Supporting Information

C-H Activation and Palladium Migration within Biaryls under Heck Reaction Conditions

Gunter Karig, Maria-Teresa Moon, Nopporn Thasana and Timothy Gallagher*

School of Chemistry, University of Bristol, Bristol BS8 1TS UK

T.Gallagher@bristol.ac.uk

General comments. ^1H and ^{13}C assignments were made using ^1H - ^1H and ^1H - ^{13}C 2D correlation spectroscopy and DEPT experiments. Where unambiguous assignments are not possible, this is indicated. The same numbering system has been employed throughout and corresponds to the following diagram, with similar systems applying to the 2- and 4-bromo derivatives.

Part A. Preparation of biaryl substrates.

1. For procedures used to prepare 4-aryl-3-bromopyridines **1a-c** and 3-aryl-2-bromopyridines **5** – see Karig, G.; Spencer, J. A.; Gallagher, T. *Organic Lett.* **2001**, 3, 835-838.

Preparation of **1a** has been described (see above)

3-Bromo-4-phenylpyridine **1b**

Isolated in 43% yield as colorless crystals; R_f 0.58 (hexane-EtOAc, 1:1); mp 47-49°C (hexanes); δ_H (300 MHz, CDCl_3) 8.82 (1 H, d, J 0.6, H-2), 8.55 (1 H, d, J 4.8, H-6), 7.40-7.53 (5 H, m, C-2', C-3', C-4'), 7.28 (1 H, dd, J 4.8, 0.6, H-5); δ_C (75.4 MHz,

CDCl₃) 152.5 (C-2), 150.4 (C-4), 148.3 (C-6), 138.2 (C-1'), 128.8 (C-4' and either C-2' or C-3'), 128.4 (C-2' or C-3'), 125.6 (C-5), 120.9 (C-3). All data were consistent with those reported in the literature (Comins, D. L.; Mantlo, N.B. *J. Heterocycl. Chem.* 1983, **20**, 1239; Shiao, M. J.; Chia, W. L.; Shing, T. L.; Chow, T. J. *J. Chem. Res.-S* 1992, 247).

3-Bromo-4-(4'-methoxyphenyl)pyridine **1c**

Isolated in 33% yield as off-white crystals; R_f 0.35 (hexane-EtOAc, 1:1); mp 77-79°C (hexane); δ_H (300 MHz, CDCl₃) 8.79 (1 H, s, H-2), 8.52 (1 H, d, *J* 5, H-6), 7.41 (2 H, AA'BB', *J* 8.9, H-2'), 7.00 (2 H, AA'BB', *J* 8.9, H-3'), 7.26 (1 H, d, *J* 5, H-5), 3.88 (3 H, s); δ_C (75.4 MHz, CDCl₃) 160.0 (C-4'), 152.6 (C-2), 149.3 (C-4), 148.3 (C-6), 130.6 (C-1'), 130.3 (C-2'), 125.7 (C-5), 121.0 (C-3), 113.8 (C-3'), 55.4 (C-5'); *m/z* (CI) 266 (⁸¹M+H⁺, 100 %); HRMS: Found: M⁺, 262.9941. C₁₂H₁₀⁷⁹BrNO requires 262.9946. ¹H NMR data and mp were consistent with those reported in the literature (Comins, D. L.; Mantlo, N.B. *J. Heterocycl. Chem.* 1983, **20**, 1239).

2. Preparation of 3-aryl -4-bromopyridines **10a** and **10b** has been described: see Karig, G.; Thasana, N.; Gallagher, T. *Synlett* **2002**, 808-810.
3. Preparation of other biaryls **12a-c**, **18a-c**, **19**.

Suzuki Reaction; General Procedure.

To a solution of requisite haloarene (see below) (0.38 mmol, 1.0 eq) in toluene (5 mL) and EtOH (1 mL) was added the appropriate boronic acid (see below) (0.57 mmol, 1.5 eq), Pd(PPh₃)₄ (0.019 mmol, 0.05 eq) and 2 M sodium carbonate solution (2 mL) and the mixture stirred vigorously and heated at reflux for 1-6 hours and the reaction was monitored by TLC. (Reactions involving 3- and 4-pyridine boronic acids were generally slower). When reaction was complete, the mixture was allowed to cool to room temperature then diluted with water. The mixture was extracted with Et₂O (3x10 mL), washed (with aq. NaHCO₃), dried (MgSO₄), and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography eluting with EtOAc/hexanes.

2-Bromo-4'-methoxybiphenyl **12a**

From 4-methoxyphenyl boronic acid and 2-bromo-1-iodobenzene and isolated in 68% yield as a pale yellow oil; R_f 0.38 (hexane-EtOAc, 6:1); δ_H (300 MHz, CDCl₃) 7.66 (1

H, dd, J 8.6, 0.7, H-3), 7.35 (2 H, AA'BB', J 8.8, H-2'), 7.30-7.35 (3 H, m, H-4, H-5, H-6), 6.96 (2 H, AA'BB', J 8.8, H-3'), 3.86 (3 H, s, OMe); δ_C (75.4 MHz, CDCl₃) 159.0 (C-4'), 142.2 (C-1), 137.1 (C-1'), 133.1, 131.4, 128.4, 127.4 (C-3, C-4, C-5, C-6), 130.6 (C-2'), 122.9 (C-2), 113.3 (C-3'), 55.3 (OMe); m/z (EI+) 277 (100 %); HRMS: Found: M^+ , 263.9975. C₁₃H₁₁⁸¹BrO requires 263.9973.

2-Bromo-4'-methoxy-4-nitrobiphenyl **12b**

From 4-methoxyphenyl boronic acid and 2-bromo-1-iodo-4-nitrobenzene and isolated in 32% yield as a yellow gum; R_f 0.40 (hexane-EtOAc, 4:1); δ_H (300 MHz, CDCl₃) 8.53 (1 H, d, J 2.4, H-3), 8.18 (1 H, dd, J 8.4, 2.4, H-5), 7.48 (1 H, d, J 8.4, H-6), 7.37 (2 H, AA'BB', J 8.9, H-2'), 6.99 (2 H, AA'BB', J 8.9, H-3'), 3.87 (3 H, s, OMe); δ_C (75.4 MHz, CDCl₃) 160.0 (C-4'), 148.7 (C-1), 146.9 (C-4), 131.6 (C-6), 131.3 (C-1'), 130.4 (C-2'), 128.4 (C-3), 123.0 (C-2), 122.3 (C-5), 113.8 (C-3'), 55.4 (OMe); m/z (CI) 310 (⁸¹M+H⁺, 60 %), 309 (⁸¹M⁺, 100), 308 (⁷⁹M+H⁺, 60), 307 (⁷⁹M⁺, 100); HRMS: Found: M+H⁺, 307.9902. C₁₃H₁₁⁷⁹BrNO₃ requires 307.9922.

2-Bromo-4-nitrobiphenyl **12c**

From phenyl boronic acid and 2-bromo-1-iodo-4-nitrobenzene isolated in 66 % yield as a pale orange solid; R_f 0.25 (hexane-DCM; 3:1); mp 84-86 °C (ethanol/petrol) (lit. (see below) mp 86 °C); δ_H (300 MHz, CDCl₃) 8.56 (1 H, d, J 2.2, H-3), 8.22 (1 H, dd, J 8.5, 2.2, H-5), 7.50 (1 H, d, J 8.5, H-6), 7.38-7.53 (5 H, m, H-2', H-3', H-4'); δ_C (75.4 MHz, CDCl₃) 149.0 (C-1), 147.3 (C-4), 139.1 (C-1'), 131.7 (C-6), 129.0 (C-2'), 128.8 (C-4'), 128.4 (C-3'), 128.3 (C-3), 123.0 (C-2), 122.3 (C-5); m/z (EI+) 279 (⁸¹M⁺, 100 %), 277 (⁷⁹M⁺, 100); HRMS: Found: M^+ , 276.9744. C₁₂H₈⁷⁹BrNO₂ requires 276.9738. This compound has been reported previously in the literature (Byron, D. J; Gray, G. W.; Ibbotson, G. A.; Worrall, B. M. *J. Chem. Soc.* **1963**, 2246) but no spectroscopic data have been described.

Preparation of **18a-c** was carried out using the general Suzuki procedure (described above) with pyridine 4-boronic acid and the requisite iodoarene.

4-(2'-Bromo-4'-nitrophenyl)pyridine **18a**

From pyridine 4-boronic acid and 2-bromo-1-iodo-4-nitrobenzene and isolated in 55% yield as a off-white crystalline solid; R_f 0.14 (hexane-EtOAc, 1:1); δ_H (300

MHz, CDCl₃) 8.76 (2 H, AA'BB', *J* 6.0, H-2), 8.59 (1 H, d, *J* 2.0, H-3'), 8.27 (1 H, dd, *J* 8.5, 2.4, H-5'), 7.50 (1 H, d, *J* 8.5, H-6'), 7.35 (2 H, AA'BB', *J* 6.0, H-3); δ_C (75.4 MHz; CDCl₃) 150.0 (C-2), 148.0, 46.6, 146.1 (C-4, C-1', C-4'), 131.3 (C-6'), 128.5 (C-3'), 123.6 (C-2', C-3, not clearly resolved), 122.6 (C-5'); *m/z* (EI+) 280 (⁸¹M⁺, 20 %), 278 (⁷⁹M⁺, 20); HRMS: Found: M⁺, 277.9708. C₁₁H₇⁷⁹BrN₂O₂ requires 277.9691.

4-(2'-Bromophenyl)pyridine **18b**

From pyridine 4-boronic acid and 2-bromo-1-iodobenzene and isolated in 32 % yield as off-white crystalline solid; R_f 0.22 (hexane-EtOAc, 1:1); δ_H (300 MHz, CDCl₃) 8.68 (2 H, AA'BB', *J* 6.2, H-2), 7.69 (1 H, dd, *J* 7.9, 1.2, H-3'), 7.40 (1 H, ddd, *J* 7.7, 7.3, 1.2, H-5'), 7.35 (2 H, AA'BB', *J* 6.2, H-3), 7.29 (1 H, dd d, *J* 7.9, 7.7, 1.9, H-4'), 7.26 (1 H, dd, *J* 7.3, 1.9, H-6'); δ_C (75.4 MHz, CDCl₃) 149.6 (C-2), 148.6 (C-4), 139.8 (C-1'), 133.4 (C-3'), 130.7, (C-4'), 129.8 (C-6'), 127.6 (C-5'), 124.2 (C-3), 121.7 (C-2'); *m/z* (EI+) 235 (⁸¹M⁺, 100 %), 233 (⁷⁹M⁺, 100); HRMS: Found: M⁺, 232.9842. C₁₁H₈⁷⁹BrN requires 232.9840.

4-(2'-Bromo-4'-methoxyphenyl)pyridine **18c**

From pyridine 4-boronic acid and 2-bromo-1-iodo-4-methoxybenzene and isolated in 38 % yield as creamy white crystals R_f 0.17 (hexane-EtOAc, 3:1); mp 92-93 °C; δ_H (300 MHz, CDCl₃) 8.65 (2 H, AA'BB', *J* 6, H-2), 7.34 (2 H, AA'BB', *J* 6, H-3), 7.24 (1 H, d, *J* 2.5, H-3'), 7.23 (1 H, d, *J* 8.6, H-6'), 6.95 (1 H, dd, *J* 8.6, 2.5, H-5'), 3.85 (3 H, s, OMe); δ_C (75.4 MHz, CDCl₃) 160.1 (C-4'), 149.5 (C-2), 148.4 (C-4), 132. (C-1'), 131.4 (C-6'), 124.5 (C-3), 122.1 (C-2'), 118.6 (C-3'), 113.9 (C-5'), 55.7 (OMe); *m/z* (EI+) 265 (⁸¹M⁺, 35 %), 263 (⁷⁹M⁺, 35); HRMS: Found: M⁺, 264.9925. C₁₂H₁₀⁸¹BrNO requires 264.9925.

3-(2'-Bromo-4'-nitrophenyl)pyridine **19**

Prepared from pyridine-3-boronic acid and 2-bromo-1-iodo-4-nitrobenzene and isolated in 40% yield as cream crystals; R_f 0.14 (hexane-EtOAc, 1:1); δ_H (300 MHz, CDCl₃) 8.72 (1 H, dd, *J* 3.5, H-6), 8.68 (1 H, d, *J* 1.6, H-2), 8.59 (1 H, d, *J* 2.0, H-3'), 8.28 (1 H, dd, *J* 8.4, 2.4, H-5'), 7.81-7.76 (1 H, m, H-4), 7.53 (1 H, d, *J* 8.4, H-6'), 7.46-7.41 (1 H, m, H-5); δ_C (75.4 MHz, CDCl₃) 150.0 and 149.4 (C-6 or C-2), 145.3/134.9/123.2 (C-1', C-2', C-4' or C-3 – these could not be assigned and one quaternary signal was not seen), 136.5/128.5/123.0/122.6 (C-4, C-5, C-3' or C-6' –

these could not be assigned), 131.7 (C-5'); m/z (EI+) 280 ($^{81}\text{M}^+$, 100 %), 278 ($^{79}\text{M}^+$, 100),; HRMS: Found: M^+ , 277.9704. $\text{C}_{11}\text{H}_7\text{N}_2\text{O}_2^{79}\text{Br}$ requires 277.9691.

Part B. Heck Reactions

General Procedure *We wish to make it clear that this procedure was followed for all of the Heck reactions described in this paper. It is important to appreciate that the Heck conditions employed may have a significant effect on the distribution of products, and in order to maintain consistency we have used the same conditions throughout.*

Some modified Heck reaction conditions were examined and these are reported in the text, but for all the results shown in Schemes 2, 3 and 5, this general procedure was used.

Bromoarene (0.11 mmol, 1.0 eq) was dissolved in dry, distilled acetonitrile (2 mL) in a sealed tube. $\text{Pd}(\text{OAc})_2$ (2.4 mg, 0.01 mmol, 0.1 eq), $\text{P}(o\text{-Tol})_3$ (6.5 mg, 0.02 mmol, 0.2 eq), triethylamine (76 μl , 0.54 mmol, 5 eq) and ethyl acrylate (35 μl , 0.32 mmol, 3 eq) were added, the tube was flushed with nitrogen, sealed and heated to 125 °C for 20 hours. The mixture was cooled to room temperature, diluted with water, extracted with CH_2Cl_2 (2x10 mL) and dried (MgSO_4). Filtration followed by evaporation *in vacuo* gave an orange oil. The crude product was assayed by ^1H NMR prior to purification by column chromatography and/or HPLC, but yields and product ratios are based on isolated compounds, homogeneous by TLC and ^1H NMR.

Numbering system used is shown below.

Products resulting from Heck reaction of 1a

Retention product 3a: R_f 0.18 (hexane–EtOAc, 1:1); mp 112–113 °C (hexane); δ_H (300 MHz, $CDCl_3$) 8.95 (1 H, s, H-2), 8.70 (1 H, d, J 5.0, H-6), 8.37 (2 H, AA'BB', J 8.9, H-2'), 7.55 (1 H, d, J 15.9, H-1''), 7.54 (2 H, AA'BB', J 8.9, H-3'), 7.31 (1 H, dd, J 4.9, 0.6, H-5), 6.52 (1 H, d, J 15.9, H-2''), 4.24 (2 H, q, J 7.2), 1.32 (3 H, t, J 7.2); δ_C (75.4 MHz, $CDCl_3$) 166.7 (C=O), 151.4 (C-6), 149.6 (C-2), 149.0/ 147.6/ 144.5 (C-4', C-4, C-1'), 139.9 (C-1''), 131.1 (C-3'), 129.0 (C-3), 124.8, 124.7 (C-2', C-5), 123.1 (C-2''), 61.8, 15.1; m/z (EI+) 298 (M^+ , 100%); HRMS: Found: M^+ , 298.0941. $C_{16}H_{14}N_2O_4$ requires 298.0954.

Crossover product 4a: R_f 0.13 (hexane–EtOAc; 1:1); mp 155–157 °C (hexane); δ_H (300 MHz; $CDCl_3$) 8.77 (2 H, AA'BB', J 6.1, H-2), 8.58 (1 H, d, J 2.2, H-6'), 8.31 (1 H, dd, J 8.6, 2.2, H-4'), 7.0 (1 H, d, J 15.9, H-2''), 7.55 (1 H, d, J 8.6, H-3'), 7.28 (2 H, AA'BB', J 6.1, H-3), 6.57 (1 H, d, J 15.9, H-2''), 4.25 (2 H, q, J 7.2), 1.32 (3 H, t, J 7.2); δ_C (75.4 MHz, $CDCl_3$) 165.7 (C=O), 150.3 (C-2), 148.2 (C-4), 145.7/ 145.4 (C-5', C-2'), 139.9 (C-1''), 134.4 (C-1'), 131.3 (C-3'), 124.0 (C-3), 124.2/ 123.4/ 122.2 (C-4', C-6', C-2''), 61.0, 14.2; m/z (CI) 299 ($M+H^+$, 100 %); HRMS: Found: $M+H^+$, 299.1028. $C_{16}H_{15}N_2O_4$ requires 299.1032.

Reduction product 2: R_f 0.16 (hexane–EtOAc, 1:1); δ_H (270 MHz, $CDCl_3$) 8.75 (2 H, AA'BB', J 6.1, H-2), 8.36 (2 H, AA'BB', J 8.9, H-3'), 7.80 (2 H, AA'BB', J 8.9, H-2'), 7.53 (2 H, AA'BB', J 6.1, H-3); δ_C (100.6 MHz, $CDCl_3$) 150.9 (C-2), 148.1/ 146.2/ 144.7 (C-4, C-1', C-4'), 128.2/ 124.6/ 121.9 (C-2', C-3', C-3). These data are consistent with those described in the literature for this compound (Ishikura, M.; Ohta, T.; Terushima, M. *Chem. Pharm. Bull.* 1985, 33, 4755).

Products resulting from Heck reaction of 1b

3b: R_f 0.23 (hexane–EtOAc, 1:1); mp 98–100 °C (hexane); δ_H (300 MHz, $CDCl_3$) 8.89 (1 H, s, H-2), 8.63 (1 H, d, J 4.4, H-6), 7.69 (1 H, J 16.1, H-1''), 7.44–7.52 (3 H, m, H-2', H-1'), 7.29–7.57 (3 H, m, H-3', H-5), 6.49 (1 H, d, J 16.1, H-2''), 4.23 (2 H, q, J 7.2), 1.30 (3 H, t, J 7.2); δ_C (75.4 MHz, $CDCl_3$) 166.3 (C=O), 150.3 (C-6), 149.3 (C-4), 148.5 (C-2), 140.6 (C-1''), 137.2 (C-1'), 129.3 (C-2'), 128.9 (C-4'), 128.9/ 128.8 (C-3', C-3), 124.4 (C-5), 120.9 (C-2''), 60.7, 14.3; m/z (CI) 254 ($M+H^+$, 100 %); HRMS: Found: $M+H^+$, 254.1177. $C_{16}H_{16}NO_2$ requires 254.1181.

4b: R_f 0.17 (hexane–EtOAc, 1:1); mp 76–77 °C (hexane); δ_H (300 MHz, $CDCl_3$) 8.69 (2 H, AA'BB', J 5.7, H-2), 7.73 (1 H, m, ArH'), 7.64 (1 H, d, J 15.9, H-1"), 7.44–7.50 (2 H, m, ArH'), 7.35 (1 H, m, H-6'), 7.27 (2 H, AA'BB', J .7, H-3), 6.42 (1 H, d, J 15.9, H-2"), 4.22 (2 H, q, J 7.1), 1.29 (3 H, t, J 7.1); δ_C (75.4 MHz, $CDCl_3$) 156.5 (C=O), 149.8 (C-2), 147.8 (C-4), 142.4 (C-1"), 139.8 (C-2'), 132.6 (C-1'), 130.1/130.0/128.9/127.1 (C-3', C-4', C-5', C-6'), 124.6 (C-3), 120.4 (C-2"), 60.6, 14.3; m/z (CI) 254 ($M+H^+$, 100 %); HRMS: Found: $M+H^+$, 254.1182. $C_{16}H_{16}NO_2$ requires 254.1181.

Products resulting from Heck reaction of 1c

Retention product 3c: R_f 0.25 (hexane–EtOAc, 1:1); mp 76–78 °C (hexane); δ_H (270 MHz, $CDCl_3$) 8.85 (1 H, s, H-2), 8.59 (1 H, d, J 4.9, H-6), 7.72 (1 H, d, J 16.1, H-1"), 7.29 (2 H, AA'BB', J 8.9, H-2'), 7.27 (1 H, d, J 4.9, H-5), 7.01 (2 H, AA'BB', J 8.9, H-3'), 6.48 (1 H, d, J 16.1, H-2"), 4.24 (2 H, q, J 7.2, H-7), 3.86 (3 H, s, OMe), 1.31 (3 H, t, J 7.2, H-8); δ_C (67.9 MHz, $CDCl_3$) 166.4 (C=O), 160.3, 150.2, 149.0, 148.7, 141.0, 130.7, 129.6, 128.7, 124.2, 120.7, 114.3, 60.6 (OMe), 55.4, 14.3; m/z (EI+) 283 (M^+ , 38 %); HRMS: Found: M^+ , 283.1208. $C_{17}H_{17}NO_3$ requires 283.1208.

Crossover product 4c: R_f 0.17 (hexane–EtOAc, 1:1); mp 54–56 °C (hexane); δ_H (300 MHz, $CDCl_3$) 8.66 (2 H, AA'BB', J 6.2, H-2), 7.63 (1 H, d, J 15.8, H-1"), 7.29 (1 H, d, J 8.5, H-3'), 7.23 (2 H, AA'BB', J 6.2, H-3), 7.19 (1 H, d, J 2.6, H-6'), 7.03 (1 H, dd, J 8.5, 2.6, H-4'), 6.41 (1 H, d, J 15.8, H-2"), 4.24 (2 H, q, J 7.2), 3.87 (3 H, s, OMe), 1.31 (3 H, t, J 7.2); δ_C (75.4 MHz, $CDCl_3$) 167.1 (C=O), 159.9 (C-5'), 149.7 (C-2), 147.3 (C-4), 142.6 (C-1"), 133.8, 132.6 (C-2', C-1'), 131.4 (C-3'), 124.7 (C-3), 120.5 (C-2"), 116.3 (C-4'), 111.7 (C-6'), 60.6, 55.5 (OMe), 14.2; m/z (EI+) 283 (M^+ , 45%); HRMS: Found: M^+ , 283.1208. $C_{17}H_{17}NO_3$ requires 283.1208.

Products resulting from Heck reaction of 5 and 19 (for yields, see text of paper)

6: Isolated as colorless crystals; R_f 0.40 (hexane–EtOAc, 1:1); mp 134–135 °C (EtOAc/Hexanes); δ_H (300 MHz, $CDCl_3$) 8.72 (1 H, dd, J 4.6, 1.6, H-6), 8.36 (2 H, AA'BB', J 8.8, H-3'), 7.67 (1 H, dd, J 7.8, 1.6, H-4), 7.59 (1 H, d, J 15.2, H-1"), 7.53 (2 H, AA'BB', J 8.8, H-2'), 7.40 (1 H, dd, J 7.8, 4.6, H-5), 7.12 (1 H, d, J 15.2, H-2"), 4.23 (2 H, q, J 7.1, H-4"), 1.29 (3 H, t, J 7.1, H-5"); δ_C (75.4 MHz, $CDCl_3$) 165.8 (C-

3"), 149.9 (C-6), 149.8 (C-1' or C-4' or C-2 or C-3), 14.7 (C-1' or C-4' or C-2 or C-3), 139.7 (C-1"), 137.8 (C-4), 136.0 (C-1' or C-4' or C-2 or C-3), 130.6 (C-2'), 124.6 (C-2"), 124.1 (C-5), 123.9 (C-3'), 123.7 (C-1' or C-4' or C-2 or C-3), 60.7, 14.2; m/z (EI+) 298 (M^+ , 10%); HRMS: Found: M^+ , 298.0945. $C_{16}H_{14}N_2O_4$ requires 298.0954.

7: Isolated as colorless crystals; R_f 0.13 (hexane–EtOAc, 1:1); mp 119–120 °C (hexane); δ_H (300 MHz, $CDCl_3$) 8.74 (1 H, br s, H-6), 8.64 (1 H, br s, H-2), 8.58 (1 H, d, J 2.2, H-6'), 8.32 (1 H, dd, J 8.4, 2.4, H-4'), 7.70–7.66 (1 H, m, H-4), 7.58 (1 H, d, J 15.9, H-1"), 7.56 (1 H, d, J 8.4, H-5), 7.49–7.44 (1 H, m, H-5), 6.69 (1 H, d, J 15.9, H-2"), 4.24 (2 H, q, J 7.1), 1.31 (3 H, t, J 7.1); δ_C (75.4 MHz, $CDCl_3$) 165.8 (C-3"), 150.1 (C-6), 149.7 (C-2), 148.0/ 144.6/ 134.7 (C-3, C-1' or C-2' or C-5' – two signals overlap), 140.2 (C-1"), 136.8 (C-4), 131.7 (C-3'), 124.2 (C-4'), 123.4 (C-5), 123.2 (C-2"), 122.2 (C-6'), 61.0, 14.2; m/z (EI+) 298 (M^+ , 2%); HRMS: Found: M^+ , 298.0950. $C_{16}H_{14}N_2O_4$ requires 298.0954.

8: Isolated as a pale yellow oil; R_f 0.23 (hexane–EtOAc, 1:1); δ_H (300 MHz, $CDCl_3$) 8.60 (1 H, dd, J 4.7, 1.7, H-6), 8.33 (2 H, AA'BB', J 8.8, H-3'), 7.55 (2 H, AA'BB', J 8.8, H-2'), 7.51 (1 H, dd, J 7.7, 1.7, H-4), 7.24 (1 H, dd, J 7.7, 1.7, H-5), 4.08 (2 H, q, J 7.2), 3.03 (2 H, t, J 7.2, H-1"), 2.81 (2 H, t, J 7.2, H-2"), 1.20 (3 H, t, J 7.2); δ_C (75.4 MHz, $CDCl_3$) 173.1 (C-3"), 156.7 (C-2), 149.1 (C-6), 146.3 (C-3 or C-1' or C-4'), 137.0 (C-4), 134.9 (C-3 or C-1' or C-4'), 130.2 (C-2'), 125.6 (C-3 or C-1' or C-4'), 123.8 (C-3'), 121.3 (C-5), 60.4, 32.4 (C-2"), 30.0 (C-1"), 14.2; m/z (EI+) 300 (M^+ , 23 %); HRMS: Found: M^+ , 300.1105. $C_{16}H_{16}N_2O_4$ requires 300.1110.

9: Isolated as cream crystals; R_f 0.09 (hexane–EtOAc, 1:1); mp 138–140 °C (hexane); δ_H (300 MHz, $CDCl_3$) 8.90 (1 H, d, J 1.8, H-2), 8.70 (1 H, dd, J 4.8, 1.3, H-6), 8.36 (2 H, AA'BB', J 9.0, H-3'), 7.97–7.92 (1 H, m, H-4), 7.77 (2 H, AA'BB', J 9.0, H-2'), 7.48–7.43 (1 H, m, H-5); δ_C (75.4 MHz, $CDCl_3$) 171.2 (C-3), 150.0 (C-6), 148.3 (C-2), 147.7/144.3 (C-4' and C-1'), 134.7 (C-4), 128.0 (C-2'), 124.4 (C-3'), 123.9 (C-5); m/z (EI+) 200 (M^+ , 71 %). These data are consistent with those described in the literature for this compound (Klemm, L. H.; Dorsey, J. J. *Heterocycl. Chem.* **1991**, 28, 1153).

Product resulting from Heck reaction of 10a

11a: Isolated as a colorless solid; $R_f = 0.26$ (1:1 EtOAc:hexane); mp 154-155 °C (EtOAc:hexane); ^1H NMR (300 MHz, C_6D_6) δ 8.44 (1 H, s, H-2), 7.84 (1 H, d, J 8.8, H-6), 7.73 (2 H, AA'BB', J 8.8, H-3'), 7.46 (d, J 15.9, H-1"), 6.88 (1 H, d, J 8.8 Hz, H-5), 6.69 (2 H, AA'BB', J 8.8, H-2'), 6.33 (1 H, d, J 15.9, H-2"), 4.01 (2 H, q, J 7.1), 0.99 (3 H, t, J 7.1); ^{13}C NMR (75 MHz, C_6D_6) δ 166.1, 142.9, 140.3, 134.7, 131.1, 128.3, 125.1, 124.7, 124.3, 61.6, 14.8; MS (EI+) m/z 298 (M^+ , 48%); HRMS: Found: 298.0953. $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_4$ requires 298.0936.

Product resulting from Heck reaction of 10b

11b: Isolated as a colorless solid; $R_f = 0.34$ (1:1 EtOAc:hexane); mp 68-69 °C (EtOAc:hexane); ^1H NMR (300 MHz, CDCl_3) δ 8.63 (1 H, s, H-2), 8.59 (1 H, d, J 8.8, H-6) 7.68 (1 H, d, J 16.0, H-1"), 7.48 (1 H, d, J 5.2, H-5), 7.28 (2 H, AA'BB', J 8.8, H-2'), 7.08 (2 H, AA'BB', J 8.8, H-3'), 6.54 (1 H, d, J 16.0, H-2"), 4.19 (2 H, q, J 7.2), 3.87 (3 H, s, OMe), 1.31 (3 H, t, J 7.2); ^{13}C NMR (75 MHz, CDCl_3) δ 166.1, 159.8, 151.3, 148.3, 141.1, 139.7, 136.7, 131.1, 128.4, 123.0, 120.2, 114.2, 60.8, 55.4, 14.2; MS (EI+) m/z 283 (M^+ , 40%); HRMS: Found: 283.1208. $\text{C}_{17}\text{H}_{17}\text{NO}_3$ requires 283.1211.

Products resulting from Heck reaction of 12a-c

13a: Isolated as colorless crystals; mp 63-65 °C (hexane); δ_{H} (300 MHz, CDCl_3) 7.76 (1 H, d, J 15.9, H-1"), 7.70-7.66 (1 H, m, H-3), 7.45-7.32 (3 H, m, H-6, H-4 and H-5), 7.24 (2 H, AA'BB', J 8.8, H-2'), 7.18 (2 H, AA'BB', J 8.8, H-3'), 6.39 (1 H, d, J 15.9, H-2"), 4.22 (2 H, q, J 7.2), 3.86 (3 H, s, OMe), 1.29 (3 H, t, J 7.2); δ_{C} (75.4 MHz, CDCl_3) 167.0 (C-3"), 159.2 (C-4'), 144.0 (C-1"), 142.6 (C-2), 132 and 132.2 (C-1 and C-1'), 131.0 (C-2'), 130.5 (C-6), 129.8 (C-5), 127.3 (C-4), 126.8 (C-3), 118.9 (C-2"), 113.8 (C-3'), 60.4, 55.4 (OMe), 14.3; m/z (EI+) 282 (M^+ , 50%); HRMS: Found: M^+ , 282.1263. $\text{C}_{18}\text{H}_{18}\text{O}_3$ requires 282.1256.

13b: Isolated as colorless crystals; R_f 0.21 (hexane–EtOAc, 4:1); mp 122-125 °C (hexane); δ_{H} (300 MHz, CDCl_3) 8.53 (1 H, d, J 2.4, H-6), 8.24 (1 H, dd, J 8.6, 2.4, H-

4), 7.72 (1 H, d, J 16.0, H-1"), 7.53 (1 H, d, J 8.6, H-3), 7.27 (2 H, AA'BB', J 8.8, H-2'), 7.02 (2 H, AA'BB', J 8.8, H-3'), 6.55 (1 H, d, J 16.0, H-2"), 4.25 (2 H, q, J 7.1), 3.88 (3 H, s, OMe), 1.32 (3 H, t, J 7.1); δ_C (75.4 MHz, CDCl₃) 166.2 (C-3"), 160.2 (C-4'), 148.4 and 147.1 (C-2 and C-1), 141.8 (C-1"), 13.0 (C-1'), 131.4 (C-3), 130.9 (C-2'), 130.0 (C-5), 124.0 (C-4), 122.1 (C-6), 121.7 (C-2"), 114.2 (C-3'), 60.8, 55.4 (OMe), 14.3; m/z (EI+) 327 (M^+ , 100%); HRMS: Found: M^+ , 327.1107. C₁₈H₁₇NO₅ requires 327.1107.

13c: Isolated as colorless crystals; R_f 0.28 (hexane–EtOAc, 4:1); mp 107–110 °C (hexane); δ_H (300 MHz, CDCl₃) 8.56 (1 H, d, J 2.4, H-6), 8.26 (1 H, dd, J 8.5, 2.4, H-4), 7.69 (1 H, d, J 16, H-1"), 7.55 (1 H, d, J 8.5, H-3), 7.52–7.43 (3 H, m, H-2' and H-4'), 7.35–7.31 (2 H, m, H-3'), 6.56 (1 H, d, J 16.0, H-2"), 4.23 (2 H, q, J 7.2), 1.31 (1 H, t, J 7.2); δ_C (75.4 MHz, CDCl₃) 166.1 (C-3"), 148.6 and 147.4 (C-2 and C-5), 141.4 (C-1"), 137.8 and 134.1 (C-1 and C-1'), 131.6 (C-3), 129.5 (C-3'), 128.9 (C-4'), 128.7 (C-2'), 124.0 (C-4), 122.0 (C-2"), 60.8, 14.2; m/z (EI+) 297 (M^+ , 45%); HRMS: Found: M^+ , 297.1002. C₁₇H₁₅NO₄ requires 297.1001.

14c: Isolated as colorless crystals; R_f 0.27 (hexane–EtOAc, 4:1); mp 79–83 °C δ_H (300 MHz, CDCl₃) 8.32 (2 H, AA'BB', J 8.9, H-3'), 7.75–7.71 (1 H, m, Ph-H), 7.60 (1 H, d, J 16.0, H-1"), 7.54–7.46 (2 H, m, Ph-H), 7.50 (2 H, AA'BB', J 8.9, H-2'), 7.39–7.31 (1 H, m, Ph-H), 6.43 (1 H, d, J 16.0, H-2"), 4.22 (2 H, q, J 7.2), 1.29 (3 H, t, J 7.2); m/z (EI+) 297 (M^+ , 50%); HRMS: Found: M^+ , 297.1017. C₁₇H₁₅NO₄ requires 297.1001. We were unable to obtain ¹³C NMR data for **14c** due to a lack of material.

Products resulting from Heck reaction of 18a-c

The products of these Heck reactions correspond to **3a-c** and **4a-c** and spectroscopic data for these compounds are described above.