Supporting Information

Ligand Effects in the Synthesis of N-Heterocycles by Intramolecular Heck Reactions.

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General experimental procedures have been described in recent papers from our laboratory. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (1223)-336033 or e-mail: deposit@ccdc.cam.ac.uk]. The assigned reference codes (CCDC numbers) are given in the Experimental paragraphs.

***N*-Benzyl-2-iodoaniline, 5.**¹ Sodium cyanoborohydride (1.72 g, 27.3 mmol, 1.2 eq.) was added to a stirred mixture of 2-iodoaniline (5.0 g, 22.8 mmol, 1.0 eq.), zinc(II) chloride (3.73 g, 27.3 mmol, 1.2 eq.) and benzaldehyde (2.78 mL, 27.3 mmol, 1.2 eq) in methanol (92 mL), and the reaction mixture was refluxed under nitrogen for 2 h. After cooling, the reaction mixture was diluted with 1M aq. NaOH (30 mL), concentrated, then extracted with diethyl ether (3 x 20 mL). The combined ether layers were washed with water, dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified by column chromatography to furnish the product as a yellow oil. Yield: 6.20 g, 91%. R_f = 0.48 (pet. ether/ethyl acetate, 5/1); $\nu_{\max}$ (thin film)/cm⁻¹ 3402 (NH); δ_H (270 MHz, CDCl₃): 4.43 (2H, close AB), 4.66 (1H, s), 6.46-6.50 (1H, m), 6.56 (1H, dd, J 1.0, 8.1), 7.16-7.21 (1H, m), 7.29-7.35 (1H, m), 7.36-7.40 (4H, m), 7.71 (1H, dd, J 1.5, 7.7); δ_C (100 MHz, CDCl₃): 48.3, 85.3, 111.0, 118.9, 127.2, 127.3, 128.9, 129.4, 138.7, 139.0, 147.1; m/z (EI) 309 (M^+ , 79%), 180 (22%), 91 (100%).

General procedure for amide coupling. A round-bottom flask was charged with carboxylic acid (2.10 mmol, 1.3 eq.), dry CH₂Cl₂ (5 mL) and a drop of DMF. The mixture was cooled to 0°C, whereupon oxalyl chloride (0.17 mL, 1.94 mmol, 1.2 eq.) was added slowly. The reaction mixture was stirred for 3 h at room temperature, then cooled to 0°C. A solution of *N*-benzyl-2-iodoaniline (0.5 g, 1.62 mmol, 1.0 eq.) in dry CH₂Cl₂ (10 mL) was then added. The reaction mixture was returned to room temperature and stirred overnight, before it was quenched by the addition of H₂O the reaction at 0°C. The organic layer was separated, washed with aq. NaHCO₃, water and brine, then dried over MgSO₄. The solution was finally evaporated to yield the crude product, which was purified by column chromatography.

But-3-enoic acid benzyl-(2-iodo-phenyl)-amide, 6. Yield: 88% as an orange oil; $R_f = 0.28$ (hexane/ethyl acetate, 5/1); $\nu_{\max}$ (thin film)/ cm^{-1} 1664 (C=O); Found: C, 53.98; H, 4.41; N, 3.58%. Calc. for $\text{C}_{17}\text{H}_{16}\text{NO}$: C, 54.13; H, 4.28; N, 3.71%; δ_{H} (270 MHz, CDCl_3): 2.67-2.78 (2H, m), 3.91 (1H, d, J 14.3), 4.93 (1H, dd, J 1.5, 17.0), 5.10 (1H, dd, J 1.5, 10.1), 5.66 (1H, d, J 14.3), 5.87-6.03 (1H, m), 6.70 (1H, dd, J 1.5, 7.9), 7.03 (1H, m), 7.17-7.26 (6H, m), 7.94 (1H, dd, J 1.2, 7.9); δ_{C} (100 MHz, CDCl_3): 39.6, 51.6, 100.5, 118.0, 127.5, 128.4, 129.1, 129.5, 129.9, 131.0, 131.5, 136.9, 140.2, 143.7, 170.5; m/z (EI) 377 (M^+ , 35%), 376 (45%), 309 (63%), 308 (65%), 250 (45%), 91 (100%).

Pent-4-enoic acid benzyl-(2-iodo-phenyl)-amide, 7. Yield: 73% as a yellow oil; $R_f = 0.36$ (hexane/ethyl acetate, 5/1); $\nu_{\max}$ (thin film)/ cm^{-1} 1664 (C=O); Found: C, 55.41; H, 4.46; N, 3.46%. Calc. for $\text{C}_{18}\text{H}_{18}\text{INO}$: C, 55.26; H, 4.64; N, 3.58%; δ_{H} (270 MHz, CDCl_3): 2.00-2.06 (2H, m), 2.35-2.43 (2H, m), 3.90 (1H, d, J 14.3), 4.90-5.00 (2H, m), 5.69 (1H, d, J 14.3), 5.68-5.80 (1H, m), 6.68 (1H, dd, J 1.5, 7.9), 7.02 (1H, m), 7.17-7.30 (6H, m), 7.94 (1H, dd, J 1.2, 7.9); δ_{C} (100 MHz, CDCl_3): 29.2, 33.9, 51.6, 100.6, 115.1, 127.5, 128.4, 129.2, 129.4, 129.8, 130.9, 137.1, 137.5, 140.2, 143.9, 171.8; m/z (EI) 391 (M^+ , 7%), 309 (16%), 308 (10%), 264 (50%), 180 (19%), 91 (100%).

Hex-5-enoic acid benzyl-(2-iodo-phenyl)-amide, 8. Yield: 81% as a white solid; $R_f = 0.26$ (hexane/ethyl acetate, 5/1); Mp 58-59°C; $\nu_{\max}$ (KBr)/ cm^{-1} 1641 (C=O); Found: C, 56.23; H, 4.84; N, 3.32 %. Calc. for $\text{C}_{19}\text{H}_{20}\text{INO}$: C, 56.31; H, 4.97; N, 3.46 %; δ_{H} (270 MHz, CDCl_3): 1.66-1.78 (2H, m), 1.92-2.04 (4H, m), 3.89 (1H, d, J 14.3), 4.86-4.97 (2H, m), 5.63-5.78 (2H, m), 6.69 (1H, dd, J 1.7, 7.7), 7.02 (1H, m), 7.17-7.30 (6H, m), 7.94 (1H, dd, J 1.2, 7.9); δ_{C} (100 MHz, CDCl_3): 24.2, 33.2, 33.8, 51.5, 100.5, 114.9, 127.5, 128.4, 129.1, 129.4, 129.8, 130.9, 137.1, 138.1, 140.2, 144.0, 172.3; m/z (EI) 405 (M^+ , 6%), 278 (44%), 180 (17%), 91 (100%).

Hept-6-enoic acid benzyl-(2-iodo-phenyl)-amide, 9. Yield: 54% as a yellow oil; $R_f = 0.33$ (hexane/ethyl acetate, 5/1); $\nu_{\max}$ (thin film)/ cm^{-1} 1644 (C=O); Found: C, 57.37; H, 5.17; N, 3.28 %. Calc. for $\text{C}_{20}\text{H}_{22}\text{INO}$: C, 57.29; H, 5.29; N, 3.34 %; δ_{H} (270 MHz, CDCl_3): 1.23-1.38 (2H, m), 1.55-1.75 (2H, m), 1.85-2.04 (4H, m), 3.95 (1H, d, J 14.3), 4.87-4.98 (2H, m), 5.68 (1H, d, J 14.3), 5.67-5.82 (1H, m), 6.68 (1H, dd, J 1.7, 7.9), 7.02 (1H, td, J 1.5, 7.7), 7.17-7.29 (6H, m), 7.94 (1H, dd, J 1.5, 7.9); δ_{C} (100 MHz, CDCl_3): 24.5, 28.5, 33.4, 34.3, 51.5,

100.5, 114.4, 127.4, 128.3, 129.1, 129.4, 129.7, 130.8, 137.1, 138.6, 140.1, 144.0, 172.4; m/z
(EI) 419 (M^+ , 10%), 292 (76%), 91 (100%).

^1H NMR spectrum of compound **10**

^{13}C NMR spectrum of compound **10**

^1H NMR spectrum of compound **11**

^{13}C NMR spectrum of compound **11**

^1H NMR spectrum of compound **12**

^{13}C NMR spectrum of compound **12**

¹H NMR spectrum of compounds **11** (peaks denoted by #) and **22** (peaks denoted by *)

¹H NMR spectrum of compound **23**

^1H NMR spectrum of the mixture of compounds **18**, **19** and **20** (see following spectra for the individual components)

^1H NMR spectrum of compound **18**

¹H NMR spectrum of compound **19**

¹H NMR spectrum of compound **20**

Crystallographic Data

Crystal data for 11: C₁₈H₁₇NO, $M = 263.33$, triclinic, $P\bar{1}$ (no. 2), $a = 8.4218(8)$, $b = 9.0810(8)$, $c = 9.1550(8)$ Å, $\alpha = 97.508(7)$, $\beta = 101.043(7)$, $\gamma = 90.621(7)^\circ$, $V = 680.84(11)$ Å³, $Z = 2$, $D_c = 1.284$ g cm⁻³, $\mu(\text{Mo-K}\alpha) = 0.079$ mm⁻¹, $T = 173$ K, colourless blocks, Oxford Diffraction Xcalibur 3 diffractometer; 4242 independent measured reflections, F^2 refinement, $R_1 = 0.049$, $wR_2 = 0.126$, 4152 independent observed absorption-corrected reflections [$|F_o| > 4\sigma(|F_o|)$], $2\theta_{\text{max}} = 65^\circ$], 181 parameters. CCDC 278201.

Crystal data for 12: C₁₉H₁₉NO, $M = 277.35$, monoclinic, $C2/c$ (no. 15), $a = 16.5637(12)$, $b = 6.9794(6)$, $c = 27.0219(18)$ Å, $\beta = 100.622(6)^\circ$, $V = 3070.3(4)$ Å³, $Z = 8$, $D_c = 1.200$ g cm⁻³, $\mu(\text{Mo-K}\alpha) = 0.074$ mm⁻¹, $T = 173$ K, colourless blocks, Oxford Diffraction Xcalibur 3 diffractometer; 5197 independent measured reflections, F^2 refinement, $R_1 = 0.059$, $wR_2 = 0.137$, 5101 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$], $2\theta_{\text{max}} = 65^\circ$], 190 parameters. CCDC 278202.

Fig. S1 The molecular structure of **11** (50% probability ellipsoids).

Fig. S2 The molecular structure of **12** (50% probability ellipsoids).

Fig. S1

Fig. S2

References

- ¹ Lizos, D. E.; Murphy, J. A. *Org. Biomol. Chem.* **2003**, *1*, 177-122.