

Supporting Information

Palladium-Catalyzed Direct Olefination of Urea Derivatives with n-Butyl Acrylate by C-H Bond Activation under Mild Reaction Conditions

Li Wang,^a Shen Liu^b, Zhi Li^b, and Yongping Yu^{b*}

^a School of Science & Engineering, Zhejiang International Studies University 310012, P. R. China

^b Institute of Materia Medica, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou 310058, P.

R. China

Fax: +86-571-88208452

E-mail: yyu@zju.edu.cn

Supporting information

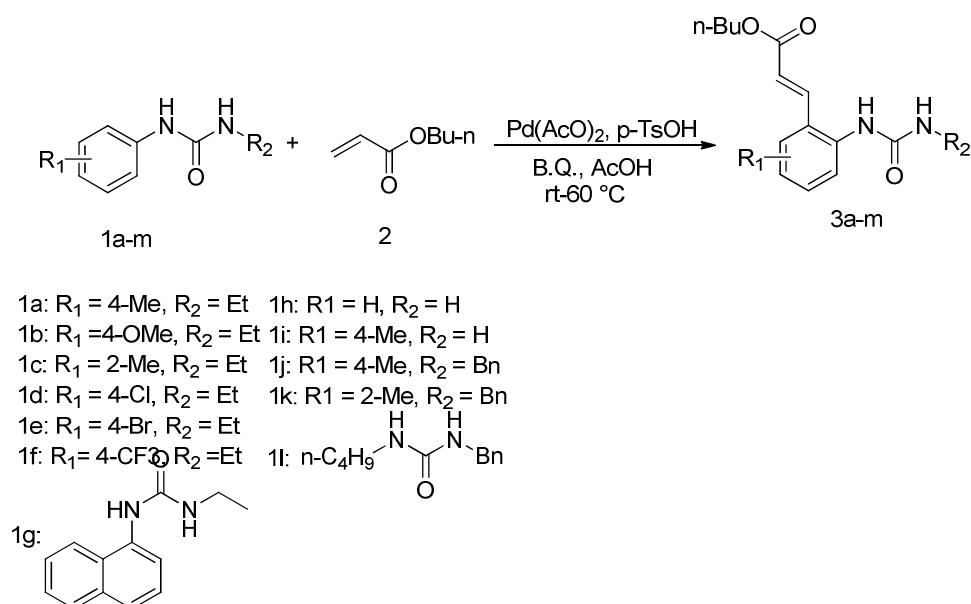
List of Contents

General Information.....	S2
General Procedure for the Synthesis of 3	S2
Characterization Data.....	S3-S7
¹ H and ¹³ C NMR spectra.....	S7-S17

General Information

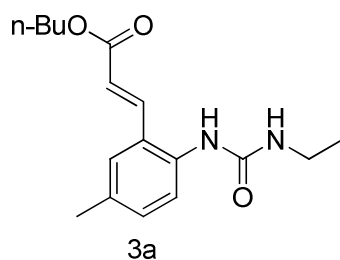
All solvents were purified according to standard methods. Purifications of reaction products were carried out by chromatography using silica gel (200–300 mesh). Melting points were recorded on a BüCHI B-540 melting point apparatus. NMR spectra were recorded for ^1H NMR at 500 MHz and for ^{13}C NMR at 125 MHz. For ^1H NMR, tetramethylsilane (TMS) served as internal standard ($\delta = 0$) and data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constant in Hz. For ^{13}C NMR, TMS ($\delta = 0$) or CDCl_3 ($\delta = 77.26$) was used as internal standard and spectra were obtained with complete proton decoupling. HRMS data were obtained using ESI ionization. The starting materials **1** is commercially available.

General Procedure for the Synthesis of **3**

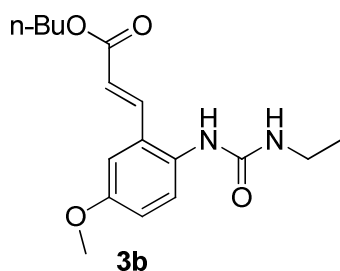


In a typical experiment, aryl urea (1.5 mmol), 10mol% $\text{Pd}(\text{OAc})_2$ (33.6 mg, 0.15 mmol), B.Q. (162 mg, 1.5 mmol) and 30mol% *p*-toluenesulfonic acid monohydrate (77.4 mg, 0.45 mmol) are weighed into a 15 mL of sealed tube charged with a magnetic stirring bar. Next, 3.0 mL acetic acid is added, followed by a solution of (0.26 mL, 1.8 mmol) *n*-butylacrylate with a micro-syringe. The sealed tube is capped and the mixture is stirred at 62 °C oil bath, the reaction time is determined by TLC. The resulting mixture is diluted in 25 mL of ethyl acetate, washed with a saturated K_2CO_3 solution (3 × 10 mL), water (3 × 10 mL), dried over Na_2SO_4 and evaporated in vacuo. The organic residue is purified by silica gel column chromatography using petroleum ether/ethyl acetate (3:1) as the eluent to afford **3** as a white solid. Recrystallization with ethyl acetate provided analytically pure product.

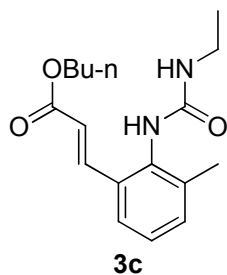
Characterization Data



A white solid; mp 139.6-140.2 °C; ^1H NMR (500 MHz, CDCl_3): δ 7.92 (d, J = 15 Hz, 1 H), 7.44 (d, J = 10 Hz, 1 H), 7.40 (s, 1 H), 7.19 (d, J = 10 Hz, 1 H), 6.78 (s, 1 H), 6.42 (d, J = 20 Hz, 1 H), 4.99 (s, 1 H), 4.18 (t, J = 10.0, 5.0 Hz, 2 H), 3.29 (m, 2 H), 2.34 (s, 3 H); 1.68 (m, 2 H), 1.45 (m, 2 H), 1.13 (t, J = 10.0, 5.0 Hz, 2 H), 0.96 (t, J = 5.0, 10.0, 2 H), ^{13}C NMR (125 MHz, CDCl_3) δ 167.1, 156.4, 139.8, 135.1, 134.6, 132.1, 129.0, 127.8, 119.6, 116.2, 64.6, 35.2, 30.8, 48.1, 20.9, 19.3, 15.2, 13.7; HRMS (ESI): m/z calcd for ($\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_3$): 304.1787; found: 304.1785.

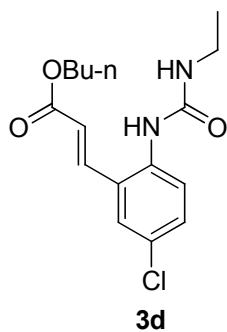


A white solid; mp 155.7-157.0 °C; ^1H NMR (500 MHz, CDCl_3): δ 7.911 (d, J = 16 Hz, 1 H), 7.383 (d, J = 9 Hz, 1 H), 7.107 (s, J = 3 Hz, 1 H), 6.963 (dd, J = 2.5 Hz, 6 Hz, 1 H), 6.422 (d, J = 16 Hz, 2 H), 4.718 (s, 1 H), 4.201 (t, J = 7.0, 6.5 Hz, 2 H), 3.837 (s, 3 H), 3.288 (m, 2 H), 1.688 (m, 2 H), 1.422 (m, 2 H), 1.122 (t, J = 7.0 Hz, 3 H), 0.96 (t, J = 7.5, 7.5 Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 166.8, 157.9, 156.6, 139.5, 130.0, 128.7, 120.3, 117.2, 111.4, 64.5, 55.6, 35.2, 30.6, 19.3, 15.2, 13.4; HRMS (ESI): m/z calcd for ($\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_4$): 320.1736; found: 320.1743.

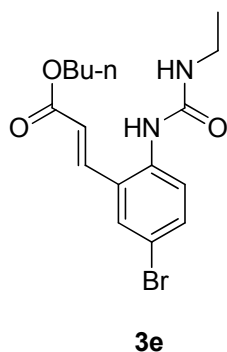


A white solid; mp 130.5-131.0 °C; ^1H NMR (500 MHz, CDCl_3): δ 7.961 (d, J = 16 Hz, 1 H), 7.383 (d, J = 7 Hz, 1 H), 7.276 (m, 2 H), 6.446 (d, J = 16 Hz, 1 H),

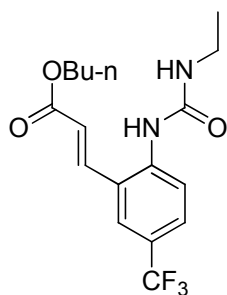
5.963 (s, 1 H), 4.220 (t, J = 6.5, 7.0 Hz, 2 H), 3.272 (m, 2 H), 2.328(s, 3 H); 1.468 (m, 2 H), 1.089 (t, J = 7.0, 7.5 Hz, 3 H), 0.982 (t, J = 7.5 Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 166.9, 156.4, 140.0, 137.7, 134.6, 133.6, 132.8, 127.9, 125.2, 120.6, 64.6, 35.4, 30.6, 19.0, 18.3, 15.7, 13.9; HRMS (ESI): m/z calcd for ($\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_3$): 304.1787; found: 304.1791.



A white solid; mp 131.3-182.5 °C; ^1H NMR (500 MHz, CDCl_3): δ 7.841 (d, J = 16 Hz, 1 H), 7.664 (d, J = 9 Hz, 1 H), 7.516 (d, J = 2.5 Hz, 1 H), 7.315 (dd, J = 6.0, 2.5 Hz, 1 H), 7.019 (s, 1 H), 6.401 (d, J = 16 Hz, 1 H), 5.186 (s, 1 H), 4.179 (t, J = 7.0, 6.5 Hz, 2 H), 3.304 (m, 2 H), 1.685 (m, 2 H); 1.460 (m, 2 H), 1.160 (t, J = 7.5, 7.0 Hz, 3 H), 0.968 (t, J = 7.5 Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 167.1, 155.6, 138.7, 136.0, 130.8, 130.2, 126.7, 126.0, 121.1, 65.1, 35.2, 30.8, 19.3, 15.4, 14.4, 13.7; HRMS (ESI): m/z calcd for ($\text{C}_{16}\text{H}_{21}\text{ClN}_2\text{O}_3$): 324.1241; found: 324.1239.

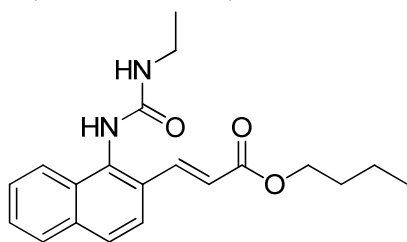


A white solid; mp 142.3-145.8 °C; ^1H NMR (500 MHz, CDCl_3): δ 7.826 (d, J = 16 Hz, 1 H), 7.666 (s, 1 H), 7.617 (d, J = 8.5 Hz, 1 H), 7.459 (dd, J = 6.5, 2.5 Hz, 1 H), 6.965 (s, 1 H), 6.401 (d, J = 15.5 Hz, 1 H), 5.147 (s, 1 H), 4.182 (t, J = 7.0, 6.5 Hz, 2 H), 3.308 (m, 2 H), 1.686 (m, 2 H); 1.448 (m, 2 H), 1.162 (t, J = 7.5, 7.0 Hz, 3 H), 0.969 (t, J = 7.5, 7.0 Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 167.2, 155.4, 138.5, 133.9, 129.8, 126.2, 121.1, 117.7, 116.2, 65.1, 35.2, 30.8, 19.3, 15.2, 13.7; HRMS (ESI): m/z calcd for ($\text{C}_{16}\text{H}_{21}\text{BrN}_2\text{O}_3$): 368.0736; found: 368.0739.



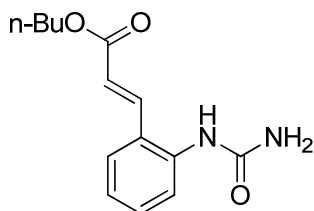
3f

A white solid; mp 173.5-174.1 °C; ^1H NMR (500 MHz, CDCl_3): δ 8.067 (d, J = 9.0 Hz, 1 H), 7.883 (d, J = 15.5 Hz, 1 H), 7.729 (s, 1 H), 7.590 (d, J = 8.5 Hz, 1 H), 7.181 (s, 1 H), 6.458 (d, J = 15.5 Hz, 1 H), 5.302 (s, 1 H), 4.204 (t, J = 7.0, 6.5 Hz, 2 H), 3.350 (m, 2 H), 1.688 (m, 2 H); 1.458 (m, 2 H), 1.202 (t, J = 7.5, 7.0 Hz, 3 H), 0.973 (t, J = 7.5 Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 167.1, 154.8, 140.5, 138.4, 127.7, 125.7, 124.1, 122.8, 121.6, 65.0, 35.3, 30.7, 19.3, 14.9, 13.7; HRMS (ESI): m/z calcd for ($\text{C}_{17}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_3$): 358.1504; found: 358.1516.



3g

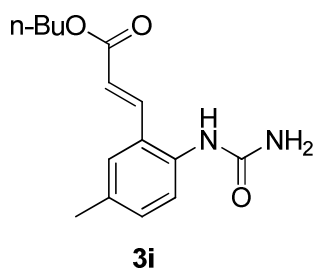
A white solid; mp 110.9-111.4 °C (dec.); ^1H NMR (500 MHz, CDCl_3): δ 8.039 (d, J = 16.0 Hz, 1 H), 7.969 (m, 1 H), 7.745 (d, J = 5.0 Hz, 1 H), 7.670 (d, J = 7.0 Hz, 1 H), 7.572 (m, 1 H), 7.463 (d, J = 5.5 Hz, 1 H), 6.964 (m, 1 H), 6.440 (d, J = 16.0 Hz, 1 H), 4.944 (s, 1 H), 4.178 (t, J = 7.0, 6.5 Hz, 2 H), 3.198 (m, 2 H), 1.689 (m, 2 H); 1.453 (m, 2 H), 1.015 (t, J = 7.5, 7.0 Hz, 3 H), 0.971 (t, J = 7.5 Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 166.8, 156.9, 139.7, 134.9, 132.5, 131.5, 130.3, 128.3, 128.2, 127.7, 127.6, 123.7, 123.1, 120.8, 64.3, 35.1, 30.5, 19.0, 15.2, 13.7; HRMS (ESI): m/z calcd for ($\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_3$): 340.1787; found: 340.1790.



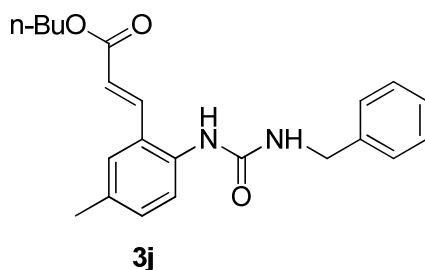
3h

A white solid; mp 169.0-171.3 °C (dec.); ^1H NMR (500 MHz, CDCl_3): δ

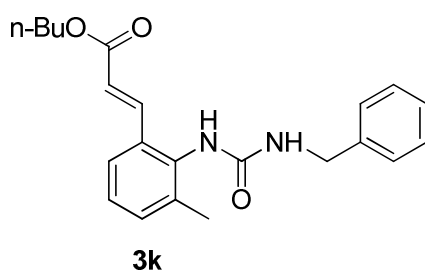
8.009 (d, $J = 15.5$ Hz, 1 H), 7.661 (d, $J = 8.5$ Hz, 1 H), 7.580 (d, $J = 7.5$ Hz, 1 H), 7.514 (s, 1 H), 7.373 (t, $J = 8.0, 7.5$ Hz, 1 H), 7.169 (t, $J = 7.5$ Hz, 1 H), 6.425 (d, $J = 16.0$ Hz, 1 H), 5.247 (s, 2 H), 4.170 (t, $J = 7.0, 6.5$ Hz, 2 H), 1.680 (m, 2 H), 1.439 (m, 2 H), 0.971 (t, $J = 7.5, 7.0$ Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 167.4, 157.1, 139.5, 137.2, 127.3, 125.5, 120.1, 119.8, 64.8, 30.8, 19.0, 13.9; HRMS (ESI): m/z calcd for ($\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_3$): 262.1317; found: 262.1320.



A white solid; mp 175.2-180.1 °C; ^1H NMR (500 MHz, CDCl_3): δ 8.209 (s, 1 H), 7.827 (d, $J = 16.0$ Hz, 1 H), 7.565 (s, 1 H), 7.510 (d, $J = 8.0$ Hz, 1 H), 7.166 (dd, $J = 6.5, 1.5$ Hz, 1 H), 6.542 (d, $J = 15.5$ Hz, 1 H), 5.980 (s, 2 H), 4.173 (t, $J = 7.0, 6.5$ Hz, 2 H), 2.271 (s, 3 H), 1.660 (m, 2 H), 1.410 (m, 2 H), 0.941 (t, $J = 7.5$ Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 166.9, 156.7, 140.7, 136.7, 133.0, 131.8, 127.4, 126.5, 124.7, 118.6, 64.1, 30.8, 20.7, 19.1, 14.1; HRMS (ESI): m/z calcd for ($\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_3$): 276.1474; found: 276.1473.



A white solid; mp 163.4-165.1 °C; ^1H NMR (500 MHz, CDCl_3): δ 8.006 (d, $J = 16.0$ Hz, 1 H), 7.513 (d, $J = 8.0$ Hz, 1 H), 7.307 (m, 8 H), 6.424 (d, $J = 16.5$ Hz, 1 H), 6.088 (s, 1 H), 4.411 (d, $J = 6.0$ Hz, 2 H), 4.235 (t, $J = 7.0, 6.5$ Hz, 2 H), 2.305 (s, 3 H), 1.728 (m, 2 H), 1.480 (m, 2 H), 0.992 (t, $J = 7.5$ Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 167.2, 156.4, 139.7, 138.9, 135.5, 134.5, 131.9, 129.8, 128.5, 127.5, 127.4, 127.2, 126.1, 119.7, 64.5, 44.4, 30.6, 21.1, 19.3, 13.9; HRMS (ESI): m/z calcd for ($\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}_3$): 366.1943; found: 366.1943.



A white solid; mp 153.0 °C (dec.); ^1H NMR (500 MHz, CDCl_3): δ 8.006 (d, $J = 16.0$ Hz, 1 H), 7.513 (d, $J = 8.0$ Hz, 1 H), 7.307 (m, 8 H), 6.424 (d, $J = 16.5$ Hz, 1 H), 6.088 (s, 1 H), 4.411 (d, $J = 6.0$ Hz, 2 H), 4.235 (t, $J = 7.0, 6.5$ Hz, 2 H), 2.305 (s, 3 H), 1.728 (m, 2 H), 1.480 (m, 2 H), 0.992 (t, $J = 7.5$ Hz, 3 H), ^{13}C NMR (125 MHz, CDCl_3) δ 166.6, 156.4, 140.0, 138.9, 137.7, 134.4, 133.6, 132.7, 128.6, 128.0, 127.4, 127.2, 125.2, 120.6, 64.6, 44.4, 30.7, 19.3, 18.3, 13.9; HRMS (ESI): m/z calcd for ($\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}_3$): 366.1943; found: 366.1941.

^1H and ^{13}C NMR spectra for the new compound

