Supporting Information

Aqueous-Phase Heck Coupling of 5-Iodouridine and Alkenes Under Phosphine-Free Conditions

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Experimental Procedures and Characterization Data

**General experimental procedures.** 5-Iodo-2'-deoxyuridine (5-IdU) was purchased from USB (Germany). TPPTS was obtained from Fluka (Germany). The alkenes and other reagents were purchased from Aldrich (U.S.A.). All reagents were and used without further purification. DCPES\(^1\) and TXPTS\(^2\) were prepared by literature methods. For all reactions, 2:1 or 1:1 H\(_2\)O:acetonitrile were combined and sparged for 30 minutes with nitrogen prior to use. The reactions were assembled in a nitrogen-filled dry box in vials closed with screw-cap septa or Schlenk-type flasks. Reaction progress was monitored by RP-HPLC equipped with UV-Vis detector (C-18 column, eluted with a gradient ranging from 10:90 MeOH/H\(_2\)O to 100% MeOH) or RP-TLC (C-18, 1:2 H\(_2\)O/MeOH eluent). Each starting material was detected at its maximum wavelength (287 nm for 5-IdU) and each product was detected at its characteristic maximum wavelength.

**General Methods for Alkenylation of 5-IdU.** Method A: 5-IdU (0.3 mmol) and Pd(OAc)\(_2\) (3.4 mg, 0.015 mmol) were placed in a round bottomed flask under nitrogen. Deoxygenated 1:1 water:acetonitrile (3 mL) was added to the reaction vessel, followed by the addition of the alkene (1.2 mmol) and triethylamine (61.0 mg, 0.600 mmol). The reaction was heated in an oil bath at 80 °C until RP-HPLC showed complete conversion. The reaction mixture was diluted to 10 mL with 1:1 water:methanol and the pH adjusted to 6-7 using 10 % aqueous HCl. After removal of solvent, the crude product was purified by chromatography (RP-SiO\(_2\), H\(_2\)O to 60:40 MeOH/H\(_2\)O).

Method B: Identical to Method A, but TPPTS (17.1 mg 0.03 mmol) was added to the flask along with Pd(OAc)\(_2\) and 5-IdU.
Butyl (E)-3-(2'-deoxyurid-5-yl)propenoate (3). Method A: Yield 68.1 mg (64%). Method B: Yield 75.0 mg (74%). H NMR (500 MHz, DMSO-d$_6$): δ 11.69 (s, 1H), 8.45 (s, 1H), 7.39 (d, $J = 15.5$ Hz, 1H), 6.88 (d, $J = 15.5$, 1H), 6.17 (dd, $J = 6.5, 6.5$ Hz, 1H), 5.29 (d, $J = 4.5$ Hz, 1H), 5.20 (t, $J = 5.0$ Hz, 1H), 4.312-4.28 (m, 1H), 4.14 (t, $J = 6.8$, 2H), 3.84 (dd, $J = 7.0, 3.5$ Hz, 1H), 3.72-3.60 (m, 2H), 2.26-2.17 (m, 2H), 1.66-1.60 (m, 2H), 1.43-1.35 (m, 2H), 0.94 (t, $J = 7.5$ Hz, 3H).

C NMR (126 MHz, DMSO-d$_6$): δ 166.7, 161.6, 149.1, 143.8, 137.8, 116.4, 108.1, 87.5, 84.7, 69.6, 63.4, 60.7, 39.9, 30.2, 18.6, 13.5. HRMS-ESI (m/z): [M+H] Calcd for C$_{16}$H$_{23}$N$_2$O$_7$, 355.1500; found, 355.1508.

3-(2'-Deoxyurid-5-yl)-2-cyclohexen-1-one (5). Method A: Yield 69.7 mg (72%). Method B: Yield 66.6 mg (71%). H NMR (500 MHz, DMSO-d$_6$): δ 11.57 (s, 1H), 8.36 (s, 1H), 6.92 (s, 1H), 6.19 (dd, $J = 6.5, 6.5$ Hz, 1H), 5.27 (d, $J = 4.5$ Hz, 1H), 5.22 (t, $J = 5.0$ Hz, 1H), 4.31-4.27 (m, 1H), 3.86-3.84 (m, 1H), 3.68-3.59 (m, 2H), 2.55-2.53 (m, 2H), 2.32-2.30 (m, 2H), 2.22-2.19 (m, 2H), 1.99-1.93 (m, 2H). C NMR (126 MHz, DMSO-d$_6$): δ 198.7, 161.3, 152.4, 149.1, 140.5, 125.1, 110.7, 87.6, 84.9, 69.9, 60.6, 40.4, 36.7, 26.4, 22.1. HRMS-ESI (m/z): [M+H] Calcd for C$_{15}$H$_{19}$N$_2$O$_6$, 323.1238; found, 323.1251.
5-((E)-2-Phenylethenyl)-2′-deoxyuridine (7).\(^3\) Method A: Yield 81.1 mg (82%). Method B: Yield 77.6 mg (81%). \(^1\)H NMR (500 MHz, DMSO-d\(_6\)): δ 11.49 (s, 1H), 8.23 (s, 1H), 7.47-7.46 (m, 2H), 7.41 (d, \(J = 16.5\) Hz, 1H), 7.36-7.33 (m, 2H), 7.25-7.22 (m, 1H), 6.91-6.87 (d, \(J = 16.5\) Hz, 1H), 6.19 (dd, \(J = 6.5, 6.5\) Hz, 1H), 5.27 (d, \(J = 4.0\) Hz, 1H), 5.19 (t, \(J = 5.0\) Hz, 1H), 4.31-4.28 (m, 1H), 3.82 (dd, \(J = 7.0, 3.5\) Hz, 1H), 3.71-3.60 (m, 2H), 2.23-2.13 (m, 2H). \(^13\)C NMR (126 MHz, DMSO-d\(_6\)): δ 162.6, 149.9, 138.6, 138.0, 129.2, 128.1, 127.8, 126.5, 121.7, 111.2, 87.9, 84.9, 70.5, 61.5, 40.5.

References


NMR Spectra