Regioselective Heck Couplings of α,β -unsaturated Tosylates and Mesylates with Electron Rich Olefins

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Supporting Information

General Methods. Solvents were dried according to standard procedures, reactions were monitored by thin-layer chromatography (TLC) analysis and flash chromatography was carried out on silica gel 60 (230-400 mesh). The chemical shifts are reported in ppm relative to solvent residual peak.¹ MS spectra were recorded on a LC TOF (ES) apparatus. All Heck couplings were carried out in 3.5 mL sample vials with a teflon sealed screwcap in a glovebox under an argon atmosphere. Dioxane was dried over sodium and distilled before use. All purchased chemicals were used as received without further purification.

General Procedure for the Preparation of Tosylate and Mesylate Substituted Heck Coupling Substrates. (2, 3, 4, 5, 6, 16, 17, 18).

The tosylate substrate **2** (5,5-dimethyl-3-oxocyclohex-1-enyl tosylate) was prepared according to a known literature procedure.²

The tosylate substrate **3** (3-oxocyclohex-1-enyl tosylate) was prepared according to a known literature procedure.³

6-Methyl-2-oxo-2H-pyran-4-yl tosylate (4).⁴ 4-Hydroxy-6-methyl-2H-pyran-2-one (500 mg, 3.97 mmol) and tosyl chloride (756 mg, 3.97 mmol) was dissolved in CH₂Cl₂ (30 mL). TEA (1.64 mL, 11.8 mmol) was added and the reaction mixture was left stirring at rt. overnight (23 h). CH₂Cl₂ (50 mL) was added and the organic phase was washed with water (25 mL) and brine (25 mL). The organic phase was dried over MgSO₄. After concentration *in vacuo* the crude product were purified by column chromatography using ethyl acetate/pentane (1:4) as eluent. This afforded 997 mg of the title compound (90 % yield) as a colorless solid. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 8.04 (d, 2H, *J* = 8.4 Hz), 7.38 (d, 2H, *J* = 8.4 Hz), 5.99 (s, 1H), 5.80 (s, 1H), 2.47 (s, 3H), 2.23 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 164.4, 163.0, 162.1, 146.8, 131.8, 130.4(2C), 128.5(2C), 100.9, 100.8, 21.9, 20.3. HRMS C₁₃H₁₂ON [M+Na⁺]; calculated: 303.0303 found: 303.0301.

¹ Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.

² Feigenbaum, A.; Pete, J. P.; Scholler, D. *J. Org. Chem.* **1984**, *49*, 2355.

³ Fu, X.; Zhang, S.; Yin, J.; McAllister, T. L.; Jiang, S. A.; Chou-Hong, T.; Thiruvengadam, K.; Zhang, F. *Tetrahedron Lett.* **2002**, *43*, 573.

⁴ Bittencourt, A. M.; Gottlieb, O. R.; Mors, W. B.; Mageswaran, M. T. M.; Ollis, W. D.; Sutherland, I. O. *Tetrahedron* **1971**, *27*, 1043.

4-Oxo-4H-chromen-2-yl tosylate (5).⁵ 4-Hydroxy coumarin (1.00 g, 6.17 mmol), TsCl (1.18 g, 6.17 mmol) and TEA (2.58 mL, 18.5 mmol) were reacted at rt. for 30 min. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (2:3) as eluent. This afforded 1.83 g of the title compound (94% yield) as a colorless solid. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 7.89 (d, 2H, J = 8.4 Hz), 7.62 (d, 1H, J = 8.0 Hz), 7.56 (t, 1H, J = 7.2 Hz), 7.39 (d, 2H, J = 8.2 Hz), 7.31-7.24 (m, 2H), 6.31 (s, 1H), 2.46 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 160.9, 157.9, 153.6, 147.0, 133.4, 131.8, 130.5(2C), 128.6(2C), 124.6, 123.3, 117.0, 115.1, 103.7, 21.9. HRMS C₁₆H₁₂O₅S [M+Na⁺]; calculated: 339.0303 found: 339.0304.

3,6-Dihydro-2-methyl-6-oxo-2H-pyran-4-yl tosylate (6). Dihydro-6-methyl-3H-pyran-2,4-dione (204 mg, 1.59 mmol), TsCl (303 mg, 1.59 mmol) and TEA (665 μ L, 4.77 mmol) were reacted at rt. for 17 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:4) as eluent. This afforded 272 mg of the title compound (61% yield) as a colorless oil. ¹H NMR (400 MHz, CD₃CN) δ (ppm) 7.87 (d, 2H, J = 8.4 Hz), 7.49 (d, 2H, J = 8.4 Hz), 5.68 (s, 1H), 4.59-4.45 (m, 1H), 2.84-2.46 (m, 5H), 1.32 (d, 3H, J = 6.4 Hz). ¹³C NMR (100 MHz, CD₃CN) δ (ppm) 165.3, 164.0, 148.2, 132.6, 131.4(2C), 129.3(2C), 107.0, 73.9, 34.4, 21.8, 20.4. HRMS C₁₃H₁₄O₅S [M+Na⁺]; calculated: 305.0460 found: 305.0463.

5,5-Dimethyl-3-oxocyclohex-1-enyl mesylate (16).⁶ Dimedone (1.24 g, 8.85 mmol), mesyl chloride (685 μ L, 8.85 mmol) and potassium carbonate were reacted at rt. for 3½ h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:3) as eluent. This afforded 1.51 g of the title compound (78% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 5.95 (s, 1H), 3.16 (s, 3H), 2.41 (s, 2H), 2.19 (s, 2H), 1.04 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 198.4, 166.1, 115.2, 50.4, 42.3, 38.9, 32.9, 28.0.

The mesylate substrate **17** (3-Oxocyclohex-1-enyl mesylate) was prepared according to a known literature procedure.⁶

3,6-Dihydro-2-methyl-6-oxo-2H-pyran-4-yl mesylate (18). Dihydro-6-methyl-3H-pyran-2,4-dione (600 mg, 4.68 mmol), mesyl chloride (362 μ L, 4.68 mmol), TEA (1.96 mL, 14.0 mmol) were reacted at rt. for 16 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (2:3) as eluent. This afforded 529 mg of the title compound (50% yield) as an amorphous solid. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 5.97 (d, 1H, J = 2.0 Hz), 4.67-4.59 (m, 1H), 3.24 (s, 3H), 2.65 (ddd, 1H, J = 17.6, 10.8, 2.0 Hz), 2.57 (dd, 1H, J = 18.0, 4.4 Hz), 1.47 (d, 3H, J = 6.4 Hz). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 164.5, 162.1, 106.0, 72.9, 39.1, 34.2, 20.5. HRMS C₇H₁₀O₅S [M+Na⁺]; calculated: 229.0147 found: 229.0144.

General Procedure for Heck Couplings with vinyl ethers. The olefin (4 equiv.), mesyl/tosyl substrate (1 equiv.), DIPEA (3 equiv.), DPPF (0.03 equiv.) were dissolved in dioxane (3 mL). Pd₂(dba)₃ (0.015 equiv.) was then added and the sample vial was fitted with a teflon sealed screwcap and removed from the glovebox. The reaction mixture was heated for the time stated for each product

⁵ Fu, X.; Zhang, S.; Jianguo, Y.; Schumacher, D. P. *Tetrahedron Lett.* **2002**, 43, 6673.

⁶ Kowalski, C. J.; Fields, K. W. *J. Org. Chem.*, **1981**, 46, 197.

at 85°C. The reaction was monitored by TLC. After completed reaction the crude reaction mixture was concentrated *in vacuo* directly onto a small amount of silica gel and purified by column chromatography.

General Procedure for Heck Couplings with enamides. The olefin (1 equiv.), mesyl/tosyl substrate (1.5 equiv.), DIPEA (2 equiv.), DPPF (0.03 equiv.) were dissolved in dioxane (3 mL). Pd₂(dba)₃ (0.015 equiv.) was then added and the sample vial was fitted with a teflon sealed screwcap and removed from the glovebox. The reaction mixture was heated for the time stated for each product at 85°C. The reaction was monitored by TLC. After completed reaction the crude reaction mixture was concentrated *in vacuo* directly onto a small amount of silica gel and purified by column chromatography.

***N*-(1-(5,5-Dimethyl-3-oxocyclohex-1-enyl)vinyl)acetamide (7) from tosylate coupling.** *N*-Vinyl acetamide (63 mg, 0.74 mmol), **2** (311 mg, 1.06 mmol), DIPEA (245 µL, 1.41 mmol), DPPF (11.7 mg, 0.021 mmol), Pd₂dba₃ (9.7 mg, 0.011 mmol) were reacted for 1 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH₂Cl₂ (1:1) as eluent. This afforded 128 mg of the title compound (83% yield) as a yellow oil. ¹H NMR (400 MHz, CD₃CN) δ (ppm) 7.70 (bs, 1H), 6.06 (s, 1H), 5.60 (s, 1H), 5.35 (s, 1H), 2.40 (s, 2H), 2.22 (s, 2H), 2.00 (s, 3H), 1.03 (s, 6H). ¹³C NMR (100 MHz, CD₃CN) δ (ppm) 200.7, 170.1, 154.8, 142.0, 124.1, 109.9, 51.7, 40.8, 34.1, 28.3, 23.9.

***N*-(1-(5,5-Dimethyl-3-oxocyclohex-1-enyl)vinyl)acetamide (7) from mesylate coupling.** *N*-Vinyl acetamide (85 mg, 0.10), **16** (327 mg, 1.50 mmol), DIPEA (350 µL, 2.00 mmol), DPPF (16.6 mg, 0.03 mmol), Pd₂dba₃ (13.7 mg, 0.015 mmol) were reacted for 1 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/CH₂Cl₂ (1:1) as eluent. This afforded 170 mg of the title compound (83% yield).

3-(1-Butoxyvinyl)-5,5-dimethylcyclohex-2-enone (8) from tosylate coupling. Butyl vinyl ether (188 µL, 1.45 mmol), **2** (106 mg, 0.36 mmol), DIPEA (180 µL, 1.08 mmol), DPPF (6.0 mg, 0.011 mmol), Pd₂dba₃ (5.0 mg, 0.0054 mmol) were reacted for 2½ h. The crude product was purified by flash chromatography on silica gel using pentane/CH₂Cl₂ (1:6) as eluent. This afforded 60 mg of the title compound (75% yield) as a colorless oil. ¹H NMR (400 MHz, CD₃CN) δ (ppm) 6.30 (s, 1H), 4.73 (d, 1H, *J* = 2.8 Hz), 4.50 (d, 1H, *J* = 2.8 Hz), 3.78 (t, 2H, *J* = 6.4 Hz), 2.41 (d, 2H, *J* = 1.2 Hz), 2.16 (s, 2H), 1.74-1.67 (m, 2H), 1.50-1.40 (m, 2H), 1.03 (s, 6H), 0.95 (t, 3H, *J* = 7.6 Hz). ¹³C NMR (100 MHz, CD₃CN) δ (ppm) 200.9, 159.4, 152.4, 123.4, 89.8, 68.5, 51.6, 39.9, 34.0, 31.7, 28.4, 20.2, 14.1. HRMS C₁₄H₂₂O₂ [M+Na⁺]; calculated: 245.1517 found: 245.1513.

3-(1-Butoxyvinyl)-5,5-dimethylcyclohex-2-enone (8) from mesylate coupling. Butyl vinyl ether (237 µL, 1.83 mmol), **16** (100 mg, 0.46 mmol), DIPEA (239 µL, 1.37 mmol), DPPF (7.6 mg, 0.014 mmol), Pd₂dba₃ (6.3 mg, 0.0069 mmol) were reacted for 17 h. The crude product was purified by flash chromatography on silica gel using pentane/CH₂Cl₂ (1:6) as eluent. This afforded 68 mg of the title compound (67% yield).

***N*-(1-(3-Oxocyclohex-1-enyl)vinyl)acetamide (9) from tosylate coupling.** *N*-Vinyl acetamide (57 mg, 0.67 mmol), **3** (250 mg, 1.00 mmol), DIPEA (232 µL, 2.00 mmol), DPPF (11.1 mg, 0.02 mmol), Pd₂dba₃ (9.46 mg, 0.01 mmol) were reacted for 1 h. The crude product was purified by flash

chromatography on silica gel using ethyl acetate/DCM (1:1) as eluent. This afforded 94.9 mg of the title compound (79% yield) as a pale yellow oil. ¹H NMR (400 MHz, CD₃CN) δ (ppm) 7.68 (bs, 1H), 6.04 (s, 1H), 5.59 (s, 1H), 5.34 (s, 1H), 2.51-2.47 (m, 2H), 2.34 (t, J = 6.0 Hz), 2.03-1.97 (m, 5H). ¹³C NMR (100 MHz, CD₃CN) δ (ppm) 200.4, 170.1, 157.2, 141.7, 125.0, 109.8, 38.0, 26.9, 23.8, 23.3. LRMS C₁₀H₁₃O₂N [M+Na⁺]; calculated: 202.0 found: 202.0.

***N*-(1-(3-Oxocyclohex-1-enyl)vinyl)acetamide (9) from mesylate coupling.** *N*-Vinyl acetamide (57 mg, 0.67 mmol), **17** (174.2 mg, 1.00 mmol), DIPEA (232 μ L, 2.00 mmol), DPPF (11.1 mg, 0.02 mmol), Pd₂dba₃ (9.46 mg, 0.01 mmol) were reacted for 5 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/DCM (1:1) as eluent. This afforded 73.3 mg of the title compound (61% yield) as a pale yellow oil.

3-(1-Butoxyvinyl)-cyclohex-2-enone (10) from tosylate coupling.⁷ Butyl vinyl ether (310 μ L, 2.40 mmol), **3** (150 mg, 0.59 mmol), DIPEA (313 μ L, 1.80 mmol), DPPF (9.96 mg, 0.018 mmol), Pd₂dba₃ (8.23 mg, 0.009 mmol) were reacted for 18 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:10) as eluent. This afforded 94.4 mg of the title compound (82% yield) as a colorless oil. ¹H NMR (400 MHz, CD₃CN) δ (ppm) 6.28 (s, 1H), 4.73 (d, 1H, J = 3.2 Hz), 5.00 (d, 1H, J = 3.2 Hz), 3.78 (t, 2H, J = 6.4 Hz), 2.50 (td, 2H, J = 6.0, 1.2 Hz), 2.35-2.31 (m, 2H), 2.03-1.97 (m, 2H), 1.74-1.67 (m, 2H), 1.49-1.41 (m, 2H), 0.95 (t, 3H, J = 7.2). ¹³C NMR (100 MHz, CD₃CN) δ (ppm) 200.63, 159.6, 154.7, 124.3, 89.8, 68.4, 38.1, 31.7, 26.0, 23.4, 20.2, 14.1. HRMS C₁₂H₁₈O₂ [M+Na⁺]; calculated: 217.1204 found: 217.1201.

3-(1-Butoxyvinyl)-cyclohex-2-enone (10) from mesylate coupling. Butyl vinyl ether (310 μ L, 2.40 mmol), **17** (104.4 mg, 0.59 mmol), DIPEA (313 μ L, 1.80 mmol), DPPF (9.96 mg, 0.018 mmol), Pd₂dba₃ (8.23 mg, 0.009 mmol) were reacted for 18 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:10) as eluent. This afforded 67.9 mg of the title compound (58% yield) as a colorless oil.

***N*-(1-(6-Methyl-2-oxo-2H-pyran-4-yl)vinyl)acetamide (11) from tosylate coupling.** *N*-Vinyl acetamide (44 mg, 0.52 mmol), **4** (200 mg, 0.72 mmol), DIPEA (165 μ L, 0.95 mmol), DPPF (7.9 mg, 0.014 mmol), Pd₂dba₃ (6.5 mg, 0.0071 mmol) were reacted for 4 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:1) as eluent. This afforded 91 mg of the title compound (91% yield) as a colorless solid. ¹H NMR (400 MHz, CD₃CN) δ (ppm) 7.84 (bs, 1H), 6.22 (s, 1H), 6.11 (s, 1H), 5.67 (s, 1H), 5.34 (s, 1H), 2.21 (s, 3H), 2.02 (s, 3H). ¹³C NMR (100 MHz, CD₃CN) δ (ppm) 170.4, 163.8, 162.9, 153.3, 139.3, 109.7, 108.2, 102.7, 23.8, 20.1. HRMS C₁₀H₁₁O₃N [M+Na⁺]; calculated: 216.0637 found: 216.0645.

4-(1-Butoxyvinyl)-6-methyl-2H-pyran-2-one (12) from tosylate coupling. Butyl vinyl ether (160 μ L, 1.43 mmol), **4** (100 mg, 0.36 mmol), DIPEA (187 μ L, 1.07 mmol), DPPF (6.0 mg, 0.011 mmol), Pd₂dba₃ (5.0 mg, 0.0054 mmol) were reacted for 23 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:20) as eluent. This afforded 63 mg of the

⁷ Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1989**, *54*, 1502.

title compound (84% yield) as a colorless oil. ^1H NMR (400 MHz, CD_3CN) δ (ppm) 6.29 (s, 1H), 4.90 (d, 1H, $J = 3.2$ Hz), 4.56 (d, 1H, $J = 3.2$ Hz), 3.82 (t, 2H, $J = 6$ Hz), 2.20 (s, 3H), 1.76-1.69 (m, 2H), 1.51-1.41 (m, 2H), 0.95 (t, 3H, $J = 7.4$ Hz). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 163.9, 162.6, 156.3, 151.2, 107.3, 101.4, 90.0, 68.9, 31.6, 20.1, 14.1.

***N*-(1-(2-Oxo-2H-chromen-4-yl)vinyl)acetamide (13) from tosylate coupling.** *N*-Vinyl acetamide (50 mg, 0.59 mmol), **5** (279 mg, 0.88 mmol), DIPEA (205 μL , 1.18 mmol), DPPF (9.8 mg, 0.018 mmol), Pd_2dba_3 (8.1 mg, 0.0088 mmol) were reacted for 6 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:1) as eluent. This afforded 98 mg of the title compound (73% yield) as a pale yellow oil. ^1H NMR (400 MHz, CD_3CN) δ (ppm) 8.26 (bs, 1H), 7.75 (dd, 1H, $J = 8.4, 1.6$ Hz), 7.60 (ddd, 1H, $J = 8.4, 7.2, 1.6$ Hz), 7.38-7.31 (m, 2H), 6.37 (s, 1H), 5.70 (s, 1H), 4.90 (s, 1H), 1.96 (s, 3H). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 169.7, 161.3, 154.5, 153.2, 138.5, 132.9, 126.9, 125.4, 119.3, 177.8, 115.4, 104.9, 23.7. HRMS $\text{C}_{13}\text{H}_{11}\text{O}_3\text{N}$ $[\text{M}+\text{Na}^+]$; calculated: 252.0637 found: 252.0632.

4-(1-Butoxyvinyl)-2H-chromen-2-one (14) from tosylate coupling. Butyl vinyl ether (245 μL , 1.90 mmol), **5** (150 mg, 0.47 mmol), DIPEA (248 μL , 1.42 mmol), DPPF (7.9 mg, 0.014 mmol), Pd_2dba_3 (6.5 mg, 0.0071 mmol) were reacted for 22 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:15) as eluent. This afforded 105 mg of the title compound (91% yield) as a colorless oil. ^1H NMR (400 MHz, CD_3CN) δ (ppm) 7.79 (dd, 1H, $J = 8.0, 1.6$ Hz), 7.57 (ddd, 1H, $J = 8.4, 7.2, 1.6$ Hz), 7.34-7.27 (m, 2H), 6.41 (s, 1H), 5.95 (d, 1H, $J = 2.8$ Hz), 5.69 (d, 1H, $J = 2.8$ Hz), 3.92 (t, 2H, $J = 6.4$ Hz), 1.76-1.69 (m, 2H), 1.49-1.39 (m, 2H), 0.94 (t, 3H, $J = 7.4$ Hz). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 161.4, 158.1, 155.0, 151.8, 132.9, 127.9, 125.2, 118.7, 117.8, 115.8, 89.9, 69.2, 31.6, 20.1, 14.1. HRMS $\text{C}_{15}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{Na}^+]$; calculated: 267.0997 found: 267.0984.

***N*-(1-(3,6-Dihydro-2-methyl-6-oxo-2H-pyran-4-yl)vinyl)acetamide (15) from tosylate coupling.** *N*-Vinyl acetamide (52 mg, 0.61 mmol), **6** (260 mg, 0.92 mmol), DIPEA (214 μL , 1.23 mmol), DPPF (10.2 mg, 0.018 mmol), Pd_2dba_3 (8.4 mg, 0.0092 mmol) were reacted for 3 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/ CH_2Cl_2 (1:1) as eluent. This afforded 65 mg of the title compound (55% yield) as a pale yellow solid. ^1H NMR (400 MHz, CD_3CN) δ (ppm) 7.75 (bs, 1H), 6.00 (s, 1H), 5.65 (s, 1H), 5.35 (s, 1H), 4.57-4.48 (m, 1H), 2.60 (dd, 1H, $J = 17.6, 3.6$ Hz), 2.38 (ddd, 1H, $J = 17.2, 11.2, 2.0$ Hz), 2.00 (s, 3H), 1.39 (d, 3H, $J = 6.0$ Hz). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 170.3, 166.3, 153.1, 139.9, 115.3, 110.8, 75.0, 32.4, 23.8, 20.8.

***N*-(1-(3,6-Dihydro-2-methyl-6-oxo-2H-pyran-4-yl)vinyl)acetamide (15) from mesylate coupling.** *N*-Vinyl acetamide (61 mg, 0.71 mmol), **18** (220 mg, 1.07 mmol), DIPEA (248 μL , 1.42 mmol), DPPF (11.8 mg, 0.021 mmol), Pd_2dba_3 (9.8 mg, 0.011 mmol) were reacted for 24 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/ CH_2Cl_2 (1:1) as eluent. This afforded 38 mg of the title compound (28% yield).

2-Methoxy-*N*-(1-(5,5-dimethyl-3-oxocyclohex-1-enyl)vinyl)acetamide (19) from mesylate coupling. *N*-Vinyl-2-methoxy acetamide (50 mg, 0.43 mmol), **16** (190 mg, 0.87 mmol), DIPEA (228 μL , 1.30 mmol), DPPF (12.0 mg, 0.022 mmol), Pd_2dba_3 (9.9 mg, 0.0011 mmol) were reacted for 4 h.

The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:1) as eluent. This afforded 59 mg of the title compound (57% yield) as a pale yellow oil. ^1H NMR (400 MHz, CD_3CN) δ (ppm) 7.99 (bs, 1H), 5.99 (s, 1H), 5.72 (s, 1H), 5.47 (s, 1H), 3.93 (s, 2H), 3.42 (s, 3H), 2.43 (s, 2H), 2.24 (s, 2H), 1.04 (s, 6H). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 200.4, 169.5, 154.4, 140.7, 123.8, 111.0, 72.7, 59.7, 51.6, 40.6, 34.1, 28.2. HRMS $\text{C}_{13}\text{H}_{19}\text{O}_3\text{N}$ $[\text{M}+\text{Na}^+]$; calculated: 260.1263 found: 260.1263.

2-Methoxy-*N*-(1-(3-oxocyclohex-1-enyl)vinyl)acetamide (20) from mesylate coupling. *N*-Vinyl-2-methoxy acetamide (88.8 mg, 0.77 mmol), **17** (269 mg, 0.154 mmol), DIPEA (262 μL , 1.54 mmol), DPPF (12.8 mg, 0.023 mmol), Pd_2dba_3 (10.6 mg, 0.0012 mmol) were reacted for 11 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/DCM (1:1) as eluent. This afforded 71.3 mg of the title compound (45% yield) as a pale yellow oil. ^1H NMR (400 MHz, CD_3CN) δ (ppm) 7.99 (bs, 1H), 5.98 (s, 1H), 5.72 (s, 1H), 5.45 (s, 1H), 3.93 (s, 2H), 3.42 (s, 3H), 2.19 (td, 2H, $J = 6.0, 1.2$ Hz), 2.35 (t, 2H, $J = 6.4$ Hz), 2.05-1.98 (m, 2H). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 200.2, 169.5, 156.8, 140.5, 124.7, 110.8, 72.7, 59.7, 38.0, 26.9, 23.2. HRMS $\text{C}_{11}\text{H}_{15}\text{O}_3\text{N}$ $[\text{M}+\text{Na}^+]$; calculated: 232.0950 found: 232.0938.

4-(1-Butoxyvinyl)-5,6-dihydro-6-methylpyran-2-one (21) from mesylate coupling. Butyl vinyl ether (376 μL , 2.91 mmol), **16** (130 mg, 0.63 mmol), DIPEA (380 μL , 2.18 mmol), DPPF (12.1 mg, 0.022 mmol), Pd_2dba_3 (10.0 mg, 0.011 mmol) were reacted for 24 h. The crude product was purified by flash chromatography on silica gel using ethyl acetate/pentane (1:15) as eluent. This afforded 55 mg of the title compound (42% yield) as a colorless oil. ^1H NMR (400 MHz, CD_3CN) δ (ppm) 6.21 (s, 1H), 4.72 (d, 1H, $J = 3.2$ Hz), 4.59 (d, 1H, $J = 3.2$ Hz), 4.58-4.50 (m, 1H), 3.86-3.77 (m, 2H), 2.64 (dd, 1H, $J = 17.6, 4$ Hz), 2.40 (ddd, 1H, $J = 17.6, 11.6, 2$ Hz), 1.77-1.70 (m, 2H), 1.52-1.39 (m, 5H), 0.97 (t, 3H, $J = 7.2$ Hz). ^{13}C NMR (100 MHz, CD_3CN) δ (ppm) 166.3, 157.4, 150.9, 114.7, 90.8, 74.8, 68.6, 31.6 (2C), 20.8, 20.1, 14.1. HRMS $\text{C}_{12}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{Na}^+]$; calculated: 233.2593 found: 233.1153.

NMR spectra

S10

S11

S12

S13

S14

S16

S17

S18

S19

S20