Supporting Information

For

Synthesis of β,γ -Unsaturated Lactams via a Magnesium Iodide-
Promoted Ring Expansion of Secondary
Methylenecyclopropyl Amides

Mark E. Scott, Christina A. Schwarz and Mark Lautens^{*}
Davenport Research Laboratories, Department of Chemistry, University of Toronto,
80 St. George Street, Toronto, Ontario, M5S 3H6, Canada
mlautens@chem.utoronto.ca

Table of Contents

Experimental procedures	SI 3
General	SI 3
Starting Material Synthesis	SI 3
General Procedure for MgI_2 -Mediated Ring Expansion	SI 13
Product Modification	SI 21
Supporting spectra	SI 22
References	SI 60

General

Melting points were recorded using a Fisher-Johns melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded using either a Varian Mercury 400 MHz or Varian Unity 500 MHz spectrometer in CDCl_3 with chemical shifts relative to tetramethylsilane (TMS, 0 ppm) unless otherwise reported. No special notation is used for equivalent carbons. IR spectra were obtained using a Nicolet DX FT IR spectrometer as thin films on NaCl plates. High-resolution mass spectra were obtained using a VG 70-250S (double focusing) mass spectrometer at 70 eV.

Diethyl ether and dichloromethane were dried and degassed using an MBRAUN MB solvent purification system. Tetrahydrofuran (THF) was distilled from Na/benzophenone prior to use. All other reagents were used as received from Sigma-Aldrich unless otherwise indicated. MgI_2 was weighed out in a glovebox to prevent the absorption of water. Neutral silica (Silicycle, Quebec, Canada) for flash chromatography was used as received. All experiments were performed under anhydrous conditions under an atmosphere of argon.

2-Methylene-cyclopropanecarboxylic acid ethyl ester,¹ 2-methylene-cyclopropanecarboxylic acid,¹ 2-methylene-cyclopropanecarboxylic acid pyrid-2-yl-amide (**1g**),² 2-methylene-cyclopropanecarboxylic acid (5-methyl-isoxazol-3-yl)-amide (**1b**),² 2-ethylidene-cyclopropanecarboxylic acid,³ *trans*-2-methyl-3-methylene-cyclopropanecarboxylic acid ethyl ester,⁴ buta-2,3-dienyl-benzene,⁵ propa-1,2-dienyl-cyclohexane,⁶ *tert*-butyl-hexa-4,5-dienyloxy-dimethyl-silane,⁷ 2-isopropylidene-cyclopropanecarboxylic acid ethyl ester,⁸ 5-methoxy-pyridin-2-ylamine⁹ and dimethyldioxirane (DMDO)¹⁰ were prepared as previously reported.

Starting Material Synthesis

2-Methylene-cyclopropanecarboxylic acid (4-methyl-thiazol-2-yl)-amide (**1a**)

To a stirred solution of 2-amino-4-methyl thiazole (1.37 g, 12 mmol) in dichloroethane (8 mL) was added 12 mL trimethylaluminum (2.0 M in toluene, 24 mmol) at room temperature over 15 minutes. Once the evolution of the methane gas subsided, the MCP ethyl ester (1.0 g, 8 mmol) was added dropwise and the solution was stirred at reflux (83 °C) for 12 hours. After cooling to room temperature, the reaction mixture was slowly added to a solution of dichloromethane (24 mL) and water (24 mL) and stirred for one hour. The reaction solution was filtered through a bed of Celite[®] and the filtrate was then washed with water, brine, dried over MgSO_4 , filtered and concentrated *in vacuo*. Flash chromatography on silica using 35% ethyl acetate in hexanes (R_f = 0.38) afforded **1a** (1.28 g, 83%) as white crystals, mp = 114 °C. IR (neat, cm^{-1}) 3158, 2943, 1681, 1550, 1348, 1308, 1264, 1167, 1103, 902, 728; δ_{H} (400 MHz, CDCl_3) 10.80 (bs, 1H), 6.56 (s, 1H), 5.66 (m, 1H), 5.63 (m, 1H), 2.39 (s, 3H), 2.36 (m, 1H), 1.98 (m, 1H), 1.79 (m, 1H); δ_{C} (100 MHz, CDCl_3) 169.3, 158.9, 146.7, 130.2, 108.6, 106.2, 20.0, 17.2, 12.1; $\text{C}_9\text{H}_{10}\text{N}_2\text{OS}$ (M^+) (EI) Requires: 194.0514. Found: 194.0516.

**2-Methylene-cyclopropanecarboxylic acid
(2-phenyl-5-p-tolyl-2H-pyrazol-3-yl)-amide (1c)**

The title compound was prepared using a modified procedure of Appendino and coworkers.¹¹ To a solution of 1-propanephosphoric acid cyclic anhydride (50 wt% in ethyl acetate, 0.4130 g, 0.65 mmol) in acetonitrile (2.5 mL), was added triethylamine (0.2063 g, 2.04 mmol) and 2-methylene-cyclopropanecarboxylic acid (0.0506 g, 0.52 mmol). The resulting solution was stirred at room temperature for 1.5 hours, after which the aminopyrazole (0.1286 g, 0.52 mmol) was added and the reaction was heated to 50 °C for two days. The brown solution was then cooled, diluted with brine and extracted with ethyl acetate (×3). The combined organic layers were dried with sodium sulfate, filtered and concentrated *in vacuo*. Flash chromatography eluting with 15% ethyl acetate in hexanes (R_f = 0.09) afforded **1c** (0.0974 g, 57%) as white crystals, mp = 164-165 °C. IR (neat, cm^{-1}) 3239, 2996, 1669, 1597, 1559, 1532, 1500, 1437, 1361, 1184, 1153, 1106, 1019, 954, 904, 824, 757, 693; δ_{H} (400 MHz, CDCl_3) 7.76 (d, 2H, J = 6.4 Hz), 7.54 (m, 4H), 7.43 (m, 2H), 7.21 (d, 2H, J = 7.9 Hz), 7.08 (bs, 1H), 5.57 (bs, 2H), 2.37 (s, 3H), 2.28 (t, 1H, J = 7.3 Hz), 1.78 (bs, 2H); δ_{C} (100 MHz, CDCl_3) 167.8, 152.2, 138.1, 136.5, 130.4, 130.2, 130.1, 129.5, 128.7, 125.8, 125.1, 106.5, 95.7, 21.5, 20.7, 12.1 $\text{C}_{21}\text{H}_{20}\text{N}_3\text{O}$ (MH^+) (ESI) Requires: 330.1600. Found: 330.1608.

**2-Methylene-cyclopropanecarboxylic acid
[3-(4-chloro-phenyl)-isoxazol-5-yl]-amide (1d)**

To a stirred solution of 2-methylene-cyclopropanecarboxylic acid (0.2629 g, 2.68 mmol) in dichloromethane (8.8 mL) at 0 °C, was added 3-(4-chloro-phenyl)-isoxazol-5-ylamine (0.6216 g, 3.78 mmol), 4-dimethylaminopyridine (0.0323 g, 0.26 mmol) and EDC·HCl (0.5140 g, 2.68 mmol). The reaction solution was then allowed to warm to room temperature and was stirred for an additional 30 hours. The reaction was quenched with saturated $\text{NaHCO}_3(\text{aq})$ and extracted with ethyl acetate (×4). The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash chromatography on silica using 33% ethyl acetate in hexanes (R_f = 0.53) afforded **1d** (0.1865 g, 25%) as a white solid, mp = 185-188 °C. IR (neat, cm^{-1}) 3213, 2956, 2925, 1694, 1683, 1612, 1539, 1510, 1429, 1354, 1202, 1172, 1093, 1015, 899, 836, 778; δ_{H} (400 MHz, CDCl_3) 8.22 (bs, 1H), 7.73 (d, 2H, J = 8.8 Hz), 7.43 (d, 2H, J = 8.8 Hz), 6.68 (s, 1H), 5.69 (m, 2H), 2.38 (m, 1H), 1.93 (dddd, 1H, J = 2.2, 2.9, 4.3, 9.7 Hz), 1.84 (m, 1H); δ_{C} (100 MHz, CDCl_3) 167.5, 163.0, 160.7, 136.4, 129.7, 129.4, 128.2, 127.7, 106.9, 87.2, 20.5, 12.5; $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_2\text{Cl}$ (MH^+) (ESI) Requires: 275.0581. Found: 275.0587.

2-Methylene-cyclopropanecarboxylic acid pyrimidin-4-ylamide (1e)

To a stirred solution of 2-methylene-cyclopropanecarboxylic acid (0.2692 g, 2.74 mmol) in dichloromethane (9.0 mL) at 0 °C, was added pyrimidin-4-ylamine (0.2611 g, 2.75 mmol), 4-dimethylaminopyridine (0.0327 g, 0.27 mmol) and EDC·HCl (0.5789 g, 3.02 mmol). The reaction solution was then allowed to warm to room temperature and was stirred for an additional 20 hours. The reaction was quenched with saturated NaHCO_{3(aq)} and extracted with ethyl acetate (×4). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash chromatography on silica using 50% ethyl acetate in hexanes (R_f = 0.24) afforded **1e** (0.3041 g, 63%) as a white solid, mp = 148-150 °C. IR (neat, cm⁻¹) 3144, 3001, 1705, 1598, 1575, 1519, 1463, 1391, 1345, 1307, 1199, 1163, 1105, 1070, 994, 907, 890, 854, 781, 670; δ_H (400 MHz, CDCl₃) 8.88 (s, 1H), 8.78 (bs, 1H), 8.63 (d, 1H, J = 5.7 Hz), 8.19 (d, 1H, J = 5.7 Hz), 5.65 (m, 2H), 2.38 (m, 1H), 1.95 (m, 1H), 1.79 (m, 1H); δ_C (100 MHz, CDCl₃) 170.8, 158.6, 158.4, 157.3, 130.0, 110.6, 106.4, 21.2, 12.1; C₉H₉N₃O (M⁺) (EI) Requires: 175.0746. Found: 175.0747.

2-Methylene-cyclopropanecarboxylic acid pyrazin-2-ylamide (1f)

To a stirred solution of amino pyrazine (1.14 g, 12 mmol) in dichloroethane (8 mL) was added 12 mL trimethylaluminum (2.0 M in toluene, 16 mmol) at room temperature over 15 minutes. Once the evolution of the methane gas subsided, the MCP ethyl ester (1.0 g, 8 mmol) was added dropwise and the solution was stirred at reflux (83 °C) for 12 hours. After cooling to room temperature, the reaction mixture was slowly added to a solution of dichloromethane (24 mL) and water (24 mL) and stirred for one hour. The reaction solution was filtered through a bed of Celite[®] and the filtrate was then washed with water, brine, dried over MgSO₄, filtered and concentrated *in vacuo*. Flash chromatography on silica using 50% ethyl acetate in hexanes (R_f = 0.38) afforded **1f** (0.58 g, 42%) as a white solid, mp = 120-121 °C. IR (neat, cm⁻¹) 3300, 1671, 1544, 1412, 1350, 1296, 1184, 1011, 905, 848, 490; δ_H (400 MHz, CDCl₃) 9.53 (d, 1H, J = 1.5 Hz), 8.34 (d, 1H, J = 2.6 Hz), 8.23 (dd, 1H, J = 2.5, 1.6 Hz), 7.94 (bs, 1H), 5.67 (m, 2H), 2.36 (m, 1H), 1.91 (m, 1H), 1.79 (m, 1H); δ_C (100 MHz, CDCl₃) 170.0, 148.3, 142.0, 140.2, 137.4, 130.2, 106.0, 20.7, 11.9; C₉H₉N₃O (M⁺) (EI) Requires: 175.0746. Found: 175.0744.

**2-Methylene-cyclopropanecarboxylic acid
(4-methyl-pyridin-2-yl)-amide (1h)**

To a stirred solution of 2-methylene-cyclopropanecarboxylic acid (0.3188 g, 3.25 mmol) in dichloromethane (4.0 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0443 g, 0.36 mmol) and 4-methyl-pyridin-2-ylamine (0.2940 g, 2.72 mmol) followed by dicyclohexylcarbodiimide (0.7052 g, 3.42 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then allowed to warm to 25 °C for 9 hours. The resulting slurry was loaded directly onto silica and purified by flash chromatography using 40% ethyl acetate in hexanes (R_f = 0.57) to afford **1h** (0.5210 g, 100%) as a white solid. IR (neat, cm^{-1}) 3253, 3206, 2995, 1692, 1612, 1570, 1534, 1416, 1346, 1295, 1184, 1106, 1038, 905, 820; δ_{H} (400 MHz, CDCl_3) 9.14 (bs, 1H), 8.12 (d, 1H, J = 5.1 Hz), 8.08 (s, 1H), 6.86 (d, 1H, J = 5.1 Hz), 5.61 (m, 2H), 2.35 (s, 3H), 2.33 (m, 1H), 1.89 (m, 1H), 1.69 (m, 1H); δ_{C} (100 MHz, CDCl_3) 170.0, 151.9, 150.3, 147.3, 130.7, 121.1, 115.1, 105.6, 21.6, 21.1, 11.5; $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}$ (MH^+) (ESI) Requires: 189.1022. Found: 189.1021.

**2-Methylene-cyclopropanecarboxylic acid
(5-iodo-pyridin-2-yl)-amide (1i)**

To a stirred solution of 2-methylene-cyclopropanecarboxylic acid (0.0584 g, 0.60 mmol) in dichloromethane (0.8 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0073 g, 0.06 mmol) and 5-iodo-pyridin-2-ylamine (0.1091 g, 0.50 mmol) followed by dicyclohexylcarbodiimide (0.1228 g, 0.60 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then allowed to warm to room temperature for 48 hours. The resulting slurry was loaded directly onto silica and purified by flash chromatography using 15% ethyl acetate in hexanes (R_f = 0.24) to afford **1i** (0.1291 g, 72%) as a white solid. IR (neat, cm^{-1}) 3289, 3079, 2932, 2854, 1675, 1563, 1518, 1457, 1295, 1171, 1106, 1084, 998, 966, 907, 834, 731; δ_{H} (400 MHz, CDCl_3) 8.65 (bs, 1H), 8.45 (d, 1H, J = 2.0 Hz), 8.07 (d, 1H, J = 8.8 Hz), 7.95 (dd, 1H, J = 8.8, 2.2 Hz), 5.63 (m, 2H), 2.33 (m, 1H), 1.90 (m, 1H), 1.73 (m, 1H); δ_{C} (100 MHz, CDCl_3) 169.9, 153.6, 150.8, 146.5, 130.3, 116.3, 106.0, 85.7, 21.1, 11.8; $\text{C}_{10}\text{H}_{10}\text{N}_2\text{OI}$ (MH^+) (ESI) Requires: 300.9832. Found: 300.9828.

**2-Methylene-cyclopropanecarboxylic acid
(5-nitro-pyridin-2-yl)-amide (1j)**

To a stirred solution of 2-methylene-cyclopropanecarboxylic acid (0.2344 g, 2.39 mmol) in dichloromethane (3.0 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0302 g, 0.25 mmol) and 5-nitro-pyridin-2-ylamine (0.2591 g, 1.86 mmol) followed by dicyclohexylcarbodiimide (0.4927 g, 2.39 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then heated to 40 °C for 43 hours. The resulting slurry was loaded directly onto silica and purified by flash chromatography using 15→33% ethyl acetate in hexanes (R_f = 0.18 in 15% ethyl acetate/hexanes) to afford **1j** (0.3317 g, 81%) as a white solid, mp = 160-162 °C. IR (neat, cm^{-1}) 3279, 1700, 1684, 1604, 1581, 1534, 1507, 1392, 1341, 1279, 1158, 1103, 1009, 907, 849, 767; δ_{H} (400 MHz, CDCl_3) 9.13 (d, 1H, J = 2.4 Hz), 8.48 (dd, 1H, J = 9.2, 2.6 Hz), 8.39 (d, 1H, J = 9.2 Hz), 8.36 (bs, 1H), 5.69 (m, 2H), 2.38 (m, 1H), 1.93 (m, 1H), 1.83 (m, 1H); δ_{C} (100 MHz, CDCl_3) 170.2, 155.3, 144.9, 140.7, 134.2, 129.9, 113.1, 106.7, 21.3, 12.4; $\text{C}_{10}\text{H}_{10}\text{N}_3\text{O}_3$ (MH^+) (ESI) Requires: 200.0716. Found: 200.0718.

**2-Methylene-cyclopropanecarboxylic acid
(5-methoxy-pyridin-2-yl)-amide (1k)**

To a stirred solution of 2-methylene-cyclopropanecarboxylic acid (0.0637 g, 0.65 mmol) in dichloromethane (0.85 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0089 g, 0.07 mmol) and 5-methoxy-pyridin-2-ylamine (0.0730 g, 0.59 mmol) followed by dicyclohexylcarbodiimide (0.13396 g, 0.65 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then allowed to warm to 25 °C for 30 hours. The resulting slurry was loaded directly onto silica and purified by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.31) to afford **1k** (0.1027 g, 85%) as a white solid, mp = 103-104 °C. IR (neat, cm^{-1}) 3243, 3007, 1683, 1588, 1532, 1475, 1394, 1348, 1279, 1255, 1177, 1107, 1031, 963, 908, 834; δ_{H} (400 MHz, CDCl_3) 8.23 (bs, 1H), 8.14 (d, 1H, J = 9.2 Hz), 7.95 (d, 1H, J = 3.1 Hz), 7.25 (dd, 1H, J = 9.0, 3.1 Hz), 5.63 (m, 2H), 3.83 (s, 3H), 2.30 (m, 1H), 1.86 (m, 1H), 1.71 (m, 1H); δ_{C} (100 MHz, CDCl_3) 169.3, 152.9, 145.2, 134.4, 130.5, 123.5, 114.7, 106.0, 56.1, 21.1, 11.7; $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}_2$ (MH^+) (ESI) Requires: 205.0971. Found: 205.0972.

***trans*-2-Methyl-3-methylene-cyclopropanecarboxylic acid pyridin-2-ylamide (**1l**)**

To a stirred solution of 2-aminopyridine (1.13 g, 12.0 mmol) in dichloroethane (8 mL) was added 12 mL trimethylaluminum (2.0 M in toluene, 16 mmol) at room temperature over 15 minutes. Once the evolution of the methane gas subsided, *trans*-2-methyl-3-methylene-cyclopropanecarboxylic acid ethyl ester (1.12 g, 10.4 mmol) was added dropwise and the solution was stirred at reflux (83 °C) for 12 hours. After cooling to room temperature, the reaction mixture was slowly added to a solution of dichloromethane (24 mL) and water (24 mL) and stirred for one hour. The reaction solution was filtered through a bed of Celite® and the filtrate was then washed with water, brine, dried over MgSO₄, filtered and concentrated *in vacuo*. Flash chromatography eluting with 10% ethyl acetate in hexanes (R_f = 0.26) afforded **1l** as a white solid (1.10 g, 60%), mp = 52-54 °C. IR (neat, cm⁻¹) 3289, 1691, 1578, 1529, 1461, 1434, 1349, 1304, 1171, 1151, 1103, 778; δ_H (400 MHz, CDCl₃) 9.35 (bs, 1H), 8.28 (m, 1H), 8.25 (d, 1H, J = 8.2 Hz), 7.69 (m, 1H), 7.03 (m, 1H), 5.60 (dd, 1H, J = 3.1, 1.1 Hz), 5.55 (s, 1H), 2.22 (m, 1H), 1.99 (t, 1H, J = 2.0 Hz), 1.26 (d, 3H, J = 6.2 Hz); δ_C (100 MHz, CDCl₃) 170.0, 152.0, 147.2, 138.4, 137.3, 119.4, 114.6, 104.2, 28.5, 19.6, 16.5; C₁₁H₁₂N₂O (M⁺) (EI) Requires: 188.0950. Found: 188.0954.

2-Ethylidene cyclopropanecarboxylic acid pyridin-2-ylamide (1m**)**

To a solution of 2-ethylidene-cyclopropanecarboxylic acid (0.1531 g, 1.37 mmol) in dichloromethane (1.7 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0167 g, 0.14 mmol) and 2-aminopyridine (0.1285 g, 1.37 mmol) followed by dicyclohexylcarbodiimide (0.2817 g, 1.37 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then allowed to warm to 25 °C for 12 hours. The resulting slurry was then loaded directly onto silica and purified by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.50) to afford **1m** (0.235 g, 87%) as a white solid and as an inseparable 2:1 mixture of olefin isomers. IR (neat, cm⁻¹) 3253, 2994, 1694, 1683, 1578, 1527, 1433, 1360, 1316, 1294, 1171, 1150, 946, 778; δ_H (400 MHz, CDCl₃) 8.30 (bs, 1H), 8.26 (d, 1H, J = 4.9 Hz), 8.22 & 8.21 (d, 1H, J = 8.4 & 8.4 Hz), 7.69 (m, 1H), 7.03 (m, 1H), 6.04 (m, 1H), 2.29 (m, 1H), 1.90 & 1.85 (m, 3H), 1.84-1.63 (m, 2H); δ_C (100 MHz, CDCl₃) 170.7, 170.4, 151.7, 147.9, 138.6, 122.2, 122.0, 119.8, 117.0, 116.5, 114.3, 21.4, 20.3, 17.2, 17.2, 12.3, 11.1; C₁₁H₁₂N₂O (M⁺) (EI) Requires: 188.0950. Found: 188.0947.

2-Phenethylidene cyclopropanecarboxylic acid pyridin-2-ylamide (**1n**)

To a refluxing solution of buta-2,3-dienyl-benzene (2.9295 g, 22.5 mmol) and $\text{Rh}_2(\text{OAc})_4$ (8.3 mg, 0.04 mmol Rh) in dichloromethane (2.3 mL), was added a solution of ethyl diazoacetate (0.7110 g, 6.23 mmol) in dichloromethane (12.7 mL) via syringe pump over 20 hours. The solution was cooled, filtered through Celite[®], and concentrated *in vacuo*. The resulting oil was purified by flash chromatography using 5% ether in pentanes ($R_f = 0.20$) to afford **SI1** and **SI2** (0.5959 g, 44%) as a slightly yellow oil and as a 2.6:1 inseparable mixture of regioisomers.

The resulting MCP ester mixture of **SI1** and **SI2** (0.5755 g, 2.66 mmol) was dissolved in methanol (10.8 mL) and water (2.7 mL) and cooled to 0 °C before K_2CO_3 (1.37 g, 9.91 mmol) was added. The resulting slurry was stirred for 6 days until judged complete by TLC. Brine (10 mL) and dichloromethane (10 mL) were added and the resulting slurry was acidified to pH = 2.0 using 2N $\text{HCl}_{(\text{aq})}$. The aqueous layer was extracted with dichloromethane (5×50 mL) and the combined organic layers were dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash chromatography using 5→40% ether in pentanes ($R_f = 0.21$ in 30% ether/pentanes) afforded the cyclopropanecarboxylic acid mixture (0.3948 g, 79%) as a yellow oil and as a 2.6:1 inseparable mixture of regioisomers.

To a solution of the cyclopropanecarboxylic acid mixture (0.0698 g, 0.37 mmol) in dichloromethane (0.5 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0045 g, 0.04 mmol) and 2-aminopyridine (0.0349 g, 0.37 mmol) followed by dicyclohexylcarbodiimide (0.0773 g, 0.37 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then allowed to warm to 25 °C for 60 hours. The resulting slurry was then loaded directly onto silica and purified by flash chromatography using 33% ethyl acetate in hexanes ($R_f = 0.43$) to afford the MCP amide mixture as a white solid (0.0525 g, 54%), and as a 1.5:1 mixture of regioisomers (**1n:SI3**). Isolation of the major isomer (**1n**) as an inseparable 3.8:1 mixture of olefin isomers could be achieved by gravity chromatography using 20% ethyl acetate in hexanes ($R_f = 0.15$). IR (neat, cm^{-1}) 3252, 3027, 1683, 1576, 1527, 1433, 1368, 1325, 1296, 1171, 1106, 1029, 778, 740, 698; δ_{H} (500 MHz, CDCl_3) 8.52 (bs, 1H), 8.26-8.16 (m, 2H), 7.69 (m, 1H), 7.31 (m, 1H), 7.24-7.12 (m, 3H), 7.03 (m, 1H), 6.16 (m, 1H), 3.60 & 3.54 (d & m, 2H, $J = 6.7$ Hz), 2.32 & 2.17 (m, 1H), 1.85 & 1.81 (m, 1H), 1.69 & 1.65 (m, 1H); δ_{C} (125 MHz, CDCl_3) 170.1, 169.9, 151.4, 147.7, 147.6, 139.9, 139.5, 138.5, 138.5, 128.8, 128.7, 128.5, 128.5, 126.3, 126.2, 122.8, 122.8, 120.1, 119.7, 119.7, 119.6, 114.2, 114.1, 38.2, 38.1, 20.9, 20.6, 11.4, 11.1; $\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}$ (MH^+) (ESI) Requires: 265.1335. Found: 265.1324.

2-Cyclohexylmethylene-cyclopropanecarboxylic acid pyridin-2-ylamide (**1o**)

To a refluxing solution of propa-1,2-dienyl-cyclohexane (2.45 g, 20.05 mmol) and $\text{Rh}_2(\text{OAc})_4$ (7.4 mg, 0.04 mmol Rh) in dichloromethane (2.0 mL), was added a solution of ethyl diazoacetate (0.5764 g, 5.05 mmol) in dichloromethane (11.3 mL) via syringe pump over 20 hours. The solution was cooled, filtered through Celite[®], and concentrated *in vacuo*. The resulting oil was purified by flash chromatography using 5% ether in hexanes ($R_f = 0.34$) to afford **SI4** and **SI5** (0.5901 g, 56%) as a clear oil and as a 3.6:1 inseparable mixture of regioisomers.

The resulting mixture of **SI4** and **SI5** (0.5901 g, 2.83 mmol) was dissolved in methanol (11.6 mL) and water (2.8 mL) and cooled to 0 °C before K_2CO_3 (1.43 g, 10.34 mmol) was added. The resulting slurry was stirred for 6 days until judged complete by TLC. Brine (10 mL) and dichloromethane (10 mL) were added and the resulting slurry was acidified to pH = 2.0 using 2N $\text{HCl}_{(\text{aq})}$. The aqueous layer was extracted with dichloromethane (5×50 mL) and the combined organic layers were dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash chromatography using 2→50% ether in pentanes ($R_f = 0.50$) afforded a 3:1 inseparable mixture of cyclopropanecarboxylic acid regioisomers (0.3999 g, 78%) as a white solid.

To a solution of the cyclopropanecarboxylic acid isomers (0.0507 g, 0.28 mmol) in dichloromethane (0.4 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0035 g, 0.03 mmol) and 2-aminopyridine (0.0266 g, 0.28 mmol) followed by dicyclohexylcarbodiimide (0.0583 g, 0.28 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then allowed to warm to 25 °C for 3 days. The resulting slurry was then loaded directly onto silica and purified by flash chromatography using 15% ethyl acetate in hexanes ($R_f = 0.24$) to afford the desired amides as a white solid (0.0526 g, 73%) and as a 5:1 mixture of regioisomers (**1o**:**SI6**). Isolation of the major isomer (**1o**) as an inseparable 3.8:1 mixture of olefin isomers could be achieved by gravity chromatography using 10% ethyl acetate in toluene ($R_f = 0.34$), mp = 109–112 °C. IR (neat, cm^{-1}) 3248, 2923, 2849, 1694, 1578, 1531, 1434, 1372, 1316, 1296, 1171, 1147, 779; δ_{H} (500 MHz, CDCl_3) 8.25 (d, 1H, $J = 4.1$ Hz), 8.20 (d, 1H, $J = 8.3$ Hz), 8.16 (bs, 1H), 7.68 (dd, 1H, $J = 8.3, 7.3$ Hz), 7.01 (dd, 1H, $J = 7.3, 4.9$ Hz), 5.96 & 5.93 (1H, d, $J = 4.4$ & 7.1 Hz), 2.32–2.17 (m, 2H), 1.90–1.62 (m, 7H), 1.60 (bs, H_2O), 1.36–1.10 (m, 5H); δ_{C} (100 MHz, CDCl_3) 170.8, 170.7, 151.7, 151.6, 147.9, 147.9, 138.6, 138.5, 127.4, 127.4, 119.8, 119.4, 118.9, 114.2, 114.2, 40.9, 40.4, 32.9, 32.7, 32.7, 32.6, 26.4, 26.2, 26.2, 26.1, 21.2, 19.9, 12.0, 11.1; $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}$ (M^+) (EI) Requires: 256.1576. Found: 256.1576.

2-[4-(tert-Butyl-dimethyl-silanyloxy)-butylidene]-cyclopropanecarboxylic acid ethyl ester (SI7)

and

2-[3-(tert-Butyl-dimethyl-silanyloxy)-propyl]-3-methylene-cyclopropanecarboxylic acid ethyl ester (SI8)

To a solution of *tert*-butyl-hexa-4,5-dienyloxy-dimethyl-silane (10.81 g, 50.89 mmol) and $\text{Rh}_2(\text{OAc})_4$ (19.0 mg, 0.08 mmol Rh) in dichloromethane (5.0 mL), was added a solution of ethyl diazoacetate (1.4781 g, 12.95 mmol) in dichloromethane (29.0 mL) via syringe pump over 20 hours. The solution was then heated to reflux for 6 hours to ensure complete decomposition of the ethyl diazoacetate, cooled, and filtered through Celite[®] and concentrated *in vacuo*. The resulting oil was purified by flash chromatography using 5% ether in pentanes ($R_f = 0.27$) to afford the title compounds (2.181 g, 56%) as a pale yellow oil and as a 4.8:1 inseparable mixture of **SI7** and **SI8**. IR (neat, cm^{-1}) 2928, 2856, 1730, 1473, 1371, 1318, 1252, 1158, 1097, 835, 771; δ_{H} (400 MHz, CDCl_3) 5.90 (m, 0.83H), 5.50 (dd, 0.17H, $J = 2.4, 2.4$ Hz), 5.46 (dd, 0.17H, $J = 2.0, 2.0$ Hz), 4.15 (dq, 0.34H, $J = 7.1, 1.5$ Hz), 4.14 (q, 1.66H, $J = 7.1$ Hz), 3.66-3.59 (m, 2H), 2.30-2.11 (m, 2.6H), 1.79-1.55 (m, 4.5H), 1.26 (t, 0.5H, $J = 7.2$ Hz), 1.25 (t, 2.5H, $J = 7.2$ Hz), 0.89 & 0.88 (s, 9H), 0.05 & 0.04 (s, 6H); δ_{C} (100 MHz, CDCl_3) 172.9, 172.7, 136.1, 121.8, 121.6, 120.0, 119.6, 104.2, 62.9, 62.8, 62.6, 60.8, 60.8, 32.3, 32.2, 32.2, 28.3, 28.0, 26.2, 25.4, 25.1, 18.5, 18.5, 17.8, 17.6, 14.5, 14.4, 11.4, 11.3, -5.1; $\text{C}_{16}\text{H}_{31}\text{O}_3\text{Si}$ (MH^+) (ESI) Requires: 321.1856. Found: 321.1847.

2-[4-(tert-Butyl-dimethyl-silanyloxy)-butylidene]-cyclopropanecarboxylic acid pyridin-2-ylamide (1p)

The resulting MCP ester mixture of **SI7** and **SI8** (0.5102 g, 1.71 mmol) was dissolved in methanol (7.0 mL) and water (1.7 mL) and cooled to 0 °C before K_2CO_3 (0.8805 g, 6.37 mmol) was added. The resulting slurry was stirred for 7 days until judged complete by TLC. Brine (10 mL) and dichloromethane (10 mL) were added and the resulting slurry was acidified to pH = 2.0

using 2N HCl_(aq). The aqueous layer was extracted with dichloromethane (5×50 mL) and the combined organic layers were dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash chromatography through a plug of silica using 40% ether in pentanes (R_f = 0.67) afforded an inseparable 3:1 mixture of regioisomers (0.4047 g, 88%) as a pale yellow oil.

To a solution of the above cyclopropanecarboxylic acid mixture (0.1666 g, 0.62 mmol) in dichloromethane (0.8 mL) at 0 °C, was added *N,N*-dimethylamino-4-pyridine (0.0080 g, 0.07 mmol) and 2-aminopyridine (0.0612 g, 0.65 mmol) followed by dicyclohexylcarbodiimide (0.1341 g, 0.65 mmol). The reaction solution was stirred at 0 °C for 30 minutes and then allowed to warm to 25 °C for 15 hours. The resulting slurry was then loaded directly onto silica and purified by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.7) to afford the desired amide mixture as a clear oil (0.1588 g, 74%) and as a 3.3:1 mixture of regioisomers (**1p:SI9**). Isolation of **1p** as an inseparable 9:1 mixture of olefin isomers could be achieved using gravity chromatography with 20% ethyl acetate in hexanes (R_f = 0.28). IR (neat, cm⁻¹) 2948, 2925, 2857, 1694, 1677, 1577, 1526, 1464, 1433, 1359, 1297, 1254, 1169, 1100, 831, 775; δ_H (400 MHz, CDCl₃) 8.25 (dm, 1H, J = 5.1 Hz), 8.19 (d, 1H, J = 8.3 Hz), 8.02 (bs, 1H), 7.68 (dd, 1H, J = 7.9, 1.8 Hz), 7.01 (dd, 1H, J = 5.9, 8.4 Hz), 6.04 (m, 1H), 3.66 & 3.60 (t, 2H, J = 6.4 & 6.6 Hz), 2.36-2.25 (m, 3H), 1.31-1.67 (m, 4H), 1.63 (bs, H₂O), 0.90 (s, 7.88H major olefin isomer), 0.85 (s, 1.12H minor olefin isomer), 0.06 & 0.05 (s, 6H); δ_C (100 MHz, CDCl₃) 170.5, 170.3, 151.5, 147.9, 138.6, 121.8, 121.5, 121.3, 119.8, 114.2, 62.8, 32.3, 32.2, 28.5, 28.2, 26.2, 26.1, 20.9, 20.7, 18.6, 11.9, 11.5, 0.2, -5.1, -5.1; C₁₉H₃₁N₂O₂Si (MH⁺) (ESI) Requires: 347.2149. Found: 347.2157.

2-Isopropylidene-cyclopropanecarboxylic acid pyridin-2-ylamide (**1q**)

To a stirred solution of 2-aminopyridine (0.2753 g, 2.93 mmol) in dichloroethane (2 mL) was added 1.95 mL trimethylaluminum (2.0 M in toluene, 3.9 mmol) at room temperature over 15 minutes. Once the evolution of the methane gas subsided, 2-isopropylidene-cyclopropanecarboxylic acid ethyl ester (0.3527 g, 2.29 mmol) was added dropwise and the solution was stirred at reflux (83 °C) for 50 hours. After cooling to room temperature, the reaction mixture was slowly added to a solution of dichloromethane (24 mL) and water (24 mL) and stirred for one hour. The reaction solution was filtered through a bed of Celite[®] and the filtrate was then washed with water, brine, dried over MgSO₄, filtered and concentrated *in vacuo*. Flash chromatography eluting with 50% ethyl acetate in hexanes (R_f = 0.44) afforded **1q** as a clear oil (0.3287 g, 71%). IR (neat, cm⁻¹) 3267, 2972, 2912, 1682, 1578, 1526, 1433, 1356, 1298, 1169, 1038, 988, 779; δ_H (500 MHz, CDCl₃) 8.26 (ddd, 1H, J = 5.0, 1.8, 0.7 Hz), 8.22 (d, 1H, J = 8.3 Hz), 8.05 (bs, 1H), 7.69 (dt, 1H, J = 7.9, 1.8 Hz), 7.02 (ddd, 1H, J = 7.3, 4.9, 1.0 Hz), 2.28 (m, 1H), 1.92 (d, 3H, J = 1.7 Hz), 1.87 (d, 3H, J = 1.5 Hz), 1.77-1.67 (m, 2H); δ_C (125 MHz, CDCl₃) 171.1, 151.6, 147.9, 138.6, 125.7, 119.8, 115.7, 114.2, 22.7, 22.6, 21.5, 12.5; C₁₂H₁₄N₂O (M⁺) (EI) Requires: 202.1106. Found: 202.1108.

General Procedure for MgI₂-Mediated Ring Expansion

To a solution of MCP amide in THF (0.004-0.005 M unless otherwise noted) was added MgI₂ (0.2 equiv. unless otherwise noted). The reaction mixture was heated at 50 °C under argon until all starting material was gone as judged by HPLC analysis of a small aliquot of the reaction solution. The reaction was then cooled to room temperature and quenched with a solution of saturated aqueous sodium sulfite (6.0 mL) for 6 hours. The aqueous layer was extracted with ethyl acetate (3×50 mL) and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered and concentrated *in vacuo*.

4-Methylene-1-(4-methyl-thiazol-2-yl)-pyrrolidin-2-one (**2a**)

The title compound was prepared according to the general procedure outlined above using **1a** (0.0580 g, 0.30 mmol) in THF (60.0 mL, 0.005 M) at 50 °C for 12 hours. Standard workup and flash chromatography with 50% ethyl acetate in hexanes (*R_f* = 0.42) afforded **2a** (0.0570 g, 98% of the *exo* isomer) as colourless crystals and as a single isomer, mp = 98 °C. IR (neat, cm⁻¹) 1698, 1494, 1376, 1318, 1236, 904, 772; δ_H (400 MHz, CDCl₃) 6.58 (s, 1H), 5.24 (d, 2H, *J* = 6.5 Hz), 4.74 (s, 2H), 3.41 (s, 2H), 2.38 (s, 3H); δ_C (100 MHz, CDCl₃) 171.0, 156.4, 147.5, 135.1, 110.6, 108.6, 53.6, 38.0, 17.3; C₉H₁₀N₂OS (M⁺) (EI) Requires 194.0514. Found: 194.0514.

4-Methylene-1-(5-methyl-isoxazol-3-yl)-pyrrolidin-2-one (**2b**)

The title compound was prepared according to the general procedure outlined above using **1b** (0.0525 g, 0.30 mmol) in THF (60.0 mL, 0.005 M) at 50 °C for 12 hours. Following standard workup, the >20:1 (*exo*:*endo*) ratio of isomers was purified by flash chromatography using 50% ethyl acetate in hexanes (*R_f* = 0.47) to afford **2b** (0.0483 g, 92% yield of the *exo* isomer) as a white solid, mp = 106-107 °C. IR (neat, cm⁻¹) 1717, 1613, 1509, 1455, 1372, 1272, 1237, 913, 791, 744; δ_H (400 MHz, CDCl₃) 6.86 (s, 1H), 5.23 (m, 2H), 4.51 (m, 2H), 3.32 (m, 2H), 2.43 (s, 3H); δ_C (100 MHz, CDCl₃) 172.1, 170.3, 158.0, 135.6, 110.6, 95.6, 52.1, 38.0, 12.8; C₉H₁₀N₂O₂ (M⁺) (EI) Requires: 178.0742. Found: 178.0747.

4-Methylene-1-(2-phenyl-5-p-tolyl-2H-pyrazol-3-yl)-pyrrolidin-2-one (2c)

The title compound was prepared according to the general procedure outlined above using **1c** (0.0368 g, 0.11 mmol) in THF (28.0 mL, 0.004 M) at 50 °C for 60 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 20% ethyl acetate in hexanes (R_f = 0.3) to afford **2c** (0.0281 g, 76% yield of the exo isomer) as a white solid. IR (neat, cm^{-1}) 2920, 2869, 1722, 1667, 1597, 1557, 1531, 1501, 1447, 1373, 1271, 1231, 1213, 1116, 955, 906, 823, 765, 695; δ_{H} (400 MHz, CDCl_3) 7.74 (d, 2H, J = 8.1 Hz), 7.53 (m, 2H), 7.46 (t, 2H, J = 7.9 Hz), 7.39 (m, 1H), 7.22 (d, 2H, J = 8.3 Hz), 6.68 (s, 1H), 5.13 (m, 1H), 5.04 (m, 1H), 4.09 (t, 2H, J = 2.0 Hz), 3.23 (s, 2H), 2.38 (s, 3H); δ_{C} (125 MHz, CDCl_3) 173.6, 152.0, 138.9, 138.2, 137.1, 135.7, 130.1, 129.6, 129.5, 128.4, 125.7, 124.1, 110.6, 101.3, 55.6, 37.1, 21.5; $\text{C}_{21}\text{H}_{20}\text{N}_3\text{O}$ (MH^+) (ESI) Requires: 330.1600. Found: 330.1609.

4-Methyl-1-(2-phenyl-5-p-tolyl-2H-pyrazol-3-yl)-1,5-dihydro-pyrrol-2-one (3c)

The minor isomer **3c** was isolated by flash chromatography using 20% ethyl acetate in hexanes (R_f = 0.20) (0.0011 g, 3% yield of the endo isomer) as a white solid. IR (neat, cm^{-1}) 2911, 2848, 1703, 1699, 1596, 1558, 1532, 1501, 1440, 1360, 1324, 1206, 1145, 950, 913, 825, 762, 697; δ_{H} (500 MHz, CDCl_3) 7.75 (d, 2H, J = 8.1 Hz), 7.55 (d, 2H, J = 8.1 Hz), 7.44 (m, 2H), 7.37 (m, 1H), 7.22 (d, 2H, J = 7.8 Hz), 6.69 (s, 1H), 5.96 (m, 1H), 3.89 (d, 2H, J = 0.7 Hz), 2.38 (s, 3H), 2.04 (d, 3H, J = 1.5 Hz); δ_{C} (125 MHz, CDCl_3) 172.1, 158.1, 151.9, 139.0, 138.1, 137.2, 130.3, 129.5, 129.5, 128.1, 125.7, 124.2, 122.4, 101.6, 57.8, 21.6, 15.8; $\text{C}_{21}\text{H}_{20}\text{N}_3\text{O}$ (MH^+) (ESI) Requires: 330.1600. Found: 330.1617.

4-Methylene-1-pyrimidin-4-yl-pyrrolidin-2-one (2e)

The title compound was prepared according to the general procedure outlined above using **1e** (0.0303 g, 0.17 mmol) in THF (42.8 mL, 0.004 M) at 50 °C for 4 hours. Following standard workup, the 17:83 (exo:endo) ratio of isomers was purified by flash chromatography using 50% ethyl acetate in hexanes (R_f = 0.44) to afford **2e** (0.0048 g, 16% yield of the exo isomer) as a white solid. IR (neat, cm^{-1}) 2926, 1994, 1723, 1590, 1556, 1473, 1398, 1377, 1219, 1196, 1122, 928, 837, 654; δ_{H} (400 MHz, CDCl_3) 8.97 (s, 1H), 8.63 (bs, 1H), 8.43 (d, 1H, J = 5.5 Hz), 5.25 (m, 1H), 5.20 (m, 1H), 4.69 (m, 2H), 3.44 (m, 2H); δ_{C} (100 MHz, CDCl_3) 174.0, 158.4, 157.6, 156.8, 134.9, 111.1, 110.6, 52.5, 39.9; $\text{C}_9\text{H}_9\text{N}_3\text{O}$ (M^+) (EI) Requires: 175.0746. Found: 175.0747.

4-Methyl-1-pyrimidin-4-yl-1,5-dihydro-pyrrol-2-one (3e)

The major isomer **3e** was isolated by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.14) (0.0233 g, 77% yield of the endo isomer) as a white solid, mp = 152-153 °C. IR (neat, cm^{-1}) 3064, 2914, 1697, 1639, 1594, 1584, 1545, 1480, 1448, 1398, 1383, 1292, 1149, 1129, 942, 855, 846, 773, 699, 663; δ_{H} (300 MHz, CDCl_3) 8.88 (d, 1H, J = 1.2 Hz), 8.57 (d, 1H, J = 6.2 Hz), 8.38 (dd, 1H, J = 5.9, 1.5 Hz), 5.96 (td, 1H, J = 2.9, 1.5 Hz), 4.53 (s, 2H), 2.19 (m, 3H); δ_{C} (100 MHz, CDCl_3) 171.6, 158.9, 158.4, 157.6, 156.6, 123.4, 109.5, 54.5, 15.8; $\text{C}_9\text{H}_{10}\text{N}_3\text{O}$ (MH^+) (ESI) Requires: 176.0818. Found: 176.0817.

4-Methylene-1-pyrazin-2-yl-pyrrolidin-2-one (2f)

The title compound was prepared according to the general procedure outlined above using **1f** (0.0526 g, 0.30 mmol) in THF (30 mL, 0.01 M) at 50 °C for 12 hours. Following standard workup, the 9:1 (exo:endo) ratio of isomers was purified by flash chromatography using 50% ethyl acetate in hexanes (R_f = 0.31) to afford **2f** (0.0384 g, 73% yield of the exo isomer) as a white solid, mp = 95 °C. IR (neat, cm^{-1}) 1705, 1479, 1414, 1372, 1219, 461; δ_{H} (400 MHz, CDCl_3) 9.78 (d, 1H, J = 1.3 Hz), 8.34-8.31 (m, 2H), 5.28 (m, 1H), 5.23 (m, 1H), 4.66 (m, 2H), 3.44 (m, 2H); δ_{C} (100 MHz, CDCl_3) 172.6, 148.2, 141.7, 139.6, 137.9, 135.3, 110.2, 52.3, 39.4; $\text{C}_9\text{H}_9\text{N}_3\text{O}$ (M^+) (EI) Requires: 175.0746. Found: 175.0745.

4-Methylene-1-pyridin-2-yl-pyrrolidin-2-one (2g)

The title compound was prepared according to the general procedure outlined above using **1g** (0.0523 g, 0.30 mmol) in THF (75.0 mL, 0.004 M) at 50 °C for 12 hours. Following standard workup, the 9:1 (exo:endo) ratio of isomers was purified by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.42) to afford **2g** (0.0434 g, 83% yield of exo isomer) as a white solid whose physical and spectral properties were in agreement with those previously reported.²

4-Methylene-1-(4-methyl-pyridin-2-yl)-pyrrolidin-2-one (2h)

The title compound was prepared according to the general procedure outlined above using **1h** (0.0400 g, 0.21 mmol) in THF (53.0 mL, 0.004 M) at 50 °C for 2.5 hours. Following standard workup, the 3:1 (exo:endo) ratio of isomers was purified by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.5) to afford **2h** (0.0270 g, 67% yield of exo isomer) as a off-white solid, mp = 86-88 °C. IR (neat, cm^{-1}) 2921, 1702, 1670, 1603, 1560, 1477, 1420, 1388, 1298, 1227, 1190, 1112, 903, 824, 754, 688; δ_{H} (400 MHz, CDCl_3) 8.29 (s, 1H), 8.21 (d, 1H, J = 5.1 Hz), 6.88 (d, 1H, J = 5.1 Hz), 5.19 (m, 1H), 5.14 (m, 1H), 4.70 (m, 2H), 3.41 (m, 2H), 2.38 (s, 3H); δ_{C} (100 MHz, CDCl_3) 172.8, 151.7, 149.3, 147.3, 136.1, 121.2, 115.5, 109.6, 53.4, 40.1, 21.6; $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}$ (MH^+) (ESI) Requires: 189.1022. Found: 189.1023.

4-Methyl-1-(4-methyl-pyridin-2-yl)-1,5-dihydro-pyrrol-2-one (3h)

The minor isomer **3h** was isolated by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.28) (0.0100 g, 25% yield of the endo isomer) as a white solid, mp = 111-112 °C. IR (neat, cm^{-1}) 3068, 2950, 1912, 1703, 1606, 1566, 1483, 1423, 1382, 1336, 1299, 1219, 1195, 1142, 1110, 1000, 948, 912, 882, 861, 807, 754, 726, 696, 619; δ_{H} (500 MHz, CDCl_3) 8.27 (m, 1H), 8.15 (d, 1H, J = 5.1 Hz), 6.83 (dm, 1H, J = 5.1 Hz), 5.93 (m, 1H), 4.53 (s, 3H), 2.37 (s, 3H), 2.15 (m, 3H); δ_{C} (125 MHz, CDCl_3) 171.1, 157.0, 151.8, 149.4, 147.2, 123.7, 120.4, 113.8, 55.4, 21.6, 15.6; $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}$ (MH^+) (ESI) Requires: 189.1022. Found: 189.1028.

1-(5-Iodo-pyridin-2-yl)-4-methylene-pyrrolidin-2-one (2i)

The title compound was prepared according to the general procedure outlined above using **1i** (0.0369 g, 0.12 mmol) in THF (29.5 mL, 0.004 M) at 50 °C for 7 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.72) to afford **2i** (0.0364 g, 99% yield of exo isomer) as a white solid as long needles, mp = 164-165 °C. IR (neat, cm^{-1}) 2919, 1705, 1667, 1566, 1462, 1384, 1365, 1308, 1279, 1217, 1130, 1083, 926, 903, 832; δ_{H} (500 MHz, CDCl_3) 8.54 (s, 1H), 8.32 (d, 1H, J = 8.9 Hz), 7.95 (dd, 1H, J = 8.9, 2.2 Hz), 5.21 (m, 1H), 5.17 (m, 1H), 4.65 (s, 2H), 3.41 (s, 2H); δ_{C} (125 MHz, CDCl_3) 172.9, 153.6, 150.6, 145.8, 135.5, 116.7, 110.0, 86.5, 53.1, 40.0; $\text{C}_{10}\text{H}_{10}\text{N}_2\text{OI}$ (MH^+) (ESI) Requires: 300.9832. Found: 300.9838.

1-(5-Nitro-pyridin-2-yl)-4-methylene-pyrrolidin-2-one (2j)

The title compound was prepared according to the general procedure outlined above using **1j** (0.0457 g, 0.21 mmol) in THF (53.0 mL, 0.004 M) at 50 °C for 4 hours. Following standard workup, the 1:3 (exo:endo) ratio of isomers was purified by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.49) to afford **2j** (0.0110 g, 24% yield of exo isomer) as a white solid. IR (neat, cm^{-1}) 2919, 2845, 1723, 1672, 1596, 1579, 1513, 1471, 1371, 1346, 1291, 1204, 1143, 1112, 1004, 901, 859, 768; δ_{H} (400 MHz, CDCl_3) 9.22 (d, 1H, J = 2.6 Hz), 8.69 (d, 1H, J = 9.2 Hz), 8.48 (dd, 1H, J = 9.2, 2.9 Hz), 5.27 (m, 1H), 5.22 (m, 1H), 4.76 (s, 2H), 3.47 (s, 2H); δ_{C} (100 MHz, CDCl_3) 173.5, 155.0, 144.5, 140.5, 134.6, 133.3, 113.9, 110.7, 53.5, 39.9; $\text{C}_{10}\text{H}_9\text{N}_3\text{O}_3$ (M^+) (EI) Requires: 219.0644. Found: 219.0647.

4-Methyl-1-(5-nitro-pyridin-2-yl)-1,5-dihydro-pyrrol-2-one (3j)

The minor isomer **3j** was isolated by flash chromatography using 33% ethyl acetate in hexanes (R_f = 0.36) (0.0357 g, 76% yield of the endo isomer) as a white solid, mp = 199-201 °C. IR (neat, cm^{-1}) 2918, 2851, 1701, 1593, 1581, 1518, 1479, 1438, 1406, 1354, 1336, 1289, 1200, 1150, 1129, 1004, 942, 849, 765, 707, 621; δ_{H} (400 MHz, CDCl_3) 9.17 (d, 1H, J = 2.6 Hz), 8.63 (d, 1H, J = 9.4 Hz), 8.45 (dd, 1H, J = 9.4, 2.6 Hz), 5.99 (m, 1H), 4.61 (s, 2H), 2.21 (m, 3H); δ_{C} (100 MHz, CDCl_3) 171.1, 159.1, 155.0, 144.8, 140.1, 133.6, 123.4, 112.2, 55.4, 15.9; $\text{C}_{10}\text{H}_{10}\text{N}_3\text{O}_3$ (MH^+) (ESI) Requires: 220.0716. Found: 220.0723.

1-(5-Methoxy-pyridin-2-yl)-4-methylene-pyrrolidin-2-one (**2k**)

The title compound was prepared according to the general procedure outlined above using **1k** (0.0298 g, 0.15 mmol) in THF (29.5 mL, 0.005 M) at 60 °C for 34 hours. Following standard workup, the 3:1 (exo:endo) ratio of isomers was purified by flash chromatography using 33% ethyl acetate in hexanes ($R_f = 0.47$) to afford **2k** (0.0125 g, 42% yield of exo isomer) as an off-white solid. IR (neat, cm^{-1}) 2954, 1700, 1667, 1575, 1491, 1442, 1388, 1294, 1269, 1241, 1227, 1136, 1125, 1029, 1009, 895, 821, 747, 629; δ_{H} (500 MHz, CDCl_3) 8.38 (d, 1H, $J = 9.2$ Hz), 8.04 (d, 1H, $J = 3.1$ Hz), 7.28 (dd, 1H, $J = 9.3, 3.2$ Hz), 5.19 (m, 1H), 5.15 (m, 1H), 4.68 (m, 2H), 3.86 (s, 3H), 3.40 (m, 2H); δ_{C} (125 MHz, CDCl_3) 172.1, 152.8, 145.3, 136.1, 133.8, 123.4, 115.5, 109.5, 56.1, 53.4, 39.9; $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}_2$ (MH^+) (ESI) Requires: 205.0971. Found: 205.0966.

4-Ethylidene-1-pyridin-2-yl-pyrrolidin-2-one (**2l** and **2m**)

The title compound was prepared according to the general procedure outlined above using *trans*-2-methyl-3-methylene-cyclopropanecarboxylic acid pyridin-2-ylamide (**1l**) (0.0560 g, 0.30 mmol) in THF (75.0 mL, 0.004 M) at 50 °C for 12 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 20% ethyl acetate in hexanes ($R_f = 0.28$) to afford **2l** (0.0460 g, 82% yield of exo isomer) as an inseparable 1.7:1 mixture of *Z* and *E* double bond isomers.¹²

The title compound was prepared according to the general procedure outlined above using 2-ethylidene cyclopropanecarboxylic acid pyridin-2-ylamide (**1m**) (0.0530 g, 0.28 mmol) in THF (76.1 mL, 0.004 M) at 50 °C for 19 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 33% ethyl acetate in hexanes ($R_f = 0.41$) to afford **2m** (0.0335 g, 63% yield of exo isomer) as an inseparable 1:1 mixture of *Z* and *E* double bond isomers.¹² IR (neat, cm^{-1}) 3060, 2920, 1710, 1588, 1469, 1436, 1380, 1346, 1307, 1222, 1150, 1125, 992, 780; δ_{H} (400 MHz, CDCl_3) 8.49 & 8.47 (dm, 1H, $J = 6.2$ Hz), 8.38 & 8.35 (dm, 1H, $J = 4.8$ Hz), 7.70 (m, 1H), 7.05 & 7.04 (t, 1H, $J = 4.8$ Hz), 5.63-5.50 (m, 1H), 4.69-4.66 (m, 2H), 3.38 & 3.32 (m, 2H), 1.73-1.66 (m, 3H); δ_{C} (100 MHz, CDCl_3) 173.3, 173.1, 151.8, 151.7, 147.6, 147.6, 137.8, 137.8, 127.0, 126.7, 119.7, 119.7, 119.5, 119.3, 115.1, 115.0, 53.0, 50.8, 39.9, 37.2, 14.7, 13.8; $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}$ (M^+) (EI) Requires: 188.0950. Found 188.0947.

4-Phenethylidene-1-pyridin-2-yl-pyrrolidin-2-one (**2n**)

The title compound was prepared according to the general procedure outlined above using **1n** (0.0334 g, 0.13 mmol) in THF (32.0 mL, 0.004 M) at 50 °C for 26.5 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 20% ethyl acetate in hexanes ($R_f = 0.34$) to afford **2n** (0.02145 g, 64% yield of exo isomer) as an inseparable 2.3:1 mixture of *Z* and *E* double bond isomers.¹² IR (neat, cm^{-1}) 2927, 2847, 1709, 1588, 1472, 1431, 1386, 1307, 1221, 1122, 782, 742, 696; δ_{H} (500 MHz, CDCl_3) 8.53 & 8.51 (1H, d, $J = 8.5$ Hz), 8.42 & 8.40 (1H, d, $J = 5.0$ Hz), 7.70-7.73 (m, 1H), 7.36-7.32 (m, 2H), 7.27-7.23 (m, 3H), 7.10 & 7.08 (ddd, 1H, $J = 7.3, 5.0, 0.9$ & 1.2 Hz), 5.80 & 5.73 (m, 1H), 4.87 & 4.76 (m, 2H), 3.50-3.44 (m, 4H); δ_{C} (125 MHz, CDCl_3) 173.0, 172.7, 151.6, 151.5, 147.6, 147.6, 140.0, 139.9, 137.9, 137.8, 128.8, 128.8, 128.4, 128.4, 127.5, 126.9, 126.5, 126.4, 123.8, 123.5, 119.8, 119.8, 115.1, 115.0, 53.0, 50.9, 39.9, 37.4, 35.7, 34.9; $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}$ (M^+) (EI) Requires: 264.1263. Found: 264.1254.

4-Cyclohexylmethylene-1-pyridin-2-yl-pyrrolidin-2-one (**2o**)

The title compound was prepared according to the general procedure outlined above using **1o** (0.0604 g, 0.24 mmol) in THF (62.0 mL, 0.004 M) at 50 °C for 24 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 15% ethyl acetate in hexanes ($R_f = 0.29$) to afford **2o** (0.0456 g, 75% yield of exo isomer) as an inseparable 2.6:1 mixture of *Z* and *E* double bond isomers¹² and as a white solid. IR (neat, cm^{-1}) 2923, 2849, 1713, 1588, 1470, 1435, 1385, 1308, 1223, 1150, 1126, 992, 932, 891, 780, 741, 684; δ_{H} (500 MHz, CDCl_3) 8.49 & 8.46 (dt, 1H, $J = 8.6, 0.9$ Hz), 8.39 & 8.36 (dm, 1H, $J = 4.8$ Hz), 7.71 (m, 1H), 7.05 (m, 1H), 5.38 & 5.33 (dm, 1H, $J = 9.2$ & 9.7 Hz), 4.71 & 4.65 (m, 2H), 3.38 & 3.34 (m, 2H), 2.21 & 2.06 (m, 1H), 1.76-1.64 (m, 5H), 1.36-1.05 (m, 5H); δ_{C} (125 MHz, CDCl_3) 173.2, 173.0, 151.6, 151.5, 147.5, 147.4, 137.7, 137.6, 131.1, 130.7, 124.1, 123.6, 119.6, 119.5, 114.9, 114.8, 52.9, 50.5, 39.8, 38.7, 37.8, 37.0, 32.8, 32.7, 26.0, 25.9, 25.9; $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}$ (MH^+) (ESI) Requires: 257.1648. Found: 257.1642.

4-[4-(tert-Butyl-dimethyl-silanyloxy)-butylidene]-1-pyridin-2-yl-pyrrolidin-2-one (2p)

The title compound was prepared according to the general procedure outlined above using **1p** (0.0343 g, 0.10 mmol) in THF (25.0 mL, 0.004 M) at 50 °C for 38 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 20% ethyl acetate in hexanes (R_f = 0.46) to afford **2p** (0.0243 g, 71% yield of exo isomer) as an inseparable 3:1 mixture of *Z* and *E* double bond isomers¹² and as a clear oil. IR (neat, cm^{-1}) 2953, 2929, 2856, 1714, 1589, 1573, 1470, 1436, 1384, 1308, 1255, 1222, 1151, 1103, 837, 778; δ_{H} (500 MHz, CDCl_3) 8.48 (dm, 1H, J = 8.5 Hz), 8.37 (m, 1H), 7.71 (m, 1H), 7.05 (m, 1H), 5.53 & 5.48 (m, 1H), 4.70 & 4.67 (s, 2H), 3.63 (t, 2H, J = 6.4 Hz), 3.39 & 3.34 (m, 2H), 2.18-2.10 (m, 2H), 1.65-1.58 (m, 2H), 0.90 & 0.90 (s, 9H), 0.06 & 0.05 (s, 6H); δ_{C} (125 MHz, CDCl_3) 173.2, 151.5, 151.4, 147.8, 147.5, 137.7, 126.3, 126.0, 124.7, 124.4, 119.6, 114.9, 114.9, 62.4, 62.4, 52.9, 50.7, 39.8, 37.2, 32.3, 32.2, 26.0, 25.7, 24.8, 18.4, -5.2; $\text{C}_{19}\text{H}_{30}\text{N}_2\text{O}_2\text{Si}$ (M^+) (EI) Requires: 346.2077. Found: 346.2069.

4-Isopropylidene-1-pyridin-2-yl-pyrrolidin-2-one (2q)

The title compound was prepared according to the general procedure outlined above using **1q** (0.04812 g, 0.24 mmol) in THF (64.3 mL, 0.004 M) at 50 °C for 48.5 hours. Following standard workup, the >20:1 (exo:endo) ratio of isomers was purified by flash chromatography using 15% ethyl acetate in hexanes (R_f = 0.29) to afford **2q** (0.01867 g, 39% yield [45% based on recovered starting material] of exo isomer) plus unreacted starting material (0.0063 g, 13%). IR (neat, cm^{-1}) 2924, 1713, 1695, 1588, 1568, 1471, 1432, 1384, 1370, 1307, 1229, 1154, 991, 778, 743, 621, 610; δ_{H} (400 MHz, CDCl_3) 8.50 (d, 1H, J = 8.4 Hz), 8.38 (d, 1H, J = 4.8 Hz), 7.70 (m, 1H), 7.05 (dd, 1H, J = 6.2, 4.8 Hz), 4.66 (s, 2H), 3.32 (m, 2H), 1.73 (s, 3H), 1.70 (s, 3H); δ_{C} (100 MHz, CDCl_3) 173.8, 151.9, 147.7, 137.8, 126.4, 119.7, 119.1, 115.1, 51.8, 38.4, 21.2, 19.8; $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}$ (MH^+) (ESI) Requires: 203.1178. Found: 203.1189.

Product Modification

5-Pyridin-2-yl-1-oxa-5-aza-spiro[2.4]heptan-6-one (9)

To a solution of 4-methylene-1-pyridin-2-yl-pyrrolidin-2-one (**2g**) (0.0315 g, 0.18 mmol) in acetone (0.25 mL) was added a solution of DMDO in acetone (8.1 mL, 0.049 M, 2.2 equiv.). The solution was stirred at room temperature for 4.5 hours until judged complete by TLC. Evaporation followed by drying under high vacuum gave analytically pure **9** as a clear oil (0.0343 g, 100%) that crystallized to a white solid upon standing, mp = 58 °C. IR (neat, cm⁻¹) 3053, 2920, 1709, 1589, 1571, 1470, 1438, 1377, 1309, 1272, 1218, 1151, 1125, 1041, 992, 916, 782, 743, 679; δ_{H} (500 MHz, CDCl₃) 8.43 (d, 1H, J = 8.5 Hz), 8.35 (dm, 1H, J = 5.0 Hz), 7.73 (ddd, 1H, J = 8.7, 7.2, 1.7 Hz), 7.07 (dd, 1H, J = 7.3, 5.1 Hz), 4.41 (AB, 1H, J = 12.9 Hz), 4.10 (AB, 1H, J = 12.7 Hz), 3.14 (AB, 1H, J = 18.8 Hz), 3.02 (AB, 1H, J = 4.4 Hz), 3.00 (AB, 1H, J = 4.4 Hz), 2.81 (AB, 1H, J = 18.6 Hz); δ_{C} (125 MHz, CDCl₃) 171.2, 151.3, 147.7, 137.9, 120.1, 115.1, 55.4, 53.0, 50.7, 39.4; C₁₀H₁₁N₂O₂ (MH⁺) (ESI) Requires: 191.0815. Found: 191.0824.

1-Pyridin-2-yl-pyrrolidine-2,4-dione (10)

To a solution of 4-methylene-1-pyridin-2-yl-pyrrolidin-2-one (**2g**) (0.0187 g, 0.11 mmol) in dichloromethane (1.0 mL) at -78 °C, was bubbled ozone until judged complete by TLC. Dimethylsulfide (1.0 mL) was then added dropwise and the reaction was allowed to warm to room temperature with stirring for two hours. The dichloromethane solution was then pipetted off, and the resulting yellow oil was washed with dichloromethane (×2). The combined dichloromethane layers were evaporated under a cone of nitrogen, and the resulting solid was triturated with ether (×2) and dried under high vacuum to afford analytically pure **10** as a white solid (0.0116 g, 61%): IR (neat, cm⁻¹) 3401, 2929, 1635, 1583, 1538, 1466, 1430, 1375, 1313, 1284, 1150, 900, 773; δ_{H} (400 MHz, DMSO-d₆ as the enol) 12.01 (bs, 1H), 8.28 (ddd, 1H, J = 4.9, 2.0, 1.0 Hz), 8.25 (d, 1H, J = 8.4 Hz), 7.72 (ddd, 1H, J = 8.6, 7.0, 2.0 Hz), 7.00 (ddd, 1H, J = 7.3, 4.9, 1.1 Hz), 4.99 (s, 1H), 4.42 (s, 2H); δ_{C} (100 MHz, DMSO-d₆) 173.9, 171.3, 151.4, 147.6, 137.8, 118.0, 112.4, 94.8, 49.9; C₉H₉N₂O₂ (MH⁺) (ESI) Requires: 177.0658. Found: 177.0655.

For full spectral characteristics see reference 2.

References

- ¹ Lai, M.-T.; Liu, L.-D.; Liu, H.-W. *J. Am. Chem. Soc.* **1991**, *113*, 7388.
- ² Lautens, M.; Han, W.; Liu, J.H.-C. *J. Am. Chem. Soc.* **2003**, *125*, 4028.
- ³ Vincens, M.; Dumont, C.; Vidal, M. *Bull. Chem. Soc. Fr.* **1974**, 2811.
- ⁴ M. Vidal, M. Vincens, P. Arnaud, *Bull. Soc. Chim. Fr.* **1972**, 665.
- ⁵ Brandsma, L.; Verkruijsse, H.D. *Synthesis of Acetylenes, Allenes and Cumulenes, A Laboratory Manual*; Elsevier: New York, 1981, pages 138-139.
- ⁶ Taherirastgar, F.; Brandsma, L. *Syn. Comm.* **1997**, *27*, 4035.
- ⁷ Llerena, D.; Buisine, O.; Aubert, C.; Malacria, M. *Tetrahedron*, **1998**, *54*, 9373.
- ⁸ Goldschmidt, Z.; Finkel, D. *J. Chem. Soc. Perkin Trans 1*, **1983**, 45.
- ⁹ Lützen, A.; Hapke, M.; Staats, H.; Bunzen, J. *Eur. J. Org. Chem.* **2003**, 3948.
- ¹⁰ Murray, R.W.; Singh, M. *Org. Syn.* **1998**, *Coll. Vol. 9*, 288.
- ¹¹ Ech-Chahad, A.; Minassi, A.; Berton, L.; Appendino, G. *Tetrahedron Lett.* **2005**, *46*, 5113.
- ¹² The absolute *E* and *Z* stereochemistry of both olefin isomers for the exo siloxy ether product were made using 2D ROESY experiment (see spectra). The stereochemistry of the remaining examples were made by analogy.