

Supporting Information for the paper

I₂-Catalyzed enantioselective ring expansion of β -lactams to γ -lactams through a novel C3–C4 bond cleavage. Direct entry to protected 3,4-dihydroxypyrrolidin-2-one derivatives

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General methods: ¹H NMR and ¹³C NMR spectra were obtained from spectrometers operating at 200 MHz, 300 MHz or 500 MHz for proton nucleus in CDCl₃ solutions, except otherwise stated. ¹H chemical shifts are reported in ppm relative to TMS (0.0 ppm) as an internal standard. ¹³C chemical shifts are reported relative to the central peak of CDCl₃ (77.0 ppm). Low and high resolution mass spectra were taken on a HP5989A spectrometer using the electronic impact (EI) or electrospray modes (ES) unless otherwise stated. Specific rotation [α]_D is given in 10⁻¹ deg cm² g⁻¹ at 20 °C, and the concentration (c) is expressed in g per 100 mL. All commercially available compounds were used without further purification.

General Procedure for the β -lactam ring expansion reaction: Synthesis of pyrrolidin-2-one derivatives **2 and **5**.** A solution of TBSCN (1.50-5.00 mmol) in anhydrous acetonitrile (3.4 mL) was added dropwise via syringe to a stirred solution of the appropriate 4-oxoazetidine-2-carbaldehyde **1** or **4** (1.00 mmol) and iodine (0.10 mmol) in the same solvent (3.4 mL) at room temperature and under argon atmosphere. The reaction mixture was stirred at room temperature until disappearance of starting material (TLC). Then, a saturated aqueous NaCl solution (10 mL) was added and the resulting mixture was extracted with DCM (5 x 20 mL). The organic layer was dried (MgSO₄), filtered and concentrated under reduced pressure. Analytically pure adducts **2** or **5**

were obtained after flash chromatography of the residue on silica gel eluting with hexanes/ethyl acetate mixtures.

(+)-(3*R*,4*S*,5*R*)-4-[[*tert*-Butyl(dimethyl)silyl]oxy]-5-cyano-3-methoxy-1-(4-methoxyphenyl)pyrrolidin-2-one, *syn*-(+)-2a. From 300 mg (1.28 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1a**, 271 mg (1.92 mmol) of TBSCN and 32 mg (0.126 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (5:1), analytically pure compound *syn*-(+)-**2a** (375 mg, 78%) was obtained as a colourless oil; $[\alpha]_D = +44.9$ (*c* 0.7, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 0.188 (s, 3H), 0.202 (s, 3H), 0.973 (s, 9H), 3.749 (s, 3H), 3.814 (s, 3H), 4.110 (d, 1H, *J* = 7.9 Hz), 4.470 (t, 1H, *J* = 7.6 Hz), 4.680 (d, 1H, *J* = 7.3 Hz), 6.937 (AA'XX', 2H), 7.433 (AA'XX', 2H); ¹³C-NMR (50 MHz, CDCl₃) δ -5.1, -4.8, 17.9, 25.5, 53.8, 55.5, 59.7, 71.9, 82.6, 114.6, 115.1, 124.1, 129.3, 158.4, 169.3; IR (CHCl₃, cm⁻¹): ν 1727; MS (EI), *m/z*: 376 (M⁺, 15), 319 (M-57, 100), 291 (M-57-28, 98). (Found: C, 60.51; H, 7.42; N, 7.54. Calc. for C₁₉H₂₈N₂O₄Si: C, 60.61; H, 7.50; N, 7.44%).

(+)-(3*R*,4*S*,5*R*)-3-Benzoyloxy-4-[[*tert*-butyl(dimethyl)silyl]oxy]-5-cyano-1-(4-methoxyphenyl)pyrrolidin-2-one, *syn*-(+)-2b. From 50 mg (0.16 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1b**, 46 mg (0.32 mmol) of TBSCN and 4 mg (0.016 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), analytically pure compound *syn*-(+)-**2b** (39 mg, 54%) was obtained as a colourless oil; $[\alpha]_D = +62.9$ (*c* 1.2, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ 0.182 (s, 6H), 0.966 (s, 9H), 3.829 (s, 3H), 4.337 (d, 1H, *J* = 7.6 Hz), 4.548 (t, 1H, *J* = 7.3 Hz), 4.705 (d, 1H, *J* = 7.1 Hz), 4.870 (d, 1H, *J* = 11.2 Hz), 5.190 (d, 1H, *J* = 11.2 Hz), 6.953 (AA'XX', 2H), 7.350-7.475 (m, 7H); ¹³C-NMR (50 MHz, CDCl₃) δ -5.0, -4.7, 17.9, 25.5, 54.1, 55.5, 71.9, 73.2, 80.0, 114.7, 115.1, 124.2, 128.1, 128.3, 128.5, 129.3, 137.0, 158.5, 169.5; IR (CHCl₃, cm⁻¹): ν 1727; MS (EI), *m/z*: 452 (M⁺, 6), 395 (M-57, 30), 346 (13), 289 (10), 250 (68), 149 (12), 91 (100). (Found: C, 66.47; H, 7.23; N, 6.35. Calc. for C₂₅H₃₂N₂O₄Si: C, 66.34; H, 7.13; N, 6.19%). From the more polar fractions compounds *syn*-**3b** (8 mg, 11%) and *anti*-**3b** (3 mg, 4%) were isolated (for data of compounds **3b** see B. Alcaide, P. Almendros, G. Cabrero and M.P. Ruiz, *J. Org. Chem.*, 2007, **72**, 7980).

(–)-(3*R*,4*S*,5*S*)-1-Benzyl-4-{{*tert*-butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxypyrrolidin-2-one, *anti*-2c, and (+)-(3*R*,4*S*,5*R*)-1-Benzyl-4-{{*tert*-butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxypyrrolidin-2-one, *syn*-2c. From 225 mg (1.03 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1c**, 218 mg (1.54 mmol) of TBSCN and 26 mg (0.102 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), both analytically pure less polar isomer *anti*-(–)-**2c** (25 mg, 7%) and the more polar one *syn*-(+)-**2c** (232 mg, 63%) were obtained. Isomer *anti*-(–)-**2c**: colourless oil; $[\alpha]_D = -1.8$ (*c* 1.1, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 0.126 (s, 3H), 0.150 (s, 3H), 0.871 (s, 9H), 3.686 (s, 3H), 3.756 (d, 1H, *J* = 5.5 Hz), 3.803 (d, 1H, *J* = 5.2 Hz), 3.970 (d, 1H, *J* = 15.0 Hz), 4.441 (t, 1H, *J* = 5.4 Hz), 5.254 (d, 1H, *J* = 15.0 Hz), 7.383-7.275 (m, 5H); ¹³C NMR (50 MHz, CDCl₃) δ –5.0, –4.9, 17.8, 25.4, 45.0, 52.3, 59.2, 75.1, 83.1, 115.4, 128.4, 128.5, 129.1, 134.1, 169.7. IR (CHCl₃, cm^{–1}): ν 1721; MS (EI), *m/z*: 345 (M⁺–15, 4), 303 (M–57, 100), 275 (M–57–28, 19), 131 (44), 91 (89). (Found: C, 63.21; H, 7.93; N, 7.92. Calc. for C₁₉H₂₈N₂O₃Si: C, 63.30; H, 7.83; N, 7.77%). Isomer *syn*-(+)-**2c**: colourless oil; $[\alpha]_D = +70.2$ (*c* 0.5, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 0.103 (s, 3H), 0.139 (s, 3H), 0.923 (s, 9H), 3.724 (s, 3H), 3.984 (d, 1H, *J* = 7.0 Hz), 3.988 (d, 1H, *J* = 14.6 Hz), 4.147 (d, 1H, *J* = 7.3 Hz), 4.230 (t, 1H, *J* = 7.1 Hz), 5.142 (d, 1H, *J* = 15.0 Hz), 7.393-7.257 (m, 5H); ¹³C NMR (50 MHz, CDCl₃) δ –5.1, –4.9, 17.9, 25.5, 45.4, 51.0, 59.5, 71.6, 82.6, 114.3, 128.5, 128.5, 129.1, 133.8, 170.1. IR (CHCl₃, cm^{–1}): ν 1721; MS (EI), *m/z*: 345 (M⁺–15, 3), 303 (M–57, 100), 275 (M–57–28, 18), 131 (10), 91 (58). (Found: C, 63.35; H, 7.69; N, 7.58. Calc. for C₁₉H₂₈N₂O₃Si: C, 63.30; H, 7.83; N, 7.77%).

(–)-(3*R*,4*S*,5*S*)-4-{{*tert*-Butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxy-1-(4-methoxybenzyl)pyrrolidin-2-one, *anti*-2d, and (+)-(3*R*,4*S*,5*R*)-4-{{*tert*-Butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxy-1-(4-methoxybenzyl)pyrrolidin-2-one, *syn*-2d. From 250 mg (1.00 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1d**, 213 mg (1.51 mmol) of TBSCN and 26 mg (0.10 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), both analytically pure less polar isomer *anti*-(–)-**2d** (31 mg, 8%) and the more polar one *syn*-(+)-**2d** (284 mg, 72%) were obtained. Isomer *anti*-(–)-**2d**: colourless oil; $[\alpha]_D = -9.1$ (*c* 1.2, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 0.129 (s, 3H), 0.146 (s, 3H), 0.870 (s, 9H), 3.680 (s, 3H), 3.734 (d, 1H, *J* = 5.5 Hz), 3.774 (d, 1H, *J* = 5.4 Hz), 3.814 (s, 3H), 3.907 (d, 1H, *J* = 14.8 Hz), 4.429 (t, 1H, *J* = 5.4 Hz), 5.187 (d, 1H, *J* = 14.8 Hz), 6.890 (AA'XX', 2H), 7.218 (AA'XX', 2H); ¹³C NMR (50 MHz, CDCl₃)

δ -5.0, -4.9, 17.8, 25.4, 44.5, 52.1, 55.3, 59.2, 75.1, 83.2, 114.5, 115.5, 126.1, 130.0, 159.7, 169.6. IR (CHCl₃, cm⁻¹): ν 1721; MS (EI), m/z : 390 (M⁺, 1), 333 (M-57, 47), 131 (5), 121 (100). (Found: C, 61.43; H, 7.93; N, 7.02. Calc. for C₂₀H₃₀N₂O₄Si: C, 61.51; H, 7.74; N, 7.17%). Isomer *syn*-(+)-**2d**: colourless oil; $[\alpha]_D = +58.5$ (c 0.9, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 0.098 (s, 3H), 0.132 (s, 3H), 0.919 (s, 9H), 3.712 (s, 3H), 3.815 (s, 3H), 3.925 (d, 1H, $J = 15.0$ Hz), 3.967 (d, 1H, $J = 7.0$ Hz), 4.124 (d, 1H, $J = 7.4$ Hz), 4.203 (t, 1H, $J = 7.1$ Hz), 5.066 (d, 1H, $J = 14.7$ Hz), 6.896 (AA'XX', 2H), 7.195 (AA'XX', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -5.2, -4.9, 17.8, 25.5, 44.8, 50.7, 55.3, 59.5, 71.6, 82.7, 114.5, 125.7, 130.0, 159.7, 170.0. IR (CHCl₃, cm⁻¹): ν 1719; MS (EI), m/z : 390 (M⁺, 1), 333 (M-57, 46), 131 (1), 121 (100). (Found: C, 61.63; H, 7.82; N, 7.21. Calc. for C₂₀H₃₀N₂O₄Si: C, 61.51; H, 7.74; N, 7.17%).

(-)-(3R,4S,5S)-1-Allyl-4-[[*tert*-butyl(dimethyl)silyl]oxy]-5-cyano-3-methoxypyrrolidin-2-one, *anti*-**2e**, and (+)-(3R,4S,5R)-1-Allyl-4-[[*tert*-butyl(dimethyl)silyl]oxy]-5-cyano-3-methoxypyrrolidin-2-one, *syn*-**2e**. From 50 mg (0.30 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1e**, 105 mg (0.74 mmol) of TBSCN and 8 mg (0.031 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), both analytically pure less polar isomer *anti*-(-)-**2e** (8 mg, 9%) and the more polar one *syn*-(+)-**2e** (51 mg, 56%) were obtained. Isomer *anti*-(-)-**2e**: pale yellow oil; $[\alpha]_D = -3.2$ (c 0.8, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ 0.176 (s, 3H), 0.188 (s, 3H), 0.916 (s, 9H), 3.561 (dd, 1H, $J = 15.4, 7.8$ Hz), 3.660 (s, 3H), 3.759 (d, 1H, $J = 5.4$ Hz), 4.045 (d, 1H, $J = 5.4$ Hz), 4.445 (t, 1H, $J = 5.2$ Hz), 4.534 (ddt, 1H, $J = 15.4, 4.6, 1.4$ Hz), 5.332 (d, 1H, $J = 10.5$ Hz), 5.350 (d, 1H, $J = 17.6$ Hz), 5.716 (dddd, 1H, $J = 17.6, 9.9, 7.8, 4.6$ Hz); ¹³C NMR (50 MHz, CDCl₃) δ -4.95, -4.90, 17.8, 25.5, 43.8, 52.7, 59.2, 75.3, 83.1, 115.5, 120.5, 130.1, 169.6; IR (CHCl₃, cm⁻¹): ν 1722; MS (EI), m/z : 295 (M⁺-15, 4), 253 (M-57, 100), 225 (M-57-28, 53), 131 (61). (Found: C, 57.95; H, 8.57; N, 9.21. Calc. for C₁₅H₂₆N₂O₃Si: C, 58.03; H, 8.44; N, 9.02%). Isomer *syn*-(+)-**2e**: pale yellow oil; $[\alpha]_D = +77.2$ (c 1.1, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ 0.163 (s, 3H), 0.170 (s, 3H), 0.950 (s, 9H), 3.639 (dd, 1H, $J = 15.1, 7.6$ Hz), 3.696 (s, 3H), 3.957 (d, 1H, $J = 6.4$ Hz), 4.312 (t, 1H, $J = 7.3$ Hz), 4.367 (d, 1H, $J = 7.1$ Hz), 4.385 (ddt, 1H, $J = 15.1, 5.0, 1.4$ Hz), 5.331 (dd, 1H, $J = 16.8$ Hz, $J = 1.0$ Hz), 5.347 (dd, 1H, $J = 10.5, 1.0$), 5.716 (m, 1H); ¹³C NMR (50 MHz, CDCl₃) δ -5.1, -4.9, 17.9, 25.5, 44.3, 51.1, 59.5, 71.8, 82.6, 114.5, 120.8, 130.1, 169.9; IR (CHCl₃, cm⁻¹): ν 1721; MS (EI), m/z :

295 (M^+ -15, 4), 253 (M-57, 100), 225 (M-57-28, 56), 131 (21). (Found: C, 58.12; H, 8.53; N, 8.97. Calc. for $C_{15}H_{26}N_2O_3Si$: C, 58.03; H, 8.44; N, 9.02%).

(+)-(3R,4S,5S)-4-{{tert-Butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxy-1-prop-2-ynylpyrrolidin-2-one, anti-2f, and (+)-(3R,4S,5R)-4-{{tert-Butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxy-1-prop-2-ynylpyrrolidin-2-one, syn-2f. From 150 mg (0.898 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1f**, 508 mg (3.595 mmol) of TBSCN and 23 mg (0.091 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), both analytically pure less polar isomer *anti*-(+)-**2f** (20 mg, 7%) and the more polar one *syn*-(+)-**2f** (138 mg, 50%) were obtained. Isomer *anti*-(+)-**2f**: colourless oil; $[\alpha]_D = +14.4$ (c 0.6, $CHCl_3$); 1H NMR (200 MHz, $CDCl_3$) δ 0.185 (s, 3H), 0.208 (s, 3H), 0.930 (s, 9H), 2.357 (t, 1H, $J = 2.6$ Hz), 3.664 (s, 3H), 3.740 (dd, 1H, $J = 17.8, 2.4$ Hz), 3.776 (d, 1H, $J = 5.9$ Hz), 4.236 (d, 1H, $J = 5.6$ Hz), 4.467 (t, 1H, $J = 5.7$ Hz), 4.756 (dd, 1H, $J = 17.7, 2.6$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ -4.92, -4.89, 17.8, 25.5, 30.8, 52.1, 59.3, 74.2, 75.3, 75.4, 83.0, 115.2, 169.2; IR ($CHCl_3$, cm^{-1}): ν 1722; MS (EI), m/z : 308 (M^+ , 1), 293 (M^+ -15, 22), 251 (M-57, 100), 223 (M-57-28, 48), 131 (58). (Found: C, 58.33; H, 7.96; N, 9.11. Calc. for $C_{15}H_{24}N_2O_3Si$: C, 58.41; H, 7.84; N, 9.08%). Isomer *syn*-(+)-**2f**: colourless oil; $[\alpha]_D = +38.7$ (c 0.9, $CHCl_3$); 1H NMR (200 MHz, $CDCl_3$) δ 0.182 (s, 6H), 0.961 (s, 9H), 2.378 (t, 1H, $J = 2.6$ Hz), 3.693 (s, 3H), 3.829 (dd, 1H, $J = 17.8, 2.4$ Hz), 3.953 (d, 1H, $J = 7.3$ Hz), 4.365 (t, 1H, $J = 7.4$ Hz), 4.623 (d, 1H, $J = 7.3$ Hz), 4.630 (dd, 1H, $J = 17.6, 2.4$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ -5.1, -4.9, 17.9, 25.5, 31.2, 50.7, 59.5, 71.9, 74.6, 75.2, 82.3, 114.2, 169.4; IR ($CHCl_3$, cm^{-1}): ν 1726; MS (EI), m/z : 293 (M^+ -15, 3), 251 (M-57, 100), 223 (M-57-28, 90), 131 (70). (Found: C, 58.53; H, 8.01; N, 8.99. Calc. for $C_{15}H_{24}N_2O_3Si$: C, 58.41; H, 7.84; N, 9.08%).

(+)-(3R,4S,5S)-3-(Benzyloxy)-4-{{tert-butyl(dimethyl)silyl}oxy}-5-cyano-1-(4-methoxybenzyl)pyrrolidin-2-one, anti-2g, and (+)-(3R,4S,5R)-3-(Benzyloxy)-4-{{tert-butyl(dimethyl)silyl}oxy}-5-cyano-1-(4-methoxybenzyl)pyrrolidin-2-one, syn-2g. From 250 mg (0.77 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1g**, 272 mg (1.93 mmol) of TBSCN and 20 mg (0.079 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), both analytically pure less polar isomer *anti*-(+)-**2g** (27 mg, 8%) and the more polar one *syn*-(+)-**2g** (195 mg, 54%) were obtained. Isomer *anti*-(+)-**2g**: colourless oil; $[\alpha]_D = +15.0$ (c 0.6, $CHCl_3$); 1H

NMR (200 MHz, CDCl₃) δ 0.090 (s, 3H), 0.098 (s, 3H), 0.839 (s, 9H), 3.794 (d, 1H, J = 5.1 Hz), 3.816 (s, 3H), 3.928 (1 d, H, J = 4.2 Hz), 3.949 (d, 1H, J = 5.4 Hz), 4.486 (t, 1H, J = 5.1 Hz), 4.803 (d, 1H, J = 11.2 Hz), 5.131 (d, 1H, J = 11.5 Hz), 5.207 (d, 1H, J = 14.9 Hz), 6.893 (AA'XX', 2H), 7.226 (AA'XX', 2H), 7.341-7.398 (m, 5H); ¹³C NMR (50 MHz, CDCl₃) δ -5.0, -4.9, 17.7, 25.4, 44.5, 52.4, 55.3, 72.7, 75.2, 80.5, 114.5, 115.5, 126.1, 128.0, 128.3, 128.4, 129.9, 136.9, 159.7, 169.8; IR (CHCl₃, cm⁻¹): ν 1721; MS (EI), m/z : 409 (M-57, 3), 360 (M-106, 11), 303 (M-57-106, 3), 121 (100), 91 (67). (Found: C, 66.83; H, 7.22; N, 6.16. Calc. for C₂₆H₃₄N₂O₄Si: C, 66.92; H, 7.34; N, 6.00%). Isomer *syn*-(+)-**2g**: colourless oil; $[\alpha]_D$ = +90.4 (c 1.1, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ 0.082 (s, 3H), 0.103 (s, 3H), 0.906 (s, 9H), 3.820 (s, 3H), 3.942 (d, 1H, J = 14.6 Hz), 4.153 (d, 1H, J = 7.1 Hz), 4.170 (d, 1H, J = 6.3 Hz), 4.282 (t, 1H, J = 6.7 Hz), 4.823 (d, 1H, J = 11.2 Hz), 5.096 (d, 1H, J = 15.1 Hz), 5.162 (d, 1H, J = 11.2 Hz), 6.898 (AA'XX', 2H), 7.209 (AA'XX', 2H), 7.343-7.413 (m, 5H); ¹³C NMR (50 MHz, CDCl₃) δ -5.1, -4.8, 17.9, 25.5, 44.8, 51.0, 55.3, 71.7, 73.0, 80.1, 114.3, 114.5, 125.7, 128.1, 128.3, 128.5, 130.0, 137.0, 159.7, 170.2; IR (CHCl₃, cm⁻¹): ν 1718; MS (EI), m/z : 409 (M-57, 17), 360 (M-106, 7), 303 (M-57-106, 1), 121 (100), 91 (44). (Found: C, 66.99; H, 7.29; N, 5.97. Calc. for C₂₆H₃₄N₂O₄Si: C, 66.92; H, 7.34; N, 6.00%).

(+)-(2*R*,3*R*)-2-[(*S*)-{*tert*-Butyl(dimethyl)silyl}oxy](cyano)methyl]-1-(4-methoxyphenyl)-4-oxoazetidin-3-yl 4-methoxybenzoate, *syn*-**3h**, and (+)-(2*R*,3*R*)-2-[(*R*)-{*tert*-Butyl(dimethyl)silyl}oxy](cyano)methyl]-1-(4-methoxyphenyl)-4-oxoazetidin-3-yl 4-methoxybenzoate, *anti*-**3h**. From 40 mg (0.11 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1h**, 80 mg (0.57 mmol) of TBSCN and 3 mg (0.012 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (5:1), both analytically pure less polar isomer *syn*-(+)-**3h** (15 mg, 27%) and the more polar one *anti*-(+)-**3h** (18 mg, 32%) were obtained. Isomer *syn*-(+)-**3h**: colourless oil; $[\alpha]_D$ = +25.2 (c 1.2, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ -0.038 (s, 3H), 0.030 (s, 3H), 0.779 (s, 9H), 3.819 (s, 3H), 3.890 (s, 3H), 4.685 (t, 1H, J = 5.1 Hz), 4.890 (d, 1H, J = 5.9 Hz), 6.382 (d, 1H, J = 5.1 Hz), 6.913 (AA'XX', 2H), 6.960 (AA'XX', 2H), 7.436 (AA'XX', 2H), 8.108 (AA'XX', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -5.64, -5.58, 17.8, 25.2, 55.4, 55.5, 58.9, 61.5, 73.1, 113.9, 114.5, 116.9, 119.5, 120.5, 129.7, 132.4, 157.1, 161.8, 164.1, 164.4; IR (CHCl₃, cm⁻¹): ν 1730, 1769; MS (EI), m/z : 496 (M⁺, 10), 439 (M-57, 2), 247 (50), 209 (18), 149 (17), 135 (100). (Found: C, 63.00; H,

6.52; N, 5.72. Calc. for C₂₆H₃₂N₂O₆Si: C, 62.88; H, 6.49; N, 5.64%). Isomer *anti*-(+)-**3h**: white solid; mp = 130-132 °C (hexanes:AcOEt); [α]_D = +54.4 (*c* 0.5, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ -0.038 (s, 3H), 0.119 (s, 3H), 0.880 (s, 9H), 3.819 (s, 3H), 3.887 (s, 3H), 4.624 (dd, 1H, *J* = 5.1, 2.2 Hz), 4.925 (d, 1H, *J* = 2.2 Hz), 6.357 (d, 1H, *J* = 5.1 Hz), 6.905 (AA'XX', 2H), 6.952 (AA'XX', 2H), 7.498 (2H, AA'XX'), 8.126 (2H, AA'XX'); ¹³C NMR (50 MHz, CDCl₃) δ -5.8, -5.4, 17.9, 25.3, 55.5, 55.5, 60.0, 60.3, 72.8, 113.9, 114.5, 116.4, 119.2, 120.4, 129.9, 132.5, 157.1, 161.5, 164.3, 164.8; IR (KBr, cm⁻¹): ν 1731, 1752; MS (EI), *m/z*: 496 (M⁺, 15), 247 (14), 209 (9), 149 (19), 135 (100). (Found: C, 62.92; H, 6.43; N, 5.79. Calc. for C₂₆H₃₂N₂O₆Si: C, 62.88; H, 6.49; N, 5.64%).

(-)-(2*S*)-{[*tert*-Butyl(dimethyl)silyl]oxy}[(2*R*,3*R*)-3-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-1-(4-methoxyphenyl)-4-oxoazetidin-2-yl]acetonitrile, *syn*-**3i**, and (-)-(2*R*)-{[*tert*-Butyl(dimethyl)silyl]oxy}[(2*R*,3*R*)-3-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-1-(4-methoxyphenyl)-4-oxoazetidin-2-yl]acetonitrile, *anti*-**2i**. From 40 mg (0.11 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**1i**, 81 mg (0.57 mmol) of TBSCN and 3 mg (0.012 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (5:1), both analytically pure less polar isomer *syn*-(-)-**3i** (27 mg, 48%) and the more polar one *anti*-(-)-**3i** (9 mg, 16%) were obtained. Isomer *syn*-(-)-**3i**: white solid; mp = 168-169 °C (hexanes:AcOEt); [α]_D = -37.9 (*c* 1.0, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ -0.176 (s, 3H), 0.068 (s, 3H), 0.811 (s, 9H), 3.814 (s, 3H), 4.834 (dd, 1H, *J* = 9.0, 5.6 Hz), 5.068 (d, 1H, *J* = 8.8), 5.735 (d, 1H, *J* = 5.6), 6.883 (AA'XX', 2H), 7.513 (AA'XX', 2H), 7.812 (AA'BB', 2H), 7.946 (AA'BB', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -5.7, -5.6, 18.0, 25.4, 54.3, 55.5, 60.6, 63.8, 114.1, 116.6, 120., 124.1, 130.2, 131.3, 134.9, 157.1, 161.1; IR (KBr, cm⁻¹): ν 1722, 1772; MS (EI), *m/z*: 491 (M⁺, 9), 434 (M-57, 41), 293 (25), 247 (100), 149 (24). (Found: C, 63.41; H, 6.02; N, 8.48. Calc. for C₂₆H₂₉N₃O₅Si: C, 63.52; H, 5.95; N, 8.55%). Isomer *anti*-(-)-**3i**: white solid; mp = 161-163 °C (hexanes:AcOEt); [α]_D = -24.0 (*c* 0.5, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ -0.228 (s, 3H), 0.032 (s, 3H), 0.691 (s, 9H), 3.818 (s, 3H), 4.723 (dd, 1H, *J* = 7.3, 5.1 Hz), 4.959 (d, 1H, *J* = 7.6 Hz), 5.663 (d, 1H, *J* = 5.1 Hz), 6.938 (AA'XX', 2H), 7.466 (AA'XX', 2H), 7.799 (AA'BB', 2H), 7.915 (AA'BB', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -5.5, -5.1, 17.8, 25.2, 55.5, 55.9, 59.4, 60.4, 114.4, 117.7, 120.6, 123.9, 128.7, 131.6, 134.8, 157.5, 160.8, 167. IR (KBr, cm⁻¹): ν 1735, 1759; MS (EI), *m/z*: 491 (M⁺, 20), 434 (M-57, 79), 293 (67), 247

(100), 149 (57). (Found: C, 63.49; H, 5.89; N, 8.67. Calc. for C₂₆H₂₉N₃O₅Si: C, 63.52; H, 5.95; N, 8.55%).

(+)-(5*S*,4*S*,3*R*)-3-Allyl-4-{{*tert*-butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxy-1-(4-methoxyphenyl)pyrrolidin-2-one, *anti*-5a, and (-)-(5*R*,4*S*,3*R*)-3-Allyl-4-{{*tert*-butyl(dimethyl)silyl}oxy}-5-cyano-3-methoxy-1-(4-methoxyphenyl)pyrrolidin-2-one, *syn*-5a. From 55 mg (0.20 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**4a**, 141 mg (1.00 mmol) of TBSCN and 5 mg (0.02 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), both analytically pure less polar isomer *anti*-(+)-**5a** (14 mg, 17%) and the more polar one *syn*-(-)-**5a** (42 mg, 50%) were obtained. Isomer *anti*-(+)-**5a**: white solid; mp = 108-110 °C (hexanes:AcOEt); [α]_D = +34.4 (*c* 0.8, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ 0.213 (s, 3H), 0.225 (s, 3H), 0.947 (s, 9H), 2.556 (dd, 1H, *J* = 14.6, 7.1 Hz), 2.789 (dd, 1H, *J* = 14.6, 7.1 Hz), 3.454 (s, 3H), 3.831 (s, 3H), 4.357 (d, 1H, *J* = 3.9 Hz), 4.602 (d, 1H, *J* = 3.9 Hz), 5.175-5.308 (m, 2H), 5.857 (ddt, 1H, *J* = 17.2, 10.1, 7.1 Hz), 6.964 (AA'XX', 2H), 7.307 (AA'XX', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -4.8, -4.7, 17.8, 25.6, 32.6, 52.1, 55.5, 56.1, 74.8, 83.4, 114.8, 116.2, 120.0, 125.5, 128.7, 130.8, 158.9, 170.0; IR (KBr, cm⁻¹): ν 1719; MS (EI), *m/z*: 416 (M⁺, 55), 359 (M-57, 41), 327 (M-57-32, 77), 304 (16), 244 (90), 210 (14), 134 (59), 89 (100). (Found: C, 63.32; H, 7.83; N, 6.63. Calc. for C₂₂H₃₂N₂O₄Si: C, 63.43; H, 7.74; N, 6.72%). Isomer *syn*-(-)-**5a**: pale yellow oil; [α]_D = -3.6 (*c* 1.8, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ 0.223 (s, 6H), 1.003 (s, 9H), 2.682-2.889 (m, 2H), 3.421 (s, 3H), 3.820 (s, 3H), 4.745 (d, 1H, *J* = 7.8 Hz), 4.841 (d, 1H, *J* = 7.6 Hz), 5.184-5.285 (m, 2H), 6.077 (ddt, 1H, *J* = 17.2, 10.1, 7.0 Hz), 6.947 (AA'XX', 2H), 7.393 (AA'XX', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -4.7, -4.6, 18.0, 25.6, 34.4, 52.0, 54.4, 55.5, 70.0, 83.1, 114.7, 115.2, 119.2, 125.0, 128.9, 131.5, 158.7, 170.1; IR (CHCl₃, cm⁻¹): ν 1719; MS (EI), *m/z*: 416 (M⁺, 27), 359 (M-57, 75), 332 (M-57-27, 62), 304 (73), 244 (73), 210 (85), 134 (80), 89 (100). (Found: C, 63.52; H, 7.79; N, 6.84. Calc. for C₂₂H₃₂N₂O₄Si: C, 63.43; H, 7.74; N, 6.72%).

(+)-(3*S*,4*S*,5*R*)-4-{{*tert*-Butyl(dimethyl)silyl}oxy}-2-(4-methoxyphenyl)-1-oxo-6-oxa-2-azaspiro[4.5]dec-8-ene-3-carbonitrile, *anti*-5b, and (+)-(3*R*,4*S*,5*R*)-4-{{*tert*-Butyl(dimethyl)silyl}oxy}-2-(4-methoxyphenyl)-1-oxo-6-oxa-2-azaspiro[4.5]dec-8-ene-3-carbonitrile, *syn*-5b. From 125 mg (0.46 mmol) of 4-oxoazetidine-2-carbaldehyde (+)-**4b**, 324 mg (2.29 mmol) of

TBSCN and 12 mg (0.047 mmol) of iodine, and after chromatography of the residue eluting with hexanes/ethyl acetate (6:1), both analytically pure less polar isomer *anti*-(+)-**5b** (34 mg, 18%) and the more polar one *syn*-(+)-**5b** (108 mg, 57%) were obtained. Isomer *anti*-(+)-**5b**: colourless oil; $[\alpha]_D = +11.2$ (*c* 1.3, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 0.176 (s, 3H), 0.195 (s, 3H), 0.918 (s, 9H), 2.395 (m, 2H), 3.828 (s, 3H), 4.338 (m, 1H), 4.338 (d, 1H, *J* = 2.2 Hz), 4.477 (d, 1H, *J* = 2.2 Hz), 4.523 (m, 1H), 5.859 (m, 2H), 6.963 (AA'XX', 2H), 7.379 (AA'XX', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -4.9, -4.9, 17.8, 23.6, 25.5, 55.5, 56.4, 63.1, 74.9, 78.0, 114.7, 115.9, 121.0, 124.8, 125.0, 129.2, 158.6, 170.5; IR (CHCl₃, cm⁻¹): ν 1723; MS (EI), *m/z*: 414 (M⁺, 55), 386 (M-28, 100), 357 (M-57, 41), 329 (M-57-28, 27), 302 (21), 222 (39). (Found: C, 63.68; H, 7.33; N, 6.89. Calc. for C₂₂H₃₀N₂O₄Si: C, 63.74; H, 7.29; N, 6.76%). Isomer *syn*-(+)-**5b**: white solid; mp = 106-108 °C (hexanes:AcOEt); $[\alpha]_D = +0.7$ (*c* 1.0, CHCl₃); ¹H NMR (200 MHz, CDCl₃) δ 0.185 (s, 3H), 0.207 (s, 3H), 0.979 (s, 9H), 2.351 (m, 1H), 2.809 (m, 1H), 3.821 (s, 3H), 4.264 (m, 1H), 4.533 (d, 1H, *J* = 7.1 Hz), 4.780 (d, 1H, *J* = 7.1 Hz), 4.833 (m, 1H), 5.867 (m, 2H), 6.940 (AA'XX', 2H), 7.435 (AA'XX', 2H); ¹³C NMR (50 MHz, CDCl₃) δ -4.9, -4.5, 18.0, 24.2, 25.6, 54.0, 55.5, 63.3, 73.5, 76.3, 114.6, 115.5, 119.8, 124.5, 125.0, 129.3, 158.4, 171.5; IR (KBr, cm⁻¹): ν 1721; MS (EI), *m/z*: 414 (M⁺, 29), 386 (M-28, 100), 357 (M-57, 67), 329 (M-57-28, 20), 302 (52), 222 (96). (Found: C, 63.79; H, 7.12; N, 6.67. Calc. for C₂₂H₃₀N₂O₄Si: C, 63.74; H, 7.29; N, 6.76%).

Desilylation of compound *syn*-(+)-2a. Synthesis of (+)-(3*R*,4*S*,5*R*)-4-hydroxy-5-cyano-3-methoxy-1-(4-methoxyphenyl)pyrrolidin-2-one, *syn*-(+)-6. A 1M solution (0.28 mL, 0.28 mmol) of tetrabutylammonium fluoride (TBAF) in THF was added, dropwise via syringe, to a solution of pyrrolidin-2-one *syn*-(+)-**2a** (65 mg, 0.17 mmol) in anhydrous THF (4.4 mL) cooled at 0°C, under argon atmosphere. The reaction mixture was stirred for 2 h at the same temperature. The resulting mixture was quenched by addition of a saturated aqueous solution of NaHCO₃ (4 mL) and the crude reaction was extracted with ethyl acetate (5 x 7 mL). The organic layer was dried (MgSO₄), filtered and the solvent was removed under reduced pressure. After flash chromatography of the residue on silica gel eluting with a hexanes/ethyl acetate (1:1) mixture, analytically pure compound *syn*-(+)-**6** (38 mg, 84%) was obtained as a white solid; mp = 152-154 °C (hexanes:AcOEt); $[\alpha]_D = +40.7$ (*c* 0.3, CHCl₃); ¹H NMR (200 MHz, *d*₆-acetone) δ 3.680 (s, 3H), 3.815 (s, 3H), 4.176 (d, 1H, *J* = 8.3 Hz), 4.651 (td, 1H, *J* = 7.9, 5.3 Hz), 5.320 (d, 1H, *J* = 7.3 Hz), 5.890 (d, 1H, *J* = 5.4 Hz), 7.002

(AA'XX', 2H), 7.547 (AA'XX', 2H); ^{13}C -NMR (50 MHz, d_6 -acetone) δ 53.1, 54.9, 58.2, 70.2, 82.2, 114.2, 115.7, 123.8, 130.1, 158.0, 169.0; IR (KBr, cm^{-1}): ν 3381, 1701; (Found: C, 59.49; H, 5.47; N, 10.76. Calc. for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_4$: C, 59.54; H, 5.38; N, 10.68%).

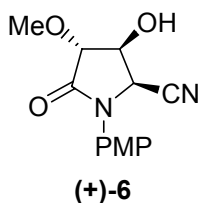
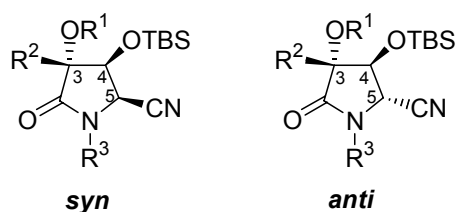


Table 2. Selected Coupling Constants (Hz) for 5-cyanopyrrolidin-2-ones **2** and **5**



Entry	Compound	<i>syn</i>		<i>anti</i>	
		$^3J_{3,4}$	$^3J_{4,5}$	$^3J_{3,4}$	$^3J_{4,5}$
1	2a	7.9	7.3	-	-
2	2b	7.6	7.1	-	-
3	2c	7.0	7.3	5.5	5.2
4	2d	7.0	7.4	5.5	5.4
5	2e	6.4	7.1	5.4	5.4
6	2f	7.3	7.3	5.9	5.6
7	2g	7.1	6.3	5.1	5.4
8	5a	-	7.7	-	3.9
9	5b	-	7.1	-	2.2