Supplementary Material for Organic & Biomolecular Chemistry

Electronic Supporting Information

Reactivity of Cyclic Sulfamidates towards Phosphonate-Stabilised Enolates: Synthesis and Applications of α-Phosphono Lactams

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(3*R*,4*S*,5*S*)-Diethyl(1,5-dimethyl-4-phenylpyrrolidin-2-on-3-yl)phosphonate (15): To a suspension of NaH (60 % dispersion in mineral oil, 160 mg, 4.00 mmol) in anhydrous DMF (10 mL) was added triethyl phosphonoacetate **3** (0.80 mL, 4.00 mmol) and the mixture was stirred for 15 minutes. Cyclic sulfamidate **10** (455 mg, 2.00 mmol) was added and the mixture was heated at 100 °C overnight. The mixture was cooled to r.t., aq. 5 M HCl (1.0 mL) was added and the mixture was stirred at r.t. for 6 h. The solution was then neutralised with saturated aq. $NaHCO_3$ and was diluted with Et_2O (30 mL). The phases were separated and the aqueous portion was extracted with Et_2O (2 × 30 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by FCC (EtOAc) afforded phosphonate **15** (202 mg, 31 %) as a colourless oil; $[\alpha]_D^{20}$ +5 (c = 1, $CHCl_3$); ν_{max} /cm^{-1} (film) 2980 (m), 2931 (m), 1693 (s), 1396 (m), 1248 (s), 1030 (s), 969 (s), 761 (m), 702 (m); δ_H (400 MHz, $CDCl_3$) 1.11 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$), 1.28 (3H, t, *J* = 7.0, $OCH_2C\underline{H}_3$), 1.32 (3H, d, *J* = 6.5, C5-C$\underline{H}_3$), 2.89 (3H, s, NC$\underline{H}_3$), 3.12 (1H, dd, *J* = 23.0 and 9.0, C3-<u>H</u>), 3.30 (1H, ddd, *J* = 18.0, 9.0 and 6.5, C4-<u>H</u>), 3.52 (1H, dq, *J* = 6.5 and 6.5, C5-<u>H</u>), 3.86-4.06 (2H, m, $OC\underline{H}_2CH_3$), 4.17-4.27 (2H, m, $OC\underline{H}_2CH_3$), 7.22-7.37 (5H, m, ArC<u>H</u>); δ_C (75 MHz, $CDCl_3$) 16.0 (d, $^3J_{PC}$ = 7.0, $OCH_2\underline{C}H_3$), 16.4 (d, $^3J_{PC}$ = 7.0, $OCH_2\underline{C}H_3$), 18.6 (C5-<u>C</u>H$_3$), 27.8 (N<u>C</u>H$_3$), 48.3 (<u>C</u>-4), 49.3 (d, $^1J_{PC}$ = 144.5, <u>C</u>-3), 62.0 (d, $^2J_{PC}$ = 6.5, $O\underline{C}H_2CH_3$), 62.9 (d, $^3J_{PC}$ = 10.0, <u>C</u>-5), 63.4 (d, $^2J_{PC}$ = 6.5, $PO\underline{C}H_2CH_3$), 127.4, 127.5 and 128.9 (Ar<u>C</u>H × 5), 141.3 (d, $^3J_{PC}$ = 4.5, Ar<u>C</u>), 168.3 (d, $^2J_{PC}$ = 2.5, <u>C</u>-2); *m/z* (CI^+) 326 ([M+H]$^+$, 100 %); HRMS: (CI^+) Found: [M+H]$^+$ 326.1514, $C_{16}H_{25}NO_4P$ requires 326.1521.

(3*R*,4*S*,5*S*)-Diisopropyl(1,5-dimethyl-2-oxo-4-phenylpyrro-lidin-3-yl)phosphonate (17): To a solution of diisopropyl ethyl phosphonoacetate **4** (219 μL, 0.92 mmol) in anhydrous *p*-dioxane (4.0 mL) was added *t*-BuOK (103 mg, 0.92 mmol) and the mixture was stirred at r.t. for 30 minutes to form a colourless solution. Cyclic sulfamidate **10** (100 mg, 0.44 mmol) was added and the mixture was heated at reflux for 18 h. After cooling to r.t., aq. 5 M HCl (0.46 mL) was added and the mixture was stirred at r.t. for 3 h. The mixture was neutralised with saturated aq. $NaHCO_3$ and then concentrated *in vacuo*. The residue was dissolved in brine (20 mL) and CH_2Cl_2 (15 mL), the organic portion was isolated and the aqueous portion was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a pale yellow oil. This residue was purified by FCC (EtOAc-MeOH 1:0 – 9:1) to afford phosphonate **17** (97 mg, 63 %) as a colourless oil; $[\alpha]_D^{20}$ +13.0 (c = 0.9, $CHCl_3$); ν_{max} /cm^{-1} (film) 2977 (m), 2933 (m), 1689 (s), 1375 (m), 1238 (s), 1105 (s); δ_H (270 MHz, $CDCl_3$) 1.13-1.35 (15H, m, OCH(C$\underline{H}_3$)$_2$ and C5-C$\underline{H}_3$), 2.88 (3H, d, *J* = 1.5, NC$\underline{H}_3$), 3.06 (1H, dd, *J* = 23.0 and 8.0, C3-<u>H</u>), 3.26 (1H, ddd, *J* = 19.0, 8.0 and 6.5, C4-<u>H</u>), 3.47 (1H, dq, *J* = 7.5 and 6.5, C5-<u>H</u>), 4.65 (1H, d septet, *J* = 7.5 and 6.0, O<u>C</u>H(CH$_3$)$_2$), 4.86 (1H, d septet, *J* = 7.5 and 6.0, O<u>C</u>H(CH$_3$)$_2$), 7.18-7.38 (5H, m, ArC<u>H</u>); δ_C (100 MHz, $CDCl_3$) 18.6 (C5-<u>C</u>H$_3$), 23.5-23.9 (m, OCH(<u>C</u>H$_3$)$_2$) × 4), 24.3 (N<u>C</u>H$_3$), 48.5 (<u>C</u>-4), 50.0 (d, $^1J_{PC}$ = 147.0, <u>C</u>-3), 62.9 (d, $^3J_{PC}$ = 8.5, <u>C</u>-5), 70.7 (d, $^2J_{PC}$ = 6.5, O<u>C</u>H(CH$_3$)$_2$), 71.9 (d, $^2J_{PC}$ = 6.5, O<u>C</u>H(CH$_3$)$_2$), 127.2, 127.5 and 128.7 (Ar<u>C</u>H × 5), 142.0 (d, $^3J_{PC}$ = 5.5, Ar<u>C</u>), 168.5 (d, $^2J_{PC}$ = 3.5, <u>C</u>-2); δ_P (162 MHz, $CDCl_3$) 21.6; *m/z* (CI^+) 354 ([M+H]$^+$, 100 %); HRMS: (CI^+) Found: [M+H]$^+$ 354.1817, $C_{18}H_{29}NO_4P$ requires 354.1834.

(3*R*,4*S*,5*R*)-Diisopropyl(1,5-dimethyl-2-oxo-4-phenylpyrr-olidin-3-yl)phosphonate (18): To a solution of diisopropyl ethyl phosphonoacetate **4** (219 μL, 0.92 mmol) in anhydrous *p*-dioxane (4.0 mL) was added *t*-BuOK (103 mg, 0.92 mmol) and the mixture was stirred at r.t. for 20 minutes to form a colourless solution. Cyclic sulfamidate **11** (100 mg, 0.44 mmol) was added and the mixture was heated at reflux for 14.5 h. After cooling to r.t., aq. 5 M HCl (0.46 mL) was added and the mixture was stirred at r.t. for 3 h. The mixture was neutralised with saturated aq. $NaHCO_3$ and then concentrated *in vacuo*. The residue was dissolved in brine (20 mL) and CH_2Cl_2 (15 mL), the organic portion was isolated and the aqueous portion was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a pale yellow oil. This residue was dissolved in PhMe (5 mL) and heated at reflux for 2 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by FCC (EtOAc-MeOH 1:0 – 9:1) to afford phosphonate **18** (84 mg, 54 %) as a colourless solid; m.p. 71-73 °C (CH_2Cl_2-hexanes); $[\alpha]_D^{20}$ +42.1 (c = 0.8, $CHCl_3$); ν_{max} /cm^{-1} (film) 2978 (m), 2931 (m), 1688 (s), 1384 (m), 1245 (s), 1104 (s); δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* = 7.0, C5-C$\underline{H}_3$), 1.18 (3H, d, *J* = 6.5, OCH(C$\underline{H}_3$)$_2$), 1.23 (3H, d, *J* = 6.0, OCH(C$\underline{H}_3$)$_2$), 1.30-1.38 (6H, m, OCH(C$\underline{H}_3$)$_2$), 2.85 (3H, d, *J* = 1.5, NC$\underline{H}_3$), 3.16 (1H, dd, *J* = 22.5 and 5.0, C3-$\underline{H}$), 3.87 (1H, ddd, *J* = 19.0, 7.0 and 5.0, C4-$\underline{H}$), 4.05 (1H, qd, *J* = 7.0 and 7.0, C5-$\underline{H}$), 4.63-4.87 (2H, m, OC$\underline{H}$(CH$_3$)$_2$), 7.10-7.15 (2H, m, ArC$\underline{H}$), 7.22-7.33 (3H, m, ArC$\underline{H}$); δ_C (100 MHz, $CDCl_3$) 15.6 (C5-$\underline{C}$H$_3$), 23.6-24.7 (m, OCH($\underline{C}$H$_3$)$_2$), 27.9 (N$\underline{C}$H$_3$), 44.7 ($\underline{C}$-4), 48.5 (d, $^1J_{PC}$ = 141.0, $\underline{C}$-3), 57.9 (d, $^3J_{PC}$ = 4.5, $\underline{C}$-5), 71.1 (d, $^2J_{PC}$ = 7.0, O$\underline{C}$H(CH$_3$)$_2$ × 4), 72.1 (d, $^2J_{PC}$ = 7.0, O$\underline{C}$H(CH$_3$)$_2$), 127.4, 128.3 and 128.5 (Ar$\underline{C}$H × 5), 139.5 (d, $^3J_{PC}$ = 9.0, Ar$\underline{C}$), 169.5 (d, $^2J_{PC}$ = 4.0, $\underline{C}$-2); δ_P (162 MHz, $CDCl_3$) 21.7; *m/z* (CI$^+$) 354 ([M+H]$^+$, 100 %); HRMS: (CI$^+$) Found: [M+H]$^+$ 354.1831, $C_{18}H_{29}NO_4P$ requires 354.1834.

(3*R,4*S**)-Diisopropyl(1,4-dibenzyl-2-oxo-pyrrolidin-3-yl)-phosphonate (19)** and **Benzyl((*E*)-3-phenylallyl)amine (21):** To a solution of diisopropyl ethyl phosphonoacetate **4** (238 μL, 1.00 mmol) in anhydrous *p*-dioxane (4.3 mL) was added *t*-BuOK (112 mg, 1.00 mmol) and the mixture was stirred at r.t. for 40 minutes to form a colourless solution. Cyclic sulfamidate **12** (150 mg, 0.50 mmol) was added and the mixture was heated at reflux for 15 h. After cooling to r.t., aq. 5 M HCl (0.50 mL) was added and the mixture was stirred at r.t. for 3 h. The mixture was neutralised with saturated aq. $NaHCO_3$ and then concentrated *in vacuo*. The residue was dissolved in brine (20 mL) and CH_2Cl_2 (15 mL), the organic portion was isolated and the aqueous portion was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a pale yellow oil. This was dissolved in PhMe (5 mL) and heated at reflux for 2 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by FCC (EtOAc-MeOH 1:0 – 9:1) to afford phosphonate **19** (121 mg, 58 %) and subsequently allylic amine **21** (7 mg, 7 %) as colourless oils.

Data for lactam **19**: ν_{max} /cm^{-1} (film) 2980 (m), 2932 (m), 1690 (s), 1386 (m), 1247 (s), 1104 (s); δ_H (400 MHz, $CDCl_3$) 1.26-1.36 (12H, m, OCH(C$\underline{H}_3$)$_2$), 2.52-2.60 (1H, m, C4-C$\underline{H}_2$Ph), 2.73 (1H, dd, *J* = 22.0 and 3.5, C3-$\underline{H}$), 2.85-2.92 (3H, m, C4-C$\underline{H}_2$Ph, C4-$\underline{H}$ and C5-$\underline{H}$), 3.40 (1H, dd, *J* = 10.0 and 7.0, C5-$\underline{H}$), 4.41 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 4.50 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 4.70-4.87 (2H, m, OC$\underline{H}$(CH$_3$)$_2$), 7.00-7.04 (2H, m, ArC$\underline{H}$), 7.16-7.37 (8H, m, ArC$\underline{H}$); δ_C (100 MHz, $CDCl_3$) 23.6-24.4 (m, OCH($\underline{C}$H$_3$)$_2$ × 4), 35.3 ($\underline{C}$-4), 40.8 (d, $^3J_{PC}$ = 11.0, C4-$\underline{C}$H$_2$Ph), 46.8 (N$\underline{C}$H$_2$Ph), 48.2 (d, $^1J_{PC}$ = 140.0, $\underline{C}$-3), 49.9 ($\underline{C}$-5), 71.1 (d, $^2J_{PC}$ = 7.5, O$\underline{C}$H(CH$_3$)$_2$), 71.8 (d, $^2J_{PC}$ = 7.5, O$\underline{C}$H(CH$_3$)$_2$), 126.7, 127.7, 128.2, 128.6, 128.7 and 129.1 (Ar$\underline{C}$H × 10), 136.2 and 138.3 (Ar$\underline{C}$), 168.8 (d, $^2J_{PC}$ = 4.0, $\underline{C}$-2); δ_P (162 MHz, $CDCl_3$) 21.9; *m/z* (CI$^+$) 430 ([M+H]$^+$, 100 %); HRMS: (CI$^+$) Found: [M+H]$^+$ 430.2141, $C_{24}H_{33}NO_4P$ requires 430.2147.

Data for allylic amine **21**: δ_H (400 MHz, $CDCl_3$) 1.63 (1H, br s, N$\underline{H}$), 3.42 (2H, d, *J* = 6.0, C1-$\underline{H}$), 3.82 (2H, s, NC$\underline{H}_2$Ph), 6.30 (1H, d t, *J* = 16.0 and 6.0, C2-$\underline{H}$), 6.53 (1H, d, *J* = 16.0, C3-$\underline{H}$), 7.18-7.39 (10H, m, ArC$\underline{H}$); *m/z* (CI$^+$) 224 ([M+H]$^+$, 100 %). The spectroscopic properties of this compound were consistent with the data available in the literature (J. Blid, P. Brandt and P. Somfai, *J. Org. Chem.*, 2004, **69**, 3043-3049.)

Diisopropyl(1-benzyl-6-methyl-2-oxopiperidin-3-yl)phos-phonate (20): To a solution of diisopropyl ethyl phosphonoacetate **4** (195 μL, 0.82 mmol) in anhydrous *p*-dioxane

(4.0 mL) was added *t*-BuOK (92 mg, 0.82 mmol) and the mixture was stirred at r.t. for 40 minutes to form a colourless solution. Cyclic sulfamidate **13** (100 mg, 0.41 mmol) was added and the mixture was heated at reflux for 15 h. After cooling to r.t., aq. 5 M HCl (0.41 mL) was added and the mixture was stirred at r.t. for 3 h. The mixture was neutralised with saturated aq. $NaHCO_3$ and then concentrated *in vacuo*. The residue was dissolved in brine (20 mL) and CH_2Cl_2 (15 mL), the organic portion was isolated and the aqueous portion was extracted with CH_2Cl_2 (2 × 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a pale yellow oil. This was dissolved in *p*-xylene (7.5 mL) and heated at reflux for 18 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by FCC (EtOAc-MeOH 1:0 – 9:1) to afford phosphonate **20** (73 mg, 50 %, 3:2 d.r. *A:B*) as a colourless oil; ν_{max} /cm^{-1} (film) 2977 (m), 2925 (m), 1635 (s), 1450 (m), 1245 (s), 1106 (s); δ_H (400 MHz, $CDCl_3$) 1.18-1.41 (30H, m, OCH(C$\underline{H}_3$)$_2$ and C6-C$\underline{H}_3$ *of A and B*), 1.43-1.54 (1H, m, C4-$\underline{H}$ *of B*), 1.70-1.86 (2H, m, C4-$\underline{H}$ *of A*), 1.93-2.08 (1H, m, C5-$\underline{H}$ *of A*), 2.09-2.37 (4H, m, C5-$\underline{H}$ *of A and B* and C4-$\underline{H}$ *of B*), 2.91-3.12 (2H, m, C3-$\underline{H}$ *of A and B*), 3.40-3.52 (2H, m, C6-$\underline{H}$ *of A and B*), 3.94 (1H, d, *J* = 15.5, NC$\underline{H}_2$Ph *of B*), 4.19 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph *of A*), 4.65-4.90 (4H, m, OC$\underline{H}$(CH$_3$)$_2$ *of A and B*), 5.14 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph *of A*), 5.50 (1H, d, *J* = 15.5, NC$\underline{H}_2$Ph *of B*), 7.19-7.34 (10H, m, ArC$\underline{H}$); δ_C (100 MHz, $CDCl_3$) 19.3 and 19.6 (C6-$\underline{C}$H$_3$ *of A and B*), 19.6 (d, $^3J_{PC}$ = 4.0, $\underline{C}$-5), 19.9 (d, $^3J_{PC}$ = 4.0, $\underline{C}$-5), 23.8-24.5 (m, OCH($\underline{C}$H$_3$)$_2$ *of A and B*), 27.9 and 28.9 ($\underline{C}$-4), 42.2 (d, $^1J_{PC}$ = 136.0, $\underline{C}$-3 *of B*), 42.4 (d, $^1J_{PC}$ = 138.0, $\underline{C}$-3 *of A*), 47.0 (N$\underline{C}$H$_2$Ph *of B*), 48.2 (N$\underline{C}$H$_2$Ph *of A*), 50.8 and 51.7 ($\underline{C}$-6 *of A and B*), 70.8 (d, $^2J_{PC}$ = 7.0, O$\underline{C}$H(CH$_3$)$_2$), 71.6 (d, $^2J_{PC}$ = 7.0, O$\underline{C}$H(CH$_3$)$_2$), 127.1 (2 signals), 127.7 (2 signals) and 128.5 (2 signals) (Ar$\underline{C}$H × 10), 137.4 and 137.7 (Ar$\underline{C}$ × 2), 165.4-165.7 (m, $\underline{C}$-2 *of A and B*); δ_P (162 MHz, $CDCl_3$) 24.3 (*B*) and 23.7 (*A*); *m/z* (CI$^+$) 368 ([M+H]$^+$, 100 %); HRMS: (CI$^+$) Found: [M+H]$^+$ 368.1988, $C_{19}H_{31}NO_4P$ requires 368.1990.

(3*Z*) and (3*E*) (5*S*)-1,5-Dibenzylethylidenepyrrolidin-2-one (23):
Procedure A (from ethyl phosphonate **14**): To a solution of phosphonate **14** (207 mg, 0.52 mmol) in anhydrous THF (4 mL) was added NaH (60 % dispersion in mineral oil, 22 mg, 0.54 mmol) and the mixture was stirred at r.t. for 15 minutes. The mixture was then cooled to -78 ^oC, acetaldehyde (56 μL, 0.50 mmol) was added in one portion *via* syringe and the resulting solution was warmed to r.t. and stirred for 2.5 h. The mixture was concentrated *in vacuo* and the resulting residue was dissolved in water (10 mL) and Et_2O (25 mL). The organic portion was isolated, washed with water (10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford a pale yellow oil. Purification by FCC (Et_2O-hexanes 1:1) afforded *Z*-**23** (57 mg, 37 %) and subsequently *E*-**23** (57 mg, 38 %) as pale yellow oils.

Procedure B (from isopropyl phosphonate **16**): To a solution of phosphonate **16** (106 mg, 0.25 mmol) in anhydrous THF (2.5 mL) was added NaH (60 % dispersion in mineral oil, 11 mg, 0.26 mmol) and the mixture was stirred at r.t. for 15 minutes. The mixture was then cooled to -78 ^oC, acetaldehyde (28 μL, 0.50 mmol) was added in one portion *via* syringe and the resulting solution was warmed to r.t. and stirred for 2 h. The mixture was diluted with brine (15 mL), extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford an orange semi-solid. This residue was purified by FCC (hexanes-EtOAc 2:1) to afford *Z*-**23** (10 mg, 14 %) and subsequently *E*-**23** (40 mg, 55 %) as colourless oils.

Data for *E*-**23**: $[\alpha]_D^{20}$ -36.4 (c = 0.4, $CHCl_3$); ν_{max} / cm^{-1} (film) 2922 (m), 1687 (s), 1665 (s), 1414 (s), 1257 (m), 1080 (m); δ_H (400 MHz, $CDCl_3$) 1.71 (3H, d, *J* = 7.0, C3-CHC$\underline{H}_3$), 2.35 (1H, d, *J* = 16.5, C4-$\underline{H}$), 2.40-2.56 (2H, m, C4-$\underline{H}$ and C5-C$\underline{H}_2$Ph), 3.14 (1H, dd, *J* = 13.5 and 4.0, C5-C$\underline{H}_2$Ph), 3.64-3.73 (1H, m, C5-$\underline{H}$), 4.12 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.17 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 6.50-6.60 (1H, m, C3-C$\underline{H}$), 7.05 (2H, d, *J* = 7.0, ArC$\underline{H}$), 7.19-7.37 (8H, m, ArC$\underline{H}$); δ_C (100 MHz, $CDCl_3$) 14.7 (C3-CH$\underline{C}$H$_3$), 28.2 ($\underline{C}$-4), 40.1 (C5-$\underline{C}$H$_2$Ph), 44.9 (N$\underline{C}$H$_2$Ph), 55.4 ($\underline{C}$-5), 126.8, 127.7, 128.3, 128.7, 128.8 and 129.2 (Ar$\underline{C}$H × 10), 128.5 (C3-$\underline{C}$H), 131.6, 136.8 and 137.1 (Ar$\underline{C}$ × 2 and $\underline{C}$-3), 168.7 ($\underline{C}$-2); *m/z* (CI$^+$) 292 ([M+H]$^+$, 100 %); HRMS: (CI$^+$) Found: [M+H]$^+$ 292.1700, $C_{20}H_{22}NO$ requires 292.1701.

Data for *Z*-**23**: $[\alpha]_D^{20}$ -45.0 (c = 0.8, $CHCl_3$); ν_{max} / cm^{-1} (film) 2923 (m), 1692 (s), 1669 (s), 1414 (s), 1249 (s), 1029 (m); δ_H (400 MHz, $CDCl_3$) 2.18 (3H, d, *J* = 7.5, C3-CHC$\underline{H}_3$), 2.34 (1H, d, *J* = 16.0, C4-$\underline{H}$), 2.45 (1H, dd, *J* = 13.0 and 9.0, C5-C$\underline{H}_2$Ph), 2.53 (1H, dddd, *J* = 16.0, 8.0, 2.5 and 2.5, C4-$\underline{H}$), 3.06 (1H, dd, *J* = 13.0 and 4.0, C5-C$\underline{H}_2$Ph), 3.60 (1H, m, C5-$\underline{H}$), 4.05 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.13 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.84-5.92 (1H, m, C3-C$\underline{H}$), 7.03 (2H, d, *J* = 7.0, ArC$\underline{H}$), 7.17-7.37 (8H, m, ArC$\underline{H}$); δ_C (100 MHz, $CDCl_3$) 13.5 (C3-CH$\underline{C}H_3$), 32.3 ($\underline{C}$-4), 39.9 (C5-$\underline{C}H_2$Ph), 44.5 (N$\underline{C}H_2$Ph), 55.4 ($\underline{C}$-5), 126.7, 127.6, 128.3, 128.6, 128.8, 129.3 and 129.4 (Ar$\underline{C}$H × 10 and $\underline{C}$-3), 132.3 (C3-$\underline{C}$H), 137.0 and 137.3 (Ar$\underline{C}$ × 2), 169.0 ($\underline{C}$-2); *m/z* (CI^+) 292 ($[M+H]^+$, 100 %); HRMS: (CI^+) Found: $[M+H]^+$ 292.1697, $C_{20}H_{22}NO$ requires 292.1701.

(3*E*)- and (3*Z*)- (5*S*)-1,5-Dibenzyl-3-butylidenepyrrolidin-2-one (24): To a suspension of NaH (60 % dispersion in mineral oil, 32 mg, 0.80 mmol) in anhydrous THF (2 mL) was added phosphonate **14** (301 mg, 0.75 mmol) as a solution in anhydrous THF (3 mL). The mixture was then cooled to –78 °C, and butanal (90 µL, 1.00 mmol) was then added. The mixture was stirred and allowed to warm to r.t. After 5 h the mixture was diluted with Et_2O (40 mL) and water (40 mL), and the phases separated. The aqueous portion was extracted with Et_2O (2 × 40 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by FCC (petrol-Et_2O 5:1 to 2:1) afforded (*Z*)-**24** (100 mg, 42 %) and subsequently (*E*)-**24** (104 mg, 43 %) as colourless oils.

Data for *Z*-**24**; $[\alpha]_D^{20}$ –73 (c = 1, $CHCl_3$); ν_{max} / cm^{-1} (film) 2959 (m), 1686 (s), 1663 (s), 1418 (s), 1256 (m); δ_H (400 MHz, $CDCl_3$) 0.93 (3H, t, *J* = 7.5, C$\underline{H}_3$), 1.41 (2H, sextet, *J* = 7.5, C$\underline{H}_2$CH$_3$), 2.35 (1H, dd, *J* = 16.0 and 1.5, C4-$\underline{H}$), 2.46 (1H, dd, *J* = 13.0 and 9, C5-C$\underline{H}_2$Ph), 2.53 (1H, ddd, *J* = 16.0, 8.0 and 1.5, C4-$\underline{H}$), 2.65-2.84 (2H, m, C$\underline{H}_2$CH$_2$CH$_3$), 3.05 (1H, dd, *J* = 13.5 and 4.0, C5-C$\underline{H}_2$Ph), 3.60 (1H, m, C5-$\underline{H}$), 4.04 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.13 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.79 (1H, tt, *J* = 8.0 and 2.0, C=C$\underline{H}$), 7.00-7.06 (2H, m, ArC$\underline{H}$), 7.16-7.37 (8H, m, ArC$\underline{H}$); δ_C (75 MHz, $CDCl_3$) 13.7 ($\underline{C}$H$_3$), 22.8 ($\underline{C}$H$_2$CH$_3$), 28.9 ($\underline{C}$H$_2$CH$_2$CH$_3$), 32.0 ($\underline{C}$-4), 39.6 (C5-$\underline{C}$H$_2$Ph), 44.3 (N$\underline{C}$H$_2$Ph), 55.1 ($\underline{C}$-5), 126.5, 127.4, 128.1, 128.4, 128.6 and 129.1 (Ar$\underline{C}$H × 10 and $\underline{C}$-3, only 6 signals observed), 136.8 and 137.0 (Ar$\underline{C}$ × 2), 137.6 (C=$\underline{C}$H), 168.6 ($\underline{C}$-2); *m/z* (CI^+) 320 ($[M+H]^+$, 100 %); HRMS: (CI^+) Found: $[M+H]^+$ 320.2015, $C_{22}H_{26}NO$ requires 320.2014.

Data for *E*-**24**; $[\alpha]_D^{20}$ –61 (c = 1, $CHCl_3$); ν_{max} / cm^{-1} (film) 2960 (m), 2930 (m), 1692 (s), 1672 (s), 1419 (s); δ_H (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* = 7.5, C$\underline{H}_3$), 1.44 (2H, sextet, *J* = 7.5, C$\underline{H}_2$CH$_3$), 1.99-2.08 (2H, m, C$\underline{H}_2$CH$_2$CH$_3$), 2.34 (1H, d, *J* = 16.0, C4-$\underline{H}$), 2.42-2.55 (2H, m, C4-$\underline{H}$ and C5-C$\underline{H}_2$Ph), 3.12 (1H, dd, *J* = 13.0 and 4.0, C5-C$\underline{H}_2$Ph), 3.68 (1H, m, C5-$\underline{H}$), 4.13 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.15 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 6.49 (1H, tt, *J* = 8.0 and 3.0, C=C$\underline{H}$), 7.01-7.07 (2H, m, ArC$\underline{H}$), 7.18-7.37 (8H, m, ArC$\underline{H}$); δ_C (75 MHz, $CDCl_3$) 13.8 ($\underline{C}$H$_3$), 21.7 ($\underline{C}$H$_2$CH$_3$), 28.1 ($\underline{C}$-4), 31.1 ($\underline{C}$H$_2$CH$_2$CH$_3$), 39.9 (C5-$\underline{C}$H$_2$Ph), 44.7 (N$\underline{C}$H$_2$Ph), 55.3 ($\underline{C}$-5), 126.6, 127.5, 128.2, 128.5, 128.6 and 129.1 (Ar$\underline{C}$H × 10 and $\underline{C}$-3, only 6 signals observed), 130.5 (Ar$\underline{C}$), 133.6 (C=$\underline{C}$H), 136.7 (Ar$\underline{C}$), 168.7 ($\underline{C}$-2); *m/z* (CI^+) 320 ($[M+H]^+$, 100 %); HRMS: (CI^+) Found: $[M+H]^+$ 320.2013, $C_{22}H_{26}NO$ requires 320.2014.

(3*Z*) and (3*E*) (4*R*,5*S*)-Ethylidene-1,5-dimethyl-4-phenyl-pyrrolidin-2-one (26): To a solution of phosphonate **17** (102 mg, 0.29 mmol) in anhydrous THF (2.5 mL) was added NaH (60 % dispersion in mineral oil, 13 mg, 0.32 mmol) and the mixture was stirred at r.t. for 15 minutes. The mixture was then cooled to -78 °C and acetaldehyde (33 µL, 0.58 mmol) was added in one portion *via* syringe and the resulting solution was warmed to r.t. and stirred for 5.5 h. The mixture was diluted with brine (20 mL), extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a colourless oil. This residue was purified by FCC (hexanes-EtOAc 1:1) to afford *Z*-**26** (35 mg, 56 %) as a colourless oil and subsequently *E*-**26** which was inseparable from oxidation product **27** (8 mg, 3:1 *E*-**26**:**27**) as a colourless oil.

Data for *Z*-**26**: $[\alpha]_D^{20}$ +62.2 (c = 0.5, $CHCl_3$); ν_{max} / cm^{-1} (film) 1912 (m), 1737 (m), 1688 (s), 1668 (s), 1393 (m), 1231 (m); δ_H (270 MHz, $CDCl_3$) 1.26 (3H, d, *J* = 6.0, C5-C$\underline{H}_3$), 2.18 (3H, dd, *J* = 7.5 and 2.5, C3-CHC$\underline{H}_3$), 2.90 (3H, s, NC$\underline{H}_3$), 3.37-3.51 (2H, m, C4-$\underline{H}$

and C5-H), 5.63 (1H, qd, *J* = 7.5 and 2.0, C3-CH), 7.14-7.38 (5H, m, ArCH); δ_C (100 MHz, $CDCl_3$) 12.9 (C3-$CH\underline{C}H_3$), 18.5 (C5-$\underline{C}H_3$), 26.9 ($N\underline{C}H_3$), 52.9 and 61.2 (C-4 and C-5), 126.7, 128.1 and 128.3 (ArCH × 5), 133.2 (C3-CH), 134.5 and 141.7 (ArC and C-3), 168.0 (C-2);*m/z* (CI^+) 216 ([M+H]$^+$, 100 %); HRMS: (CI^+) Found: [M+H]$^+$ 216.1379, $C_{14}H_{18}NO$ requires 216.1388. Geometric assignment of this compound was based upon a diagnostic field gradient nOe observed between C4-H and C3-CH.

Data for *E*-**26**: δ_H (400 MHz, $CDCl_3$) 1.32 (3H, d, *J* = 9.5, C5-$C\underline{H}_3$), 1.48 (3H, dd, *J* = 10.5 and 2.5, C3-CHC$\underline{H}_3$), 2.92 (3H, s, NC$\underline{H}_3$), 3.34-3.43 (1H, m, C5-H), 3.56-3.62 (1H, m, C4-H), 6.70 (1H, qd, *J* = 10.5 and 4.0, C3-C$\underline{H}$CH$_3$), 7.14-7.46 (5H, m, ArCH); *m/z* (CI^+) 216 ([M+H]$^+$, 100 %). Full characterisation is not given as this material could not be obtained in pure form (*vide supra*). Geometric assignment of this compound was based upon a diagnostic field gradient nOe observed between C4-H and C3-CHC$\underline{H}_3$.

2,4,6-Trivinylcyclotriboroxane pyridyl complex: To a solution of trimethylborate (10.0 mL, 84.9 mmol) in anhydrous THF (75 mL) at -78 ^oC was added dropwise, *via* cannula, a solution of vinyl magnesium bromide (1.0 M, 50.0 mmol) over 45 minutes. The mixture was stirred at -78 ^oC for 1.25 h and then aq. 1 M HCl (25 mL) was added dropwise over 5 minutes to form a fine, colourless precipitate. The mixture was warmed to r.t., diluted with brine (20 mL) and extracted with Et_2O (4 × 50 mL). The combined organic extracts were washed with water (2 × 50 mL), brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo* to *ca.* 25 mL. Pyridine (10 mL) was added and the mixture was stirred at r.t. for 4 h. Concentration *in vacuo* and then Kugelrohr distillation (*ca.* 75 ^oC, 0.01 mmHg) afforded the vinyl boroxane (2.92 g, 73 %) as a colourless solid; m.p. 47-49 ^oC (CH_2Cl_2-hexanes) [Lit., 46-48 ^oC]; δ_H (400 MHz, $CDCl_3$) 5.81 (3H, dd, *J* = 11.0 and 7.0), 5.98-6.04 (6H, m), 7.63 (2H, dd, *J* = 7.0), 8.04 (1H, t, *J* = 7.0), 8.83 (2H, d, *J* = 5.0); δ_C (100 MHz, $CDCl_3$) 125.4, 131.4, 138.1 (br), 140.8 and 144.0; δ_B (96 MHz, $CDCl_3$) 18.9. The spectroscopic properties of this compound were consistent with the data available in the literature.[12]

(*S*)-1,5-Dibenzyl-3-(3-nitrophenyl)-1,5-dihydropyrrol-2-one (32): A solution of vinyl triflate **29** (40 mg, 0.10 mmol), K_3PO_4 (32 mg, 0.15 mmol), 3-nitrobenzene boronic acid (18 mg, 0.11 mmol) and freshly prepared $Pd(PPh_3)_4$ (6 mg, 5 mol %) in *p*-dioxane (1.5 ml) and water (0.5 ml) was heated under microwave conditions for 5 minutes (90 °C max, 150 W, Powermax). The mixture was cooled to r.t. and extracted with Et_2O (4 x 2 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a yellow oil. This residue was purified by FCC (petrol-Et_2O 3:1-2:1) to yield arylated lactam **32** (28 mg, 73 %) as an amorphous yellow solid; m.p. 98-99°C (Et_2O-petrol); $[\alpha]_D^{20}$ –36.4 (c = 1.7, $CHCl_3$); ν_{max} / cm $^{-1}$ (film) 3029 (w), 1678 (s), 1525 (s), 1409 (m), 1347 (s), 1078 (m); δ_H (400 MHz, $CDCl_3$) 2.59 (1H, dd, *J* = 13.0 and 9.0, C5-C$\underline{H}_2$Ph), 3.21 (1H, dd, *J* = 13.0 and 5.0, C5-C$\underline{H}_2$Ph), 4.10-4.17 (1H, m, C5-H), 4.20 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.23 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 7.05 (2H, d, *J* = 7.0, ArCH), 7.13 (1H, d, *J* = 1.5, C4-H), 7.18-7.32 (7H, m, ArCH), 7.49 (1H, dd, *J* = 8.5, ArCH), 8.10 (1H, d, *J* = 8.5, ArCH), 8.23 (1H, d, *J* = 8.5, ArCH), 8.56 (1H, s, ArCH); δ_C (100 MHz, $CDCl_3$) 37.6 (C5-$\underline{C}H_2$Ph), 44.4 (N$\underline{C}H_2$Ph), 60.5 (C-5), 122.0, 123.2, 127.2, 127.8, 128.0, 128.8, 128.9, 129.0, 129.4, 133.0 (ArCH x 14), 133.1, 134.2, 135.7 (ArC x 3), 137.0 (C-3), 142.4 (C-4), 148.3 (ArC), 169.1 (C-2); HRMS: (ESI^+) Found [M+H]$^+$ 385.1541, $C_{24}H_{21}N_2O_3$ requires 385.1547. The enantiomeric purity of this compound was determined by chiral HPLC (Chiralpak AD-H, isocratic hexane - *i*-PrOH 95:5, 1.0 mL/min, 20 ^oC); t_R (major) = 39.1 min and t_R (minor) = 49.8 min.

(*S*)-1,5-Dibenzyl-3-pyridin-3-yl-1,5-dihydropyrrol-2-one (33): A solution of vinyl triflate **29** (40 mg, 0.10 mmol), K_3PO_4 (32 mg, 0.15 mmol) and pyridine-3-boronic acid (14 mg, 0.11 mmol) and freshly prepared $Pd(PPh_3)_4$ (6 mg, 5 mol %) in *p*-dioxane (1.5 ml) and water (0.5 ml) was heated under microwave conditions for 5 minutes (90 °C max, 150 W, Powermax). The mixture was cooled to r.t. and extracted with Et_2O (4 x 2 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a yellow oil. This residue was purified by FCC (petrol-Et_2O 1:1–1:4) to yield pyridyl lactam **33** (13 mg, 38 %) as a yellow oil; $[\alpha]_D^{20}$ –32.4 (c = 0.4, $CHCl_3$); ν_{max} / cm $^{-1}$ (film) 3090 (w), 2922 (m), 1683 (s), 1410 (m), 1261 (m); δ_H (400 MHz, $CDCl_3$) 2.65 (1H, dd, *J*

= 13.5 and 9.5, C5-C$\underline{H}_2$Ph), 3.29 (1H, dd, *J* = 13.5 and 5.5, C5-C$\underline{H}_2$Ph), 4.15-4.20 (1H, m, C5-$\underline{H}$), 4.26 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 5.30 (1H, d, *J* = 15.0, NC$\underline{H}_2$Ph), 7.08-7.14 (3H, m, ArC$\underline{H}$ and C4-$\underline{H}$), 7.22-7.39 (9H, m, ArC$\underline{H}$), 8.29 (1H, dd, *J* = 8.0 and 1.5, ArC$\underline{H}$), 8.56 (1H, dd, *J* = 4.5 and 1.5, ArC$\underline{H}$), 8.91 (1H, s, ArC$\underline{H}$); δ_c (100 MHz, $CDCl_3$) 37.9 (C5-$\underline{C}H_2$Ph), 44.5 (N$\underline{C}H_2$Ph), 60.7 ($\underline{C}$-5), 123.7, 127.2, 127.8, 128.1, 128.8, 128.9, 129.15 (Ar$\underline{C}$H × 11), 133.7 (Ar$\underline{C}$ x 2), 134.7 (Ar$\underline{C}$H), 136.0 and 137.2 ($\underline{C}$-3 and Ar$\underline{C}$), 141.5 ($\underline{C}$-4), 148.2 and 149.4 (Ar$\underline{C}$H × 2), 169.5 ($\underline{C}$-2); HRMS: (ESI$^+$) Found $[M+H]^+$ 341.1652, $C_{23}H_{21}N_2O$ requires 341.1648. The enantiomeric purity of this compound was determined by chiral HPLC (Chiralcel OJ-H, isocratic hexane - *i*-PrOH 80:20, 1.0 mL/min, 20 ^oC); t_R (major) = 28.0 min and t_R (minor) = 23.5 min.