Supporting Information

Cyclic Sulfamides as Vehicles for the Synthesis of Substituted Lactams

John F. Bower, Jakub Švenda, Andrew J. Williams, Jonathan P. H. Charmant, Ron M. Lawrence, Peter Szeto and Timothy Gallagher*

*School of Chemistry, University of Bristol, Bristol, BS8 1TS, UK.
GlaxoSmithKline, Medicines Research Centre, Stevenage, SG1 2NY, UK.*

T.Gallagher@bristol.ac.uk

General comments

Starting materials were sourced from commercial suppliers and were used as received. All reactions that involved air or moisture sensitive compounds were performed in oven dried glassware using anhydrous solvent and under an atmosphere of dry nitrogen. MgO was flame dried under high vacuum immediately prior to use. 'Petrol' refers to the fraction of petroleum ether boiling in the range 40-60 °C. Column chromatography was carried out using Merck 60 silica (40 - 62 µm). Melting points are uncorrected. Infra-red spectra were recorded on a Perkin Elmer FT-IR spectrometer either as a neat film or as a pure solid compressed onto a diamond window. Selected absorption maxima are quoted to the nearest wave number. ¹H NMR coupling constants are quoted to the nearest 0.5 Hz.

(i) Synthesis of Cyclic Sulfamides

For the preparation and characterisation data of 1,2-cyclic sulfamides (**2a**, **2b**, **2d**) see earlier work.¹ **2e** {[α]_D²⁰ -19.6 (c = 1.6, CHCl₃)} was prepared in an analogous manner and its enantiomer is a known compound.² The enantiomer of **2e**, which is described² as being derived from 1S, 2S-(+)-pseudoephedrine, is also reported to have a negative rotation {[α]_D -11.2 (c = 2.14, CHCl₃)}. This data is inconsistent with our observations, but we have checked the rotation of the 1R, 2R-(-)-pseudoephedrine (purchased from Acros) that we have used as our starting material.

(±) 4-Methyl[1,2,3]oxathiazinane-2,2-dioxide

This compound was prepared using methods described for structurally related compounds as reported by Du Bois³. To vigorously stirred, ice-cooled (0 °C) chlorosulfonyl isocyanate (12.16 mL, 139.4 mmol) was added formic acid (5.27 mL, 139.4 mmol). After 5 minutes a colourless precipitate formed and this was diluted by addition of CH₂Cl₂ (80 mL) to form a fine suspension which was allowed to warm slowly to r.t. overnight. The mixture was cooled to 0 °C and a solution of anhydrous *n*-BuOH (8.49 mL, 92.9 mmol) and anhydrous pyridine (11.27 mL, 139.4 mmol) in CH₂Cl₂ (65 mL) was added dropwise over 30 minutes. The mixture was allowed to warm to r.t. and was stirred for 24 hours. The reaction was quenched by addition of water and was extracted with CH₂Cl₂. The organics were combined, washed with brine solution, dried (Na₂SO₄), and concentrated *in vacuo* to afford the intermediate sulfamic acid butyl ester (12.74 g, 90 %) as a colourless oil. *This compound was used in the next step without further purification.* δ_{H} (270 MHz, CDCl₃) 0.94 (3H, t, J = 7.0), 1.43 (2H, tq, J = 7.0 and 7.0), 1.72 (2H, tt, J = 7.0 and 7.0), 4.21 (2H, t, J = 7.0), 4.79 (2H, br s). To a solution of sulfamate ester (1.06 g, 7.05 mmol) in CH₂Cl₂ at r.t. was added sequentially MgO (645 mg, 16.0 mmol), PhI(OAc)₂ (2.46 g, 7.6 mmol) and Rh₂(OAc)₄ (92 mg, 0.21 mmol) to form a green suspension which was heated at reflux for 15 hours. The reaction mixture was allowed to cool to r.t. and filtered through Celite[®]. Concentration *in vacuo* followed by flash chromatography (Et₂O-hexanes 1:1) afforded the unprotected sulfamidate (546 mg, 52 %) as a pale yellow oil which crystallised on standing; m.p. 85-86 °C (CH₂Cl₂-petrol); ν_{max} / cm⁻¹ (film) 3260 (br, m), 1420 (m), 1350 (s), 1179 (s), 1081 (m), 1013 (m), 958 (m), 866 (s), 769 (s); δ_{H} (270 MHz, CDCl₃) 1.26 (3H, d, J = 6.5, C4-CH₃), 1.66-1.78 (2H, m, C5-H₂), 3.83 (1H, m, C4-H), 4.06 (1H, br s, NH), 4.56 (1H, ddd, J = 10.5, 3.0 and 3.0, C6-H), 4.69 (1H, m, C6-H); δ_{C} (100 MHz, CDCl₃) 20.8 (CH₃), 31.3 (C-5), 52.1 (C-4), 72.3 (C-6);

m/z (EI^+) 151 ($[\text{M}]^+$, 55 %); HRMS: (EI^+) Found: $[\text{M}]^+$ 151.1926, $\text{C}_4\text{H}_9\text{NO}_3\text{S}$ requires 151.1928.

(±) 3-Benzyl-4-methyl-[1,2,3]oxathiazinane-2,2-dioxide (2c)

This compound was prepared using the *N*-alkylation conditions described by Tewson.⁴ To a solution of unprotected sulfamidate (2.14 g, 14.4 mmol), BnBu_3NCl (224 mg, 0.72 mmol) and BnBr (6.83 mL, 57.4 mmol) in CH_2Cl_2 (48 mL) at r.t. was added aq. NaOH (14.4 mL, 40 wt %) to form a yellow solution which was stirred at r.t. for 16.5 hours. The organics were isolated and the aqueous phase was extracted with CH_2Cl_2 . The organics were combined and washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography (petrol- Et_2O 2:1) to afford the protected sulfamidate (**2c**) (1.87 g, 55 %) as a colourless crystalline solid; m.p. 57 °C (ether-petrol); ν_{max} / cm^{-1} 1455 (m), 1340 (s), 1160 (s), 1024 (m), 944 (m), 845 (m), 869 (m), 833 (m), 819 (s); δ_{H} (400 MHz, CDCl_3) 1.25 (3H, d, $J = 7.0$, CH_3), 1.70-1.87 (2H, m, C5-H_2), 4.08 (1H, m, C4-H), 4.26 (1H, d, $J = 15.5$, PhCH_2N), 4.49 (1H, d, $J = 15.5$, PhCH_2N), 4.57-4.69 (2H, m, C6-H_2), 7.25-7.40 (5H, m, ArCH); δ_{C} (100 MHz, CDCl_3) 19.0 (CH_3), 27.3 (C-5), 49.4 (CH_2N), 55.1 (C-4), 71.0 (C-6), 127.6, 127.7 and 128.6 ($\text{ArCH} \times 5$), 137.5 (ArC); m/z (EI^+) 241 ($[\text{M}]^+$, 18 %), 226 (15), 176 (30), 132 (30), 91 (100); HRMS: (EI^+) Found: $[\text{M}]^+$ 241.0770, $\text{C}_{11}\text{H}_{15}\text{NO}_3\text{S}$ requires 241.0773.

(ii) Synthesis of substituted lactams

Ethyl (3*RS*, 5*R*) 1,5-dibenzylpyrrolidine-2-one-3-carboxylate (3a)

To a suspension of NaH (40 mg, 60 % dispersion in oil, 1.00 mmol) in THF (2 mL) was added diethyl malonate (0.152 mL, 1.00 mmol), and the mixture stirred for 20 minutes. Sulfamidate (**2a**) (152 mg, 0.50 mmol) was then added and the mixture heated to 50 °C for 20 hours. The mixture was cooled to r.t., conc. H₂SO₄ (2 drops) and water (2 drops) were added and the mixture was stirred for 48 hours. The mixture was neutralised by the addition of saturated aq. NaHCO₃ solution and was then partitioned between EtOAc and water. The phases were separated and the aqueous portion was extracted with EtOAc. The combined organics were dried (Na₂SO₄) and concentrated *in vacuo*. Purification by column chromatography (petrol-Et₂O 1:1) afforded the title compound (**3a**) (120 mg, 71 %, 3:2 d.r. *A:B*) as a colourless oil; ν_{max} / cm⁻¹ (film) 3028 (m), 2982 (m), 2931 (m), 1737 (s), 1693 (s), 1454 (m), 1257 (m), 1180 (m), 734 (m), 702 (m); δ_{H} (400 MHz, CDCl₃) 1.28 (3H, td, *J* = 7.0 and 1.0, OCH₂CH₃ of *A*), 1.34 (3H, td, *J* = 7.0 and 1.0, OCH₂CH₃ of *B*), 1.95-2.18 (3H, m, C4-H × 3), 2.28 (1H, dt, *J* = 13.0 and 7.5, C4-H of *A*), 2.54-2.63 (2H, m, PhCH₂C × 2), 2.99 (1H, dd, *J* = 13.5 and 4.5, PhCH₂C of *A*), 3.18-3.29 (2H, m, PhCH₂C × 1 and C3-H of *A*), 3.43 (1H, dd, *J* = 9.0 and 7.5, C3-H of *B*), 3.60 (1H, m, C5-H of *B*), 3.78 (1H, m, C5-H of *A*), 4.10 (1H, d, *J* = 15.0, PhCH₂N of *A*), 4.12 (1H, d, *J* = 15.0, PhCH₂N of *B*), 4.20 (2H, q, *J* = 7.5, OCH₂), 4.22-4.31 (2H, m, OCH₂), 5.06 (1H, d, *J* = 15.0, PhCH₂N of *B*), 5.15 (1H, d, *J* = 15.0, PhCH₂N of *A*), 7.01-7.09 (4H, m, ArCH), 7.20-7.38 (16H, m, ArCH); δ_{C} (75 MHz, CDCl₃) 14.1 and 14.2 (OCH₂CH₃ × 2), 27.7 (C-4 of *B*), 28.2 (C-4 of *A*), 39.1 (PhCH₂C of *A*), 39.9 (PhCH₂C of *B*), 44.8 (PhCH₂N of *A*), 45.0 (PhCH₂N of *B*), 47.5 (C-3 of *A*), 48.1 (C-3 of *B*), 56.4 (C-5 of *A*), 57.1 (C-5 of *B*), 61.6 (OCH₂ of *A*), 61.8 (OCH₂ of *B*), 126.8, 126.9, 127.7, 127.8, 128.0, 128.1, 128.6, 128.7, 128.8, 128.8, 129.2 and 129.2 (ArCH × 20), 135.9, 136.2, 136.3 and 136.9 (ArC × 4), 170.1, 170.3 and 170.4 (C=O × 4); *m/z* (CI⁺) 338 ([M+H]⁺, 30 %); HRMS: (CI⁺) Found: [M+H]⁺ 338.1752, C₂₁H₂₄NO₃ requires 338.1756.

(5R) 1,5-Dibenzylpyrrolidine-2-one (4a)⁵

To a solution of **3a** (120 mg, 0.36 mmol) in DMF (2 mL) was added NaCl (24 mg, 0.40 mmol) and water (10 μ L, 0.54 mmol). The mixture was then heated to reflux overnight. The mixture was cooled to r.t., diluted with water and EtOAc and the phases separated. The aqueous portion was extracted with EtOAc, and the combined organics were dried (Na_2SO_4) and concentrated *in vacuo* to afford the title compound (**4a**) (68 mg, 71 %) as a colourless oil; δ_{H} (400 MHz, CDCl_3) 1.58-1.90 (2H, m, C4- $\underline{\text{H}}_2$), 2.14-2.24 (2H, m, C3- $\underline{\text{H}}_2$) 2.48 (1H, dd, $J = 13.0$ and 8.5 , PhCH_2C), 2.92 (1H, dd, $J = 13.0$ and 4.5 , PhCH_2C), 3.56 (1H, m, C5- $\underline{\text{H}}$), 3.92 (1H, d, $J = 15.0$, PhCH_2N), 5.02 (1H, d, $J = 15.0$, PhCH_2N), 6.93-7.00 (2H, m, ArCH), 7.12-7.28 (8H, m, ArCH); δ_{C} (75 MHz, CDCl_3) 23.6 ($\underline{\text{C}}\text{-4}$), 29.7 ($\underline{\text{C}}\text{-3}$), 39.0 (PhCH_2C), 44.3 (PhCH_2N), 57.8 ($\underline{\text{C}}\text{-5}$), 126.6, 127.4, 127.9, 128.5, 128.6 and 129.1 ($\text{ArCH} \times 10$), 136.5 and 136.9 ($\text{ArC} \times 2$), 175.2 ($\underline{\text{C}}\text{-2}$). The spectroscopic data for this compound were consistent with those reported in the literature.⁵

Ethyl (3R, 4S, 5S) 1,5-dimethyl-4-phenylpyrrolidine-2-one-3-carboxylate (3b)

To a suspension of NaH (80 mg, 60 % dispersion in oil, 2.00 mmol) in DMF (5 mL) was added, dropwise, diethyl malonate (304 μ L, 2.00 mmol). After stirring at r.t. for 30 minutes, sulfamidate (**2b**) (228 mg, 1.00 mmol) was added and the reaction was heated to 100 $^{\circ}\text{C}$ overnight. The mixture was cooled to r.t., aq. HCl (0.50 mL, 5 M) was added, and the mixture was stirred for 10 hours at r.t. The solution was then neutralised by the addition of saturated aq. NaHCO_3 and diluted by the addition of Et_2O . The phases were then separated and the aqueous portion was extracted with Et_2O . The combined organics were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by column chromatography (Et_2O -petrol 2:1) afforded the title compound (**3b**) (157 mg, 60 %) as a colourless crystalline solid; m.p. 119-120 $^{\circ}\text{C}$ (Et_2O -petrol); $[\alpha]_{\text{D}}^{20} +76$ ($c = 1$, CHCl_3); $\nu_{\text{max}} / \text{cm}^{-1}$ (solid) 2974 (m), 1733 (s), 1684 (s), 1401 (m), 1242 (m), 1178 (s), 1121 (m), 751 (m), 703 (s); δ_{H} (400 MHz, CDCl_3) 1.24 (3H, t, $J =$

7.0, OCH₂CH₃), 1.29 (3H, d, *J* = 6.5, C5-CH₃), 2.89 (3H, s, NCH₃), 3.40 (1H, dd, *J* = 10.0 and 8.5, C4-H), 3.54-3.65 (2H, m, C3-H and C5-H), 4.11-4.28 (2H, m, OCH₂), 7.22-7.38 (5H, m, ArCH); δ_C (100 MHz, CDCl₃) 14.2 (OCH₂CH₃), 18.1 (C3-CH₃), 27.8 (NCH₃) 50.9 (C-4), 56.6 and 60.9 (C-3 and C-5), 61.6 (OCH₂CH₃), 127.7 and 129.0 (ArCH ×), 139.3 (ArC), 168.7 and 169.5 (C-2 and COOEt); *m/z* (Cl⁺) 262 ([M+H]⁺, 35 %), 216 (25), 57 (100); HRMS: (Cl⁺) Found: [M+H]⁺ 262.1442, C₁₅H₂₀NO₃ requires 262.1443.

The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.

ORTEP view of ethyl (3*R*, 4*S*, 5*S*) 1,5-dimethyl-4-phenylpyrrolidine-2-one-3-carboxylate (**3b**)

Ethyl (3*R, 6*R**) and (3*R**, 6*S**) 1-benzyl-6-methylpiperidine-2-one-3-carboxylate (3c)**

To a suspension of NaH (16 mg, 60 % dispersion in oil, 0.40 mmol) in DMF (2 mL) was added diethyl malonate (61 μ L, 0.40 mmol). After stirring for 15 minutes, sulfamidate (**2c**) (48 mg, 0.20 mmol) was added and the mixture was then heated to 100 °C for 24 hours. The reaction mixture was cooled to r.t., aq. HCl (0.20 mL, 5 M) was added and the mixture was stirred for 5 hours before neutralisation with saturated aq. NaHCO₃ solution. The mixture was diluted with Et₂O and the phases were separated. The aqueous portion was extracted with Et₂O and the organics were combined and washed with water. The solution was then dried (Na₂SO₄) and concentrated *in vacuo*. The resulting oil was dissolved in ethanol (1 mL) which was then added to an ethanolic solution of sodium ethoxide (2 mL, 0.2 M). The mixture was then heated to reflux for 9 hours. The mixture was cooled to r.t., aq. NH₄Cl solution was added, followed by Et₂O. The phases were separated and the aqueous portion was extracted with Et₂O. The organics were combined, washed with water and then brine. The solution was then dried (Na₂SO₄) and concentrated *in vacuo*. Purification by column chromatography (Et₂O-petrol 2:1) afforded the title compound (**3c**) (31 mg, 57 %, 1:1 d.r.) as a colourless oil; δ_{H} (400 MHz, CDCl₃) 1.22 (3H, d, J = 7.5, C6-CH₃), 1.26 (3H, d, J = 7.5, C6-CH₃), 1.32 (6H, t, J = 7.5, OCH₂CH₃ $\times$ 2), 1.50-1.90 (4H, m), 1.95-2.25 (4H, m), 3.43-3.53 (4H, m, C3-H $\times$ 2 and C6-H $\times$ 2), 3.99 (1H, d, J = 15.0, PhCH₂N), 4.15 (1H, d, J = 15.0, PhCH₂N), 4.18-4.33 (4H, m, OCH₂CH₃ $\times$ 2), 5.17 (1H, d, J = 15.0, PhCH₂N), 5.45 (1H, d, J = 15.0, PhCH₂N), 7.19-7.38 (10H, m, ArCH); δ_{C} (75 MHz, CDCl₃) 14.1 and 14.2 (OCH₂CH₃), 19.5, 19.6, 21.5 and 21.8 (C-4 and C6-CH₃), 27.6 and 28.3 (C-5), 47.1 (2 signals), 47.7, 48.0, 48.6, 49.5, 50.8 and 51.4 (C-3, PhCH₂N and OCH₂Me), 61.3 (C-6), 127.2, 127.5, 127.7 and 128.5 (ArCH), 137.2 and 137.5 (ArC), 166.2, 166.4, 171.3 and 171.4 (C-2 and COOEt); m/z (CI⁺) 276 ([M+H]⁺, 100 %); HRMS: (CI⁺) Found: 276.1590, C₁₆H₂₂NO₃ requires 276.1600.

(3*R, 6*R**) and (3*R**, 6*S**) 1-Benzyl-6-methylpiperidine-2-one -3-carboxylic acid**

To a solution of ester (**3c**) (120 mg, 0.44 mmol) in methanol (1 mL) was added KOH (34 mg, 0.61 mmol) and water (1.5 mL). The mixture was then heated for 3.5 hours to reflux. The mixture was cooled to r.t, aq. HCl (2 M) was added and the mixture was diluted with EtOAc. The phases were separated and the aqueous portion was extracted with EtOAc. The combined organics were washed with brine and dried (Na₂SO₄). Concentration *in vacuo* afforded the acid (77 mg, 71 %, 5:3 d.r. *A*:*B*) as a colourless oil which was used in the next step without further purification. *Only partial characterisation data are given*; $\nu_{\max}$ / cm⁻¹ (film) 2972 (br, s), 2500-3000 (br, m), 1739 (s), 1598 (s), 1452 (s), 1184 (m), 734 (m), 704 (m); δ_{H} (400 MHz, CDCl₃) 1.28 (6H, m, C6-CH₃ of *A* and *B*), 1.64 (1H, m, of *B*), 1.80 (1H, m, of *A*), 1.85-2.00 (2H, m, of *A* and *B*), 2.12-2.38 (4H, m, 2H of *A* and 2H of *B*), 3.28-3.45 (2H, m, C3-H of *A* and *B*), 3.51 (1H, m, C6-H of *B*), 3.63 (1H, m, C6-H of *A*), 4.03 (1H, d, *J* = 15.0, PhCH₂N of *A*), 4.22 (1H, d, *J* = 15.0, PhCH₂N of *B*), 5.25 (1H, d, *J* = 15.0, PhCH₂ of *B*), 5.31 (1H, d, *J* = 15.0, PhCH₂N of *A*), 7.18-7.38 (10H, m, ArCH of *A* and *B*); δ_{C} (75.5 MHz, CDCl₃) 18.7 (C-4 of *A*), 18.9 (C6-CH₃ of *A*), 19.8 (C6-CH₃ of *B*), 20.0 (C-4 of *B*), 27.9 (C-5 of *A*), 29.2 (C-5 of *B*), 44.6 (C-3 of *B*), 44.9 (C-3 of *A*), 47.8 (PhCH₂N of *B*), 48.7 (PhCH₂N of *A*), 51.9 (C-6 of *A*), 52.4 (C-6 of *B*), 127.5, 127.7, 127.8, 127.9 and 128.9 (ArCH of *A* and *B*), 135.9 and 136.0 (ArC of *A* and *B*), 169.6, 169.7, 170.0 and 170.6 (C-2 and COOH of *A* and *B*); *m/z* (CI⁺) 407 ([2M-2CO₂+H]⁺, 25 %), 248 ([M+H]⁺, 3), 204 ([M-CO₂+H]⁺, 100).

(±) 1-Benzyl-6-methylpiperidin-2-one (4c**)⁶**

A solution of carboxylic acid (20 mg, 0.08 mmol) in 1,4-dioxane (2 mL) was heated to reflux for 24 hours. The solvent was then removed *in vacuo* to afford the title compound (**4c**) (16 mg, 100 %) as a colourless oil; $\nu_{\max}$ / cm^{-1} (film) 2946 (m), 1635 (s), 1452 (m), 1335 (m), 1259 (m), 1184 (m), 706 (m); δ_{H} (400 MHz, CDCl_3) 1.20 (3H, $J = 7.0$, C6-CH₃), 1.56-2.00 (4H, m, C4-H₂ and C5-H₂), 2.46-2.54 (2H, m, C3-H₂), 3.47 (1H, m, C6-H), 4.00 (1H, d, $J = 15.0$, PhCH₂N), 5.33 (1H, d, $J = 15.0$, PhCH₂N), 7.21-7.35 (5H, m, ArCH); δ_{C} (75.5 MHz, CDCl_3) 17.5 (C-4), 19.6 (C6-CH₃), 30.3 (C-5), 32.2 (C-3), 47.1 (PhCH₂N), 51.0 (C-6), 127.1, 127.7 and 128.5 (ArCH $\times 5$), 137.8 (ArC), 170.3 (C-2); m/z (Cl^+) 204 ($[\text{M}+\text{H}]^+$, 100 %); HRMS: (Cl^+) Found: $[\text{M}+\text{H}]^+$ 204.1381, $\text{C}_{13}\text{H}_{18}\text{NO}$ requires 204.1388. *The spectroscopic data for this compound were consistent with those reported in the literature.*⁶

Diethyl (5S) (1,5-Dibenzylpyrrolidin-2-on-3-yl)phosphonate (6a)

To a solution of triethyl phosphonoacetate (**5**) (1.30 mL, 6.6 mmol) in THF (30 mL) was added *t*-BuOK (739 mg, 6.6 mmol) and the resulting mixture was heated at 40 °C for 20 minutes to form a colourless solution. Sulfamidate (**2a**) (1.00 g, 3.3 mmol) was added and the reaction mixture was heated at 40 °C for 13 hours. The mixture was allowed to cool to r.t., aq. HCl (3.4 mL, 5 M) was added and the mixture was stirred for 3 hours. The reaction mixture was neutralised by addition of saturated aq. NaHCO_3 , diluted by addition of brine and extracted with CH_2Cl_2 . The organics were combined, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in toluene (40 mL) and heated at reflux for 16 hours. The reaction mixture was allowed to cool to r.t., concentrated *in vacuo* and excess triethyl phosphonoacetate (**5**) was removed by vacuum distillation (*ca.* 70 °C, 0.01 mmHg). The residue was purified by flash chromatography (EtOAc) to afford the product (**6a**) (1.27 g, 96 %, 2:1 d.r. *A:B*) as a colourless oil; $\nu_{\max}$ / cm^{-1} (solid) 2983 (m), 2930 (m), 1689 (s), 1454 (m), 1249 (s), 1024 (s), 968 (s), 737 (m), 703 (m); δ_{H} (400 MHz, CDCl_3) 1.23-1.41 (6H, m, OCH_2CH_3 of *A* and *B*), 1.97-2.34 (4H, m, C4-H₂ of *A* and *B*), 2.55 (1H, dd, $J = 13.0$ and 8.5, PhCH₂C of *A*), 2.66 (1H, dd, $J = 13.0$ and 10.0, PhCH₂C of *B*), 2.85-3.14

(3H, m, PhCH₂C of A and C3-H of A and B), 3.21 (1H, dd, $J = 13.0$ and 4.5 , PhCH₂C of B), 3.64 (1H, m, C5-H of B), 3.78 (1H, m, C5-H of A), 4.02 (1H, d, $J = 15.0$, PhCH₂N of A), 4.10-4.36 (5H, m, PhCH₂N of B and OCH₂ of A and B), 5.03 (1H, d, $J = 15.0$, PhCH₂N of B), 5.15 (1H, d, $J = 15.0$, PhCH₂N of A), 7.00-7.09 (4H, m, ArCH), 7.19-7.38 (16H, m, ArCH); δ_C (75.5 MHz, CDCl₃) 16.3-16.6 (4C, m, OCH₂CH₃ $\times$ 4), 25.5 (d, $^2J_{PC} = 4.0$, C-4 of B), 26.1 (d, $^2J_{PC} = 3.5$, C-4 of A), 39.2 (PhCH₂C of A), 39.7 (PhCH₂C of B), 40.0 (d, $^1J_{PC} = 144.5$, C-3 of A), 40.5 (d, $^1J_{PC} = 146.0$, C-3 of B), 44.6 (PhCH₂N of A), 44.9 (PhCH₂N of B), 56.3 (d, $^3J_{PC} = 5.0$, C-5 of A), 57.3 (d, $^3J_{PC} = 6.0$, C-5 of B), 62.1-63.3 (4C, m, OCH₂CH₃ $\times$ 4), 126.7, 126.9, 127.6, 127.7, 127.9, 128.1, 128.6, 128.7 (3 signals) and 129.2 (ArCH $\times$ 20), 135.9, 136.2, 136.3 and 137.0 (ArC $\times$ 4), 169.5 (d, $^2J_{PC} = 3.5$, C-2 of A and B); δ_P (121 MHz, CDCl₃) 24.9 (B) and 25.2 (A); m/z (CI⁺) 402 ([M+H]⁺, 100 %); HRMS: (CI⁺) Found: [M+H]⁺ 402.1830, C₂₂H₂₉NO₄P requires 402.1834.

(S) 1,5-Dibenzyl-3-methylenepyrrolidin-2-one (7a)

To a solution of heterocyclic phosphonate (**6a**) (1.210 g, 3.02 mmol) in THF (15 mL) was added, portionwise, at r.t., NaH (127 mg, 3.17 mmol, 60 % dispersion in mineral oil) to form a light brown suspension. Paraformaldehyde (191 mg, 6.04 mmol) was added and the mixture was stirred at r.t. for 3.5 hours. Aq. HCl (8 mL, 2 M) was added, the mixture was diluted with brine and extracted with CH₂Cl₂. The organics were combined, dried (Na₂SO₄) and concentrated *in vacuo*. The residue was purified by flash chromatography (Et₂O-hexanes 2:1) to afford the product (**7a**) (544 mg, 65 %) as a colourless oil which crystallised on standing; m.p. 90.5-92 °C (Et₂O-petrol); $[\alpha]_D^{20}$ -71.0 ($c = 1.6$, CHCl₃); ν_{max} / cm⁻¹ (film) 3028 (w), 2924 (w), 1684 (s), 1659 (s), 1416 (s), 730 (s), 694 (s); δ_H (300 MHz, CDCl₃) 2.41-2.70 (3H, m, C4-H $\times$ 2 and C5-CH₂Ph), 3.08-3.19 (1H, dd, $J = 13.5$ and 4.0 , C5-CH₂Ph), 3.69 (1H, dddd, $J = 12.5$, 8.0 , 4.0 and 3.5 , C5-H), 4.14 (1H, d, $J = 15.0$, NCH₂Ph), 5.20 (1H, d, $J = 15.0$, NCH₂Ph), 5.31 (1H, t, $J = 2.0$, C3-CH₂), 6.04 (1H, t, $J = 2.0$, C3-CH₂), 7.06 (2H, dd,

$J = 6.5$ and 1.5 , ArCH), 7.19-7.42 (8H, m, ArCH); δ_C (100 MHz, $CDCl_3$) 30.7 (C4-CH₂Ph), 39.9 (C-4), 45.1 (NCH₂Ph), 55.3 (C-5), 116 (C3-CH₂), 126.7, 127.6, 128.2, 128.6, 128.7 and 129.1 (ArCH $\times$ 10), 136.4, 136.8 and 138.9 (ArC and C-3), 168.1 (C-2); m/z (CI^+) 278 ($[M+H]^+$, 100 %); HRMS: (CI^+) Found: $[M+H]^+$ 278.1541, $C_{19}H_{19}NO$ requires 278.1545; Anal. Calcd for $C_{19}H_{19}NO$: C, 82.19; H, 7.12; N, 4.76. Found: C, 82.28; H, 6.90; N, 5.05);

(5S) 1,5-Dibenzyl-3-cyclohexylidenepyrrolidin-2-one (7b)

To a suspension of NaH (32 mg, 60 % dispersion in oil, 0.80 mmol) in THF (5 mL) was added phosphonate (**6a**) (301 mg, 0.75 mmol) and the mixture was stirred for 30 minutes at r.t. Cyclohexanone (104 μ L, 1.00 mmol) was then added dropwise, and the mixture was stirred for 3 hours. The solution was then diluted with Et₂O and water and the phases separated. The aqueous portion was extracted with Et₂O, and then the organics were combined, dried (Na₂SO₄) and concentrated *in vacuo*. Purification by column chromatography (petrol-Et₂O 4:1) afforded the title compound (**7b**) (188 mg, 73 %) as a colourless crystalline solid; m.p. 94-97 °C; $[\alpha]_D^{20}$ -55 ($c = 1$, $CHCl_3$); ν_{max} / cm^{-1} (solid) 2920 (m), 2850 (m), 1674 (s), 1655 (s), 1434 (m), 1420 (s), 1262 (s), 738 (s), 700 (s); δ_H (400 MHz, $CDCl_3$) 1.45-1.75 (6H, m), 1.97-2.11 (2H, m), 2.35 (1H, m), 2.43-2.55 (2H, m), 2.89-3.16 (3H, m), 3.60 (1H, m, C5-H), 4.08 (1H, d, $J = 15.0$, PhCH₂N), 5.14 (1H, d, $J = 15.0$, PhCH₂N), 7.00-7.06 (2H, m, ArCH), 7.18-7.35 (8H, m, ArCH); δ_C (100 MHz, $CDCl_3$) 26.5, 27.9, 28.2 (2 signals), 30.0, 33.4, 40.0 and 44.6 (CH₂ $\times$ 8), 54.5 (C-5), 120.2 (C-3), 126.6, 127.5, 128.3, 128.6, 128.7 and 129.3 (ArCH $\times$ 10), 137.3 (ArC $\times$ 2), 150.1 (cyclohexyl-C), 169.4 (C-2); m/z (EI^+) 345 ($[M]^+$, 20 %), 254 ($[M-Bn]^+$ 100); HRMS: (EI^+) Found: $[M]^+$ 345.2094, $C_{24}H_{27}NO$ requires 345.2093.

(3E)- and (3Z)- (5S) 1,5-Dibenzyl-3-butylidenepyrrolidin-2-one (7c)

To a suspension of NaH (32 mg, 60 % dispersion, 0.80 mmol) in THF (2 mL) was added heterocyclic phosphonate (**6a**) (301 mg, 0.75 mmol) as a solution in 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 hours the mixture was diluted with Et_2O and water, and the phases separated. The aqueous portion was extracted with Et_2O then the organics were combined, dried (Na_2SO_4) and concentrated *in vacuo*. Purification by column chromatography (petrol- Et_2O 5:1 to 2:1) afforded the title compounds (*E*)-(**7c**) and (*Z*)-(**7c**) (1:1 ratio, 204 mg, 85 %) as colourless oils.

First eluted from the column was (*Z*)-(**7c**); $[\alpha]_{\text{D}}^{20} -73$ ($c = 1$, CHCl_3); $\nu_{\text{max}} / \text{cm}^{-1}$ (film) 2959 (m), 1686 (s), 1663 (s), 1418 (s), 1256 (m), 754 (s), 700 (s); δ_{H} (400 MHz, CDCl_3) 0.93 (3H, t, $J = 7.5$, CH_3), 1.41 (2H, sextet, $J = 7.5$, CH_2Me), 2.35 (1H, dd, $J = 16.0$ and 1.5 , C4-H), 2.46 (1H, dd, $J = 13.0$ and 9 , PhCH_2C), 2.53 (1H, ddd, $J = 16.0$, 8.0 and 1.5 , C4-H), 2.65-2.84 (2H, m, $\text{CH}_2\text{CH}_2\text{Me}$), 3.05 (1H, dd, $J = 13.5$ and 4.0 , PhCH_2C), 3.60 (1H, m, C5-H), 4.04 (1H, d, $J = 15.0$, PhCH_2N), 5.13 (1H, d, $J = 15.0$, PhCH_2N), 5.79 (1H, tt, $J = 8.0$ and 2.0 , $\text{C}=\text{CH}$), 7.00-7.06 (2H, m, ArCH), 7.16-7.37 (8H, m, ArCH); δ_{C} (75 MHz, CDCl_3) 13.7 (CH_3), 22.8 (CH_2Me), 28.9 ($\text{CH}_2\text{CH}_2\text{Me}$), 32.0 (C-4), 39.6 (PhCH_2C), 44.3 (PhCH_2N), 55.1 (C-5), 126.5, 127.4, 128.1, 128.4, 128.6 and 129.1 ($\text{ArCH} \times 10$), 136.8 and 137.0 ($\text{ArC} \times 2$), 137.6 ($\text{C}=\text{CH}$), 168.6 (C-2); m/z (CI^+) 320 ($[\text{M}+\text{H}]^+$, 100 %); HRMS: (CI^+) Found: $[\text{M}+\text{H}]^+$ 320.2015, $\text{C}_{22}\text{H}_{26}\text{NO}$ requires 320.2014.

Further elution from the column provided (*E*)-(**7c**); $[\alpha]_{\text{D}}^{20} -61$ ($c = 1$, CHCl_3); $\nu_{\text{max}} / \text{cm}^{-1}$ (film) 2960 (m), 2930 (m), 1692 (s), 1672 (s), 1419 (s), 753 (s), 701 (s); δ_{H} (400 MHz, CDCl_3) 0.90 (3H, t, $J = 7.5$, CH_3), 1.44 (2H, sextet, $J = 7.5$, CH_2CH_3), 1.99-2.08 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.34 (1H, d, $J = 16.0$, C4-H), 2.42-2.55 (2H, m, C4-H and PhCH_2C), 3.12 (1H, dd, $J = 13.0$ and 4.0 , PhCH_2C), 3.68 (1H, m, C5-H), 4.13 (1H, d,

$J = 15.0$, PhCH_2N), 5.15 (1H, d, $J = 15.0$, PhCH_2N), 6.49 (1H, tt, $J = 8.0$ and 3.0 , $\text{C}=\text{CH}$), 7.01-7.07 (2H, m, ArCH), 7.18-7.37 (8H, m, ArCH); δ_{C} (75 MHz, CDCl_3) 13.8 (CH_3), 21.7 (CH_2Me), 28.1 ($\text{C}-4$), 31.1 ($\text{CH}_2\text{CH}_2\text{Me}$), 39.9 (PhCH_2C), 44.7 (PhCH_2N), 55.3 ($\text{C}-5$), 126.6, 127.5, 128.2, 128.5, 128.6 and 129.1 ($\text{ArCH} \times 10$), 130.5 (ArC), 133.6 ($\text{C}=\text{CH}$), 136.7 (ArC), 168.7 ($\text{C}-2$); m/z (CI^+) 320 ($[\text{M}+\text{H}]^+$, 100 %); HRMS: (CI^+) Found: $[\text{M}+\text{H}]^+$ 320.2013, $\text{C}_{22}\text{H}_{26}\text{NO}$ requires 320.2014.

Diethyl (3R, 4S, 5S) (1,5-dimethyl-4-phenylpyrrolidin-2-on-3-yl)phosphonate (6b)

To a suspension of NaH (160 mg, 60 % dispersion in oil, 4.00 mmol) in DMF (10 mL) was added dropwise triethyl phosphonoacetate (**5**) (0.80 mL, 4.00 mmol) and the mixture was stirred for 15 minutes. Sulfamidate (**2b**) (455 mg, 2.00 mmol) was then added and the mixture was then heated to 100 °C overnight. The mixture was cooled to r.t., aq. HCl (1.0 mL, 5 M) was added and the mixture was stirred at r.t. for 6 hours. The solution was then neutralised by the addition of NaHCO_3 solution, and was diluted with Et_2O . The phases were separated and the aqueous portion was extracted with Et_2O . The organics were combined, dried (Na_2SO_4) and concentrated *in vacuo*. Purification by column chromatography (EtOAc) afforded the title compound (**6b**) (202 mg, 31 %) as a colourless oil; $[\alpha]_{\text{D}}^{20} +5$ ($c = 1$, CHCl_3); $\nu_{\text{max}}/\text{cm}^{-1}$ (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_2CH_3), 1.28 (3H, t, $J = 7.0$, OCH_2CH_3), 1.32 (3H, d, $J = 6.5$, C5-CH_3), 2.89 (3H, s, NCH_3), 3.12 (1H, dd, $J = 23.0$ and 9.0 , C3-H), 3.30 (1H, ddd, $J = 18.0$, 9.0 and 6.5 , C4-H), 3.52 (1H, qd, $J = 6.5$ and 1.0 , C5-H), 3.86-4.06 (2H, m, OCH_2CH_3), 4.17-4.27 (2H, m, OCH_2CH_3), 7.22-7.37 (5H, m, ArCH); δ_{C} (75 MHz, CDCl_3) 16.0 (d, $^3J_{\text{PC}} = 7.0$, POCH_2CH_3), 16.4 (d, $^3J_{\text{PC}} = 7.0$, POCH_2CH_3), 18.6 (C5-CH_3), 27.8 (NCH_3), 48.3 ($\text{C}-4$), 49.3 (d, $^1J_{\text{PC}} = 144.5$, $\text{C}-3$), 62.0 (d, $^2J_{\text{PC}} = 6.5$, POCH_2CH_3), 62.9 (d $^3J_{\text{PC}} = 10.0$, $\text{C}-5$), 63.4 (d, $^2J_{\text{PC}} = 6.5$, POCH_2CH_3), 127.4, 127.5 and 128.9 ($\text{ArCH} \times 5$), 141.3 (d, $^3J_{\text{PC}} = 4.5$, ArC), 168.3 (d,

$^2J_{PC} = 2.5$, C-2); m/z (Cl^+) 326 ($[M+H]^+$, 100 %); HRMS: (Cl^+) Found: $[M+H]^+$ 326.1514, $C_{16}H_{25}NO_4P$ requires 326.1521.

(5S) 1,5-Dibenzyl-3-(4-nitrophenyl)pyrrolidin-2-one (9a)

To a solution of ethyl *p*-nitrophenylacetate (**8**) (276 mg, 1.32 mmol) in DMF (6 mL) was added NaH (53 mg, 1.32 mmol, 60 % dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 15 minutes to form a purple solution. Sulfamidate (**2a**) (200 mg, 0.66 mmol) was added and the reaction mixture was stirred at r.t. for 15.5 hours. Aq. HCl (0.7 mL, 5 M) was added to form a yellow suspension which was stirred at r.t. for 3 hours. The reaction mixture was neutralised by addition of saturated aq. $NaHCO_3$ and extracted with Et_2O . The organics were combined, washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in toluene (5 mL) and heated at 100 °C for 2.5 hours. The mixture was cooled to r.t. and concentrated *in vacuo*. The residue was purified by flash chromatography (Et_2O -petrol 3:2) to afford the product (**9a**) (225 mg, 88 %, 3:2 d.r. *A:B*) as a yellow oil; ν_{max} / cm^{-1} (film) 3029 (w), 2863 (w), 1682 (s), 1516 (s), 1344 (s), 853 (m), 732 (s), 698 (s); δ_H (400 MHz, $CDCl_3$) 1.76 (1H, ddd, $J = 13.0$, 12.0 and 9.0, C4-H of *B*), 2.04 (1H, ddd, $J = 13.0$, 10.0 and 9.5, C4-H of *A*), 2.35 (1H, ddd, $J = 13.0$, 9.5 and 2.5, C4-H of *A*), 2.41 (1H, ddd, $J = 13.0$, 10.0 and 7.0, C4-H of *B*), 2.54 (1H, dd, $J = 13.0$ and 10.0, C5-CH₂Ph of *B*), 2.76 (1H, dd, $J = 13.5$ and 8.0, C5-CH₂Ph of *A*), 3.05 (1H, dd, $J = 13.5$ and 4.5, C5-CH₂Ph of *A*), 3.25 (1H, dd, $J = 13.0$ and 4.0, C5-CH₂Ph of *B*), 3.54 (1H, dd, $J = 9.5$ and 9.5, C3-H of *A*), 3.74 (1H, dd, $J = 10.0$ and 10.0, C3-H of *B*), 3.68-3.84 (2H, m, C5-H of *A* and *B*), 4.03 (1H, d, $J = 15.0$, NCH₂Ph of *A*), 4.25 (1H, d, $J = 14.5$, NCH₂Ph of *B*), 5.17 (1H, d, $J = 14.5$, NCH₂Ph of *B*), 5.21 (1H, d, $J = 15.0$, NCH₂Ph of *A*), 7.01 (2H, d, $J = 8.5$, C8-H of *B*), 7.12 (2H, d, $J = 8.5$, C8-H of *A*), 7.21-7.44 (20H, m, ArCH of *A* and *B*), 8.15 (2H, d, $J = 8.5$, C9-H of *A*), 8.17 (2H, d, $J = 8.5$, C9-H of *B*); δ_C (100 MHz, $CDCl_3$) 33.0 (C-4 of *A*), 34.1 (C-4 of *B*), 38.7 (C5-CH₂Ph of *A*), 40.1 (C5-CH₂Ph of *B*), 45.1 (NCH₂Ph of *A*), 45.2 (NCH₂Ph of *B*),

46.3 (C-3 of A), 47.7 (C-3 of B), 56.0 (C-5 of A), 56.4 (C-5 of B), 123.9 (2 signals), 127.0, 127.1, 127.9, 128.0, 128.2, 128.3, 128.8, 128.9 (2 signals), 129.0 (2 signals), 129.1, 129.2 and 129.3 (28 × ArCH), 136.2, 136.4 (2 signals) and 136.7 (ArC), 147.0, 147.1 and 147.2 (2 signals) (C-8 and C-9), 173.4 (C-2 of A), 174.0 (C-2 of B); m/z (Cl^+) 387 ($[\text{M}+\text{H}]^+$, 100 %); HRMS: (Cl^+) Found: $[\text{M}+\text{H}]^+$ 387.1696, $\text{C}_{24}\text{H}_{23}\text{N}_2\text{O}_3$ requires 387.1709.

(4S, 5S) 1,5-Dimethyl-3-(4-nitrophenyl)-4-phenylpyrrolidin-2-one (9b)

To a solution of ethyl *p*-nitrophenylacetate (**8**) (384 mg, 1.84 mmol) in DMF (6 mL) was added NaH (74 mg, 1.84 mmol, 60 % dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 15 minutes to form a purple solution. Sulfamidate (**2b**) (200 mg, 0.92 mmol) was added and the reaction mixture was heated at 60 °C for 19 hours. The mixture was allowed to cool to r.t. and aq. HCl (0.9 mL, 5 M) was added to form a red emulsion which was stirred at r.t. for 3 hours. The reaction mixture was neutralised by addition of saturated aq. NaHCO_3 and extracted with Et_2O . The organics were combined, washed with water, dried (MgSO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography (EtOAc -hexanes 2:1) to afford the product (**9b**) (205 mg, 72 %, 5:2 d.r. *A:B*) as a yellow oil; ν_{max} / cm^{-1} (film) 2966 (w), 1689 (s), 1517 (s), 1361 (s), 701(m); δ_{H} (400 MHz, CDCl_3) 1.30 (3H, d, $J = 6.5$, C5-CH₃ of A), 1.38 (3H, d, $J = 6.5$, C5-CH₃ of B), 2.88 (1H, dd, $J = 11.0$ and 9.0, C4-H of A), 2.98 (3H, s, NCH₃ of A), 3.08 (3H, s, NCH₃ of B), 3.48 (1H, dd, $J = 9.0$ and 5.5, C4-H of B), 3.70 (1H, dq, $J = 9.0$ and 6.5, C5-H of A), 3.93 (1H, d, $J = 11.0$, C3-H of A), 3.96 (1H, qd, $J = 6.5$ and 5.5, C5-H of B), 4.21 (1H, d, $J = 9.0$, C3-H of B), 6.76 (2H, dd, $J = 5.5$ and 2.0, ArCH of B), 6.94 (2H, d, $J = 9.0$, C7-H of B), 7.17 (2H, d, $J = 9.0$, C7-H of A), 7.04-7.14 (3H, m ArCH of B), 7.22-7.39 (5H, ArCH of A), 7.91 (2H, d, $J = 9.0$, C8-H of B), 8.11 (2H, d, $J = 9.0$, C8-H of A); δ_{C} (100 MHz, CDCl_3) 18.0 (C5-CH₃ of B), 18.1 (C5-CH₃ of A), 27.7 (NCH₃ of B), 27.9 (NCH₃ of A), 52.7 (C-3 of B), 53.1 (C-4 of B), 56.3 (C-3 of A), 57.8 (C-4 of

A), 59.2 (C-5 of B), 60.6 (C-5 of A), 123.1, 123.8, 127.4, 128.0 (2 signals), 128.1, 128.5, 129.1, 129.4 and 130.3 ($18 \times \text{ArCH}$), 137.4 (ArC of B), 138.1 (ArC of A), 143.8, 145.8, 146.6 and 147.2 (C-6 and C-9 of A and B), 172.2 (C-2 of A), 172.4 (C-2 of B); m/z (Cl^+) 311 ($[\text{M}+\text{H}]^+$, 100 %); HRMS: (Cl^+) Found: $[\text{M}+\text{H}]^+$ 311.1392, $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}_3$ requires 311.1396.

(3R*, 6R*) and (3R*, 6S*) 1-Benzyl-6-methyl-3-(4-nitrophenyl)piperidin-2-one
(9c)

To a solution of ethyl *p*-nitrophenylacetate (**8**) (0.82 mmol, 171 mg) in DMF (3 mL) at r.t. was added NaH (33 mg, 0.82 mmol, 60 % dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 15 minutes to form a deep purple solution. Sulfamidate (**2c**) was added (100 mg, 0.41 mmol) and the mixture was heated at 60 °C for 14.5 hours. The reaction mixture was allowed to cool to r.t. and aq. HCl (0.5 mL, 5 M) was added to form an orange emulsion which was stirred at r.t. for 3 hours. The reaction mixture was neutralised by addition of saturated aq. NaHCO_3 and extracted into Et_2O . The organics were combined, washed with water, dried (MgSO_4) and concentrated *in vacuo*. The residue was dissolved in MeOH (8 mL), NaCN (2 mg, 10 mol %) was added and the mixture heated at 50 °C for 46 hours. The mixture was allowed to cool to r.t. and concentrated *in vacuo*. The residue was purified by flash chromatography (Et_2O -petrol 2:1 – 3:1) to afford the product (**9c**) (68 mg, 51 %, 5:2 d.r. A:B) as a yellow oil; ν_{max} / cm^{-1} (film) 3063 (w), 2942 (br m), 1633 (s), 1515 (s), 1352 (s), 853 (m), 699 (s); δ_{H} (400 MHz, CDCl_3) 1.29 (3H, d, $J = 6.5$, C6- CH_3 of B), 1.35 (3H, d, $J = 6.5$, C6- CH_3 of A), 1.62 (1H, dddd, $J = 13.5, 9.0, 6.5$ and 3.0 , C5-H of B), 1.74 (1H, dddd, $J = 13.5, 5.5, 3.5$ and 3.5 , C4-H of A), 1.89 (1H, dddd, $J = 13.5, 9.0, 7.5$ and 3.0 , C4-H of A), 1.93-2.04 (2H, m, C4-H of A and C5-H of B), 2.05-2.19 (2H, m, C5-H of A), 2.28 (1H, dddd, $J = 13.5, 9.5, 6.5$ and 3.5 , C4-H of B), 3.58-3.68 (2H, m, C6-H of A and B), 3.78-3.86 (2H, m, C3-H of A and B), 4.03 (1H, d, $J = 15.0$, NCH_2Ph of A), 4.12 (1H, d, $J = 15.0$, NCH_2Ph of B), 5.37 (2H, d, $J = 15.0$, NCH_2Ph of

A and B), 7.24-7.44 (14H, m, ArCH), 8.14-8.22 (4H, m, ArCH); δ_C (100 MHz, CDCl₃) 19.8 (C6-CH₃ of *A*), 20.6 (C6-CH₃ of *B*), 26.6 (C-5 of *A*), 27.0 (C-4 of *B*), 28.7 (C-5 of *B*), 28.8 (C-4 of *A*), 47.3 (NCH₂Ph of *B*), 48.2 (NCH₂Ph of *A*), 49.3 (2 signals) (C-3 of *A and B*), 51.4 (C-6 of *A*), 51.8 (C-6 of *B*), 123.7, 123.8, 127.5 (2 signals), 128.0, 128.1, 128.7 (2 signals) and 129.3 (2 signals) (ArCH $\times$ 18), 137.6, 137.7, 146.9 (2 signals), 149.5 and 149.7 (ArC $\times$ 6), 169.9 (C-2 of *A*), 169.9 (C-2 of *B*); m/z (CI⁺) 325 ([M+H]⁺, 100 %); HRMS: (CI⁺) Found: [M+H]⁺ 325.1541, C₁₉H₂₁N₂O₃ requires 325.1552.

(3S*, 4R*) 1,4-Dibenzyl-3-(4-nitrophenyl)pyrrolidin-2-one (9d)

To a solution of ethyl *p*-nitrophenylacetate (**8**) (276 mg, 1.32 mmol) in DMF (6 mL) was added NaH (53 mg, 1.32 mmol, 60 % dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 15 minutes to form a purple solution. Sulfamidate (**2d**) (200 mg, 0.66 mmol) was added and the reaction mixture was heated at 60 °C for 15 hours. The mixture was allowed to cool to r.t. and aq. HCl (0.7 mL, 5 M) was added to form an orange emulsion which was stirred at r.t. for 3 hours. The reaction mixture was neutralised by addition of saturated aq. NaHCO₃ and extracted with Et₂O. The organics were combined, washed with water, dried (MgSO₄) and concentrated *in vacuo*. The residue was dissolved in toluene (5 mL) and heated at 100 °C for 2.5 hours. Solvent was removed *in vacuo* and the residue was purified by flash chromatography (Et₂O-petrol 2:1) to afford the product (**9d**) (167 mg, 66 %) as a pale yellow powder; m.p. 119-120 °C (Et₂O-petrol); $\nu_{\max}$ / cm⁻¹ (film) 3034 (m), 2951 (m), 1689 (s), 1512 (s), 1439 (m), 1345 (s), 696 (s); δ_H (400 MHz, CDCl₃) 2.61-2.76 (2H, m, C4-H and C4-CH₂Ph), 2.81-2.93 (1H, m, C4-CH₂Ph), 3.08 (1H, dd, J = 10.0 and 7.5, C5-H), 3.31 (1H, dd, J = 10.0 and 7.5, C5-H), 3.54 (1H, d, J = 8.5, C3-H), 4.48 (1H, d, J = 14.5, NCH₂Ph), 4.53 (1H, d, J = 14.5, NCH₂Ph), 6.99 (2H, d, J = 8.0, ArCH), 7.14-7.40 (10H, m, ArCH), 8.16 (2H, d, J = 8.0, ArCH); δ_C (100 MHz, CDCl₃) 39.4 (C4-CH₂Ph), 43.3 (C-4), 47.2 (NCH₂Ph), 50.4 (C-5), 54.9 (C-3), 123.9,

126.9, 127.9, 128.3, 128.7 (2 signals), 128.9 and 129.4 ($\text{ArCH} \times 14$), 136.2, 138.1, 146.4 and 147.2 (ArC), 172.9 (C-2); m/z (Cl^+) 387 ($[\text{M}+\text{H}]^+$, 100 %); HRMS: (Cl^+) Found: $[\text{M}+\text{H}]^+$ 387.1702, $\text{C}_{24}\text{H}_{23}\text{N}_2\text{O}_2$ requires 387.1709. *The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.*

ORTEP view of (3*S**, 4*R**) 1,4-Dibenzyl-3-(4-nitrophenyl)pyrrolidin-2-one (**9d**)

(3*S*, 4*S*, 5*R*) 1,5-Dimethyl-3-(4-nitrophenyl)-4-phenylpyrrolidin-2-one (9e)

To a solution of ethyl *p*-nitrophenylacetate (**8**) (384 mg, 1.84 mmol) in DMF (6 mL) was added NaH (74 mg, 1.84 mmol, 60 % dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 15 minutes to form a purple solution. Sulfamidate (**2e**) (200 mg, 0.92 mmol) was added and the reaction mixture was heated at 60 °C for 19 hours. The mixture was allowed to cool to r.t. and aq. HCl (0.9 mL, 5 M) was added to form a brown emulsion which was stirred at r.t. for 3 hours. The reaction

mixture was neutralised by addition of saturated aq. NaHCO₃ and extracted with Et₂O. The organics were combined, washed with water, dried (MgSO₄) and concentrated *in vacuo*. The residue was purified by flash chromatography (EtOAc-hexanes 2:1) to afford the product (**9e**) (127 mg, 45 %) as a pale yellow oil; $[\alpha]_D^{20} +210$ (c = 0.8, CHCl₃); $\nu_{\max} / \text{cm}^{-1}$ (film) 2971 (w), 2927 (w), 1686 (s), 1517 (s), 1346 (s), 701(m); δ_{H} (400 MHz, CDCl₃) 0.91 (3H, d, J = 6.0, C5-CH₃), 2.98 (3H, s, NCH₃), 3.86-3.98 (2H, m, C4-H and C5-H), 4.22 (1H, d, J = 11.5, C3-H), 7.20-7.29 (3H, m, ArCH), 7.31-7.37 (2H, m, ArCH), 7.44 (2H, d, J = 9.0, ArCH), 8.11 (2H, d, J = 9.0, ArCH); δ_{C} (100 MHz, CDCl₃) 14.4 (C5-CH₃), 28.4 (NCH₃), 49.7 (C-3), 51.2 (C-4), 58.3 (C-5), 123.7, 127.7, 128.2, 128.9 and 129.6 (9 × ArCH), 136.4 (ArC), 145.5 and 147.2 (C-6 and C-9), 172.1 (C-2); m/z (CI⁺) 311 ([M+H]⁺, 100 %); HRMS: (CI⁺) Found: [M+H]⁺ 311.1392, C₁₈H₁₉N₂O₃ requires 311.1396.

(5S) 1,5-Dibenzyl-3-phenylpyrrolidin-2-one (12)

To a solution of phenylacetic acid methyl ester (**10**) (190 μL , 1.32 mmol) in DMF (6 mL) was added NaH (53 mg, 1.32 mmol, 60 % dispersion in mineral oil) and the resulting mixture was stirred at r.t. for 20 minutes to form a pale pink suspension. Sulfamidate (**2a**) (200 mg, 0.66 mmol) was added and the reaction mixture was stirred at r.t. for 20.5 hours. Aq. HCl (0.7 mL, 5 M) was added to form a colourless suspension which was stirred at r.t. for 3 hours. The reaction mixture was neutralised by addition of saturated aq. NaHCO₃ and extracted with Et₂O. The organics were combined, washed with water, dried (MgSO₄) and concentrated *in vacuo*. The residue was dissolved in toluene (5 mL) and heated at 100 °C for 2 hours. The mixture was cooled to r.t. and concentrated *in vacuo* and the residue was purified by flash chromatography (Et₂O-petrol 3:2) to afford the product (**12**) (165 mg, 73 %, 2:1 d.r. A:B) as a colourless oil; $\nu_{\max} / \text{cm}^{-1}$ (film) 3028 (w), 2926 (w), 1682 (s), 1417 (m), 1243 (m), 692 (s); δ_{H} (400 MHz, CDCl₃) 1.81 (1H, ddd, J = 13.0, 10.5 and 8.5, C4-H of B), 2.06 (1H, ddd, J = 13.0, 9.0 and 9.0, C4-H of A), 2.31 (1H, ddd, J = 13.0, 9.0

and 3.0, C4-H of A), 2.37 (1H, ddd, $J = 13.0, 9.5$ and 7.0 , C4-H of B), 2.51 (1H, dd, $J = 13.0$ and 10.0 , C5-CH₂Ph of B), 2.74 (1H, dd, $J = 13.5$ and 8.5 , C5-CH₂Ph of A), 3.08 (1H, dd, $J = 13.5$ and 4.5 , C5-CH₂Ph of A), 3.29 (1H, dd, $J = 13.0$ and 4.0 , C5-CH₂Ph of B), 3.55 (1H, dd, $J = 9.0$ and 9.0 , C3-H of A), 3.63-3.74 (2H, m, C5-H and C3-H of B), 3.78 (1H, dddd, $J = 9.0, 8.5, 4.5$ and 3.0 , C5-H of A), 4.05 (1H, d, $J = 14.5$, NCH₂Ph of A), 4.29 (1H, d, $J = 15.0$, NCH₂Ph of B), 5.19 (1H, d, $J = 15.0$, NCH₂Ph of B), 5.26 (1H, d, $J = 14.5$, NCH₂Ph of A), 7.01-7.48 (30H, m, ArCH of A and B); δ_C (100 MHz, CDCl₃) 33.6 (C-4 of A), 34.9 (C-4 of B), 39.0 (C5-CH₂Ph of A), 40.5 (C5-CH₂Ph of B), 45.0 (NCH₂Ph of A), 45.2 (NCH₂Ph of B), 46.6 (C-3 of A), 48.0 (C-3 of B), 56.2 (C-5 of A), 56.7 (C-5 of B), 126.8, 126.9, 127.0 (2 signals), 127.7, 127.8, 128.1, 128.2, 128.3 (2 signals), 128.7 (3 signals), 128.8 and 128.9 (2 signals) ($30 \times$ ArCH), 136.9 (3 signals), 137.2, 139.8 and 139.9 (ArC), 174.9 (C-2 of A), 175.5 (C-2 of B); m/z (CI⁺) 342 ([M+H]⁺, 100 %); HRMS: (CI⁺) Found: [M+H]⁺ 342.1856, C₂₄H₂₄NO requires 342.1858.

(5S) 1,5-Dibenzyl-3-(4-methoxyphenyl)pyrrolidin-2-one (13)

To a solution of methyl (4-methoxyphenyl)acetate (213 μ L, 1.32 mmol) in DMF (6 mL) was added NaH (53 mg, 1.32 mmol, 60 % dispersion in mineral oil) and the resulting suspension was stirred at r.t. for 15 minutes to form a pale yellow suspension. Sulfamidate (**2a**) (200 mg, 0.66 mmol) was added and the reaction mixture was stirred at r.t. for 18.5 hours. Aq. HCl (0.7 mL, 5 M) was added to form a pale yellow emulsion which was stirred at r.t. for 3 hours. The reaction mixture was neutralised by addition of saturated aq. NaHCO₃ solution and extracted with Et₂O. The organics were combined, washed with water, dried (MgSO₄) and concentrated *in vacuo*. The residue was dissolved in toluene (5 mL) and heated at 100 °C for 2.5 hours. The reaction mixture was allowed to cool to r.t., concentrated *in vacuo* and the residue was purified by flash chromatography (Et₂O-petrol 3:2) to afford the product

(13) (160 mg, 65 %, 1:1 d.r. *A:B*) as a colourless oil which crystallised upon standing; m.p. 109-114 °C (Et₂O-petrol); $\nu_{\max}$ / cm⁻¹ (film) 3003 (w), 2932 (w), 1682 (s), 1512 (s), 1244 (s), 1177 (m), 1030 (m), 733 (m), 699 (s); δ_{H} (400 MHz, CDCl₃) 1.74 (1H, ddd, J = 13.0, 10.0 and 9.0, C4-H of *B*), 2.01 (1H, ddd, J = 13.0, 9.0 and 9.0, C4-H of *A*), 2.26 (1H, ddd, J = 13.0, 9.0 and 2.5, C4-H of *A*), 2.33 (1H, ddd, J = 13.0, 9.5 and 7.0, C4-H of *B*), 2.48 (1H, dd, J = 13.0 and 10.0, C5-CH₂Ph of *B*), 2.69 (1H, dd, J = 13.5 and 8.5, C5-CH₂Ph of *A*), 3.05 (1H, dd, J = 13.5 and 4.5, C5-CH₂Ph of *A*), 3.25 (1H, dd, J = 13.0 and 4.0, C5-CH₂Ph of *B*), 3.48 (1H, dd, J = 9.0 and 9.0, C3-H of *A*), 3.59 (1H, dd, J = 10.0 and 9.5, C3-H of *B*), 3.65 (1H, m, C5-H of *B*), 3.73 (1H, m, C5-H of *A*), 3.77 (3H, s, Ar-OCH₃), 3.80 (3H, s, Ar-OCH₃), 4.00 (1H, d, J = 15.0, NCH₂Ph of *A*), 4.25 (1H, d, J = 15.0, NCH₂Ph of *B*), 5.15 (1H, d, J = 15.0, NCH₂Ph of *B*), 5.22 (1H, d, J = 15.0, NCH₂Ph of *A*), 6.82-6.92 (4H, m, ArCH), 7.01 (2H, d, J = 6.5, ArCH), 7.07-7.43 (22H, m, ArCH); δ_{C} (100 MHz, CDCl₃) 33.5 (C-4 of *A*), 34.8 (C-4 of *B*), 38.8 (C5-CH₂Ph of *A*), 40.3 (C5-CH₂Ph of *B*), 44.8 (NCH₂Ph of *A*), 45.0 (NCH₂Ph of *B*), 45.6 (C-3 of *A*), 47.1 (C-3 of *B*), 55.2 (2 signals) (Ar-OCH₃), 56.0 (C-5 of *A*), 56.4 (C-5 of *B*), 114.1 (2 signals), 126.6, 126.7, 127.5, 127.6, 128.5, 128.6, 128.7 (3 signals), 128.8, 129.0, 129.1 and 129.2 (2 signals) (28 × ArCH), 131.7, 131.8, 136.7 (3 signals), 137.1, and 158.6 (2 signals) (ArC), 175.0 and 175.6 (C-2); m/z (CI⁺) 372 ([M+H]⁺, 100 %); HRMS: (CI⁺) Found: [M+H]⁺ 372.1956, C₂₅H₂₆NO₂ requires 372.1964.

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