

## Experimental section

**General:** Unless otherwise noted, all reactions were run under nitrogen atmosphere and distilled solvents were transferred by syringe. Tetrahydrofuran (THF) and ether were distilled from sodium/benzophenone immediately before use; dimethoxyether (DME) was distilled from  $\text{LiAlH}_4$ ;  $\text{CH}_2\text{Cl}_2$  was distilled from  $\text{P}_2\text{O}_5$ ;  $\text{Et}_3\text{N}$  was distilled from  $\text{BaO}$ . Final reaction mixture solutions were dried over  $\text{Na}_2\text{SO}_4$ . Chromatography was on 230-400 mesh silica gel; TLC on aluminum-backed silica plates. Melting points are uncorrected. Mass spectral data, HRMS (EI and FAB), were obtained by the Université de Montréal Mass Spectroscopy facility.  $^1\text{H}$  NMR (300/400 MHz) and  $^{13}\text{C}$  NMR (75/100 MHz) spectra were recorded in  $\text{CDCl}_3$ . Chemical shifts are reported in ppm ( $\delta$  units). Coupling constants are given in Hz. Chemical shifts for aromatic carbons are not reported for compounds possessing PhF groups.

### **(2*R*,4*S*)-tert-Butyl 2-Oxo-3-PhF-1,2,3-oxathiazainane-4-carboxylate ((2*R*)-7) and (2*S*,4*S*)-tert-Butyl 2-Oxo-3-PhF-1,2,3-oxathiazainane-4-carboxylate ((2*S*)-7).**

A solution of (2*S*)-tert-butyl-2-[*N*-(PhF)amino]-4-hydroxybutanoate (**6**, 2 g, 4.7 mmol) in 100 mL of dichloromethane was cooled to 0 °C, treated with 1.3 g of imidazole (19.1 mmol) followed by 1.4 mL of triethylamine (10.3 mmol), stirred for 10 min, then treated with 0.39 mL of thionyl chloride (5.3 mmol). After stirring for an additional 1 h, the solution was diluted with 80 mL of water, and the phases were separated. The aqueous phase was extracted with dichloromethane (2 × 50 mL). The combined organic fractions were washed with water (2 × 50 mL), dried, filtered, and evaporated to a residue that was purified by chromatography on silica gel with a gradient of 0-10% EtOAc in hexane as eluant to provide 1.6 g (71%) of (2*R*)-7 and 0.5 g (23%) of (2*S*)-7. First to elute was (2*S*)-7:  $R_f$  = 0.36 (30% EtOAc in hexane); mp 166-167 °C;  $[\alpha]_D^{20}$  212° (*c* 0.34,  $\text{CH}_3\text{Cl}$ );  $^1\text{H}$  NMR  $\delta$  1.27 (m, 1 H), 1.62 (s, 9 H), 1.76 (m, 1 H), 3.17 (dd, 1 H,  $J$  = 2.5, 5.4), 3.55 (m, 1 H), 4.91 (m, 1 H), 7.20-7.78 (m, 13 H);  $^{13}\text{C}$  NMR  $\delta$  22.6, 27.9, 49.3, 54.6, 76.6, 81.7, 169.9; HRMS calcd for  $\text{C}_{27}\text{H}_{27}\text{O}_4\text{NNaS}$  ( $M+\text{Na}$ ) 484.1559, found 484.1560. Second to elute was (2*R*)-7:  $R_f$  = 0.27 (20% EtOAc in hexane); mp 172-173 °C;  $[\alpha]_D^{20}$  132° (*c* 0.33,  $\text{CH}_3\text{Cl}$ );  $^1\text{H}$  NMR  $\delta$  1.40 (s, 9 H), 2.18 (m, 1 H), 2.68 (m, 1 H), 3.31 (dd, 1 H,  $J$  = 3.4, 4.3), 3.94 (ddd, 1 H,  $J$  = 9.7, 10.9, 16.4), 4.37 (m, 1 H), 7.20-8.27 (m, 13 H);  $^{13}\text{C}$  NMR  $\delta$  26.6, 27.8, 54.3, 57.0, 76.8, 81.3, 170.6; HRMS calcd for  $\text{C}_{27}\text{H}_{27}\text{O}_4\text{NNaS}$  ( $M+\text{Na}$ ) 484.1559, found 484.1541.

**(4*S*)-tert-Butyl 2,2-Dioxo-3-PhF-1,2,3-oxathiazainane-4-carboxylate (2).** A solution of sulfimidite (2*R*)-7 (1 g, 2.2 mmol) in 50 mL of acetonitrile was cooled to 0 °C and treated with 20 mg of ruthenium (III) chloride monohydrate followed by 940 mg of sodium periodate (4.4 mmol). After stirring for 15 min, the reaction mixture was treated with 40 mL of water, stirred for an additional 6 h at 0 °C and diluted with 40 mL of ether. The phases were separated and the aqueous phase was extracted with ether (3 × 30 mL). The combined organic fractions were washed with 30 mL of saturated aqueous sodium bicarbonate and 30 mL of brine, dried, filtered, and evaporated to a residue that crystallized to provide 936 mg (89%) of **2**: mp 188-188.5 °C;  $[\alpha]_D^{20}$  268° (*c* 0.37,

CH<sub>3</sub>Cl); <sup>1</sup>H NMR δ 1.10 (m, 1 H), 1.66 (s, 9 H), 1.74 (m, 1 H), 3.86 (m, 1 H), 4.15 (m, 1 H), 4.88 (m, 1 H), 7.20-8.11 (m, 13 H); <sup>13</sup>C NMR δ 22.4, 28.0, 58.3, 70.7, 78.6, 82.6, 168.3; HRMS calcd for C<sub>27</sub>H<sub>27</sub>O<sub>5</sub>NSNa (M+Na) 500.1508, found 500.1489.

**(2S)-tert-Butyl [N-(PhF)Amino]-4-azido-butanoate (9a).** A solution of sulfamidate **2** (17 mg, 0.04 mmol) in 2 mL of DMF was treated with 10 mg of NaN<sub>3</sub> (0.16 mmol) and stirred for 24 h. The mixture was diluted with 20 mL of CHCl<sub>3</sub>, poured into 1 M KH<sub>2</sub>PO<sub>4</sub> (5 mL) and extracted with CHCl<sub>3</sub>, washed with water (2 × 10 mL), dried, filtered and evaporated under vacuum. The residue was purified by chromatography on silica gel with an eluant of 0-10% EtOAc in hexane. Evaporation of the collected fractions provided 13 mg (83%) of **9a** as a thick clear oil: [α]<sub>D</sub><sup>20</sup> -211° (c 0.43, CH<sub>3</sub>Cl); <sup>1</sup>H NMR δ 1.22 (s, 9 H), 1.60 (m, 2 H), 2.58 (dd, 1 H, J = 4.6, 7.7), 3.41 (m, 2 H), 7.21-7.72 (m, 13 H); <sup>13</sup>C NMR δ 27.7, 34.2, 48.0, 53.5, 72.8, 81.0, 174.4; HRMS calcd for C<sub>27</sub>H<sub>29</sub>N<sub>4</sub>O<sub>3</sub> (MH<sup>+</sup>) 441.2291, found 441.2305.

**(2S)-tert-Butyl [N-(PhF)Amino]-4-(1-imidazol)butanoate (9b).** A suspension of NaH (prewashed with hexane, 60 wt % in oil, 85 mg, 2.1 mmol) in 10 mL of DMF was treated with 145 mg of imidazole (2.1 mmol), stirred for 10 min, treated with sulfamidate **2** (50 mg, 0.9 mmol), heated at 60 °C for 18 h, cooled to room temperature, and poured into 1 M NaH<sub>2</sub>PO<sub>4</sub> (20 mL). The mixture was extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (2 × 15 mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 0-6% MeOH in EtOAc. Concentration of the collected fractions provided 83.2 mg (50%) of **9b** as a thick clear oil; [α]<sub>D</sub><sup>20</sup> -165° (c 0.7, CHCl<sub>3</sub>); <sup>1</sup>H NMR δ 1.18 (s, 9 H), 1.75 (m, 1 H), 1.80 (m, 1 H), 2.45 (dd, 1 H, J = 4.9, 14.0), 3.24 (brd, 1 H), 3.78 (m, 1H), 4.15 (m, 1 H), 6.75 (s, 1H), 6.92 (s, 1 H), 7.20 – 7.80 (m, 14 H); <sup>13</sup>C NMR δ 28.0, 37.1, 44.1, 54.1, 73.1, 81.6, 174.5; HRMS calcd for C<sub>29</sub>H<sub>32</sub>O<sub>2</sub>N<sub>4</sub> (MH<sup>+</sup>) 454.5816, found 454.5822. Performance of the same reaction without NaH in DMF (15 mL) at 60 °C for 24 h gave **9b** in 55% yield: [α]<sub>D</sub><sup>20</sup> -164° (c 0.8, CHCl<sub>3</sub>). When the reaction was conducted without NaH in CH<sub>3</sub>CN (15 mL) at 75°C for 30 h, **9b** was obtained in 65% yield.

**(2S)-tert-Butyl [N-(PhF)Amino]-4-(morpholine)butanoate (9c).** A suspension of NaH (prewashed with hexane, 60 wt % in oil, 25 mg, 0.52 mmol) in 10 mL of DMF was treated with 46 mg of morpholine (0.52 mmol), stirred for 10 min, treated with sulfamidate **2** (50 mg, 0.10 mmol), heated at 60 °C for 24 h, cooled to room temperature, and poured into 1 M NaH<sub>2</sub>PO<sub>4</sub> (20 mL). The mixture was extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with brine (2 × 15 mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 50-75% EtOAc in hexane. Concentration of the collected fractions provided 43.2 mg (85%) of **9c** as a thick clear oil: [α]<sub>D</sub><sup>20</sup> -217° (c 0.2, CHCl<sub>3</sub>); <sup>1</sup>H NMR δ 1.18 (s, 9 H), 1.58 (m, 2 H), 2.35 (m, 6 H), 2.58 (dd, 1 H, J = 5.3, 7.0), 3.18 (brd, 1 H), 3.65 (m, 4 H), 7.12-7.72 (m, 13 H); <sup>13</sup>C NMR δ 28.0, 32.4, 53.8, 54.7, 55.6, 67.1, 73.2, 80.7, 175.3; HRMS

calcd for  $C_{31}H_{37}O_3N_2$  ( $MH^+$ ) 485.2804, found 485.2795. When the reaction was conducted without NaH in 30 mL of  $CH_3CN$  at  $75^\circ C$  for 30 h, **9c** was obtained in 95% yield:  $[\alpha]_D^{20} -217^\circ$  (c 0.1,  $CHCl_3$ ).

**(2S)-tert-Butyl [N-(PhF)Amino]-4-(piperidine)butanoate (9d).** A suspension of NaH (prewashed with hexane, 60 wt % in oil, 25 mg, 0.52 mmol) in 10 mL of DMF was treated with 45 mg of piperidine (0.52 mmol), stirred for 10 min, treated with sulfamidate **2** (50 mg, 0.10 mmol), heated at  $60^\circ C$  for 30 h, cooled to room temperature, and poured into 1 M  $NaH_2PO_4$  (20 mL). The mixture was extracted with EtOAc ( $3 \times 15$  mL). The combined organic phases were washed with brine ( $2 \times 15$  mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 5-10% MeOH in EtOAc. Concentration of the collected fractions provided 40.4 mg (80%) of **9d** as a thick clear oil:  $[\alpha]_D^{20} -130^\circ$  (c 0.6,  $CHCl_3$ );  $^1H$  NMR  $\delta$  1.17 (s, 9 H), 1.35 (m, 2 H), 1.49 (m, 8 H), 2.13 (m, 4 H), 2.61 (dd, 1 H,  $J = 5.3, 7.0$ ), 3.16 (brd, 1 H), 7.10-7.77 (m, 13 H);  $^{13}C$  NMR  $\delta$  24.4, 25.9, 28.1, 32.3, 54.7, 55.1, 56.1, 73.2, 80.7, 175.2; HRMS calcd for  $C_{32}H_{39}O_2N_2$  ( $MH^+$ ) 483.3011, found 483.3026. When the reaction was carried conducted without NaH in 30 mL of  $CH_3CN$  at  $75^\circ C$  for 36 h, **9d** was obtained in 90% yield.

**(2S)-tert-Butyl [N-(PhF)Amino]-4-(aniline)butanoate (9e).** A solution of sulfamidate **2** (150 mg, 0.31 mmol) in 50 mL of  $CH_3CN$  was treated with 146 mg of aniline (1.55 mmol), heated at  $75^\circ C$  for 30 h, cooled to room temperature, poured into 1 M  $KH_2PO_4$  (30 mL) and extracted with EtOAc ( $3 \times 30$  mL). The combined organic phase was washed with brine ( $2 \times 20$  mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 10-20% EtOAc in hexane. Concentration of the collected fractions provided 131 mg (85%) of **9e** as a thick clear oil:  $[\alpha]_D^{20} -146^\circ$  (c 0.6,  $CHCl_3$ );  $^1H$  NMR  $\delta$  1.21 (s, 9 H), 1.66 (t, 2 H,  $J = 5.4$ ), 2.65 (dd, 1 H,  $J = 5.9, 6.8$ ), 3.20 (t, 2 H,  $J = 5.3$ ), 3.18 (brd, 1 H), 6.57- 7.75 (m, 18 H);  $^{13}C$  NMR  $\delta$  28.0, 34.6, 40.7, 54.6, 73.2, 81.0, 175.6; HRMS calcd for  $C_{33}H_{35}O_2N_2$  ( $MH^+$ ) 491.2095, found 491.2083

**(2S)-tert-Butyl [N-(PhF)Amino]-4-(isobutylamine)butanoate (9f).** A solution of sulfamidate **2** (50 mg, 0.10 mmol) in 30 mL of  $CH_3CN$  was treated with 22 mg of isobutylamine (0.30 mmol), heated at  $75^\circ C$  for 30 h, cooled to room temperature, poured into 1 M  $KH_2PO_4$  (15 mL), and extracted with EtOAc ( $3 \times 20$  mL). The combined organic phase was washed with brine ( $2 \times 15$  mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 5-10% MeOH in AcOEt. Concentration of the collected fractions provided 43 mg (91%) of **9f** as a thick clear oil:  $[\alpha]_D^{20} -176^\circ$  (c 0.6,  $CHCl_3$ );  $^1H$  NMR  $\delta$  0.89 (d, 3 H,  $J = 6.6$ ), 0.90 (d, 3 H,  $J = 6.6$ ), 1.18 (s, 9 H), 1.55 (m, 2 H), 1.75 (m, 1 H), 2.38 (d, 2 H,  $J = 7.2$ ), 2.55 (dd, 1 H,  $J = 5.5, 7.4$ ), 2.68 (m, 2H), 3.05 (brd, 1H), 6.80-7.77 (m, 13 H);  $^{13}C$  NMR  $\delta$  20.9, 28.0, 28.3, 34.9, 46.7, 54.9, 57.6, 73.2, 80.9, 175.3; MS  $C_{31}H_{39}O_2N_2$  ( $MH^+$ )  $m/e$  471.4, 241.1, 173.2, 86.0.

**(2S)-N-PhF-S-Cyanohomocysteine *tert*-Butyl Ester (9g).** A solution of sulfamidate **2** (80 mg, 0.167 mmol) in 30 mL of CH<sub>3</sub>CN was treated with potassium thiocyanate 35 mg (0.36 mmol), heated at 75 °C for 30 h, cooled to room temperature, poured into 1 M KH<sub>2</sub>PO<sub>4</sub> (15 mL), and extracted with EtOAc (3 × 20 mL). The combined organic phase was washed with brine (2 × 15 mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 10-20% AcOEt in hexane. Concentration of the collected fractions provided 52 mg (68%) of **9g** as clear oil:  $[\alpha]_D^{20}$  -209° (*c* 0.45, CHCl<sub>3</sub>); <sup>1</sup>H NMR δ 1.22 (s, 9 H), 1.81 (m, 2 H), 2.57 (dd, 1 H, *J* = 4.0, 8.2), 2.90 (m, 1 H), 3.20 (m, 1 H), 3.25 (brd, 1 H), 7.15 - 7.75 (m, 13 H); <sup>13</sup>C NMR δ 28.0, 31.2, 35.5, 54.5, 73.1, 81.8, 112.8, 174.3; HRMS calcd for C<sub>28</sub>H<sub>29</sub>O<sub>2</sub>N<sub>2</sub>S (MH<sup>+</sup>) 457.1916, found 457.1935.

**(2S)-N-PhF-S-Phenylhomocysteine *tert*-Butyl Ester (9h).** A suspension of NaH (prewashed with hexane, 60 wt % in oil, 85 mg, 2.1 mmol) in 10 mL of DMF was treated with 22 mg of thiophenol (0.30 mmol), stirred for 10 min, treated with sulfamidate **2** (50 mg, 0.10 mmol), heated at 60 °C for 36 h, cooled to room temperature, and poured into 1 M NaH<sub>2</sub>PO<sub>4</sub> (20 mL). The mixture was extracted with EtOAc (3 × 15 mL). The combined organic phases were washed with brine (2 × 15 mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 10-20% EtOAc in hexane. Concentration of the collected fractions provided 83.2 mg (56%) of **9h** as a thick clear oil:  $[\alpha]_D^{20}$  -310° (*c* 0.15, CHCl<sub>3</sub>); <sup>1</sup>H NMR δ 1.16 (s, 9 H), 1.66 (m, 2 H), 2.58 (dd, 1 H, *J* = 3.7, 6.3), 2.83 (m, 1 H), 3.00 (m, 1 H), 3.18 (brd 1H), 7.09-7.74 (m, 18 H); <sup>13</sup>C NMR δ 28.0, 29.8, 35.3, 55.5, 73.2, 81.1, 174.9; HRMS calcd for C<sub>33</sub>H<sub>34</sub>O<sub>2</sub>NS (MH<sup>+</sup>) 508.2321, found 508.2308. When the reaction was performed in the absence of NaH in CH<sub>3</sub>CN (30 mL) at 75° C for 30 h, **9i** was not formed and starting material was recovered.

**(2S)-N-PhF-O-Phenylhomoserine *tert*-Butyl Ester (9i).** A suspension of NaH (prewashed with hexane, 60 wt % in oil, 85 mg, 2.1 mmol) in 10 mL of DMF was treated with with 200 mg of phenol (2.1 mmol), stirred for 10 min, treated with sulfamidate **2** (50 mg, 0.10 mmol), heated at 60 °C for 60 h, cooled to room temperature, and poured into 1 M NaH<sub>2</sub>PO<sub>4</sub> (15 mL). The mixture was extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with brine (2 × 15 mL), dried, filtered, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 10-20% EtOAc in hexane. The Concentration of the collected fractions provided provided 83.2 mg (56%) of **9i** as a thick clear oil;  $[\alpha]_D^{20}$  -178° (*c* 0.7, CHCl<sub>3</sub>); <sup>1</sup>H NMR δ 1.15 (s, 9 H), 1.76 (m, 2 H), 2.61 (dd, 1 H, *J* = 1.5, 5.2), 3.08 (brd 1H), 3.95 (m, 2 H), 6.65- 7.62 (m, 18 H); <sup>13</sup>C NMR δ 28.0, 35.0, 53.5, 64.4, 73.1, 81.0, 175.3; HRMS calcd for C<sub>33</sub>H<sub>34</sub>O<sub>3</sub>N (MH<sup>+</sup>) 492.2539, found 492.2561

**(2S)-*tert*-Butyl 2-Amino-4-(morpholine)butanoate.** A solution of (2S)-*tert*-Butyl 2-[N-(PhF)amino]-4-(morpholine)butanoate (**9c**, 50 mg, 1 mmol, prepared from nucleophilic addition with NaH) in MeOH (30 mL) was placed into a hydrogenation vessel and treated with palladium-on-carbon (10 wt %, 28 mg). The vessel was filled, vented and filled three times with hydrogen and

the mixture was stirred under 10 atm of hydrogen for 72 h. The mixture was filtered on Celite™ and washed with MeOH (10 mL). The combined organic phase was washed with hexane until no more protecting PhF group was observed by TLC. The methanolic solution was then evaporated to provide 25 mg (97%) of (2*S*)-*tert*-butyl 2-amino-4-(morpholine)butanoate as a thick clear oil:  $[\alpha]_D^{20}$  23.1° (*c* 0.5, CHCl<sub>3</sub>); <sup>1</sup>H NMR δ 1.52 (s, 9 H), 2.42 (m, 2 H), 2.75 (m, 7 H), 3.78 (m, 4 H), 4.25 (brd, 2 H).

**L- and D,L-*N*-(*p*-Toluenesulfonyl)proline.** *p*-Toluenesulfonyl chloride (830 mg, 4.36 mmol) was added to a solution of either L or D,L-proline (500 mg, 4.36 mmol) in 10 mL of 1 N NaOH (8.7 mmol). After stirring for 4 h at room temperature, the mixture was acidified with 2 N HCl to pH 2 and extracted with ether. The organic layer was dried and evaporated to give 1.10 g (94%) of a white solid: mp 85-86 °C; <sup>1</sup>H NMR δ 1.58 (m, 1 H), 1.95 (m, 1 H), 2.15 (m, 2 H), 2.45 (s, 3 H), 3.24 (dd, 1 H, *J* = 7.6, 16.1), 3.54 (m, 1 H), 4.26 (dd, 1 H, *J* = 3.5, 8.1), 7.35 (d, 2H, *J* = 8.1), 7.77 (d, 2 H, *J* = 8.1); <sup>13</sup>C NMR δ 21.8, 24.9, 30.7, 49.1, 60.6, 127.8, 130.1, 134.2, 144.4, 176.2; MS: *m/e* 410.2 (*m*+1), 307.1, 289.1, 257.1, 241.1, 154.1; HRMS calcd for C<sub>12</sub>H<sub>16</sub>ClO<sub>3</sub>NS (MH<sup>+</sup>) 270.0722, found 270.0831. L-*N*-(*p*-Toluenesulfonyl)proline:  $[\alpha]_D^{20}$  -96.5° (*c* 0.5, CHCl<sub>3</sub>).

**L- and D,L-*N*-(*p*-Toluenesulfonyl)proline Chloride.** A solution of 500 mg (1.86 mmol) of either L or D,L-*N*-(*p*-toluenesulfonyl)proline in 5 mL of dry CH<sub>2</sub>Cl<sub>2</sub> was treated with 0.45 mL of oxalyl chloride and 2 drops of DMF, stirred for 1 h at room temperature and evaporated to a residue that was dissolved in benzene, washed with saturated NaHCO<sub>3</sub> and brine, dried, and evaporated to give 1.1 g (94%) of the acid chloride as white solid: mp 65-67 °C; <sup>1</sup>H NMR δ 1.82 (m, 1 H), 1.98 (m, 1H), 2.20 (m, 2 H), 2.45 (s, 3 H), 3.34 (m, 1 H), 3.52 (m, 1 H), 4.60 (dd, 1 H, *J* = 5.4, 7.3), 7.35 (d, 2 H, *J* = 8.1), 7.77 (d, 2 H, *J* = 8.1); <sup>13</sup>C NMR δ 22.0, 21.8, 24.5, 30.8, 48.8, 68.9, 127.7, 130.0, 144.4, 174.2; HRMS calcd for C<sub>12</sub>H<sub>15</sub>ClO<sub>3</sub>NS (MH<sup>+</sup>) 287.0383, found 287.0407. L-*N*-(*p*-Toluenesulfonyl)proline chloride:  $[\alpha]_D^{20}$  -102.0° (*c* 0.5, CHCl<sub>3</sub>).

**Enantiomeric Purity of (2*S*)-*tert*-Butyl 2-amino-4-(morpholine)butanoate.** A solution of (2*S*)-*tert*-butyl 2-amino-4-(morpholine)butanoate (12.3 mg, 0.05 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was treated with Et<sub>3</sub>N (7.8 μL), L or D,L-*N*-(*p*-toluenesulfonyl)prolyl chloride (16 mg, 0.06 mmol) at room temperature. After stirring for 1 h, the solution was diluted with ethyl acetate (10 mL), washed with saturated NaHCO<sub>3</sub> (2 x 2 mL) and brine (5 mL), dried, and concentrated under vacuum to a crude oil that was directly examined by <sup>1</sup>H NMR spectroscopy. The limits of detection were determined by measuring the diastereomeric *tert*-butyl ester singlets at 1.86 and 1.88 ppm in CDCl<sub>3</sub> in the 400 MHz <sup>1</sup>H NMR spectra. Purification by chromatography using a gradient of 5-10 % methanol in EtOAc as eluant gave the dipetide having the following spectrum: (2*S*)-*tert*-Butyl 2-[L-*N*-(*p*-toluenesulfonyl)prolinamido]-4-(morpholine)butanoate: <sup>1</sup>H NMR (C<sub>6</sub>D<sub>6</sub>) δ 1.57 (s, 9 H), 2.01 (s, 3 H), 2.14 (m, 2 H), 2.30 (m, 2 H), 2.38 (m, 6 H), 2.45 (m, 1 H), 2.57 (m, 1 H), 3.10 (m, 1H), 3.45 (m, 1 H), 3.81 (m, 4 H), 4.36 (dd, 1 H, *J* = 3.5, 8.6), 4.90 (dd, 1 H, *J* = 5.8, 13.2), 6.95 (d, 2H, *J* = 8.0), 7.77 (d, 2H, *J* = 8.0), 8.2 (brd, 1H).

**(2S)-2-Amino-4-(piperidine)butanoic acid (10d)** (2S)-*tert*-Butyl 2-[*N*-(PhF)amino]-4-(piperidine)-butanoate (**9d**, 105 mg, 0.22 mmol) was dissolved in 20 mL of CH<sub>2</sub>Cl<sub>2</sub>, treated with 2 mL of TFA, and heated at a reflux for 18 h. The volatiles were removed by evaporation on a rotary evaporator, the residue was then digested into 10 mL of H<sub>2</sub>O and filtered. The aqueous solution was washed with hexanes (2 × 20 mL) and then evaporated to a solid (45 mg) that was further purified by ion exchange chromatography on 4 g of Dowex tetra-alkyl ammonium resin (hydroxide form) eluting with 0.01N HCl. Evaporation of the ninhydrin positive fractions gave **10d** (28 mg, 68%) as its hydrochloride:  $[\alpha]_D^{20}$  15.3° (*c* 0.9, MeOH); <sup>1</sup>H NMR (CD<sub>3</sub>OD) δ 1.83 (m, 6 H), 2.40 (m, 2 H), 2.80 (m, 2H), 3.40 (m, 2 H), 3.53 (m 2 H), 4.14 (t, 1 H, *J* = 5.8); <sup>13</sup>C NMR (CD<sub>3</sub>OD) δ 23.0, 24.7, 26.6, 52.0, 54.9, 55.0, 55.1, 170.9.