A SECOND GENERATION SYNTHESIS OF POLYPYRROLINONE NONPEPTIDOMIMETICS: PRELUDE TO THE SYNTHESIS OF POLYPYRROLINONES ON SOLID SUPPORT

(SUPPORTING INFORMATION)

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MATERIALS AND METHODS

All reactions were carried out in oven-dried or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent or high performance liquid chromatography (HPLC) grade. Diethyl ether and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under argon prior to use. Dichloromethane was freshly distilled from calcium hydride before use. Triethylamine and diisopropylethylamine were distilled from calcium hydride and stored over potassium hydroxide. HPLC grade benzene was purchased from J.T. Baker and stored over 4 Å molecular sieves. Anhydrous dimethylformamide and dimethyl sulfoxide were purchased from Aldrich and used without purification. *n*-Butyllithium was purchased from Aldrich and standardized by titration with diphenylacetic acid.

Unless otherwise stated, all reactions were magnetically stirred and monitored by thin layer chromatography using 0.25 mm E. Merck pre-coated silica gel plates. Flash column chromatography was performed with the indicated solvents using silica gel-60 (particle size 0.040-0.062 mm) supplied by E. Merck. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated.

All melting points were determined on a Bristoline heated-stage microscope or a Thomas-Hoover apparatus and are corrected. The IR and NMR spectra were obtained for $CHCl_3$ and $CDCl_3$ solutions respectively unless otherwise noted. Infrared spectra were recorded with a Perkin-Elmer Model 283B spectrometer using polystyrene as an external standard. Proton and carbon-13 NMR spectra were recorded on a Bruker AM-500 spectrometer and obtained at 305 K unless otherwise noted. Chemical shifts are reported relative to chloroform (δ 7.24 for proton and δ 77.0 for carbon-13). Optical rotations were obtained with a Perkin-Elmer model 241 polarimeter in the solvent indicated. High-resolution mass spectra were obtained at the University of Pennsylvania Mass Spectrometry Service Center on either a VG micromass 70/70H high resolution double-focusing electron impact/chemical ionization spectrometer or a VG ZAB-E spectrometer. Microanalyses were performed by Robertson Laboratories, Madison, New Jersey. Single-crystal X-ray diffraction structure determination were performed at the University of Pennsylvania using an Enraf Nonius CAD-4 automated diffractometer.

Preparation of Cbz-protected amino aldehyde (+)-14a. To a 0 °C solution of (-)-**13a** (2.30 g, 11.55 mmol) in THF (40 mL) was added *i*-Pr_2NEt (2.41 mL, 1.79 g, 13.86 mmol) followed by benzyl

chloroformate (1.81 mL, 2.17 g, 12.7 mmol). The mixture was warmed to rt, stirred for 4 h, cooled back to 0 °C, and quenched by addition of 2 N aqueous HCl (20 mL). The resulting biphasic mixture was warmed to rt, extracted with EtOAc (2 x 50 mL), and the combined organic phases washed with 2 N aqueous HCl (10 mL), saturated aqueous $NaHCO_3$ (15 mL), brine (15 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (EtOAc/hexanes, 5:95) to afford the Cbz-protected amino ester (3.56 g, 93% yield) as a colorless oil: $[\alpha]_D^{23}$ +16.8° (*c* 1.0, $CHCl_3$); IR (KBr) 3600, 3500, 1720, 1500 cm-^{1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.25 (m, 5H), 5.78 (bs, 1H), 5.88 (d, 1H, *J* = 12.4 Hz), 5.01 (d, 1H, *J* = 12.4 Hz), 4.86 (t, 1H, *J* = 6.7 Hz), 3.71 (s, 3H), 3.12 (dd, 1H, *J* = 6.2, 7.2 Hz), 2.64 (dd, 1H, *J* = 6.2, 7.2 Hz), 2.48 (heptet, 1H, *J* = 6.4 Hz), 1.62 (s, 3H), 1.53 (s, 3H), 0.97 (d, 3H, *J* = 6.9 Hz), 0.89 (d, 3H, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.38, 154.21, 136.87, 135.08, 128.44, 127.93, 127.86, 118.36, 67.47, 66.10, 52.20, 33.80, 31.02, 25.96, 17.82, 17.77; high-resolution mass spectrum (CI, NH_3) *m/z* 334.2026 [$(M + H)^+$], calcd for $C_{19}H_{28}NO_4$ 334.2018.

A solution of Cbz-protected amino ester (6.8 g, 20.4 mmol) in CH_2Cl_2 (70 mL) was cooled to -78 °C, and ozone was bubbled into the reaction until a blue color persisted. After excess ozone was purged with argon, PPh_3 (5.88 g, 22.43 mmol) was added, and the solution was warmed to rt, stirred for 14 h, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (EtOAc/hexanes, 20:80) to afford (+)-**14a** (5.95 g, 95% yield) as a colorless oil: $[\alpha]_D^{23}$ +0.19° (*c* 1.1, $CHCl_3$); IR (KBr) 3620, 3400, 1730, 1225 cm-^{1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.33-7.29 (m, 5H), 5.89 (bs, 1H), 5.05-4.98 (m, 2H), 3.79 (bs, 1H), 3.74 (s, 3H), 3.07 (d, 1H, *J* = 17.7 Hz), 2.35 (heptet, 1H, *J* = 7.0 Hz), 0.91 (d, 3H, *J* = 6.6 Hz), 0.90 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.2, 172.0, 154.7, 136.3, 128.5, 128.1, 127.8, 66.5, 63.2, 52.7, 46.2, 34.6, 17.5, 17.2; high-resolution mass spectrum (CI, NH_3) *m/z* 308.1493 [$(M + H)^+$], calcd for $C_{16}H_{22}NO_5$ 308.1498.

Cbz-protected amino aldehyde (+)-14b. Following the procedure described above for (+)-**14a**; flash chromatography (EtOAc/hexanes, 20:80) afforded (+)-**14b** (5.90 g, 96% yield for two steps); compound (+)-**14b** has physical and spectroscopic properties identical to literature values.[4b]

Preparation of Cbz-protected amino lactone (-)-15a. Typical procedure for reduction with $NaCNBH_3$. To a 0 °C solution of (+)-**14a** (2.15 g, 7.0 mmol) in MeOH (10 mL) was added $NaBH_3CN$ (0.65 g, 10.5 mmol) in small portions over a period of 10 min. To this mixture 2N HCl in MeOH (55 mL) was added and the mixture was warmed to rt, stirred for 3 h, diluted with EtOAc (400 mL), and basified to pH 9 with saturated aqueous $NaHCO_3$. The resulting biphasic mixture was extracted with EtOAc (2 x 200 mL), and the combined organic phases washed with brine (100 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (EtOAc/hexanes, 40:60) to afford (-)-**15a** (1.6 g, 78% yield) as a white crystalline solid: mp 73-75 °C; $[\alpha]_D^{23}$ -3.6° (*c* 0.67, $CHCl_3$); IR (KBr) 3447, 1772, 1719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.29 (m, 5 H), 5.17 (bs, 1 H), 5.12-5.04 (m, 2H), 4.52 (bs, 1H), 4.23-4.14 (m, 1H), 2.64-2.54 (m, 1H), 2.45-2.38 (m, 1H), 2.14-2.07 (m, 1H), 1.02 (d, 3H, *J* = 6.9 Hz), 0.99 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 155.2, 135.8, 128.5, 128.3, 128.2, 67.1, 65.6, 62.6, 33.9, 29.1, 17.1, 16.4; high-resolution mass spectrum (CI, NH_3) *m/z* 278.1394 [$(M + H)^+$], calcd for $C_{15}H_{20}NO_4$ 278.1392.

Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 65.43; H, 6.69; N, 4.90.

Cbz-protected amino lactone (-)-15b. Following the procedure described above for (-)-**15a**; flash chromatography (EtOAc/hexanes, 40:60) afforded (-)-**15b** (1.45 g, 80% yield) as a white solid: mp 62-63 °C; $[\alpha]_D^{23}$ -3.1° (*c* 0.45, $CHCl_3$); IR (KBr) 3418, 1777, 1719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.29 (m, 5 H), 5.30 (bs, 1 H), 5.12-5.06 (m, 2H), 4.46 (bs, 1H), 4.25 (dd, 1H, *J* = 8.8, 16.6 Hz), 2.72-2.68 (m, 1H), 2.54-2.50 (m, 1H), 1.86-1.79 (m, 2H), 1.70-1.63 (m, 1H), 0.97 (d, 3H, *J* = 6.3 Hz), 0.94 (d, 3H, *J* = 6.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 154.8, 136.0, 128.5, 128.2, 128.1, 66.9, 65.5, 58.8, 43.6, 34.3, 24.3, 24.0, 23.6; high-resolution mass spectrum (CI, NH_3) *m/z* 292.1560 [$(M + H)^+$], calcd for $C_{16}H_{22}NO_4$ 292.1549.

Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.97; H, 7.27; N, 4.81. Found: C, 65.94; H, 7.30; N, 4.78.

Preparation of amino lactone (-)-1a. Typical procedure for removal of the Cbz protecting group. A heterogeneous mixture of (-)-**15a** (3.43 g, 12.4 mmol) and Pd(C) (0.05 g) in EtOH (110 mL) was treated with H_2 (balloon) for 1 h. The crude mixture was filtered through a short silica column to remove the catalyst and the filtrate was concentrated *in vacuo*. Purification by flash chromatography (EtOAc) afforded (-)-**1a**

(1.48 g, 83% yield) as a colorless oil: $[\alpha]_D^{23}$ -46.3° (*c* 0.54, $CHCl_3$); IR (neat) 3350, 2960, 1770, 1220 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.34-4.30 (m, 1 H), 4.24-4.20 (m, 1H), 2.37-2.31 (m, 1H), 1.97-1.91 (m, 2H), 1.03 (d, 3H, *J* = 6.8 Hz), 0.95 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.6, 64.9, 61.0, 34.0, 31.8, 17.6, 16.2; high-resolution mass spectrum (CI, NH_3) *m/z* 144.1020 $[(M + H)^+]$, calcd for $C_7H_{14}NO_2$ 144.1025.

Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15. Found: C, 58.31, H, 9.02.

Amino lactone (-)-1b. Following the procedure described above for (-)-**1a**; flash chromatography (EtOAc) afforded (-)-**1b** (0.58 g, 84% yield) as a colorless oil: $[\alpha]_D^{23}$ -36.3° (*c* 3.1, $CHCl_3$); IR (neat) 3460, 1770, 1220 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.30-4.24 (m, 1 H), 4.19-4.13 (m, 1H), 2.29-2.24 (m, 1H), 2.08-2.03 (m, 1H), 1.84-1.77 (m, 1H), 1.60 (dd, 1H, *J* = 5.3, 14.3 Hz), 1.43 (dd, 1H, *J* = 7.1, 14.4 Hz), 0.93 (d, 3H, *J* = 6.6 Hz), 0.90 (d, 3H, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.9, 64.6, 57.4, 45.7, 35.6, 24.6, 24.1, 23.6; high-resolution mass spectrum (CI, NH_3) *m/z* 158.1178 $[(M + H)^+]$, calcd for $C_8H_{16}NO_2$ 158.1181.

Anal. Calcd for $C_8H_{15}NO_2$: C, 61.12; H, 9.62. Found: C, 60.89, H, 9.54.

Preparation of monohydroxy pyrrolinone (-)-18. Solutions of aminolactone (-)-**1a** (68 mg, 0.47 mmol) and aldehyde (-)-**16** (138 mg, 0.43 mmol) in toluene (5 mL each) were combined and concentrated in *vacuo*, and the residue azeotropically dehydrated with additional toluene (3 x 10 mL). The resultant oil was dissolved in THF (15 mL), and this solution was added via cannula to a solution of KHMDS (6.9 mL, 3.44 mmol, 0.5 M in toluene) and 18-c-6 (909 mg, 3.44 mmol) in THF (35 mL) at 0 °C. The resultant reddish solution was stirred at 0 °C for 2 h, at rt for 3 h, cooled back to 0 °C, and quenched by addition of 5% aqueous $NaHSO_4$ (10 mL). The mixture was then warmed to rt, stirred for another 20 min, and then extracted with EtOAc (3 x 25 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine (15 mL each), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Flash chromatography (EtOH/EtOAc/hexanes 10:40:50) afforded (-)-**18** (148 mg, 77% yield) as a white solid: mp 190 °C dec; $[\alpha]_D^{23}$ -10.2° (*c* 0.48, $CHCl_3$); IR ($CHCl_3$) 3447, 1751, 1685, 1636 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, 1H, *J* = 3.8 Hz), 7.23-7.19 (m, 3 H), 7.04-7.00 (m, 2H), 6.27 (bs, 1 H), 5.87 (bs, 1H), 3.79 (d, 1H, *J* = 13.2 Hz), 3.70 (s, 3H), 3.49-3.42 (m, 2H), 3.29 (d, 1H, *J* = 13.1 Hz), 2.50 (bs, 1H), 2.07-1.94 (m, 2H), 1.81-1.76 (m, 1H), 1.42 (s, 9H), 0.95 (d, 3H, *J* = 6.9 Hz), 0.74 (d, 3H,

J = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.1, 172.0, 163.7, 154.7, 135.6, 130.0, 128.1, 127.0, 112.8, 79.4, 73.2, 60.0, 58.7, 52.6, 39.3, 37.2, 34.1, 28.4, 16.9, 15.9; high-resolution mass spectrum (ES, Na^+) *m/z* 447.2476 [$(M + H)^+$], calcd for $C_{24}H_{35}N_2O_6$ 447.2495.

Anal. Calcd for $C_{24}H_{34}N_2O_6$: C, 64.55; H, 7.67. Found: C, 64.25; H, 7.33.

Unsaturated lactam (-)-20. mp 169-170 °C; $[\alpha]_D^{23}$ -8.4° (*c* 0.87, $CHCl_3$); IR (KBr) 3374, 1718, 1702, 1171 cm-^{1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.21 (m, 3 H), 7.15-7.12 (m, 2H), 6.66 (d, 1H, *J* = 5.2 Hz), 5.60 (d, 1H, *J* = 5.2 Hz), 4.93 (bs, 1H), 4.18-4.10 (m, 1H), 4.03-3.98 (m, 1H), 3.12-3.04 (m, 1H), 3.06 (d, 1H, *J* = 12.9 Hz), 2.89 (d, 1H, *J* = 12.8 Hz), 2.38-2.31 (m, 1H), 2.27-2.22 (m, 1H), 1.40 (s, 9H), 1.00 (d, 3H, *J* = 6.8 Hz), 0.88 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4, 173.5, 154.1, 133.8, 130.8, 130.3, 128.1, 127.3, 111.1, 80.2, 65.8, 65.7, 64.4, 42.9, 33.2, 29.0, 28.3, 17.1, 16.7; high-resolution mass spectrum (CI, NH_3) *m/z* 414.2148 [M^+], calcd for $C_{23}H_{30}N_2O_5$ 414.2155.

Anal. Calcd for $C_{23}H_{30}N_2O_5$: C, 66.65; H, 7.30. Found: C, 66.55; H, 7.28.

Preparation of monopyrrolinone aldehyde (-)-19. **Typical procedure for the Swern oxidation of hydroxy pyrrolinones.** To a solution of $(COCl)_2$ (0.31 mL, 0.61 mmol, 2.0 M in CH_2Cl_2) in CH_2Cl_2 (15 mL) at -70 °C was added DMSO (0.1 mL, 95 mg, 1.22 mmol). The resulting solution was stirred for 15 min, cooled to -78 °C, and then a solution of monohydroxy pyrrolinone (-)-**18** (182 mg, 0.41 mmol) in CH_2Cl_2 (10 mL) added via cannula. The reaction was stirred for another 15 min at -78 °C and then DBU (0.30 mL, 310 mg, 2.03 mmol) added via syringe. The solution was warmed to rt, stirred for 20 min, cooled back to 0 °C, and quenched by addition of water (5 mL). The resulting biphasic mixture was extracted with CH_2Cl_2 (2 x 20 mL). The combined organic extracts were washed with aqueous $NaHCO_3$/brine (1:1, v/v, 2 x 5 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Flash chromatography (EtOAc/hexanes, 80:20) afforded (-)-**19** (154 mg, 85% yield) as a yellow solid; (-)-**19** has physical and spectroscopic properties identical to literature values.[1d]

Preparation of bishydroxy pyrrolinone (-)-21. **Typical procedure for the synthesis of hydroxy pyrrolinones.** Solutions of aminolactone (-)-**1b** (52 mg, 0.33 mmol) and aldehyde (-)-**19** (119 mg,

0.27 mmol) in $CHCl_3$ (5 mL each) were combined and concentrated in *vacuo*, and the residue azeotropically dehydrated with benzene (10 mL). The resultant oil was dissolved in THF (10 mL), followed by addition of trimethylorthoformate (10 mL). The solution was stirred at rt for 14 h and then concentrated in *vacuo*, and the residue azeotropically dehydrated with toluene (15 mL). The resultant oil was dissolved in THF (13 mL) and this solution added via cannula to a 0 °C solution of KHMDS (4.1 mL, 2.1 mmol, 0.5 M in toluene) and 18-c-6 (650 mg, 2.46 mmol) in THF (20 mL). The reaction was stirred at 0 °C for 2 h, at rt for 4 h, cooled back to 0 °C, and quenched by addition of 5% aqueous $NaHSO_4$ (20 mL). The mixture was warmed to rt, stirred for another 20 min and then extracted with EtOAc (3 x 25 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and brine (15 mL each), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Flash chromatography (EtOH/EtOAc/hexanes 10:40:50) afforded (-)-**21** (120 mg, 77% yield) as a white solid: mp 115-118 °C; $[\alpha]_D^{23}$ -98.7° (*c* 0.64, $CHCl_3$); IR (KBr) 3460, 3300, 1710, 1640, 1460 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.23 (bs, 2H), 7.52 (s, 1H), 7.23-7.14 (m, 3 H), 7.04-6.99 (m, 2H), 6.43 (bs, 1 H), 6.25 (bs, 1H), 3.87-3.69 (m, 3H), 3.72 (s, 3H), 3.40 (d, 1H, *J* = 13.2 Hz), 2.32 (bs, 1H), 2.04-1.98 (m, 1H), 1.83 (t, 2H, *J* = 5.6 Hz), 1.74-1.65 (m, 2H), 1.58-1.53 (m, 1H), 1.40 (s, 9H), 0.93 (d, 3H, *J* = 6.9 Hz), 0.83 (d, 3H, *J* = 6.5 Hz), 0.79 (d, 3H, *J* = 6.7 Hz), 0.76 (d, 3H, *J* = 6.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.4, 201.0, 172.8, 164.1, 161.3, 154.2, 136.1, 130.1, 128.0, 126.7, 110.6, 107.7, 79.0, 71.4, 70.6, 60.4, 58.7, 52.4, 43.7, 39.8, 39.1, 37.9, 28.4, 24.6, 24.0, 23.8, 17.3, 16.0; high-resolution mass spectrum (ES, Na^+) *m/z* 606.3146 [$(M + Na)^+$], calcd for $C_{32}H_{45}N_3O_7Na$ 606.3155.

Anal. Calcd for $C_{32}H_{45}N_3O_7$: C, 65.84; H, 7.77. Found: C, 65.53; H, 7.48.

Bispyrrolinone aldehyde (-)-22. Following the procedure described above for (-)-**19**; flash chromatography (EtOAc/hexanes, 80:20) afforded (-)-**22** (94 mg, 80% yield); compound (-)-**22** has physical and spectroscopic properties identical to literature values.[1d]

Trishydroxy pyrrolinone. Following the procedure described above for (-)-**21**; flash chromatography (EtOH/EtOAc/hexanes 10:40:50) afforded trishydroxy pyrrolinone (46 mg, 48% yield) as a yellow soild: mp 130-135 °C; $[\alpha]_D^{23}$ -58.0° (*c* 0.5, $CHCl_3$); IR (KBr) 3619, 1718, 1654, 1578 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (bs,

2H), 8.14 (bs, 1H), 7.48 (bs, 1H), 7.42 (bs, 1H), 7.20-7.16 (m, 3 H), 7.00-6.97 (m, 2H), 6.55 (bs, 1 H), 6.11 (bs, 1H), 3.87-3.80 (m, 1H), 3.78-3.72 (m, 1H), 3.71 (s, 3H), 3.64 (d, 1H, *J* = 12.0 Hz), 3.43 (d, 1H, *J* = 13.1 Hz), 1.96-1.90 (m, 1H), 1.84-1.78 (m, 2H), 1.68-1.48 (m, 6H), 1.40 (s, 9H), 0.85 (d, 3H, *J* = 6.8 Hz), 0.84 (d, 3H, *J* = 6.4 Hz), 0.80 (d, 3H, *J* = 6.4 Hz), 0.78 (d, 3H, *J* = 6.7 Hz), 0.73 (d, 3H, *J* = 6.7 Hz), 0.68 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.9, 202.6, 201.0, 172.7, 163.9, 161.8, 160.5, 154.3, 136.1, 130.2, 127.9, 126.7, 110.7, 109.4, 107.2, 79.0, 71.2, 70.6, 68.7, 60.7, 58.7, 52.4, 47.4, 43.5, 40.1, 39.3, 37.8, 28.4, 24.7, 24.6, 24.3, 24.1, 23.9, 23.7, 17.1, 15.9; high-resolution mass spectrum (ES, Na^+) *m/z* 721.4162 [$(M + H)^+$], calcd for $C_{40}H_{57}N_4O_8$ 721.4176.

Trispyrrolinone aldehyde (-)-23. Following the procedure described above for (-)-**19**; flash chromatography (EtOAc/hexanes, 80:20) afforded (-)-**23** (28 mg, 65% yield); compound (-)-**23** has physical and spectroscopic properties identical to literature values.[1d]

Tetrapyrrolinone (-)-25. Following the previously described procedure;[1d] flash chromatography (EtOAc/hexanes, 50:50) afforded (-)-**25** (20 mg, 64% yield); compound (-)-**25** has physical and spectroscopic properties identical to literature values.[1d]