SUPPORTING INFORMATION

Synthesis of Novel Pyran β -Amino Acid and 5,6-Dihydro-2H-pyran β -Aminoxy Acid from Carbohydrate Derivatives

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CONTENTS

S2-S15: Experimental section

S16-S36: ^1H and ^{13}C NMR spectra of all new compounds

(2*R*, 3*S*)-1-(*tert*.-Butyldiphenylsilyloxy)-3-(4-methoxybenzyloxy) hex-5-en-2-ol (6):

To a cooled (0 °C) solution of **5** (10.0 g, 39.68 mmol) in CH₂Cl₂ (100 mL), imidazole (8.10 g, 119.12 mmol) and dibutyltin oxide (0.02 g, 0.08 mmol) were added and stirred. After 30 min, TBDPSCl (10.2 mL, 39.6 mmol) was added and stirred at room temperature for 2 h. The reaction mixture was evaporated and purified the residue by column chromatography (60-120 Silica gel, 11% ethyl acetate in pet. ether) to afford **6** (16.5 g, 85%) as a colorless liquid. $[\alpha]_D^{20} = +51.24$, (*c* 1.2, CHCl₃); IR (neat): ν 3021, 1730, 1514, 1498, 1374, 1247, 1214, 1045, 926, 743, 667 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.67-7.64 (m, 4H, ArH), 7.46-7.33 (m, 6H, ArH), 7.10 (d, 2H, *J* = 8.5 Hz, ArH), 6.78 (d, 2H, *J* = 8.7 Hz, ArH), 5.95-5.81 (m, 1H, olefinic), 5.17-5.10 (m, 2H, olefinic), 4.52 (d, 1H, *J* = 10.9 Hz, benzylic), 4.34 (d, 1H, *J* = 10.9 Hz, benzylic), 3.82-3.78 (m, 1H, OCH), 3.78 (s, 3H, OCH₃), 3.76-3.68 (m, 2H, OCH), 3.56-3.50 (q, 1H, *J* = 5.6 Hz, OCH), 2.49 (d, 1H, *J* = 3.6 Hz, OH), 2.43-2.32 (m, 2H, CH₂), 1.06 (s, 9H, 3 x CH₃); ¹³C NMR (75 MHz, CDCl₃): δ 159.0, 135.4, 134.7, 132.9, 130.2, 129.6, 129.2, 127.6, 117.0, 113.5, 78.3, 72.4, 71.5, 64.6, 54.9, 34.4, 26.7, 19.1; HRMS (ESI): *m/z* calculated for C₃₀H₃₈O₄SiNa [M+Na]⁺ 513.2430, found 513.2431.

(4*S*, 5*R*)-6-(*tert*.-Butyldiphenylsilyloxy)-4-(4-methoxybenzyloxy)hexane-1,5-diol (7):

To a stirred solution of cyclohexene (15.1 g, 184.1 mmol) in anhydrous THF (90 mL) BH₃.DMS (8.61 mL, 91.7 mmol) was added at 0 °C and stirred for 2 h at 0 °C. A solution of **6** (15.0 g, 30.6 mmol) in THF (75 mL) was added to the reaction mixture at the same temperature and allowed to stir for an additional 2 h. 2N Sodium hydroxide (60 mL) and 30% hydrogen peroxide (30 mL) were added at 0 °C and allowed to stir at room temperature for 3 h. It was, extracted with EtOAc (2 x 200 mL) and washed with brine (150 mL). Organic

layer was dried (Na₂SO₄), evaporated and purified the residue by column chromatography (60-120 Silica gel, 19% ethyl acetate in pet. ether) to furnish alcohol **4** (12.1 g, 78%) as a colorless liquid. $[\alpha]_D^{20} = +45.15$, (*c* 1.2, CHCl₃); IR (neat): ν 3418, 3137, 3003, 2947, 2881, 1764, 1391, 1023, 655 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.71-7.61 (m, 4H, ArH), 7.45-7.34 (m, 6H, ArH), 7.11 (d, 2H, *J* = 8.5 Hz, ArH), 6.8 (d, 2H, *J* = 8.5 Hz, ArH), 4.46-4.40 (m, 2H, benzylic), 4.14-4.10 (m, 1H, OCH), 3.87-3.75 (m, 2H, OCH₂), 3.78 (s, 3H, OCH₃), 3.60-3.56 (m, 2H, OCH₂), 3.51-3.48 (m, 1H, OCH), 1.80-1.56 (m, 6H, 2 x CH₂, 2 x OH), 1.07 (s, 9H, 3 x CH₃); ¹³C NMR (75 MHz, CDCl₃): δ 159.2, 135.5, 129.7, 129.4, 127.7, 113.7, 78.5, 72.6, 71.6, 64.8, 62.7, 55.1, 28.1, 26.8, 26.1, 19.1; HRMS (ESI): *m/z* calculated for C₃₀H₄₀O₅SiNa [M+Na]⁺ 531.2536, found 531.2537.

***tert.*-Butyl(((2*R*,3*S*)-3-(4-methoxybenzyloxy)tetrahydro-2H-pyran-2-yl)-methoxy) diphenylsilane (**8**):**

To a solution of **7** (11.0 g, 21.6 mmol) in CH₂Cl₂ (165 mL) at 0 °C, Et₃N (6 mL, 43.3 mmol) and *p*-TsCl (4.11 g, 21.6 mmol) were added and stirred at room temperature for 2 h. The reaction mixture was washed with water (80 mL), brine (80 mL) and dried (Na₂SO₄). Evaporation of solvent furnished **4** as a colorless oil, which was immediately used for the next reaction without further purification.

A solution of **4** (9.0 g, 13.60 mmol) in MeOH (45 mL) was treated with K₂CO₃ (5.62 g, 40.72 mmol) and stirred at room temperature for 2 h. MeOH was evaporated under reduced pressure and residue was extracted with EtOAc (3 x 70 mL). Organic layer was washed with water (70 mL) and brine (70 mL). Solvent was dried (Na₂SO₄), evaporated and purified the residue by column chromatography (Silica gel 60-120 mesh, 8% ethyl acetate in pet. ether) to furnish **8** (4.5 g, 67%) as a colorless liquid. $[\alpha]_D^{20} = +39.84$, (*c* 1.2, CHCl₃); IR (neat): ν 3021, 1730, 1374, 1247, 1045, 667 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.75-7.70 (m, 4H, ArH),

7.42-7.31 (m, 6H, ArH), 7.12 (d, 2H, $J = 8.5$ Hz, ArH), 6.8 (d, 2H, $J = 8.5$ Hz, ArH), 4.52 (d, 1H, $J = 10.9$ Hz, benzylic), 4.35 (d, 1H, $J = 10.9$ Hz, benzylic), 3.91 (d, 2H, $J = 2.6$ Hz, OCH₂), 3.77 (s, 3H, OCH₃), 3.54-3.43 (m, 1H, OCH), 3.37-3.20 (m, 2H, OCH₂), 2.28-2.23 (m, 1H, OCH), 1.68-1.60 (m, 2H, CH₂), 1.49-1.36 (m, 2H, CH₂), 1.06 (s, 9H, 3 x CH₃); ¹³C NMR (CDCl₃, 150 MHz): δ 159.0, 135.8, 135.7, 129.5, 129.2, 127.6, 127.5, 113.7, 81.8, 73.0, 70.6, 67.5, 64.0, 55.3, 29.7, 29.4, 26.9, 19.4; HRMS (ESI): m/z calculated for C₃₀H₃₈O₄SiNa [M+Na]⁺ 513.2435, found 513.2431.

((2*R*, 3*S*)-3-(4-Methoxybenzyloxy) tetrahydro-2H-pyran-2-yl)methanol

(9):

To a cooled (0 °C) solution of **8** (3.50 g, 7.14 mmol) in dry THF (20 mL) under nitrogen atmosphere, 1.0 M solution of TBAF in THF (7.8 mL, 7.86 mmol) was added and stirred for 2 h. It was diluted with water (30 mL) and extracted with EtOAc (2 x 25 mL). The combined organic layers were washed with water (2 x 25 mL), brine (25 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (60-120 Silica gel, 11% ethyl acetate in pet. ether) to give **9** (1.50 g, 83%) as a liquid. $[\alpha]_D^{20} = +31.15$, (c 1.2, CHCl₃); IR (neat): ν 3411, 2884, 1783, 1219, 1098, 772, 639 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.3 (d, 2H, $J = 8.7$ Hz, ArH), 6.86 (d, 2H, $J = 8.3$ Hz, ArH), 4.55 (d, 1H, $J = 11.3$ Hz, benzylic), 4.42 (d, 1H, $J = 10.9$ Hz, benzylic), 3.97-3.82 (m, 2H, OCH₂), 3.80 (s, 3H, OCH₃), 3.70-3.65 (m, 1H, OCH), 3.41-3.20 (m, 2H, OCH₂), 2.30-2.24 (m, 2H, OCH, OH), 1.76-1.51 (m, 2H, CH₂), 1.47-1.33 (m, 2H, CH₂); ¹³C NMR (CDCl₃, 75 MHz): δ 159.3, 130.4, 129.2, 113.7, 80.7, 73.7, 70.3, 67.6, 63.0, 55.1, 29.0, 25.1; HRMS (ESI): m/z calculated for C₁₄H₂₀O₄Na [M+Na]⁺ 275.1251, found 275.1253.

(2*S*, 3*S*)-3-(4-Methoxybenzyloxy) tetrahydro-2H-pyran-2-carboxylic acid

(10):

To a stirred solution of **9** (1.0 g, 3.97 mmol) in CH₂Cl₂:H₂O (1:1, 5 mL), TEMPO (0.19 g, 1.19 mmol) and BAIB (3.83 g, 11.89 mmol) were added at 0 °C and stirred for 2 h. The reaction mixture was diluted with water (15 mL) and extracted with CH₂Cl₂ (2 x 25 mL). Organic layers were washed with sat. aq hypo (15 mL), brine (15 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (Silica gel, 60-120 mesh, 20-25% ethyl acetate in pet. ether) to give acid **10** (0.8 g, 76%) as a colorless syrup. $[\alpha]_D^{20} = +25.19$, (*c* 1.2, CHCl₃); IR (neat): ν 3050, 2938, 2374, 1723, 1441, 1373, 1246, 1035, 961, 666 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.24 (d, 2H, *J* = 6.7 Hz, ArH), 6.86 (d, 2H, *J* = 6.8 Hz, ArH), 4.60 (d, 1H, *J* = 10.9 Hz, benzylic), 4.48 (d, 1H, *J* = 11.3 Hz, benzylic), 4.01 (d, 1H, *J* = 11.3 Hz, OCH), 3.9 (td, 1H, *J* = 1.8, 8.2 Hz, OCH), 3.79 (s, 3H, OCH₃), 3.65 (td, 1H, *J* = 2.6, 10.1 Hz, OCH), 3.48 (td, 1H, *J* = 1.8, 10.9 Hz, OCH), 1.79-1.62 (m, 2H, CH₂), 1.49-1.32 (m, 2H, CH₂); ¹³C NMR (75 MHz, CDCl₃): 172.8, 159.5, 129.5, 129.4, 114.0, 78.3, 73.9, 70.8, 67.2, 55.2, 28.5, 23.6; HRMS (ESI): *m/z* calculated for C₁₄H₁₈O₅Na [M+Na]⁺ 289.1043, found 289.1046.

(2S, 3S)-Methyl 3-(4-methoxybenzyloxy) tetrahydro-2H-pyran-2-carboxylate (3):

A solution of **10** (0.7 g, 2.63 mmol) in Et₂O (20 mL) was treated with ethereal diazomethane [prepared from 0.81 g of N-nitrosomethyl urea and 50% KOH in water (30 mL)]. The reaction mixture was stirred at 0 °C for 30 min, evaporated solvent and purified the residue by column chromatography (Silica gel, 9% ethyl acetate in pet. ether) to give **3** (0.65 g) in 89% yield as a syrup; $[\alpha]_D^{20} = +19.12$, (*c* 1.2, CHCl₃); IR (Neat): ν 3021, 1731, 1374, 1247, 1098, 1045, 744, 667 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 7.20 (d, 2H, *J* = 8.7 Hz, ArH), 6.85 (d, 2H, *J* = 8.3 Hz, ArH), 4.50 (d, 1H, *J* = 11.3 Hz, benzylic), 4.45 (d, 1H, *J* =

11.3 Hz, benzylic), 4.01-3.94 (m, 1H, OCH), 3.80 (s, 3H, OCH₃), 3.76 (s, 3H, COOCH₃), 3.66-3.40 (m, 2H, OCH), 2.20-2.12 (m, 1H, OCH), 1.79-1.46 (m, 4H, OCH₂); ¹³C NMR (75 MHz, CDCl₃): 170.6, 159.2, 130.1, 129.2, 113.7, 79.6, 74.0, 70.7, 67.2, 55.2, 52.0, 28.5, 23.7; HRMS (ESI): *m/z* calculated for C₁₅H₂₀O₅ [M+Na]⁺ 303.1200, found 303.1202.

(2*S*, 3*S*)-Methyl 3-hydroxytetrahydro-2H-pyran-2-carboxylate (11):

To a solution of **3** (0.50 g, 1.79 mmol) in aq. CH₂Cl₂:H₂O (19:1), (15 mL), DDQ (0.60 g, 2.68 mmol) was added and stirred at room temperature for 2 h. The reaction mixture was quenched with sat. NaHCO₃ solution (10 mL), filtered and washed with CH₂Cl₂ (20 mL). The filtrate was washed with water (20 mL), brine (20 mL) and dried (Na₂SO₄). Solvent was evaporated under reduced pressure and purified the residue by column chromatography (60-120 Silica gel, 14% ethyl acetate in pet. ether) to furnish **3** (0.24 g, 86%) as a yellow liquid. [α]_D²⁰ = +13.69, (*c* 1.2, CHCl₃); IR (neat): ν 3020, 2931, 2855, 1731, 1441, 1246, 1093, 1045, 667 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 4.05 (d, 1H, *J* = 11 Hz, OCH), 3.84 (s, 3H, OCH₃), 3.78-3.71 (m, 2H, OCH₂), 3.45-3.40 (m, 1H, OCH), 2.21-2.16 (m, 1H, OH), 1.78-1.70 (m, 3H, CH₂), 1.55-1.45 (m, 1H, CH); ¹³C NMR (75 MHz, CDCl₃): δ 171.9, 80.0, 68.0, 67.5, 52.7, 31.0, 24.3; HRMS (ESI): *m/z* calculated for C₇H₁₂O₄Na [M+Na]⁺ 183.0628, found 183.0627.

(2*S*, 3*R*)-Methyl 3-azidotetrahydro-2H-pyran-2-carboxylate (12):

To a solution of **11** (0.15 g, 0.94 mmol) in CH₂Cl₂ (10 mL) at 0 °C, Et₃N (0.19 g, 1.90 mmol) and *p*-TsCl (0.18 g, 0.95 mmol) were added and stirred at room temperature for 2 h. Work up as described for **4** furnished **11a** as a colorless oil, which was used for the next reaction without further purification.

To a solution of **11a** in DMF (5 mL), NaN₃ (0.12 g, 1.91 mmol) was added and stirred at 70 °C for 3 h. The reaction mixture was cooled to room temperature, treated with water (8 mL) and extracted with ether (2 x 10 mL). Organic layers were washed with brine (10 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 10% ethyl acetate in pet. ether) to give **12** (0.10 g, 85%) as a colorless liquid. $[\alpha]_D^{20} = -132.11$, (*c* 1.2, CHCl₃); IR (KBr): ν 2971, 2945, 2105, 1736, 1437, 1370, 1272, 1085, 976, 868, 751, 666 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz): δ 4.08 (d, 1H, *J* = 11 Hz, OCH), 4.01 (m, 1H, OCH), 3.77 (s, 3H, OCH₃), 3.50 (t, 1H, *J* = 11.4 Hz, OCH), 1.98-1.83 (m, 3H, CH₂), 1.71-1.55 (m, 2H, CH₂); ¹³C NMR (75 MHz, CDCl₃): δ 170.6, 80.3, 68.2, 53.1, 52.0, 27.9, 24.1; HRMS (ESI): *m/z* calculated for C₇H₁₁N₃O₂Na [M+Na]⁺ 208.0613, found 208.0616.

(2S,3R)-Methyl 3-(tert.-butoxycarbonylamino)tetrahydro-2H-pyran-2-carboxylate (1):

A mixture of **12** (0.08 g, 0.43 mmol) and 10% Pd-C (cat.) in MeOH (1.5 mL) was stirred at room temperature under hydrogen atmosphere for 4 h. It was filtered and washed with EtOAc (10 mL). The filtrate was evaporated under reduced pressure to furnish amine **13**, which was used for the next reaction without further purification.

To a solution of the above amine **13** in CH₂Cl₂ (10 mL), Et₃N (0.15 mL, 0.99 mmol) and (Boc)₂O (0.17 mL, 0.75 mmol) were added at 0 °C and stirred for 5 h. The reaction mixture was treated with water (10 mL) and extracted with CH₂Cl₂ (2 x 15 mL). Organic layer was washed with brine (10 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 12% ethyl acetate in pet. ether) to furnish **1** (0.11 g, 85%) as a colorless syrup; $[\alpha]_D^{20} = -103.94$, (*c* 1.2, CHCl₃); IR (KBr): ν 3290, 2975, 2936, 1754, 1705, 1540, 1446, 1370, 1290, 1209, 1175, 1115, 1094,

1066, 689 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 4.64 (brs, 1H, NH), 4.10-3.95 (m, 2H, OCH), 3.76 (s, 3H, COOCH_3), 3.50-3.39 (m, 2H, OCH), 2.13-2.0 (m, 2H, OCH), 1.78-1.68 (m, 2H, CH_2), 1.42 (s, 9H, Boc); ^{13}C NMR (75 MHz, CDCl_3): δ 170.1, 155.1, 80.1, 79.6, 66.7, 52.4, 48.2, 29.3, 28.3, 23.9; HRMS (ESI): m/z calculated for $\text{C}_{12}\text{H}_{21}\text{NO}_5\text{Na}$ $[\text{M}+\text{Na}]^+$ 282.1350, found 282.1352.

(3*R*,5*R*,6*S*,6*R*)-2,2-Dimethyl-5-vinyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-ol

(16):

To a stirred solution of **17** (22.0 g, 84.61 mmol) in dry CH_2Cl_2 (100 mL), Ph_3P (88.67 g, 338.46 mmol), imidazole (23.01 g, 338.44 mmol) and I_2 (63.96 g, 253.83 mmol) were added at 0 $^\circ\text{C}$ and allowed to stir for 4 h. The reaction mixture was quenched with sat. NaOH (5 mL) and extracted with CH_2Cl_2 (2 x 50 mL). The combined organic layers were washed with hypo (2 x 25 mL), brine (25 mL) and dried (Na_2SO_4). Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 5% ethyl acetate in pet. ether) to furnish **16** (12.3 g, 64%) as a colorless oil; $[\alpha]_D^{20} = -87.04$ (c 0.1, CHCl_3); IR (CHCl_3): ν 3467, 3395, 2919, 2851, 1735, 1661, 1481, 1377, 1217, 1163, 1076, 1020, 932, 885, 861, 777 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.9 (m, 2H, olefinic), 5.8 (d, 1H, $J = 4.1$ Hz, C_1H), 5.39 (td, 1H, $J = 1.1, 1.1$ Hz, olefinic), 5.28 (d, 1H, $J = 1.1$ Hz, olefinic), 5.25 (dd, 1H, $J = 1.1$ Hz, olefinic), 5.1 (dd, 1H, $J = 1.5, 10.2$ Hz, olefinic), 4.53 (dd, 1H, $J = 2.2, 6.4$ Hz, C_4H), 4.5 (d, 1H, $J = 3.7$ Hz, C_2H), 4.04 (dq, 2H, $J = 5.2, 10.2$ Hz, OCH), 3.76 (d, 1H, $J = 3.0$ Hz, C_3H), 1.48 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (75 MHz, CDCl_3 , 295 K) δ 133.9, 132.1, 118.6, 117.1, 111.1, 104.6, 83.1, 82.7, 81.3, 70.9, 26.5, 25.9; HRMS (ESI): m/z calculated for $\text{C}_{12}\text{H}_{19}\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 249.1102, found 249.1111.

(3*R*,5*R*,6*S*,6*R*)(Allyloxy)-2,2dimethylvinyltetrahydrofuro[2,3*d*][1,3]dioxole (18):

To a stirred solution of **16** (12.3 g, 54.42 mmol) in dry toluene (50 mL), Grubbs-I catalyst (10 mol%) was added and stirred at reflux for 3 h. The reaction mixture was stirred for an additional 1 h at room temperature in open air. It was filtered through celite, washed with toluene (2 x 20 mL) and evaporated the solvent. The residue on purification by column chromatography (60-120 mesh Silica gel, 10% ethyl acetate in pet. ether) afforded **18** (9.6 g, 90%) as a brown syrup; $[\alpha]_D^{20} = -22.7$ (*c* 0.1, CHCl₃); IR (CHCl₃): ν 2987, 2937, 1737, 1645, 1449, 1288, 1163, 954, 831 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.0 (s, 2H, olefinic), 5.89 (d, 1H, *J* = 3.7 Hz, C₁H), 4.52 (d, 1H, *J* = 3.7 Hz, C₄H), 4.31 (m, 1H, C₂H), 4.12 (m, 2H, OCH), 3.88 (d, 1H, *J* = 2.6 Hz, C₃H), 1.48 (s, 3H, Me), 1.31 (s, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 131.7, 121.4, 111.1, 104.9, 84.1, 78.5, 70.6, 64.3, 26.5, 25.9; HRMS (ESI): *m/z* calculated for C₁₀H₁₅O₄ [M+H]⁺ 199.0964, found 199.0963.

(2*S*,3*R*,3*R*,7*R*)-3,3*a*,5,7*a*-Tetrahydro-2*H*-furo[3,2-*b*]pyran-2,3-diol (19):

A solution of **18** (9.6 g, 48.48 mmol) in 60% aq. AcOH (60 mL) was stirred at reflux for 3 h. The reaction mixture was neutralized with solid NaHCO₃ and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried (Na₂SO₄), evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 50% ethyl acetate in pet. ether) to afford **19** (5.36 g, 70%) as a yellow liquid. $[\alpha]_D^{20} = -69.5$ (*c* 0.2, CHCl₃); IR (CHCl₃): ν 3436, 3395, 2921, 1726, 1644, 1531, 1449, 1219, 1036, 832, 689 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.99 (s, 2H, olefinic), 5.51 (d, 0.6 H, *J* = 3.8 Hz, C₁H), 5.1 (s, 0.4 H, C₄H), 4.34 (bs, 1H, C₂H), 4.21 (s, 0.3 H, OCH), 4.12 (m, 1.6 H, OCH), 3.99 (d, 1H, *J* = 16.5 Hz, C₃H), 3.92 (d, 1H, *J* = 19.8 Hz, OCH), 3.07 (bs, 2H, OH); ¹³C NMR (75 MHz, CDCl₃) δ 131.3,

129.7, 123.4, 121.9, 103.5, 96.4, 80.5, 79.4, 76.2, 72.0, 69.3, 64.0, 29.6. HRMS (ESI): m/z calculated for $C_7H_{11}O_4Na$ $[M+Na]^+$ 181.0476, found 181.0478.

(2*R*,3*R*)-2-(Hydroxymethyl)-3,6-dihydro-2H-pyran-3-ol (20):

To a solution of **19** (5.36 g, 33.92 mmol) in acetone:H₂O (32 mL:5:1) at 0 °C, NaIO₄ (8.87 g, 40.7 mmol) was added and allowed to stir at room temperature for 1 h. Solvent was evaporated and extracted the reaction mixture into CH₂Cl₂ (2 x 25 mL). Organic layer was dried (Na₂SO₄), evaporated and used the crude aldehyde for the next reaction without purification.

To a solution of the above aldehyde (5.3 g, 33.92 mmol) in MeOH:H₂O (26.5 mL:3:1), NaBH₄ (1.28 g, 33.92 mmol) was added portion wise at 0 °C. The reaction mixture was treated with NH₄Cl (3 mL) and extracted with EtOAc (2 x 50 mL). Organic layer was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 30% ethyl acetate in pet. ether) to afford **20** (2.6 g, yield 60%) as yellow syrup; $[\alpha]_D^{20} = -20.0$, (c 0.2, CHCl₃); IR (CHCl₃): ν 3746, 3379, 3336, 2919, 2850, 1711, 1657, 1552, 1460, 1333, 1219, 1088, 1062, 1017, 856, 772, 673, 636, 594 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.91 (m, 2H, olefinic), 4.19 (1H, d, $J = 16.9$ Hz, OCH), 4.08 (1H, d, $J = 16.9$ Hz, OCH), 3.87 (bs, 1H, OH), 3.73 (m, 2H, OCH), 3.57 (brs, 1H, OH), 3.47 (m, 2H, OCH); ¹³C NMR (75 MHz, CDCl₃): δ 129.9, 126.1, 78.0, 65.7, 62.6, 62.1; HRMS (ESI): m/z calculated for $C_6H_{10}O_3Na$ $[M+Na]^+$ 153.1418, found 153.1423.

(4*R*,8*R*)-2-(4-Methoxyphenyl)-4,4a,6,8a-tetrahydropyrano[3,2-d][1,3]dioxine (15):

To a stirred solution of **20** (2.6 g, 20.0 mmol) in dry CH₂Cl₂ (100 mL), *p*-anisaldehyde dimethyl acetal (5.46 g, 30.0 mmol) and PTSA (cat.) were added at 0 °C and

stirred at room temperature for 3 h. The reaction mixture was neutralized with Et₃N (3 mL) and extracted with CH₂Cl₂ (3 x 20 mL). The combined organic layers were washed with water (50 mL), brine (50 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 10% ethyl acetate in pet. ether) to give **15** (4.46 g, 90%) as a pale yellow solid; m.p. 90 °C; $[\alpha]_D^{20} = -20.8$ (*c* 0.3, CHCl₃); IR (CHCl₃): ν 3424, 3395, 3018, 2920, 2850, 1695, 1681, 1599, 1578, 1215, 1023, 771, 596 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.39 (d, 2H, *J* = 8.6 Hz, ArH), 6.81 (d, 2H, *J* = 8.6 Hz, ArH), 6.05 (m, 2H, olefinic), 5.47 (s, 1H, benzylic), 4.48-4.1 (m, 6H, OCH), 3.77 (s, 3H, OCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 159.8, 132.0, 130.5, 127.5, 122.8, 113.4, 100.7, 70.3, 68.8, 68.6, 65.8, 55.1; HRMS (ESI): *m/z* calculated for C₁₄H₁₇O₄Na [M+Na]⁺ 271.0946, found 271.0952.

((2*R*,3*R*)-3-(4-Methoxybenzyloxy)-3,6-dihydro-2H-pyran-2-yl)methanol

(21):

To a stirred solution of **15** (4.46 g, 17.98 mmol) in dry CH₂Cl₂ (70 mL) at 0 °C DIBAL-H (25.53 mL, 35.96 mmol, 2 M solution in toluene) was added drop wise. After 1 h, methanol (15 mL) followed by saturated aq. sodium potassium tartarate solution (15 mL) was added to the reaction mixture, filtered through a pad of celite and washed with EtOAc (2 x 100 mL). The combined organic layers were dried (Na₂SO₄), evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 15% ethyl acetate in pet. ether) to furnish **21** (4.13 g, 92%) as a light yellow liquid; $[\alpha]_D^{20} = -22.5$ (*c* 0.2, CHCl₃); IR (CHCl₃): ν 3019, 2924, 2852, 1731, 1665, 1612, 1513, 1467, 1214, 1091, 1035, 928, 745, 667, 626 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.2 (d, 2H, *J* = 8.1 Hz, ArH), 6.88 (d, 2H, *J* = 8.1 Hz, ArH), 6.05 (s, 2H, olefinic), 4.62 (d, 1H, *J* = 11.3 Hz, benzylic), 4.47 (d, 1H, *J* = 11.3 Hz, benzylic), 4.34 (d, 1H, *J* = 17.2 Hz, OCH), 4.16 (d, 1H, *J*

= 17.2 Hz, OCH), 3.94 (m, 1H, OCH), 3.78 (m, 5H, OCH), 3.62 (m, 1H, OCH₂), 2.21 (brs, 1H, OH); ¹³C (75 MHz, CDCl₃) δ 159.1, 131.4, 130.1, 129.3, 123.1, 113.7, 77.5, 70.0, 68.4, 65.7, 62.7, 55.1; HRMS (ESI): *m/z* calculated for C₁₄H₁₈O₄Na [M+Na]⁺ 273.1102, found 273.1094.

(2*S*,3*R*)-3-(4-Methoxybenzyloxy)-3,6-dihydro-2H-pyran-2-carboxylic acid (22):

To a solution of the alcohol **21** (4.13 g, 15.64 mmol) in CH₂Cl₂:H₂O (20 mL:1:1), TEMPO (0.73 g, 4.69 mmol) followed by BAIB (15.10 g, 46.92 mmol) were added at 0 °C and stirred at room temperature for 1 h. Work up as described for **10** and purification of the residue by column chromatography (60-120 mesh Silica gel, 70% ethyl acetate in pet. ether) furnished **22** (4.0 g, 60%) as a light yellow syrup. [α]_D²⁰ = -32.6 (*c* 0.2, CHCl₃); IR (CHCl₃): ν 3019, 2924, 2852, 1731, 1665, 1612, 1513, 1467, 1214, 1091, 1035, 928, 745, 667, 626 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 9.73 (s, 1H, COOH), 7.11 (d, 2H, *J* = 6.0 Hz, ArH), 6.71 (d, 2H, *J* = 6.0 Hz, ArH), 5.78 (brs, 2H, olefinic), 4.48 (m, 2H, benzylic), 4.14 (m, 3H, OCH), 3.76 (m, 1H, OCH), 3.68 (m, 1H, OCH), 3.64 (s, 3H, OCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 159.1, 132.2, 130.0, 129.6, 128.6, 123.5, 113.6, 71.7, 68.5, 65.8, 55.1; HRMS (ESI): *m/z* calculated for C₁₄H₁₇O₅Na [M+Na]⁺ 287.0895, found 287.0896.

(2*S*,3*R*)-Methyl 3-(4-methoxybenzyloxy)-3,6-dihydro-2H-pyran-2-carboxylate (14):

To a solution of acid **22** (4.0 g, 15.15 mmol) in Et₂O (10 mL) at 0 °C, a solution of CH₂N₂ [prepared from 3.8 g of N-nitrosomethyl urea and 50% KOH in water (30 mL)] in Et₂O (100 mL) was added until the persistence of yellow color in the reaction mixture. After 30 min, ether was evaporated and purified the residue by column chromatography (60-120

mesh Silica gel, 10% ethyl acetate in petroleum ether) to afford **14** (2.5 g, 60%, over 3 steps) as a colorless syrup; $[\alpha]_D^{20} = -136.6$, (*c* 0.1, CHCl₃); IR (CHCl₃): ν 3019, 2921, 2851, 1740, 1692, 1627, 1609, 1531, 1514, 1464, 1377, 1250, 1214, 1182, 1095, 1036, 929, 752, 667, 627, 578 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.2 (d, 2H, *J* = 8.3 Hz, ArH), 6.85 (d, 2H, *J* = 8.3 Hz, ArH), 6.01 (m, 2H, olefinic), 4.61 (d, 1H, *J* = 11.3 Hz, benzylic), 4.49 (d, 1H, *J* = 11.3 Hz, benzylic), 4.42 (m, 1H, OCH), 4.18 (m, 3H, OCH), 3.79 (s, 6H, COOCH₃, OCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 169.5, 159.1, 131.0, 130.3, 129.3, 123.0, 113.6, 77.2, 70.3, 68.5, 65.8, 55.2, 52.0; HRMS (ESI): *m/z* calculated for C₁₅H₁₉O₅Na [M+Na]⁺ 301.1051, found 301.1042.

(2*S*,3*R*)-Methyl 3-hydroxy-3,6-dihydro-2H-pyran-2-carboxylate (23):

To a stirred solution of **14** (2.5 g, 8.99 mmol) in CH₂Cl₂:H₂O (4 mL:19:1), DDQ (2.24 g, 9.89 mmol) was added and stirred at room temperature for 2 h. Work up as described for **11** and purification of the residue by column chromatography (60-120 mesh Silica gel, 17% ethyl acetate in pet. ether) furnished **23** (1.02 g, 72%) as a colorless oil; $[\alpha]_D^{20} = -319.07$, (*c* 0.07, CHCl₃); IR (CHCl₃): ν 3020, 2926, 2854, 1740, 1609, 1524, 1426, 1214, 928, 742, 667, 628 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.05 (m, 2H, olefinic), 4.4 (d, 1H, *J* = 16.5 Hz, OCH), 4.21 (m, 3H, OCH), 3.83 (s, 3H, COOCH₃), 2.08 (d, 1H, *J* = 9.7 Hz, OH); ¹³C NMR (75 MHz, CDCl₃) δ 169.4, 130.2, 125.7, 66.0, 63.3, 61.9, 52.3; HRMS (ESI): *m/z* calculated for C₇H₁₁O₄Na [M+Na]⁺ 181.0476, found 181.0487.

Methyl-2-((2*S*,3*S*)-3-(1,3-dioxoisindolin-2-yloxy)-3,6-dihydro-2H-pyran-2-yl)-2-oxo acetate (24):

To a solution of Ph₃P (2.53 g, 9.68 mmol) and N-hydroxy phthalimide (1.55 g, 9.68 mmol) in THF (5 mL), a solution of **23** (1.02 g, 6.45 mmol) in dry THF (5 mL) was added at

0 °C. DIAD (1.95 mL, 6.55 mmol) was added to the reaction mixture and stirred for 6 h. Solvent was evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 22% ethyl acetate in pet. ether) to afford **24** (1.36 g, 70%) as yellow syrup; $[\alpha]_D^{20} = +74.19$, (c 0.09, CHCl_3); IR (CHCl_3): ν 3020, 2923, 2852, 2313, 1788, 1734, 1550, 1499, 1482, 1450, 1374, 1216, 1107, 1017, 979, 929, 87, 777, 667, 624 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.85 (m, 2H, ArH), 7.78 (m, 2H, ArH), 6.14 (m, 2H, olefinic), 4.94 (m, 2H, OCH), 4.48 (m, 1H, OCH), 4.27 (m, 1H, OCH), 3.78 (s, 3H, COOCH_3); ^{13}C NMR (75 MHz, CDCl_3) δ 169.4, 163.8, 134.5, 133.4, 128.7, 123.5, 119.5, 78.1, 74.3, 69.8, 52.3; HRMS (ESI): m/z calculated for $\text{C}_{15}\text{H}_{14}\text{NO}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ 326.0640, found 326.0655.

Boc-(R)- β -Ala-(S)-Ama-OMe (26):

A solution of **24** (1.36 g, 4.48 mmol) and $\text{N}_2\text{H}_4\cdot\text{H}_2\text{O}$ (0.61 mL, 13.46 mmol) in $\text{CH}_3\text{OH}:\text{CH}_2\text{Cl}_2$ (6.8 mL; 4:1) was stirred at room temperature. After 2 h, solvent was evaporated and CH_2Cl_2 was added to the residue. The organic layer was washed with 5% NaHCO_3 solution (10 mL) and brine (10 mL). It was dried (Na_2SO_4) and evaporated to afford *(2S, 3S)-methyl 3-(aminoxyl)-3,6-dihydro-2H-pyran-2-carboxylate*, which was used directly in the next step.

A solution of acid **25** (0.37 g, 1.98 mmol), HOBt (0.26 g, 1.98 mmol) and EDCI (0.37 g, 1.98 mmol) in CH_2Cl_2 (2 mL) was stirred at 0 °C under N_2 atmosphere for 15 min and treated with a solution of **2** (0.22 g, 1.32 mmol) in CH_2Cl_2 (1 mL) and DIPEA (0.34 mL, 1.5 mmol). The reaction mixture was stirred at room temperature for 5 h, quenched with sat. aq. NH_4Cl solution (10 mL) at 0 °C and diluted with CHCl_3 (10 mL). It was sequentially washed with 1 N HCl (10 mL), NaHCO_3 (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4), evaporated and purified the residue by column chromatography (60-120 mesh Silica gel, 50% ethyl acetate in pet. ether) to afford **26** (0.23 g,

52%) as a syrup; $[\alpha]_D^{20} = +83.46$, (c 1.3, CHCl_3); IR (CHCl_3): ν 3328, 3301, 3270, 2960, 2922, 1746, 1682, 1514, 1367, 1169, 1073, 1019, 859, 717 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 9.85 (brs, 1H, NH-aminoxy), 6.02 (m, 2H, olefinic), 5.31 (d, 1H, $J = 7.9$ Hz, NH-amine), 4.58 (d, 1H, $J = 10.9$ Hz, OCH), 4.46 (d, 1H, $J = 17.3$ Hz, OCH), 4.22 (d, 1H, $J = 16.9$ Hz, OCH), 3.76 (s, 3H, COOCH_3), 1.43 (s, 9H, Boc), 1.34 (d, 3H, $J = 6.7$, CH_3). ^{13}C NMR (75 MHz, CDCl_3): δ 170.8, 169.9, 155.5, 132.2, 120.6, 80.3, 75.9, 73.4, 63.4, 63.3, 52.4, 47.4, 28.2, 17.6; HRMS (ESI): m/z calculated for $\text{C}_{15}\text{H}_{25}\text{NO}_7\text{Na}$ $[\text{M}+\text{Na}]^+$ 367.1481, found 367.1493.

Figure S1. ^1H NMR Spectrum of **6** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **6** (75 MHz, CDCl_3).

Figure S2. ^1H NMR Spectrum of **7** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **7** (75 MHz, CDCl_3).

Figure S3. ^1H NMR Spectrum of **8** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **8** (75 MHz, CDCl_3)

Figure S4. ^1H NMR Spectrum of **9** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **9** (75 MHz, CDCl_3).

Figure S5. ^1H NMR Spectrum of **10** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **10** (75 MHz, CDCl_3).

Figure S6. ¹H NMR Spectrum of **3** (300 MHz, CDCl₃).

¹³C NMR Spectrum of **3** (75 MHz, CDCl₃).

Figure S7. ^1H NMR Spectrum of **11** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **11** (75 MHz, CDCl_3)

Figure S8. ^1H NMR Spectrum of **12** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **12** (75 MHz, CDCl_3).

Figure S9. ^1H NMR Spectrum of **1** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **1** (75 MHz, CDCl_3).

Figure S10. ^1H NMR Spectrum of **16** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **16** (75 MHz, CDCl_3).

Figure S11. ^1H NMR Spectrum of **18** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **18** (75 MHz, CDCl_3).

Figure S12. ^1H NMR Spectrum of **19** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **19** (75 MHz, CDCl_3).

Figure S13. ¹H NMR Spectrum of **20** (300 MHz, CDCl₃).

¹³C NMR Spectrum of **20** (75 MHz, CDCl₃).

Figure S14. ^1H NMR Spectrum of **15** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **15** (75 MHz, CDCl_3).

Figure S15. ¹H NMR Spectrum of **21** (300 MHz, CDCl₃).

¹³C NMR Spectrum of **21** (75 MHz, CDCl₃).

Figure S16. ¹H NMR Spectrum of **22** (300 MHz, CDCl₃).

¹³C NMR Spectrum of **22** (75 MHz, CDCl₃).

Figure S17. ¹H NMR Spectrum of **14** (300 MHz, CDCl₃).

¹³C NMR Spectrum of **14** (75 MHz, CDCl₃)

Figure S18. ^1H NMR Spectrum of **23** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **23** (75 MHz, CDCl_3).

Figure S19. ^1H NMR Spectrum of **24** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **24** (75 MHz, CDCl_3).

Figure S20. ^1H NMR Spectrum of **26** (300 MHz, CDCl_3).

^{13}C NMR Spectrum of **26** (75 MHz, CDCl_3).