Supporting Information to Accompany:

Synthesis of Cyclic and Acyclic β -Amino Acids via Chelation-Controlled 1,3-Dipolar Cycloaddition

Roger Hanselmann,* Jiacheng Zhou, Philip Ma and Pat N. Confalone

Bristol-Myers Squibb Pharma Company, Experimental Station, E336/36, P.O. Box
80336, Wilmington, DE 19880-0336

Table of Contents

	<u>Page</u>		<u>Page</u>
- General Methods	2	- ^1H and ^{13}NMR of compound 5	15
- Synthesis of 5	2	- ^1H and ^{13}NMR of compound 8	16
- Synthesis of 8	3	- ^1H and ^{13}NMR of compound 10	17
- Synthesis of 10	4	- ^1H and ^{13}NMR of compound 12	18
- Synthesis of 12	5	- ^1H and ^{13}NMR of compound 13	19
- Synthesis of 13	6	- ^1H and ^{13}NMR of compound 14	20
- Synthesis of 14	7	- ^1H and ^{13}NMR of compound 15	21
- Synthesis of 15	8	- ^1H and ^{13}NMR of compound 16	22
- Synthesis of 16	9	- ^1H and ^{13}NMR of compound 17	23
- Synthesis of 17	11	- ^1H and ^{13}NMR of compound 18	24
- Synthesis of 18	12	- ^1H and ^{13}NMR of compound 19	25
- Synthesis of 19	13	- ^1H and ^{13}NMR of compound 20	26
- Synthesis of 20	14		

General Methods: Reagents and solvents were purchased from commercial sources and utilized without further purification unless otherwise stated. Thin layer chromatography (TLC) was performed on Merck SilG 60 F254. Spots were made visible with UV light and staining with KMnO₄ solution (prepared by dissolving 3 g. KMnO₄, 20 g. K₂CO₃ and 0.5 g. NaOH in 300 ml water). HPLC was performed using an analytical column (Phenomenex, ultracarb. 5C8, 250 x 4.6mm 5 micron) and UV detection at 220 nm. The products were eluted utilizing a solvent gradient (water/ 0.1%TFA: 90% to 20% within 20 min. and acetonitrile/0.1% TFA: 10% to 80% within 20 min.).

To a suspension of (*R*)-*N*-hydroxyphenylglycinol (0.92 g, 6.02 mmol) in CH₂Cl₂ (21 ml) was added MgBr₂ (1.11 g, 6.02 mmol). After stirring the mixture for 15 min., 2-propanol (0.46 ml, 6.02 mmol) was added and after stirring for an additional 10 min. a solution of **3** (1.00 g, 5.02 mmol) in CH₂Cl₂ (5 ml) was added. The mixture was stirred at 35°C overnight, poured into 5% aqueous NaHCO₃/ice and extracted with CH₂Cl₂ (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-hexanes 1:1, to yield **5** as white crystals (1.59 g, 95%). Mp. 86-88°C; [α]_D²⁵ +90.8° (c0.472, MeOH); ¹H NMR (300 MHz, CDCl₃): δ 1.37 (9H, s), 3.09-3.27 (4H, m), 3.41-3.50 (1H, m), 3.61-3.72 (3H, m), 3.77-3.82 (1H, m), 4.04 (1H,

dd, $J = 11.7, 6.6\text{Hz}$), 4.23-4.35 (1H, m), 7.23-7.32 (5H, m); ^{13}C NMR (75 MHz, CDCl_3): δ 28.4, 45.1, 50.2, 50.9, 67.7, 69.2, 70.5, 71.8, 79.6, 128.3, 128.4, 128.9, 137.8, 154.1; IR: (KBr) 3466, 2975, 1695, 1404 cm^{-1} ; MS (ES) m/z : 335 ($\text{M}^+ + 1\text{H}$, 100%); ES-HRMS m/z : ($\text{M}^+ + 1\text{H}$) calcd. for $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_4$ 335.1971; found 335.1961.

To a suspension of *N*-hydroxyphenylglycinol (1.87 g, 12.23 mmol) in anhydrous THF (55 ml) was added anhydrous MgBr_2 (2.25 g, 12.23 mmol). The solution was stirred at room temperature for 10 min. 2-Propanol (0.94 ml, 12.23 mmol) was added and after an additional 10 min. of stirring, a solution of **7** (1.00 g, 10.19 mmol) in 6 ml anhydrous THF was added. The mixture was stirred at 65°C for 2 days, poured into 5% aqueous NaHCO_3 /ice and extracted with ethyl acetate (3x). The combined organic extract was washed with water (2x), brine (1x), dried over Na_2SO_4 and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate - hexanes 1:2, to yield **8** as beige crystals (2.25 g, 95%). Mp. 88-90°C; $[\alpha]^{25}_{\text{D}} +44.9^\circ$ (c0.350, MeOH); ^1H NMR (300 MHz, CDCl_3): δ 1.25-1.82 (6H, m), 2.91-3.03 (1H, m), 3.22 (1H, dd, $J = 9.1, 3.6\text{Hz}$), 3.34 (1H, dd, $J = 13.2, 5.5\text{Hz}$), 3.58-3.71 (2H, m), 3.87 (1H, dd, $J = 7.3, 3.0\text{Hz}$), 4.04-4.12 (1H, m), 7.26-7.33 (5H, m); ^{13}C NMR (75 MHz, CDCl_3): δ 25.3, 32.5, 33.7, 47.2, 68.6, 70.6, 71.3, 72.7, 128.0, 128.4, 128.7, 138; IR: (KBr) 3329,

2948, 1062 cm^{-1} ; MS (AP) m/z : 234 ($\text{M}^+ + 1\text{H}$, 100%); ES-HRMS m/z : ($\text{M}^+ + 1\text{H}$) calcd. for $\text{C}_{14}\text{H}_{20}\text{NO}_2$ 234.1495; found 234.1496.

To a suspension of *N*-hydroxyphenylglycinol (1.84 g, 11.99 mmol) in anhydrous CH_2Cl_2 (55 ml) was added anhydrous MgBr_2 (2.21 g, 11.99 mmol). The suspension was stirred at room temperature for 10 min.. 2-Propanol (0.92 ml, 11.99 mmol) was added and after an additional 10 min. of stirring, a solution of **9** (1.00 g, 9.99 mmol) in anhydrous CH_2Cl_2 (5 ml) was added. The mixture was stirred at 40°C for 1h, poured into 5% aqueous NaHCO_3 /ice and extracted with CH_2Cl_2 (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na_2SO_4 and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-hexanes 4:1, to yield **10** as white crystals (2.1 g, 89%). Mp. 65-67°C; $[\alpha]_D^{25} +33.1^\circ$ (c0.464, MeOH); ^1H NMR (300 MHz, CDCl_3): δ 3.02 (1H, dd, $J = 8.7, 4.4\text{Hz}$), 3.17-3.25 (1H, m), 3.46 (1H, d, $J = 4.8\text{Hz}$), 3.64-3.82 (4H, m), 3.89 (1H, dd, $J = 6.9, 3.3\text{Hz}$), 4.07-4.15 (1H, m), 4.04-4.12 (1H, m), 4.29 (1H, dd, $J = 8.8, 7.4\text{Hz}$), 7.29-7.38 (5H, m); ^{13}C NMR (75 MHz, CDCl_3): δ 48.4, 68.1, 70.8, 71.2 (2x), 73.1, 73.3, 128.4, 128.9, 137.8; IR: (KBr) 3438, 2863, 704 cm^{-1} ; MS (ES) m/z : 236 ($\text{M}^+ + 1$, 100%); ES-HRMS m/z : ($\text{M}^+ + 1$) calcd. for $\text{C}_{13}\text{H}_{18}\text{NO}_3$ 236.1286; found 236.1289.

To a suspension of *N*-hydroxyphenylglycinol (567 mg, 3.7 mmol) in anhydrous THF (18 ml) was added anhydrous MgBr₂ (681 mg, 3.7 mmol). The solution was stirred at room temperature for 10 min.. 2-Propanol (0.28 ml, 3.7 mmol) was added and after an additional 10 min. of stirring, 2-allyloxybenzaldehyde (500 mg, 3.08 mmol) was added. The mixture was stirred at 65°C for 5 days, poured into 5% aqueous NaHCO₃/ice and extracted with ethyl acetate (3x). The combined organic extract was washed with water (2x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate - hexanes 1:1, to yield **12** as beige crystals (759 mg, 83%). Mp. 137-140°C; [α]²⁵_D +7.3° (c0.301, MeOH); ¹H NMR (300 MHz, CDCl₃): δ 3.16-3.26 (2H, m), 3.74 (1H, d, *J*= 11Hz), 3.97-4.03 (2H, m), 4.05-4.22 (4H, m), 4.45 (1H, dd, *J*= 9.8, 7.6Hz), 6.76 (1H, dd, *J*= 8.1, 1.1Hz), 6.86-6.92 (1H, m), 7.06-7.14 (2H, m), 7.30-7.49 (5H, m); ¹³C NMR (75 MHz, CDCl₃): δ 39.7, 60.4, 64.7, 68.0, 68.1, 69.4, 116.8, 121.8, 122.7, 128.4, 128.6, 128.7, 129.2, 130.0, 138.5, 155.9; IR: (KBr) 3524, 1488, 1248cm⁻¹; MS (ES)*m/z* : 298 (M⁺+1H, 100%); ES-HRMS *m/z* : (M⁺+1H) calcd. for C₁₈H₂₀NO₃ 298.1440; found 298.1444.

A solution of aqueous 37 wt% formaldehyde (0.56 ml, 7.18 mmol), *N*-hydroxy-phenylglycinol (1.00 g, 6.53 mmol) in EtOH (10 ml) was stirred over night at room temperature, evaporated, dissolved in CH₂Cl₂ and washed with brine (1x), dried over Na₂SO₄ and evaporated. The residue was dissolved in THF (33 ml), anhydrous MgBr₂ (1.20 g, 6.53 mmol) added and stirred for 15 min. at room temperature. To the mixture was added allyl alcohol (0.44 ml, 6.53 mmol), stirred at 40°C for 2h, poured into 5% aqueous NaHCO₃/ice and extracted with ethyl acetate (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-MeOH 95:5, yielding **13** as a clear oil (1.31 g, 90%). $[\alpha]^{25}_{\text{D}} -12.8^{\circ}$ (c0.268, MeOH); ¹H NMR (300 MHz, CDCl₃): δ 2.06-2.20 (2H, m), 2.89-3.02 (1H, m), 3.55-3.87 (5H, m), 4.05-4.15 (1H, m), 4.16-4.24 (1H, m) 7.27-7.36 (5H, m); ¹³C NMR (75 MHz, CDCl₃): δ 29.4, 54.0, 63.5, 67.6, 73.1, 79.5, 128.1, 128.7(2x), 138.2; IR: (neat) 3373, 2934, 2879, 1044cm⁻¹; MS (ES)*m/z* : 224 (M⁺+1H, 100%); ES-HRMS *m/z* : (M⁺+1H) calcd. for C₁₂H₁₈NO₃ 224.1286; found 224.1298.

To a suspension of *N*-hydroxyphenylglycinol (500 mg, 3.26 mmol) in anhydrous THF (16 ml) was added anhydrous MgBr₂ (601 mg, 3.26 mmol). After stirring for 10 min. at room temperature, 2-propanal (0.26 ml, 3.59 mmol) was added and after an additional 10 min. of stirring, allyl alcohol (0.24 ml, 3.59 mmol) was added. The mixture was stirred at 65°C for 3 days, poured into 5% aqueous NaHCO₃/ice and extracted with ethyl acetate (2x). The combined organic extract was washed with water (2x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-MeOH 95:5, to yield **14** as a clear oil (770 mg, 94%). $[\alpha]^{25}_{\text{D}} -16.2^{\circ}$ (c0.424, MeOH); ¹H NMR (600 MHz, CDCl₃): δ 0.98 (3H, t, *J*= 7.4Hz), 1.40-1.47 (1H, m), 1.65-1.71 (1H, m), 2.01 (1H, ddd, *J*= 12.3, 7.1, 1.2Hz), 2.67 (1H, ddd, *J*= 12.3, 9.7, 6.5), 3.21 (1H, dd, *J*= 14.0, 7.1Hz), 3.81 (1H, dd, *J*= 12.4, 2.5Hz), 3.92-4.01 (3H, m), 4.12 (1H, dd, *J*= 12.4, 2.5Hz), 4.26 (1H, t, *J*= 7.0Hz), 4.45-4.48 (2H, m), 7.47-7.56 (5H, m); ¹³C NMR (75 MHz, CDCl₃): δ 11.1, 26.8, 32.6, 62.4, 65.9, 69.0, 71.9, 81.2, 128.1, 128.7, 128.9, 138.8; IR: (neat) 3362, 2960, 2934, 2875, 1453cm⁻¹; MS (ES)*m/z* : 252 (*M*⁺+1H, 100%); ES-HRMS *m/z* : (*M*⁺+1H) calcd. for C₁₄H₂₂NO₃ 252.1600; found 252.1591.

To a solution of **5** (500 mg, 1.5 mmol) in MeOH (25 ml) was added 20 wt.% Pd(OH)₂ on carbon (500 mg). The mixture was hydrogenated at 1 atm. over night, filtered over Hyflo and evaporated. The residue was dissolved in THF-water 2:1 (15 ml), NaHCO₃ (314 mg, 3.74 mmol) and benzyl chloroformate (0.24 ml, 1.65 mmol) was added at 0°C. The mixture was stirred at room temperature over night, poured into 1M HCl/ice and extracted with ethyl acetate (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate - hexanes 2:1, to yield the alcohol as white crystals (375 mg, 72%). Mp. 90-92°C; [α]_D²⁵ -7.0° (c0.388, MeOH); ¹H NMR (300 MHz, CDCl₃): δ 1.44 (9H, s), 2.43-2.61 (1H, m), 2.80-2.96 (1H, m), 3.33-3.78 (6H, m), 4.23-4.38 (1H, m), 5.13 (2H, s), 5.18-5.31 (1H, m), 7.32-7.40 (5H, m); ¹³C NMR of major rotamer (75 MHz, CDCl₃): δ 28.5, 45.1, 46.2, 51.3, 52.2, 59.7, 67.5, 79.9, 128.3, 128.5, 128.7, 135.9, 154.4, 157.5; IR: (KBr) 3308, 2975, 1693cm⁻¹; MS (AP)*m/z* : 351 (M⁺+1H, 100%); ES-HRMS *m/z* : (M⁺+1H) calcd. for C₁₈H₂₇N₂O₅ 351.1920; found 351.1904.

To a mixture of the alcohol (100 mg, 0.285 mmol) in MeCN (3 ml) and sodium phosphate buffer (1.7 ml, 0.67 M, pH 6.7) was added Tempo (4.45 mg, 0.029 mmol), aqueous NaClO₂ solution (97 mg 80%, 0.856 mmol in 0.6 ml water) and dilute bleach

(0.2 ml of a 0.5 % aqueous solution) at 35°C. The mixture was stirred at 35°C for 6h, at room temperature over night and quenched with ice/water (15 ml). The pH was adjusted to 8.5 with 1N NaOH and 0.5M Na₂SO₃ (2 ml) was added. The aqueous mixture was washed with ethyl acetate (1x) and acidified with conc. HCl and extracted with ethyl acetate (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na₂SO₄ and evaporated, to yield **15** as white crystals (99 mg, 95%). Mp. 124-127°C (dec.); [α]²⁵_D -16.7° (c0.388, MeOH); ¹H NMR (300 MHz, d-DMSO at 90°C): δ 1.40 (9H, s), 3.17-3.24 (2H, m), 3.40-3.51 (2H, m), 3.56 (1H, dd, J = 11.0, 7.5Hz), 4.33-4.40 (1H, m), 5.04 (2H, s), 7.21-7.26 (1H, m), 7.27-7.37 (5H, m), 12.41 (1H, br.s); ¹³C NMR (75 MHz, d-DMSO at 90°C): δ 27.8, 45.7, 50.4, 51.2 (br.), 65.1, 78.0, 127.1, 127.2, 127.8, 136.7, 153.1, 155.2, 171.0; IR: (KBr) 2975, 1748, 1672cm⁻¹; MS (ES) m/z : 365 (M⁺+1H, 100%); ES-HRMS m/z : (M⁺+1H) calcd. for C₁₈H₂₅N₂O₆ 365.1712; found 365.1721.

To a solution of **8** (700 mg, 3.0 mmol) in MeOH (48 ml) was added 20 wt.% Pd(OH)₂ on carbon (800 mg). The mixture was hydrogenated at 1 atm. over night, filtered over Hyflo, evaporated and purified through a plug of silica gel, eluting with ethyl acetate-hexanes 2:1 then MeOH. The residue was dissolved in THF-water 2:1 (30 ml). NaHCO₃ (630 mg, 7.5 mmol) and di-*t*-butyl dicarbonate (721 mg, 3.3 mmol) was added at 0°C. The

mixture was stirred at room temperature over night, poured into 1M HCl/ice, and extracted with ethyl acetate (3x). The combined organic extract was washed with water (2x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-hexanes 1:2, to yield the alcohol as white crystals (450 mg, 70%). Mp. 131-134°C; [α]²⁵_D -26.4° (c0.386, MeOH); ¹H NMR (300 MHz, CDCl₃): δ 1.06-1.17 (1H, m), 1.46 (9H, s), 1.48-1.78 (3H, m), 1.93-2.04 (1H, m), 2.07-2.20 (1H, m), 3.35-3.43 (1H, m), 3.54-3.63 (1H, m), 3.94-3.98 (1H, m), 4.07-4.13 (1H, m), 4.51-4.59 (1H, m); ¹³C NMR (75 MHz, CDCl₃): δ 21.7, 24.8, 28.4, 32.3, 48.1, 52.9, 62.3, 80.1, 157.2; IR: (KBr) 3277, 2975, 1673, 1541 cm⁻¹; MS (AP)*m/z* : 216 (M⁺+1H, 85%); ES-HRMS *m/z* : (M⁺+1H) calcd. for C₁₁H₂₂NO₃ 216.1600; found 216.1595.

To a solution of the alcohol (126 mg, 0.585 mmol) in MeCN-water 1:1 (8 ml) was added RuCl₃-hydrate (6 mg, 0.029 mmol) and NaIO₄ (376 mg, 1.755 mmol) at 0°C. The mixture was stirred at room temperature for 2h, poured into 5% aqueous NaHCO₃/ice and extracted with ethyl acetate (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na₂SO₄ and decolorized with activated carbon (*ca.* 5 mg), filtered over Hyflo and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-MeOH 95:5, to yield **16** as white crystals (110 mg, 82%). Mp. 124-127°C; [α]²⁵_D -25.2° (c0.544, CHCl₃). Compound **16** had the same spectroscopic properties as reported.

To a solution of **10** (500 mg, 2.13 mmol) in MeOH (20 ml) was added 20 wt.% Pd(OH)₂ on carbon (600 mg). The mixture was hydrogenated at 1 atm. over night, filtered over Hyflo and evaporated. The residue was dissolved in THF-water 2:1 (15 ml). NaHCO₃ (446 mg, 5.31 mmol) and benzyl chloroformate (0.34 ml, 2.34 mmol) was added at 0°C. The mixture was stirred at room temperature over night, poured into 1M HCl/ice and extracted with ethyl acetate (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-hexanes 2:1, to yield the alcohol as white crystals (350 mg, 66%). Mp. 107-109°C; $[\alpha]_D^{25}$ -14.0° (c0.394, MeOH); ¹H NMR (300 MHz, CDCl₃): δ 2.58-2.75 (1H, m), 3.35-3.43 (2H, m), 3.48-3.68 (2H, m), 3.74 (1H, dd, *J*= 9.5, 1.4Hz), 3.88-3.95 (2H, m), 4.30-4.39 (1H, m), 5.14 (2H, s), 5.29-5.32 (1H, m), 7.32-7.41 (5H, m); ¹³C NMR (75 MHz, CDCl₃): δ 46.5, 53.4, 59.6, 67.4, 67.7, 73.4, 128.3, 128.4, 128.6, 136.0, 157.5; IR: (KBr) 3294, 1702, 1555cm⁻¹; MS (AP)*m/z* : 252 (M⁺+1H, 100%); ES-HRMS *m/z* : (M⁺+1H) calcd. for C₁₃H₁₈NO₄ 252.1235; found 252.1230.

To a mixture of the alcohol (100 mg, 0.398 mmol) in MeCN (3 ml) and sodium phosphate buffer (1.5 ml, 0.67 M, pH 6.7) was added Tempo (3.73 mg, 0.024 mmol), aqueous NaClO₂ solution (135 mg 80%, 1.19 mmol in 0.6 ml water) and dilute bleach (0.2 ml of a 0.5% aqueous solution) at 35°C. The mixture was stirred at 35°C for 7h, at room temperature over night and quenched with ice/water (15 ml). The pH was adjusted

to 8.5 with 1N NaOH and 0.5M Na₂SO₃ (2 ml) was added. The aqueous mixture was washed with ethyl acetate (1x) and acidified with conc. HCl and extracted with ethyl acetate (2x). The combined organic extract was washed with water (1x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was crystallized with ethyl acetate-hexanes 1:3 (4 ml), filtered and dried under vacuum, to yield **17** as white crystals (101 mg, 96%). Mp. 177-179°C; [α]_D²⁵ -44.4° (c0.408, MeOH); ¹H NMR (300 MHz, d-DMSO): δ 3.15-3.24 (1H, m), 3.53 (1H, dd, J = 8.8, 4.7Hz), 3.87-3.95 (3H, m), 4.40-4.49 (1H, m), 5.02 (1H, d, J = 13.3Hz), 5.03 (1H, d, J = 13.3Hz), 7.29-7.39 (5H, m), 7.56 (1H, d, J = 8.4Hz), 12.42 (1H, br.s); ¹³C NMR (75 MHz, d-DMSO): δ 48.1, 53.3, 65.8, 68.5, 72.3, 128.1, 128.2, 128.8, 137.5, 156.2, 171.9; IR: (KBr) 3245, 1741, 1685, 1565cm⁻¹; MS (AP) m/z : 266 (M⁺+1H, 100%); ES-HRMS m/z : (M⁺+1H) calcd. for C₁₃H₁₆NO₅ 266.1028; found 266.1011.

To a solution of **13** (300 mg, 1.34 mmol) in MeOH (15 ml) was added 20 wt.% Pd(OH)₂ on carbon (300 mg). The mixture was hydrogenated at 1 atm. over night, filtered over Hyflo and evaporated. The residue was dissolved in THF-water 2:1 (9 ml), NaHCO₃ (198 mg, 2.35 mmol) and benzyl chloroformate (0.20ml, 1.41 mmol) was added at 0°C. The mixture was stirred at room temperature over night, poured into 1M HCl/ice and extracted with ethyl acetate (2x). The combined organic extract was washed with water

(1x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-MeOH 95:5, to yield **18** as white crystals (194 mg, 61%). Mp. 64-66°C; $[\alpha]^{25}_{\text{D}} +1.3^{\circ}$ (c0.482, CHCl₃); **18** had the same spectroscopic properties as reported.

To a solution of **14** (300 mg, 1.19 mmol) in MeOH (15 ml) was added 20 wt.% Pd(OH)₂ on carbon (200 mg). The mixture was hydrogenated at 1 atm. over night, filtered over Hyflo and evaporated. The residue was dissolved in THF-water 2:1 (15 ml), NaHCO₃ (251 mg, 2.98 mmol) and di-*t*-butyl dicarbonate (287 mg, 1.31 mmol) was added at 0°C. The mixture was stirred at room temperature over night, poured into 1M HCl/ice, and extracted with ethyl acetate (3x). The combined organic extract was washed with water (2x), brine (1x), dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate-MeOH 95:5, to yield the alcohol as white crystals (190 mg, 68%). Mp. 70-72°C; $[\alpha]^{25}_{\text{D}} -6.2^{\circ}$ (c0.478, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃): δ 0.96 (3H, t, *J*= 7.5Hz), 1.16-1.25 (1H, m), 1.45 (9H, s), 1.46-1.63 (2H, m), 2.37 (1H, dd, *J*= 8.3, 3.8Hz), 3.42-3.61 (2H, m), 3.63-3.79 (2H, m), 4.42 (1H, d, *J*=9.1Hz), 4.49 (1H, d, *J*= 3Hz); ¹³C NMR (75 MHz, CDCl₃): δ 10.8, 28.4, 28.8, 40.0, 48.9, 66.6, 68.5, 80.2, 157.5; IR: (KBr) 3342, 2968, 2934, 1685cm⁻¹; MS

(AP) m/z : 234 (M^++1H , 100%); CI-HRMS m/z : (M^++1H) calcd. for $C_{11}H_{24}NO_4$ 234.1705; found 234.1696.

To a solution of the alcohol (84.7 mg, 0.36 mmol) in MeCN-water 1:1 (7 ml) was added $RuCl_3$ -hydrate (3.7 mg, 0.018 mmol) and $NaIO_4$ (385 mg, 1.80 mmol) at 0°C. The mixture was stirred at room temperature for 45 min., poured into 5% aqueous $NaHCO_3$ /ice and extracted with ethyl acetate (3x). The combined organic extract was washed with water (1x), brine (1x), dried over Na_2SO_4 and decolorized with activated carbon (*ca.* 5 mg), filtered over Hyflo and evaporated, yielding **19** as white crystals (72 mg, 92%). Mp. 88-89°C; $[\alpha]^{25}_D$ -22.9° (c0.380, CH_2Cl_2); **19** had the same spectroscopic properties as reported.

To a solution of **12** (390 mg, 1.31 mmol) in AcOH (11 ml) was added 20 wt.% $Pd(OH)_2$ on carbon (300 mg). The mixture was hydrogenated at 1 atm. over night, filtered over Hyflo and evaporated. The residue was dissolved twice in toluene (2x10 ml) and evaporated. The residue was purified by flash column chromatography on silica gel, eluting with ethyl acetate - hexanes 1:1, to yield **20** as white crystals (118 mg, 55%). $[\alpha]^{25}_D$ $+17.2^\circ$ (c0.312, MeOH); **20** had the same spectroscopic properties as reported.

^1H and ^{13}C NMR of compound 5:

^1H and ^{13}C NMR of compound **8**:

^1H and ^{13}C NMR of compound **10**

^1H and ^{13}C NMR of compound **12**

^1H and ^{13}C NMR of compound **13**

^1H and ^{13}C NMR of compound **14**

^1H and ^{13}C NMR of compound **15** (at 90C in DMSO-d)

^1H and ^{13}C NMR of compound **16**

^1H and ^{13}C NMR of compound **17**

^1H and ^{13}C NMR of compound **18**

^1H and ^{13}C NMR of compound **19**

^1H and ^{13}C NMR of compound **20**