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Rapid Communication

Synthesis of two novel chiral building blocks for *anti*- and *syn*-1,3-diols

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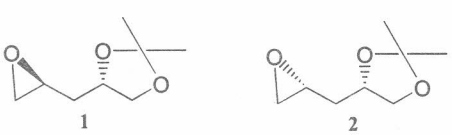
Two novel chiral building blocks **1** and **2** for *anti*- and *syn*-1,3-diols have been synthesized starting from the readily available and inexpensive D-(+)-xylose.

Many natural compounds such as polyene macrolide antibiotics and 1α,25-dihydroxyvitamin D_3 analogues contain 1,3-diol units.[1-4] This unit is synthesized usually from the chiral building block of 1,3-diol[1], the synthesis of which has attracted much interest in recent years[2,5]. Herein, we report the synthesis of two novel chiral building blocks **1** and **2** starting from the readily available and inexpensive D-(+)-xylose. The synthetic routes are outlined in **Scheme I** and **Scheme II**.

D-(+)-Xylose **3** was converted to diacetyllactone **5** by a modified Bock's method[6]. Reduction of **5** with BH_3 in THF gave a known tetraol **6**[7], where a pair of 1,3-dihydroxy groups was protected with 2,2-dimethoxypropane to give the acetonide **7**. The acetonide **7** was treated with TsCl and NaOH to afford the first target compound **1**(**Scheme I**)

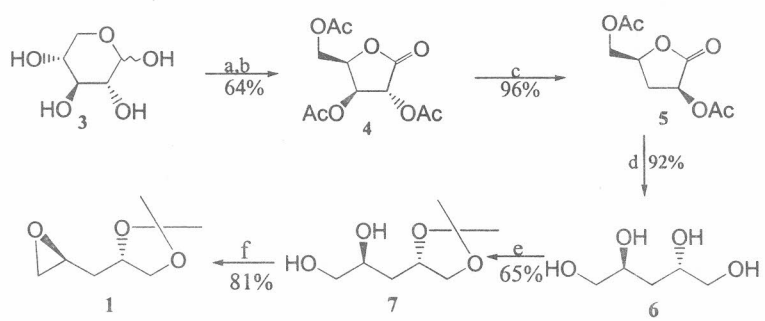
We then turned our attention to the synthesis of the second target **2** (**Scheme II**). The primary hydroxy group of **7** was protected with TBDPSCl to yield silyl ether **8**, which was tosylated with TsCl to give **9**. The compound **9** was finally treated with TBAF to afford the second target compound **2**.



Experimental Section

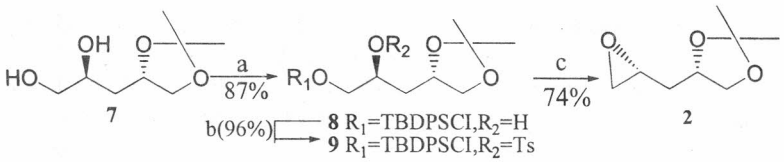
General. Melting points reported are uncorrected. Optical rotations were determined on a Perkin-Elmer model 241 polarimeter. Elemental analyses were carried out using a model Carbo-Erba 1106 analyser. IR spectra were recorded on a Beckman IR-4230 spectrometer. H^1 NMR spectra recorded on a Brucker AM 500 spectrometer at 500 MHz using TMS as internal standard. Mass spectra were recorded on HP 5988 spectrometer.

(3*R*,4*S*,5*R*)-3,4-Diacetoxy-5-acetoxymethyl-2-tetrahydrofuranone 4. To D(+)-xylose (7.5 g, 50 mmoles) in 80 mL H_2O were added dropwise K_2CO_3 (15 g,110 mmoles) in 20 mL H_2O and Br_2 (16 g, 100 mmoles) by two dropping funnels alternately in 30 min to keep *p*H 6-9 during addition. After stirring at room temperature for 22 hr, the reaction



(a) Br_2, K_2CO_3, H_2O,room temperature, 22 hr. (b) AcOH, Ac_2O, 50-55 °C, 24 hr. (c) Pd/C, H_2, AcOEt, Et_3N, room temperature, 24 hr. (d)BH_3, THF, room temperature, 36 hr. (e) 2,2-Dimethoxypropane,Camphorsulfonic acid, Acetone,. 0 °C, 2.5 hr. (f) TsCl, NaOH, THF, room temperature, 4 hr.

Scheme I



(a) TBDPSCl, Imid., DMF, room temperature, 8 hr. (b) TsCl, Et_3N, DMAP, CH_2Cl_2, room temperature, 48 hr. (c) TBAF, THF, room temperature, 9 hr.

Scheme II

solution was concentrated to give a light brown residue. The residue was added to 60 mL of HOAc-Ac_2O (1:5) . The reaction mixture was heated to 50-55 °C, and then stirred for another 24 hr. Usual work-up and purification afforded 8.72 g of **4** as a white solid in 64 % yield, mp 95-96 °C; $[\alpha]_D^{20}$ +71.9° (*c* 2.39, $CHCl_3$), {lit.[6] mp 94-95 °C; $[\alpha]^{20}{}_D$ +71.8° (*c* 3.0, $CHCl_3$)}; IR(KBr): 2963, 1805, 1749, 1372, 1221, 1074 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.67 (1H, d, *J* = 7.9 Hz), 5.60 (1H; t, *J* = 7.9 Hz), 5.00 (1H, ddd, *J* = 2.9,7.9,7.9 Hz), 4.36 (1H, dd, *J* = 2.9, 13.9 Hz), 4.25 (1H, dd, *J* = 2.9, 13.9 Hz), 2.18 (3H, s), 2.10 (3H, s), 2.09 (3H, s).

(3*S*, 5*S*)-3-Acetoxy-5-acetoxymethyl-2-tetrahydrofuranone 5. To a solution of **4** (6.15 g, 22.44 mmoles) in 60 mL dry EtOAc and 30 mL Et_3N was added 1.2g 10% Pd/C. The mixture was hydrogenated with a balloon with H_2 at room temperature for 24 hr. Usual work-up and purification afforded 4.67 g of **5** as a white solid in 96% yield, mp 70-71 °C; $[\alpha]_D^{20}$ +53.9° (*c* 2.67, $CHCl_3$) {lit.[6] mp 69-71 °C, $[\alpha]_D^{20}$ +51.2° (*c* 1.3, $CHCl_3$)}; IR(KBr): 2954, 1792, 1745, 1438, 1375, 1231, 1197, 1104, 1019 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.50 (1H, dd, *J* = 8.8, 10.3 Hz), 4.68 (1H, m, 10 lines), 4.38 (1H, dd, *J* = 3.1, 12.5 Hz), 4.19 (1H, dd, *J* = 5.9, 12.5 Hz), 2.79 (1H, ddd, *J* = 5.9, 8.9, 12.5 Hz), 2.18 (3H, s), 2.10 (3H, s), 2.05 (1H, m).

(2*S*,4*S*)-Pentane-1,2,3,4-tetraol 6. To a solution of **5** (3 g, 13.89 mmoles) in 50 mL THF was added dropwise BH_3 in THF (83 mL, 83 mmoles). The reaction mixture was stirred at 56-60 °C for 36 hr. Usual work-up and purification afforded 1.74g of **6** as a white solid in 92 % yield, mp 106-107 °C; $[\alpha]_D^{20}$ –48.1° (*c* 1.39, CH_3OH), {lit.[7] mp 106-107 °C; $[\alpha]_D^{20}$ –46° (*c* 1.03, CH_3OH)}; ^1H NMR (D_2O): δ 3.92 (2H, m), 3.58 (2H, dd, *J* = 3.76, 13.6 Hz), 3.48 (2H, dd, *J* = 6.8, 11.7 Hz), 1.50 (2H, dd, *J* = 5.8, 7.2 Hz).

(2'*S*, 5*S*)-5-(2',3'-Dihydroxypropyl)-2,2-dimethyl-1,3-dioxane 7. To a solution of **6** (400 mg, 2.94 mmoles) in 4 mL acetone and 4 mL 2,2-dimethoxypropane was added 60 mg camphorsulfonic acid at 0 °C. The reaction mixture was stirred at room temperature for 2.5 hr. Work-up and purification afforded 336 mg of **7** as a colourless oil in 65 % yield; $[\alpha]_D^{20}$ –3.75° (*c* 0.39, $CHCl_3$). Anal. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15%. Found: C, 54.55; H, 9.12; IR(neat): 3404, 2987, 2936, 1381, 1220, 1158, 1056 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.35 (1H, m), 4.10 (1H, dd, *J* = 6.0, 8.0 Hz), 3.92 (1H, m), 3.69 (1H, m), 3.58 (1H, dd, *J* = 8.0, 8.0 Hz), 3.50 (1H, m), 2.73 (1H, d, *J* = 4.5 Hz ,D_2O, exchangeable), 2.15 (1H, t, *J* = 5.8 Hz, D_2O, exchangeable), 1.76 (1H, ddd, *J* = 4.1, 8.7, 14.2 Hz), 1.68 (1H, ddd, *J* = 3.7, 7.9, 14.2 Hz), 1.42 (3H, s), 1.36 (3H, s); MS: m/z 177(M^+ + 1, 2 %), 161 (100), 145 (15), 119 (20), 101 (70), 83 (20).

(2'*S*, 5*S*)-2, 2-Dimethyl-5-(2', 3'-epoxypropyl)-1, 3-dioxane 1. To a suspension of NaH (48 mg, 2 mmoles) in 4 mL THF was added dropwise **7** (176 mg, 1 mmole) in 1 mL THF . After stirring at room temperature for 1 hr, TsCl (209 mg, 1.1 mmoles) was added at 0 °C, and the reaction mixture stirred at room temperature for another 4 hr. Usual work-up and purification yielded 128 mg of **1** as a colourless oil in 81 % yield; $[\alpha]_D^{20}$ –17.9° (*c* 1.10, $CHCl_3$). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92 %. Found: C, 60.78; H, 8.96 %; IR(neat): 2987, 2936, 1370, 1215, 1158, 1056 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.27 (1H, m), 4.12 (1H, dd, *J* = 6.0, 8.0 Hz), 3.56 (1H, dd, *J* = 7.3, 8.0 Hz), 3.02 (1H, m), 2.82 (1H, dd, *J* = 4.7, 4.7 Hz), 2.51 (1H, dd, *J* = 2.7, 4.7 Hz), 1.98 (1H, ddd, *J* = 4.0, 7.5, 14.0 Hz), 1.55 (1H, ddd, *J* = 5.4, 7.6, 14.0 Hz), 1.42 (3H, s), 1.36 (3H, s); MS: m/z 159(M^+ + 1, 20 %), 143 (100), 135 (20), 127 (5), 113 (10), 87 (5).

(2'*S*, 5*S*)-2, 2-Dimethyl-5,3'-diphenyl-*t*-butylsilyl-oxy-2'-hydroxyl-1,3-dioxane 8. To a solution of **7** (125 mg, 0.71 mmole) and imid.(198 mg, 2.92 mmoles) in 4 mL dry DMF was added dropwise TBDPSCl (220 mg, 0.8 mmoles) at 0 °C. The reaction mixture was stirred at room temperature for 8 hr. On usual work-up and purification it gave 255 mg of **8** as a colourless oil in 87% yield; $[\alpha]_D^{20}$ +1.30° (*c* 1.10, $CHCl_3$). Anal. Calcd for $C_{24}H_{34}O_4Si$: Found: C, 69.48; H, 8.31 %; IR(neat): 3440, 2932, 1427, 1110, 824, 740, 702 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.64 (4H, m), 7.40 (6H, m), 4.30 (1H, m), 4.05 (1H, dd, *J* = 6.0, 8.1 Hz), 3.92 (1H, m), 3.67 (1H, dd, *J* = 4.0, 10.1 Hz), 3.50 (2H, m), 2.64 (1H, d, *J* = 3.8 Hz, D_2O, exchangeable), 1.65 (2H, m), 1.42 (3H, s), 1.35 (3H, s), 1.07 (9H, s); MS: m/z 399(M^+ – 15, 3%), 357 (2), 299 (5), 221 (70), 199 (100), 139 (40).

(2'*S*, 5*S*)-2, 2-Dimethyl-5-[3'-(diphenyl- *t* –butyl - silyloxy)-2'-tolylsulfonyloxy]-1,3-dioxane 9. To a solution of **8**(190 mg, 0.46 mmoles), DMAP (10 mg) and 1.5 mL Et_3N in 4 mL CH_2Cl_2 was added TsCl(396 mg, 2 mmoles). The reaction mixture was stirred at room temperature for 48

hr. On usual work up it gave 250 mg of **9** as a colourless oil in 96% yield; $[\alpha]_D^{20}$ –29.66° (*c* 1.00, $CHCl_3$). Anal. Calcd for $C_{31}H_{40}O_6SSi$: C, 65.46; H, 7.09. Found: C, 65.50; H, 7.11 %; IR(neat): 2931, 1407, 1368, 1176, 1112, 1062, 893, 815, 742, 703 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.22-7.70 (14H, m), 4.71 (1H, m), 3.98 (2H, m), 3.70 (2H, ddd, *J* = 4.9, 11.0, 15.3 Hz), 3.48 (1H, dd, *J* = 6.9, 7.4 Hz), 2.40 (3H, s), 1.91 (2H, dd, *J* = 6.4, 6.4 Hz), 1.38 (3H, s), 1.22 (3H, s), 1.02 (9H, s); MS: m/z 553(M^+ – 15, 4 %), 353 (100), 293 (30), 199 (35), 141(70), 101 (70), 83 (20).

(2'*R*, 5*S*)-2,2-Dimethyl-5-(2', 3'-epoxypropyl)-1, 3-dioxane(2). To a solution of **9** (235 mg, 0.41 mmole) in 1 mL THF was added dropwise TBAF (3 mL, 1*M* in THF) at room temperature. The reaction mixture was stirred at room temperature for 9 hr. On usual work-up and purification gave 48 mg of **2** as a colourless oil in 74 % yield; $[\alpha]_D^{20}$ +19.58° (*c* 1.90, $CHCl_3$). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.71; H, 8.89 %; IR(neat): 2986, 1370, 1215, 1157, 1056 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.21 (1H, m), 4.09 (1H, dd, *J* = 5.8, 8.0 Hz), 3.63 (1H, dd, *J* = 8.0, 8.0 Hz), 3.04 (1H, m), 2.75 (1H, dd, *J* = 4.7, 4.7 Hz), 2.52 (1H, dd, *J* = 2.8, 4.7 Hz), 1.85 (2H, m), 1.41 (3H, s), 1.34 (3H, s); MS: m/z 159(M^+ + 1, 30%), 143 (100), 135 (10), 127 (5), 113 (10), 87 (5).

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