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A Short Route to Homochiral *D*- and *L*-Hexose Precursors from (*R*)-Methyl-*p*-Tolylsulfoxide

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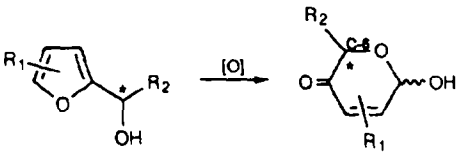
Abstract: Homochiral *D*- and *L*-hexose precursors have been prepared in good overall yield from (*R*)-methyl-*p*-tolylsulfoxide as the sole asymmetric inductor. The process involves sequential condensation of the sulfoxide with ethyl 2-furancarboxylate, stereoselective sulfoxide-monitored carbonyl reduction, Pummerer rearrangement of the sulfinyl group, reduction of the resulting aldehydes and ring-oxidation of the corresponding furfuryl alcohols.

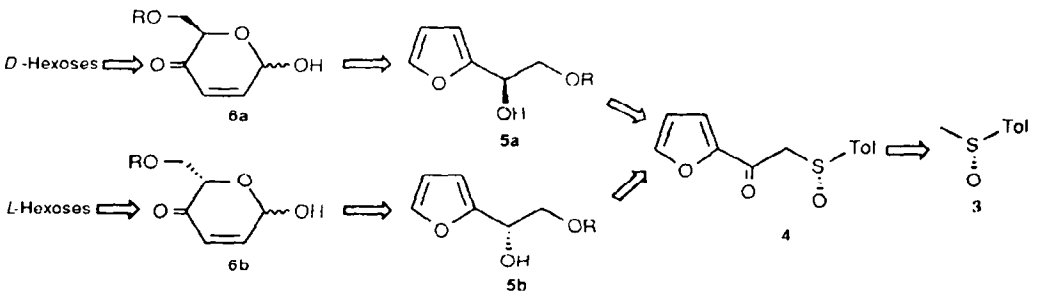
It is well known that when furylcarbinols of general structure **1** are treated with any of several oxidizing agents such as peracids[1a], PCC[1b] and Br_2[1c,d], the furan ring undergoes an oxidation-rearrangement sequence producing the hydropyranone derivative **2**. This protocol has been successfully used for the construction of various natural products including carbohydrates[2], macrolides and related compounds[3], pheromones[4] and alkaloids[5]. The key feature of the *furan approach* to the synthesis of natural products relies upon the preparation of an optically pure furylcarbinol whose stereochemistry at the hydroxylic carbon atom will be further transferred to the C-6 center in the hydropyranone nucleus (Scheme 1). Although many methods to prepare optically active 2-furylcarbinols have been described[6], some of the current strategies suffer from limitations in the easy access to the two possible enantiomers of the furfuryl alcohol. Here we report a new method for the synthesis of both enantiomers of optically active furylcarbinols which employs (*R*)-methyl-*p*-tolylsulfoxide as the sole chiral auxiliary. This strategy has been applied to the synthesis of *D*- and *L*-hexose precursors.



1 **2**

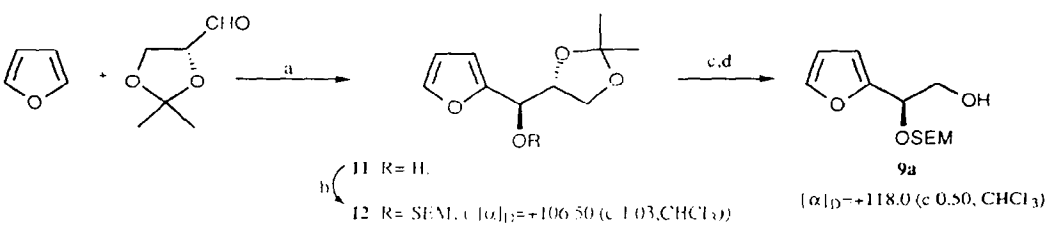
Scheme 1

The essential features of our protocol are summarized in the antithetic sequence depicted in Scheme 2 wherein chiral β-ketosulfoxide **4** was envisaged as the key intermediate. The two precursors of *D*- and *L*-hexoses, **6a** and **6b**, would be obtained (by oxidation of the furan ring) from the two possible enantiomers of monoprotected diols **5a** and **5b**, which are derived from the same ketosulfoxide **4** by sequential enantioselective reduction of the prochiral keto group, desulfuration by a Pummerer type rearrangement, and reduction of the corresponding aldehyde.



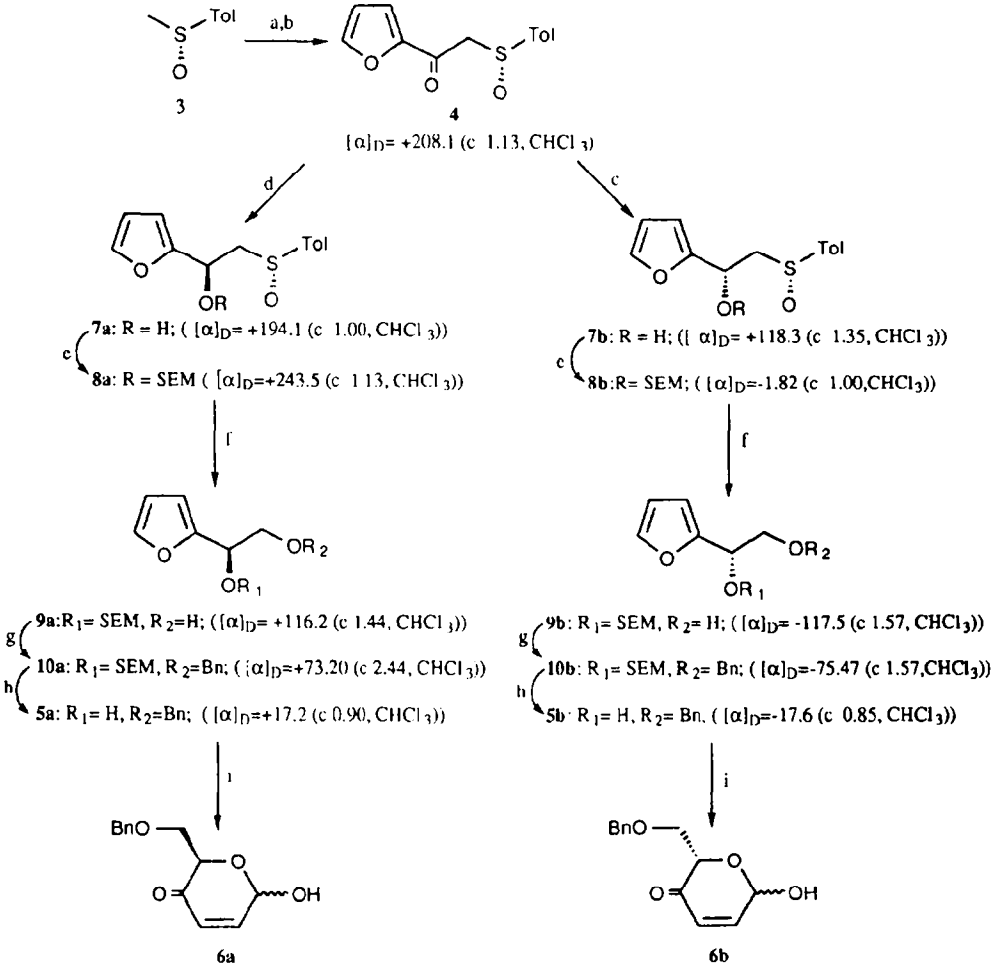
Scheme 2

The above plan was put into practice as follows (Scheme 4): Condensation of ethyl 2-furancarboxylate with the anion of (*R*)-methyl-*p*-tolylsulfoxide **3** yielded ketosulfoxide **4**. Treatment of this ketosulfoxide with DIBALH or DIBALH / $ZnCl_2$, according to the methodology developed by Solladie[7], afforded the two possible diastereomers of β-hydroxysulfoxides **7a** and **7b** in ≥95% d.e. (^{1}Hnmr). Each diastereomer was further freed of the less than 2% of the other epimer at hydroxylic carbon by flash chromatography. Stereochemistry at the newly created stereogenic center, *i.e.* the hydroxylic carbon atom in the 2-furylcarbinol, was assigned taking into account i) the nature of the reducing agent[7,8]; ii) ^{1}Hnmr and ^{13}Cnmr spectroscopic analysis[9,10]; iii) our previous experience of the conformational behavior of different β-hydroxysulfoxides[10]. Additionally, the configuration for **9a** was chemically correlated as follows (Scheme 3): (*R*)-(+)-Isopropylidene-*D*-glyceraldehyde was allowed to react with furan in the presence of monochloroacetic acid yielding **11** according to Zamojski[6a]. After protection of the free hydroxyl group as SEM ether, hydrolysis of the acetal followed by cleavage of the diol functionality and SBH reduction of the aldehyde afforded monoprotected diol **9a**, equal in all respects (^{1}Hnmr, $[\alpha]_D$ and ms) to that prepared from hydroxysulfoxide **7a**, as shown in Scheme 4.



a: $ClCH_2COOH$ /Δ; yield 96%. b ClSEM / $^iPr_2NEt$, yield 96% c TFA /CH_3CN/H_2O; yield 76% d: i) $NaIO_4$ / EtOH / H_2O. ii) $NaBH_4$; Combined yield 81%.

Scheme 3



a: LDA (1.8 eq). b: Ethyl 2-furancarboxylate (1.5 eq); yield: 75%. c: DIBALH / $ZnCl_2$ / -78°C; yield: 80%. d: DIBALH / -78°C; yield: 85%. e: CISEM (2.5 eq) / $^iPr_2NEt$; yield: 95% for **8a** and 95% for **8b**. f: i) TFAA / Collidine / acetonitrile. ii) $NaHCO_3$ / H_2O. iii) $NaBH_4$; Combined yield: 88% for **9a** and 88% for **9b**. g. BrBn / NaOH / TBABr; yield: 95% for **10a** and 94% for **10b**. h: TBAF / DMPU / molecular sieves, yield. 93% for 5a and 80% for **5b**. i: Br_2 / CH_3CN / H_2O; yield: 89% for **6a** and 80% for **6b**.

Scheme 4

With β-hydroxysulfoxides **7a** and **7b**, the two possible epimers of 2-furylcarbinols have been efficiently obtained and the stereochemistry assigned according to general rules extracted from the literature. In order to prove that our approach for the preparation of both enantiomers of chiral 2-furylmethanols could be applied to the preparation of *D*- and *L*-hexoses, removal of the sulfoxide group was now mandatory. To this aim, hydroxysulfoxides **7a** and **7b** were smoothly transformed into the SEM ethers **8a** and **8b** according to standard procedures[11], and the resulting protected β-hydroxysulfoxides were submitted to Pummerer's conditions rearrangement[12]. Treatment of **8a** and **8b** with TFAA in acetonitrile in the presence of collidine as base effected the desired rearrangement in five minutes. The corresponding trifluoroacetylsulfides were

hydrolyzed *in situ* ($NaHCO_3$) and reduced ($NaBH_4$) affording **9a** and **9b**. Benzylation of monoprotected diols followed by unraveling of the furfuryl hydroxy group by the action of fluoride ion, according to the protocol recently described by Lipshutz[13], gave both the enantiomers of furfuryl diols **5a** and **5b**[14]. Oxidation of the furan nucleus employing bromine in acetonitrile[1d] effected the transformation of both the enantiomers of 2-furylmethanol **5a** and **5b** into the precursors of *D*- and *L*-hexoses **6a** and **6b**, respectively.

Since Achmatowicz and coworkers have previously shown that hex-2-en-uloses **6a** and **6b** can be stereoselectively converted to sugars with the *allo*, *altro*, *manno*, *gluco*, *galacto* and *ido* configurations[2a], our sequence implies a formal synthesis of *D*- and *L*-isomers of these sugars.

Thus, we have developed an efficient protocol for the preparation of both precursors of D- and L-hexoses in which the chirality of (*R*)-methyl-p-tolylsulfoxide can be transferred to the C-6 carbon atom of hydropyranones in an effective and high-yielding process. Application of this methodology to the preparation of natural products is under way in our laboratory, and the results will be published in due course.

Experimental

Melting points were determined in open capillary tubes on a Gallenkamp apparatus and are uncorrected. ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50.3 MHz) spectra were registered on a Bruker AC-200 spectrometer. All NMR spectra were obtained using $CDCl_3$ as solvent and TMS as internal standard. Chemical shifts are reported in ppm, and coupling constants in Hz. Optical rotations were taken on a Perking-Elmer 241-MC polarimeter in an 1dm tube; concentrations are given in g/100 mL. Infrared spectra were recorded on a Bomen Michelson 100, FT-IR spectrophotometer. High resolution mass measurements were performed on a Kratos MS-80-RFA spectrometer. Routine monitoring of reactions was performed using Merck 60 F 254 silica gel, aluminum supported TLC plates. For flash chromatography, silica gel 60 (230-400 mesh ASTM, E.Merck) was used. All reactions were run under an atmosphere of dry argon using flame-dried glassware and freshly distilled and dried solvents. The organic extracts were dried over anhydrous sodium sulfate and concentrated *in vacuo*.

[(S) *R*]-1-(2-furyl)-1-oxo-2-*p*-tolylsulfinylethane, (4).

^{n}Butyllithium (17.51 mmol, 7.000 mL of a 2.5 M solution in hexanes) was added dropwise at 0°C to a stirred solution of 2.461 mL of $^i Pr_2NH$ (17.51 mmol, 1.772 g) in 25 mL of THF. The mixture was kept for 15 min at 0°C, cooled to -78°C, and (*R*)-methyl-*p*-tolylsulfoxide (9.72 mmol, 1.500 g) in 15 mL of THF was dropwise added. The mixture was stirred during 30 min and ethyl-2-furancarboxylate (14.59 mmol, 2.044 g) in THF (10 mL) added dropwise. After 10 min the mixture was quenched with saturated ammonium chloride solution (50 mL). The organic layer was separated and the aqueous solution acidified with 10% sulfuric acid solution to pH 3-4 and extracted with CH_2Cl_2 (3 x 50 mL). After evaporation of the solvent, the residue was purified by flash chromatography (hexane-ethyl acetate, 1:1) to give 1.810 g (75% yield) of ketoester **4** as a white solid. mp: 118-9°C; $[\alpha]_D$= + 208.1 (c 1.13, $CHCl_3$). ^{1}H NMR, δ: 7.70-7.20 (m, 6H), 6.55 (dd, 1H, J= 4.36 and 2.18 Hz), 4.24 (AB system, 2H, J=-13.07 Hz), 2.40 (s, 3H) ppm; ^{13}C NMR, δ: 178.9, 152.4, 147.5, 142.0, 140.4, 129.9, 124.1, 119.2, 112.7, 65.7, 21.2 ppm; I.R. (KBr) (cm^{-1}): 3117, 1642, 1556, 1466, 1400, 1379, 1312, 1206, 1085, 1041, 993, 915, 823, 806; HRMS (EI) 248.0492 M$^+$, Calcd. for $C_{13}H_{12}O_3S$: 248.0507. Anal. Calcd. for $C_{13}H_{12}O_3S$: C, 62.55; H, 4.86. Found: C, 62.88; H, 4.87.

[1*S*, (S) *R*]-1-(2-furyl)-2-*p*-tolylsulfinylethanol, (7a).

To a cold (-78°C) solution of 1.000 g (4.03 mmol) of ketosulfoxide **4** in 100 mL of THF under argon was dropwise added 16.120 mL (16.12 mmol) of a 1M solution of DIBALH in THF diluted with 30 mL of THF. After stirring at -78°C for 5h, the reaction mixture was quenched with saturated $NaHCO_3$ solution, stirred for 15 min and acidified with 1M HCl solution to pH 4-5. The aqueous solution was extracted with methylene chloride and the organic layer was washed with brine. The organic phase was dried over sodium sulfate and evaporated under reduced pressure to yield compound **7a** as a 98:2 mixture of [1*S*, (S) *R*] and [1*R*, (S) *R*] isomers from which diastereomerically pure **7a**-[1*S*, (S) *R*] was isolated as a white solid (85% yield) by flash chromatography using ^{i}PrOH hexane (2:8) as eluent. mp: 113.5-4.5°C, $[\alpha]_D$= +194.1 (c 1.00, $CHCl_3$); ^{1}H NMR, δ: 7.70-7.30 (m, 6H), 6.30 (m, 1H), 5.27 (ddd, 1H, X fragment from an ABMX system, J_{AX}= 2.50Hz, J_{BX}= 9.55 Hz, J_{MX}= 4.02 Hz), 4.13 (d, 1H, M fragment from an ABMX system, J_{MX}= 4.02 Hz), 3.41 (dd, 1H, B fragment from an ABMX system, J_{BX}= 9.55 Hz, J_{AB}= -13.50 Hz), 3.00 (dd, 1H, A

fragment from an ABMX system, J_{AX}= 2.50 Hz, J_{AB}= -13.50 Hz), 2.43 (s, 3H) ppm; ^{13}C NMR, δ: 154.4, 142.4, 141.8, 139.8, 130.2, 124.1, 110.4, 106.9, 63.6, 60.2, 21.4 ppm; I.R. (KBr) (cm^{-1}): 3577, 3234, 3106, 2916, 1493, 1397, 1331, 1300, 1235, 1219, 1197, 1156, 1081, 1069, 940, 789, 699; HRMS (EI) 250.0680 M$^+$. Calcd. for $C_{13}H_{14}O_3S$: 250.0664. Anal. Calcd. for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64. Found: C, 62.21; H, 5.77.

[1 *R*, (S) *R*]-1-(2-furyl)-2-*p*-tolylsulfinylethanol, (7b).

To 0.660 g (4.84 mmol) of anhydrous $ZnCl_2$ in 30 mL of THF, a solution of 1.000 g (4.03 mmol) of ketosulfoxide **4** in 70 mL of THF was added. After stirring during 30 min at room temperature, the solution was cooled to -78°C and 16.120 mL (16.12 mmol) of a 1M solution of DIBALH in THF diluted with 30 mL of THF, was dropwise added and stirred for 5h. The reaction mixture was quenched with saturated sodium bicarbonate solution, stirred for 15 min and acidified with 1M HCl solution to pH 4-5. The aqueous solution was extracted with methylene chloride and the organic layer was washed with brine. The organic phase was dried (Na_2SO_4) and evaporated to yield compound **7b** as a 95:5 mixture of [1 *R*, (S) *R*] and [1 *S*, (S) *R*] isomers from which diastereomerically pure **7b**-[1 *R*, (S) *R*] was isolated as a white solid (80 % yield) by flash chromatography (^{i}PrOH-hexane, 2:8). mp: 96.5-7.5°C; $[\alpha]_D$= + 118.3 (c 1.35, $CHCl_3$); ^{1}H NMR, δ: 7.70-7.25 (m, 6H), 6.35 (m, 1H), 5.35 (m, 1H), 3.89 (bs, 1H), 3.50-2.99 (m, 2H), 2.43 (s, 3H) ppm; ^{13}C NMR, δ: 154.4, 142.4, 141.7, 139.8, 130.2, 124.1, 110.4, 107.0, 65.1, 61.3, 21.4 ppm; I.R. (KBr) (cm^{-1}): 3272, 2887, 1502, 1493, 1412, 1305, 1221, 1159, 1081, 1065, 1019, 1007, 985, 861, 808, 744; HRMS (EI) 250.0648 M$^+$. Cald. for $C_{13}H_{14}O_3S$: 250.0664. Anal. Calcd. for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64. Found: C, 62.01; H, 5,65.

[1 *S*, (S) *R*]-1-(2-furyl)-1-*O*-[(2'-trimethylsilylethoxy) methyl]-2-*p*-tolylsulfinylethanol, (8a).

To a solution of 625 mg (2.50 mmol) of hydroxysulfoxide **7a** in 1.25 mL of dry CH_2Cl_2, 2.177 mL (12.50 mmol; 1.616 g) of diisopropylethylamine and 1.106 mL (6.25 mmol; 1.042 g) of β-(trimethylsilyl) ethoxymethyl chloride (SEMCl) were successively added. After stirring the reaction mixture for 5h at 40°C, 50 mL of methylene chloride was added and the mixture was successively washed with 1M HCl solution, saturated sodium bicarbonate solution and finally with brine. The organic layer was dried over sodium sulfate and the solvent removed at reduced pressure. The residue was column chromatographed using a 4:1 mixture of hexane-ethyl acetate as eluent to give 903 mg (95% yield) of **8a** as a white solid. mp: 47-8°C. $[\alpha]_D$= +243.5 (c 1.13, $CHCl_3$); ^{1}H NMR, δ: 7.70-7.30 (m, 5H), 6.30 (m, 2H), 5.22 (dd, 1H, X fragment of an ABX system, J_{AX}= 3.46 Hz, J_{BX}= 10.29 Hz), 4.70 (s, 2H), 4.02-3.38 (m, 2H), 3.45-2.88 (m, 2H, AB fragment from an ABX system; J_{AB}= -13.17), 2.37 (s, 3H), 1-04-0.82 (m, 2H), 0.00 (s, 9H) ppm; ^{13}C NMR, δ: 151.8, 142.8, 141.7, 141.3, 129.9, 123.9, 110.2, 109.1, 92.7, 65.7, 65.1, 63.2, 21.2, 18.0, -0.1, -1.5 ppm; I.R. (KBr) (cm^{-1}): 2949, 2891, 1496, 1402, 1248, 1150, 1094, 920, 750; HRMS (EI) 380.1495 M$^+$. Cald. for $C_{19}H_{28}O_4SSi$: 380.1477; Anal. Cald. for $C_{19}H_{28}O_4SSi$: C, 59.96; H, 7.42. Found: C, 59.71; H, 7.47.

[1 *R*, (S) *R*]-1-(2-furyl)-1-*O*-[2'-(trimethylsilylethoxy) methyl]-2-*p*-tolylsulfinylethanol, (8b).

Was prepared according to the experimental procedure used for **8a** from [1 *R*, (S) *R*]-1-(2-furyl)-2-p-tolylsulfinylethanol **7b**. Yield 95%. Oil: $[\alpha]_D$= -1.82 (c 1.00, $CHCl_3$), ^{1}H NMR, δ: 7.65-7.20 (m, 5H), 6.40 (m, 2H), 4.96 (t, 1H, J= 7.16 Hz), 4.58 (s, 2H), 3.72-3.15 (m, 4H), 2.40 (s, 3H), .87 (m, 2H), 0.00 (s, 9H) ppm; ^{13}C NMR, δ: 151.5, 143.0, 141.5, 129.9, 124.2, 110.3, 109.7, 92.8, 66.8, 65.7, 62.2, 21.2, 18.1, -1.5 ppm; I.R. (film) (cm^{-1}): 3114, 2951, 2890, 1495, 1402, 1248, 1151, 1094, 1057, 1040, 1017, 925, 859, 836, 748; HRMS (EI) 380.1478 M$^+$. Calcd. for $C_{19}H_{28}O_4SSi$: 380.1477; Anal.Cald. for $C_{19}H_{28}O_4SSi$: C, 59.96; H, 7.42. Found: C, 59.87; H, 7.45.

(*R*)-1-(2-furyl)-1-*O*-[2'-(trimethylsilylethoxy) methyl]-1,2-ethanediol, (9a).

To an acetonitrile solution (50 mL) of sulfoxide **8a** (800 mg; 2.10 mmol) and collidine (6.30 mmol; 764 mg; 840 µL), was added an acetonitrile solution (5 mL) of trifluoracetic anhydride (6.30 mmol; 1.323 g; 876 µL) at 0°C under argon. After stirring of the reaction mixture at 0°C for 30 min, an aqueous solution (20 mL) of sodium hydrogen carbonate (10.50 mmol, 882 mg) followed by 397 mg (10.50 mmol) of sodium borohydride was added. The reaction mixture was stirred at room temperature for 10 min. The solvent was removed under reduced pressure and the reaction crude extracted into methylene chloride. The organic phase was successively washed with 1N HCl solution, saturated sodium bicarbonate and brine and dried over sodium sulfate. The solvent was removed and the residue column chromatographed (hexane-ethyl acetate, 4:1) to afford 478 mg (88 % yield) of pure **9a** as an oil: $[\alpha]_D$ = +116.2 (c 1.44, $CHCl_3$); ^{1}H NMR, δ: 7.40 (t, 1H, J=1.34 Hz), 6.33 (d, 2H, J= 1.34 Hz), 4.72 (m, 2H), 4.10-3.48 (m, 4H), 2.15 (bs, 1H), 1.82 (t, 2H, J= 8.50

Hz), 0.00 (s, 9H) ppm; ^{13}C NMR, δ: 152.1, 142.4, 110.1, 108.3, 93.5, 73.7, 65.6, 64.3, 18.1, -1.5 ppm; I.R. (film) (cm^{-1}): 3452, 2952, 2889, 1251, 1151, 1107, 1062, 1027, 862, 845, 747; Anal. Cald. for $C_{12}H_{22}O_4Si$: C, 55.78; H, 8.58. Found: C, 55.56, H, 8.42.

(*S*)-1-(2-furyl)-1-*O*-[2'-(trimethylsilylethoxy) methyl]-1,2-ethanediol, (9b).
Was obtained according to the procedure used for **9a** from [1*R*, (S)*R*]-1-(2-furyl)-1-*O*-[2'-trimethylsilylethoxy) methyl]-2-*p*-tolylsulfinylethanol, **8b**. Yield 88%. Oil: $[\alpha]_D$ = -117.5 (c 1.57, $CHCl_3$); ^{1}H NMR, δ: 7.40 (t, 1H, J=1.34 Hz), 6.33 (d, 2H, J= 1.34 Hz), 4.72 (m, 2H), 4.10-3.48 (m, 4H), 2.15 (bs, 1H), 1.82 (t, 2H, J= 8.50 Hz), 0.00 (s, 9H) ppm; ^{13}C NMR, δ: 152.1, 142.4, 110.1, 108.3, 93.5, 73.7, 65.6, 64.3, 18.1, -1.5 ppm; I.R. (film) (cm^{-1}): 3452, 2952, 2889, 1251, 1151, 1107, 1062, 1027, 862, 843, 747; Anal. Cald. for $C_{12}H_{22}O_4Si$: C, 55.78, H, 8.58. Found: C, 55.89, H, 8.55.

(*R*)-1-(2-furyl)-1-*O*-[2'-(trimethylsilylethoxy) methyl]-2-*O*-benzyl-1,2-ethanediol, (10a).
To a mixture of 10 mL of a methylene chloride solution of alcohol **9a** (517 mg, 2.00 mmol) and 10 mL of a 50 % aqueous solution of sodium hydroxide was added 357 μL of benzyl bromide (3.00 mmol; 513 mg) and a catalytic amount of tetra *n*-butyl ammonium bromide. After vigorous stirring of the reaction mixture overnight, the organic layer was decanted, dried (Na_2SO_4) and evaporated. Flash chromatography of the residue gave 622 mg (95 % yield) of pure **10a** as an oil. $[\alpha]_D$ = +73.20 (c 2.44, $CHCl_3$); ^{1}H NMR, δ: 7.35 (m, 6H), 6.31 (d, 2H, J= 1.37 Hz), 4.88 (t, 1H, J= 5.50 Hz), 4.70 (s, 2H), 4.56 (s, 2H), 3.97-3.35 (m, 4H), 0.90 (m, 2H), 0.00 (s, 9H) ppm. ^{13}C NMR, δ: 152.6, 142.3, 138.4, 128.3, 127.5, 110.1, 108.3, 93.1, 73.4, 71.8, 10.6, 65.2, 18.1, -1.5 ppm; I.R. (film) (cm^{-1}); 2947, 2886, 1248, 1150, 1103, 1025, 859, 835, 738, 696; HRMS (EI) 348.1739 M$^+$. Cald. for $C_{19}H_{28}O_4Si$: 348.1757; Anal. Calcd. for $C_{19}H_{28}O_4Si$: C, 65.48; H, 8.10. Found: C, 65.25; H, 7.95.

(*S*)-1-(2-furyl)-1-*O*-[2'-(trimethylsilylethoxy) methyl]-2-*O*-benzyl-1,2-ethanediol, (10b).
Was prepared from (*S*)-1-(2-furyl)-1-*O*-[2'-(trimethylsilylethoxy) methyl]-1,2-ethanediol, **9b** following the same experimental procedure described for **10a**. Yield 94%. Oil: $[\alpha]_D$ = -75.47 (c 1.57, $CHCl_3$); ^{1}H NMR, δ: 7.35 (m, 6H), 6.31 (d, 2H, J= 1.37 Hz), 4.88 (t, 1H, J= 5.50 Hz), 4.70 (s, 2H), 4.56 (s, 2H), 3.97-3.35 (m, 4H), 0.90 (m, 2H), 0.00 (s, 9H) ppm. ^{13}C NMR, δ: 152.6, 142.3, 138.4, 128.3, 127.5, 110.1, 108.3, 93.1, 73.4, 71.8, 10.6, 65.2, 18.1, -1.5 ppm; I.R. (film) (cm^{-1}); 2947, 2886, 1248, 1150, 1103, 1025, 859, 835, 738, 696; HRMS (EI) 348.1747 M$^+$. Cald for $C_{19}H_{28}O_4Si$: 348.1757; Anal. Calcd. for $C_{19}H_{28}O_4Si$: C, 65.48; H, 8.10. Found: C, 65.45 ; H, 8.15.

(*R*)-1-(2-furyl)-2-*O*-benzyl-1,2-ethanediol, (5a).
An 1M solution of TBAF in THF (5 mL) was added to the SEM ether **10a** (349 mg; 1.00 mmol) and the solution concentrated *in vacuo*. The resulting oil was dissolved in dry DMPU (0.5 mL) and crushed, activated 4Å molecular sieves (350 mg) were added. The reaction mixture was heated to 80°C with stirring continued for 2h. The flask was then cooled, and the contents diluted with Et_2O and extracted (3 X 50 mL) from water (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (hexane-ethyl acetate, 4:1) afforded 203 mg (93 %) yield of pure **5a** as an oil. $[\alpha]_D$ = +17.2 (c 0.90, $CHCl_3$)[14]; ^{1}H NMR, δ: 7.32 (m, 6H), 6.30 (m, 2H), 4.91 (t, 1H, J= 5.74 Hz), 4.60 (s, 2H), 3.74 (d, 2H, J= 5.74 Hz), 2.70 (bs, 1H) ppm; ^{13}C NMR, δ: 154.0, 142.0, 137.9, 128.4, 127.7, 110.2, 106.8, 73.4, 72.7, 67.0 ppm; I.R. (film) (cm^{-1}): 3427, 2908, 2863, 1557, 1540, 1502, 1454, 1362, 1211, 1147, 1094, 1008, 738, 698.

(*S*)-1-(2-furyl)-2-*O*-benzyl-1,2-ethanediol, (5b).
Was prepared according to the procedure used for **5a** from (*S*)-1-(2-furyl)-1-*O*-[2'-(trimethylsilylethoxy) methyl]-2-*O*-benzyl-1,2-ethanediol, **10b**. Yield 80%. Oil: $[\alpha]_D$ = -17.6 (c 0.85, $CHCl_3$)[14]; ^{1}H NMR, δ: 7.32 (m, 6H), 6.30 (m, 2H), 4.91 (t, 1H, J= 5.74 Hz), 4.60 (s, 2H), 3.74 (d, 2H, J= 5.74 Hz), 2.70 (bs, 1H) ppm; ^{13}C NMR, δ: 154.0, 142.0, 137.9, 128.4, 127.7, 110.2, 106.8, 73.4, 72.7, 67.0 ppm; I.R. (film) (cm^{-1}): 3427, 2908, 2863, 1557, 1540, 1502, 1454, 1362, 1211, 1147, 1094, 1008, 738, 698

6-*O*-benzyl-2,3-dideoxy-α and β-*D*-*glycero*-hex-2-enopyranos-4-ulose, (6a).
To a solution of **5a** (220 mg; 1.00 mmol) in an acetonitrile-water mixture (10 mL; 9:1 v/v) cooled to -5°C, bromine (1.10 mmol; 176 mg; 56.4 μL) was added with vigorous stirring. The resulting solution was

allowed to warm gradually to room temperature and solid sodium hydrogen carbonate (3.00 mmol; 252 mg) was added. The reaction mixture was extracted with ether (2 X 50 mL). The organic layer was washed with brine, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was column chromatographed (hexane-ethyl acetate, 3:1) to give 208 mg (89% yield) of pure **6a** as a mixture of α and β anomers. Oil: $[\alpha]_D$= + 62.0 (after 5h, c 1.00, $CHCl_3$). Lit. 14: +61.6 (after 5 h, c 1.32, $CHCl_3$).

6-*O*-benzyl-2,3-dideoxy-α and β-*L-glycero*-hex-2-enopyranos-4-ulose, (6b).

Under the reaction conditions identical with those used for the preparation of **6a**, compound **5b** afforded **6b** (80% yield) as a colorless oil: $[\alpha]_D$=- 61.8 (after 5 h, c 1.50, $CHCl_3$). Lit. 14: -61.7 (after 6 h, c 0.94, $CHCl_3$).

Chemical correlation of the configuration for 9a.

To a solution of 0.202 g (1.00 mmol) of (1 *R*, 2 *R*)-1-(2-furyl)-2,3-*O*-isopropylidene-1,2,3-propanetriol, **11** (prepared according to Zamojski[6a]) in 1.25 mL of dry methylene chloride, 0.685 mL (4.00 mmol) of diisopropylethylamine and 0.349 mL (6.25 mmol) of β-(trimethylsilyl) ethoxymethyl chloride (SEMCl) were successively added. After stirring the reaction mixture for 2h at 40ºC, 50 mL of methylene chloride was added and the mixture was successively washed with 1M HCl solution, saturated sodium bicarbonate solution and finally with brine. The organic layer was dried over sodium sulfate and the solvent removed at reduced pressure. The residue was column chromatographed using a 20:1 mixture of hexane-ethyl acetate as eluent to afford 322 mg (96% yield) of **12** as an oil. $[\alpha]_D$= +106.5 (c 1.03, $CHCl_3$); HRMS (EI) 328.1673 M^+. Cald. for $C_{16}H_{28}O_5Si$: 328.1706.

A solution of (1 *R*, 2 *R*)-1-(2-furyl)-1-*O*-[(2'-trimethylsilylethoxy) methyl]-2,3-*O*-isopropylidene-1,2,3-propanetriol, **12**, in an acetonitrile-water mixture (5 mL; 4:1, v/v), 0.310 mL of trifluoracetic acid was added. After stirring the reaction mixture for 24 h at room temperature, the solution was neutralized with solid sodium hydrogen carbonate and extracted into methylene chloride. The organic layer was dried (Na_2SO_4) and the solvent removed *in vacuo*. The residue was purified by flash chromatography (ethyl ether-hexane, 15:1) to give 106 mg (76% yield) of (1 *R*, 2 *R*)-1-(2-furyl)-1-*O*-[(2'-trimethylsilylethoxy) methyl]-1,2,3-propanetriol as an oil. $[\alpha]_D$= +24.0 (c 0.92, CH_2Cl_2); HRMS (EI) 288.1378 M^+. Cald. for $C_{13}H_{24}O_5Si$: 288.1393.

To 180 mg (0.62 mmol) of the precursor diol derivative in 0.30 mL of water containing 5 drops of methanol; 134 mg (0.62 mmol) of sodium periodate was added. After stirring for 30 min, the reaction mixture was cooled to 0ºC and 2 mL of methanol and 24 mg (0.62 mmol) of sodium borohydride were added. The mixture was stirred for 1 h at 0ºC and extracted into methylene chloride. The organic phase was dried over sodium sulfate and the solvent removed under reduced pressure. The residue was flash chromatographed (ethyl ether-hexane, 2:1) to afford 130 mg (81% yield) of **9a**, equal in all respects to that prepared by Pummerer's rearrangement from **8a**. $[\alpha]_D$= +118.0 (c 0.50, $CHCl_3$).

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