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A SIMPLE STEREOCONTROLLED SYNTHESES OF OPTICALLY ACTIVE DEOXYSUGARS L-RHODINOSE AND D-AMICETOSE

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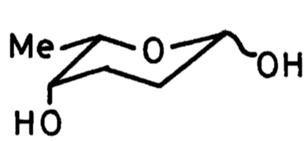
Facile stereoselective syntheses of 2,3,6-trideoxysugars, L-rhodinose and D-amicetose, were achieved from highly diastereoselective nucleophilic addition of methyl group to (S)-2-benzyloxy-5-hexenal, which was easily obtained from optically pure (S)-glycidyl sulfide.

The key role played by deoxysugars in the biological action of many medicinally active compounds has encouraged synthetic chemists to develop diverse strategies for their preparation.[1)] 2,3,6-Trideoxy-L-*threo*-hexopyranose (L-rhodinose 1)[2,3)] and 2,3,6-trideoxy-D-*erythro*-hexopyranose (D-amicetose 2)[4)] were components of many antibiotics from *Streptomyces* and *Micromonospora spp.* There have been a few syntheses of these deoxysugars from naturally abundant sugars[3ab,4a)] *via* lengthy and troublesome transformations, and from non-carbohydrate precursors.[3c,4b)] From the viewpoint of the synthesis of various deoxysugars, it is desired to develop the simple method involving useful chiral precursor with wide applicability and predictable stereoselective reactions.

We now wish to report expedient stereoselective syntheses of 1 and 2 *via* diastereoselective nucleophilic addition of methyl group to (S)-2-benzyloxy-5-hexenal (3), which was easily obtained from (S)-glycidyl sulfide (4). In our previous paper, 4 obtained readily by the Baker's yeast mediated reduction of 3-hydroxy-1-phenylthio-2-propanone has been shown to be a versatile chiral building block for optically active secondary alcohols.[5)] In the present sugar syntheses, β-hydroxy sulfide 5 produced by nucleophilic ring-opening of 4 is converted into β-hydroxy aldehyde derivative 3 which undergoes diastereoselective addition of organometallics to provide 1,2-diol derivatives (7 and 8).

Thus glycidyl sulfide 4 ($[\alpha]^{23}_{D}$ -34.1° (c 1.06, $CHCl_3$), 100% ee) was treated with allylmagnesium bromide (1.5 eq) in the presence of copper (I) iodide (20 mol %) in THF at -30 °C for 2 h gave the β-hydroxy sulfide 5 in 80% yield, $bp_{0.85}$ 135 °C (bath temp), $[\alpha]^{23}_{D}$ -17.8° (c 1.34, THF). After protection of the hydroxy group of 5 (BnBr, NaH, cat. n-Bu_4NBr, THF, rt, 89%), the benzyl ether 6 was oxidized



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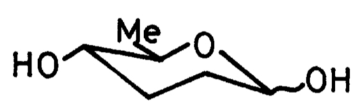

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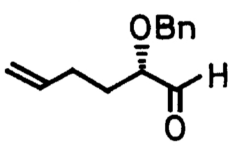

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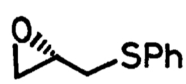

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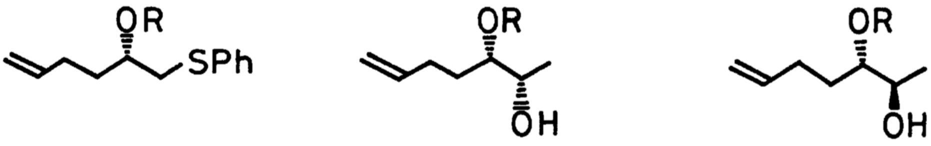

5 R=H
6 R=Bn

7 R=Bn
9 R=H

8 R=Bn
10 R=H

with $NaIO_4$, followed by the Pummerer reaction and reduction with diisobutylaluminum hydride, after aqueous workup and bulb-to-bulb distillation,[6] to give the α-benzyloxy aldehyde 3 in 73% yield, $bp_{0.7}$ 130 °C (bath temp), $[\alpha]_D^{23}$ -76.4° (c 0.55, THF).

Diastereoselective *syn*-addition of methyl group to 3 (chelation control) was accomplished by the reaction of methylmagnesium bromide in the influence of $ZnBr_2$[7] in THF at 0 °C for 1 h to give the *syn*-diol derivative 7 in 66% yield with remarkably high diastereoselectivity (7 : 8 = 250 : 1, determined by glc on PEG-20M 50m capillary column). Purification by TLC on silica-gel and debenzylation (lithium in liquid ammonia) afforded the *syn*-diol 9 in 76% yield, $[\alpha]_D^{23}$ -21.3° (c 0.35, EtOH). On the other hand, addition of $MeTi(OiPr)_3$ to 3 (non-chelation control)[8] predominantly yielded the *anti*-diol derivative 8 (7 : 8 = 1 : 6.7) which was purified by TLC on silica-gel, followed by debenzylation to give the *anti*-diol 10 in 35% yield, $bp_{0.5}$ 140 °C (bath temp), $[\alpha]_D^{23}$ -25.5° (c 0.54, EtOH).

Finally, ozonolysis of 9 at -78 °C in MeOH, followed by reductive workup with Me_2S at room temperature afforded L-rhodinose (1) in 76% yield, $bp_{0.65}$ 100 °C (bath temp), $[\alpha]_D^{23}$ -11.0° (c 0.45, acetone), lit[2] $[\alpha]_D$ -11 ± 1.6°. D-Amicetose (2) was obtained from 10 by the same procedure in a yield of 70%, $bp_{0.5}$ 100 °C (bath temp), $[\alpha]_D^{23}$ +40.6° (c 0.35, acetone), lit[4a] $[\alpha]_D$ +43.6°.

Thus two types of deoxysugar of biological importance were readily synthesized in short steps and in good overall yields from optically pure (S)-glycidyl sulfide, which was easily prepared by the Baker's yeast reduction of 3-hydroxy-1-phenylthio-2-propane.[9]

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