Stereospecific Synthesis from Non-carbohydrate Precursors of the Deoxy- and Methyl-branched Deoxy-sugars L-Amicetose, L-Mycarose, and L-Olivomycose

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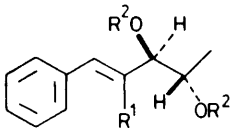
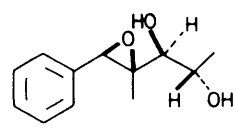
Summary 2,3,6-Trideoxy-L-*erythro*-hexose (L-amicetose) (**12**), 2,6-dideoxy-3-*C*-methyl-L-*ribo*-hexose (L-mycarose) (**13**), and 2,6-dideoxy-3-*C*-methyl-L-*arabino*-hexose (L-olivomycose) (**14**) have been synthesized from the corresponding lactones (**9**), (**10**), and (**11**), obtained, in turn, upon cleavage with ozone of the aromatic ring of suitable derivatives of the aromatic, C_6–C_5 optically active methyl diols (**1**) and (**2**) prepared from the C_6–C_3 $\alpha\beta$-unsaturated aldehydes and fermenting baker's yeast.

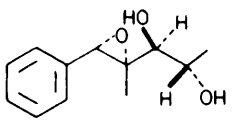
DEOXY- and methyl-branched deoxy-sugars have received wide interest[1] because of their occurrence as glucoside components of many antibiotics from *Streptomyces* and *Micromonospora* spp. Most of these compounds are synthetically available[1b] in the natural and/or unnatural enantiomeric form through procedures which involve either regioselective removal of oxygen function(s) from suitable derivatives of natural carbohydrate or a resolution step at some stage in the sequence when optically inactive materials are used.



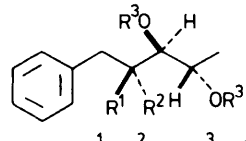
(1) $R^1 = R^2 = H$
(2) $R^1 = Me$; $R^2 = H$
(3) $R^1 = H$; $R^2 = COMe$



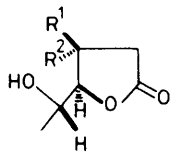
(4)



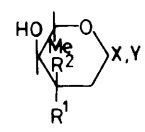
(5)



(6) $R^1 = R^2 = H$; $R^3 = COMe$
(7) $R^1 = OH$; $R^2 = Me$; $R^3 = COMe$
(8) $R^1 = Me$; $R^2 = OH$; $R^3 = COMe$



(9) $R^1 = R^2 = H$
(10) $R^1 = OH$; $R^2 = Me$



(11) $R^1 = Me$; $R^2 = OH$; X,Y = O
(12) $R^1 = R^2 = H$; X,Y = H,OH
(13) $R^1 = Me$; $R^2 = OH$; X,Y = H,OH
(14) $R^1 = OH$; $R^2 = Me$; X,Y = H,OH

We report now the synthesis of the deoxy- and methyl-branched deoxy-sugars L-amicetose (**12**),[2] L-mycarose (**13**),[3] and L-olivomycose (**14**)[4] from the corresponding C_6 lactones obtained, in turn, from suitable transformation products of the aromatic C_6–C_5 methyl diols (**1**) and (**2**), prepared in fermenting baker's yeast[5] from C_6–C_3 unsaturated aldehydes, upon cleavage with ozone of the aromatic ring. This conversion would provide a configurational assignment for compounds (**1**) and (**2**), and a stereospecific synthesis of carbohydrates from non-carbohydrate precursors.

Thus, the diacetate (**3**)[5] was hydrogenated (10% Pd–C) to the oily (**6**), $[\alpha]$ −12·6°,† which upon ozonolysis in 80% formic acid at 0 °C, and oxidative work-up, followed by treatment with 10% NaOH and continuous extraction (ethyl acetate) of the acidified solution, gave a γ-lactone ($\nu_{C=O}$ 1765 cm^{-1}), $[\alpha]$ −9·4°, shown by g.l.c. and comparison with authentic samples of the lactones of *erythro*-[6] and *threo*‡-4,5-dihydroxy-hexanoic acids to contain *ca.* 95% of the *erythro*-form. The optically active lactone was shown to be compound (**9**), since it was converted, according to known procedures,[6] into the oily 2,3,6-trideoxy-*erythro*-hexose, $[\alpha]$ −43·1° (*c* 1, acetone). Its 2,4-dinitrophenylhydrazone had m.p. 157 °C, $[\alpha]$ +9·8° (*c* 0·8, pyridine). Comparison of these physical properties with those in the literature[2,7] for L-amicetose and derivatives allows the assignment of structure (**12**) to the synthetic deoxy-sugar and the (2*S*,3*R*) absolute configuration depicted in (**1**) to the methyl diol obtained from cinnamaldehyde and fermenting baker's yeast.

The methyl diol (**2**), upon treatment with 1·1 mol. equiv. of 3-chloroperoxybenzoic acid (CH_2Cl_2, K_2CO_3, 0 °C), gave a mixture from which an epoxide, m.p. 84 °C, $[\alpha]$ −24·0°, separated in *ca.* 40% yield from ethyl acetate–hexane. This material was acetylated and converted upon hydrogenation (10% Pd–C) into the oily (**7**), $[\alpha]$ −36·6°. The residue from which the epoxide yielding (**7**) had been separated was hydrogenated to give in *ca.* 65% yield a sparingly soluble material which was acetylated to the crystalline (**8**), $[\alpha]$ −52°. Compounds (**7**) and (**8**) can be distinguished on t.l.c. The main difference between (**7**) and (**8**) in their ^1H n.m.r. spectra is in the ≥C-Me absorption; δ 1·05 and 1·18, respectively (100 MHz, $CDCl_3$). The acetate (**8**) was converted, upon ozonolysis, as reported above, in *ca.* 40% yield into a γ-lactone, $[\alpha]$ −45° (*c* 0·5, tetrahydrofuran), showing i.r. and ^1H n.m.r. spectra, and chromatographic behaviour identical with those of an authentic sample of (±)-3-epimycaroselactone.[8] Its optical rotation indicated it to be 2,6-dideoxy-3-*C*-methyl-L-*arabino*-hexonolactone (**10**) (lit.,[8] $[\alpha]$ for the D-enantiomer, +39·9°). Reduction[8] of (**10**) gave L-olivomycose (**14**),

† If not otherwise indicated, optical rotations are measured in $CHCl_3$, *c* = 1, at 20 °C.

‡ Prepared by hydroxylation with $KMnO_4$ of (*E*)-hex-4-enoic acid.

m.p. 108—110 °C, $[\alpha]$ −20·8 (*c* 1, water, 24 h), these physical properties being in agreement with those in the literature.[4,9]

The aromatic ring of (**7**) was similarly oxidatively destroyed to give, eventually, a δ-lactone, recognized, by direct comparison with an authentic sample of synthetic racemic material,[10] as mycaroselactone (**11**). Reduction of the lactone (**11**) with di-isobutylaluminium hydride[8] gave L-mycarose (**13**), identified by its m.p., 127 — 130 °C, and optical rotation, $[\alpha]$ −29° (water), values in agreement with those in the literature.[11]

The above results thus indicate the (2*S*,3*R*) absolute configuration for the diol (**2**) and structures (**4**) and (**5**) for the epoxides from which (**7**) and (**8**) are derived. Experiments designed to increase the stereospecificity in the epoxidation of (**2**) and other types of functionalizations of the hydroxy-group-activated double bond of (**1**) and (**2**) which should allow other deoxy- and methyl-branched amino-deoxy-sugars to be obtained from (**1**) and (**2**) are in progress.

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