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A CONVENIENT SYNTHESIS OF TOLYPOSAMINE DERIVATIVES

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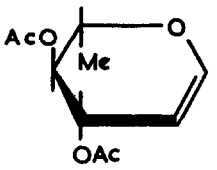
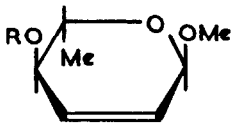
The antibiotic tolypomycin Y obtained (1) from Streptomyces tolypophorus is composed of a quinone (tolypomycinone) and a water soluble amino-sugar (tolyposamine) to which the structure 4-amino-2,3,4,6-tetradeoxy-L-erythro-hexose has been assigned on the basis of chemical and spectroscopic evidence. This assignment is substantiated by the following stereospecific synthesis of a derivative of tolyposamine.

We have recently shown (2) that 3,4-di-O-acetyl-L-rhamnal(I) undergoes an allylic rearrangement with boron trifluoride in methanolic dichloromethane to give methyl 4-O-acetyl-2,3,6-trideoxy-α-L-erythro-hex-2-enopyranoside(II), which was converted into the allylic sulphonate(III), m.p. 47-49° (from ether-hexane), $[\alpha]_D$ - 149° (c 0.9, $CHCl_3$), on deacetylation and methanesulphonylation. Treatment of the allylic sulphonate(III) with sodium iodide in aqueous acetone at room temperature yielded methyl 4-iodo-2,3,4,6-tetradeoxy-α-L-threo-hex-2-enopyranoside(IV), m.p. 62.5-63.5° (from aqueous methanol), $[\alpha]_D$ + 526° (c 1, $CHCl_3$). The configuration at C-4 of the latter compound was confidently assigned on the basis of the rotational data and n.m.r. spectroscopy, thereby excluding the possibility of further displacement on the initially formed iodo-compound.

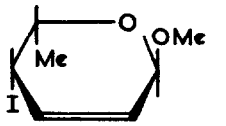
Displacement of the iodo-group from (IV) was achieved with azide ion in aqueous acetone at ca 70° to give a highly volatile azide (V) (ν_{max} 2100 cm^{-1}), which was transformed into methyl 4-benzamido-2,3,4,6-tetradeoxy-α-L-erythro-hexopyranoside (methyl N-benzoyl-α-tolyposaminide) (VI), m.p. 132-133,5° (from ethyl acetate-light petroleum), $[\alpha]_D$ - 150 ± 1° (c 0.8, EtOH), following hydrogenation over a platinum catalyst and N-benzoylation using benzoic anhydride in methanol. Although the physical constants of the synthetic material differ slightly from those [m.p. 136-140°, $[\alpha]_D$-139° (c 0.5, EtOH)] reported (1) for natural methyl N-benzoyl-α-tolyposaminide, the infrared spectra (KBr discs)



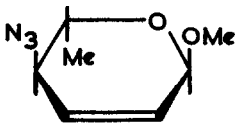
I



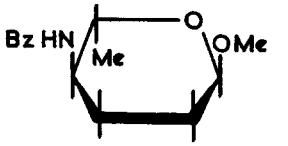
II R=Ac
III R=Ms



IV



V



VI

of the two materials are indistinguishable.

A convenient synthesis of tolyposamine derivatives is naturally important in studies directed towards a total synthesis of tolypomycin. An added incentive derives from the recent use (3) of racemic tolyposamine derivatives in a total synthesis of kasugamycin, although the overall yield of the antibiotic obtained was disappointingly low. The use of optically pure D-tolyposamine derivatives, prepared by a route corresponding to that described above, might serve to improve the efficiency of the reactions leading to synthetic kasugamycin and its homologues.

We are grateful to Dr. T. Kishi for providing us with the infrared spectrum of mothyl N-benzoyl-α-tolyposaminide.

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