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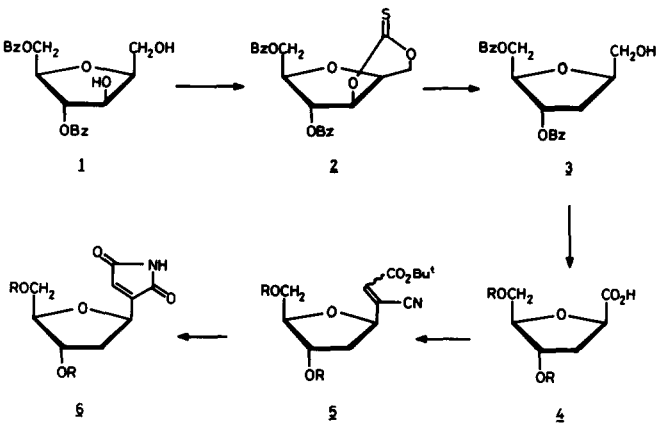
A SYNTHESIS OF β-2'-DEOXYSHOWDOMYCIN

Azeez M. Mubarak and Daniel M. Brown*
University Chemical Laboratory, Cambridge CB2 1EW

A stereospecific synthesis of the 2'-deoxy analogue of showdomycin, 2-(2'-deoxy-β-D-ribofuranosyl)-maleimide, from 2,5-anhydro-D-glucitol is described.

A number of 2'-deoxynucleoside analogues show selective antiviral and antitumour activity, while some antibiotic C-ribonucleosides also show the latter activity.[1] 2'-Deoxy-C-nucleosides represent an obvious structural extension for studies of this type.[2] The synthesis of such compounds from a chiral precursor has up to now involved either modification of an existing ribosyl-C-nucleoside, or the use of 2-deoxyribose as starting material.[2,3]

We described earlier the 4,6-di-O-benzoate (1) of 2,5-anhydro-D-glucitol, itself readily accesible from D-mannitol.[4] (1) was converted by thiocarbonyldiimidazole to its 1,3-O-thiocarbonate (2;80%),[5] m.p. 144-146° and thence by tributylstannane reduction in hot toluene[6] to the 2,5-anhydro-3-deoxy-D-ribo-hexitol (3;62%), needles, m.p. 69-71°. The latter represents in principle a convenient progenitor of β-D-2'-deoxyribo-C-nucleosides, exemplified here by its conversion to 2'-deoxyshowdomycin (6;R=H).[7]



Oxidation of (3)with pyridinium dichromate in DMF[8] led to the acid (4;R=Bz), obtained as an oil (86%). Following Kalvoda,[9] it was treated successively with thionyl chloride, hydrogen cyanide and the Wittig reagent $Ph_3P{=}CH.CO_2Bu^t$, affording the isomeric tert. butyl propenoates (5;R=Bz) in a favourable Z:E ratio (7:3). The mixture was treated with trifluoroacetic acid-trifluoroacetic anhydride to give the maleimide (6;R=PhCO) as hygroscopic crystals (68%), $[\alpha]_D^{20}$+ 15(c 2 in $CHCl_3$). Showdomycin is exceptionally unstable to mild base.[10] Correspondingly, debenzoylation of (6) by the usual methods failed. But by using NaOMe-MeOH in dry benzene, conditions under which the kinetically more inert maleimide anion was present[11] and where the product quickly precipitated, 2'-deoxyshowdomycin (6;R=H; 30%) was obtained. It had λ_{max}221nm(lit.[7] 222nm) and an m.s. fragmentation pattern identical with the (±)-form.[7] An alternative synthesis using (4;R=Ac) gave (5;R=Ac)(Z:E, 1:1) which with HCl-MeOH afforded (6;R=H). Throughout these synthetic series no evidence of anomerisation was found. The n.m.r. spectrum of (6;R=H) is very closely similar to that of β-D-2'-deoxypseudouridine.[2,3a,12]

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References and Footnotes

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