A Novel Approach to Aminocyclitol Analogues from Azidotrideoxyhex-5-enopyranosides

István Pelyvás, Ferenc Sztaricskai, and Rezső Bognár

Research Group of Antibiotics of the Hungarian Academy of Sciences, Debrecen, H-4010 Hungary

Application of the Ferrier's carbocyclic ring closure to methyl 3-azido-2,3,6-trideoxyhex-5-enopyranosides leads to cyclitol derivatives (**3**) and (**5**) suitable for the convenient synthesis of 1,3-diaminocyclitol-type aminoglycoside antibiotic analogues.

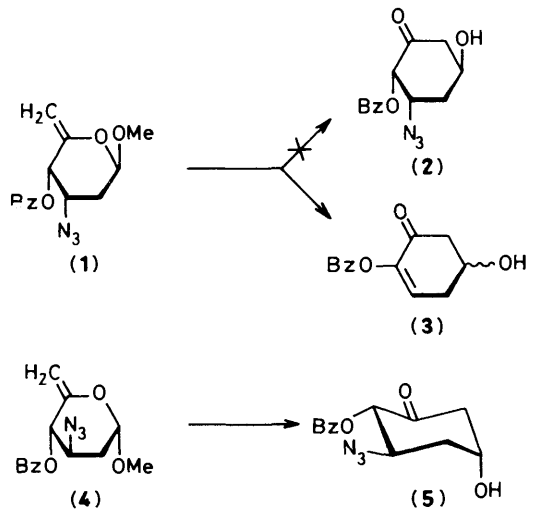
In 1979 Ferrier[1] reported the transformation of methyl 3,4-di-*O*-benzoyl-6-deoxy-2-*O*-*p*-tolylsulphonyl-α-D-*xylo*-hex-5-enopyranoside into 2L-2,4,5/3-2,3-dibenzoyloxy-5-hydroxy-4-*O*-*p*-tolylsulphonylcyclohexanone, and the reaction was shown to proceed *via* an intramolecular aldol ring closure in the presence of mercury(II) chloride.

This procedure for the synthesis of cyclitols from neutral sugars has been applied to the simple conversion of monosaccharides[2] into cyclohexanones, as well as of disaccharides[3] into glycosides containing the cyclohexanone aglycone moiety. Thus, the method has opened up new prospects for the total synthesis of aminocyclitol antibiotics.

As no amino- or azido-functionalized di- or tri-deoxyhex-5-enopyranosides have been utilized for this transformation, methyl 3-azido-4-*O*-benzoyl-2,3,6-trideoxy-β-D-*erythro*-hex-5-enopyranoside (**1**),[4] an intermediate in our synthesis[4,5] of D-ristosamine, was treated with an equimolar amount of $HgCl_2$ in hot aqueous acetone for four hours. Instead of the

Table 1. ^{13}C N.m.r. data (50.3 MHz) for compounds (**3**) and (**5**).

Compound	Solvent	Chemical shifts δ (p.p.m.)						
		C-1	C-2	C-3	C-4	C-5	C-6	Ester C=O
(**3**)	$CDCl_3$	190.3	128.9	132.8	33.7	66.4	46.9	166.0
(**5**)	$(CD_3)_2CO$	200.2	81.5	60.7	37.0	65.9	47.5	165.7



Bz = PhCO

expected 2L-2,3/5-3-azido-2-benzoyloxy-5-hydroxycyclohexanone (**2**) we isolated the unsaturated 2-benzoyloxy-5-hydroxycyclohex-2-enone (**3**) {78%; m.p. 124—125 °C; $[\alpha]_D$ + 27.8° ($CHCl_3$); M^+ 232; δ 6.74 (3-H), 4.75 (5-OH)}.† During the transformation the C-3 azide and C-4 hydrogen functions of (**1**), being *trans* to each other, are presumably eliminated in the form of hydrazoic acid. It is believed that this undesired elimination arises from the above-mentioned steric arrangement.

This latter assumption is strongly supported by the observation that no such elimination occurs under similar conditions in the case of the α-D-*threo* isomer (**4**)[6] of (**1**), in which the 3-N_3 and 4-H groups are *cis*; instead the product was 2L-2,5/3-2-*O*-benzoyl-3-azido-5-hydroxycyclohexanone (**5**) {82%; m.p. 182—183 °C; $[\alpha]_D$ −126.6° ($CHCl_3$); M^+ 275; δ 4.45 (5-OH)}.‡

Compound (**5**), containing both functions needed for the conversion into a 1,3-diaminocyclitol analogue, seems to be an appropriate material for the chemical and muta-synthesis of novel aminocyclitol antibiotic derivatives.

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† All new compounds gave satisfactory elemental analyses and were adequately identified by i.r., ^1H and ^{13}C n.m.r., and mass spectral analyses.

‡ ^1H N.m.r. (200 MHz, [$^2H_6$]acetone) coupling constants [*J*(H, H), Hz] for compound (**5**): (2,3) 10.7, (3, 4e) 4.5, (3, 4a) 11.0, (4e, 5) 5.0, (4a, 5) 2.0, (5, 6e) 3.0, (5, 6a) 4.0, (4e, 6e) 2.5.