Synthesis of 2,3,5-Tri-*O*-benzyl-α- (and β-)-D-ribofuranosylethyne, Potential Intermediates for the Synthesis of *C*-Nucleosides

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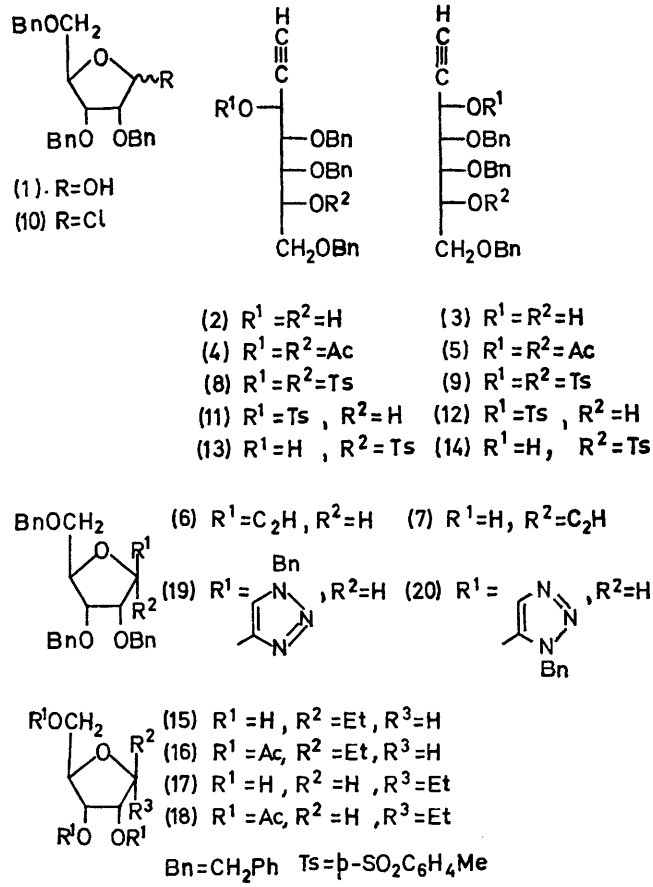
Summary Two methods are described for the synthesis of the anomers of 2,3,5-tri-*O*-benzyl-D-ribofuranosyelthyne; the β-anomer has been converted into 1,2,3-triazole derivatives by reaction with benzyl azide.

WE have been interested in the preparation of D-ribofuranosyl derivatives of acetylene as potential intermediates for the synthesis of naturally occurring *C*-nucleoside antibiotics[1,2] and related compounds[3-6] by 1,3-dipolar additions[7] and other reactions.

In the first method, the ribofuranose (**1**)[8] was treated with ethynylmagnesium bromide in tetrahydrofuran.[9] The crude product was shown to be a mixture of epimers (**2**) and (**3**) by the n.m.r. spectrum of the derived mixture of diacetates (**4**) and (**5**); the isomer ratio, calculated both from the relative intensities of the acetylenic proton signals and from those of the *C*-methyl groups, was 7:3. That the predominant diol isomer had the D-*altro*-configuration (**2**) is shown later. The mixture of diols (**2**) and (**3**) was treated with toluene-*p*-sulphonyl chloride in pyridine and the resulting mixture chromatographed on silica gel. The major product, which crystallised after nine months, was the ribofuranosyl-ethyne (**6**)† [51% from (**1**)], m.p. 63—64°, $[\alpha]_D$ + 9·7° (*c* 4·9 in $CHCl_3$), together with a small amount of the impure syrupy anomer (**7**) (8%) and a mixture of disulphonates (**8**) and (**9**) (16%). The formation of cyclic, sulphur-free products was to be expected from the work of Rabinsohn and Fletcher;[10] Gero[11] has recently described further examples. The assignment of the β-D-*ribo*-configuration (**6**) to the major product required some proof, and this was provided by the second method of synthesis now to be described.

The ribofuranosyl chloride (**10**)[12] reacted with ethynylmagnesium bromide[13] in tetrahydrofuran to yield, after chromatography on silica gel, the β-D-*ribo*-compound (**6**) (8%), $[\alpha]_D$ + 13·0° (*c* 2·5 in $CHCl_3$), whose n.m.r. spectrum was indistinguishable from that of the compound assigned this structure above. The major product was the α-anomer (**7**)† (61%), m.p. 52—53°, $[\alpha]_D$ + 79·7° (*c* 2·2 in $CHCl_3$). These two products were assigned the D-*ribo*-configuration from their mode of formation from the chloride (**10**), and the anomeric configurations were assigned by Hudson's rule.



† This compound gave correct elemental analysis and spectroscopic data.

It was no surprise that the α-anomer (**7**) was the major product in the reaction from the chloride (**10**).[12] Thus, the two methods of synthesis are complementary, the first giving a reasonable yield of the β-anomer and the second yielding mainly the α-anomer.

In the formation of the β-D-*ribo*-isomer (**6**) in the first synthesis it is assumed that monosulphonylation of the D-*altro*-diol (**2**) occurs to give the sulphonate (**11**) which undergoes ring closure by attack of the C-6 hydroxy-group at C-3, with inversion. The diol (**2**) is therefore the major product from the initial Grignard reaction. The impure α-D-*ribo*-compound would arise similarly from the D-*allo*-diol (**3**) to form the sulphonate (**12**), followed by ring closure. There was evidence (t.l.c.) for the formation of small amounts of other sulphonate-free products. We assume these to be cyclic compounds of the L-*lyxo*-configuration arising from the monosulphonates (**13**) and (**14**).

When the acetylene (**6**) was hydrogenated (5% Pd–C), β-D-ribofuranosyl ethane (**15**),† $[\alpha]_D$ + 0·9° (*c* 1·14 in H_2O), was formed in high yield; the derived triacetate (**16**)† had $[\alpha]_D$ + 6·2° (*c* 1·78 in MeOH). Similarly, from the acetylene (**7**) was formed the crystalline α-D-ribofuranosylethane (**17**),† m.p. 94—95°, $[\alpha]_D$ + 32·7° (*c* 1·5 in H_2O); triacetate (**18**),† $[\alpha]_D$ + 43·9° (*c* 0·7 in MeOH). The specific rotations of compounds (**16**)—(**18**) agree with the earlier assignments of anomeric configuration to (**6**) and (**7**).

The acetylene (**6**) was heated with benzyl azide[14,15] to give, in very high yield, a mixture of isomeric triazoles (**19**)† and (**20**).† The isomers were separated by treatment with ethanol, from which one of them crystallised virtually quantitatively (41%), m.p. 125—126°, $[\alpha]_D$ + 13° (*c* 1·38 in $CHCl_3$). The other isomer (49%) was a syrup, $[\alpha]_D$ − 20·5° (*c* 1·95 in $CHCl_3$). Analytical and spectral data (n.m.r. and mass spectrum) left no doubt that the two compounds were isomeric, but no decision could be made between the two structures.

The ribosylacetylenes (**6**) and (**7**) should be versatile intermediates for the elaboration of the heterocyclic ring systems present in the *C*-nucleosides showdomycin,[1] formycin B,[2] and variants of these structures.

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