Synthesis of D-Ribofuranosyl Derivatives of Methyl Propiolate as C-Nucleoside Precursors

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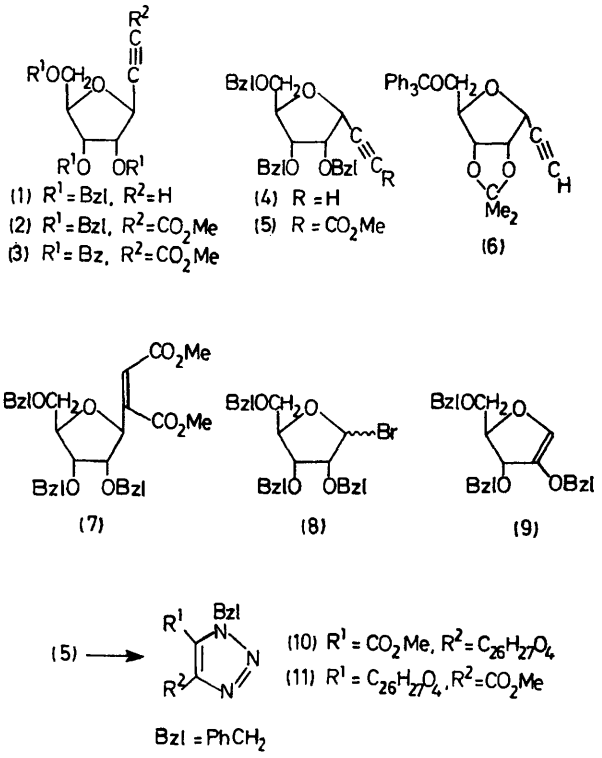
Summary The synthesis of methyl 4,7-anhydro-5,6,8-tri-*O*-benzyl-2,3-dideoxy-D-*allo*-oct-2-ynoate (**2**) and its D-*altro* isomer (**5**) is reported; the ester (**5**) reacts with benzyl azide to give two isomeric triazoles (**10**) and (**11**).

WE have been interested in the exploitation of ribofuranosylethynes, such as (**1**), (**4**), and (**6**), as intermediates for the synthesis of *C*-nucleosides.[1-3] We have previously described the synthesis of the maleic ester (**7**),[3] and now report the synthesis of the acetylenic esters (**2**) and (**5**), compounds which should readily undergo cycloadditions and thus make available a range of *C*-nucleosides. A previous attempt[4] to synthesise the ester (**3**) was unsuccessful, yielding instead a 1,2 acetal, formed as a consequence of participation by a benzoyl group at C-2. Our own attempts to prepare (**2**) by normal carboxylation reactions, or using the method described by Heck,[5] have been unsuccessful.

The ribofuranosyl bromide (**8**)[6] in methylene chloride was stirred for 50 min with AgC ≡ CCO_2Me[4] (1·16 mol. equiv.). Chromatography on silica gel yielded the enol ether (**9**) (10%), $[\alpha]_D$ − 1·8° ($CHCl_3$), whose 100 MHz ^1H n.m.r. spectrum included a signal at δ 5·08 (s, 1-H). Further elution yielded the ester (**2**) (21%), $[\alpha]_D$ + 16·0° ($CHCl_3$); ν_{max} 2240 (C≡C) and 1718 cm^{-1} (C=O); δ (100 MHz; $CDCl_3$) 3·68 (3H, s, OMe). Finally, further elution yielded the ester (**5**) (42%) m.p. 38—39°, $[\alpha]_D$ + 84·3° ($CHCl_3$); ν_{max} 2240 (C≡C) and 1712 cm^{-1} (C=O); δ (100 MHz; $CDCl_3$) 3·74 (3H, s, OMe).

The tentative assignment of the anomeric configuration in the esters (**2**) and (**5**), made by application of Hudson's rules, was confirmed by conversion into the known ethynes (**1**) and (**4**).[1,2] The ester (**2**) was stirred with KOH (1·04 mol. equiv.) in aqueous dioxan at room temperature, yielding the salt of the parent acid which, on acidification and heating in boiling benzene for 18 h, yielded the β-ethyne (**1**)[1,2] (60%) m.p. 62—63°, $[\alpha]_D$ + 7·3° ($CHCl_3$). A similar sequence of reactions was performed on the ester (**5**) yielding the α-ethyne (**4**)[1,2] (77%), m.p. 50—51°, $[\alpha]_D$ + 80·6° ($CHCl_3$).

Since we had expected that the acetylenic esters (**2**) and (**5**) would readily undergo cycloadditions we have examined the reaction of (**5**) with benzyl azide. The ester (**5**) in dry benzene was heated under reflux for 5·5 h with benzyl azide (4 mol. equiv.). Chromatography on silica gel yielded first the unchanged ester (**5**) (9·9%), followed by the two isomeric triazoles (**10**) and (**11**). The first eluted triazole was isolated as a syrup (51%), $[\alpha]_D$ + 12·8° ($CHCl_3$); ν_{max} 1712 cm^{-1} (C=O); *m/e* 619 (M^+). The isomeric triazole was also isolated as a syrup (34%), $[\alpha]_D$ − 44·3° ($CHCl_3$); ν_{max} 1723 cm^{-1} (C=O). The mass spectrum was similar to that of the isomeric triazole. It has not yet been possible to assign individual structures to the two triazoles.



All new compounds gave satisfactory analytical data.

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