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Preliminary communication

Synthesis of D-ribofuranosyl derivatives of dimethyl maleate and of ethyl acetate as C-nucleoside precursors*

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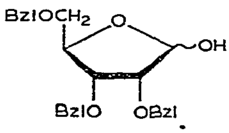
We have been interested in the exploitation of 2,3,5-tri-*O*-benzyl-D-ribofuranose (**1**) as a starting material for the synthesis of *C*-nucleosides[1]. There have been recent publications on the preparation of tri-*O*-benzyl-D-ribofuranosyl derivatives of esters[2-5] which prompt us to report some related studies.

The ethyne **2**, dissolved in methanol, was stirred overnight with palladium chloride (1.01 mol. equiv.) and mercuric chloride (1.01 mol. equiv.) in the presence of carbon monoxide (1 atm)[6]. The major product, isolated by chromatography on silica gel, was the maleic ester **3** (80%), ν_{max} 1735 cm^{-1} (C=O). The 100-MHz p.m.r. spectrum of **3** ($CDCl_3$) included signals at δ 3.68 (s, OMe), 3.72 (s, OMe), 4.75 (dd, H-1, $J_{1,2}$ 4.5, $J_{allylic}$ 1.5 Hz), 6.33 (d, C*H*CO_2Me, $J_{allylic}$ 1.5 Hz). The maleate stereochemistry was assigned by analogy with the results of Heck[6] and by comparison of the allylic coupling constant in the p.m.r. spectrum of **3** with those of **4**[2], **5**[7], and **6**[7]; the values of $J_{allylic}$ are 2.0, 2.0, and 0.5 Hz, respectively. The overall yield of **3** from D-ribose (28%) compares favourably with that of similar intermediates used for the synthesis of showdomycin[2,8] and we are now engaged in the completion of this synthesis.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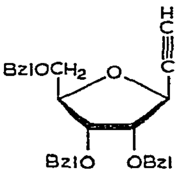
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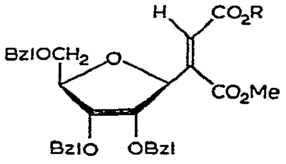
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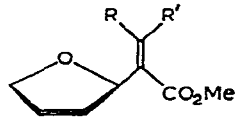
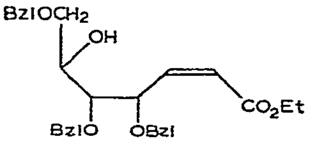
4 R = Et


5 R = H, R′ = CO_2Me
6 R = CO_2Me, R′ = H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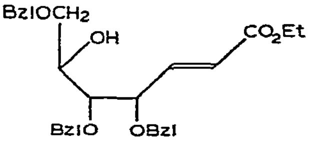
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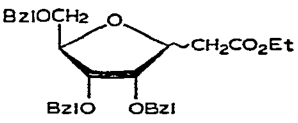
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We have also been interested in the synthesis of *C*-ribofuranosyl derivatives of ethyl acetate. Such compounds have recently been synthesised by Hanessian and his co-workers[3,9], ester protection being employed for the sugar hydroxyl groups. In recent years, the Wittig reaction has been applied extensively in carbohydrate chemistry[10], and also to syntheses of potential *C*-nucleoside intermediates[11]. Our interest was attracted by the reported reaction of stabilised Wittig reagents with free sugars[12,13], normally carried out using *N,N*-dimethylformamide as solvent, in which cyclic compounds are major products.

Treatment of **1** with carbethoxymethylenetriphenylphosphorane[14] in anhydrous 1,2-dimethoxyethane, in the presence of a catalytic amount of benzoic acid, yielded two isomeric olefins, **7** and **8**, in 90% yield. Fractionation of the mixture by chromatography on silica gel yielded first **7**, $[\alpha]_D$ +10.4° (ethanol), and then **8**, $[\alpha]_D$ +35.4° (ethanol), in the ratio 2:3. The 100 MHz p.m.r. spectrum of **7** ($CDCl_3$) included signals at δ 6.42 (dd, H-3) and 5.98 (d, H-2) ($J_{2,3}$ 12 Hz), while that of **8** had signals at δ 7.08 (dd, H-3) and 6.12 (dd, H-2) ($J_{2,3}$ 15.6, $J_{2,4}$ 1.5 Hz), showing that **7** and **8** are indeed the cis and trans olefins, respectively.

When **7** or **8** was treated with a catalytic amount of sodium ethoxide in ethanol, cyclisation took place within 1 min, to give the anomeric mixture **9** as an oil, $[\alpha]_D$ +10.2° (ethanol), in quantitative yield. The p.m.r. spectrum of **9** (220 MHz, $CDCl_3$) showed signals at δ 1.18 (t, CH_3), 1.22 (t, CH_3), 2.52 (q, CH_2CH_3), and 2.77 (q, CH_2CH_3); the relative intensity of the methylene proton signals indicated that the anomers were present in approximately equal amounts. The two anomers cannot be separated by chromatography. The reactions described make the anomeric esters **9** available from D-ribose in 63% yield.

The ring closure clearly involves nucleophilic addition to the double bond in **7** and **8**. It might have been expected that different anomer ratios in **9** would result when **7** and **8** were each subjected to ring closure under conditions of kinetic control, but we have no evidence that this is the case. The two olefins do not cyclise under acidic conditions. Ring closure may also be brought about by heating **7** or **8** in *N,N*-dimethylformamide. It now seems logical to assume that when the Wittig reactions involving free sugars are carried out in *N,N*-dimethylformamide as solvent[12,13], cyclic products arise from first-formed olefinic intermediates and no special mechanism[13] need be invoked for their formation.

All new compounds gave satisfactory analytical and spectroscopic data. We thank Heriot-Watt University for a post-graduate studentship (to P.D.T.), and the Science Research Council for n.m.r. spectra measured at the PCMU, Harwell.

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