C-Nucleoside Studies. Part I. Synthesis of [2,3,5-Tri-*O*-benzyl-α(and β)-D-ribofuranosyl]ethyne [1]

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Ethynylmagnesium bromide reacted with 2,3,5-tri-*O*-benzyl-D-ribofuranose (1) in tetrahydrofuran to give, in quantitative yield, a mixture of 4,5,7-tri-*O*-benzyl-1,2-dideoxy-D-*altro*- and D-*allo*-hept-1-ynitol [(2) and (7)] in the ratio 7:3. Treatment of the mixture with toluene-*p*-sulphonyl chloride in pyridine afforded (2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)ethyne (13) (52%) and its α-anomer (16) (13%), together with 4,5,7-tri-*O*-benzyl-1,2-dideoxy-3,6-bis-*O*-*p*-tolylsulphonyl-D-*altro*-hept-1-ynitol (4) (16%). 2,3,5-Tri-*O*-benzyl-D-ribofuranosyl chloride (12) and ethynylmagnesium bromide gave the ethynes (13) and (16) in 8 and 63% yield, respectively.

Hydrogenation of the ethynes (13) and (16) (Pd–C) afforded β-D-ribofuranosylethane (15) and the crystalline anomer (18), respectively, together with 5,6,7-trideoxy-L-*ribo*-heptitol (27), characterised as the tetra-acetate (28).

The β-ethyne (13), on treatment with benzyl azide, was converted into 1-benzyl-4(and 5)-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-1,2,3-triazole [(30) and (31)] in approximately equal amounts.

NATURALLY occurring D-ribofuranosyl derivatives have been described in which the carbohydrate unit is linked to a heterocycle by a C–C rather than the more usual C–N bond.[2] Such compounds are termed *C*-nucleosides. Pseudouridine, the first of these compounds to be discovered,[3] is a component of transfer ribonucleic acid. The other, more recently discovered, compounds are active as antibiotics and antitumour agents. The synthesis of these compounds has attracted a great deal of attention and syntheses of pseudouridine,[4-7] showdomycin,[8,9] oxoformycin,[10,11] formycin B,[12] formycin,[13] and pyrazomycin [14] have already been described. In addition, a number of

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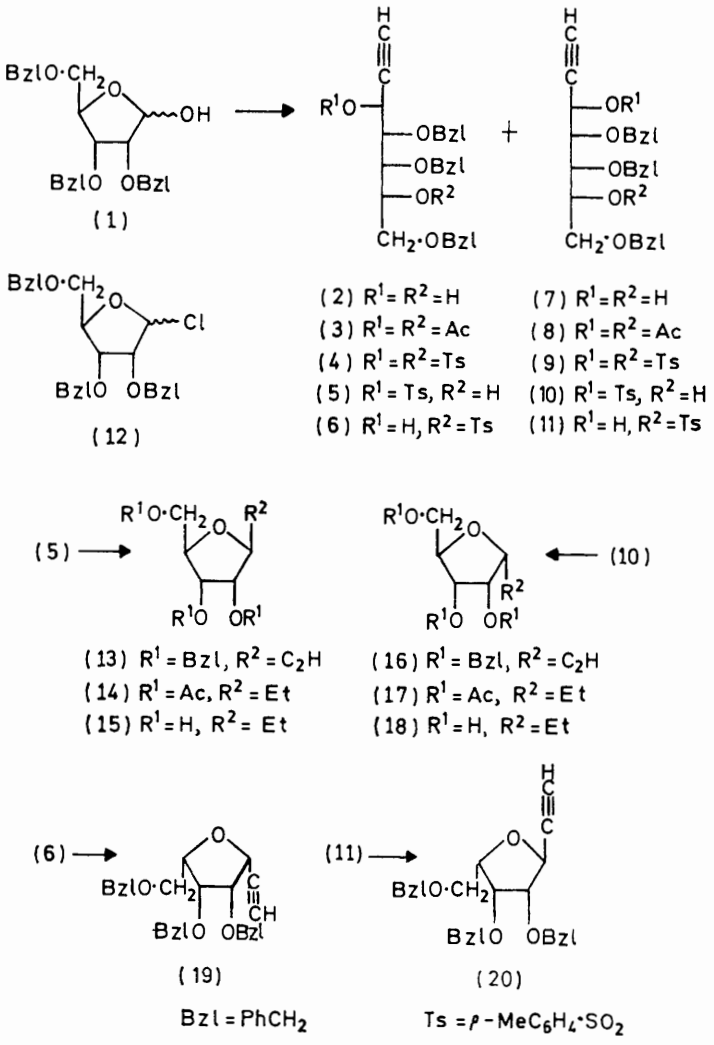
syntheses of potential value for preparation of *C*-nucleosides and their analogues have been explored.[15-29]

We wished to develop general methods of synthesis in this field, leading not only to the naturally occurring *C*-nucleosides themselves, but also to analogues of potential value as antibiotics. In the first instance our objective has been the preparation of β-D-ribofuranosylethyne and its derivatives.

Acetylenic derivatives of carbohydrates have been known for many years [30] and were exploited by Raphael in the immediate post-war period.[31] More recently Horton and his colleagues have studied a number of reactions of ethynylmagnesium bromide with *aldehydo*-sugars,[32,33] and other sugar derivatives containing a free carbonyl group, partly aimed at the synthesis of *C*-nucleoside analogues by 1,3-dipolar additions to the acetylenic function.[25,34]

We chose 2,3,5-tri-*O*-benzyl-D-ribofuranose (1) as a readily available intermediate,[35-37] in the expectation that it would react as a free aldehyde in the presence of a Grignard reagent.[32,38] When the hemiacetal (1) was treated with an excess of ethynylmagnesium bromide in tetrahydrofuran a mixture of the two diols (2) and (7) was obtained in virtually quantitative yield. Acetylation afforded a syrupy mixture of diacetates (3) and (8) whose 100 MHz n.m.r. spectrum showed two signals due to acetylenic protons, in the ratio 7 : 3 and two pairs of signals due to *O*-acetyl groups, in the same ratio. The diacetate mixture eventually crystallised and a pure diacetate, shown by n.m.r. to be the major component, was obtained from it by recrystallisation from ethanol. After this part of the work was complete, Chilton and his colleagues [27] showed that 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose undergoes a similar reaction with ethynylmagnesium bromide.

Our initial attempts to bring about cyclisation of the heptynediols (2) and (7) used acid catalysis.[39] Dilute sulphuric acid in dioxan formed only products of lower R_F value on t.l.c., and toluene-*p*-sulphonic acid in hot benzene gave a complex mixture of products. Treatment with dimethyl sulphoxide [40] at various temperatures gave no useful results, and it was therefore decided to study the ring closure of toluene-*p*-sulphonate esters. Ring closure of the heptynitols (2) and



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(7) to yield products of D-*ribo*-configuration, (13) and (16), required preferential sulphonylation at O-3, as

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in the sulphonates (5) and (10), followed by base-catalysed intramolecular nucleophilic displacement with inversion at C-3. A similar process involving the 6-sulphonates (6) and (11) would lead to the cyclic products (19) and (20), respectively, of the L-*lyxo*-configuration. It was expected that *p*-tolylsulphonylation would occur preferentially at O-3 because of the relatively small bulk of the ethynyl group. When the mixture of diols (2) and (7) was treated with 1·1 mol. equiv. of toluene-*p*-sulphonyl chloride in pyridine at room temperature for 5 days, little reaction occurred. Complete conversion of the mixture of diols into products was achieved by heating in pyridine at 60° with 2·2 mol. equiv. of the acid chloride. Three major products were detected by t.l.c. and were purified by chromatography on silica gel.

The most polar product did not crystallise. It gave analytical and spectroscopic data corresponding to the disulphonates (4) and (9) (16% yield). In the n.m.r. spectrum ($CDCl_3$; 100 MHz) the acetylenic proton signal was masked by the CH_3 signals of the toluene groups. Addition of a few drops of pyridine caused the acetylenic signal to appear at lower field and it was clearly observed in the 220 MHz spectrum. There was no evidence of heterogeneity of the signals due to the acetylenic proton or the toluene methyl groups, even in the presence of pyridine. Subsequent work, described below, showed the product to consist of only the D-*altro*-isomer (4).

The other two compounds crystallised and were sulphur-free. They have been shown to be the β-D-ribofuranosylethyne (13) [52% from (1)] and the α-D-ribofuranosylethyne (16) [13% from (1)]. The two compounds gave analytical and spectroscopic data consistent with the isomeric structures (13), (16), (19), and (20). In order to distinguish between the D-*ribo*-structures (13) and (16) on the one hand and the L-*lyxo*-structures on the other, an unambiguous synthesis of the former pair of isomers was sought.

Phenylethynylmagnesium bromide reacts with tetra-*O*-acetyl-α-D-glucopyranosyl bromide to give a mixture of the anomeric glycosylacetylenes,[25,41] a reaction complicated by the presence of labile ester groups. As expected, the benzyl ether group was ideally suited for protection to these conditions, and when the ribofuranosyl chloride (12) [42] was treated with ethynylmagnesium bromide in tetrahydrofuran two main products were detected by t.l.c. Separation by chromatography yielded the same two isomers that had been isolated previously, showing that the latter were derivatives of D-ribofuranose, (13) and (16). Of the two ribofuranosylethynes the major product (63%) had $[\alpha]_D$ +79·7° and the minor (8%) $[\alpha]_D$ +13·0°. Direct application of Hudson's rule to these compounds [25] indicates that the former compound has the α-D-structure (16) and the latter is the β-D-isomer (13). In support of this conclusion it is known that the chloride (12) yields predominantly α-D-isomers by nucleophilic attack at C-1 and is itself probably β in configuration.[42]

These assignments at the anomeric centre were confirmed by a study of the hydrogenation products from the two isomers. Catalytic hydrogenation, followed by acetylation and purification of the main product by chromatography yielded the ribofuranosylethanes (14) and (17); subsequent deacetylation afforded the triols (15) and (18). The specific rotations of compounds (14), (15), (17), and (18) are in complete agreement with the earlier assignments of structures. It is notable, too, that the specific rotations of the ribofuranosylethanes (14) and (15) (6·2 and 0·9°, respectively) are of low magnitude, reflecting the greater symmetry of the β-D-series.

The two methods of synthesis are complementary, making both the ribofuranosylethynes (13) and (16) available in reasonable quantity for further elaboration. We now return to some points of interest arising from the first synthesis.

The formation of cyclic products by treatment of the heptynitols with toluene-*p*-sulphonyl chloride in pyridine was not unexpected.[43-46] Of particular relevance is the report that 1,4-anhydro-2,3,5-tri-*O*-benzyl-D-arabinitol is formed from the parent diol.[44] The β-D-ribofuranosylethyne (13) clearly arose from the D-*altro*-component (2) of the mixture, by way of the 3-sulphonate (5), whereas the α-anomer (16) was produced *via* the D-*allo*-diol (7) and its 3-sulphonate (10). As expected, when the crystalline diacetate (3) of the major component of the heptynitol mixture was deacetylated and the pure diol (2) was subjected to cyclisation conditions the β-D-ribofuranosylethyne (13) was the only cyclic compound formed, together with the disulphonate (4). The latter was indistinguishable from the disulphonate isolated earlier from the sulphonylation of the mixture of diols (2) and (7). The origin of the disulphonate is of some interest. If sulphonylation at O-3 in the diols (2) and (7) were not exclusive, then some of the 6-sulphonates (6) and (11) would be produced. Cyclisation of the D-*altro*-sulphonate is probably unfavourable because of the all-*cis*-arrangement of groups in the transition state leading to the β-L-*lyxo*-isomer (19),[39,45,47] and further sulphonylation to yield the disulphonate (4) may take preference over ring closure. None of the D-*allo*-disulphonate (9) was detected, nor was the α-L-lyxofuranosylethyne (20). In an attempt to increase the regioselectivity of sulphonylation at O-3 the hindered mesitylenesulphonyl chloride [48] was used, but the

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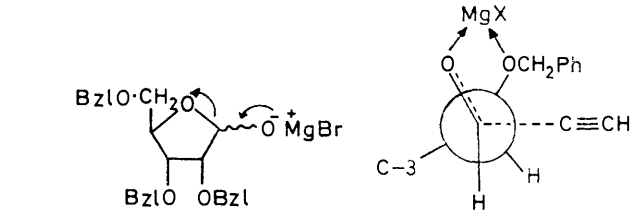
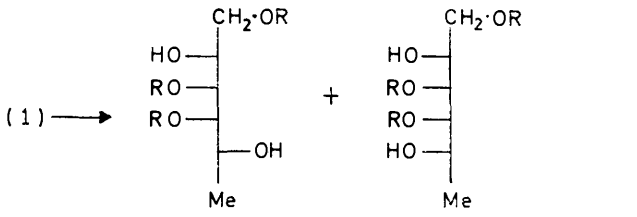
reaction was very slow and further heating caused gross decomposition.

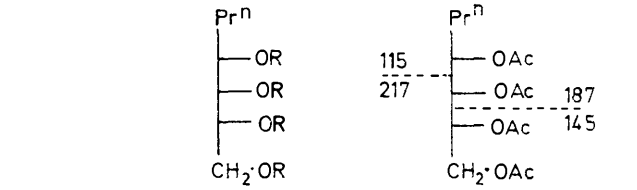
The preferential formation of the D-*altro*-diol (**2**) from the ribofuranose (1) is in keeping with experimental findings in the glyceraldehyde series,[49,50] and is consistent with the rules devised by Cram [51,52] and by Karabatsos.[53] It is assumed that ring opening to the *aldehydo*-form takes place, by way of the anion (21). The transition state, represented by (22), shows nucleophilic attack at C-1 from the side opposite to the bulky carbon chain. In the present work it was found that the reaction of the ribofuranose (1) with methylmagnesium



(21) (22)



(23) R = Bzl (25) R = Bzl
(24) R = H (26) R = H



(27) R = H (29)
(28) R = Ac

Bzl = $PhCH_2$

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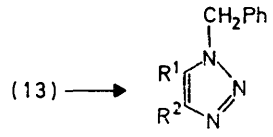
iodide in ether was even more stereoselective, affording the D-*talo*-isomer (23) in preference to the L-*allo*- (25) (9 : 1). The products were examined after hydrogenolysis to the parent deoxyhexitols, (24) and (26), as described in the Experimental section.

During the hydrogenation of the ethynes (13) and (16) it was noticed that a second product, apparently the same compound in each case, was produced. The product was isolated from the hydrogenation of the α-ethyne (16) by conversion into a peracetate, which was shown by n.m.r. and mass spectrometry to be the tetra-acetate (28). The presence of an n-propyl group was clearly shown by a three-proton triplet at δ 0·89 together with a four-proton multiplet at δ 1·2—1·7. In the mass spectrum the peak of highest mass (*m/e* 273) arose from the loss of an acetate radical from the molecular ion. Peaks at *m/e* 115, 145, 187, and 217 correspond to the scission of carbon–carbon bonds between neighbouring acetoxy-groups,[54] as shown in formula (29). The minor product is therefore the tetraol (27), arising by hydrogenolytic cleavage of the C–O bond between the ring oxygen atom and C-1 of the ribose system, probably at the allyl ether stage.

1,3-Dipolar addition was first used in the carbohydrate field in 1957,[55,56] and applied to the synthesis of nucleoside analogues.[56,57] As a model reaction in our own system we have treated the ethyne (13) with benzyl azide at 100°. After chromatography and crystallisation two isomeric triazoles, (30) and (31), were obtained, one crystalline (41%) and the other a



(30) R^1 = H, R^2 = tri-*O*-benzyl-β-D-ribofuranosyl

(31) R^1 = tri-*O*-benzyl-β-D-ribofuranosyl, R^2 = H

SCHEME 3

syrup (49%). It has not been possible to assign individual structures to the two compounds. It would have been predicted, from arguments based on steric effects,[34] that the isomer (30) would preponderate, and it is clear that other factors, presumably polar in nature, are also involved. Other workers have described the formation of two isomers in similar reactions.[58]

EXPERIMENTAL

I.r. spectra were measured for potassium bromide discs or chloroform films using a Perkin-Elmer 257 spectrophotometer. Mass spectra were recorded with an A.E.I. MS902 or MS30 spectrometer. N.m.r. spectra were measured for 10% solutions (w/v) on a Perkin-Elmer R 12B spectrometer at 60 MHz, a Varian HA-100D spectrometer at 100 MHz, and a Varian HR-220 spectrometer at 220 MHz. Tetramethylsilane was used as internal standard in deuteri-

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ated organic solvents, and sodium 3-trimethylsilylpropane-1-sulphonate in deuterium oxide. Specific rotations refer to room temperature (20—25°) and were measured using a Bendix-NPL automatic polarimeter 143D (path length 1 cm).

Evaporations were carried out under reduced pressure by means of a rotary evaporator. Light petroleum refers to the fraction of b.p. 60—80°. Adsorption chromatography was carried out using silica gel (Merck; 70—230 mesh ASTM). For t.l.c. Kieselgel G (Merck) was used as adsorbent; carbohydrates were generally detected by anisaldehyde–sulphuric acid.[59] G.l.c. of trimethylsilyl ethers [60] was performed with a Perkin-Elmer F11 gas chromatograph using a flame-ionisation detector (2 m column of 2·5% silicone OV1 on Chromosorb G; operating temperature 170°; nitrogen carrier gas pressure 15 lb in^{-2}).

Reaction of 2,3,5-*Tri*-O-*benzyl*-D-*ribofuranose* (1) *with Ethynylmagnesium Bromide.*—A solution of the sugar (1) (2·0 g) in dry tetrahydrofuran (25 ml) was added during 30 min to a stirred solution of ethynylmagnesium bromide [61] in tetrahydrofuran (0·45M; 210 ml). Acetylene was bubbled through the mixture during the addition and for a further 3 h. Next day the mixture was concentrated (60 ml) and diluted with ether (60 ml). The organic phase was washed successively with aqueous 10% ammonium chloride (3 × 80 ml) and water (3 × 80 ml), dried ($MgSO_4$), and evaporated to give a syrupy mixture of 4,5,7-tri-*O*-benzyl-1,2-dideoxy-D-*altro*- and D-*allo*-hept-1-ynitol [(2) and (7)] (2·1 g, 99%); $\nu_{max.}$ (film) 3440 (OH), 3290 (≡C–H), and 2100 cm^{-1} (C≡C); δ (60 MHz; $CDCl_3$) 2·5 (1H, d, acetylenic), 3·4—4·9 (14H, m), and 7·25 (15H, m, Ph).

The above mixture (152 mg) in pyridine (3 ml) was treated overnight with acetic anhydride (0·7 g). The product was isolated by means of chloroform to yield a pale-yellow syrup (0·15 g, 84%) composed of 3,6-di-*O*-acetyl-4,5,7-tri-*O*-benzyl-1,2-dideoxy-D-*altro*- and D-*allo*-hept-1-ynitol [(3) and (8)]; $\nu_{max.}$ (film) 3270 (≡C–H), 2110 (C≡C), and 1745 cm^{-1} (C=O); δ (100 MHz; $CDCl_3$) 1·97, 2·03, and 2·08 (6H, OAc), 2·47 and 2·49 (1H, C≡CH), 2·4—5·2 (10H, m), 5·48 (1H, m), 5·73 (1H, m), and 7·28 (15H, m, Ph). A ten-fold expansion of the n.m.r. spectrum revealed the presence of two doublets at 2·47 and 2·49, in the ratio 7 : 3, and four lines between 1·97 and 2·08. The ratio of the areas of the two outer peaks to the area of the two inner peaks was 7 : 3.

After several months the mixture crystallised. Repeated recrystallisation from ethanol afforded the pure D-altro-*diacetate* (3) (30 mg, 17%), m.p. 64—65°, $[\alpha]_D$ −29·6° (*c* 1·08 in $CHCl_3$); $\nu_{max.}$ (KBr) 3280 (≡C–H), 2110 (C≡C), 1735 cm^{-1} (C=O); δ (100 MHz; $CDCl_3$) 1·96 (3H, s, AcO), 2·06 (3H, s, AcO), 2·46 (1H, d, $J_{1,3}$ 2·25 Hz, H-1), 3·68 (2H, d, $J_{6,7}$ 4·5 Hz, H-7), 3·8—4·1 (2H, m, H-4 and H-5), 4·4—4·8 (6H, m, $PhCH_2$), 5·46 (1H, $J_{5,6}$ 9·0 Hz, H-6), 5·7 (1H, dd, $J_{3,4}$ 5·0 Hz, H-3), and 6·9—7·4 (15H, m, Ph) (Found: C, 72·35; H, 6·45. $C_{32}H_{34}O_7$ requires C, 72·4; H, 6·5%).

Deacetylation of the diacetate (3) (0·218 g) in methanol (10 ml) using methanolic 0·1M-sodium methoxide (0·2 ml) afforded the pure *diol* (2) as a clear syrup (0·181 g, 98%), $[\alpha]_D$ +16·4° (*c* 1·04 in $CHCl_3$); $\nu_{max.}$ (film) 3440 (OH), 3290 (≡C–H), and 2100 cm^{-1} (C≡C); δ (100 MHz; $CDCl_3$) 2·47 (1H, d, ≡C–H), 2·8 (2H, s, OH), 3·55 (2H, d), 3·84 (2H, m), 4·15 (1H, q), 4·46 (2H, s, $PhCH_2$), 4·58—4·87 (5H, m), and 7·28 (15H, m, Ph).

Treatment of 4,5,7-*Tri*-O-*benzyl*-1,2-*dideoxy*-D-altro- *and* D-allo-*hept*-1-*ynitol* [(2) *and* (7)] *with Toluene*-p-*sulphonyl Chloride.*—A solution of toluene-*p*-sulphonyl chloride (7·22 g, 2·2 mol. equiv.) in dry, ethanol-free chloroform (50 ml) was added during 2 h to a stirred solution of the mixed diols [(2) and (7)] (8·32 g) in dry pyridine (70 ml) at 60°. The resulting solution was kept at 60° for a further 6 h, then cooled, and a few chips of ice were added. After 3 h the product was isolated using chloroform to yield a dark crimson syrup (8·7 g), shown by t.l.c. (1 : 1 light petroleum–ether) to consist of three components. The syrup (2·4 g) was chromatographed on silica gel.

Elution with light petroleum–ether (17 : 3) gave (2,3,5-*tri*-O-*benzyl*-β-D-*ribofuranosyl*)*ethyne* (13), which crystallised after nine months. Recrystallised from ethanol the ethyne (1·17 g, 52%) had m.p. 63—64°, $[\alpha]_D$ +9·7° (*c* 4·9 in $CHCl_3$); $\nu_{max.}$ (KBr) 3250 (≡C–H) and 2110 cm^{-1} (C≡C); δ (100 MHz; $CDCl_3$) 2·49 (1H, d, *J* 2 Hz, ≡CH), 3·5—4·8 (12H, m), and 7·2—7·4 (15H, m, Ph); *m/e* 351 (*M* − Ph, weak) and 337 (*M* − C_7H_7, weak) (Found: C, 78·4; H, 6·4. $C_{28}H_{28}O_4$ requires C, 78·5; H, 6·6%).

Elution with light petroleum–ether (4 : 1) gave (2,3,5-*tri*-O-*benzyl*-α-D-*ribofuranosyl*)*ethyne* (16) (0·3 g, 13%). After recrystallation from ethanol–water (3 : 1) it had m.p. 52—53°; $\nu_{max.}$ (KBr) 3220 (≡C–H) and 2110 cm^{-1} (C≡C); δ (100 MHz; $CDCl_3$) 2·57 (1H, d, *J* 2 Hz, ≡CH), 3·4—5·0 (12H, m), and 7·26 (15H, s, Ph); *m/e* 351 (*M* − Ph, weak) and 337 (*M* − C_7H_7, weak) (Found: C, 78·4; H, 6·5%).

Elution with light petroleum (3 : 1) gave 4,5,7-*tri*-O-*benzyl*-1,2-*dideoxy*-2,6-*bis*-O-p-*tolylsulphonyl*-D-altro-*hept*-1-*ynitol* (4) as a syrup (0·64 g, 16%); $\nu_{max.}$ (film) 3280 (≡C–H), 2130 (C≡C), and 1195, 1180, and 1340 cm^{-1} (all OTs); δ (100 MHz; $CDCl_3$) 2·34—2·38 (7H, m, $ArCH_3$ and H-1), 3·6—5·4 (12H, m), and 7·0—7·8 (23H, m, Ar). When the n.m.r. spectrum was measured at 220 MHz the acetylenic doublet could be observed between the two *C*-methyl signals. Addition of pyridine (3 drops) caused the acetylenic signal to appear at lower field (Found: C, 66·7; H, 5·55; S, 8·7. $C_{42}H_{42}O_9S_2$ requires C, 66·8; H, 5·6; S, 8·5%).

Treatment of 4,5,7-*Tri*-O-*benzyl*-1,2-*dideoxy*-D-altro-*hept*-1-*ynitol* (2) *with Toluene*-p-*sulphonyl Chloride.*—The pure D-*altro*-diol (2) (0·126 g) in dry pyridine (1·3 ml) was treated with toluene-*p*-sulphonyl chloride (0·17 g, 2·2 mol. equiv.) in pure chloroform (1·2 ml), as in the previous experiment. The crude product (0·142 g) was subjected to chromatography as before. Elution with light petroleum–ether (4 : 1) gave the β-ethyne (13) (69 mg, 55%), m.p. 63—64° (from ethanol), indistinguishable (i.r., t.l.c., mixed m.p.) from the compound prepared above. Elution with light petroleum–ether (7 : 3) gave the disulphonate (4) as a syrup (42 mg, 19%), indistinguishable [t.l.c., n.m.r. (100 MHz)] from the disulphonate above.

Reaction of 2,3,5-*Tri*-O-*benzyl*-D-*ribofuranosyl Chloride* (12) *with Ethynylmagnesium Bromide.*—A solution of the chloride (12) [42] (1·62 g) in dry tetrahydrofuran (20 ml) was added during 0·5 h to 0·48M-ethynylmagnesium bromide [61] in dry tetrahydrofuran (180 ml). Acetylene was passed through the Grignard solution during the addition and for a further 3 h. The resulting solution was concentrated to 60 ml and diluted with ether (60 ml). The ethereal

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solution was washed with ice-cold aqueous 10% ammonium chloride (3 × 80 ml) and water (3 × 80 ml), dried (Na_2SO_4), and evaporated to give a deep red syrup (1·612 g), which was chromatographed on silica gel. Elution with light petroleum–ether (12 : 1) gave the β-ethyne (13) as a syrup (0·108 g, 8%), $[\alpha]_D$ +13·0° (*c* 2·5 in $CHCl_3$), indistinguishable [i.r., n.m.r. (100 MHz), t.l.c.] from the β-ethyne above. Elution with light petroleum–ether (4 : 1) gave the α-ethyne (16) (0·994 g, 63%), m.p. 52—53° (from aqueous ethanol), $[\alpha]_D$ +79·7° (*c* 2·2 in $CHCl_3$), indistinguishable (m.p., i.r., n.m.r., t.l.c.) from the α-ethyne above.

Catalytic Hydrogenation of (2,3,5-*Tri*-O-*benzyl*-α- *and* β-D-*ribofuranosyl*)*ethyne*.—(*a*) The α-ethyne (16) (0·99 g) in methanol (40 ml) was hydrogenated for 12 h at room temperature and a slight overpressure of hydrogen over 5% palladium–charcoal (0·25 g). The mixture was filtered and evaporated to yield a clear syrup (0·39 g), which was treated with pyridine (15 ml) and acetic anhydride (7·0 ml) overnight. The product was isolated by means of chloroform to give a syrup (0·61 g). T.l.c. (2 : 3 light petroleum–ether) showed two spots, the slower moving being the major component. The mixture was chromatographed on silica gel.

Elution with light petroleum–ether (4 : 1) gave 1,2,3,4-tetra-*O*-acetyl-5,6,7-trideoxy-L-*ribo*-heptitol (28) as a syrup (0·031 g), purified by distillation (140° and 10^{-2} mmHg); $\nu_{max.}$ (film) 1755 cm^{-1} (C=O); δ (100 MHz; $CDCl_3$) 0·89 (3H, t, C–CH_3), 1·2—1·7 (4H, m, CH_2–CH_2), 2·04 (12H, m, OAc), 4·0—4·5 (2H, m), and 4·9—5·4 (3H, m); *m/e* 273 (*M* − OAc, weak), 217 (weak), 187 (medium), 145 (strong), 115 (strong), and 43 (Ac^+, strong).

Light petroleum–ether (7 : 3) eluted the major component, (2,3,5-*tri*-O-*acetyl*-α-D-*ribofuranosyl*)*ethane* (17) as a syrup (0·343 g, 52%). Purified by distillation (140° and 10^{-2} mmHg) it had $[\alpha]_D$ +43·9° (*c* 0·7 in MeOH); δ (100 MHz; $CDCl_3$) 0·91 (3H, t, C–CH_3), 1·4—1·8 (2H, m, C–CH_2–C), 2·04, 2·08, and 2·12 (9H, all s, OAc), 4·04 (1H, m, H-1), 4·14—4·40 (3H, m), 5·16—5·36 (1H, m, H-3), and 5·46 (1H, q, H-2); *m/e* 288 (M^+, weak), 259 (*M* − Et, weak), and 215 (*M* − CH_2OAc, weak) (Found: C, 53·7; H, 7·1. $C_{13}H_{20}O_7$ requires C, 54·2; H, 7·0%).

Methanolic 0·1M-sodium methoxide (0·3 ml) was added to a solution of the triacetate (17) (0·28 g) in dry methanol (5 ml). After 20 h the solution was neutralised (CO_2) and passed through a short column of Amberlite MB1 ion-exchange resin, with methanol as eluant. Evaporation of the eluate gave crystalline α-D-ribofuranosylethane (18) (0·157 g, 100%), m.p. 94—95° (from propanol–light petroleum), $[\alpha]_D$ +32·7° (*c* 1·5 in H_2O). δ (60 MHz; D_2O) 1·0 (3H, t, C–CH_3), 1·65 (2H, m, C–CH_2–C), and 3·7—4·5 (6H, m) (Found: C, 51·9; H, 8·6. $C_7H_{14}O_4$ requires C, 51·8; H, 8·7%).

(*b*) The β-ethyne (13) (0·65 g) in methanol (35 ml) was hydrogenated over 5% palladium–charcoal in the same manner as in (*a*). The acetylated product, prepared and isolated as before, consisted of two compounds (t.l.c. in 2 : 3 light petroleum–ether). The minor component, present in very small amount, was indistinguishable from the tetra-acetate (28) described in (*a*). The crude syrup (0·424 g) was chromatographed on silica gel. Elution with benzene–ether (19 : 1) gave (2,3,5-*tri*-O-*acetyl*-β-D-*ribofuranosyl*)*ethane* (14) as a syrup (0·382 g, 87%), which was further purified by distillation (140° and 0·2 mmHg); $[\alpha]_D$ +6·2° (*c* 1·78 in MeOH); $\nu_{max.}$ (film) 1745 cm^{-1} (C=O); δ (100 MHz; $CDCl_3$) 0·96 (3H, t, C–CH_3), 1·62 (2H, m, C–CH_2–C), 2·06 (9H, m, OAc), 3·91 (1H, q, H-1), 4·0—4·5 (3H, m), 4·96 (1H, t, H-2), and 5·12 (1H, t, H-3).

The triacetate (14) (0·145 g) was deacetylated as in (*a*) to give β-D-ribofuranosylethane (15) (80 mg, 98%) as a syrup, $[\alpha]_D$ +0·9° (*c* 1·14 in H_2O); δ (100 MHz; D_2O) 0·96 (3H, t, C–CH_3), 1·6 (2H, m, C–CH_2–C), and 3·5—4·2 (6H, m) (Found: C, 51·8; H, 8·8%).

Reaction of 2,3,5-*Tri*-O-*benzyl*-D-*ribofuranose* (1) *with Methylmagnesium Iodide*.—A solution of the furanose (1) (1·5 g) in dry ether (30 ml) was added during 45 min to stirred ethereal 0·57M-methylmagnesium iodide (130 ml) and the mixture was left overnight. The solution was heated under reflux for 1 h, evaporated to 30 ml, and diluted with chloroform (200 ml). The solution was washed successively with 2M-sulphuric acid (3 × 100 ml), saturated aqueous potassium hydrogen carbonate (2 × 100 ml), M-sodium thiosulphate (2 × 50 ml), and water (3 × 100 ml), dried (Na_2SO_4), and evaporated to give a syrup [1·33 g, 85% calc. as a mixture of diols (23) and (25)]; δ (100 MHz; $CDCl_3$) 1·19 (3H, d, CH_3), 2·86 (2H, s, OH), 3·5—4·8 (12H, m), and 7·3 (15H, d, Ph). At a four-fold sweep width expansion of the n.m.r. spectrum, the doublet at δ 1·19 was resolved into three lines.

The mixture (0·23 g) in methanol (20 ml) was hydrogenolysed over 5% palladium–charcoal (100 mg). After filtration through a short column of Amberlite MB3 ion-exchange resin the solution was evaporated to give a partially crystalline mixture of polyols (24) and (26) (86 mg, 99%). Repeated crystallisation from ethanol–ether gave 6-deoxy-D-talitol (24) (40 mg, 46%), m.p. 104—106° (lit.,[62] 105—107°) (Found: C, 43·5; H, 8·5. Calc. for $C_6H_{14}O_5$: C, 43·4; H, 8·5%).

The original mixture was analysed by g.l.c. of the trimethylsilyl ethers.[60] An authentic sample of 6-deoxy-D-allitol [the enantiomer of the polyol (26)] was made by sequential acidic hydrolysis and reduction with sodium borohydride of methyl 6-deoxy-β-D-allofuranoside.[63] Crystallised from ethyl acetate it had m.p. 94—96° (lit.,[64] 62—63°) (Found: C, 43·6; H, 8·6%). Analysis of the mixture showed that the talitol (24) (retention time 31·1 min) and the allitol (26) (26·7 min) were present in the ratio 9 : 1.

Reaction of (2,3,5-*Tri*-O-*benzyl*-β-D-*ribofuranosyl*)*ethyne with Benzyl Azide*.—A mixture of the β-ethyne (13) (0·4 g) and freshly distilled benzyl azide [65] (0·5 g, 4 mol. equiv.) was heated at 100° for 3·5 h, then chromatographed on silica gel. Elution with benzene–ether (9 : 1) gave a mixture of triazoles (30) and (31) as a partially crystalline residue. Two crystallisations from ethanol afforded 1-benzyl-4 or 5-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)-1,2,3-triazole [(30) or (31)] (0·215 g, 41%), m.p. 125—126°, $[\alpha]_D$ +13° (*c* 1·38 in $CHCl_3$); δ (100 MHz; $CDCl_3$) 3·4—4·7 (12H, m), 5·08—5·44 (3H, m), and 7·53 (20H, m, Ph); *m/e* 561 (M^+, weak), 484 (*M* − Ph, weak), 470 (*M* − C_7H_7, medium), and 188 (*N*-benzyltriazole +30, medium) (Found: C, 74·9; H, 6·3; N, 7·6. Calc. for $C_{35}H_{35}N_3O_4$: C, 74·9; H, 6·2; N, 7·5%).

The mother liquors from the first crystallisation were evaporated to a pale yellow syrup consisting of the isomeric

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triazole [(31) or (30)] (0·253 g, 49%), $[\alpha]_D$ −20·5° (*c* 1·95 in $CHCl_3$); δ (100 MHz; $CDCl_3$) 3·4—4·7 (12H, m), 4·97 (1H, d, H-4 or H-5), 5·54 (2H, s, NCH_2), and 7·28 (20H, m, Ph); *m/e* 561 (M^+, weak), 484 (M − Ph, weak), and 470 (M − C_7H_7, weak) (Found: C, 74·7; H, 7·5; N, 6·2%).

We thank the S.R.C. for a research studentship (M. J. P.), for a grant towards the MS30 mass spectrometer, and for n.m.r. and mass spectra measured at the PCMU, Harwell.

[4/658 *Received*, 1*st April*, 1974]