C-Nucleoside Studies. Part 6.[1] Synthesis of 3-[2,3,5-Tri-*O*-benzyl-β-(and α)-D-ribofuranosyl]prop-2-yn-1-ol and Related Compounds; a New Synthesis of 3(5)-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole

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Treatment of 2,3,5-tri-*O*-benzyl-β-D-ribofuranosylethyne (2) with a large excess of paraformaldehyde and potassium hydroxide in ethanol gave 3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)prop-2-yn-1-ol (5) in 70% yield. Oxidation of (5) with chromic oxide (Jones reagent) afforded the carboxylic acid (4) (75%), esterification of which with diazomethane gave the known ester (7). Similar reactions and correlations have been carried out in the α-series.

Reaction of the Grignard reagent (14) of 3-(tetrahydropyran-2-yloxy)propyne with 2,3,5-tri-*O*-benzyl-D-ribofuranose (19) followed by ring closure and removal of the tetrahydropyranyl ether group gave the alcohol (5) in 52% overall yield.

Careful oxidation of (5) gave the corresponding aldehyde (3) which yielded the known pyrazole (1) (72%) on treatment with hydrazine. When 1,2-dideoxy-4,5:7,8-di-*O*-isopropylidene-D-*manno*-oct-1-yn-3-ulofuranose (22) was treated with hydrazine, 3(5)-(1,2:4,5-di-*O*-isopropylidene-D-*manno*-pentahydroxypentyl)pyrazole (23) was isolated in 93% yield.

THE discovery [2,3] of the antibiotics formycin, formycin B, and pyrazofurin (pyrazomycin) and its α-anomer,[4] all of which contain the pyrazole ring, has stimulated interest in the synthesis of *C*-ribofuranosylpyrazoles,[1,5-15] and in particular 3-β-D-ribofuranosylpyrazoles.[1,5-8,10,12,14]

[1] Part 5, J. G. Buchanan, A. R. Edgar, M. J. Power, and G. C. Williams, *Carbohydrate Res.*, 1977, **55**, 225; preliminary communications, *idem.*, *Nucleic Acids Research Special Publ. No.* 1, 1975, s69; *J.C.S. Chem. Comm.*, 1975, 501.

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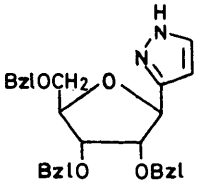
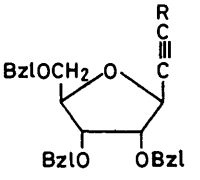
We have recently described [1] the synthesis of 3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole (1) by dipolar addition of diazomethane to 2,3,5-tri-*O*-benzyl-β-D-ribofuranosylethyne (2). This paper describes another synthesis of the pyrazole (1) by reaction of the acetylenic aldehyde (3) with hydrazine, together with some related chemistry.

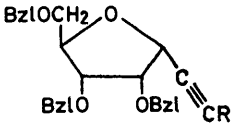


(1)

Bzl = $PhCH_2$



(2) R=H
(3) R=CHO
(4) R=CO_2H
(5) R=CH_2·OH
(6) R=CH_2·OAc
(7) R=CO_2Me



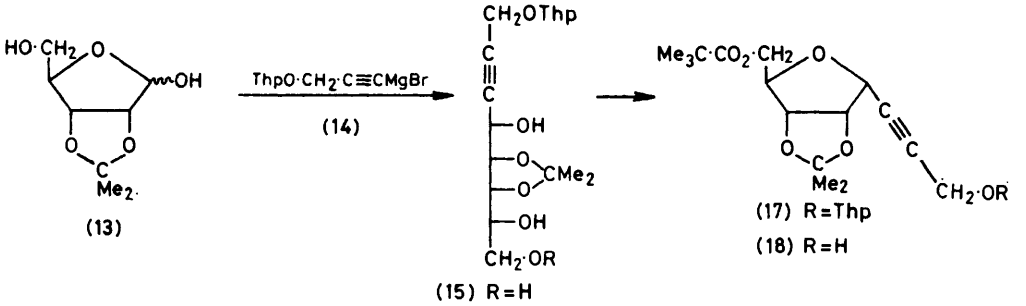
(8) R=H
(9) R=CH_2·OH
(10) R=CH_2·OAc
(11) R=CO_2H
(12) R=CO_2Me

Part 5 [1] described unsuccessful attempts to convert the ethyne (2) into derivatives of the propiolic acid (4) by carboxylation and similar reactions of metal salts. We have now found that when an ethanolic solution of the ethyne (2) is treated with a large excess of paraformaldehyde and potassium hydroxide the alcohol (5) can be obtained in 70% yield as a syrup after purification *via* the acetate (6). One factor which may contribute to the success of this reaction is that the hydroxymethyl group in the product (5) does not activate the triple bond towards Michael addition, enabling a polar solvent and more strenuous reaction conditions to be used.

methyl ester (7), whose specific rotation in chloroform (−11.6°) agrees with that reported by Moffatt (−8.7°) [11] rather than our own published value (+16.0°).

Similarly, in the α-series, the ethyne (8) could be converted into the alcohol (9), which was purified *via* the acetate (10). Oxidation of the alcohol (9) with Jones reagent gave the acid (11) (85%), treatment of which with diazomethane afforded the known crystalline ester (12) in 82% yield.

An alternative route to the hydroxymethyl derivatives has been examined. In an exploratory reaction, 2,3-*O*-isopropylidene-D-ribose (13) was treated with an excess of the Grignard reagent (14) derived from the tetrahydropyranyl ether of prop-2-yn-1-ol.[17-19] T.l.c. showed that all the sugar (13) had reacted, and only one product, the acetylene (15), was detected. By analogy with the corresponding reaction between the sugar (13) and ethynylmagnesium bromide [20] the D-*allo*-configuration, as shown in (15), is assumed for the major isomer.



(13)

ThpO·CH_2·C≡CMgBr

(14)

(15) R=H
(16) R=Me_3C·CO

(17) R=Thp
(18) R=H

Thp = tetrahydropyran-2-yl

The alcohol (5) was oxidised by Jones reagent [16] to the acid (4) (75%), decarboxylation of which gave the ethyne (2) (93%), showing that no anomerisation or other rearrangement had taken place. Treatment of the acid (4) with diazomethane afforded the known [1,11]

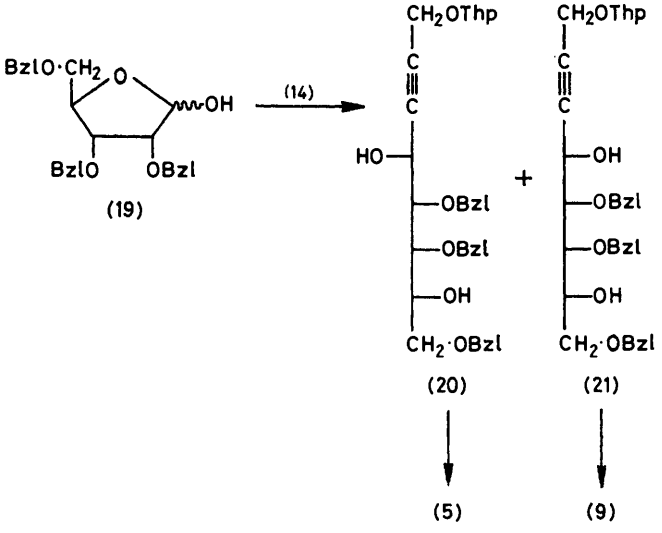
The diastereoisomeric forms of (15), arising through the chirality of the tetrahydropyranyl residue, were not separated by t.l.c.

When the acetylene (15) was treated with pivaloyl chloride (0.75 mol. equiv.) in pyridine, the major product (32%) was the pivalate (16), which was cyclised

[16] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.
[17] H. B. Henbest, E. R. H. Jones, and I. M. S. Walls, *J. Chem. Soc.*, 1950, 3646.
[18] P. D. Landor, S. D. Landor, and E. S. Pepper, *J. Chem. Soc.* (*C*), 1967, 185.
[19] G. A. MacAlpine, R. A. Raphael, A. Shaw, A. W. Taylor, and H.-J. Wild, *J.C.S. Perkin I*, 1976, 410.
[20] J. G. Buchanan, A. D. Dunn, and A. R. Edgar, *J.C.S. Perkin I*, 1975, 1191.

by means of toluene-*p*-sulphonyl chloride in pyridine.[20] Reaction was rapid, a further indication [20] of the D-*allo*-configuration in (15), leading to the α-D-*ribo*-structure (17) for the cyclic product. Careful acidic hydrolysis removed the tetrahydropyranyl group preferentially, to give the crystalline alcohol (18).

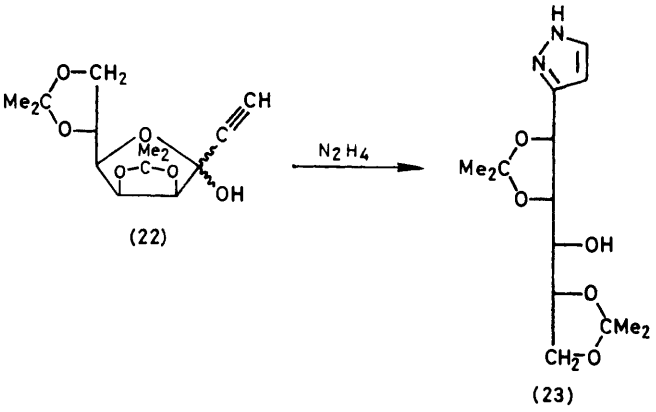
When 2,3,5-tri-*O*-benzyl-D-ribofuranose (19) was treated with an excess of the Grignard reagent (14) two products were detected by t.l.c. By analogy with the reaction of the furanose (19) with ethynylmagnesium bromide [21] and with a Grignard reagent derived from propiolic acid,[11] major and minor components were assigned D-*altro*- and D-*allo*-configurations, (20) and (21), respectively. Ring closure of the mixed diols was effected with toluene-*p*-sulphonyl chloride in pyridine,[20,21] and the protecting tetrahydropyranyl group removed with acidic methanol. The presence of the ethynes (5) and (9) was shown by t.l.c. By chromatography the pure β-D-ribofuranosylethyne (5) was isolated in 52% yield, together with a mixture of α- and β-ethynes [(9) and (5)] (22%) which did not afford the pure α-isomer (9) on further chromatography. This is a useful alternative method for preparing the β-ethyne (5).



In exploring methods for converting the alcohol (5) into the aldehyde (3) we originally envisaged the use of manganese dioxide, which had proved successful in earlier work.[20,22] Although some of the required aldehyde (3) was formed by oxidation in benzene solution, the yield was low (13%) and starting material (29%) was the only other compound recovered. Oxidation with nickel peroxide [23,24] gave an improved yield (38%) with 29% recovered starting material. After studying a number of other oxidation methods we found that the most reliable was the use of Jones reagent, with recovery of unchanged alcohol by chromatography. After two oxidation cycles the yield of aldehyde (3) was 53%.

[21] J. G. Buchanan, A. R. Edgar, and M. J. Power, *J.C.S. Perkin I*, 1974, 1943.
[22] J. G. Buchanan, A. D. Dunn, and A. R. Edgar, *J.C.S. Perkin I*, 1976, 68.

The aldehyde (3) was converted into the pyrazole (1) in 72% yield by treatment with hydrazine. This method gives overall yields similar to those of the earlier synthesis of (1) from the ethyne (2). We have also studied the reaction of the masked acetylenic ketone (22) with hydrazine. The crystalline 3-substituted pyrazole (23) was readily obtained in 93% yield.



A recent review [15] of *C*-nucleoside synthesis contains a number of inaccuracies and misinterpretations in relation to our earlier work. We wish to point out that the assignment [20,21] of anomeric configurations to the ethynes (2) and (8) rests on secure degradative evidence [20,22] and does not rely entirely on Hudson's rules. Other aspects of the reactions leading to (2) and (8) have been misquoted [15] and we advise the reader to consult the original literature.[21]

EXPERIMENTAL

The general methods used were mainly as outlined in Part 2.[20] Adsorption chromatography was also carried out using Kieselgel H type 60 (Merck); for t.l.c. we used mainly precoated aluminium-backed plates [Kieselgel HF_{254} type 60 (Merck)].

^1H N.m.r. spectra at 220 MHz were measured with a Varian HR220 spectrometer at the P.C.M.U., Harwell.

For oxidations using chromic oxide (Jones reagent [16]) a stock solution of chromium trioxide (3.258 g) in water (36 ml) and concentrated sulphuric acid (2.75 ml) was prepared and used as required.

3-(2,3,5-Tri-O-benzyl-β-D-ribofuranosyl)prop-2-ynyl Acetate (6).—The ethyne (2) (2.0 g), potassium hydroxide (5.51 g), and paraformaldehyde (13 g) in ethanol (90 ml) were heated under reflux for 1.25 h. More potassium hydroxide (20 g) and paraformaldehyde (13 g) were added gradually during the next 3.5 h, with continuous heating. The solution was cooled to room temperature, neutralised (2M-hydrochloric acid), concentrated *in vacuo*, diluted with water (200 ml), acidified with 2M-hydrochloric acid, and extracted with chloroform (3 × 250 ml). The combined extracts were dried ($MgSO_4$) and evaporated to yield a syrup, which was chromatographed on silica gel (46 g). Light petroleum–ether (5 : 1) eluted unchanged ethyne (2)

[23] K. Nakagowa, R. Konaka, and T. Nakata *J. Org. Chem.*, 1962, **27**, 1597.
[24] R. E. Atkinson, R. F. Curtis, D. M. Jones, and J. A. Taylor, *J. Chem. Soc.* (*C*), 1969, 2173.

(276 mg, 14%). Elution with light petroleum–ether (2 : 1) gave a syrup (1.896 g) consisting mainly of the alcohol (5), a sample (168 mg) of which was treated with acetic anhydride (2 g) and pyridine (6 ml) for 5 h at room temperature. The product was isolated with chloroform and chromatographed on silica gel. Elution with light petroleum–ether (5 : 1) gave the *acetate* (6) [159 mg, 77% from (2)] as a pure syrup, $[\alpha]_D$ 0° (*c* 3.11 in $CHCl_3$); $\nu_{max.}$ (film) 1 742 cm^{-1} (C=O); δ (60 MHz; $CDCl_3$) 2.03 (3 H, s, COMe), 3.46—4.87 (14 H, m), and 7.22—7.50 (15 H, m, Ph); *m/e* 500w (*M*), 427w (*M* — Ph), and 409s (*M* — CH_2Ph) (Found: C, 74.3; H, 6.3. $C_{31}H_{32}O_6$ requires C, 74.4; H, 6.4%).

3-(2,3,5-*Tri*-O-*benzyl*-β-D-*ribofuranosyl*)*prop*-2-*yn*-1-*ol* (5). —(*a*) The acetate (6) (99 mg) was treated with sodium methoxide (26 mg, 2.4 mol. equiv.) in methanol (8 ml) for 1 h at room temperature. The solution was passed through a short column of Amberlite IR-120 (H^+) resin with methanol as eluant. Evaporation of the eluate gave the *alcohol* (5) (82 mg, 90%) as a pure syrup, $[\alpha]_D$ −5.9° (*c* 2.0 in $CHCl_3$); $\nu_{max.}$ (film) 3 402 cm^{-1} (OH); δ (100 MHz; $CDCl_3$) 1.72br (1 H, s, exch. in D_2O, OH), 3.60 (2 H, m, H-5′), 3.96—4.84 (12 H, m), and 7.20—7.48 (15 H, m, Ph); *m/e* 458w (*M*), 381w (*M* — Ph), and 367s (*M* — CH_2Ph) (Found: C, 75.8; H, 6.7. $C_{29}H_{30}O_5$ requires C, 76.0; H, 6.55%).

(*b*) A solution of ethylmagnesium bromide [from magnesium (0.408 g) and ethyl bromide (2.96 g, 1.6 mol. equiv.) in dry tetrahydrofuran (5 ml) under nitrogen] was heated to 70 °C and 3-(tetrahydropyran-2-yloxy)propyne (3.3 g, 1.4 mol. equiv.) in dry tetrahydrofuran (10 ml) was added with stirring over 45 min. After a further 2 h at 70—80 °C the solution was cooled to 50 °C and a solution of the ribofuranose (19) (1.0 g) in tetrahydrofuran (10 ml) was added during 15 min. The mixture was stirred for a further 30 min at 50 °C, cooled to room temperature, and evaporated. The residue was dissolved in chloroform and treated with aqueous 10% ammonium chloride and water, and the chloroform layer was dried ($MgSO_4$), and evaporated. The resulting syrup (4.8 g) was shown by t.l.c. [light petroleum–ether (3 : 5)] to contain two products (R_F *ca.* 0.3) and no tribenzylribofuranose (19). Chromatography on silica gel (35 g) and elution with light petroleum–ether (2 : 1) gave 3-(tetrahydropyran-2-yloxy)propyne (2.92 g); the mixed diols [(20) and (21)] were then eluted by light petroleum–ether (1 : 2). The crude syrupy diols (1.64 g) showed δ (60 MHz; $CDCl_3$) 1.6 (*ca.* 6 H, m), 2.8—5.0 (*ca.* 19 H, m), and 7.35 (*ca.* 15 H, m).

A solution of the diols (1.64 g) in dry pyridine (10 ml) was treated with toluene-*p*-sulphonyl chloride (1.3 g, *ca.* 2.5 mol. equiv.) in pyridine (5 ml), added during 20 min at 50—60 °C. After 3 h at this temperature water was added and the product was isolated with chloroform. The resulting dark syrup (1.46 g), a mixture consisting mainly of the tetrahydropyranyl ethers of (5) and (9), showed δ (60 MHz; $CDCl_3$) 1.7 (*ca.* 6 H, m), 3.3—4.8 (*ca.* 17 H, m), and 7.3 (*ca.* 15 H, m).

The above mixture (1.46 g) in methanol (10 ml) was treated with toluene-*p*-sulphonic acid (10 mg) overnight. After neutralisation with sodium carbonate the product was isolated with chloroform to give a syrup (1.33 g) shown by t.l.c. [light petroleum–ether (1 : 4)] to consist mainly of the hydroxymethyl compounds (5) and (9). Chromatography on silica gel (10 g) and elution with light petroleum–ether (2 : 1) gave the major product (5) [0.57 g, 52% from (19)] as a pure syrup, $[\alpha]_D$ −3.2° (*c* 2.53 in $CHCl_3$), followed by a mixture (0.24 g) of (5) and (9), which did not afford pure (9) on further chromatography.

The i.r. spectrum and the ^1H n.m.r. spectrum (100 MHz) of the hydroxymethyl compound (5) were indistinguishable from those given in (*a*). Further resolution of the n.m.r. spectrum was obtained at 220 MHz ($CDCl_3$): δ 2.20 (1 H, s, OH), 3.57 (2 H, m, H-5′), 4.02 (2 H, m, 2 ring H), 4.17 (3 H, m, ring H and H-1), 4.53 (2 H, ABq, $PhCH_2$), 4.54 (2 H, ABq, $PhCH_2$), 4.64 (2 H, ABq, $PhCH_2$), 4.70 (1 H, m, ring H), and 2.7 (15 H, m, Ph).

3-(2,3,5-*Tri*-O-*benzyl*-β-D-*ribofuranosyl*)*propiolic Acid* (4). —Chromic acid solution (9 ml, 8.7 mol. equiv. Cr^{IV}) was added to the alcohol (5) (396 mg) in acetone (9 ml) during 1 h, and the mixture was stirred at room temperature for 3 h. Water (80 ml) was added and the acidic product isolated with chloroform. The resulting syrup was chromatographed on silica gel (19 g). Light petroleum–ether (2 : 1) eluted a minor impurity. Elution with chloroform–acetic acid (49 : 1) gave the *acid* (4) as a syrup (305 mg, 75%), $[\alpha]_D$ −6.6° (*c* 2.42 in $CHCl_3$); $\nu_{max.}$ (film) 3 680—2 400 (acid OH), 2 234 (C≡C), and 1 722 cm^{-1} (C=O); δ (60 MHz; $CDCl_3$) 3.5—5.0 (12 H, m), 7.17—7.46 (15 H, m, Ph), and 7.61 (1 H, exch. in D_2O, CO_2H); *m/e* 428m (*M* − CO_2) (Found: C, 73.6; H, 6.2. $C_{29}H_{28}O_6$ requires C, 73.7; H, 5.9%).

Decarboxylation of the Acid (4).—The acid (4) (81 mg) in benzene (12 ml) was heated under reflux for 2 h. Analytical t.l.c. [light petroleum–ether (1 : 1)] indicated almost complete conversion into a less polar product. Evaporation left a syrup which crystallised on addition of a seed of the ethyne (2). The product (68 mg, 93%) was indistinguishable from (2) by m.p., mixed m.p., t.l.c., and i.r. and ^1H n.m.r. spectra.

Esterification of the Acid (4).—The acid (4) (80 mg) was treated with diazomethane (1 mol. equiv.) in ether for 30 min at room temperature. Evaporation left a syrup which was dissolved in light petroleum–ether (3 : 1) and filtered through a short column of silica gel. The resulting homogeneous syrup (74 mg, 90%) was indistinguishable from an authentic sample [1] by i.r., ^1H n.m.r., and mass spectra and t.l.c. It had $[\alpha]_D$ −11.6° (*c* 2.57 in $CHCl_3$) [lit.[1] +16.0°; lit.[11] −8.7° (see Discussion section)].

3-(2,3,5-*Tri*-O-*benzyl*-α-D-*ribofuranosyl*)*prop*-2-*ynyl Acetate* (10).—The ethyne (8) (551 mg) in ethanol (25 ml) was heated under reflux for 2 h, during which time potassium hydroxide (6.95 g) and paraformaldehyde (7.79 g) were gradually added simultaneously. The mixture was processed as for the β-compound (5) to give a syrup which was chromatographed on silica gel (10 g). Elution with light petroleum–ether (2 : 1, then 1 : 1) gave the major product (9), an impure syrup (512 mg) which was treated with acetic anhydride (10 ml) and pyridine (18 ml) for 2 h at room temperature. The product was isolated with chloroform and chromatographed on silica gel (10 g). Light petroleum–ether (5 : 1) eluted the *acetate* (10) (456 mg, 71%), which slowly crystallised. Recrystallisation from ethanol gave the pure acetate (10), m.p. 68.5—69°, $[\alpha]_D$ +80.5° (*c* 1.23 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 744 cm^{-1} (C=O); δ (60 MHz; $CDCl_3$) 2.02 (3 H, s, COMe), 3.50—4.90 (14 H, m), and 7.20—7.53 (15 H, m, Ph); *m/e* 500w (*M*), 441w (*M* — OAc), and 409s (*M* — CH_2Ph) (Found: C, 74.35; H, 6.35. $C_{31}H_{32}O_6$ requires C, 74.4; H, 6.4%).

3-(2,3,5-*Tri*-O-*benzyl*-α-D-*ribofuranosyl*)*prop*-2-*yn*-1-*ol* (9). —The acetate (10) (375 mg) and sodium methoxide (33 mg,

0.81 mol. equiv.) in methanol (15 ml) were stirred at room temperature for 1 h. The mixture was neutralised with Amberlite IR-120(H^+) resin and the solution was evaporated to give a syrup which was chromatographed on silica gel (5 g). Elution with light petroleum–ether (1 : 1) afforded the *alcohol* (9) as a homogeneous syrup (328 mg, 96%), $[\alpha]_D$ +84.6° (*c* 1.07 in $CHCl_3$); $\nu_{max.}$ (film) 3 443 cm^{-1} (OH); δ (60 MHz; $CDCl_3$) 1.96br (1 H, s, exch. in D_2O, OH), 3.48—3.68 (2 H, m), 3.94—5.00 (12 H, m), and 7.22—7.56 (15 H, m, Ph); *m/e* 367s (*M* − CH_2Ph) (Found: C, 76.2; H, 6.4. $C_{29}H_{30}O_5$ requires C, 76.0; H, 6.55%).

3-(2,3,5-*Tri*-O-*benzyl*-α-D-*ribofuranosyl*)*propiolic Acid* (11).—Chromic acid solution (6.3 ml, 10.1 mol. equiv. Cr^{VI}) was added during 45 min to the alcohol (9) (242 mg) in acetone (5 ml) and the mixture stirred for 2.7 h at room temperature. The solution was diluted with water (50 ml) and the product isolated by extraction with chloroform. Chromatography, as for the β-isomer (4), gave the pure *acid* (11) (212 mg, 85%) as a syrup, $[\alpha]_D$ +77.7° (*c* 1.99 in $CHCl_3$); $\nu_{max.}$ (film) 3 660—2 400 (acid OH), 2 240 (C≡C), and 1 708 cm^{-1} (C=O); δ (60 MHz; $CDCl_3$) 3.43—4.96 (12 H, m), 7.19—7.61 (15 H, m, Ph), and 8.81br (1 H, s, exch. in D_2O, CO_2H) (Found: C, 74.1; H, 5.6. $C_{29}H_{28}O_6$ requires C, 73.7; H, 5.9%).

Esterification of the Acid (11).—The acid (11) (202 mg) was treated with diazomethane (0.9 mol. equiv.) in ether (7 ml) for 30 min at room temperature. Evaporation gave a syrup which was chromatographed on silica gel (4 g). Elution with light petroleum–ether (4 : 1) afforded the methyl ester (12) (170 mg, 82%), which crystallised from ether–light petroleum. It was indistinguishable from the authentic ester [1] (mixed m.p., ^1H n.m.r. spectrum, and t.l.c.).

3-(2,3-O-*Isopropylidene*-5-O-*pivaloyl*-α-D-*ribofuranosyl*)-*prop*-2-*yn*-1-*ol* (18).—A solution of ethylmagnesium bromide [from magnesium (10.8 g) and ethyl bromide (48 ml) in dry tetrahydrofuran (300 ml) under nitrogen] was heated to 60 °C, and 3-(tetrahydropyran-2-yloxy)propyne (63 g) in dry tetrahydrofuran (40 ml) was added dropwise with constant stirring. The addition took place over 1.25 h and the solution was heated for a further 1.5 h. 2,3-*O*-Isopropylidene-D-ribose (13) (9.8 g) in dry tetrahydrofuran (75 ml) was added dropwise to the solution with constant stirring. T.l.c. (10 min after complete addition) indicated that no starting material remained. After a further 1 h aqueous ammonium chloride (10%; 100 ml) was added, the mixture was filtered through Celite, and the residue was washed thoroughly with ethyl acetate. The combined filtrates were dried over a large quantity of magnesium sulphate, filtered, and evaporated to give a dark brown syrup (*ca.* 75 g), which was chromatographed on silica gel (200 g). Elution with light petroleum–benzene (1 : 1) gave unchanged tetrahydropyranyl ether. Ether eluted the crude triol (15) as a syrup (16.98 g).

A solution of the triol (15) (4.0 g) in dry pyridine (25 ml) was treated with pivaloyl chloride (1.10 g, 0.75 mol. equiv.) for 1.5 h at room temperature. T.l.c. indicated the presence of a complex mixture, including one major product and some unchanged triol. By means of chloroform the products were isolated as a syrup (3.35 g), which was chromatographed on silica gel (35 g). Light petroleum–ether (11 : 9) eluted the pivalate (16) as a thick colourless syrup [1.63 g, 32% based on (13)]; $\nu_{max.}$ (film) 3 420 (OH), 1 735 (C=O), 1 405 (CMe_3), and 1 390 and 1 375 cm^{-1} (CMe_2); δ (100 MHz; $CDCl_3$) 1.26 (9 H, s, CMe_3), 1.37—1.90 (12 H, m), and 3.36—4.90 (13 H, m, decreased to 11 H by D_2O exchange).

A solution of the ester (16) (1.63 g) in dry pyridine (20 ml) was heated to 85—90 °C for 1.5 h with toluene-*p*-sulphonyl chloride (1.9 g, 2.5 mol. equiv.). The excess of reagent was destroyed with water and the product isolated with chloroform. The resulting syrup was chromatographed on silica gel. Light petroleum–ether (7 : 3) eluted the cyclic compound (17), obtained as a colourless syrup (1.21 g, 78%); $\nu_{max.}$ (film) 1 735 (C=O), 1 400 (CMe_3), and 1 385 and 1 375 cm^{-1} (CMe_2).

A solution of the tetrahydropyranyl ether (17) (1.457 g) in 80% acetic acid (v/v) (30 ml) was heated at 50—60 °C for 10 min. T.l.c. indicated that no starting material remained. Evaporation left a residue, which was chromatographed on silica gel (10 g). Light petroleum–ether (6 : 4) eluted the *alcohol* (18) as a syrup which crystallised rapidly (758 mg, 66%), m.p. 89—89.5°, $[\alpha]_D$ −65.7° (*c* 0.785 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 280br (OH), 1 740 (C=O), 1 400 (CMe_3), and 1 390 and 1 380 cm^{-1} (CMe_2); δ (100 MHz; $CDCl_3$) 1.23 (9 H, s, CMe_3), 1.38 (3 H, s, CMe_2), 1.58 (3 H, s, CMe_2), 2.28 (1 H, t, *J* 7 Hz, exch. in D_2O, OH), 4.0—4.4 (5 H, m), and 4.6—4.8 (3 H, m); *m/e* 297 (*M* − CH_3) (Found: C, 61.7; H, 7.7. $C_{16}H_{24}O_6$ requires C, 61.5; H, 7.7%).

3-(2,3,5-*Tri*-O-*benzyl*-β-D-*ribofuranosyl*)*propynal* (3).—(*a*) The alcohol (5) (730 mg) and a suspension of freshly ground manganese dioxide (1.4 g) were stirred in benzene (50 ml) at room temperature for 46 h. More manganese dioxide (2.8 g) was added and stirring continued for 2 h. The manganese dioxide was filtered off and washed with ether. The combined filtrate and washings, on evaporation, left a syrup (310 mg), which was chromatographed on silica gel (8 g). Light petroleum–ether (5 : 1) eluted the *aldehyde* (3) (96 mg, 13%) as a homogeneous syrup, $[\alpha]_D$ −8.6° (*c* 1.62 in $CHCl_3$); $\nu_{max.}$ (film) 2 730 (CH, aldehyde), 2 200 (C≡C), and 1 666 cm^{-1} (C=O); δ (60 MHz; $CDCl_3$) 3.47—5.00 (12 H, m), 7.27—7.54 (15 H, m, Ph), and 9.14 (1 H, s, CHO); *m/e* 456m (*M*), 379w (*M* − Ph), and 365s (*M* − CH_2Ph) (Found: C, 76.4; H, 6.1%; *M*, 456.1943. $C_{29}H_{28}O_5$ requires C, 76.3; H, 6.1%; *M*, 456.1937). Elution with light petroleum–ether (1 : 1) gave unchanged alcohol (5) (213 mg, 29%) as the only other component.

(*b*) A continuously stirred mixture of the alcohol (5) (450 mg) and nickel peroxide (400 mg) in benzene (15 ml) was heated at 60 °C for 1 h. Analytical t.l.c. indicated the presence of the aldehyde (3) but mainly the alcohol (5). More nickel peroxide (1 g) was added and stirring continued at 60 °C for 1.5 h. After cooling to room temperature and diluting with ether (30 ml) the mixture was filtered and the residue washed with ether. The crude syrup (300 mg) obtained on evaporation was chromatographed on silica gel (14 g). Elution with light petroleum–ether (6 : 1) gave the aldehyde (3) (168 mg, 38%) as a syrup, indistinguishable from the product described in (*a*). Further elution with ether gave unchanged alcohol (5) (132 mg, 29%).

(*c*) Chromic acid solution (0.5 ml, 0.57 mol. equiv. Cr^{VI}) was added during 1.5 h to a solution of the alcohol (5) (336 mg) in acetone (9 ml) at room temperature. The reaction was monitored by t.l.c. [light petroleum–ether (1 : 1)]. In the early stages of addition only the aldehyde (3) and the alcohol (5) were present but at the end some acid (4) was detected. The solution was diluted with water and the products were isolated with chloroform. Chromatography on silica gel (10 g) and elution with light petroleum–ether (6 : 1) gave pure aldehyde (3) (125 mg). Further elution with light petroleum–ether (1 : 1) gave

unchanged (5) (152 mg, 45%). A similar oxidation of (5) (152 mg) with 0.3 ml (0.76 mol. equiv.) of the chromic acid solution gave, after chromatography, compounds (3) (52 mg) and (5) (53 mg, 35%). The total yield of (3) was 177 mg (53%), its structure being confirmed by i.r. and t.l.c. comparison with the product described in (*a*).

3(5)-(2,3,5-*Tri*-O-*benzyl*-β-D-*ribofuranosyl*)*pyrazole* (1).—The aldehyde (3) (92 mg), hydrazine hydrate (2 ml), and methanol (3 ml) were heated (40—45 °C) for 35 min. The product was isolated with chloroform to give a syrup which was chromatographed on silica gel (2 g). Light petroleum–ether (1 : 1) eluted the pyrazole (1) (68 mg, 72%), which was recrystallised from ether–hexane. The sample was indistinguishable (m.p., t.l.c., and i.r. and ^{1}H n.m.r. spectra) from the pyrazole (1) obtained by the reaction of (2) with diazomethane.[1]

3(5)-1,2:4,5-*Di*-O-*isopropylidene*-D-manno-*pentahydroxypentyl*)*pyrazole* (23).—The ketose (22) (80 mg) in ethanol (10 ml) was heated under reflux with hydrazine hydrate (110 mg) for 30 min. The solvent was removed *in vacuo* to leave a colourless syrup which crystallised. Recrystallisation from ether containing a small amount of ethyl acetate gave the pure *pyrazole* (23), (78 mg, 93%), m.p. 169°, $[\alpha]_D$ −52° (*c* 1.0 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 300 (OH, NH), 1 530 (C=N), and 1 390, 1 385, and 1 375 cm^{-1} (CMe_2); δ (100 MHz; $CDCl_3$) 1.32 (6 H, s), 1.46 (3 H, s), and 1.61 (3 H, s) (all CMe_2), 3.20br [1 H, s, becoming d ($J_{3',4'}$ 7 Hz) on D_2O exchange, H-3'], 3.86—4.24 (4 H, m, becoming 3 H on D_2O exchange), 4.43 (1 H, d, $J_{1',2'}$ 7 Hz, H-2'), 5.36 (1 H, d, $J_{1',2'}$ 7 Hz, H-1'), 6.29 [1 H, d, $J_{4,5(3)}$ 2 Hz, H-4], and 7.44 [1 H, d, $J_{4,5(3)}$ 2 Hz, H-5(3)]; *m/e* 298 (*M*) and 283 (*M* − CH_3) (Found: C, 56.2; H, 7.3; N, 9.5. $C_{14}H_{22}N_2O_5$ requires C, 56.4; H, 7.4; N, 9.4%).

We thank Professor J. K. N. Jones, F.R.S., for a discussion and the S.R.C. for research studentships (to A. D. D., R. J. H., and G. C. W.) and for n.m.r. and mass spectra measured at the P.C.M.U., Harwell. We also thank Organon Laboratories Ltd. for a grant.

[7/324 *Received*, 23*rd February*, 1977]