C-Nucleoside Studies. Part 9.[1] Synthesis of 3(5)-α-D-Ribofuranosylpyrazole and Related Compounds

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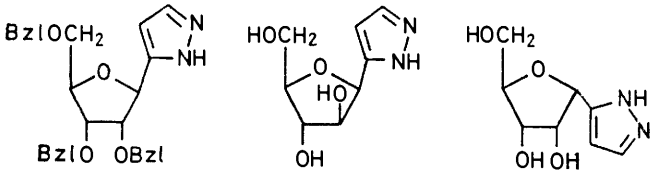
3-(1,2:4,5-Di-*O*-isopropylidene-D-*allo*-1,2,3,4,5-pentahydroxypentyl)-1-(2,4-dinitrophenyl)pyrazole (8) was prepared in four steps (40% overall yield) from 2,3:5,6-di-*O*-isopropylidene-D-allose (4). Treatment of (8) with acetone and concentrated sulphuric acid formed a mixture of (8) and its 1,3:4,5- (12) and 2,3:4,5-di-*O*-isopropylidene (13) isomers. On treatment with methanesulphonyl chloride in pyridine, the isomer (13) formed an unstable methanesulphonate ester which spontaneously underwent cyclisation with loss of acetone to give 1-(2,4-dinitrophenyl)-3-(2,3-*O*-isopropylidene-α-D-ribofuranosyl)pyrazole (21).

Reaction of 2,3,5-tri-*O*-benzyl-D-ribofuranosyl chloride with 3,3-diethoxyprop-1-ynylmagnesium bromide, and treatment of the major product with aqueous acid and hydrazine, yielded 3(5)-(2,3,5-tri-*O*-benzyl-α-D-ribofuranosyl)pyrazole (25), which could be converted in 3 steps (62% overall yield) into (21).

Treatment of (25) with boron trichloride and subsequent methanolysis produced 3(5)-α-D-ribofuranosylpyrazole (3) in 61% yield.

SINCE the discovery [2,3] of the *C*-nucleoside antibiotics formycin, formycin B, and pyrazofurin (pyrazomycin) together with its α-anomer,[4] all of which contain the pyrazole ring, there has been considerable interest in the synthesis of *C*-pentofuranosylpyrazoles.[5,6] Previous papers in this series [7] have described syntheses of 3(5)-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole (1), from

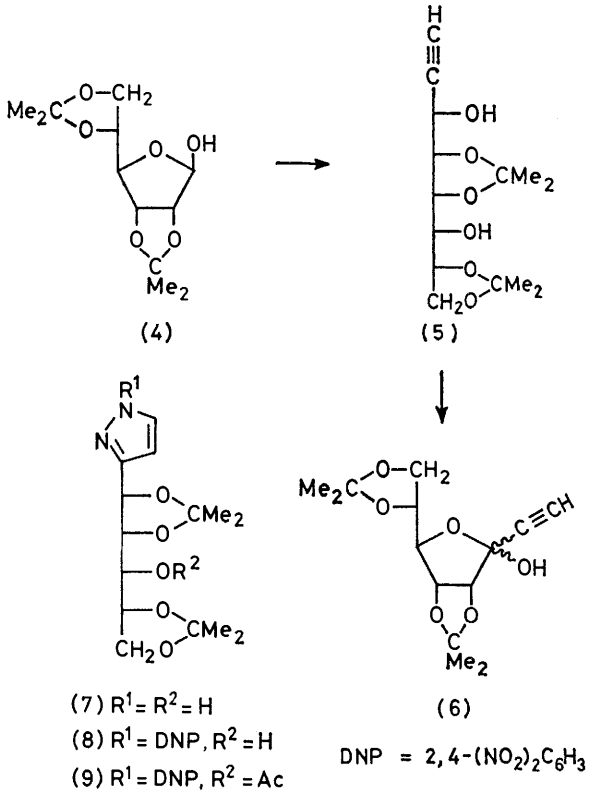


(1) (2) (3)

suitably protected derivatives of D-ribose, and we have recently described [1] a complementary approach to *C*-pentofuranosyl heterocycles in which a hexose sugar was used as a precursor for 3(5)-β-D-arabinofuranosylpyrazole (2). We now describe the application of both these approaches to the synthesis of 3(5)-α-D-ribofuranosylpyrazole (3).

Reaction of 2,3:5,6-di-*O*-isopropylidene-D-allofuranose (4) [8,9] with ethynylmagnesium bromide produced, after chromatography, a single addition product in 84% yield, to which, on the basis of previous evidence,[10] we assign the D-*glycero*-D-*allo*-stereochemistry (5). Selective oxidation of the propynylic alcohol with activated manganese dioxide [10] produced the ketose (6), which on treatment with hydrazine hydrate in ethanol gave the pyrazole (7) in 91% yield. When (7) was treated with 1-fluoro-2,4-dinitrobenzene and triethylamine in refluxing benzene [1,11] the 2,4-dinitrophenyl derivative (8) was produced in 84% yield.

We have shown in previous work [1] that the di-*O*-isopropylidene-D-*manno*-pentahydroxypentylpyrazole (10) was smoothly isomerised to its isomer (11) on treatment with acetone and sulphuric acid, a result which we ascribed to the greater stability of the isomer (11) containing a *trans*-fused (αT) dioxolan ring.[12,13] Perhaps not surprisingly there was no such clear-cut thermodynamic preference in the case of the D-*allo*-compound (8). When the pyrazole (8) was equilibrated with acetone containing concentrated sulphuric acid, a mixture was produced from which was isolated starting material (8) (25%) and another material (55%) which, although chromatographically homogeneous in several solvent systems, was shown clearly by ^{1}H n.m.r. spectro-



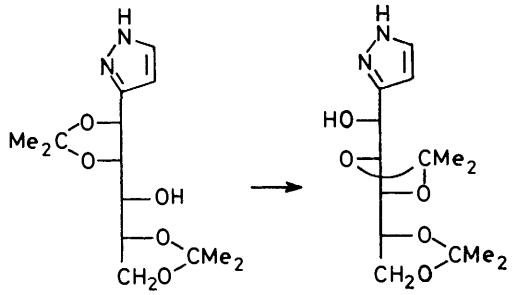
(4) (5)

(7) $R^1 = R^2 = H$
(8) R^1 = DNP, R^2 = H
(9) R^1 = DNP, R^2 = Ac

(6)

scopy to be a mixture. On the basis of evidence given below, we believe this mixture to contain two components, the 1,3:4,5-di-*O*-isopropylidene derivative (12) and the 2,3:4,5-isomer (13) in roughly equal amounts.

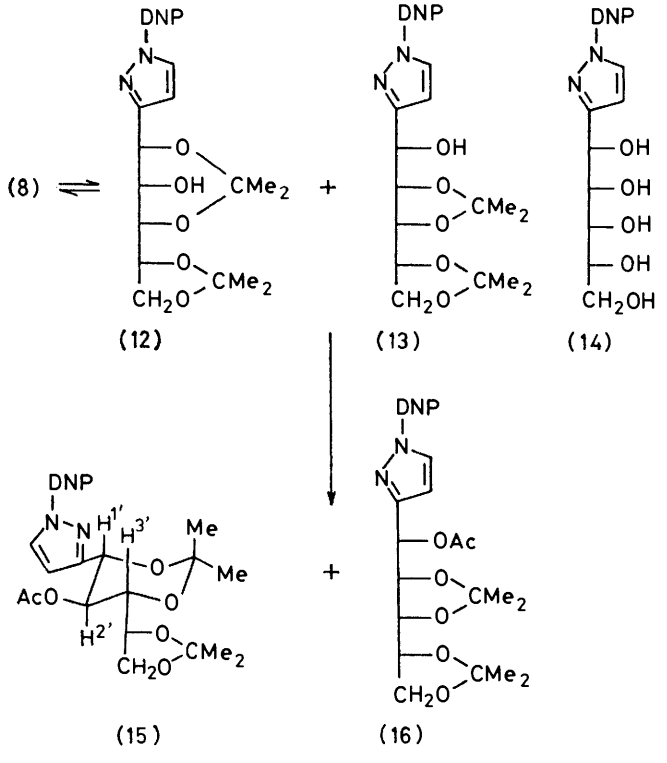
A closely similar distribution of products was obtained when compound (8) was hydrolysed by hydrochloric acid in ethanol, and the resultant pentahydroxy-compound (14) was treated with acetone and sulphuric acid.



(10) (11)

When the mixture of di-*O*-isopropylidene derivatives (12) and (13) was treated with acetic anhydride and pyridine, the resultant acetates (15) (55%) and (16) (45%) could be separated by chromatography on silica. Equally, the 1,2:4,5-isomer (8) was cleanly converted into its acetate (9) under the same conditions.

The structures of the acetates (9), (15), and (16), and thus of their alcohol precursors, follow from their ^{1}H n.m.r. spectra. The acetate (9) showed, as expected, two deshielded sugar protons, a doublet at δ 5.32

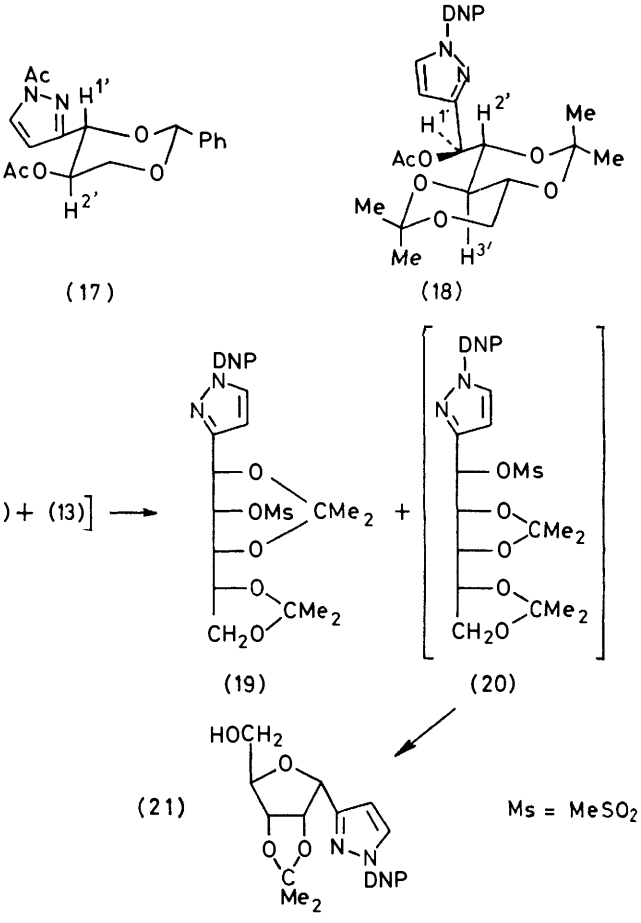


(12) (13) (14)

(15) (16)

assigned to H-1′, and a double doublet at δ 4.95 due to H-3′. The acetate (15) showed (in hexadeuteriobenzene solution) two deshielded sugar protons, a doublet (J 9.5 Hz) at δ 4.97, assigned to H-1′, and a triplet (J 9.5 Hz) at δ 5.28, assigned to H-2′. These large coupling constants, $J_{1',2'}$ and $J_{2',3'}$, are consistent with the *trans*-diaxial arrangement of H-1′, H-2′, and H-3′ expected in structure (15), and in excellent agreement with corresponding ^{1}H n.m.r. data for the benzylidene acetal (17) reported by Horton *et al.*[14]

The acetate (16) showed only one deshielded sugar proton, a doublet at δ 6.04. This chemical shift is



(17) (18)

(19) (20)

(21)

Ms = $MeSO_2$

appropriate for a proton deshielded by both an acetoxy-group and a heterocyclic ring; thus the acetoxy-group must be on C-1′, and two possible structures can be considered, the 2,3:4,5-arrangement (16), or the isomeric 2,4:3,5-structure (18). When the ^{1}H n.m.r. spectrum of (16) was recorded with irradiation at δ 6.04 (H-1′), a double doublet at δ 4.64 collapsed to a doublet (J 4.5 Hz). This signal is thus due to H-2′, and the coupling constant ($J_{2',3'}$ 4.5 Hz) is inconsistent with the *trans*-diaxial arrangement of these protons expected in isomer (18); the compound is thus assigned the structure (16). Other chemical modifications of alcohol (13) discussed below support this assignment.

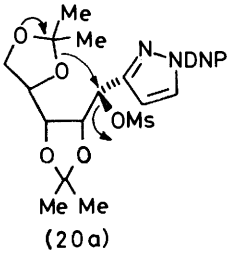
We expected on the basis of our previous findings that conversion of the hydroxy-group of compound (13) into a good leaving group, such as a sulphonate ester, should give a suitable precursor for cyclisation to an α-D-ribofuranosylpyrazole. In the event, this cyclisation occurred very readily. Thus, treatment of the mixture

of alcohols (12) and (13) with methanesulphonyl chloride in pyridine gave a mixture of two products, resolvable on thin-layer chromatography. When this mixture was applied to a silica column, the product of higher mobility was isolated as a pure crystalline solid, which was shown by its ^{1}H n.m.r. spectrum to be the 2-*O*-methylsulphonyl-1,3:4,5-di-*O*-isopropylidene-pentahydroxypentylpyrazole (19). In particular, the coupling constants $J_{1',2'}$ and $J_{2',3'}$ had the same large values (9.2 Hz) as for the analogous acetate (15). The more polar compound, presumed to be the isomeric mesylate (methanesulphonate) (20), was, however, eluted from the column contaminated with another compound of still lower R_F value. When kept for 24 h in the dark, this mixture was entirely transformed into the new compound and chromatography afforded it in a pure state. On the basis of its spectroscopic properties this material is assigned the structure 1-(2,4-dinitrophenyl)-3-(2,3-*O*-isopropylidene-α-D-ribofuranosyl)pyrazole (21) [30% yield, based on the mixture (12) + (13)]. In particular, in the ^{1}H n.m.r. spectrum, the coupling constant ($J_{1',2'}$ 3.2 Hz) is typical of the values found for isopropylidene acetals of α-D-ribofuranosyl nucleosides [15] while the absence of observable coupling between H-3′ and H-4′ also supports the α-D-configuration; [16] the β-D-ribofuranosyl isomer would be expected to have $J_{3',4'}$ 5 Hz. The structure was confirmed by the independent synthesis described below. Product (21) is presumably formed by displacement of the mesyloxy-group in (20) by O-4′, shown in structure (20a), and subsequent loss of the terminal isopropylidene group. We discuss some implications of this reaction later.

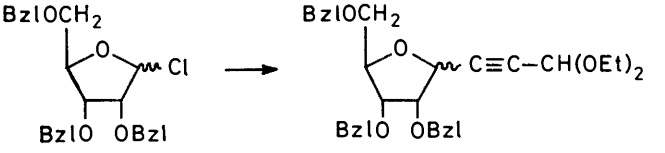
Since a mixture of three isomers was produced on equilibration of the di-*O*-isopropylidene compound (8) with acetone and acid, we considered that this method did not provide a viable route to the α-D-ribofuranosyl-pyrazole (3). Accordingly, we have developed a higher-yielding and more direct route to this compound, described below.

Treatment of 2,3,5-tri-*O*-benzyl-D-ribofuranosyl chloride [17] (22) with the Grignard reagent derived from 3,3-diethoxypropyne [18] yielded as major product the α-alkyne (23), together with a small amount of its β-anomer (24).[19] We expected, in the light of previous experience,[20] that the major product of this reaction should be the α-anomer (23), and this prediction was confirmed when acidic hydrolysis followed by treatment with hydrazine gave rise, in 74% yield, to the pyrazole (25) which was shown to be different from its β-isomer.[6,7]

When the pyrazole (25) was treated with 1-fluoro-2,4-dinitrobenzene and triethylamine in benzene, the DNP-derivative (26) was formed in 87% yield. Reaction of (26) with boron trichloride at low temperatures, followed by methanolysis, cleanly removed the benzyl groups to give the triol (27) which was fully characterised as its triacetate (28). The triol (27) was converted into the isopropylidene derivative (21) using acetone and conc. sulphuric acid; the material obtained in this way had spectroscopic properties fully in agreement with the same compound prepared by the other route described above, although in this preparation the compound was obtained as a crystalline solid.



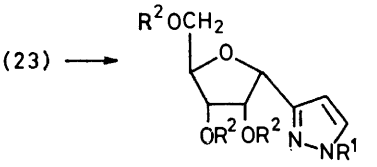
(20a)



(22)

(23) α-isomer

(24) β-isomer



(25) R^1=H, R^2=Bzl

(26) R^1=DNP, R^2=Bzl

(27) R^1=DNP, R^2=H

(28) R^1=DNP, R^2=Ac

When the tri-*O*-benzyl-α-D-ribofuranosyl-pyrazole (25) was treated with boron trichloride in dichloromethane at −78 °C, and the resultant borate esters were decomposed with methanol, 3(5)-α-D-ribofuranosyl-pyrazole (3) was isolated as a crystalline solid in 61% yield after ion-exchange chromatography.

The spontaneous loss of an isopropylidene group from the methanesulphonate (20) calls for some comment. Isopropylidene acetals are widely used for protection of carbohydrate diols during synthesis under non-acidic conditions. They are, of course, susceptible to acidic hydrolysis, but cleavage or rearrangement may occur in the presence of other electrophilic species, *e.g.* phosphorus pentachloride,[21] triphenyl phosphite halides,[22] glycosyl halides,[23] Vilsmeier reagents,[24] triethyloxonium fluoroborate,[25] and triphenylmethyl fluoroborate.[26] Some mechanisms for the rearrangements have been discussed.[27]

In the present instance of the conversion of (20) into (21), C-1′ in the mesylate, shown in (20a), acts as an internal electrophilic centre and can lead, in the presence of moisture, to the monoisopropylidene compound (21). Tronchet [28] has given an example of the cleavage of an acetal assisted by a neighbouring carbonyl group.

Similar processes [29-32] are known to occur in other acetals in which a 1,3-dioxolan ring is not involved. It is interesting that the 4,5-isopropylidene group in (20), having served its purpose as a protecting group, undergoes self-destruction during the final stage of the synthesis.

EXPERIMENTAL

The general methods used were as stated in Part 2.[10a] Adsorption chromatography was carried out using Kieselgel H type 60 (Merck); an external pressure was applied to the top of columns. T.l.c. was carried out on pre-coated aluminium-backed plates [Kieselgel HF_{254} type 60 (Merck)].

1,1,2,2-*Tetrahydro*-1,2-*dideoxy*-4,5:7,8-*di*-O-*isopropylidene*-D-glycero-D-allo-*octitol* (5).—Ethylmagnesium bromide [from magnesium (10 g) and ethyl bromide (12 ml)] in dry tetrahydrofuran (200 ml) was added dropwise to tetrahydrofuran (200 ml), previously saturated with acetylene. During the addition, and for 1 h afterwards, constant stirring was maintained, and acetylene was passed through the solution. 2,3:5,6-Di-*O*-isopropylidene-D-allofuranose (4) [8,9] (10 g) was added in portions, with passage of acetylene, and the mixture was stirred for 24 h. After treatment with 10% aqueous ammonium chloride (25 ml), the mixture was filtered through Celite, and the precipitate washed well with ethyl acetate. The combined filtrates were dried with a large quantity of sodium sulphate, filtered, and evaporated to leave a syrup which was dissolved in ether. The solution was washed with water, dried, and evaporated and the resultant syrup (10.6 g) was chromatographed on silica, with benzene–ethyl acetate (2 : 1) as eluant to give the *diol* (5) as a colourless syrup (9.2 g, 84%), $[\alpha]_D$ +1.08° (*c* 1.85 in $CHCl_3$); $\nu_{max.}$ (film) 3 420 (OH), 3 280 (≡C–H), and 2 120 cm^{-1} (C≡C); δ(100 MHz; $CDCl_3$) 1.38 (3 H, s), 1.40 (3 H, s), and 1.48 (6 H, s) (all CMe_2), 2.08 (1 H, s, exchangeable with D_2O, OH), 2.57 (1 H, d, *J* 2 Hz, ≡CH), 3.38 (1 H, d, exchangeable with D_2O; OH), and 3.9—4.8 (7 H, m) (Found: C, 59.0; H, 8.0. $C_{14}H_{22}O_6$ requires C, 58.7; H, 7.7%).

1,1,2,2-*Tetrahydro*-1,2-*dideoxy*-4,5:7,8-*di*-O-*isopropylidene*-D-allo-*oct*-3-*ulose* (6).—The diol (5) (6.8 g) and freshly-prepared activated manganese dioxide [10] (80 g) were stirred in benzene (800 ml) at room temperature for 0.5 h. The suspension was filtered, and the solid washed with benzene (3 × 80 ml). The filtrate and washings were evaporated to give a solid residue, which on recrystallisation from benzene–light petroleum yielded the *ketose* (6) (4.2 g, 61%), m.p. 124—125 °C, $[\alpha]_D$ −69.4° (*c* 1.48 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 470 (OH), 3 285 (≡C–H), 2 120 (C≡C), 1 388, and 1 378 cm^{-1} (CMe_2); δ(100 MHz; $CDCl_3$) 1.37 (6 H, s), 1.47 (3 H, s), and 1.55 (3 H, s) (all CMe_2), 2.75 (1 H, s, ≡C–H), 3.8—4.3 (4 H, m), 4.63 (1 H, d, *J* 6 Hz, H-5), and 4.90 (1 H, d, *J* 6 Hz, H-4) (Found: C, 59.0; H, 7.1. $C_{14}H_{20}O_6$ requires C, 59.2; H, 7.0%).

3(5)-(1,2:4,5-*Di*-O-*isopropylidene*-D-allo-1,2,3,4,5-*pentahydroxypentyl*)*pyrazole* (7).—The ketose (6) (2.0 g) and hydrazine hydrate (2.72 ml) were heated under reflux in ethanol for 0.5 h. Evaporation and chromatography of the residue on silica gel, with ethyl acetate as eluant, gave a syrup which slowly crystallised. Recrystallisation from ether–light petroleum gave the *pyrazole* (7) (1.9 g, 91%), m.p. 107—108 °C, $[\alpha]_D$ −6.6° (*c* 5.0 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 300 (OH, NH), 1 528 (C=N), 1 372, and 1 380 cm^{-1} (CMe_2); δ(100 MHz; $CDCl_3$) 1.37 (3 H, s), 1.42 (6 H, s), and 1.57 (3 H, s) (all CMe_2), 3.67 (1 H, dd, *J* 9 and 2.2 Hz, H-3′), 4.0—4.2 (4 H, m), 5.48 (1 H, d, *J* 6 Hz, H-1′), 6.02 (1 H, d, *J* 1.5 Hz, H-4), and 7.58 [1 H, d, *J* 1.5 Hz, H-5(3)] (Found: C, 56.3; H, 7.2; N, 9.3. $C_{14}H_{22}N_2O_5$ requires C, 56.4; H, 7.4; N, 9.4%).

1-(2,4-*Dinitrophenyl*)-3-(1,2:4,5-*di*-O-*isopropylidene*-D-allo-1,2,3,4,5-*pentahydroxypentyl*)*pyrazole* (8).—A solution of the pyrazole (7) (1.5 g) and 1-fluoro-2,4-dinitrobenzene (0.976 g) in benzene (60 ml) containing triethylamine (1 ml) was heated under reflux for 20 h. Evaporation, chromatography on silica gel, and elution with benzene–ethyl acetate (2 : 1) gave the *DNP-derivative* (8) (1.95 g, 84%) as a yellow syrup, $[\alpha]_D$ +73.1° (*c* 0.46 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 450 (OH), 1 545 and 1 350 (NO_2), 1 375, and 1 385 cm^{-1} (CMe_2); δ(100 MHz; $CDCl_3$) 1.36, 1.40, 1.43, and 1.60 (each 3 H, s, CMe_2), 2.68 (1 H, d, *J* 2 Hz, exchangeable with D_2O, OH), 3.76 (1 H, m, becomes dd, *J* 9 and 2 Hz on D_2O exchange, H-3′), 4.0—4.3 (4 H, m), 5.46 (1 H, d, *J* 6 Hz, H-1′), 6.73 (1 H, d, *J* 2.5 Hz, H-4), 7.87 (1 H, d, *J* 2.5 Hz, H-5), 7.85 (1 H, d, *J* 9 Hz, H-6″), 8.64 (1 H, dd, *J* 9 and 2 Hz, H-5″), and 8.80 (1 H, d, *J* 2 Hz, H-3″)* (Found: C, 52.0; H, 5.3; N, 12.0. $C_{20}H_{24}N_4O_9$ requires C, 51.7; H, 5.2; N, 12.1%).

1-(2,4-*Dinitrophenyl*)-3-(D-allo-1,2,3,4,5-*pentahydroxypentyl*)*pyrazole* (14).—A solution of the di-isopropylidene derivative (8) (1.0 g) in ethanol (5 ml) was treated with hydrochloric acid (1.5 ml), and the mixture was kept in the dark at room temperature; a precipitate slowly formed. After 8 h, the solid was filtered off, washed with cold ethanol, and recrystallised from ethanol to give the *pentitol* (14) (0.7 g, 85%), m.p. 148—149 °C, $[\alpha]_D$ +28.2° (*c* 1.06 in MeOH); $\nu_{max.}$ 3 425 (OH), 1 550 (NO_2), 1 535 (C=N), and 1 355 cm^{-1} (NO_2); δ[100 MHz; $(CD_3)_2SO$] 3.2—4.0 (5 H, m, exchangeable with D_2O, OH), 5.44 (1 H, d, *J* 5 Hz, H-1′), 6.68 (1 H, d, *J* 2.5 Hz, H-4), 8.12 (1 H, d, *J* 9 Hz, H-6″), 8.40 (1 H, d, *J* 2.5 Hz, H-5), 8.62 (1 H, dd, *J* 9 and 2 Hz, H-5″), and 8.84 (1 H, d, *J* 2 Hz, H-3″) (Found: C, 44.0; H, 4.1; N, 14.6. $C_{14}H_{16}N_4O_9$ requires C, 43.75; H, 4.2; N, 14.6%).

3-(2-O-*Acetyl*-1,3:4,5-*di*-O-*isopropylidene*-D-allo-1,2,3,4,5-*pentahydroxypentyl*)-1-(2,4-*dinitrophenyl*)*pyrazole* (15) *and* 3-(1-O-*Acetyl*-2,3:4,5-*di*-O-*isopropylidene*-D-allo-1,2,3,4,5-*pentahydroxypentyl*)-1-(2,4-*dinitrophenyl*)*pyrazole* (16).—(a) The pyrazole (8) (0.6 g), dissolved in dry acetone (24 ml) containing conc. sulphuric acid (0.15 ml), was stirred at room temperature for 8 h. After neutralisation with anhydrous sodium carbonate, the mixture was filtered, and the solids washed well with acetone. Evaporation of the filtrate yielded a syrup (0.58 g). Chromatography on silica gel and elution with benzene–ethyl acetate (2 : 1) gave a mixture of the alcohols (12) and (13) (0.33 g, 55%); further elution with the same solvent then gave a syrup (0.15 g, 25%), identical (i.r., t.l.c.) with the starting material (8). The alcohol mixture (12) and (13) (0.3 g) was set aside in dry pyridine (3 ml) and acetic anhydride (0.75 ml) for 16 h. Isolation with chloroform yielded a syrup (0.32 g) which on chromatography on silica, with benzene–ethyl acetate (3 : 1) as eluant, yielded the 2-O-*acetyl*-1,3:4,5-*di*-O-*isopropylidene derivative* (15) (0.164 g, 55%), as a syrup, $[\alpha]_D$ −20.8° (*c* 0.72 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 750 (C=O), 1 545 and 1 350 (NO_2), 1 385, and 1 370 cm^{-1} (CMe_2);

* Unprimed numbers refer to the pyrazole hydrogen atoms, primed (′) numbers to the sugar residue, and double primed (″) numbers to the DNP substituent throughout.

δ(100 MHz; $CDCl_3$) 1.32, 1.40, 1.47, and 1.60 (each 3 H, s, CMe_2), 1.97 (3 H, s, COMe), 3.8—4.2 (4 H, m), 4.8—5.1 (2 H, m, H-1′, H-2′), 6.68 (1 H, d, *J* 2.2 Hz, H-4), 7.73 (1 H, d, *J* 9 Hz, H-6″), 7.77 (1 H, d, *J* 2.2 Hz, H-5), 8.48 (1 H, dd, *J* 9 and 2 Hz, H-5″), and 8.62 (1 H, d, *J* 2 Hz, H-3″); δ(100 MHz; C_6D_6), *inter alia*, 4.97 (1 H, d, *J* 9.5 Hz, H-1′) and 5.28 (1 H, t, *J* 9.5 Hz, H-2′) (Found: C, 52.3; H, 5.05; N, 11.2. $C_{22}H_{26}N_4O_{10}$ requires C, 52.2; H, 5.2; N, 11.1%).

Further elution with the same solvent then yielded the 1-O-*acetyl*-2,3:4,5-*di*-O-*isopropylidene derivative* (16) (0.145 g, 45%) as a yellow foam, $[\alpha]_D$ −13.7° (*c* 0.80 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 750 (C=O), 1 550 (C=N, NO_2), 1 350 (NO_2), 1 375, and 1 385 cm^{-1} (CMe_2); δ(100 MHz; $CDCl_3$) 1.33 (6 H, s), 1.35 (3 H, s), and 1.40 (3 H, s) (all CMe_2), 2.05 (3 H, s, COMe), 3.80—4.30 (4 H, m), 4.64 (1 H, dd, $J_{1',2'}$ 8.5, $J_{2',3'}$ 4.5 Hz, H-2′), 6.04 (1 H, *J* 8.5 Hz, H-1′), 6.64 (1 H, d, *J* 2.2 Hz, H-4), 7.77 (1 H, d, *J* 2.2 Hz, H-5), 7.78 (1 H, d, *J* 9 Hz, H-6″), 8.47 (1 H, dd, *J* 9 and 2.2 Hz, H-5″), and 8.63 (1 H, d, *J* 2.2 Hz, H-3″) (Found: C, 52.0; H, 5.1; N, 11.2%).

(b) The pentitol (14) (0.34 g) was stirred in dry acetone (12 ml) containing conc. sulphuric acid (0.1 ml) at room temperature for 6 h. After neutralisation (sodium carbonate), filtration and evaporation, the residue was chromatographed on silica gel. Benzene–ethyl acetate (2 : 1) eluted first the mixture of (12) and (13) (0.23 g, 55%), followed by the 1,2:4,5-di-*O*-isopropylidene derivative (8) (0.13 g, 31%). Treatment of the mixture of (12) and (13) with acetic anhydride and pyridine produced a result identical with that in (a).

3-(3-O-*Acetyl*-1,2:4,5-*di*-O-*isopropylidene*-D-allo-1,2,3,4,5-*pentahydroxypentyl*)-1-(2,4-*dinitrophenyl*)*pyrazole* (9).—The alcohol (8) (90 mg) was treated with pyridine (1 ml) and acetic anhydride (0.25 ml) at room temperature for 16 h. Isolation with chloroform, chromatography of the residue on silica gel, and elution with benzene–ethyl acetate (3 : 1) yielded the *acetate* (9) (81 mg, 82%) as a yellow foam, $[\alpha]_D$ +140.2° (*c* 0.68 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 758 (C=O), 1 550 (NO_2), 1 385, 1 375 (CMe_2), and 1 350 cm^{-1} (NO_2); δ(100 MHz; $CDCl_3$) 1.28 (6 H, s), 1.42 (3 H, s), and 1.60 (3 H, s) (all CMe_2), 1.75 (3 H, s, COMe), 3.9—4.6 (4 H, m), 4.95 (1 H, dd, *J* 9 and 2 Hz, H-3′), 5.32 (1 H, d, *J* 6.5 Hz, H-1′), 6.57 (1 H, d, *J* 2.5 Hz, H-4), 7.75 (1 H, d, *J* 2.5 Hz, H-5), 7.80 (1 H, d, *J* 9 Hz, H-6″), 8.48 (1 H, dd, *J* 9 and 2.2 Hz, H-5″), 8.64 (1 H, d, *J* 2.2 Hz, H-3″) (Found: C, 52.2; H, 5.0; N, 11.3. $C_{22}H_{26}N_4O_{10}$ requires C, 52.2; H, 5.2; N, 11.1%).

1-(2,4-*Dinitrophenyl*)-3-(2-O-*methylsulphonyl*-1,3:4,5-*di*-O-*isopropylidene*-D-allo-1,2,3,4,5-*pentahydroxypentyl*)-*pyrazole* (19) *and* 1-(2,4-*Dinitrophenyl*)-3-(2,3-O-*isopropylidene*-α-D-*ribofuranosyl*)*pyrazole* (21).—The mixture of alcohols (12) and (13) (0.2 g, 0.43 mmol) in dry pyridine (3 ml) was treated with methanesulphonyl chloride (0.1 ml, 1.29 mmol) at room temperature for 17 h. Water was added and the product isolated with chloroform. The orange syrup was shown by t.l.c. (benzene–ethyl acetate; 2 : 1) to be a mixture of 2 major products, R_F 0.54 and 0.41. The mixture was applied to a silica gel column; elution with the solvent system above and crystallisation from benzene–light petroleum yielded first the 2-O-*methylsulphonyl compound* (18) (0.125 g, 53%), m.p. 174—175 °C, $[\alpha]_D$ +8.8° (*c* 0.34 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 540 (NO_2), 1 375, 1 370 (CMe_2), 1 355, 1 350, and 1 340 cm^{-1} (NO_2, SO_2); δ(100 MHz; $CDCl_3$) 1.35, 1.43, 1.48, and 1.60 (each 3 H, s, CMe_2), 2.78 (3 H, s, SO_2Me), 3.90—4.45 (4 H, m), 4.62 (1 H, t, *J* 9.2 Hz, H-2′), 5.03 (1 H, d, *J* 9.2 Hz, H-1′), 6.72 (1 H, d, *J* 2.2 Hz, H-4), 7.73 (1 H, d, *J* 2.2 Hz, H-5), 7.95 (1 H, d, *J* 9 Hz, H-6″), 8.50 (1 H, dd, *J* 9 and 2.2 Hz, H-5″), 8.65 (1 H, d, *J* 2.2 Hz, H-3″) (Found: C, 46.6; H, 4.9; N, 10.2; S, 6.1. $C_{21}H_{26}N_4O_{11}S$ requires C, 46.5; H, 4.8; N, 10.3; S, 5.9%). Further elution yielded a second fraction which on evaporation gave a syrup (50 mg) which was found by t.l.c. to be contaminated with a slower-moving material, R_F 0.18; more of this material (30 mg) was obtained by continued elution of the column. After 24 h, t.l.c. showed that the second fraction contained only the slower-moving material. Re-chromatography of the combined fractions yielded the α-D-*ribofuranosyl compound* (21) (49 mg, 30%) as a yellow foam, $\nu_{max.}$ 3 450 (OH), 1 540 (NO_2), 1 390, 1 370 (CMe_2), and 1 295 cm^{-1} (NO_2); δ(100 MHz; $CDCl_3$) 1.30, 1.50 (each 3 H, s, CMe_2), 2.35 (1 H, s, exchangeable with D_2O, OH), 3.65 (2 H, d, *J* 5.5 Hz, H-5′), 4.25 (1 H, t, $J_{4',5'}$, 5.5, $J_{3',4'}$ *ca.* 0, H-4′), 4.65—4.90 (2 H, m, H-2′, H-3′), 5.10 (1 H, d, *J* 3.2 Hz, H-1′), 6.67 (1 H, d, *J* 2.5 Hz, H-4), 7.70 (1 H, d, *J* 2.5 Hz, H-5), 7.75 (1 H, d, *J* 9 Hz, H-6″), 8.40 (1 H, dd, *J* 9 and 2.2 Hz, H-5″), and 8.56 (1 H, d, *J* 2.2 Hz, H-3″); *m/e* 391 (*M* − CH_3) and 263 (heterocycle + 30) (Found: C, 50.5; H, 4.8; N, 14.0. $C_{17}H_{18}N_4O_8$ requires C, 50.3; H, 4.5; N, 13.8%).

Reaction of 2,3,5-*Tri*-O-*benzyl*-D-*ribofuranosyl Chloride with* 3,3-*Diethoxyprop*-1-*ynylmagnesium Bromide*.—To a solution of ethylmagnesium bromide [from magnesium (1.9 g) and ethyl bromide (8.73 g)] in dry tetrahydrofuran (THF) (150 ml) was added at 55 °C a solution of 3,3-diethoxypropyne (11.19 g) in THF (100 ml) over 0.5 h. The mixture was heated at 55 °C for a further 1 h, and 2,3,5-tri-*O*-benzyl-D-ribofuranosyl chloride [from 2,3,5-tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-β-D-ribofuranose [17] (22.5 g)] in THF (100 ml) was added dropwise over 0.5 h. After a further 1.5 h at 50 °C, THF was removed *in vacuo*, and the residue partitioned between dichloromethane and saturated aqueous ammonium chloride. The washed and dried organic layer was evaporated to leave a syrup, which was chromatographed on silica gel. Elution with light petroleum–ether (15 : 1) yielded first an unknown compound, possibly an elimination product (1.34 g), followed by the β-acetal [19] (24) (2.73 g, 13%), as a syrup.

Further elution with light petroleum–ether (7 : 1) yielded the α-acetal (23) (10.2 g, 49%), m.p. 34—35 °C; δ(100 MHz; $CDCl_3$) 1.15 (6 H, 2 overlapping t, Me), 3.0—5.0 (16 H, m), 5.20 [1 H, s, $CH(OEt)_2$], and 7.2 (15 H, m, Ar) (Found: C, 75.1; H, 7.3. $C_{33}H_{38}O_6$ requires C, 74.7; H, 7.2%).

3(5)-(2,3,5-*Tri*-O-*benzyl*-α-D-*ribofuranosyl*)*pyrazole* (25).—To a solution of the α-acetal (23) (10.2 g) in glacial acetic acid (270 ml) was added 2M-hydrochloric acid (80 ml). The mixture was stirred for 0.5 h after which hydrazine hydrate (15 ml) in acetic acid (50 ml) was added over 0.5 h. After the addition, the mixture was refluxed for 1 h. To the cooled solution was added dilute sodium hydroxide solution (80 ml), and the mixture partitioned between water (3 l) and dichloromethane (3 × 1 l). Evaporation of the dried organic layers gave an oil which on chromatography on silica with light petroleum–ether (1 : 4) as eluant yielded the *pyrazole* (25) (6.5 g, 74%) as a syrup, $[\alpha]_D$ +38.7° (*c* 0.81 in $CHCl_3$); $\nu_{max.}$ (film) 3 240 cm^{-1} (NH); δ(100 MHz; $CDCl_3$) 3.0—5.0 (11 H, m), 5.12 (1 H, s, H-1′), 6.2 (1 H, br s, H-4), 7.1 (15 H, m, Ar), 7.4 [1 H, br s, H-5(3)], and 8.5 (1 H, br s, exchangeable with D_2O, NH) (Found: C, 73.9; H, 6.1; N, 5.8. $C_{29}H_{30}N_2O_4$ requires C, 74.0; H, 6.2; N, 6.0%).

1-(2,4-*Dinitrophenyl*)-3-(2,3,5-*tri*-O-*benzyl*-α-D-*ribofuranosyl*)*pyrazole* (26).—A solution of the pyrazole (25) (5.5 g), 1-fluoro-2,4-dinitrobenzene (4.84 ml), and triethylamine (5.06 ml) in benzene (200 ml) was heated under reflux for 8 h. Evaporation and chromatography of the residue on silica gel, with light petroleum–ether (1 : 1) as eluant, yielded the *DNP-derivative* (26) (6.5 g, 87%) as a yellow syrup, $[\alpha]_D$ −6.90° (*c* 1.60 in $CHCl_3$); $\nu_{max.}$ 1 620 (Ar), 1 540, and 1 350 cm^{-1} (NO_2); δ(60 MHz; $CDCl_3$) 3.5—5.0 (11 H, m), 5.2 (1 H, d, *J* 2 Hz, H-1′), 6.7 (1 H, d, 2 Hz, H-4), 7.3 (15 H, m, Ph), 7.5 (1 H, d, *J* 9 Hz, H-6″), 7.7 (1 H, d, *J* 2 Hz, H-5), and 8.2—8.6 (2 H, m, H-3″, H-5″) (Found: C, 66.1; H, 5.0; N, 9.0: $C_{35}H_{32}N_4O_8$ requires C, 66.0; H, 6.0; N, 8.8%).

1-(2,4-*Dinitrophenyl*)-3-(2,3,5-*tri*-O-*acetyl*-α-D-*ribofuranosyl*)*pyrazole* (28).—To a solution of boron trichloride (50 ml) in dichloromethane (150 ml) at −78 °C was added a solution of the pyrazole (26) (3.41 g) in dichloromethane (150 ml) over 0.5 h. After a further 5 h at −78 °C, dichloromethane–methanol (1 : 1; 250 ml) was added over 0.5 h, at −78 °C. The mixture was allowed to warm to room temperature, and stirred overnight. The solvents were removed *in vacuo*, and the residue co-distilled with methanol (3 × 300 ml). Chromatography on silica gel, eluting with ethyl acetate, gave the triol (27) (1.60 g), as a foam. A portion (1 g) of this material was left overnight as a solution in pyridine (20 ml) and acetic anhydride (10 ml). Solvents were removed *in vacuo*. Chromatography on silica gel, with light petroleum–ethyl acetate (2 : 1) as eluant, gave the *triacetate* (28) (1.19 g, 71%) as a glassy solid, $[\alpha]_D$ +4.4° (*c* 1.2 in $CHCl_3$); $\nu_{max.}$ (film) 1 750 (ester), 1 615 (Ar), 1 540, and 1 350 cm^{-1} (NO_2); δ(100 MHz; $CDCl_3$) 2.00, 2.04, and 2.11 (each 3 H, s, Me), 4.1—4.6 (3 H, m, H-2′, H-3′, H-4′), 5.3—5.7 (3 H, m, H-1′, H-5′), 6.64 (1 H, d, *J* 2 Hz, H-4), 7.72 (1 H, d, *J* 2 Hz, H-5), 7.84 (1 H, d, *J* 8 Hz, H-6″), 8.52 (1 H, dd, *J* 8 and 2 Hz, H-5″), and 8.68 (1 H, d, *J* 2 Hz, H-3″) (Found: C, 48.9; H, 4.1; N, 11.25. $C_{20}H_{20}N_4O_{11}$ requires C, 48.8; H, 4.1; N, 11.4%).

1-(2,4-*Dinitrophenyl*)-3-(2,3-O-*isopropylidene*-α-D-*ribofuranosyl*)*pyrazole* (21).—A solution of the pyrazole (27) (0.1 g), from the foregoing preparation, in acetone (5 ml) and concentrated sulphuric acid (0.05 ml), was left at room temperature for 2 h. Neutralisation (Na_2CO_3), filtration, and evaporation gave a crude product (0.11 g), which, after chromatography on silica gel, with light petroleum–ether (1 : 4), as eluant and crystallisation from light petroleum–ether, gave the isopropylidene derivative (20) [98 mg, 71% from (26)], m.p. 81—85 °C, $[\alpha]_D$ −124.6° (*c* 0.65 in $CHCl_3$), with spectroscopic properties identical with the material just described.

3(5)-α-D-*Ribofuranosylpyrazole* (3).—To a solution of boron trichloride (17 ml) in dichloromethane (50 ml) at −78 °C was added dropwise over 0.5 h, a solution of 3(5)-tri-*O*-benzyl-α-D-ribofuranosylpyrazole (1.0 g) in dichloromethane (50 ml). The mixture was stirred for 5 h at −78 °C, and dichloromethane–methanol (1 : 1; 200 ml) added over 0.5 h. The mixture was stirred at room temperature overnight, solvents were removed *in vacuo*, and the residue was co-distilled with methanol (3 × 100 ml). The resultant syrup was applied to a column (20 ml) of Amberlite IR—400 (OH^-) resin. Elution with a gradient of 10—50% methanol in water, evaporation, and recrystallisation from methanol–ether gave 3(5)-α-D-*ribofuranosylpyrazole* (3) (0.25 g, 61%), m.p. 123—125 °C, $[\alpha]_D$ −15.2° (*c* 0.85 in MeOH); $\nu_{max.}$ 3 500 cm^{-1} (OH, NH); δ(100 MHz; D_2O) 3.5—5.0 (5 H, m), 5.3 (1 H, d, *J* 3 Hz, H-1′), 6.52 (1 H, d, *J* 2 Hz, H-4), and 7.78 [1 H, d, *J* 2 Hz, H-3(5)] (Found: M^+, 200.079 7; $C_8H_{12}N_2O_4$ requires 200.076 8; heterocycle $+CH_2O$, 97.040 2; $C_4H_5N_2O$ requires 97.038 2).

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