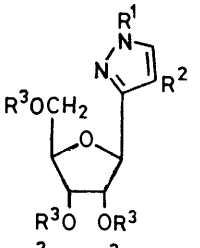
C-Nucleoside Studies. Part 10.[1,2] A New Synthesis of 3-(2,3,5-Tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole and its Conversion into 4-Nitro-3(5)-β-D-ribofuranosylpyrazole

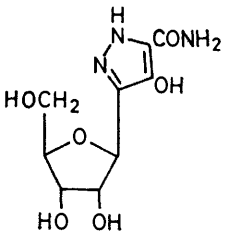
By **J. Grant Buchanan,* Alan R. Edgar, Roderick J. Hutchison, Alan Stobie,** and **Richard H. Wightman,**
Department of Chemistry, Heriot-Watt University, Riccarton, Currie, Edinburgh EH14 4AS

1,1-Diethoxy-3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)prop-2-yne (12) has been synthesised from 2,3,5-tri-*O*-benzyl-D-ribofuranose in 52% yield. Acidic hydrolysis followed by reaction with hydrazine affords 3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole (1) in 71% yield. Mild methods have been devised for nitration of pyrazole derivatives at C-4, leading to a synthesis of 4-nitro-3(5)-β-D-ribofuranosylpyrazole (3) from (1) in 56% overall yield.

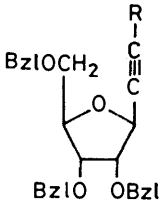
In earlier papers[3,4] we have described the synthesis of 3-(2,3,5-tri-*O*-benzyl-β-D-ribofuranosyl)pyrazole (1). One of our objectives has been to prepare 4-amino-3-β-D-ribofuranosylpyrazole (2) which is related to the *C*-nucleoside antibiotic pyrazofurin (pyrazomycin) (9).[5] We thought that the amine (2), as its 5′-phosphate,



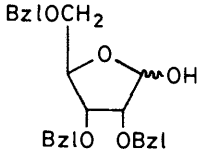
(1) $R^1 = R^2 = H$, $R^3 = Bzl$
(2) $R^1 = R^3 = H$, $R^2 = NH_2$
(3) $R^1 = R^3 = H$, $R^2 = NO_2$
(4) $R^1 = DNP$, $R^2 = H$, $R^3 = Bzl$
(5) $R^1 = DNP$, $R^2 = R^3 = H$
(6) $R^1 = DNP$, $R^2 = H$, $R^3 = Ac$
(7) $R^1 = DNP$, $R^2 = NO_2$, $R^3 = Ac$
(8) $R^1 = R^3 = Ac$, $R^2 = NHAc$



(9)



(10) R = CHO
(11) R = CH_2OH
(12) R = $CH(OEt)_2$

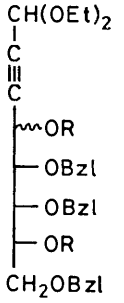


(13)

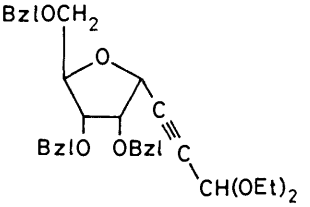
Bzl = $PhCH_2$
DNP = 2,4-$(NO_2)_2C_6H_3$

might be a biochemical precursor of formycin and pyrazofurin by analogy with the *de novo* biosynthesis of purine nucleotides.[6] The nitropyrazole (3) was an obvious synthetic target. This paper describes a new, improved synthesis of the pyrazole (1), together with nitration studies leading to (3). The amine (2) proved to be too unstable for feeding experiments. The nitropyrazole (3) has recently been used in a new synthesis of formycin.[2]

One synthesis[4] of the pyrazole (1) involved reaction between hydrazine and the acetylenic aldehyde (10) which was obtained by oxidation of the primary alcohol (11) with chromic oxide. The oxidation step required great care and gave a total yield of only 42% after chromatography. We have therefore explored the use of 3,3-diethoxypropynylmagnesium bromide[7-9] for the preparation of the acetal (12). Reaction of 2,3,5-tri-*O*-benzyl-D-ribofuranose (13) with the Grignard reagent afforded a mixture of epimeric diols[10] (14) which was



(14) R = H
(15) R = Ts



(16)

partially purified by chromatography. Treatment with toluene-*p*-sulphonyl chloride in pyridine[10] then gave a mixture of the ribofuranosyl derivatives (12) and (16) together with the disulphonate(s) (15). The course of similar reactions has been discussed at some length.[10,11] After chromatography the yields of the pure β- (12) and α-acetal (16) were 52 and 9% respectively. The disulphonates were not obtained in analytically pure form, but the presence of toluenesulphonate groups was evident from the i.r. and ^1H n.m.r. spectra.

In earlier work[4] the substituted propynal (10) was converted into the pyrazole (1) (72%) by reaction with hydrazine. The acetal (12) was therefore hydrolysed using hydrochloric acid in acetic acid and the resulting aldehyde (10) treated *in situ* with hydrazine to give the pyrazole (1) in 71% yield. The β-configuration in (12)

is firmly established by this conversion and it is interesting that the yields of β- and α-isomers [(12) and (16)] are very similar to those observed in earlier work involving reaction of the ribofuranose (13) with other acetylenic Grignard reagents, followed by cyclisation.[4,10]

In attempting a synthesis of the 4-nitro-derivative (3) several factors had to be considered. It is well known that treatment of pyrazoles with a mixture of nitric and sulphonic acids ('mixed acid') gives exclusively the 4-nitro-derivative,[12-14] but the conditions required are vigorous, probably because of the formation of the pyrazolium cation.[15-17] Using mixed acid, Moffatt and his co-workers [18] were unable to nitrate the pyrazole ring of the ribosylpyrazole (17) even under forcing conditions.

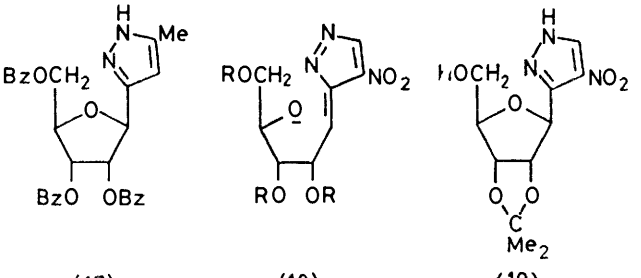
Nitration of pyrazoles under mild conditions has been accomplished using acetyl nitrate,[17,19-22] formed *in situ* from nitric acid and acetic anhydride. Under these conditions a neutral pyrazole molecule is the probable substrate. In pyrazoles unsubstituted on nitrogen the product is normally an *N*-nitropyrazole,[21,22] but *N*-arylpyrazoles give the 4-nitropyrazole in fair yield.[17,19,20]

An extensive study of the nitration of *N*-benzylpyrazoles [23] and *N*-(2,4-dinitrophenyl)pyrazoles [24] with acetyl nitrate showed that both these protecting groups were suitable, but the dinitrophenyl group was preferred because it could easily be removed [25] under basic conditions after nitration had been achieved. Treatment of the pyrazole (1) with 1-fluoro-2,4-dinitrobenzene in the presence of triethylamine [25] afforded the dinitrophenyl derivative (4) in 82% yield. Reaction of this compound with acetyl nitrate was unsatisfactory and it appeared that nitration and possibly acetolysis of the benzyl ether groups occurred under these conditions.[23]

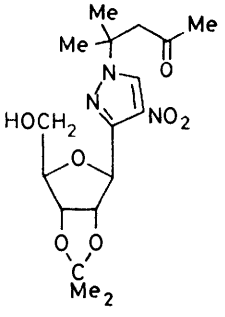
The triacetate (6) seemed a more suitable potential substrate for nitration by acetyl nitrate because the protecting groups would be stable to the acidic conditions but removable by methanolic sodium methoxide. The benzyl groups in the ether (4) were selectively cleaved by boron trichloride [25,26] to give the triol (5) which afforded the triacetate (6) on acetylation. The most satisfactory reagent for nitration proved to be copper(II) nitrate–acetic anhydride [27,28] which gave the 4-nitro-compound (7) in 93% yield. The location of the nitro-group at C-4 was clear from the ^{1}H n.m.r. spectra of (6) and (7). Whereas in (6) the H-4 signal appears at δ 6.57 and H-5 at δ *ca.* 7.7, H-4 is absent from the spectrum of (7) and the H-5 signal, deshielded by the 4-nitro-group, appears at δ 8.5. Treatment of the triacetate (7) with sodium methoxide gave the triol (3) with simultaneous removal of dinitrophenyl and ester groups. There was some evidence (t.l.c.) that the dinitrophenyl group was removed before the ester groups.

The amine (2), produced by catalytic hydrogenation of the nitro-compound (3), proved to be very unstable in the presence of air, in keeping with the behaviour of simpler 4-aminopyrazoles and their salts.[23,29] It was converted, *in situ*, into the penta-acetyl derivative (8).

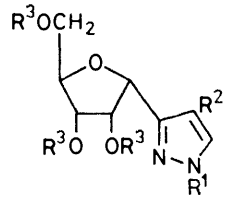
We felt it necessary to establish unambiguously the β-configuration in the triol (3), since the basic reaction conditions of the deprotection step opened the possibility for anomerisation *via* an intermediate of type (18). To this end the triol (3) was converted into its 2,3-*O*-isopropylidene derivative (19) for detailed n.m.r. examination. Interestingly, acid-catalysed condensation of (3) with acetone overnight gave a high yield of the crystalline adduct (20), presumably formed by Michael addition of pyrazole nitrogen to 4-methylpent-3-en-2-one, itself



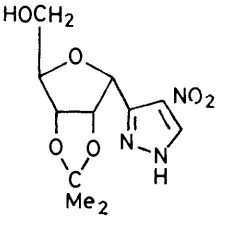
(17) (18) (19)



(20)



(21) R^1 = DNP, R^2 = H, R^3 = Ac
(22) R^1 = DNP, R^2 = NO_2, R^3 = Ac
(23) R^1 = R^3 = H, R^2 = NO_2



(24)

produced by self-condensation of acetone. When this adduct was treated with sodium methoxide in methanol it cleanly lost the substituent on nitrogen to give the isopropylidene derivative (19).

The ^{1}H n.m.r. spectrum of (19) showed a significant coupling (J 3 Hz) between H-3′ and H-4′, with the signal for H-4′ appearing as a quartet due to approximately equal coupling with protons at positions 3′ and 5′. This behaviour is typical of the isopropylidene derivatives of nucleosides of β-configuration.[30] Also, the chemical shift difference (Δδ) between the two methyl signals of the isopropylidene group has a value, 0.2 p.p.m., typical of

a β-configuration.[31] However, the value of 2.5 Hz observed for the coupling between H-1′ and H-2′ was rather larger than might have been expected for a compound of β-configuration.[32,33] That epimerisation had not occurred, and that (19) and thus (3) had the pyrazole β-oriented, was conclusively established by synthesis of the corresponding α-compound (24).

The synthetic route used paralleled that carried out in the β-series. Thus, the α-triacetate (21) [1] was nitrated with copper(II) nitrate–acetic anhydride to give the 4-nitro derivative (22) in 78% yield. This material was deprotected with sodium methoxide to give the α-triol (23) which was directly treated with acetone and sulphuric acid for a fairly short time (2.5 h), to give the α-isopropylidene derivative (24).

This product was clearly different from the β-compound (19) by all physical properties measured. In particular, its ^{1}H n.m.r. spectrum showed no observable coupling between H-3′ and H-4′, with the latter signal appearing as a triplet; this behaviour is typical of α-oriented nucleosides.[30] The chemical shift differences ($\Delta\delta$) between the isopropylidene signals was small (0.04 p.p.m.), again typical of an α-configuration,[31] whilst $J_{1',2'}$ had a value (5 Hz) larger than for the β-isomer (19).

EXPERIMENTAL

The general methods used were as stated in Part 2.[11] Adsorption chromatography was carried out using Kieselgel H type 60 (Merck); an external pressure was applied to the tops of columns. For t.l.c. precoated aluminium-backed plates [Kieselgel HF_{254} type 60 (Merck)] were used.

1,1-Diethoxy-3-[2,3,5-tri-O-benzyl-β(and α)-D-ribofuranosyl]prop-2-yne [(12) *and* (16)].—A solution of ethylmagnesium bromide [from magnesium (0.285 g) and ethyl bromide (2.07 g, 1.6 mol. equiv.)] in dry tetrahydrofuran (10 ml) was heated to 50—60 °C and a solution of 1,1-diethoxyprop-2-yne [34] (2.75 g, 1.2 mol. equiv.) in dry tetrahydrofuran (10 ml) was added with stirring during 45 min. After a further 1 h at 50 °C a solution of 2,3,5-tri-*O*-benzyl-D-ribofuranose (13) (1.0 g, 0.2 mol. equiv.) was added during 20 min. The mixture was stirred for a further 30 min, cooled to room temperature, and evaporated. The residue was dissolved in chloroform (50 ml) and shaken with aqueous 10% ammonium chloride (50 ml) followed by water (50 ml). The dried (Na_2SO_4) chloroform solution was evaporated to give a mobile dark red oil shown by t.l.c. to consist mainly of unchanged diethoxypropyne and two compounds of R_F value similar to that of (13). The mixture was chromatographed on silica gel. Light petroleum–ether (2 : 1) eluted unchanged diethoxypropyne (1.63 g) and light petroleum–ether (1 : 2) eluted a mixture of epimeric diols (14) as a syrup (1.58 g, >100%) showing δ(60 MHz; $CDCl_3$) 1.18 (*ca.* 6 H, t, *J* 6.7 Hz, 2 Me), 2.8—5.0 (*ca.* 18 H, m), 5.29 [1 H, d, *J* 1.1 Hz, C*H*(OEt)$_2$], and 7.3 (*ca.* 15 H, m, Ar).

The impure diols (14) (1.58 g) in dry pyridine (10 ml) were treated with toluene-*p*-sulphonyl chloride [1.13 g, 2.5 mol. equiv. based on (13)] during 20 min at 60—70 °C. After 1.5 h at *ca.* 60 °C t.l.c. indicated that the diols had disappeared, being replaced by two major products of lower polarity. After hydrolysis of the excess of acid chloride the product was isolated using chloroform to give a dark syrup (1.37 g) which was chromatographed on silica gel. Elution with light petroleum–ether (5 : 1) gave first the β-*acetal* (12) as a pure syrup (660 mg, 52%), $[\alpha]_D$ −0.9° (*c* 2.24 in $CHCl_3$); $\nu_{max.}$ (film) 2 240 cm^{-1} (C≡C); δ(60 MHz; $CDCl_3$) 1.20 (6 H, t, *J* 6.7 Hz; 2 Me), 3.2—4.9 (16 H, m), 5.29 [1 H, d, *J* *ca.* 1 Hz, C*H*(OEt)$_2$], and 7.3 (15 H, m, Ar); *m/e* 530 (1%, M^+), 485 (7%, M^+ − OEt), 439 (4%, M^+ − C_7H_7), 393 [8%, M^+ − C:CCH(OEt)$_2$], and 91 (100%, C_7H_7) (Found: C, 74.7; H, 7.3. $C_{33}H_{38}O_6$ requires C, 74.7; H, 7.2%).

Further elution of the column with light petroleum–ether (5 : 1) gave first a mixture of (12) and (16) (42 mg) followed by the α-acetal [1] (16) (113 mg, 9%) as a pure syrup which later crystallised, but did not recrystallise readily on a small scale.

Elution of the column with light petroleum–ether (2 : 1) gave a syrupy mixture of two components (270 mg); $\nu_{max.}$ (film) 2 250 (C≡C) and 1 180 cm^{-1} (SO_2); δ(60 MHz; $CDCl_3$) 2.35, 2.40 (6 H, 2s, 2 *Me* C_6H_4), 5.30 [1 H, m, C*H*(OEt)$_2$], and 7.0—8.0 (23 H, m, Ar).

Finally, elution with light petroleum–ether (1 : 1) afforded unchanged (13) (113 mg, 11%) as a syrup which crystallised as needles, m.p. 48—50 °C, identified by comparison with an authentic sample.

On a large scale, tri-*O*-benzyl-D-ribofuranose (13) (40 g) gave a mixture of diols (14) (50 g) which was treated with toluene-*p*-sulphonyl chloride in pyridine to give the β-acetal (12) (23 g, 46%).

3(5)-(2,3,5-Tri-O-benzyl-β-D-ribofuranosyl)pyrazole (1).—The acetal (12) (10 g) was dissolved in glacial acetic acid (270 ml) and hydrochloric acid (2M; 80 ml) and stirred at room temperature for 30 min. To this was added a solution of hydrazine hydrate (15 ml) in glacial acetic acid (50 ml) dropwise during 15 min. The dark red solution was heated under reflux. It became colourless and heating was continued for 1 h. The solution was cooled in ice and basified with ice-cold concentrated aqueous sodium hydroxide. The product was isolated using dichloromethane to give a crude syrup (9.2 g) which was chromatographed on silica gel. Light petroleum–ether (3 : 1) eluted the pyrazole (1) (8.0 g, 71%) which was recrystallised from benzene–light petroleum to give the pure pyrazole (1) (7.5 g), indistinguishable from an authentic sample.[3,4]

1-(2,4-Dinitrophenyl)-3-(2,3,5-tri-O-benzyl-β-D-ribofuranosyl)pyrazole (4).—The pyrazole (1) (0.37 g) was dissolved in dry benzene (50 ml) and triethylamine (0.15 g, 4 mol. equiv.) and heated under reflux overnight with 1-fluoro-2,4-dinitrobenzene (0.3 g, 4 mol. equiv.). The solvent was removed to leave a dark syrup (0.54 g) which was chromatographed on silica gel. Light petroleum–ether (2 : 1) eluted unchanged fluorodinitrobenzene (50 mg) followed by the DNP-*derivative* (4) as a red syrup (408 mg, 82%); $\nu_{max.}$ (film) 1 535 and 1 345 cm^{-1} (NO_2); δ(60 MHz; $CDCl_3$) 3.3—4.8 (11 H, m, 5 ring H + 3 CH_2Ph), 5.19 (1 H, d, *J* 4.4 Hz, H-1′), 6.58 (1 H, d, *J* 2.7 Hz, H-4), 7.3 (15 H, m, Ar), 7.69 (1 H, d, *J* 2.7 Hz, H-3), 7.75 (1 H, dd, *J* 10 and 0.5 Hz, H-6″), 8.49 (1 H, dd, *J* 10 and 2.4 Hz, H-5″), and 8.67 (1 H, dd, *J* 2.4 and 0.5 Hz, H-3″) * (Found: C, 66.0; H, 5.0; N, 8.9. $C_{35}H_{32}N_4O_8$ requires C, 66.0; H, 5.1; N, 8.8%).

1-(2,4-Dinitrophenyl)-3-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)pyrazole (6).—To a solution of boron trichloride

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

(84 ml) in dry dichloromethane (550 ml) at −78 °C was added dropwise over 0.5 h a solution of the tribenzyl ether (4) (21.1 g) in dichloromethane (550 ml). The mixture was maintained at −78 °C for 5 h, methanol–dichloromethane (1 : 1; 1.4 l) was added, and the mixture allowed to warm to room temperature over 2 h. The solvents were removed *in vacuo*, and the residue codistilled with methanol (500 ml) 4 times. To the resultant triol (5) was added pyridine (400 ml) and acetic anhydride (200 ml). The mixture was stirred overnight, solvents were removed *in vacuo*, and the residue chromatographed on silica gel with light petroleum–ethyl acetate (2 : 1) as eluant to yield the *triacetate* (6) as a yellow syrup (16.1 g, 98%), $[\alpha]_D$ +12.7° (*c* 0.55 in $CHCl_3$); $\nu_{max.}$ (film) 1 750 (ester), 1 610 (Ar), 1 540, and 1 350 cm^{-1} (NO_2); δ(60 MHz; $CDCl_3$) 2.10 (3 H, s, Me), 2.15 (6 H, s, Me), 4.3 (3 H, m, sugar), 5.0—5.5 (3 H, m, sugar), 6.57 (1 H, d, *J* 3 Hz, H-4), 7.6—7.9 (2 H, m, H-5, H-6″), and 8.3—8.6 (2 H, m, H-3″, H-5″) (Found: C, 48.6; H, 4.2; N, 11.45; $C_{20}H_{20}N_4O_{11}$ requires C, 48.8; H, 4.1; N, 11.4%).

1-(2,4-*Dinitrophenyl*)-3-(2,3,5-*tri*-O-*acetyl*-β-D-*ribofuranosyl*)-4-*nitropyrazole* (7).—A mixture of copper(II) nitrate trihydrate (4 g) and acetic anhydride (30 ml) was stirred for 1.5 h. The triacetate (6) (2.0 g) was added and the mixture stirred at room temperature for 48 h, with addition of more copper nitrate (2 g) after 24 h. After addition of water (100 ml), the mixture was extracted with ethyl acetate. The washed organic layer was evaporated to dryness and the residue chromatographed over silica gel, with light petroleum–ethyl acetate (2 : 1) as eluant to yield the *nitro-derivative* (7) (2.02 g, 93%) as an amorphous yellow solid, $[\alpha]_D$ +18.5° (*c* 0.54 in $CHCl_3$); $\nu_{max.}$ (film) 1 750 (ester), 1 610 (Ar), 1 550 and 1 350 cm^{-1} (NO_2); δ(100 MHz; $CDCl_3$) 2.08 (9 H, s, Me), 4.0—4.4 (3 H, m, H-4′, H-5′), 5.1—5.7 (3 H, m, H-1′, H-2′, H-3′), 7.78 (1 H, d, *J* 8 Hz, H-6″), and 8.4—8.7 (3 H, m, H-5, H-3″, H-5″) (Found: C, 44.7; H, 3.6; N, 13.2. $C_{20}H_{19}N_5O_{13}$ requires C, 44.7; H, 3.5; N, 13.0%).

4-*Nitro*-3-(β-D-*ribofuranosyl*)*pyrazole* (3).—To the triacetate (7) (2.02 g) in methanol (50 ml) was added a solution of sodium methoxide (from 0.25 g of sodium) in methanol (25 ml). After 1 h, acetic acid was added to neutrality and the solvents were removed *in vacuo*. The products in methanol were evaporated to dryness with silica gel. The resultant silica gel was applied to the top of a column of more silica, and the column eluted with ethyl acetate–methanol (10 : 1) to yield the *triol* (3) (0.70 g, 76%) as an oil, $[\alpha]_D$ +57.9° (*c* 1.07 in water); $\nu_{max.}$ (film) 3 300 (OH) cm^{-1}; δ(60 MHz; D_2O) 3.8—4.8 (5 H, m, H-2′—5′), 5.47 (1 H, d, *J* 5 Hz, H-1′), and 8.4 (1 H, s, H-5) (Found: C, 39.2; H, 4.6; N, 17.0. $C_8H_{11}N_3O_6$ requires C, 39.2; H, 4.5; N, 17.1%).

4-*Acetamido*-1-*acetyl*-3-(2,3,5-*tri*-O-*acetyl*-β-D-*ribofuranosyl*)*pyrazole* (8).—To a stirred suspension of palladium on charcoal (5%; 20 mg) in acetic acid (5 ml) under hydrogen was added a solution of the triol (3) (0.10 g) in acetic acid (3 ml). The mixture was stirred for 12 h, and then filtered under nitrogen, and the catalyst washed with acetic acid. The residue after evaporation was dissolved in pyridine (10 ml) and acetic anhydride (5 ml), and the solution left under nitrogen overnight. Evaporation and chromatography on silica gel with light petroleum–ethyl acetate (3 : 2) as eluant gave the *penta-acetyl derivative* (8) (0.14 g, 81%) as an oil, $[\alpha]_D$ +12.3° (*c* 0.57 in $CHCl_3$); $\nu_{max.}$ (film) 3 400 (NH), 1 750 (ester), 1 695, and 1 550 cm^{-1} (amide); δ(100 MHz; $CDCl_3$) 2.02, 2.10 (each 3 H, s, Me), 2.15 (6 H, s, Me), 2.60 (3 H, s, pyrazole Ac), 4.4 (3 H, m, sugar), 5.2 (2 H, m, sugar), 5.60 (1 H, t, *J* 5 Hz, sugar), 8.2 (1 H, s, exchangeable with D_2O, NH), and 8.82 (1 H, s, H-5) (Found: C, 51.1; H, 5.6; N, 9.3; M^+, 425.1441. $C_{18}H_{23}N_3O_9$ requires C, 50.8; H, 5.4; N, 9.9%; M^+, 425.143 4).

1-(1,1-*Dimethyl*-3-*oxobutyl*)-3-(2,3-O-*isopropylidene*-β-D-*ribofuranosyl*)-4-*nitropyrazole* (20).—Concentrated sulphuric acid (0.5 ml) was added to a solution of the triol (3) (0.64 g) in dry acetone (50 ml). After 18 h the mixture was neutralised with sodium carbonate, filtered, and evaporated. Chromatography over silica with light petroleum–ethyl acetate (1 : 1) as eluant and crystallisation from benzene–light petroleum gave the *isopropylidene derivative* (20) (0.774 g, 77%), m.p. 91—92 °C; $\nu_{max.}$ (KBr) 3 300 (OH), 1 720 (C=O), 1 540, and 1 340 cm^{-1} (NO_2); δ(60 MHz; $CDCl_3$) 1.37, 1.62 (each 3 H, s, CMe_2), 1.70 (6 H, s, CMe_2), 2.07 (3 H, s, COMe), 3.05 (2 H, s, $-CH_2-$), 3.7 (2 H, m, H-5′), 4.4 (1 H, m, H-4′), 4.9 (2 H, m, H-2′, H-3′), 5.73 (1 H, d, 2 Hz, H-1′), and 8.36 (1 H, s, H-5) (Found: C, 53.1; H, 6.5; N, 11.25. $C_{17}H_{25}N_3O_7$ requires C, 53.3; H, 6.5; N, 11.0%).

3-(2,3-O-*Isopropylidene*-β-D-*ribofuranosyl*)-4-*nitropyrazole* (19).—To a solution of (20) (0.774 g) in methanol (40 ml) was added sodium methoxide (from 0.150 g of sodium) in methanol (20 ml). After 18 h, the solution was neutralised with acetic acid, evaporated, and the residue partitioned between ethyl acetate and sodium hydrogen carbonate solution. The dried organic layer was evaporated, and the residue crystallised from dichloromethane to give the *isopropylidene derivative* (19) (0.50 g, 87%), m.p. 181—182 °C; $[\alpha]_D$ +20.8° (*c* 0.72 in acetone); $\nu_{max.}$ (KBr) 3 200 (OH,NH), 1 510, and 1 380 cm^{-1} (NO_2); δ[100 MHz; $(CD_3)_2CO$] 1.32, 1.56 (each 3 H, s, CMe_2), 2.8br (1 H, s, OH), 3.66 (1 H, dd, *J* 12 and 4.5 Hz, H-5′$_a$), 3.86 (1 H, dd, *J* 12, 4 Hz, H-5′$_b$), 4.22 (1 H, q, *J* 4 Hz, H-4′), 4.84 (1 H, dd, *J* 6 and 3 Hz, H-3′), 4.97 (1 H, dd, *J* 6 and 2.5 Hz, H-2′), 5.64 (1 H, d, *J* 2.5 Hz, H-1′), and 8.36 (1 H, s, H-5) (Found: C, 46.2; H, 5.3; N, 14.8. $C_{11}H_{15}N_3O_6$ requires C, 46.3; H, 5.3; N, 14.7%).

1-(2,4-*Dinitrophenyl*)-4-*nitro*-3-(2,3,5-*tri*-O-*acetyl*-α-D-*ribofuranosyl*)*pyrazole* (22).—Copper(II) nitrate trihydrate (2 g) and acetic anhydride (15 ml) were stirred for 1.5 h; the α-triacetate (21) [1] (1.0 g) was added, followed after 14 h by further copper nitrate (1 g). After a further 24 h, water (50 ml) was added, and the product isolated with ethyl acetate. The residue after solvent removal was chromatographed on silica gel, with light petroleum–ethyl acetate (2 : 1) as eluant to give the *nitropyrazole* (22) (0.85 g, 78%) as an amorphous yellow solid, $[\alpha]_D$ −36.4° (*c* 0.60 in $CHCl_3$); $\nu_{max.}$ (film) 1 750 (ester), 1 620 (Ar), 1 555, and 1 350 cm^{-1} (NO_2); δ(100 MHz; $CDCl_3$) 1.96, 2.02, 2.08 (each 3 H, s, Me), 4.0—4.6 (3 H, m, H-4′, H-5′), 5.2—5.9 (3 H, m, H-1′—3′), 7.76 (1 H, d, *J* 8 Hz, H-6″), 8.4—8.6 (2 H, m, H-5, H-5″), and 8.74 (1 H, d, *J* 2 Hz, H-3″) (Found: C, 44.8; H, 3.5; N, 13.8. $C_{20}H_{19}N_5O_{13}$ requires C, 44.7; H, 3.54; N, 13.0%).

3-(2,3-O-*Isopropylidene*-α-D-*ribofuranosyl*)-4-*nitropyrazole* (24).—A solution of sodium methoxide (from 0.1 g of sodium) in methanol (12 ml) was added to the triacetyl derivative (22) (0.74 g) in methanol (25 ml). After 1 h, the mixture was neutralised with acetic acid, and evaporated to dryness. The product was preadsorbed on silica gel using methanol, and applied to the top of a column of silica gel. The column was eluted with light petroleum–

ether (1 : 1) to remove dinitroanisole and then with ethyl acetate–methanol (10 : 1) to yield the triol (23) (0.28 g).

A portion (0.09 g) of this material was dissolved in dry acetone (5 ml). Concentrated sulphuric acid (0.05 ml) was added, and after 2.5 h the mixture was neutralised by addition of solid sodium carbonate. After filtration and solvent removal, chromatography on silica gel with light petroleum–ether (1 : 2) as eluant, followed by crystallisation from chloroform gave the *α-isopropylidene compound* (24) (0.07 g, 56%), m.p. 136—137 °C, $[\alpha]_D$ −171.4° (*c* 0.88 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 400, 3 200 (OH,NH), 1 520, and 1 325 cm^{-1} (NO_2); δ[100 MHz; $(CD_3)_2CO$] 1.20 and 1.24 (each 3 H, s, CMe_2), 3.80 (2 H, d, *J* 4 Hz, H-5′), 4.36 (1 H, t, *J* 4 Hz, H-4′), 5.00 (1 H, d, *J* 5 Hz, H-3′), 5.24 (1 H, t, *J* 5 Hz, H-2′), 5.82 (1 H, d, *J* 5 Hz, H-1′), and 8.16 (1 H, s, H-5) (Found: C, 46.0; H, 5.1; N, 14.7. $C_{11}H_{15}N_3O_6$ requires C, 46.3; H, 5.3; N, 14.7%).

We thank the S.R.C. for Studentships (to R. J. H. and A. S.).

[9/1986 *Received*, 17*th December*, 1979]

REFERENCES

[1] Part 9, J. G. Buchanan, M. E. Chacón-Fuertes, A. Stobie, and R. H. Wightman, preceding paper.
[2] Preliminary communication: J. G. Buchanan, A. R. Edgar, R. J. Hutchison, A. Stobie, and R. H. Wightman, *J. Chem. Soc., Chem. Commun.*, 1980, 237.
[3] J. G. Buchanan, A. R. Edgar, M. J. Power, and G. C. Williams, *Carbohydr. Res.*, 1977, **55**, 225.
[4] J. G. Buchanan, A. D. Dunn, A. R. Edgar, R. J. Hutchison, M. J. Power, and G. C. Williams, *J. Chem. Soc., Perkin Trans.* 1, 1977, 1786.
[5] K. Gerzon, R. H. Williams, M. Hoehn, M. Gorman, and D. C. Delong, Abstracts, 2nd International Congress of Heterocyclic Chemistry, Montpellier, France, July 1969, 30C; R. J. Suhadolnik, 'Nucleoside Antibiotics,' Wiley–Interscience, New York, 1970.
[6] J. M. Buchanan and S. C. Hartman, *Adv. Enzymol.*, 1959, **21**, 199; L. N. Lukens and J. M. Buchanan, *J. Biol. Chem.*, 1959, **234**, 1799.
[7] M. Ohzeki, T. Mizoguchi, K. Koga, and S. Yamada, *Chem. Pharm. Bull.*, 1977, **25**, 2676.
[8] K. Heyns and K.-M. Grühn, *Tetrahedron Lett.*, 1978, 2861.
[9] K. Heyns, K.-M. Grühn, and W. Rust, *Tetrahedron Lett.*, 1978, 4015.
[10] J. G. Buchanan, A. R. Edgar, and M. J. Power, *J. Chem. Soc., Perkin Trans.* 1, 1974, 1943.
[11] J. G. Buchanan, A. D. Dunn, and A. R. Edgar, *J. Chem. Soc., Perkin Trans.* 1, 1975, 1191.
[12] E. Buchner and M. Fritsch, *Justus Liebigs Ann. Chem.*, 1893, **273**, 256.
[13] L. Knorr, *Justus Liebigs Ann. Chem.*, 1894, **279**, 188.
[14] R. Hüttel, F. Büchele, and P. Jochum, *Chem. Ber.*, 1955, **88**, 1577.
[15] M. W. Austin, J. R. Blackborow, J. H. Ridd, and B. V. Smith, *J. Chem. Soc.*, 1965, 1051.
[16] A. G. Burton, P. P. Forsythe, C. D. Johnson, and A. R. Katritzky, *J. Chem. Soc.* (*B*), 1971, 2365.
[17] M. R. Grimmett, S. R. Hartshorn, K. Schofield, and J. B. Weston, *J. Chem. Soc., Perkin Trans.* 2, 1972, 1654.
[18] D. B. Repke, H. P. Albrecht, and J. G. Moffatt, *J. Org. Chem.*, 1975, **40**, 2481.
[19] D. Dal Monte, A. Mangini, and R. Passerini, *Gazz. Chim. Ital.*, 1956, **86**, 797.
[20] M. A. Khan, B. M. Lynch, and Y.-Y. Hung, *Can. J. Chem.*, 1963, **41**, 1540.
[21] R. Hüttel and F. Büchele, *Chem. Ber.*, 1955, **88**, 1586.
[22] J. W. A. M. Janssen and C. L. Habraken, *J. Org. Chem.*, 1971, **36**, 3081.
[23] R. J. Hutchison, Ph.D. Thesis, Heriot-Watt University, 1977.
[24] T. R. B. Ogunro, B.Sc. Dissertation, Heriot-Watt University, 1977.
[25] J. G. Buchanan, M. E. Chacón-Fuertes, and R. H. Wightman, *J. Chem. Soc., Perkin Trans.* 1, 1979, 244.
[26] G. Trummlitz, D. B. Repke, and J. G. Moffatt, *J. Org. Chem.*, 1975, **40**, 3352.
[27] J. B. Menke, *Rec. Trav. Chim. Pays-Bas.*, 1925, **44**, 141, 269.
[28] A. V. Topchiev, 'Nitration of Hydrocarbons and Other Organic Compounds,' trans. C. Mathews, Pergamon, London, 1959, pp. 291—298.
[29] N. I. Carruthers, B.Sc. Dissertation, Heriot-Watt University, 1977.
[30] M. MacCoss, M. J. Robins, B. Rayner, and J.-L. Imbach, *Carbohydr. Res.*, 1977, **59**, 575.
[31] B. Rayner, C. Tapiero, and J.-L. Imbach, *Carbohydr. Res.*, 1976, **47**, 195 and references therein.
[32] H. Maehr, T. H. Williams, M. Leach, and A. Stempel, *Helv. Chim. Acta*, 1974, **57**, 212.
[33] S. De Bernardo and M. Weigele, *J. Org. Chem.*, 1976, **41**, 287.
[34] L. Brandsma, 'Preparative Acetylenic Chemistry,' Elsevier, Amsterdam, 1971, p. 118.