C-Nucleoside Studies. Part 12.[1] Synthesis of 3-α- and 3-β-(D-Xylofuranosyl)pyrazoles

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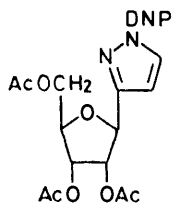
3-(2,3:4,5-Di-*O*-isopropylidene-D-*gulo*-pentahydroxypentyl)pyrazole (13) was prepared in four steps (45% overall yield) from D-gulonolactone (9). Treatment with 1-fluoro-2,4-dinitrobenzene and triethylamine followed by reaction with methanesulphonyl chloride in pyridine afforded 1-(2,4-dinitrophenyl)-3-(1-*O*-methylsulphonyl-2,3:4,5-di-*O*-isopropylidene-D-*gulo*-pentahydroxypentyl)pyrazole (15) which, on treatment with boron trichloride and subsequent methanolysis, followed by exposure to methanolic ammonia, yielded 3-(α-D-xylofuranosyl)pyrazole (5). Oxidation of the pyrazole (13) and subsequent hydride reduction afforded, stereoselectively, 3-(2,3:4,5-di-*O*-isopropylidene-D-*ido*-pentahydroxypentyl)pyrazole (18); treatment of this in the same manner as the pyrazole (13) yielded 3-(β-D-xylofuranosyl)pyrazole (7).

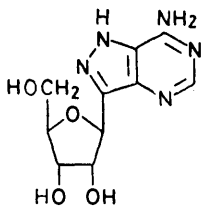
The reactions of sodium benzoate in dimethylformamide with 1-methylsulphonyl-3-(1-*O*-methylsulphonyl-2,3:4,5-di-*O*-isopropylidene-D-*gulo*-pentahydroxypentyl)pyrazole (24) and with its D-*ido*-isomer (27) appear to involve a common fulvene-type intermediate (30).

We have recently reported [2] a convenient synthesis of a protected derivative, compound (1), of 3-(β-D-ribofuranosyl)pyrazole, and from this intermediate we have completed novel total syntheses of the naturally occurring *C*-nucleoside antibiotics [3] formycin (2) [1,2,4] and pyrazofurin (3).[5] Both formycin and pyrazofurin show antitumour and antiviral activity, with the latter showing promise of becoming of clinical use in man.[6] Furthermore, it is now known that very promising antiviral activity is shown by a number of nucleosides with altered configuration in the pentofuranosyl ring, with 9-(β-D-arabinofuranosyl)adenine (ara-A), in particular, in widespread clinical use against herpes encephalitis.[6] Such considerations make it highly desirable to have available routes to analogues of the *C*-nucleoside antibiotics with modified configurations of the sugar ring. We have earlier reported a stereospecific synthesis of 3-(β-D-arabinofuranosyl)pyrazole (4) and we now report stereoselective syntheses of 3-(α-D-xylofuranosyl)pyrazole (5) and its 3-β-isomer (7), together with some interesting observations concerning the stereochemistry of displacement reactions at C-1′ of some pentahydroxypentylpyrazole derivatives.

As in our previous work,[7] a hexose derivative of appropriate stereochemistry was used as starting material and the commercially available D-gulono-γ-lactone (9) seemed appropriate. The lactone was converted into its di-*O*-isopropylidene derivative (10) in very high yield by a modification of the literature procedure.[8] It is well established that the reaction of organolithium reagents with lactones in equimolar amounts gives the lactol as the major product;[9] when the lactone (10) was allowed to react with lithium acetylide in tetrahydrofuran (THF) at low temperatures,[10] the acetylenic lactol (11) was obtained in 72% yield after chromatography. When the lactol (11) was heated under reflux with hydrazine hydrate in ethanol,[7] the crystalline pyrazole (12) was produced in 88% yield, and when a solution of this material in acetone containing sulphuric acid was left for several hours, clean isomerisation occurred to give the 2,3:4,5-*O*-isopropylidene derivative (13). This isomerisation reflects the greater stability of isomer (13) in which the central dioxolan ring has the two bulky substituents in a *trans*-arrangement and parallels our earlier findings in an isomeric series.[7] That this isomerisation product (13) contained two five-membered dioxolan



(1)



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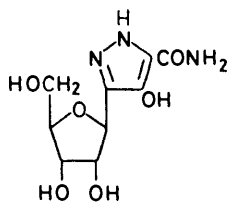

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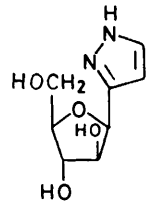

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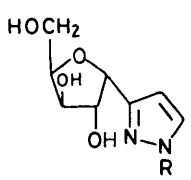
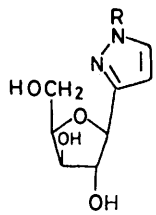
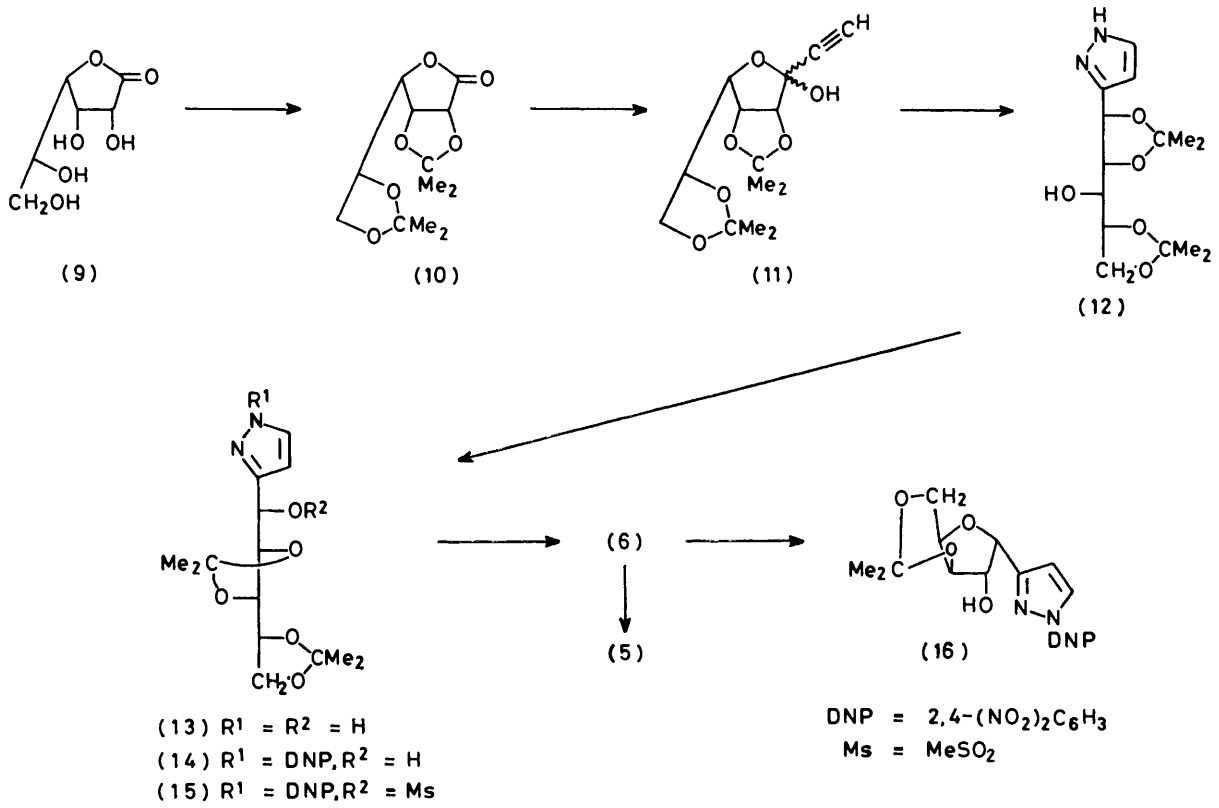


(5) R = H
(6) R = DNP



(7) R = H
(8) R = DNP

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



rings, as opposed to six-membered dioxan rings, was confirmed by measurement of its ^{13}C n.m.r. spectrum.[11]

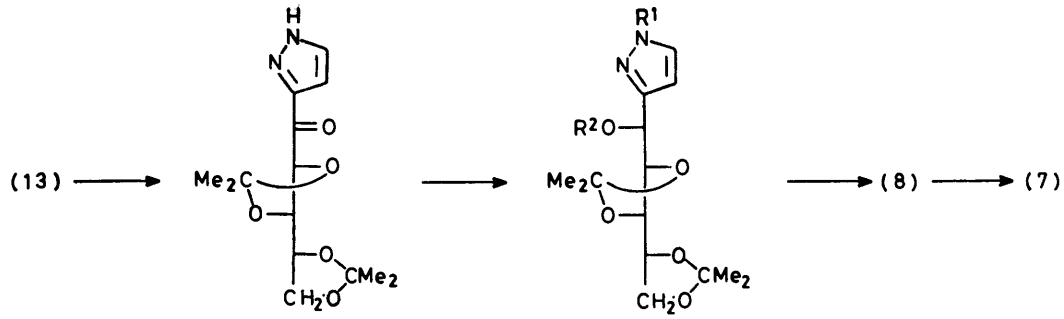
Our earlier studies [7] indicated the need both to introduce a good leaving group at C-1′ of compound (13) in order to effect cyclisation with inversion of configuration, giving an α-xylofuranose system of type (5), and to protect the pyrazole ring. Thus, the pyrazole (13) was treated with 1-fluoro-2,4-dinitrobenzene and triethylamine in refluxing benzene to give the 2,4-dinitrophenyl (DNP)-protected compound (14) (81%) and this, on treatment with methanesulphonyl chloride in pyridine, gave the crystalline methanesulphonate (15). Cyclisation was effected with boron trichloride, followed by methanolysis of the resultant borate complexes,[7] to give a single triol (6).

It was necessary to establish that in the cyclisation to give (6) a furanose ring had, indeed, been formed and that the product had an α-configuration. As regards ring size, ^1H n.m.r. data were unhelpful, and the presence of a furanoid ring was shown chemically by the ready formation of the isopropylidene derivative (16) on treatment with acetone and sulphuric acid. An alternative pentopyranose structure would not have been expected to form an isopropylidene derivative, since vicinal hydroxy-groups would be in a *trans*-arrangement; the formation of 3,5-*O*-isopropylidene derivatives of xylofuranosides is, however, well known.[12] The α-configuration, inferred from the method of formation and the absence of any other cyclisation products, was confirmed by the separate synthesis of the β-isomer described below.

When the DNP-derivative (6) was treated with a solution of ammonia in methanol, the protecting group was cleanly removed; ion-exchange chromatography yielded 3-(α-D-xylofuranosyl)pyrazole (5) as a syrup in 76% yield.

To adapt this synthetic sequence for the preparation of the potentially more interesting β-D-*xylo*-isomer (7), it was clearly necessary to invert the stereochemistry at C-1′ in compound (13) and subsequent intermediates. This was most conveniently accomplished by oxidation of the pyrazole (13) with dimethyl sulphoxide (DMSO)–acetic anhydride, to give the ketone (17), and subsequent reduction with 9-borabicyclo[3.3.1]nonane (9-BBN). The reduction was stereoselective (>3 : 1) in favour of the desired D-*ido*-isomer (18), which was isolated, by chromatography and subsequent crystallisation, in 58% yield; the mother liquors were richer in the D-*gulo*-isomer (13) and these could be recycled. The D-*gulo*- (13) and D-*ido*- (18) isomers, although inseparable on t.l.c., were distinguished by ^1H n.m.r. spectroscopy, with, in particular, the doublets for 1′-H being of slightly different chemical shift, as well as by melting point, optical rotation, and ^{13}C n.m.r. spectroscopy. The origin of the stereoselectivity in the reduction is discussed below in connection with other results. Use of sodium borohydride reduction was also possible, but with rather lower stereoselectivity (*ca.* 3 : 1).

Additional indication of the inversion of configuration in the conversion of isomer (13) into isomer (18) was obtained by hydrolysis of the di-isopropylidene derivatives to give the pentitols (22) and (23), respectively.



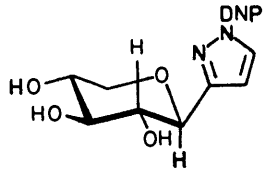
(17)

DNP = $2,4\text{-}(NO_2)_2C_6H_3$
Ms = $MeSO_2$

(18) $R^1 = R^2 = H$
(19) R^1 = DNP, R^2 = H
(20) R^1 = DNP, R^2 = Ms

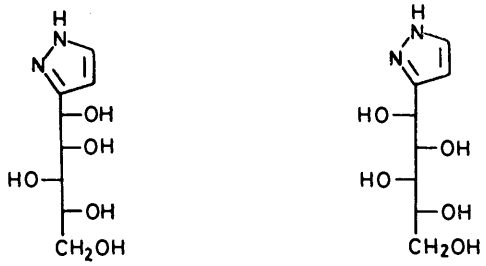
Compound (22) had $[\alpha]_D$ +22.6° (H_2O), whilst compound (23) had a specific rotation of −3.0°. These signs of rotation are in agreement with the rotation rules of Richtmyer and Hudson [13] and El Khadem.[14]

The synthesis of 3-(β-D-xylofuranosyl)pyrazole (7) was then completed in a manner analogous to that used for the α-isomer. Preparation of the DNP-derivative (19) was followed by treatment with methanesulphonyl



(21)

DNP = $2,4\text{-}(NO_2)_2C_6H_3$



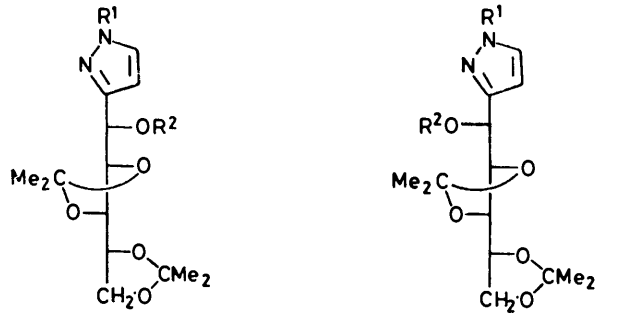
(22) (23)

DNP = $2,4\text{-}(NO_2)_2C_6H_3$

chloride in pyridine to give the crystalline mesylate (20) (85%). Cyclisation was again effected by treatment with boron trichloride and subsequent methanolysis, and again only a single cyclised product was obtained, which was different from the α-isomer (6). The β-D-furanosyl structure (8) was strongly supported by the ^1H n.m.r. spectrum, in which 1′-H appeared as a doublet with $J_{1,2}$ 3.5 Hz. For the alternative pyranose structure (21), with a *trans*-diaxial arrangement of 1′-H and 2′-H, a substantially larger coupling would have been expected.[15]

Treatment of the pyrazole (8) with methanolic ammonia and subsequent ion-exchange chromatography gave 3-(β-D-xylofuranosyl)pyrazole (7) in 70% yield. It is noteworthy that, in comparing the ^1H n.m.r. spectra of α- and β-D-xylofuranosylpyrazoles (5) and (7), the signal for 1′-H of the α-anomer (5) appeared further downfield than the comparable signal in the spectrum of the β-anomer (7). It has been generally observed both for *N*-nucleosides [16] and for *C*-nucleosides [17] that a *cis*-arrangement of the substituent at C-1′ and the hydroxy-group at C-2′ leads to the appearance of 1′-H at lower field than in the other anomer. This evidence further confirms our structural assignments for the α- and β-isomers (5) and (7), respectively.

We also investigated, as an alternative way of inverting the stereochemistry at C-1′ of the pyrazole (13) to yield the D-*ido*-isomer (18), the reaction of a sulphonate ester of compound (13) with sodium benzoate in dimethylformamide (DMF).[18] We envisaged that an S_N2-type displacement would give a clean inversion of the stereochemistry, but in the event the reaction took a rather different course. Thus, the D-*gulo*-alcohol (13) was treated with an excess of methanesulphonyl chloride to give the *NO*-disulphonyl derivative (24).



(24) $R^1 = R^2$ = Ms
(25) R^1 = H, R^2 = Bz
(26) $R^1 = R^2$ = Bz

(27) $R^1 = R^2$ = Ms
(28) $R^1 = R^2$ = Bz
(29) R^1 = H, R^2 = Bz

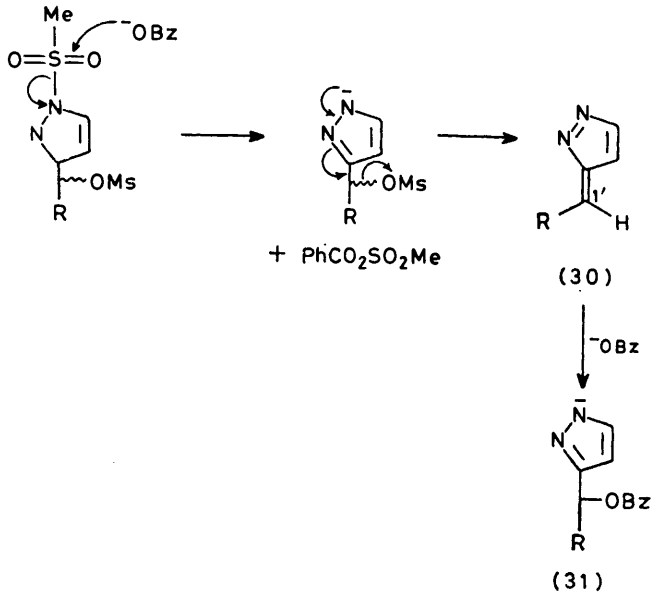
Ms = $MeSO_2$, Bz = PhCO

This material was heated with sodium benzoate in DMF at 100 °C; careful monitoring of the reaction by t.l.c. indicated the gradual disappearance of starting material and appearance of a single product. The product was isolated by chromatography, in 82% yield, as an oil and it appeared, on spectroscopic evidence, to be a homogeneous monobenzoate. Surprisingly, however, basic hydrolysis of this monobenzoate gave a crystalline alcohol identical with compound (13), and it thus appeared that the monobenzoate had structure (25), and had been formed by replacement of methanesulphonate by benzoate with retention of configuration. To confirm this conclusion, alcohol (13) was converted into the crystalline dibenzoyl derivative (26) which, on treatment with piperidine in methanol, gave the oily monobenzoate (25). The monobenzoate prepared in this unambiguous way was identical ($[\alpha]_D$ and i.r. and ^{1}H n.m.r. spectroscopy) with the material obtained from the sodium benzoate reaction. Furthermore, treatment of the product of the benzoate reaction with benzoyl chloride gave the crystalline dibenzoyl derivative (26), identical with the material prepared directly from compound (13).

In the light of this result, it was of interest to investigate the reaction of the D-*ido*-disulphonate (27) with sodium benzoate in DMF. The disulphonate was readily obtained by standard methods, as a crystalline solid. When the disulphonate (27) was treated with sodium benzoate in DMF at 100 °C, the starting material reacted cleanly to give a mixture of two products. These were separated by chromatography; the less polar material was obtained (27%) as a crystalline solid identical with the D-*gulo*-dibenzoyl derivative (26), whilst the more polar product was obtained as an oil (56%), identical with the D-*gulo*-monobenzoate (25). Hydrolysis of the oily monobenzoate gave the crystalline alcohol (13). Furthermore, benzoylation of the D-*ido*-alcohol (17) gave a non-crystalline dibenzoyl compound (28) which, on treatment with piperidine in methanol gave the monobenzoate (29). These materials were clearly distinguishable by spectroscopy from the analogous compounds in the D-*gulo*-series, in particular, in the ^{1}H n.m.r. spectra by the chemical shift of the 1′-H protons. The D-*ido*-bis(methylsulphonyl) compound (27) thus reacts with sodium benzoate in DMF with clean inversion of configuration at C-1′.

We rationalise these findings in terms of the mechanism shown in the Scheme. Since we could not detect any intermediates during the substitution, we postulate an initial slow removal of the *N*-methylsulphonyl group by the benzoate ion, followed by rapid elimination of the methylsulphonyloxy-group at C-1′ to give a fulvene-type intermediate (30), this same intermediate being formed from either precursor (24) or (27). Examination of a molecular model of intermediate (30) clearly indicates that attack of an external nucleophile at C-1′ should, on steric grounds, occur preferentially from the *si*-face, giving the D-*gulo*-product. The formation of the dibenzoyl compound (26) from the reaction of the disulphonyl compound (27) can be explained by the benzoylation of anion (31), either by the mixed benzoic methanesulphonic anhydride formed in the first step or by benzoic anhydride subsequently formed.

The ketone (17) has, like intermediate (30), a trigonal centre at C-1′, and similar examination of a molecular model indicates that hydride attack should occur from the *si*- face to give, predominantly, an alcohol of D-*ido*-configuration, as was observed experimentally, and described earlier in this paper.



SCHEME

Methods developed during earlier work [1,2,4,5] should make possible the conversion of the xylofuranosylpyrazoles (5) and (6) into xylofuranosyl analogues of pyrazofurin and formycin, and further analogues with modifications in the heterocyclic ring should also be easily accessible. Work along these lines is in progress.

EXPERIMENTAL

General methods used were as stated in Part 2.[19] Adsorption chromatography was carried out using Kieselgel H type 60 (Merck); an external pressure was applied to the top of columns. For t.l.c., pre-coated aluminium-backed plates [Kieselgel HF_{254} type 60 (Merck)] were used. ^{13}C N.m.r. spectra were recorded at 20 MHz on a Varian CFT-20 spectrometer.

2,3:5,6-*Di*-O-*isopropylidene*-D-*gulono*-1,4-*lactone* (10).—To a stirred solution of D-gulono-1,4-lactone (Sigma) (10 g) in acetone (500 ml) containing anhydrous copper(II) sulphate (45 g) was added concentrated sulphuric acid (1 ml). After 12 h, the mixture was neutralised with anhydrous sodium carbonate, filtered, and evaporated. The resultant white solid was crystallised from benzene–light petroleum to yield the *di-isopropylidene derivative* (10) (14.37 g, 99%), m.p. 153—154 °C (lit.,[8] 153—153.5 °C).

1,2-*Dideoxy*-1,1,2,2-*tetradehydro*-4,5:7,8-*di*-O-*isopropylidene*-D-gulo-*oct*-3-*ulose* (11).—Dry acetylene gas was bubbled through dry THF (50 ml), for 15 min at room tempera-

ture and 15 min at −78 °C. n-Butyl-lithium in ether (21.2 mmol) was then added in drops, with stirring. Passage of acetylene through the solution was continued for 0.5 h, after which time the lactone (10) (5 g), dissolved in the minimum quantity of dry THF (50 ml) was added to it. The mixture was stirred at −78 °C for 0.5 h, after which the passage of acetylene was discontinued and the solution maintained at −78 °C for a further 0.5 h. The solution was then allowed to warm to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (50 ml) and to this was added a 10% (w/v) ammonium chloride solution (20 ml). The aqueous layer was then extracted with dichloromethane until no product was evident by t.l.c. The dried dichloromethane solution was concentrated under reduced pressure, and the resultant brown syrup was chromatographed on silica gel. Elution with light petroleum–ether (3 : 1) and crystallisation from benzene–light petroleum afforded the *ethyne* (11) (3.99 g, 72%), m.p. 119—121 °C, $[\alpha]_D$ −36.6° (*c* 1.9 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 390 (OH), 3 240 (≡CH), 2 110 (C≡C), and 1 385 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.32 (3 H, s), 1.38 (3 H, s), 1.44 (3 H, s), and 1.51 (3 H, s) (all CMe_2), 2.62 and 2.72 [1 H, 2 s (ratio 1 : 5), ≡CH], 3.48—3.88 (2 H, m), 4.0—4.54 (3 H, m, collapses to 2 H, m, on D_2O shake), and 4.56—5.80 (2 H, m) (Found: C, 59.05; H, 7.2. $C_{14}H_{20}O_6$ requires C, 59.14; H, 7.09%).

(1,2:4,5-*Di*-O-*isopropylidene*-D-gulo-*pentahydroxypentyl*)-*pyrazole* (12).—The ethyne (11) (8 g) dissolved in ethanol (265 ml) was heated under reflux with hydrazine hydrate (11.0 g, 10.72 ml) for 0.5 h. Evaporation and crystallisation from benzene–light petroleum gave the pure *pyrazole* (12) (7.39 g, 88%), m.p. 120—121 °C, $[\alpha]_D$ +37.5° (*c* 0.72 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 300 (OH, NH), 1 530 (C=N), and 1 390 and 1 370 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.38 (6 H, s), 1.48 (3 H, s), and 1.64 (3 H, s) (all CMe_2), 3.3—3.46 (1 H, m), 3.62—4.3 (6 H, m, becomes 5 H, m, on D_2O shake), 5.4 (1 H, d, *J* 8 Hz, 1′-H), 6.36 (1 H, d, *J* 2 Hz, 4-H), and 7.54 (1 H, d, *J* 2 Hz, 5-H); for ^{13}C n.m.r. data see ref. 11 (Found: C, 56.6; H, 7.3; N, 9.45. $C_{14}H_{22}N_2O_5$ requires C, 56.36; H, 7.43; N, 9.38%).

3-(2,3:4,5-*Di*-O-*isopropylidene*-D-gulo-*pentahydroxypentyl*)*pyrazole* (13).—A solution of the pyrazole (12) (5.5 g) in dry acetone (275 ml) containing concentrated sulphuric acid (2.75 ml) was left for 7 h, when t.l.c. of a neutralized sample showed the presence of a major new product. Neutralization with anhydrous sodium carbonate, filtration, and evaporation yielded a brownish oil. This was chromatographed on silica gel [light petroleum–acetone (7 : 1) as eluant]. Crystallisation from ether and recrystallisation from ether–light petroleum gave the *pyrazole* (13) (4.0 g, 72%), m.p. 115—116 °C, $[\alpha]_D$ −17.7° (*c* 0.7 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 400 (OH,NH), 1 540 (C=N), and 1 385 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.35 (3 H, s), 1.38 (3 H, s), and 1.41 (6 H, s) (all CMe_2), 3.66—4.36 (6 H, m, becomes 5 H, m, on D_2O shake), 4.92 (1 H, d, *J* 5 Hz, 1′-H), 6.30 (1 H, s, 4-H), and 7.48 (1 H, s, 5-H); for ^{13}C n.m.r. data see ref. 11 (Found: C, 56.25; H, 7.7; N, 9.45. $C_{14}H_{22}N_2O_5$ requires C, 56.36; H, 7.43; N, 9.38%).

1-(2,4-*Dinitrophenyl*)-3-(2,3:4,5-*di*-O-*isopropylidene*-D-gulo-*pentahydroxypentyl*)*pyrazole* (14).—A solution of the pyrazole (13) (2.25 g) and 1-fluoro-2,4-dinitrobenzene (1.53 g) in dry benzene (10 ml) containing triethylamine (1.57 ml) was heated under reflux for 2 h. The solution was concentrated under reduced pressure to give an oil. Chromatography on silica gel [gravity column and light petroleum–ether (1 : 1) as eluant] and crystallisation of the resultant solid from methanol–water gave the *DNP-derivative* (14) (2.85 g, 81%), m.p. 59 °C, $[\alpha]_D$ −25.6° (*c* 0.78 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 440 (OH), 1 540 (C=N), 1 550 and 1 350 (NO_2), and 1 385 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.35 (3 H, s), 1.39 (3 H, s), and 1.44 (6 H, s) (all CMe_2), 3.28 (1 H, d, *J* 6 Hz, disappears on D_2O shake, OH), 3.76—4.13 (4 H, m), 4.26 (1 H, t, *J* 5 Hz, 2′-H), 4.89 (1 H, t, *J* 5 Hz, 1′-H, collapses to a doublet on D_2O shake, *J* 5 Hz), 6.69 (1 H, d, *J* 3 Hz, 4-H), 7.75—7.91 (2 H, m, 5- and 6″-H), 8.51 (1 H, dd, *J* 9 and 2 Hz, 5″-H), and 8.63 (1 H, d, *J* 2 Hz, 3″-H) (Found: C, 51.65; H, 5.2; N, 12.1. $C_{20}H_{24}N_4O_9$ requires C, 51.72; H, 5.2; N, 12.06%).

1-(2,4-*Dinitrophenyl*)-3-(1-O-*methylsulphonyl*-2,3:4,5-*di*-O-*isopropylidene*-D-gulo-*pentahydroxypentyl*)*pyrazole* (15).—Methanesulphonyl chloride (1.2 ml) was added in drops to a stirred solution of the pyrazole (14) (2.3 g) in dry pyridine (25 ml). The solution was left overnight in the dark, and a few drops of water were then added to destroy excess of reagent. After 0.5 h, the mixture was partitioned between water and dichloromethane. The washed and dried organic extracts were evaporated to leave a brown oil, which was chromatographed on silica [light petroleum–ether (1 : 1) as eluant]. Crystallisation from methanol–water gave the *methylsulphonyl derivative* (15) (1.64 g, 70%), m.p. 90 °C, $[\alpha]_D$ +1.9° (*c* 1.03 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 550 (NO_2), 1 540 (C=N), 1 385 and 1 375 (both CMe_2), and 3 120, 3 080, 1 615, and 1 505 cm^{-1} (aromatic); δ (100 MHz, $CDCl_3$) 1.36 (6 H, s) and 1.44 (6 H, s) (both CMe_2), 2.97 (3 H, s, SO_2Me), 3.88—4.24 (4 H, m), 4.34 (1 H, dd, *J* 6 and 2 Hz, 2′-H), 5.76 (1 H, d, *J* 6 Hz, 1′-H), 6.80 (1 H, d, *J* 2 Hz, 4-H), 7.76—8.92 (2 H, m, 5- and 6″-H), 8.56 (1 H, dd, *J* 9 and 2 Hz, 5″-H), and 8.70 (1 H, d, *J* 2 Hz, 3″-H) (Found: C, 46.7; H, 5.1; N, 10.6; S, 6.05. $C_{21}H_{26}N_4O_{11}S$ requires C, 46.49; H, 4.83; N, 10.32; S, 5.90%).

1-(2,4-*Dinitrophenyl*)-3-(α-D-*xylofuranosyl*)*pyrazole* (6).—To a stirred solution of boron trichloride (20 g) in dry dichloromethane (160 ml), at −78 °C, was added a cold solution of the pyrazole (15) (2 g) in dichloromethane (10 ml), by syringe through a septum. This mixture was maintained at −78 °C for 2 h and was then allowed to warm to room temperature. At the same time a mixture of dichloromethane–methanol (1 : 1, 100 ml) was added in drops to the solution. When the solution was at room temperature it was evaporated to dryness and the residue was co-distilled three times with methanol (100 ml). The oil obtained was chromatographed on silica gel [ether–ethyl acetate (6 : 1) as eluant] to give the *xylofuranosylpyrazole* (6) as a yellow syrup (0.6 g, 52%), $[\alpha]_D$ −34.5° (*c* 0.87 in EtOH); $\nu_{max.}$ (film) 3 400 (OH), 1 550 and 1 345 (NO_2), 1 540 (C=N), and 1 610 and 1 505 cm^{-1} (aromatic); δ (100 MHz; [$^2H_5$]pyridine) 4.36—4.52 (2 H, m), 4.76—5.16 (3 H, m), 5.87 (1 H, d, *J* 4 Hz, 1′-H), 6.16 (3 H, s, disappears on D_2O shake, 3 × OH), 7.08 (1 H, d, *J* 3 Hz, 4-H), 7.92 (1 H, d, *J* 9 Hz, 6″-H), 8.26 (1 H, d, *J* 3 Hz, 5-H), 8.48 (1 H, dd, *J* 9 and 2 Hz, 5″-H), and 8.85 (1 H, d, *J* 2 Hz, 3″-H) (Found: C, 45.65; H, 4.1; N, 15.3. $C_{14}H_{14}N_4O_8$ requires C, 45.90; H, 3.85; N, 15.29%).

3-(α-D-*Xylofuranosyl*)*pyrazole* (5).—The protected pyrazole (6) (0.6 g), dissolved in methanol (15 ml) saturated with ammonia, was stirred for 35 h at room temperature. The solution was evaporated to dryness and water (5 ml) was added to the residue. The aqueous layer was washed with ethyl acetate (3 × 10 ml) and then passed down freshly generated Amberlite IR 400 (OH^-) resin (20 ml). Elution

with water–methanol (8 : 1) gave the *product* (5) as a clear oil (0.25 g, 76%), $[\alpha]_D$ −3.1° (*c* 1.12 in H_2O); $\nu_{max.}$ (film) 3 300 (OH,NH) and 1 540 cm^{-1} (C=N); δ (100 MHz, D_2O) 3.68—3.86 (2 H, m), 4.2—4.44 (3 H, m), 5.26 (1 H, d, *J* 3.5 Hz, 1′-H), 6.31 (1 H, d, *J* 2 Hz, 4-H), and 7.56 [1 H, d, *J* 2 Hz, 5-H]; *m/e* 200 $(M)^+$, 1.69 $(M - CH_2OH)^+$, 97 (heterocycle + 30)$^+$ (Found: C, 47.85; H, 6.2; N, 14.1. $C_8H_{12}N_2O_4$ requires C, 48.00; H, 6.02; N, 13.99%).

The Acetonation of (6).—The xylofuranosylpyrazole (6) (0.1 g) in acetone (3 ml), containing a drop of concentrated sulphuric acid, was left for 3 h after which t.l.c. showed the absence of starting material. The solution was neutralized with anhydrous sodium carbonate, filtered, and the solvent was removed. The resulting brown oil was chromatographed on silica gel. Elution with ether–ethyl acetate (9 : 1) gave the isopropylidene compound (16) as a golden yellow syrup (0.0 9 g, 96%), $[\alpha]_D$ −71.2° (*c* 0.95 in EtOH); $\nu_{max.}$ (film) 3 400 (OH), 1 355 (CMe_2), 1 550 and 1 345 (NO_2), 1 540 (C=N), and 3 110, 3 090, 1 610, and 1 505 cm^{-1} (aromatic); δ (100 MHz; [$^2H_5$]pyridine) 1.64 (6 H, s, CMe_2), 4.12—4.22 (2 H, m), 4.48—4.62 (1 H, m), 4.66—4.72, (2 H, m), 4.96 (1 H, s, disappears on D_2O shake, OH), 5.86 (1 H, d, *J* 4 Hz, 1′-H), 7.12 (1 H, d, *J* 3 Hz, 4-H), 7.92 (1 H, d, *J* 9 Hz, 6″-H), 8.30 (1 H, d, *J* 3 Hz, 5-H), 8.50 (1 H, dd, *J* 9 and 2 Hz, 5″-H), and 8.94 (1 H, d, *J* 2 Hz, 3″-H).

3-(2,3:4,5-*Di*-O-*isopropylidene*-1-*oxo*-D-xylo-*tetrahydroxypentyl*)*pyrazole* (17).—A solution of the alcohol (13) (1.4 g) in DMSO (91 ml) and acetic anhydride (12 ml) was left for 24 h. The solution was then concentrated under reduced pressure to give a golden brown oil. This was dissolved in methanol (50 ml) and piperidine (0.1 ml) was added. The solution was stirred for 5 min and then concentrated under reduced pressure to give a brown oil, which was chromatographed on silica gel. Elution with light petroleum–ether (4 : 1) gave the *ketone* (17) as a clear oil (1.04 g, 75%), $[\alpha]_D$ −22.7° (*c* 6.3 in $CHCl_3$); $\nu_{max.}$ (film) 3 250 (NH), 1 690 (C=O), and 1 385 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.41 (3 H, s), 1.42 (3 H, s), 1.45 (3 H, s), and 1.57 (3 H, s) (all CMe_2), 3.84—4.16 (2 H, m), 4.24—4.48 (2 H, m), 5.04 (1 H, d, *J* 6 Hz, 2′-H), 7.08 (1 H, d, *J* 2 Hz, 4-H), and 7.66 (1 H, d, *J* 2 Hz, 5-H) (Found: C, 56.65; H, 6.9; N, 9.25. $C_{14}H_{20}N_2O_5$ requires C, 56.74; H, 6.80; N, 9.45%).

3-(2,3:4,5-*Di*-O-*isopropylidene*-D-ido-*pentahydroxypentyl*)*pyrazole* (18).—(a) The ketone (17) (2.56 g) was dissolved in dry THF (67 ml) and to this was added a 0.5M THF solution of 9-BBN (34.29 ml). This solution was left for 4 h, after which methanol (2.95 ml) was added and the solution left for a further 0.5 h. Concentration of the solution under reduced pressure gave a brown oil which was chromatographed on silica gel. Elution with light petroleum–acetone (4 : 1) gave the product (17), impure. Further chromatography on silica gel [light petroleum–acetone (3 : 1) as eluant] gave a white solid, which was recrystallised from dichloromethane; the first crop of crystals (0.37 g, 18%) was found, by ^1H n.m.r., to be a mixture of the D-*ido*-(18) and D-*gulo*-(13) isomers (2 : 1); the second crop, (1.594 g, 58%) was the pure D-ido-*pyrazole* (18), m.p. 136—138 °C, $[\alpha]_D$ −32.8° (*c* 0.61 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 480 (NH), 3 280 (OH), 1 530 (C=N), and 1 385 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.34 (3 H, s), 1.39 (3 H, s), and 1.44 (6 H, s) (all CMe_2), 3.63—4.15 (5 H, m, becomes 4 H, m, on D_2O shake), 4.27—4.43 (1 H, m, 2′-H), 4.85 (1 H, d, *J* 4 Hz, 1′-H), 6.35 (1 H, s, 4-H), and 7.53 s, 5-H); δ_C($CDCl_3$) 25.40, 25.99, 27.12 (×2) (Me), 109.48, and 110.07 (*C*Me_2) (Found: C, 56.2; H, 7.8; N, 9.4. $C_{14}H_{22}N_2O_5$ requires C, 56.36; H, 7.43; N, 9.38%).

(b) An excess of sodium borohydride was added to the ketone (17) (0.09 g) in ethanol (2 ml) and the mixture was stirred for 20 min. Solvent was removed under reduced pressure and water (5 ml) was added to the residue. The product was extracted into chloroform (3 × 10 ml) and the extracts dried ($MgSO_4$). Evaporation gave a colourless solid (0.084 g, 92%) which was shown, by ^1H n.m.r. spectroscopy, to be a mixture of the D-*ido*- and D-*gulo*-isomers [(18) and (13)] in the ratio 3 : 1.

3-(D-gulo-*Pentahydroxypentyl*)*pyrazole* (22).—The pyrazole (13) (1.0 g) was heated under reflux with 0.5M aqueous hydrochloric acid (100 ml) for 0.5 h. The solution was then neutralized with freshly generated Amberlite IR 400 (OH^-) resin. Filtration, evaporation to dryness, and crystallisation from methanol gave the *pentitol* (22) (0.588 g, 80%), m.p. 148—150 °C, $[\alpha]_D$ +22.6° (*c* 0.84 in H_2O); $\nu_{max.}$ (KBr) 3 500, 3 400, 3 340, 3 240, 3 180 (OH, NH), and 1 530 cm^{-1} (C=N); δ (100 MHz, D_2O) 3.56—3.96 (5 H, m), 4.8 (1 H, s, 1′-H), 6.32 (1 H, d, *J* 2 Hz, 4-H), and 7.56 (1 H, d, *J* 2 Hz, 5-H) (Found: C, 44.15; H, 6.45; N, 12.8. $C_8H_{14}N_2O_5$ requires C, 44.03; H, 6.46; N, 12.83%).

3-(D-ido-*Pentahydroxypentyl*)*pyrazole* (23).—The pyrazole (18) (0.4 g) in 0.5M aqueous hydrochloric acid (20 ml) was heated under reflux for 0.5 h. The solution was then neutralized using freshly generated Amberlite IR 400 (OH^-) resin and concentrated under reduced pressure to give an oil. This was chromatographed on regenerated Amberlite IR 400 (OH^-) resin (10 ml) [water–methanol (8 : 1) as eluant], to give the *pentitol* (23) as an oil (0.24 g, 82%), $[\alpha]_D$ −3.02° (*c* 1.32 in H_2O); $\nu_{max.}$ (film) 3 300 (OH,NH) and 1 540 (C=N); δ (100 MHz, D_2O) 3.4—4.08 (6 H, m), 6.54 (1 H, s, 4-H), and 6.87 (1 H, s, 5-H) (Found: C, 44.65; H, 5.95; N, 12.55. $C_8H_{14}N_2O_5$ requires C, 44.03; H, 6.46; N, 12.83%).

1-(2,4-*Dinitrophenyl*)-3-(2,3:4,5-*di*-O-*isopropylidene*-D-ido-*pentahydroxypentyl*)*pyrazole* (19).–A solution of the pyrazole (18) (1.4 g) and 1-fluoro-2,4-dinitrobenzene (0.873 g) in dry benzene (70 ml) containing triethylamine (0.88 ml) was heated under reflux for 2 h. The solution was concentrated under reduced pressure to give a brown oil, which was chromatographed on silica gel using a gravity column. Elution with light petroleum–ether (1 : 1) gave the *DNP-derivative* (19) as a yellow oil (1.6 g, 73%), $[\alpha]_D$ −22.4° (*c* 0.766 in $CHCl_3$); $\nu_{max.}$ (film) 3 440 (OH) 3 120, 3 090, 1 610, 1 505, and 835 (aromatic), 1 550 (NO_2), 1 540 (C=N), and 1 380 and 1 370 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.31 (3 H, s), 1.38 (3 H, s), and 1.43 (6 H, s) (all CMe_2), 3.28—4.00 (5 H, m, becomes 4 H, m, on D_2O shake), 4.42 (1 H, dd, *J* 7 and 4.5 Hz, 2′-H), 4.53 (1 H, d, *J* 4.5 Hz, 1′-H), 6.56 (1 H, d, *J* 2 Hz, 4-H), 7.67 (1 H, d, *J* 9 Hz, 6″-H), 7.68 (1 H, d, *J* 2 Hz, 5-H), 8.36 (1 H, dd, *J* 9 and 2 Hz, 5″-H), and 8.50 (1 H, d, *J* 2 Hz, 3″-H) (Found: C, 51.45; H, 5.35; N, 12.05. $C_{20}H_{24}O_9$ requires C, 51.72; H, 5.2; N, 12.06%).

1-(2,4-*Dinitrophenyl*)-3-(1-O-*methylsulphonyl*-2,3:4,5-*di*-O-*isopropylidene*-D-ido-*pentahydroxypentyl*)*pyrazole* (20).—Methanesulphonyl chloride (0.4 ml) was added in drops to a stirred solution of the pyrazole (19) (0.764 g) in dry pyridine (8.5 ml). The solution was left in the dark for 8 h, when a few drops of water were added to destroy excess of the reagent. After 0.5 h, the mixture was partitioned between water and dichloromethane. The washed and dried organic extracts were evaporated to leave a brown oil. Chromatography on silica [light petroleum–ether (1 : 1) as eluant]

and crystallisation twice from dichloromethane–light petroleum gave the *methanesulphonate* (20) (0.76 g, 85%), m.p. 126 °C, $[\alpha]_D$ −60° (*c* 0.205 in $CHCl_3$); $\nu_{max.}$ (KBr) 3 120, 3 080, 1 610, and 1 500 (aromatic), 1 560 (NO_2), 1 540 (C=N), 1 385 and 1 375 (both CMe_2), and 1 350 cm^{-1} (SO_2); δ (100 MHz, $CDCl_3$) 1.29 (3 H, s), 1:38 (3 H, s), and 1.44 (6 H, s) (all CMe_2), 2.99 (3 H, s, OSO_2Me), 3.52—4.08 (4 H, m), 4.37 (1 H, t, *J* 6 Hz, 2′-H), 5.57 (1 H, d, *J* 6 Hz, 1′-H), 6.68 (1 H, d, *J* 2 Hz, 4-H), 7.84 (1 H, d, *J* 9 Hz, 6″-H), 7.73 (1 H, d, *J* 2 Hz, 5-H), 8.40 (1 H, dd, *J* 9 and 3 Hz, 5″-H), and 8.54 (1 H, d, *J* 3 Hz, 3″-H) (Found: C, 46.05; H, 4.85; N, 10.35; S, 5.45. $C_{21}H_{26}N_4O_{11}S$ requires C, 46.49; H, 4.83; N, 10.32; S, 5.90%).

1-(2,4-*Dinitrophenyl*)-3-(β-D-*xylofuranosyl*)*pyrazole* (8).—To a solution of boron trichloride (6 g) in dry dichloromethane (50 ml) at −78 °C was added the pyrazole (20) (0.6 g) dissolved in the minimum quantity of dry dichloromethane. The mixture was stirred for 2 h and then the solution was allowed to warm to room temperature, whilst dichloromethane–methanol (1 : 1, 28.3 ml) was added in drops. The solution was then evaporated to dryness and the residue co-distilled with methanol (3 × 40 ml) to leave a golden oil. Chromatography on silica gel [ether–ethyl acetate (2 : 1) as eluant] gave a yellow solid, which was crystallised from ethyl acetate–light petroleum to yield the *xylofuranosylpyrazole* (8) (0.244 g, 60%), m.p. 142—143 °C, $[\alpha]_D$ +12.9° (*c* 1.16 in EtOH); $\nu_{max.}$ (KBr) 3 080 and 1 610 (aromatic), 3 340 (OH), 1 545 (NO_2), and 1 530 cm^{-1} (C=N); δ (100 MHz, [$^2H_5$]pyridine) 4.28—4.56 (2 H, m), 4.64—4.88 (2 H, m), 4.92—5.08 (1 H, m), 5.44 (1 H, d, *J* 3.5 Hz, 1′-H), 6.38 (3 H, s, disappears on D_2O, 3 × OH), 7.02 (1 H, d, *J* 2 Hz, 4-H), 7.77 (1 H, d, *J* 9 Hz, 6″-H), 8.15 (1 H, d, *J* 2 Hz, 5-H), 8.34 (1 H, dd, *J* 9 and 2 Hz, 5″-H), and 8.80 (1 H, d, *J* 2 Hz, 3″-H) [Found: $(M - H_2O)^+$ 348.0742. $C_{14}H_{12}N_4O_7$ requires 348.0699].

3-(β-D-*Xylofuranosyl*)*pyrazole* (7).—The protected pyrazole (8) (0.21 g) was added to methanol (15 ml) saturated with ammonia and the solution was left at room temperature for 36 h. Evaporation gave a yellow oil, which was dissolved in water (10 ml); the solution was washed with ethyl acetate (3 × 10 ml) and then concentrated under reduced pressure. Chromatography on freshly generated Amberlite IR 400 (OH^-) resin (10 ml) and elution with water–methanol (8 : 1) gave the β-*xylofuranosylpyrazole* (7) as a clear oil (0.08 g, 70%), $[\alpha]_D$ −33.1° (*c* 0.69 in H_2O); $\nu_{max.}$ (film) 3 260 (OH,NH) and 1 530 cm^{-1} (C=N); δ (100 MHz, D_2O) 3.76—3.92 (2 H, m), 4.12—4.40 (3 H, m), 4.78 (1 H, d, *J* 3.5 Hz, 1′-H), 6.4 (1 H, d, *J* 2 Hz, 4-H), and 7.6 (1 H, d, *J* 2 Hz, H-5) (Found: C, 47.95; H, 6.25; N, 13.7. $C_8H_{12}N_2O_4$ requires C, 48.00; H, 6.02; N, 13.99%).

1-*Methylsulphonyl*-3-(1-O-*methylsulphonyl*-2,3:4,5-*di*-O-*isopropylidene*-D-gulo-*pentahydroxypentyl*)*pyrazole* (24).—To a solution of the pyrazole (13) (1 g) in dry pyridine (10.25 ml) was added methanesulphonyl chloride (1.08 ml), in drops, and the solution was left overnight. The reaction was worked up in the normal way and, after evaporation to dryness, a yellow solid was obtained. This, upon crystallisation from ether–light petroleum gave the *dimesylate* (24) (1.11 g, 73%), m.p. 132 °C, $[\alpha]_D$ −121.1° (*c* 0.19 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 530 (C=N), 1 385 (CMe_2), and 1 175 cm^{-1} (SO_2); δ (100 MHz, $CDCl_3$) 1.36 (6 H, s) and 1.44 (6 H, s) (both CMe_2), 3.02 (3 H, s, OSO_2Me), 3.36 (3 H, s, NSO_2Me), 3.8—4.2 (4 H, m), 4.48—4.72 (1 H, m, 2′-H), 5.82 (1 H, d, *J* 5 Hz, 1′-H), 6.68 (1 H, d, *J* 3 Hz, 4-H), and 8.08 (1 H, d, *J* 3 Hz, 5-H) (Found: C, 42.0; H, 5.5; N, 6.2; S, 13.85. $C_{16}H_{26}N_2O_9S_2$ requires C, 42.28; H, 5.76; N, 6.16; S, 14.10%).

1-*Benzoyl*-3-(1-O-*benzoyl*-2,3:4,5-*di*-O-*isopropylidene*-D-gulo-*pentahydroxypentyl*)*pyrazole* (26).—A solution of the pyrazole (13) (0.2 g) in dry pyridine (6 ml) and benzoyl chloride (0.16 ml) was stirred overnight and then worked-up using standard procedures. Chromatography of the product, obtained after work-up, on silica gel and elution with light petroleum–ether (1 : 1) gave a white solid, which upon crystallisation from ether–light petroleum gave the *dibenzoate* (26) (0.192 g, 56%), m.p. 122 °C, $[\alpha]_D$ −41.4° (*c* 1.16 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 540 (C=N), 1 740 and 1 715 (C=O), 3 060 and 1 600 (aromatic), and 1 385 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.28 (3 H, s), 1.32 (3 H, s), 1.40 (3 H, s), and 1.44 (3 H, s) (all CMe_2), 3.84—4.28 (4 H, m), 4.64 (1 H, dd, *J* 7 and 5 Hz, 2′-H), 6.30 (1 H, d, *J* 5 Hz, 1′-H), 6.66 (1 H, d, *J* 3 Hz, 4-H), 7.32—7.72 (6 H, m, Ph), 8.0—8.2 (4 H, m, Ph), and 8.39 (1 H, d, *J* 3 Hz, 5-H) (Found: C, 66.5; H, 6.1; N, 5.6. $C_{28}H_{30}N_2O_7$ requires C, 66.39; H, 5.96; N, 5.53%).

3-(1-O-*Benzoyl*-2,3:4,5-*di*-O-*isopropylidene*-D-gulo-*pentahydroxypentyl*)*pyrazole* (25).—The dibenzoate (26) (0.1 g) was suspended in dry methanol (5 ml) and piperidine (0.035 ml) was added, with stirring. The suspended solid dissolved immediately upon addition of piperidine and after 5 min, t.l.c. [light petroleum–ether (1 : 1)] showed only one product. Concentration of the solution under reduced pressure and chromatography of the resultant clear oil [light petroleum–ether (1 : 1) as eluant] gave the *monobenzoate* (25) as a clear oil (0.06 g, 76%), $[\alpha]_D$ −27.0° (*c*. 1.59 in $CHCl_3$); $\nu_{max.}$ (film 3 300 (NH), 3 060, 1 600, 1 580, and 1 500 (aromatic), 1 540 (C=N), 1 720 (C=O), and 1 380 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.29 (3 H, s), 1.35 (3 H, s), and 1.42 (6 H, s) (all CMe_2), 3.76—4.20 (4 H, m), 4.56—4.76 (1 H, m, 2′-H), 6.37 (1 H, d, *J* 6 Hz, 1′-H), 6.45 (1 H, d, *J* 2 Hz, 4-H), 7.32—7.68 (4 H, m), and 8.0—8.18 (2 H, m, *o*-H of Ph) (Found: C, 63.05; H, 6.8; N, 6.9. $C_{21}H_{26}N_2O_6$ requires C, 62.67; H, 6.51; N, 6.96%).

Reaction of the Dimesylate (24) *with Sodium Benzoate and Identification of the Product*.—The dimesylate (24) (0.2 g) was heated in dry DMF (20 ml) with sodium benzoate (0.182 g), for 5.5 h at 100 °C, after which t.l.c. showed the presence of a single spot that was not the starting material. The solvent was then removed under reduced pressure using *p*-xylene. Chromatography of the resultant solid on silica gel [light petroleum–ether (1 : 1) as eluant] gave the monobenzoate (25) as a clear oil (0.132 g, 82%). This was identical by optical rotation {$[\alpha]_D$ −26.8° (*c* 1.045 in $CHCl_3$)} and ^1H n.m.r. and i.r. spectroscopy with the monobenzoate (25) that had been prepared by the unambiguous route described above.

The mono-*O*-benzoyl compound (0.071 g) was dissolved in dry dichloromethane and to this was added benzoyl chloride (0.021 ml) and dry pyridine (0.015 ml). The mixture was left overnight, washed with water (2 ml), dried ($MgSO_4$), filtered, and the filtrate was concentrated under reduced pressure to give a brown oil. This was chromatographed on silica gel [light petroleum–ether (1 : 1) as eluant] to give a white solid which was recrystallised from ether–light petroleum to afford a dibenzoate (0.064 g, 73%), which was identical {m.p. 122 °C, $[\alpha]_D$ −46.2° (*c* 0.585 in $CHCl_3$), ^1H n.m.r. and i.r. spectroscopy, and t.l.c.} with the D-*gulo*-dibenzoate (26) prepared unambiguously from the pyrazole (13), as described above.

To the monobenzoate (0.1 g) in methanol (5 ml) was

added potassium hydroxide (0.1 g) and the mixture was stirred overnight. After evaporation and partition between water and dichloromethane, the organic layer was dried, filtered, and concentrated under reduced pressure to give a brown oil. This was chromatographed on silica gel [light petroleum–acetone (6 : 1) as eluant] to give a clear oil. This crystallised from ether and was recrystallised from ether–light petroleum to give a white solid (0.063 g, 65%), which was identical {m.p. 115—116 °C, $[\alpha]_D$ −12.5° (*c* 2.095 in $CHCl_3$), ^1H n.m.r. and i.r. spectroscopy, and t.l.c.} with the D-*gulo*-alcohol (13).

1-*Methylsulphonyl*-3-(1-O-*methylsulphonyl*-2,3:4,5-*di*-O-*isopropylidene*-D-ido-*pentahydroxypentyl*)*pyrazole* (27).—To a solution of the pyrazole (18) (0.2 g) in dry pyridine (2.04 ml) was added in drops methanesulphonyl chloride (0.17 ml) and the solution was left for 8.5 h. The reaction was worked up in the usual way and, after concentration under reduced pressure, a brown oil was obtained. Chromatography on silica gel [light petroleum–ether (1 : 2) as eluant] gave a white crystalline solid, which was recrystallised from dichloromethane–light petroleum to give the *dimethanesulphonate* (27) (0.232 g, 76%), m.p. 137—139 °C, $[\alpha]_D$ −46.2° (*c* 0.52 in $CHCl_3$); $\nu_{max.}$ (KBr) 1 530 (C=N), 1 385 and 1 375 (both CMe_2), and 1 350 cm^{-1} (SO_2); δ (100 MHz, $CDCl_3$) 1.13 (3 H, s), 1.20 (3 H, s), and 1.27 (6 H, s) (all CMe_2), 3.05 (3 H, s, OSO_2Me), 3.26 (3 H, s, NSO_2Me), 3.77—4.25 (4 H, m), 4.43 (1 H, dd, *J* 8.5 and 5.5 Hz, 2′-H), 5.73 (1 H, d, *J* 5.5 Hz, 1′-H), 6.73 (1 H, d, *J* 2 Hz, 4-H), and 8.09 (1 H, d, *J* 2 Hz, 5-H) [Found: $(M - Me)^+$ 439.0818. $C_{15}H_{23}N_2O_9S_2$ requires 439.0835].

Reaction of the Dimethylsulphonate (27) *with Sodium Benzoate*.—To a solution of the dimesylate (27) (0.3 g) in dry DMF (4 ml) was added sodium benzoate (0.274 g). The mixture was heated, with stirring, at 100 °C for 1.5 h, when t.l.c. showed the presence of two products and no starting material. The solution was then evaporated to dryness using *p*-xylene to form an azeotrope. The white resi*due* was partitioned between water and dichloromethane. The dichloromethane solution was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give a clear oil. This was chromatographed on silica gel [light petroleum–ether (5 : 1) as eluant] and crystallised from ether–light petroleum to give a white solid (0.09 g, 27%) which was found to be identical {m.p. 122 °C, $[\alpha]_D$ −52.6° (*c* 2.05 in $CHCl_3$), and ^1H n.m.r. and i.r. spectroscopy} with the D-*gulo*-dibenzoate (26).

Further elution with ether gave a clear oil (0.15 g, 56%) as the second product. This was found to be identical {$[\alpha]_D$ −26.4° (*c* 1.07 in $CHCl_3$) and ^1H n.m.r. and i.r. spectroscopy} with the D-*gulo*-monobenzoate (25). This monobenzoate (0.137 g) was dissolved in methanol (2 ml); to this solution was added sodium hydroxide (0.02 g) and the mixture was stirred overnight. The solution was evaporated to dryness; the residue was dissolved in water (3 ml) and the solution was extracted with dichloromethane (3 × 15 ml). The dichloromethane solution was dried ($MgSO_4$), filtered, and the filtrate concentrated under reduced pressure to give an oil. Chromatography on silica gel [light petroleum–acetone (2 : 1) as eluant] and crystallisation from ether–light petroleum gave a white solid (0.06 g, 59%), identical {m.p. 114—115 °C, $[\alpha]_D$ −18.4° (*c* 2.23 in chloroform), ^1H n.m.r. spectroscopy, and t.l.c.} with the D-*gulo*-pyrazole (13).

1-*Benzoyl*-3-(1-O-*benzoyl*-2,3:4,5-*di*-O-*isopropylidene*-D-ido-*pentahydroxypentyl*)*pyrazole* (28).—To a solution of the alcohol (18) (0.258 g) in dry pyridine (6 ml) was added benzoyl chloride (0.2 ml). The solution was left overnight and was then worked-up in the usual way to give a brown oil, chromatography of which on silica gel [light petroleum–ether (6 : 1) as eluant] gave the *dibenzoate* (28) as a clear oil (0.244 g, 56%), $[\alpha]_D$ −2.0° (*c* 1.00 in $CHCl_3$); $\nu_{max.}$ (film) 3 060, 1 600, 1 580, 1 490, and 710 (aromatic), 1 730 and 1 720 (C=O), 1 540 (C=N), and 1 380 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.34 (3 H, s), 1.40 (3 H, s), and 1.48 (6 H, s) (all CMe_2), 3.84—4.20 (4 H, m), 4.48—4.72 (1 H, m, 2′-H), 6.32 (1 H, d, *J* 4.5 Hz, 1′-H), 6.65 (1 H, d, *J* 2 Hz, 4-H), 7.32—7.68 (6 H, m, *m*- and *p*-H of Ph), 8.00—8.20 (4 H, m, *o*-H of Ph), and 8.29 (1 H, d, *J* 2 Hz, 5-H) (Found: C, 66.25; H, 5.85; N, 5.55. $C_{28}H_{30}N_2O_7$ requires C, 66.39; H, 5.96; N, 5.53%).

3-(1-O-*Benzoyl*-2,3:4,5-*di*-O-*isopropylidene*-D-ido-*pentahydroxypentyl*)*pyrazole* (29).—To the pyrazole (18) (0.22 g) dissolved in dry pyridine (2.0 ml) was added benzoyl chloride (0.176 ml), and this solution was left at room temperature for 6 h. The solution was then worked-up in the usual way and, after concentration under reduced pressure a brown oil was obtained. This was dissolved in methanol (10 ml), piperidine (0.1 ml) was added, and the solution was stirred for 5 min. It was then concentrated under reduced pressure to give an oil, which was chromatographed on silica gel [ether as eluant]. The *monobenzoate* (29) was obtained as a clear oil (0.29 g, 97%), $[\alpha]_D$ −27.2° (*c* 1.77 in $CHCl_3$); $\nu_{max.}$ (film) 3 300 (NH), 3 060, 1 600, 1 580, and 710 (aromatic), 1 720 (C=O), 1 530 (C=N), and 1 380 and 1 375 cm^{-1} (both CMe_2); δ (100 MHz, $CDCl_3$) 1.29 (3 H, s), 1.40 (3 H, s), and 1.48 (6 H, s) (all CMe_2), 3.66—4.16 (4 H, m), 4.68 (1 H, t, *J* 6 Hz, 2′-H), 6.41 (1 H, d, *J* 6 Hz, 1′-H), 6.51 (1 H, s, 4-H), 7.28—7.56 (3 H, m, *m*- and *p*-H of Ph), 7.72 (1 H, s, 5-H), 8.04—8.20 (2 H, m, *o*-H of Ph), and 10.58 (1 H, s, disappears on D_2O shake, NH) (Found: C, 62.35; H, 6.1; N, 7.1. $C_{21}H_{26}N_2O_6$ requires C, 62.67; H, 6.51; N, 6.96%).

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REFERENCES

[1] Part 11, J. G. Buchanan, A. Stobie, and R. H. Wightman, *Can. J. Chem.*, 1980, **58**, 2624.
[2] J. G. Buchanan, A. R. Edgar, R. J. Hutchison, A. Stobie, and R. H. Wightman, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2567.
[3] G. D. Daves, jun., and C. C. Cheng, *Prog. Med. Chem.*, 1976, **13**, 303, and references therein; R. J. Suhadolnik, *Prog. Nucleic Acid Res. Mol. Biol.*, 1979, **22**, 193, and references therein.
[4] J. G. Buchanan, A. R. Edgar, R. J. Hutchison, A. Stobie, and R. H. Wightman, *J. Chem. Soc., Chem. Commun.*, 1980, 237.
[5] J. G. Buchanan, A. Stobie, and R. H. Wightman, *J. Chem. Soc., Chem. Commun.*, 1980, 916.
[6] E. de Clercq and P. F. Torrence, *J. Carbohydr. Nucleosides, Nucleotides*, 1978, **5**, 187, and references therein.
[7] J. G. Buchanan, M. E. Chacón-Fuertes, and R. H. Wightman, *J. Chem. Soc., Perkin Trans. 1*, 1979, 244.
[8] L. M. Lerner, B. D. Kohn, and P. Kohn, *J. Org. Chem.*, 1968, **33**, 1780.
[9] *E.g.* E. W. Colvin, S. Malchenko, R. A. Raphael, and J. S. Roberts, *J. Chem. Soc., Perkin Trans. 1*, 1978, 658; A. J. Duggan, M. A. Adams, P. J. Brynes, and J. Meinwald, *Tetrahedron Lett.*, 1978, 4323, and references therein.
[10] M. M. Midland, *J. Org. Chem.*, 1975, **40**, 2250.
[11] J. G. Buchanan, M. E. Chacón-Fuertes, A. R. Edgar, S. J. Moorhouse, D. I. Rawson, and R. H. Wightman, *Tetrahedron Lett.*, 1980, **21**, 1793.
[12] P. A. Levene and A. L. Raymond, *J. Biol. Chem.*, 1933, **102**, 317; M. Kiso and A. Hasegawa, *Carbohydr. Res.*, 1976, **52**, 95.

[13] N. K. Richtmyer and C. S. Hudson, *J. Am. Chem. Soc.*, 1942, **64**, 1793.
[14] H. El Khadem and Z. M. El-Shafei, *Tetrahedron Lett.*, 1963, 1887; H. S. El Khadem in ' Synthetic Methods for Carbohydrates,' ed. H. S. El Khadem, American Chemical Society 1977, p. 77.
[15] *E.g.* G. Kotowycz and R. U. Lemieux, *Chem. Rev.*, 1973, **73**, 669.
[16] L. B. Townsend in ' Synthetic Procedures in Nucleic Acid Chemistry,' ed. W. W. Zorbach and R. S. Tipson, Wiley–Interscience, New York, Vol. 2, 1973, p. 330.
[17] H. Ohrui, G. H. Jones, J. G. Moffatt, M. L. Maddox, A. T. Christensen, and S. K. Byram, *J. Am. Chem. Soc.*, 1975, **97**, 4602; G. Trummlitz, D. B. Repke, and J. G. Moffatt, *J. Org. Chem.*, 1975, **40**, 3352.
[18] *E.g.* C. L. Stevens, D. Chitharanjan, K. G. Taylor, and P. M. Pillai, *J. Org. Chem.*, 1975, **40**, 2471.
[19] J. G. Buchanan, A. D. Dunn, and A. R. Edgar, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1191.