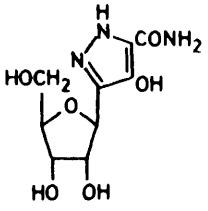
C-Nucleoside Studies. Part 14.[1] A New Synthesis of Pyrazofurin

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

Treatment of 3-cyano-4-nitro-5-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)pyrazole (4) with benzyl bromide and triethylamine gave as major product the 1-benzyl-5-cyano-isomer (5), whilst similar treatment of 5-cyano-3-methyl-4-nitropyrazole (7) gave exclusively 1-benzyl-3-cyano-5-methyl-4-nitropyrazole (8). This was converted into 4-amino-1-benzyl-3-carboxamido-5-methylpyrazole (10); attempts to convert (10) into a 4-hydroxypyrazole *via* the diazonium salt were unsuccessful, but photolysis of the diazonium salt (11) in aqueous trifluoroacetic acid–dioxan gave 1-benzyl-3-carboxamido-5-methylpyrazole (13) in 67% yield.

Treatment of 4-amino-3-cyano-5-methylpyrazole (14) with nitrous acid and subsequent neutralisation gave a diazopyrazole which on photolysis in aqueous acetone yielded 3-cyano-4-hydroxy-5-methylpyrazole (16) in 79% overall yield. Application of the same sequence to 4-amino-3-cyano-5-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-pyrazole (2) gave the 4-hydroxy-compound (17) (87% overall), which was converted in two steps into pyrazofurin (1).

PYRAZOFURIN (pyrazomycin) (1), one of the *C*-nucleoside antibiotics,[2] was isolated in 1969 from the culture filtrate of a strain of *Streptomyces candidus* (NRRL 3601).[3] It shows considerable activity against a number of viruses [4] and tumours,[5] and is currently undergoing clinical evaluation as an antitumour agent.[6] Two previous chemical syntheses have been reported, by widely different routes,[7,8] and here we report a further novel synthesis of pyrazofurin, as part of our programme of synthesis of *C*-nucleoside antibiotics and their analogues *via* acetylenic intermediates.[9,10]



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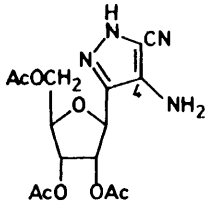

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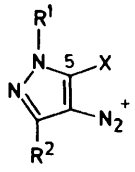
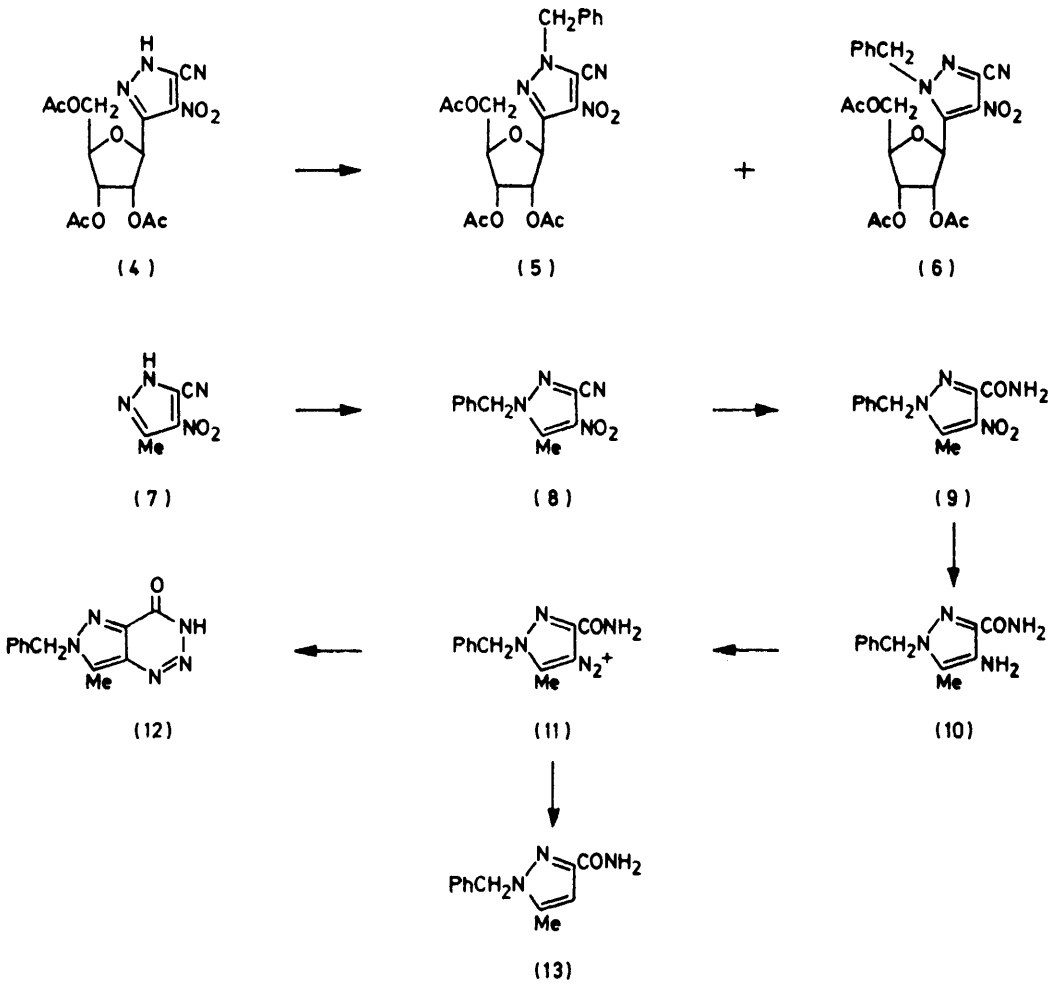


(3) X = CN or $CONH_2$

During our synthesis of the *C*-nucleoside antibiotic formycin [11] we had prepared the 4-aminopyrazole (2), and it appeared that replacement of nitrogen with oxygen at C-4 in this compound should lead to the synthesis of pyrazofurin. A classical method of carrying out such a conversion in aromatic systems involves nucleophilic substitution of a diazonium salt, but the use of this procedure for the synthesis of 4-hydroxypyrazoles is not well documented, owing presumably to the unusual stability of pyrazole diazonium salts.[12] We felt, however, that an electron-withdrawing group at C-5 in a 1-alkylpyrazole-4-diazonium salt of type (3) might facilitate nucleophilic displacement of nitrogen, and that the benzyl group might be suitable as an *N*-alkyl group which could be easily introduced and subsequently removed. We thus investigated the behaviour of 4-nitropyrazole (4), the precursor of (2), on benzylation.

Treatment of (4) with benzyl bromide and triethylamine in refluxing benzene produced a mixture of two products, which could be separated by chromatography. Spectroscopy and analysis indicated that the two products were isomeric *N*-benzyl derivatives; the major product (73%) showed a singlet in the aromatic region of its ^1H n.m.r. spectrum, whilst the minor product (15%) showed a complex multiplet; the spectra of the two products were otherwise very similar. In order to assign structures to these two products, 5-cyano-3-methyl-4-nitropyrazole (7) was treated with benzyl bromide under similar conditions. In this case a single crystalline product was isolated (75% yield), the ^1H n.m.r. spectrum of which showed a complex multiplet in the aromatic region. It seems reasonable to assume that the two products with complex aromatic signals have similar substitution patterns; furthermore, the triacetylribofuranosyl and methyl groups are similar in their electronic effects, but considerably different in their steric bulk. It thus follows that the exclusive product of benzylation of (7) must be the 1-benzyl-3-cyano-isomer (8), corresponding to the minor product (6) obtained from (4), whilst the major product from benzylation of (4) is the 1-benzyl-5-cyano-isomer (5), in which the bulky triacetylribofuranosyl group has directed substitution towards the cyano-group. We note that the methylation of (7) with dimethyl sulphate gives the 1,5-dimethyl isomer,[13] a result analogous to our findings on its benzylation.

In order to conserve the valuable compound (4), we investigated further reactions using (8) as a model compound; it was recognised that the difference in substitution pattern between (8) and (5) made it an imperfect model, but we felt that nucleophilic displacements in diazonium salts derived from (5) should be easier than such substitutions in salts derived from (8). The nitrile



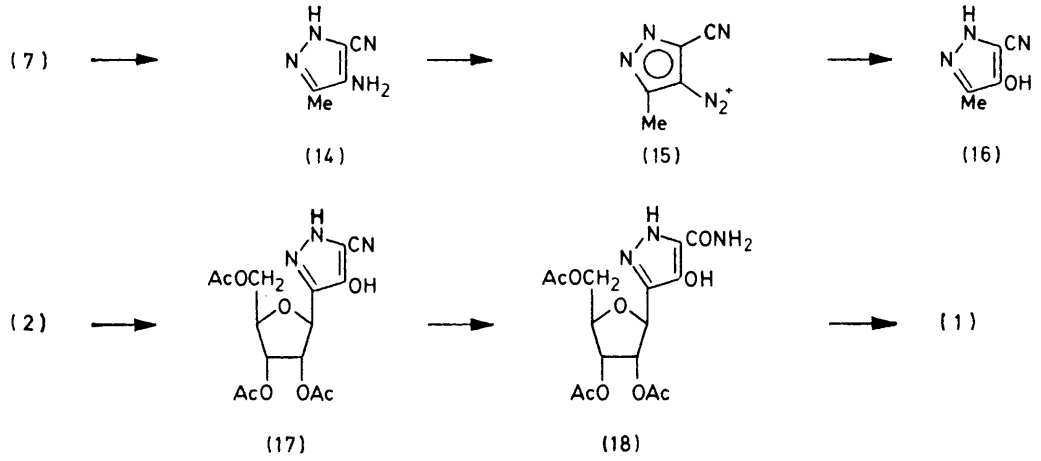
(8) was initially converted into the amide (9) by treatment with alkaline hydrogen peroxide; the electron-withdrawing effect of the nitro-group made this a rapid reaction under mild conditions. Reduction with zinc and acetic acid then gave the aminopyrazole (10) in 80% yield.

It was envisaged that cyclisation of the diazonium cation (11) to the triazinone (12) might prove a complication to the desired displacement.[14,*] The triazinone (12) was therefore synthesised intentionally by treatment of the amine (10) with sodium nitrite in a mixture of water, dioxan, and trifluoroacetic acid (TFA) followed by addition of potassium hydrogen carbonate. Diazotisation of (10) was then carried out by treatment with sodium nitrite under a variety of conditions, using TFA,[15] or mixtures of TFA and aqueous dioxan. In each case a persistent ultraviolet absorption maximum at 261 nm was observed; the triazinone (12) had an absorption maximum at 290 nm under these conditions, and thus was not being formed in the acidic solutions; it could be isolated readily in each case after addition of an excess of hydrogencarbonate. The absorption maximum at 261 nm is thus assumed to be due to the stable diazonium cation (11); this maximum persisted even at reflux in aqueous TFA, with no conversion either into hydroxypyrazole, or to triazinone without prior neutralisation.

Photolytic decomposition of the diazonium salt (11) also did not give a 4-hydroxypyrazole. Irradiation of (11) in aqueous TFA at wavelengths >260 nm gave no reaction, and at wavelengths <260 nm, a complex product resulted. However, on irradiation in TFA–aqueous dioxan with visible light the diazo-group was replaced with hydrogen to yield 1-benzyl-3-carboxamido-5-methylpyrazole (13) in 67% yield. The n.m.r. spectrum of this material contained a 1-proton singlet at δ 6.52, characteristic of the H-4 in a pyrazole ring. Faced with these failures to prepare a hydroxypyrazole *via* a diazonium salt, this approach was abandoned in favour of the successful route described below, involving diazopyrazoles.

When a 4-aminopyrazole with no substituent on nitrogen is diazotised and then the diazonium salt solution rendered alkaline, a neutral zwitterionic diazopyrazole is

* Very recent results with the related system 5-diazoimidazole-4-carboxamide (J. K. Horton and M. F. G. Stevens, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1433; M. F. G. Stevens, personal communication) indicate that photolysis at controlled pH might avoid cyclisation.



produced.[16] Although 4-diazopyrazoles seem to be thermally stable, there was precedent for photochemical replacement of the diazo-group with the hydroxy- or acetoxy-group.[17] Application of such a sequence to the aminopyrazole (2) should preferentially involve replacement of the diazo-group prior to hydrolysis of the nitrile. If a diazoamide were formed it would be liable to undergo cyclisation to a triazinone.[14] As a model compound, 4-amino-5-cyano-3-methylpyrazole (14) [14] was prepared by catalytic hydrogenation of (7). When (14) was treated with sodium nitrite in aqueous acetic acid, subsequent basification and extraction with ethyl acetate gave a crystalline diazopyrazole (15) which on photolysis in aqueous acetone with a medium-pressure mercury lamp and Pyrex filter evolved nitrogen to yield the 4-hydroxypyrazole (16) in 79% yield from (14).

This sequence was now applied to the ribofuranosylpyrazole (2); this was prepared from (4) by dithionite reduction, which proved more reliable than the catalytic hydrogenation previously used. Diazotisation of (2) and subsequent neutralisation gave a diazopyrazole which was not purified but photolysed directly to give hydroxypyrazole (17) in 87% overall yield.

It was now necessary to convert the nitrile group of (17) into an amide. Since pyrazofurin and derivatives are known to anomerise under acidic and basic conditions,[8] a mild method was desirable. Various transition metals are known to catalyse nitrile hydrolysis,[18,19] and we felt that the adjacent hydroxy-group would particularly favour this method of hydrolysis through formation of a cyclic chelate. In the event, hydrolysis was completed within 1 h at reflux in glacial acetic acid in the presence of nickel acetate tetrahydrate,[19] tri-*O*-acetyl pyrazofurin (18) being isolated in 65% yield after chromatography. Deacetylation with ammonia in methanol gave the pyrazofurin (1) in 75% yield; after crystallisation from water the synthetic material was identical (m.p., mixed m.p., i.r. and u.v. spectra, t.l.c., and optical rotation) with natural material.

EXPERIMENTAL

General methods were as stated in Part 2.[20] 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 precoated aluminium-backed plates [Kieselgel HF_{254} type 60 (Merck)].

Reaction of Compound (4) *with Benzyl Bromide.*—A solution of the nitro-compound (4) [11] (0.55 g, as the benzene solvate), triethylamine (0.58 ml), and benzyl bromide (0.34 ml) in benzene was heated under reflux for 0.75 h, cooled, and added to water (100 ml). The organic layer was washed with dilute sulphuric acid (20 ml) and water (20 ml), dried, and evaporated. The residue was chromatographed on silica gel, eluting with benzene–acetone (100 : 1 v/v) to give first 1-*benzyl*-5-*cyano*-4-*nitro*-3-(2,3,5-*tri*-O-*acetyl*-β-D-*ribofuranosyl*)*pyrazole* (5) (0.445 g, 73%) as a clear syrup; $\nu_{max.}$ (film) 2 240 (C≡N), 1 750 (ester), and 1 510 and 1 360 cm^{-1} (NO_2); δ (100 MHz, $CDCl_3$) 1.96, 2.02, and 2.06 (9 H, 3 s, Me), 3.96—4.4 (3 H, m, H-4′ and -5′), 5.24—5.68 (5 H, m, H-1′—3′, CH_2), and 7.28 (5 H, s, Ph) (Found: C, 54.6; H, 4.6; N, 11.6. $C_{22}H_{22}N_4O_9$ requires C, 54.3; H, 4.5; N, 11.5%).

Further elution with benzene–acetone (100 : 1 v/v) gave a mixture of (5) and its isomer (6) (0.025 g, 4%), followed by the pure 1-*benzyl*-3-*cyano-isomer* (6) (0.09 g, 15%) as a clear syrup; $\nu_{max.}$ (film) 2 250 (C≡N), 1 750 (ester), and 1 510 and 1 360 cm^{-1} (NO_2); δ (100 MHz, $CDCl_3$) 1.92 (6 H, s, Me), 2.09 (3 H, s, Me), 4.2—4.36 (3 H, m, H-5′ and -4′) 5.00—5.36 (2 H, m, H-2′ and -3′), 5.40—5.68 (3 H, m, H-1′ and CH_2), and 7.0—7.4 (5 H, m, Ph) (Found: C, 54.5; H, 4.6; N, 11.5. $C_{22}H_{22}N_4O_9$ requires C, 54.3; H, 4.5; N, 11.5%).

1-*Benzyl*-3-*cyano*-5-*methyl*-4-*nitropyrazole* (8).—To the pyrazole (7) (1 g) in benzene (50 ml) was added triethylamine (2.8 ml) and benzyl bromide (1.68 ml). The mixture was heated under reflux for 0.5 h, added to water (50 ml) and the organic layer was washed with dilute sulphuric acid and then water. The dried organic layer was evaporated and the residue chromatographed on silica gel, eluting with ether; the crude product, contaminated with benzyl bromide, was crystallised from ether–light petroleum to give the N-*benzyl compound* (8) (1.2 g, 75%), m.p. 94—96 °C; $\nu_{max.}$ (KBr) 2 240 (C≡N), and 1 500 and 1 360 cm^{-1} (NO_2); δ (100 MHz, $CDCl_3$) 2.6 (3 H, s, Me), 5.31 (2 H, s, CH_2), and 7.0—7.36 (5 H, m, Ph) (Found: C, 59.2; H, 4.1; N, 23.1. $C_{12}H_{10}N_4O_2$ requires C, 59.5; H, 4.1; N, 23.1%).

1-*Benzyl*-3-*carboxamido*-5-*methyl*-4-*nitropyrazole* (9).—To the nitrile (8) (0.2 g) in water (5 ml) and dioxan (6 ml) containing potassium carbonate (0.5 g) was added hydrogen peroxide (1.14 ml, 30%), at 0 °C. The reaction was allowed to reach room temperature and stirred for 1.25 h. Water

(20 ml) and ethyl acetate (20 ml) were added and the dried organic layer was evaporated to leave a solid, which was crystallised from ethyl acetate–light petroleum to give the *amide* (9) (0.19 g, 89%) as white crystals, m.p. 161—163 °C; $\nu_{max.}$ (KBr) 3 500—3 400 (NH), 3400—3 000 (NH), and 1 660 and 1 650 cm^{-1} (amide); δ [100 MHz, $(CD_3)_2CO$] 2.48 (3 H, s, Me), 5.33 (2 H, s, CH_2), 6.1—7.08br (2 H, s, NH_2), and 7.17 (5 H, s, Ph) (Found: C, 55.5; H, 4.7; N, 21.6. $C_{12}H_{12}N_4O_3$ requires C, 55.4; H, 4.6; N, 21.5%).

4-*Amino*-1-*benzyl*-3-*carboxamido*-5-*methylpyrazole* (10).—To a stirred suspension of zinc (1 g) in acetic acid (15 ml) was added the nitro-compound (9) (0.5 g) in acetic acid (5 ml). The reaction was stirred at room temperature for 1.75 h, a further portion of zinc (0.5 g) being added after 1.25 h. The acetic acid was evaporated off and water (20 ml) and ethyl acetate (50 ml) were added to the residue. This mixture was filtered and the filtrate was washed with ethyl acetate. The combined ethyl acetate fractions were washed with saturated sodium hydrogencarbonate, dried, and evaporated to leave a solid residue which was crystallised from ethyl acetate–light petroleum to yield the *amino-compound* (10) (0.354 g, 80%), m.p. 160—162 °C; $\nu_{max.}$ (KBr) 3 500—3 000 (NH), and 1 670 and 1 650 cm^{-1} (amide); δ [100 MHz, $(CD_3)_2SO$] 2.00 (3 H, s, Me), 4.12—4.68br (2 H, s, NH_2), 5.14 (2 H, s, CH_2), and 6.60—7.36 (7 H, m, Ph and NH_2) (Found: C, 62.4; H, 6.0; N, 24.4. $C_{12}H_{14}N_4O$ requires C, 62.6; H, 6.1; N, 22.4%).

6-*Benzyl*-7-*methylpyrazolo*[4,3-*d*]-1,2,3-*triazin*-4-*one* (12).—The amino-compound (10) (0.20 g) was dissolved in a mixture of water (5 ml), dioxan (5 ml), and trifluoroacetic acid (1 ml) at 0 °C. Sodium nitrite (0.061 g) in water (3 ml) was added slowly to this cooled solution; stirring was continued at 0 °C for 0.25 h and then at room temperature for 0.5 h. The reaction mixture was added to water (20 ml) and neutralised ($KHCO_3$). Extraction of the aqueous medium with ethyl acetate followed by drying and evaporation of the organic layer gave a solid which was crystallised from dichloromethane to give the *triazinone* (12) (0.19 g, (91%), m.p. 204—206 °C; $\nu_{max.}$ (KBr) 3 300—3 020 (NH), and 1 750—1 600 cm^{-1} (C=O); $\lambda_{max.}$ (H_2O containing 10% TFA) 241 and 290 nm; δ [100 MHz, $(CD_3)_2SO$] 2.67 (3 H, s, Me), 5.61 (2 H, s, CH_2), 7.24 (5 H, s, Ph), and 13.96br (1 H, s, NH) (Found: C, 59.5; H, 4.4; N, 29.2. $C_{12}H_{11}N_5O$ requires C, 59.7; H, 4.6; N, 29.1%).

1-*Benzyl*-3-*carboxamido*-5-*methylpyrazole* (13).—To a solution of the amino-compound (10) (0.1 g) in an ice-cold mixture of water (2 ml), dioxan (2 ml), and TFA (0.4 ml) was slowly added sodium nitrite (0.0304 g) in water (1 ml). Stirring was continued at 0 °C for 0.25 h then at room temperature for 0.5 h after which the solution of diazonium salt (11) was exposed to a strong visible light source for 2 days. Addition of water (20 ml), neutralisation ($KHCO_3$), isolation with ethyl acetate, and crystallisation from toluene gave the *pyrazole* (13) (0.06 g, 67%), m.p. 136—139 °C; $\nu_{max.}$ (KBr) 3 500—3 300 and 3 220—3 020 (NH), and 1 665 cm^{-1} (amide); δ (100 MHz, $CDCl_3$) 2.17 (3 H, s, Me), 5.10 (2 H, s, CH_2), 5.72—6.16br (1 H, s, NH), 6.52 (1 H, s, H-4), 6.6—6.84br (1 H, s, NH), and 6.85—7.37 (5 H, m, Ph) (Found: C, 67.1; H, 6.2; N, 19.8. $C_{12}H_{13}N_3O$ requires C, 67.0; H, 6.1; N, 19.5%).

5-*Cyano*-4-*hydroxy*-3-*methylpyrazole* (16).—The aminopyrazole (14) [14] (0.462 g) was dissolved in acetic acid (10 ml); to this solution just above its freezing point was added sodium nitrite (0.296 g) in water (1.5 ml). The solution was stirred at 0 °C for 0.25 h and at room temperature for 0.25 h. The solvents were evaporated below 30 °C, water (50 ml) was added, and the solution was made basic ($KHCO_3$). The solution was exhaustively extracted with ethyl acetate, the dried organic extracts being evaporated to give a solid residue which was crystallised from dichloromethane–light petroleum to give the crude diazopyrazole (15) (0.393 g), m.p. 109—111 °C, $\nu_{max.}$ (KBr) 2 240 (C≡N) and 2 170 cm^{-1} (N_2^+); $\lambda_{max.}$ (H_2O) 217, 242, and 283 nm. A portion of the crude diazopyrazole (0.1 g) was dissolved in acetone–water (3 : 1 v/v) (20 ml). The solution was deoxygenated by passing nitrogen through it for 0.25 h, and then irradiated using a medium-pressure mercury lamp and Pyrex filters. Gas evolution commenced after 1.5 h and was complete after 24 h. The volatile solvents were evaporated off and water (20 ml) and ethyl acetate (20 ml) were added to the aqueous residue. The aqueous layer was extracted further with ethyl acetate (2 × 10 ml); the combined ethyl acetate fractions were dried and evaporated to leave a yellow solid residue which was crystallised from toluene to give the *hydroxy-compound* (16) (0.093 g, 79%), an analytical sample of which was prepared by vacuum sublimation, m.p. 210 °C (with decomposition); $\nu_{max.}$ (KBr) 3 700—2 300 (OH and NH) and 2 250 cm^{-1} (C≡N); δ [100 MHz, $(CD_3)_2CO$] 2.16 (3 H, s, Me) and 7.0—12.0vbr (2 H, s, OH and NH) (Found: C, 48.6; H, 4.2; N, 34.0. $C_5H_5N_3O$ requires C, 48.8; H, 4.1; N, 34.1%).

4-*Amino*-3-*cyano*-5-(2,3,5-*tri*-O-*acetyl*-β-D-*ribofuranosyl*)-*pyrazole* (2).—The nitropyrazole (4) [11] (0.5 g) was added to a solution of sodium dithionite (0.75 g) in water–ethanol (1 : 2 v/v) (60 ml) containing potassium hydrogen carbonate (0.75 g). The reaction was stirred at room temperature for 1 h and the ethanol removed under vacuum. The aqueous residue was added to water (20 ml) and ethyl acetate (40 ml); the dried organic layer was evaporated, and the residue was chromatographed on silica gel, eluting with ether to yield the *amino-compound* (2) (0.328 g, 71%), identical in all respects to the product from catalytic hydrogenation.[11]

3(5)-*Cyano*-4-*hydroxy*-5(3)-(2,3,5-*tri*-O-*acetyl*-β-D-*ribofuranosyl*)*pyrazole* (17).—To a solution of the aminopyrazole (2) (0.819 g) in acetic acid (50 ml) just above its freezing point was added sodium nitrite (0.18 g) in water (2.0 ml). The solution was stirred at 0 °C for 0.25 h and then at room temperature for 0.25 h. The solvents were evaporated at <30 °C, water (100 ml) was added, and the solution made basic ($KHCO_3$). The solution was extracted with ethyl acetate; evaporation of the organic layer gave the crude diazopyrazole (0.9 g); $\nu_{max.}$ (film) 2 235 (C≡N) and 2 180 cm^{-1} (N_2^+). This was dissolved in acetone–water (3 : 1 v/v) (40 ml). This solution was deoxygenated by passing nitrogen through it for 0.25 h, and then irradiated using a medium-pressure mercury lamp and Pyrex filters. Evolution of gas commenced after 1.5 h and was complete after 24 h. The volatile solvents were evaporated off and water (50 ml) and dichloromethane (50 ml) were added to the aqueous residue. The combined dichloromethane extracts were dried and evaporated. The residue was chromatographed on silica gel, eluting with benzene–ether (1 : 1 v/v) to give the *hydroxypyrazole* (17) (0.705 g, 87%) as a clear glass, $[\alpha]_D$ −5.77 (*c*, 1.45 in $CHCl_3$); $\nu_{max.}$ (film) 3 700—3 060 (NH and OH), 2 235 (C≡N), and 1 745 cm^{-1} (ester); δ (100 MHz, $CDCl_3$) 2.12 (6 H, s, Me), 2.15 (3 H, s, Me), 4.16—4.60 (3 H, m, H-4′ and -5′), 4.96—5.48 (3 H, m, H-1′—3′), and 10.00—13.00vbr (1 H, s, OH) (Found: C, 49.1; H, 4.7; N, 11.0. $C_{15}H_{17}N_3O_8$ requires C, 49.1; H, 4.6; N, 11.4%).

2′,3′,5′-*Tri*-O-*acetylpyrazofurin* (18).—To a solution of

the nitrile (17) (0.4 g) in glacial acetic acid (60 ml) was added nickel acetate tetrahydrate (1.6 g). The mixture was refluxed for 1 h, cooled, and added to water (100 ml) containing disodium ethylenediaminetetra-acetate (3 g). The product was isolated using dichloromethane. The residue after removal of solvents was chromatographed on silica gel, eluting with dichloromethane–acetone (4 : 1 v/v) to give the *amide* (18) as a glass (0.275 g, 65%), $[\alpha]_D$ −8.96° (*c*, 0.67 in $CHCl_3$); $\nu_{max.}$ (film) 3 700—3 000 (OH and NH), 1 740 (ester), and 1 660, 1 610, and 1 535 cm^{-1} (amide); $\lambda_{max.}$ (EtOH) 205 nm (ε 9 700); $\lambda_{max.}$ (0.01M-KOH) 208 (ε 15 000) and 310 nm (6 400); δ (100 MHz, $CDCl_3$) 2.11 (9 H, s, Me), 4.02—4.68 (3 H, m, H-4′ and -5′), 5.00—5.76 (3 H, m, H-1′ and -3′), 6.04—7.08br (2 H, s, NH_2), and 10.00—12.00vbr (1 H, s, OH) (Found: C, 46.8; H, 5.1; N, 10.9. $C_{15}H_{19}N_3O_9$ requires C, 46.8; H, 4.9; N, 10.9%).

Pyrazofurin (1).—A solution of the triacetate (18) (0.2 g) in methanol (10 ml) and concentrated ammonia (5 ml) was stirred at room temperature for 9 h. The solvents were evaporated off under vacuum and the residue was dissolved in methanol and evaporated to dryness in the presence of silica gel. The resultant silica gel was applied to the top of a column of further silica and the column was eluted with ethyl acetate for 2 h to remove acetamide. Elution with ethyl acetate–water–acetone–methanol (6 : 1 : 1 : 1 v/v) and precipitation from methanol with ethyl acetate gave pyrazofurin (1) (0.101 g, 75%) as an amorphous white solid. Crystallisation from water at 0 °C gave crystalline pyrazofurin (1), m.p. 111—113° (lit.,[8] 111—115 °C); mixed m.p. with authentic material 111—113 °C; $[\alpha]_D$ −48.4° (*c*, 0.31 in H_2O) [lit.,[8] −49.6° (*c*, 0.7984 in H_2O)]; the i.r. and u.v. spectra were superimposable on those of authentic material; δ (360 MHz, D_2O) 3.69 (1 H, dd, *J* 12.32 and 4.23 Hz, H-5′a), 3.74 (1 H, dd, *J* 12.32 and 3.31 Hz, H-5′b), 4.02 (1 H, m, H-4′), 4.165 (1 H, dd, *J* 5.24 and 3.95 Hz, H-3′) 4.34 (1 H, dd, *J* 5.50 and 7.14 Hz, H-2′), and 4.875 (1 H, d, *J* 7.14 Hz, H-1′) [Found: M^+, 259.0804. $C_9H_{13}N_3O_6$ requires *M*, 259.0804. Found: *m/e*, 156.0406; $C_5H_6N_3O_3$ (heterocycle + CH_2O) requires 156.0409].

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