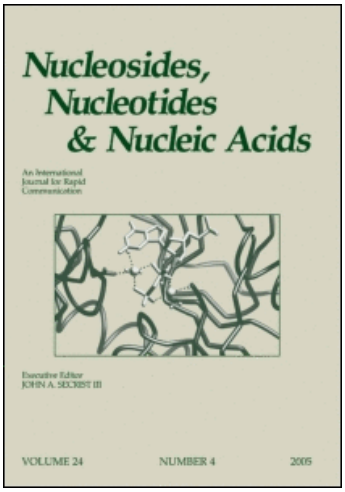

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R. F. Whale[a]; P. L. Coe[a]; R. T. Walker[a]
[a] School of Chemistry, University of Birmingham, Birmingham

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THE SYNTHESIS OF 5-SUBSTITUTED-2,4-DIMETHOXYPYRIMIDINES AND SOME RELATED NUCLEOSIDE ANALOGUES

R.F. Whale, P. L. Coe and R.T. Walker*

School Of Chemistry, University of Birmingham,
PO Box 363, Birmingham, B15 2TT

Abstract: The reaction of 5-formyl-2,4-dimethoxypyrimidine with active methylene compounds in the Knoevenagel reaction and the subsequent nucleoside formation reactions of some of the products was investigated. A new synthesis of (*E*)-5-(2-bromovinyl)uracil and an improved synthesis of 5-formyl-2',3'-isopropylidene uridine are reported.

A decade ago, the synthesis[1] and antiviral activity[2,3] were reported of (*E*)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU) and it was found to be the most potent and selective inhibitor of Herpes Simplex Virus Type 1 (HSV-1) and Varicella-Zoster virus (VZV) at minimum inhibitory concentrations (MIC) of 0.007 and 0.002 $\mu g\ ml^{-1}$ respectively. With this lead, many subsequent substituted 5-vinylic pyrimidine nucleosides were synthesized[4-8] and although some analogues were almost as active, none was found to be better. Although the majority of the analogues synthesized have been pyrimidine 2'-deoxy nucleosides, some 5-substituted vinylic pyrimidine ribonucleosides are known. These include the cyanovinyl[9], phenylvinyl[10] and carboethoxy[8] compounds.

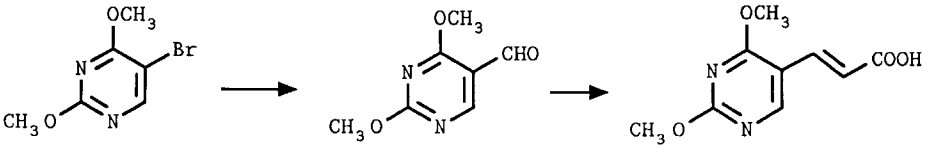
In a previous study,[11] it had been found that (*E*)-5-(2-bromovinyl)uridine and (*E*)-5-(2-carbomethoxyvinyl)uridine had slight activity against the Yellow Fever virus (ID_{50} 60.10 and 20.93 $\mu g\ ml^{-1}$ corresponding to therapeutic indices of 8.32 and 23.89 respectively).

With this lead and the fact that so few pyrimidine ribonucleosides are known, we undertook the synthesis of a series of substituted 5-vinyl uridine analogues and in a previous paper[12] we reported the synthesis of

a series of esters analogous to (*E*)-5-(2-carbomethoxyvinyl)uridine and some amides derived from this ester *via* ammonolysis. We report here some work that was undertaken on 5-substituted 2,4-dimethoxypyrimidines as precursors for both substituted uracils and nucleosides and work on some related nucleoside analogues towards the synthesis of a nitrovinyl side-chain, of which we report here our preliminary results.

Results and Discussion

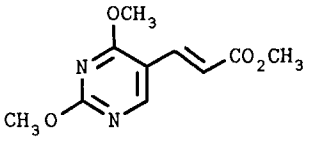
5-Formyl-2,4-dimethoxypyrimidine (2) was prepared according to the method of Noble[13] in which 5-bromo-2,4-dimethoxypyrimidine (1) was treated with n-butyl lithium at -78°C under nitrogen and the resulting 2,4-dimethoxypyrimidin-5-yl lithium then reacted with an excess of ethyl



1 2 3

formate. Reaction of 2 with the anion of malonic acid in the Doebner-Verley modification of the Knoevenagel reaction to produce cinnamic acid-type compounds such as the acid (3) proceeded rapidly when 2 equivalents of malonic acid were used. This is analogous to the preparation of (*E*)-5-(2-carboxyvinyl)uracil.[14]

Compound 3 reacted readily with thionyl chloride upon gentle heating, although if heated for too long the acidic conditions dealkylate the dimethoxypyrimidine system.[15] The crude acid chloride was then reacted with methanol to give the methyl ester (4) and with an aqueous solution of ammonia or methylamine to give the amides (5) and (6) respectively. Reaction of the acid chloride with sodium azide gave the acyl azide (7).



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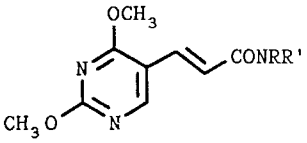
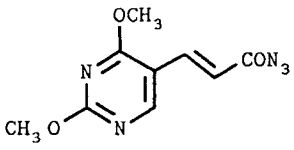


5 R = R' = H
6 R = H, R' = Me



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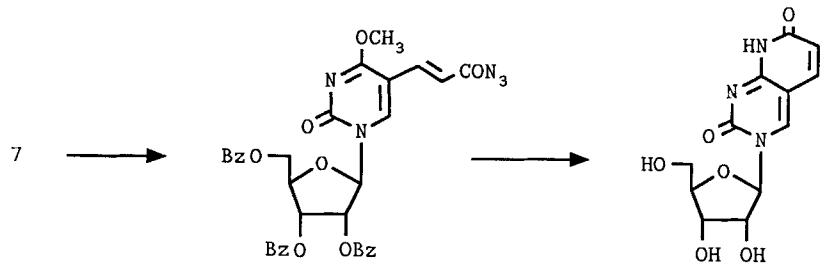
To form a nucleoside, the Hilbert-Johnson reaction involves the reaction of a chlorosugar with a dialkoxypyrimidine. The chlorosugar of 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose was prepared *in situ* from stannic chloride and then reacted with 7 to give the fully protected acyl azide (8) in 52% yield.

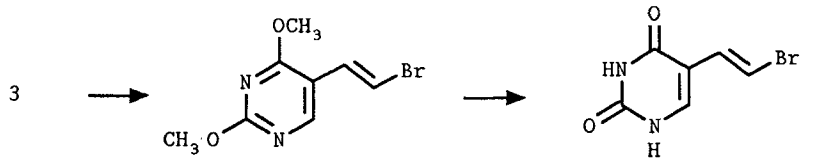
Deprotection of 8 with ammonia in methanol gave the cyclic pyridopyrimidine (9), a compound with a blue fluorescence (UV 254 nm) previously made by photochemical cyclisation of (*E*)-5-(2-carbomethoxyvinyl)cytidine[16] and whose use as an oligonucleotide probe has been investigated.[17] The corresponding 2'-deoxynucleoside has found use as an oligonucleotide probe.[18] Initial displacement of the 4-methoxy group by ammonia would give the cytidine nucleoside, the NH_2 group of which could attack the acyl group and give 9 by elimination of azide ion. 2,4-Dmethoxypyrimidines can be converted to the corresponding uracil and 4-O-alkyl nucleosides to the corresponding dealkylated compound by sodium iodide in glacial acetic acid.[19] This method is not applicable to 7 and 8



8 9

due to the thermal instability of acyl azides, 8 is particularly unstable when heated.

(*E*)-5-(2-Bromovinyl)uracil (11) has previously been synthesized either by bromination of 5-vinyluracil[20] or by the decarboxylative bromination of (*E*)-5-(2-carboxyvinyl)uracil.[14] The first method, however

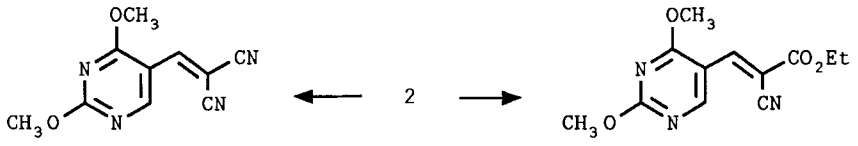


10 11

starts from 5-acetyluracil which is not commercially available, is not easy to prepare and can give an inseparable mixture of both (*E*) and (*Z*) isomers and the second method can give an inseparable mixture of product and starting material.

The decarboxylative bromination of 3 by N-bromosuccinimide to 10 proceeds rapidly in DMF to give exclusively the (*E*) isomer. Subsequent dealkylation of 10 was achieved by sodium iodide in glacial acetic acid to give (*E*)-5-(2-bromovinyl)uracil (11) as a white finely crystalline solid; this route provides 11 of high purity with a melting point/decomposition that depends on the rate of heating.

5-Formyl-2,4-dimethoxypyrimidine (2) was found to react readily with other active methylene compounds in the Knoevenagel reaction. The reaction with malononitrile to give 12 was extremely rapid and proceeded



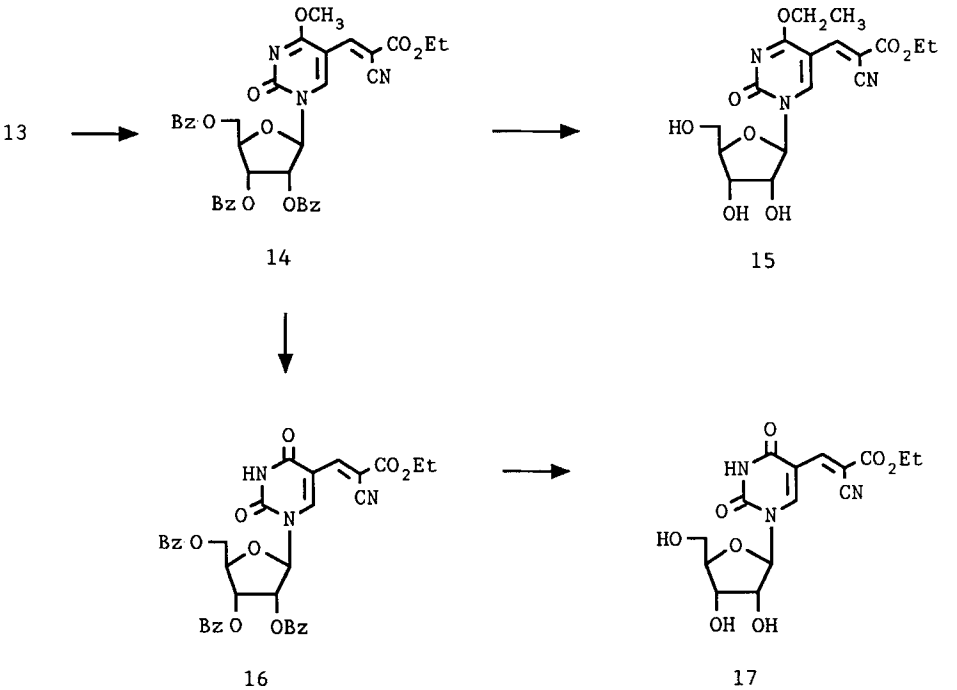
12 13

in high yield although attempts to use this pyrimidine in the Hilbert-Johnson reaction failed. It is known that dialkoxypyrimidines

with strongly electron-withdrawing substituents in the 5-position do not condense well with halosugars.[21]

The reaction of 2 with ethyl cyanoacetate was also rapid and gave 13 in good yield. Although the side-chain of this compound is strongly electron-withdrawing, it is not as strong as that for the 2,2-dicyanovinyl chain of compound 12 and therefore condensation with an *in situ*-generated chlorosugar gave the expected condensation product 14 as the only nucleosidic product. It was found that although the sugar of 14 could be successfully debenzoylated with catalytic ethoxide in ethanol, the 4-O-methyl group was replaced by a 4-O-ethyl group to give compound 15. The 4-O-methyl group could be removed from 14 by sodium iodide in acetic acid to give 16 and treatment of this with ethoxide in ethanol then gave the fully deprotected nucleoside, 17. The deprotection of the 4-O-ethyl group of 15 with sodium iodide/acetic acid was not attempted due to the expected lack of solubility of 17 in chloroform in the extraction and washing of the acetic acid removal stage.

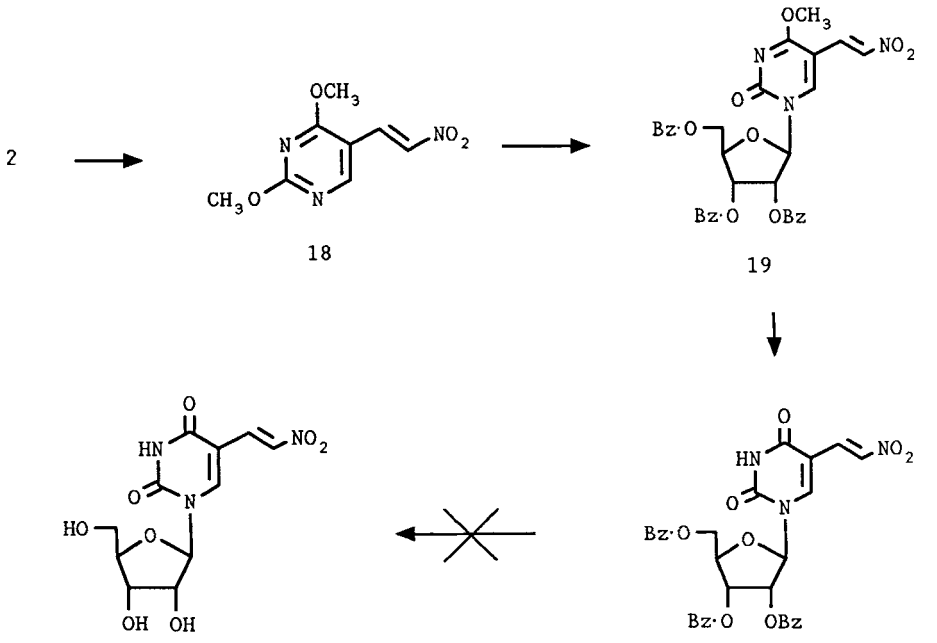
The aldehyde 2 was found not to react with nitromethane under



piperidine- or n-butylamine-catalysis, but with triethylamine an intermediate 1-hydroxy-2-nitroethyl compound was obtained which could be

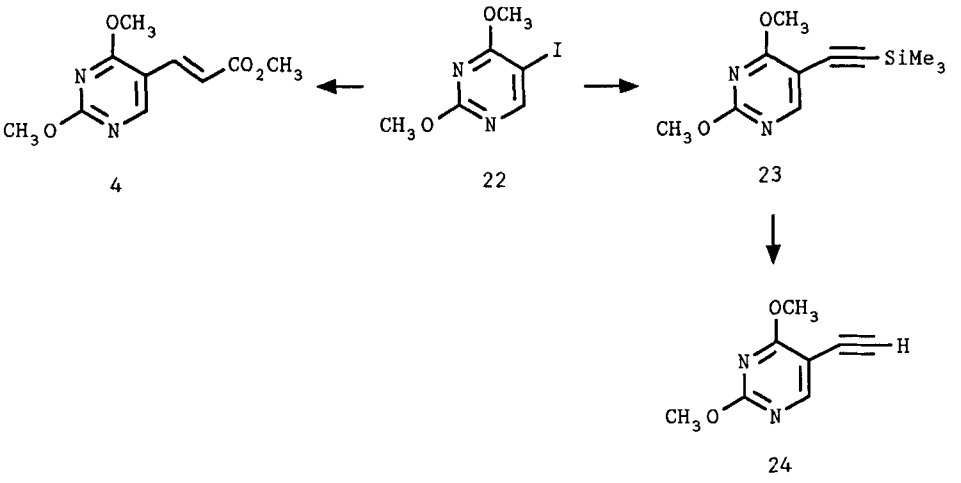
immediately acetylated with added acetic anhydride. Spontaneous elimination of acetic acid then gave the compound with the required nitrovinyl side-chain, 18. In an analogous manner to the formation of compound 14, (*E*)-5-(2-nitrovinyl)-2,4-dimethoxypyrimidine (18) was reacted with the halosugar. The 4-O-methyl group of the resulting condensation product (19) was removed by sodium iodide in acetic acid to give 20. However, attempts to deprotect the sugar of 20 with methoxide/methanol, potassium carbonate/methanol or triethylamine/ethanol to give (*E*)-5-(2-nitrovinyl)uridine (21) caused decomposition of the side-chain to give deep green coloured solutions of undetermined composition.

The Heck reaction has been widely used to couple 5-iodopyrimidine



nucleosides with a compound containing an activated double bond such as allylic compounds and acrylic acid esters. 5-Iodo-2,4-dimethoxypyrimidine (22) was synthesized according to the published procedure[22,23] in which 5-iodouracil was chlorinated to 2,4-dichloro-5-iodopyrimidine by phosphoryl chloride in the presence of *N,N*-dimethylaniline and then reacted with sodium methoxide in methanol. 2,4-Dichloro-5-iodopyrimidine can cause blistering of the skin and an alternative synthesis[24] of 22

involves iodination of 2,4-dimethoxypyrimidine using *N*-iodosuccinimide in trifluoroacetic acid/trifluoroacetic anhydride and although gives an excellent yield the reagents would probably be too expensive for the large scale synthesis of 22. Compound 22 was reacted with methyl acrylate using a palladium (II) acetate, triphenyl phosphine and triethylamine catalyst system to give the ester 4 in 78% yield. This compares with the synthesis of 4 *via* the acid chloride of 3 in 42% yield.

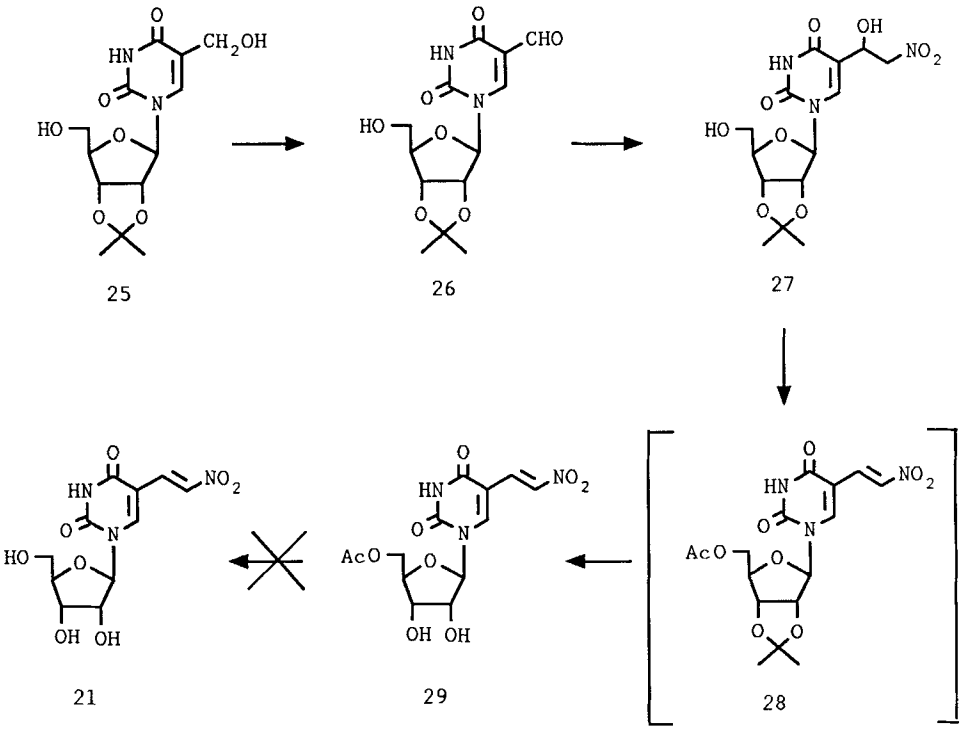


4 22 23 24

It is known that reaction of the powerfully vesicant 5-(α-chlorovinyl)-2,4-dichloropyrimidine when treated with methoxide/methanol gives 2,4-dimethoxy-5-ethynylpyrimidine (24) which can be silylated to 23 using t-butyl lithium/chlorotrimethylsilane.[25] As 5-iodopyrimidine nucleosides are known to couple readily with terminal acetylenes such as trimethylsilylacetylene[26] an alternative synthesis of 24, useful for large scale preparations, involved the coupling of 5-iodo-2,4-dimethoxypyrimidine (22) to trimethylsilylacetylene using *bis*(triphenylphosphine)palladium (II) chloride/copper (I) iodide catalysis. The reaction proceeded cleanly in excellent yield. 2,4-Dimethoxy-5-ethynylpyrimidine (24) was obtained from 23 by treatment with tetrabutylammonium fluoride in THF.

The synthesis and reactions of the aldehyde 5-formyl-2',3'-isopropylideneuridine (26) were also investigated in order to produce a

compound having a vinylic side chain from an aldehyde at the nucleoside level. 2',3'-Isopropylideneuridine can be readily hydroxymethylated in the 5-position using paraformaldehyde/aqueous potassium hydroxide[27] to give 25. Although this can be oxidised by manganese dioxide to 26 in 37%

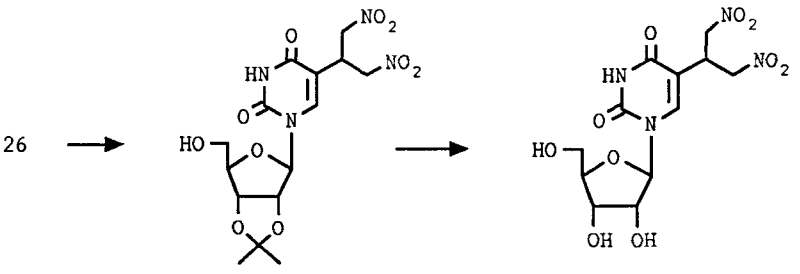


yield[28] we report here the use of an homogenous pyridinium dichromate/DMF/dichloromethane system which consistently effected this oxidation in 63% yield.

Treatment of 26 with ethoxide/ethanol/nitromethane at room temperature gave a 9% yield of the 1-hydroxy-2-nitroethyl compound 27. The formation of α-hydroxy-β-nitroethyl compounds in the Henry reaction[29] is catalysed by alkoxides or amines and occurs when spontaneous elimination of water to give the nitro-olefin does not occur. The less the aromaticity of the aldehyde the less likely spontaneous elimination of water is to occur, thus for the pseudo-aromatic 5-position the hydroxy compound 27 is isolable. In order to increase the yield of 27, sodium hydride was used to generate the anion of nitromethane and the required product was obtained in 64% yield. In an effort to generate the

nitro-olefin side chain, the hydroxy compound 27 was treated with acetic anhydride in an analogous manner to the preparation of 18 and the acetylated side-chain hydroxyl of 27 spontaneously eliminated acetic acid. However, the 5'-hydroxyl group was not surprisingly acetylated at the same time and compound 28 resulted. The 5'-*O*-acetyl-2',3'-isopropylidine-(*E*)-5-(2-nitrovinyl)uridine (*28*) was not isolated but was treated directly with 50% aqueous trifluoroacetic acid to give 5'-*O*-acetyl-(*E*)-5-(2-nitrovinyl)uridine (29). As mentioned earlier, we found that a 5-nitrovinyl side-chain pyrimidine nucleoside with the sugar protected with base-labile protecting groups such as the benzoate esters of 20 could not be deprotected under basic conditions and this was confirmed by 29 which could not be deprotected to (*E*)-5-(2-nitrovinyl)uridine (21) with potassium carbonate/methanol without causing decomposition, an alternative methodology using acid labile protecting groups will be reported later.

When compound 26 was heated under reflux with an excess of ethoxide/nitromethane the initially formed compound containing the nitrovinyl side-chain underwent Michael addition of the nitromethane anion to give 30. When only 1 equivalent of ethoxide/nitromethane was



30 31

used, compound 30 was again formed and starting material remained. The unsaturated side-chain is thus more reactive than the starting material towards $^{-}CH_2NO_2$ and this reactivity has been demonstrated by the lability of the nitrovinyl side-chain in the presence of base. The use of aqueous trifluoroacetic acid brought about smooth conversion of 30 to the deprotected nucleoside 31.

Our work reported here has approached the goal of nucleoside synthesis from two directions, namely from 2,4-dimethoxypyrimidines and

from preformed nucleosides. Although we did not set out to determine a more advantageous route to the nucleosides, we found for instance that a nitrovinyl side-chain was more readily obtained from a pyrimidine than a nucleoside due to the formers greater aromaticity even though the resulting compound (20) could not be deprotected. On the other hand, 17 could no doubt be obtained *via* 26 although this material is not as readily available in as large a quantity as 2.

BIOLOGICAL RESULTS

Biological testing was done by the United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD and The Wellcome Research Laboratories, Beckenham, Kent, UK, against a series of viruses including Vaccinia Virus, Vesicular Stomatitis Virus HSV-1 and HSV-2. None of the compounds tested (9,15,17,27,29,31) showed any significant activity.

EXPERIMENTAL

Ultraviolet spectra were recorded with a Perkin Elmer 552 spectrophotometer and were run in spectroscopic grade ethanol. Mass spectra were determined with a Kratos MS80 mass spectrometer with a DS55 data system employing automatic digital readout of data. For Fast Atom Bombardement (FAB) a 3-NOBA matrix with Na doping was used. The ^{1}H-NMR spectra (s=singlet, d=doublet, t=triplet, b=broad, m=multiplet, q=quartet) were recorded on either a Jeol FX90 (90 MHz) or a Jeol GX270 (270 MHz) spectrometer. Precoated Merck silica gel 60 F_{254} plates were used for TLC and the spots were examined with UV light (254nm) and a sulphuric acid-cysteine spray. Column chromatography was performed using Kieselgel 60, 70-230 mesh ASTM, type 7734, supplied by E. Merck A.G., Darmstadt, Germany. Columns were packed under gravity. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. Dimethylformamide was dried over P_2O_5 and distilled under high vacuum, pyridine and triethylamine were refluxed over CaH_2 then distilled and 1,4-dioxan and THF were dried with potassium/benzophenone then distilled.

5-Formyl-2,4-dimethoxypyrimidine[13] (2) A solution of n-butyl lithium (480 ml, 1.6 M, 736.0 mmol) in n-hexane was added dropwise over 10 minutes to a stirred suspension of 5-bromo-2,4-dimethoxypyrimidine (160 g, 730.5 mmol) in dry diethyl ether (2400 ml) at -70 °C under dry nitrogen. Ethyl formate (280.0 g, 3.77 mol), which had been fractionated from calcium hydride, was added to the pale yellow suspension of 2,4-dimethoxypyrimidin-5-yl lithium and the resulting orange solution stirred at -70 C for 2 hours. The reaction mixture was then allowed to warm slowly to room temperature, quenched with water (2000 ml) and extracted twice with ether (2 X 1000 ml). The organic layers were combined, dried ($MgSO_4$) and the solvent removed under reduced pressure and the residue purified by column chromatography with elution in hexane/ethyl acetate (90:10) followed by recrystallization from hexane containing some ethyl acetate (75.15 g, 61 %). M.pt. 111-112 °C (Lit[30]

123 °C). UV λ_{max} 279.9 nm, ϵ=9340. ^{1}H-NMR δ(DMSO-d_6) 10.05(1-H,s,CHO), 8.75(1-H,s,H-6), 4.08(3-H,s,OCH_3), 4.02(3-H,s,OCH_3). FAB mass spectrum m/e 169 $(M+H)^+$. Elemental analysis $C_7H_8N_2O_3$ calculated C, 50.0; H, 4.80; N, 16.7; found C, 50.1; H, 4.5; N, 16.9

(*E*)-5-(2-Carboxyvinyl)-2,4-dimethoxypyrimidine (3) 5-formyl-2,4-dimethoxypyrimidine (10.52 g, 62.60 mmol) was dissolved in dry pyridine (60 ml) and malonic acid (13.02 g, 126.20 mmol) and freshly redistilled piperidine (2 ml) added. The mixture was heated on a steam bath for 10 hours then the solvent was removed *in vacuo*. The resulting oil was coevaporated with water and the white solid recrystallized firstly from water then from methanol to give the product, in two crops (7.53 g, 57%). M.pt. 260-265 °C (d). UV λ_{max} 298.0 nm, ϵ=19290. ^{1}H-NMR δ(DMSO-d_6) 12.00(1-H,bs,COOH), 8.68(1-H,s,H-6), 7.50(1-H,d,vinylic H, J=16Hz), 6.55(1-H,d,vinylic H,J=16Hz), 4.02(3-H,s,OCH_3), 3.95(3-H,s,OCH_3). EI mass spectrum m/e 210 (M). Elemental analysis $C_9H_{10}N_2O_4$ calculated C, 51.42; H, 4.79; N, 13.33; found C, 51.3; H, 4.8; N, 13.1

(*E*)-5-(2-Carbomethoxyvinyl)-2,4-dimethoxypyrimidine (4) **Method A** A solution of 3 ((0.10 g, 0.47 mmol) in thionyl chloride (40ml) was heated under reflux for 20 minutes then the excess of thionyl chloride was removed *in vacuo*. The resulting yellow solid was suspended in dry ether (20 ml) and dry methanol (5 ml) added. After 20 minutes at room temperature, the excess of methanol was removed and the yellowish solid purified by short column chromatography with elution in 70:30 hexane/ethyl acetate followed by recrystallization from hexane to give fine white needles (0.046 g, 42%). M.pt. 120-121 °C. UV λ_{max} 293.0nm, ϵ=18430. ^{1}H-NMR δ(DMSO-d_6) 8.73(1-H,s,H-6), 7.58(1-H,d,vinylic H, J=16Hz), 6.65 (1-H,d,vinylic H, J=16Hz), 4.03(3-H,s,OCH_3), 3.95 (1-H,s,OCH_3), 3.71(3-H,s,CO_2CH_3). EI mass spectrum m/e 224 (M). Elemental analysis $C_{10}H_{12}N_2O_4$ C, 53.59; H, 5.39; N, 12.49; found C, 53.4; H, 5.2; N; 12.6

Method B A solution of palladium (II) acetate (0.042 g, 0.18 mmol), triphenylphosphine (0.098 g, 0.37 mmol) and dry triethylamine (1 ml) in dry dioxan (10 ml) was heated to 70 °C and to the resulting deep red-coloured solution of the activated catalyst were added 5-iodo-2,4-dimethoxy-pyrimidine[22,23] (1.00 g, 3.76 mmol) and methyl acrylate (0.64 g, 7.43 mmol). The solution was stirred under reflux for 1 hour, then silica gel added, the solvent removed *in vacuo* and the product isolated by short column chromatography as above followed by recrystallization from hexane to give fine white needles (0.66 g, 78%) with identical spectroscopic and analytical data to those obtained above.

(*E*)-5-(2-Aminocarbonylvinyl)-2,4-dimethoxypyrimidine (5) A solution of 3 (0.75 g, 3.56 mmol) in thionyl chloride (40 ml) was heated under gentle reflux for 20 minutes then evaporated to dryness *in vacuo*. To the resulting yellow solid were added dry ether (20 ml) then concentrated aqueous ammonia solution (2 ml) with vigorous stirring. After standing at room temperature for 10 minutes the reaction mixture was evaporated to dryness and recrystallized from water to give fine white needles (0.23 g, 31%). M.pt. 196-198 °C. UV λ_{max} 288.0nm, ϵ=18580. ^{1}H-NMR δ(DMSO-d_6) 8.55(1-H,s,H-6), 7.55(1-H,bs,N-H), 7.38(1-H,d,vinylic H, J=16HZ), 7.08(1-H,bs,N-H), 6.71(1-H,d,vinylic H,J=16Hz), 4.02(3-H,s,OCH_3), 3.40(3-H,s,OCH_3). EI mass spectrum m/e 209 (M). Elemental analysis $C_9H_{11}N_3O_3$ calculated C, 51.67; H, 5.29; N, 20.08; found C, 51.4; H, 5.2; N, 19.9

(*E*)-5-(2-Methylaminocarbonylvinyl)-2,4-dimethoxypyrimidine (6) A solution of 3 (0.20 g, 0.95 mmol) in thionyl chloride (40 ml) was heated under gentle reflux for 20 minutes then evaporated to dryness. To the resulting yellow solid was added dry ether (20 ml) and a solution of methyl amine (2 ml). After 10 minutes the solution was evaporated to dryness and the yellow solid recrystallized from water (0.10 g, 47%). M.pt. 194-196°C. UV λ_{max} 273.0nm, ϵ=20840. ^{1}H-NMR δ(DMSO-d_6) 8.53(1-H,s,H-6), 8.07(1-H,bd,N-H), 7.50(1-H,d,vinylic H,J=16Hz), 6.72(1-H,d,vinylic H,J=16Hz), 4.02(3-H,s,OCH_3), 3.95(3-H,s,OCH_3), 2.70(3-H,s,NCH_3). EI mass spectrum m/e 223 (M). Elemental analysis $C_{10}H_{13}N_3O_3$ calculated C, 53.80; H, 5.87;, N, 18.82; found C, 53.7; H, 6.0; N, 18.5

(*E*)-5-(2-Azidocarbonylvinyl)-2,4-dimethoxypyrimidine (7) A solution of 3 (0.40 g, 1.90 mmol) in freshly redistilled thionyl chloride (8 ml) was heated under reflux for 10 minutes. The excess of the thionyl chloride was then evaporated *in vacuo* and the yellow solid dissolved in dry THF (10 ml) and added dropwise to a stirred solution of sodium azide (0.18 g) in 50:50 water/acetone. The solution was stirred for 10 minutes and the solvent then removed under reduced pressure. The yellow oil obtained was purified by column chromatography with elution in 80:20 toluene/acetone followed by recrystallization from hot acetone which was kept overnight at 4°C to give long fine white needles (0.32 g, 72%). M.pt 108-109°C (d). UV λ_{max} 311.5nm, ϵ= 19720. ^{1}H-NMR δ(DMSO-d_6) 8.75(1-H,s,H-6), 7.64 (1-H,d,vinylic H,J=16Hz), 6.63(1-H,d,vinylic H,J=16Hz), 4.02(3-H,s,OCH_3), 3.95(3-H,s,OCH_3). EI mass spectrum m/e 235 (M), 207 (M-N_2). Elemental analysis $C_9H_9N_5O_3$ calculated C, 45.96; H, 3.86; N, 29.77; found C, 46.2; H, 3.8; N, 29.6

1-(2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl)-4-methoxy-5-[(*E*)-azidocarbonylvinyl]-2-(1*H*) pyrimidinone (8) To a solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (1.73 g, 3.40 mmol) in dry dichloromethane (5 ml) was added stannic chloride (0.90 g, 3.40 mmol) and the solution stirred at 0 °C while a solution of 7 (0.81 g, 3.40 mmol) in dry dichloromethane (4 ml) was added in one portion. The solution was allowed to warm to room temperature and stirred for 7 hours. The organic solution was poured into ice/water (30 ml) and separated and sequentially washed with hydrochloric acid (2M, 5 x 15 ml), aqueous sodium bicarbonate (3 x 15 ml) and water (15 ml). The organic layer was dried ($MgSO_4$), filtered then evaporated *in vacuo* and the resulting white foam purified by column chromatography with elution in 90:10 toluene/acetone to give a white foam (1.19 g, 52%). UV λ_{max} 310.0nm, ϵ=21560. ^{1}H-NMR δ(DMSO-d_6) 8.76(1-H,s, H-6), 8.03-7.40(16-H,m, aromatic H, 1 vinylic H), 6.51(1-H,d,vinylic H,J=16Hz), 6.30(1-H,d,H-1'), 4.87-4.74(4-H,m,H-2',H-3',H-5'), 4.04-3.93 (1-H,m,H-4'), 3.99(3-H,s,OCH_3). FAB mass spectrum m/e 666 $(M+H)^+$. Elemental analysis $C_{34}H_{27}N_5O_{10}.H_2O$ calculated C, 59.73; H, 4.27; N, 10.24; found C, 60.0; H, 4.5; N, 9.9

3-β-D-Ribofuranosyl-2,7-dioxopyrido[2,3-*d*]pyrimidine (9) To 8 (0.322 g, 0.483 mmol) was added dry methanol saturated at 0°C with dry ammonia gas (25 ml) and the yellow solution stirred at room temperature for 48 hours. After releasing the pressure, the solution was heated under gentle reflux for 3 hours then evaporated to dryness and the product isolated by column chromatography with elution in 70:30 chloroform/methanol (0.1 g, 70%). M.pt. 239-240°C (d) (Lit[16] 240°C). UV λ_{max} 331.0nm, ϵ=12200 (Lit[16] 300 nm, ϵ = 17000. ^{1}H-NMR δ(DMSO-d_6) 11.75(1-H,bs,N-H), 9.05(1-H,s, H-4), 7.60(1-H,d,H-5,J=10Hz), 6.19(1-H,d,H-6,J=10Hz), 5.81(1-H,d,H-1'), 5.60(1-H,d,2'-OH), 5.38(1-H,t,5'-OH), 5.10(1-H,d,3'-OH), 4.30-3.60(5-H,m,H-2',H-3',H-4',H-5'). FAB mass spectrum m/e 296 $(M+H)^+$. Elemental analysis $C_{12}H_{13}N_3O_6$ calculated C, 48.82; H, 4.44; N, 14.23; found C, 48.5; H, 4.1; N, 13.9

(*E*)-5-(2-Bromovinyl)-2,4-dimethoxypyrimidine (10) To a solution of 3 (0.30 g, 1.43 mmol) in dry DMF (5 ml) was added potassium carbonate (0.45 g, 5.25 mmol). After stirring at room temperature for 15 minutes, a solution of *N*-bromosuccinimide (0.258 g, 1.45 mmol) in dry DMF (4 ml) was added dropwise over 10 minutes then filtered immediateley and the precipitate washed with dry DMF. The filtrate was evaporated under high vacuum and the oil purified by column chromatography with elution in 70:30 hexane/ethyl acetate followed by recrystallization from hexane to give fine white needles (0.156 g). A second crop (0.08 g) gave a total of 0.236 g (67%). M.pt. 91-92 °C. UV λ_{max} 260.0nm, ϵ=19560. ^{1}H-NMR δ(DMSO-d_6) 8.45(1-H,s,H-6), 7.24(1-H,d,vinylic H, J=14Hz), 7.02(1-H,d, vinylic H,J=14Hz), 3.98(3-H,s,OCH_3), 3.89(3-H,s,OCH_3). FAB mass spectrum m/e 245/247 $(M+H)^+$. Elemental analysis $C_8H_9BrN_2O_2$ calculated C, 39.2; H, 3.70; N, 11.43; found C, 38.9; H, 3.6; N, 11.5

(*E*)-5-(2-Bromovinyl)uracil (11) To 10 (5.49 g, 22.40 mmol) in glacial acetic acid (30 ml) was added sodium iodide (7.38 g, 49.28 mmol) and the solution heated at 100 °C for 30 minutes after which time the product had crystallized from solution. The deep red-coloured suspension was allowed to cool and was then filtered and washed with acetone (6 x 100 ml) then ether (3 x 100 ml) to give a fine white crystalline solid (4.03 g, 83%). M.pt. darkens and decomposes from 195 °C (Lit[31] 220 °C, d). UV λ_{max} 290.0nm, ϵ=9950. ^{1}H-NMR δ(DMSO-d_6) 11.20(2-H,bs,2 N-H), 7.65 (1-H,s,H-6), 7.29(1-H,d,vinylic H,J=14Hz), 6.83(1-H,d,vinylic H,J=14Hz). Elemental analysis $C_6H_5BrN_2O_2$ calculated C, 33.20; H, 2.32; N, 12.91; found C, 33.2; H, 2.1; N, 12.6

5-(2,2-Dicyanovinyl)-2,4-dimethoxypyrimidine (12) To a suspension of 2 (1.50 g, 8.92 mmol) in ethanol (30 ml) was added malononitrile (0.585 g, 8.90 mmol) then piperidine (0.1 ml). The yellow solution was stirred at room temperature for 20 minutes after which time some of the product had started to crystallize from solution. The solvent was removed *in vacuo* and the product isolated by short column chromatography with elution in 80:20 hexane/ethyl acetate followed by recrystallization from ethanol to give fine lemon-yellow coloured crystals (1.72 g, 89%). M.pt. 100-101 °C. UV λ_{max} 334.0 nm, ϵ=12590. ^{1}H-NMR δ(DMSO-d_6) 8.95(1-H,s,vinylic H), 8.32(1-H,s,H-6), 4.01(6-H,s,2 OCH_3). EI mass spectrum m/e 216 (M). Elemental analysis $C_{10}H_8N_4O_2$ calculated C, 55.56; H, 3.70; N, 25.90; found C, 55.6; H, 3.5; N, 25.9

5-(2-Carboethoxy-2-cyanovinyl)-2,4-dimethoxypyrimidine (13) To a suspension of 2 (0.50 g, 2.97 mmol) in ethanol (10 ml) was added ethyl cyanoacetate (0.336 g, 2.97 mmol) and piperidine (0.1 ml). The resulting yellow solution was stirred at room temperature for 1.5 hours after which time the solvent was removed *in vacuo* and the product isolated by short column chromatography with elution in 70:30 hexane/ethyl acetate followed by recrystallization from ethanol to give pale yellow needles (0.62 g, 79%). M.pt. 73-75 °C. UV λ_{max} 350.5nm, ϵ=20360. ^{1}H-NMR δ(DMSO-d_6) 9.08(1-H,s,vinylic H), 8.21(1-H,s,H-6), 4.30(2-H,q,OCH_2), 4.05(3-H,s,OCH_3), 4.00(3-H,s,OCH_3), 1.32(3-H,t,CH_3). FAB mass spectrum m/e 264 $(M+H)^+$. Elemental analysis $C_{12}H_{13}N_3O_4$ calculated C, 54.75; H, 4.97; N, 15.96; found C, 54.8; H, 5.0; N, 16.0

5-(2-Carboethoxy-2-cyanovinyl)-1-(2,3,5-tri-*O*-benzoyl)-β-*D*-ribofuranosyl-4-methoxy-2(1*H*)-pyrimidinone (14) To a solution of 1-*O*-acetyl-2,3,5-tri--*O*-benzoyl-β-*D*-ribofuranose (1.09 g, 2.16 mmol) in dry dichloromethane (3 ml) was added stannic chloride (0.56 g, 2.3 mmol) and the solution

stirred at 0 °C for 30 minutes. Then, a solution of 13 (0.54 g, 2.05 mmol) in dry dichloromethane (3 ml) was added all at once. After 24 hours, the reaction mixture was poured into water (30 ml), separated and the organic layer washed with hydrochloric acid (4M, 2 x 40 ml) and aqueous sodium bicarbonate (1M, 3 x 40 ml), dried ($MgSO_4$), and then evaporated to dryness. The product was isolated by short column chromatography with elution in 96:4 toluene/acetone to give a pale-yellow foam (0.87 g, 61%). UV λ_{max} 337.0 nm, ϵ=16700. ^{1}H-NMR δ(DMSO-d_6) 9.25 (1-H,s,H-6), 8.05-7.19(16-H,m, Ph,vinylic), 6.29(1-H,d,H-1'), 6.08(2-H, q,H-5'), 5.00(1-H,m, H-4'), 4.67-4.61(2-H,m,H-2',H-3'), 4.16(2-H,q, CO_2CH_2), 3.99(3-H,s,OCH_3), 1.24(3-H,t,CH_3). FAB mass spectrum m/e 694 $(M+H)^+$. Elemental analysis $C_{37}H_{31}N_3O_{11}$ calculated C, 64.1; H, 4.5; N, 6.05; found C, 64.4; H, 4.3; N, 5.9

5-(2-Carboethoxy-2-cyanovinyl)-1-(β-*D*-ribofuranosyl)-4-ethoxy-2(1*H*)pyrimidinone (15) To 14 (0.50 g, 0.72 mmol) in dry ethanol (40 ml) was added a solution of sodium ethoxide (0.25 g) in dry ethanol (10 ml). After stirring for 4 hours, glacial acetic acid (0.3 ml) was added and the solution evaporated *in vacuo*. The product was isolated by column chromatography with elution in 90:10 chloroform/methanol followed by recrystallization from ethanol (0.16 g, 56%). M.pt. 175-176 °C. UV λ_{max} 337.5 nm, ϵ=20860. ^{1}H-NMR δ(DMSO-d_6) 9.15(1-H,s,H-6), 8.10(1-H,s,vinylic H), 5.85(1-H,d, H-1'), 5.60(1-H,d,2'-OH), 5.10(2-H,m,3'-OH,5'-OH), 4.50-4.15(4-H,m,2 OCH_2), 4.10-3.80(3-H,m,H-2',H-3',H-4'), 3.70 (2-H,m,H-5'), 1.30(6-H,m,2 CH_3). FAB Mass spectrum m/e 396 $(M+H)^+$. Elemental analysis $C_{17}H_{21}N_3O_8$ calculated C, 51.64; H, 5.35; N, 10.62; found C, 51.9; H, 5.1; N, 10.7

5-(2-Carboethoxy-2-cyanovinyl)-2',3',5'-tri-*O*-benzoyluridine (16) To 14 (1.00 g, 1.44 mmol) in glacial acetic acid (15 ml) was added sodium iodide (0.88 g, 5.80 mmol) and the solution was stirred at 100 °C for 3 hours. The darkly coloured reaction mixture was evaporated to dryness, dissolved in chloroform and extracted with aqueous sodium bicarbonate (1M, 2 x 200 ml) and then dried ($MgSO_4$). The residue was purified by short column chromatography to give a pale yellow foam (0.82 g, 84%). UV λ_{max} 341.0 nm, ϵ=13830. ^{1}H-NMR δ(DMSO-d_6) 12.08(1-H,s,N-H), 9.06(1-H, s,H-6), 8.10-7.20(16-H,m,3 Ph,vinylic H), 6.29(1-H,d,H-1'), 6.10(2-H,m, H-5'), 4.95(1-H,m,H-4'), 4.63)2-H,m,H-2',H-3'), 4.15(2-H,q,CO_2CH_3), 1.21(3-H,t,CH_3). FAB mass spectrum m/e 680 $(M+H)^+$. Elemental analysis $C_{36}H_{29}N_3O_{11}$ calculated C, 63.62; H, 4.30; N, 6.18; found C, 63.3; H, 4.4; N, 5.9

5-(2-Carboethoxy-2-cyanovinyl)uridine (17) To 16 (3.88 g, 5.70 mmol) was added a solution of sodium (0.20 g) in dry ethanol (50 ml) and the orange solution stirred at room temperature for 2 hours. The reaction mixture was quenched with glacial acetic acid (1 ml) and then evaporated *in vacuo*. The product was isolated by short column chromatography with elution in 80:20 chloroform/methanol followed by recrystallization from methanol to give fine yellow crystals (0.99 g, 47%). M.pt. 196-198 °C. UV λ_{max} 342.0 nm, ϵ=16110. ^{1}H-NMR δ(DMSO-d_6) 12.00(1-H,bs,N-H), 8.87(1-H,s, H-6), 8.15(1-H, s,vinylic H), 5.85(1-H,d,H-1'), 5.50(1-H,bs,2'-OH), 5.30 (1-H,bs,5'-OH), 5.00(1-H,bs,3'-OH), 4.45-4.15(2-H,q,OCH_2), 5.15-3.80 (3-H,m,H-2', H-3',H-4'), 3.70-3.50(2-H,m,H-5'), 1.25(3-H,t,CH_3). FAB mass spectrum m/e 368 $(M+H)^+$. Elemental analysis $C_{15}H_{17}N_3O_8.0.5H_2O$ calculated C, 47.8; H, 4.82; N, 11.16; found C, 48.0; H, 4.8; N, 10.9

(*E*)-5-(2-Nitrovinyl)-2,4-dimethoxypyrimidine (18) To 2 (4.00 g, 23.79 mmol) in ethanol (300 ml) and nitromethane (28.0 g, 0.46 mmol) was added triethylamine (2 ml) and the solution stirred at room temperature for 1 hour. The solvent was removed *in vacuo* and acetic anhydride (50 ml) added. After 6 hours, the yellowish solution was evaporated to dryness then coevaporated with methanol and the orange residue purified by short column chromatography with elution in 80:20 hexane/ethyl acetate followed by recrystallization from ethanol to give, in two crops, long fine lemon-yellow crystals which turn orange on exposure to light (3.39 g, 67%). M.pt. 142-144 °C. UV λ_{max} 316.0 nm, ϵ=14930. ^{1}H-NMR δ(DMSO-d_6) 8.80(1-H,s,H-6), 8.10(1-H,d,vinylic H, J=16Hz), 7.92(1-H,d,vinylic H,J=16Hz), 4.06(3-H, s,OCH_3), 3.95(3-H,s,OCH_3). FAB mass spectrum m/e 212 $(M+H)^+$. Elemental analysis $C_8H_9N_3O_4$ calculated C, 45.50; H, 4.29; N, 19.89; found C, 45.5; H, 4.1; N, 19.9

(*E*)-5-(2-Nitrovinyl)-1-(2,3,5-tri-*O*-benzoyl)-β-D-ribofuranosyl-4-methoxy-2(1*H*)pyrimidinone (19) To a stirred solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (3.58 g, 7.10 mmol) in dry dichloromethane (8 ml) at 0 °C was added stannic chloride (1.85 g, 7.10 mmol) and 18 (1.50 g, 7.10 mmol). The reaction mixture was stirred at 0 °C for 1 hour then at room temperature for 5 hours then poured onto ice/water (100 ml) and washed with dilute hydrochloric acid (4M, 2 x 100 ml), aqueous sodium bicarbonate then water and dried ($MgSO_4$). The product was isolated by short column chromatography with elution in 60:40 hexane/ethyl acetate to give a yellow foam (2.10 g, 46%). M.pt 107-109 °C. UV λ_{max} 323.0 nm, ϵ=15050. ^{1}H-NMR δ(DMSO-d_6) 8.83(1-H,s,H-6), 8.00-7.83(17-H,m, 2 vinylics, 3 Ph), 6.28(1-H,d,H-1'), 5.99(2-H,m,H-5'), 4.89(1-H,m,H-4'), 4.82-4.68(2-H,m,H-2',H-3'), 4.02(3-H,s,OCH_3). FAB mass spectrum m/e 642 $(M+H)^+$. Elemental analysis $C_{33}H_{27}N_3O_{11}$ calculated C, 61.78; H,4.24; N, 6.55 found C, 61.6; H, 4.3; N, 6.5

(*E*)-5-(2-Nitrovinyl)-2',3',5'-tri-*O*-benzoyluridine. (20) To a stirred solution of 19 (1.30 g, 2.03 mmol) in acetic acid (20 ml) was added sodium iodide (3.00 g, 20.0 mmol) and the solution heated at 100 °C for 1 hour. The darkly coloured solution was evaporated to dryness *in vacuo*, extracted with chloroform (2 x 100 ml) and washed with aqueous sodium bicarbonate (2 x 100 ml) and dried ($MgSO_4$). The product was isolated by short column chromatography with elution in 90:10 toluene/acetone as a yellow foam (1.26 g, 99%). M.pt 202-203 °C. UV λ_{max} 325.0 nm, ϵ=16560. ^{1}H-NMR δ(DMSO-d_6) 12.00(1-H,bs,N-H), 8.60(1-H,s,H-6), 8.25-7.16(17-H,m,3 Ph, 2 vinylics), 6.25(1-H,d,H-1'), 6.00(2-H,m,H-5'), 4.90-4.60 (3-H,m, H-2', H-3',H-4'). FAB mass spectrum m/e 650 $(M+Na)^+$. Elemental analysis $C_{32}H_{25}N_3O_{11}$ calculated C; 61.24; H, 4.01; N, 6.69; found C, 61.3; H, 3.9; N, 6.6

2,4-Dimethoxy-5-trimethylsilylethynylpyrimidine (23) To dry triethylamine (150 ml) under an atmosphere of dry nitrogen were added *bis*(triphenylphosphine)palladium (11) chloride (0.76 g, 1.08 mmol), copper (1) iodide (0.76 g, 4.00 mmol), 5-iodo-2,4-dimethoxypyrimidine (13.5 g, 50.7 mmol) and trimethylsilylacetylene (10.0 g, 101.5 mmol) and the grey suspension heated at 50 °C for 4 hours. The mixture was evaporated to dryness *in vacuo* and the product isolated by short column chromatography with elution in 80:20 hexane/ethyl acetate followed by recrystallization from ethanol to give long off-white coloured crystals which were further purified by distillation in a sublimation apparatus to give a white crystalline powder (10.20 g, 85%). M.pt. 72-74 °C (Lit[24] 73-74 °C). UV λ_{max} 282.0 nm, ϵ=10780. ^{1}H-NMR δ(DMSO-d_6) 8.44(1-H,s,H-6), 3.97(3-H,s,OCH_3), 3.91(3-H,s,OCH_3), 0.21(9-H,s,$SiMe_3$). EI mass spectrum m/e 236 (M). Elemental analysis $C_{11}H_{16}N_2O_2Si$ calculated C, 55.9; H, 6.82; N, 11.85; found C, 56.0; H, 7.0; N, 12.0

2,4-Dimethoxy-5-ethynylpyrimidine (24) To a solution of 23 (0.81 g, 3.42 mmol) in dry THF (5 ml) was added a solution of tetrabutylammonium fluoride (1.08 g, 3.42 mmol) dissolved in dry THF (5 ml). The brown darkly coloured solution was stirred at room temperature for 5 minutes then methanol (5 ml) and silica gel (10 g) added. The reaction mixture was then absorbed onto the silica *in vacuo* and the product isolated by column chromatography with elution in 80:20 hexane/ethyl acetate followed by recrystallization from hexane to remove final traces of colour to give white crystals (0.34 g, 60%). M.pt. 83-84 °C (Lit[25] 83-84 °C, methanol or 82-84 °C[32], chloroform/60-80 petroleum ether). UV λ_{max} 277.0 nm, ϵ=7420 (Lit 255.0 nm, ϵ=4200). ^{1}H-NMR δ(DMSO-d_6) 8.47(1-H,s,H-6), 4.42(1-H,s,CH), 3.95 (3-H,s,OCH_3), 3.92(3-H,s,OCH_3). EI mass spectrum m/e 164 (M). Elemental analysis $C_8H_8N_2O_2$ calculated C, 58.53; H, 4.91; N, 17.06; found C, 58.5; H, 4.8; N, 17.2

5-Hydroxymethyl-2',3'-isopropylidineuridine (25) A solution of 2',3'-isopropylidineuridine (Sigma Chemical Company, Ltd, 10.00 g, 35.17 mmol) and paraformaldehyde (2.20 g) in 0.5M aqueous potassium hydroxide (70 ml) was heated to 50 °C for 2 days after which time TLC in 90:10 chloroform/methanol showed the absence of starting material. The solution was adjusted to pH 7 with glacial acetic acid and the solvent removed by evaporation *in vacuo*. The resulting viscous oil was dissolved in chloroform (100 ml), dried ($MgSO_4$), concentrated to a small volume and purified by short column chromatography with elution in 90:10 chloroform/methanol to give a white foam which is homogenous by TLC and ^{1}H-NMR and which can be used directly in the next step, (9.50 g, 86%). UV λ_{max} 264.0nm, ϵ=10255. ^{1}H-NMR δ(DMSO-d_6) 11.40 (1-H,s,N-H), 7.65(1-H, s,H-6), 5.85(1-H,d,H-1'), 5.14-4.65(4-H,m,H-2', H-3',2 OH), 4.10 (3-H, m,H-4',$\underline{CH_2}$OH), 3.55(2-H,t,H-5'), 1.46(3-H,s,CH_3), 1.28(3-H,s,CH_3). FAB mass spectrum m/e 315 $(M+H)^+$.

5-Formyl-2',3'-isopropylidineuridine (26) To a solution of pyridinium dichromate (33.21 g, 88.3 mmol) in dry DMF (40 ml) was added a solution of 25 (18.50 g, 58.86 mmol) in dry dichloromethane/DMF (7:1, 230 ml) and the resulting solution stirred at room temperature for 1 hour or until the black solution showed total conversion to a faster running nucleoside product by TLC in 95:5 chloroform/ethanol. The solvent was removed under high vacuum and the resulting black oil purified by column chromatography with elution in 95:5 chloroform/ethanol then recrystallization from ethanol to give white crystals (11.53 g, 63%). M.pt. 153-155 °C (Lit[28] 157-159 °C). UV λ_{max} 288.4nm, ϵ=10330. ^{1}H-NMR δ(DMSO-d_6) 11.88(1-H,s,N-H), 9.73(1-H,s,CHO), 8.68(1-H,s,H-6), 5.85(1-H.,d,H-1'), 5.15(1-H,t,5'-OH), 4.94(1-H,m,H-2'), 4.73(1-H,m,H-3'), 3.23(1-H,m,H-4'), 3.57(2-H,m,H-5'), 1.45(3-H,s,CH_3), 1.25(3-H,s,CH_3). FAB mass spectrum m/e 313 $(M+H)^+$. Elemental analysis $C_{13}H_{16}N_2O_7$ calculated C, 50.00;, H, 5.16; N, 8.97; found C, 50.0; H, 5.1; N, 9.2

5-(1-Hydroxy-2-nitroethyl)-2',3'-isopropylidineuridine (27) To a stirred solution of 26 (0.300 g, 0.96 mmol) in dry THF (5 ml) and dry nitromethane (5 ml) was added sodium hydride (0.182 g, 3.0 mmol) and the resulting yellow solution stirred at room temperature for 20 minutes. The solution was carefully acidified with glacial acetic acid (0.2 ml) and the product isolated by column chromatography with elution in 95:5 chloroform/methanol (0.23 g, 64%). M.pt. 110-114 °C. UV λ_{max} 262.8nm, ϵ=9820. ^{1}H-NMR δ(DMSO-d_6) 11.61(1-H,s,N-H), 7.83(1-H,d,H-6), 5.98(1-H, t,CH($\underline{OH}$)), 5.85 (1-H,d,H-1'), 5.07(2-H,m,H-2',5'-OH), 4.90(1-H,m,H-3'), 4.77(2-H,m, CH_2NO_2), 4.51(1-H,t,CH), 4.08(1-H,m,H-4'), 3.57(2-H,t,H-5'), 1.47(3-H, s,CH_3), 1.29(3-H,s,CH_3). FAB mass spectrum m/e 374 $(M+H)^+$. Elemental analysis $C_{14}H_{19}N_3O_9$ calculated C, 45.04; H, 5.13; N, 11.25; found C, 45.0; H, 5.1; N, 11.2

5'-*O*-Acetyl-(*E*)-5-(2-nitrovinyl)uridine (29) A solution of 27 (0.32 g, 0.86 mmol) in acetic anhydride (10 ml) was stirred at room temperature for 2 days after which time TLC showed complete conversion to a faster running nucleoside on TLC. The solvent was removed *in vacuo* and the yellow foam treated with 50% aqueous trifluoroacetic acid (10 ml). After 50 minutes the solution was evaporated to dryness and the product isolated by short column chromatography with elution in 90:10 chloroform/methanol followed by recrystallization from ethanol to give the product (0.07 g, 23%). M.pt. 145-148 °C. UV λ_{max} 329.0 nm, ϵ=17980. ^{1}H-NMR δ(DMSO-d_6) 11.95(1-H,bs,N-H), 8.44(1-H,s,H-6), 8.22(1-H,d,vinylic H,J=16Hz), 7.97(1-H,d,vinylic H,J=16 Hz), 5.78(1-H,d,H-1'), 5.48(1-H,d, 2'-OH), 5.32(1-H, d,3'-OH), 4.45-3.83(5-H,m,H-2', H-3',H-4'H-5'), 2.05-(3-H,s,ester CH_3). FAB mass spectrum m/e 358 $(M+H)^+$. Elemental analysis $C_{13}H_{15}N_3O_9$ calculated C, 43.70; H, 4.23; N, 11.76; found C, 43.4; H, 3.9; N, 11.6

5-(1-Nitromethyl-2-nitro)ethyl-2',3'-isopropylidineuridine (30) Sodium (0.116 g, 5.0 mmol) was dissolved in dry ethanol (15 ml) then nitromethane (0.30 g, 5.04 mmol) and 26 (0.315 g, 1.00 mmol) were added. The solution was heated under gentle reflux for 1.5 hours then adjusted to pH 7 with AcOH and evaporated *in vacuo*. The product was isolated by short column chromatography with elution in 95:5 chloroform/ethanol then recrystallization from ethanol to give colourless crystals (0.27 g, 64%). M.pt. 195-197 °C. UV λ_{max} 265.5nm, ϵ=8470. ^{1}H-NMR δ(DMSO-d_6) 11.70(1-H,s,N-H), 7.95(1-H,s,H-6), 5.76(1-H,s,H-1'), 5.14(1-H,t,5'-OH),, 4.87(5-H,m,CH_2NO_2, H-4'), 4.75(1-H,m,CH), 4.10-4-00(2-H,m,H-2',H-3'), 3.57(2-H,m,H-5'), 1.48(3-H,s,CH_3), 1.29(3-H,s,CH_3). FAB mass spectrum m/e 417 $(M+H)^+$. Elemental analysis $C_{15}H_{20}N_4O_{10}$ calculated C, 43.27; H, 4.84; N, 13.46 found C, 43.3; H, 4.7; N, 13.2

5-(1-Nitromethyl-2-nitro)ethyluridine (31) A solution of 30 (0.0986 g, 0.236 mmol) in 50% aqueous trifluoroacetic acid (5 ml) was stirred at room temperature for 30 minutes and was then evaporated to dryness under high vacuum and the product isolated by column chromatography followed by recrystallization from ethanol to give white crystals (0.062 g, 70%). M.pt. 97-98 °C. UV λ_{max} 268.0nm, ϵ=8850. ^{1}H-NMR δ(DMSO-d_6) 11.69(1-H, bs,N-H), 8.05(1-H, s,H-6), 5.74(1-H,d,H-1'), 5.42(1-H,d,2'-OH), 5.18 (1-H,t,5'-OH), 4.90(4-H,d,2 CH_2NO_2), 4.35(1-H,t,3'-OH), 4.25-3.50(6-H, m,H-2', H-3',H-4',H-5',CH). FAB mass spectrum m/e 377 $(M+H)^+$. Elemental analysis $C_{12}H_{16}N_4O_{10}$ calculated C, 38.3; H, 4.3; N, 14.9; found C, 38.2; H, 4.6; N, 14.6

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