Synthesis of 1-(Hydroxyalkoxy)pyrimidines, a Novel Series of Acyclic Nucleoside Analogues

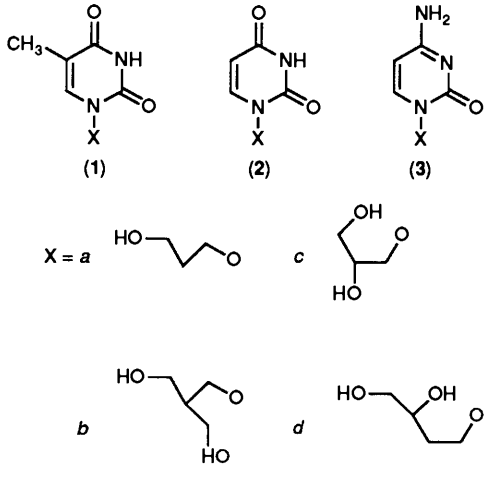
Michael R. Harnden, L. John Jennings, and Ann Parkin *
Smith Kline Beecham Pharmaceuticals, Biosciences Research Centre, Great Burgh, Yew Tree Bottom Road, Epsom, Surrey KT 18 5XQ

Syntheses of 1-(3-hydroxypropoxy), 1-[3-hydroxy-2-(hydroxymethyl)propoxy], 1-(2,3-dihydroxypropoxy), and 1-(3,4-dihydroxybutoxy) derivatives of thymine (**1a–d**) and uracil (**2a–d**) are described. These acyclonucleosides were obtained by cyclisation of appropriately functionalised ureas with either ethyl 3,3-diethoxy-2-methylpropionate (**4**) or methyl 3,3-dimethoxypropionate (**5**). The uracils (**2a–d**) were converted into cytosine analogues (**3a–d**) *via* intermediate 4-(1,2,4-triazol-1-yl) derivatives. (*E*)-5-(2-Bromovinyl) (**36**) and 5-vinyl (**37**) analogues of (**2a**) were prepared by palladium(II)-catalysed cross-coupling reactions on the 5-iodo derivative (**32**). The 5-fluoro-1-(hydroxyalkoxy)uracils (**41**) and (**42**) were obtained by alkylation of 5-fluoro-1-hydroxyuracil with a suitably functionalised halide. None of this series of acyclonucleosides showed activity in antiviral tests in cell cultures.

Since the discovery of acyclovir (ACV, Zovirax), a selective antiherpes virus agent,[1–3] considerable interest has been focussed on the preparation of novel acyclic analogues of nucleosides.[4,5] As a result of this research, a number of derivatives of guanine have been identified as potential antiviral drugs.[4–6] Some analogous acyclopyrimidines have also been synthesised,[4,5,7–11] the majority of which have shown no significant antiviral activity. However 1-[(1,3-dihydroxy-2-propoxy)methyl]cytosine (BW A1117U) has shown the same order of activity as its corresponding guanine analogue ganciclovir against human cytomegalovirus (CMV) and Epstein Barr virus (EBV).[12]

Our recent research has led us to the synthesis of acyclonucleosides in which the acyclic substituent is linked to the heterocyclic base by means of a nitrogen–oxygen bond. We have recently reported on the preparation of several guanine derivatives with potent antiherpes virus activity.[13–16]

In this paper we describe the synthesis of a series of 1-alkoxypyrimidines (**1a–d**), (**2a–d**), and (**3a–d**). In each case, the

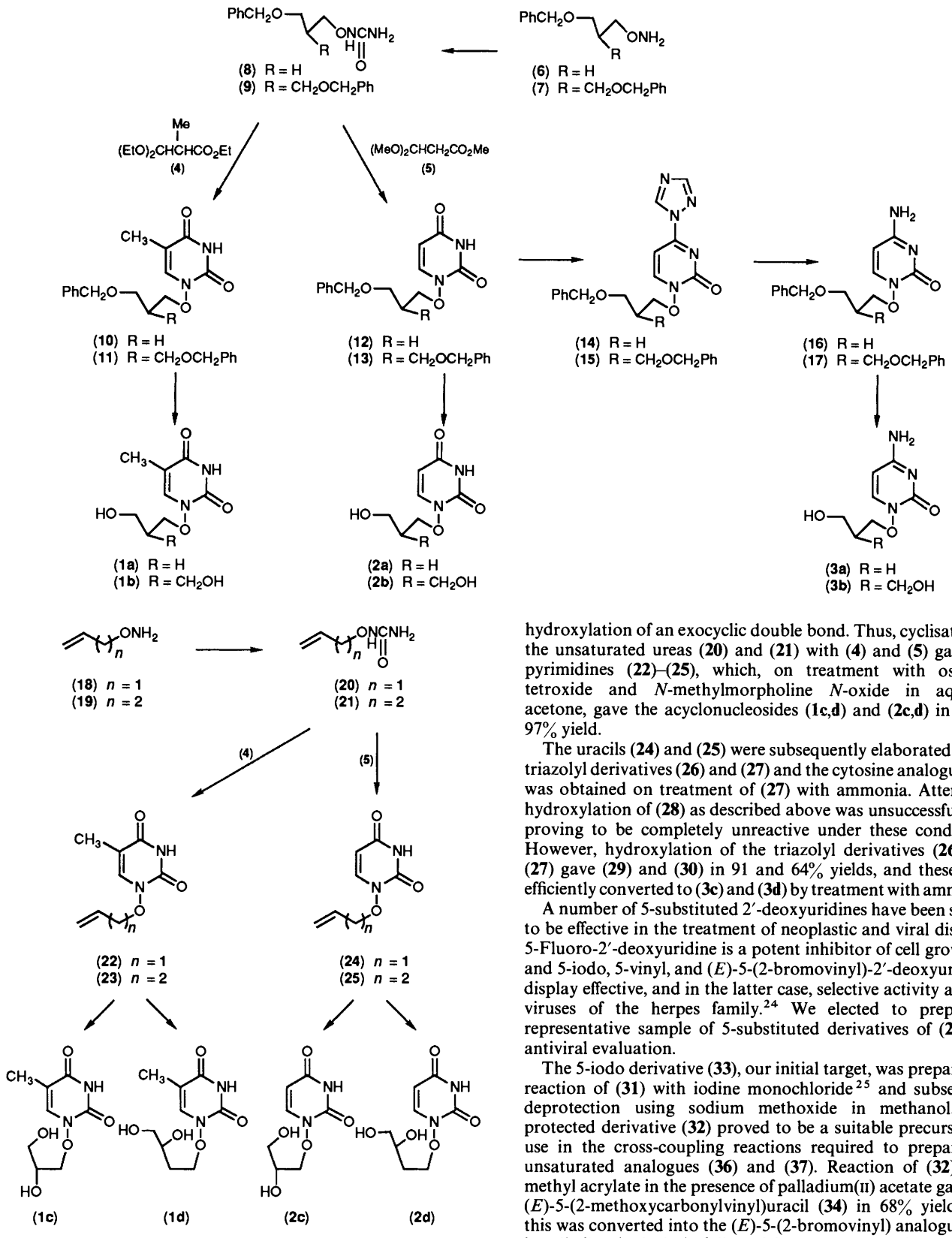


alkoxy substituent is structurally related to a portion of a nucleoside ribose moiety. Within this series is included compound (**3b**), which is closely related structurally to the antiviral acyclocytosine BW A1117U. Additionally, we report the preparation of several 5-substituted derivatives of (**2a**), related to known antiviral 2′-deoxyuridines. The antiviral activity of these compounds in cell cultures has been investigated.

Results and Discussion

Since oxidation of pyrimidines has not yet been achieved selectively at N-1 we elected to develop a general route to 1-alkoxypyrimidines using an adaptation of a published procedure for the syntheses of 1-benzyloxythymine and benzyloxyuracil.[18,19] This involved reaction of a suitably functionalised urea with either ethyl 3,3-diethoxy-2-methylpropionate[20] (**4**) or methyl 3,3-dimethoxypropionate (**5**). For the preparation of compounds (**10**)–(**13**) the ureas (**8**) and (**9**) were obtained in high yields by reaction of the alkoxy amines (**6**) and (**7**)[13] with aqueous acidic sodium cyanate. Attempted cyclisation of the ureas with (**4**) and (**5**) in refluxing sodium ethoxide in ethanol[18,19] gave poor yields of the required pyrimidines. A more satisfactory procedure was subsequently developed, involving preliminary formation of the anions of (**8**) and (**9**) using sodium hydride in dimethyl sulphoxide, followed by reaction with (**4**) or (**5**) at ambient or moderate (60 °C) temperatures, giving yields of up to 70% of cyclised products. Debenzylation of (**10**)–(**13**) was carried out by hydrogenolysis over 10% palladium on charcoal under acidic conditions. To avoid cleavage of the nitrogen–oxygen bond during this process, the reaction was carefully monitored, both by hydrogen uptake and by thin layer chromatography, and yields of 80–90% of the acyclonucleosides (**1a,b**) and (**2a,b**) were achieved.

For the preparation of the required cytosine derivatives we adopted methodology which has been developed for conversion of a number of uracil nucleosides into cytosine analogues.[21,22] This involved reaction of (**12**) and (**13**) with 1,2,4-triazole and phosphorus oxychloride or (4-chlorophenyl) phosphodichloridate to form the 4-(1,2,4-triazol-1-yl) derivatives (**14**) and (**15**). On treatment with ammonia the protected cytosines (**16**) and (**17**) were obtained in good yields. Debenzylation of cytosine nucleosides has often proved problematic due to their tendency towards cleavage to the parent base under conditions of catalytic reduction.[12] In the cases of (**16**) and (**17**), deprotection using atmospheric pressure hydrogenolysis over palladium on charcoal under acidic conditions occurred extremely rapidly. We were able to arrest the reaction without cleavage of the 1-alkoxy substituent and obtained the acyclonucleosides (**3a**) and (**3b**) in 80% yield.

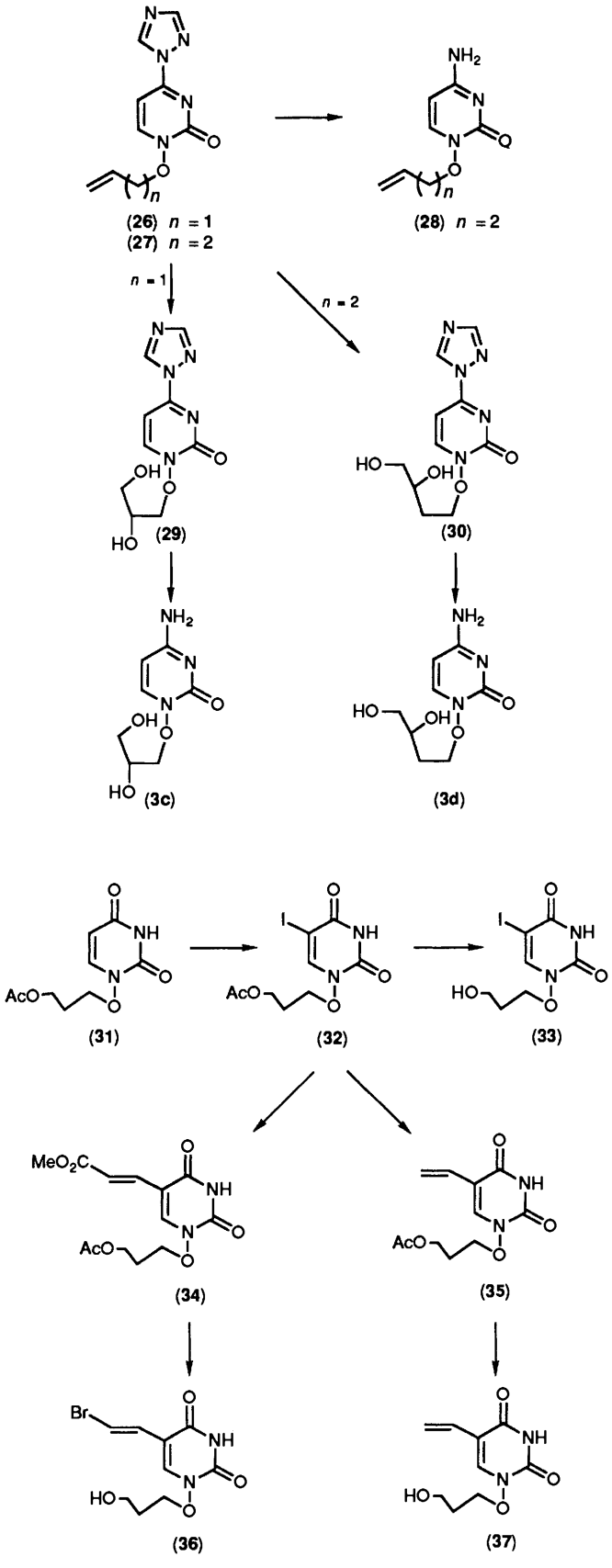


This general synthetic method was extended to the preparation of other 1-(hydroxyalkoxy)pyrimidines, (**1c,d**), (**2c,d**), and (**3c,d**). In these syntheses the need for protecting groups was obviated by introducing the hydroxy functionalities of the acyclic substituents at a later stage in the synthesis, by hydroxylation of an exocyclic double bond. Thus, cyclisation of the unsaturated ureas (**20**) and (**21**) with (**4**) and (**5**) gave the pyrimidines (**22**)–(**25**), which, on treatment with osmium tetroxide and *N*-methylmorpholine *N*-oxide in aqueous acetone, gave the acyclonucleosides (**1c,d**) and (**2c,d**) in up to 97% yield.

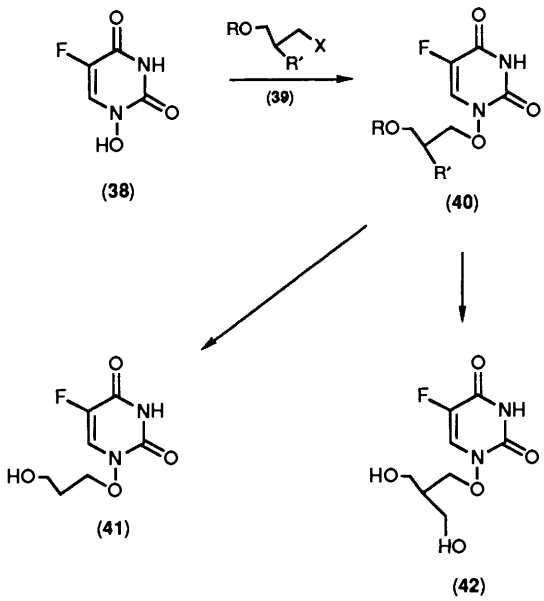
The uracils (**24**) and (**25**) were subsequently elaborated to the triazolyl derivatives (**26**) and (**27**) and the cytosine analogue (**28**) was obtained on treatment of (**27**) with ammonia. Attempted hydroxylation of (**28**) as described above was unsuccessful, (**28**) proving to be completely unreactive under these conditions. However, hydroxylation of the triazolyl derivatives (**26**) and (**27**) gave (**29**) and (**30**) in 91 and 64% yields, and these were efficiently converted to (**3c**) and (**3d**) by treatment with ammonia.

A number of 5-substituted 2′-deoxyuridines have been shown to be effective in the treatment of neoplastic and viral diseases. 5-Fluoro-2′-deoxyuridine is a potent inhibitor of cell growth,[23] and 5-iodo, 5-vinyl, and (*E*)-5-(2-bromovinyl)-2′-deoxyuridines display effective, and in the latter case, selective activity against viruses of the herpes family.[24] We elected to prepare a representative sample of 5-substituted derivatives of (**2a**) for antiviral evaluation.

The 5-iodo derivative (**33**), our initial target, was prepared by reaction of (**31**) with iodine monochloride[25] and subsequent deprotection using sodium methoxide in methanol. The protected derivative (**32**) proved to be a suitable precursor for use in the cross-coupling reactions required to prepare the unsaturated analogues (**36**) and (**37**). Reaction of (**32**) with methyl acrylate in the presence of palladium(II) acetate gave the (*E*)-5-(2-methoxycarbonylvinyl)uracil (**34**) in 68% yield, and this was converted into the (*E*)-5-(2-bromovinyl) analogue (**36**) by alkaline hydrolysis followed by treatment with *N*-bromosuccinimide.[26] In a related reaction sequence, the 5-vinyl derivative (**35**) was prepared in 57% yield by reaction of (**32**) with vinyl acetate in the presence of preactivated diacetatobis(triphenylphosphine)palladium(II) catalyst.[27] Deprotection with ammonia gave the required acyclopyrimidine (**37**).



The 5-fluoro analogues (**40a**) and (**40b**) were prepared by alkylation of 5-fluoro-1-hydroxyuracil (**38**).[28] After initial formation of a dianion of (**38**), reaction with the appropriately



For (**39**), (**40**) **a**; R = COPh, R^1 = H, X = Br
b; R = CH_2Ph, R^1 = CH_2OCH_2Ph, X = I

functionalised halides (**39a**) and (**39b**) gave the uracils (**40a**) and (**40b**) in 32 and 65% yields. Conventional deprotection techniques afforded the final products (**41**) and (**42**) in 56 and 76% yields.

The acyclonucleosides (**1a–d**), (**2a–d**), (**3a–d**), (**33**), (**36**), (**37**), (**41**), and (**42**) were tested for activity against viruses of the herpes family in cell culture. No significant activity was noted against herpes simplex virus types 1 and 2, varicella zoster, cytomegalovirus or Epstein-Barr virus, and, at concentrations up to 100 μg/ml, none of the compounds was toxic for the cell monolayers used in the tests.

Experimental

IR spectra were recorded on a Perkin-Elmer 580 instrument; UV spectra were recorded on a Cary 219 spectrometer. NMR spectra were recorded on a JEOL GX270 spectrometer. Mass spectrometry was performed using a VG 70–70 instrument operating at 70 e.V. M.p.s were determined using a Reichert–Kofler apparatus and are uncorrected. Elemental analysis was carried out on a Carlo Erba model 1106 analyser. Organic solutions of products were dried using magnesium sulphate and chromatography was performed on Merck 7736 60 H silica gel. All compounds were homogeneous by TLC on silica gel $60F_{254}$ coated aluminium sheets. Compound (**18**) was commercially available (Aldrich) and details of the preparation of compound (**19**) together with its full characterisation appear in ref. 13.

General Procedure for the Preparation of Compounds (**8**), (**9**), (**20**), *and* (**21**).—Sodium cyanate (1.3 mmol) was added in portions to a solution of the alkoxy amine hydrochloride (1 mmol) in 0.5M hydrochloric acid (2 ml) at 0 °C. After addition the mixture was stirred at room temperature for 30 min.

Work-up method A. The mixture was extracted with chloroform (10 ml), and the organic extract was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure.

Work-up method B. The solvent was removed under reduced pressure, co-evaporating with methanol. The solid residue was extracted with chloroform at reflux temperature, filtered, dried, and evaporated under reduced pressure.

N-(3-*Benzyloxypropoxy*)*urea* (**8**) was obtained as a white solid by method A and purified by crystallisation from ethyl acetate (93%, 82 mmolar scale), m.p. 70–71 °C; ν_{max}(KBr) 3 440, 3 200, 2 890, 1 660, 1 595, and 1 450 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.84 (2 H, m, $CH_2CH_2CH_2$), 3.5 (3 H, t, *J* 6.3 Hz, CH_2OCH_2Ph), 3.75 (2 H, t, *J* 6.3 Hz, CH_2ONH), 4.45 (2 H, s, OCH_2Ph), 6.31 (2 H, s, D_2O exchangeable, NH_2), 7.33 (5 H, m, C_6H_5), and 8.95 (1 H, s, NH) (Found: C, 59.0; H, 7.2; N, 12.4. $C_{11}H_{16}N_2O_3$ requires C, 58.9; H, 7.2; N, 12.5%).

N-[3-*Benzyloxy*-2-(*benzyloxymethyl*)*propoxy*]*urea* (**9**) was obtained as an oil by method A, after purification by chromatography on silica gel, eluting with ethyl acetate–hexane (2:1) (80%, 3 mmolar scale); ν_{max}(KBr) 3 415, 3 380, 3 289, 3 202, 3 089, 3 064, 3 031, 2 918, 2 872, 1 662, 1 600, 1 540, 1 496, 1 479, 1 454, and 1 429 cm^{-1}; δ_H($CDCl_3$) 2.34 (1 H, m, CH), 3.56 (4 H, m, 2 × CH_2OCH_2Ph), 3.96 (2 H, d, *J* 5.5 Hz, CH_2ONH), 4.49 (4 H, s, 2 × OCH_2Ph), 5.45 (2 H, br s, NH_2), and 7.30 (11 H, m, 2 × C_6H_5 plus D_2O exchangeable NH); *m/z* (FAB +ve ion, thioglycerol), MH^+ 345.

N-(*Prop*-2-*enyloxy*)*urea* (**20**) was obtained as a white solid by method B and purified by crystallisation from ethyl acetate–hexane (97%, 90 mmolar scale), m.p. 84–85 °C; ν_{max}(KBr) 3 400, 3 270, 3 190, 3 080, 2 985, 2 945, 2 915, 2 850, 1 615, 1 600, 1 460, 1 436, and 1 415 cm^{-1}; δ_H[$(CD_3)_2SO$] 4.18 (2 H, d, *J* 7 Hz, CH_2), 5.21 [1 H, dd, *J* 10 and 1 Hz, (*Z*)-H of $=CH_2$], 5.30 [1 H, dd, *J* 17 and 1 Hz, (*E*)-H of $=CH_2$], 5.97 (1 H, m, =CH), 6.35 (2 H, s, D_2O exchangeable, NH_2), and 8.96 (1 H, s, D_2O exchangeable, NH) (Found: C, 41.4; H, 6.7; N, 24.0. $C_4H_8N_2O_2$ requires C, 41.4; H, 6.9; N, 24.1%).

N-(*But*-3-*enyloxy*)*urea* (**21**) was obtained as a white solid by method B and purified by crystallisation from ethyl acetate (84%, 16 mmolar scale), m.p. 95–96 °C; ν_{max}(KBr) 3 413, 3 277, 3 181, 3 083, 3 002, 2 974, 2 958, 2 928, 2 863, 1 665, 1 596, 1 471, and 1 432 cm^{-1}; δ_H($CDCl_3$) 2.42 (2 H, m, CH_2), 3.92 (2 H, d, *J* 6.5 Hz, CH_2ON), 5.15 (2 H, m, $=CH_2$), 5.54 (2 H, br s, D_2O exchangeable, NH_2), 5.80 (1 H, m, =CH), and 7.60 (1 H, s, D_2O exchangeable, NH) (Found: C, 46.1; H, 7.8; N, 21.3. $C_5H_{10}N_2O_2$ requires C, 46.1; H, 7.7; N, 21.5%).

General Method for the Preparation of Compounds (**10**)–(**13**) *and* (**22**)–(**25**).—A dispersion of sodium hydride in oil (60%; 1.5 mmol) was washed with two portions of dry ether under nitrogen. After decanting the solvent, the solid was suspended in dry dimethyl sulphoxide (1 ml) and the urea (1 mmol) was added. After being stirred at room temperature for 4 h, the mixture was treated with the appropriate propionate (1 mmol) and either stirred at room temperature or heated at 60 °C. The mixture was evaporated under reduced pressure and the residue treated with methanol (2 ml) and acidified by addition of saturated methanolic hydrogen chloride. After being heated at reflux temperature for 40 min the mixture was filtered, the filtrate evaporated under reduced pressure, and the residual oil chromatographed on silica gel.

1-(3-*Benzyloxypropoxy*)*thymine* (**10**) was obtained as a gum in 34% yield (7 mmolar scale) after the reaction mixture had been stirred overnight at room temperature and the product chromatographed on silica gel, eluting with ethyl acetate–hexane (1:3); ν_{max}(film) 3 200, 3 060, 2 960, 2 870, 1 700, and 1 450 cm^{-1}; δ_H($CDCl_3$) 1.86 (3 H, d, *J* 1 Hz, CH_3), 2.02 (2 H, m, $CH_2CH_2CH_2$), 3.63 (2 H, t, *J* 6.3 Hz, CH_2OCH_2Ph), 4.27 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.53 (2 H, s, OCH_2Ph), 7.18 (1 H, q, *J* 1 Hz, 6-H), 7.34 (5 H, m, C_6H_5), and 9.72 (1 H, s, D_2O exchangeable, NH) (Found: C, 62.3; H, 6.3; N, 9.4. $C_{15}H_{18}N_2O_4$ requires C, 62.05; H, 6.25; N, 9.65%).

1-[3-*Benzyloxy*-2-(*benzyloxymethyl*)*propoxy*]*thymine* (**11**) was obtained as a gum in 35% yield (3 mmolar scale) after the reaction mixture had been stirred overnight at room temperature and the product chromatographed on silica gel, eluting the ethyl acetate–hexane (1:1); ν_{max}(film) 3 180, 3 060, 3 030, 2 950, 2 920, 2 860, 1 720, 1 680, 1 495, 1 455, and 1 420 cm^{-1}; δ_H($CDCl_3$) 1.83 (3 H, d, *J* 1 Hz, CH_3), 2.40 (1 H, m, CH), 3.63 (4 H, d, *J* 6 Hz, 2 × CH_2OCH_2Ph), 4.26 (2 H, d, *J* 6 Hz, CH_2ON), 4.51 (4 H, s, 2 × OCH_2Ph), 7.13 (1 H, q, *J* 1 Hz, 6-H), 7.33 (10 H, m, 2 × C_6H_5), and 8.48 (1 H, s, D_2O exchangeable, NH) (Found: C, 67.3; H, 6.5; N, 6.8. $C_{23}H_{26}N_2O_5$ requires C, 67.3; H, 6.4; N, 6.8%).

1-(3-*Benzyloxypropoxy*)*uracil* (**12**) was obtained in 72% yield (10 mmolar scale) after the reaction mixture had been heated at 60 °C overnight and the product chromatographed on silica gel, eluting with ethyl acetate–hexane (3:2), and recrystallised from acetone–diethyl ether; m.p. 78–80 °C; ν_{max}(KBr) 3 450, 3 120, 1 730, 1 450, and 1 410 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.90 (2 H, m, $CH_2CH_2CH_2$), 3.56 (2 H, t, *J* 6.3 Hz, CH_2OCH_2Ph), 4.16 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.50 (2 H, s, OCH_2Ph), 5.45 (1 H, d, *J* 8 Hz, 5-H), 7.33 (5 H, m, C_6H_5), 7.90 (1 H, d, *J* 8 Hz, 6-H), and 11.46 (1 H, s, D_2O exchangeable, NH) (Found: C, 60.9; H, 5.8; N, 10.2. $C_{14}H_{17}N_2O_4$ requires C, 60.85; H, 5.8; N, 10.1%).

1-[3-*Benzyloxy*-2-(*benzyloxymethyl*)*propoxy*]*uracil* (**13**) was obtained in 56% yield (7 mmolar scale) after the reaction mixture had been stirred at room temperature overnight and the product chromatographed on silica gel, eluting with ethyl acetate–hexane (1:1), and recrystallised from ethyl acetate; m.p. 88–89 °C; ν_{max}(film) 3 180, 3 080, 3 050, 3 020, 2 940, 2 900, 2 850, 1 730, 1 680, 1 620, 1 560, 1 490, 1 450, and 1 415 cm^{-1}; δ_H($CDCl_3$) 2.40 (1 H, m, CH), 3.63 (4 H, m, 2 × CH_2OCH_2Ph), 4.26 (2 H, d, *J* 6 Hz, CH_2ON), 4.51 (4 H, s, 2 × OCH_2Ph), 5.50 (1 H, d, *J* 8 Hz, 5-H), 7.20 (1 H, d, *J* 8 Hz, 6-H), 7.30 (10 H, m, 2 × C_6H_5), and 9.05 (1 H, s, D_2O exchangeable, NH) (Found: C, 66.4; H, 6.3; N, 6.95. $C_{22}H_{24}N_2O_5$ requires C, 66.65; H, 6.1; N, 7.0%).

1-(*Prop*-2-*enyloxy*)*thymine* (**22**) was obtained in 56% yield (9 mmolar scale) after the reaction mixture had been heated at 60 °C overnight and the product chromatographed on silica gel, eluting with ethyl acetate–hexane (1:1), and recrystallised from ethyl acetate–hexane; m.p. 74–75 °C; ν_{max}(KBr) 3 431, 3 168, 3 074, 3 031, 2 959, 2 929, 2 892, 2 824, 1 717, 1 675, 1 467, 1 445, and 1 423 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.74 (3 H, d, *J* 1 Hz, CH_3), 4.58 (2 H, d, *J* 7 Hz, CH_2), 4.29 (2 H, m, $=CH_2$), 6.02 (1 H, m, =CH), 7.83 (1 H, q, *J* 1 Hz, 6-H), and 11.47 (1 H, s, D_2O exchangeable, NH) (Found: C, 52.7; H, 5.35; N, 15.4. $C_8H_{10}N_2O_3$ requires C, 52.7; H, 5.5; N, 15.4%).

1-(*But*-3-*enyloxy*)*thymine* (**23**) was obtained in 37% yield (4 mmolar scale) after the reaction mixture had been heated at 60 °C for 7 h, and the product chromatographed on silica gel, eluting with ethyl acetate–hexane (2:1), and recrystallised from ethyl acetate–hexane; m.p. 82–83 °C; ν_{max}(KBr) 3 429, 3 194, 3 069, 2 981, 2 926, 2 853, 2 826, 1 734, 1 714, 1 684, 1 665, 1 467, 1 452, 1 424, and 1 409 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.75 (3 H, d, *J* 1 Hz, CH_3), 2.40 (2 H, m, CH_2CH_2ON), 4.12 (2 H, t, *J* 6.5 Hz, CH_2ON), 5.08 [1 H, dd, *J* 1.5 and 10.5 Hz, (*Z*)-H of $=CH_2$], 5.18 [1 H, dd, *J* 1.5 and 17 Hz, (*E*)-H of $=CH_2$], 5.60 (1 H, m, =CH), 7.82 (1 H, q, *J* 1 Hz, 6-H), and 11.45 (1 H, s, D_2O exchangeable, NH) (Found: C, 55.05; H, 5.8; N, 14.3. $C_9H_{12}N_2O_3$ requires C, 55.1; H, 6.2; N, 14.3%).

1-(*Prop*-2-*enyloxy*)*uracil* (**24**) was obtained in 60% yield (35 mmolar scale) after the reaction mixture had been heated at 60 °C overnight and the product chromatographed on silica gel, eluting with ethyl acetate–hexane (2:1), and crystallised from ethyl acetate–hexane; m.p. 130–131 °C; ν_{max}(KBr) 3 431, 3 118, 3 102, 3 085, 2 985, 2 904, 2 805, 1 771, 1 745, 1 720, 1 665, 1 646, 1 615, 1 453, 1 426, and 1 410 cm^{-1}; δ_H[$(CD_3)_2SO$] 4.68 (2 H, d, *J* 6.5 Hz, CH_2), 5.49 (3 H, m, 5-H plus $=CH_2$), 6.10 (1 H, m, =CH), 8.01 (1 H, d, *J* 8 Hz, 6-H), and 11.56 (1 H, s, D_2O exchangeable, NH) (Found: C, 50.0; H, 4.8; N, 16.8. $C_7H_8N_2O_3$ requires C, 50.0; H, 4.8; N, 16.7%).

1-(*But*-3-*enyloxy*)*uracil* (**25**) was obtained in 50% yield (8

mmolar scale) after the reaction mixture had been stirred overnight at room temperature and the product chromatographed on silica gel, eluting with ethyl acetate–hexane (1:2), and crystallised from ethyl acetate–hexane; m.p. 108–108.5 °C; ν_{max}(KBr) 3 424, 3 117, 3 100, 3 077, 3 005, 2 925, 2 825, 2 805, 1 768, 1 745, 1 712, 1 669, 1 642, 1 617, 1 433, 1 426, and 1 412 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.40 (2 H, m, CH_2CH_2ON), 4.13 (2 H, t, *J* 6.5 Hz, CH_2ON), 5.13 (1 H, m, =CH_2), 5.47 (1 H, d, *J* 8 Hz, 5-H), 5.85 (1 H, m, =CH), 7.92 (1 H, d, *J* 8 Hz, 6-H), and 11.46 (1 H, s, D_2O exchangeable, NH) (Found: C, 52.9; H, 5.45; N, 15.3. $C_8H_{10}N_2O_3$ requires C, 52.7; H, 5.5; N, 15.4%).

1-(3-*Benzyloxypropoxy*)-4-(1,2,4-*triazol*-1-*yl*)*pyrimidin*-2(1H)-*one* (**14**).—Phosphorus oxychloride (0.5 ml, 5.3 mmol) was added to a solution of 1,2,4-triazole (1.2 g, 1.8 mmol) in acetonitrile (5 ml). The mixture was cooled to 0 °C and treated with triethylamine (2.5 ml, 18 mmol) and a solution of compound (**12**) (0.49 g, 1.8 mmol) in acetonitrile (5 ml). The mixture was stirred overnight at room temperature and treated with additional triazole (1.2 g, 1.8 mmol), phosphorus oxychloride (0.5 ml, 5.3 mmol) and triethylamine (2.5 ml, 18 mmol). After the reaction mixture had been stirred for 48 h triethylamine (2.5 ml) and water (1 ml) were added and the solvent removed under reduced pressure. The residue was dissolved in chloroform (50 ml), and the solution washed with water (20 ml), dried, and evaporated under reduced pressure. The residue was chromatographed on silica gel, eluting with ethyl acetate–hexane (2:1) to give the *title compound* (**14**) as a solid which was crystallised from ethyl acetate (0.2 g, 34%), m.p. 103–105 °C; ν_{max}(KBr) 3 440, 3 140, 3 085, 3 035, 2 940, 2 920, 2 880, 2 860, 2 850, 2 840, 2 800, 1 700, 1 615, 1 537, 1 515, 1 495, 1 480, 1 455, 1 435, and 1 412 cm^{-1}; δ_H($CDCl_3$) 2.08 (2 H, m, $CH_2CH_2CH_2$), 3.68 (2 H, t, *J* 6 Hz, CH_2OCH_2Ph), 4.46 (4 H, t, *J* 6 Hz, CH_2ON), 4.55 (2 H, s, OCH_2Ph), 6.90 (1 H, d, *J* 7 Hz, 5-H), 7.36 (5 H, m, C_6H_5), 7.86 (1 H, d, *J* 7 Hz, 6-H), 8.12 (1 H, s, CH), and 9.21 (1 H, s, CH) (Found: C, 58.35; H, 5.3; N, 21.2. $C_{16}H_{17}N_5O_3$ requires C, 58.7; H, 5.2; N, 21.4%).

1-[3-*Benzyloxy*-2-(*benzyloxymethyl*)*propoxy*]-4-(1,2,4-*triazol*-1-*yl*)*pyrimidin*-2(1H)-*one* (**15**) was prepared by the method described for (**14**) and was obtained after chromatography on silica gel, eluting with ethyl acetate–hexane (2:1) as an oil (73%, 1 mmolar scale); ν_{max}(film) 3 120, 3 090, 3 060, 2 910, 2 860, 1 700, 1 620, 1 545, 1 510, 1 460, and 1 410 cm^{-1}; δ_H($CDCl_3$) 2.46 (1 H, m, CH), 3.67 (4 H, m, 2 × CH_2OCH_2Ph), 4.43 (2 H, d, *J* 6 Hz, CH_2ON), 4.53 (4 H, s, 2 × OCH_2Ph), 6.84 (1 H, d, *J* 7 Hz, 5-H), 7.35 (10 H, m, 2 × C_6H_5), 7.77 (1 H, d, *J* 7 Hz, 6-H), 8.12 (1 H, s, CH), and 9.21 (1 H, s, CH) (Found: C, 64.25; H, 5.7; N, 15.3. $C_{24}H_{25}N_5O_4$ requires C, 64.4; H, 5.6; N, 15.65%).

1-(3-*Hydroxypropoxy*)*thymine* (**1a**).—A solution of compound (**10**) (0.7 g, 2.4 mmol) in methanol (20 ml) and saturated methanolic hydrogen chloride (0.25 ml) was treated with 5% palladium—charcoal catalyst (20 mg) and hydrogenated at atmospheric pressure and room temperature until uptake of hydrogen ceased (5–10 min). The mixture was filtered through a glass fibre pad, and the catalyst washed with tetrahydrofuran. The filtrate was neutralised with ammonia (*d* 0.880) and the solvent was removed under reduced pressure. The residue was dissolved in chloroform, dried, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel, eluting with ethyl acetate–hexane (1:3) to give the *title compound* (**1a**) as a solid which was crystallised from ethanol (450 mg, 93%), m.p. 145–146 °C; λ_{max}(MeOH) 270 (ε 8 972) nm; ν_{max}(KBr) 3 450, 3 070, 3 000, 2 830, 1 730, 1 680, 1 470, and 1 430 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.75 (5 H, m, CH_3, $CH_2CH_2CH_2$), 3.52 (2 H, t, *J* 6.1 Hz, CH_2OH), 4.15 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.55 (1 H, s, D_2O exchangeable, OH), 7.8 (1 H, q, *J* 1.1 Hz, 6-H), and 11.44 (1 H, s, D_2O exchangeable, NH) (Found: C, 48.5; H, 6.1; N, 14.0. $C_8H_{12}N_2O_4$ requires C, 48.0; H, 6.0; N, 14.0%).

1-[3-*Hydroxy*-2-(*hydroxymethyl*)*propoxy*]*thymine* (**1b**) was prepared on a 0.65 mmolar scale using the method described for (**1a**). After hydrogenation for 30 min, and chromatography on silica gel, eluting with chloroform–methanol (10:1), (**1b**) was obtained as a glass (83%) which was crystallised as a hygroscopic solid from a small volume of isopropyl alcohol, m.p. 91–93 °C; λ_{max}(H_2O) 270 (ε 9 400) nm; ν_{max}(KBr) 3 343, 3 062, 2 985, 2 973, 2 948, 2 928, 2 896, 1 715, 1 698, 1 676, 1 663, 1 460, 1 431, and 1 401 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.75 (3 H, d, *J* 1 Hz, CH_3), 1.88 (1 H, m, CH), 3.48 (4 H, br m, 2 × CH_2OH), 4.07 (2 H, d, *J* 6 Hz, CH_2ON), 4.53 (2 H, br s, 2 × D_2O exchangeable, OH), 7.83 (1 H, q, *J* 1 Hz, 6-H), and 11.46 (1 H, br s, D_2O exchangeable, NH) (Found: C, 47.2; H, 6.2; N, 12.1. $C_9H_{14}N_2O_5$ requires C, 47.0; H, 6.1; N, 12.2%).

1-(3-*Hydroxypropoxy*)*uracil* (**2a**).—A solution of compound (**12**) (440 mg, 1.59 mmol) in methanol (25 ml) and methanolic hydrogen chloride (0.25 ml) was treated with 5% palladium–charcoal catalyst (10–15 mg) and hydrogenated at atmospheric pressure and room temperature until uptake of hydrogen ceased (4 min). The mixture was filtered through a glass fibre pad and the filtrate was treated with 1–2 drops of ammonia (*d* 0.880). The solvent was removed under reduced pressure and the residue purified by chromatography on silica gel, eluting with chloroform–methanol (97:3) to give the *title compound* (**2a**) as a solid which was crystallised from acetone–diethyl ether, (270 mg, 91%), m.p. 91–92 °C; λ_{max}(EtOH) 266 nm (ε 9 356); ν_{max}(KBr) 3 360, 3 120, 2 980, 2 300, 1 710, 1 665, 1 450, and 1 410 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.76 (2 H, m, $CH_2CH_2CH_2$), 3.52 (2 H, t, *J* 6.3 Hz, CH_2OH), 4.14 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.56 (1 H, br s, D_2O exchangeable, OH), 5.5 (1 H, d, *J* 8 Hz, 5-H), 7.95 (1 H, d, *J* 8 Hz, 6-H), and 11.45 (1 H, br s, D_2O exchangeable, NH) (Found: C, 44.9; H, 5.4; N, 14.9. $C_7H_{10}N_2O_4$ requires C, 45.15; H, 5.4; N, 15.05%).

1-[3-*Hydroxy*-2-(*hydroxymethyl*)*propoxy*]*uracil* (**2b**) was prepared on a 0.8 mmolar scale by the method described for (**2a**). After hydrogenation for 30 min and chromatography on silica gel, eluting with chloroform–methanol (10:1), (**2b**) was obtained as a solid (80%) which was crystallised from ethanol, m.p. 110–111 °C; λ_{max}(H_2O) 266 nm (ε 9 720); ν_{max}(KBr) 3 300, 3 260, 3 100, 3 040, 2 970, 2 960, 2 920, 2 890, 2 840, 1 720, 1 665, 1 655, 1 465, and 1 430 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.88 (1 H, m, CH), 3.48 (4 H, m, 2 × CH_2OH), 4.09 (2 H, d, *J* 6 Hz, CH_2), 4.53 (2 H, br, D_2O exchangeable, OH's), 5.49 (1 H, d, *J* 8 Hz, 5-H), 7.94 (1 H, d, *J* 8 Hz, 6-H), and 11.47 (1 H, br s, D_2O exchangeable, NH) (Found: C, 44.2; H, 5.6; N, 12.8. $C_8H_{12}N_2O_5$ requires C, 44.45; H, 5.6; N, 12.9%).

1-(3-*Hydroxypropoxy*)*cytosine* (**3a**).—A solution of compound (**16**) (0.26 g, 0.95 mmol) in methanol (14 ml) and saturated methanolic hydrogen chloride (1 ml) was treated with 5% palladium–charcoal catalyst (60 mg). The mixture was hydrogenated at atmospheric pressure and room temperature for 3 min, filtered through a glass fibre pad, neutralised by addition of ammonia (*d* 0.880), evaporated under reduced pressure and chromatographed on silica gel, eluting with chloroform–methanol (10:1) of increasing polarity to (5:1) to give the *title compound* (**3a**) as a solid which was crystallised from methanol (140 mg, 80%), m.p. 152–153 °C; λ_{max}(H_2O) 274 nm (ε 8 480); ν_{max}(KBr) 3 408, 3 393, 3 104, 3 047, 2 963, 2 939, 2 896, 1 660, 1 623, 1 518, 1 484, and 1 470 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.73 (2 H, m, $CH_2CH_2CH_2$), 3.52 (2 H, m, CH_2OH), 4.10 (2 H, t, *J* 6.5 Hz, CH_2ON), 4.61 (1 H, t, *J* 5.5 Hz, D_2O exchangeable, OH), 5.58 (1 H, d, *J* 7.5 Hz, 5-H), 7.15 (2 H, br, D_2O exchangeable, NH_2), and 7.81 (1 H, d, *J* 7.5 Hz, 6-H) (Found: C,

45.2; H, 6.1; N, 22.55. $C_7H_{11}N_3O_3$ requires C, 45.4; H, 6.0; N, 22.7%).

1-[3-*Hydroxy*-2-(*hydroxymethyl*)*propoxy*]*cytosine* (**3b**) was prepared on a 0.35 mmolar scale using the method described for (**3a**). After hydrogenation for 9 min, and chromatography on silica gel, eluting with chloroform–methanol (10:1) of increasing polarity to (5:1), (**3b**) was obtained as a glass (79%) which was converted into its hydrochloride salt by treatment with methanolic hydrogen chloride and crystallised from methanol, m.p. 171–173 °C; $\lambda_{max}(H_2O)$ 274 nm (ε 8 644); ν_{max}(KBr) 3 333, 3 158, 3 121, 3 095, 2 943, 2 881, 2 810, 2 758, 1 741, 1 715, 1 676, 1 620, 1 577, 1 533, 1 470, 1 456, 1 418, and 1 404 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 1.90 (1 H, m, CH), 3.50 (4 H, m, 2 × CH_2OH), 3.80 (>2 H, br, 2 × D_2O exchangeable OH plus H_2O), 4.15 (2 H, d, *J* 6 Hz, CH_2ON), 5.94 (1 H, d, *J* 8 Hz, 5-H), 8.25 (1 H, d, *J* 8 Hz, 6-H), 8.31 (1 H, s, D_2O exchangeable, NH), and 9.30 (1 H, s, D_2O exchangeable, NH) (Found: C, 37.7; H, 5.5; N, 15.9. $C_8H_{14}ClN_3O_4 \cdot 0.25H_2O$ requires C, 37.5; H, 5.7; N, 16.4%).

(R,S)1-(2,3-*Dihydroxypropoxy*)*thymine* (**1c**).—A solution of compound (**22**) (0.85 g, 4.6 mmol) in acetone (24 ml) and water (8 ml) was treated with a small crystal of osmium tetroxide. After being stirred at room temperature for 10 min, the solution was treated with *N*-methylmorpholine *N*-oxide (0.92 g, 6.8 mmol) and stirred at room temperature for 3 days. The solvent was removed under reduced pressure and the residue chromatographed on silica gel, eluting with chloroform–methanol (5:1) to give, after recovery of unchanged starting material (0.39 g), *the title compound* (**1c**) as an oil (0.36 g, 68%), which solidified with time and was crystallised from ethanol, m.p. 105–106 °C; $\lambda_{max}(H_2O)$ 270.5 nm (ε 9 060); ν_{max}(film) 3 387, 3 206, 3 057, 2 949, 2 931, 2 890, 2 819, 1 706, 1 678, 1 462, 1 440, and 1 420 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 1.76 (3 H, s, CH_3), 3.39 (2 H, m, CH_2OH), 3.73 (1 H, m, CH), 3.94 (1 H, dd, *J* 7 and 10 Hz, CH of CH_2ON), 4.17 (1 H, dd, *J* 3 and 10 Hz, CH of CH_2ON), 4.68 (1 H, t, *J* 5.5 Hz, D_2O exchangeable, CH_2OH), 5.01 (1 H, d, *J* 5.5 Hz, D_2O exchangeable, CHO*H*), 7.81 (1 H, s, 6-H), and 11.47 (1 H, s, D_2O exchangeable, NH) (Found: C, 44.5; H, 5.55; N, 12.6. $C_8H_{12}N_2O_5$ requires C, 44.45; H, 5.6; N, 13.0%).

(R,S)1-(3,4-*Dihydroxybutoxy*)*thymine* (**1d**) was prepared from compound (**23**) by the method described for (**1c**) and was obtained after chromatography on silica gel, eluting with chloroform–methanol (5:1) as a glass (0.25 g, 97%) which was crystallised from isopropyl alcohol, m.p. 94–96 °C; $\lambda_{max}(H_2O)$ 271 nm (ε 7 900); ν_{max}(KBr) 3 390, 2 957, 2 928, 2 852, 2 814, 1 721, 1 654, 1 463, 1 451, and 1 424 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 1.56 (1 H, m, CH of CH_2CH_2ON), 1.75 (3 H, s, CH_3), 1.80 (1 H, m, CH of CH_2CH_2ON), 3.30 (2 H, m, CH_2OH), 3.58 (1 H, m, CH), 4.15 (2 H, m, CH_2ON), 4.56 (1 H, t, *J* 5 Hz, D_2O exchangeable, OH), 4.65 (1 H, d, *J* 5 Hz, D_2O exchangeable, OH), 7.84 (1 H, s, 6-H), and 11.45 (1 H, s, D_2O exchangeable, NH) (Found: C, 45.0; H, 6.0; N, 11.6. $C_9H_{14}N_2O_5 \cdot H_2O$ requires C, 45.2; H, 6.3; N, 11.7%).

(R,S)1-(2,3-*Dihydroxypropoxy*)*uracil* (**2c**) was prepared from compound (**24**) by the method described for (**1c**) and was obtained after chromatography on silica gel, eluting with chloroform–methanol (5:1) as a solid (95%, 14 mmolar scale) which was recrystallised from ethanol; m.p. 104–105 °C; $\lambda_{max}(H_2O)$ 266 nm (ε 9 630); ν_{max}(KBr) 3 407, 3 099, 3 033, 2 806, 1 715, 1 658, 1 453, and 1 410 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 3.35 (>2 H, m, CH_2OH plus H_2O), 3.72 (1 H, m, CH), 3.96 (1 H, dd, *J* 7 and 10.5 Hz, CH of CH_2ON), 4.18 (1 H, dd, *J* 3.5 and 10.5 Hz, CH of CH_2ON), 4.68 (1 H, br, D_2O exchangeable, OH), 5.02 (1 H, br, D_2O exchangeable, OH), 5.48 (1 H, d, *J* 8 Hz, 5-H), 7.90 (1 H, d, *J* 8 Hz, 6-H), and 11.47 (1 H, br, D_2O exchangeable, NH) (Found: C, 41.6; H, 4.8; N, 13.6. $C_7H_{10}N_2O_5$ requires C, 41.6; H, 5.0; N, 13.9%).

(R,S)1-(3,4-*Dihydroxybutoxy*)*uracil* (**2d**) was prepared from compound (**25**) by the method described for (**1c**) and was obtained after chromatography on silica gel, eluting with chloroform–methanol (5:1) as a solid (84%, 2.2 mmolar scale) which was crystallised from ethanol, m.p. 138–139 °C; $\lambda_{max}(H_2O)$ 266 nm (ε 9 600); ν_{max}(KBr) 3 372, 3 097, 3 036, 2 962, 2 940, 2 924, 2 862, 2 818, 1 716, 1 688, 1 661, 1 605, 1 456, and 1 414 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 1.58 (1 H, m, CH of CH_2CH_2ON), 1.85 (1 H, m, CH of CH_2CH_2ON), 3.30 (>2 H, m, CH_2OH plus H_2O), 3.58 (1 H, m, C*H*OH), 4.18 (2 H, m, CH_2ON), 4.56 (1 H, br s, D_2O exchangeable, CH_2OH), 4.65 (1 H, d, *J* 5 Hz, D_2O exchangeable, OH), 5.48 (1 H, d, *J* 8 Hz, 5-H), 7.95 (1 H, d, *J* 8 Hz, 6-H), and 11.46 (1 H, br s, D_2O exchangeable, NH) (Found: C, 44.2; H, 5.6; N, 12.8. $C_8H_{12}N_2O_5$ requires C, 44.5; H, 5.6; N, 13.0%).

1-(*Prop*-2-*enyloxy*)-4-(1,2,4-*triazol*-1-*yl*)*pyrimidin*-2(1H)-*one* (**26**).—(4-Chlorophenyl) dichlorophosphate (2 ml, 12 mmol) was added to a solution of 1,2,4-triazole (1.23 g, 17.8 mmol) in dry acetonitrile (30 ml) and triethylamine (8.2 ml, 60 mmol) at 0 °C. The mixture was treated with a solution of compound (**24**) (1 g, 6 mmol) in dry acetonitrile (10 ml). After being stirred at room temperature for 24 h the deep red mixture was treated with water (1 ml), the solvent evaporated under reduced pressure, and the residue partitioned between chloroform (100 ml) and water (50 ml). The organic phase was dried and evaporated under reduced pressure and the residue was chromatographed on silica gel, eluting with ethyl acetate–hexane (4:1) to give *the title compound* (**26**) as a solid which was crystallised from ethyl acetate–hexane (0.5 g, 38%), m.p. 159–160 °C; ν_{max}(KBr) 3 427, 3 127, 3 107, 3 096, 3 027, 3 006, 2 917, 1 692, 1 648, 1 617, 1 544, 1 515, 1 510, 1 466, 1 456, 1 433, and 1 413 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 4.78 (2 H, d, *J* 6 Hz, CH_2), 5.40 (2 H, m, $=CH_2$), 6.06 (1 H, m, =CH), 6.88 (1 H, d, *J* 7 Hz, 5-H), 8.40 (1 H, s, CH), 8.72 (1 H, d, *J* 7 Hz, 6-H), and 9.40 (1 H, s, CH) (Found: C, 49.65; H, 4.1; N, 32.0. $C_9H_9N_5O_2$ requires C, 49.2; H, 4.1; N, 32.0%).

1-(*But*-3-*enyloxy*)-4-(1,2,4-*triazol*-1-*yl*)*pyrimidin*-2(1H)-*one* (**27**) was prepared from compound (**25**) by the method described for (**26**) and was obtained after chromatography on silica gel, eluting with ethyl acetate–hexane (2:1) as a solid (64%, 4.4 mmolar scale) which was crystallised from ethyl acetate, m.p. 130 °C (sublimes); ν_{max}(KBr) 3 437, 3 129, 3 110, 2 980, 2 911, 2 858, 1 686, 1 642, 1 616, 1 546, 1 512, 1 460, and 1 411 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 2.48 (2 H, m, CH_2CH_2ON), 4.32 (2 H, t, *J* 6.6 Hz, CH_2ON), 5.12 [1 H, dd, J 1.5 and 9 Hz, (*Z*)-CH of $=CH_2$], 5.22 [1 H, dd, *J* 1.5 and 17 Hz, (*E*)-H of $=CH_2$], 5.88 (1 H, m, =CH), 6.90 (1 H, d, *J* 7 Hz, 5-H), 8.41 (1 H, s, CH), 8.73 (1 H, d, *J* 7 Hz, 6-H), and 9.41 (1 H, s, CH) (Found: MH^+, 234.0993. $C_{10}H_{11}N_5O_2$ requires MH^+, 234.0991).

(R,S)1-(2,3-*Dihydroxypropoxy*)-4-(1,2,4-*triazol*-1-*yl*)-*pyrimidin*-2(1H)-*one* (**29**) was prepared from compound (**26**) by the method described for (**1c**) and was obtained, after chromatography on silica gel, eluting with chloroform–methanol (5:1), as a solid (91%, 0.9 mmolar scale) which was crystallised from ethyl acetate–methanol, m.p. 178–179 °C; ν_{max}(KBr) 3 399, 3 104, 2 950, 2 887, 1 683, 1 617, 1 548, 1 519, 1 457, and 1 412 cm^{-1}; $\delta_H[(CD_3)_2SO]$ 3.42 (2 H, m, CH_2OH), 3.80 (1 H, m, CH), 4.15 (1 H, dd, *J* 7 and 10.5 Hz, CH of CH_2ON), 4.39 (1 H, dd, *J* 3 and 10.5 Hz, CH of CH_2ON), 4.75 (1 H, br, D_2O exchangeable, OH), 5.13 (1 H, br, D_2O exchangeable, OH), 6.92 (1 H, d, *J* 7 Hz, 5-H), 8.40 (1 H, s, CH), 8.73 (1 H, d, *J* 7 Hz, 6-H), and 9.41 (1 H, s, CH); *m/z* (FAB, +ve ion, thioglycerol) MH^+ 254.

(R,S)1-(3,4-*Dihydroxybutoxy*)-4-(1,2,4-*triazol*-1-*yl*)*pyrimidin*-2(1H)-*one* (**30**) was prepared from compound (**27**) by the method described for (**1c**) and was obtained after chromatography on silica gel, eluting with chloroform–methanol (30:1), eluting as the second component (64%, 0.73

mmolar scale); ν_{max}(KBr) 3 344, 3 104, 2 920, 2 852, 1 693, 1 618, 1 551, 1 520, 1 457, and 1 416 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.65 (1 H, m, CH of CH_2CH_2ON), 1.92 (1 H, m, CH of CH_2CH_2ON), 3.32 (2 H, m, CH_2OH), 3.64 (1 H, m, CHOH), 4.36 (2 H, m, CH_2ON), 4.59 (1 H, t, *J* 6 Hz, D_2O exchangeable, OH), 4.71 (1 H, d, *J* 5 Hz, D_2O exchangeable, OH), 5.71 (1 H, d, *J* 7.4 Hz, 5-H), 8.41 (1 H, s, CH), 8.76 (1 H, d, *J* 7.4 Hz, 6-H), and 9.41 (1 H, s, CH) (Found: C, 44.8; H, 5.1; N, 26.4. $C_{10}H_{13}N_5O_4$ requires C, 44.9; H, 4.9; N, 26.2%).

General Procedure for the Preparation of Compounds (**16**), (**17**), (**28**), (**3c**), *and* (**3d**).—A solution of the corresponding (1,2,4-triazol-1-yl)pyrimidine derivative (1 mmol) in dioxane (5 ml) and ammonia (*d*, 0.880; 5 ml) was stirred at room temperature for 24 h. The solvent was removed under reduced pressure.

1-(3-*Benzyloxypropoxy*)*cytosine* (**16**) was obtained from compound (**14**) after chromatography on silica gel, eluting with ethyl acetate–methanol (10:1) as a solid (74%, 1.2 mmolar scale) which was crystallised from ethyl acetate, m.p. 151–152 °C; ν_{max}(KBr) 3 353, 3 134, 3 095, 3 065, 2 958, 2 919, 2 890, 2 853, 2 804, 1 648, 1 620, 1 518, 1 483, 1 455, and 1 420 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.87 (2 H, m, $CH_2CH_2CH_2$), 3.56 (2 H, t, *J* 6 Hz, CH_2OCH_2Ph), 4.11 (2 H, t, *J* 6 Hz, CH_2ON), 4.48 (2 H, s, OCH_2Ph), 5.56 (1 H, d, *J* 7 Hz, 5-H), 7.15 (2 H, br, D_2O exchangeable, NH_2), 7.33 (5 H, m, C_6H_5), and 7.75 (1 H, d, *J* 7 Hz, 6-H) (Found: C, 61.3; H, 6.3; N, 15.5. $C_{14}H_{17}N_3O_3$ requires C, 61.1; H, 6.3; N, 15.3%).

1-[3-*Benzyloxy*-2-(*benzyloxymethyl*)*propoxy*]*cytosine* (**17**) was obtained from compound (**15**) after chromatography on silica gel, eluting with ethyl acetate–methanol (20:1) as a solid (97%, 0.7 mmolar scale) which was crystallised from ethyl acetate, m.p. 154–155 °C; ν_{max}(KBr) 3 340, 3 100, 3 040, 2 920, 2 860, 1 650, 1 520, 1 480, and 1 455 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.25 (1 H, m, CH), 3.55 (4 H, d, *J* 6 Hz, 2 × CH_2OCH_2Ph), 4.09 (2 H, d, *J* 6 Hz, CH_2ON), 4.47 (4 H, s, 2 × OCH_2Ph), 5.55 (1 H, d, *J* 7 Hz, 5-H), 7.15 (2 H, br, D_2O exchangeable, NH_2), 7.3 (10 H, m, 2 × C_6H_5), and 7.69 (1 H, d, *J* 7 Hz, 6-H) (Found: C, 67.1; H, 6.4; N, 10.7. $C_{22}H_{25}N_3O_4$ requires C, 66.8; H, 6.4; N, 10.6%).

1-(*But*-3-*enyloxy*)*cytosine* (**28**) was obtained from compound (**27**) after chromatography on silica gel eluting with chloroform–methanol (20:1) as a solid (88%, 2 mmolar scale) which was crystallised from ethyl acetate, m.p. 156–160 °C; ν_{max}(KBr) 3 352, 3 182, 3 054, 2 981, 2 957, 2 887, 1 670, 1 637, 1 515, 1 489, 1 428, and 1 414 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.36 (1 H, m, CH_2CH_2ON), 4.10 (2 H, t, *J* 6.5 Hz, CH_2ON), 5.07 [1 H, dd, *J* 2 and 10 Hz, (*Z*)-H of $=CH_2$], 5.13 [1 H, dd, *J* 2 and 17 Hz, (*E*)-H of $=CH_2$], 5.57 (1 H, d, *J* 7.4 Hz, 5-H), 5.85 (1 H, m, =CH), 7.11 (1 H, br s, D_2O exchangeable, NH), 7.17 (1 H, br s, D_2O exchangeable, NH), and 7.76 (1 H, d, *J* 7.4 Hz, 6-H) (Found: C, 53.5; H, 6.2; N, 23.2. $C_8H_{11}N_3O_2$ requires C, 53.0; H, 6.1; N, 23.2%).

(R,S)1-(2,3-*Dihydroxypropoxy*)*cytosine* (**3c**) was obtained from compound (**29**) after chromatography on silica gel, eluting with chloroform–methanol (5:1) as a solid (87%, 0.67 mmolar scale) which was converted into its hydrochloride salt by treatment with methanolic hydrogen chloride and crystallised from methanol, m.p. 144–145 °C; $\lambda_{max}(H_2O)$ (hydrochloride) 274 nm (ε 8 470); ν_{max}(KBr) (free base) 3 351, 3 192, 3 090, 2 963, 2 946, 2 936, 2 920, 2 881, 1 671, 1 655, 1 620, 1 520, 1 485, and 1 461 cm^{-1}; δ_H(free base) [$(CD_3)_2SO$] 3.38 (2 H, m, CH_2OH), 3.68 (1 H, m, CH), 3.90 (1 H, dd, *J* 7 and 10 Hz, CH of CH_2ON), 4.18 (1 H, dd, *J* 3 and 10 Hz, CH of CH_2ON), 5.65 (1 H, d, *J* 7 Hz, 5-H), 7.22 (1 H, br, D_2O exchangeable, NH of NH_2), 7.26 (1 H, br, D_2O exchangeable, NH of NH_2), and 7.86 (1 H, d, *J* 7 Hz, 6-H) (Found: C, 35.4; H, 5.15; N, 17.3. $C_7H_{12}ClN_3O_4$ requires C, 35.4; H, 5.1; N, 17.3%).

(R,S)1-(3,4-*Dihydroxybutoxy*)*cytosine* (**3d**) was obtained from compound (**30**) after chromatography on silica gel, eluting with chloroform–methanol (5:1) as a glass (89%, 0.4 mmolar scale) which was converted into its hydrochloride salt by treatment with methanolic hydrogen chloride and crystallised from methanol, m.p. 140–141 °C; $\lambda_{max}(H_2O)$ 274 nm (ε 8 650); ν_{max}(KBr) 3 295, 3 107, 3 049, 2 964, 2 772, 1 742, 1 675, 1 640, 1 539, 1 486, 1 462, and 1 441 cm^{-1}; δ_H[$(CD_3)_2SO$] (free base) 1.55 (1 H, m, CH of CH_2CH_2ON), 1.80 (1 H, m, CH of CH_2CH_2ON), 3.30 (2 H, m, CH_2OH), 3.60 (1 H, m, CHOH), 4.14 (2 H, m, CH_2ON), 4.54 (1 H, t, *J* 5.5 Hz, D_2O exchangeable, CH_2OH), 4.74 (1 H, d, *J* 5 Hz, D_2O exchangeable, CHOH), 5.58 (1 H, d, *J* 7.4 Hz, 5-H), 7.13 (1 H, s, D_2O exchangeable, NH of NH_2), 7.18 (1 H, s, D_2O exchangeable, NH of NH_2), and 7.81 (1 H, d, *J* 7.4 Hz, 6-H) (Found: C, 38.0; H, 5.6; N, 16.5. $C_8H_{14}ClN_3O_4$ requires C, 38.2; H, 5.6; N, 16.7%).

1-(3-*Acetoxypropoxy*)*uracil* (**31**).—A solution of compound (**2a**) (5.7 g, 30.6 mmol) in dry pyridine (25 ml) at room temperature was treated with acetic anhydride (25 ml) and the mixture was heated at reflux for 2 h. The cooled solution was evaporated under reduced pressure and the residue purified by chromatography on silica gel, eluting with ethyl acetate–hexane (1:1) to give *the title compound* (**31**) as a solid which was crystallised from acetone (6.9 g, 98%), m.p. 127–129 °C; ν_{max}(KBr) 3 420, 3 100, 3 020, 2 820, 1 725, 1 675, 1 470, and 1 415 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.0 (2 H, m, $CH_2CH_2CH_2$), 2.01 (3 H, s, CH_3), 4.14 (4 H, m, $CH_2CH_2CH_2$), 5.5 (1 H, d, *J* 8.2 Hz, 5-H), 7.95 (1 H, d, *J* 8.2 Hz, 6-H), and 11.5 (1 H, s, D_2O exchangeable, NH) (Found: C, 47.5; H, 5.2; N, 12.2. $C_9H_{12}N_2O_5$ requires C, 47.4; H, 5.3; N, 12.3%).

1-(3-*Acetoxypropoxy*)-5-*iodouracil* (**32**).—A solution of compound (**31**) (6.9 g, 29 mmol) in dry dichloromethane (75 ml), was treated with a solution of iodine monochloride (7.0 g, 43.5 mmol) in dry dichloromethane (50 ml) and the dark red solution was then heated at reflux for 2 h. The cooled solution was diluted with dichloromethane (100 ml) and washed with 5% aqueous sodium thiosulphate (2 × 75 ml), water (2 × 50 ml), dried, and evaporated under reduced pressure to give (**32**) as a yellow solid which was crystallised from methanol–diethyl ether to give the *title compound* (**32**) as colourless crystals (10.2 g, 97%), m.p. 172–174 °C; ν_{max}(KBr) 3 120, 3 080, 3 030, 1 720, 1 650, and 1 410 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.93 (2 H, m, $CH_2CH_2CH_2$), 2.01 (3 H, s, CH_3), 4.2 (4 H, m, $CH_2CH_2CH_2$), 8.5 (1 H, s, 6-H), and 11.8 (1 H, s, D_2O exchangeable, NH) (Found: C, 30.4; H, 3.3; N, 7.9. $C_9H_{11}IN_2O_5$ requires C, 30.5; H, 3.1; N, 7.9%).

1-(3*Hydroxypropoxy*)-5-*iodouracil* (**33**).—A solution of compound (**32**) (0.35 g, 0.98 mmol) in methanol (10 ml) was treated with 0.1M sodium methoxide solution in methanol (5 ml) and left at room temperature for 2 h. The solution was neutralised with Amberlite IR 120 (H) ion exchange resin, filtered, and evaporated under reduced pressure. The residual oil was purified by chromatography on silica gel, eluting with chloroform–methanol (97:3) to give the *title compound* (**33**) as a solid which was crystallised from methanol (240 mg, 78%), m.p. 168–170 °C; λ_{max}(MeOH) 288 nm (ε 7 806); ν_{max}(KBr) 3 470, 3 050, 2 960, 2 805, 1 720, 1 680, and 1 410 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.75 (2 H, m, $CH_2CH_2CH_2$), 3.52 (2 H, m, CH_2OH), 4.15 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.55 (1 H, t, *J* 5 Hz, D_2O exchangeable, OH), 8.5 (1 H, s, 6-H), and 11.8 (1 H, s, D_2O exchangeable, NH) (Found: C, 27.3; H, 2.9; N, 9.1. $C_7H_9IN_2O_4$ requires C, 26.9; H, 2.9; N, 9.0%).

(E)-1-(3-*Acetoxypropoxy*)-5-(2-*methoxycarbonyl vinyl*)*uracil* (**34**).—A solution of compound (**32**) (1.0 g, 2.82 mmol) in anhydrous *N*,*N*-dimethylformamide (20 ml) was treated with

triethylamine (0.8 g, 7.9 mmol), palladium(II) acetate (30 mg, 0.13 mmol), and methyl acrylate (0.48 g, 5.58 mmol) and heated at 50 °C for 5 h. The solution was filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on silica gel, eluting with chloroform to give the *title compound* (**34**) as a solid which was crystallised from methanol–diethyl ether (0.6 g, 68%), m.p. 187–189 °C; ν_{max}(KBr) 3 080, 3 030, 2 850, 1 735, 1 710, 1 695, 1 620, 1 470, and 1 437 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.9 (2 H, m, $CH_2CH_2CH_2$), 2.0 (3 H, s, $COCH_3$), 3.67 (3 H, s, CO_2CH_3), 4.2 (4 H, m, $CH_2CH_2CH_2$), 6.8 (1 H, d, *J* 15.6 Hz, =CH), 7.3 (1 H, d, *J* 15.6 Hz, =CH), 8.66 (1 H, s, 6-H), and 11.8 (1 H, s, D_2O exchangeable, NH) (Found: C, 49.7; H, 5.2; N, 9.0. $C_{13}H_{16}N_2O_7$ requires C, 50.0; H, 5.2; N, 9.0%).

1-(3-*Acetoxypropoxy*)-5-*vinyluracil* (**35**).—A mixture of palladium(II) acetate (32 mg, 0.14 mmol), triphenylphosphine (73.5 mg, 0.28 mmol), and methylamine (2 ml, 28 mmol) in anhydrous *N*,*N*-dimethylformamide (10 ml) was heated to 70 °C and stirred until the appearance of a deep red colour indicated activation of the catalyst. A mixture of compound (**32**) (1.0 g, 2.82 mmol) and vinyl acetate (10 ml, 115 mmol) was added and the reaction was stirred at 70 °C for 18 h. The mixture was cooled, filtered, and evaporated under reduced pressure to give a dark oil which was purified by chromatography on silica gel, eluting with hexane–acetone (3:1) to give the *title compound* (**35**) as a solid which was crystallised from acetone–diethyl ether (0.4 g, 57%), m.p. 143–145 °C; ν_{max}(KBr) 3 015, 1 730, 1 660, 1 465, and 1 412 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.95 (2 H, m, $CH_2CH_2CH_2$), 2.01 (3 H, s, CH_3), 4.14 (4 H, m, $CH_2CH_2CH_2$), 5.14 [1 H, dd, *J* 11.5 and 2 Hz, (*Z*)-H of $=CH_2$], 6.0 [1 H, dd, *J* 17.6 and 2 Hz, (*E*)-H of $=CH_2$], 6.3 (1 H, dd, *J* 17.6 and 11.5 Hz, =CH), 8.21 (1 H, s, 6-H), and 11.6 (1 H, s, D_2O exchangeable, NH) (Found: C, 51.5; H, 5.5; N, 10.8. $C_{11}H_{14}N_2O_5$ requires C, 52.0; H, 5.55; N, 11.0%).

(E)-5-(2-*Bromovinyl*)-1-(3-*hydroxypropoxy*)*uracil* (**36**).—A solution of compound (**34**) (0.65 g, 1.9 mmol) in 0.5M aqueous sodium hydroxide (20 ml) was left at room temperature for 2 h. The solution was neutralised with Amberlite IR 120 (H) ion exchange resin, filtered, and the solvent removed under reduced pressure. The residue was dissolved in water (15 ml) and potassium acetate (0.4 g, 4 mmol) was added. The solution was heated to 70 °C, treated with *N*-bromosuccinimide (0.35 g, 1.96 mmol), and stirred for 2 h without further heating. The solvent was removed under reduced pressure and the residue purified by chromatography on silica gel, eluting with ethyl acetate to give the *title compound* (**36**) as a solid which was crystallised from acetone (0.12 g, 21%); m.p. 148–150 °C, λ_{max}(EtOH) 298 (ε 12 322) and 251 nm (ε 13 359); ν_{max}(KBr) 3 410, 3 010, 2 840, 1 730, 1 710, 1 685, 1 595, and 1 440 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.75 (2 H, m, $CH_2CH_2CH_2$), 3.5 (2 H, m, CH_2OH), 4.17 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.56 (1 H, br s, D_2O exchangeable, OH), 6.8 (1 H, d, *J* 13.5 Hz, =CH), 7.25 (1 H, d, *J* 13.5 Hz, =CH), 8.25 (1 H, s, 6-H), and 11.75 (1 H, br s, D_2O exchangeable, NH) (Found: C, 37.4; H, 3.9; N, 9.5. $C_9H_{11}BrN_2O_4$ requires C, 37.1; H, 3.8; N, 9.6%).

1-(3-*Hydroxypropoxy*)-5-*vinyluracil* (**37**).—A solution of compound (**35**) (0.4 g, 1.57 mmol) in dioxane (3 ml) was treated with a 50% solution of ammonia (*d* 0.880) in water (3 ml) and stirred at room temperature for 18 h. The solvent was removed under reduced pressure and the residue purified by chromatography on silica gel, eluting with ethyl acetate to give the *title compound* (**37**) as a solid which was crystallised from acetone–diethyl ether (100 mg, 30%), m.p. 135–136 °C; λ_{max}(EtOH) 290 (ε 7 020) and 237 nm (ε 8 427); ν_{max}(KBr) 3 415, 3 160, 3 100, 3 060, 3 020, 2 940, 1 720, 1 670, 1 605, 1 460, and 1 420 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.78 (2 H, m, $CH_2CH_2CH_2$), 3.52 (2 H, m, CH_2OH), 4.17 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.56 (1 H, m, D_2O exchangeable, OH), 5.14 [1 H, dd, *J* 11.5 and 2 Hz, (*Z*)-H of $=CH_2$], 6.0 [1 H, dd, *J* 17.6 and 2 Hz, (*E*)-H of $=CH_2$], 6.3 (1 H, dd, *J* 17.6 and 11.5 Hz, =CH), 8.19 (1 H, s, 6-H), and 11.59 (1 H, s, D_2O exchangeable, NH) (Found: C, 51.1; H, 5.7; N, 12.8. $C_9H_{12}N_2O_4$ requires C, 50.9; H, 5.7; N, 13.2%).

3-*Benzyloxy*-2-*benzyloxymethyl*-1-*iodopropane* (**39b**).—A solution of 3-benzyloxy-2-(benzyloxymethyl)propan-1-ol[13] (5 g, 17 mmol) and triethylamine (3.6 ml, 26 mmol) in dichloromethane (50 ml) at 0 °C was treated dropwise with methanesulphonyl chloride (2 ml, 26 mmol). After being stirred at 0 °C for 30 min, the solution was warmed to room temperature and extracted with 2M hydrochloric acid (50 ml). The organic phase was washed with brine, dried, and evaporated under reduced pressure to give the crude mesylate as an oil. A solution of the oil in acetone (200 ml) was treated with sodium iodide (13 g, 87 mmol) and the mixture was refluxed for 4 h. The solvent was removed under reduced pressure and the residue dissolved in ethyl acetate (50 ml), washed with water (30 ml), dried, and evaporated under reduced pressure. The residual oil was chromatographed on silica gel, eluting with ethyl acetate–hexane (1:7) to give the *title compound* (**39b**) as an oil (4.2 g, 62%); ν_{max}(film) 3 088, 3 064, 3 030, 2 859, 2 792, 1 605, 1 586, 1 496, 1 477, 1 454, and 1 423 cm^{-1}; δ_H($CDCl_3$) 1.57 (1 H, m, CH), 3.07 (6 H, m, 3 × CH_2), 4.07 (4 H, s, 2 × OCH_2Ph), 7.0 (10 H, s, 2 × C_6H_5) (Found: C, 54.4; H, 5.6; I, 32.1. $C_{18}H_{21}IO_2$ requires C, 54.6; H, 5.3; I, 32.0%).

1-(3-*Benzoyloxypropoxy*)-5-*fluorouracil* (**40a**).—Sodium hydride (80%; 90 mg, 3.0 mmol) was added to a solution of 5-fluoro-1-hydroxyuracil (**38**) (220 mg, 1.5 mmol) in dry dimethyl sulphoxide (20 ml) under nitrogen and the mixture was then heated at 50 °C for 1 h. Potassium iodide (10 mg) and 1-benzoyloxy-3-bromopropane (400 mg, 1.6 mmol) were added and the mixture was heated at 50 °C for 18 h. The solvent was removed under reduced pressure and the residue dissolved in methanol and neutralised with Amberlite IR 120 (H) ion exchange resin. The solution was filtered and evaporated under reduced pressure and the residue was purified by chromatography on silica gel, eluting with chloroform–methanol (99:1) to give the *title compound* (**40a**) as a solid which was crystallised from diethyl ether (150 mg, 32%), m.p. 134–136 °C; ν_{max}(KBr) 3 400, 3 185, 3 060, 2 840, 1 720, 1 650, 1 600, and 1 453 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.1 (2 H, m, $CH_2CH_2CH_2$), 4.26 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.41 (2 H, t, *J* 6.3 Hz, CH_2OCOPh), 7.6–8.0 (5 H, m, C_6H_5), 8.53 (1 H, d, *J* 6 Hz, 6-H), and 12.1 (1 H, br s, D_2O exchangeable, NH) (Found: C, 54.75; H, 4.3; N, 9.05. $C_{14}H_{13}FN_2O_5$ requires C, 54.5; H, 4.25; N, 9.1%).

1-[3-*Benzyloxy*-2-(*benzyloxymethyl*)*propoxy*]-5-*fluorouracil* (**40b**).—Sodium hydride (80%; 62 mg, 2.05 mmol) was added to a solution of 5-fluoro-1-hydroxyuracil (**38**) (150 mg, 1.02 mmol) in dry dimethylformamide (25 ml) under nitrogen and the mixture was heated at 50 °C for 1 h. It was then treated with compound (**39b**) (400 mg, 1.0 mmol) and stirred overnight at 50 °C. The solvent was removed under reduced pressure and the residue dissolved in methanol and neutralised with Amberlite IR 120 (H) ion exchange resin. The solution was filtered and evaporated under reduced pressure and the residue was purified by chromatography on silica gel, eluting with chloroform–methanol (98:2) to give the *title compound* (**40b**) as a colourless gum (280 mg, 65%); ν_{max}(film) 3 180, 3 060, 2 860, 1 710, 1 451, and 1 350 cm^{-1}; δ_H[$(CD_3)_2SO$] 2.28 (1 H, m, CH), 3.55 (4 H, d, *J* 6.3 Hz, 2 × CH_2OCH_2Ph), 4.15 (2 H, d, *J* 6.3 Hz, CH_2ON), 4.5 (4 H, s, 2 × $OCH_2C_6H_5$), 7.3 (10 H, m, 2 × C_6H_5), 8.4 (1 H, d, *J* 6.1 Hz, 6-H), and 12.0 (1 H, br s, D_2O exchangeable, NH)

(Found: C, 63.8; H, 5.6; N, 6.9. $C_{22}H_{23}FN_2O_5$ requires C, 63.75; H, 5.9; N, 6.8%).

5-Fluoro-1-(3-hydroxypropoxy)uracil (**41**).—A solution of compound (**40a**) (150 mg, 0.48 mmol) in methanol (25 ml) was treated with potassium t-butoxide (20 mg, 0.17 mmol) at room temperature. The mixture was stirred for 3 h and then neutralised with Amberlite IR 120 (H) ion exchange resin, filtered through a glass fibre pad, and evaporated under reduced pressure. The residue was crystallised from acetone–diethyl ether to give the *title compound* (**41**) (55 mg, 56%), m.p. 160–162 °C; λ_{max}(MeOH) 272 nm (ε 7 710); ν_{max}(KBr) 3 480, 3 440, 3 070, 3 010, 2 840, 1 710, 1 660, 1 443, and 1 400 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.76 (2 H, m, $CH_2CH_2CH_2$), 3.51 (2 H, t, *J* 6.3 Hz, CH_2OH), 4.14 (2 H, t, *J* 6.3 Hz, CH_2ON), 4.56 (1 H, br s, D_2O exchangeable, OH), 8.5 (1 H, d, *J* 6 Hz, 6-H), and 12.0 (1 H, br, D_2O exchangeable, NH) (Found: C, 41.1; H, 4.5; N, 13.6. $C_7H_9FN_2O_4$ requires C, 41.2; H, 4.4; N, 13.7%).

5-Fluoro-1-[3-hydroxy-2-(hydroxymethyl)propoxy]uracil (**42**).—A solution of compound (**40b**) (280 mg, 0.67 mmol) in methanol (20 ml) and saturated methanolic hydrogen chloride (0.25 ml) was treated with 5% palladium–charcoal catalyst (25 mg) and hydrogenated at atmospheric pressure and room temperature until uptake of hydrogen ceased (5 min). The mixture was filtered through a glass fibre pad, neutralised with ammonia (*d* 0.880), and evaporated under reduced pressure. The residue was purified by crystallisation from acetone–diethyl ether to give the *title compound* (**42**) (120 mg, 76%), m.p. 137–139 °C; λ_{max}(EtOH) 272 nm (ε 7 400); ν_{max}(KBr) 3 360, 3 060, 2 980, 2 800, 1 693, 1 650, and 1 275 cm^{-1}; δ_H[$(CD_3)_2SO$] 1.87 (1 H, m, CH), 3.5 (4 H, m, 2 × CH_2OH), 4.1 (2 H, d, *J* 6 Hz, CH_2ON), 4.53 (2 H, t, *J* 5.5 Hz, 2 × D_2O exchangeable, OH), 8.47 (1 H, d, *J* 6 Hz, 6-H), and 12.0 (1 H, br s, D_2O exchangeable, NH) (Found: C, 40.3; H, 4.7; N, 11.6. $C_8H_{11}FN_2O_5$ requires C, 40.0; H, 4.8; N, 11.7%).

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