SYNTHESIS AND ANTIVIRAL ACTIVITY OF ACYCLIC NUCLEOSIDE ANALOGUES OF 5-METHOXYMETHYL-6-METHYLURACIL AND 4-ALKYLAMINO-5-METHOXYMETHYL-6-METHYL-2(1*H*)-PYRIMIDINONES

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The uracil derivatives 1-(2-hydroxyethoxymethyl/allyl/2,3-dihydroxypropyl)-5-methoxymethyl-6-methyluracils (*Vb*, *VIII*, *XI*) and 4-alkylamino-1-(2-hydroxyethoxymethyl/allyl/2,3-dihydroxypropyl)-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*VIa* – *VIc*, *IXa* – *IXc*, *XIIa* – *XIIc*) were synthesized from versatile intermediates 1-(2-benzoyloxyethoxymethyl/allyl/2,3-dihydroxypropyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IVa*, *VII*, *X*), respectively. The compounds *IVb*, *Vb*, *VIa* – *VIc*, *VIII*, *IXa* – *IXc*, *XIIa* – *XIIc* were evaluated against Ranikhet disease virus (RDV) at the dose of (0.1 μg/ml); compounds *VIa*, *VIb*, *IXa*, *XIIb* showed 57, 100, 40, 80% inhibition, respectively.

Considerable attention has been paid to the novel group of nucleoside and nucleotide analogues, in which the sugar moiety is replaced by an acyclic chain. This has resulted in a number of interesting compounds. The most important antiviral drugs discovered are the acyclic analogues of guanosine, 9-(2-hydroxyethoxymethyl)guanine[1] (ACV) active against herpesvirus, and 9-(*S*)-(2,3-dihydroxypropyl)adenine[2] (DHPA) active against both DNA and RNA viruses. It has been found that a number of acyclic nucleosides of 5-benzyluracil[3] are specific and fairly potent inhibitor of uridine phosphorylase. Some 1-substituted uracils containing additional substituents at 5,6-position have also been found to be potent inhibitors of thymidine phosphorylase[4].

As a part of our programme of evaluating acyclic nucleosides[5] we report in this communication the synthesis and antiviral activity of 1-(2-hydroxyethoxymethyl)-5-methoxymethyl-6-methyluracil (*Vb*), 1-(2,3-dihydroxypropyl)-5-methoxymethyl-6-methyluracil (*XI*), 1-(2-hydroxyethoxymethyl-5-methoxymethyl-6-methylcytosine

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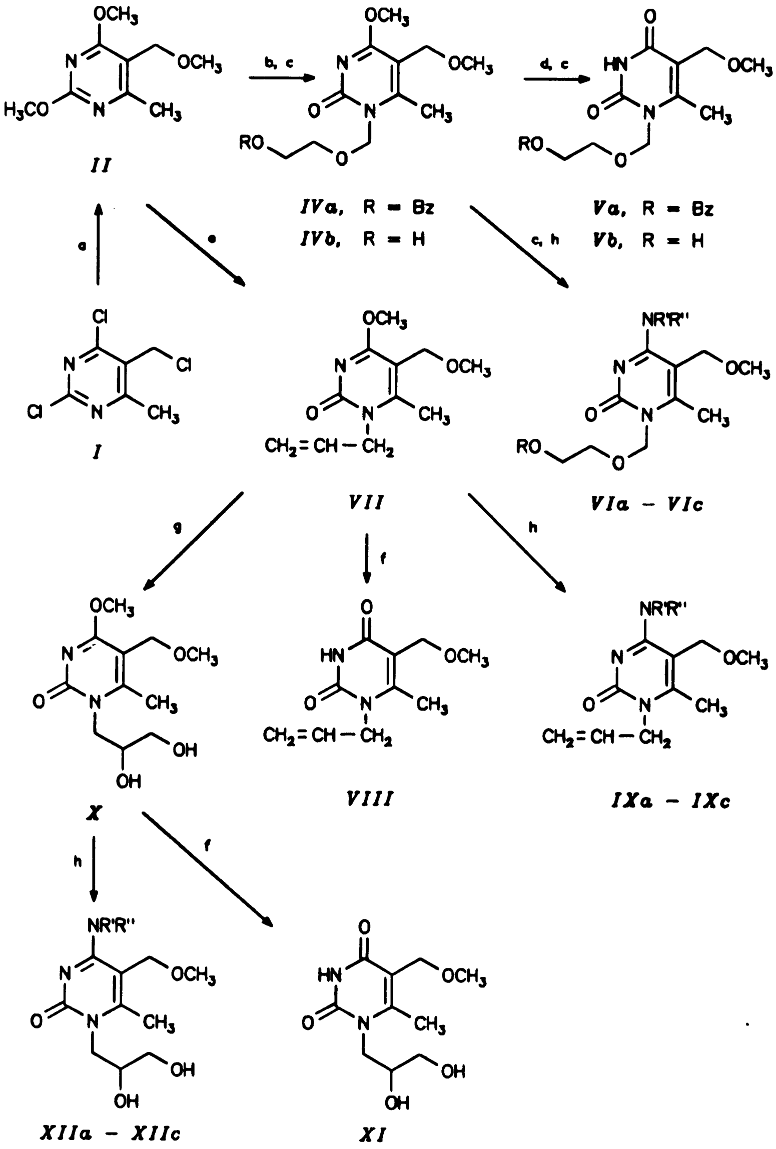
(*VIa*) and 1-(2,3-dihydroxypropyl)-5-methoxymethyl-6-methylcytosine (*XIIa*) and their analogues (see Scheme 1).

2,4-Dimethoxy-5-methoxymethyl-6-methylpyrimidine (*II*) was prepared by treatment of 5-chloromethyl-2,4-dichloro-6-methylpyrimidine[6] (*I*) with sodium methoxide in methanol in 73% yield. The dichloropyrimidine *I* was obtained in three steps from 6-methyluracil by the literature procedure[7]. Reaction of the 2,4-dimethoxy-5-methoxymethyl-6-methylpyrimidine (*II*) with 2-benzoyloxy-1-chloromethoxyethane[8] (*III*) or allyl bromide by modified Hilbert–Johnson procedure[9] afforded versatile intermediates 1-(2-benzoyloxyethoxymethyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IVa*) and 1-allyl-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*VII*). Treatment of *IVa* with hydrogen chloride[10] in chloroform gave the corresponding protected 5-methoxymethyl-6-methyluracil derivative (*Va*). Deprotection of the *IVa* and *Va* with methanolic ammonia furnished 1-(2-hydroxyethoxymethyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IVb*) and 1-(2-hydroxyethoxymethyl)-5-methoxymethyl-6-methyluracil (*Vb*), respectively. Hydroxylation of the compound *VII* with sodium chlorate and osmium tetraoxide[11] in aqueous methanol afforded racemic diol, 1-(2,3-dihydroxypropyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*X*). Demethylation of *VII* and *X* with aqueous sodium hydroxide gave uracil derivatives *VIII* and *XI*. The site of glycosylation was confirmed to be N-1 by direct comparison of the UV spectrum of *Vb* (λ_{max} (MeOH): 210, 265 nm; (MeOH + NaOH): 202, 264 nm) with the UV spectrum of the 5,6-dimethyluridine[12] (λ_{max} (pH 1 – 4): 268 nm; λ_{max} (pH 14): 271 nm) which in turn resemble to the 1-methyluracil[13]. Amination of *IVa*, *VII* and *X* with methanolic ammonia in steel bomb afforded the corresponding cytosine analogues *VIa*, *IXa* and *XIIa*, respectively. Compounds *IVa*, *VII* and *X* were also treated with methylamine or ethylamine to determine if alkyl substitution on the 4-amino group would have any effect on the antiviral activity. Thus, 4-alkylamino-1-(2-hydroxyethoxymethyl)-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*VIb* and *VIc*), 1-allyl-4-alkylamino-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IXb* and *IXc*) and 4-alkylamino-1-(2,3-dihydroxypropyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*XIIb* and *XIIc*) were synthesized in good yields, by the reaction of the *VIa*, *VII* and *X* with methylamine and ethylamine.

The compounds *IVb*, *Vb*, *VIa* – *VIc*, *VIII*, *IXa* – *IXc*, *XI*, *XIIa* – *XIIc* were evaluated for antiviral activity against Ranikhet disease virus (RDV) in chorio-allantoic membrane (CAM) cultures at the dose of 0.1 μg/culture, 0.064 HA/ml by the method described earlier[14]. The compounds *VIa*, *VIb*, *IXa* and *XIIb* showed 57, 100, 40, and 80% inhibition, respectively. The remaining compounds were found to exhibit either low order of activity or were inactive.



a NaOMe, MeOH; b $BzOCH_2CH_2OCH_2Cl$ (*III*), CH_2Cl_2, Na_2CO_3; c $MeOH-NH_3$;
d $CHCl_3$, HCl; e $CH_2=CHCH_2Br$, CH_2Cl_2, Na_2CO_3; f aq. NaOH;
g aq. NaOH, $NaClO_3$, OsO_4; h NHR'R''.

In formulae *VI*, *IX*, *XII* : *a*, R' = R'' = H; *b*, R' = H, R'' = CH_3;
c, R' = H, R'' C_2H_5

SCHEME 1

EXPERIMENTAL

Melting points are uncorrected. Compounds were routinely checked for their homogeneity by TLC on silica gel or GF-254 plates and their spots were located under UV lamp or by iodine vapours or by spraying with Dragendorff's reagent. UV absorption spectra (λ_{max}, nm) were recorded on Perkin-Elmer Lambda-15 and Hitachi-320 model. IR spectra ($\tilde{\nu}_{max}$, cm^{-1}) were recorded on Perkin–Elmer 157 or Acculab 1 model. ^{1}H NMR spectra (δ, ppm) were recorded on Perkin–Elmer R-32 or EM360L instruments using TMS as internal reference. Mass spectra were run on Jeol JMS-D 300 using direct inlet system.

2,4-Dimethoxy-5-methoxymethyl-6-methylpyrimidine (*II*)

A solution of *I* (ref.[6a])(5.0 g, 23.6 mmol) in dry methanol (20 ml) was added slowly to NaOMe (3.8 g, 70.9 mmol). The reaction mixture was refluxed for 0.5 h and cooled. The separated solid was filtered and washed with ether (50 ml). The combined filtrate was evaporated under reduced pressure to give 3.4 g (73%) of pyrimidine *II*, as an oil. UV spectrum (MeOH): 219, 259. ^{1}H NMR spectrum ($CDCl_3$): 2.36 s, 3 H (6-CH_3); 3.25 s, 3 H (5-CH_2OCH_3); 3.87 s, 6 H (4-OCH_3 and 2-OCH_3); 4.30 s, 2 H (5-CH_2). Mass spectrum (*m*/*z*): 198(M$^+$). For $C_9H_{14}N_2O_3$ (198.2) calculated: 54.53% C, 7.11% H, 14.3% N; found: 54.49% C, 7.30% H, 14.02% N.

1-(2-Benzoyloxyethoxymethyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IVa*)

2-Benzoyloxy-1-chloromethoxyethane[8] (*III*) (4.6 g, 21.2 mmol) in CH_2Cl_2 (20 ml) was slowly added to the mixture of *II* (3.5 g, 17.7 mmol), Na_2CO_3 (2.3 g, 21.2 mmol in CH_2Cl_2 (100 ml). The reaction mixture was stirred at room temperature for 4 h. The resulting mixture was filtered and the residue washed with CH_2Cl_2 (100 ml). The filtrate was evaporated under reduced pressure to give a syrup which was chromatographed on a SiO_2 column. Elution with benzene–ethyl acetate (8 : 2) and evaporation of the appropriate fractions gave 3.3 g (52%) of pyrimidinone *IVa*, m.p. 110 °C (C_6H_6). UV spectrum (MeOH) or (MeOH + HCl): 221, 274; (MeOH + NaOH): 211, 275; ^{1}H NMR spectrum ($CDCl_3$): 2.35 s, 3 H (6-CH_3); 3.21 s, 3 H (5-CH_2OCH_3); 3.86 s, 3 H (4-OCH_3); 3.92 m, 2 H (3'-H), 4.05 s, 2 H (5-CH_2); 4.30 m, 4 H (4'-H); 5.45 s, 2 H (1'-H); 750 m, 3 H (C_6H_5); 7.87 – 8.00 m, 2 H (C_6H_5). Mass spectrum (*m*/*z*): 362 (M$^+$).

1-(2-Benzoyloxyethoxymethyl)-4-methoxy-5-methoxymethyl-6-methyluracil (*Va*)

A solution of *IVa* (2.0 g, 5.5 mmol) in $CHCl_3$ (325 ml) was saturated with HCl at 10 °C and the reaction mixture was allowed to stand at room temperature for 10 h. The hydrogen chloride and $CHCl_3$ was removed under reduced pressure and the residue was chromatographed on SiO_2 column. Elution with benzene–ethyl acetate (8 : 2) gave 1.5 g (78%) of methyl uracil *Va*, m.p. 106 °C. IR spectrum (KBr): 1 700, 1 660 (C=O). UV spectrum (MeOH) or (MeOH + HCl): 224, 265; (MeOH + NaOH): 211, 265. ^{1}H NMR spectrum ($CDCl_3$): 2.34 s, 3 H (6-CH_3); 3.25 s, 3 H (5-CH_2OCH_3); 3.87 m, 2 H (3'-H); 4.14 s, 2 H (5-CH_2); 4.32 m, 2 H (4'-H); 5.35 s, 2 H (1'-H); 7.30 – 7.50 m, 3 H (C_6H_5); 7.84 – 8.00 m, 2 H (C_6H_5). Mass spectrum (*m*/*z*): 348 (M$^+$).

1-(2-Hydroxyethoxymethyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IVb*)

A mixture of *IVa* (0.6 g, 1.7 mmol) and MeOH–NH_3 (20 ml) was kept at 0 °C for 24 h. The excess of MeOH and NH_3 was removed under reduced pressure. The product was chromatographed on a SiO_2 column. Elution of the column with $CHCl_3$–MeOH (98 : 2) and evaporation of the appropriate fractions furnished 0.13 g (30%) of the title compound, as an oil. ^{1}H NMR spectrum ($CDCl_3$); 2.35 s, 3 H (6-CH_3); 3.26 s, 3 H (5-CH_2OCH_3); 3.64 s, 4 H (3'-H and 4'-H); 3.89 s, 3 H (4-OCH_3); 4.18 s, 2 H (5-CH_2); 5.45 s , 2 H (1'-H). Mass spectrum (*m/z*): 258 (M^+). For $C_{11}H_{18}N_2O_5$ (258.3) calculated: 51.15% C, 7.02% H, 10.84% N; found: 51.31% C, 6.82% H, 10.64% N.

1-(2-Hydroxyethoxymethyl)-5-methoxymethyl-6-methyluracil (*Vb*)

Title compound was prepared from *Va* (1.0 g, 2.9 mmol) and MeOH–NH_3 (40 ml), by the method described for *IVb*. Methyluracil *Vb* was obtained in 54% yield, m.p. 110 °C (ethyl acetate–hexane). ^1H NMR spectrum ($CDCl_3$): 2.36 s, 3 H (6-CH_3); 3.26 s, 3 H (5-CH_2OCH_3); 3.63 s, 4 H (3'-H and 4'-H); 4.20 s, 2 H (5-CH_2); 5.31 s, 2 H (1'-H). Mass spectrum (*m/z*); 244 (M^+). For $C_{10}H_{16}N_2O_5$ (244.3) calculated: 49.17% C, 6.60% H, 11.47% N; found: 49.13% C, 6.32% H, 11.49% N.

1-(2-Hydroxyethoxymethyl)-5-methoxymethyl-6-methylcytosine (*VIa*)

A mixture of *IVa* (1.0 g, 2.8 mmol) and MeOH–NH_3 (30 ml) was heated in a steel bomb at 100 °C for 16 h. The excess of MeOH and NH_3 was evaporated under reduced pressure and the residue was chromatographed on a SiO_2 column. Elution of the column with $CHCl_3$–MeOH (9 : 1) and evaporation of the appropriate fractions afforded 0.54 g (80%) of cytosine *VIa*, m.p. 187 °C. IR spectrum (KBr): 3 400 (OH, NH_2). ^1H NMR spectrum ($CDCl_3$ + $(CD_3)_2SO$): 2.34 s, 3 H (6-CH_3); 3.22 s, 3 H (5-CH_2OCH_3); 3.50 s, 4 H (3'-H and 4'-H); 4.16 s, 2 H (5-CH_2); 5.31 s, 2 H (1'-H); 5.51 s, 1 H (5-H); 6.70 bs, 2 H (exchanges with D_2O, NH_2). Mass spectrum (*m/z*): 243 (M^+). For $C_{10}H_{17}N_3O_4$ (243.3 calculated: 49.37% C, 7.05% H, 17.27% N; found: 49.54% C, 7.12% H, 17.61% N.

This procedure was also applied for the preparation of 1-allyl-5-methoxymethyl-6-methylcytosine (*IXa*) and 1-(2,3-dihydroxypropyl)-5-methoxymethyl-6-methylcytosine (*XIIa*), were prepared by the same procedure starting from 1-substituted-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinones (*VII* and *X*). Characteristic data of compounds *IXa* and *XIIa* are listed in Table I.

1-(2-Hydroxyethoxymethyl)-4-methylamino-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*VIb*)

A mixture of *IVa* (0.9 g, 2.2 mmol) and CH_3NH_2 (10 ml of 33% aqueous solution) was heated at 100 °C for 8 h. The excess of CH_3NH_2 was removed under reduced pressure. The residue was coevaporated with EtOH (50 ml). The product thus obtained was chromatographed on a SiO_2 column, elution with $CHCl_3$–MeOH (8 : 2) and evaporation of the appropriate fractions gave 0.4 g (68%) of compound *VIb*, as an oil. ^1H NMR spectrum ($CDCl_3$): 2.32 s, 3 H (6-CH_3); 2.82 d, 3 H ($NHCH_3$); 3.24 s, 3 H (5-CH_2OCH_3); 3.42 s, 4 H (3'-H and 4'-H); 4.22 s, 2 H (5-CH_2); 5.38 s, 2 H (1'-H); 6.20 bs, 1 H (exchanges with D_2O, NH). Mass spectrum (*m/z*): 257 (M^+). For $C_{11}H_{19}N_3O_4$ (257.3) calculated: 51.35% C, 7.44% H, 16.33% N; found: 51.26% C, 7.51% H, 16.20% N.

Similarly 1-(2-hydroxyethoxymethyl)-4-ethylamino-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*VIc*), 1-allyl-4-alkylamino-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IXb* – *IXc*) and 4-alkylamino-1-(2,3-dihydroxypropyl)-5-methoxymethyl -6-methyl-2(1*H*)-pyrimidinone (*XIIb* – *XIIc*) were prepared from corresponding 1-(benzoylethoxymethyl/allyl/dihydroxypropyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*IVa*, *VIIa* and *X*) by reacting with methylamine and ethylamine solutions. Characteristic data of compounds *VIc*, *IXb* – *IXc* and *XIIb* – *XIIc* are presented in Table I.

1-Allyl-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*VII*)

A mixture of *I* (5.0 g, 25.3 mmol), allyl bromide (3.7 g, 30.3 mmol) anhydrous Na_2CO_3 (3.2 g, 30.3 mmol) and CH_3CN (100 ml) was refluxed with the exclusion of moisture at 140 °C bath for 8 h. The resulting mixture was cooled, filtered and the solid was washed with CH_3CN (100 ml). The filtrate and washings were combined and evaporated under reduced pressure to give a syrup which was chromatographed on a

TABLE I

Physical and spectral data of cytosines *IXa*, *XIIa* and 4-alkylaminopyrimidinones *VIc*, *IXb*, *IXc*, *XIIb*, *XIIc*

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found			Spectra data
			% C	% H	% N	
VIc	oil 56	$C_{12}H_{21}N_3O_4$ (271.3)	53.12 53.39	7.80 7.76	15.48 15.31	MS (*m/z*): 271 (M^+). ^1H NMR ($CDCl_3$): 1.10 t, 3 H (4-$NHCH_2CH_3$); 3.34 – 3.50 m, 2 H (4-$NHCH_2$); 5.40 s, 2 H (1′-H); 6.10 bs,1 H (exchanges with D_2O, NH)
IXa	157 – 159[a] 65	$C_{10}H_{15}N_3O_2$ (209.2)	57.59 57.26	7.22 7.32	20.08 19.62	MS (*m/z*): 209 (M^+). ^1H NMR ($CDCl_3$): 4.45 – 4.55 m, 2 H (1′-H); 5.00 – 5.15 m, 2 H (3′-H); 5.60 – 5.80 m, 1 H (2′-H); 6.50 bs, 2 H (D_2O exchangeable, NH_2)
IXb	119 – 121[a] 87	$C_{11}H_{17}N_3O_2$ (223.3)	59.17 59.39	7.67 7.72	18.82 18.94	MS (*m/z*): 223 (M^+). ^1H NMR ($CDCl_3$): 2.95 bs, 3 H ($NHCH_3$); 4.50 – 4.65 m, 2 H (1′-H); 6.15 bs, 1 H (D_2O exchangeable, NH)
IXc	102 – 104[a] 86	$C_{12}H_{19}N_3O_2$ (237.3)	60.77 60.79	8.07 8.12	17.70 17.49	MS (*m/z*): 237 (M^+). ^1H NMR ($CDCl_3$): 1.15 t, 3 H (4-$NHCH_2CH_3$); 3.35 – 3.56 m, 2 H (4-$NHCH_2$); 4.50 – 4.62 m, 2 H (1′-H); 6.04 bs, 1 H (D_2O exchangeable, NH)
XIIa	171 – 173[b] 74	$C_{10}H_{17}N_3O_4$ (243.3)	49.37 49.56	7.04 7.29	17.27 17.23	MS (*m/z*): 243 (M^+). ^1H NMR ($CDCl_3$ + $(CD_3)_2SO$): 3.30 – 3.45 m, 2 H (1′-H); 3.62 – 3.95 m, 3 H (2′-H and 3′-H); 6.50 bs, (D_2O exchangeable, NH_2)
XIIb	157 – 159[b] 68	$C_{11}H_{19}N_3O_4$ (257.3)	51.35 51.52	7.44 7.30	16.33 16.50	MS (*m/z*): 257 (M^+). ^1H NMR ($CDCl_3$ + $(CD_3)_2SO$): 2.88 d, 3 H (4-$NHCH_3$); 3.22 – 3.50 m, 2 H (1′-H); 6.20 bs, 1 H (D_2O exchangeable, NH)
XIIc	99 – 101[a] 69	$C_{12}H_{21}N_3O_4$ (271.3)	53.12 53.26	7.80 7.82	15.48 15.66	MS (*m/z*): 271 (M^+). ^1H NMR ($CDCl_3$):1.10 t, 3 H (4-$NHCH_2CH_3$); 3.30 – 3.55 m, 4 H (1′-H and 4-$NHCH_2$); 6.08 bs, 1 H (D_2O exchangeable, NH)

[a] Ethyl acetate–hexane; [b] methanol–water.

SiO_2 column, elution with C_6H_6–EtOAc (8 : 2) and evaporation of the appropriate fractions gave 3.1 g (55%) of pyrimidinone *VII*, m.p. 106 °C. UV spectrum λ_{max} (MeOH): 205, 271; ^1H NMR spectrum ($CDCl_3$): 2.35 s, 3 H (6-CH_3); 3.28 s, 3 H (5-CH_2OCH_3); 3.90 s, 3 H (4-OCH_3); 4.22 s, 2 H (5-CH_2); 4.50 – 4.65 m, 2 H (1'-H); 5.02 – 5.25 m, 2 H (3'-H); 5.65 – 6.06 m, 1 H (2'-H). Mass spectrum (*m*/*z*): 224 (M^+); for $C_{11}H_{16}N_2O_3$ calculated (224.3).

1-Allyl-5-methoxymethyl-6-methyluracil (*VIII*)

A mixture of pyrimidinone *VII* (0.5 g, 2.2 mmol) and 2 M aqueous NaOH (15 ml) was stirred at 50 °C for 24 h. The resulting mixture was cooled, neutralized with AcOH and concentrated under reduced pressure to dryness. The product was dissolved in H_2O (100 ml), extracted with EtOAc (250 ml), the extracts dried with Na_2SO_4 and concentrated in vacuo to dryness. The product was crystallized from Et_2O; yield 0.24 g (51%), m.p. 140 °C. ^1H NMR spectrum ($CDCl_3$): 2.37 s, 3 H (6-CH_3); 3.27 s, 3 H (5-CH_2OCH_3); 4.25 s, 2 H (5-CH_2); 4.40 – 4.53 m, 2 H (1'-H); 5.10 – 5.25 m, 2 H (3'-H); 5.60 – 6.00 m, 1 H (2'-H). Mass spectrum (*m*/*z*): 210 (M^+). For $C_{10}H_{14}N_2O_3$ (210.2) calculated: 57.12% C, 6.71% H, 13.32% N; found: 57.39% C, 6.82% H, 13.45% N.

1-(2,3-Dihydroxypropyl)-4-methoxy-5-methoxymethyl-6-methyl-2(1*H*)-pyrimidinone (*X*)

Osmium tetraoxide (0.08 g, 0.3 mmol) was added to the stirred solution of pyrimidinone *VII* (5.0 g, 22.3 mmol) and $NaClO_3$ (3.09 g, 29.0 mmol) in 50% aqueous MeOH (200 ml). Stirring was continued for 24 h. The resulting mixture was filtered through Celite pad and the solid was washed with H_2O (100 ml). The filtrate and washings were combined and solvent removed under reduced pressure to dryness. The crude product was chromatographed on a SiO_2 column, elution $CHCl_3$–MeOH (9 : 1) and evaporation of the appropriate fractions gave 3.8 g (66%) of dihydroxypropyl *X*, m.p. 96 °C ethyl acetate–hexane). IR spectrum (KBr) : 3 300 (OH), 1 610 (C=O). UV spectrum λ_{max} (MeOH): 205, 279; (MeOH–NaOH): 208, 278.^1H NMR spectrum ($CDCl_3$): 2.41 s, 3 H (6-CH_3); 3.27 s, 3 H (5-CH_2OCH_3); 3.45 – 3.65 m, 2 H (1'-H), 3.85 s, 3 H (4-OCH_3); 3.85 – 4.06 m, 3 H (2'-H and 3'-H); 4.20 s, 2 H (5-CH_2). Mass spectrum (*m*/*z*); 258 (M^+). For $C_{11}H_{18}N_2O_5$ (258.3) calculated: 51.15% C, 7.02% H, 10.85% N; found: 51.36% C, 7.37% H, 11.09% N.

1-(2,3-Dihydroxypropyl)-5-methoxymethyl-6-methyluracil (*XI*)

A mixture of *X* (0.5 g, 1.9 mmol) and 2 M aqueous NaOH (30 ml) was stirred at room temperature for 24 h. The resulting mixture was worked up as described for *VIII*. The crude product was chromatographed on a SiO_2 column, elution with $CHCl_3$–MeOH (8 : 2) and evaporation of the appropriate fractions gave 0.23 g (48%) of methyluracil *XI*, m.p. 130 °C. IR spectrum (KBr): 3 240 (OH), 1 660 (C=O). UV spectrum λ_{max} (MeOH): 212, 270; (MeOH–NaOH): 212, 272. ^1H NMR spectrum ($CDCl_3$ + $(CD_3)_2SO$): 2.33 s, 3 H (6-CH_3); 3.20 s, 3 H (5-CH_2OCH_3); 3.30 – 3.45 m, 2 H (1'-H); 3.74 – 4.05 m, 3 H (2'-H and 3'-H); 4.15 s, 2 H (5-CH_2). Mass spectrum (*m*/*z*): 244 (M^+). For $C_{10}H_{16}N_2O_5$ (244.3) calculated: 49.17% C, 6.60% H, 11.47% N; found : 49.32% C, 6.84% H, 11.41% N.

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