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Studies on the Synthesis of Pyrimidine Deoxynucleosides. I. Synthesis of 2′,3′-Dideoxyuridine and 1-(3-Ethylthio-3-deoxy-β-D-xylofuranosyl)uracil

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Treatment of 2,2′-anhydro-1-(3,5-di-*O*-acetyl-β-D-arabinofuranosyl)uracil (II) with sodium ethanethiol afforded 1-(3-ethylthio-3-deoxy-β-D-xylofuranosyl)uracil (IV) in 90% yield. Hydrogenation of 2,2′-anhydro-1-(5-*O*-benzoyl-3-*O*-mesyl-β-D-arabinofuranosyl)-uracil (III) with Raney nickel resulted in formation of the 5,6-dihydro derivative (VI). 5′-*O*-Benzoyl-2′-bromo-2′-deoxy-3′-*O*-mesyluridine (VII) was hydrogenated in the presence of Pd·$BaSO_4$ or Raney nickel to yield 5′-*O*-benzoyl-2′,3′-dideoxyruidine (VIII). VIII was treated with alkali to give 2′,3′-dideoxyuridine (IX) in 50% overall yield from uridine. The mechanism of the reductive elimination of the *cis*-bromohydrin mesylate (VII) was presented. The treatment of VII with sodium methoxide in methanol gave 1-(2-bromo-2,3-dideoxy-2-ene-β-D-glyceropentofuranosyl)uracil (XII) which was converted to IX by the catalytic hydrogenation. Bromination of IX afforded 5-bromo-2′,3′-dideoxy-uridine (XIV).

During the course of our attempts to develop new routes for the syntheses of 2′-deoxyuridine (I) we investigated the use of 2,2′-anhydro-1-(3,5-di-*O*-acetyl-β-D-arabinofuranosyl)-uracil (II)[2] and of 2,2′-anhydro-(5-*O*-benzoyl-3-*O*-mesyl-β-D-arabinofuranosyl)uracil (III)[3] as starting materials. While neither of these compounds yielded I, they did lead to the syntheses of some interesting nucleoside analogs.

In an attempt to introduce an ethylthio group into the 2′-position, we subjected compound II to fission of the anhydro linkage by use of sodium ethanethiol according to a modification of the method of Brown, *et al.*[4] The reaction mixture which revealed a single ultraviolet absorbing spot on a paper chromatogram was desalted with activated charcoal. A white powder was obtained which was identical with 1-(3-ethylthio-3-deoxy-β-D-xylofuranosyl)-

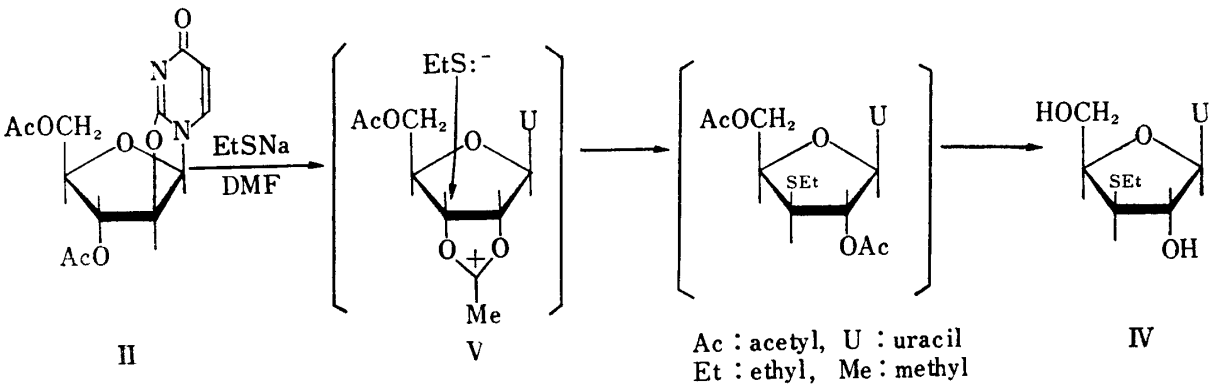


Chart 1

1) Location: *Juso-Nishino-cho, Higashiyodogawa-ku, Osaka.*
2) Y. Furukawa and M. Honjo, *Chem. Pharm. Bull.* (Tokyo), **16**, 2274 (1968).
3) J.F. Codington, R. Recher and J.J. Fox, *J, Am. Chem. Soc.*, **82**, 2794 (1960).
4) D.M. Brown, D.B. Parihar, A. Todd and S. Varadarajan, *J. Chem. Soc.*, **1958**, 3028.

uracil (IV, Chart 1) on the basis of elemental analysis and the nuclear magnetic resonance (NMR) spectrum.[5] The H_3' signal in IV was shifted to considerably higher field (δ=3.55 ppm) which is consistent with the introduction of an ethylthio function into the 3'-position. The reaction may be interpreted as follows: The ethanthiol anion attacks the 2',3'-acetoxonium ion (V) at position 3' (the 2'-position is sterically more hindered by the uracil moiety) and, after deacetylation, affords the xylo nucleoside (IV).[6,7]

The aforementioned reaction thus led to an alternative synthesis of the same compound (IV) which was previously prepared by Brown, *et al.*[4] by treatment of 2,2'-anhydro-1-β-D-arabinofuranosyluracil with sodium ethanethiol. Their reaction mechanism assumed the intermediary formation of 2',3'-epoxyribofuranosyluracil. Our synthesis of IV from II appears to be superior to theirs in view of the higher yields obtained and the ability to isolate product without the use of counter-current distribution techniques. Kowollik and Langen[8] recently reported the synthesis of IV from uridine by four steps *via* 1-(3-*O*-mesyl-2,5-di-*O*-trityl-β-D-ribofuranosyl)uracil. Their overall yield, however, was low and their process required tedious purification procedures.

Studies with compound III (Chart 2) required the development of methods for the hydrolytic removal of the 3'-*O*-mesyl group. Compound III was treated by the method of Kenner and Murray[9] who had subjected 1:2,5:6-diisopropylidene-3-*O*-tosyl-D-glucose to hydrogenation with Raney nickel in ethanol to obtain 1:2,5:6-diiospropylidene-D-glucose in high yields. The reaction of III took up two mole equivalents of hydrogen resulting in a considerable decrease of the optical density at 250 mμ. The hydrogenation product was obtained as colorless crystals, and the structure, 5,6-dihydro-2,2'-anhydro-1-(5-*O*-benzoyl-3-*O*-mesyl-β-D-arabinofuranosyl)uracil (VI), was assigned on the basis of the elementary analysis and the NMR spectrum (both signals of 5,6-vinyl protons of uracil moiety disappeared and two triplet signals of methylene protons appeared at δ=2.56 and 3.66 ppm, whose chemical shifts and coupling constants were consistent with those of 5,6-dihydrouridine[10]). The following reactions were then attempted with the aim of removing the 3'-*O*-mesyl group from III[3]:III→5'-*O*-benzoyl-2'-bromo-2'-deoxy-3'-*O*-mesyluridine (VII) →5'-*O*-benzoyl-2'-deoxy-3'-*O*-mesyluridine →2,3'-anhydro-1- (5-*O*-benzoyl-2-deoxy-β-D-xylofuranosyl) uracil→3',5'-di-*O*-benzoyl-2'-deoxyuridine →2'-deoxyuridine. III was thus treated by a modification of method of Fox, *et al.*[11] to afford VII, in 93% yield. VII was subjected to debromination by catalytic hydrogenation in ethanol in the presence of palladised barium sulfate[12] (or Raney nickel) and sodium acetate. The reaction took up two mole equivalents of hydrogen. The reaction mixture was purified by silica gel column chromatography to afford colorless needles, in 72% yield. This substance did not contain sulfur and was assigned the structure, 5'-*O*-benzoyl-2',3'-dideoxyuridine (VIII), on the basis of the elementary analysis and the NMR spectrum (signals of four protons appearing at δ=1.7—2.7 ppm were in accord with those[13] of 2'- and 3'-protons of 2',3'-dideoxyuridine), and its conversion to 2',3'-dideoxyuridine (IX) by the treatment with sodium methoxide (Chart 2). This appears to be the first example, not only in the carbohydrate area, but also in the nucleoside field of a unique reductive elimination of a *cis*-bromohydrin mesylate.

5) The NMR spectrum of our sample was in good agreement with that of an authentic sample, which was kindly provided by Dr. Kowollik (Institut für Biochemie der Deutschen Akademie der Wissenschaften zu Berlin).
6) The oxonium ion mechanism postulated here is akin to that described by Fox and Watanabe[7] for the conversion of a 2,3'-anhydro-1-(2,5-di-*O*-benzoyl-β-D-xylosyl)uracil to tri-*O*-benzoylxylofuranosyluracil using benzoate ion as the nucleophile.
7) J.J. Fox and K.A. Watanabe, *Chem. Pharm. Bull.* (Tokyo), **17**, 211 (1969).
8) G. Kowollik and P. Langen, *Chem. Ber.*, **101**, 235 (1968).
9) G.W. Kenner and M.A. Murray, *J. Chem. Soc.*, **1949**, S 178.
10) A.R. Hanze, *J. Am. Chem. Soc.*, **89**, 6720 (1967).
11) J.F. Codington, I.L. Doerr and J.J. Fox, *J. Org. Chem.*, **29**, 558 (1964).
12) D.M. Brown, D.B. Parihar, C.B. Reese and A. Todd, *J. Chem. Soc.*, **1958**, 3035.
13) See the experimental.

This reductive elimination seemed to proceed *via* the intermediary formation of the 2,3′-anhydro derivative. This assumption, however, was ruled out by the fact that thin-layer chromatography (TLC) using silica gel showed only the starting material, after VII had been left in ethanol at room temperature for two hours[14] in the presence of sodium acetate. In order to examine the effect of the presence of the bromine atom on the hydrogenation, a compound having no bromine atom [5′-*O*-benzoyl-3′-*O*-mesyl-2′-deoxyuridine (X)] was synthesized in two steps from 5′-*O*-trityl-3′-*O*-mesyl-2′-deoxyuridine,[15] and subjected to catalytic hydrogenation under the same conditions as in case of VII. The powdery substance obtained by treatment of the reaction product proved to be an equimolar mixture of X and 5,6-dihydro-5′-*O*-benzoyl-3′-*O*-mesyl-2′-deoxyuridine (XI) in the light of the elementary analysis and the NMR spectrum (Chart 3). These observations suggest that the cleavage of the mesyloxy group of VII

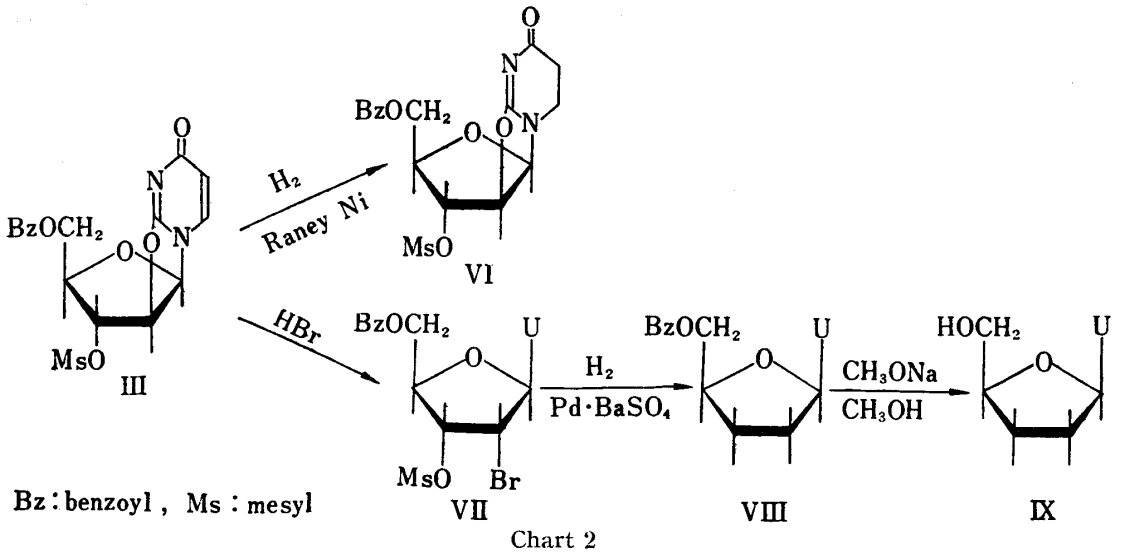


Chart 2

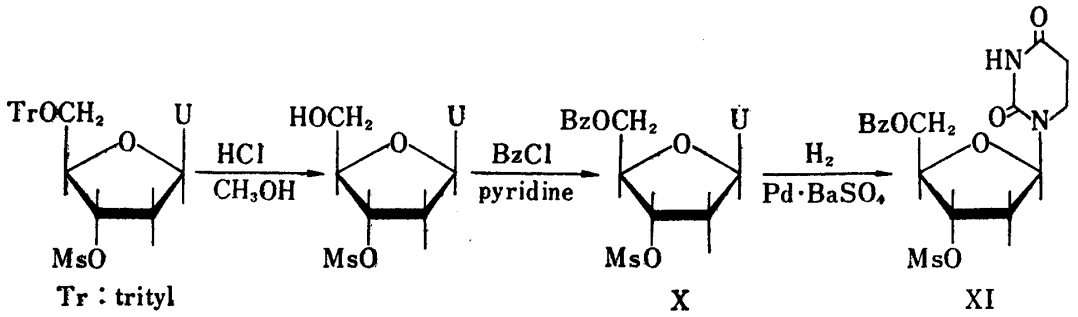


Chart 3

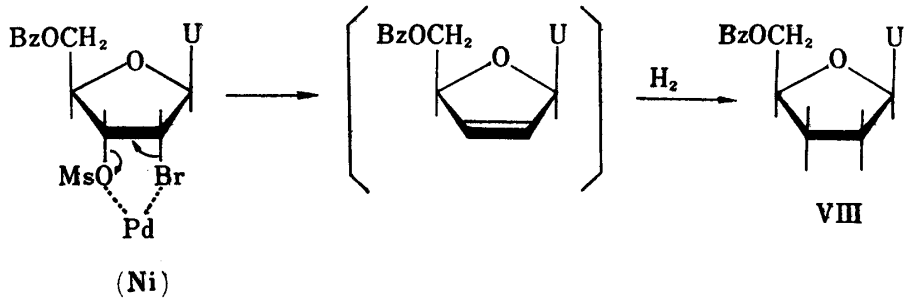


Chart 4

14) When VII was left for 20 hours under the similar conditions, 2,2′-anhydro linkage was formed in 20% yield, but no appreciable amount of 2,3′-anhydro compound was detectable.

15) J.P. Horwitz, J. Chua, M.A. Da Rooge, M. Noel and I.L. Klundt, *J. Org. Chem.*, **31**, 205 (1966).

occurs prior to, or at the same time as, the elimination of the bromine atom. If the former is the case, 5′-*O*-benzoyl-2′-bromo-2′,3′-dideoxyuridine should be formed as the intermediate. VII was thus subjected to the catalytic hydrogenation under the conditions as described above except that the reaction was interrupted when one mole equivalent of hydrogen had been absorbed. The reaction mixture was purified by silical gel column chromatography to isolate VII and VIII (45% and 36% in yields, respectively). This indicates a concomitant loss of both 2′-bromine and 3′-mesyloxy group. A possible interpretation of the concomitant cleavage is that Pd or Ni may coordinate with VII to cause *cis*-elimination giving rise an intermediary unsaturated compound followed by the hydrogenation of the double bond[16] (Chart 4).

In order to remove the 5′-*O*-benzoyl group, VII was refluxed in methanol with sodium methoxide from which colorless crystals were obtained in 83% yield. The structure of this compound was assigned 1-(2-bromo-2,3-dideoxy-2-ene-β-D-glyceropentofuranosyl)uracil (XII) on the basis of the elementary analysis, the NMR spectrum (one vinyl proton signal appeared at $\delta=6.71$ ppm which by a decoupling experiment was assigned to 3′-proton) and its conversion to IX by catalytic hydrogenation (68% in yield). XII was the only product to be isolated. Paper chromatography of the mother liquor revealed formation of no other products having different *Rf* values. Horwitz, *et al.* were the first to prepare the 2′,3′-unsaturated compound, 1-(5-*O*-trityl-2,3-dideoxy-2-ene-β-D-glycero-pentofuranosyl) uracil, by the treatment of 2,3′-anhydro-1-(2-deoxy-5-*O*-trityl-β-D-lyxo-furanosyl)uracil or 2′-deoxy-3′-*O*-mesyl-5′-*O*-trityluridine in dimethylsulfoxide with potassium *t*-butoxide and they proposed an *E* 2 elimination mechanism for the former reaction.[15] The mechanism of our reaction could be accounted for by either a direct *E* 2 elimination or the intermediary formation of 2,3′-anhydro compound (XIII) followed by the *E* 2 elimination (Chart 5).

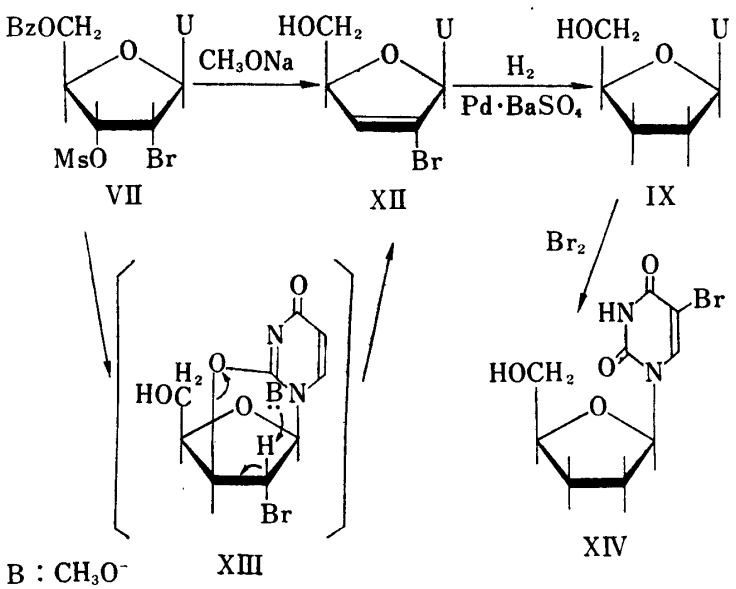


Chart 5

Robins, *et al.* pointed out the possibility that a 2′,3′-dideoxynucleoside may be a chain terminator for the biosynthesis of deoxyribonucleic acid.[17] The synthesis of IX through five steps from 2′-deoxyuridine (I) has already been reported by Pfitzner and Moffatt[18] and by Horwitz, *et al.*[15,19] We have succeeded in the synthesis of IX in five steps in an overall yield of about 50% starting from uridine which is more readily available than 2′-deoxyuridine (I).

16) VII was shaken in ethanol in the presence of palladised barium sulfate or inactivated Raney nickel and sodium acetate with exclusion of hydrogen. The reaction mixture was separated by silica gel column chromatography to recover VII without formation of any detectable amount of the 2′,3′-unsaturated compound. This implies that the reductive elimination can be initiated by the participation of hydrogen.

17) M.J. Robins and R.K. Robins, *J. Am. Chem. Soc.*, **86**, 3585 (1964); M.J. Robins, J.R. McCarthy, Jr. and R.K. Robins, *Biochemistry*, **5**, 224 (1966).

18) K.E. Pfitzner and J.G. Moffatt, *J. Org. Chem.*, **29**, 1508 (1964).

19) 2′,3′-Dideoxy-5-fluorouridine was synthesized by a method analogous to that of Horwitz, *et al.*[15] to test the biological activity.[20]

20) T.A. Khwaja and C. Heidelberger, *J. Med. Chem.*, **10**, 1066 (1967).

Bromination of IX according to the method of Chang and Welch[21] afforded 5-bromo-2′,3′-dideoxyuridine (XIV) in 61% yield. The biological activity of XIV is under testing.

Experimental[22]

1-(3-Ethylthio-3-deoxy-β-D-xylofuranosyl)uracil (IV)——A solution of II (900 mg, 2.9 mmoles) in DMF (135 ml), after the addition of EtSNa (4.5 g), was left at 37° for 15 hr. The reaction mixture was evaporated to dryness *in vacuo*, the residue dissolved in H_2O (200 ml), the solution adjusted to pH 7 with AcOH, and passed through the column of activated charcoal (5 g). The column was washed with H_2O, then eluted with 50% EtOH containing 2% conc. NH_4OH. The eluate was evaporated to dryness *in vacuo* to yield a viscous substance which became a white powder after drying at 90° (770 mg, 90%), UV mμ: $\lambda_{max}^{H_2O}$ 262, $\lambda_{min}^{H_2O}$ 232, $\lambda_{max}^{pH\,11}$ 262, $\lambda_{min}^{pH\,11}$ 237, $[\alpha]_D^{24}+6.4°$($c=1.22$, H_2O), PC (H_2O: BuOH 14:86, v/v): *Rf* 0.64. *Anal.* Calcd. for $C_{11}H_{16}O_5N_2S\cdot 1/2H_2O$: C, 44.50; H, 5.86; N, 9.42; S, 10.80. Found: C, 44.57; H, 5.79; N, 9.82; S, 10.93. NMR (D_2O): 1.28 (3H, triplet, $J=7.5$ cps, CH_3), 2.71 (2H, quartet, $J=7.5$ cps, CH_2), 3.55 (1H, quartet, $J_{2',3'}=5.0$ cps, $H_{3'}$), 4.43 (1H, quartet, $J_{1'2'}=4.5$ cps, $J_{2',3'}=5.0$ cps, $H_{2'}$), 4.95 (2H, doublet, $J=4.5$ cps, $H_{5'}$), 5.87 (doublet, $J=4.5$ cps, $H_{1'}$), 5.92 (doublet, $J=8.0$ cps, H_5), 7.99 (doublet, $J=8.0$ cps, H_6).

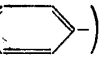
5,6-Dihydro-2,2′-anhydro-1-(5-*O*-benzoyl-3-*O*-mesyl-β-D-arabinofuranosyl)uracil (VI)——To a solution of III[3] (910 mg, 2.23 mmoles) in 50% EtOH (250 ml) was added Raney nickel (W-6, 4 ml). The mixture was shaken in H_2 atmosphere at 760 mmHg and room temperature for 4 hr (H_2 absorbed, 100 ml). The catalyst was filtered off, the filtrate evaporated to dryness, and the residue recrystallized from H_2O (20 ml) to yield colorless needles, mp 158—160° (360 mg, 40%). *Anal.* Calcd. for $C_{17}H_{18}O_8N_2S$: C, 49.74; H, 4.42; N, 6.83; S, 7.81. Found: C, 50.15; H, 4.47; N, 6.75; S, 7.56. NMR ($CDCl_3$): 2.58 (2H, triplet, $J=8.0$ cps, H_5), 3.24 (3H, singlet, CH_3), 3.64 (2H, triplet, $J=8.0$ cps, H_6), 5.93 (1H, doublet, $J=5.5$ cps, $H_{1'}$), 7.3—8.1 (5H, multiplet, ).

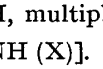
5′-*O*-Benzoyl-2′,3′-dideoxyuridine (VIII)——i) To a solution of VII (1.62 g, 3.31 mmoles) in EtOH (220 ml) were added 10% Pd·$BaSO_4$ (800 mg) and AcONa (656 mg). The mixture was subjected to catalytic hydrogenation in H_2 atmosphere for 1 hr (H_2 absorbed, 170 ml, 6.95 mmoles). The catalyst was filtered off, the filtrate evaporated *in vacuo* to dryness, the residue dissolved in $CHCl_3$ and the solution placed on a column of silica gel (40 g) and the column eluted with $CHCl_3$. The UV absorbing fraction (the 1st fraction was discarbed) was evaporated *in vacuo* to dryness and recrystallized from EtOAc to yield colorless needles, mp 143—144° (750 mg, 72%). *Anal.* Calcd. for $C_{16}H_{16}O_5N_2$: C, 60.75; H, 5.11; N, 8.86. Found: C, 60.70; H, 4.97; N, 8.84. NMR ($CDCl_3$): 1.7—2.7 (4H, multiplet, $H_{2',3'}$), 6.08 (1H, quartet, $H_{1'}$), 5.57 (1H, doublet, $J=8.0$ cps, H_5), 7.3—8.2 (6H, multiplet, H_6 and ), 9.80 (1H, broad singlet, NH). ii) To a solution of VII (245 mg, 0.5 mmole) in EtOH (25 ml) was added Raney nickel (0.1 ml) and AcONa (82 mg). The mixture was subjected to catalytic hydrogenation for 1 hr. The reaction mixture was similarly treated as described above to yield a viscous substance of which the *Rf* value (TLC, silica gel, EtOAc) and the NMR spectrum ($CDCl_3$) were similar to those of the sample obtained by the method i), respectively.

The Formation of 2,2′-Anhydro-1-(5-*O*-benzoyl-3-*O*-mesyl-β-D-arabinofuranosyl)uracil (III) from 5′-*O*-Benzoyl-2′-bromo-2′-deoxy-3′-*O*-mesyluridine (VII)——A solution of AcONa (220 mg) in H_2O (3 ml) was added to a solution of VII (600 mg) in EtOH (50 ml) and the mixture was left at room temperature for 2 hr. TLC (silical gel, $CHCl_3$:MeOH=10:1, v/v, all TLC in this item were performed under the similar conditions) revealed a single UV absorbing spot of the same *Rf* value=0.6 as that of VII. When the above described mixture was kept for further 18 hr, a new UV absorbing spot was detected at *Rf* value=0.3 by TLC. Colorless needles crystallized, which after cooling were separated by filtration, mp 228—230° (decomp.) [(lit,[5] mp 226—227° (decomp.)]. *Rf* 0.3. This sample was found to be identical with III by comparison of the IR spectrum (KBr) and by mixed melting point.

5′-*O*-Benzoyl-3′-*O*-mesyl-2′-deoxyuridine (X).——A solution of 5′-*O*-trityl-3′-*O*-mesyl-2′-deoxyuridine[15] (7 g, 12.7 mmoles) in MeOH (300 ml), after the addition of 10% HCl–MeOH (30 ml), was refluxed for 10 min. The solvent was removed *in vacuo* and the residue extracted with a mixture of H_2O (150 ml) and ether (150 ml). The aqueous layer was evaporated to dryness *in vacuo*, the residue (3′-*O*-mesyl-2′-deoxyuridine) dissolved in pyridine (40 ml), the solution mixed with benzoylchloride (1.96 g) and kept at 55—60° for 40 hr. The solvent was evaporated *in vacuo* and the residue extracted with a mixture of $CHCl_3$ (100 ml) and H_2O (100 ml). An insoluble material was filtered off, the $CHCl_3$ layer evaporated to dryness *in vacuo*, the residue dissolved in $CHCl_3$ and the solution adsorbed to a column (3.2×30 cm) of silica gel (100 g). The column was eluted first with $CHCl_3$ (3 liters) and then with $CHCl_3$–EtOAc (1:1, v/v). The latter UV absorbing eluate

21) P.K. Chang and A.D. Welch, *Biochem. Pharmacol.*, **6**, 50 (1961).
22) All melting points were uncorrected, NMR spectrum was measured using Me_4Si as an external reference and chemical shift was expressed in δ values.

(3.5 liters, TOD_{260}[23] 63,000) was evaporated to dryness *in vacuo* to yield colorless powder (2.7 g, 52%). $[\alpha]_D^{22}$ +6.0° (c=5.0, acetone). *Anal.* Calcd. for $C_{17}H_{18}O_8N_2S$: C, 49.75; H, 4.43; N, 6.83; S, 7.82. Found: C, 49.04; H, 4.30; N, 6.46; S, 7.77. NMR ($CDCl_3$): 2.3—2.8 (2H, multiplet, $H_{2'}$), 3.09 (3H, singlet, CH_3), 5.58 (1H, doublet, J=8.0 cps, H_5), 6.19 (1H, triplet, J=6.5 cps, $H_{1'}$), 7.2—8.2 (6H, multiplet, H_6 and  -), 10.0 (1H, broad singlet, >NH).

Hydrogenation of 5′-*O*-Benzoyl-3′-*O*-mesyl-2′-deoxyuridine (X)——To a solution of X (410 mg, 1 mmole) in EtOH (53 ml) were added 10% Pd·$BaSO_4$ (270 mg) and AcONa (220 mg). The mixture was shaken in H_2 atmosphere at 760 mmHg and room temperature for 1 hr (H_2 absorbed, 5 ml). The catalyst was filtered off, the filtrate evaporated to dryness *in vacuo*, the residue dissolved in $CHCl_3$, the solution put onto a column (2.0×22 cm) of silica gel (30 g), the column washed with $CHCl_3$ (200 ml) and eluted with EtOAc (250 ml). A UV absorbing eluate was evaporated to dryness *in vacuo* to afford colorless powder (420 mg, 102% recovery). *Anal.* Calcd. for $C_{17}H_{19}O_8N_2S$ (an equimolar mixture of X and XI): C, 49.74; H, 4.67; N, 6.82; S, 7.80. Found: C, 48.39; H, 4.67; N, 6.54; S, 7.66. NMR ($CDCl_3$): 2.2—2.8 [3H, $H_{2'}$ (X and XI) and H_5 (XI)], 3.08 (3H, singlet, CH_3), 3.18—3.5 [1H, multiplet, H_6 (XI)], 5.58 [0.5H, doublet, J=8.0 cps, H_5 (X)], 6.05—6.45 [1H, multiplet, $H_{1'}$ (X and XI)], 7.25—8.15 (5.5H, multiplet,  - (X and XI), H_6 (XI)), 8.55 (0.5H, singlet, >NH (XI)], 9.68 [0.5H, broad singlet, >NH (X)].

A Limited Hydrogenation of 5′-*O*-Benzoyl-2′-bromo-2′-deoxy-3′-*O*-mesyluridine (VII)——To a solution of VII (810 mg, 1.66 mmoles) in EtOH (80 ml) were added 10% Pd·$BaSO_4$ (250 mg) and AcONa (328 mg). The mixture was shaken in H_2 atmosphere at 760 mmHg, until one mole equivalent of H_2 (40 ml, 1.65 mmoles) had been absorbed. The catalyst was filtered off, the filtrate evaporated to dryness *in vacuo*, the residue dissolved in $CHCl_3$, half volume of the solution put onto a column (2.6×33 cm) of silica gel (50 g), and the column was eluted with $CHCl_3$ to yield 2 fractions. The 1st (760 ml, TOD_{260} 4010) was evaporated to dryness *in vacuo* to afford colorless powder (200 mg, 45%), which was identified with the starting material (VII) on the basis of the elementary analysis and the NMR spectrum. The 2nd (800 ml, TOD_{260} 3050) was evaporated to dryness *in vacuo* to give colorless powder (95 mg, 36%), which was identified with VIII on the basis of the elementary analysis and the NMR spectrum. No UV absorbing substance other than VII and VIII was detected in the reaction mixture.

1-(2-Bromo-2,3-dideoxy-2-ene-β-D-glyceropentofuranosyl)uracil (XII)——A solution of VII (1.35 g, 2.76 mmoles) in 2.3% MeONa–MeOH (20 ml) was refluxed for 1 hr. The solvent was evaporated *in vacuo*, the residue dissolved in H_2O, the solution passed through columns of IR-120 (H^+) (10 ml) and Dowex-1 (HCO_3^-) (20 ml) successively and the columns washed with H_2O. The effluent and the washings were combined and evaporated to dryness *in vacuo*. The residue was recrystallized from H_2O to afford colorless needles (660 mg, 83%). UV mμ (ε): $\lambda_{max}^{H_2O}$ 258.5 (9.74×10³), $\lambda_{min}^{H_2O}$ 230.5, $\lambda_{max}^{pH\,1}$ 258.5 (9.68×10³), $\lambda_{max}^{pH\,13}$ 259.5 (7.11×10³), $\lambda_{min}^{pH\,13}$ 244. *Anal.* Calcd. for $C_9H_9O_4N_2Br$: C, 37.36; H, 3.14; N, 9.69; Br, 27.64. Found: C, 37.48; H, 3.05; N, 9.79; Br, 27.84. NMR (100 Mc, d_6-DMSO): 3.59 (2H, doublet, J=3.0 cps, $H_{5'}$), 4.76 (1H, quartet, J=2.0, 3.0 cps, $H_{4'}$), 5.62 (1H, quartet, J=2.0, 8.0 cps, H_5), 6.63 (1H, triplet, J=2.0 cps, $H_{1'}$), 6.72 (1H, quartet, J=2.0, 3.5 cps, $H_{3'}$), 7.78 (1H, doublet, J=8.0 cps, H_6), 11.36 (1H, broad singlet, >NH). Paper chromatography (BuOH:H_2O=86:14, v/v, ascending method) of the mother liquor revealed a single UV absorbing spot of the same *Rf* value (0.71) as that of XII.

2′,3′-Dideoxyuridine (IX)——i) From 5′-*O*-Benzoyl-2′,3′-dideoxyuridine (VIII): A solution of VIII (300 mg, 0.95 mmoles) in 2.3% MeONa–MeOH (4 ml) was refluxed for 1 hr. The solvent was evaporated *in vacuo*, the residue dissolved in H_2O_2 passed through columns of IR-120 (H^+) (2 ml) and Dowex-1 (HCO_3^-) (4 ml) successively and the columns wahsed with H_2O. The effluent and the washings were combined and evaporated to dryness *in vacuo*. The residue was dissolved in acetone (5 ml) and an insoluble material was filtered off. Ether was added dropwise to the filtrate to yield colorless crystalls, mp 115° (lit., mp 116—117°,[18] mp 117.5—118.5°[15]) (140 mg, 70%). UV mμ: $\lambda_{max}^{pH\,7}$ 262, $\lambda_{min}^{pH\,7}$ 231, $\lambda_{max}^{pH\,12}$ 262, $\lambda_{min}^{pH\,12}$ 242. *Anal.* Calcd. for $C_9H_{12}O_4N_2$: C, 50.74; H, 5.70; N, 13.13. Found: C, 50.90; H, 5.70; N, 13.20. NMR (D_2O): 1.6—2.8 (4H, multiplet, $H_{2'}$,$_{3'}$), 6.15 (1H, quartet, $H_{1'}$), 5.94 (1H, doublet, J=8.0 cps, H_5), 8.0 (1H, doublet, J=8.0 cps, H_6). ii) From 1-(2-Bromo-2,3-dideoxy-2-ene-β-D-glyceropentofuranosyl)uracil (XII): To a solution of XII (578 mg, 2 mmoles) in EtOH (100 ml) were added 10% Pd·$BaSO_4$ (400 mg) and AcONa (328 mg). The mixture was shaken in H_2 atmosphere at 760 mmHg for 2 hr (H_2 absorbed, 90 ml, 3.7 mmoles). The catalyst was filtered off, the filtrate evaporated to dryness *in vacuo*, the residue dissolved in H_2O, the solution treated with a column of activated charcoal (5 g) to remove inorganic salts, and the eluate further evaporated to dryness *in vacuo*. The residue was recrystallized from acetone to afford colorless needles (290 mg, 68%). The UV absorbing, NMR and IR spectra of the sample were all in accord with those of the sample obtained by the method i). *Anal.* Calcd. for $C_9H_{12}O_4N_2$: C, 50.74; H, 5.70; N, 13.13. Found: C, 50.59; H, 5.70; N, 13.22.

5-Bromo-2′,3′-dideoxyuridine (XIV)——To a solution of IX (416 mg, 2 mmoles) in pyridine (9 ml) was added a solution of Br_2 (0.35 g, 2.18 mmoles) in CCl_4 (1.2 ml). The mixture was stirred at room temperature

23) TOD_{260}=Optical density at 260 mμ×ml.

for 2 hr and evaporated to dryness *in vacuo*. The residue was dissolved in MeOH (4 ml) and the solution re-evaporated to dryness. The process was repeated three times and the crystalline residue was recrystallized from 20% MeOH (4 ml) to yield colorless needles, mp 178—179° (350 mg, 61% yield). UV mμ: $\lambda_{max}^{H_2O}$ 280, $\lambda_{min}^{H_2O}$ 242. $[\alpha]_D^{23}$ +36.0° (c=0.5 in 0.1N NaOH). *Anal.* Calcd. for $C_9H_{11}O_4N_2Br$: C, 37.12; H, 3.81; N, 9.62; Br, 27.44. Found: C, 36.93; H, 3.93; N, 9.43; Br, 26.94. NMR (d_6-DMSO): 1.7—2.4 (4H, multiplet, $H_{2',3'}$), 5.94 (1H, quartet, $H_{1'}$), 8.55 (1H, singlet, H_6), 11.65 (1H, broad singlet, >NH).

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