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Nucleosides. CXLIV. Some Reactions of 2′-*O*-Triflyl-2,3′-anhydroxylosyluracil with Nucleophilic Reagents. Synthesis of 2′-Chloro-2′,3′-dideoxyuridinene. Studies Directed toward the Synthesis of 2′-Deoxy-2′-substituted *arabino* Nucleosides. (5)[1]

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Treatment of 2,3′-anhydro-1-(5-*O*-acetyl-2-*O*-triflyl-β-D-xylofuranosyl)uracil with LiCl in hexamethylphosphoric triamide afforded the 2′-"up" chloride of the anhydronucleoside, *i.e.*, the 2′-triflate group was directly displaced by the chloride nucleophile. All attempts to hydrolyze the 2,3′-anhydro linkage resulted in the formation of 2′-chloro-2′,3′-didehydro-dideoxynucleoside.

Keywords——nucleoside; anhydronucleoside; reaction mechanism; 2,3′-anhydro-1-(2-*O*-triflyl-β-D-xylofuranosyl)uracil; 2,3′-anhydro-1-(2-chloro-2-deoxy-β-D-lyxofuranosyl)uracil; 1-(2-chloro-2,3-didehydro-2,3-dideoxy-β-D-glyceropento-2-enofuranosyl)uracil; 2′-chloro-2′,3′-dideoxyuridinene

In the preceding report,[1] we described that our attempts to displace the 2′-triflate group of 2,5′-anhydro-3′-*O*-acetyl-2′-*O*-triflyluridine with various nucleophiles resulted in the formation of 5′-substituted-2,2′-anhydro-3′-*O*-acetyl-β-D-arabinosyluracils instead of 2′-substituted-2,5′-anhydroarabinosyluracils, due mainly to instability of the 2,5′-anhydro-linkage. Now it became interesting to investigate the course of reaction of a 2′-*O*-triflyl-2,3′-anhydro-xylosyluracil with nucleophilic reagents for two reasons: if the 2,3′-anhydrolinkage was more reactive than the 2′-triflate group, the initial product would be 3′-substituted uridine which would be further converted into a 3′-substituted-2,2′-anhydro-arabinosyluracil, whereas if the 2′-position was more susceptible to nucleophilic attack than the 3′-position, the reaction would lead to the formation of 2′-substituted-2,3′-anhydro-lyxosyluracil which may then be converted into a 2′-substituted-arabinofuranosyluracil.

Our starting material for the present investigation, *i.e.*, 5′-*O*-protected-2,3′-anhydro-1-(β-D-xylofuranosyl)uracil (**4**) (Chart 1) was prepared from 3′-*O*-mesyl-2′,5′-di-*O*-trityluridine (**1**).[2,3] Treatment of **1** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in *N*,*N*-dimethylformamide (DMF) afforded the 2,3′-anhydronucleoside **2** in 91% yield. The 5′-*O*-trityl group of **2** was selectively removed in 80% acetic acid to give 2,3′-anhydro-1-(2′-*O*-trityl-β-D-xylofuranosyl)uracil (**3a**) which was acylated with acetic anhydride or benzoyl chloride in pyridine to give **3b** and **3c**, respectively. De-*O*-tritylation of **3b** and **3c** with 10% trifluoroacetic acid in chloroform (v/v) afforded the corresponding 5′-*O*-protected 2,3′-anhydroxylosyluracils **4b** and **4c**. Compound **4b** was hydrolyzed in 80% acetic acid to 1-(5-*O*-acetyl-β-D-xylofuranosyl)uracil (**8b**) which was further converted into the known compound 1-(β-D-xylofuranosyl)uracil.[4] Tritylation of 2,3′-anhydro-1-(β-D-xylofuranosyl)uracil (**4a**)[2] with trityl chloride in pyridine gave 5′-*O*-trityl-2,3′-anhydroxylosyluracil **4d**. Treatment of **4b—d** with triflyl chloride in methylene chloride in the presence of *p*-dimethylaminopyridine (DMAP) and triethylamine afforded the corresponding 2′-*O*-triflyl derivatives **5b—d** in high

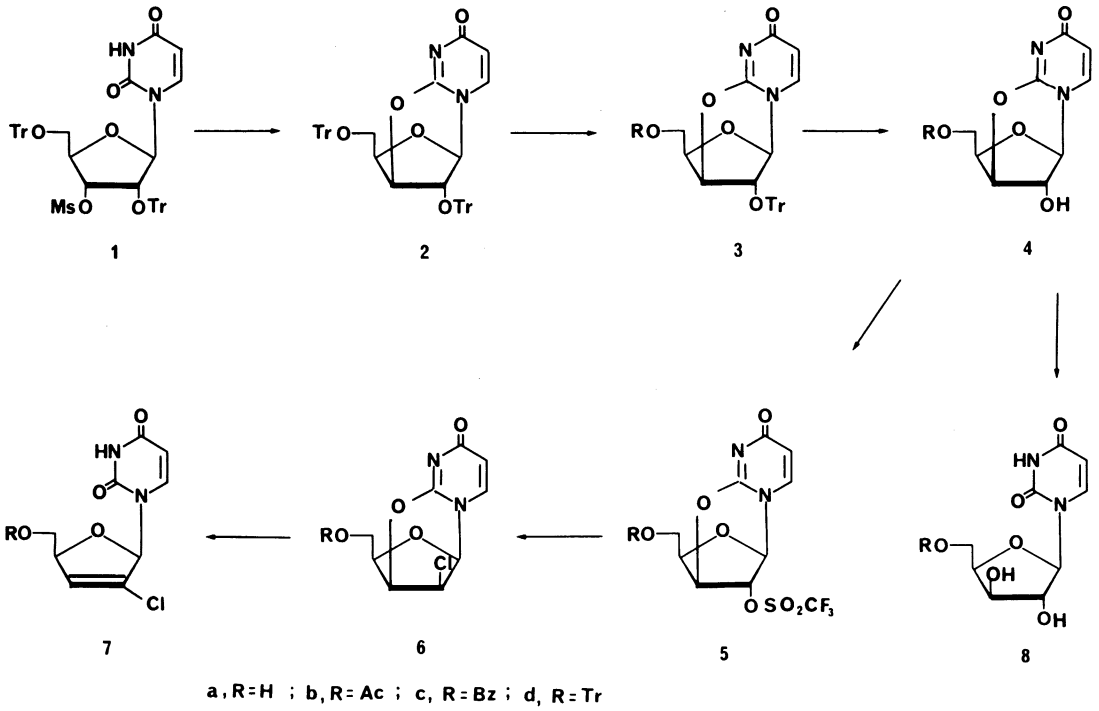

Chart 1

yield.[5]

Reaction of **5b** and **5c** with lithium chloride in hexamethylphosphoric triamide (HMPA) at 100 °C afforded the corresponding 2′-chloro-2′-deoxy-2,3′-anhydrolyxosyluracils **6b** and **6c** as major products. The ultraviolet (UV) spectra of these products are typical for those of 2,3′-anhydronucleosides.[2,4,6] Compound **6b** was not identical to the known 2,2′-anhydro-1-(5′-*O*-acetyl-3′-chloro-3′-deoxy-β-D-arabinofuranosyl)uracil.[7] Apparently, the 2′-triflate was directly displaced by chloride. Our attempts to open the 2,3′-anhydro linkage of **6b** and **6c** in base resulted in the formation of 2′-chloro-2′,3′-dideoxy-2′,3′-didehydrouridine (2′-chlorouridinene) (**7a**). Compound **7a** was analyzed correctly for $C_9H_9ClN_2O_4$ and showed one each of olefinic proton, and dissociable NH signals. The relatively large $J_{1',3'}$ and small $J_{1',4'}$ values (each 1.5 Hz) are consistent with the β-2-enofuranosyl structure.[8,9] The formation of **7** from **6** clearly established the *lyxo* structure for **6**, since proton and oxide must have been removed from C-2′ and C-3′, respectively, by a *trans* elimination mechanism. Formation of 2′,3′-dideoxy-2′,3′-didehydronucleosides from 2,3′-anhydro-2′-deoxynucleosides by a similar mechanism has been reported by Horwitz *et al.*[10] Acid catalyzed solvolysis[11] of **6b** with sodium benzoate and benzoic acid in DMF led to the formation of the olefins **7b** and no 2′-chloro-arabinosyluracil was obtained.

Experimental

2,3′-Anhydro-1-(2,5-di-*O*-trityl-β-D-xylofuranosyl)uracil (2)——To a solution of 3′-*O*-mesyl-2′,5′-di-*O*-trityluridine[2] (**1**, 18.75 g, 23 mmol) in DMF (150 ml) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (4 ml), and the mixture was heated at 100 °C for 3 h. A second charge of DBU (4 ml) was added, and heating continued for three more hours. The mixture was concentrated *in vacuo*, and the residue chromatographed on a silica gel column to give **2** (15 g, 91%), mp 224—225 °C. ^{1}H-NMR (DMSO-d_6) δ: 3.17 (m, 2H, H-5′,5″), 4.36—4.56 (m, 3H, H-2′,3′,4′), 4.88 (s, 1H, H-1′), 5.74 (d, 1H, H-5, $J_{5,6}$=7.3 Hz), 7.15—7.42 (m, 31H, H-6 and Tr). The melting point was undepressed

upon admixture with an authentic sample.[2)]

2,3′-Anhydro-1-(2-*O*-trityl-β-D-xylofuranosyl)uracil (3a)——A solution of **2** (2.8 g, 3.9 mmol) in 80% HOAc (150 ml) was stirred overnight at room temperature, and then concentrated *in vacuo*. Traces of HOAc were azeotropically removed with toluene and EtOH. Upon trituration of the residue with EtOH, **3a** crystallized (1.7 g, 92%), mp 284—285 °C. ^{1}H-NMR (DMSO-d_6) δ: 3.50 (t, 2H, H-5′,5″, changed to d upon addition of D_2O), 4.37—4.59 (m, 3H, H-2′,3′,4′), 4.90 (s, 1H, H-1′), 5.07 (t, 1H, OH), 5.68 (d, 1H, H-5, $J_{5,6}$=7.3 Hz), 7.15 (d, 1H, H-6), 7.33—7.44 (m, 15H, Tr). *Anal.* Calcd for $C_{28}H_{24}N_2O_5$: C, 71.78; H, 5.16; N, 5.98. Found: C, 71.71; H, 5.21; N, 5.81.

2,3′-Anhydro-1-(5-*O*-acetyl-2-*O*-trityl-β-D-xylofuranosyl)uracil (3b)——A mixture of **3a** (4.68 g, 10 mmol) and Ac_2O (10 ml) in pyridine (70 ml) was stirred at room temperature for 3 h, and then the reaction quenched by dilution with EtOH (20 ml). The mixture was concentrated *in vacuo*, the residue dissolved in $CHCl_3$ (500 ml) and the solution washed with water (3 × 200 ml), dried (Na_2SO_4), and concentrated to *ca.* 100 ml. EtOH (300 ml) was added, and the mixture concentrated until crystals started to precipitate. The mixture was kept at *ca.* 4 °C overnight, and then the crystalline product **3b** was collected by filtration (5.0 g, 98%), mp 110—115 °C. ^{1}H-NMR (DMSO-d_6) δ: 1.91 (s, 3H, Ac), 4.14—4.27 (m, 2H, H-5′,5″), 4.42 (s, 1H, H-2′), 4.59—4.72 (m, 2H, H-3′,4′), 4.95 (s, 1H, H-1′), 5.69 (d, 1H, H-5, $J_{5,6}$=7.6 Hz), 7.12 (d, 1H, H-6), 7.33—7.44 (m, 15H, Tr). *Anal.* Calcd for $C_{30}H_{25}N_2O_6 \cdot 1/2H_2O$: C, 69.49; H, 5.25; N, 5.40. Found: C, 69.39; H, 5.33; N, 5.25.

By following the same procedure but using BzCl instead of Ac_2O, 2,3-anhydro-1-(5-*O*-benzoyl-2-*O*-trityl-β-D-xylofuranosyl)uracil (**3c**) was obtained (5.16 g, 90%), mp 158—160 °C. ^{1}H-NMR (DMSO-d_6) δ: 4.42 (m, 3H, H-2′,5′,5″), 4.69 (m, 1H, H-4′), 4.88—5.00 (m, 2H, H-1′,3′), 5.67 (d, 1H, H-5, $J_{5,6}$=7.3 Hz), 7.09—7.94 (m, 21H, Tr, Bz, H-6). *Anal.* Calcd for $C_{35}H_{28}N_2O_6 \cdot 3/2H_2O$: C, 70.10; H, 5.20; N, 4.67. Found: C, 70.22; H, 5.05; N, 4.48. The presence of H_2O was shown in ^{1}H-NMR at δ 3.32.

2,3′-Anhydro-1-(5-*O*-acetyl-β-D-xylofuranosyl)uracil (4b)——Compound **3b** (510 mg, 1.0 mmol) was dissolved in 10% $CF_3CO_2H/CHCl_3$ (6 ml). After 5 min at room temperature, the mixture was diluted with benzene (50 ml) and then concentrated *in vacuo*. The residue was triturated with Et_2O, and the solid crystallized from EtOH–Et_2O to give **4b** (250 mg, 93%), mp 204—205 °C. ^{1}H-NMR (DMSO-d_6) δ: 1.92 (s, 3H, Ac), 4.20 (dd, 1H, H-5′, $J_{5',5''}$=12.2, $J_{4',5'}$=5.5 Hz), 4.35 (dd, 1H, H-5″, $J_{4',5''}$=4.5 Hz), 4.63 (m, 1H, H-4′), 4.76 (s, 1H, H-2′), 5.03 (br s, 1H, H-3′), 5.65 (s, 1H, H-1′), 5.85 (d, 1H, H-5, $J_{5,6}$=7.3 Hz), 6.45 (d, 1H, OH), 7.67 (d, 1H, H-6). *Anal.* Calcd for $C_{11}H_{12}N_2O_6$: C, 49.25; H, 4.51; N, 10.44. Found: C, 49.35; H, 4.72; N, 10.17.

In a similar manner, **3c** (600 mg, 1.05 mmol) was converted into 2,3′-anhydro-1-(5-*O*-benzoyl-β-D-xylofuranosyl)uracil (**4c**) (300 mg, 83%), mp 227—230 °C. ^{1}H-NMR (DMSO-d_6) δ: 422 (dd, 1H, H-5′, $J_{5',5''}$=11.6, $J_{4',5'}$=7.4 Hz), 4.49 (dd, 1H, H-5″, $J_{4',5''}$=4.0 Hz), 4.70—4.80 (m, 2H, H-2′,4′), 5.13 (s, 1H, H-3′), 5.68 (s, 1H, H-1′), 5.80 (d, 1H, H-5, $J_{5,6}$=7.4 Hz), 7.42—7.95 (m, 6H, H-6 and Bz). *Anal.* Calcd for $C_{16}H_{14}N_2O_6$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.46; H, 4.58; N, 8.22.

2,3′-Anhydro-1-(5-*O*-trityl-β-D-xylofuranosyl)uracil (4d)——A mixture of **4a**[2)] (1.13 g, 5 mmol) and TrCl (1.6 g, 6 mmol) in pyridine (75 ml) was heated at 70 °C for 5 h. The reaction was quenched by dilution with EtOH (5 ml), and the mixture concentrated *in vacuo*. The residue was chromatographed on a silica gel column using $CHCl_3$–EtOH (6 : 1, v/v) as the eluent to give **4d** (1.6 g, 69%), mp 240—245 °C (dec). ^{1}H-NMR (DMSO-d_6) δ: 3.18 (d, 2H, H-5′,5″), 4.61—4.74 (m, 2H, H-2′,4′), 5.01 (s, 1H, H-3′), 5.67 (s, 1H, H-1′), 5.85 (d, 1H, H-5, $J_{5,6}$=7.3 Hz), 6.43 (d, 1H, OH), 7.34 (m, 15H, Tr), 7.69 (d, 1H, H-6). *Anal.* Calcd for $C_{28}H_{24}N_2O_5 \cdot 1/2H_2O$: C, 70.43; H, 5.28; N, 5.86. Found: C, 70.51; H, 5.48; N, 5.72. A small amount of H_2O in the analytical sample was detected by ^{1}H-NMR.

1-(5-*O*-Acetyl-β-D-xylofuranosyl)uracil (8b)——Compound **4b** (255 mg, 0.5 mmol) was dissolved in 80% HOAc (10 ml), and the solution heated at 100 °C for 2 h. After evaporation of the solvent, the residue was chromatographed on a silica gel column ($CHCl_3$–EtOH 9 : 1, v/v) to give **8b** (112 mg, 79%), mp 141—143 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.04 (s, 3H, Ac), 3.97 (m, 2H, H-5′,5″), 4.29 (m, 3H, H-2′,3′,4′), 5.68 (d, 1H, H-5, $J_{5,6}$=8.2 Hz), 5.60 (d, 1H, OH), 5.68 (s, 1H, H-1′), 5.85 (d, 1H, OH), 7.74 (d, 1H, H-6). *Anal.* Calcd for $C_{11}H_{14}N_2O_7$: C, 46.16; H, 4.93; N, 9.78. Found: C, 45.96; H, 4.95; N, 9.62.

Triflation of 4b—d——To a stirred suspension of **4** (1 mmol), DMAP (122 mg, 1 mmol) and Et_3N (202 mg, 2 mmol) in CH_2Cl_2 (20 ml) was added dropwise a solution of TflCl (236 mg, 2 mmol) in CH_2Cl_2 (5 ml). The suspension dissolved and from the clear solution, crystalline product precipitated out. Crystals were collected by filtration and washed with CH_2Cl_2 to give: 2,3′-Anhydro-1-(5-*O*-acetyl-2-*O*-triflyl-1-β-D-xylofuranosyl)uracil (**5b**) (384 mg, 96%), mp 205—207 °C (dec.). ^{1}H-NMR (DMSO-d_6) δ: 1.88 (s, 3H, Ac), 4.28 (dd, 1H, H-5′, $J_{5',5''}$=12.5, $J_{4',5'}$=4.8 Hz), 4.43 (dd, 1H, H-5″, $J_{4',5''}$=4.8 Hz), 4.71 (m, 1H, H-4′), 5.67 (s, 1H, H-3′), 5.93 (d, 1H, H-5, $J_{5,6}$= 7.6 Hz), 6.33 (s, 1H, H-2′), 6.57 (s, 1H, H-1′), 7.71 (d, 1H, H-6). *Anal.* Calcd for $C_{12}H_{11}F_3N_2O_8S$: C, 36.00; H, 2.77; N, 7.00; S, 8.01. Found: C, 35.92; H, 2.80; N, 6.98; S, 8.23. 2,3′-Anhydro-1-(5-*O*-benzoyl-2-*O*-triflyl-1-β-D-xylofuranosyl)uracil (**5c**) (356 mg, 77%), mp 210—211 °C (dec.). ^{1}H-NMR (DMSO-d_6) δ: 4.52 (dd, 1H, H-5′, $J_{5',5''}$= 11.9, $J_{4',5'}$=6.1 Hz), 4.62 (dd, 1H, H-5″, $J_{4',5''}$=4.9 Hz), 4.89 (m, 1H, H-4′), 5.75—5.90 (m, 2H, H-3′,5), 6.39 (s, 1H, H-1′), 6.65 (s, 1H, H-2′), 7.48—8.25 (m, 6H, Bz and H-6). *Anal.* Calcd for $C_{17}H_{13}F_3N_2O_8S$: C, 44.16; H, 2.83; N, 6.06; S, 6.93. Found: C, 44.27; H, 2.88; N, 6.03; S. 6.90. 2,3′-Anhydro-1-(2-*O*-triflyl-5-*O*-trityl-1-β-D-xylofuranosyl)uracil (**5d**) was obtained in crystalline form after chromatographic purification on a silica gel column using $CHCl_3$–EtOH (95 : 5, v/v) as the eluent (480 mg, 80%), mp 193—194 °C (dec.). ^{1}H-NMR (DMSO-d_6) δ: 3.21 (d,

2H, H-5′,5″), 4.67 (m, 1H, H-4′), 5.67 (m, 1H, H-3′), 5.88 (d, 1H, H-5, $H_{5,6}$ = 7.3 Hz), 6.36 (s, 1H, H-1′), 6.57 (s, 1H, H-2′), 7.32 (m, 15H, Tr), 7.73 (d, 1H, H-6). *Anal.* Calcd for $C_{29}H_{23}F_3N_2O_7S$: C, 58.00; H, 3.86; N, 4.66; S, 5.34. Found: C, 58.28; H, 4.01; N, 4.47; S, 5.28.

2,3′-Anhydro-1-(5-*O*-acetyl-2-chloro-2-deoxy-β-D-lyxofuranosyl)uracil (6b)——A mixture of **5b** (400 mg, 1 mmol) and LiCl (430 mg, 10 mmol) in HMPA (10 ml) was heated at 110 °C for 36 h. The reaction was quenched by addition of water (100 ml), and the mixture was extracted with EtOAc (3 × 100 ml). The organic extracts were combined, dried (Na_2SO_4), evaporated *in vacuo*, and the residue triturated with pyridine (20 ml) and filtered. The filtrate was condensed *in vacuo*, and the residue chromatographed on a silica gel column using $CHCl_3$–Me_2CO (2 : 1, v/v) followed by $CHCl_3$–Me_2CO (1 : 1, v/v). Compound **6b** was crystallized from EtOH–Et_2O (177 mg, 63%), mp 205—207 °C. ^{1}H-NMR (DMSO-d_6) δ: 1.91 (s, 3H, Ac), 4.20 (dd, 1H, H-5′, $J_{5',5''}$ = 12.2, $J_{4',5'}$ = 5.3 Hz), 4.32 (dd, 1H, H-5″, $J_{4',5''}$ = 4.5 Hz), 4.62 (m, 1H, H-4′), 5.31—5.34 (m, 2H, H-2′,3′), 5.94 (d, 1H, H-5, $J_{5,6}$ = 7.4 Hz), 6.04 (d, 1H, H-1′, $J_{1',2'}$ = 4.1 Hz), 7.74 (d, 1H, H-6). *Anal.* Calcd for $C_{11}H_{11}ClN_2O_5$: C, 46.09; H, 3.87; Cl, 12.36; N, 9.72. Found: C, 46.05; H, 3.81; Cl, 12.35; N, 9.69.

In a similar manner, **5c** (1.0 g, 2.16 mmol) was converted into 2,3′-anhydro-1-(5-*O*-benzoyl-2-chloro-2-deoxy-β-D-lyxofuranosyl)uracil (**6c**) (350 mg, 48%), mp 203—205 °C. ^{1}H-NMR (DMSO-d_6) δ: 4.45 (dd, 1H, H-5′, $J_{5',5''}$ = 11.9, $J_{4',5'}$ = 6.6 Hz), 4.52 (dd, 1H, H-5″, $J_{4',5''}$ = 6.1 Hz), 4.77 (m, 1H, H-4′), 5.33—5.50 (m, 2H, H-2′,3′), 5.86 (d, 1H, H-5, $J_{5,6}$ = 7.3 Hz), 6.08 (d, 1H, H-1′, $J_{1',2'}$ = 3.8 Hz), 7.41—7.94 (m, 6H, Bz and H-6). *Anal.* Calcd for $C_{16}H_{13}ClN_2 \cdot 1/2H_2O$: C, 53.72; H, 3.94; Cl, 9.91; N, 7.83. Found: C, 53.87; H, 3.92; Cl, 9.83; N, 7.83.

5′-*O*-Acetyl-2′-chloro-2′,3′-didehydro-2′,3′-dideoxyuridine (5′-*O*-Acetyl-2′-chlorouridinene) (7b)——A mixture of **6b** (143 mg, 0.5 mmol), NaOBz (288 mg, 2 mmol) and HOBz (122 mg, 1 mmol) in DMF (15 ml) was heated under reflux with stirring for 5 h, and then partitioned between EtOAc and H_2O (100 ml each). The organic layer was washed with H_2O, dried (Na_2SO_4), concentrated *in vacuo* and the residue crystallized from EtOH to give **7b** (110 mg, 77%), mp 215—217 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.05 (s, 3H, Ac), 4.21 (d, 2H, H-5′,5″), 5.08 (m, 1H, H-4′), 5.79 (d, 1H, H-5, $J_{5,6}$ = 7.9 Hz), 6.88 (t, H-1′, $J_{1',3'} = J_{1',4'}$ = 1.8 Hz). 6.77 (dd, 1H, H-3′, $J_{1',3'}$ = 1.8, $J_{3',4'}$ = 3.3 Hz), 7.51 (d, 1H, H-6), 11.54 (s, 1H, NH). *Anal.* Calcd for $C_{11}H_{11}ClN_2O_5$: C. 46.09; H, 3.87; N, 9.77. Found: C, 46.07; H, 3.82; N, 9.69.

2′-Chloro-2′,3′-didehydro-2′,3′-dideoxyuridine (2′-Chlorouridinene) (7a)——Compound **6b** (100 mg, 0.04 mmol) was dissolved in 1 N NaOH (3 ml). After 1 h at room temperature, the solution was neutralized with 1 N HCl and then concentrated *in vacuo*. The residue was triturated with EtOH (3 × 5 ml) and insoluble solid was removed by filtration. The combined filtrates were concentrated, and the residue crystallized from EtOH to give **7a** (65 mg, 65%), mp 155—157 °C. ^{1}H-NMR (DMSO-d_6) δ: 3.62 (m, 2H, H-5′,5″), 4.88 (m, 1H, H-4′), 5.15 (t, 1H, OH), 5.70 (d, 1H, H-5, $J_{5,6}$ = 7.9 Hz), 6.60 (t, 1H, H-1′, $J_{1',3'} = J_{1',4'}$ = 1.5 Hz), 6.75 (dd, 1H, H-3′, $J_{1',3'}$ = 1.5, $J_{3',4'}$ = 3.3 Hz), 7.84 (d, 1H, H-6), 11.47 (s, 1H, NH). *Anal.* Calcd for $C_9H_9ClN_2O_4$: C, 44.19; H, 5.71; Cl, 14.49; N, 11.45. Found: C, 44.19; H, 3.82; Cl, 14.50; N, 11.33.

2′-*O*-*tert*-Butyldimethylsilyl-5′-*O*-dimethoxytrityl-3′-*O*-mesyluridine——To a solution of 2′-*O*-*tert*-butyldimethylsilyl-5′-*O*-dimethoxytrityluridine[3] (1.3 g, 2 mmol) in pyridine (10 ml) was added MsCl (192 μl, 4.5 mmol), and the mixture kept at *ca.* 4 °C for 20 h, and then at room temperature for 8 h. The reaction was quenched by addition of MeOH (10 ml), and the mixture concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (100 ml), and the solution washed with water, dried (Na_2SO_4), concentrated *in vacuo*, and the residue chromatographed on a silica gel column (Et_2O–hexane, 2 : 1) to give the title compound (1.26 g, 87%) as a foam. ^{1}H-NMR (DMSO-d_6) δ: 0.03 (s, 3H, SiMe), 0.08 (s, 3H, SiMe), 0.83 (s, 9H, *tert*-Bu), 3.16 (s, 3H, Ms), 3.43 (m, 2H, H-5′,5″), 3.75 (s, 6H, OMe), 4.30 (m, 1H, H-4′), 4.56 (t, 1H, H-2′, $J_{1',2'} = J_{2',3'}$ = 5.7 Hz), 5.01 (m, 1H, H-3′), 5.45 (d, 1H, H-5, $J_{5,6}$ = 8.0 Hz), 5.77 (d, 1H, H-1′), 6.90—7.35 (14H, Tr), 7.70 (d, 1H, H-6), 11.5 (s, 1H, NH). *Anal.* Calcd for $C_{37}H_{46}N_2O_{10}SSi$: C, 60.14; H, 6.27; N, 3.79. Found: C, 60.28; H, 6.08: N, 3.60.

2,3′-Anhydro-1-(2-*O*-*tert*-butyldimethylsilyl-5-*O*-dimethoxytrityl-β-D-xylofuranosyl)uracil——The 3′-*O*-mesylate (738 mg, 1 mmol) as prepared above, was dissolved in MeCN (15 ml). DBU 228 mg, 1.5 mmol) was added to the solution, and the mixture was heated under reflux for 8 h. After concentration of the mixture *in vacuo*, the residue was chromatographed on a silica gel column using $CHCl_3$–EtOH (39 : 1, v/v) as the eluent to give the title compound (30 mg, 4.7%) as a foam. ^{1}H-NMR (DMSO-d_6) δ: 0.17 (s, 3H, Me), 0.18 (s, 3H, Me), 0.88 (s, 9H, *tert*-Bu), 3.17 (m, 2H, H-5′,5″), 3.72 (s, 6H, OMe), 4.43 (m, 1H, H-4′), 5.00 (s, 2H, H-2′,3′), 5.71 (s, 1H, H-1′), 5.83 (d, 1H, H-5, $J_{5,6}$ = 7.4 Hz), 6.84—7.34 (m, 13H, aromatic), 7.70 (d, 1H, H-6). *Anal.* Calcd for $C_{36}H_{42}N_2O_7Si$: C, 67.26; H, 6.58; N, 4.36. Found: C, 67.52; H, 6.29; N, 4.29.

A significant amount (500 mg, 68%) of the starting material was recovered from the column.

2,3′-Anhydro-1-(2-*O*-mestyl-5-*O*-trityl-β-D-xylofuranosyl)uracil——To a solution of **4d** (234 mg, 0.5 mmol) in tetrahydrofuran (THF) (20 ml) was added NaH (70 mg, 50% in oil), then MsCl in THF (75 mg, 0.65 mmol in 5 ml). The mixture was stirred at room temperature, concentrated *in vacuo*. The residue was dissolved in $CHCl_3$, (50 ml), washed (water), dried (Na_2SO_4), concentrated, and the residue chromatographed on a silica gel column ($CHCl_3$–EtOH 9 : 1, v/v) to give 2,3′-anhydro-1-(2-*O*-mesyl-5-*O*-trityl-β-D-xylofuranosyl)uracil (165 mg, 60%), mp 150—152 °C. ^{1}H-NMR (DMSO-d_6) δ: 3.19 (m, 2H, H-5′,5″), 3.32 (s, 3H, Ms), 4.61 (m, 1H, H-4′), 5.45 (brs, 1H, H-3′), 5.86 (d, 1H, H-5, $J_{5,6}$ = 7.3 Hz), 5.93 (s, 1H, H-1′), 6.14 (s, 1H, H-2′), 7.32 (m, 15H, Tr), 7.75 (d, 1H, H-6). *Anal.* Calcd

for $C_{29}H_{26}N_2O_7S \cdot 2H_2O$: C, 59.78; H, 5.19; N, 4.80; S, 5.50. Found: C, 59.78; H, 4.96; N, 4.69; S, 5.33.

In a similar manner, 2,3′-anhydro-*tert*-(2-*O*-tosyl-5-*O*-trityl-β-D-xylofuranosyl)uracil was prepared (320 mg, 51%) mp 133—135 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.44 (s, 3H, MePh), 3.15 (d, 2H, H-5′,5″), 4.54 (m, 1H, H-4′), 5.22 (br s, 1H, H-3′), 5.83 (d, 1H, H-5, $J_{5,6}$ = 7.4 Hz), 5.88 (s, 1H, H-1′), 6.03 (s, 1H, H-2′), 7.30 (m, 15H, Tr), 7.54—7.69 (d, 2H, MePh), 7.69 (d, 1H, H-6), 7.45 (d, 2H, MePh). *Anal.* Calcd for $C_{35}H_{30}N_2O_7 \cdot H_2O$: C, 65.62; H, 5.03; N, 4.37; S, 5.00. Found: C, 65.97; H, 5.03; N, 4.26; S. 5.03.

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References

1) Nucleosides 143 (preceding paper).
2) N. C. Young and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 3060 (1961).
3) 2′-*O*-Dimethyl-*tert*-butylsilyl-5′-*O*-dimethoxytrityluridine [G. H. Hakimelachi, Z. A. Proba and K. K. Ogilvie, *Can. J. Chem.*, **60**, 1106 (1982)] could be quantitatively mesylated. Treatment of the 3′-mesylate with DBU, however, afforded the desired 2,3′-anhydroxylosyluracil in only 5% yield. 2′-*O*-Desilylation prior to DBU treatment did not improve the yield of 2,3′-anhydronucleoside.
4) J. F. Codington, R. Fecher and J. J. Fox, *J. Am. Chem. Soc.*, **82**, 2794 (1960).
5) No sulfonylation products were obtained when **4h—d** were treated with MsCl, TsCl or TflCl in pyridine. Compound **4d** could be mesylated or tosylated in THF in the presence of NaH, but triflation under these conditions yielded an intractable mixture.
6) R. Fecher, J. F. Codington and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 1889 (1961).
7) T. Naito, M. Hirota, Y. Nakai, T. Kobayashi and M. Kanao, *Chem. Pharm. Bull.*, **13**, 1258 (1965).
8) R. U. Lemieux, K. A. Watanabe and A. A. Pavia, *Can. J. Chem.*, **47**, 4413 (1969).
9) A. Matsuda, C. K. Chu, U. Reichman, K. Pankiewicz, K. A. Watanabe and J. J. Fox, *J. Org. Chem.*, **46**, 3603 (1981).
10) J. P. Horwitz, J. Chua, I. L. Klundt, M. A. DaRooge and M. Noel, *J. Am. Chem. Soc.*, **86**, 1896 (1964); J. P. Horwitz, J. Chua, M. A. DaRooge, M. Noel and I. L. Klundt, *J. Org. Chem.*, **31**, 205 (1966).
11) J. J. Fox and N. C. Miller, *J. Org. Chem.*, **28**, 936 (1963).