Pergamon

Tetrahedron 55 (1999) 5319–5344

TETRAHEDRON

Face Selective 6,1'-(1-Oxo)ethano Bridge Formation of Uracil Nucleosides under Hypoiodite Reaction Conditions

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Received 10 February 1999; accepted 8 March 1999

Abstract: Synthesis of novel spiro uracil nucleosides with an anomeric orthoester structure in a stereoselective manner under the hypoiodite reaction conditions of Heusler-Kalvoda and Suárez is fully described. While 2'-deoxy-6-(hydroxymethyl)uridine **2** and 2'-deoxy-6-[(1-hydroxy-1-methyl)ethyl]uridine **4** gave β- and α-spiro nucleosides in 43-68% yields with low β/α selectivity (1/1.3~3/1), the secondary alcohols **3a** and **3b** showed 68-79% chemical yields with significantly better β/α selectivity (6.5/1~1/46). The β/α orientation of the 6-(hydroxyalkyl)uridine counterparts **6-8**, **16-17**, and **19** seemed to be controlled not only by the 2'-substituent but also by the chirality at the C7-stereocenter of the C6-side chain like in the 2'-deoxyuridine series. The transition state geometries of the reaction were postulated based on the X-ray crystallographic structures of cyclized products **20**α and **24**β.

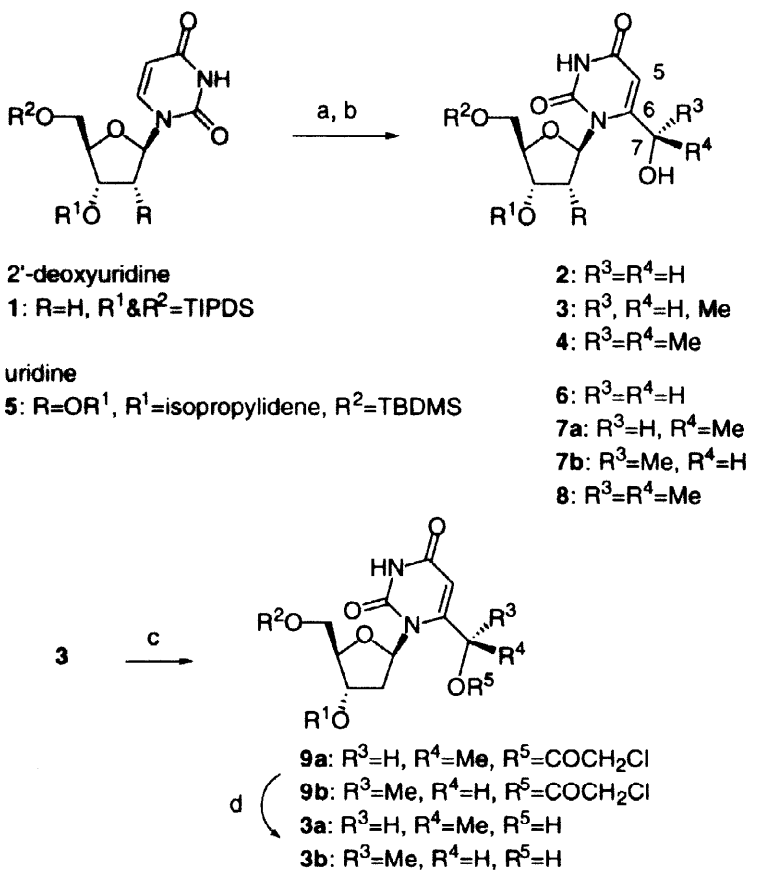
Introduction

Much attention has been focused on the nucleoside anomeric radical formation as one of the important DNA and RNA degradation mechanisms by certain anticancer drugs and oxygen radicals.[1] A number of C1'-elongated nucleosides showing interesting biological activities have been isolated as natural products, and several modes for introducing a functional group into the nucleoside anomeric position have been explored extensively. We have studied the method for generating nucleoside anomeric radicals and the synthetic utility of such species as the reactive intermediate to create a novel framework of nucleosides with C1'-modification.[2] In a preliminary communication,[3a] we have reported the hypoiodite reaction[4] on 2'-deoxy-6-(hydroxyalkyl)- and 6-(hydroxyalkyl)uridines (**2-4** and **6-7**).[5] Anomeric hydrogen was abstracted by the C6-alkoxy radical, which was generated by irradiation of a hypoiodite intermediate, *via* radical 1,5-translocation,[2a,b,g] and the subsequent stereoselective cyclization afforded spiro nucleosides having an anomeric orthoester structure.[3,6] We wish to report in detail this radical reaction with additional results from the substrates 6-(hydroxyalkyl)uridines **8**, **16-17**, and **19**, some of which provided β-spiro nucleosides predominantly.[7]

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00232-X

Results and Discussion

Preparation of substrates. To introduce the hydroxyalkyl group into the 6-position of uridines, 3',5'-*O*-(tetraisopropyldisiloxan-1,3-diyl)-2'-deoxyuridine **1** and 5'-*O*-TBDMS-2',3'-*O*-(isopropylidene)uridine **5** were first lithiated with LDA, respectively, and subsequently treated with an appropriate electrophile: 1) DMF to introduce a 6-formyl group, then $NaBH_4$ reduction of the resulting aldehyde for **2** (53%)[5a] and **6** (79%)[5b]; 2) acetaldehyde to give the secondary alcohols **3** and **7**; or 3) acetone for the tertiary alcohols **4** (24%) and **8** (20%). Although the secondary alcohol **7** could be separated into each diastereomer [**7a** (25%) and **7b** (37%)] by HPLC, the 2'-deoxyuridine derivative **3** was obtained as an inseparable mixture. Subsequently, the mixture of alcohols was converted to chloroacetate **9**, which enabled the separation of **9a** (24%) and **9b** (30%) by HPLC. Each chloroacetate was treated with NH_3/MeOH to afford depicted (7*R*)-alcohol **3a** and (7*S*)-alcohol **3b** in quantitative yields (Scheme 1).



Scheme 1. *Reagents and conditions*: a) LDA (3 eq), THF, −78 °C, 30 min; b) for **2** and **6**: DMF (11 eq), then $NaBH_4$ (3 eq), for **3** and **7**: acetaldehyde (5-11 eq), for **4** and **8**: acetone (30 eq); c) $(ClCH_2CO)_2O$ (3 eq), DMAP (5 eq), CH_2Cl_2, rt, 15 min, HPLC purification; d) saturated NH_3 in MeOH, rt, 5 min.

The stereochemistry at C7 of the secondary alcohol **3b** was unambiguously determined as *S*-configuration by X-ray crystallographic analysis (Figure 1).[3a] The C7-configurations of **7a** and **7b** were consistent with ^{1}H NMR evidence of their *O*-methylmandelates[8a] and Mosher's esters.[8b,c] For example, chemical shifts of H5 and C7-Me in (*S*)-*O*-methylmandelate of **7a** are 5.59 and 1.43 ppm, and those in (*S*)-*O*-methylmandelate of **7b** are 5.32 and 1.56 ppm, respectively. In addition, **7a** and **7b** were converted to their (*S*)-MTPA esters, and $\Delta\delta$ values of H5, C7-Me, and H1' were calculated[8c] as δ[**7b**·(*S*)-MTPA] – δ[**7a**·(*S*)-MTPA]: H5, +0.06; C7-Me, –0.05; and H1', +0.06 ppm. These results suggest that **7a** has (*7R*)-configuration and **7b** possesses (*7S*)-configuration.

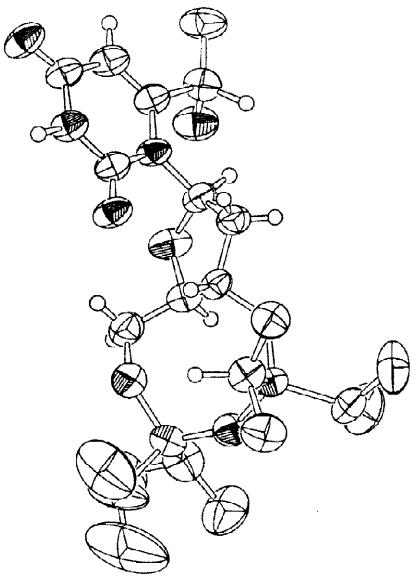
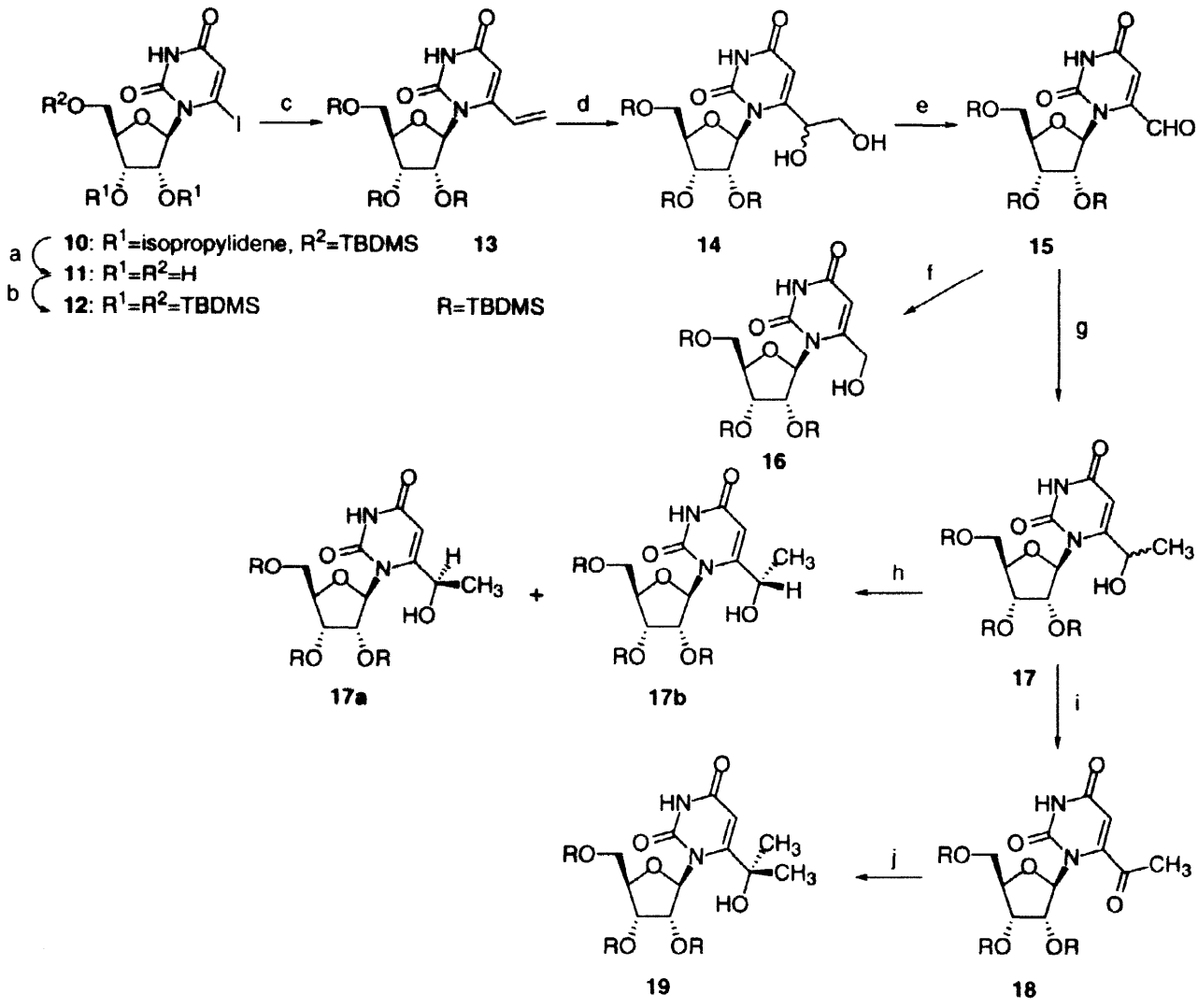


Figure 1. ORTEP drawing of **3b**.

2',3',5'-Tris-*O*-TBDMS-6-(hydroxyalkyl)uridines **16**, **17**, and **19** were also synthesized to compare the stereoselectivity of the cyclization. It is known that direct lithiation toward 2',3',5'-tris-*O*-(TBDMS)uridine is not effective;[9a,b] therefore, we planned to yield these compounds *via* the 6-formyluridine derivative **15**. 6-Iodouridine **11**,[9c] which was obtained by deprotection of **10** in an acidic condition, was protected by the TBDMS groups to afford **12** in 89% yield. Stille coupling with tributyl(vinyl)tin[10] in the presence of CuI[11] and $Pd(CH_3CN)_2Cl_2$ as a catalyst gave 6-vinyluridine **13** in 91% yield. Dihydroxylation of the vinyl group using *cat.* OsO_4/NMO, followed by periodate oxidation of the resulting vicinal diol gave aldehyde **15** in 76% yield in two steps.

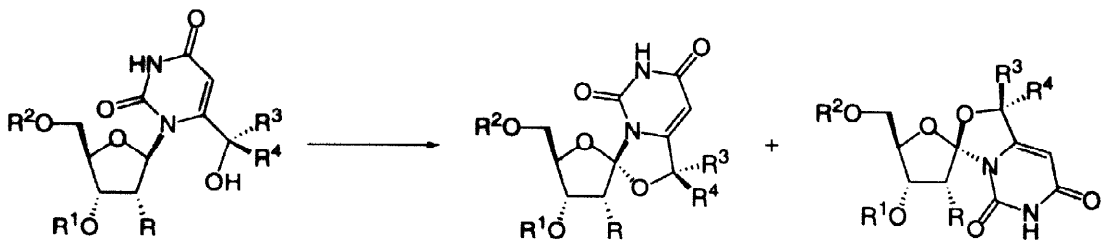
Reduction of **15** by $NaBH_4$ afforded the primary alcohol **16** in quantitative yield. Methylation with MeMgBr in THF provided a diastereomeric mixture of the secondary alcohols, which was chloroacetylated to isolate each diastereomer, in yields of 43 and 32%, by HPLC. Deacylation with NH_3/MeOH gave **17a** (97%) and **17b** (89%), respectively. Stereochemistry at C7 was determined based on chemical conversion from **3a** or **3b**.[12] Moffatt oxidation of **17** afforded ketone **18** in 86% yield, and subsequent methylation with MeLi in Et_2O gave the tertiary alcohol **19** in 27% yield (Scheme 2).

The H1' resonance of the *tert*-alcohols **8** and **19** appeared at δ 6.98 ppm in $CDCl_3$, while that of the other primary and secondary alcohols was in a range of 5.49-5.82 ppm. This remarkable deshielding effect, which was reflected by proximity of the tertiary hydroxyl group to H1', was also observed in the 2'-deoxyuridine case.[3a]



Scheme 2. *Reagents and conditions*: a) 50% CF_3CO_2H; b) TBDMSCl (5 eq), imidazole (8 eq), DMF; c) $Bu_3SnCH{=}CH_2$ (1.85 eq), 10 mol% $Pd(CH_3CN)_2Cl_2$, CuI (0.2 eq), THF, rt; d) *cat.* OsO_4, NMO (1.6 eq), acetone-H_2O (6:1); e) $NaIO_4$ (1.1 eq), dioxane-H_2O (6:1); f) $NaBH_4$ (3 eq), MeOH; g) MeMgBr (10 eq), THF; h) $(ClCH_2CO)_2O$ (3 eq), DMAP (3 eq), CH_2Cl_2, followed by HPLC separation; then saturated NH_3 in MeOH; i) DCC (3 eq), Cl_2CHCO_2H (0.15 eq), DMSO; j) MeLi (15 eq), Et_2O.

Cyclization reaction of alcohols in hypoiodite reaction conditions. The hypoiodite reaction of alcohols thus obtained above was carried out under the conditions of Heusler-Kalvoda [$Pb(OAc)_4/I_2/CaCO_3/h\nu$: method A][4b] and the reaction conditions of Suárez [(diacetoxyiodo)benzene (DIB)/$I_2/h\nu$: method B][4d-g] (Scheme 3).



2'-deoxyuridines: R=H, R^1&R^2=TIPDS

2: R^3=R^4=H	**20β**: R^3=R^4=H	**20α**: R^3=R^4=H
3a: R^3=H, R^4=Me	**21β**: R^3=H, R^4=Me	**21α**: R^3=H, R^4=Me
3b: R^3=Me, R^4=H	**22β**: R^3=Me, R^4=H	**22α**: R^3=Me, R^4=H
4: R^3=R^4=Me	**23β**: R^3=R^4=Me	**23α**: R^3=R^4=Me
	24β: R^1=R^2=R^3=R^4=H	**25α**: R^3=Me, R^1=R^2=R^4=H
	26β: R^3=R^4=Me, R^1=R^2=H	

uridines: R=OR^1, R^1=isopropylidene, R^2=TBDMS

6: R^3=R^4=H	**27β**: R^3=R^4=H	**27α**: R^3=R^4=H
7a: R^3=H, R^4=Me	**28β**: R^3=H, R^4=Me	**28α**: R^3=H, R^4=Me
7b: R^3=Me, R^4=H	**29β**: R^3=Me, R^4=H	**29α**: R^3=Me, R^4=H
8: R^3=R^4=Me	**30β**: R^3=R^4=Me	**30α**: R^3=R^4=Me

R=OR^1, R^1=R^2=TBDMS

16: R^3=R^4=H	**31β**: R^3=R^4=H	
17a: R^3=H, R^4=Me	**32β**: R^3=H, R^4=Me	
17b: R^3=Me, R^4=H	**33β**: R^3=Me, R^4=H	**33α**: R^3=Me, R^4=H
19: R^3=R^4=Me	**34β**: R^3=R^4=Me	**34α**: R^3=R^4=Me
	35β: R^1=R^2=R^3=R^4=H	

Scheme 3. *Reagents and conditions*: method A: $Pb(OAc)_4$ (4 eq), I_2 (0.6 eq), $CaCO_3$ (4 eq), *hv* (250W tungsten lamp), cyclohexane-CH_2Cl_2 (6:1 or 3:1); method B: DIB (2.4-3.0 eq), I_2 (0.6 eq), *hv* (250W tungsten lamp), cyclohexane-CH_2Cl_2 (6:1 or 3:1).

The cyclized products were purified by silica gel column chromatography and subsequent HPLC. The results are summarized in Table 1.[3a,b,7] It was found that DIB was the better oxidant than $Pb(OAc)_4$ for this cyclization reaction, in terms of not only chemical yield but also face selectivity. Although reaction time was shorter, the acidic condition of the $Pb(OAc)_4$ system would result in poor chemical balance.

To determine the anomeric stereochemistly of the cyclized products in uridine series **27-34**, the anisotropic effect of the fixed C2 carbonyl group toward H2' and H4' could be taken into account as in the 2'-deoxyuridine cases.[3a] For example, in β-spiro nucleoside **27β**, chemical shifts of H2' and H4' in $CDCl_3$ are 5.46 and 4.28 ppm, respectively, and those for the corresponding α-nucleoside **27α** are 4.68 and 4.72 ppm. The free nucleoside **35β** from **34β** was recrystallized from EtOH to subject to X-ray crystallographic analysis, and the C1'-stereochemistly was clarified (data not shown, ORTEP drawing of Chatgilialoglu's group, see

reference 3c). Namely, H2' is deshielded by the C2 carbonyl in β-spiro nucleosides, and H4' is influenced by the same effect in α-spiro nucleosides (Table 2).

Table 1. Hypoiodite reaction of 6-(hydroxyalkyl)uridine derivatives.

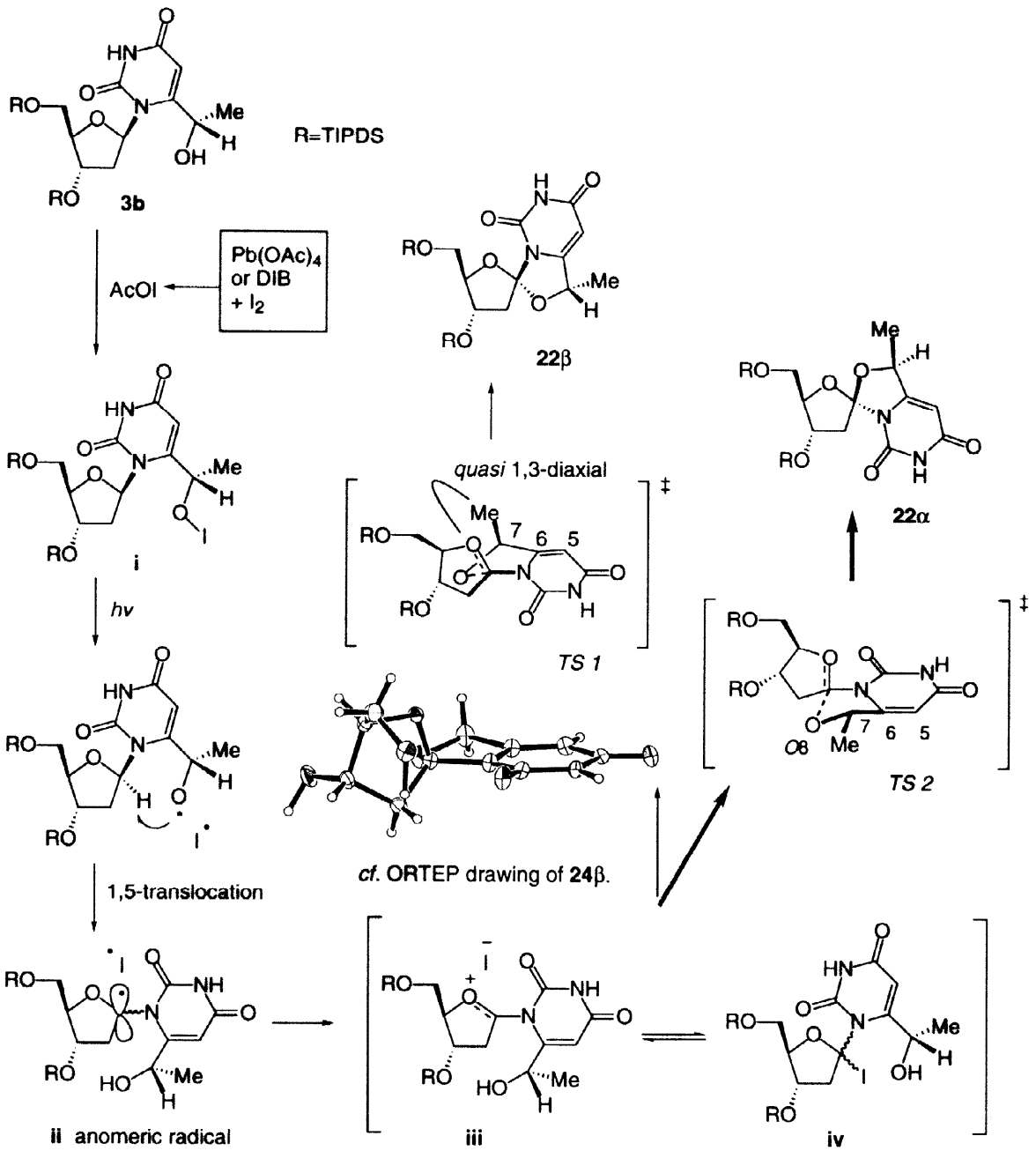
entry	substrate	method[a]	irradiation time (min)[b]	cyclized products (% yield by HPLC separation)		combined yield (%)	anomeric β/α ratio
1	**2**	A	15	**20β** (19)	**20α** (24)	43	1/1.3
2	**2**	B	60	**20β** (25)	**20α** (43)	68	1/1.7
3	**3a**	A	18	**21β** (62)	**21α** (9.5)	71.5	6.5/1
4	**3a**	B	45	**21β** (60)	**21α** (8.5)	68.5	7.0/1
5	**3b**	A	15	**22β** (2.0)	**22α** (67)	69	1/33.3
6	**3b**	B	45	**22β** (1.7)	**22α** (78)	80	1/45.7
7	**4**	A	15	**23β** (46)	**23α** (15)	61	3.0/1
8	**4**	B	45	**23β** (44)	**23α** (22)	66	2.0/1
9	**6**	A	20	**27β** (19)	**27α** (1.7)	21	11.1/1
10	**6**	B	30	**27β** (42)	**27α** (1.2)	43	34.6/1
11	**7a**	A	10	**28β** (53)	**28α** (3.8)	57	13.8/1
12	**7a**	B	60	**28β** (62)	**28α** (1.8)	64	34.4/1
13	**7b**	A	20	**29β** (18)	**29α** (12)	30	1.5/1
14	**7b**	B	87	**29β** (39)	**29α** (14)	53	2.7/1
15	**8**	A	15	**30β** (40)	**30α** (19)	59	2.1/1
16	**8**	B	55	**30β** (69)	**30α** (11)	80	6.5/1
17	**16**	B	95	**31β** (55)	-	55	β-only
18	**17a**	B	65	**32β** (61)	-	61	β-only
19	**17b**	B	80	**33β** (38)	**33α** (19)	57	2.0/1
20	**19**	B	150	**34β** (55)	**34α** (9.5)	64.5	5.8/1

Table 2. ^{1}H NMR chemical shifts of spiro nucleosides (ppm).

spiro compounds	H2'	H4'	β or α
27β	5.46	4.28	β
27α	4.68	4.72	α
28β	5.50	4.25	β
28α	4.46	4.70	α
29β	5.32	4.31	β
29α	4.71	4.71	α
30β	5.41	4.26	β
30α	4.68	4.69	α
31β	5.21	3.95	β
32β	5.11	4.06	β
33β	4.92	4.16	β
33α	4.12	4.42	α
34β	5.10	4.07	β
34α	4.05	4.20	α

in $CDCl_3$

Scheme 4. The plausible reaction mechanism.



The plausible reaction mechanism. The following reaction steps would be involved as shown in Scheme 4: 1) hypoiodite (**i**) formation at the C7-hydroxyl group; 2) photo-cleavage of the O-I bond to generate an alkoxy radical and an iodine atom; 3) 1,5-translocation to provide an anomeric radical (**ii**); 4) oxidation of the anomeric carbon by the iodine to produce an oxonium cation (**iii**), or radical coupling between the C1'-radical and the iodine to form a C1'-iodo intermediate (**iv**), which would reach equilibrium with **iii**; and 5) rise to the transition state (*TS1* or *TS2*) for cyclization. The origin of the chiral induction of the cyclization (β/α=1/46)

of the secondary alcohol **3b** is explained based on the X-ray result of deprotected **24β**. On the newly forming oxazolidine ring in the transition states, C1', N1, C6, and C7 atoms are placed on the same plane as the uracil ring, and only O8 is forced to be located below the plane due to the anomeric effect of the furanose ring oxygen (O4').[13] The ORTEP drawing of **24β** shows that the *pro-S* hydrogen and the O4' atom are mutually in the *quasi* 1,3-diaxial disposition. If this hydrogen were replaced by a methyl group as in **3b**, there would be an enhanced steric repulsion between (*7S*)-Me and O4'; therefore, the *TS2* (leading to **22α**) should be more favorable than *TS1*. The reverse has been discussed in reference 3a using the X-ray result of compound **20α**.

The presence of the 2'-α-*O*-substituent plays an important role as a stereo-directing group for the β-cyclization throughout all uridine derivatives (Table 1, entries 9-20), especially in the primary alcohols. When the steric demand from the 2'-α-*O*-substituent matched the C7-configuration (*7R*), a high β/α ratio was again observed (entries 11-12 and 17-18). In contrast, when mismatched [(*7S*)-alcohols: entries 13-14, and 19], the ratio decreased significantly. The tertiary alcohols **8** and **19** gave spiro products with low face selectivity but in high yield as in the 2'-deoxy case of **4**[3a] (entries 15-16 and 20). We recognized that proximity between the tertiary hydroxyl group and H1' is most likely one of the important factors to encourage the 1,5-translocation and cyclization steps.

Regarding differences of β/α ratios between methods A and B, especially in the uridine series (entries 9-16), it could be assumed that the proportion of S_N1 *vs.* S_N2 process for the cyclization step is different between the two methods. Uridine's 2'-oxygen may destabilize the oxonium cation **iii** due to its negative inductive effect, and the population of the intermediate **iv** would be enriched in the equilibrium relative to the 2'-deoxyuridine case.[14]

Additionally, it was found that 6-(phenylhydroxymethyl)-3',5'-*O*-TIPDS-2'-deoxyuridine[5a] was a poor substrate for the cyclization conditions. All cyclized products in method B were obtained in lower than 5% yield (data not shown).

Deprotection of cyclized compounds. Some of the spiro nucleosides (**20β**, **22α**, **23β**, and **31β**) synthesized in this study were readily deprotected in the conventional way (Bu_4NF in THF), which furnished the corresponding free nucleosides (**24β**, **25α**, **26β**, and **35β**) in high yields.

Conclusions

We have disclosed a practical synthesis of novel anomeric spiro uracilnucleosides with the orthoester structure utilizing the hypoiodite reaction, in which the alkoxy radical-induced H1' abstraction process is involved. Based on X-ray crystallographic results of the products, the geometries of the transition states have been proposed to explain remarkable stereoselectivity of the cyclization.

The possibility of introducing such an acid labile component, with base moiety fixed in

syn-conformation, into oligo nucleotides is currently under investigation.

Experimental Section

General Information. Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H NMR spectra were measured at 23 °C with a JEOL JNM-GX 400 or a JEOL ramda 500 spectrometer. Chemical shifts were reported in ppm on the δ scale relative to the internal standard (Me_4Si). Mass spectra (MS) were taken on a JEOL SX-102A spectrometer in FAB mode (*m*-nitrobenzylalcohol as a matrix). Ultraviolet spectra (UV) were recorded on a JASCO Ubest-55 spectrophotometer. A commercially available hexane solution of BuLi was titrated before use with diphenyl acetic acid in THF. THF was distilled from benzophenone ketyl. Column chromatography was carried out on silica gel (Silica Gel 60, Merck). Thin layer chromatography (TLC) was performed on silica gel (precorted silica gel plate F_{254}, Merck). Preparative HPLC was carried out on a Shimadzu LC-6AD with a Shim-pack PREP-SIL(H)·KIT column (2×25 cm).

Synthesis of the secondary alcohols 3a and 3b. To a THF (23 mL) solution of LDA (13.7 mmol), 3',5'-*O*-(tetraisopropyldisiloxan-1,3-diyl)-2'-deoxyuridine **1** (2.15 g, 4.57 mmol) in THF (23 mL) was added *via* a syringe while maintaining the temperature below −70 °C. After stirring for 30 min at −78 °C, freshly distilled acetaldehyde (2.8 mL, 50.3 mmol) was added and the mixture was stirred for 1 h at the same temperature. After the addition of AcOH (2.6 mL, 45.4 mmol), the mixture was partitioned between EtOAc (450 mL) and water (75 mL). The organic layer was separated and washed with saturated aqueous $NaHCO_3$, H_2O, and brine (50 mL each), successively, and dried over Na_2SO_4. Purification by column chromatography on silica gel (17-40% EtOAc in hexane) gave a diastereomeric mixture of alcohols **3a** and **3b** (1.50 g, 64%) as a colorless oil, which was used for the subsequent chloroacetylation for separation.

Chloroacetylation of the secondary alcohols. To the solution of the diastereomeric mixture of alcohols **3a** and **3b** (341.5 mg, 0.663 mmol) and DMAP (405.2 mg, 3.32 mmol) in CH_2Cl_2 (12 mL), monochloroacetic anhydride (340.1 mg, 1.99 mmol) in CH_2Cl_2 (12 mL) was added. The solution was stirred at rt for 15 min, and 1.2 mL of EtOH was added to quench the reaction. The mixture was partitioned between EtOAc (200 mL) and water (80 mL), the organic layer was washed with 0.5 M HCl, saturated aqueous $NaHCO_3$, H_2O, and brine (50 mL each), successively, and dried over Na_2SO_4. Silica gel column chromatography (10-33% EtOAc in hexane) followed by HPLC (EtOAc:hexane=1:1) gave **9a** (retention time (t_R) 9.2 min, 147.5 mg, solid, 38%) and **9b** (t_R 10.2 min, 184.4 mg, powder, 47%). Data for each alcohol is as follows:

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6-[(1*R*)-1-chloroacetoxyethyl]-2'-deoxyuridine (9a). mp 146.5-147.5 °C (hexane-Et_2O). UV (MeOH) λ_{max} 261 nm (ε 10300), λ_{min} 231 nm (ε 2600). ^{1}H NMR ($CDCl_3$) δ 8.00 (1H, br), 5.82 (1H, q, $J_{7,CH3}$=6.8 Hz), 5.81～5.78 (2H, m), 5.01 (1H, dt, $J_{2',3'}$=$J_{3',4'}$=7.0, $J_{2',3'}$=8.8 Hz), 4.13 (2H, s), 4.01～3.96 (2H, m), 3.79 (1H, dt, $J_{4',5'}$=7.0 and 4.8 Hz), 2.95 (1H, ddd, $J_{1',2'}$=3.1, J_{gem}=13.4 Hz), 2.38 (1H, ddd, $J_{1',2'}$=9.3 Hz), 1.65

(3H, d), 1.19~0.87 (28H, m). FAB MS *m/z* 615, 613 $(M+Na)^+$, 593, 591 $(M+H)^+$, and 549, 547 $(M-iPr)^+$. Anal. Calcd for $C_{25}H_{43}ClN_2O_8Si_2$: C, 50.79; H, 7.33; N, 4.74. Found: C, 50.69; H, 7.41; N, 4.62.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6-[(1*S*)-1-chloroacetoxyethyl]-2'-deoxyuridine (9b). UV (MeOH) λ_{max} 264 nm (ε 10300), λ_{min} 231 nm (ε 2400). ^1H NMR ($CDCl_3$) δ 8.07 (1H, br), 6.25 (1H, $J_{1',2'}$=5.1 and 9.0), 5.81 (1H, s), 5.80 (1H, q, $J_{7,CH3}$=6.2), 4.87 (1H, dt, $J_{2',3'}=J_{3',4'}$=6.6, $J_{2',3'}$=9.2 Hz), 4.09 (2H, s), 4.04 (1H, dd, $J_{4',5'}$=3.7, J_{gem}=12.1 Hz), 3.99 (1H, dd, $J_{4',5'}$=5.5 Hz), 3.75 (1H, ddd), 2.89 (1H, ddd, J_{gem}=13.6 Hz), 2.39 (1H, ddd), 1.61 (3H, d), 1.10~0.90 (28H, m). FAB MS *m/z* 615, 613 $(M+Na)^+$, 593, 591 $(M+H)^+$, and 549, 547 $(M-iPr)^+$. Anal. Calcd for $C_{25}H_{43}ClN_2O_8Si_2$: C, 50.79; H, 7.33; N, 4.74. Found: C, 50.89; H, 7.29; N, 4.69.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6-[(1*R*)-1-hydroxyethyl]-2'-deoxyuridine (3a). Compound **9a** (169.1 mg, 0.286 mmol) was dissolved in saturated NH_3 in MeOH (15 mL). After 5 min, the solution was concentrated and the residue was purified on a silica gel column (20-40% EtOAc in hexane) to yield **3a** (139.3 mg, 95%) as an oil, which was gradually solidified. Recrystallization from hexane-EtOAc gave an analytical sample: mp 175.0-175.5 °C (hexane-EtOAc). UV (MeOH) λ_{max} 261 nm (ε 11000), λ_{min} 229 nm (ε 2500). ^1H NMR ($CDCl_3$) δ 8.26 (1H, br), 6.10 (1H, dd, $J_{1',2'}$=3.4 and 9.3 Hz), 5.84 (1H, br), 4.98 (1H, dt, $J_{2',3'}=J_{3',4'}$=7.0, $J_{2',3'}$=8.9 Hz), 4.80 (1H, br), 4.02 (1H, dd, $J_{4',5'}$=7.0, J_{gem}=11.6 Hz), 3.99 (1H, dd, $J_{4',5'}$=3.7 Hz), 3.79 (1H, dt), 2.86 (1H, ddd, J_{gem}=13.4 Hz), 2.65 (1H, br), 2.38 (1H, ddd), 1.55 (3H, d, $J_{7,CH3}$=6.3 Hz), 1.17~0.88 (28H, m). FAB MS *m/z* 537 $(M+Na)^+$, 515 $(M+H)^+$, and 471 $(M-iPr)^+$. Anal. Calcd for $C_{23}H_{42}N_2O_7Si_2$: C, 53.67; H, 8.22; N, 5.44. Found: C, 53.92; H, 8.32; N, 5.36.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6-[(1*S*)-1-hydroxyethyl]-2'-deoxyuridine (3b). This compound (160.5 mg) was obtained from **9b** (184.4 mg, 0.312 mmol) by the same procedure for **3a** in the quantitative yield. The resulting solid was recrystallized from hexane-EtOAc to give an analytical sample: mp 173.0-174.5 °C (hexane-EtOAc). UV (MeOH) λ_{max} 262 nm (ε 12300), λ_{min} 230 nm (ε 2500). ^1H NMR ($CDCl_3$) δ 8.58 (1H, br), 5.99 (1H, dd, $J_{1',2'}$=3.7 and 9.5 Hz), 5.88 (1H, d, $J_{5,NH}$=2.4 Hz), 4.97 (1H, dt, $J_{2',3'}=J_{3',4'}$=6.9, $J_{2',3'}$=8.9 Hz), 4.85 (1H, m), 4.01 (1H, dd, $J_{4',5'}$=6.9, J_{gem}=11.6 Hz), 3.98 (1H, dd, $J_{4',5'}$=4.3 Hz), 3.79 (1H, dt), 3.07 (1H, d, $J_{7,OH}$=4.3 Hz), 2.91 (1H, ddd, J_{gem}=13.4 Hz), 2.35 (1H, ddd), 1.50 (3H, d, $J_{7,CH3}$=6.7 Hz), 1.20~0.89 (28H, m). FAB MS *m/z* 537 $(M+Na)^+$, 515 $(M+H)^+$, and 471 $(M-iPr)^+$. Anal. Calcd for $C_{23}H_{42}N_2O_7Si_2$: C, 53.67; H, 8.22; N, 5.44. Found: C, 53.50; H, 8.40; N, 5.38.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6-[(1-hydroxy-1-methyl)ethyl]-2'-deoxyuridine (4). To a THF (27 mL) solution of LDA (16.4 mmol), **1** (2.57 g, 5.46 mmol) in THF (27 mL) was added *via* a syringe while maintaining the temperature below −70 °C. After stirring for 30 min at −78 °C, freshly distilled acetone (12 mL, 164 mmol) was added and the mixture was stirred for 1 h at the same temperature. After the addition of AcOH (3.1 mL, 54.6 mmol),

the mixture was partitioned between EtOAc (300 mL) and water (100 mL). The organic layer was separated and washed with saturated aqueous $NaHCO_3$, H_2O, and brine (100 mL each), successively, and dried over Na_2SO_4. Purification by column chromatography on silica gel (10-33% EtOAc in hexane) gave alcohol **4** (677.3 mg, 24%) as a solid along with recovered **1** (1.88 g, 73%). Recrystallization from hexane-EtOAc gave an analytically pure sample: mp 150.0-151.0 °C (hexane-EtOAc). UV (MeOH) λ_{max} 264 nm (ε 10500), λ_{min} 231 nm (ε 2300). ^1H NMR ($CDCl_3$) δ 8.11 (1H, br), 6.86 (1H, dd, $J_{1',2'}$=3.7 and 9.5 Hz), 5.71 (1H, d, $J_{5,NH}$=2.2 Hz), 5.00 (1H, dt, $J_{2',3'}$=$J_{3',4'}$=6.6, $J_{2',3'}$=9.2 Hz), 4.06 (1H, dd, $J_{4',5'}$=7.7, J_{gem}=11.4 Hz), 3.99 (1H, dd, $J_{4',5'}$=3.7 Hz), 3.80 (1H, ddd), 2.85 (1H, ddd, J_{gem}=13.6 Hz), 2.49 (1H, br), 2.36 (1H, ddd), 1.67 and 1.62 (6H, each as s), 1.20~0.98 (28H, m). FAB MS *m/z* 551 $(M+Na)^+$, 529 $(M+H)^+$, and 485 $(M-iPr)^+$. Anal. Calcd for $C_{24}H_{44}N_2O_7Si_2$: C, 54.51; H, 8.39; N, 5.30. Found: C, 54.56; H, 8.61; N, 5.28.

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6-(hydroxymethyl)uridine (6). To a THF (23.5 mL) solution of LDA (14.1 mmol), 5'-*O*-(*tert*-butyldimethylsilyl)-2',3'-*O*-(isopropylidene)uridine **5** (1.88 g, 4.72 mmol) in THF (23.5 mL) was added *via* a syringe while maintaining the temperature below −70 °C. After stirring for 30 min at −78 °C, anhydrous DMF (4.0 mL, 51.9 mmol) was added and the mixture was stirred for 1 h at the same temperature. After the addition of AcOH (2.7 mL, 47.2 mmol), the mixture was partitioned between EtOAc (300 mL) and water (50 mL). The organic layer was separated and washed with saturated aqueous $NaHCO_3$, H_2O, and brine (50 mL each), successively, and dried over Na_2SO_4. After evaporation of the solvent, the residual oil was dissolved in MeOH (100 mL) and $NaBH_4$ (535.7 mg, 14.2 mmol) was added portionwise. After stirring for 3 h, AcOH (0.81 mL, 14.2 mmol) was added and the mixture was concentrated *in vacuo*. The residue was partitioned between EtOAc (300 mL) and saturated aqueous $NaHCO_3$ (50 mL). The organic layer was separated and washed with H_2O and brine (50 mL each), successively, and dried over Na_2SO_4. Purification by column chromatography on silica gel (17-60% EtOAc in hexane) gave alcohol **6** (1.59 g, 79%) as a solid: UV (MeOH) λ_{max} 260 nm (ε 9800), λ_{min} 228 nm (ε 2800). ^1H NMR ($CDCl_3$) δ 9.27 (1H, br), 5.81 (1H, br), 5.78 (1H, d, $J_{1',2'}$=1.3 Hz), 5.18 (1H, dd, $J_{2',3'}$ =6.6 Hz), 4.80 (1H, dd, $J_{3',4'}$=4.6 Hz), 4.53 (2H, d, $J_{7,OH}$=6.6 Hz), 4.15 (1H, dt, $J_{4',5'}$=4.6 and 7.2 Hz), 3.88 (1H, dd, J_{gem}=11.0 Hz), 3.83 (1H, dd), 3.39 (1H, t), 1.55 and 1.33 (6H, each as s), 0.89 (9H, s), 0.08 and 0.07 (6H, each as s). FAB MS *m/z* 451 $(M+Na)^+$, 429 $(M+H)^+$, 413 $(M-Me)^+$, and 371 $(M-{}^tBu)^+$. Anal. Calcd for $C_{20}H_{34}N_2O_7Si$: C, 53.25; H, 7.53; N, 6.54. Found: C, 53.48; H, 7.46; N, 6.41.

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6-[(*R*)-1-hydroxy-ethyl]-uridine (7a) and 5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6-[(*S*)-1-hydroxyethyl]uridine (7b). To a THF (28.5 mL) solution of LDA (15.3 mmol), compound **5** (2.02 g, 5.07 mmol) in THF (28.5 mL) was added *via* a syringe while maintaining the temperature below −70 °C. After stirring for 30 min at −78 °C, freshly distilled acetaldehyde

(1.4 mL, 25.5 mmol) was added and the mixture was stirred for 1 h at the same temperature. After the addition of AcOH (2.9 mL, 50.7 mmol), the mixture was partitioned between EtOAc (300 mL) and water (50 mL). The organic layer was separated and washed with saturated aqueous $NaHCO_3$, H_2O, and brine (50 mL each), successively, and dried over Na_2SO_4. Purification by column chromatography on silica gel (10-33% EtOAc in hexane) gave a diastereomixture of alcohols **7a** and **7b**, which was separated by HPLC (33% hexane in EtOAc) to yield **7a** (t_R 10.7 min, 564.5 mg, foam, 25%) and **7b** (t_R 10.2 min, 826.4 mg, foam, 37%).

7a: UV (MeOH) λ_{max} 260 nm (ε 10100), λ_{min} 230 nm (ε 2800). ^1H NMR ($CDCl_3$) δ 9.24 (1H, br), 6.04 (1H, d, $J_{1',2'}$=1.2 Hz), 5.82 (1H, d, $J_{5,NH}$=2.1 Hz), 5.18 (1H, dd, $J_{2',3'}$=6.5 Hz), 4.83 (1H, dq, $J_{7,CH3}$=6.7, $J_{7,OH}$=4.9 Hz), 4.80 (1H, dd, $J_{3',4'}$=4.7 Hz), 4.14 (1H, dt, $J_{4',5'}$=5.1 and 7.2 Hz), 3.86 (1H, dd, J_{gem}=10.8 Hz), 3.83 (1H, dd), 3.41 (1H, d), 1.57 (3H, d), 1.55 and 1.34 (6H, each as s), 0.89 (9H, s), 0.06 (6H, s). FAB MS *m/z*: 465 $(M+Na)^+$, 443 $(M+H)^+$, 427 $(M-Me)^+$, and 385 $(M-{}^tBu)^+$. Anal. Calcd for $C_{20}H_{34}N_2O_7Si$: C, 54.28; H, 7.74; N, 6.33. Found: C, 54.42; H, 7.72; N, 6.25.

7b: UV (MeOH) λ_{max} 260 nm (ε 10700), λ_{min} 230 nm (ε 2700). ^1H NMR ($CDCl_3$) δ 8.86 (1H, br), 5.87 (1H, d, $J_{5,NH}$=2.1 Hz), 5.79 (1H, br), 5.21 (1H, dd, $J_{1',2'}$=1.2, $J_{2',3'}$=6.4 Hz), 4.85 (1H, dq, $J_{7,OH}$=4.6, $J_{7,CH3}$=6.7 Hz), 4.77 (1H, dd, $J_{3',4'}$= 4.3 Hz), 4.17 (1H, dt, $J_{4',5'}$=4.4 and 8.5 Hz), 3.94 (1H, dd, J_{gem}=11.0 Hz), 3.84 (1H, dd), 3.43 (1H, d), 1.67 (3H, d), 1.51 and 1.33 (6H, each as s), 0.09 (6H, s). FAB MS *m/z* 465 $(M+Na)^+$, 443 $(M+H)^+$, 427 $(M-Me)^+$, and 385 $(M-{}^tBu)^+$. Anal. Calcd for $C_{20}H_{34}N_2O_7Si$: C, 54.28; H, 7.74; N, 6.33. Found: C, 54.32; H, 7.95; N, 6.24.

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6-[(1-hydroxy-1-methyl)-ethyl]uridine (8). To a THF (21 mL) solution of LDA (12.6 mmol), compound **5** (1.68 g, 4.22 mmol) in THF (21 mL) was added *via* a syringe while maintaining the temperature below −70 °C. After stirring for 30 min at −78 °C, freshly distilled acetone (9.3 mL, 127 mmol) was added and the mixture was stirred for 1 h at the same temperature. After quenching with AcOH (2.4 mL, 42.2 mmol), the mixture was partitioned between EtOAc (300 mL) and water (50 mL). The organic layer was separated and washed with saturated aqueous $NaHCO_3$, H_2O, and brine (50 mL each), successively, and dried over Na_2SO_4. Purification by column chromatography on silica gel (10-33% EtOAc in hexane) gave alcohol **8** (392.9 mg, 20%) as a foam, along with recovered **5** (1.24 g, 74%). Compound **8**: UV (MeOH) λ_{max} 261 nm (ε 13000), λ_{min} 231 nm (ε 5900). ^1H NMR ($CDCl_3$) δ 9.02 (1H, br), 6.97 (1H, d, $J_{1',2'}$=1.4 Hz), 5.61 (1H, d, $J_{5,NH}$=2.4 Hz), 5.15 (1H, dd, $J_{2',3'}$=6.7 Hz), 4.75 (1H, dd, $J_{3',4'}$=4.6 Hz), 4.15 (1H, dt, $J_{4',5'}$=4.6 and 8.6 Hz), 4.00 (1H, dd, J_{gem}=10.7 Hz), 3.86 (1H, dd), 3.67 (1H, br), 1.63 and 1.61 (6H, each as s), 1.54 and 1.33 (6H, each as s), 0.88 (9H, s), 0.09 and 0.06 (6H, each as s). FAB MS *m/z* 479 $(M+Na)^+$, 457 $(M+H)^+$, 441 $(M-Me)^+$, and 399 $(M-{}^tBu)^+$. Anal. Calcd for $C_{21}H_{36}N_2O_7Si$: C, 55.29; H, 8.08; N, 5.93. Found: C, 55.24; H, 7.95; N, 6.14.

(−)-Mandelate esters of 7a and 7b. Freshly distilled oxalyl chloride (60 μL, 0.688 mmol) was added to the solution of DMF (80 μL, 1.03 mmol) in CH_3CN (5 mL) at 0 °C under Ar, and

the mixture was stirred for 5 min, and then (–)-*O*-methylmandelic acid (114.3 mg, 0.688 mmol) was added and the mixture was stirred for 5 min. After the addition of a diastereomeric mixture of **7a** and **7b** (304.5 mg, 0.688 mmol) in pyridine (1 mL) while stirring for 1.5 h, the mixture was partitioned between Et_2O (100 mL) and saturated aqueous $CuSO_4$ (30 mL). The organic layer was washed with saturated aqueous $NaHCO_3$, H_2O, and brine (30 mL each), and dried over Na_2SO_4. Partial purification by silica gel column chromatography (10-33% EtOAc in hexane) and subsequent HPLC (33% EtOAc in hexane) gave (–)-mandelates with t_R of 16.7 min (77.3 mg, foam, 19%) and with t_R of 18.5 min (111.7 mg, foam, 27%).
(–)-Mandelate with t_R of 16.7 min: ^{1}H NMR ($CDCl_3$) δ 8.71 (1H, br), 7.39~7.44, (5H, m), 5.81 (1H, q, $J_{7,CH3}$=6.3 Hz), 5.75 (1H, s), 5.59 (1H, s), 5.18 (1H, d, $J_{2',3'}$=6.5 Hz), 4.83 (1H, s), 4.79 (1H, dd, $J_{3',4'}$=4.8 Hz), 4.13 (1H, dt, $J_{4',5'}$=4.9 and 7.2 Hz), 3.83 (1H, dd, J_{gem}=11.2 Hz), 3.78 (1H, dd), 3.42 (3H, s), 1.43 (3H, d), 1.51 and 1.33 (6H, each as s), 0.87 (9H, s), 0.07 (6H, s). FAB MS *m/z* 613 $(M+Na)^+$, 591 $(M+H)^+$, 575 $(M-Me)^+$, and 533 $(M-{}^tBu)^+$.
(–)-Mandelates with t_R of 18.5 min: ^{1}H NMR ($CDCl_3$) δ 8.42 (1H, br), 7.34~7.44, (5H, m), 5.83 (1H, s), 5.75 (1H, dq, $J_{7,CH3}$= 6.4 Hz), 5.32 (1H, s), 5.21 (1H, d, $J_{2',3'}$=6.3 Hz), 4.83 (1H, s), 4.81 (1H, dd, $J_{3',4'}$=4.6 Hz), 4.06 (1H, ddd, $J_{4',5'}$=4.9 and 6.0 Hz), 3.82 (1H, dd, J_{gem}=10.6 Hz), 3.76 (1H, dd), 3.41 (3H, s), 1.56 (3H, d), 1.54 and 1.34 (6H, each as s), 0.88 (9H, s), 0.04 (6H, s). FAB MS *m/z* 613 $(M+Na)^+$, 591 $(M+H)^+$, 575 $(M-Me)^+$, and 533 $(M-{}^tBu)^+$.

(*S*)-MTPA esters of 7a and 7b. To the CH_2Cl_2 (12 mL) solution of **7** (55.3 mg, 0.125 mmol) and 4-(dimethylamino)pyridine (58.2 mg, 0.476 mmol), (–)-MTPA chloride (44.9 μL, 0.240 mmol) was added at 0 °C under Ar, and the solution was stirred at rt for 15 min. After evaporation of the solvent, the residue was purified on preparative TLC plates (33% EtOAc in hexane) to yield (*S*)-MTPA esters with R_f0.6 (15.8 mg, foam, 19%) and with R_f0.7 (23.0 mg, oil, 28%). ^{1}H NMR data for these compounds are as follows:
(*S*)-MTPA ester with R_f0.6: ^{1}H NMR ($CDCl_3$) δ 9.35 (1H, br), 7.39~7.50 (5H, m), 5.97 (1H, q, $J_{7,CH3}$=6.4 Hz), 5.72 (1H, s), 5.58 (1H, s), 5.20 (1H, d, $J_{2',3'}$=6.6 Hz), 4.82 (1H, dd, $J_{3',4'}$=4.8 Hz), 4.10 (1H, ddd, $J_{4',5'}$=5.5 and 6.6 Hz), 3.83 (1H, dd, J_{gem}=11.1 Hz), 3.79 (1H, dd), 3.57 (3H, s), 1.67 (3H, d), 1.55 and 1.33 (6H, each as s), 0.89 (9H, s), 0.05 (6H, s).
(*S*)-MTPA ester with R_f0.7: ^{1}H NMR ($CDCl_3$) δ 9.47 (1H, br), 7.43~7.51 (5H, m), 6.04 (1H, dq, $J_{7,CH3}$=6.6 Hz), 5.78 (1H, s), 5.64 (1H, s), 5.21 (1H, d, $J_{2',3'}$=6.2 Hz), 4.80 (1H, dd, $J_{3',4'}$=5.3 Hz), 4.13 (1H, ddd, $J_{4',5'}$=5.5 and 7.0 Hz), 3.81 (1H, dd, J_{gem}=11.2 Hz), 3.77 (1H, dd), 3.54 (3H, s), 1.62 (3H, d), 1.54 and 1.33 (6H, each as s), 0.86 (9H, s), 0.03 and 0.02 (6H, each as s).

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6-iodouridine (10).
Compound **5** (2.52 g, 6.32 mmol) was lithiated by LDA (19.0 mmol) in THF according to the same procedure for the preparation of **6**, and I_2 (1.92 g, 7.56 mmol) in THF (35.5 mL) was added as an electrophile below –70 °C. After 1 h stirring at –78 °C, AcOH (3.6 mL, 63 mmol) was added to quench the reaction, and the mixture was concentrated *in vacuo* to *ca.* 15 mL, which was partitioned between EtOAc (500 mL) and saturated aqueous $NaHCO_3$ (200 mL),

and the organic phase was washed with H_2O and brine (200 mL each), and dried over Na_2SO_4. Silica gel column chromatography (10-33% EtOAc in hexane) gave **5** (2.44 g, 74%) as a pale yellow foam: UV (MeOH) λ_{max} 266 nm (ε 6900), λ_{min} 241 nm (ε 4500). ^{1}H NMR ($CDCl_3$) δ 9.11 (1H, br), 6.45 (1H, s), 6.09 (1H, d, $J_{1',2'}$=1.4 Hz), 5.18 (1H, dd, $J_{2',3'}$=6.4 Hz), 4.81 (1H, dd, $J_{3',4'}$=4.4 Hz), 4.17 (1H, ddd, $J_{4',5'}$=5.6 and 7.1 Hz), 3.81 (1H, dd, J_{gem}=10.8 Hz), 3.78 (1H, dd), 1.34 and 1.56 (6H, each as s), 0.89 (9H, s), 0.05 and 0.04 (6H, each as s). FAB MS *m/z* 547 $(M+Na)^+$, 525 $(M+H)^+$, 509 $(M-Me)^+$, and 467 $(M-{}^tBu)^+$. Anal. Calcd for $C_{18}H_{29}IN_2O_6Si \cdot 1/2H_2O$: C, 54.77; H, 8.70; N, 4.56. Found: C, 54.57 H, 8.90 N, 4.49.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-iodouridine (12). Compound **10** (2.12 g, 4.04 mmol) was dissolved in 50% CF_3COOH (50 mL) and the solution was stirred at rt for 18 h in the dark. The mixture was concentrated *in vacuo* with EtOH-toluene, and the residue was partially purified by silica gel column chromatography (50% benzene-MeOH) to yield **11** (1.55 g, quant.), which was used without further purification. Compound **11** (560 mg, 1.5 mmol) was dissolved in DMF (10 mL), and imidazole (817 mg, 12.0 mmol) and TBDMSCl (1.36 g, 9.0 mmol) were added. The reaction mixture was stirred at rt overnight in the dark. The mixture was partitioned between EtOAc (150 mL) and saturated aqueous $NaHCO_3$ (50 mL), and the organic phase was washed with H_2O and brine (50 mL each), and dried over Na_2SO_4. Silica gel column chromatography (10-17% EtOAc in hexane) gave **12** (953.7 mg, 89%) as a foam: UV (MeOH) λ_{max} 268 nm (ε 6200), λ_{min} 239 nm (ε 3200). ^{1}H NMR ($CDCl_3$) δ 8.38 (1H, br), 6.36 (1H, d, $J_{5,NH}$=1.8 Hz), 5.81 (1H, d, $J_{1',2'}$=6.4 Hz), 5.02 (1H, dd, $J_{2',3'}$=4.6 Hz), 4.12 (1H, dd, $J_{3',4'}$=1.7 Hz), 3.83 (1H, ddd, $J_{4',5'}$=4.9 and 8.3 Hz), 3.68 (1H, dd, J_{gem}=10.8 Hz), 3.56 (1H, dd), 0.84, 0.82, and 0.80 (27H, each as s), 0.02, −0.04, −0.05, −0.08, −0.10, and −0.12 (18H, each as s). FAB MS *m/z* 736 $(M+Na)^+$, 714 $(M+H)^+$, 698 $(M-Me)^+$, and 656 $(M-{}^tBu)^+$. Anal. Calcd for $C_{27}H_{53}IN_2O_6Si_3 \cdot 2/3H_2O$: C, 44.44; H, 7.34; N, 3.61. Found: C, 44.81; H, 7.54; N, 3.87.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-vinyluridine (13). The mixture of compound **12** (106.8 mg, 0.150 mmol), $Pd(CH_3CN)_2Cl_2$ (3.9 mg, 15.0 μmol), CuI (5.7 mg, 0.03 mmol), and $Bu_3SnCHCH_2$ (88 μL, 0.30 mmol) in THF (4 mL) was stirred 1.5 h. The reaction mixture was passed through a celite pad, and the eluate was concentrated *in vacuo*. The residue was partitioned between EtOAc (100 mL) and saturated aqueous $NaHCO_3$ (30 mL), and the organic phase was washed with H_2O and brine (30 mL each), and dried over Na_2SO_4. Silica gel column chromatography (10-17% EtOAc in hexane) gave **13** (83.6 mg, 91%) as a colorless oil: UV (MeOH) λ_{max} 276 nm (ε 5600), λ_{min} 243 nm (ε 2600). ^{1}H NMR ($CDCl_3$) δ 9.05 (1H, br), 6.62 (1H, dd, $J_{7,8a}$=11, $J_{7,8b}$=17 Hz), 5.80 (1H, d), 5.72 (1H, d, $J_{5,NH}$=2.6 Hz), 5.59 (1H, d), 5.53 (1H, d, $J_{1',2'}$=6.0 Hz), 5.01 (1H, dd, $J_{2',3'}$=3.3 Hz), 4.25 (1H, dd, $J_{3',4'}$=4.9 Hz), 3.91 (1H, dt, $J_{4',5'}$=4.9 and 7.2 Hz), 3.82 (1H, dd, J_{gem}=10.9 Hz), 3.68 (1H, dd), 0.91, 0.89, and 0.83 (27H, each as s), 0.10, 0.08, 0.06, 0.03, and −0.06 (18H, each as s). FAB MS *m/z* 635 $(M+Na)^+$, 613 $(M+H)^+$, 597 $(M-Me)^+$, and 555 $(M-{}^tBu)$. Anal. Calcd for $C_{29}H_{56}N_2O_6Si_3$: C, 56.60; H, 9.33; N, 4.27. Found: C, 56.82; H, 9.21; N, 4.57.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-(1,2-dihydroxyethyl)uridine (14). To the acetone-H_2O (6:1, 35 mL) solution of compound **13** (1.12 g, 1.83 mmol), 4-methylmolpholine *N*-oxide (350.9 mg, 3.00 mmol) and 2% OsO_4 in H_2O (0.23 mL) were added. The solution was stirred at rt overnight and partitioned between EtOAc (350 mL) and H_2O (100 mL). The organic layer was washed with brine (80 mL) and dried over Na_2SO_4. Silica gel column chromatography (20-50% EtOAc in hexane) gave vicinal diol **14** (1.00 g, 85%) as a foam: UV (MeOH) λ_{max} 262 nm (ε 7200), λ_{min} 231 nm (ε 2100). ^1H NMR ($CDCl_3$) δ 8.46 and 8.50 (1H, each as br), 6.00 and 6.03 (1H, each as s), 5.63 (0.5H, d, $J_{1',2'}$=7.2 Hz), 5.48 (0.5H, d, $J_{1',2'}$=7.2 Hz), 5.28 (0.5H, dd, $J_{2',3'}$=4.6 Hz), 5.21 (0.5H, dd, $J_{2',3'}$=4.6 Hz), 4.79 (0.5H, dd, $J_{7,8}$=3.5 and 6.3 Hz), 4.73 (0.5H, dd, $J_{7,8}$=3.5 and 6.3 Hz), 4.21 (0.5H, dd, $J_{3',4'}$=1.5 Hz), 4.19 (0.5H, d), 3.95 (2H, m), 3.83 (1H, dd, J_{gem}=11.4 Hz), 3.76 (1H, dd, $J_{4',5'}$=8.2, J_{gem}=11.8 Hz), 3.71 (1H, dd, $J_{4',5'}$=5.2, J_{gem}=11.8 Hz), 3.63 (0.5H, dd, J_{gem}=11.4 Hz), 0.93, 0.92, 0.90, 0.89, 0.86 and 0.85 (27H, each as s), 0.11, 0.09, 0.08, 0.07, 0.06, 0.04, −0.03, and −0.04 (18H, each as s). FAB MS *m/z* 647 $(M+H)^+$, 631 $(M-Me)^+$, and 589 $(M-{}^tBu)$. Anal. Calcd for $C_{29}H_{56}N_2O_7Si_3$: C, 54.00; H, 8.75; N, 4.34. Found: C, 53.93; H, 9.08; N, 4.26.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-formyluridine (15). Diol **14** (1.01 g, 1.65 mmol) was dissolved in dioxane-H_2O (3:1, 40 mL) and $NaIO_4$ (400.4 mg, 1.87 mmol) was added. The solution was stirred at rt overnight and partitioned between EtOAc (350 mL) and H_2O (100 mL). The organic layer was washed with brine (80 mL) and dried over Na_2SO_4. Silica gel column chromatography (10-17% EtOAc in hexane) gave aldehyde **15** (959.3 mg, 95%) as a foam: UV (MeOH) λ_{max} 262 nm (ε 8600), λ_{min} 232 nm (ε 2100). ^1H NMR ($CDCl_3$) δ 10.07 (1H, s), 9.71 (1H, br), 6.19 (1H, d, $J_{1',2'}$=7.5 Hz), 6.17 (1H, s), 4.53 (1H, dd, $J_{2',3'}$=5.0 Hz), 4.19 (1H, dd, $J_{3',4'}$=2.1 Hz), 4.01 (1H, ddd, $J_{4',5'}$=3.7 and 4.6 Hz), 3.80 (1H, dd, J_{gem}=11.3 Hz), 3.73 (1H, dd), 0.92, 0.91, and 0.83 (27H, each as s), 0.10, 0.09, 0.08, and 0.02 (6H, each as s). FAB MS *m/z* 638 $(M+Na)^+$, 615 $(M+H)^+$, 599 $(M-Me)^+$, and 557 $(M-{}^tBu)^+$. Anal. Calcd for $C_{28}H_{53}N_2O_7Si_3$: C, 54.77; H, 8.70; N, 4.56. Found: C, 54.57; H, 8.90; N, 4.49.

2', 3', 5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-(hydroxymethyl)uridine (16). To the MeOH (2 mL) solution of aldehyde **15** (111.9 mg, 0.182 mmol), $NaBH_4$ (20.7 mg, 0.546 mmol) was added and the mixture was stirred for 2 h. After the addition of AcOH (31 μL, 0.54 mmol), the mixture was partitioned between EtOAc (100 mL) and saturated aqueous $NaHCO_3$ (30 mL). The organic layer was washed with H_2O and brine (30 mL each) and dried over Na_2SO_4. Silica gel column chromatography (20-50% EtOAc in hexane) gave alcohol **16** (110.1 mg, 98%) as a solid: UV (MeOH) λ_{max} 260 nm (ε 7000), λ_{min} 230 nm (ε 2000). ^1H NMR ($CDCl_3$) δ 8.80 (1H, br), 6.36 (1H, d, $J_{5,NH}$=1.8 Hz), 5.49 (1H, d, $J_{1',2'}$=6.6 Hz), 5.10 (1H, dd, $J_{2',3'}$=4.6 Hz), 4.49 (2H, d, $J_{7,OH}$=6.4 Hz), 4.23 (1H, dd, $J_{3',4'}$=2.1 Hz), 3.96 (1H, ddd, $J_{4',5'}$=4.9 and 6.6 Hz), 3.80 (1H, dd, J_{gem}=10.9 Hz), 3.70 (1H, dd), 0.92, 0.89, and 0.85 (27H, s), 0.11, 0.10, 0.07, 0.06, 0.04, and −0.04 (18H, each as s). FAB MS *m/z* 639 $(M+Na)^+$, 617 $(M+H)^+$, 601 $(M-Me)^+$, and 559 $(M-{}^tBu)^+$. Anal. Calcd for $C_{28}H_{56}N_2O_7Si_3$: C, 54.51; H, 9.15; N, 4.54. Found: C,54.87; H, 9.22; N, 4.51.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-[(*R*)-(1-hydroxy)ethyl]uridine (17a) and 2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-[(*S*)-(1-hydroxy)ethyl]uridine (17b). To the THF (15 mL) solution of MeMgBr (10.1 mmol), aldehyde **15** (1.24 g, 2.02 mmol) in THF (15 mL) was added at 0 °C, and the solution was stirred at rt overnight. The mixture was diluted with EtOAc (300 mL) and washed with saturated aqueous NH_4Cl, $NaHCO_3$, H_2O, and brine (100 mL each). After drying with Na_2SO_4, column chromatography on silica gel (10-25% EtOAc in hexane) gave a diastereomeric mixture of alcohols **17a** and **17b** (1.27 g, quant.). The mixture (712.3 mg, 1.13 mmol) in CH_2Cl_2 (25 mL) reacted with chloroacetic anhydride (579.6 mg, 3.39 mmol) in the presence of 4-dimethylaminopyridine (414.2 mg, 3.39 mmol) at rt. EtOH (3 mL) was added and the mixture was partitioned between EtOAc (250 mL) and saturated aqueous $NaHCO_3$ (80 mL), the organic phase was washed with H_2O and brine (80 mL each), and dried over Na_2SO_4. Purification by silica gel column chromatography ($CHCl_3$) and subsequent HPLC (25% EtOAc in hexane) gave chloroacetates **36b** (t_R 12.7 min, 252.4 mg, foam, 32%) and **36a** (t_R 13.7 min, 336.8 mg, foam, 43%). The former compound (252.4 mg, 0.357 mmol) was treated with saturated NH_3 in MeOH (10 mL) to yield **17b** (201.1 mg, solid, 89%), and the latter (336.8 mg, 0.476 mmol) was also converted to **17a** (292.6 mg, solid, 97%) in the same way.

36a: UV (MeOH) λ_{max} 262 nm (ε 9400), λ_{min} 230 nm (ε 2800). ^1H NMR ($CDCl_3$) δ 9.51 (1H, br), 5.88 (1H, d, $J_{5,NH}$=2.1 Hz), 5.83 (1H, q, $J_{7,CH3}$=6.6 Hz), 5.49 (1H, d, $J_{1',2'}$=7.3 Hz), 5.28 (1H, dd, $J_{2',3'}$=4.6 Hz), 4.18 (1H, dd, $J_{3',4'}$=1.2 Hz), 4.10 and 4.12 (2H, each as d, J_{gem}=15.1 Hz), 3.93 (1H, ddd, $J_{4',5'}$=4.9 and 8.5 Hz), 3.76 (1H, dd, J_{gem}=10.7 Hz), 3.67 (1H, dd), 1.62 (3H, d), 0.91, 0.88, and 0.83 (27H, s), 0.11, 0.09, 0.06, 0.05, 0.04, and −0.04 (18H, each as s). FAB MS *m/z* 731, 729 $(M+Na)^+$ and 651, 649 $(M-{}^tBu)^+$. Anal. Calcd for $C_{31}H_{59}ClN_2O_8Si_3$: C, 52.62; H, 8.41; N, 3.96. Found: C, 53.01; H, 8.42; N, 3.87.

36b: UV (MeOH) λ_{max} 262 nm (ε 9700), λ_{min} 232 nm (ε 2700). ^1H NMR ($CDCl_3$) δ 9.08 (1H, br), 5.83 (1H, d, $J_{5,NH}$=2.1 Hz), 5.77 (1H, q, $J_{7,CH3}$=6.7 Hz), 5.51 (1H, d, $J_{1',2'}$=6.7 Hz), 5.19 (1H, dd, $J_{2',3'}$=4.3 Hz), 4.24 (1H, dd, $J_{3',4'}$=1.7 Hz), 4.10 and 4.12 (2H, each as d, J_{gem}=15.1 Hz), 3.92 (1H, dt, $J_{4',5'}$=4.8 and 8.8 Hz), 3.78 (1H, dd, J_{gem}=10.7 Hz), 3.65 (1H, dd), 1.67 (3H, d), 0.93, 0.89, and 0.85 (27H, s), 0.12, 0.10, 0.06, 0.05, 0.04, and −0.01 (18H, each as s). FAB MS *m/z* 731, 729 $(M+Na)^+$ and 651, 649 $(M-{}^tBu)^+$. Anal. Calcd for $C_{31}H_{59}ClN_2O_8Si_3$: C, 52.62; H, 8.41; N, 3.96. Found: C, 52.63; H, 8.41; N, 3.88.

17a: UV (MeOH) λ_{max} 260 nm (ε 14000), λ_{min} 230 nm (ε 4700). ^1H NMR ($CDCl_3$) δ 8.28 (1H, br), 5.97 (1H, d, $J_{5,NH}$=2.1 Hz), 5.56 (1H, d, $J_{1',2'}$=7.3 Hz), 5.38 (1H, dd, $J_{2',3'}$=4.4 Hz), 4.47 (1H, dq, $J_{7,OH}$=3.7, $J_{7,CH3}$ =6.4 Hz), 4.21 (1H, dd, $J_{3',4'}$=0.8 Hz), 3.96 (1H, ddd, $J_{4',5'}$=4.7 and 9.0 Hz), 3.79 (1H, dd, J_{gem}=10.8 Hz), 3.69 (1H, dd), 2.64 (1H, d), 1.55 (3H, d), 0.93, 0.90, and 0.85 (27H, s), 0.12, 0.10, 0.07, 0.06, 0.05, and −0.03 (18H, each as s). FAB MS *m/z* 654 $(M+Na)^+$, 632 $(M+H)^+$, 616 $(M-Me)^+$, and 574 $(M-{}^tBu)^+$. Anal. Calcd for $C_{29}H_{58}N_2O_7Si_3$: C, 55.19; H, 9.27; N, 4.44. Found: C, 55.36; H, 9.35; N, 4.38.

17b: UV (MeOH) λ_{max} 260 nm (ε 10700), λ_{min} 230 nm (ε 2700). ^1H NMR ($CDCl_3$) δ 8.11 (1H, br), 5.97 (1H, d, $J_{5,NH}$=2.2 Hz), 5.65 (1H, d, $J_{1',2'}$=7.3 Hz), 5.19 (1H, dd, $J_{2',3'}$=4.3 Hz), 4.81 (1H, dq, $J_{7,OH}$=3.7, $J_{7,CH3}$=6.3 Hz), 4.20 (1H, dd, $J_{3',4'}$=0.8 Hz), 3.94 (1H, dt, $J_{4',5'}$=5.2 and 8.9 Hz),

3.76 (1H, dd, J_{gem}=10.7 Hz), 3.70 (1H, dd), 2.46 (1H, d), 1.55 (3H, d), 0.93, 0.90, and 0.85 (27H, s), 0.12, 0.10, 0.07, 0.06, 0.04, and −0.03 (18H, each as s). FAB MS *m/z* 654 $(M+Na)^+$, 632 $(M+H)^+$, 616 $(M-Me)^+$, and 574 $(M-{}^tBu)^+$. Anal. Calcd for $C_{29}H_{58}N_2O_7Si_3$: C, 55.19; H, 9.27; N, 4.44. Found: C, 55.14; H, 9.39; N, 4.39.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-acetyluridine (18). The mixture of compound **17** (730.2 mg, 1.16 mmol) and DCC (1.19 g, 5.79 mmol) in DMSO (24 mL) was treated with dichloroacetic acid (14.5 μL, 0.175 mmol) at rt for 4 h. The mixture was partitioned between EtOAc (250 mL) and saturated aqueous $NaHCO_3$ (100 mL), the organic phase was washed with H_2O and brine (100 mL each), and dried over Na_2SO_4. Purification by silica gel column chromatography (10-25% EtOAc in hexane) gave 6-acetyluridine **18** (628.5 mg, 86%) as a foam: UV (MeOH) λ_{max} 270 nm (ε 7200), λ_{min} 238 nm (ε 2600). ^1H NMR ($CDCl_3$) δ 8.76 (1H, br), 5.63 (1H, d, $J_{5,NH}$=2.4 Hz), 5.52 (1H, d, $J_{1',2'}$=6.7 Hz), 4.86 (1H, dd, $J_{2',3'}$=4.6 Hz), 4.21 (1H, dd, $J_{3',4'}$=2.0 Hz), 3.93 (1H, dd, $J_{4',5'}$=5.8 and 7.5 Hz), 3.70 (1H, J_{gem}=10.8 Hz), 3.65 (1H, dd), 2.50 (3H, s), 0.90, 0.89, and 0.87 (27H, s), 0.09, 0.08, 0.07, 0.06, and 0.05 (18H, each as s). FAB MS *m/z* 629 $(M+H)^+$, 613 $(M-Me)^+$, and 571 $(M-{}^tBu)^+$. Anal. Calcd for $C_{29}H_{56}N_2O_7Si_3$: C, 55.37; H, 8.97; N, 4.45. Found: C, 55.56; H, 8.72; N, 4.43.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6-[(1-hydroxy-1-methyl)ethyl]uridine (19). To the Et_2O (10 mL) solution of ketone **18** (203.1 mg, 0.323 mmol), MeLi in Et_2O (1.62 mmol) was added at −78 °C, and the solution was stirred at −40 °C for 6 h. The mixture was partitioned between EtOAc (100 mL) and saturated aqueous NH_4Cl (50 mL), the organic phase was washed with H_2O and brine (50 mL each), and dried over Na_2SO_4. Purification by silica gel column chromatography (10-25% EtOAc in hexane) gave *tert*-alcohol **19** (55.1 mg, 26%) as a solid along with the starting material **18** (91.7 mg, 45%). Compound **19**: UV (MeOH) λ_{max} 261 nm (ε 7200), λ_{min} 230 nm (ε 2000). ^1H NMR ($CDCl_3$) δ 8.33 (1H, br), 6.39 (1H, d, $J_{1',2'}$=8.2 Hz), 5.97(1H, d, $J_{5,NH}$=2.4 Hz), 5.42 (1H, dd, $J_{2',3'}$= 4.1 Hz), 4.21 (1H, d), 3.93 (1H, dd, $J_{4',5'}$=5.0 and 9.3 Hz), 3.75 (1H, dd, J_{gem}=10.7 Hz), 3.71 (1H, dd), 2.45, (1H, br), 1.68 (6H, s), 0.93, 0.90, and 0.83 (27H, s), 0.12, 0.09, 0.07, 0.06, 0.03, and −0.04 (18H, each as s). FAB MS *m/z* 667 $(M+Na)^+$, 645 $(M+H)^+$, 629 $(M-Me)^+$, and 587 $(M-{}^tBu)^+$. Anal. Calcd for $C_{30}H_{60}N_2O_7Si_3$: C, 55.86; H, 9.38; N, 4.34. Found: C, 55.74; H, 9.53; N, 4.31.

Cyclization reaction of alcohols. The typical procedures of method A and B are described for compound **2**. *Method A*: The mixture of $CaCO_3$ (97.3 mg, 0.972 mmol), I_2 (37.0 mg, 0.146 mmol), and $Pb(OAc)_4$ (431.0 mg, 0.972 mmol) in cyclohexane (24 mL) was stirred at rt for 5 min. Alcohol **2** (121.5 mg, 0.243 mmol) in CH_2Cl_2 (4 mL) was added to the mixture above, and the resulting deep violet mixture was stirred and irradiated with a 250W-tungsten lamp until the color disappeared (*ca.* 8 min). The reaction mixture was partitioned between EtOAc (80 mL) and 0.2N $Na_2S_2O_3$ (30 mL). The organic layer was washed with water, saturated aqueous $NaHCO_3$, H_2O, and brine (30 mL each), successively, and dried over Na_2SO_4. Silica gel column

chromatography (10-40% EtOAc in hexane) followed by HPLC (hexane EtOAc=1:1) gave cyclized compounds **20β** (t_R 14.6 min, 23.2 mg, solid, 19%) and **20α** (t_R 16.3 min, 29.1 mg, solid, 24%). *Method B*: The mixture of DIB (105.4 mg, 0.328 mmol) and I_2 (38.1 mg, 0.150 mmol) in cyclohexane (13.7 mL) was stirred at rt for 5 min. Alcohol **2** (136.5 mg, 0.273 mmol) in CH_2Cl_2 (4.6 mL) was added to the mixture, which was stirred and irradiated with a 250W-tungsten lamp for 15 min with refluxing of the solvent. Additional DIB (52.7 mg, 0.164 mmol) was added three times every 15 min, and finally the color of iodine disappeared. The reaction mixture was partitioned between EtOAc (20 mL) and 0.2N $Na_2S_2O_3$ (5 mL). The organic layer was washed with water, saturated aqueous $NaHCO_3$, H_2O, and brine (5 mL each), successively, and dried over Na_2SO_4. Silica gel column chromatography (10-40% EtOAc in hexane) followed by HPLC (hexane EtOAc=1:2) gave cyclized compounds **20β** (t_R 10.8 min, 33.9 mg, 25%) and **20α** (t_R 11.4 min, 58.5 mg, 43%). Recrystallization from hexane-EtOAc afforded analytically pure samples. Physical data for these compounds are as follows:

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-(1-oxoethano)-2'-deoxyuridine (20β). mp 241.5-242.0 °C (hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 11700), λ_{min} 227 nm (ε 2100). ^{1}H NMR ($CDCl_3$) δ 8.14 (1H, br), 5.55 (1H, br), 4.94 (1H, dt, $J_{2',3'}$=8.4, $J_{3',4'}$=7.6 Hz), 4.92 (1H, dd, $J_{5,7}$=1.5, J_{gem}=14.6 Hz), 4.84 (1H, dd, $J_{5,7}$=1.2 Hz), 4.00 (1H, dd, $J_{4',5'}$=3.1, J_{gem}=12.2 Hz), 3.95 (1H, dd, $J_{4',5'}$=5.2), 3.89 (1H, ddd), 3.20 (1H, dd, J_{gem}=14.0 Hz), 2.49 (1H, dd), 1.13～0.92 (28H, m). FAB MS *m/z* 521 $(M+Na)^+$, 499 $(M+H)^+$ and 455 $(M-iPr)^+$. Anal. Calcd for $C_{22}H_{38}N_2O_7Si_2$: C, 52.98; H, 7.68; N, 5.62. Found: C, 52.73; H, 7.71; N, 5.51.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-(1-oxoethano)-α-2'-deoxyuridine (20α). mp 209.0-210.5 °C (hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 11300), λ_{min} 227 nm (ε 2000). ^{1}H NMR ($CDCl_3$) δ 8.52 (1H, br), 5.56 (1H, br), 4.97 (1H, dd, $J_{5,7}$=1.5, J_{gem}=14.6 Hz), 4.80 (1H, ddd, $J_{5,7}$=1.2 Hz), 4.65 (1H, ddd, $J_{2',3'}$=7.0 and 10.7, $J_{3',4'}$=7.9 Hz), 4.22 (1H, ddd, $J_{4',5'}$=3.4 and 4.3 Hz), 3.97 (1H, dd, J_{gem}=12.8 Hz), 3.92 (1H, dd), 3.43 (1H, dd, J_{gem}=12.5 Hz), 2.42 (1H, dd), 1.12～0.91 (28H, m). FAB MS *m/z* 521 $(M+Na)^+$, 499 $(M+H)^+$ and 455 $(M-iPr)^+$. Anal. Calcd for $C_{22}H_{38}N_2O_7Si_2$: C, 52.98; H, 7.68; N, 5.62. Found: C, 53.12; H, 7.80; N, 5.62.

The following two compounds **21β** and **21α** were obtained from alcohol **3a** by both methods A and B. *Method A*: Alcohol **3a** (162.7 mg, 0.325 mmol) gave **21β** (103.2 mg, 62%) and **21α** (15.9 mg, 9.5%), which were separated by HPLC (hexane-EtOAc=1:1; **21β** t_R 10.9 min, **21α** t_R 14.3 min); *Method B*: Alcohol **3a** (167.7 mg, 0.326 mmol) gave **21β** (100.1 mg, 60%) and **21α** (14.2 mg, 8.5%). Physical data for these compounds are as follows:

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-[(2*R*)-2-methyl-1-oxoethano]-2'-deoxyuridine (21β). mp 180.0-181.0 °C (hexane-EtOAc). UV (MeOH) λ_{max} 259 nm (ε 11000), λ_{min} 227 nm (ε 2000). ^{1}H NMR ($CDCl_3$) δ 8.01 (1H, br), 5.45 (1H, dd, $J_{5,7}$=1.5, $J_{5,NH}$=2.3 Hz), 5.10 (1H, dq, $J_{7,CH3}$=6.6 Hz), 4.93 (1H, ddd, $J_{2',3'}$=8.2 and 8.9, $J_{3',4'}$=7.6 Hz), 3.99 (1H, dd, $J_{4',5'}$=3.4, J_{gem}=12.4 Hz), 3.95 (1H, dd, $J_{4',5'}$=5.2 Hz), 3.88 (1H, ddd), 3.19 (1H, dd, J_{gem}=14.0 Hz), 2.48 (1H, dd), 1.52 (3H, d), 1.13～0.90 (28H, m). FAB MS *m/z* 535 $(M+Na)^+$, 513 $(M+H)^+$ and 469 $(M-iPr)^+$. Anal. Calcd for $C_{23}H_{40}N_2O_7Si_2 \cdot 1/4H_2O$: C, 53.41; H, 7.89; N, 5.42. Found: C,

53.25; H, 7.95; N, 5.37.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-[(2*R*)-2-methyl-1-oxoethano]-α-2'-deoxyuridine (21α). mp 209.0-213.5 °C (hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 11400), λ_{min} 228 nm (ε 2200). ^{1}H NMR ($CDCl_3$) δ 7.92 (1H, br), 5.47 (1H, t, $J_{5,7}$=$J_{5,NH}$=1.7 Hz), 4.99 (1H, dq, $J_{7,CH3}$=6.7 Hz), 4.62 (1H, ddd, $J_{2',3'}$=10.7 and 7.0, $J_{3',4'}$=7.9 Hz), 4.22 (1H, ddd, $J_{4',5'}$=3.4 and 4.9 Hz), 3.99 (1H, dd, J_{gem}=12.5 Hz), 3.92 (1H, dd), 3.28 (1H, dd, J_{gem}=12.2 Hz), 2.39 (1H, dd), 1.56 (3H, d), 1.13~0.93 (28H, m). FAB MS *m/z* 513 $(M+H)^+$ and 469 $(M-iPr)^+$. Anal. Calcd for $C_{23}H_{40}N_2O_7Si_2$: C, 53.88; H, 7.86; N, 5.46. Found: C, 53.54; H, 7.91; N, 5.38.

The following two compounds **22β** and **22α** were obtained from alcohol **3b** by both methods A and B. *Method A*: Alcohol **3b** (145.9 mg, 0.283 mmol) gave **22β** (2.9 mg, 2.0%) and **22α** (96.5 mg, 67%), which were separated by HPLC (hexane-EtOAc=1:1; **22β** t_R 10.7 min, **22α** t_R 11.7 min); *Method B*: Alcohol **3b** (178.6 mg, 0.347 mmol) gave **22β** (3.1 mg, 1.7%) and **22α** (138.3 mg, 78%). Physical data for these compounds are as follows:

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-[(2*S*)-2-methyl-1-oxoethano]-2'-deoxyuridine (22β). mp 201.0-202.0 °C (hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 11000), λ_{min} 227 nm (ε 2100). ^{1}H NMR ($CDCl_3$) δ 7.83 (1H, br), 5.46 (1H, t, $J_{5,7}$=$J_{5,NH}$=1.5 Hz), 5.10 (1H, dq, $J_{7,CH3}$=6.6 Hz), 4.93 (1H, ddd, $J_{2',3'}$=8.1 and 8.8, $J_{3',4'}$=7.7 Hz), 4.00 (1H, dd, $J_{4',5'}$=3.3, J_{gem}=12.5 Hz), 3.95 (1H, dd, $J_{4',5'}$=4.8 Hz), 3.88 (1H, ddd), 3.19 (1H, dd, J_{gem}=13.9 Hz), 2.48 (1H, dd), 1.52 (3H, d), 1.12~0.91 (28H, m). FAB MS *m/z* 535 $(M+Na)^+$, 513 $(M+H)^+$, and 469 $(M-iPr)^+$. Anal. Calcd for $C_{23}H_{40}N_2O_7Si_2$: C, 53.88; H, 7.86; N, 5.46. Found: C, 53.75; H, 8.00; N, 5.39.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-[(2*S*)-2-methyl-1-oxoethano]-α-2'-deoxyuridine (22α). mp 229.0-230.5 °C (hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 11300), λ_{min} 228 nm (ε 2200). ^{1}H NMR ($CDCl_3$) δ 8.62 (1H, br), 5.48 (1H, t, $J_{5,7}$=$J_{5,NH}$=1.5 Hz), 5.14 (1H, dq, $J_{7,CH3}$=6.6 Hz), 4.65 (1H, dt, $J_{2',3'}$= $J_{3',4'}$=7.5, $J_{2',3'}$=10.6 Hz), 4.21 (1H, ddd, $J_{4',5'}$=3.3 and 4.8 Hz), 4.00 (1H, dd, J_{gem}=12.5 Hz), 3.90 (1H, dd), 3.51 (1H, dd, J_{gem}=12.5 Hz), 2.39 (1H, dd), 1.48 (3H, d), 1.12~0.92 (28H, m). FAB MS *m/z* 535 $(M+Na)^+$, 513 $(M+H)^+$, and 469 $(M-iPr)^+$. Anal. Calcd for $C_{23}H_{40}N_2O_7Si_2$: C, 53.88; H, 7.86; N, 5.46. Found: C, 53.61; H, 7.91; N, 5.40.

The following two compounds **23β** and **23α** were obtained from alcohol **4** by both methods A and B. *Method A*: Alcohol **4** (198.8 mg, 0.376 mmol) gave **23β** (90.9 mg, 46%) and **23α** (30.2 mg, 15%), which were separated by HPLC (hexane-EtOAc=1:1; **23β** t_R 10.0 min, **23α** t_R 11.5 min); *Method B*: Alcohol **4** (85.7 mg, 0.162 mmol) gave **23β** (37.3 mg, 44%) and **23α** (19.1 mg, 22%). Physical data for these compounds are as follows:

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-[2,2-dimethyl-1-oxoethano]-2'-deoxyuridine (23β). mp 240.0-241.0 °C (hexane). UV (MeOH) λ_{max} 259 nm (ε 11400), λ_{min} 228 nm (ε 2100). ^{1}H NMR ($CDCl_3$) δ 8.08 (1H, br), 5.40 (1H, d, $J_{5,NH}$=1.8 Hz), 4.93 (1H, q, $J_{2',3'}$=$J_{3',4'}$=8.4 Hz), 4.02~3.97 (2H, m), 3.94~3.89 (1H, m), 3.14 and 2.46 (2H, each as dd,

J_{gem}=14.3 Hz), 1.61 and 1.59 (6H, each as s), 1.13~0.90 (28H, m). FAB MS *m/z* 527 $(M+H)^+$ and 483 $(M-iPr)^+$. Anal. Calcd for $C_{24}H_{42}N_2O_7Si_2$: C, 54.72; H, 8.04; N, 5.32. Found: C, 54.47; H, 8.10; N, 5.24.

3',5'-*O*-(Tetraisopropyldisiloxan-1,3-diyl)-6,1'-[2,2-dimethyl-1-oxoethano]-α-2'-deoxyuridine (23α). mp 238.0-238.5 °C (hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 11600), λ_{min} 228 nm (ε 2300). ^1H NMR ($CDCl_3$) δ 8.19 (1H, br), 5.43 (1H, d, $J_{5,NH}$=1.8 Hz), 4.62 (1H, dt, $J_{2',3'}=J_{3',4'}$=7.5, $J_{2',3'}$=10.7 Hz), 4.20 (1H, ddd, $J_{4',5'}$=3.4 and 5.5 Hz), 3.97 (1H, dd, J_{gem}=12.5 Hz), 3.88 (1H, dd), 3.42 (1H, dd, J_{gem}=12.5 Hz), 2.35 (1H, dd), 1.56 and 1.50 (6H, each as s), 1.12~0.92 (28H, m). FAB MS *m/z* 527 $(M+H)^+$ and 483 $(M-iPr)^+$. Anal. Calcd for $C_{24}H_{42}N_2O_7Si_2$: C, 54.72; H, 8.04; N, 5.32. Found: C, 54.61; H, 8.14; N, 5.20.

Cyclization reaction of ribo series. Compound **6** (103.6 mg, 0.24 mmol) was treated with the same procedure for compound **2** in *Method A*. Silica gel column chromatography (10-33% EtOAc in hexane) and subsequent HPLC (EtOAc:hexane=1:1) gave following two cyclized compounds **27β** (t_R 16.6 min, 19.4 mg, 19%) and **27α** (t_R 19.4 min, 1.8 mg, 1.7%). In *Method B*, alcohol **6** (500.4 mg, 1.17 mmol) was converted to **27β** (207.1 mg, 41.5%) and **27α** (5.9 mg, 1.2%).

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6,1'-[(1-oxa)ethano]uridine (27β). mp 241.5-242.0 °C (hexane-EtOAc). UV (MeOH) λ_{max} 259 nm (ε 11000), λ_{min} 227 nm (ε 2100). ^1H NMR ($CDCl_3$) δ 8.48 (1H, br), 5.59 (1H, d, $J_{5,7}$=1.5 Hz), 5.46 (1H, d, $J_{2',3'}$=6.6 Hz), 5.05 (1H, dd, J_{gem}=14.6 Hz), 4.98 (1H, dd), 4.81 (1H, dd, $J_{2',3'}$=6.6, $J_{3',4'}$=2.9 Hz), 4.28 (1H, dd, $J_{4',5'}$=6.2 Hz), 3.78 (2H, d), 1.59, 1.38 (6H, each as s), 0.89 (9H, s), 0.07, 0.06 (6H, each as s). FAB MS *m/z* 449 $(M+Na)^+$, 427 $(M+H)^+$, 411 $(M-Me)^+$, and 369 $(M-{}^tBu)^+$. Anal. Calcd for $C_{19}H_{30}N_2O_7Si$: C, 53.50; H, 7.09; N, 6.57. Found: C, 53.36; H, 7.07; N, 6.39.

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-α-6,1'-[(1-oxa)ethano]-uridine (27α). mp 247.0-247.5 °C (hexane-EtOAc). UV (MeOH) λ_{max} 259 nm (ε 10800), λ_{min} 226 nm (ε 2000). ^1H NMR ($CDCl_3$) δ 7.91 (1H, br), 5.53 (1H, d, $J_{5,7}$=1.5 Hz), 4.97 (1H, dd, $J_{2',3'}$=7.0, $J_{3',4'}$=2.6 Hz), 4.93 (1H, dd, J_{gem}=14.5 Hz), 4.75 (1H, dd), 4.72 (1H, dd, $J_{4',5'}$=5.7 Hz), 4.68 (1H, d), 3.78 (2H, d), 1.54 and 1.32 (6H, each as s), 0.90 (9H, s), 0.08 and 0.07 (6H, each as s). FAB MS *m/z* 449 $(M+Na)^+$, 427 $(M+H)^+$, 411 $(M-Me)^+$, and 369 $(M-{}^tBu)^+$. Anal. Calcd for $C_{19}H_{30}N_2O_7Si$: C, 53.50; H, 7.09; N, 6.57. Found: C, 53.21; H, 7.05; N, 6.40.

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6,1'-[(2*R*)-2-methyl-1-oxaethano]uridine (28β) and 5'-*O*-(*tert*-butyldimethylsilyl)-2',3'-*O*-isopropylidene-α-6,1'-[(2*R*)-2-methyl-1-oxaethano]uridine (28α). The secondary alcohol **7a** (177.5 mg, 0.401 mmol) was treated with *Method A* and the subsequent HPLC purification (EtOAc:hexane=1:1) gave compounds **28β** (t_R 10.3 min, 91.1 mg, powder, 52%) and **28α** (t_R 13.1 min, 6.4 mg, powder, 3.6%). These compounds **28β** (155.4 mg, 62%) and **28α** (4.6 mg, 1.8%) were also obtained from compound **7a** (250.2 mg, 0.565 mmol) by *Method B*. Physical data for compound **28β**: UV (MeOH) λ_{max} 258 nm (ε 7300), λ_{min} 227 nm (ε 1500). ^1H NMR ($CDCl_3$) δ

8.96 (1H, br), 5.50 (1H, d, $J_{2',3'}$=6.4 Hz), 5.50 (1H, d, $J_{5,7}$=1.7 Hz), 5.24 (1H, dq, $J_{7,CH3}$=6.7 Hz), 4.77 (1H, dd, $J_{3',4'}$=2.4 Hz), 4.25 (1H, dd, $J_{4',5'}$=6.4 Hz), 3.76 (2H, d), 1.59 and 1.37 (6H, each as s), 1.56 (3H, d), 0.88 (9H, s), 0.06 and 0.05 (6H, each as s). FAB MS *m/z* 463 $(M+Na)^+$,441 $(M+H)^+$, 425 $(M-Me)^+$, and 383 $(M-{}^tBu)^+$. Anal. Calcd for $C_{20}H_{32}N_2O_7Si$: C, 54.53; H, 7.32; N, 6.36. Found: C, 54.30; H, 7.40; N, 6.15.

Physical data for compound **28α**: UV (MeOH) λ_{max} 258 nm (ε 8400), λ_{min} 228 nm (ε 1800). ^1H NMR ($CDCl_3$) δ 7.96 (1H, br), 5.44 (1H, d, $J_{5,7}$=1.1 Hz), 5.15 (1H, dq, $J_{7,CH3}$=6.7 Hz), 4.95 (1H, dd, $J_{2',3'}$=7.3, $J_{3',4'}$=2.4 Hz), 4.71 (1H, d), 4.70~4.68 (1H, m), 3.77~3.76 (2H, m), 1.56 and 1.33 (6H, each as s), 1.52 (3H, d), 0.90 (9H, s), 0.08 (6H, s). FAB MS *m/z* 463 $(M+Na)^+$, 441 $(M+H)^+$, 425 $(M-Me)^+$, and 383 $(M-{}^tBu)^+$. Anal. Calcd for $C_{20}H_{32}N_2O_7Si$: C, 54.53; H, 7.32; N, 6.36. Found: C, 54.21; H, 7.44; N, 6.18.

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6,1'-[(2*S*)-2-methyl-1-oxaethano]uridine (29β) and 5'-*O*-(*tert*-butyldimethylsilyl)-2',3'-*O*-isopropylidene-α-6,1'-[(2*S*)-2-methyl-1-oxaethano]uridine (29α). The secondary alcohol **7b** (146.4 mg, 0.331 mmol) was treated with *Method A* and the subsequent HPLC purification (EtOAc:hexane=1:1) gave compounds **29β** (t_R 18.3 min, 29.2 mg, 20%) and **29α** (t_R 17.0 min, 19.2 mg, 13%) as white powder. These compounds **29β** (41.0 mg, 40%) and **29α** (15.0 mg, 15%) were also obtained from compound **7b** (103.3 mg, 0.233 mmol) by *Method B*. Physical data for compound **29β**: UV (MeOH) λ_{max} 258 nm (ε 12800), λ_{min} 228 nm (ε 2600). ^1H NMR ($CDCl_3$) δ 8.73 (1H, br), 5.50 (1H, br), 5.32 (1H, d, $J_{2',3'}$=6.3 Hz), 5.18 (1H, dq, $J_{5,7}$=1.3, $J_{7,CH3}$=7.0 Hz), 4.79 (1H, dd, $J_{3',4'}$=2.9 Hz), 4.31 (1H, dd, $J_{4',5'}$= 6.4 Hz), 3.79 (2H, d), 1.62 (3H, d), 1.60 and 1.37 (6H, each as s), 0.89 (9H, s), 0.06 and 0.05 (6H, each as s). FAB MS *m/z* 463 $(M+Na)^+$, 441 $(M+H)^+$, 425 $(M-Me)^+$, and 383 $(M-{}^tBu)^+$. Anal. Calcd for $C_{20}H_{32}N_2O_7Si$: C, 54.53; H, 7.32; N, 6.36. Found: C, 54.47; H, 7.41; N, 6.25.

Physical data for compound **29α**: UV (MeOH) λ_{max} 258 nm (ε 7200), λ_{min} 228 nm (ε 1700). ^1H NMR ($CDCl_3$) δ 7.97 (1H, br), 5.45 (1H, br), 5.15 (1H, dd, $J_{5,7}$=1.3, $J_{7,CH3}$=6.6 Hz), 4.95 (1H, dd, $J_{2',3'}$=7.3, $J_{3',4'}$=2.6 Hz), 4.71 (1H, d), 4.69 (1H, m), 3.77 (2H, d, $J_{4',5'}$=3.7 Hz), 1.58 and 1.32 (6H, each as s), 1.52 (3H, d), 0.91 (9H, s), 0.07 (6H, s). FAB MS *m/z* 463 $(M+Na)^+$, 441 $(M+H)^+$, 425 $(M-Me)^+$, and 383 $(M-{}^tBu)^+$. Anal. Calcd for $C_{20}H_{32}N_2O_7Si$: C, 54.53; H, 7.32; N, 6.36. Found: C, 54.55; H, 7.52; N, 6.29.

5'-*O*-(*tert*-Butyldimethylsilyl)-2',3'-*O*-isopropylidene-6,1'-(2,2-dimethyl-1-oxaethano)uridine (30β) and 5'-*O*-(*tert*-butyldimethylsilyl)-2',3'-*O*-isopropylidene-α-6,1'-(2,2-dimethyl-1-oxaethano)uridine (30α). The tertiary alcohol **8** (175.0 mg, 0.383 mmol) was treated with *Method A* and the subsequent HPLC purification (EtOAc:hexane=1:1) gave compounds **30β** (t_R 10.6 min, 69.3 mg, powder, 40%) and **30α** (t_R 13.0 min, 33.2 mg, powder, 19%). Compound **8** (376.1 mg, 0.831 mmol) was converted to **30β** (261.6 mg, 69%) and **30α** (40.9 mg, 11%) by *Method B*. Physical data for compound **30β**: UV (MeOH) λ_{max} 259 nm (ε 8400), λ_{min} 227 nm (ε 2300). ^1H NMR ($CDCl_3$) δ 9.16 (1H, br), 5.44 (1H, d, $J_{5,7}$=1.5 Hz), 5.41

(1H, d, $J_{2',3'}$=6.4 Hz), 4.75 (1H, dd, $J_{3',4'}$=2.2 Hz), 4.26 (1H, dd, $J_{4',5'}$=6.6 Hz), 3.77 (2H, d), 1.63 and 1.59 (6H, each as s), 1.56 and 1.36 (6H, each as s), 0.88 (9H, s), 0.06 (6H, s). FAB MS *m/z* 477 $(M+Na)^+$, 455 $(M+H)^+$, 439 $(M-Me)^+$, and 397 $(M-{}^tBu)^+$. Anal. Calcd for $C_{21}H_{34}N_2O_7Si$: C, 55.48; H, 7.54; N, 6.16. Found: C, 55.30; H, 7.65; N, 6.06.

Physical data for compound **30α**: UV (MeOH) λ_{max} 259 nm (ε 7000), λ_{min} 227 nm (ε 1500). ^1H NMR ($CDCl_3$) δ 8.44 (1H, br), 5.40 (1H, d, $J_{5,7}$=1.8 Hz), 4.94 (1H, dd, $J_{2',3'}$=7.1, $J_{3',4'}$=2.7 Hz), 4.70~4.67 (2H, m), 3.76 (2H, d, $J_{4',5'}$=3.6 Hz), 1.54 (6H, s), 1.53 and 1.31 (6H, each as s), 0.90 (9H, s), 0.07 (6H, s). FAB MS *m/z* 477 $(M+Na)^+$, 455 $(M+H)^+$, 439 $(M-Me)^+$, and 397 $(M-{}^tBu)^+$. Anal. Calcd for $C_{21}H_{36}N_2O_7Si$: C, 55.48; H, 7.54; N, 6.16. Found: C, 55.27; H, 7.55; N, 6.14.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6,1'-(1-oxaetano)uridine (31β). This compound was obtained from **16** (204.7 mg, 0.332 mmol) according to *Method B* as a solid (112.2 mg, 55%) which was recrystallized from hexane-EtOAc: mp 249.0-249.3 °C. UV (MeOH) λ_{max} 260 nm (ε 8000), λ_{min} 227 nm (ε 1800). ^1H NMR ($CDCl_3$) δ 8.13 (1H, br), 5.56 (1H, m), 5.01 (1H, d, $J_{2',3'}$=5.2 Hz), 5.00 (1H, dd, $J_{5,7}$=1.5, J_{gem}= 15.0 Hz), 4.85 (1H, dd), 4.24 (1H, dd, $J_{3',4'}$=0.9 Hz), 4.13 (1H, ddd, $J_{4',5'}$=5.2 and 8.6 Hz), 3.76 (1H, dd, J_{gem}=10.7 Hz), 3.70 (1H, dd), 0.92, 0.91 and 0.86 (27H, each as s), 0.11, 0.09, 0.08, 0.07, 0.05, and −0.05 (18H, each as s). FAB MS *m/z* 637 $(M+Na)^+$, 615 $(M+H)^+$, and 557 $(M-{}^tBu)^+$. Anal. Calcd for $C_{28}H_{54}N_2O_7Si_3$: C, 54.77; H, 8.70; N, 4.56. Found: C, 54.86; H, 9.08; N, 4.56.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6,1'-[(2*R*)-2-methyl-1-oxaethano]uridine (32β). This compound was obtained from **17a** (106.0 mg, 0.168 mmol) by *Method B* as a solid (65.7 mg, 62%): mp 87.0-88.0 °C (solidified from hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 7600), λ_{min} 227 nm (ε 1600). ^1H NMR ($CDCl_3$) δ 9.27 (1H, br), 5.49 (1H, s, H5), 5.17 (1H, dq, $J_{5,7}$=1.5, $J_{7,CH3}$=6.4 Hz), 5.11 (1H, d, $J_{2',3'}$=5.2 Hz), 4.25 (1H, dd, $J_{3',4'}$=1.3 Hz), 4.06 (1H, ddd, $J_{4',5'}$=5.3 and 8.5 Hz), 3.71 (1H, dd, J_{gem}=10.8 Hz), 3.67 (1H, dd), 1.49 (3H, d), 0.91, 0.89, and 0.86 (27H, s), 0.10, 0.07, 0.06, 0.05, 0.04, and −0.04 (18H, each as s). FAB MS *m/z* 652 $(M+Na)^+$, 630 $(M+H)^+$, and 571 $(M-{}^tBu)^+$. Anal. Calcd for $C_{29}H_{56}N_2O_7Si_3$: C, 55.37; H, 8.97; N, 4.45. Found: C, 55.24; H, 9.09; N, 4.40.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6,1'-[(2*S*)-2-methyl-1-oxaethano]uridine (33β) and 2',3',5'-tris-*O*-(*tert*-butyldimethylsilyl)-α-6,1'-[(2*S*)-2-methyl-1-oxaethano]uridine (33α). These compounds were obtained from **17b** (106.9 mg, 0.170 mmol) by *Method B*. Purification of HPLC (EtOAc:hexane=1:1) gave **33β** (t_R 10.1 min, 40.1 mg, 38%) as a foam and **33α** (t_R 13.4 min, 20.8 mg, 19%) as a solid. **33β**: UV (MeOH) λ_{max} 259 nm (ε 8100), λ_{min} 228 nm (ε 1900). ^1H NMR ($CDCl_3$) δ 8.73 (1H, br), 5.49 (1H, dq, $J_{7,CH3}$=6.6 Hz), 5.48 (1H, d, $J_{5,NH}$=1.7 Hz), 4.93 (1H, d, $J_{2',3'}$=5.2 Hz), 4.20 (1H, dd, $J_{3',4'}$=0.6 Hz), 4.16 (1H, dd, $J_{4',5'}$=5.2 and 9.2 Hz), 3.75 (1H, dd, J_{gem}=10.7 Hz), 3.70 (1H, dd), 1.54 (3H, d), 0.92, 0.90, and 0.85 (27H, s), 0.10, 0.07, 0.06, 0.04, and −0.06 (18H, each as s). FAB MS *m/z* 630 $(M+H)^+$ and 571 $(M-{}^tBu)^+$. Anal. Calcd for $C_{29}H_{56}N_2O_7Si_3$: C, 55.37; H, 8.97; N, 4.45. Found: C, 55.35; H, 9.01; N,

4.41. **33α**: mp 185.5-187.0 °C (solidified from hexane-EtOAc). UV (MeOH) λ_{max} 260 nm (ε 7900), λ_{min} 229 nm (ε 2000). ^{1}H NMR ($CDCl_3$) δ 8.73 (1H, br), 5.49 (1H, dq, $J_{7,CH3}$=6.6 Hz), 5.48 (1H, d, $J_{5,NH}$=1.7 Hz), 4.93 (1H, d, $J_{2',3'}$=5.2 Hz), 4.20 (1H, dd, $J_{3',4'}$=0.6 Hz), 4.16 (1H, dd, $J_{4',5'}$=5.2 and 9.2 Hz), 3.75 (1H, dd, J_{gem}=10.7 Hz), 3.70 (1H, dd), 1.54 (3H, d), 0.92, 0.90, and 0.85 (27H, s), 0.14, 0.10, 0.07, 0.06, and -0.07 (18H, each as s). FAB MS *m/z* 630 $(M+H)^+$, 614 $(M-Me)^+$, and 571 $(M-{}^tBu)^+$. Anal. Calcd for $C_{29}H_{56}N_2O_7Si_3$: C, 55.37; H, 8.97; N, 4.45. Found: C, 55.35; H, 9.01; N, 4.41.

2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-6,1'-[2,2-dimethyl-1-oxaethano]uridine (34β) and 2',3',5'-Tris-*O*-(*tert*-butyldimethylsilyl)-α-6,1'-[2,2-dimethyl-1-oxaetano]uridine (34α). These compounds were obtained from **19** (120.4 mg, 0.187 mmol) by *Method B*. Purification of HPLC (EtOAc:hexane=1:1) gave **34β** (t_R 9.8 min, 67.9 mg, powder, 56%) and **34α** (t_R 11.7 min, 11.4 mg, powder, 9.5%). **34β**: UV (MeOH) λ_{max} 260 nm (ε 7200), λ_{min} 227 nm (ε 1900). ^{1}H NMR ($CDCl_3$) δ 9.10 (1H, br), 5.44 (1H, s), 5.10 (1H, d, $J_{2',3'}$=5.0 Hz), 4.20 (1H, dd, $J_{3',4'}$=0.8 Hz), 4.07 (1H, dd, $J_{4',5'}$=5.8 and 8.5 Hz), 3.69 (1H, dd, J_{gem}=10.5 Hz), 3.66 (1H, dd), 1.50 and 1.57 (6H, each as s), 0.91, 0.90, and 0.86 (27H, s), 0.09, 0.07, 0.06, 0.04, and -0.03 (18H, s). FAB MS *m/z* 585 $(M-{}^tBu)^+$. Anal. Calcd for $C_{30}H_{58}N_2O_7Si_3$: C, 56.03; H, 9.09; N, 4.36. Found: C, 55.86; H, 9.11; N, 4.20. **34α**: UV (MeOH) λ_{max} 260 nm (ε 11000), λ_{min} 229 nm (ε 2400). ^{1}H NMR ($CDCl_3$) δ 7.97 (1H, br), 5.38 (1H, s), 4.69 (1H, dt, $J_{3',4'}$=8.0, $J_{4',5'}$=2.1 Hz), 4.32 (1H, dd, $J_{2',3'}$=5.2 Hz), 4.05 (1H, d), 3.89 (1H, dd, J_{gem}=12.2 Hz), 3.72 (1H, dd), 1.51 and 1.52 (6H, each as s), 0.91, 0.89, and 0.87 (27H, s), 0.12, 0.10, 0.07, 0.06, 0.05, and 0.04 (18H, s). FAB MS *m/z* 643 $(M+H)^+$ and 585 $(M-{}^tBu)^+$. Anal. Calcd for $C_{30}H_{58}N_2O_7Si_3$: C, 56.03; H, 9.09; N, 4.36. Found: C, 56.06; H, 9.05; N, 4.34.

Deprotection of the silyl protecting groups. Four free spiro nucleosides were obtained by TBAF treatment in THF and fully characterized. The typical procedure is described for compound **24β**. To the THF solution (3 mL) of **20β** (33.9 mg, 0.0680 mmol), TBAF (35.5 mg, 0.136 mmol) was added. After 6 h stirring, silica gel (350 mg) was added and the whole mixture was concentrated *in vacuo*. The residue was applied on a silica gel column and the deprotected compound was eluted (1-4% MeOH in CH_2Cl_2) to yield solid of **24β** (14.1 mg, 81%), which was recrystallized from $CHCl_3$-EtOH.

6,1'-(1-Oxoethano)-2'-deoxyuridine (24β). mp 192.0-193.0 °C ($CHCl_3$-EtOH). UV (MeOH) λ_{max} 259 nm (ε 10800), λ_{min} 227 nm (ε 2100). ^{1}H NMR (DMSO-*d6*) δ 11.29 (1H, br), 5.58 (1H, br), 5.30 (1H, d, $J_{3',OH}$=5.5 Hz), 4.97 (1H, dd, $J_{5,7}$=1.1, J_{gem}=15.0 Hz), 4.87 (1H, dd, $J_{5,7}$=1.3 Hz), 4.74 (1H, t, $J_{5',OH}$=5.9), 4.25 (1H, ddt, $J_{2',3'}$=$J_{3',4'}$=6.7, $J_{2',3'}$=8.2 Hz), 3.81 (1H, dt, $J_{4',5'}$=6.7 and 3.3 Hz), 3.59 (1H, ddd, J_{gem}=12.1 Hz), 3.44 (1H, ddd), 3.12 (1H, dd, J_{gem}=14.3 Hz), 2.13 (1H, dd). FAB MS *m/z* 257 $(M+H)^+$. Anal. Calcd for $C_{10}H_{12}N_2O_6$: C, 46.88; H, 4.72; N, 10.93. Found: C, 46.91; H, 4.60; N, 10.85.

6,1'-[(2*S*)-2-Methyl-1-oxoethano]-α-2'-deoxyuridine (25α). This compound (28.2 mg)

was obtained from **22α** (56.1 mg, 0.109 mmol) by the same procedure described for **24β** in 95.7% yield. The resulting white powder was recrystallized from $CHCl_3$-EtOH for an analytical sample: mp 184.0-185.0 °C ($CHCl_3$-EtOH). UV (MeOH) λ_{max} 259 nm (ε 10700), λ_{min} 227.4 nm (ε 2400). ^1H NMR (DMSO-d_6) δ 11.39 (1H, br), 5.65 (1H, d, $J_{5,7}$=1.5 Hz), 5.45 (1H, d, $J_{3',OH}$=6.2 Hz), 5.13 (1H, dq, $J_{7,CH3}$=6.6 Hz), 4.75 (1H, t, $J_{5',OH}$=5.9 Hz), 4.14 (1H, ddt, $J_{2',3'}$=8.4 and 7.5, $J_{3',4'}$=6.2 Hz), 3.97 (1H, dt, $J_{4',5'}$=6.2 and 3.3 Hz), 3.56 (1H, ddd, J_{gem}=12.1 Hz), 3.38 (1H, ddd), 3.10 (1H, dd, J_{gem}=13.6 Hz), 2.36 (1H, dd), 1.41 (3H, d). FAB MS *m/z* 271 $(M+H)^+$. Anal. Calcd for $C_{11}H_{14}N_2O_6$: C, 48.89; H, 5.22; N, 10.37. Found: C, 48.86; H, 5.24; N, 10.22.

6,1'-[2,2-Dimethyl-1-oxoethano]-2'-deoxyuridine (26β). This compound (26.0 mg) was obtained from **23β** (48.2 mg, 0.0915 mmol) by the same procedure described for **24β** in the quantitative yield. The resulting white foam was recrystallized from $CHCl_3$-EtOH for an analytical sample: mp 187.5-188.5 °C ($CHCl_3$-EtOH). UV (MeOH) λ_{max} 259 nm (ε 11000), λ_{min} 228 nm (ε 2200). ^1H NMR (DMSO-d_6) δ 11.27 (1H, br), 5.69 (1H, d, $J_{5,NH}$=2.1 Hz), 5.21 (1H, d, $J_{3',OH}$=5.2 Hz), 4.66 (1H, t, $J_{5',OH}$=5.8 Hz), 4.24 (1H, ddt, $J_{2',3'}$=$J_{3',4'}$=6.4, $J_{2',3'}$=8.1 Hz), 3.82 (1H, dt, $J_{4',5'}$=6.4 and 3.4 Hz), 3.58 (1H, ddd, J_{gem}=11.9 Hz), 3.40 (1H, ddd), 3.09 (1H, dd, J_{gem}=14.0 Hz), 2.07 (1H, dd), 1.52 and 1.42 (6H, each as s). FAB MS *m/z* 307 $(M+Na)^+$ and 285 $(M+H)^+$. Anal. Calcd for $C_{12}H_{16}N_2O_6$: C, 50.70; H, 5.67; N, 9.85. Found: C, 50.33; H, 5.56; N, 9.61.

6,1'-(1-Oxaetano)uridine (35β). The 1 M solution of TBAF in THF (0.63 mL, 0.63 mmol) was added to the THF (5 mL) solution of **34β** (108.6 mg, 0.177 mmol) at 0 °C. The mixture was stirred at rt for 18 h. Purification on a silica gel column (1-10% MeOH in $CHCl_3$) followed by recrystallization from EtOH gave **35β** (45.3 mg, 94%). Physical data of **35β** is as follows: mp 183.0-185.0 °C (EtOH). UV (MeOH) λ_{max} 260 nm (ε 8400), λ_{min} 228 nm (ε 1600). ^1H NMR (DMSO-d_6) δ 11.4 (1H, br), 5.62 (1H, t, $J_{5,7}$=$J_{5,NH}$=1.4 Hz), 5.14 (1H, d, $J_{3',OH}$=4.3 Hz), 5.05 (1H, d, $J_{2',OH}$=9.2 Hz), 5.00 (1H, dd, J_{gem}=15.1 Hz), 4.92 (1H, dd), 4.74 (1H, dd, $J_{2',3'}$=6.1 Hz), 4.67 (1H, dd, $J_{5',OH}$=5.2 and 7.0 Hz), 4.02 (1H, m), 4.00 (1H, dt, $J_{3',4'}$=1.6, $J_{4',5'}$=5.1 and 5.5 Hz), 3.52 (1H, ddd, J_{gem}=11.7 Hz), 3.45 (1H, ddd). FAB MS *m/z*: 273 $(M+H)^+$. Anal. Calcd for $C_{10}H_{12}N_2O_7 \cdot 1/2H_2O$: C, 42.71; H, 9.96; N, 4.66. Found: C, 42.85; H, 9.83; N, 4.50.

Acknowledgment. The authors would like to thank Ms. Suzanne Knowlton (Showa University) for proofreading this manuscript and Miss Rumiko Takamatsu (Showa University) for her technical assistance. This work was partially supported by the High-Technology Research Center Project from the Ministry of Education, Science, Sports and Culture of Japan.

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