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Alkyl Addition Reaction of Pyrimidine 2′-Ketonucleosides: Synthesis of 2′-Branched-Chain Sugar Pyrimidine Nucleosides (Nucleosides and Nucleotides. LXXXI[1])

AKIRA MATSUDA,*,[a] HIROKO ITOH,[a] KENJI TAKENUKI,[a] TAKUMA SASAKI,[b] and TOHRU UEDA[a]

Faculty of Pharmaceutical Sciences, Hokkaido University,[a] Kita-12, Nishi-6, Kita-ku, Sapporo 060, Japan and Cancer Research Institute, Kanazawa University,[b] Takara-machi, Kanazawa 920, Japan

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The reaction of 4-ethoxy-1-(3,5-*O*-tetraisopropyldisiloxanyl-1,3-diyl-β-D-*erythro*-pentofuran-2-ulosyl)-2(1*H*)-pyrimidinone (**11**) with various organometallic reagents yielded corresponding 2′-branched-chain sugar pyrimidine nucleosides. Only in the reactions with MeMgBr and EtMgBr was the more hindered β-attack observed to afford the 2′-alkyl ribofuranosides (**13a, b**). In the reaction of **11** with MeLi, Me_3Al, or PhMgBr, 2′-methyl or phenyl arabinosides (**12a, b, c**) were obtained stereoselectively. Conversion of these pyrimidine nucleosides into cytosine derivatives is also described and their antileukemic and antiviral activities are discussed.

Keywords——2′-branched-chain sugar pyrimidine nucleoside; nucleoside; Grignard reagent; antileukemic activity; pyrimidine 2′-ketonucleoside; CD spectrum; 2′-alkylcytidine; 2′-methylcytidine; 2′-ethylcytidine

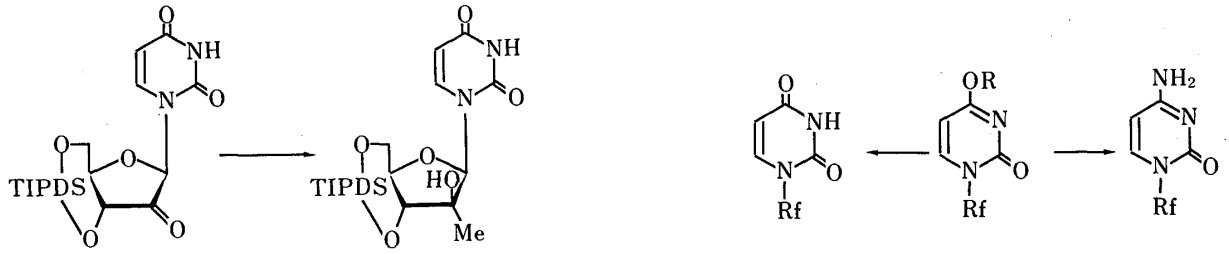
1-β-D-Arabinofuranosylcytosine (ara-C) is probably one of the most potent drugs for treatment of human acute leukemia.[2] However, ara-C is rapidly deaminated to a chemotherapeutically inactive 1-β-D-arabinofuranosyluracil (ara-U) by cytidine deaminase. One approach to circumvent this enzymatic inactivation has been to introduce certain other substituents into the 2′-*arabino* position in place of the hydroxyl group of ara-C. It is of great interest that 2′-amino- and 2′-azido-2′-deoxy-β-D-arabinofuranosylcytosines[3] were found to be resistant to cytidine deaminase while 2′-deoxy-2′-fluoro-β-D-arabinofuranosylcytosine[4,5] was a substrate to some extent. These three nucleosides inhibited the growth of mouse leukemic cells *in vitro*. However, these nucleosides have been synthesized by condensation of appropriately modified sugars with nucleobases, which required a lengthy manipulation.[6] If the requisite substituents could be introduced directly into the 2′-"up"-position of naturally occurring pyrimidine nucleosides, this method should be a versatile alternative. Up to now, such procedures have not been devised because the close proximity of the C-2 carbonyl group to the C-2′ leaving group in the *ribo* configuration of the sugar residue usually results in the formation of O^2,2′-cyclonucleoside during the nucleophilic substitution at the 2′-position.[7]

Branched-chain sugar nucleosides have been synthesized for evaluation of their biological activities.[8] However, the methods so far reported were rather lengthy, involving formation of a requisite branched-chain sugar then condensation with a nucleobase. Stereoselective alkyl addition of a carbonyl group is one of the most useful techniques in synthetic organic chemistry. Application of this methodology to nucleoside chemistry seems to be a straightforward route for the synthesis of branched-chain sugar nucleosides. Although Cook and Moffatt originally synthesized 3′,5′-di-*O*-trityl-2′-ketouridine from uridine by Moffatt oxidation, they reported that the alkyl addition of the carbonyl group was unsuccessful due to its

alkaline lability.[9] Since then, only a few alkyl additions have been applied to ketonucleosides.[10] However, we have recently successfully utilized 3′,5′-*O*-(tetraisopropyldisiloxan-1,3-diyl)-2′-ketouridine (**1**) as a starting material for the Wittig reaction,[11] nitromethylation[12] or epoxidation with diazomethane,[13] and for carbon-bridged cyclonucleoside synthesis.

In this report, we describe the reaction of the ketonucleoside with various organometallic reagents and conversion of these 2′-branched-chain nucleosides into biologically interesting cytosine derivatives together with the preliminary results on their antileukemic and antiviral activities *in vitro*. A preliminary account of this work has appeared.[14]

A preliminary examination of the reaction of **1** with MeMgI in Et_2O at 0 °C resulted in immediate precipitation and the formation of the methyl addition product (**2**) in low yield.[15] This may be due to the formation of metal complexes between N^3 and O^4 of the uracil moiety. Therefore, it seemed necessary to protect the base moiety to avoid such metal complex formation. Among several methods for protection of the uracil moiety in the nucleosides, we selected 4-*O*-alkylation, since the O^4-alkyl derivative (**4**) can be converted to cytosine (**5**) or uracil (**3**) derivatives after derivatization of the sugar moiety.

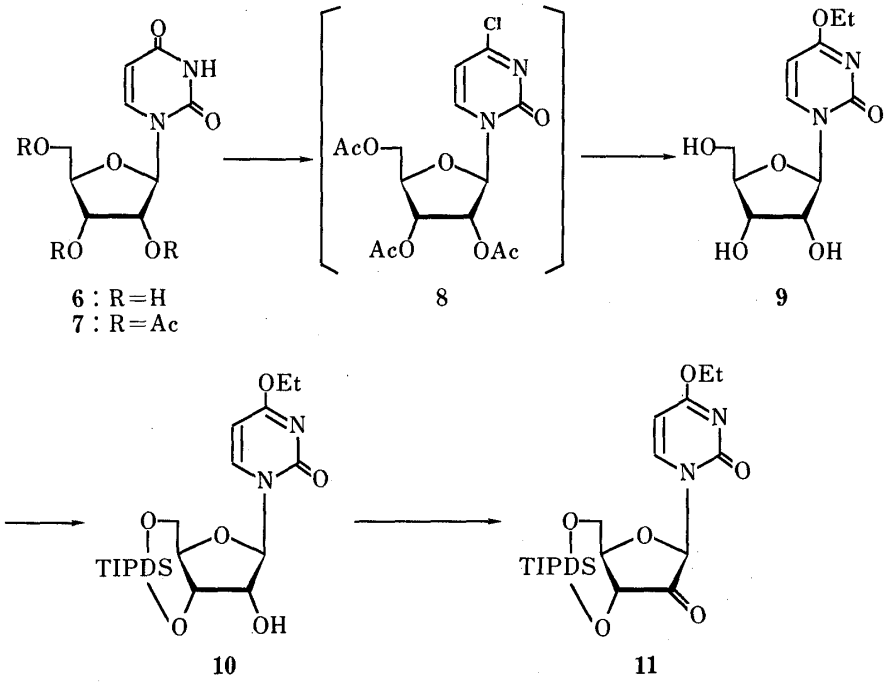


1 **2** **3** **4** **5**

Chart 1

The starting 4-ethoxy-2(1*H*)-pyrimidinone-2′-ketonucleoside (**11**) was prepared by the route shown in Chart 1. Treatment of tri-*O*-acetyluridine (**7**) with the Vilsmeier–Haake reagent in $CHCl_3$[16] gave a 4-chloro derivative (**8**), which, without purification, was treated with NaOEt to afford 4-ethoxy-1-(β-D-ribofuranosyl)-2(1*H*)-pyrimidinone (**9**) in 84% yield. Compound **9** was converted to the 3′,5′-tetraisopropyldisiloxanyl (TIPDS) derivative (**10**) by a standard method in 86% yield as an oil. Compound **10** was then subjected to the Swern oxidation[17] to furnish the 2′-keto derivative (**11**) in 84% yield as crystals after purification by silica gel column chromatography. Other oxidation methods, such as the use of the dimethylsulfoxide (DMSO)–dicyclohexylcarbodiimide (DCC) or CrO_3–pyridine–Ac_2O system, gave lower yields of **11**. The proton nuclear magnetic resonance (^{1}H-NMR) spectral pattern of **11** is quite similar to that of **1**, showing a singlet at δ 4.94 due to H-1′ and a doublet at δ 5.18 due to H-3′.

The reaction of **11** with MeMgBr (3 eq) in tetrahydrofuran (THF) at −50 °C proceeded smoothly without formation of a precipitate to give products showing three spots on a thin layer chromatography (TLC) plate; these products were separated by column chromatography. The first-eluted product (**12a**), obtained as an oil (55% yield), showed a molecular ion peak at *m/z* 528 in its mass spectrum. In the ^{1}H-NMR spectrum of **12a**, a 2′-*tert*-alcohol peak at δ 2.73 as a singlet and the signal of the 2′-methyl protons at δ 1.21 as a singlet were observed. The second compound (**13a**), which was crystallized from EtOH (21% yield), showed a peak of 2′-*tert*-alcohol at δ 2.83 as a singlet, while the 2′-methyl proton signal overlapped with the isopropyl proton signals at around δ 1.03—1.14 in its ^{1}H-NMR spectrum. The stereochemistry at the 2′-position of these compounds was not determined at this stage. Therefore, deblocking of the sugar silyl groups was carried out in THF with tetra-*n*-



6 : R=H
7 : R=Ac

8

9

10

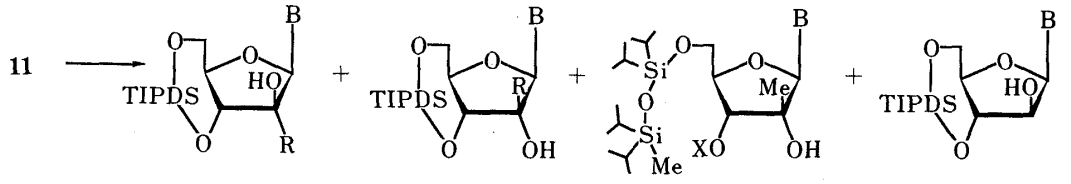
11

Chart 2

butylammonium fluoride (TBAF) as shown in Chart 4. The compound **19a** obtained from **13a** showed a positive periodate-benzidine spray test while the compound **16a** from **12a** was negative. These results together with the formation of a 2′,3′-cyclic borate complex of **19a**, which migrated as a monoanion on paper electrophoresis, implied that **19a** has a ribofuranosyl structure whereas **16a** has an arabinofuranosyl structure.

In the ^{1}H-NMR spectrum of the third component (**14a**), which was obtained as an oil in 20% yield, signals due to two dissociable protons at δ 3.06 (doublet) and 5.26 (singlet) along with two distinct methyl protons at δ 0.03 and δ 1.13 (each singlet) were seen. In the mass spectrum, an $(M-Me)^+$ peak was observed at *m/z* 529. Reaction of **14a** with methanesulfonyl chloride in pyridine gave a 3′-*O*-mesylate (**14b**). Furthermore, after treatment of **14a** with TBAF, the compound obtained showed the same physical properties as the authentic **19a**. These results revealed that **13a** once formed was cleaved selectively at the Si of the 3′-end position by an excess of methyl carbanions to afford **14a**. It is interesting to note that in the case of the 2′(*S*)-methyl derivative (**12a**), such a 3′-end-cleaved compound is hardly detectable. All together, the ratio of the methylated products (**12a** : **13a**+**14a**) is about 1 : 0.7. Although it is generally recognized that the α-face of the 2′-ulose seems to be less hindered, it is of interest that in this case the more hindered β-attack by the Grignard reagent is observed.

In order to improve the β-stereoselectivity, we set up several experiments whose results



12a : R=Me
12b : R=Et
12c : R=Ph

13a : R=Me
13b : R=Et

14a : X=H
14b : X=Ms

15

B=4-ethoxy-2(1*H*)-pyrimidinon-1-yl

Chart 3

TABLE I. Reaction of Compound **11** with Various Organometallic Reagents

Entry	Reagent	Conditions	R	Isolated yields (%)			
				12	**13**	**14**	**15**
1	MeMgBr	THF, −50 °C	Me	55.3	20.9	19.8	0
2	MeMgBr	Et_2O, −50 °C	Me	51.9	42.6	0	0
3	MeMgBr	Et_2O, −78 °C	Me	53.3	40.0	0	0
4	MeMgBr +MAT	Toluene, Et_2O, −78 °C	Me	77.7	17.4	0	0
5	MeMgBr $+BF_3 \cdot OEt_2$	Et_2O, −78 °C	Me	48.8	36.9	0	0
6	MeLi	Et_2O, −78 °C	Me	88.0	0	0	0
7	Me_3Al	$CHCl_3$, −50 °C	Me	82.2	0	0	0
8	EtMgBr	Et_2O, −50 °C	Et	12.6	43.3	0	24.9
9	Et_3Al	$CHCl_3$, −50 °C	H	0	0	0	94.6
10	PhMgBr	Et_2O, −78 °C	Ph	84.0	0	0	0

are summarized in Table I. In contrast to entry 1, the reaction in Et_2O (entry 2) proceeded effectively to give **12a** and **13a** in a ratio of 1 : 0.8 without formation of the 3′-end cleavage product. No changes of the product ratio was observed when the reaction was performed at −78 °C (entry 3). If the less-hindered α-face were blocked by methylaluminum bis(2,4,6-*tert*-butylphenoxide) (MAT), which was introduced recently by Yamamoto *et al.*[18] to increase the axial attack of carbanions in 4-*tert*-butylcyclohexanone, the β-stereoselectivity would be more favored. However, rather inverse selectivity was observed, as shown in Table I (entry 4). Also, the use of $BF_3 \cdot OEt_2$ did not improve the stereoselectivity. On the other hand, in the reaction of **11** with MeLi in THF or Me_3Al in $CHCl_3$ only the α-face attack was observed and the methylated product (**12a**) was exclusively obtained in yields of 88% and 82%, respectively (entries 6 and 7).

Introduction of an ethyl group at the 2′-position of **11** was next examined. Treatment of **11** with EtMgBr in Et_2O (entry 8) gave three nucleosidic products. The β-ethylated nucleoside (**13b**) was mainly obtained, along with the α-ethylated product (**12b**) in rather low yield as compared with the case of entry 2. However, formation of arabinofuranosyl nucleoside (**15**), which would be due to the reduction of the 2′-carbonyl by the β-hydride of the ethyl Grignard reagent, was observed in a considerable amount (entry 8). As expected, reaction with Et_3Al afforded predominantly **15** (entry 9). From these results, there seems to be a chelation-controlled process, in which the Grignard reagent would chelate between the 2′-carbonyl oxygen and the 3′-oxygen atom in **11**, resulting in β-attack to give the 2′-alkylribofuranosides, competing with a non-chelation process which would prefer the less-hindered α-attack to the 2′-alkylarabinofuranosylnucleosides. However, when the alkyl group became bulkier, such as PhMgBr, the 2′-arabinofuranosyl nucleoside (**12c**) was the sole product (entry 10).

The protected 2′-branched-chain nucleosides synthesized in this study were then converted into biologically interesting cytosine nucleosides. Compounds **12b, c**, **13b** and **15** were treated with TBAF in THF to furnish the corresponding free nucleosides (**16b—d**, **19b**, respectively) in good yields. The configuration at the 2′-position of these nucleosides was determined in the same manner as described above. These compounds (**16a, b**, **19a, b**) were further reacted with NH_3/MeOH at 100 °C in a sealed tube to give the corresponding cytosine derivatives (**18a, b**, **20a, b**). A uracil nucleoside (**17**) was obtained from **12a** by alkaline hydrolysis.

In summary, the introduction of a carbon unit at the 2′-position of cytidines has thus been accomplished. This approach should be applicable for the synthesis of 3′-branched

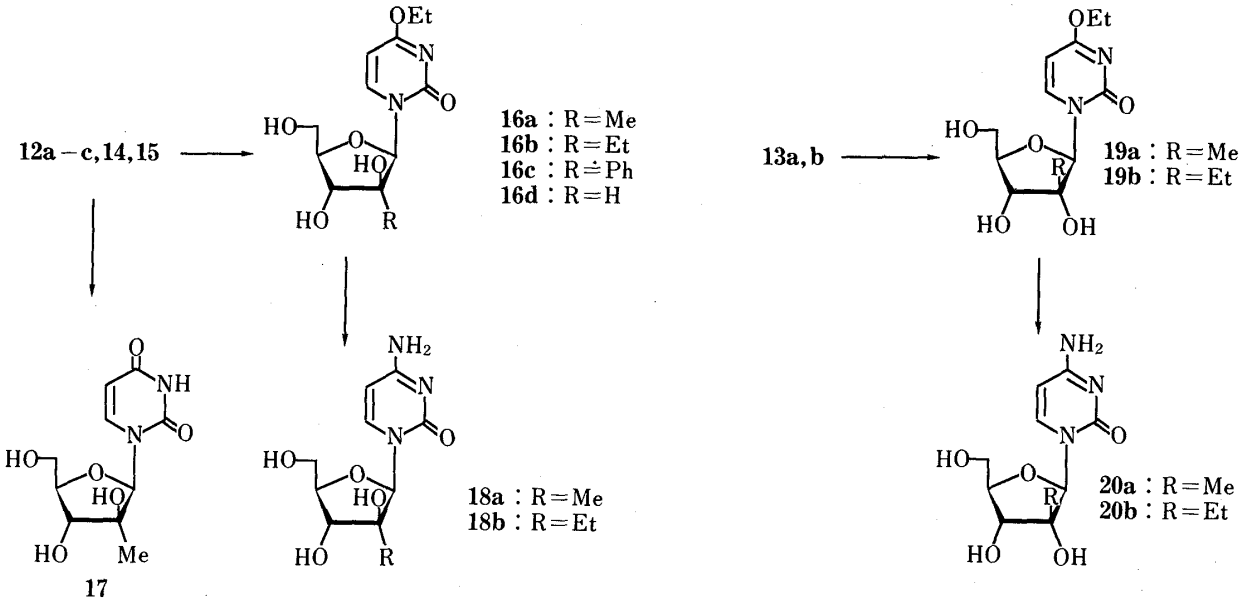


Chart 4

nucleosides as well. It should be noted that the molar ellipticities (θ) of 2′-alkylribonucleosides are always larger than those of the corresponding 2′-alkylarabinofuranosides. This may be a reflection of the bulkiness of the 2′-*ara*-substituents, the alkyl groups being larger than the hydroxyl group.

Antileukemic activities of these 2′-branched-chain nucleosides were tested toward murine L1210 cells *in vitro*. Among them, the most potent inhibitor of the cell growth was 2′(*R*)-methylcytidine (**20a**, $IC_{50}=15\,\mu g/ml$). The ethyl derivative (**20b**) was much less potent (45% inhibition at 400 μg/ml concentration). Though 2′(*S*)-methylcytidine (**18a**) is an analogue of 1-β-D-arabinofuranosylcytosine, a prominent antileukemic antimetabolite in clinical use, the inhibitory activity was only 30% even at 400 μg/ml concentration. None of the compounds showed antiviral activity[19] against herpes simplex type 1 or 2 at the concentration of 100 μg/ml. To improve the activity, the deletion of the hydroxyl group of **18** and **20** seemed desirable and experiments along these lines are currently being undertaken.

Experimental

Melting points were determined on a Yanagimoto MP-3 micro-melting point apparatus and are uncorrected. The ^{1}H-NMR spectra were recorded on a JEOL FT100FT or FX-270FT spectrometer with tetramethylsilane as an internal standard. Chemical shifts are reported in parts per million (δ), and signals are expressed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad). All exchangeable protons were confirmed by addition of D_2O. Ultraviolet (UV) absorption spectra were recorded with a Shimadzu UV-240 spectrophotometer. Mass spectrum (MS) were measured on a JEOL D-300 spectrometer. Circular dichroism (CD) spectra were recorded on a JASCO J-500A spectropolarimeter at room temperature. TLC was performed on Merck Kieselgel F_{254} precoated plates. Silica gel used for column chromatography was Merck Kieselgel 60 (70—230 mesh).

2′,3′,5′-Tri-*O*-acetyluridine (7)——Triethylamine (114 ml, 820 mmol) was added to a mixture of uridine (50 g, 205 mmol), 4-dimethylaminopyridine (250 mg) and acetic anhydride (77.5 ml, 820 mmol) in acetonitrile (400 ml). An exothermic reaction occurred and the mixture was stirred for 1 h at ambient temperature. The mixture was quenched by addition of MeOH (35 ml) with stirring for further 10 min, then concentrated *in vacuo*. The resulting oil was partitioned between H_2O (300 ml) and $CHCl_3$ (300 ml × 2). The organic phase was dried (Na_2SO_4) and evaporated to dryness to give an oily material which was crystallized from aqueous EtOH to afford 70.6 g (93%) of **7**, mp 128—129 °C, lit.[20] mp 128—130 °C.

4-Ethoxy-1-(β-D-ribofuranosyl)-2(1*H*)-pyrimidinone (9)——A mixture of **7** (3.35 g, 9.05 mmol), thionyl chloride (8.1 ml, 112 mmol) and *N*,*N*-dimethylformamide (DMF, 0.5 ml) in anhydrous $CHCl_3$ (50 ml) was heated under reflux for 6.5 h. The yellow-colored solution was evaporated to dryness *in vacuo* and coevaporated with toluene (50 ml × 2).

The residue was dissolved in EtOH (20 ml) and 1 N NaOEt (30 ml) was added to the solution at 0 °C. The mixture was stirred for 1 h at room temperature then heated under reflux for 2 h. The precipitate was removed by filtration and the filtrate was concentrated to a small volume, to which silica gel (*ca.* 30 g) was added. The mixture was evaporated to dryness and the residue was placed on top of a silica gel column (4 × 30 cm) which was washed with 8% EtOH in $CHCl_3$ and then eluted with 16% EtOH in $CHCl_3$. The main UV-absorbing fractions were combined and evaporated to leave a solid which was crystallized from EtOH to give 2.08 g (84.2%) of **9**, mp 136—137.5 °C. MS *m/z*: 272 (M^+), 141 $(B+2)^+$. NMR (DMSO-d_6): 1.28 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.65 (2H, m, 5′-H), 3.92 (3H, m, 2′,3′,4′-H), 4.29 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.03 (1H, d, 2′-OH), 5.15 (1H, t, 5′-OH), 5.44 (1H, d, 3′-OH), 5.77 (1H, d, 1′-H, $J_{1',2'}=2.7$ Hz), 6.02 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 8.30 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{11}H_{16}N_2O_6\cdot 1/3\,H_2O$: C, 46.97; H, 6.09; N, 9.96. Found: C, 46.91; H, 6.02; N, 9.98. This compound is slightly hygroscopic.

4-Ethoxy-1-(3,5-*O*-TIPDS-1,3-diyl-β-D-ribofuranosyl)-2(1*H*)-pyrimidinone (10)——Compound **9** (1.28 g, 5 mmol) was dissolved in pyridine (15 ml), and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (1.74 g, 5.5 mmol) was added. The reaction mixture was stirred at 0 °C for 2 h, then at room temperature for 3 h. H_2O (5 ml) was added to the mixture, which was concentrated to dryness *in vacuo*. The residue was partitioned between H_2O (30 ml) and $CHCl_3$ (50 ml × 2). The organic phase was separated, dried (Na_2SO_4) and evaporated to dryness to leave an oily residue which was chromatographed over a silica gel column (2 × 25 cm) with 40% EtOAc in hexane as the eluent. The main UV-absorbing fractions were combined and evaporated to dryness to leave an oily product (2.22 g, 86.3%). MS *m/z*: 514 (M^+), 471 $(M-\text{iso-Pr})^+$, 141 $(B+2)^+$. NMR ($CDCl_3$): 0.99—1.10 (28H, m, iso-Pr), 1.36 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.16 (1H, d, 2′-OH), 4.04—4.29 (5H, m, 2′,3′,4′,5′-H), 4.43 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.77 (1H, s, 1′-H), 5.84 (1H, d, 5-H, $J_{5,6}=7.5$ Hz), 7.97 (1H, d, 6-H, $J_{5,6}=7.5$ Hz). This compound was used without further purification.

4-Ethoxy-1-(3,5-*O*-TIPDS-1,3-diyl-β-D-*erythro*-pentofuran-2-ulosyl)-2(1*H*)-pyrimidinone (11)——Dimethylsulfoxide (4.8 ml, 66.9 mmol) was added dropwise over 20 min to a solution of oxalyl chloride (2.7 ml, 31.1 mmol) in CH_2Cl_2 (40 ml) at −70 °C under argon. To this mixture, a solution of **10** (12.3 g, 23.9 mmol) in CH_2Cl_2 (50 ml) was added dropwise over 20 min. The whole was stirred for a further 2 h, then triethylamine (20 ml, 143 mmol) was added at once. The reaction mixture was stirred for a further 1 h, then the cooling bath was removed. After warming to room temperature, the mixture was washed with H_2O (20 ml × 2). The organic phase was separated, dried (Na_2SO_4) and concentrated to dryness to leave an oily residue which was purified on a silica gel column (5 × 28 cm) eluted with 20% EtOAc in hexane. The main UV-absorbing fractions were combined and evaporated to dryness. The residue obtained was crystallized from hexane to give 10.2 g (83.6%) of **11**, mp 157.5—159 °C. MS *m/z*: 512 (M^+), 469 $(M-\text{iso-Pr})^+$ NMR ($CDCl_3$): 1.04—1.13 (28H, m, iso-Pr), 1.34 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.95—4.18 (3H, m, 4′,5′-H), 4.41 (2H, q, 4-$O\underline{CH_2}CH_3$), 4.94 (1H, s, 1′-H), 5.18 (1H, d, 3′-H, $J_{3',4'}=7.6$ Hz), 5.88 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 7.36 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{24}H_{39}N_2O_7Si_2$: C, 53.87; H, 7.86; N, 5.46. Found: C, 53.73; H, 7.87; N, 5.57.

Reaction of 11 with MeMgBr in THF (Entry 1)——A 1 M solution of MeMgBr in THF (6 ml, 6 mmol) was added dropwise over 5 min to a solution of **11** (1.01 g, 1.97 mmol) in THF (40 ml) at −50 °C under argon. The mixture was stirred for 1.5 h at −50 °C, then aqueous 1 N NH_4Cl solution (10 ml) was added. After warming to room temperature, the mixture was partitioned between EtOAc (100 ml) and H_2O (30 ml × 2) and the organic phase was dried (Na_2SO_4) then concentrated to dryness. The residue was purified on a silica gel column (2 × 20 cm) which was eluted with 20% EtOAc in hexane. From this fraction, **12a** (576 mg, 55.3%) was obtained as an oil. Elution was continued with 40% EtOAc in hexane to afford **13a** (218 mg, 20.9%), which was crystallized from hexane–EtOAc. Then the column was eluted with 80% EtOAc in hexane to give **14a** (206 mg, 19.8%) as an oil.

Physical Data for 4-Ethoxy-1-(2-methyl-3,5-*O*-TIPDS-1,3-diyl-β-D-arabinofuranosyl)-2(1*H*)-pyrimidinone (**12a**): MS *m/z*: 528 (M^+), 485 $(M-\text{iso-Pr})^+$, 141 $(B+2)^+$. NMR (270 MHz, $CDCl_3$): 1.03—1.14 (28H, m, iso-Pr), 1.21 (3H, s, 2′-Me), 1.33 (3H, t, 4-$OCH_2\underline{CH_3}$), 2.73 (1H, s, 2′-OH), 3.99—4.27 (4H, m, 3′,4′,5′-H), 4.43 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.85 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 6.13 (1H, s, 1′-H), 7.95 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{24}H_{44}N_2O_7Si_2$: C, 54.51; H, 8.39; N, 5.30. Found: C, 54.39; H, 8.32; N, 5.17.

Physical Data for 4-Ethoxy-1-(2-methyl-3,5-*O*-TIPDS-1,3-diyl-β-D-ribofuranosyl)-2(1*H*)-pyrimidinone (**13a**): mp 179—180.5 °C. MS *m/z*: 528 (M^+), 485 $(M-\text{iso-Pr})^+$, 141 $(B+2)^+$. NMR (270 MHz, $CDCl_3$): 1.03—1.14 (28H, m, iso-Pr), 1.36 (3H, t, 4-$OCH_2\underline{CH_3}$), 2.83 (1H, s, 2′-OH), 3.74—4.20 (4H, m, 3′,4′,5′-H), 4.43 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.79 (1H, s, 1′-H), 5.89 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 8.11 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{24}H_{44}N_2O_7Si_2$: C, 54.51; H, 8.39; N, 5.30. Found: C, 54.50; H, 8.49; N, 5.15.

Physical Data for 4-Ethoxy-1-[2-methyl-5-*O*-(3-methyl-1,1,3,3-tetraisopropyldisiloxan-1-yl)-β-D-ribofuranosyl]-2(1*H*)-pyrimidinone (**14a**): MS *m/z*: 529 $(M-Me)^+$, 501 $(M-\text{iso-Pr})^+$, 141 $(B+2)^+$. NMR ($CDCl_3$): 0.03 (3H, s, Si-Me), 0.99—1.06 (28H, m, iso-Pr), 1.13 (3H, s, 2′-Me), 1.37 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.06 (1H, d, 3′-OH), 4.02—4.83 (4H, m, 3′,4′,5′-H), 4.45 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.26 (1H, s, 2′-OH), 5.29 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 5.94 (1H, s, 1′-H), 8.08 (1H, d, 6-H, $J_{5,6}=7.3$ Hz).

4-Ethoxy-1-[3-*O*-mesyl-2-methyl-5-*O*-(3-methyl-1,1,3,3-tetraisopropyldisiloxan-1-yl)-β-D-ribofuranosyl]-2(1*H*)-pyrimidinone (14b)——A solution of **14a** (173 mg, 0.32 mmol) in pyridine (10 ml) was added to mesyl chloride (100 μl, 1.5 mmol) and the mixture was stirred at room temperature for 4 h. H_2O (0.5 ml) was added, and the whole was concentrated to dryness, then the residue was partitioned between EtOAc (30 ml) and H_2O (10 ml × 2). The separated organic phase was dried (Na_2SO_4) and purified on a silica gel column (2 × 18 cm). Compound **14b** was eluted with

20% hexane in EtOAc: yield 175 mg (oil, 87.8%), MS *m/z*: 607 $(M-Me)^+$, 579 $(M-iso\text{-}Pr)^+$, 141 $(B+2H)^+$. NMR ($CDCl_3$): 0.06 (3H, s, Si-Me), 1.00—1.06 (28H, m, iso-Pr), 1.18 (3H, s, 2′-Me), 1.38 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.19 (3H, s, SO_2Me), 3.98 (1H, dd, 5′-Ha, $J_{4',5'a}=2.9$ Hz, $J_{5'a,5'b}=11.7$ Hz), 4.15 (1H, dd, 5′-Hb, $J_{4'5'b}=2.2$ Hz, $J_{5'a,5'b}=11.7$ Hz), 4.29 (1H, m, 4′-H), 4.46 (2H, q, 4-$O\underline{CH_2}CH_3$), 4.88 (1H, s, 2′-OH), 4.91 (1H, d, 3′-H, $J_{3',4'}=5.1$ Hz), 5.90 (1H, s, 1′-H), 5.93 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 7.89 (1H, d, 6-H, $J_{5,6}=7.3$ Hz).

Reaction of 11 with MeMgBr in Et_2O (Entries 2 and 3) or in the Presence of $BF_3\cdot OEt_2$ (Entry 5)——A 3 M solution of MeMgBr (2 ml, 6 mmol) was added dropwise over 5 min to a solution of **11** (1.0 g, 1.95 mmol) in Et_2O (40 ml) at −50 °C (or −78 °C in the case of entries 3 and 5) under argon. The reaction mixture was stirred for 2 h at −50 °C. The same work-up and purification procedures as described for entry 1 were carried out to give **12a** (535 mg, 51.9%) and **13a** (439 mg, 42.6%) in entry 2.

Entry 3: From 2.0 g (3.9 mmol) of **11**, **12a** (1.1 g, 53.3%) and **13a** (825 mg, 40%) were obtained.

Entry 5: From 300 mg (0.59 mmol) of **11** in the presence of $BF_3\cdot OEt_2$ (370 μl, 3 mmol), **12a** (168 mg, 48.8%) and **13a** (114 mg, 36.9%) were obtained.

Reaction of 11 with MeMgBr in the Presence of MAT (Entry 4)——A 15% solution of Me_3Al in hexane (1.9 ml, 3 mmol) was added to a solution of 2,4,6-tri-*tert*-butylphenol (1.32 g, 5 mmol) in toluene (10 mmol) under argon. The mixture was stirred at room temperature for 1 h then cooled to −78 °C. To this mixture, a solution of **11** (512 mg, 1 mmol) in Et_2O (10 ml) was added, followed by dropwise addition (over 5 min) of a 3 M solution of MeMgBr (3 ml, 9 mmol). The mixture was stirred for a further 1.5 h at −78 °C then quenched by addition of aqueous 1 M NH_4Cl solution (15 ml). The mixture was washed with H_2O (10 ml × 2), dried (Na_2SO_4), and evaporated *in vacuo*. The residue was purified on a silica gel column (2.5 × 20 cm) as described above to give 411 mg (77.7%) of **12a** and 92 mg (17.4%) of **13a**.

Reaction of 11 with MeLi (Entry 6)——A 1.6 M solution of MeLi in Et_2O (0.88 ml, 1.2 mmol) was added dropwise over 5 min to a solution of **11** (500 mg, 0.98 mmol) in Et_2O (20 ml) at −78 °C under argon. The reaction mixture was stirred for 40 min. The same work-up procedure as described for entry 1 was carried out. The crude product was chromatographed (40% EtOAc in hexane) to give **12a** (456 mg, 88%).

Reaction of 11 with Me_3Al (Entry 7)——A 15% solution of Me_3Al in hexane (1.9 ml, 3 mmol) was added dropwise to a solution of **11** (513 mg, 1 mmol) in $CHCl_3$ (20 ml) at −50 °C under argon. The mixture was stirred for 40 min. Work-up and purification as described for entry 1 afforded **12a** (435 mg, 82.2%).

Reaction of 11 with EtMgBr in Et_2O (Entry 8)——A 3 M solution of EtMgBr in Et_2O (2.5 ml, 7.5 mmol) was added dropwise to a solution of **11** (1.0 g, 1.95 mmol) in Et_2O (40 ml) at −50 °C under argon. The mixture was stirred for 1.5 h. The same work-up procedure as described for entry 1 was carried out. The crude products were chromatographed over a silica gel column (3 × 22 cm). Compound **12b** (oil, 133 mg, 12.6%) was eluted first from the column with 5% EtOAc in hexane, followed by compound **13b** (oil, 458 mg, 43.3%) with 10% EtOAc in hexane. Compound **15** was eluted with 20% EtOAc in hexane: yield 250 mg (oil, 24.9%).

Physical Data for 4-Ethoxy-1-(2-ethyl-3,5-*O*-TIPDS-1,3-diyl-β-D-ribofuranosyl)-2(1*H*)-pyrimidinone (**13b**): MS MS *m/z*: 542 (M^+), 499 $(M-iso\text{-}Pr)^+$, 141 $(B+2)^+$. NMR ($CDCl_3$): 1.10 (31H, m, iso-Pr, 2′-$CH_2\underline{CH_3}$), 1.36 (3H, t, 4-$OCH_2\underline{CH_3}$), 2.01 (2H, m, 2′-$\underline{CH_2}CH_3$), 2.98 (1H, s, 2′-OH), 4.12 (4H, m, 3′,4′,5′-H), 4.42 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.84 (1H, s, 1′-H), 5.98 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 8.16 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{25}H_{46}N_2O_7Si_2$: C, 55.32; H, 8.54; N, 5.16. Found: C, 55.17; H, 8.70; N, 5.02.

Physical Data for 4-Ethoxy-1-(2-ethyl-3,5-*O*-TIPDS-1,3-diyl-β-D-ribufuranosyl)-2(1*H*)-pyrimidinone (**13b**): MS *m/z*: 542 (M^+), 499 $(M-iso\text{-}Pr)^+$, 141 $(B+2)^+$. NMR ($CDCl_3$): 0.92 (3H, t, 2′-$CH_2\underline{CH_3}$), 1.10 (28H, m, iso-Pr), 1.36 (3H, t, 4-$OCH_2\underline{CH_3}$), 1.58 (2H, m, 2′-$\underline{CH_2}CH_3$), 2.77 (1H, s, 2′-OH), 4.16 (4H, m, 3′,4′,5′-H), 4.43 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.84 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 6.12 (1H, s, 1′-H), 7.79 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{25}H_{46}N_2O_7Si_2$: C, 55.32; H, 8.54; N, 5.16. Found: C, 55.15; H, 8.56; N, 4.93.

Physical Data for 4-Ethoxy-1-(3,5-*O*-TIPDS-1,3-diyl-β-D-arabinofuranosyl)-2(1*H*)-pyrimidinone (**15**): MS *m/z*: 514 (M^+), 471 $(M-iso\text{-}Pr)^+$, 141 $(B+2)^+$. NMR ($CDCl_3$): 0.99—1.10 (28H, m, iso-Pr), 1.37 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.18 (1H, d, 2′-OH), 3.86—4.64 (5H, m, 2′,3′,4′,5′-H), 4.43 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.91 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 6.11 (1H, d, 1′-H, $J_{1',2'}=6.1$ Hz), 8.08 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{23}H_{42}N_2O_7Si_2$: C, 53.66; H, 8.23; N, 5.44. Found: C, 53.47; H, 8.20; N, 5.43.

Reaction of 11 with Et_3Al (Entry 9)——A 15% solution of Et_3Al in hexane (2.9 ml, 3 mmol) was added dropwise to a solution of **11** (512 mg, 1 mmol) in $CHCl_3$ (20 ml) at −50 °C under argon. The reaction mixture was stirred for 30 min at −50 °C. Work-up and purification were carried out as described under entry 1 to afford **15** (oil, 487 mg, 94.6%).

Reaction of 11 with PhMgBr (Entry 10)——A 2 M solution of PhMgBr in THF (2 ml, 4 mmol) was added dropwise to a solution of **11** (512 mg, 1 mmol) in Et_2O (20 ml) at −78 °C under argon. The reaction mixture was stirred for 1 h. Work-up and purification were carried out as described above to afford 4-ethoxy-1-(2-phenyl-3,5-*O*-TIPDS-β-D-arabinofuranosyl)-2(1*H*)-pyrimidinone (**12c**), which was crystallized from hexane–EtOAc: yield 455 mg (84%), mp 179—180 °C. MS *m/z*: 590 (M^+). NMR ($CDCl_3$): 1.07—1.13 (28H, m, iso-Pr), 1.30 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.59 (1H, s, 2′-OH), 3.67—4.33 (4H, m, 3′,4′,5′-H), 4.44 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.95 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 6.34 (1H, s, 1′-H), 7.32—7.64 (5H, m, Ph), 8.39 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{29}H_{46}N_2O_7Si_2$: C, 58.95; H,

7.85; N, 4.74. Found: C, 58.70; H, 7.84; N, 4.98.

2′-Methyl-1-β-D-arabinofuranosyluracil (17)——A solution of **12a** (500 mg, 0.95 mmol) in THF (15 ml) was treated with 1 N NaOH (5 ml) at room temperature for 23 h then at 60 °C for 1.5 h. The reaction mixture was neutralized with AcOH and evaporated to dryness. The residue was purified on a silica gel column (2 × 20 cm), which was eluted with 16% EtOH in $CHCl_3$. The main UV-absorbing fractions were combined and evaporated to dryness to leave a residue, which was crystallized from Et_2O to give **17** (132 mg, 53.6%), mp 137—138 °C. MS *m/z*: 258 (M^+), 240 $(M-H_2O)^+$, 112 $(B+1)^+$. NMR (CD_3OD): 1.28 (3H, s, 2′-Me), 3.81—3.88 (4H, m, 3′,4′,5′-H), 6.64 (1H, d, 5-H, $J_{5,6}=8.3$ Hz), 7.96 (1H, s, 1′-H), 7.86 (1H, d, 6-H, $J_{5,6}=8.3$ Hz). UV $\lambda_{max}^{H_2O}$ (ε): 263 nm (12820). CD (H_2O) [θ]: +25350 (265 nm); −10840 (235 nm), −9090 (215 nm). *Anal.* Calcd for $C_{10}H_{14}N_2O_6 \cdot 0.5H_2O$: C, 44.96; H, 5.66; N, 10.48. Found: C, 44.76; H, 5.68; N, 10.18.

Deprotection of TIPDS Group——General Procedure: A solution of tetra-*n*-butylammonium fluoride (2.2 eq) was added to a solution of **12a—c**, **13a, b**, **14** or **15** in THF. The reaction was almost completed within 20 min. The reaction mixture was neutralized with AcOH and mixed with silica gel. The mixture was evaporated to dryness *in vacuo* and the residue was placed on a silica gel column which was eluted with 10—16% EtOH in $CHCl_3$ to afford the free nucleoside.

4-Ethoxy-1-(2-methyl-β-D-arabinofuranosyl)-2(1*H*)-pyrimidinone (16a)——From 576 mg of **12a**, 269 mg (86.4%) of **16a** was obtained, mp 212—213 °C (MeOH). MS *m/z*: 286 (M^+), 268 $(M-H_2O)^+$, 141 $(B+2)^+$, 113 $(B-Et)^+$. NMR (DMSO-d_6): 1.17 (3H, s, 2′-Me), 1.29 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.57—3.64 (4H, m, 3′,4′,5′-H), 4.29 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.17 (1H, t, 5′-OH), 5.17 (1H, s, 2′-OH), 5.47 (1H, d, 3′-OH), 5.94 (1H, s, 1′-H), 5.98 (1H, d, 5-H, $J_{5,6}=7.5$ Hz), 7.94 (1H, d, 6-H, $J_{5,6}=7.5$ Hz). UV $\lambda_{max}^{H_2O}$ (ε): 275 nm (7280). *Anal.* Calcd for $C_{12}H_{18}N_2O_6$: C, 50.35; H, 6.34; N, 9.78. Found: C, 50.17; H, 6.24; N, 9.75.

4-Ethoxy-1-(2-methyl-β-D-ribofuranosyl)-2(1*H*)-pyrimidinone (19a)——a) From 206 mg of **13a**, **19a** was obtained (92 mg, EtOH, 94.5%), mp 135—136.5 °C. MS *m/z*: 286 (M^+), 141 $(B+2)^+$, 113 $(B-Et)^+$. NMR (DMSO-d_6): 0.94 (3H, s, 2′-Me), 1.28 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.66—3.78 (4H, m, 3′,4′,5′-H), 4.29 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.09 (1H, d, 3′-OH), 5.13 (1H, s, 2′-OH), 5.90 (1H, s, 1′-H), 6.01 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 8.39 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). UV $\lambda_{max}^{H_2O}$ (ε): 275 nm (6910). *Anal.* Calcd for $C_{12}H_{18}N_2O_6$: C, 50.35; H, 6.34; N, 9.78. Found: C, 50.50; H, 6.45; N, 9.74. b) From compound **14** (150 mg), 70 mg (89%) of **19a** was obtained.

4-Ethoxy-1-(2-ethyl-β-D-arabinofuranosyl)-2(1*H*)-pyrimidinone (16b)——From 335 mg of **12b**, **16b** was obtained (123 mg, foam, 63.1%). MS *m/z*: 300 (M^+), 282 $(M-H_2O)^+$, 141 $(B+2)^+$. NMR (CD_3OD): 0.98 (3H, t, 2′-$CH_2\underline{CH_3}$), 1.35 (3H, t, 4-$OCH_2\underline{CH_3}$), 1.00—2.04 (2H, m, 2′-$\underline{CH_2}CH_3$), 3.80—4.28 (4H, m, 3′,4′,5′-H), 4.39 (2H, q, 4-$O\underline{CH_2}CH_3$), 6.00 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 6.18 (1H, s, 1′-H), 8.07 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). UV $\lambda_{max}^{H_2O}$ (ε): 275 nm (5690). *Anal.* Calcd for $C_{13}H_{20}N_2O_6$: C, 51.99; H, 6.71; N, 9.33. Found: C, 51.81; H, 6.64; N, 9.21.

4-Ethoxy-1-(2-ethyl-β-D-ribofuranosyl)-2(1*H*)-pyrimidinone (19b)——From 1.04 g of **13b**, **19b** was obtained (450 mg, foam, 78.9%). MS *m/z*: 300 (M^+), 282 $(M-H_2O)^+$, 253 $(M-H_2O-Et)^+$, 141 $(B+2)^+$. NMR (CD_3OD): 0.92 (3H, t, 2′-$CH_2\underline{CH_3}$), 1.36 (3H, t, 4-$OCH_2\underline{CH_3}$), 1.17—1.48 (2H, m, 2′-$\underline{CH_2}CH_3$), 3.64—4.05 (4H, m, 3′,4′,5′-H), 4.39 (2H, q, 4-$O\underline{CH_2}CH_3$), 6.05 (1H, d, 5-H, $J_{5,6}=7.6$ Hz), 6.11 (1H, s, 1′-H), 8.31 (1H, d, 6-H, $J_{5,6}=7.6$ Hz). UV $\lambda_{max}^{H_2O}$ (ε): 275 nm (6650). *Anal.* Calcd for $C_{13}H_{20}N_2O_6$: C, 51.99; H, 6.71; N, 9.33. Found: C, 51.80; H, 6.82; N, 9.21.

4-Ethoxy-1-(2-phenyl-β-D-arabinofuranosyl)-2(1*H*)-pyrimidinone (16c)——From 118 mg of **12c**, 68 mg of **16c** was obtained; yield 98% (EtOAc), mp 181—182 °C. MS *m/z*: 348 $(M)^+$. NMR (DMSO-d_6): 1.25 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.71—4.02 (4H, m, 3′,4′,5′-H), 4.24 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.36 (1H, d, 3′-OH), 5.52 (1H, t, 5′-OH), 5.99 (1H, d, 5-H, $J_{5,6}=7.6$ Hz), 6.01 (1H, s, 2′-OH), 6.68 (1H, s, 1′-H), 7.25—7.60 (5H, m, 2′-Ph), 8.23 (1H, d, 6-H, $J_{5,6}=7.6$ Hz). *Anal.* Calcd for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.84; H, 5.86; N, 8.06.

4-Ethoxy-1-(β-D-arabinofuranosyl)-2(1*H*)-pyrimidinone (16d)——mp 166—167 °C. MS *m/z*: 272 (M^+). NMR (DMSO-d_6): 1.22 (3H, t, 4-$OCH_2\underline{CH_3}$), 3.60 (2H, m, 5′-H), 3.93 (3H, m, 2′,3′,4′-H), 4.29 (2H, q, 4-$O\underline{CH_2}CH_3$), 5.05 (1H, t, 5′-OH), 5.46 (2H, m, 2′,3′-OH), 5.97 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 6.03 (1H, d, 1′-H, $J_{1',2'}=4.4$ Hz), 7.92 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). *Anal.* Calcd for $C_{11}H_{16}N_2O_6$: C, 48.53; H, 5.92; N, 10.29. Found: C, 48.37; H, 6.00; N, 10.31.

Conversion of 16a, b and 19a, b into Cytosine Nucleosides——General Procedure: Compound (**16a**, **16b**, **19a**, or **19b**) was dissolved in NH_3/MeOH (presaturated at 0 °C), and the solution was heated in a steal container for 48 h at 100 °C.

2′-Methyl-1-β-D-arabinofuranosylcytosine Hydrochloride (18a)——From 260 mg of **16a**, 220 mg of free nucleoside (**18a**) was obtained as a foam, which was dissolved in 3% HCl/EtOH (2 ml). The hydrochloride (211 mg) was obtained, mp 195—197 °C. NMR (D_2O): 1.38 (3H, s, 2′-Me), 3.90—4.04 (4H, m, 3′,4′,5′-H), 6.01 (1H, s, 1′-H), 6.23 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 8.09 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). UV $\lambda_{max}^{0.5N\ HCl}$ (ε): 280 nm (15630). CD (H_2O) [θ]: +27860 (274 nm), −19850 (218 nm). *Anal.* Calcd for $C_{10}H_{15}N_3O_5 \cdot HCl$: C, 40.89; H, 5.49; N, 14.31. Found: C, 40.67; H, 5.61; N, 14.08.

2′-Methyl-1-β-D-ribofuranosylcytosine (20a)——From 250 mg of **19a**, 214 mg (95.6%, MeOH) of **20a** was obtained, mp 239.5—242 °C, lit.[21] mp 243—244 °C. MS *m/z*: 257 (M^+), 239 $(M-H_2O)^+$, 112 $(B+2)^+$. NMR (D_2O): 1.12 (3H, s, 2′-Me), 3.73—4.10 (4H, m, 3′,4′,5′-H), 6.04 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 6.06 (1H, s, 1′-H), 7.85 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). UV $\lambda_{max}^{0.5N\ HCl}$ (ε): 280 nm (12190). CD (H_2O) [θ]: +35760 (271 nm), −19100 (216 nm). *Anal.* Calcd for $C_{10}H_{15}N_3O_5$: C, 46.69; H, 5.88; N, 16.33. Found: C, 46.68; H, 5.92; N, 16.22.

2′-Ethyl-1-β-D-arabinofuranosylcytosine Hydrochloride (18b)——From 50 mg of **16b**, 54 mg of free nucleoside (**18b**) was obtained as a foam. MS *m/z*: 271 (M^+), 253 $(M-H_2O)^+$, 112 $(B+2)^+$. NMR (DMSO-d_6 + D_2O): 1.24 (3H, t, 2′-$CH_2\underline{CH_3}$), 0.87—1.80 (2H, m, 2′-$\underline{CH_2}CH_3$), 3.62—3.90 (4H, m, 3′,4′,5′-H), 5.89 (1H, s, 1′-H), 6.21 (1H, d, 5-H, $J_{5,6}=7.8$ Hz), 7.97 (1H, d, 6-H, $J_{5,6}=7.8$ Hz). This compound was crystallized from 3% HCl/EtOH (2 ml) to afford 60 mg of the hydrochloride, mp 205—207 °C. UV $\lambda_{max}^{0.5N\ HCl}$ (ε): 279 nm (12110). CD (H_2O) [θ]: +29100 (273 nm), −16800 (219 nm). *Anal.* Calcd for $C_{11}H_{17}N_3O_5 \cdot HCl$: C, 42.93; H, 5.89; N, 13.65. Found: C, 42.69; H, 5.94; N, 13.34.

2′-Ethyl-1-β-D-ribofuranosylcytosine (20b)——From 250 mg of **19b**, 214 mg (94%, EtOH) of **20b** was obtained, mp 190—191 °C. MS *m/z*: 271 (M^+), 112 $(B+2)^+$. NMR (DMSO-d_6 + D_2O): 0.79 (3H, t, 2′-$CH_2\underline{CH_3}$), 0.86—1.39 (2H, m, 2′-$\underline{CH_2}CH_3$), 3.19—3.72 (4H, m, 3′,4′,5′-H), 5.71 (1H, d, 5-H, $J_{5,6}=7.3$ Hz), 5.96 (1H, s, 1′-H), 7.80 (1H, d, 6-H, $J_{5,6}=7.3$ Hz). UV $\lambda_{max}^{0.5N\ HCl}$ (ε): 280 nm (12820). CD (H_2O) [θ]: +39390 (271 nm), −18180 (216 nm). *Anal.* Calcd for $C_{11}H_{17}N_3O_5$: C, 48.70; H, 6.32; N, 15.48. Found: C, 48.77; H, 6.53; N, 14.99.

Paper Electrophoresis——Paper electrophoresis was carried out using Toyo filter paper (No. 51A) in borate buffer (0.2 M boric acid–sodium borate, pH 6.0, 700 V, 100 min).

Relative Migration: Cytidine, 1.0; 1-β-D-arabinofuranosylcytosine, 0.17; **16a**, 0.14; **16b**, 0.15; **16c**, 0.15; **16d**, 0.14; **19a**, 0.97; **19b**, 1.08.

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