Pergamon

Tetrahedron 56 (2000) 5363–5371

TETRAHEDRON

An Intramolecular Anionic Migration of a Stannyl Group from the 6-Position of 1-(2-Deoxy-D-*erythro*-pent-1-enofuranosyl)uracil to the 2′-Position: Synthesis of 2′-Substituted 1′,2′-Unsaturated Uridines

Hiroki Kumamoto, Satoru Shindoh, Hiromichi Tanaka,* Yoshiharu Itoh, Kazuhiro Haraguchi, Eisen Gen, Atsushi Kittaka, Tadashi Miyasaka, Masato Kondo and Kazuo T. Nakamura

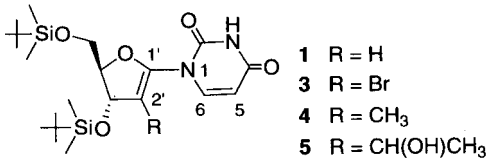
School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan

Received 10 February 2000; accepted 22 May 2000

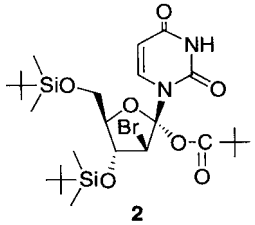
Abstract—Lithiation of 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl)uracil (**1**) takes place exclusively at the 6-position of the uracil base. The 6-tributylstannyl (or 6-trimethylsilyl) derivative prepared by quenching the C6-lithiated species with Bu_3SnCl (or Me_3SiCl) was found to undergo an intramolecular anionic migration to the 2′-positon of the furanoid glycal portion. By manipulation of the 2′-stannyl group, 2′-halogeno and 2′-carbon-substituted 1′,2′-unsaturated uridines were prepared for the first time. In contrast to the reported instability of **1** during deprotection, the 2′-substituted analogs synthesized in the present study gave the corresponding free nucleosides uniformly in high yields upon treatment with NH_4F in MeOH.

Introduction

In 1974, Robins et al. reported the synthesis of an unsaturated-sugar nucleoside of unique structure, 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl)uracil (**1**).[1,2] However, presumably due to the reported instability of **1** during deprotection, chemistry regarding this class of nucleosides[3] had been unexploited until recently with the exception of simple catalytic hydrogenation.



1 R = H
3 R = Br
4 R = CH_3
5 R = $CH(OH)CH_3$



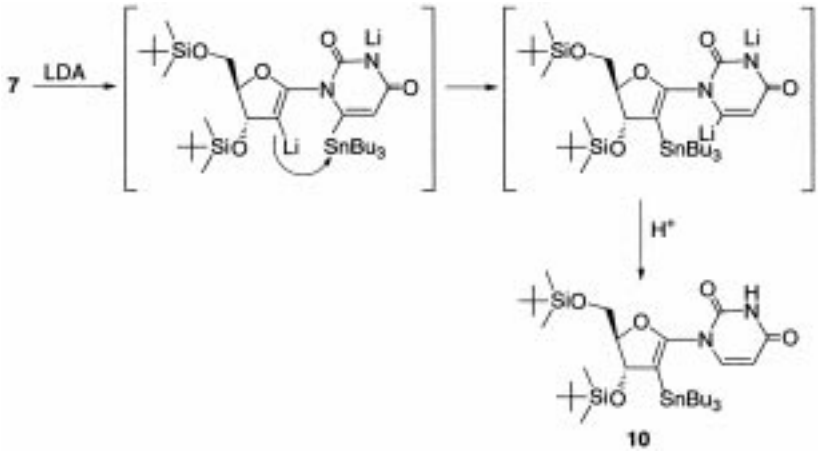
2

Previously, we reported an electrophilic addition (bromopivaloyloxylation) to **1** which gave **2** as the main adduct.[4] Compound **2** was shown to be a useful substrate for C–C bond formation at the anomeric position, through its reactions with organosilicon and organoaluminum reagents.[4] Radical-initiated 1,2-acyloxy migration of **2**, which generates an anomeric radical, was also reported.[5,6] It was also found that heating **2** in refluxing xylene containing solid $NaHCO_3$ gave, albeit in variable yields, the 2′-bromo derivative **3**.[7] Compound **3**, upon halogen–lithium exchange reaction in the presence of MeI or CH_3CHO (in situ trapping), gave the respective 2′-carbon-substituted product **4** or **5**, although simultaneous formation of **1** was inevitably observed.

During these studies, we noticed that UV absorption maxima (λ_{max}) of the 2′-substituted derivatives in MeOH (**3**: λ_{max} 255 nm; **4**: λ_{max} 255 nm; **5**: λ_{max} 253 nm) appeared at much shorter wavelength than that of **1** (λ_{max} 276 nm). This finding led us to assume that the base and glycal portions of **1** could be in mutually coplanar disposition to a certain extent, while the presence of a 2′-substituent, *ortho* to the N1–C1′ pivot bond, would impede such coplanarity in the case of **3**–**5**. If the reported instability of **1** during desilylation is due to its conformational feature, which may provide the molecule with the propensity to undergo aromatization at the glycal portion, the 2′-substituted analogs could be desilylated without intervention of such elimination pathway. This assumption, however, remained to

Keywords: lithiation; migration; nucleosides; tin and compounds.
* Corresponding author. Tel.: +81-3-3784-8186; fax: +81-3-3784-8252; e-mail: hirotnk@pharm.showa-u.ac.jp

0040–4020/00/$ - see front matter
PII: S0040-4020(00)00441-5



Scheme 1.

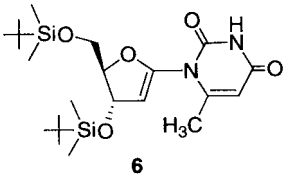
be confirmed because of poor reproducibility of the conversion from **2** to **3**.

In the present paper, we report an alternative route to the modification of **1** at the 2′-position based on lithiation chemistry. Also reported here is the fact that desilylation of the resulting 2′-substituted analogs can be carried out by a conventional method without any side reaction.[8]

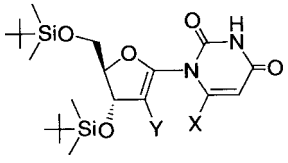
Stannyl migration observed during LDA lithiation of 1

Since our first report on the lithiation of 2′,3′-*O*-isopropylideneuridine,[9] continuous efforts have been devoted to the lithiation chemistry of nucleosides to show its generality and usefulness for modification of the base moiety.[10] One typical example would be the regiospecific C6-lithiation of 5′-*O*-protected 2′,3′-*O*-isopropylideneuridine with LDA.[11] The C6-lithiated species generated in this reaction reacts with a wide range of electrophiles, including carbon-electrophiles, which contrasts with the existing nucleophilic substitution (addition–elimination mechanism) of 5-halogenouridine.[12] Later, it was found that the conformation of the sugar portion, which alters the steric environment around the 6-position, has a significant effect on the C6-lithiation.[13]

In accord with the case of 5′-*O*-protected 2′,3′-*O*-isopropylideneuridine, when **1** was lithiated with LDA (3 equiv.) in THF below −70°C and then treated with MeOD, deuterium was incorporated solely into the 6-position of the uracil ring (D-incorporation 70%; recovery 90%). Quenching of the above-generated C6-lithiated species with MeI gave the 6-methyl derivative **6** in 67% yield. However, upon reacting with Bu_3SnCl (3 equiv.), the same C6-lithiated species gave the 2′,6-bis-stannylated product **8** in 10% yield in addition to the expected **7** (75%). Similarly, the 2′,6-bis-trimethylsilyl derivative **9** (70%) was formed from **1** by using a combination of LDA (4 equiv.) and Me_3SiCl (5 equiv.).



6



7 X = $SnBu_3$, Y = H
8 X = Y = $SnBu_3$
9 X = Y = $SiMe_3$

The observed formation of the bis-stannylated (or bis-silylated) product was initially considered to be simply a consequence of intervention of the C2′-lithiated species of **7** which reacted with Bu_3SnCl (or Me_3SiCl). To see if the 2′-position had actually been lithiated during the formation of **8**, we carried out LDA (3 equiv.) lithiation of **7** and subsequent deuteration with MeOD.

As a result of HPLC (hexane/EtOAc=5/1) analysis of the reaction mixture, it appeared that one slower-running product (*Rt*: 15.1 min) was formed in addition to **7** (*Rt*: 14.0 min). From the fact that ^1H NMR spectrum of this product was devoid of a resonance corresponding to H-2′, and that it showed the presence of one tributylstannyl group, the structure was determined to be **10** (isolated yield: 24%). A further structural confirmation came from its conversion to **3** by treatment with NBS, as described later. An additional piece of information from the ^1H NMR spectrum of **10** is that a 96% D-incorporation was observed at the 6-position, which was calculated by comparing integration of H-6 with that of H-3′ (a doublet, δ 4.99 ppm). On the other hand, no D-incorporation was observed at the 2′-position of the recovered **7** (recovery: 49%). These results suggest that the C2′-lithiation of **7** had been followed by an instantaneous migration of the 6-stannyl group as depicted in Scheme 1.[14]

Optimization of reaction conditions for stannyl migration

To find out optimum reaction conditions required for conversion of **7** to **10**, several reactions were carried out, and the results are summarized in Table 1. In these reactions, a mixture of **7** and **10** obtained by flash silica gel column chromatography was analyzed by ^1H NMR spectroscopy.

Table 1. Preparation of the 2′-stannyl derivative **10** and **7** via anionic stannyl migration (all reactions were carried out by using 3 equiv. of the respective lithiating agent (in THF, below −70°C))

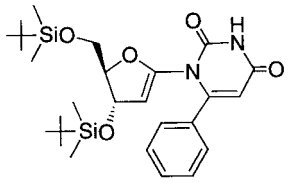
Entry	Lithiating agent	HMPA (equiv.)	Reation time (h)	Combined yield (%)[a] of **10** and **7**	Ratio of **10**/**7**[b]
1	LDA	–	0.5	73	1/2
2	LDA	10	0.5	72	3/1
3	LTMP	–	0.5	68	1/1
4	LTMP	10	0.5	73	5/1
5	LTMP	10	1.0	77	96/4
6	LTMP	10	3.0	62[c]	100/0

[a] The yields refer to those obtained after silica gel flash column chromatography.
[b] Calculated based on ^{1}H NMR spectroscopy by integrating H-5 of **7** and **10**.
[c] Compound **1** was isolated in 11% yield.

The comparison of entries 1 and 2 indicates that the presence of HMPA as an additive encourages the formation of **10**. The fact that use of a more basic lithiating agent LTMP gave better results than LDA (entry 1 vs. entry 3; entry 2 vs. entry 4) would be additional support for involvement of the C2′-lithiated species in these reactions. Although complete conversion to **10** was possible by prolonging the reaction time (entry 6), the observed lower yield led us to employ entry 5 for the preparation of **10**. It may deserve a mention that, in these entries, protodestannylation of **10** leading to **1** is certainly involved during silica gel column chromatography, and thus, the yields of **10** given in Table 1 are somewhat underestimated. In fact, when the reaction mixture resulting from entry 5 was subjected to a simple extractive workup and then reacted with iodine in THF, the 2′-iodo derivative (**15**) was isolated in a higher yield of 87%.

Evidence for C2′-lithiation and intramolecular reaction mechanism

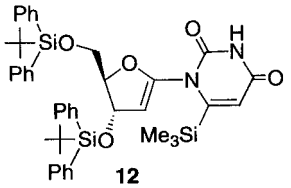
Since lithiations in the β-position of vinyl ethers have been reported only for those substrates having a β-halogen atom,[15,16] such as (*E*)-2-chlorovinyl ethyl ether, we required evidence for the C2′-lithiation in the present furanoid glycal system. As mentioned earlier, LDA lithiation of **1** occurred only at the 6-position. One would anticipate that, under the circumstance where the 6-position of **1** has already been deprotonated, generation of the C2′-lithiated species becomes difficult because of anionic repulsion. We, therefore, selected the 6-phenyl derivative **11** as a substrate, which was prepared by the Stille reaction between **7** and PhI (72% yield: $Pd(PPh_3)_4$/CuI/THF, for 23 h at room temperature).



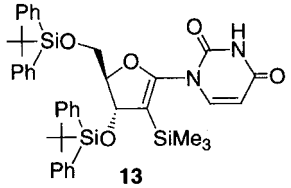
11

Lithiation-based deuterations of **11** were next carried out and the results are given in Table 2. Although concurrent deuteration at the 5-position of the uracil ring was observed in all entries, it is evident that the C2′-lithiated species had been generated under these lithiation conditions. It is also clear that factors advantageous for the above-mentioned stannyl migration, the use of LTMP and the presence of HMPA, certainly increase the C2′-lithiation level.

The present stannyl migration proceeds conceivably in an intramolecular manner as shown in Scheme 1. Taking the aforementioned formation of the 6,2′-bis-trimethylsilyl derivative **9** into consideration, it would be reasonable to anticipate that the silyl version of this migration could also be operative. To confirm the intramolecular mechanism, an equimolar mixture of **7** and **12**, which mutually differ both in the 6-substituent and in the sugar-protecting group, was reacted with LTMP (3 equiv.) in the presence of HMPA (10 equiv.). Among four products isolated from this reaction (**10**: 72%, **1**: 10%, **13**: 10%, and **14**: 50%),[17] none appeared to be a product arising from cross reaction between **7** and **12**.



12



13

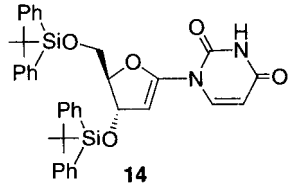
Table 2. Lithiation-based deuteration of **11** (lithiations carried out by using 5 equiv. of the respective lithiating agent (in THF, below −70°C) were immediately followed by quenching with MeOD)

Entry	Lithiating agent	HMPA (equiv.)	Recovery (%)[a]	D-incorporation (%)	
				C2′	C5
1	LDA	–	91	9	9
2	LTMP	–	100	19	48
3	LTMP	10	90	68	8

[a] The recoveries refer to those obtained after silica gel flash column chromatography.

Table 3. UV absorption maxima of **15**–**22** in MeOH

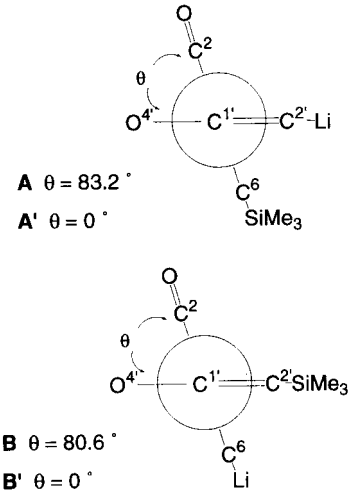
Compound	C2′-substituent	λ_{max} (nm) in MeOH
15	I	252
3	Br	255
16	Cl	254
17	F	261
18	Ph	253
19	CH_2Ph	254
20	Vinyl	251
4	Me	255



14

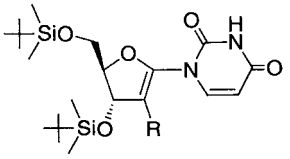
To see if the observed anionic migration is a thermodynamically controlled process, a putative reaction was selected in which 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]-6-(trimethylsilyl)uracil plays as a model starting material, and stabilities of lithiated species (**A** and **B**) involved in this reaction were calculated using CHARMm[18] program.

As a result, the 2′-lithio-6-trimethylsilyl derivative **A** (13.3 kcal/mol) was estimated to be 5.6 kcal/mol less stable than the rearranged 6-lithiated species **B** (7.7 kcal/mol), although their conformation about the N1–C1′ pivot bond is very similar (θ=83.2° and 80.6°, respectively). Comparison was also made of their transition states (**A**′ and **B**′) wherein the base and glycal portions lie mutually coplanar. Again, it was shown that the migration of the silyl group is a thermodynamically favored process (**A**′ 37.3 kcal/mol vs. **B**′ 21.0 kcal/mol).



Synthesis of the 2′-substituted derivatives

By manipulation of the 2′-stannyl group of **10**, synthesis of 2′-halogeno and 2′-carbon-substituted derivatives was carried out.[19] Iodination proceeded simply by reacting with iodine in THF at room temperature to give **15** in 93% yield. Similarly, the 2′-bromo derivative **3** was obtained in 90% yield by using NBS. Chlorination with NCS to yield **16** (83%) was performed at refluxing temperature of THF. Fluorination was conducted by applying a protocol reported by Tius et al.[20] (XeF_2/AgOTf/4-dimethylaminopyridine). Although the starting material **10** disappeared within 5 min, a complex mixture of products resulted, from which the 2′-fluoro derivative **17** was isolated only in 29% yield.



15 R = I **18** R = Ph
3 R = Br **19** R = CH_2Ph
16 R = Cl **20** R = vinyl
17 R = F **4** R = Me

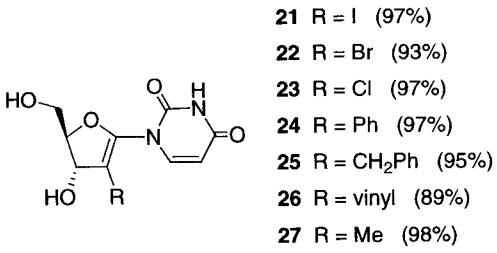
For the introduction of carbon-substituents, the Stille reaction[21] was employed by using either **10** or **15**. The reaction between **10** and PhI, when carried out in DMF(80°C, 5 min) in the presence of $Pd(PPh_3)_4$ and CuI, gave the 2′-phenyl derivative **18** in 66% yield. Similar reaction of **10** with benzyl bromide (in HMPA, 80°C, 14 h) gave **19** in 29 % yield. Since destannylation of **10** leading to **1** was observed during prolonged reaction time, it would be better to use **15** whenever organotin reagents are available. Thus, the Stille reaction between **15** and tributylvinyltin carried out in refluxing THF for 22 h gave the 2′-vinyl derivative **20** in 80% yield. Although the use of **15** and Me_4Sn in a similar reaction (in DMF, 60°C for 120 h) leads to the formation of the 2′-methyl derivative **4** (67%), Sn–Li exchange reaction of **10** was found to be advantageous in terms of reaction time. Thus, when **10** was treated with BuLi in THF in the presence of an excess amount of MeI, **4** was formed in 69% yield within 0.5 h.

The UV absorption maxima of these 2′-substituted compounds are listed in Table 3. All compounds show a hypsochromic shift of λ_{max} as compared with that of the 2′-unsubstituted compound (**1**:λ_{max} 276 nm). Within the 2′-halogenated compounds, there can be seen a trend that this hypsochromic shift becomes larger according to the increase in the size of halogen atom. This finding is well in accord with our aforementioned assumption concerning conformational difference between **1** and its 2′-substituted derivatives. It can also be assumed that the presence of a substituent at the 6-position of **1**, which is also *ortho* to the N1–C1′ pivot bond, should cause a similar conformational change. This appeared to be the case: the λ_{max} of the 6-methyl derivative **6** prepared in early stage of this study appeared at 257 nm.

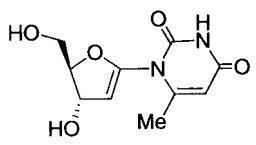
Desilylation of the 2′-substituted derivatives

Deprotection of the 2′-substituted 1′,2′-unsaturated uridines synthesized in the present study was carried out with NH_4F in refluxing MeOH,[22] and the resulting products **21**–**27** were isolated by usual silica gel column chromatography (3–5% MeOH in $CHCl_3$). As being evident from uniformly high isolated yields given in parentheses, no appreciable side

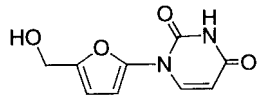
reaction seems to be involved in these instances. The desilylation of the 6-methyl derivative **6** also proceeded without any problem as can be expected its λ_{max}, giving the corresponding free nucleoside **28** in almost quantitative yield.



21 R = I (97%)
22 R = Br (93%)
23 R = Cl (97%)
24 R = Ph (97%)
25 R = CH_2Ph (95%)
26 R = vinyl (89%)
27 R = Me (98%)



28 (99%)



29

In contrast to these, when **1** was allowed to react under the above desilylation conditions, none of the corresponding free nucleoside was obtained but the furan derivative **29** and uracil were isolated in 22 and 76% yields, respectively.[23]

Conclusion

The lithiation study of 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl)uracil (**1**) revealed that the 6-tributylstannyl (or trimethylsilyl) group undergoes an intramolecular anionic migration to the 2′-position of the furanoid glycal. Manipulation of the resulting 2′-stannyl group has disclosed the first entry to the 2′-halogeno (**3** and **15**–**17**) and 2′-carbon-substituted (**4** and **18**–**20**) 1′,2′-unsaturated uridines. Based on the comparison of UV absorption maxima, an assumption was made that the reported instability of **1** during deprotection could possibly be due to its considerably coplanar conformation of the base and the glycal portions, which may differ from the 2′-substituted derivatives. We believe that the successful deprotection of the 2′-substituted derivatives accomplished in this study provides support for this assumption.

Experimental

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were measured at 23°C (internal standard, Me_4Si) with JNM-LA500 (500 MHz) spectrometer. Mass spectra (MS) were taken in FAB mode (*m*-nitrobenzyl alcohol as a matrix) with JMS-SX 102A spectrometer. Ultraviolet (UV) spectra were recorded on a JASCO Ubest-55 spectrophotometer. Column chromatography was carried out on silica gel (Silica Gel 60, Merck). Thin layer chromatography (TLC) was performed on silica gel (precoated silica gel plate F_{254}, Merck). HPLC was carried out on a Shimadzu LC-6AD with a Shim-pack PREP-SIL (H)·KIT column (2×25 cm).

Halogen–lithium exchange reaction of 3 for the preparation of 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-methyl-D-*erythro*-pento-1-enofuranosyl]uracil (4). To a THF (10 mL) solution containing **3** (111.2 mg, 0.21 mmol) and MeI (0.13 mL, 2.10 mmol), BuLi (1.34 M in hexane, 0.47 mL, 0.63 mmol) was added dropwise, while maintaining the temperature below −70°C. After stirring for 15 min, the reaction mixture was quenched with AcOH, evaporated to remove the solvent, and then partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Silica gel column chromatography (hexane/EtOAc=3/1) of the organic layer gave **4** (solid, 74.9 mg, 76%) and **1** (10.5 mg, 11%).

Physical data of **4** are as follows: mp 146–150°C; UV (MeOH) λ_{max} 255 nm (ϵ 9000), λ_{min} 235 nm (ϵ 7000); ^1H NMR ($CDCl_3$) δ 0.07, 0.08, 0.11, and 0.12 (12H, each as s), 0.89 and 0.91 (18H, each as s), 1.60 (3H, s), 3.68 (1H, dd, J=11.0 and 5.8 Hz), 3.77 (1H, dd, J=11.0 and 5.3 Hz), 4.29–4.32 (1H, m), 4.80 (1H, d, J=3.3 Hz), 5.74 (1H, d, J=7.9 Hz), 7.22 (1H, d, J=7.9 Hz), 8.31 (1H, br); FAB-MS *m/z* 469 (M^++H). Anal. Calcd for $C_{22}H_{40}N_2O_5Si_2$: C, 56.37; H, 8.60; N, 5.98. Found: C, 56.57; H, 8.61; N, 5.99.

Halogen–lithium exchange reaction of 3 for the preparation of 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-(1-hydroxyethyl)-D-*erythro*-pento-1-enofuranosyl]-uracil (5). To a mixture of **3** (62.4 mg, 0.12 mmol) and MeCHO (0.07 mL, 1.2 mmol) in THF (3 mL), BuLi (1.57 M in hexane) was added dropwise in three portions (0.23 mL×3, 1.08 mmol) under positive pressure of dry Ar, while maintaining the temperature below −70°C. After stirring for 15 min, the reaction mixture was quenched with AcOH, evaporated to remove the solvent, and then partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Silica gel column chromatography of the organic layer followed by HPLC (hexane/EtOAc=2/1) separation gave the major diastereomer (syrup, 30.3 mg, 51%) and the minor diastereomer (syrup, 13.3 mg, 24%) of **5**.

Physical data of the major diastereomer of **5** are as follows: UV (MeOH) λ_{max} 253 nm (ϵ 11800), λ_{min} 235 nm (ϵ 11000); ^1H NMR ($CDCl_3$) δ 0.08, 0.17, and 0.19 (12H, each as s), 0.90 and 0.91 (18H, each as s), 1.35 (3H, d, J=6.2 Hz), 2.72 (1H, br), 3.63 (1H, dd, J=10.8 and 6.4 Hz), 3.79 (1H, dd, J=10.8 and 5.0 Hz), 4.38 (2H, m), 5.16 (1H, d, J=2.2 Hz), 5.79 (1H, d, J=8.1 Hz), 7.32 (1H, d, J=8.1 Hz), 8.57 (1H, br); FAB-MS *m/z* 499 (M^++H). Anal. Calcd for $C_{23}H_{42}N_2O_6Si_2$: C, 55.39; H, 5.62; N, 8.49. Found: C, 55.77; H, 5.32; N, 8.80.

Physical data of the minor diastereomer of **5** are as follows: ^1H NMR ($CDCl_3$) δ 0.07 and 0.15 (12H, each as s), 0.89 and 0.90 (18H, each as s), 1.34 (3H, d, J=7.0 Hz), 2.87 (1H, br), 3.61 (1H, dd, J=10.9 and 6.4 Hz), 3.74 (1H, dd, J=10.9 and

5.5 Hz), 4.35 (1H, m), 4.47 (1H, dd, J=13.4 and 7.0 Hz), 5.06 (1H, d, J=1.8 Hz), 5.79 (1H, d, J=8.1 Hz), 7.27 (1H, d, J=8.1 Hz), 9.53 (1H, br); FAB-MS m/z 499 (M^++H). Anal. Calcd for $C_{23}H_{42}N_2O_6Si_2$: C, 55.39; H, 5.62; N, 8.49. Found: C, 55.78; H, 5.26; N, 8.72.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]-6-methyluracil (6). Compound **1** (100 mg, 0.22 mmol) in THF (5 mL) was added dropwise to a THF (5 mL) solution of LDA (0.66 mmol) under positive pressure of dry Ar, while maintaining the temperature below −70°C. After 5 min, MeI (137 μL, 2.2 mmol) was added neat to the resulting solution, and the mixture was stirred for 5 min. The reaction mixture was treated with saturated aqueous NH_4Cl, extracted with EtOAc, and then chromatographed on a silica gel column (hexane/EtOAc=5/1). This gave **6** (69 mg, 67%) as a solid: mp 174–176°C; UV (MeOH) λ_{max} 257 nm (ϵ 12300), λ_{min} 231 nm (ϵ 5500); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09, and 0.10 (12H, each as s), 0.88 and 0.90 (18H, each as s), 2.33 (3H, d, J=0.91 Hz), 3.66 (1H, dd, J=11.0 and 6.7 Hz), 3.80 (1H, dd, J=11.0 and 5.5 Hz), 4.43–4.46 (1H, m), 5.02 (1H, d, J=2.4 Hz), 5.14 (1H, d, J=2.4 Hz), 5.59 (1H, d, J=0.91 Hz), 8.27 (1H, br); FAB-MS m/z 469 (M^++H). Anal. Calcd for $C_{22}H_{40}N_2O_5Si_2$: C, 56.37; H, 8.60; N, 5.98. Found: C, 56.48; H, 8.82; N, 6.03.

Lithiation-based stannylation of 1: formation of 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]-6-(tributylstannyl)uracil (7) and 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-(tributylstannyl)-D-*erythro*-pent-1-enofuranosyl]-6-(tributylstannyl)uracil (8). These compounds were obtained by the procedure described for the preparation of **6**. The following amounts of reagents and **1** (470 mg, 1.03 mmol) in THF (5 mL) were used: LDA (3.10 mmol) in THF (10 mL) and Bu_3SnCl (840 μL, 3.10 mmol). After addition of Bu_3SnCl, the reaction was continued for 5 min. Silica gel column chromatography (hexane/EtOAc=15/1–10/1) of the EtOAc extract gave **8** (oil, 106 mg, 10%) and **7** (oil, 577 mg, 75%).

Physical data of **7** are as follows: UV λ_{max} 266 nm (ϵ 9900), λ_{min} 238 nm (ϵ 6300); ^{1}H NMR ($CDCl_3$) δ 0.07–0.10 (12H, m), 0.87–0.94 (27H, m), 1.12–1.52 (18H, m), 3.61 (1H, dd, J=10.7 and 7.3 Hz), 3.78 (1H, dd, J=10.7 and 6.1 Hz), 4.35–4.38 (1H, m), 5.01 (1H, t, J=2.8 Hz), 5.14 (1H, d, J=2.8 Hz), 5.80 (1H, d, J=2.1 Hz), 8.06 (1H, br); FAB-MS m/z 745 (M^++H). Anal. Calcd for $C_{33}H_{64}N_2O_5Si_2Sn$: C, 53.29; H, 8.67; N, 3.77. Found: C, 53.13; H, 8.64; N, 3.66.

^{1}H NMR data of **8** are as follows: UV λ_{max} 268 nm (ϵ 9000), λ_{min} 242 nm (ϵ 5800); ^{1}H NMR ($CDCl_3$) δ 0.06 and 0.07 (12H, each as s), 0.85–0.95 and 1.10–1.50 (72H, each as m), 3.55 (1H, dd, J=10.4 and 7.2 Hz), 3.72 (1H, dd, J=10.4 and 6.4 Hz), 4.29–4.33 (1H, m), 4.95 (1H, t, J=2.0 Hz), 5.78 (1H, s), 7.96 (1H, br). FAB-MS m/z 1033 (M^++H). Anal. Calcd for $C_{45}H_{90}N_2O_5Si_2Sn_2$: C, 52.34; H, 8.78; N, 2.71. Found: C, 52.05; H, 9.18; N, 2.45.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-(trimethylsilyl)-D-*erythro*-pent-1-enofuranosyl]-6-(trimethylsilyl)uracil (9). This compound was obtained by the procedure described for the preparation of **6**. The following amounts of reagents and **1** (736 mg, 1.62 mmol) in THF (5 mL) were used: LDA (6.48 mmol) in THF (15 mL) and Me_3SiCl (1.03 mL, 16.2 mmol). After addition of Me_3SiCl, the reaction was continued for 5 min. Silica gel column chromatography (hexane/EtOAc=10/1) of the EtOAc extract gave **9** (foam, 678 mg, 70%):UV λ_{max} 266 nm (ϵ 10700), λ_{min} 239 nm (ϵ 4500); ^{1}H NMR ($CDCl_3$) δ 0.06–0.24 (21H, m), 0.36 (9H, s), 0.88 and 0.91 (18H, each as s), 3.52 (1H, t, J=10.1 Hz), 3.73 (1H, dd, J=10.1 and 5.8 Hz), 4.37–4.40 (1H, m), 4.95 (1H, d, J=1.2 Hz), 5.01 (1H, d, J=1.8 Hz), 8.44 (1H, br); FAB-MS m/z 599 (M^++H). Anal. Cald for $C_{27}H_{54}N_2O_5Si_4$: C, 54.13; H, 9.09; N, 4.68. Found: C, 53.88; H, 9.45; N, 4.60.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-(tributylstannyl)-D-*erythro*-pent-1-enofuranosyl]uracil (10). To a THF (5 mL) solution containing LTMP (1.2 mmol) and HMPA (696 μL, 4.0 mmol), **7** (300 mg, 0.4 mmol) dissolved in THF (5 mL) was added dropwise under positive pressure of dry Ar, while maintaining the temperature below −70°C. The reaction mixture was stirred for 1 h and then treated with saturated aqueous NH_4Cl. Extraction with EtOAc followed by silica gel column chromatography (hexane/EtOAc=10/1) gave **10** (216 mg, 72%) as a syrup: UV (MeOH) λ_{max} 257 nm (ϵ 7500), λ_{min} 241 nm (ϵ 6800); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.11, and 0.13 (12H, each as s), 0.86 (9H, t, J=7.3 Hz), 0.89 and 0.90 (18H, each as s), 1.24–1.32 (6H, m), 1.41–1.48 (6H, m), 3.60 (1H, dd, J=10.4 and 7.0 Hz), 3.76 (1H, dd, J=10.4 and 5.1 Hz), 4.37–4.40 (1H, m), 4.99 (1H, d, J=2.1 Hz), 5.73 (1H, d, J=8.2 Hz), 7.25 (1H, d, J=8.2 Hz), 8.38 (1H, br); FAB-MS m/z 745 (M^++H). Anal. Calcd for $C_{33}H_{64}N_2O_5Si_2Sn$: C, 53.29; H, 8.67; N, 3.77. Found: C, 53.38; H, 8.79; N, 3.78.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]-6-phenyluracil (11). A mixture of **7** (400 mg, 0.53 mmol), $Pd(PPh_3)_4$ (58 mg, 0.053 mmol), CuI (20 mg, 0.11 mmol), PhI (182 μL, 1.6 mmol) in THF (5 mL) was stirred, under positive pressure of dry Ar, for 23 h at room temperature. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=4/1) of the organic extract gave **11** (203 mg, 72%) as a foam: UV λ_{max} 268 nm (ϵ 12900), λ_{min} 238 nm (ϵ 6300); ^{1}H NMR ($CDCl_3$) δ −0.11, −0.04, and 0.04 (12H, each as s), 0.77 and 0.87 (18H, each as s), 3.24 (1H, dd, J=10.5 and 8.2 Hz), 3.57 (1H, dd, J=10.5 and 5.8 Hz), 4.18–4.21 (1H, m), 4.73 (1H, t, J=2.5 Hz), 4.86 (1H, d, J=2.5 Hz), 5.73 (1H, s), 7.38–7.46 (5H, m), 8.55 (1H, br); FAB-MS m/z 531 (M^++H). Anal. Cald for $C_{27}H_{46}N_2O_5Si_2$: C, 61.09; H, 7.98; N, 5.28. Found: C, 61.03; H, 8.12; N, 5.23.

1-[3,5-Bis-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]-6-(trimethylsilyl)uracil (12). To a mixture of Me_3SiCl (1.05 mL, 8.2 mmol) and **14** (635 mg, 0.82 mmol) in THF (5 mL), lithium hexamethyldisilazide (1.0 M THF solution, 4.1 mL, 4.1 mmol) was added dropwise under positive pressure of dry Ar, while maintaining the temperature below −70°C. After stirring for 20 min, the reaction mixture was quenched by adding saturated aqueous NH_4Cl. Extraction with EtOAc followed by silica gel column chromatography (hexane/EtOAc=5/1) gave **12**

(614 mg, 92%) as a foam: UV λ_{max} 265 nm (ϵ 12300), λ_{min} 239 nm (ϵ 4900); ^{1}H NMR ($CDCl_3$) δ 0.41 (9H, s), 0.95 and 1.04 (18H, each as s), 3.32 (1H, dd, J=11.3 and 3.7 Hz), 3.56 (1H, dd, J=11.3 and 7.9 Hz), 4.60 (1H, ddd, J=7.9, 3.7, and 3.0 Hz), 4.82 (1H, dd, J=3.0 and 2.8 Hz), 4.96 (1H, d, J=2.8 Hz), 5.91 (1H, d, J=2.4 Hz), 7.24–7.60 (20H, m), 7.98 (1H, br). FAB-MS m/z 775 (M^++H). Anal. Calcd for $C_{44}H_{54}N_2O_5Si_3$: C, 68.18; H, 7.02; N, 3.61. Found: C, 68.13; H, 6.88; N, 3.62.

1-[3,5-Bis-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-2-*C*-trimethylsilyl-D-*erythro*-pent-1-enofuranosyl]uracil (13). Physical data of this compound (foam) are as follows: UV λ_{max} 258 nm (ϵ 10800), λ_{min} 239 nm (ϵ 8000); ^{1}H NMR ($CDCl_3$) δ 0.15 (9H, s), 0.95 and 1.04 (18H, each as s), 2.78 (1H, dd, J=11.6 and 4.0 Hz), 3.28 (1H, dd, J=11.6 and 3.1 Hz), 4.33–4.35 (1H, m), 5.32 (1H, d, J=2.4 Hz), 5.52 (1H, d, J=7.9 Hz), 6.80 (1H, d, J=7.9 Hz), 7.29–7.75 (20H, m); FAB-MS m/z 775 (M^++H). Anal. Calcd. for $C_{44}H_{54}N_2O_5Si_3$: C, 68.18; H, 7.02; N, 3.61. Found: C, 67.95; H, 7.07; N, 3.66.

1-[3,5-Bis-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil (14). Physical data of this compound (foam) are as follows: UV λ_{max} 271 nm (ϵ 10800), λ_{min} 246 nm (ϵ 6200); ^{1}H NMR ($CDCl_3$) δ 0.94 and 1.07 (18H, each as s), 3.33 (1H, dd, J=11.6 and 5.8 Hz), 3.43 (1H, dd, J=11.6 and 3.7 Hz), 4.51 (1H, ddd, J=5.8, 3.7, and 2.8 Hz), 5.02 (1H, dd, J=3.1 and 2.8 Hz), 5.45 (1H, d, J=3.1 Hz), 5.68 (1H, d, J=8.2 Hz), 7.30–7.43 (10H, m), 7.47 (1H, d, J=8.2 Hz), 7.50–7.73 (10H, m). FAB-MS m/z 703 (M^++H). Anal. Calcd for $C_{41}H_{46}N_2O_5Si_2$: C, 70.05; H, 6.60; N, 3.98. Found: C, 69.93; H, 6.57; N, 4.01.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-iodo-D-*erythro*-pent-1-enofuranosyl]uracil (15). A mixture of **10** (994 mg, 1.34 mmol) and iodine (410 mg, 1.61 mmol as I_2) in THF (15 mL) was stirred for 40 min at room temperature. The reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ and then extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=5/1) of the organic extract gave **15** (725 mg, 93%) as a solid: mp 159–160°C; UV (MeOH) λ_{max} 252 nm (ϵ 8000), λ_{min} 243 nm (ϵ 7800); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09, 0.10, 0.15, and 0.21 (12H, each as s), 0.90 and 0.92 (18H, each as s), 3.73 (1H, dd, J=11.0 and 5.8 Hz), 3.81 (1H, dd, J=11.0 and 4.9 Hz), 4.48–4.51 (1H, m), 4.90 (1H, d, J=3.1 Hz), 5.79 (1H, dd, J=8.0 and 2.4 Hz), 7.17 (1H, d, J=8.0 Hz), 8.12 (1H, br); FAB-MS m/z 581 (M^++H). Anal. Calcd for $C_{21}H_{37}IN_2O_5Si_2$: C, 43.44; H, 6.42; N, 4.74. Found: C, 43.68; H, 6.44; N, 4.74.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-bromo-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil (3). A mixture of **10** (1.20 g, 1.61 mmol) and NBS (340 mg, 1.93 mmol) in THF (9 mL) was stirred for 30 min at room temperature. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and then extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=5/1) of the organic extract gave **3** (781 mg, 90%) as a solid: mp 145–148°C; UV (MeOH) λ_{max} 255 nm (ϵ 6300), λ_{min} 235 nm (ϵ 5400); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09, 0.14, and 0.18 (12H, each as s), 0.90 and 0.91 (18H, each as s), 3.74 (1H, dd, J=11.0 and 6.0 Hz), 3.82 (1H, dd, J=11.0 and 4.9 Hz), 4.44–4.47 (1H, m), 4.94 (1H, d, J=3.1 Hz), 5.79 (1H, dd, J=8.1 and 2.3 Hz), 7.19 (1H, d, J=8.1 Hz), 8.50 (1H, br); FAB-MS m/z 534 (M^++H). Anal. Calcd for $C_{21}H_{37}BrN_2O_5Si_2$: C, 47.27; H, 6.99; N, 5.25. Found: C, 47.42; H, 6.95; N, 5.24.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-chloro-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil (16). A mixture of **10** (355 mg, 0.48 mmol) and NCS (77 mg, 0.58 mmol) in THF (5 mL) was refluxed for 30 min and then stirred at room temperature for 17 h. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and then extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=5/1) of the organic extract gave **16** (194 mg, 83%) as a foam: UV (MeOH) λ_{max} 254 nm (ϵ 6500), λ_{min} 233 nm (ϵ 5800); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09, 0.14, and 0.16 (12H, each as s), 0.90 and 0.92 (18H, each as s), 3.73 (1H, dd, J=11.0 and 5.9 Hz), 3.81 (1H, dd, J=11.0 and 4.9 Hz), 4.41–4.44 (1H, m), 4.93 (1H, d, J=3.1 Hz), 5.79 (1H, d, J=8.0 Hz), 7.19 (1H, d, J=8.0 Hz), 8.29 (1H, br); FAB-MS m/z 489 (M^++H for ^{35}Cl). Anal. Calcd for $C_{21}H_{37}ClN_2O_5Si_2$: C, 51.56; H, 7.62; N, 5.73. Found: C, 51.57; H, 7.70; N, 5.70.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-fluoro-D-*erythro*-pent-1-enofuranosyl]uracil (17). A CH_2Cl_2 (15 mL) solution containing **10** (376 mg, 0.50 mmol), DMAP (183 mg, 1.5 mmol), XeF_2 (254 mg, 1.5 mmol), and AgOTf (385 mg, 1.5 mmol) was stirred at room temperature for 5 min. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and then extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=6/1) of the organic extract gave **17** (46 mg, 29%) as a foam: UV (MeOH) λ_{max} 261 nm (ϵ 10400), λ_{min} 233 nm (ϵ 6700); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09, 0.13, and 0.14 (12H, each as s), 0.90 and 0.91 (18H, each as s), 3.71 (1H, dd, J=11.1 and 6.0 Hz), 3.80 (1H, dd, J=11.1 and 5.0 Hz), 4.29–4.33 (1H, m), 5.08 (1H, d, J=3.2 Hz), 5.79 (1H, d, J=8.0 Hz), 7.22 (1H, d, J=8.0 Hz), 8.80 (1H, br); FAB-MS m/z 473 (M^++H). Anal. Calcd for $C_{21}H_{37}FN_2O_5Si_2$: C, 53.36; H, 7.89; N, 5.93. Found: C, 53.63; H, 8.01; N, 5.85.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-phenyl-D-*erythro*-pent-1-enofuranosyl]uracil (18). To a DMF (5.0 mL) solution of **10** (175 mg, 0.235 mmol), $Pd(PPh_3)_4$ (25 mg, 0.023 mmol), and PhI (80 μL, 0.70 mmol), CuI (12 mg, 0.06 mmol) was added under positive pressure of dry Ar, and the whole mixture was heated immediately at 80°C for 5 min. The reaction mixture was partitioned between saturated aqueous $NaHCO_3$ and EtOAc. Silica gel column chromatography (hexane/EtOAc=4/1) of the organic layer gave **18** (83 mg, 66%) as a syrup: UV (MeOH) λ_{max} 252 nm (ϵ 12000), λ_{min} 230 nm (ϵ 7400); ^{1}H NMR ($CDCl_3$) δ 0.02, 0.07, and 0.10 (12H, each as s), 0.84 and 0.91 (18H, each as s), 3.76 (1H, dd, J=10.6 and 6.7 Hz), 3.87 (1H, dd, J=10.6 and 5.0 Hz), 4.47–4.50 (1H, m), 5.30 (1H, d, J=2.5 Hz), 5.68 (1H, d, J=8.2 Hz), 7.08 (1H, d, J=8.2 Hz), 7.21–7.32 (5H, m), 8.15 (1H, br); FAB-MS m/z 531 (M^++H). Anal. Calcd for $C_{27}H_{42}N_2O_5Si_2$: C, 61.09; H, 7.98; N, 5.28. Found: C, 60.75; H, 8.03; N, 5.24.

1-[2-*C*-Benzyl-3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil (19). To a HMPA (10 mL) solution of **10** (450 mg, 0.61 mmol), $Pd(PPh_3)_4$ (140 mg, 0.12 mmol), and benzyl bromide (145 μL, 1.2 mmol), CuI (12 mg, 0.06 mmol) was added under positive pressure of dry Ar, and the whole mixture was heated at 80°C for 14 h. The reaction mixture was partitioned between saturated aqueous $NaHCO_3$ and EtOAc. Silica gel column chromatography (hexane/EtOAc=10/1) of the organic layer gave **19** (94 mg, 29%) as a solid: mp 130–131°C; UV (MeOH) λ_{max} 254 nm (ϵ 12000), λ_{min} 239 nm (ϵ 11000); ^{1}H NMR ($CDCl_3$) δ 0.02, 0.04, and 0.05 (12H, each as s), 0.89 and 0.90 (18H, each as s), 3.32 (1H, d, *J*=16.0 Hz), 3.43 (1H, d, *J*=16.0 Hz), 3.65 (1H, dd, *J*=10.7 and 6.4 Hz), 3.78 (1H, dd, *J*=10.7 and 5.2 Hz), 4.34–4.37 (1H, m), 4.80 (1H, d, *J*=2.7 Hz), 5.59 (1H, d, *J*=7.9 Hz), 7.05 (1H, d, *J*=7.9 Hz), 7.15–7.25 (5H. m), 8.74 (1H, br); FAB-MS *m/z* 545 (M^++H). Anal. Calcd for $C_{28}H_{44}N_2O_5Si_2$: C, 61.73; H, 8.14; N, 5.14. Found: C, 61.57; H, 8.10; N, 5.09.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-vinyl-D-*erythro*-pent-1-enofuranosyl]uracil (20). A mixture of **15** (936 mg, 1.60 mmol), $PdCl_2(PPh_3)_2$ (112 mg, 0.16 mmol), CuI (30 mg, 0.16 mmol), and tributylvinyltin (1.4 mL, 4.8 mmol) in THF (20 mL) was refluxed for 22 h under positive pressure of dry Ar. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=4/1) of the organic extract gave **20** (620 mg, 80%) as a foam: UV (MeOH) λ_{max} 251 nm (ϵ 13000), λ_{min} 224 nm (ϵ 7600); ^{1}H NMR ($CDCl_3$) δ 0.08, 0.09, 0.15, and 0.16 (12H, each as s), 0.89 and 0.90 (18H, each as s), 3.64 (1H, dd, *J*=10.7 and 7.0 Hz), 3.79 (1H, dd, *J*=10.7 and 5.2 Hz), 4.40–4.43 (1H, m), 5.11 (1H, dd, *J*=11.1 and 1.2 Hz), 5.15 (1H, d, *J*=1.8 Hz), 5.25 (1H, dd, *J*=17.4 and 1.2 Hz), 5.77 (1H, d, *J*=8.0 Hz), 6.12 (1H, dd, *J*=17.4 and 11.1 Hz), 7.21 (1H, d, *J*=8.0 Hz), 8.41 (1H, br); FAB-MS *m/z* 482 (M^++H). Anal. Calcd for $C_{23}H_{40}N_2O_5Si_2$: C, 57.46; H, 8.39; N, 5.83. Found: C, 57.58; H, 8.54; N, 5.79.

1-[3,5-Bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-2-*C*-methyl-D-*erythro*-pent-1-enofuranosyl]uracil (4). *Method A*: A mixture of **15** (264 mg, 0.46 mmol), $PdCl_2(MeCN)_2$ (25 mg, 0.09 mmol), CuI (10 mg, 0.05 mmol), and Me_4Sn (820 μL, 5.9 mmol) in DMF (2.0 mL) was heated at 60°C for 120 h under positive pressure of dry Ar. The reaction mixture was treated with saturated aqueous $NaHCO_3$ and extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=1/1) of the organic extract gave **4** (145 mg, 67%). *Method B*: To a cooled THF (15 mL) solution containing **10** (810 mg, 1.09 mmol) and MeI (680 μL, 10.9 mmol), BuLi (1.34 M in hexane, 1.63 mL, 2.18 mmol) was added dropwise, while maintaining the temperature below −70°C. The same amount of BuLi was added further twice (after 15 and 30 min). The reaction mixture was treated with saturated aqueous NH_4Cl and then extracted with EtOAc. Silica gel column chromatography of the organic extract gave **4** (350 mg, 69%).

General procedure for desilylation

A mixture of the respective 2′-substituted 1-[3,5-bis-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-D-*erythro*-pent-1-enofuranosyl]uracil and NH_4F (15 equiv.) in MeOH was refluxed until complete disappearance of the starting material (12–24 h). Silica gel column chromatography (3–5% MeOH in $CHCl_3$) of the reaction mixture gave **21**–**27**.

1-[2-Deoxy-2-iodo-D-*erythro*-pent-1-enofuranosyl]uracil (21). This compound was isolated in 97% yield as a solid: mp 104–109°C; UV (MeOH) λ_{max} 250 nm (ϵ 9000), λ_{min} 243 nm (ϵ 8800); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.53 (2H, d, *J*=5.2 Hz), 4.34–4.36 (1H, m), 4.58 (1H, d, *J*=4.3 Hz), 5.75 (1H, d, *J*=7.9 Hz), 7.51 (1H, d, *J*=7.9 Hz); FAB-MS *m/z* 353 (M^++H). Anal. Calcd for $C_9H_9IN_2O_5$: C, 30.70; H, 2.58; N, 7.97. Found: C, 30.83; H, 2.38; N, 7.76.

1-[2-Bromo-2-deoxy-2-D-*erythro*-pent-1-enofuranosyl]-uracil (22). This compound was isolated in 93% yield as a solid: mp 93–100°C; UV (MeOH) λ_{max} 255 nm (ϵ 10600), λ_{min} 233 nm (ϵ 9000); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.56 (2H, d, *J*=5.2 Hz), 4.33–4.36 (1H, m), 4.66 (1H, d, *J*=4.0 Hz), 5.75 (1H, d, *J*=8.0 Hz), 7.53 (1H, d, *J*=8.0 Hz); FAB-MS *m/z* 305 and 307 (M^++H). Anal. Calcd for $C_9H_9BrN_2O_5$: C, 35.43; H, 2.97; N, 9.18. Found: C, 35.36; H, 2.87; N, 8.98.

1-[2-Chloro-2-deoxy-2-D-*erythro*-pent-1-enofuranosyl]-uracil (23). This compound was isolated in 97% yield as a solid: mp 95–100°C; UV (MeOH) λ_{max} 255 nm (ϵ 9200), λ_{min} 235 nm (ϵ 7100); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.58 (2H, d, *J*=5.2 Hz), 4.33–4.35 (1H, m), 4.67 (1H, d, *J*=3.6 Hz), 5.78 (1H, d, *J*=8.0 Hz), 7.56 (1H, d, *J*=8.0 Hz); FAB-MS *m/z* 261 (M^++H for ^{35}Cl). Anal. Calcd for $C_9H_9ClN_2O_5$: C, 41.48; H, 3.48; N, 10.75. Found: C, 41.24; H, 3.43; N, 10.47.

1-[2-Deoxy-2-*C*-phenyl-D-*erythro*-pent-1-enofuranosyl]-uracil (24). This compound was isolated in 97% yield as a solid: mp 110–120°C; UV (MeOH) λ_{max} 260 nm (ϵ 17800), λ_{min} 231 nm (ϵ 9000); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.54 (2H, d, *J*=5.2 Hz), 4.33–4.37 (1H, m), 5.06 (1H, d, *J*=3.2 Hz), 5.77 (1H, d, *J*=8.0 Hz), 7.18–7.34 (5H, m), 7.50 (1H, d, *J*=8.0 Hz); FAB-MS *m/z* 303 (M^++H). Anal. Calcd for $C_{15}H_{14}N_2O_5 \cdot 1/2H_2O$: C, 57.88; H, 4.86; N, 9.00. Found: C, 58.16; H, 4.48; N, 8.97.

1-[2-*C*-Benzyl-2-deoxy-D-*erythro*-pent-1-enofuranosyl]-uracil (25). This compound was isolated in 95% yield as a solid: mp 184–187°C; UV (MeOH) λ_{max} 256 nm (ϵ 9000), λ_{min} 237 nm (ϵ 6700); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.45 (2H, m), 3.64 (2H, m), 4.32–4.36 (1H, m), 4.59 (1H, d, *J*=3.4 Hz), 5.58 (1H, d, *J*=8.0 Hz), 7.12–7.25 (5H, m), 7.32 (1H, d, *J*=8.0 Hz); FAB-MS *m/z* 317 (M^++H). Anal. Calcd for $C_{16}H_{16}N_2O_5 \cdot 1/5H_2O$: C, 60.07; H, 5.17; N, 8.76. Found: C, 60.11; H, 4.78; N, 8.64.

1-[2-Deoxy-2-*C*-vinyl-D-*erythro*-pent-1-enofuranosyl]-uracil (26). This compound was isolated in 89% yield as a solid which gave no distinct mp (melted between 150 and 180°C); UV (MeOH) λ_{max} 251 nm (ϵ 13100), λ_{min} 225 nm (ϵ 6300); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.47–3.55 (2H, m), 4.26–4.28 (1H, m), 4.87 (1H, d, *J*=3.4 Hz), 4.98 (1H, dd, *J*=11.1 and 1.8 Hz), 5.30 (1H,

dd, J=17.4 and 1.8 Hz), 5.70 (1H, d, J=7.9 Hz), 6.11 (1H, dd, J=17.4 and 11.1 Hz), 7.50 (1H, d, J=7.9 Hz); FAB-MS m/z 253 (M^++H). Anal. Calcd for $C_{11}H_{12}N_2O_5$: C, 52.38; H, 4.80; N, 11.11. Found: C, 51.98; H, 4.77; N, 10.79.

1-[2-Deoxy-2-*C*-methyl-D-*erythro*-pent-1-enofuranosyl]-uracil (27). This compound was isolated in 98% yield as a solid: mp 81–86°C; UV (MeOH) λ_{max} 257 nm (ϵ 10000), λ_{min} 233 nm (ϵ 6700); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 1.56 (3H, d, J=0.8 Hz), 3.52 (2H, d, J=5.6 Hz), 4.18–4.23 (1H, m), 4.54 (1H, dd, J=0.8 and 4.0 Hz), 5.75 (1H, d, J=8.0 Hz), 7.55 (1H, d, J=8.0 Hz); FAB-MS m/z 241 (M^++H). Anal. Calcd for $C_{10}H_{12}N_2O_5 \cdot 1/2H_2O$: C, 48.19; H, 5.25; N, 11.24. Found: C, 47.89; H, 5.22; N, 11.40.

1-[2-Deoxy-D-*erythro*-pent-1-enofuranosyl]-6-methyl-uracil (28). This compound was obtained from **6** as a solid by the general procedure described above: mp 155–159°C; UV (MeOH) λ_{max} 257 nm (ϵ 11200), λ_{min} 231 nm (ϵ 4400); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 2.16 (3H, s), 3.47–3.55 (2H, m), 4.26–4.29 (1H, m), 4.71 (1H, br), 5.25 (1H, d, J=2.0 Hz), 5.61 (1H, s); FAB-MS m/z 241 (M^++H). Anal. Calcd for $C_{10}H_{12}N_2O_5$: C, 50.00; H, 5.04; N, 11.66. Found: C, 50.30; H, 4.69; N, 11.72.

Desilylation of 1

A mixture of **1** (404 mg, 0.88 mmol) and NH_4F (490 mg, 13.2 mmol) in MeOH (15 mL) was heated at 60°C for 21 h with stirring. The reaction mixture was evaporated and then applied on a silica gel column. Elution with $CHCl_3$ and with 10% MeOH in $CHCl_3$ gave **29** (40 mg, 22%, solid) and uracil (75 mg, 76%), respectively. Physical data of **29** are as follows: mp 163–165°C; UV (MeOH) λ_{max} 251 nm (ϵ 8800), λ_{min} 238 nm (ϵ 8400); ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 4.38 (2H, s), 5.71 (1H, d, J=8.0 Hz), 6.39 (1H, d, J=3.2 Hz), 6.45 (1H, J=3.2 Hz), 7.71 (1H, d, J=8.0 Hz); FAB-MS m/z 209 (M^++H). Anal. Calcd for $C_9H_8N_2O_4$: C, 51.93; H, 3.87; N, 13.46. Found: C, 51.80; H, 3.48; N, 13.40.

Acknowledgements

The authors would like to thank Dr Martin J. Slater (Glaxo-Wellcome Medicine Research Centre, UK) for proof-reading this manuscript.

References

1. Robins, M. J.; Trip, E. M. *Tetrahedron Lett.* **1974**, 3369.
2. For an alternative high-yield preparation of **1**: Haraguchi, K.; Tanaka, H.; Maeda, H.; Itoh, Y.; Saito, S.; Miyasaka, T. *J. Org. Chem.* **1991**, *56*, 5401.
3. (a) Robins, M. J.; Jones, R. A. *J. Org. Chem.* **1974**, *39*, 113. (b) Robins, M. J.; Jones, R. A.; Mengel, R. *J. Am. Chem. Soc.* **1976**, *98*, 8213. (c) Ranganathan, R. *Tetrahedron Lett.* **1977**, 1291. (d) Fraser, A.; Wheeler, P.; Cook, P. D.; Sanghvi, Y. S. *J. Heterocycl. Chem.* **1993**, *30*, 1277.
4. (a) Haraguchi, K.; Itoh, Y.; Tanaka, H.; Yamaguchi, K.; Miyasaka, T. *Tetrahedron Lett.* **1993**, *34*, 6913. (b) Itoh, Y.; Haraguchi, K.; Tanaka, H.; Gen, E.; Miyasaka, T. *J. Org. Chem.* **1995**, *60*, 656. (c) Yoshimura, Y.; Kano, F.; Miyazaki, S.; Ashida, N.; Sakata, S.; Haraguchi, K.; Itoh, Y.; Tanaka, H.; Miyasaka, T. *Nucleosides Nucleotides* **1996**, *15*, 305.
5. Itoh, Y.; Haraguchi, K.; Tanaka, H.; Matsumoto, K.; Nakamura, K. T.; Miyasaka, T. *Tetrahedron Lett.* **1995**, *36*, 3867.
6. For a similar reaction sequence utilizing 9-(2-deoxy-D-*erythro*-pent-1-enofuranosyl)adenine, see: (a) Haraguchi, K.; Matsumoto, K.; Itoh, Y.; Tanaka, H.; Miyasaka, T. *Nucleic Acids Symp. Ser.* **1994**, *31*, 29. (b) Gimisis, T.; Ialongo, G.; Chatgilialoglu, C. *Tetrahedron* **1998**, *54*, 573.
7. Haraguchi, K.; Tanaka, H.; Gen, E., unpublished result.
8. A part of the present study has been published as a communication: Kumamoto, H.; Shindoh, S.; Tanaka, H.; Gen, E.; Haraguchi, K.; Kittaka, A.; Miyasaka, T. *Tetrahedron Lett.* **1998**, *39*, 3761.
9. Tanaka, H.; Nasu, I.; Miyasaka, T. *Tetrahedron Lett.* **1979**, 4755.
10. For a review article, see: Tanaka, H.; Hayakawa, H.; Haraguchi, K.; Miyasaka, T.; Walker, R. T.; De Clercq, E.; Baba, M.; Stammers, D. K.; Stuart, I. D. In *Advances in Antiviral Drug Design*; De Clercq, E., Ed.; JAI Press: Greenwich, Vol. 3, 1999, pp 93–144.
11. (a) Tanaka, H.; Hayakawa, H.; Miyasaka, T. *Chem. Pharm. Bull.* **1981**, *29*, 3565. (b) Tanaka, H.; Hayakawa, H.; Miyasaka, T. *Tetrahedron* **1982**, *38*, 2635. (c) Yamamoto, Y.; Seko, T.; Rong, F. G.; Nemoto, H. *Tetrahedron Lett.* **1989**, *30*, 7191. (d) Tanaka, H.; Hayakawa, H.; Shibata, S.; Haraguchi, K.; Miyasaka, T.; Hirota, K. *Nucleosides Nucleotides* **1992**, *11*, 319.
12. (a) Inoue, H.; Ueda, T. *Chem. Pharm. Bull.* **1978**, *26*, 2657. (b) Rosenthal, A.; Dodd, R. H. *Carbohydr. Res.* **1980**, *85*, 15.
13. Hayakawa, H.; Tanaka, H.; Maruyama, Y.; Miyasaka, T. *Chem. Lett.* **1985**, 1401.
14. For migration of stannyl group in the lithiation of heterocycles: (a) Kato, K.; Hayakawa, H.; Tanaka, H.; Kumamoto, H.; Miyasaka, T. *Tetrahedron Lett.* **1995**, *36*, 6507. (b) Kelly, T. R.; Lang, F. *Tetrahedron Lett.* **1995**, *36*, 9293. (c) Kato, K.; Hayakawa, H.; Tanaka, H.; Kumamoto, H.; Shindoh, S.; Shuto, S.; Miyasaka, T. *J. Org. Chem.* **1997**, *62*, 6833.
15. Ficini, J.; Depezay, J. C. *Tetrahedron Lett.* **1968**, 937.
16. Lau, K. S. Y.; Schlosser, M. *J. Org. Chem.* **1978**, *43*, 1595.
17. The yields were calculated, respectively, from **7** and **12**.
18. Brooks, B. R.; Bruccoleri, R. E.; Olason, B. D.; States, D. J.; Swaminathan, S.; Karplus, M. *J. Comput. Chem.* **1983**, *4*, 187.
19. Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*, Butterworths: London, 1987.
20. (a) Tius, M. A.; Kawakami, J. K. *Synth. Commun.* **1992**, *22*, 1461. (b) Tius, M. A. *Tetrahedron* **1995**, *51*, 6605.
21. For a review of the Stille reaction, see: Mitchell, T. N. *Synthesis* **1992**, 803.
22. Zhang, W.; Robins, M. J. *Tetrahedron Lett.* **1992**, *33*, 1177.
23. When **1** was desilylated under the conditions reported in Ref. 1 (Bu_4NF/pyridine/room temperature for 26 h), the free nucleoside was obtained in 49% yield after Florisil® column chromatography (3% MeOH in $CHCl_3$), together with **29** (yield: 6%). ^{1}H NMR and FAB-MS data of the free nucleoside are as follows: ^{1}H NMR (DMSO-d_6, after addition of D_2O) δ 3.52–3.54 (2H, m), 4.26–4.31 (1H, m), 4.74–4.75 (1H, m), 5.39 (1H, d, J=2.8 Hz), 5.77 (1H, d, J=8.0 Hz), 7.86 (1H, d, J=8.0 Hz); FAB-MS m/z 227 (M^++H).