An Efficient Method for the Preparation of 1′α-Branched-Chain Sugar Pyrimidine Ribonucleosides from Uridine: The First Conversion of a Natural Nucleoside into 1′-Substituted Ribonucleosides**

Tetsuya Kodama, Satoshi Shuto,* Makoto Nomura, and Akira Matsuda*[a]

Abstract: The 1′α-phenylselenouridine derivative **13** was successfully synthesized by enolization of the 3′,5′-*O*-TIPDS-2′-ketouridine **8**, and was subjected to a radical reaction with a vinylsilyl tether—an efficient procedure for preparing 1′α-branched-chain sugar pyrimidine nucleosides. Successive treatment of **8** with LiHMDS and PhSeCl in THF at $< -70\,^{\circ}C$ gave the desired 1′-phenylseleno products in 85% yield as an anomeric mixture of the 1′α-product **11** and the 1′β-product **12** (**11**/**12** = 2.5:1). Highly stereoselective reduction at the 2′-carbonyl of the 1′α-product **11** occurred from the β-face by using $NaBH_4/CeCl_3$ in MeOH, and subsequent introduction of a dimethylvinylsilyl tether at the 2′-hydroxyl gave the radical reaction substrate **14**. The photochemical radical atom-transfer reaction of **14** by using a high-pressure mercury lamp proceeded effectively in benzene to give the *exo*-cyclized PhSe-transferred product **18**, in which $(PhSe)_2$ proved to be essential as an additive for radical atom-transfer cyclization reactions. Subsequent phenylseleno-group elimination of **18** gave the sugar-protected 1′α-vinyluridine. With this procedure, 1′α-vinyluridine (**22**) and -cytidine (**25**), designed to be potential antitumor agents, were successfully synthesized. This study is the first example of functionalization at the anomeric 1′-position of a nucleoside by starting from a natural nucleoside to produce a *ribo*-type 1′-modified nucleoside.

Keywords: glycosides · nucleosides · radical reactions · selenium · silicon

Introduction

In recent years, we have been engaged in the study of branched-chain sugar nucleosides and have developed stereoselective synthetic methods for several of these biologically important targets in medicinal chemistry.[1] In the course of these studies, we have prepared a variety of sugar-modified nucleoside analogs, and have found that 1-(2-deoxy-2-methylene-β-D-*erythro*-pentofuranosyl)cytosine (DMDC, **1**),[2] 1-(2-*C*-cyano-2-deoxy-β-D-*arabino*-pentofuranosyl)cytosine (CNDAC, **2**),[3] and 1-(3-*C*-ethynyl-β-D-*ribo*-pentofuranosyl)-cytosine (ECyd, **3**)[4] are potent antitumor nucleosides, which significantly inhibit the growth of various human solid tumor cells both in vitro and in vivo. We have also identified 2′-deoxy-4′-*C*-ethynylcytidine (**4**)[5a] and 4′-*C*-vinylthymidine (**5**)[5b] as potent antiviral and/or antitumor agents.

We are also interested in the biological activity of 1′-branched-chain sugar ribonucleosides **I** (Scheme 1), since the antitumor antibiotics angustmycin C (**6**)[6] and hydantocidin (**7**),[7] which have herbicidal and plant-growth regulatory effects, are included in this class of nucleosides and have been isolated from bacterial broths. A variety of procedures for preparing branched-chain sugar nucleosides have been developed. However, examples of reported 1′-branched-chain sugar nucleosides are limited,[8] and the biological activities of these nucleosides have not been systematically investigated;[9] perhaps because of the lack of efficient synthetic methods for producing them. The 1′-branched-chain sugar nucleosides have been synthesized by introduction or construction of a nucleobase at the 1-position of the corresponding α-*C*-glycosidic precursors, the preparation of which required rather long reaction steps.[10]

With this in mind, we decided to develop an efficient method for preparing the 1′α-branched-chain sugar ribonucleosides **I**, starting from natural nucleosides and using a radical cyclization reaction, which is a highly versatile method for forming C–C bonds. Since silicon-containing tethers are very useful for the regio- and stereoselective introduction of a carbon substituent based on a temporary silicon connection, there is a growing interest in their use in intramolecular radical cyclization reactions.[11] We have developed a regio-

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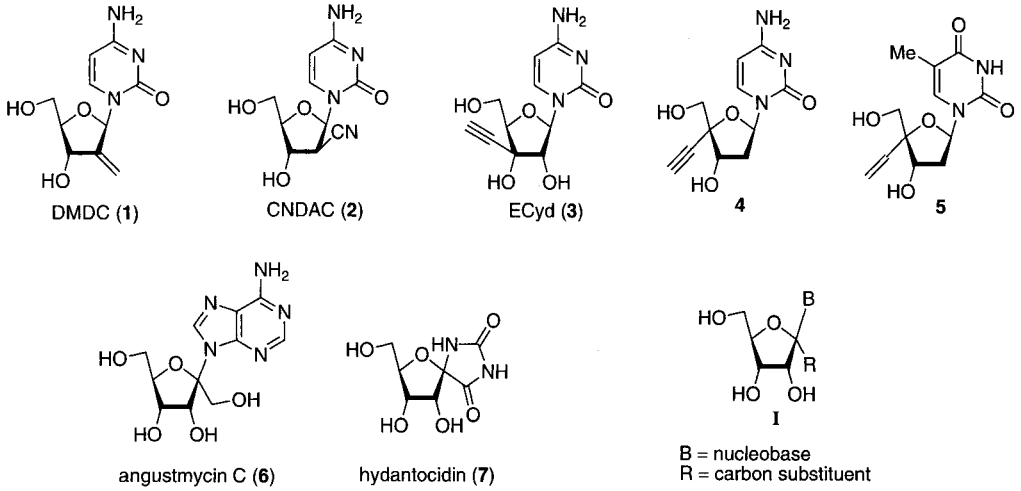
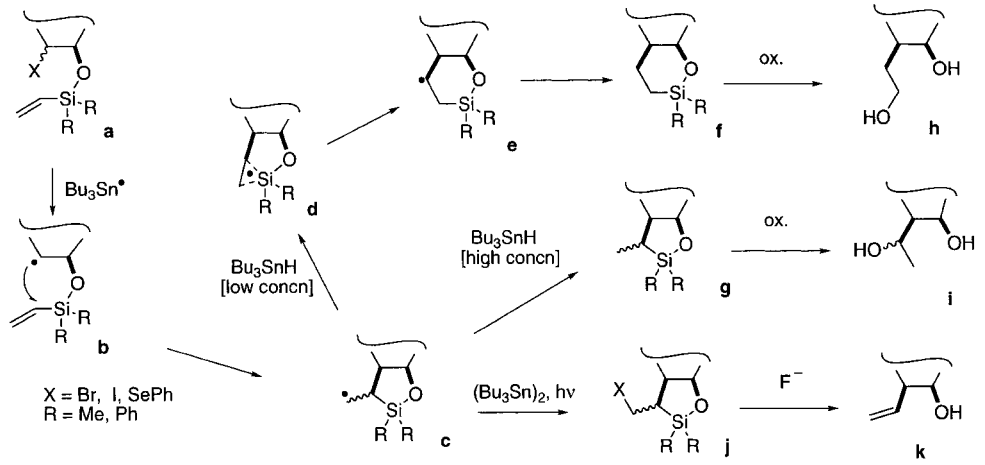


Scheme 1. Branched-chain nucleosides with biological activity.



Scheme 2. General scheme for the radical cyclization reaction with a vinylsilyl group as a temporary connecting tether.

and stereoselective method for introducing three kinds of C_2 substituents, namely 1-hydroxyethyl, 2-hydroxyethyl, and vinyl groups at the position β to a hydroxyl group in halohydrins or in α-phenylselenoalkanols **a** by using an intramolecular radical cyclization reaction with a dimethyl- or a diphenylvinylsilyl group as a temporary connecting radical-acceptor tether (Scheme 2).[12] Thus, the selective introduction of both 1-hydroxyethyl and 2-hydroxyethyl groups can be achieved, depending on the concentration of nBu$_3$SnH in the reaction system, via a 5-*exo*-cyclization intermediate **g** or a 6-*endo*-cyclization intermediate **f**, respectively, after oxidative ring-cleavage by reacting the cyclization products together under Tamao oxidation conditions.[13] A vinyl group can also be introduced by irradiation of the vinylsilyl ether in the presence of (nBu$_3$Sn)$_2$, followed by treatment of the resulting atom-transfer 5-*exo*-cyclization product **j** with the fluoride ion.[12d] The results of our investigation of the radical cyclization mechanism suggest that the kinetically favored 5-*exo*-cyclized radical **c**, formed from radical **b**, was trapped when the concentration of nBu$_3$SnH was high enough to give **g**. At lower concentrations of nBu$_3$SnH and at higher reaction temperatures, the radical **c** rearranged into the more stable, ring-enlarged 4-oxa-3-silacyclohexyl radical **e** via a pentavalent-like silicon radical transition state **d**, which was then trapped with nBu$_3$SnH to give **f**.[12g]

We recently applied this method to the synthesis of 4′α-branched-chain sugar nucleosides.[5b, 12a–c] The 4′-phenylselenonucleosides **II**, which were prepared from natural 2′-deoxyribonucleosides by the procedure developed by Giese and co-workers,[14] were used successfully in the synthesis of a variety of 4′α-branched-chain sugar nucleosides **III** through a radical reaction with a temporary connecting vinylsilyl tether (Scheme 3). Among these, 4′α-ethynyl-2′-deoxycytidine (**4**) and 4′α-vinylthymidine (**5**) showed potent antiviral and/or antitumor effects.[5] Consequently, the 1′-phenylselenonucleosides should also be highly useful precursors for the synthesis of the biologically important 1′α-branched-chain sugar nucleosides.

In this report, we describe the synthesis of 1′-phenylselenouridines by enolization of a sugar-protected 2′-ketouridine[15] and its radical reaction with a vinylsilyl tether to produce 1′α-branched-chain sugar pyrimidine nucleosides.

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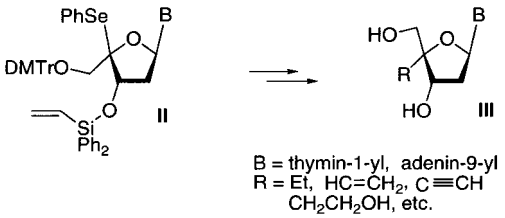
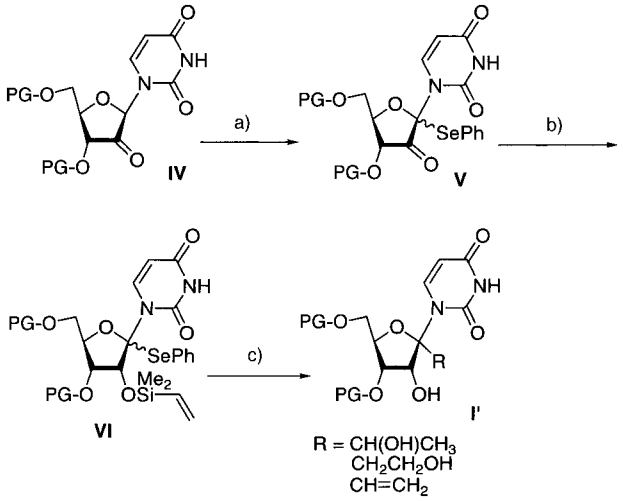


Scheme 3. Synthesis of 4′-branched 2′-deoxynucleosides by radical cyclization reactions with a vinylsilyl group as a temporary connecting tether.

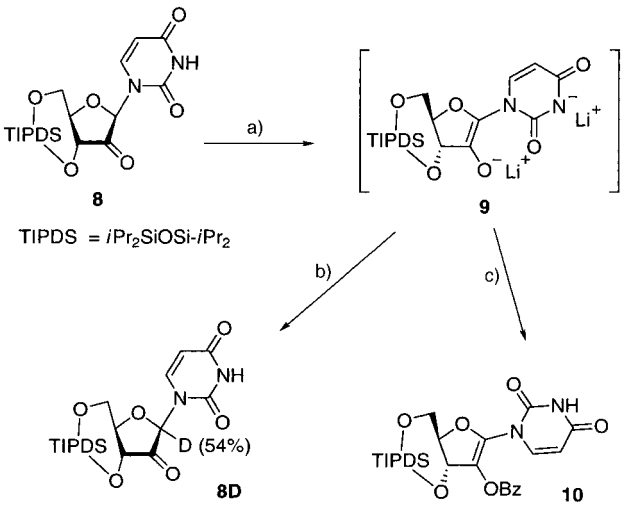
Results and Discussion

Synthetic plan: Scheme 4 shows our synthetic plan. In order to provide the substrate for the radical reaction, a method for introducing a phenylseleno group at the 1′-positon of nucleosides was needed. We assumed that treatment of the 2′-ketouridine derivative **IV**, readily prepared from uridine, with a strong base would produce the corresponding 1′-enolate and that the subsequent reaction with PhSeCl as electrophile would give the 1′-phenylseleno-2′-ketouridine derivative **V**. The stereoselective hydride reduction of the 2′-carbonyl from the β-face, followed by introduction of a dimethylvinylsilyl tether at the 2′-hydroxyl, would provide the desired radical reaction substrate **VI**. The radical reaction of **VI** and subsequent Tamao oxidation or elimination of the phenylseleno group of the product would afford the corresponding sugar-protected 1′-branched-chain sugar nucleosides **I′**.



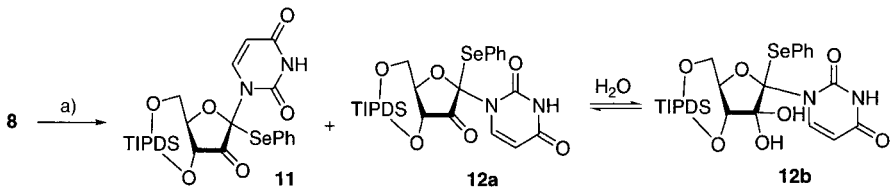
Scheme 4. Strategy for synthesizing 1′α-branched-chain ribonucleosides via 1′-phenylselenouridine derivatives. a) 1. base, 2. PhSeCl. b) 1. reduction, 2. $Me_2Si(CH=CH_2)Cl$. c) 1. radical reaction, 2. Tamao oxidation or elimination.

Enolization at the 1′-position: The 3′,5′-*O*-TIPDS-2′-ketouridine **8** (TIPDS = 1,1,3,3-tetraisopropyldisiloxane-1,3-diyl), first prepared by our group,[16] has been widely used for the synthesis of 2′-modified nucleosides by nucleophilic addition reactions at the 2′-carbonyl.[17] We first examined, by deuterium-labeling experiments, whether enolization at the 1′-position of **8** occurred (Scheme 5). A mixture of **8** and lithium hexamethyldisilazide (LiHMDS) (2.1 equiv) in THF was stirred at $< -70\,^{\circ}C$ for 1 h, then quenched with CD_3CO_2D/CD_3OD. The 2′-ketouridine **8D** was obtained in about 90% yield,[18] in which 54% of the 1′-protons had been replaced by deuterium atoms based on the ^1H NMR spectrum. A similar experiment with lithium diisopropylamide (LDA) as the base also gave the 1′-deuterium-labeled product **8D** (yield 72%, deuterium incorporation 50%). Furthermore, when the reaction mixture of **8** and LiHMDS (2.1 equiv) in THF was treated with BzCl at $< -70\,^{\circ}C$, the enol-*O*-benzoate **10** was obtained in 73% yield. These experiments clearly showed that the 1′-enolate **9** was produced under these conditions, as predicted. As far as we know, this is the first example demonstrating enolization at the 1′-position of a 2′-ketonucleoside.[19]



Scheme 5. Enolization of 3′,5′-*O*-TIPDS-2′-ketouridine (**8**). a) LiHMDS, THF. b) CD_3CO_2D, CD_3OD; ca. 90%. c) BzCl; 73%.

Introduction of a phenylseleno group at the 1′-position: Introduction of a phenylseleno group at the 1′-position of **8** through its enolization was next investigated (Scheme 6), and the results are summarized in Table 1. The reactions were carried out as follows. A mixture of **8** and a base in a solvent was stirred at $< -70\,^{\circ}C$ for 1 h. Two equivalents of PhSeCl were added, and the resulting mixture was further stirred at the same temperature for 1 h. The reaction products were



Scheme 6. Introduction of a phenylseleno group at the 1′-positon of 3′,5′-*O*-TIPDS-2′-ketouridine (**8**). a) 1. base, 2. PhSeCl.

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Table 1. The introduction of a phenylseleno group at the 1′-position of **8**.[a]

	base (equiv)	solvent	yield (**11** + **12** [%])	ratio (**11**/**12**)[b]	**8** (recovered [%])
1	LiHMDS (1.5)	THF	47	2.9:1	47
2	LiHMDS (2.1)	THF	85	2.5:1	6
3	LiHMDS (3.0)	THF	73	2.7:1	16
4	LiHMDS (4.0)	THF	5	only **12**	57
5	LiHMDS (2.1)	DME	85	2.7:1	9
6	LiHMDS (2.1)	Et_2O	53	2.4:1	36
7	LiHMDS (2.1)	THF/HMPA (9:1)	75	1.4:1	3
8	LDA (2.1)	THF	62	2.6:1	12
9	NaHMDS (2.1)	THF	76	1.2:1	10
10	KHMDS (2.1)	THF	79	1:3.0	6

[a] solvent at $< -70\,^{\circ}C$ for 1 h, PhSeCl (2 equiv) was added, and the resulting mixture was further stirred at the same temperature for 1 h. [b] The ratio was obtained from their isolated yield, after purification by neutral silica gel column chromatography.

purified by neutral silica-gel column chromatography. The reaction was first performed with 1.5 equivalents of LiHMDS to give the desired 1′-phenylseleno product in 47% yield as an anomeric mixture of the 1′α-phenylseleno product **11** and the corresponding β-product **12** (**11**/**12** = 2.9:1, entry 1). It is worth noting that the 1′β-phenylseleno product **12** was in equilibrium between the 2′-keto form **12a** and its 2′-hydrate **12b**. The stereochemistry was confirmed by NOE analysis of **12b**, as shown in Figure 1a. When 2.1 or 3.0 equivalents of LiHMDS were used, the yields increased significantly (entry 2, yield 85%; entry 3, yield 73%).[20] However, when 4.0 equivalents of the base were used, a poorer yield resulted (entry 4).[21] In all these reactions, the 1′α-phenylseleno product **11** was obtained selectively as the major product. The

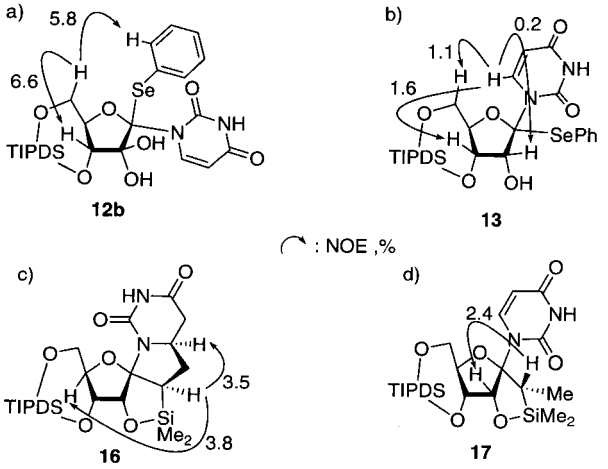


Figure 1. NOE experimental data of compounds **12b**, **13**, **16**, and **17**.

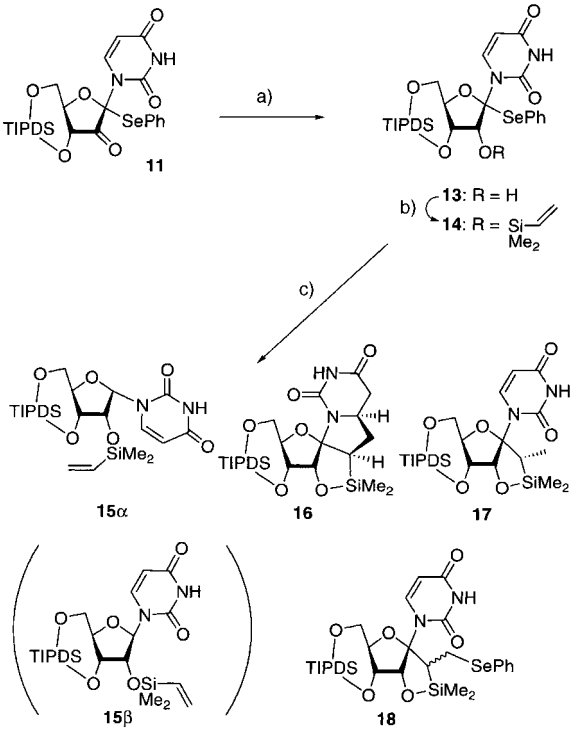
effect of the solvent on the reaction was next examined. Although 1,2-dimethoxyethane (DME) was suitable for this reaction (entry 5) and gave results similar to the reaction in THF, the yield decreased when Et_2O was used (entry 6). The anomeric ratio did not change when using DME or Et_2O, but the facial selectivity was almost lost when THF/HMPA (hexamethylphosphoramide) was the solvent (entry 7, yield 75%, **11**/**12** = 1.4:1). Although the yield decreased with LDA as the base, the 1′-phenylseleno products were obtained in excellent yields similar to those with LiHMDS, when NaHMDS or KHMDS was used (entries 9 and 10). It is interesting to note that the α-selectivity is lost when the counterion of HMDS is changed to sodium. Furthermore, the stereoselectivity was reversed to give the 1′β-phenylseleno derivative **12** as the major product (**11**/**12** = 1:3.0) when potassium was used as the counterion.

These results with different counterions, together with the results in the presence of HMPA (entry 7), suggest that the 1′α-phenylseleno product **11** is probably produced through a chelation-controlled reaction pathway.[22] While the structure of the chelation intermediate has not been elucidated, one might postulate a chelation of Li^+ between the 2′-enol oxygen and 2-carbonyl oxygen of the uracil moiety.

Synthesis of the substrate for the radical reactions: The 1′α-phenyseleno product **11**, obtained in pure form after neutral silica gel column chromatography, was subjected to reduction at the 2′-keto moiety with hydride reagents, such as $NaBH_4$, $LiBH_4$, $NaBH_3CN$, diisobutylaluminum hydride (DIBAL-H), or $LiAl(OEt)_3H$. We investigated various reaction conditions and found that the 2′-carbonyl group of **11** was chemo- and stereoselectively reduced from the β-face when it was treated with $NaBH_4$ in the presence of $CeCl_3$ in MeOH[23] at $< -70\,^{\circ}C$ to give the desired sugar-protected 1′-phenylselenouridine **13** in 90% yield as the sole product.[24] The stereochemistry of **13** was confirmed by NOE experiments, as shown in Figure 1b.

The vinylsilyl tether was introduced at the 2′-hydroxy group by treating **13** with a dimethylvinylchlorosilane, 4-(dimethylamino) pyridine (DMAP), and Et_3N in toluene to give **14**, the substrate for the radical reaction, as shown in Scheme 7.

The radical reaction under reductive conditions: The radical reactions of the 1′α-phenylselenouridine derivative **14**, bearing a dimethylvinylsilyl tether at the 2′-position, were first performed under reductive conditions with nBu$_3$SnH. However, the results were undesirable. Treatment of **14** with nBu$_3$SnH (3.0 equiv) in the presence of 2,2′-azobis*iso*butyronitrile (AIBN, 0.3 equiv) in benzene at 60 °C or 2,2′-azobis-(2,4-dimethyl-4-methoxyvaleronitrile) (V-70, 0.3 equiv) at 0 °C gave the 1′-reduced product **15** as the major product (43% at 60 °C, 33% at 0 °C). The anomeric configuration was assigned as α, since this compound was not identical to the uridine derivative **15*β*** that was prepared by silylation at the 2′-hydroxyl of 3′,5′-*O*-TIPDS-uridine. The radical reactions with $(TMS)_3SiH$ as the reducing agent were also unsuccessful. For example, when **14** was treated with $(TMS)_3SiH$ (3.0 equiv) and AIBN (0.3 equiv) in benzene at 60 °C, a tandem cyclization occurred to give the pentacyclic product **16** as the major product in 37% yield, along with 5-*exo*-cyclized **17** (13%) and its atom-transfer product **18**



Scheme 7. Radical reactions of 1′α-phenylselenouridine derivative **14** with a vinylsilyl group at the 2′-hydroxyl under reductive conditions. a) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH. b) $Me_2Si(CH{=}CH_2)Cl$, DMAP, Et_3N, toluene. c) $n$$Bu_3SnH$ or $(TMS)_3SiH$, AIBN or V-70, benzene or CH_2Cl_2.

(3%). The stereochemistries of **16** and **17** were confirmed by NOE experiments, as shown in Figure 1c and d.

The introduction of a vinyl group by radical atom-transfer cyclization: We next investigated the introduction of a vinyl group at the 1′α-position of uridine by radical atom-transfer cyclization[25] and subsequent elimination of the phenylseleno group, which we recently developed.[12d] When the radical atom-transfer cyclization reaction was performed by irradiation of a solution of **14** in benzene with a high-pressure mercury lamp through a Pyrex filter at room temperature, the starting material **14** disappeared within 4 h. The product, without purification, was immediately treated with aqueous H_2O_2 in THF at room temperature (method A) or treated successively with tetrabutylammonium fluoride (TBAF) in THF and with Ac_2O/DMAP/Et_3N in MeCN at room temperature (method B). The results are summarized in Table 2. The photoreaction was first performed without an additive, and the product was oxidatively eliminated by method A to give the desired 1′α-vinyl product in 12% yield as a mixture of 2′-*O*-silyl **20** and de-silylated **19** (entry 1).

The effect of additives on the photoreaction was next examined. Addition of hexabutylditin [$(n$$Bu_3Sn)_2$], which proved effective in our previous study,[12d] did not work in this system (entry 2). We found that when diphenyldiselenide [$(PhSe)_2$] was added, the yield of the 1′α-vinyl product increased (entry 3, yield 47%). We also discovered that β-elimination with TBAF (method B) was superior to the above oxidative elimination with H_2O_2 (method A). When the

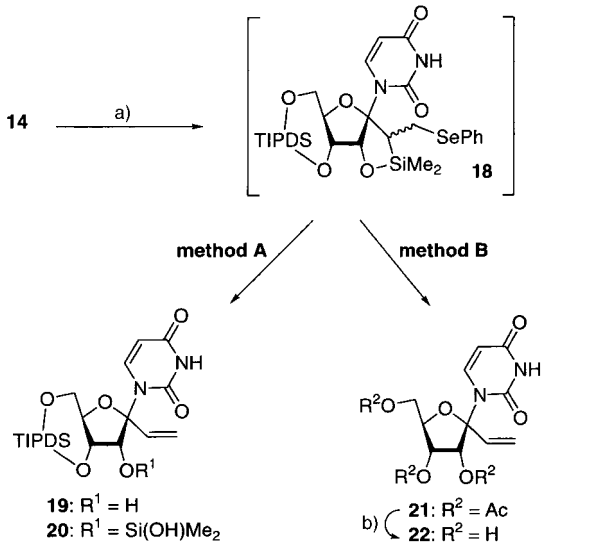
Table 2. Synthesis of 1′α-vinyluridine derivatives by a radical atom-transfer reaction of **14**.[a]

	additive (equiv)	elimination method[b]	products	yield [%]
1	none	A	**19** + **20**	12
2	$(n$$Bu_3Sn)_2$ (0.1)	A	**19** + **20**	18
3	$(PhSe)_2$ (0.1)	A	**19** + **20**	47
4	none	B	**21**	47
5	$(PhSe)_2$ (0.1)	B	**21**	48
6	$(PhSe)_2$ (0.3)	B	**21**	70
7	$(PhSe)_2$ (0.7)	B	**21**	77
8	$(PhSe)_2$ (1.0)[c]	B	**21**	69

[a] A solution of **14** (and an additive) in benzene was irradiated with a high pressure mercury lamp (300 W) with Pyrex filter at room temperature for 4 h (entry 8, for 24 h). [b] A: The radical atom-transfer cyclization product was treated with H_2O_2 in aqueous THF at room temperature. B: The radical atom-transfer cyclization product was successively treated with TBAF in THF and with Ac_2O/DMAP/Et_3N in MeCN at room temperature. [c] After 24 h, a part of the starting material **14** remained was detected by ^1H NMR spectrum of the reaction mixture.

product formed by irradiation without an additive was treated by method B, the 1′α-vinyl product was isolated in 47% yield as the tri-*O*-acetate **21** (entry 4). The photoreaction in the presence of 0.1 equiv of $(PhSe)_2$ and subsequent treatment by method B gave **21** in 48% yield. When 0.3 or 0.7 equiv of $(PhSe)_2$ was used as an additive in the photoreaction, the yield increased (entry 6, yield 70%; entry 7, yield 77%). As far as we know, this is the first example in which $(PhSe)_2$ proved to be an effective additive for radical atom-transfer cyclization reactions. However, the use of 1.0 equiv of $(PhSe)_2$ resulted in a slower reaction (entry 8).

These results suggest the reaction pathways summarized in Scheme 8. The 5-*exo* cyclization of the anomeric radical **A**, produced by UV irradiation of **14**, gives the radical **B** (Scheme 9). In the reaction without $(PhSe)_2$, at least three



Scheme 8. Synthesis of 1′α-vinyluridine (**22**) by a photochemical radical atom-transfer cyclization reaction. a) *hν*, additive, benzene. Method A: aq. H_2O_2, THF. Method B: 1. TBAF, THF. 2. Ac_2O, DMAP, Et_3N, MeCN. b) Et_3N, MeOH.

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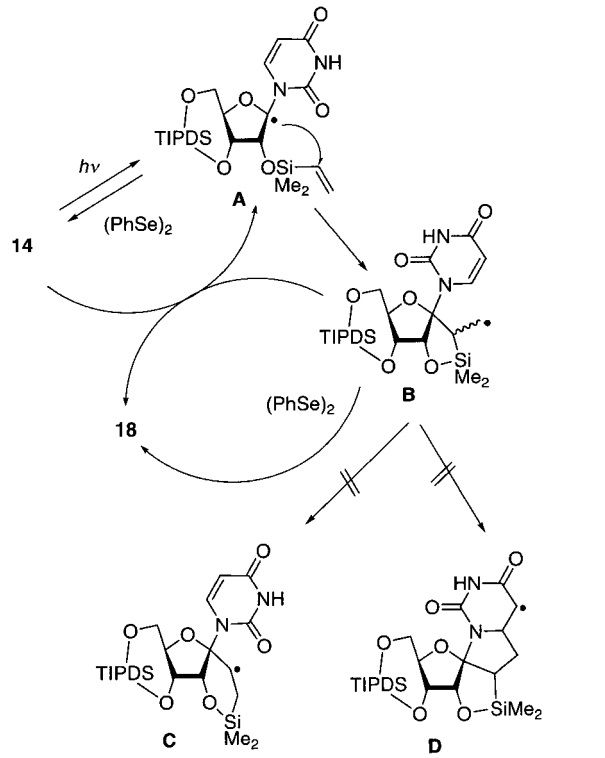
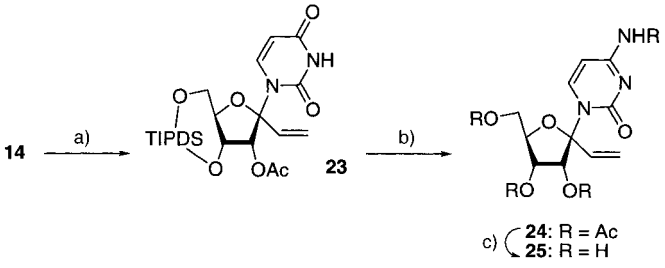


Scheme 9. A possible reaction mechanism for the radical atom-transfer cyclization reaction with $(PhSe)_2$ as an additive.

molecules, that is, the desired PhSe-transferred product **18**, the ring-enlarged radical **C**, and the tandem-cyclized radical **D**, can be formed from **B**, which may explain the poorer yields of the desired product **18**. When $(PhSe)_2$ is present, the 5-*exo*-cyclized radical **B** is likely to be trapped by $(PhSe)_2$; therefore the side reactions producing the radicals **C** or **D** are inhibited and the yield of the desired **18** increases. However, high concentrations of $(PhSe)_2$ may also trap the anomeric radical A to give back the starting material **14**, which competes with the 5-*exo*-cyclization producing **B**. This may be why the atom-transfer reaction (entry 8) proceeded so slowly when 1.0 equiv of $(PhSe)_2$ was used.

The synthesis of 1′α-vinyluridine and -cytidine: Removal of the acetyl groups of **21** with Et_3N/MeOH gave the target 1′α-vinyluridine **22** in high yield. The corresponding cytidine derivative **25** was synthesized as shown in Scheme 10. Successive treatment of **14** under the conditions for photochemical radical atom-transfer cyclization with $(PhSe)_2$ as an additive and for oxidative elimination with H_2O_2 gave a mixture of **19** and **20**, which, without purification, was further treated successively with saturated NH_3 in MeOH and Ac_2O/DMAP/Et_3N in MeCN to give 2′-*O*-Ac-3′,5′-*O*-TIPDS-1′α-vinyluridine (**23**) in 52% overall yield from **14**. The 1′α-*C*-vinyluridine derivative **23** was treated with 2,4,6-triisopropylbenzenesulfonyl chloride (TPSCl)/DMAP/Et_3N in MeCN followed by ammonolysis[26] to give the corresponding cytidine derivative, which was isolated as the tetraacetate **24** in 78% yield. Removal of the acetyl groups of **24** with saturated NH_3 in MeOH afforded the 1′α-*C*-vinylcytidine (**25**).



Scheme 10. Synthesis of 1′α-vinylcytidine (**25**) by a photochemical radical atom-transfer cyclization reaction. a) 1. *hν*, $(PhSe)_2$, benzene; 2. bq. H_2O_2, aq. THF; 3. NH_3, MeOH; 4. Ac_2O, DMAP, Et_3N, MeCN. b) 1. TPSC1, DMAP, Et_3N, MeCN; 2. 25% NH_4OH; 3. TBAF, THF; 4. Ac_2O, DMAP, Et_3N, MeCN.

Conclusion

We have successfully introduced a phenylseleno group at the 1′-position of the 2′-ketouridine derivative **8** by its enolization with LiHMDS. Subsequent chemo- and stereoselective reduction of the 2′-keto moiety gave the sugar-protected 1′-phenylselenouridine **13**, which is a highly useful precursor for the preparation of various 1′α-modified pyrimidine nucleosides of biological interest. After introduction of a dimethylvinylsilyl tether at the 2′-hydroxyl of **13**, the photochemical radical atom-transfer reaction with $(PhSe)_2$ as an effective additive, followed by elimination of the phenylseleno group gave the protected 1′α-vinyluridines. 1′α-Vinyluridine (**22**) and -cytidine (**25**) were successfully synthesized by using this procedure. This study is the first example of functionalization at the anomeric 1′-position of a nucleoside, starting from a natural nucleoside, to produce a *ribo*-type 1′-modified nucleoside.

Experimental Section

General: NMR Chemical shifts are reported in ppm downfield from TMS and *J* values are given in hertz. The ^1H NMR assignments reported for key compounds[27] are in agreement with the COSY spectra. Thin layer chromatography was done on Merck coated plate $60F_{254}$. Silica gel chromatography was done on Merck silica gel 5715 or Kanto Chemical silica gel 60N (neutral). Reactions were carried out under an argon atmosphere.

Deuterium labeling experiment with 8: A solution of LiHMDS (1.0 M in THF, 1.05 mL, 1.05 mmol) was added dropwise to a solution of **8** (242 mg, 0.50 mmol) in THF (5.5 mL) at below −70 °C, and the mixture was stirred at the same temperature for 1 h. After dropwise addition of a mixture of CD_3CO_2D (120 μL) and CD_3OD (120 μL), the resulting mixture was warmed to room temperature. The whole was partitioned between AcOEt and H_2O, and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (hexane/AcOEt 2:1) to give crude **8D** as a white solid (233 mg, 96%) containing a trace amount of an unknown compound, which may be the corresponding α-isomer. The rate of deuterium incorporation at the 1′-positon was determined as 54%, based on the ^1H NMR spectrum of pure **8D** recrystallized from hexane/AcOEt. M.p. 175–180 °C (went yellow and melted); ^1H NMR ($CDCl_3$, 270 MHz) $\delta = 8.15$ (br s, D_2O exchangeable, 1H), 7.14 (d, $J = 7.9$ Hz, 1H), 5.75 (dd, $J = 7.9$, 2.1 Hz, 1H), 5.05 (d, $J = 9.0$ Hz, 1H), 4.98 (s, 0.46H), 4.13 (dd, $J = 12.6$, 4.6 Hz, 1H), 4.13 (dd, $J = 12.6$, 3.3 Hz, 1H), 3.93 (ddd, $J = 9.0$, 4.6 Hz, 3.3, 1H), 1.13–0.98 (m, 28H); FAB-HRMS calcd for $C_{21}H_{36}DN_2O_7Si_2$ 486.2202; found 486.2197 $[M+H]^+$.

2′-*O*-Enol benzoate 10: A solution of LiHMDS (1.0 M in THF, 1.05 mL, 1.05 mmol) was added dropwise to a solution of **8** (242 mg, 0.50 mmol) in THF (5.5 mL) at below −70 °C, and the mixture was stirred at the same temperature for 1 h. After dropwise addition of a solution of BzCl (122 μL, 1.05 mmol) in THF (1.5 mL), the resulting mixture was stirred at the same

temperature for 1 h. AcOH (100 μL) was added, and the mixture was warmed to room temperature. The mixture was partitioned between AcOEt and H_2O, and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (hexane/AcOEt 4:1, 3:1, 2:1, and 1:1) to give **10** as a white foam. Yield: 214 mg, 73%; ^{1}H NMR ($CDCl_3$, 500 MHz) $\delta = 8.27$ (br s, D_2O exchangeable, 1H), 8.06 (m, 2H), 7.61 (m, 1H), 7.46 (m, 2H), 7.38 (d, $J =$ 8.1 Hz, 1H), 5.77 (dd, $J = 8.1$, 2.3 Hz, 1H), 5.66 (d, $J = 5.1$ Hz, 1H), 4.58 (ddd, $J = 11.2$, 4.8, 5.1 Hz, 1H), 4.19 (dd, $J = 11.2$, 4.8 Hz, 1H), 3.97 (dd, $J =$ 11.2, 11.2 Hz, 1H), 1.12–0.88 (m, 28H); ^{13}C NMR ($CDCl_3$, 125 MHz) $\delta =$ 163.54, 162.54, 147.41, 141.49, 136.30, 133.93, 130.28, 130.17, 128.63, 128.38, 126.53, 122.64, 103.28, 86.50, 75.36, 63.91, 17.57, 17.44, 17.40, 17.37, 16.87, 16.81, 16.78, 13.45, 13.42, 13.05, 12.34; FAB-HRMS calcd for $C_{28}H_{41}N_2O_8Si_2$ 589.2402; found 589.2416 $[M+H]^+$.

Introduction of a phenylseleno group at the 1′-position of 8 (General procedure): A solution of MHMDS in THF (M = Li and Na) or toluene (M = K) was added dropwise to a solution of **8** (242 mg, 0.50 mmol) in THF (5.5 mL) at below −70 °C, and the mixture was stirred at the same temperature for 1 h. After dropwise addition of a solution of PhSeCl (192 mg, 1.0 mmol) in THF (1.5 mL), the resulting mixture was stirred at the same temperature for 1 h. AcOH (ca. 150 μL) was added, and the mixture was warmed to room temperature. The mixture was partitioned between AcOEt and H_2O, the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (hexane/AcOEt 4:1, 3:1, 2:1, and 1:1) to give **11** (as a pale yellow foam), a mixture of **12a** and **12b** (as a yellow solid) and **8** (as a white foam). **11**: ^{1}H NMR ($CDCl_3$, 500 MHz) $\delta = 8.51$ (d, $J = 8.3$ Hz, 1H), 8.08 (br s, D_2O exchangeable, 1H), 7.55 (m, 2H), 7.42 (m, 1H), 7.36 (m, 2H), 5.79 (dd, $J =$ 8.3, 2.3 Hz, 1H), 4.95 (d, $J = 7.6$ Hz, 1H), 4.03–3.99 (m, 3H), 1.13–1.00 (m, 28H); ^{13}C NMR ($CDCl_3$, 100 MHz) $\delta = 197.82$, 162.53, 149.09, 143.17, 136.12, 122.99, 129.58, 125.27, 102.43, 96.34, 80.83, 71.47, 63.02, 17.41, 17.29, 17.25, 16.95, 16.89, 16.86, 16.77, 13.37, 13.07, 12.56, 12.51; FAB-HRMS calcd for $C_{27}H_{41}N_2O_7SeSi_2$ 641.1618; found 641.1615 $[M+H]^+$; elemental analysis calcd (%) for $C_{27}H_{40}N_2O_7SeSi_2$ (639.8): C 50.69, H 6.30, N 4.38: found: C 50.56, H 6.31, N 4.33.

Purification of 12a and 12b: a mixture of **12a** and **12b** (740 mg) was treated with hot AcOEt/hexane to give pure **12b** as white crystals (620 mg, M.p. 159.5–160.5 °C). The filtrate was then evaporated and triturated with AcOEt/hexane to give pure **12a** as a white powder (30 mg). **12a**: ^{1}H NMR ($CDCl_3$, 500 MHz) $\delta = 8.27$ (d, $J = 8.3$ Hz, 1H), 8.08 (br s, D_2O exchangeable, 1H), 7.59 (m, 2H), 7.45 (m, 1H), 7.37 (m, 2H), 5.76 (dd, $J = 8.3$ Hz, 1.2, 1H), 4.64 (d, $J = 9.1$ Hz, 1H), 4.52 (ddd, $J = 9.1$, 4.8, 3.0 Hz, 1H), 3.93 (dd, $J = 12.7$, 3.0 Hz, 1H), 3.67 (dd, $J = 12.7$, 4.8 Hz, 1H), 1.13–0.95 (m, 28H); FAB-HRMS calcd for $C_{27}H_{41}N_2O_7SeSi_2$: 641.1618; found 641.1661 $[M+H]^+$. **12b**: ^{1}H NMR ($CDCl_3$, 500 MHz) $\delta = 8.46$ (br s, D_2O exchangeable, 1H; N3-H), 7.49 (m, 2H; *o*-SePh), 7.39 (m, 1H; *p*-SePh), 7.27 (m, 2H; *m*-SePh), 6.95 (d, $J = 8.3$ Hz, 1H; H6), 6.48 (s, D_2O exchangeable, 1H; 2′OH), 5.35 (dd, $J = 8.3$, 2.3 Hz, 1H; H5), 4.84 (d, $J = 7.8$ Hz, 1H; H3′), 4.21 (dd, $J = 12.9$ Hz, 7.0, 1H; H5′a), 4.06–4.04 (m, 2H; H4′, H5′b), 3.92 (s, D_2O exchangeable, 1H; O2′H), 1.20–1.01 (m, 28H; isopropyl ×4); NOE (400 MHz, $CDCl_3$): irradiated H5′, observed *o*-SePh (5.8%), H3′ (6.6%); ^{13}C NMR ($CDCl_3$, 125 MHz) $\delta = 162.83$, 150.36, 139.66, 138.58, 129.63, 128.84, 125.69, 103.52, 100.49, 100.14, 83.72, 75.64, 62.69, 17.51, 17.47, 17.45, 17.29, 17.01, 17.00, 16.79, 16.76, 13.41, 13.14, 12.82, 12.44; FAB-HRMS calcd for $C_{27}H_{42}N_2O_8SeSi_2Na$: 681.1543; found 681.1567 $[M+Na]^+$.

1-[1-*C*-Phenylseleno-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-*ribo*-pentofuranosyl]uracil (13): A mixture of $CeCl_3 \cdot 7H_2O$ (7.45 g, 20.0 mmol) and $NaBH_4$ (454 mg, 12.0 mmol) in MeOH (40 mL) was stirred at −70 °C for 1 h. A solution of **11** (6.40 g, 10.0 mmol) in MeOH (55 mL) was added to the resulting solution, and the mixture was stirred at the same temperature for 10 min. After addition of aqueous tartaric acid (5%, 10 mL), the mixture was warmed to room temperature and partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (hexane/AcOEt 3:1) to give **13** as a white foam. Yield: 5.80 g, 90%; ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta = 8.39$ (br s, D_2O exchangeable, 1H; N3-H), 7.48 (m, 2H; *o*-SePh), 7.36 (m, 1H; *p*-SePh), 7.23 (m, 2H; *m*-SePh), 7.06 (d, $J = 8.6$ Hz, 1H; H6), 5.20 (d, $J = 8.6$ Hz, 1H; H5), 4.62 (dd, $J = 6.6$, 2.0 Hz, 1H; H2′), 4.33 (ddd, $J = 8.6$, 2.6, 2.6 Hz, 1H; H4′), 4.23 (dd, $J = 8.6$, 6.6 Hz, 1H; H3′), 4.13 (dd, $J = 13.2$, 2.6 Hz, 1H; H5′a), 4.11 (dd, $J = 13.2$, 2.6 Hz, 1H; H5′b), 3.71 (br s, D_2O exchangeable, 1H; 2′OH), 1.08–0.85 (m, 28H; isopropyl ×4); NOE (400 MHz, $CDCl_3$): irradiated H6, observed H5′ (1.1%), H3′ (1.6%), H2′ (0.2%); ^{13}C NMR ($CDCl_3$, 100 MHz) $\delta = 163.18$, 148.98, 139.21, 138.53, 129.45, 128.81, 125.86, 106.59, 100.11, 80.16, 75.53, 68.55, 59.75, 17.34, 17.20, 16.98, 16.91, 16.79, 13.39, 13.19, 12.98, 12.62, 12.40; FAB-HRMS calcd for $C_{27}H_{43}N_2O_7SeSi_2$ 643.1774; found 643.1800 $[M+H]^+$; elemental analysis calcd (%) for $C_{27}H_{42}N_2O_7SeSi_2 \cdot H_2O$ (659.8): C 49.15, H 6.72, N 4.25; found C 49.25, H 6.43, N 4.25.

1-[1-*C*-Phenylseleno-2-*O*-dimethylvinylsilyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-*ribo*-pentofuranosyl]uracil (14): A mixture of **13** (642 mg, 1.0 mmol), DMAP (25 mg, 0.20 mmol), Et_3N (881 μL, 6.3 mmol), and chlorodimethylvinylsilane (828 μL, 6.0 mmol) in toluene (5 mL) was stirred at room temperature for 30 min. After addition of MeOH (0.5 mL) at 0 °C, the resulting mixture was stirred at room temperature for 10 min and partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography ($CHCl_3$/AcOEt 8:1 then 4:1) to give **14** as a white foam. Yield: 705 mg, 97%; ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta = 7.84$ (br s, D_2O exchangeable, 1H), 7.51 (d, $J = 7.9$ Hz, 1H), 7.35–7.17 (m, 5H), 6.34 (dd, $J = 20.4$, 14.3 Hz, 1H), 6.08 (dd, $J = 14.3$, 4.0 Hz, 1H), 5.90 (dd, $J = 20.4$, 4.0 Hz, 1H), 5.13 (dd, $J = 7.9$, 2.0 Hz, 1H), 5.06 (d, $J = 4.0$ Hz, 1H), 4.34 (d, $J = 9.2$ Hz, 1H), 4.20 (d, $J = 13.8$ Hz, 1H), 4.01–3.93 (m, 2H), 1.08–0.81 (m, 28H), 0.40 (s, 3H), 0.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) $\delta =$ 163.22, 148.18, 139.62, 138.21, 137.28, 133.49, 129.29, 128.66, 126.17, 104.78, 99.51, 80.67, 77.39, 68.32, 58.71, 17.46, 17.32, 17.15, 17.08, 17.06, 16.91, 13.47, 13.05, 12.89, 12.73, −1.16, −1.22; FAB-HRMS calcd for $C_{31}H_{51}N_2O_7SeSi_3$ 727.2170; found 727.2187 $[M+H]^+$; elemental analysis calcd (%) for $C_{31}H_{50}N_2O_7SeSi_3$ (726.0): C 51.29, H 6.94, N 3.86; found C 51.24, H 6.98, N 3.85.

Radical reaction of 14 under reductive conditions: A solution of **14** (44 mg, 0.060 mmol), nBu$_3$SnH or (TMS)$_3$SiH (0.18 mmol), and AIBN (3 mg, 0.015 mmol) or V-70 (6 mg, 0.018 mmol) in benzene or CH_2Cl_2 (0.6 mL) was stirred at 60 °C or at 0 °C. After **14** had disappeared, as shown by TLC, the solvent was evaporated, and the residue was purified by column chromatography ($CHCl_3$/AcOEt 20:1, 10:1, 5:1 then 1:1) to give **15α**, **16**, **17**, and **18**, respectively, in a pure form. **15α**: ^{1}H NMR ($CDCl_3$, 500 MHz) $\delta =$ 9.05 (br s, 1H, D_2O exchangeable, N3-H), 7.39 (d, $J = 8.1$ Hz, 1H; H6), 6.11 (d, $J = 3.1$ Hz, 1H; H1′), 6.03–5.95 (m, 2H; CH=CH_2 and CH=CH$_2$), 5.75–5.67 (m, 1H; CH=CH$_2$), 5.71 (d, $J = 8.1$ Hz, 1H; H5), 4.43 (dd, $J = 3.5$, 3.1 Hz, 1H; H2′), 4.34 (dd, $J = 9.3$, 3.5 Hz, 1H; H3′), 4.15–4.09 (m, H5′a, 2H; H4′), 3.94 (dd, $J = 13.2$, 2.3 Hz, 1H; H5′b), 1.10–0.96 (m, 28H; isopropyl ×4), 0.14 (s, 3H; SiCH$_3$), 0.12 (s, 3H; SiCH$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) $\delta = 163.37$, 150.16, 141.83, 136.34, 133.99, 100.52, 85.74, 81.53, 72.70, 70.63, 59.69, 17.39, 17.29, 17.26, 17.14, 17.07, 17.03, 16.89, 13.57, 13.34, 13.03, 12.84, 12.71, −1.79, −1.84; FAB-HRMS calcd for $C_{25}H_{47}N_2O_7Si_3$ 571.2692; found 571.2706 $[M+H]^+$. **16**: ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta =$ 7.25 (br s, D_2O exchangeable, 1H; N3-H), 4.95 (dd, $J = 8.6$, 5.9 Hz, 1H; H3′), 4.69 (d, $J = 5.9$ Hz, 1H; H2′), 4.17–4.06 (m, 2H; H5′a, H6), 3.98 (dd, $J = 12.3$, 3.0 Hz, 1H; H5′b), 3.68 (m, 1H; H4′), 2.79 (dd, $J = 16.5$, 4.2 Hz, 1H; H5a), 2.39 (dd, $J = 16.5$, 13.1 Hz, 1H; H5b), 2.31 (ddd, $J = 12.7$, 8.6, 5.1 Hz, 1H; H7′a), 1.89 (dd, $J = 12.7$, 8.6 Hz, 1H; H6′), 1.49 (ddd, $J = 12.7$, 12.7, 10.5 Hz, 1H; H7′b), 1.14–0.97 (m, 28H; isopropyl ×4), 0.39 (s, 3H; SiCH$_3$), 0.30 (s, 3H; SiCH$_3$); NOE (400 MHz, $CDCl_3$) irradiated H6′, observed H6 (3.5%), H4′ (3.8%); FAB-HRMS calcd for $C_{25}H_{47}N_2O_7Si_3$: 571.2692; found 571.2702 $[M+H]^+$. **17**: ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta =$ 8.25 (br s, D_2O exchangeable, 1H; N3-H), 8.03 (d, $J = 8.3$ Hz, 1H; H6), 5.69 (dd, $J = 8.3$, 2.4 Hz, 1H; H5), 5.17 (d, $J = 3.3$ Hz, 1H; H2′), 4.22 (d, $J =$ 13.7 Hz, 1H; H5′a), 4.17 (dd, $J = 9.4$, 3.3 Hz, 1H; H3′), 4.00 (dd, $J = 9.4$, 2.3 Hz, 1H; H4′), 3.93 (dd, $J = 13.7$, 2.3 Hz, 1H; H5′b), 2.37 (q, $J = 7.3$ Hz, 1H; H6′), 0.91 (d, $J = 7.3$ Hz, 3H; H7′), 1.25–0.81 (m, 28H; isopropyl ×4), 0.39 (s, 3H; SiCH$_3$a), 0.26 (s, 3H; SiCH$_3$b); NOE (400 MHz, $CDCl_3$): irradiated H6′, observed H2′ (2.4%); FAB-HRMS calcd for $C_{25}H_{47}N_2O_7Si_3$ 571.2692; found 571.2695 $[M+H]^+$. For **18**: ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta = 8.00$ (d, $J = 8.5$ Hz, 1H), 7.91 (br s, D_2O exchangeable, 1H), 7.36–7.22 (m; SePh), 5.70 (dd, $J = 8.5$, 2.0 Hz, 1H), 5.03 (d, $J = 3.3$ Hz, 1H), 4.24 (d, $J = 13.6$ Hz, 1H), 4.11 (dd, $J = 9.2$, 3.3 Hz, 1H), 4.03 (dd, $J = 9.2$, 2.0 Hz, 1H), 3.94 (dd, $J = 13.6$, 2.0 Hz, 1H), 3.03 (dd, $J = 11.8$, 7.3 Hz, 1H), 2.95 (dd, $J = 11.8$, 8.9 Hz, 1H), 2.76 (dd, $J = 8.9$, 7.8 Hz, 1H), 1.08–0.97 (m, 28H), 0.44 (s, 3H), 0.32 (s, 3H); FAB-HRMS calcd for $C_{31}H_{51}N_2O_7SeSi_3$ 727.2170; found 727.2159 $[M+H]^+$.

1-[2-*O*-Dimethylvinylsilyl-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-*ribo*-pentofuranosyl]uracil (15β): Compound **15β** was obtained as

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a white foam from 1-[3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-ribofuranosyl]uracil (244 mg, 0.50 mmol, as a foam) as described for the synthesis of **14**, after purification by column chromatography (hexane/AcOEt 4:1). Yield: 285 mg, quant.; ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta = 8.83$ (br s, D_2O exchangeable, 1H; N3-H), 7.95 (d, $J = 7.9$ Hz, 1H; H6), 6.19 (dd, $J = 19.8$, 15.2 Hz, 1H; C*H*=CH_2), 6.03 (dd, $J = 15.2$, 4.6 Hz, 1H; CH=CH_2), 5.85 (dd, $J = 19.8$, 4.6 Hz, 1H; CH=CH_2), 5.66 (dd, $J = 7.9$, 2.0 Hz, 1H; H5), 5.61 (s, 1H; H1′), 4.25 (dd, $J = 13.9$ Hz, ca. 0, 1H; H5′a), 4.23–4.14 (m, 2H; H2′, H4′), 4.08 (dd, $J = 9.2$, 4.0 Hz, 1H; H3′), 3.97 (dd, $J = 13.9$, 2.0 Hz, 1H; H5′b), 1.10–1.00 (m, 28H; isopropyl × 4), 0.28 (s, 3H; $SiCH_3$), 0.27 (s, 3H; $SiCH_3$).

Radical atom-transfer cyclization and subsequent elimination:

Method A: A stirring solution of **14** (44 mg, 0.060 mmol) and an additive (0.006 mmol) in benzene (0.6 mL) was irradiated with a high-pressure mercury lamp (300 W) at room temperature for 4 h. The solvent was evaporated, and a mixture of the residue and H_2O_2 (30% in H_2O, 27 μL, 0.24 mmol) in THF (7 mL) was stirred at room temperature for 35 min. After addition of aqueous saturated $Na_2S_2O_3$ (100 μL), the mixture was partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography ($CHCl_3$/AcOEt 2:1, 1:1, 1:2, and AcOEt) to give a mixture of **19** and **20** (**19**/**20** = 1:5 based on the ^{1}H NMR). ^{1}H NMR ($CDCl_3$, 270 MHz) of the mixture. For **19**, $\delta = 8.45$ (br s, D_2O exchangeable, 1H), 7.99 (d, $J = 8.6$ Hz, 1H), 6.11 (dd, $J = 17.2$, 10.6 Hz, 1H), 5.68 (dd, $J = 8.6$, 2.0 Hz, 1H), 5.52 (dd, $J = 17.2$, 1.3 Hz, 1H), 5.38 (dd, $J = 10.6$, 1.3 Hz, 1H), 4.80 (d, $J = 4.0$ Hz, 1H), 4.29 (dd, $J = 9.2$, 4.6 Hz, 1H), 4.25 (d, $J = 13.2$ Hz, 1H), 4.16 (d, $J = 9.2$ Hz, 1H), 3.99 (dd, $J = 13.2$, 2.6 Hz, 1H), 2.79 (br s, 1H), 1.08–0.98 (m, 28H). For **20**, $\delta = 9.55$ (br s, D_2O exchangeable, 1H), 8.05 (d, $J = 7.9$ Hz, 1H), 6.52 (dd, $J = 17.2$, 10.6 Hz, 1H), 5.70 (dd, $J = 7.9$, 2.0 Hz, 1H), 5.40 (d, $J = 17.2$ Hz, 1H), 5.29 (d, $J = 10.6$ Hz, 1H), 5.04 (d, $J = 2.6$ Hz, 1H), 4.26 (dd, $J = 13.9$, 0.7 Hz, 1H), 4.16–4.15 (m, 2H), 3.96 (dd, $J = 13.9$, 2.0 Hz, 1H), 3.72 (br s, D_2O exchangeable, 1H), 1.08–0.96 (m, 28H), 0.24 (s, 3H), 0.20 (s 3H); FAB-HRMS of the mixture: calcd for $C_{23}H_{41}N_2O_7Si_2$ 513.2452; found 513.2447 ([*M*+H]$^+$ for **19**); calcd for $C_{25}H_{47}N_2O_8Si_3$ 587.2640; found 587.2639 ([*M*+H]$^+$ for **20**).

Method B: A stirring solution of **14** (1.02 g, 1.4 mmol) and $(PhSe)_2$ (0–1.4 mmol) in benzene (14 mL) was irradiated with a high-pressure mercury lamp (300 W) at room temperature for 4 h (Table 2 entry 8, 24 h). The solvent was evaporated, and a mixture of the residue and TBAF (1.0 M in THF, 7.0 mL, 7.0 mmol) was stirred at room temperature for 1 h. After the solvent was evaporated, a mixture of the residue, DMAP (32 mg, 0.26 mmol), Et_3N (1.95 mL, 14 mmol), and Ac_2O (1.32 mL, 14 mmol) in MeCN (10 mL) was stirred at room temperature for 70 min. After addition of MeOH (0.5 mL), the resulting solution was partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (hexane/AcOEt 1:1, 1:2, then 1:4) to give **21** as a white foam. ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta = 8.25$ (br s, D_2O exchangeable, 1H), 7.78 (d, $J = 8.6$ Hz, 1H), 6.28 (d, $J = 4.6$ Hz, 1H), 6.26 (dd, $J = 17.2$, 11.2 Hz, 1H), 5.70 (dd, $J = 8.6$ Hz, ca. 0, 1H), 5.53 (dd, $J = 17.2$, 1.3 Hz, 1H), 5.37 (dd, $J = 11.2$, 1.3 Hz, 1H), 5.33 (dd, $J = 7.3$, 4.6 Hz, 1H), 4.49 (m, 1H), 4.38 (dd, $J = 12.4$, 2.6 Hz, 1H), 4.27 (dd, $J = 12.4$, 4.0 Hz, 1H), 2.13 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) $\delta = 170.03$, 169.22, 168.63, 162.75, 149.62, 139.49, 131.78, 118.00, 101.61, 97.36, 79.81, 74.29, 69.76, 61.75, 20.79, 20.59, 20.47; FAB-HRMS calcd for $C_{17}H_{21}N_2O_9$: 397.1247; found 397.1252 [*M*+H]$^+$; elemental analysis calcd (%) for $C_{17}H_{20}N_2O_9 \cdot 0.8H_2O$ (410.8): C 49.71, H 5.30, N 6.82; found C 49.67, H 5.02, N 6.77.

1-(1-*C*-Ethenyl-β-D-*ribo*-pentofuranosyl)uracil (22): A mixture of **21** (198 mg, 0.50 mmol), Et_3N (2 mL, 15 mmol), and MeOH (3 mL) was stirred at room temperature for 90 h. The solvent was evaporated, and the residue was purified by column chromatography ($CHCl_3$/MeOH 15:1, 10:1 then 5:1) to give a solid. The solid was dissolved in H_2O, which was freeze-dried to give **22** as a white cotton. Yield: 84 mg, 62%; ^{1}H NMR ([D_6]DMSO, 400 MHz) $\delta = 11.13$ (br s, D_2O exchangeable, 1H; N3-H), 8.08 (d, $J = 8.2$ Hz, 1H; H6), 6.40 (dd, $J = 17.5$, 10.6 Hz, 1H; C*H*=CH_2), 5.51 (d, $J = 4.9$ Hz, 1H; 2′OH), 5.50 (d, $J = 8.2$ Hz, 1H; H5), 5.18 (dd, $J = 17.5$, 1.3 Hz, 1H; CH=CH_2), 5.18 (dd, $J = 10.6$, 1.3 Hz, 1H; CH=CH_2), 4.98 (t, $J = 5.5$ Hz, 1H; 5′-OH), 4.87 (d, $J = 6.6$ Hz, 1H; 3′-OH), 4.63 (dd, $J = 4.9$, 4.5 Hz, 1H; H2′), 3.95–3.84 (m, H4′, 2H; H3′), 3.73 (ddd, $J = 12.5$, 5.5, 2.3 Hz, 1H; H5′a), 3.50 (ddd, $J = 12.5$, 5.5, 4.6 Hz, 1H; H5′b); ^{13}C NMR ([D_6]DMSO, 100 MHz) $\delta = 163.45$, 150.32, 140.64, 134.77, 115.68, 99.90, 97.61, 83.56, 74.45, 68.65, 59.43; FAB-HRMS calcd for $C_{11}H_{15}N_2O_6$ 271.0930; found 271.0916 [*M*+H]$^+$; elemental analysis calcd (%) for $C_{11}H_{14}N_2O_6 \cdot 0.2H_2O$ (273.9): C 48.25, H,5.30, N 10.23; found C 48.04, H 5.31, N 10.10.

1-[2-*O*-Acetyl-1-*C*-ethenyl-3,5,-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-β-D-*ribo*-pentofuranosyl]uracil (23): A stirring solution of **14** (1.02 g, 1.4 mmol) and $(PhSe)_2$ (306 mg, 0.98 mmol) in benzene (14 mL) was irradiated with a high-pressure mercury lamp (300 W) at room temperature for 4 h, and then the solvent was evaporated. A mixture of the residue and H_2O_2 (30% in H_2O, 630 μL, 5.6 mmol) in THF (14 mL) was stirred at room temperature for 15 min, and then aqueous saturated $Na_2S_2O_3$ (1 mL) was added. The resulting mixture was partitioned between AcOEt and H_2O, and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. Saturated NH_3 in MeOH (10 mL) was added to a solution of the residue in MeOH (5 mL), and the mixture was stirred at room temperature for 1 h. After the solvent was evaporated, a mixture of the residue, DMAP (17 mg), Et_3N (390 μL, 2.8 mmol), and Ac_2O (264 μL, 2.8 mmol) was stirred at room temperature for 2.5 h. After addition of MeOH (0.3 mL), the resulting mixture was partitioned between AcOEt and H_2O, and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (hexane/AcOEt 3:1) to give **23** as a pale brown foam. Yield: 402 mg, 52%; ^{1}H NMR ($CDCl_3$, 270 MHz) $\delta = 8.40$ (br s, D_2O exchangeable, 1H), 7.97 (d, $J = 9.2$ Hz, 1H), 6.43 (dd, $J = 17.2$, 10.6 Hz, 1H), 6.17 (d, $J = 4.6$ Hz, 1H), 5.68 (d, $J = 9.2$ Hz, 1H), 5.53 (d, $J = 17.2$ Hz, 1H), 5.33 (d, $J = 10.6$ Hz, 1H), 4.33 (dd, $J = 9.9$, 4.6 Hz, 1H), 4.26 (d, $J = 13.2$ Hz, 1H), 4.08 (br d, $J = 9.9$ Hz, 1H), 3.98 (dd, $J = 13.2$, 2.0 Hz, 1H), 2.12 (s, 3H), 1.08–0.92 (m, 28H); FAB-HRMS calcd for $C_{25}H_{43}N_2O_8Si_2$ 555.2558; found 555.2557 [*M*+H]$^+$.

N^4-Acetyl-1-(2,3,5-tri-*O*-acetyl-1-*C*-ethenyl-β-D-*ribo*-pentofuranosyl)cytosine (24): A mixture of **23** (361 mg, 0.65 mmol), TPSCl (395 mg, 1.3 mmol), DMAP (159 mg, 1.3 mmol), and Et_3N (182 μL, 1.3 mmol) in MeCN (6 mL) was stirred at room temperature for 5 h. After addition of NH_3 (25% in H_2O, 6 mL), the resulting mixture was stirred at room temperature for 2.5 h and then partitioned between AcOEt and H_2O, and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. A mixture of the residue and TBAF (1.3 mL, 1.3 mmol, 1M) in THF (4 mL) was stirred at room temperature for 1 h, and then the solvent was evaporated. A mixture of the residue, DMAP (16 mg), Et_3N (906 μL, 6.5 mmol), and Ac_2O (613 μL, 6.5 mmol) in MeCN (6 mL) was stirred at room temperature for 12 h. After addition of MeOH (0.3 mL), the resulting mixture was partitioned between AcOEt and H_2O, and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography ($CHCl_3$, $CHCl_3$/MeOH 20:1 then 10:1) to give **24** as a white foam. Yield: 200 mg, 78%; ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta = 9.49$ (br s, D_2O exchangeable, 1H), 8.20 (d, $J = 7.7$ Hz, 1H), 7.40 (d, $J = 7.7$ Hz, 1H), 6.47 (dd, $J = 17.1$, 10.8 Hz, 1H), 6.32 (d, $J = 4.8$ Hz, 1H), 5.51 (d, $J = 17.1$ Hz, 1H), 5.33 (d, $J = 10.8$ Hz, 1H), 5.23 (dd, $J = 7.7$, 4.8 Hz, 1H), 4.50 (m, 1H), 4.39 (dd, $J = 13.0$, 2.4 Hz, 1H), 4.29 (dd, $J = 13.0$, 3.7 Hz, 1H), 2.27, 2.13 (each s, each 3H), 2.07 (s, 3H), 2.02 (s, 3H); FAB-HRMS calcd for $C_{19}H_{24}N_3O_9$ 438.1512; found 438.1487 [*M*+H]$^+$.

1-(1-*C*-Ethenyl-β-D-*ribo*-pentofuranosyl)cytosine (25): Saturated NH_3 in MeOH (2.5 mL) was added to a solution of **24** (198 mg, 0.5 mmol) in MeOH (3 mL) at 0 °C, and the resulting mixture was stirred at the same temperature for 30 min and at room temperature for 15 h. The solvent was evaporated, and the residue was purified by column chromatography ($CHCl_3$/MeOH 5:1, then 3:1) to give a solid. This solid was dissolved in H_2O, and the resulting solution was freeze-dried to give **25** as a white cotton. Yield: 76 mg, 80%; ^{1}H NMR ([D_6]DMSO, 400 MHz) $\delta = 8.00$ (d, $J = 7.3$ Hz, 1H, H6), 7.08 (br s, D_2O exchangeable, 1H; NH4), 7.02 (br s, D_2O exchangeable, 1H; NH4), 6.43 (dd, $J = 17.2$, 10.6 Hz, 1H; C*H*=CH_2), 5.65 (d, $J = 7.3$ Hz, 1H; H5), 5.55 (br s, 1H; OH), 5.07 (dd, $J = 10.6$, 1.8 Hz, 1H; CH=CH_2), 5.04 (dd, $J = 17.2$, 1.8 Hz, 1H; C*H*=CH_2), 4.88 (br s, total 2H; OH), 4.53 (d′, $J = 4.0$ Hz, 1H; H2), 3.95 (m, 1H; H4′), 3.86 (dd, $J = 5.9$, 4.0 Hz, 1H; H3′), 3.61 (dd, $J = 11.9$, 3.3 Hz, 1H; H5′a), 3.45 (dd, $J = 11.9$, 4.0 Hz, 1H; H5′b); ^{13}C NMR ([D_6]DMSO, 100 MHz) $\delta = 165.62$, 155.57, 141.35, 135.95, 114.59, 97.64, 92.78, 84.38, 75.44, 69.78, 60.21; FAB-HRMS calcd for $C_{11}H_{16}N_3O_5$ 270.1090; found 271.1095 [*M*+H]$^+$; elemental analysis calcd (%) for $C_{11}H_{15}N_3O_5 \cdot 0.8H_2O$ (283.7): C 46.58, H 5.90, N 14.81; found C 46.35, H 5.46, N 14.85.

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[1] S. Ichikawa, S. Shuto, N. Minakawa, A. Matsuda, *J. Org. Chem*. **1997**, *62*, 1368 – 1375, and references therein.

[2] a) K. Takenuki, A. Matsuda, T. Ueda, T. Sasaki, A. Fujii, K. Yamagami, *J. Med. Chem*. **1988**, *31*, 1063 – 1064; b) A. Matsuda, K. Takenuki, M. Tanaka, T. Sasaki, T. Ueda, *J. Med. Chem*. **1991**, *34*, 812 – 819; c) K. Yamagami, A. Fujii, M. Arita, T. Okumoto, S. Sakata, A. Matsuda, T. Ueda, *Cancer Res.* **1991**, *51*, 2319 – 2323; d) T. Ono, A. Fujii, M. Hosoya, T. Okumoto, S. Sakata, A. Matsuda, T. Sasaki, *Biochem. Pharmacol*. **1996**, *52*, 1279 – 1285.

[3] a) A. Matsuda, Y. Nakajima, A. Azuma, M. Tanaka, T. Sasaki, *J. Med. Chem*. **1991**, *34*, 2917 – 2919; b) A. Azuma, Y. Nakajima, N. Nishizono, N. Minakawa, M. Suzuki, K. Hanaoka, T. Kobayashi, M. Tanaka, T. Sasaki, A. Matsuda, *J. Med. Chem*. **1993**, *36*, 4183 – 4189; c) M. Tanaka, A. Matsuda, T. Terao, T. Sasaki, *Cancer Lett*. **1992**, *64*, 67 – 74; d) A. Azuma, K. Hanaoka, A. Kurihara, T. Kobayashi, S. Miyauchi, N. Kamo, M. Tanaka, T. Sasaki, A. Matsuda, *J. Med. Chem*. **1995**, *38*, 3391 – 3397; e) A. Matsuda, A. Azuma, *Nucleosides Nucleotides* **1995**, *14*, 461 – 471; f) K. Hanaoka, M. Suzuki, T. Kobayashi, F. Tanzawa, K. Tanaka, T. Shibayama, S. Miura, T. Ikeda, H. Iwabuchi, A. Nakagawa, Y. Mitsuhashi, M. Hisaoka, M. Kaneko, A. Tomida, Y. Wataya, T. Nomura, T. Sasaki, A. Matsuda, T. Tsuruo, S. Kurakata, *Int. J. Cancer* **1999**, *82*, 226 – 236.

[4] a) A. Matsuda, H. Hattori, M. Tanaka, T. Sasaki, *Bioorg. Med. Chem. Lett*. **1996**, *6*, 1887 – 1892; b) S. Tabata, M. Tanaka, A. Matsuda, M. Fukushima, T. Sasaki, *Oncology Rep*. **1996**, *3*, 1029 – 1034; c) H. Hattori, M. Tanaka, M. Fukushima, T. Sasaki, A. Matsuda, *J. Med. Chem*. **1996**, *39*, 5005 – 5011; d) H. Hattori, E. Nozawa, T. Iino, Y. Yoshimura, S. Shuto, Y. Shimamoto, M. Nomura, M. Fukushima, M. Tanaka, T. Sasaki, A. Matsuda, *J. Med. Chem*. **1998**, *41*, 2892 – 2902; e) S. Takatori, H. Kanda, K. Takenaka, Y. Wataya, A. Matsuda, M. Fukushima, Y. Shimamoto, M. Tanaka, T. Sasaki, *Cancer Chemother. Pharmacol*. **1999**, *44*, 97 – 104.

[5] a) M. Nomura, S. Shuto, M. Tanaka, T. Sasaki, S. Mori, S. Shigeta, A. Matsuda, *J. Med. Chem*. **1999**, *42*, 2901 – 2908; b) I. Sugimoto, S. Shuto, S. Mori, S. Shigeta, A. Matsuda, *Bioorg. Med. Chem. Lett*. **1999**, *9*, 385 – 388.

[6] H. Yüntsen, K. Ohkuma, Y. Ishii, *J. Antibiot*. **1956**, *9A*, 195 – 201.

[7] a) M. Nakajima, K. Itoi, Y. Y. Takamatsu, T. Kinoshita, T. Okazaki, Kawakubo, M. Shindo, T. Honma, M. Tohjigamor, T. Haneishi, *J. Antibiot*. **1991**, *44*, 293 – 300; b) H. Haruyama, T. Takayama, T. Kinoshita, M. Kondo, M. Nakajima, T. Haneishi, *J. Chem. Soc. Perkin Trans. 1* **1991**, 1637 – 1640; c) S. Mio, H. Sano, M. Shindo, T. Honma, S. Sugai, *Agric. Biol. Chem*. **1991**, *55*, 1105 – 1109.

[8] For examples see: a) K. Mahmood, A. Vasella, B. Bernet, *Helv. Chem. Acta* **1991**, 74, 1555 – 1584; b) R. D. Elliott, S. Niwas, J. M. Riordan, J. A. Montgomery, J. A. Secrist III, *Nucleosides Nucleotides* **1992**, *11*, 97 – 119; c) V. Faivre-Buet, A. Grouiller, G. Descotes, *Nucleosides Nucleotides* **1992**, *11*, 1651 – 1660; d) V. Uteza, G.-H. Chen, J. L.-Q. Toui, G. Descotes, B. Fenet, G. Gouiller, *Tetrahedron* **1993**, *34*, 8579 – 8588; e) H. Hayakawa, M. Miyazawa, H. Tanaka, T. Miyasaka, *Nucleosides Nucleotides* **1994**, *13*, 297 – 308.

[9] 2′-Deoxy-1′-pivaloyluridine proved useful for producing a radical at the 1′-position of 2′-deoxyuridine residue in oligonucleotides. This system was applied to studying the mechanism of oxidative damage to DNA: J. -T. Hwang, M. M. Greenberg, *J. Am. Chem. Soc.* **1999**, *121*, 4311 – 4315, and references therein.

[10] 2′-Deoxy-1′-modified uridines have been synthesized from uridine by electrophilic addition reactions on 1′,2′-unsaturated uridine derivatives: Y. Itoh, K. Haraguchi, H. Tanaka, E. Gen, T. Miyasaka, *J. Org. Chem*. **1995**, *60*, 656 – 662.

[11] a) H. Nishiyama, T. Kitajima, M. Matsumoto, K. Itoh, *J. Org. Chem*. **1984**, *49*, 2298 – 2300; b) G. Stork, M. Kahn, *J. Am. Chem. Soc.* **1985**, *107*, 500 – 501; c) E. Magnol, M. Malacria, *Tetrahedron Lett*. **1986**, *27*, 2255 – 2256; d) M. Koreeda, I. A. George, *J. Am. Chem. Soc.* **1986**, *108*, 8098 – 8100; e) K. Tamao, K. Maeda, T. Yamaguchi, Y. Ito, *J. Am. Chem. Soc.* **1989**, *111*, 4984 – 4985; f) R. D. Walkup, R. R. Kane, N. U. Obeyesekere, *Tetrahedron Lett*. **1990**, *31*, 1531 – 1534; g) M. Koreeda, L. G. Hamann, *J. Am. Chem. Soc.* **1990**, *112*, 8175 – 8177; h) A. G. Myers, D. Y. Gin, K. L. Widdowson, *J. Am. Chem. Soc.* **1991**, *113*, 9661 – 9663; i) J. H. Hutchinson, T. S. Daynard, J. W. Gillard, *Tetrahedron Lett*. **1991**, *32*, 573 – 576; j) W.-J. Koot, R. van Ginkel, M. Kranenburg, H. Hiemstra, S. Louwrier, M. J. Moolenaar, W. N. Speckamp, *Tetrahedron Lett*. **1991**, *32*, 401 – 404; k) G. Stork, H. S. Suh, G. Kim. *J. Am. Chem. Soc.* **1991**, *113*, 7054 – 7056; l) Z. Xi, P. Agback, J. Plavec, A. Sandstrom, J. B. Chattopadhyaya, *Tetrahedron* **1992**, *58*, 349 – 370; m) A. Martinez-Grau, D. P. Curran, *J. Org. Chem*. **1995**, *60*, 8332 – 8333; n) M. Bols, T. Skrydstrup, *Chem. Rev.* **1995**, *95*, 1253 – 1277; o) L. Fensterbark, M. Malacria, S. M. Sieburth, *Synthesis* **1997**, 813 – 854; p) H. Abe, S. Shuto, A. Matsuda, A. *Tetrahedron Lett*. **2000**, *41*, 2391 – 2394; q) S. Shuto, M. Terauchi, Y. Yahiro, H. Abe, S. Ichikawa, A. Matsuda, *Tetrahedron Lett*. **2000**, *41*, 4151 – 4155; r) H. Abe, S. Shuto, A. Matsuda, A. *J. Org.Chem*. **2000**, *65*, 4315 – 4325.

[12] a) S. Shuto, M. Kanazaki, S. Ichikawa, A. Matsuda, *J. Org. Chem*. **1997**, *62*, 5676 – 5677; b) S. Shuto, M. Kanazaki, S. Ichikawa, N. Minakawa, A. Matsuda, *J. Org. Chem*. **1998**, *63*, 746 – 754; c) Y.Ueno, Y. Nagasawa, I. Sugimoto, N. Kojima, M. Kanazaki, S. Shuto, A. Matsuda, *J. Org. Chem*. **1998**, *63*, 1660 – 1667; d) I. Sugimoto, S. Shuto, A. Matsuda, *J. Org. Chem*. **1999**, *64*, 7153 – 7157; e) Y. Yahiro, S. Ichikawa, S. Shuto, A. Matsuda, *Tetrahedron Lett*. **1999**, *40*, 5527 – 5531; f) I. Sugimoto, S. Shuto, A. Matsuda, *Synlett* **1999**, 1766 – 1768; g) S. Shuto, I. Sugimoto, H. Abe, A. Matsuda, *J. Am. Chem. Soc*. **2000**, *122*, 1343 – 1351; h) M. Kanazaki, Y. Ueno, S. Shuto, A. Matsuda, *J. Am. Chem. Soc.* **2000**, *122*, 2422 – 2432; i) S. Shuto, Y. Yahiro, S. Ichikawa, A. Matsuda, *J. Org. Chem*. **2000**, *65*, 5547 – 5557.

[13] K. Tamao, N. Ishida, M. Kumada, *J. Org. Chem*. **1983**, *48*, 2120 – 2122.

[14] B. Giese, P. Erdmann, T. Schafer, U. Schwitter, *Synthesis* **1994**, 1310 – 1312.

[15] A preliminary account of enolization of 2′-ketouridine derivatives has appeared: T. Kodama, S. Shuto, M. Nomura, A. Matsuda, *Tetrahedron Lett*. **2000**, *41*, 3643 – 3646.

[16] T. Ueda, S. Shuto, H. Inoue, *Nucleosides Nucleotides* **1984**, *3*, 173 – 182.

[17] See refs. [2a,b, 3a,b], and references therein.

[18] It included a trace of an inseparable, unknown compound, which might be the corresponding α-anomer.

[19] The 3′-lithium enolate of a 3′-deoxy-2′-ketouridine derivative has been reported: K. Haraguchi, H. Tanaka, Y. Itoh, T. Miyasaka, *Tetrahedron Lett*. **1991**, *32*, 777 – 780.

[20] When 3′,5′-bis-*O*-TBS-2′-ketouridine was treated under conditions identical to those in entry 3, it gave a mixture of 1′α- and 1′β-phenylseleno products in a ratio of about 1:1 in 56% yield. Although we also tried to use 3′,5′-*O*-di-*tert*-butylsilene-2′-ketouridine as the substrate, it was too unstable to be obtained in pure form.

[21] The 1′-phenylseleno group is likely to be replaced by lithium in the presence of an excess of LiHMDS, since the substrate **8** was obtained in 90% yield when **11** was treated again with LiHMDS (4 equiv) at $< -70\,^{\circ}C$ in THF.

[22] Introduction of carbon substituents at the 1′-position via the enolate **9** was examined, but it was unsuccessful.

[23] J. -L. Luche, *J. Am. Chem. Soc.* **1978**, *100*, 2226 – 2227.

[24] The reduction of a 1′α-methoxycarbonylethyl-2′-ketouridine derivative, synthesized from D-fructose, with $NaBH_4$ has been reported, in which the corresponding *arabino*- and *ribo*-type products were obtained in a ratio of 1:5 in 87% yield: a) Y. Yoshimura, T. Ueda, A. Matsuda, *Tetrahedron Lett*. **1991**, *32*, 4549 – 4552; b) Y. Yoshimura, B. A. Otter, T. Ueda, A. Matsuda, *Chem. Pharm. Bull*. **1992**, *40*, 1761 – 1769.

[25] For examples see: a) D. P. Curran, C.-T. Chang, *Tetrahedron Lett*. **1987**, *28*, 2477 – 2480; b) D. P. Curran, E. Bosch, J. Kaplan, M. Newcomb, *J. Org. Chem*. **1989**, *54*, 1826 – 1831; c) D. P. Curran, C.-T. Chang, *J. Org. Chem*. **1989**, *54*, 3140 – 3157; d) L. Belvisi, C. Gennari, G. Poli, C. Scolastico, B. Salom, M. Vassallo, *Tetrahedron* **1992**, *48*, 3945 – 3960.

[26] A. Matsuda, H. Okajima, A. Masuda, A. Kakefuda, Y. Yoshimura, T. Ueda, *Nucleosides Nucleotides* **1992**, *11*, 197 – 226.

[27] The side-chain carbons at the 1′-position were numbered 6′ and 7′ for NMR assignments.

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  0947-6539/01/0711-2340 $ 17.50+.50/0