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Radical-mediated furanose ring reconstruction from 2′,3′-*seco*-uridine

Hiroki Kumamoto,[a] Junko Ogamino,[a] Hiromichi Tanaka,[a,*] Hisaki Suzuki,[a] Kazuhiro Haraguchi,[a] Tadashi Miyasaka,[a] Tsutomu Yokomatsu[b] and Shiroshi Shibuya[b]

[a]*School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan*
[b]*School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan*

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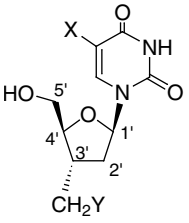
Abstract—Starting from 5′-*O*-trityl-2′,3′-*seco*-uridine, reconstruction of a furanose structure was carried out by the following sequence of reactions: (1) regioselective introduction of a phenylselenenyl group to the 2′-position of the 2′,3′-*seco*-uridine, (2) oxidation and subsequent Wittig reaction of the 3′-hydroxyl group and (3) intramolecular radical reaction (5-*exo-trig* ring closure) leading to 3′-*C*-carbon-substituted 2′,3′-dideoxyuridine. Also studied is the Pummerer reaction of the 2′-phenylseleno derivative of 2′,3′-*seco*-uridine. The resulting product, an α-(acyloxy)phenylselenide, also serves as a substrate for the radical cyclization to allow the introduction of a hydroxyl group at the 2′-position of the reconstructed furanose ring.

1. Introduction

3′-*C*-Branched 2′,3′-dideoxyribonucleosides of general structure **1** have attracted much attention due to their structural similarity to the anti-HIV agent AZT (3′-azido-3′-deoxythymidine) as well as their usefulness as building blocks of nuclease-resistant antisense oligonucleotides.[1] Syntheses of **1** have been accomplished by initial construction of sugar structures which were then condensed with nucleobases,[2] or by radical-mediated 3′-*C*-allylation of 2′-deoxyuridine or thymidine derivatives.[3]



1 X = H, Me
Y = CH=CH$_2$, C≡CH, CN, CO$_2$R, PO(OR)$_2$

The latter method, by further manipulation of the 3′-*C*-allyl group, allowed the preparations of 3′-*C*-cyanomethyl and 3′-*C*-propargyl derivatives.[4] An additional unique approach to **1** (X=Me, Y=CO$_2$Et) utilizing 5′-*O*-protected 2′,3′-*seco*-(ribofuranosyl)thymine (**2**) has been reported by Chattopadhyaya et al. (Scheme 1).[5] In this approach, the 2′-*O*-silyl derivative **3** was separated from **4** and **5**, and was then converted to the radical precursor **8** which underwent a highly diastereoselective 5-*exo-trig* ring closure leading to **9**.

In 1988, we reported that a phenylselenide anion prepared by reducing (PhSe)$_2$ with LiAlH$_4$ serves as a highly efficient species for the introduction of a phenylselenenyl group to the 2′-position, through cleavage of the anhydro bond of O^2,2′-cyclouridine.[6] We anticipated that the regioselective preparation of the 2′-phenylselenenyl-2′,3′-*seco*-uridines would be possible starting with a readily accessible O^2,2′-cyclo derivative of 2′,3′-*seco*-uridine, and that such compounds, upon radical cyclization, would give **1** as reported by Chattopadhyaya et al.

In the present study, the regioselective introduction of a phenylselenenyl group to the 2′-position of 2′,3′-*seco*-uridine and the radical-mediated reconstruction of the furanose ring were studied in detail. The choice of phenylselenenyl group is not only as a precursor of a simple 2′-alkyl radical but also due to its possibility to undergo a Pummerer reaction, the product of which would permit generation of an α-acyloxyalkyl radical.

2. Preparation of substrates for radical reaction

The 2′,3′-*seco*-uridine **10**, prepared from 5′-*O*-trityluridine, was converted to the O^2,2′-cyclo derivative **11** according to the published procedure.[7] Preparation of **12** by selective ring opening of **11** was then examined (Scheme 2).

Keywords: nucleosides; radicals and radical reactions; selenium and compounds; steric and strain effects.
* Corresponding author. Tel.: +81-3-3784-8186; fax: +81-3-3784-8252; e-mail: hirotnk@pharm.showa-u.ac.jp

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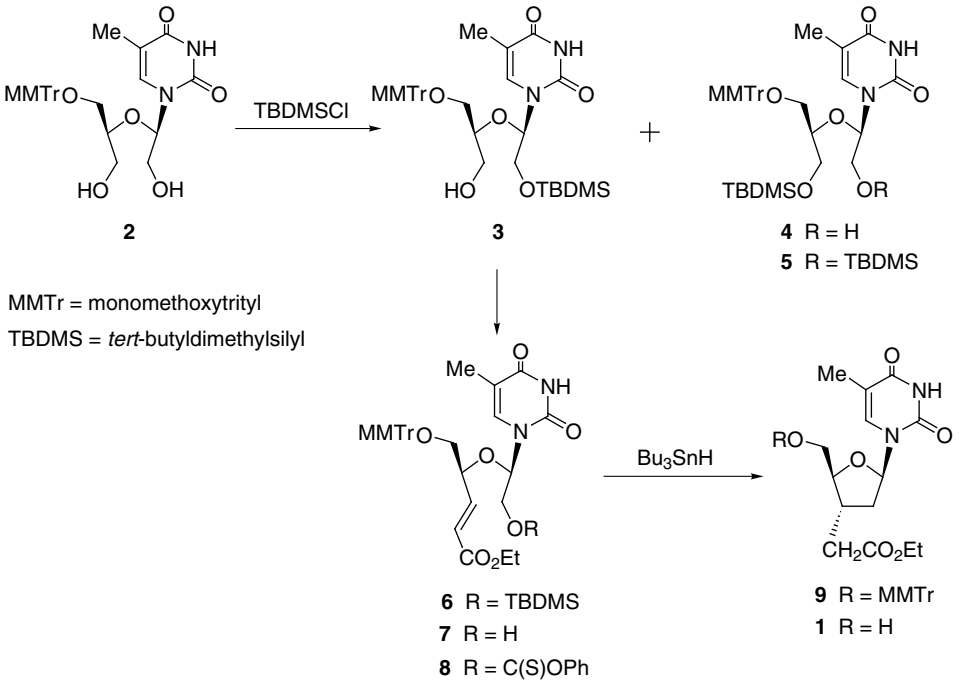
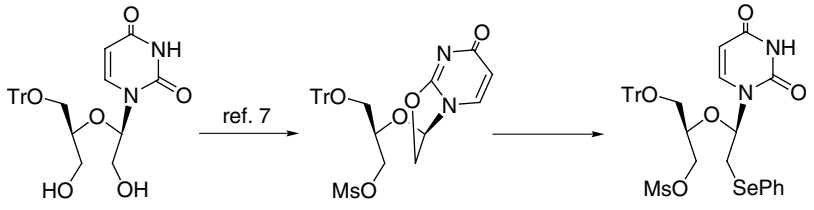


2 **3** **4** R = H, **5** R = TBDMS

6 R = TBDMS, **7** R = H, **8** R = C(S)OPh

9 R = MMTr, **1** R = H

Scheme 1.



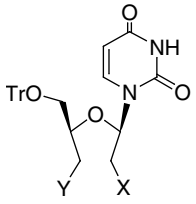
10 **11** **12**

Scheme 2.

When sodium benzeneselenolate, prepared from Na and $(PhSe)_2$ in THF in the presence of 18-crown-6,[8] was reacted with **11** (room temperature, for 19 h), several products (**13**, 3%; **14**, 5%; **15**, 5%) were formed in addition to **12** (7%) and the recovered **11** (44%). The formation of **13** and **14**[7] is a likely consequence of aryl-*O*-fission of the O^2,2′-anhydro bond which yields 2-phenylseleno-4-pyrimidone intermediate that could be hydrolyzed during work-up. The reaction of **11** with a selenide anion generated by reducing $(PhSe)_2$ with $NaBH_4$ in EtOH–THF[9] (room temperature, for 16 h) improved the yield of **12** (49%), but again a considerable amount of **11** (26%) was recovered together with a by-product **16** (6%).

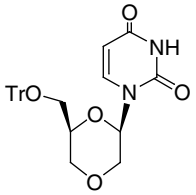
In contrast to these results, when phenylselenide anion derived from $(PhSe)_2/LiAlH_4/THF$[6] was used, the desired **12** was obtained exclusively in 94% yield. This reaction is completed within 15 min at −20°C, which also contrasts with the above two examples. Compound **12** was converted to the 3′-hydroxyl derivative **17** by treatment with NaOAc in 5% aqueous DMF (100°C for 3 h, 93%) followed by NH_3/MeOH (room temperature for 42 h, 97%).

To introduce radical-acceptors to the 3′-position, oxidation of **17** under several conditions and subsequent Wittig reaction with Ph_3PCHCO_2Me were examined (Scheme 3). When the Swern oxidation[10] was applied, the desired **18** (32%) was accompanied by its 4′-epimer **19** (14%), presumably due to Et_3N which was used for quenching the oxidation. The use of $(i\text{-}Pr)_2NEt$ prevented the formation of **19**; however, poor reproducibility of the yield of **18** (37–69%) led us to examine two other oxidation methods, the



13 X = OH, Y = OMs

16 X = Y = SePh



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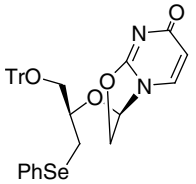

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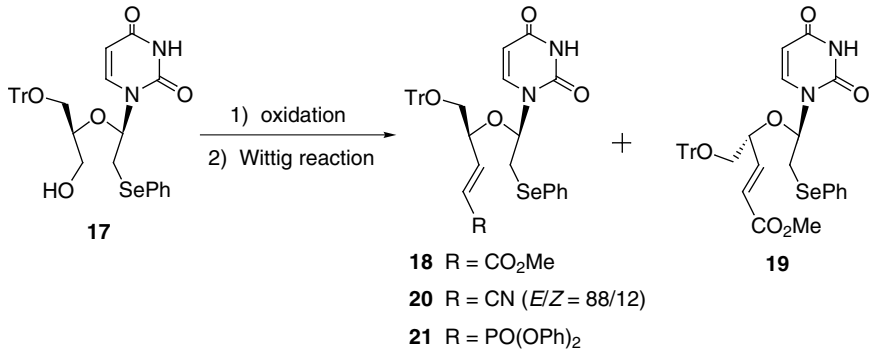


Scheme 3.

Pfitzner–Moffatt oxidation[11] and the Dess–Martin oxidation.[12] Although both methods gave more than 70% yield of **18** without epimerization at the 4′-position, the latter method appeared to be superior due to its simplicity of work-up procedure.

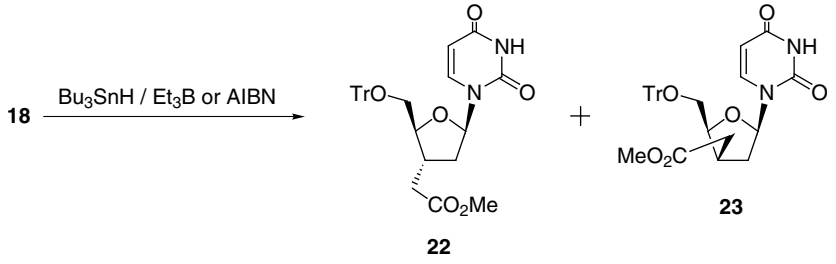
Thus, when the 3′-aldehyde obtained by the Dess–Martin oxidation of **17** was reacted in CH_3CN with Ph_3PCHCO_2Me, **18** was obtained in 73% isolated yield. The (*E*)-configuration of **18** was confirmed by ^1H NMR spectroscopy (*J*-value of the olefinic protons: 15.9 Hz). Occasionally, a small amount (<1–3%) of the (*Z*)-isomer (*J*-value of the olefinic protons: 11.8 Hz) was observed in **18**. The same reaction sequence was applied to the preparation of **20** (76%, *E*/*Z*=88:12) and **21** (44%).

3. Reconstruction of furanose ring by radical cyclization

By using **18** as a substrate, reconstruction of the furanose ring leading to 2′,3′-dideoxy-3′-*C*-carbon-substituted uridine was investigated (Scheme 4). The radical-mediated cyclization, carried out by adding a mixture of Bu_3SnH and AIBN via a motor-driven syringe, proceeded in 5-*exo*-*trig* manner in high yield with a high diastereoselectivity (**22**/**23**), irrespective of the reaction temperature (Table 1).[13] Although the reaction time varies significantly depending on the temperature, no detectable amount of reduced product was formed in all entries. The highly efficient cyclization observed here is certainly due to the nucleophilic character[14] of the 2′-alkyl radical, which favors reaction with electron-deficient olefins.

As pointed out by Chattopadhyaya et al.,[5] the observed dominant formation of the *erythro* isomer **22** would be explicable based on the fact that the radical species involved in this reaction is a '2,4-*cis*-disubstituted 5-hexenyl radical'[15] and, thus, both substituents (uracil base and 4′-CH_2OTr) would favor pseudo-equatorial positions (conformer **A** in Fig. 1) in the transition state that resembles the chair form of cyclohexane. An additional factor working here in disfavor of **B** may be a 1,3-allylic strain[16] between the vinylic hydrogen alpha to the methoxycarbonyl group and the 4′-CH_2OTr substituent. To see which substituent (uracil base or 4′-CH_2OTr) is more demanding in the pseudo-equatorial position, the cyclization of the (4′*R*)-epimer **19** was also carried out under the conditions of entry 4 in Table 1.

As shown in Scheme 5, the reaction of **19** not only gave the simple furanose-reconstructed products, **24** (51%) and **25** (21%),[17] but also the 6,3′-methano derivative **26** (7%: as a



Scheme 4.

Table 1. Radical-mediated cyclization of **18**

Entry	Reagents (equiv.)	Solvent	Temperature (°C)	Time (h)	Yield (%)	Ratio of **22**/**23**
1	Bu_3SnH (1.5), Et_3B (1.2)	Benzene	rt	68	84	97:3
2	Bu_3SnH (1.5), Et_3B (1.2)	Benzene	50	28	80	98:2
3	Bu_3SnH (2.0), AIBN (0.2)	Benzene	80	20	90	97:3
4	Bu_3SnH (1.5), AIBN (0.1)	Toluene	110	1	92	97:3

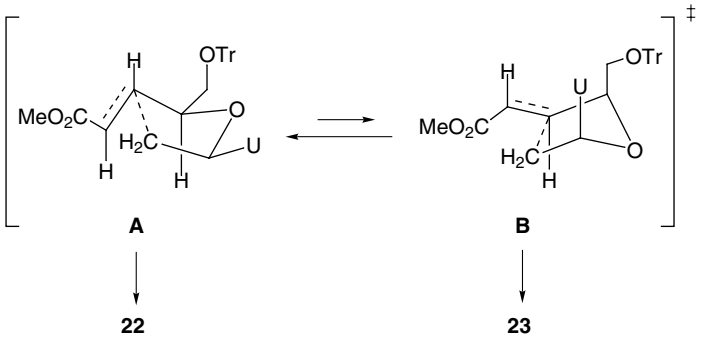
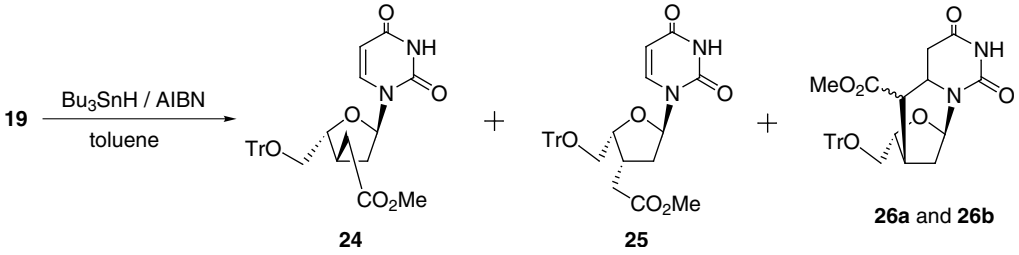


Figure 1. Transition structures of the radical derived from **18**.



Scheme 5.

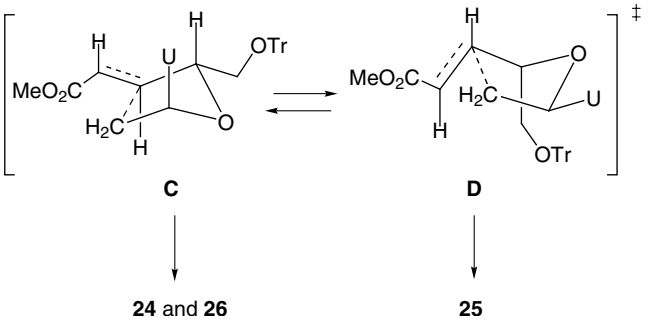
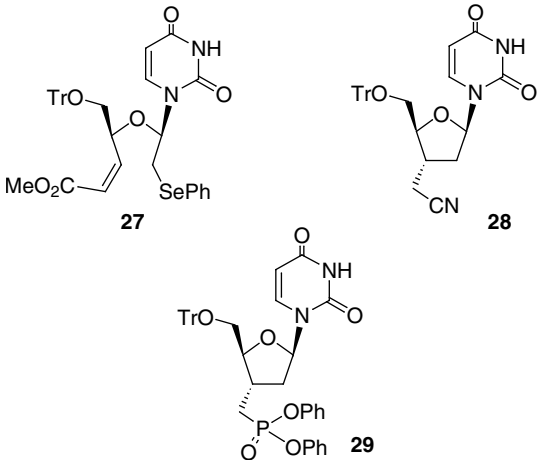


Figure 2. Transition structures of the radical derived from **19**.

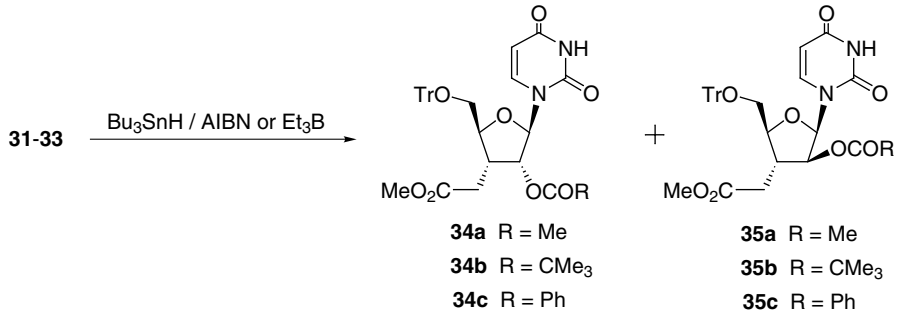
mixture of two diastereomers).[18] One could say that the transition state conformation **C** (Fig. 2) is preferred simply because the 4′-CH_2OTr group is more bulky than the base moiety. However, the observed stereochemical outcome may also be explicable in terms of 1,3-allylic strain: in the conformer **D**, an unfavorable disposition of the vinylic hydrogen and the 4′-CH_2OTr results, as was seen in the conformer **B** in Fig. 1.

We next examined the influence of the configuration of the olefinic structure. Oxidation of **17** with DMSO–DCC followed by the Horner–Emmons reaction employing LHMDS and $(CF_3CH_2O)_2P(O)CH_2CO_2Me$[19] gave a mixture of **18** and its (*Z*)-isomer **27** (total yield 74%, *E*/*Z*=1.0:4.6).

The desired (*Z*)-isomer **27** was isolated by HPLC purification of the mixture. When **27** was subjected to the radical reaction under the conditions of entry 4 in Table 1, almost the same results as the case of **18** were obtained (93% yield, ratio of **22**/**23**=99:1). However, when the reaction of **27** was carried out in benzene at room temperature, the cyclized product **22**[20] was obtained only in 35% yield after 68 h, which contrasts with the case of **18** (entry 1 in Table 1). TLC analysis (hexane/EtOAc=2:3) of the reaction mixture showed that, in addition to **22** (35% yield, R_f 0.19) and the starting material **27** (29% yield, R_f 0.43), an additional product (R_f 0.49) was formed in this reaction. The ^1H NMR spectrum of this product confirmed its structure to be the (*E*)-isomer **18** (18% yield). It is conceivable, therefore, that the radical-mediated isomerization of **27** to **18** is a slow process and that the cyclization of **27** takes place at least in part through **18**.[21]



The cyclization of other substrates **20** and **21** under the optimized reaction conditions (entry 4 in Table 1) also gave the corresponding furanose-reconstructed products **28** (93% yield, *erythro*/*threo*=97:3) and **29** (95% yield, *erythro*/*threo*=99:1), respectively, in a highly diastereoselective manner.

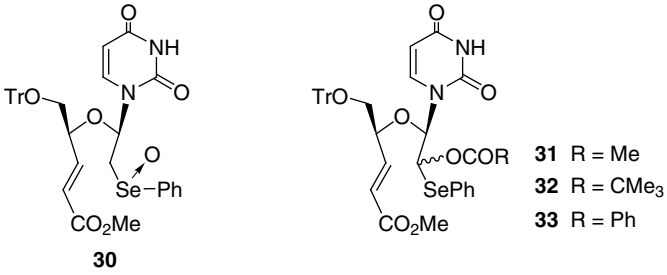


Scheme 6.

4. Pummerer products derived from 2′-phenylseleno-2′,3′-*seco*-uridine and their use as substrates for radical-mediated reconstruction of furanose ring

Although a selenium version of the Pummerer reaction has been known,[22] one concern regarding this reaction is concomitant formation of elimination products caused by enhanced reactivity of selenoxides. In our earlier works on selenoxide elimination using uridine derivatives,[6b] it was observed that their phenylselenoxides are stable enough to be isolated when the β-position is occupied with an electronegative atom such as oxygen.[23]

Since the β-position to the selenium atom of 2′-phenylseleno-2′,3′-*seco*-uridines carries an oxygen atom as well as the base moiety, we reasoned that the selenoxide derived from these compounds could be stable and that their Pummerer reaction would give α-(acyloxy)phenylselenides, that can serve as substrates for the radical cyclization, without forming 1′,2′-unsaturated 2′,3′-*seco*-uridines. This appeared to be the case. When **18** was oxidized with *m*-CPBA in CH_2Cl_2, the corresponding selenoxide **30** was isolated in 91% yield as a mixture of two diastereomers. When the seleno-Pummerer reaction using **30** was carried out in CH_2Cl_2 with acid anhydrides, the α-(acyloxy)phenylselenides **31**–**33** were obtained uniformly in high yields (78–89%) as a mixture of two diastereomers.



We next studied the radical reactions of **31**–**33** to reconstruct the furanose ring having a hydroxyl group at the 2′-position (Scheme 6). The results are summarized in Table 2. Despite the fact that an acyloxy substituent decreases the nucleophilicity of carbon-radicals,[24] these substrates uniformly gave high yields of cyclized products. From Table 2, it can also be seen that, irrespective of the substrate used, the major product was the isomer **34** having 3′-deoxyribofuranosyl configuration.[25] To see the effect of reaction temperature on the stereoselectivity about the 2′-position (the ratio of **34/35**), the reaction of **33** was carried out at lower temperatures (entries 4–6); however, no significant change was observed even at −50°C.

Table 2. Radical-mediated cyclization of **31**–**33**

Entry	Substrate	Initiator (equiv.)	Solvent	Temp.	Time (h)	Yield (%)	Ratio of **34/35**
1	**31**	AIBN (0.2)	toluene	110°C	1	90	68/32
2	**32**	AIBN (0.2)	toluene	110°C	1	82	59/41
3	**33**	AIBN (0.2)	toluene	110°C	1	94	69/31
4	**33**	Et_3B (1.2)	benzene	r.t.	24	91	74/26
5	**33**	Et_3B (1.2)	benzene	0°C	24	94	75/25
6	**33**	Et_3B (1.2)	toluene	−50°C	24	76	77/23

All reactions were carried out by using 2.0 equiv of Bu_3SnH.

Table 3. Radical-mediated cyclization of the two diastereomers of **31**

Entry	Substrate	Initiator (equiv.)	Solvent	Temp.	Time (h)	Yield (%)	Ratio of **34/35**
1	**31a**	AIBN (0.2)	toluene	110°C	1	74	66/34
2	**31a**	Et_3B (1.2)	benzene	r.t.	24	93	71/29
3	**31b**	AIBN (0.2)	toluene	110°C	1	98	68/32
4	**31b**	Et_3B (1.2)	benzene	r.t.	24	97	71/29

All reactions were carried out by using 2.0 equiv of Bu_3SnH.

An additional factor, which possibly alters the stereoselectivity of these reactions, would be the configuration about the 2′-position of the substrates **31**–**33**.[26] To examine this possibility, each diastereomer of **31** was isolated by silica gel column chromatography, and these were separately used as substrates for the radical cyclization. In Table 3, the major isomer and the minor one are referred to as **31a** and **31b**, respectively. When a comparison is made between the yields of entries 1 and 3, it is apparent that the major diastereomer **31a** is less reactive than **31b**. In terms of the stereoselectivity, however, both substrates gave exactly the same results irrespective of the reaction temperature. These results suggest that, although accessibility of tin radical to the 2′-phenylseleno group may differ depending on the configuration (the steric environment around the 2′-position), both diastereomers eventually generate the same sp^2-hybridized radical intermediate.[27]

5. Conclusion

Following regioselective preparation of 2′,3′-*seco*-uridines having a phenylselenenyl group at the 2′-position, 3′-*C*-branched 2′,3′-dideoxyribonucleosides (**1**) were synthesized based on radical-mediated reconstruction of the furanose ring. The observed dominant formation of the *erythro* isomer can be explained in terms of the stability of the chair-like transition structure, in which 1,3-pseudo-diaxial interaction between the base and the 4′-CH_2OTr as well as 1,3-allylic strain of the olefinic portion could be working as determinants of the stereochemistry.

Successful seleno-Pummerer reaction of the selenoxide derived from **18** exemplified the utility of the present approach by the synthesis of 3′-*C*-branched nucleosides having a hydroxyl group at the 2′-position.

6. Experimental

6.1. General

^{1}H NMR spectra were measured at 23°C (internal standard, Me_4Si) with JNM-LA500 (500 MHz) or JNM-GX400 (400 MHz) spectrometers. Mass spectra (MS) were taken in FAB mode (*m*-nitrobenzyl alcohol as a matrix) with a JMS-SX 102A spectrometer. For compounds containing Se, ion peaks corresponding to ^{80}Se are shown. 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).

6.1.1. Reaction of 11 with NaSePh. A mixture of $(PhSe)_2$ (228 mg, 0.73 mmol) and Na (33 mg, 1.43 mmol) in THF (7 mL) was refluxed for 4 h under positive pressure of dry Ar. To the resulting solution, **11** (500 mg, 0.91 mmol) and 18-crown-6 (12 mg, 0.045 mmol) were added at room temperature, and stirred for 19 h. The reaction mixture was treated with 20% AcOH in MeOH and then partitioned between $CHCl_3$ and H_2O. Silica gel column chromatography (10% MeOH in $CHCl_3$) of the organic layer gave the recovered **11** (219 mg, 44%). Fractions containing **12** and **14** were combined and subjected to HPLC separation (hexane/EtOAc=1:2). This gave **12** (t_R 12 min, 47 mg, 7%) and **14** (t_R 15 min, 19 mg, 5%).

Physical data of **12**: UV (MeOH) λ_{max} 263 nm (ϵ 11 100), λ_{min} 244 nm (ϵ 7700); ^{1}H NMR ($CDCl_3$) δ 2.94 (3H, s, SO_2Me), 3.12 (1H, dd, *J*=6.4 and 13.6 Hz, H-5′), 3.20–3.22 (2H, m, H-2′), 3.28 (1H, dd, *J*=6.0 and 13.6 Hz, H-5′), 3.63–3.66 (1H, m, H-4′), 4.27 (1H, dd, *J*=2.4 and 11.2 Hz, H-3′), 4.40 (1H, dd, *J*=3.2 and 11.2 Hz, H-3′), 5.42 (1H, d, *J*=8.0 Hz, H-5), 6.02 (1H, t, *J*=6.0 Hz, H-1′), 7.19 (1H, d, *J*=8.0 Hz, H-6), 7.20–7.35 and 7.49–7.50 (20H, each as m, Ph), 9.01 (1H, br, NH); FAB-MS *m/z* 707 (M^++H). Anal. calcd for $C_{35}H_{34}N_2O_7SSe$: C, 59.57; H, 4.86; N, 3.97. Found: C, 59.47; H, 4.49; N, 3.97.

Physical data of **14**: see Ref. 5.

Fractions containing **13** and **15** were combined and subjected to HPLC separation ($CHCl_3$/MeOH=30:1). This gave **15** (t_R 15 min, 29 mg, 5%) and **13** (t_R 16 min, 14 mg, 3%).

Physical data of **13**: UV (MeOH) λ_{max} 260 nm (ϵ 8600), λ_{min} 243 nm (ϵ 5300); ^{1}H NMR ($CDCl_3$) δ 3.03 (3H, s, SO_2Me), 3.20–3.27 (2H, m, H-2′), 3.68–3.75 (2H, m, H-3′ and H-4′), 3.80 (1H, dd, *J*=5.2 and 12.4 Hz, H-3′), 4.34 (1H, dd, *J*=5.2 and 11.6 Hz, H-5′), 4.49 (1H, dd, *J*=2.8 and 11.6 Hz, H-5′), 5.56 (1H, d, *J*=8.0 Hz, H-5), 5.91 (1H, t, *J*=5.2 Hz, H-1′), 7.21–7.35 (16H, m, Ph and H-6); FAB-MS *m/z* 567 (M^++H). Anal. calcd for $C_{29}H_{30}N_2O_8S$: C, 61.47; H, 5.34; N, 4.94. Found: C, 61.32; H, 5.28; N, 4.78.

Physical data of **15**: UV (MeOH) $\lambda_{shoulder}$ 262 nm (ϵ 8400); ^{1}H NMR ($CDCl_3$) δ 2.86 (1H, dd, *J*=8.0 and 13.2 Hz, H-3′), 3.03 (1H, dd, *J*=4.0 and 13.2 Hz, H-3′), 3.27 (1H, dd, *J*=7.2 and 11.2 Hz, H-5′), 3.42 (1H, dd, *J*=4.0 and 11.2 Hz, H-5′), 3.71–3.77 (1H, m, H-4′), 4.48 (1H, dd, *J*=2.8 and 10.4 Hz, H-2′), 4.62 (1H, dd, *J*=6.4 and 10.4 Hz, H-2′), 5.72 (1H, d, *J*=7.4 Hz, H-5), 5.78 (1H, dd, *J*=2.8 and 6.4 Hz, H-1′), 7.17 (1H, d, *J*=7.4 Hz, H-6), 7.25–7.36 and 7.37–7.43 (20H, each as m, Ph); FAB-MS *m/z* 611 (M^++H). Anal. calcd for $C_{34}H_{30}N_2O_4Se$: C, 66.99; H, 4.96; N, 4.60. Found: C, 66.62; H, 5.07; N, 4.40.

6.1.2. Reaction of 11 with $(PhSe)_2$/$NaBH_4$. Under positive pressure of dry Ar, an EtOH (5 mL) solution containing $(PhSe)_2$ (240 mg, 0.77 mmol) was treated with $NaBH_4$ (45 mg, 1.19 mmol) at room temperature for 10 min. To this was added **11** (500 mg, 0.91 mmol) in THF (5 mL), and the reaction mixture was stirred at room temperature for 16 h. The mixture was quenched by adding 20% AcOH in MeOH and evaporated. The resulting residue was chromatographed on a silica gel column. Elution with hexane/EtOAc=2:1–1:4 gave **16** (39 mg, 6%, foam) and **12** (315 mg, 49%). Elution with 10% MeOH in $CHCl_3$ gave the recovered **11** (130 mg, 26%).

Physical data of **16**: UV (MeOH) λ_{max} 265 nm (ϵ 14 700),

λ_{min} 245 nm (ϵ 11 200); ^{1}H NMR ($CDCl_3$) δ 3.03–3.13 (4H, m, H-2′ and H-3′), 3.19 (1H, dd, J=6.2 and 10.4 Hz, H-5′), 3.26 (1H, dd, J=4.4 and 10.4 Hz, H-5′), 3.61–3.63 (1H, m, H-4′), 5.36 (1H, d, J=8.0 Hz, H-5), 5.92 (1H, t, J=5.6 Hz, H-1′), 7.19–7.32, 7.37–7.40, and 7.44–7.47 (26H, each as m, Ph and H-6), 8.06 (1H, br, NH); FAB-MS m/z 807 (M^++H). Anal. calcd for $C_{40}H_{36}N_2O_4Se_2$: C, 62.67; H, 4.73; N, 3.65. Found: C, 62.76; H, 4.49; N, 3.66.

6.1.3. Reaction of 11 with $(PhSe)_2$/$LiAlH_4$. Under positive pressure of dry Ar, a THF (30 mL) solution containing $(PhSe)_2$ (1.36 g, 4.37 mmol) was treated with $LiAlH_4$ (124 mg, 3.28 mmol) at room temperature for 15 min and then cooled to −20°C. To this was added **11** (3.0 g, 5.47 mmol), and the reaction mixture was stirred at −20°C for 15 min. After being quenched with 10% AcOH in MeOH, the whole reaction mixture was chromatographed on a silica gel column (hexane/EtOAc=1:4) to give **12** (3.61 g, 94%).

6.1.4. 2′-Deoxy-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (17). A mixture of **12** (2.24 g, 3.17 mmol) and NaOAc (1.3 g, 15.8 mmol) in 5% aqueous DMF (20 mL) was heated at 100°C for 3 h. The reaction mixture was partitioned between EtOAc and H_2O. Silica gel column chromatography (hexane/EtOAc=1:1) of the organic layer gave 3′-*O*-acetyl-2′-deoxy-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (1.97 g, 93%) as a foam. Physical data of this compound are as follows: UV (MeOH) λ_{max} 263 nm (ϵ 11 400), λ_{min} 244 nm (ϵ 7800); ^{1}H NMR ($CDCl_3$) δ 1.97 (3H, s, Ac), 3.08–3.24 (4H, m, H-2′ and H-5′), 3.63–3.68 (1H, m, H-4′), 4.08 (1H, dd, J=6.2 and 12.0 Hz, H-3′), 4.30 (1H, dd, J=3.6 and 12.0 Hz, H-3′), 5.42 (1H, d, J=8.0 Hz, H-5), 6.08 (1H, t, J=6.0 Hz, H-1′), 7.21–7.36 and 7.48–7.50 (21H, each as m, Ph and H-6), 8.19 (1H, br, NH); FAB-MS m/z 671 (M^++H). Anal. calcd for $C_{36}H_{34}N_2O_6Se$: C, 64.57; H, 5.12; N, 4.18. Found: C, 64.26; H, 4.72; N, 4.10. The above acetate (1.95 g, 2.91 mmol) in THF (20 mL) was treated with saturated NH_3 in MeOH (60 mL) in a sealed tube for 42 h. The reaction mixture was evaporated and chromatographed on a silica gel column (hexane/EtOAc=1:4). This gave **17** (1.78 g, 97%) as a foam: UV (MeOH) λ_{max} 263 nm (ϵ 11 300), λ_{min} 245 nm (ϵ 7900); ^{1}H NMR ($CDCl_3$, after addition of D_2O) δ 3.11 (1H, dd, J=7.6 and 13.6 Hz, H-2′), 3.17 (1H, dd, J=4.4 and 13.6 Hz, H-2′), 3.21 (1H, dd, J=4.4 and 10.4 Hz, H-5′), 3.30 (1H, dd, J=6.4 and 10.4 Hz, H-5′), 3.48–3.51 (1H, m, H-4′), 3.61 (1H, dd, J=4.8 and 12.8 Hz, H-3′), 3.78 (1H, dd, J=3.6 and 12.8 Hz, H-3′), 5.47 (1H, d, J=8.0 Hz, H-5), 5.93 (1H, dd, J=4.4 and 7.6 Hz, H-1′), 7.22–7.30, 7.34–7.36, and 7.51–7.54 (20H, each as m, Ph), 7.42 (1H, d, J=8.0 Hz, H-6); FAB-MS m/z 629 (M^++H). Anal. calcd for $C_{34}H_{32}N_2O_5Se{\cdot}0.5H_2O$: C, 64.15; H, 5.23; N, 4.40. Found: C, 64.48; H, 4.94; N, 4.28.

6.1.5. Swern oxidation of 17 and subsequent reaction with Ph_3PCHCO_2Me: formation of 3′-*C*-(*E*)-(carbomethoxy)methylene-2′,3′-dideoxy-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (18) and its 4′-epimer (19). Under positive pressure of dry Ar, $(COCl)_2$ (102 μL, 1.70 mmol) was added to a CH_2Cl_2 (7 mL) solution of DMSO (200 μL, 2.83 mmol) at −80°C, and the mixture was stirred for 5 min. Compound **17** (711 mg, 1.13 mmol) in CH_2Cl_2 (7 mL) was added to the above solution. After stirring for 30 min at −80°C, the reaction was quenched by adding Et_3N (1.57 mL, 11.3 mmol), and the mixture was stirred for 30 min at room temperature. The reaction mixture was partitioned between saturated aqueous NH_4Cl and CH_2Cl_2. The separated organic layer was dried ($MgSO_4$), evaporated, and taken up into CH_3CN (7 mL). The resulting CH_3CN solution was reacted with Ph_3PCHCO_2Me (568 mg, 1.7 mmol) at room temperature overnight. The reaction mixture was evaporated and passed through a short column of silica gel (hexane/EtOAc=3:2). HPLC separation (hexane/EtOAc=2:3) of the mixture gave **18** (t_R 10 min, 247 mg, 32%, foam) and **19** (t_R 12 min, 106 mg, 14%, foam).

Physical data of **18**: UV (MeOH) λ_{max} 263 nm (ϵ 11 900), λ_{min} 244 nm (ϵ 8600); ^{1}H NMR ($CDCl_3$) δ 3.13 (1H, dd, J=3.2 and 10.9 Hz, H-5′), 3.19 (1H, dd, J=5.4 and 13.6 Hz, H-2′), 3.26 (1H, dd, J=5.4 and 13.6 Hz, H-2′), 3.36 (1H, dd, J=7.6 and 10.8 Hz, H-5′), 3.72 (3H, s, CO_2Me), 3.83–3.87 (1H, m, H-4′), 5.47 (1H, dd, J=2.0 and 8.0 Hz, H-5), 5.79 (1H, t, J=5.4 Hz, H-1′), 5.97 (1H, dd, J=1.0 and 15.9 Hz, C*H*CO_2Me), 6.61 (1H, dd, J=3.6 and 15.9 Hz, C*H*=CHCO_2Me), 7.19–7.31, 7.35–7.38 and 7.46–7.48 (20H, each as m, Ph), 7.58 (1H, d, J=8.0 Hz, H-6), 8.80 (1H, br, NH); FAB-MS m/z 683 (M^++H). Anal. calcd for $C_{37}H_{34}N_2O_6Se$: C, 65.20; H, 5.03; N, 4.11. Found: C, 64.93; H, 4.89; N, 4.09.

Physical data of **19**: UV (MeOH) λ_{max} 263 nm (ϵ 11 600), λ_{min} 244 nm (ϵ 8400); ^{1}H NMR ($CDCl_3$) δ 3.19 (1H, dd, J=6.2 and 13.6 Hz, H-2′), 3.24–3.32 (3H, m, H-2′ and H-5′), 3.69 (3H, s, CO_2Me), 4.06–4.09 (1H, m, H-4′), 5.55 (1H, d, J=8.2 Hz, H-5), 5.86 (1H, dd, J=1.4 and 15.8 Hz, C*H*CO_2Me), 6.19 (1H, t, J=6.2 Hz, H-1′), 6.61 (1H, dd, J=6.2 and 15.8 Hz, C*H*=CHCO_2Me), 7.16–7.70 (21H, m, Ph and H-6), 8.29 (1H, br, NH); FAB-MS m/z 683 (M^++H). Anal. calcd for $C_{37}H_{34}N_2O_6Se{\cdot}0.5H_2O$: C, 64.35; H, 5.11; N, 4.06. Found: C, 64.74; H, 4.82; N, 3.83.

6.1.6. Dess–Martin oxidation of 17 and subsequent reaction with Ph_3PCHCO_2Me. Under positive pressure of dry Ar, a mixture of **17** (1.0 g, 1.59 mmol) and the Dess–Martin reagent 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (810 mg, 1.91 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 15 min. The reaction mixture was filtered, and the filtrate was partitioned between saturated aqueous NH_4Cl and CH_2Cl_2. The organic layer was evaporated and taken up into CH_3CN (10 mL). The resulting CH_3CN solution was reacted with Ph_3PCHCO_2Me (797 mg, 2.39 mmol) at room temperature overnight. After evaporation of the solvent, the reaction mixture was chromatographed on a silica gel column (hexane/EtOAc=1:1) to give **18** (796 mg, 73%).

6.1.7. 3′-*C*-Cyanomethylene-2′,3′-dideoxy-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (20). Under positive pressure of dry Ar, a THF (8 mL) solution of (cyanomethyl)tributylphosphonium chloride (797 mg, 2.87 mmol) was treated with LHMDS (1 M THF solution, 2.6 mL, 2.58 mmol) for 30 min. To this was added a THF (8 mL) solution of the aldehyde prepared from **17** (600 mg, 0.96 mmol) and the

Dess–Martin reagent (425 mg, 1.05 mmol) as described for the preparation of **18**. The reaction mixture was stirred for 30 min at room temperature, and then partitioned between EtOAc and H_2O. Silica gel column chromatography (hexane/EtOAc=2:1) of the organic layer gave **20** (471 mg, 76%, foam) as a mixture of two geometrical isomers (*E*/*Z*=88:12): UV (MeOH) λ_{max} 263 nm (ϵ 11 400), λ_{min} 245 nm (ϵ 8200); ^{1}H NMR ($CDCl_3$) for (*E*)-isomer δ 3.13 (1H, dd, *J*=5.5 and 13.5 Hz, H-2′), 3.15 (1H, dd, *J*=4.3 and 11.0 Hz, H-5′), 3.20 (1H, dd, *J*=6.4 and 13.5 Hz, H-2′), 3.32 (1H, dd, *J*=7.0 and 11.0 Hz, H-5′), 3.74–3.77 (1H, m, H-4′), 5.52 (1H, d, *J*=8.0 Hz, H-5), 5.59 (1H, dd, *J*=1.5 and 16.5 Hz, CHCN), 5.76 (1H, dd, *J*=5.5 and 6.4 Hz, H-1′), 6.41 (1H, dd, *J*=6.1 and 16.5 Hz, C*H*=CHCN), 7.24–7.31, 7.33–7.36 and 7.48–7.51 (20H, each as m, Ph), 7.39 (1H, d, *J*=8.0 Hz, H-6); ^{1}H NMR ($CDCl_3$) for (*Z*)-isomer δ 3.18 (1H, dd, *J*=5.2 and 13.6 Hz, H-2′), 3.18 (1H, dd, *J*=4.0 and 10.4 Hz, H-5′), 3.28 (1H, dd, *J*=6.4 and 13.6 Hz, H-2′), 3.33 (1H, dd, *J*=6.8 and 10.4 Hz, H-5′), 4.37–4.41 (1H, m, H-4′), 5.55 (1H, d, *J*=8.4 Hz, H-5), 5.55 (1H, dd, *J*=1.2 and 11.2 Hz, CHCN), 5.85 (1H, dd, *J*=5.2 and 6.4 Hz, H-1′), 6.33 (1H, dd, *J*=8.4 and 11.2 Hz, C*H*=CHCN), 7.20–7.33, 7.35–7.39, and 7.46–7.50 (20H, each as m, Ph), 7.42 (1H, d, *J*=8.4 Hz, H-6); FAB-MS *m*/*z* 650 (M^++H). Anal. calcd for $C_{36}H_{31}N_3O_4Se$: C, 66.66; H, 4.82; N, 6.48. Found: C, 66.44; H, 4.69; N, 6.37.

6.1.8. 2′,3′-Dideoxy-3′-*C*-(*E*)-(bisphenoxyphosphono)-methylene-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (21). To a CH_3CN (10 mL) solution containing the aldehyde, prepared from **17** (550 mg, 0.88 mmol) and the Dess–Martin reagent (410 mg, 0.96 mmol) as described for the preparation of **18**, was added $Ph_3PCHP(O)(OPh)_2$[28] (890 mg, 1.75 mmol). The reaction mixture was stirred at room temperature overnight. Evaporation of the solvent followed by silica gel column chromatography (hexane/EtOAc=1:1) of the resulting residue gave **21** (327 mg, 44%, foam): UV (MeOH) λ_{max} 262 nm (ϵ 12 700), λ_{min} 244 nm (ϵ 8900); ^{1}H NMR ($CDCl_3$) δ 3.09 (1H, dd, *J*=3.2 and 11.1 Hz, H-5′), 3.09 (1H, dd, *J*=5.6 and 13.5 Hz, H-2′), 3.18 (1H, dd, *J*=5.6 and 13.5 Hz, H-2′), 3.26 (1H, dd, *J*=7.4 and 11.1 Hz, H-5′), 3.82–3.85 (1H, m, H-4′), 5.41 (1H, d, *J*=8.0 Hz, H-5), 5.72 (1H, t, *J*=5.6 Hz, H-1′), 6.19 (1H, ddd, *J*=1.0, 17.2 and 23.3 Hz, C*H*P(O)(OPh)$_2$), 6.64 (1H, ddd, *J*=6.0, 23.3 and 23.3 Hz, C*H*=CHP(O)(OPh)$_2$), 7.12–7.49 (31H, m, Ph and H-6); FAB-MS *m*/*z* 857 (M^++H). Anal. calcd for $C_{47}H_{41}N_2O_7PSe$: C, 65.96; H, 4.83; N, 3.27. Found: C, 66.25; H, 5.05; N, 3.47.

6.1.9. Radical-mediated cyclization of 18: formation of 1-[3-*C*-(carbomethoxy)methyl-2,3-dideoxy-5-*O*-trityl-β-D-*erythro*-pentofuranosyl]uracil (22) and its *threo*-isomer (23). To a toluene (8.2 mL) solution of **18** (281 mg, 0.41 mmol) kept at 110°C, a mixture of AIBN (6.8 mg, 0.04 mmol) and Bu_3SnH (166 μL, 0.62 mmol) in toluene (5.5 mL) was added by a syringe-pump over 1 h under Ar atmosphere. Evaporation of the solvent followed by silica gel column chromatography (hexane/EtOAc=1:1) of the residue gave a mixture of **22** and **23** (**22**/**23**=97:3 based on integration of H-6, total yield 200 mg, 92%) as foam. HPLC separation (hexane/EtOAc=1:2) of the mixture gave pure **22** (t_R 19.4 min, foam) and **23** (t_R 17.3 min, foam).

Physical data of **22**: UV (MeOH) λ_{max} 263 nm (ϵ 9600), λ_{min} 242 nm (ϵ 5100); ^{1}H NMR ($CDCl_3$) δ 2.13–2.23 (1H, m, H-2′), 2.20 (1H, dd, *J*=9.0 and 16.0 Hz, C*H*$_2$CO$_2$Me), 2.31 (1H, dd, *J*=5.1 and 16.0 Hz, C*H*$_2$CO$_2$Me), 2.40 (1H, ddd, *J*=2.6, 7.6 and 13.9 Hz, H-2′), 2.73–2.83 (1H, m, H-3′), 3.34 (1H, dd, *J*=3.3 and 11.1 Hz, H-5′), 3.60 (1H, dd, *J*=2.6 and 11.1 Hz, H-5′), 3.63 (3H, s, CO_2Me), 3.77–3.81 (1H, m, H-4′), 5.35 (1H, d, *J*=8.2 Hz, H-5), 6.11 (1H, dd, *J*=2.6 and 6.9 Hz, H-1′), 7.25–7.35 and 7.40–7.43 (15H, each as m, Ph), 8.00 (1H, d, *J*=8.2 Hz, H-6), 8.43 (1H, br, NH); FAB-MS *m*/*z* 527 (M^++H). Anal. calcd for $C_{31}H_{30}N_2O_6$·0.5H_2O: C, 69.52; H, 5.83; N, 5.23. Found: C, 69.33; H, 5.69; N, 5.15.

Physical data of **23**: UV (MeOH) λ_{max} 261 nm, λ_{min} 241 nm; ^{1}H NMR ($CDCl_3$) δ 1.18 (1H, ddd, *J*=8.6, 12.0 and 12.2 Hz, H-2′), 2.42 (1H, dd, *J*=7.4 and 16.6 Hz, C*H*$_2$CO$_2$Me), 2.50 (1H, dd, *J*=8.2 and 16.6 Hz, C*H*$_2$CO$_2$Me), 2.54 (1H, ddd, *J*=5.5, 6.8 and 12.2 Hz, H-2′), 2.91–2.99 (1H, m, H-3′), 3.14 (1H, dd, *J*=4.0 and 10.8 Hz, H-5′), 3.52 (1H, dd, *J*=4.0 and 10.8 Hz, H-5′), 3.56 (3H, s, CO_2Me), 4.41 (1H, dt, *J*=4.0 and 8.1 Hz, H-4′), 5.33 (1H, d, *J*=8.3 Hz, H-5), 6.16 (1H, dd, *J*=5.5 and 8.6 Hz, H-1′), 7.22–7.42 (15H, m, Ph), 7.78 (1H, d, *J*=8.3 Hz, H-6), 8.90 (1H, br, NH); HRFAB-MS *m*/*z* 527.2227 (M^++H), calcd for $C_{31}H_{31}N_2O_6$ (M^++H) 527.2182.

6.1.10. Radical-mediated cyclization of 19: formation of 24, 25 and 26. To a toluene (4.0 mL) solution of **19** (138.9 mg, 0.203 mmol) kept at 110°C, a mixture of AIBN (6.7 mg, 0.041 mmol) and Bu_3SnH (109 μL, 0.406 mmol) in toluene (1.8 mL) was added by a syringe-pump over 1 h under Ar atmosphere. Evaporation of the solvent followed by silica gel column chromatography of the residue gave a mixture of **26a** and **26b** (elution with hexane/EtOAc=2:1, 7.2 mg, 7% yield, **26a**/**26b**=1:1), and then a mixture of **24** and **25** (elution with hexane/EtOAc=1:1, 77.3 mg, 72% yield, **24**/**25**=2.4:1). Isolation of pure compounds was carried out by preparative TLC (hexane/EtOAc=1:2) for **26a** and **26b**, and by HPLC (hexane/EtOAc=2:3) for **24** (t_R 30 min) and **25** (t_R 34 min).

Physical data of **24**: UV (MeOH) λ_{max} 261 nm (ϵ 11 000), λ_{min} 242 nm (ϵ 6000); ^{1}H NMR ($CDCl_3$) δ 1.77 (1H, ddd, *J*=6.8, 10.0 and 13.4 Hz, H-2′), 2.29 (1H, dd, *J*=8.6 and 15.9 Hz, C*H*$_2$CO$_2$Me), 2.44 (1H, dd, *J*=5.2 and 15.9 Hz, C*H*$_2$CO$_2$Me), 2.57–2.67 (1H, m, H-3′), 2.83 (1H, ddd, *J*=6.4, 7.6 and 13.4 Hz, H-2′), 3.23 (1H, dd, *J*=4.8 and 10.6 Hz, H-5′), 3.31 (1H, dd, *J*=4.0 and 10.6 Hz, H-5′), 3.61 (3H, s, CO_2Me), 4.05 (1H, ddd, *J*=4.0, 4.8 and 8.5 Hz, H-4′), 5.77 (1H, d, *J*=8.0 Hz, H-5), 6.08 (1H, dd, *J*=6.4 and 6.8 Hz, H-1′), 7.22–7.32 and 7.43–7.48 (16H, m, Ph and H-6), 9.15 (1H, br, NH); FAB-MS *m*/*z* 527 (M^++H). Anal. calcd for $C_{31}H_{30}N_2O_6$·0.25H_2O: C, 70.11; H, 5.79; N, 5.27. Found: C, 70.09; H, 5.48; N, 5.23.

Physical data of **25**: UV (MeOH) λ_{max} 262 nm (ϵ 11 600), λ_{min} 242 nm (ϵ 6100); ^{1}H NMR ($CDCl_3$) δ 2.27 (1H, ddd, *J*=1.8, 7.5 and 13.5 Hz, H-2′), 2.39 (1H, dd, *J*=7.0 and 17.0 Hz, C*H*$_2$CO$_2$Me), 2.45 (1H, dd, *J*=7.8 and 17.0 Hz, C*H*$_2$CO$_2$Me), 2.55 (1H, ddd, *J*=6.4, 11.5 and 13.5 Hz, H-2′), 2.69–2.80 (1H, m, H-3′), 2.87 (1H, dd, *J*=2.8 and

11.0 Hz, H-5′), 3.43 (1H, dd, *J*=4.0 and 11.0 Hz, H-5′), 3.53 (3H, s, CO_2Me), 4.60 (1H, m, H-4′), 5.74 (1H, d, *J*=8.4 Hz, H-5), 6.30 (1H, dd, *J*=1.8 and 6.4 Hz, H-1′), 7.22–7.34 and 7.42–7.45 (16H, m, Ph and H-6), 8.68 (1H, br, NH); FAB-MS *m/z* 527 (M^++H). Anal. calcd for $C_{31}H_{30}N_2O_6$: C, 70.71; H, 5.74; N, 5.32. Found: C, 70.67; H, 5.38; N, 5.28.

^{1}H NMR and HRFAB-MS data of **26a**: ^{1}H NMR ($CDCl_3$) δ 1.89–1.95 (1H, m, H-2′), 2.22 (1H, d, *J*=12.0 Hz, H-2′), 2.53 (1H, dd, *J*=4.8 and 16.7 Hz, H-5), 2.75–2.79 (2H, m, H-3′ and H-6′), 2.97 (1H, dd, *J*=12.8 and 16.7 Hz, H-5), 3.04 (1H, dd, *J*=6.4 and 10.2 Hz, H-5′), 3.23 (1H, dd, *J*=5.2 and 10.2 Hz, H-5′), 3.74 (3H, s, CO_2Me), 3.94 (1H, dt, *J*=4.8 and 12.8 Hz, H-6), 4.08 (1H, dd, *J*=5.2 and 6.4 Hz, H-4′), 6.31 (1H, d, *J*=4.8 Hz, H-1′), 7.22–7.33 and 7.40–7.43 (15H, m, Ph), 7.67 (1H, br, NH); HRFAB-MS *m/z* 527.2214 (M^++H), calcd for $C_{31}H_{31}N_2O_6$ (M^++H) 527.2182.

^{1}H NMR and HRFAB-MS data of **26b**: ^{1}H NMR ($CDCl_3$) δ 1.65 (1H, d, *J*=12.0 Hz, H-2′), 2.08 (1H, dt, *J*=5.2 and 12.0 Hz, H-2′), 2.38 (1H, dd, *J*=13.0 and 16.7 Hz, H-5), 2.56 (1H, dd, *J*=2.4 and 10.4 Hz, H-6′), 2.90–2.98 (3H, m, H-5′, H-5, and H-3′), 3.20 (1H, dd, *J*=4.6 and 9.5 Hz, H-5′), 3.78 (3H, s, CO_2Me), 4.06–4.13 (1H, m, H-6), 4.26 (1H, dd, *J*=4.6 and 7.2 Hz, H-4′), 6.25 (1H, d, *J*=4.4 Hz, H-1′), 7.22–7.32 and 7.36–7.39 (15H, m, Ph), 7.66 (1H, br, NH); HRFAB-MS *m/z* 527.2175 (M^++H), calcd for $C_{31}H_{31}N_2O_6$ (M^++H) 527.2182.

6.1.11. 3′-*C*-(*Z*)-(Carbomethoxy)methylene-2′,3′-dideoxy-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (27). To a DMSO (3 mL) solution of **17** (301.8 mg, 0.48 mmol), DCC (298 mg, 1.44 mmol) and dichloroacetic acid (20 μL, 0.24 mmol) were added and the mixture was stirred for 2 h at room temperature under positive pressure of dry Ar. Filtration of the oxidation mixture was followed by participation between EtOAc and H_2O. The organic layer was dried ($MgSO_4$), evaporated to dryness, and dissolved in THF (3 mL). Under positive pressure of dry Ar, the above THF solution was added at below −78°C to a mixture of 18-crown-6 (636 mg, 2.41 mmol), $(CF_3CH_2O)_2P(O)CH_2CO_2Me$ (102 μL, 0.48 mmol), and LHMDS (24% THF solution, 481 μL, 0.48 mmol) in THF (7 mL). After stirring for 1 h, $(CF_3CH_2O)_2P(O)CH_2CO_2Me$ (51 μL, 0.24 mmol) was added, and the mixture was stirred for 15 min. The reaction mixture was diluted with H_2O, and extracted with EtOAc. Silica gel column chromatography (hexane/EtOAc=3:2) of the extract gave a mixture (242.3 mg, 74%, *E*/*Z*=1.0:4.6) of **18** and **27**. Compound **27** (t_R 12 min) was separated from **18** (t_R 10 min) by HPLC (hexane/EtOAc=2:3): UV (MeOH) λ_{max} 263 nm (ε 12 100), λ_{min} 244 nm (ε 8600); ^{1}H NMR ($CDCl_3$) δ 3.15 (1H dd, *J*=3.2 and 10.2 Hz, H-5′), 3.19 (1H, dd, *J*=4.4 and 13.6 Hz, H-2′), 3.24 (1H, dd, *J*=6.0 and 13.6 Hz, H-2′), 3.26 (1H, dd, *J*=7.6 and 10.2 Hz, H-5′), 3.66 (3H, s, CO_2Me), 5.34–5.38 (1H, m, H-4′), 5.57 (1H, dd, *J*=2.0 and 8.0 Hz, H-5), 5.81 (1H, dd, *J*=4.4 and 6.0 Hz, H-1′), 5.96 (1H, dd, *J*=0.8 and 11.8 Hz, C*H*CO_2Me), 6.06 (1H, dd, *J*=8.4 and 11.8 Hz, C*H*=CHCO_2Me), 7.18–7.40 (20H, m, Ph), 7.67 (1H, d, *J*=8.0 Hz, H-6), 8.03 (1H, br, NH); FAB-MS *m/z* 683 (M^++H). Anal. calcd for $C_{37}H_{34}N_2O_6Se$: C, 65.20; H, 5.03; N, 4.11. Found: C, 65.04; H, 4.75; N, 4.13.

6.1.12. 1-[3-*C*-Cyanomethyl-2,3-dideoxy-5-*O*-trityl-β-D-*erythro*-pentofuranosyl]uracil (28). UV (MeOH) λ_{max} 262 nm (ε 9500), λ_{min} 243 nm (ε 5300); ^{1}H NMR ($CDCl_3$) δ 2.18 (1H, dd, *J*=7.0 and 17.1 Hz, CH_2CN), 2.31 (1H, dd, *J*=4.8 and 17.1 Hz, CH_2CN), 2.35–2.39 (2H, m, H-2′), 2.61–2.71 (1H, m, H-3′), 3.40 (1H, dd, *J*=3.0 and 11.4 Hz, H-5′), 3.73 (1H, dd, *J*=3.0 and 11.4 Hz, H-5′), 3.85 (1H, dt, *J*=3.0 and 9.0 Hz, H-4′), 5.42 (1H, d, *J*=8.2 Hz, H-5), 6.11 (1H, dd, *J*=3.6 and 6.0 Hz, H-1′), 7.24–7.43 (15H, m, Ph), 7.95 (1H, d, *J*=8.2 Hz, H-6), 8.57 (1H, br, NH); FAB-MS *m/z* 494 (M^++H). Anal. calcd for $C_{30}H_{27}N_3O_4{\cdot}0.5H_2O$: C, 71.70; H, 5.62; N, 8.36. Found: C, 71.80; H, 5.35; N, 8.36.

6.1.13. 1-[2,3-Dideoxy-3-*C*-(diphenoxy)phosphonomethyl-5-*O*-trityl-β-D-*erythro*-pentofuranosyl]uracil (29). UV (MeOH) λ_{max} 261 nm (ε 10 400), λ_{min} 242 nm (ε 5600); ^{1}H NMR ($CDCl_3$) δ 1.90 (1H, ddd, *J*=10.4, 15.4 and 18.0 Hz, CH_2PO), 2.17 (1H, ddd, *J*=4.0, 15.4 and 20.2 Hz, CH_2PO), 2.36 (1H, ddd, *J*=7.0, 11.0 and 14.1 Hz, H-2′), 2.58 (1H, ddd, *J*=2.0, 7.3 and 14.1 Hz, H-2′), 2.93–3.00 (1H, m, H-3′), 3.38 (1H, dd, *J*=2.8 and 11.2 Hz, H-5′), 3.62 (1H, dd, *J*=2.8 and 11.2 Hz, H-5′), 3.82 (1H, ddd, *J*=2.8 and 9.3 Hz, H-4′), 5.38 (1H, d, *J*=8.0 Hz, H-5), 6.14 (1H, dd, *J*=2.0 and 7.0 Hz, H-1′), 7.09–7.42 (25H, m, Ph), 7.97 (1H, d, *J*=8.0 Hz, H-6), 8.47 (1H, br, NH); FAB-MS *m/z* 739 (M^++K). Anal. calcd for $C_{41}H_{37}N_2O_7P$: C, 70.28; H, 5.32; N, 4.00. Found: C, 70.20; H, 5.03; N, 4.00.

6.1.14. Oxidation of 18: formation of the selenoxide 30. A solution of **18** (724.2 mg, 1.06 mmol) in CH_2Cl_2 (10 mL) was cooled at 0°C. To this solution, *m*-CPBA (275 mg, 1.59 mmol) was added and the reaction mixture was stirred for 10 min. The mixture was neutralized by adding Et_3N, and then partitioned between saturated aqueous $NaHCO_3$ and CH_2Cl_2. Silica gel column chromatography ($CHCl_3$/MeOH=50:1) of the organic layer gave **30** (675.1 mg, 91%) as a mixture of two diastereomers (ca. 1.0:0.9): FAB-MS *m/z* 737 (M^++K). An aliquot of this mixture was purified by HPLC ($CHCl_3$/MeOH=10:1) for ^{1}H NMR measurement to give the major isomer (t_R 8.1 min) and the minor one (t_R 8.6 min).

Physical data of the major isomer: UV (MeOH) λ_{max} 258 nm (ε 10 800), λ_{min} 244 nm (ε 8800); ^{1}H NMR ($CDCl_3$) δ 3.18–3.24 (3H, m, H-2′ and H-5′), 3.38 (1H, dd, *J*=7.4 and 10.6 Hz, H-5′), 3.74 (3H, s, CO_2Me), 3.91–3.95 (1H, m, H-4′), 5.59 (1H, d, *J*=8.4 Hz, H-5), 6.01 (1H, dd, *J*=0.8 and 15.8 Hz, C*H*CO_2Me), 6.06 (1H, t, *J*=7.2 Hz, H-1′), 6.66 (1H, dd, *J*=7.2 and 15.8 Hz, C*H*=CHCO_2Me), 7.23–7.43, 7.51–7.52 and 7.77–7.79 (21H, each as m, Ph and H-6). Anal. calcd for $C_{37}H_{34}N_2O_7Se{\cdot}0.5H_2O$: C, 62.89; H, 4.85; N, 3.96. Found: C, 62.79; H, 4.80; N, 3.92.

Physical data of the minor isomer: UV (MeOH) λ_{max} 258 nm (ε 11 200), λ_{min} 244 nm (ε 9200); ^{1}H NMR ($CDCl_3$) δ 3.18–3.44 (4H, m, H-2′ and H-5′), 3.75 (3H, s, CO_2Me), 3.82–3.87 (1H, m, H-4′), 5.60 (1H, d, *J*=8.0 Hz, H-5), 5.86–5.90 (2H, m, H-1′ and C*H*=CHCO_2Me), 6.58 (1H, dd, *J*=7.6 and 15.6 Hz, H-3′), 7.23–7.38, 7.50–7.51 and 7.70–7.74 (21H, each as m, Ph and H-6). Anal. calcd for

$C_{37}H_{34}N_2O_7Se{\cdot}H_2O$: C, 62.10; H, 4.79; N, 3.91. Found: C, 62.14; H, 4.92; N, 3.73.

6.1.15. 2′-*O*-Acetyl-3′-*C*-(*E*)-(carbomethoxy)methylene-3′-deoxy-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (31). A mixture of **30** (373.4 mg, 0.53 mmol) and Ac_2O (151 μL, 1.60 mmol) in CH_2Cl_2 (6 mL) was stirred for 19.5 h at room temperature. The reaction mixture was neutralized by adding Et_3N, and then partitioned between saturated aqueous $NaHCO_3$ and CH_2Cl_2. Silica gel column chromatography (hexane/EtOAc=1:1) of the organic layer gave **31** (foam, 351.5 mg, 89%) as a mixture of two diastereomers (ca. 1.0:0.6). Further purification of **31** by silica gel column chromatography (hexane/EtOAc=1:1) enabled the isolation of the major isomer **31a** and the minor isomer **31b**.

Physical data of **31a**: UV (MeOH) λ_{max} 261 nm (ε 11 200), λ_{min} 244 nm (ε 7800); ^{1}H NMR ($CDCl_3$) δ 2.07 (3H, s, Ac), 3.18 (1H, dd, *J*=4.8 and 10.8 Hz, H-5′), 3.43 (1H, dd, *J*=8.4 and 10.8 Hz, H-5′), 3.73 (3H, s, CO_2Me), 3.97–4.00 (1H, m, H-4′), 5.59 (1H, d, *J*=8.0 Hz, H-5), 5.78 (1H, d, *J*=4.0 Hz, H-1′), 6.15 (1H, dd, *J*=1.2 and 16.0 Hz, C*H*CO_2Me), 6.26 (1H, d, *J*=4.0 Hz, H-2′), 6.64 (1H, dd, *J*=6.4 and 16.0 Hz, C*H*=$CHCO_2Me$), 7.24–7.40 and 7.51–7.60 (20H, each as m, Ph), 7.91 (1H, d, *J*=8.0 Hz, H-6), 7.95 (1H, br, NH); FAB-MS *m/z* 741 (M^++H). Anal. calcd for $C_{39}H_{36}N_2O_8Se$: C, 63.33; H, 4.91; N, 3.79. Found: C, 63.23; H, 4.83; N, 3.82.

Physical data of **31b**: UV (MeOH) λ_{max} 260 nm (ε 11 600), λ_{min} 244 nm (ε 8100); ^{1}H NMR ($CDCl_3$) δ 2.04 (3H, s, Ac), 3.14 (1H, dd, *J*=3.1 and 10.9 Hz, H-5′), 3.41 (1H, dd, *J*=7.8 and 10.9 Hz, H-5′), 3.74 (3H, s, CO_2Me), 3.91–3.94 (1H, m, H-4′), 5.50 (1H, dd, *J*=1.6 and 8.3 Hz, H-5), 5.95 (1H, d, *J*=5.2 Hz, H-1′), 6.04 (1H, dd, *J*=1.0 and 15.9 Hz, C*H*CO_2Me), 6.38 (1H, d, *J*=5.2 Hz, H-2′), 6.65 (1H, dd, *J*=6.8 and 15.9 Hz, C*H*=$CHCO_2Me$), 7.24–7.32, 7.36–7.38 and 7.55–7.59 (21H, each as m, Ph and H-6), 8.68 (1H, br, NH); FAB-MS *m/z* 741 (M^++H). Anal. calcd for $C_{39}H_{36}N_2O_8Se$: C, 63.33; H, 4.91; N, 3.79. Found: C, 63.34; H, 4.83; N, 3.84.

6.1.16. 3′-*C*-(*E*)-(Carbomethoxy)methylene-3′-deoxy-2′-*O*-pivaloyl-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (32). This compound (foam, a mixture of two diastereomers, ca. 1.0:0.7) was prepared in 78% yield from **30** by the procedure described for the preparation of **31**: FAB-MS *m/z* 782 (M^++H). ^{1}H NMR ($CDCl_3$) for the major isomer δ 1.10 (9H, s, CMe_3), 3.17 (1H, dd, *J*=3.0 and 10.9 Hz, H-5′), 3.42 (1H, dd, *J*=7.8 and 10.9 Hz, H-5′), 3.74 (3H, s, CO_2Me), 3.86–3.90 (1H, m, H-4′), 5.58 (1H, d, *J*=8.0 Hz, H-5), 5.86 (1H, d, *J*=5.8 Hz, H-1′), 6.04 (1H, dd, *J*=1.0 and 15.9 Hz, C*H*CO_2Me), 6.27 (1H, d, *J*=5.8 Hz, H-2′), 6.66 (1H, dd, *J*=7.0 and 15.9 Hz, C*H*=$CHCO_2Me$), 7.23–7.32, 7.35–7.39, and 7.57–7.61 (20H, each as m, Ph), 7.67 (1H, d, *J*=8.0 Hz, H-6), 8.22 (1H, br, NH). ^{1}H NMR ($CDCl_3$) for the minor isomer δ 1.12 (9H, s, CMe_3), 3.13 (1H, dd, *J*=2.8 and 10.8 Hz, H-5′), 3.46 (1H, dd, *J*=8.0 and 10.8 Hz, H-5′), 3.74 (3H, s, CO_2Me), 3.90–3.94 (1H, m, H-4′), 5.48 (1H, d, *J*=8.4 Hz, H-5), 5.99 (1H, d, *J*=5.2 Hz, H-1′), 6.04 (1H, dd, *J*=1.4 and 15.9 Hz, C*H*CO_2Me), 6.40 (1H, d, *J*=5.2 Hz, H-2′), 6.64 (1H, dd, *J*=7.0 and 15.9 Hz, C*H*=$CHCO_2Me$), 7.23–7.32, 7.35–7.39, and 7.57–7.61 (21H, each as m, Ph and H-6), 8.38 (1H, br, NH).

6.1.17. 2′-*O*-Benzoyl-3′-*C*-(*E*)-(carbomethoxy)methylene-3′-deoxy-2′-phenylseleno-5′-*O*-trityl-2′,3′-*seco*-uridine (33). This compound (foam, a mixture of two diastereomers, ca. 1.0:0.7) was prepared in 88% yield from **30** by the procedure for the preparation of **31**: FAB-MS *m/z* 801 (M^++H); ^{1}H NMR ($CDCl_3$) for the major isomer δ 3.19 (1H, dd, *J*=3.2 and 10.8 Hz, H-5′), 3.46 (1H, dd, *J*=7.8 and 10.8 Hz, H-5′), 3.70 (3H, s, CO_2Me), 3.94–3.98 (1H, m, H-4′), 5.57 (1H, dd, *J*=2.0 and 8.0 Hz, H-5), 5.96 (1H, d, *J*=5.0 Hz, H-1′), 6.10 (1H, dd, *J*=1.0 and 15.8 Hz, C*H*CO_2Me), 6.48 (1H, d, *J*=5.0 Hz, H-2′), 6.71 (1H, dd, *J*=6.8 and 15.8 Hz, C*H*=$CHCO_2Me$), 7.21–8.13 (26H, m, Ph and H-6), 8.47 (1H, br, NH); ^{1}H NMR ($CDCl_3$) for the minor isomer δ 3.11 (1H, dd, *J*=2.8 and 10.8 Hz, H-5′), 3.42 (1H, dd, *J*=8.0 and 10.8 Hz, H-5′), 3.73 (3H, s, CO_2Me), 3.94–3.98 (1H, m, H-4′), 5.40 (1H, dd, *J*=2.0 and 8.0 Hz, H-5), 6.05 (1H, dd, *J*=1.4 and 15.8 Hz, C*H*CO_2Me), 6.09 (1H, d, *J*=5.6 Hz, H-1′), 6.62 (1H, d, *J*=5.6 Hz, H-2′), 6.63 (1H, dd, *J*=7.0 and 15.8 Hz, C*H*=$CHCO_2Me$), 7.21–8.13 (26H, m, Ph and H-6), 8.65 (1H, br, NH).

6.1.18. 2′-*O*-Acetyl-3′-deoxy-3′-*C*-(carbomethoxy)methyl-5′-*O*-trityluridine (34a) and its 2′-epimer (35a). These compounds were obtained as a foam. Separation of **34a** and **35a** was carried out by silica gel column chromatography (hexane/EtOAc=2:3).

Physical data of **34a**: UV (MeOH) λ_{max} 260 nm (ε 9600), λ_{min} 242 nm (ε 5700); ^{1}H NMR ($CDCl_3$) δ 2.08 (1H, dd, *J*=5.4 and 16.7 Hz, CH_2CO_2Me), 2.11 (3H, s, Ac), 2.35 (1H, dd, *J*=9.6 and 16.7 Hz, CH_2CO_2Me), 2.95–3.03 (1H, m, H-3′), 3.34 (1H, dd, *J*=3.2 and 11.2 Hz, H-5′), 3.61 (3H, s, CO_2Me), 3.67 (1H, dd, *J*=2.4 and 11.2 Hz, H-5′), 3.99–4.03 (1H, m, H-4′), 5.38 (1H, dd, *J*=8.2 Hz, H-5), 5.51 (1H, dd, *J*=1.6 and 6.0 Hz, H-2′), 5.92 (1H, d, *J*=1.6 Hz, H-1′), 7.25–7.34 and 7.39–7.45 (15H, each as m, Ph), 7.88 (1H, d, *J*=8.2 Hz, H-6), 8.83 (1H, br, NH); FAB-MS *m/z* 585 (M^++H). Anal. calcd for $C_{33}H_{32}N_2O_8$: C, 67.80; H, 5.52; N, 4.79. Found: C, 67.59; H, 5.38; N, 4.77.

Physical data of **35a**: UV (MeOH) λ_{max} 260 nm (ε 10 100), λ_{min} 242 nm (ε 5900); ^{1}H NMR ($CDCl_3$) δ 1.96 (3H, s, Ac), 2.47 (2H, d, *J*=6.4 Hz, CH_2CO_2Me), 2.69–2.76 (1H, m, H-3′), 3.33 (1H, dd, *J*=4.2 and 10.9 Hz, H-5′), 3.56 (1H, dd, *J*=3.2 and 10.8 Hz, H-5′), 3.60 (3H, s, CO_2Me), 3.92–3.96 (1H, m, H-4′), 5.35 (1H, dd, *J*=5.6 and 6.0 Hz, H-2′), 5.45 (1H, d, *J*=8.2 Hz, H-5), 6.23 (1H, d, *J*=5.6 Hz, H-1′), 7.22–7.35 and 7.40–7.44 (15H, each as m, Ph), 7.79 (1H, d, *J*=8.2 Hz, H-6), 8.12 (1H, br, NH); FAB-MS *m/z* 585 (M^++H). Anal. calcd for $C_{33}H_{32}N_2O_8$: C, 67.80; H, 5.52; N, 4.79. Found: C, 67.75; H, 5.37; N, 4.80.

6.1.19. 3′-Deoxy-3′-*C*-(carbomethoxy)methyl-2′-*O*-pivaloyl-5′-*O*-trityluridine (34b) and its 2′-epimer (35b). These compounds were obtained as a mixture: FAB-MS *m/z* 627 (M^++H).

Compound **34b**: ^{1}H NMR ($CDCl_3$) δ 1.21 (9H, s, Bu-*t*), 2.08 (1H, dd, *J*=5.8 and 16.7 Hz, CH_2CO_2Me), 2.36 (1H, dd,

J=9.2 and 16.7 Hz, CH_2CO$_2$Me), 2.96–3.30 (1H, m, H-3′), 3.35 (1H, dd, J=3.2 and 11.4 Hz, H-5′), 3.60 (3H, s, CO$_2$Me), 3.65 (1H, dd, J=2.8 and 11.4 Hz, H-5′), 3.96–4.00 (1H, m, H-4′), 5.42 (1H, d, J=8.2 Hz, H-5), 5.45 (1H, dd, J=1.6 and 6.0 Hz, H-2′), 5.85 (1H, d, J=1.6 Hz, H-1′), 7.25–7.34 and 7.40–7.43 (15H, each as m, Ph), 7.82 (1H, d, J=8.2 Hz, H-6), 8.18 (1H, br, NH).

Compound **35b**: ^{1}H NMR (CDCl$_3$) δ 1.05 (9H, s, Bu-*t*), 2.49 (2H, d, J=6.4 Hz, CH_2CO$_2$Me), 2.63–2.72 (1H, m, H-3′), 3.30 (1H, dd, J=4.8 and 10.8 Hz, H-5′), 3.55 (1H, dd, J=2.8 and 10.8 Hz, H-5′), 3.61 (3H, s, CO$_2$Me), 4.00 (1H, ddd, J=2.8, 4.8 and 8.0 Hz, H-4′), 5.31 (1H, t, J=5.4 Hz, H-2′), 5.47 (1H, d, J=8.2 Hz, H-5), 6.25 (1H, d, J=5.4 Hz, H-1′), 7.25–7.34 and 7.41–7.44 (15H, each as m, Ph), 7.78 (1H, d, J=8.2 Hz, H-6), 8.18 (1H, br, NH).

6.1.20. 2′-*O*-Benzoyl-3′-deoxy-3′-*C*-(carbomethoxy)methyl-5′-*O*-trityluridine (34c) and its 2′-epimer (35c). These compounds were obtained as a mixture: FAB-MS *m/z* 647 (M^++H).

Compound **34c**: ^{1}H NMR (CDCl$_3$) δ 2.18 (1H, dd, J=5.8 and 16.6 Hz, CH_2CO$_2$Me), 2.98 (1H, dd, J=9.0 and 16.6 Hz, CH_2CO$_2$Me), 3.09–3.17 (1H, m, H-3′), 3.40 (1H, dd, J=3.0 and 11.2 Hz, H-5′), 3.53 (3H, s, CO$_2$Me), 3.69 (1H, dd, J=2.4 and 11.2 Hz, H-5′), 4.13–4.17 (1H, m, H-4′), 5.41 (1H, d, J=8.2 Hz, H-5), 5.75 (1H, dd, J=1.6 and 6.2 Hz, H-2′), 6.05 (1H, d, J=1.6 Hz, H-1′), 7.25–7.35, 7.42–7.47, 7.57–7.61 and 7.99–8.02 (20H, each as m, Ph), 7.89 (1H, d, J=8.2 Hz, H-6), 8.60 (1H, br, NH).

Compound **35c**: ^{1}H NMR (CDCl$_3$) δ 2.55 (1H, dd, J=6.2 and 16.5 Hz, CH_2CO$_2$Me), 2.62 (1H, dd, J=6.4 and 16.5 Hz, CH_2CO$_2$Me), 2.82–2.88 (1H, m, H-3′), 3.35 (1H, dd, J=4.4 and 10.8 Hz, H-5′), 3.57 (3H, s, CO$_2$Me), 3.60 (1H, dd, J=3.2 and 10.8 Hz, H-5′), 4.02–4.06 (1H, m, H-4′), 5.48 (1H, d, J=8.2 Hz, H-5), 5.58 (1H, t, J=5.4 Hz, H-2′), 6.35 (1H, d, J=5.4 Hz, H-1′), 7.20–7.30, 7.32–7.46, 7.58–7.60 and 7.79–7.81 (20H, each as m, Ph), 7.85 (1H, d, J=8.2 Hz, H-6), 8.21 (1H, br, NH).

References

1. For an example, see: Morr, M.; Ernst, L.; Schomburg, D. *Liebigs Ann. Chem.* **1991**, 615–631.
2. (a) Lavallée, J.-F.; Just, G. *Tetrahedron Lett.* **1991**, *32*, 3469–3472. (b) Yokomatsu, T.; Shimizu, T.; Yuasa, Y.; Shibuya, S. *Synlett* **1995**, 1280–1282. (c) Yokomatsu, T.; Sada, T.; Shimizu, T.; Shibuya, S. *Tetrahedron Lett.* **1998**, *39*, 6299–6302.
3. (a) Chu, C. K.; Doboszewski, B.; Schmidt, W.; Ullas, G. V.; Roey, P. V. *J. Org. Chem.* **1989**, *54*, 2767–2769. (b) De Mesmaeker, A.; Lebreton, J.; Waldner, A.; Fritsch, V.; Wolf, R. M.; Freier, S. M. *Synlett* **1993**, 733–736. (c) Lebreton, J.; Waldner, A.; Lesueur, C.; De Mesmaeker, A. *Synlett* **1994**, 137–140.
4. Fiandor, J.; Tam, S. Y. *Tetrahedron Lett.* **1990**, *31*, 597–600.
5. Papchikhin, A.; Chattopadhyaya, J. *Tetrahedron* **1994**, *50*, 5279–5286.
6. (a) Haraguchi, K.; Tanaka, H.; Hayakawa, H.; Miyasaka, T. *Chem. Lett.* **1988**, 931–934. (b) Haraguchi, K.; Tanaka, H.; Maeda, H.; Itoh, Y.; Saito, S.; Miyasaka, T. *J. Org. Chem.* **1991**, *56*, 5401–5408.
7. Jones, A. S.; Walker, R. T.; Wyatt, P. G.; Balzarini, J.; De Clercq, E. *J. Chem. Res. (M)* **1985**, 3520–3532.
8. Liotta, D.; Santiesteban, H. *Tetrahedron Lett.* **1977**, 4369–4372.
9. Liotta, D.; Markiewicz, W.; Santiesteban, H. *Tetrahedron Lett.* **1977**, 4365–4368.
10. For the Swern oxidation, see: Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165–185.
11. Pfitzner, K. E.; Moffatt, J. G. *J. Am. Chem. Soc.* **1965**, *87*, 5661–5670.
12. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287.
13. The depicted stereochemistry was confirmed based on NOE experiments: **22** (15% between H-3′ and H-2′β; 2% between H-1′ and H-4′), **23** (9% between H-3′ and H-4′; 1% between H-1′ and H-4′).
14. Giese, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 753–764.
15. Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925–3941.
16. Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841–1860.
17. The depicted stereochemistry was confirmed based on NOE experiments: **24** (2% between H-4′ and H-2′β; 3% between H-5′ and H-3′; 7% between H-1′ and H-3′), **25** (7% between H-3′ and H-2′β; 9% between H-4′ and H-3′).
18. The stereochemistry of the two isomeric 2′,3′-dideoxy-6,3′-methano-5,6-dihydrouridines (**26a** and **26b**) is not known. It has been reported, however, that the 3′-methyl radical derived from 1-[5-*O*-benzoyl-2,3-dideoxy-3-*C*-iodomethyl-β-D-*threo*-pentofuranosyl]-5-chlorouracil reacts with the C^6 exclusively at the *si*-face: Ueda, T.; Shuto, S. *Nucleosides Nucleotides* **1984**, *3*, 295–302.
19. Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405–4408.
20. No trace amount of **23** was detected by ^{1}H NMR spectroscopy.
21. The isomerization would be initiated with attack of tin radical to the carbonyl oxygen of the methoxycarbonyl group: Enholm, E. J.; Whitley, P. E. *Tetrahedron Lett.* **1995**, *36*, 9157–9160.
22. For an example: Marshall, J. A.; Royce, Jr., R. D. *J. Org. Chem.* **1982**, *47*, 693–698.
23. Haraguchi, K.; Saito, S.; Tanaka, H.; Miyasaka, T. *Nucleosides Nucleotides* **1992**, *11*, 483–493.
24. Giese, B.; Mehl, W. *Tetrahedron Lett.* **1991**, *32*, 4275–4278.
25. The depicted stereochemistry was confirmed based on NOE experiments, which is exemplified by **34a** and **35a**: **34a** (4% between H-6 and H-3′; 3% between H-6 and H-2′; 2% between H-1′ and H-4′), **35a** (5% between H-6 and H-3′; 13% between H-1′ and H-2′; 2% between H-1′ and H-4′).
26. An enantioselective radical reduction has been reported: Buckmelter, A. J.; Kim, A. I.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2000**, *122*, 9386–9390.
27. An alternative possible explanation is that sp^3-hybridized radicals derived from **31a** and **31b** are at equilibrium with a low inversion barrier; see Ref. 26.
28. For the preparation of Ph$_3$P=CHP(O)(OPh)$_2$, see: Jones, G. H.; Hamamura, E. K.; Moffatt, J. G. *Tetrahedron Lett.* **1968**, 5731–5734.