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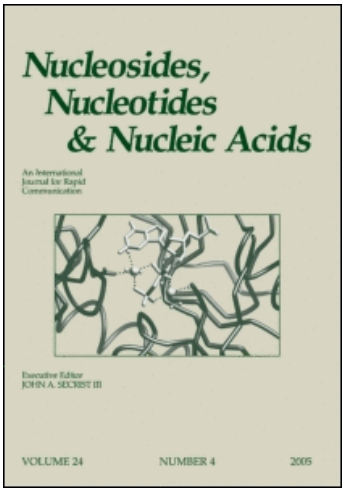

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Pummerer Rearrangement of Selenium-Containing Uracil Nucleosides

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PUMMERER REARRANGEMENT OF SELENIUM-CONTAINING URACIL NUCLEOSIDES

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Abstract: Pummerer-type rearrangement of uracil nucleosides having a phenylseleno group in the 2'-, 3'-, and 5'-positions took place upon oxidation with MCPBA in CH_2Cl_2 followed by treatment with acid anhydrides to yield α-acyloxyselenides.

Recent reports from our laboratory show that reduction of $(PhSe)_2$ with $LiAlH_4$ furnishes a highly nucleophilic phenylselenide anion which is capable of cleaving various types of anhydro structures in uracil nucleosides.[1-3] Since oxidative elimination of selenides proceeds in a highly stereospecific manner under mild reaction conditions,[4] nucleosides bearing a phenylseleno group in the sugar portion have recently been used as starting materials for the preparation of 2',3'-didehydro-2',3'-dideoxy derivatives such as D4T.[5-8] The selenium-containing nucleosides also serve as versatile synthons for C-C bond forming reactions in the sugar moiety.[9,10]

During our study on the utilization of $(PhSe)_2/LiAlH_4$ for synthetic purpose in nucleoside field, O^2,2'-cyclouridine derivative **1** was converted to 3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-deoxy-2'-phenylselenouridine (**2**)[11] in high yield (Chart 1). In this article, Pummerer-type rearrangement of selenoxides derived from uracil

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This paper is dedicated to the memory of Professor Tohru Ueda.

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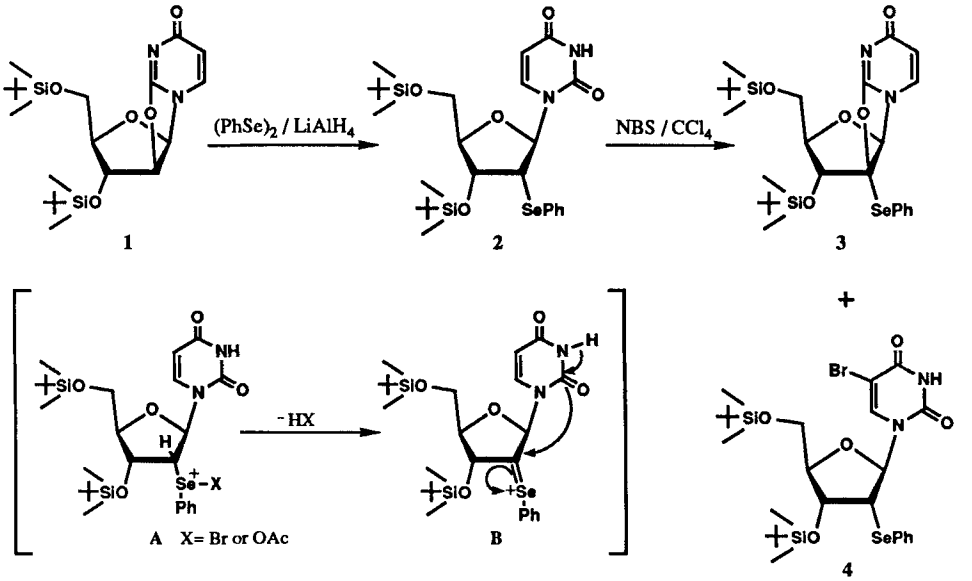

Chart 1

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nucleosides such as **2** is described. The resulting products are stable acylated *O*,*Se*-hemiacetals and, as such, their utilization as a masked carbonyl equivalent would be expected.

Our present study was initiated with an attempt to brominate the 2'-position of **2**.[12] However, as shown in Chart 1, when **2** was treated with *N*-bromosuccinimide in CCl_4 at room temperature for 24 h, two products formed turned out to be **3** (42%) and **4** (40%). Formation of the O^2,2'-cyclonucleoside (**3**) can be rationalized by assuming sequential formation of intermediates **A** (X= Br) and **B**. The latter would subsequently undergo overwhelmingly advantageous intramolecular attack of the C-2 carbonyl group to produce **3**.

To improve the yield of **3**, we thought that acetylation of selenoxide derived from **2** with Ac_2O, which does not react at the C-5 position, would form **A** (X= OAc) more efficiently and acetate anion generated in this step could act as a base in the two consecutive proton abstractions (H-2' of **A** and N^3-H of **B**). Compound **2** was oxidized with MCPBA (1.2 equiv) in CH_2Cl_2 at room temperature to

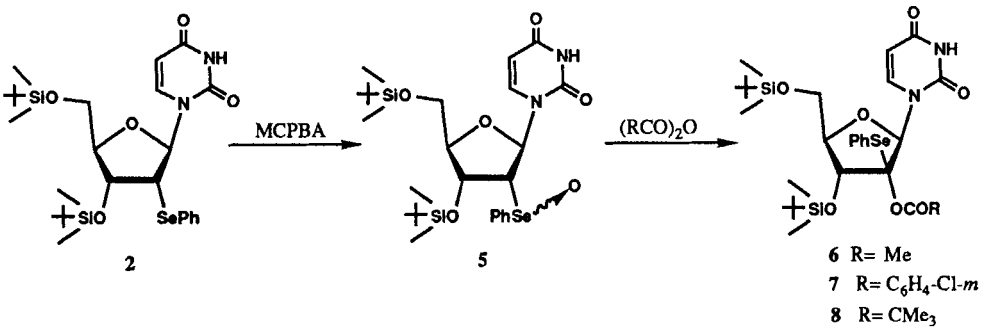
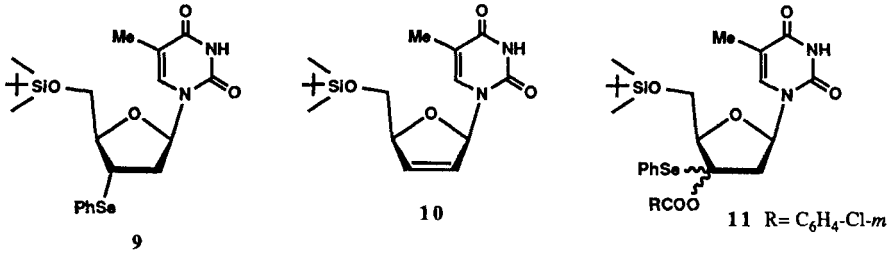


Chart 2

give **5**, which was then treated in a one-pot manner with Ac_2O (10 equiv) for 12 h. ^1H NMR spectrum of a product isolated by silica gel column chromatography showed the presence of D_2O-exchangeable NH proton (δ: 7.88 ppm) and one methyl group (δ: 2.15 ppm). Together with its MS spectrum [*m/z*: 670 (M^+)], the structure of this product was determined to be **6**, which apparently resulted from Pummerer-type rearrangement[13,14] of the selenoxide **5**. The yield was 62%. Another product obtained in this reaction was **7** (25%).[15] When a diastereomeric mixture of **5** was isolated by short column chromatography and then treated with Ac_2O, **6** was obtained in an improved yield of 80%. Similar treatment of **5** with pivalic anhydride gave **8** in 73% yield.

From the ^1H NMR spectra of **6** and **8**, it was clear that these products consisted of practically only one isomer. Stereochemistry about the 2'-position was examined in the case of **8** by measuring its NOESY spectrum, wherein a NOE correlation was observed between the $COCMe_3$ and H-1'.[16]

The expected synthetic utility of the Pummerer product led us to extend the reaction to other phenylseleno derivatives. We have already reported that the selenoxide of **9** has a higher propensity to



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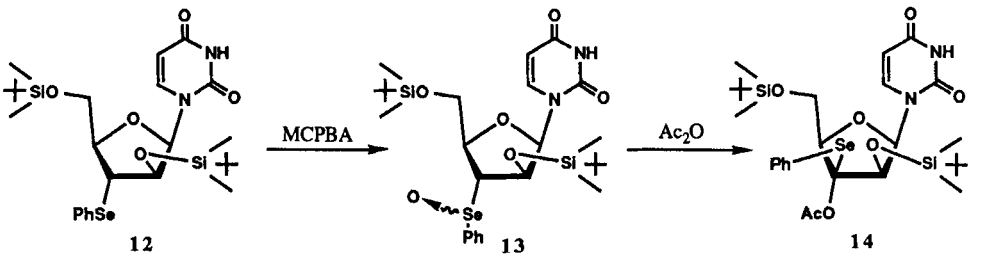

12 13 14

Chart 3

undergo *syn*-elimination.[8] Consequently, even when the MCPBA oxidation of **9** was carried out at 0 °C, the main reaction path was its conversion to a D4T analogue **10.** Although an additional product assumed to be **11**[17] was isolated after addition of Ac_2O and warming the reaction mixture to room temperature, we were unable to obtain the desired 3'-acetoxylated product of **9**.

The rearrangement at the 3'-position was, therefore, examined by using **12** which was prepared from the reaction of 1-(2,3-anhydro-5-*O*-trityl-β-D-lyxofuranosyl)uracil with $(PhSe)_2/LiAlH_4$.[8] Although the corresponding selenoxide (**13**) had been expected to be stable due to the presence of two electronegative β-oxygen atoms ($O^{1'}$ and $O^{2'}$), the isolated **13** was found to be considerably susceptible to the *syn*-elimination between the 3'- and 4'-positions. Thus, treatment of freshly prepared **13** with Ac_2O (5 equiv, in CH_2Cl_2 overnight at room temperature) gave **14** in only 44% yield. As can be anticipated from the fact that α-face of the selenonium intermediate derived from **13** is much less hindered, the stereochemistry of **14** about the 3'-position was deduced as depicted — a NOE correlation was observed between H-4' and COMe.

Finally, 5'-phenylselenide **15**, prepared by anhydro bond cleavage of 2',3'-bis-*O*-(*tert*-butyldimethylsilyl)-O^2,5'-cyclouridine with $(PhSe)_2/NaBH_4$,[8,18] was converted to **16** (78%). Selenoxide **16** is stable and can be kept at room temperature for at least one week. Treatment of **16** with Ac_2O under similar reaction conditions to the case of **13** gave a mixture of two products (**17**) containing an acetoxy group in 61% yield. These were separated by preparative

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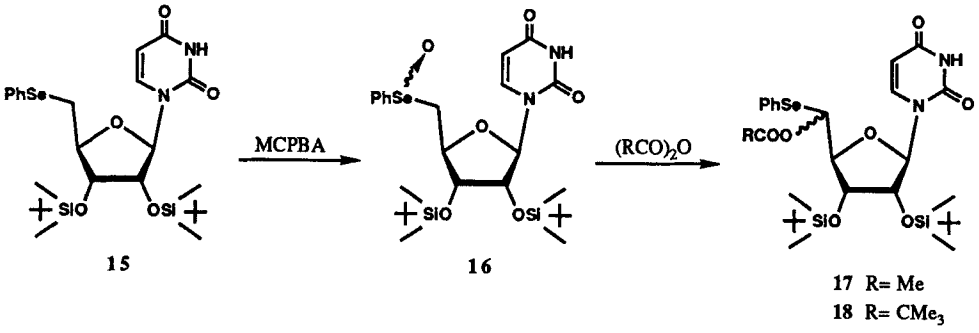

Chart 4

TLC and confirmed to be diastereomeric each other (*ca.* 1:1.7) based on ^{1}H NMR and MS spectrometries. Similarly, **18** was obtained as an inseparable mixture of two diastereomers (*ca.* 2:1) in 59% yield.[19]

In conclusion, the present work shows that selenium-containing nucleosides can be transformed to α-acyloxy selenides through Pummerer rearrangement. By the use of the Pummerer products, it would be possible to generate an oxygen-stabilized carbenium ion or radical upon cleavage of their C-Se bond and, therefore, they could serve as an useful synthon for C-C bond formation in the sugar portion of nucleosides. We are currently investigating along this line.

EXPERIMENTAL

Melting points were determined with a Yanagimoto micro-melting point apparatus and are uncorrected. ^{1}H NMR spectra were measured with tetramethylsilane as an internal standard, with either a JEOL JNM-FX 100 (100 MHz) or a JEOL JNM-GX 400 (400 MHz) NMR spectrometer. Mass spectra were taken on a JEOL JMS-D 300 spectrometer. UV spectra were recorded on a Shimadzu UV-240 spectrophotometer. Column chromatography was carried out on a silica gel (Wakogel® C-200). TLC was performed on precoated silica gel plates F_{254}, Merck.

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Reaction of 2 with NBS A CH_2Cl_2 (4 ml) solution of **2** (40 mg, 0.07 mmol) was treated with NBS (23 mg, 0.13 mmol) at room temperature for 12 h. Neutralization with Et_3N followed by column chromatography (17-25% EtOAc in hexane) gave **4** (16 mg, 40%) as a syrup and crude **3** contaminated with succinimide. The crude **3** was dissolved in $CHCl_3$ and washed with cold 0.1 *N* NaOH. This gave pure **3** (19 mg, 42%), which was crystallized from EtOAc-hexane (mp 228-229 °C). *Anal.* Calcd for $C_{27}H_{42}N_2O_5SeSi_2$: C, 53.20; H, 6.95; N, 4.60. Found: C, 53.39; H, 7.02; N, 4.54. UV absorption in MeOH: $\lambda_{shoulder}$ 246 nm (ε 8100). ^1H NMR ($CDCl_3$) δ: 0.18 and 0.31 (12H, each as s, SiMe), 0.80 and 0.98 (18H, each as s, SiBu-*t*), 3.69 (2H, m, CH_2-5'), 4.04 (1H, m, H-4'), 4.67 (1H, d, $J_{3',4'}$= 6.3 Hz, H-3'), 5.71 (1H, s, H-1'), 5.77 (1H, d, $J_{5,6}$= 7.3 Hz, H-5), 6.83 (1H, d, H-6), 7.30 (3H, m, Ph), 7.64 (2H, m, Ph). MS *m/z*: 553 (M^+–Bu-*t*).

Physical data of **4** are as follows. *Anal.* Calcd for $C_{27}H_{43}BrN_2O_5SeSi_2$: C, 46.97; H, 6.28; N, 4.06. Found: C, 46.71; H, 6.34; N, 3.92. UV absorption in MeOH: λ_{max} 273 nm (ε 8600), λ_{min} 243 nm (ε 3100). ^1H NMR ($CDCl_3$) δ: 0.13 (3H, s, SiMe), 0.15 (6H, s, SiMe), 0.20 (3H, s, SiMe), 0.96 (18H, s, SiBu-*t*), 3.55 (1H, dd, $J_{1',2'}$= 9.3, $J_{2',3'}$= 4.9 Hz, H-2'), 3.80 (2H, m, CH_2-5'), 4.04 (1H, m, H-4'), 4.50 (1H, d, H-3'), 6.52 (1H, d, H-1'), 7.22 (3H, m, Ph), 7.45 (3H, m, Ph and H-6), 8.52 (1H, br, NH). MS *m/z*: 692 and 690 (M^+), 635 and 633 (M^+–Bu-*t*).

2'-*O*-Acetyl-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-phenylselenouridine (6) A mixture of **2** (500 mg, 0.82 mmol) and MCPBA (169 mg, 0.98 mmol) in CH_2Cl_2 (25 ml) was stirred at room temperature for 5 h. The reaction mixture was neutralized with Et_3N and partitioned between $CHCl_3$ and aqueous saturated $NaHCO_3$. The organic layer was dried (Na_2SO_4) and evaporated to dryness. Column chromatography (2% EtOH in $CHCl_3$) of the residue gave **5**, which was dissolved in CH_2Cl_2 (25 ml) and treated with Ac_2O (387 μl, 4.1 mmol) at room temperature overnight. The mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. Column chromatography (20% EtOAc in hexane) of the organic layer gave **6** (445 mg, 80%) as a foam, which was analytically pure. *Anal.* Calcd for $C_{29}H_{46}N_2O_7SeSi_2$: C, 52.02; H, 6.92; N, 4.18. Found: C, 52.39; H, 7.01; N, 4.49. UV absorption in MeOH: λ_{max} 263 nm (ε 11200), λ_{min} 239 nm (ε 5600). ^1H NMR ($CDCl_3$) δ: 0.12 and 0.18 (12H, each as s,

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SiMe), 0.91 and 0.94 (18H, each as s, SiBu-*t*), 2.15 (3H, s, OAc), 3.75 (1H, dd, J_{gem}= 11.7, $J_{4',5'}$= 2.4 Hz, H-5'), and 3.97 (1H, dd, $J_{4',5'}$= 2.9 Hz, H-5'), 4.26 (1H, m, H-4'), 4.39 (1H, d, $J_{3',4'}$= 5.8 Hz, H-3'), 5.66 (1H, dd, $J_{5,6}$= 8.3, $J_{5,NH}$= 1.9 Hz, H-5), 6.81 (1H, s, H-1'), 7.28 (3H, m, Ph), 7.45 (2H, m, Ph), 7.72 (1H, d, H-6), 7.88 (1H, br, NH). MS *m/z*: 670 (M^+), 613 (M^+–Bu-*t*), 553 (M^+–Bu-*t*–AcOH), 112 (B+1).

2'-*O*-(*m*-Chlorobenzoyl)-3',5'-bis-*O*-(*tert*-butyldimethylsilyl)-2'-phenylselenouridine (7) This compound was obtained as a foam in 25% yield from **2** when treatment with Ac_2O was carried out without isolating **5**. *Anal.* Calcd for $C_{34}H_{47}ClN_2O_7SeSi_2$: C, 53.30; H, 6.18; N, 3.66. Found: C, 53.37; H, 6.39; N, 3.53. UV absorption in MeOH: λ_{max} 260 nm (ε 12100), λ_{min} 249 nm (ε 11100). ^1H NMR ($CDCl_3$) δ: 0.04 and 0.12 (6H, each as s, SiMe), 0.15 (6H, s, SiMe), 0.70 and 0.98 (18H, each as s, SiBu-*t*), 3.90 (2H, m, CH_2-5'), 4.29 (1H, m, H-4'), 4.68 (1H, d, $J_{3',4'}$= 4.4 Hz, H-3'), 5.65 (1H, dd, $J_{5,6}$= 8.3, $J_{5,NH}$= 2.4 Hz, H-5), 6.83 (1H, s, H-1'), 7.11-8.01 (11H, m, Ph, H-6, and NH). MS *m/z*: 711 and 709 (M^+–Bu-*t*).

3',5'-Bis-*O*-(*tert*-butyldimethylsilyl)-2'-phenylseleno-2'-*O*-pivaloyluridine (8) This compound was prepared from **2** in 73% yield as a foam by the procedure described for the preparation of **6**. *Anal.* Calcd for $C_{32}H_{52}N_2O_7SeSi_2$: C, 54.01; H, 7.37; N, 3.94. Found: C, 54.26; H, 7.56; N, 3.86. UV absorption in MeOH: λ_{max} 262 nm (ε 11400), λ_{min} 238 nm (ε 6300). ^1H NMR ($CDCl_3$) δ: 0.12 and 0.18 (12H, each as s, SiMe), 0.90 and 0.97 (18H, each as s, SiBu-*t*), 1.24 (9H, s, $COCMe_3$), 3.74 (1H, dd, J_{gem}= 11.8, $J_{4',5'}$= 1.9 Hz, H-5'), 3.97 (1H, dd, $J_{4',5'}$= 2.4 Hz, H-5'), 4.31 (1H, m, H-4'), 4.43 (1H, d, $J_{3',4'}$= 5.8 Hz, H-3'), 5.66 (1H, dd, $J_{5,6}$= 8.1, $J_{5,NH}$= 2.2 Hz, H-5), 6.66 (1H, s, H-1'), 7.23-7.56 (5H, m, Ph), 7.64 (1H, br, NH), 7.75 (1H, d, H-6). MS *m/z*: 655 (M^+–Bu-*t*), 553 (M^+–Bu-*t*–Me_3CCO_2H), 112 (B+1).

1-[2,5-Bis-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-3-phenylseleno-β-D-arabinofuranosyl]uracil (12) A mixture of 1-(3-deoxy-3-phenylseleno-β-D-arabinofuranosyl)uracil[8] (1.0 g), *tert*-butyldimethylsilyl chloride (1.37 g), and imidazole (619 mg) in DMF (20 ml) was stirred overnight at 110 °C. The reaction mixture was partitioned between H_2O and EtOAc. Column chromatography (33% EtOAc in hexane) of the organic layer gave **12** (1.59 g) as an analytically pure syrup in quantitative yield. *Anal.* Calcd for

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$C_{27}H_{44}N_2O_5SeSi_2 \cdot H_2O$: C, 51.51; H, 7.37; N, 4.45. Found: C, 51.68; H, 7.26; N, 4.47. UV absorption in MeOH: λ_{max} 264 nm (ε 11800), λ_{min} 232 nm (ε 5000). ^1H NMR ($CDCl_3$) δ: 0.01 and 0.08 (12H, each as s, SiMe), 0.75 and 0.86 (18H, each as s, SiBu-*t*), 3.55 (1H, t, $J_{1',2'} = J_{2',3'} =$ 5.0 Hz, H-2'), 3.80 (2H, m, CH_2-5'), 3.98 (1H, m, H-4'), 4.44 (1H, t, H-3'), 5.62 (1H, dd, $J_{5,NH} =$ 1.9, $J_{5,6} =$ 8.3 Hz, H-5), 6.18 (1H, d, H-1'), 7.28 (3H, m, Ph), 7.61 (2H, m, Ph), 7.63 (1H, d, H-6), 8.41 (1H, br, NH). MS *m/z*: 555 (M^+–Bu-*t*).

1-[3-*O*-Acetyl-2,5-bis-*O*-(*tert*-butyldimethylsilyl)-3-phenylseleno-β-D-arabinofuranosyl]uracil (14) This compound was prepared from **12** *via* **13** by the procedure similar to that of the preparation of **6**. MCPBA oxidation of **12** was carried out for 30 min to give **13** which was isolated in 92% yield by column chromatography (2% EtOH in $CHCl_3$). Without being characterized, **13** was treated with Ac_2O (5 eq) in CH_2Cl_2 overnight at room temperature. Column chromatography (17% EtOAc in hexane) of the reaction mixture gave **14** in 44% yield as an analytically pure solid. *Anal.* Calcd for $C_{29}H_{46}N_2O_7SeSi_2$: C, 52.02; H, 6.92; N, 4.18. Found: C, 52.00; H, 6.89; N, 4.18. UV absorption in MeOH: λ_{max} 264 nm (ε 12600), λ_{min} 235 mn (ε 7000). ^1H NMR ($CDCl_3$) δ: 0.09 and 0.38 (12H, each as s, SiMe), 0.92 (18H, s, SiBu-*t*), 1.70 (3H, s, OAc), 4.12 (2H, m, CH_2-5'), 4.47 (1H, dd, $J_{4',5'} =$ 3.9 and 4.4 Hz, H-4'), 5.16 (1H, d, $J_{1',2'} =$ 3.4 Hz, H-2'), 5.70 (1H, dd, $J_{5,NH} =$ 1.7, $J_{5,6} =$ 8.5 Hz, H-5), 6.16 (1H, d, H-1'), 7.26-7.69 (6H, m, Ph and H-6), 8.26 (1H, br, NH). MS *m/z*: 670 (M^+), 613 (M^+–Bu-*t*), 553 (M^+–Bu-*t*–AcOH), 112 (B+1).

5'-*O*-Acetyl-2',3'-bis-*O*-(*tert*-butyldimethylsilyl)-5'-phenylselenouridine (17) This compound was prepared from **15** *via* **16** by the procedure similar to that of the preparation of **6**. MCPBA oxidation of **15** was carried out for 3 h to give **16** which was isolated in 78% yield by column chromatography (2% EtOH in $CHCl_3$). Treatment of **16** with Ac_2O (5 equiv) was carried out in CH_2Cl_2 overnight at room temperature. Column chromatography (17% EtOAc in hexane) gave **17** as a mixture of two diastereomers (*ca.* 1:1.7) in 61% yield. Preparative TLC (hexane:EtOAc= 7:2) of the mixture gave a more polar isomer (major product) as an analytically pure foam. *Anal.* Calcd for $C_{29}H_{46}N_2O_7SeSi_2$: C, 52.02; H, 6.92; N, 4.18. Found: C, 52.19; H, 7.09; N, 3.95. UV absorption in MeOH: λ_{max} 260 nm (ε

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11000), λ_{min} 235 nm (ε 5500). ^{1}H NMR ($CDCl_3$) δ: 0.02 (6H, s, SiMe), 0.04 and 0.06 (6H, each as s, SiMe), 0.86 and 0.87 (18H, each as s, SiBu-*t*), 2.05 (3H, s, OAc), 3.95 (1H, t, $J_{2',3'}$= $J_{3',4'}$= 4.4 Hz, H-3'), 4.14 (1H, t, $J_{3',4'}$= $J_{4',5'}$= 4.4 Hz, H-4'), 4.41 (1H, t, $J_{1',2'}$= $J_{2',3'}$= 4.4 Hz, H-2'), 5.70 (1H, d, $J_{5,6}$= 8.3 Hz, H-5), 5.85 (1H, d, H-5'), 6.35 (1H, d, H-1'), 7.29 (3H, m, Ph), 7.66 (3H, m, Ph and H-6), 8.55 (1H, br, NH). MS *m/z*: 613 (M^+–Bu-*t*), 112 (B+1).

^{1}H NMR data of the other isomer are given below. ^{1}H NMR ($CDCl_3$) δ: 0.04 (6H, s, SiMe), 0.05 and 0.07 (6H, each as s, SiMe), 0.86 and 0.89 (18H, each as s, SiBu-*t*), 2.08 (3H, s, Ac), 4.07 (1H, dd, $J_{2',3'}$= 2.4, $J_{3',4'}$= 4.7 Hz, H-3'), 4.19 (1H, dd, $J_{1',2'}$= 5.0 Hz, H-2'), 4.35 (1H, dd, $J_{4',5'}$= 6.8 Hz, H-4'), 5.75 (1H, d, $J_{5,6}$= 8.0 Hz, H-5), 5.85 (1H, d, H-5'), 6.37 (1H, d, H-1'), 7.29-7.37 (4H, m, H-6 and Ph), 7.65-7.67 (2H, m, Ph), 8.88 (1H, br, NH).

2',3'-*O*-(*tert*-Butyldimethylsilyl)-5'-phenylseleno-5'-pivaloyluridine (18) This compound was prepared from **16** by the procedure described for the preparation of **17**. Column chromatography (17-20% EtOAc in hexane) of the reaction mixture gave **18** (a mixture of two diastereomers, *ca.* 2:1) in 59% yield as an analytically pure syrup. *Anal.* Calcd for $C_{32}H_{52}N_2O_7SeSi_2$: C, 54.01; H, 7.37; N, 3.94. Found: C, 54.00; H, 7.60; N, 3.87. UV absorption in MeOH: λ_{max} 261 nm (ε 13000), λ_{min} 230 nm (ε 6000). The following ^{1}H NMR data of each isomer are collected based on COSY spectrum of the mixture. ^{1}H NMR ($CDCl_3$) of the major isomer δ: 0.03 and 0.04 (6H, each as s, SiMe), 0.07 (6H, s, SiMe), 0.86 and 0.89 (18H, each as s, SiBu-*t*), 1.16 (9H, s, $COCMe_3$), 3.96 (1H, t, $J_{2',3'}$= $J_{3',4'}$= 4.4 Hz, H-3'), 4.08 (1H, t, $J_{3',4'}$= $J_{4',5'}$= 4.4 Hz, H-4'), 4.45 (1H, t, $J_{1',2'}$= $J_{2',3'}$= 4.4 Hz, H-2'), 5.74 (1H, d, $J_{5,6}$= 8.1 Hz, H-5), 5.90 (1H, d, H-5'), 6.42 (1H, d, H-1'), 7.28-7.35 (3H, m, Ph), 7.62-7.68 (3H, m, H-6 and Ph), 9.48 (1H, br, NH). ^{1}H NMR ($CDCl_3$) of the minor isomer δ: 0.03 and 0.04 (6H, each as s, SiMe), 0.07 (6H, s, SiMe), 0.86 and 0.89 (18H, each as s, SiBu-*t*), 1.24 (9H, s, CO-CMe_3), 4.05 (1H, dd, $J_{2',3'}$= 2.0, $J_{3',4'}$= 4.4 Hz, H-3'), 4.17 (1H, dd, $J_{1',2'}$= 5.8, $J_{2',3'}$= 2.0 Hz, H-2'), 4.33 (1H, dd, $J_{4',5'}$= 6.8 Hz, H-4'), 5.74 (1H, d, $J_{5,6}$= 8.1 Hz, H-5), 5.89 (1H, d, H-5'), 6.42 (1H, d, H-1'), 7.28-7.35 (3H, m, Ph), 7.62-7.68 (3H, m, H-6 and Ph), 9.29 (1H, br, NH). MS *m/z*: 712 (M^+), 655 (M^+–Bu-*t*), 553 (M^+–Bu-*t*–Me_3CCO_2H).

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REFERENCES AND NOTES

1) K. Haraguchi, H. Tanaka, H. Hayakawa, and T. Miyasaka, *Chem. Lett.*, **1988**, 931.

2) K. Haraguchi, H. Tanaka, and T. Miyasaka, *Synthesis*, **1989**, 434.

3) The combination of $(PhSe)_2$ and $LiAlH_4$ has been used for the preparation of aryl difluoromethyl selenides: H. Suzuki, M. Yoshinaga, K. Takaoka, and Y. Hiroi, *Synthesis*, **1985**, 497.

4) For an example: K. B. Sharpless and R. F. Rauer, *J. Am. Chem. Soc.*, **95**, 2697 (1973).

5) J.-M. Vial, P. Agback, and J. Chattopadhyaya, *Nucleosides and Nucleotides*, **9**, 245 (1990).

6) C. K. Chu, J. R. Babu, J. W. Beach, S. K. Ahn, H. Huang, L. S. Jeong, and S. J. Lee, *J. Org. Chem.*, **55**, 1418 (1990).

7) N. D. P. Cosford and R. F. Schinazi, *J. Org. Chem.*, **56**, 2161 (1991).

8) K. Haraguchi, H. Tanaka, H. Maeda, Y. Itoh, S. Saito, and T. Miyasaka, *J. Org. Chem.*, **56** (1991), in press.

9) J.-C. Wu and J. Chattopadhyaya, *Tetrahedron*, **45**, 4507 (1989); *Idem*, *ibid.*, **46**, 2587 (1990); W. Tong, Z. Xi, C. Gioeli, and J. Chattopadhyaya, *ibid.*, **47**, 3431 (1991).

10) K. Haraguchi, H. Tanaka, Y. Itoh, and T. Miyasaka, *Tetrahedron Lett.*, **32**, 777 (1991); K. Haraguchi, Y. Itoh, H. Tanaka, and T. Miyasaka, *Tetrahedron Lett.*, **32**, 3391 (1991).

11) For the preparations and physical data of **2**, **9**, **10**, **15**, and **16**, see reference 8.

12) For an example of α-chlorination of sulfides with *N*-chlorosuccinimide: D. L. Tuleen and T. B. Stephens, *J. Org. Chem.*, **34**, 31 (1969).

13) For an example of the Pummerer-type rearrangement of selenoxides: J. A. Marshall and R. D. Royce, Jr., *J. Org. Chem.*, **47**, 693 (1982).

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14) For a mechanistically related α-fluorination of nucleoside 5'-sulfoxides with diethylaminosulfur trifluoride: M. J. Robins and S. F. Wnuk, *Tetrahedron Lett.*, **29**, 5729 (1988); E. T. Jarvi, J. R. McCarthy, S. Mehdi, D. P. Matthews, M. L. Edwards, N. J. Prakash, T. L. Bowlin, P. S. Sunkara, and P. Bey, *J. Med. Chem.*, **34**, 647 (1991).

15) A Pummere-type rearrangement has been observed during oxidation of certain selenides with organic peracids: G. Galambos and V. Simonidesz, *Tetrahedron Lett.*, **23**, 4371 (1982).

16) In the case of **6**, no significant NOESY correlation was observed between the COMe and other protons. The stereochemistry of **6** is, therefore, tentative.

17) ^{1}H NMR data of **11** are given below. ^{1}H NMR ($CDCl_3$) δ: 0.20 (6H, s, SiMe), 0.98 (9H, s, SiBu-*t*), 1.94 (3H, s, 5-Me), 2.32 (1H, dd, J_{gem}= 13.4, $J_{1',2'a}$= 9.2 Hz, H-2'a), 2.72 (1H, dd, $J_{1',2'b}$= 4.9 Hz, H-2'b), 4.04 (1H, dd, J_{gem}= 11.6, $J_{4',5'a}$= 3.3 Hz, H-5'a), 4.10 (1H, dd, $J_{4',5'b}$= 3.3 Hz, H-5'b), 4.77 (1H, t, H-4'), 6.06 (1H, dd, H-1'), 7.30-7.34 (2H, m, Ph), 7.38-7.43 (2H, m, Ph), 7.55-7.60 (4H, m, Ph), 7.99 (1H, m, Ph), 8.09 (1H, s, H-6), 9.45 (1H, br, NH).

18) D. Liotta, W. Markiewicz, and H. Santiesteban, *Tetrahedron Lett.*, **1977**, 4365.

19) Formation of two unknown products was observed during the treatment of **16** with Ac_2O or pivalic anhydride.

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