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An Efficient Method for the Synthesis of Selenium Modified Nucleosides: Its application to the synthesis of *Se*-adenosyl-L-selenomethionine (SeAM)

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In this paper, we report that a versatile method for the synthesis of 5′-selenium modified nucleosides has been explored on the basis of 2-(trimethylsilyl)ethyl (TSE) seleno group as a selenating donor. We demonstrate the broad utility of this method through direct introduction of various functional groups into a 5′-TSE-selenonucleosides. This original method offers additional advantages for the preparation of these compounds, such as highly functional group tolerance, ready availability of various electrophilic reagents, mild conditions, simple operation, and good yields. The utility of this approach is further demonstrated by the synthesis of *Se*-adenosyl-L-selenomethionine (SeAM) as chemical reporter for methyltransferases.

Introduction

In recent years, modified nucleosides have proved to be useful in biochemistry, molecular biology, gene therapy, and drug discovery.[1] The modification of the nucleobase or ribose oxygen moiety in nucleoside with other elements such as carbon, nitrogen, sulfur, selenium is a promising alternative to conventional cancer chemotherapy and viral infections.[2] Moreover, the selenium modification of ribose moiety has been extensively studied for structural determination of nucleic acids. For example, the substitution of the 2′ and 5′-oxygen atom in nucleotides by selenium is successfully used in the 3-D structural study of DNA and RNA for multi-wavelength anomalous dispersion (MAD)[3] in X-ray crystallography and labeled nucleic acid[4]. Therefore, the functional group transformation at the exocyclic C-5′ position of nucleosides by the replacement of the 5′-oxygen is attractive due to the biological importance of these molecules.[5] For example, 5′-thiouridine derivatives is useful for selective inhibitors against α-1,3-galactosyl transferases.[6] Moreover, the selective DOT1L methyltransferase inhibitor,[7] which was designed on the basis of the cofactor *S*-adenosyl-L-methionine (SAM) is attractive due to the potential therapeutic target for the drug discovery of the anti-cancer drug known as the epigenetic drugs.

In this context, the synthesis of selenium-modified nucleosides has attracted attention. However, few reports are available in the literature for the synthesis of 5′-selenonucleosides due to difficulties involved in their preparations. Based on our knowledge, 5′-selenonucleosides or these diselenides have been synthesized by Sivapriya's group[8a], Braga's group,[8b] Belostotskii's group[8c] and Huang's group.[4] Sivapriya's method is based on the use of tetraethylammonium tetraselenotungstate as a selenium transfer reagent. Braga's method exploited in situ selenolate anion generated by the reduction of the symmetrical diorganodiselenide with sodiumborohydride in ethanol. Belostotskii et al. synthesized 5′-selenocyanate by nucleophilic substitution of tosylated nucleoside with tetrabutylammonium selenocyanate. Huang et al. exploited in situ 2-cyanoethyl selenide generated by the reduction of symmetrical 2-cyanoethyl diselenide.[9] The active form of 2-cyanoethyl diselenide is 2-cyanoethyl ethaneselenolate, which is generated by treatment with 0.05M K_2CO_3 in MeOH. In particular, Huang's method is efficient for the synthesis of organoselenium compounds. However, only several examples of simple electrophile as benzylhalides and α-haloamide were demonstrated and the reaction required high dilution condition that may reduce volume efficiency. Therefore, utilizing the previous methods for introduction of a selenium atom into a nucleic acid molecule, requires the preparation of diselenide having a necessary functional group. While these methods have proved adequate for the synthesis of simple functional groups, they are associated with the lack of functional group compatibility due to inherent problems. To address this challenge, we report a new, versatile method for the synthesis of 5′-selenium modified nucleosides by the use of 2-(trimethylsilyl)ethyl (TSE) seleno group.

In our strategy outlined in Scheme 1, the TSE seleno group serves as a convenient protecting group for the selenol functional group because this protecting group was easily converted into a corresponding selenolate anion via treatment with tetrabutyl ammonium fluoride (TBAF). The driving force

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behind this reaction is the extreme Si-F single bond strength of 582 kJ/mol[10] by the high affinity of Si to F.

Results and discussion

2-(Trimethylsilyl)ethyl (TSE) diselenide **1**[11] (Fig.1) prepared from 2-(bromoethyl)trimethyl silane with selenolate anion was generated in situ by reduction of elemental selenium with diisobutyl aluminium hydride (DIBAL) or sodium borohydride. Another selenating reagent **2** was synthesized by the reaction of potassium *p*-methylseleno benzoate[12] with (2-bromoethyl) trimethylsilane. Previously, we reported the stereoselective synthesis of α- and β-selenoglycosides[13] using potassium *p*-methylseleno benzoate. Furthermore, appealing the usefulness of **2**, we explored a general synthetic approach to the variety of selenium-containing β-lactam[14] using selenating reagent **2**. The active form of **2** is 2-(trimethylsilyl) ethaneselenolate, which is generated by treatment with amine in the presence of Cs_2CO_3. This anion reacted smoothly with the electrophilic part of target reactants, following the introduction of the 2-(trimethylsilyl) ethylseleno moiety; therefore, we applied it to the synthesis of 5′-TSE-selenonucleosides using these selenating reagents (**1** and **2**).

Our synthetic route for 5′-TSE-selenouridine is shown in Scheme 2. According to the previously reported procedure, the 2′,3′-*O*-isopropylidene uridine **4**[15] was synthesized from commercially available and inexpensive uridine **3**, which was smoothly converted to the key intermediate 2′,3′-*O*-isopropylidene-2,5′-anhydrouridine (cyclouridine) **5**[16] through Mitsunobu reaction[17] using DIAD and PPh_3 provided a yield of 94%. It is noteworthy to mention that compound **5** was stable in the freezer at -20°C for half a year. Next, the ring-opening reaction of cyclouridine **5** with **2** in the presence of *N*-methylhydrazine and Cs_2CO_3 in DMF provided the 2-(trimethylsilyl)ethane seleno group substituted uridine **6** in a yield of 97% via ring-opening reaction (Method A). Since there was no reaction, no product was formed in the absence of Cs_2CO_3. Therefore, Cs_2CO_3 accelerated selenium nucleophilicity for this ring-opening reaction. Furthermore, an excellent regioselectivity[18] was observed for reaction with cyclouridine **5** at the ribose C-5′ position by nucleophilic substitution of an activated selenolate anion. Additionally, the chemical shifts of C-5′ selenium of compound **6** in ^{77}Se NMR was observed at 181.9 ppm, indicating the presence of selenide function.[19] In the case of the reaction between **5** and TSE selenolate anion, which was generated by reductive cleavage of selenating reagent **1** with sodium borohydride in ethanolic DMF afforded the 5′-TSE-selenouridine **6** a yield of 95% (Method B) was observed. The structure of **6** was further confirmed by single-crystal X-ray crystallography (See Supporting Information). Finally, 5′-TSE-selenouridine **6** was treated with BzCl in the presence of Et_3N[20] to provide the *N*-Benzoylated 5′-TSE-selenouridine **7** in a yield of 94%.

As indicated in Table 1, we prepared various derivatives of **7** and **15**. For the scope of this methodology, uridine and adenosine were selected as representative compounds of pyrimidine and purine nucleosides, respectively. All electrophiles were added to the solution of **7** or **15** in DMF at room temperature and the mixture was stirred at room temperature to bring the reactions to completion. In this reaction, the 2-(trimethylsilyl)ethyl (TSE) group was removed with TBAF, followed by nucleophilic attack of the generated selenolate anion to an existing electrophile. We first examined alkylation with alkyl halide which led to the corresponding alkylated selenide **8a-8i** and **9a-9f** in good yield (61-93%, entries 1-9 and 46-75%, entries 19-24). The reaction with isobutylene oxide yielded the corresponding alcohol **8j** via ring-opening reaction (70%, entry 10). S_NAr reaction with 2-fluoronitrobenzene and 4-fluoronitrobenzene afforded a good yield of aryl selenide **8k** and **8l** (60% and 63%, entries 11, 12). Furthermore, we succeeded in the introduction of active functionalized groups such as ketone (**8m**: 60% and **8n**: 80%, entries 13, 14), ester (**8o**: 90% and **8p**: 77%, entries 15, 16), nitrile (**8q**: 67%, entry 17) with good to excellent yields. Reduction-labile functional groups, including nitro, epoxide, ketone, ester, and nitrile, remain intact under the reaction conditions. Consequently, this result indicated an extensive precedent for introduction of selenium functionality. We demonstrated the construction of selenomethionine structures (**8r**: 73% and **9g**: 72%, entries 18, 25). In this reaction, epimerization of the α-carbon did not occur during the course of the reaction. As a result, TSE approaches enabled a relatively straightforward access to a large variety of 5′-selenium modified nucleosides and synthetic methodologies for the construction of complex organic molecules.

With the successful results in hand, we next turned our attention to the synthesis of *Se*-uridyl-L-selenohomocysteine, *Se*-adenosyl-L-selenohomocysteine (SeAH) and *Se*-adenosyl-L-selenomethionine (SeAM). *S*-adenosyl-L-methionine (SAM) is an important molecule with the most diverse methyl donor for enzymatic methylations by SAM-dependent methyl transferases.[21] Recently, SeAM has been reported to have a significantly better methylation activity than SAM, thus making it a useful probe.[21] In addition, SeAH is important as the synthetic precursor of SeAM-analogues. Few strategies have been exploited for the synthesis of SeAH and SeAM. However, these methods commonly required highly flammable Na/NH_3 reduction for the generation of a selenolate anion from L-selenomethionine or *Se*-benzyl-selenohomocysteine.[22] Very recently, as an improved method, Luo et al. reported a large-scale protection-free synthesis of SeAH and SeAM,[23] wherein they successfully avoided the use of air-reactive metal. Therefore, this method provides several advantages over the precedents, involving practicality and safety. However, this route requires much purification by using expensive resin and lacks the functional group compatibility as mentioned previously. Furthermore, the use and low yield preparation of unstable[24] 5′-iodo-5′-deoxyadenosine as a precursor of SeAH seem to need improvement. Therefore, the present method is applied to the synthesis of *Se*-uridyl-L-selenohomocysteine, SeAH and SeAM.

As depicted in Scheme 3, we investigated the deprotection of selenomethionine functionalized uridine. The methyl ester and *N*-Bz group of **8r** were hydrolyzed to provide the Boc-

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protected *Se*-uridyl-L-selenohomocysteine **10** in a yield of 90%. Lastly, the deprotection of Boc-group and isopropylidene conducted in acidic conditions provided fully deprotected *Se*-uridyl-L-selenohomocysteine **11** in a yield of 93%.

As another example of a synthetic application, we investigated the synthesis of SeAH **18** and SeAM **19** (Scheme 4). Our synthesis of SeAH **18** commenced with the synthesis of 5′-TSE-selenoadenosine **15** starting from commercially available and inexpensive adenosine **12**. First, 5′-chloro-5′-deoxyadenosine **13**[25] was prepared from **12** via Appel reaction. Subsequently, 2′- and 3′-hydroxyl groups of **13** was protected with isopropylidene group, yielding 2′,3′-*O*-isopropylidene-5′-chloro-5′-deoxyadenosine **14**, following a reported method.[25] Next, the reaction between **14** and TSE selenolate anion, which was generated by reductive cleavage of selenating reagent **1** with sodium borohydride in ethanolic DMF afforded the **15** in a yield of 65% (Method B). In the use of selenating reagent **2** as a nucleophilic substitution reaction, a little lower yield (46%) was observed, due to difficulty in separating from the byproduct derived from the selenating reagent **2** (Method A). Next, the 2-(trimethylsilyl)ethyl group was removed with TBAF, followed by nucleophilic attack to Boc-protected iodohomoserine **16**,[26] giving selenomethionine **9g** in a yield of 72%. The methyl ester of **9g** was hydrolyzed to give the Boc-protected *Se*-Adenosyl-L-selenohomocysteine **17** in a yield of 91%. The deprotection of Boc-group and isopropylidene conducted in acidic conditions provided fully deprotected SeAH **18** in a yield of 97%.

Finally, we demonstrated the *Se*-alkylation of SeAH **18** with methyl iodide in the presence of silver (I) perchlorate, followed by salt formation with 10% TFA aq., which gave the corresponding SeAM **19** in 73% yield. The structure of **19** was confirmed by ^{1}H and ^{13}C NMR spectra compared to previous report.[21b, 23] The appearance of a newly formed methylseleno group of **19** was observed at 2.81 ppm and 2.77 ppm, respectively (47 : 53, *Se*-epimers). Furthermore, the ^{77}Se NMR of the selenonium **19** shifted downfield (δ = 325.5 ppm, 325.0 ppm : *Se*-epimers) compared to the selenide **18** (δ = 130.0 ppm).

Conclusions

In summary, an efficient method for the synthesis of 5′-selenium modified nucleosides has been explored based on the idea of direct functionalization of 2-(trimethylsilyl)ethyl (TSE) seleno groups. This method allows for rapid and easy access to a variety of 5′-selenium modified nucleosides that would be more difficult to access with traditional methods; thereby the 2-(trimethylsilyl)ethyl group appears very attractive for introduction of the selenium functionality in the synthesis of 5′-selenium modified nucleosides. Furthermore, this method was successfully applied to the synthesis of highly functionalized biological important nucleosides such as SeAH and SeAM. As a result, we expect this simple protocol to be of broad utility for the synthesis and development of new selenium-modified nucleosides. We believe that this method would be very useful for the future drug discovery of methyltransferase inhibitors and the development of epigenetic cancer therapies.

Experimental

General methods

Commercially available reagents were used without further purification. Compound **1**[11], **2**[14], **4**[15], **5**[16], **13**[25], **14**[25,] **16**[26] were synthesized according to the previously reported procedure.[25] All reactions were performed in a dry solvent under an argon atmosphere. Transfer of air- and moisture-sensitive reagents were performed via cannula under a positive pressure of argon atmosphere. DMF was degassed by argon bubbling prior to use. Analytical thin- layer chromatography (TLC) analysis was performed on Merck TLC (silica gel 60F_{254} on glass plate). The developed chromatography was analyzed by UV lamp (254 nm) or by spraying 10 % H_2SO_4 solution in EtOH, 20 % phosphomolybdic acid solution in EtOH, or ninhydrin reagent, followed by heating. Silica gel 60N (spherical, neutral) manufactured by Kanto Chemical Co. Inc. was used for flash column chromatography. NMR spectra were recorded on JEOL JNM-ECS400 (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz, ^{77}Se NMR: 75 MHz), JEOL JNM-ECA500 (^{1}H NMR: 500 MHz, ^{13}C NMR: 125 MHz, ^{77}Se NMR: 94 MHz) and JEOL JNM-ECA600 (^{1}H NMR: 600 MHz, ^{13}C NMR: 150 MHz, ^{77}Se NMR: 113 MHz) spectrometers. Chemical shifts of ^{1}H NMR are reported in δ values referred to $CHCl_3$ (δ 7.26 ppm), CH_3OH (δ 3.31 ppm), or D_2O (δ 4.79 ppm) as an internal standard and the following abbreviation were used as follows: s: singlet, d: doublet, t: triplet, m: multiplet. Chemical shifts of ^{13}C NMR are reported in δ values referred to $CHCl_3$ (δ 77.1 ppm), CH_3OH (δ 49.0 ppm) as an internal standard. The ^{77}Se NMR chemical shifts are reported in ppm (δ) relative to the external standard. High-resolution mass spectra (HRMS) was measured with a Waters UPLC system (Aquity UPLC XevoQTof). Melting points were measured by a Yanagimoto micromelting point apparatus. IR spectra were measured on JASCO FT/IR-410 Fourier Transform Infrared Spectrometer in $CHCl_3$ or MeOH. Optical rotations were measured with a JASCO P-2300.

Typical procedure for the direct functionalization of 2-(trimethylsilyl)ethyl (TSE) seleno groups

To a stirred solution of **7** (27.6 mg, 0.05 mmol) and methyl iodide (16 μL, 0.25 mmol) in DMF (0.5 mL) was added 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol) at rt. The mixture was stirred for 1 h at rt (TLC monitoring; EtOAc:n-hexane = 1:1), then the reaction mixture was diluted with EtOAc, and the solution was washed with water and brine, dried over Na_2SO_4, and then concentrated. The residue was purified by column chromatography on silica gel (EtOAc:n-hexane = 1:2) to afford **8a** (18.5 mg, 80%) as a white foam.

***N*-Benzoyl-5′-deoxy-5′-methylseleno-2′,3′-*O*-isopropyridene uridine (8a)**: white foam (18.5 mg, 80% yield)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.92 (m, 2H, Ph), 7.69-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.43 (d, 1H, *J* = 8.2 Hz, H-6), 5.86 (d, 1H, *J* = 8.2 Hz, H-5), 5.65 (d, 1H, *J* = 1.8 Hz, H-1′), 5.05

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(dd, 1H, *J* = 6.4, 1.8 Hz, H-2'), 4.74 (dd, 1H, *J* = 6.4, 4.1 Hz, H-3'), 4.31 (ddd, 1H, *J* = 6.9, 6.9, 4.1 Hz, H-4'), 2.79 (d, 2H, *J* = 6.8 Hz, H-5'), 2.06-2.02 (m, 3H, -SeC$\underline{H}_3$), 1.55 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (C=O), 162.0 (C-4), 149.2 (C-2), 142.3 (C-6), 135.4, 131.4, 130.7, 129.4 (Ph), 114.8 (-$\underline{C}(CH_3)_2$), 102.8 (C-5), 95.3 (C-1'), 87.4 (C-4'), 84.6 (C-2'), 83.9 (C-3'), 27.5 (C-5'), 27.2 (-C($\underline{C}H_3)_2$), 25.4 (-C($\underline{C}H_3)_2$), 5.5 (-Se$\underline{C}H_3$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 49.9; IR (film): 1748, 1709, 1673; $[\alpha]^{20}_D$ +3.1 (*c* 0.55, $CHCl_3$); HRMS (ESI): calcd for $C_{20}H_{22}N_2O_6SeNa$ $[M+Na]^+$: 489.0541, found: 489.0539.

***N*-Benzoyl-5'-deoxy-5'-ethylseleno-2',3'-*O*-isopropyridene uridine (8b)**: white foam (17.7 mg, 74% yield)

The reaction was conducted with **7** (27.6 mg, 0.05 mmol), ethyl iodide (20 μL, 0.25 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.92 (m, 2H, Ph), 7.68-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.44 (d, 1H, *J* = 8.6 Hz, H-6), 5.85 (d, 1H, *J* = 8.2 Hz, H-5), 5.67 (d, 1H, *J* = 2.3 Hz, H-1'), 5.03 (dd, 1H, *J* = 6.9, 1.8 Hz, H-2'), 4.74 (dd, 1H, *J* = 6.8, 4.2 Hz, H-3'), 4.31 (ddd, 1H, *J* = 6.4, 6.4, 4.1 Hz, H-4'), 2.82 (d, 2H, *J* = 6.4 Hz, H-5'), 2.61 (q, 2H, *J* = 7.8 Hz, -SeC$\underline{H}_2$CH$_3$), 1.55 (s, 3H, CH_3), 1.37 (t, 3H, *J* = 7.8 Hz, -SeCH$_2$C$\underline{H}_3$), 1.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (C=O), 162.0 (C-4), 149.2 (C-2), 142.2 (C-6), 135.4, 131.4, 130.7, 129.4 (Ph), 114.8 (-$\underline{C}(CH_3)_2$), 102.8 (C-5), 95.0 (C-1'), 87.4 (C-4'), 84.6 (C-2'), 83.8 (C-3'), 27.2 (-C($\underline{C}H_3)_2$), 25.5 (C-5'), 25.4 (-C($\underline{C}H_3)_2$), 18.7 (-Se$\underline{C}$H$_2$CH$_3$), 15.8 (-SeCH$_2\underline{C}H_3$); ^{77}Se NMR (113 MHz, $CDCl_3$): δ 161.5; IR (film): 1748, 1709, 1670; $[\alpha]^{20}_D$ +1.6 (*c* 0.58, $CHCl_3$); HRMS (ESI): calcd for $C_{21}H_{24}N_2O_6SeNa$ $[M+Na]^+$: 503.0697, found: 503.0697.

***N*-Benzoyl-5'-deoxy-5'-isopropylseleno-2',3'-*O*-isopropyridene uridine (8c)**: white foam (15.8 mg, 64% yield)

The reaction was conducted with **7** (27.6 mg, 0.05 mmol), isopropyl iodide (20 μL, 0.25 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.92 (m, 2H, Ph), 7.68-7.64 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.45 (d, 1H, *J* = 8.2 Hz, H-6), 5.86 (d, 1H, *J* = 8.2 Hz, H-5), 5.67 (d, 1H, *J* = 2.3 Hz, H-1'), 5.02 (dd, 1H, *J* = 6.9, 2.3 Hz, H-2'), 4.74 (dd, 1H, *J* = 6.8, 4.1 Hz, H-3'), 4.32 (ddd, 1H, *J* = 6.4, 6.4, 4.1 Hz, H-4'), 3.18-3.11 (m, 1H, -C$\underline{H}$(CH$_3)_2$), 2.89-2.80 (m, 2H, H-5'), 1.54 (s, 3H, CH_3), 1.41-1.36 (m, 6H, -CH(C$\underline{H}_3)_2$), 1.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (C=O), 162.1 (C-4), 149.2 (C-2), 142.2 (C-6), 135.4, 131.4, 130.7, 129.4 (Ph), 114.9 (-$\underline{C}(CH_3)_2$), 102.8 (C-5), 94.8 (C-1'), 87.4 (C-4'), 84.7 (C-2'), 83.8 (C-3'), 30.4 (-$\underline{C}$H(CH$_3)_2$), 27.2 (-C($\underline{C}H_3)_2$), 25.4 (-C($\underline{C}H_3)_2$), 24.9 (C-5'), 24.6 (-CH($\underline{C}H_3)_2$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 254.9; IR (film): 1749, 1709, 1671; $[\alpha]^{20}_D$ +3.2 (*c* 0.65, $CHCl_3$); HRMS (ESI): calcd for $C_{22}H_{26}N_2O_6SeNa$ $[M+Na]^+$: 517.0854, found: 517.0855.

***N*-Benzoyl-5'-deoxy-5'-benzylseleno-2',3'-*O*-isopropyridene uridine (8d)**: white foam (21.9 mg, 81% yield)

The reaction was conducted with **7** (27.6 mg, 0.05 mmol), benzyl bromide (12 μL, 0.1 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93-7.91 (m, 2H, Ph), 7.67-7.63 (m, 1H, Ph), 7.51-7.47 (m, 2H, Ph), 7.40 (d, 1H, *J* = 8.2 Hz, H-6), 7.30-7.19 (m, 5H, Ph, overlap with $CDCl_3$), 5.84 (d, 1H, *J* = 8.2 Hz, H-5), 5.64 (d, 1H, *J* = 2.3 Hz, H-1'), 4.97 (dd, 1H, *J* = 6.9, 2.3 Hz, H-2'), 4.60 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.22 (ddd, 1H, *J* = 6.4, 6.4, 4.6 Hz, H-4'), 3.82-3.78 (m, 2H, -SeC$\underline{H}_2$Ph), 2.81-2.70 (m, 2H, H-5'), 1.53 (s, 3H, CH_3), 1.31 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (C=O), 162.0 (C-4), 149.1 (C-2), 142.2 (C-6), 138.8 (Ph), 135.4, 131.4, 130.7, 129.4, 129.0, 128.8, 127.2 (Ph), 114.8 (-$\underline{C}(CH_3)_2$), 102.8 (C-5), 94.9 (C-1'), 87.1 (C-4'), 84.5 (C-2'), 83.8 (C-3'), 28.2 (-Se$\underline{C}$H$_2$Ph), 27.2 (-C($\underline{C}H_3)_2$), 25.8 (C-5'), 25.4 (-C($\underline{C}H_3)_2$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 221.4; IR (film): 1749, 1709, 1673; $[\alpha]^{20}_D$ +1.2 (*c* 0.67, $CHCl_3$); HRMS (ESI): calcd for $C_{26}H_{26}N_2O_6SeNa$ $[M+Na]^+$: 565.0854, found: 565.0856.

***N*-Benzoyl-5'-deoxy-5'-(4-methylbenyl)seleno-2',3'-*O*-isopropyridene uridine (8e)**: white foam (41.4 mg, 93% yield)

The reaction was conducted with **7** (44.1 mg, 0.08 mmol), 4-methylbenzyl bromide (44.4 mg, 0.24 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (240 μL, 0.24 mmol).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93-7.92 (m, 2H, Ph), 7.67-7.64 (m, 1H, Ph), 7.50-7.48 (m, 2H, Ph), 7.42 (d, 1H, *J* = 8.3 Hz, H-6), 7.15-7.14 (m, 2H, Ph), 7.09-7.08 (m, 2H, Ph), 5.84 (d, 1H, *J* = 7.6 Hz, H-5), 5.65 (d, 1H, *J* = 2.0 Hz, H-1'), 4.96-4.95 (m, 1H, H-2'), 4.58 (dd, 1H, *J* = 6.2, 4.1 Hz, H-3'), 4.23 (ddd, 1H, *J* = 6.2, 6.2, 4.1 Hz, H-4'), 3.77 (s, 2H, -SeC$\underline{H}_2$Ph), 2.78 (dd, 1H, *J* = 13.1, 6.9 Hz, H-5'a), 2.71 (dd, 1H, *J* = 13.1, 6.2 Hz, H-5'b), 2.31 (s, 3H, PhC$\underline{H}_3$), 1.52 (s, 3H, CH_3), 1.30 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.4 (C=O), 162.0 (C-4), 149.1 (C-2), 142.1 (C-6), 136.8, 135.7, 135.4, 131.3, 130.6, 129.4$_4$, 129.3$_6$, 128.9 (Ph), 114.8 (-$\underline{C}(CH_3)_2$), 102.7 (C-5), 94.7 (C-1'), 86.9 (C-4'), 84.5 (C-2'), 83.7 (C-3'), 27.9 (-Se$\underline{C}$H$_2$Ph), 27.2 (-C($\underline{C}H_3)_2$), 25.7 (C-5'), 25.3 (-C($\underline{C}H_3)_2$), 21.2 (PhC$\underline{H}_3$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 220.6; IR (film): 1749, 1709, 1674; $[\alpha]^{20}_D$ +4.6 (*c* 0.72, $CHCl_3$); HRMS (ESI): calcd for $C_{27}H_{28}N_2O_6SeNa$ $[M+Na]^+$: 579.1010, found: 579.1012.

***N*-Benzoyl-5'-deoxy-5'-(4-nitrobenyl)seleno-2',3'-*O*-isopropyridene uridine (8f)**: pale yellow foam (28.6 mg, 61% yield)

The reaction was conducted with **7** (44.1 mg, 0.08 mmol), 4-nitrobenzyl bromide (51.8 mg, 0.24 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (240 μL, 0.24 mmol).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11-8.09 (m, 2H, Ph), 7.94-7.92 (m, 2H, Ph), 7.69-7.65 (m, 2H, Ph), 7.52-7.48 (m, 2H, Ph), 7.40-7.33 (m, 3H, H-6, Ph), 5.86 (d, 1H, *J* = 8.3 Hz, H-5), 5.54 (d, 1H, *J* = 1.8 Hz, H-1'), 5.09-5.08 (m, 1H, H-2'), 4.68 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.19 (ddd, 1H, *J* = 6.9, 6.9, 4.1 Hz, H-4'), 3.85-3.82 (m, 2H, -SeC$\underline{H}_2$Ph), 2.80-2.71 (m, 2H, H-5'), 1.52 (s, 3H, CH_3), 1.32 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3 (C=O), 162.0 (C-4), 149.1 (C-2), 147.0, 147.0 (Ph, overlap), 143.0 (C-6), 135.6, 131.2, 130.7, 129.8, 129.4, 124.0 (Ph), 114.8 (-$\underline{C}(CH_3)_2$), 102.9 (C-5), 96.4 (C-1'), 88.0 (C-4'), 84.5 (C-2'), 83.9 (C-3'), 27.2 (-C($\underline{C}H_3)_2$), 27.0 (-Se$\underline{C}$H$_2$Ph), 25.9 (C-5'), 25.3 (-C($\underline{C}H_3)_2$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 243.3; IR (film): 1749, 1709, 1671; $[\alpha]^{20}_D$ +16.5 (*c* 0.20, $CHCl_3$); HRMS (ESI): calcd for $C_{26}H_{25}N_3O_8SeNa$ $[M+Na]^+$: 610.0705, found: 610.0703.

***N*-Benzoyl-5'-deoxy-5'-allylseleno-2',3'-*O*-isopropyridene uridine (8g)**: white foam (20.8 mg, 85% yield)

The reaction was conducted with **7** (27.6 mg, 0.05 mmol), allyl bromide (13 μL, 0.15 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).

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^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.92 (m, 2H, Ph), 7.69-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.42 (d, 1H, *J* = 8.2 Hz, H-6), 5.89-5.78 (m, 2H, H-5, -SeCH$_2$C<u>H</u>CH$_2$), 5.65 (d, 1H, *J* = 2.3 Hz, H-1'), 5.04-4.97 (m, 3H, H-2', -SeCH$_2$CHC<u>H$_2$</u>), 4.73 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.28 (ddd, 1H, *J* = 6.9, 6.9, 4.1 Hz, H-4'), 3.21-3.19 (m, 2H, -SeC<u>H$_2$</u>CHCH$_2$), 2.81-2.71 (m, 2H, H-5'), 1.55 (s, 3H, CH_3), 1.34 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (<u>C</u>OPh), 162.0 (C-4), 149.1 (C-2), 142.3 (C-6), 135.4 (Ph), 134.4 (Allyl), 131.2, 130.6, 129.3 (Ph), 117.1 (Allyl), 114.7 (-<u>C</u>(CH$_3$)$_2$), 102.6 (C-5), 94.9 (C-1'), 87.1 (C-4'), 84.5 (C-2'), 83.7 (C-3'), 27.2 (-C(<u>C</u>H$_3$)$_2$), 26.9 (C-5'), 25.3 (-C(<u>C</u>H$_3$)$_2$), 25.0 (Allyl); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 157.2; IR (film): 1749, 1710, 1670; $[\alpha]^{20}_D$ +6.6 (*c* 0.55, $CHCl_3$); HRMS (ESI): calcd for $C_{22}H_{24}N_2O_6SeNa$ $[M+Na]^+$: 515.0697, found: 515.0700.

***N*-Benzoyl-5'-deoxy-5'-propargylseleno-2',3'-*O*-isopropyridene uridine (8h)**: white foam (25.3 mg, 86% yield)
The reaction was conducted with **7** (33.1 mg, 0.06 mmol), propargyl bromide (13.6 μL, 0.18 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (180 μL, 0.18 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.92 (m, 2H, Ph), 7.69-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.40 (d, 1H, *J* = 8.3 Hz, H-6), 5.86 (d, 1H, *J* = 8.3 Hz, H-5), 5.64 (d, 1H, *J* = 2.3 Hz, H-1'), 5.07-5.05 (m, 1H, H-2'), 4.78 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.39-4.35 (m, 1H, H-4'), 3.24-3.22 (m, 2H, -SeC<u>H$_2$</u>CCH), 3.04-3.02 (m, 2H, H-5'), 2.26 (s, 1H, -SeCH$_2$CC<u>H</u>), 1.54 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (<u>C</u>OPh), 162.0 (C-4), 149.1 (C-2), 142.4 (C-6), 135.5, 131.3, 130.7, 129.4 (Ph), 114.9 (-<u>C</u>(CH$_3$)$_2$), 102.8 (C-5), 95.3 (C-1'), 87.5 (C-4'), 84.6 (C-2'), 83.9 (C-3'), 80.4 (-SeCH$_2$<u>C</u>CH), 72.1 (-SeCH$_2$C<u>C</u>H), 27.2 (-C(<u>C</u>H$_3$)$_2$), 26.3 (C-5'), 25.4 (-C(<u>C</u>H$_3$)$_2$), 8.0 (-Se<u>C</u>H$_2$CCH); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 220.2; IR (film): 3288 (alkyne), 1748, 1709, 1671; $[\alpha]^{20}_D$ +13.6 (*c* 0.48, $CHCl_3$); HRMS (ESI): calcd for $C_{22}H_{22}N_2O_6SeNa$ $[M+Na]^+$: 513.0541, found: 513.0546.

***N*-Benzoyl-5'-deoxy-5'-(2-methoxyethyl)seleno-2',3'-*O*-isopropyridene uridine (8i)**: white foam (75.6 mg, 74% yield)
The reaction was conducted with **7** (113.1 mg, 0.2 mmol), 2-bromoethyl methyl ether (57 μL, 0.6 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (600 μL, 0.6 mmol).
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.93-7.92 (m, 2H, Ph), 7.68-7.65 (m, 1H, Ph), 7.52-7.49 (m, 2H, Ph), 7.43 (d, 1H, *J* = 8.2 Hz, H-6), 5.85 (d, 1H, *J* = 8.2 Hz, H-5), 5.66 (s, 1H, H-1'), 5.02 (d, 1H, *J* = 5.5 Hz, H-2'), 4.74 (dd, 1H, *J* = 6.8, 4.1 Hz, H-3'), 4.32 (ddd, 1H, *J* = 6.2, 6.2, 4.1 Hz, H-4'), 3.61-3.59 (m, 2H, -SeCH$_2$C<u>H$_2$</u>OCH$_3$), 3.34 (s, 3H, -SeCH$_2$CH$_2$OC<u>H$_3$</u>), 2.87 (d, 2H, *J* = 6.2 Hz, H-5'), 2.77-2.75 (m, 2H, -SeC<u>H$_2$</u>CH$_2$OCH$_3$), 1.54 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.4 (<u>C</u>OPh), 162.0 (C-4), 149.1 (C-2), 142.3 (C-6), 135.4, 131.3, 130.6, 129.4 (Ph), 114.8 (-<u>C</u>(CH$_3$)$_2$), 102.8 (C-5), 94.9 (C-1'), 87.4 (C-4'), 84.6 (C-2'), 83.7 (C-3'), 72.7 (-SeCH$_2$<u>C</u>H$_2$OCH$_3$), 58.7 (-SeCH$_2$CH$_2$O<u>C</u>H$_3$), 27.2 (-C(<u>C</u>H$_3$)$_2$), 26.3 (C-5'), 25.4 (-C(<u>C</u>H$_3$)$_2$), 24.2 (-Se<u>C</u>H$_2$CH$_2$OCH$_3$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 116.2; IR (film): 1749, 1709, 1673; $[\alpha]^{20}_D$ +12.4 (*c* 0.12, $CHCl_3$); HRMS (ESI): calcd for $C_{22}H_{26}N_2O_7SeNa$ $[M+Na]^+$: 533.0803, found: 533.0803.

***N*-Benzoyl-5'-deoxy-5'-(2,2-dimethylethane-2-ol)seleno-2',3'-*O*-isopropyridene uridine (8j)**: white foam (36.5 mg, 70% yield)
The reaction was conducted with **7** (55.2 mg, 0.1 mmol), isobutylene oxide (88.8 μL, 1 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (300 μL, 0.3 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96-7.93 (m, 2H, Ph), 7.70-7.66 (m, 1H, Ph), 7.54-7.50 (m, 2H, Ph), 7.40 (d, 1H, *J* = 8.2 Hz, H-6), 5.86 (d, 1H, *J* = 8.2 Hz, H-5), 5.61 (s, 1H, H-1'), 5.09-5.07 (m, 1H, H-2'), 4.77-4.74 (m, 1H, H-3'), 4.33-4.30 (m, 1H, H-4'), 2.88-2.73 (m, 4H, H-5', -SeC<u>H$_2$</u>C(CH$_3$)$_2$OH), 2.34 (br s, 1H, -SeCH$_2$C(CH$_3$)$_2$O<u>H</u>), 1.55 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.28-1.27 (m, 6H, -SeCH$_2$C(C<u>H$_3$</u>)$_2$OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (<u>C</u>OPh), 162.1 (C-4), 149.2 (C-2), 142.7 (C-6), 135.5, 131.3, 130.7, 129.4 (Ph), 114.8 (-<u>C</u>(CH$_3$)$_2$), 102.8 (C-5), 95.7 (C-1'), 87.7 (C-4'), 84.6 (C-2'), 83.8 (C-3'), 70.2 (-SeCH$_2$<u>C</u>(CH$_3$)$_2$OH), 41.7 (-Se<u>C</u>H$_2$C(CH$_3$)$_2$OH), 29.0 (-SeCH$_2$C(<u>C</u>H$_3$)$_2$OH), 28.0 (C-5'), 27.2 (-C(<u>C</u>H$_3$)$_2$), 25.4 (-C(<u>C</u>H$_3$)$_2$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 68.4; IR (film): 3491 (OH), 1748, 1709, 1672; $[\alpha]^{20}_D$ +12.8 (*c* 0.57, $CHCl_3$); HRMS (ESI): calcd for $C_{23}H_{28}N_2O_7SeNa$ $[M+Na]^+$: 547.0959, found: 547.0953.

***N*-Benzoyl-5'-deoxy-5'-(2-nitrophenyl)seleno-2',3'-*O*-isopropyridene uridine (8k)**: yellow foam (17.2 mg, 60% yield)
The reaction was conducted with **7** (27.6 mg, 0.05 mmol), 2-fluoronitrobenzene (10.5 μL, 0.1 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).
^{1}H NMR (600 MHz, $CDCl_3$): δ 8.28-8.27 (m, 1H, Ph), 7.93-7.92 (m, 2H, Ph), 7.62-7.60 (m, 1H, Ph), 7.47-7.45 (m, 4H, Ph), 7.33-7.30 (m, 2H, H-6, Ph), 5.82 (d, 1H, *J* = 8.2 Hz, H-5), 5.56 (d, 1H, *J* = 1.4 Hz, H-1'), 5.15 (d, 1H, *J* = 6.2 Hz, H-2'), 4.83 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.41-4.38 (m, 1H, H-4'), 3.25-3.18 (m, 2H, H-5'), 1.51 (s, 3H, CH_3), 1.32 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.3 (<u>C</u>OPh), 162.0 (C-4), 149.3 (C-2), 147.0 (Ph), 143.0 (C-6), 135.5, 133.9, 132.3, 131.2, 130.6, 129.4, 129.2, 126.6, 126.0 (Ph), 114.8 (-<u>C</u>(CH$_3$)$_2$), 102.8 (C-5), 96.7 (C-1'), 86.9 (C-4'), 84.6 (C-2'), 84.4 (C-3'), 28.5 (C-5'), 27.1 (-C(<u>C</u>H$_3$)$_2$), 25.3 (-C(<u>C</u>H$_3$)$_2$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 329.2; IR (film): 1749, 1709, 1672; $[\alpha]^{20}_D$ +81.0 (*c* 0.54, $CHCl_3$); HRMS (ESI): calcd for $C_{25}H_{23}N_3O_8SeNa$ $[M+Na]^+$:596.0548, found: 596.0548.

***N*-Benzoyl-5'-deoxy-5'-(4-nitrophenyl)seleno-2',3'-*O*-isopropyridene uridine (8l)**: yellow foam (18.0 mg, 63% yield)
The reaction was conducted with **7** (27.6 mg, 0.05 mmol), 4-fluoronitrobenzene (10.6 μL, 0.1 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06-8.04 (m, 2H, Ph), 7.95-7.93 (m, 2H, Ph), 7.68-7.64 (m, 1H, Ph), 7.52-7.47 (m, 4H, Ph), 7.29 (d, 1H, *J* = 8.3 Hz, H-6), 5.84 (d, 1H, *J* = 8.3 Hz, H-5), 5.51 (d, 1H, *J* = 1.4 Hz, H-1'), 5.16-5.14 (m, 1H, H-2'), 4.80 (dd, 1H, *J* = 6.4, 4.1 Hz, H-3'), 4.33 (ddd, 1H, *J* = 6.9, 6.9, 4.1 Hz, H-4'), 3.33-3.22 (m, 2H, H-5'), 1.51 (s, 3H, CH_3), 1.32 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3 (<u>C</u>OPh), 161.9 (C-4), 149.2 (C-2), 146.5 (Ph), 143.2 (C-6), 140.6, 135.6, 131.2, 130.7, 130.6, 129.4, 124.0 (Ph), 114.7 (-<u>C</u>(CH$_3$)$_2$), 102.9 (C-5), 97.1 (C-1'), 87.6 (C-4'), 84.7 (C-2'), 84.1 (C-3'), 29.1 (C-5'), 27.1 (-C(<u>C</u>H$_3$)$_2$), 25.3 (-C(<u>C</u>H$_3$)$_2$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 283.9; IR (film): 1749, 1709, 1672; $[\alpha]^{20}_D$ +42.3 (*c* 0.40, $CHCl_3$); HRMS (ESI): calcd for $C_{25}H_{23}N_3O_8SeNa$ $[M+Na]^+$:596.0548, found: 596.0555.

***N*-Benzoyl-5'-deoxy-5'-(2-oxopropyl)seleno-2',3'-*O*-isopropyridene uridine (8m)**: white foam (15.2 mg, 60% yield)

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The reaction was conducted with **7** (27.6 mg, 0.05 mmol), bromoacetone (41.9 μL, 0.5 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97-7.95 (m, 2H, Ph), 7.69-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.38 (d, 1H, *J* = 8.2 Hz, H-6), 5.86 (d, 1H, *J* = 8.2 Hz, H-5), 5.60 (d, 1H, *J* = 1.8 Hz, H-1'), 5.07-5.05 (m, 1H, H-2'), 4.72 (dd, 1H, *J* = 6.4, 4.1 Hz, H-3'), 4.30 (ddd, 1H, *J* = 6.9, 6.9, 4.6 Hz, H-4'), 3.30-3.22 (m, 2H, -SeC$\underline{H}_2$COCH$_3$), 2.86-2.84 (m, 2H, H-5'), 2.31 (s, 3H, -SeCH$_2$COC$\underline{H}_3$), 1.55 (s, 3H, CH$_3$), 1.33 (s, 3H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7 (-SeCH$_2$$\underline{C}OCH_3$), 168.5 ($\underline{C}$OPh), 162.1 (C-4), 149.2 (C-2), 142.6 (C-6), 135.5, 131.3, 130.7, 129.4 (Ph), 114.8 (-$\underline{C}$(CH$_3$)$_2$), 102.8 (C-5), 95.6 (C-1'), 87.5 (C-4'), 84.6 (C-2'), 83.9 (C-3'), 32.3 (-Se$\underline{C}$H$_2$COCH$_3$), 27.7 (-SeCH$_2$CO$\underline{C}$H$_3$), 27.2 (-C($\underline{C}$H$_3$)$_2$), 26.4 (C-5'), 25.4 (-C($\underline{C}$H$_3$)$_2$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 166.9; IR (film): 1748, 1708, 1668; $[\alpha]^{20}_D$ +5.6 (*c* 0.43, $CHCl_3$); HRMS (ESI): calcd for $C_{22}H_{24}N_2O_7SeNa$ $[M+Na]^+$: 531.0646, found: 531.0643.

***N*-Benzoyl-5'-deoxy-5'-(2-oxo-2-phenylethyl)seleno-2',3'-*O*-isopropyridene uridine (8n)**: white foam (36.4 mg, 80% yield)
The reaction was conducted with **7** (44.1 mg, 0.08 mmol), 2-bromoacetophenone (47.8 mg, 0.24 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (240 μL, 0.24 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.92 (m, 4H, Ph), 7.65-7.56 (m, 2H, Ph), 7.50-7.45 (m, 4H, Ph), 7.39 (d, 1H, *J* = 8.2 Hz, H-6), 5.81 (d, 1H, *J* = 8.2 Hz, H-5), 5.64 (m, 1H, H-1'), 5.02-5.00 (m, 1H, H-2'), 4.70 (dd, 1H, *J* = 6.8, 4.1 Hz, H-3'), 4.34 (m, 1H, H-4'), 3.89-3.82 (m, 2H, -SeC$\underline{H}_2$COPh), 2.94-2.92 (m, 2H, H-5'), 1.53 (s, 3H, CH$_3$), 1.31 (s, 3H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.8 (-SeCH$_2$$\underline{C}$OPh), 168.4 ($\underline{C}$OPh), 162.0 (C-4), 149.1 (C-2), 142.3 (C-6), 135.4, 135.1, 133.6, 131.3, 130.7, 129.3, 128.9, 128.8 (Ph), 114.8 (-$\underline{C}$(CH$_3$)$_2$), 102.8 (C-5), 95.0 (C-1'), 87.2 (C-4'), 84.6 (C-2'), 83.8 (C-3'), 27.3 (-Se$\underline{C}$H$_2$COPh), 27.2 (-C($\underline{C}$H$_3$)$_2$), 26.9 (C-5'), 25.4 (-C($\underline{C}$H$_3$)$_2$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 179.2; IR (film): 1748, 1708, 1670; $[\alpha]^{20}_D$ +0.09 (*c* 0.45, $CHCl_3$); HRMS (ESI): calcd for $C_{27}H_{26}N_2O_7SeNa$ $[M+Na]^+$: 593.0803, found: 593.0804.

***N*-Benzoyl-5'-deoxy-5'-(methyl-2-acetate)seleno-2',3'-*O*-isopropyridene uridine (8o)**: white foam (23.6 mg, 90% yield)
The reaction was conducted with **7** (27.6 mg, 0.05 mmol), methyl bromoacetate (18.6 μL, 0.2 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.93 (m, 2H, Ph), 7.69-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.38 (d, 1H, *J* = 8.2 Hz, H-6), 5.86 (d, 1H, *J* = 8.2 Hz, H-5), 5.63 (d, 1H, *J* = 2.3 Hz, H-1'), 5.06-5.05 (m, 1H, H-2'), 4.74 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.34 (ddd, 1H, *J* = 6.9, 6.9, 4.1 Hz, H-4'), 3.70 (s, 3H, -SeCH$_2$CO$_2$C$\underline{H}_3$), 3.25-3.17 (m, 2H, -SeC$\underline{H}_2$CO$_2$CH$_3$), 3.05-2.97 (m, 2H, H-5'), 1.55 (s, 3H, CH$_3$), 1.33 (s, 3H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6 (-SeCH$_2$$\underline{C}O_2CH_3$), 168.4 ($\underline{C}$OPh), 162.0 (C-4), 149.1 (C-2), 142.5 (C-6), 135.4, 131.2, 130.6, 129.3 (Ph), 114.7 (-$\underline{C}$(CH$_3$)$_2$), 102.7 (C-5), 95.2 (C-1'), 87.3 (C-4'), 84.5 (C-2'), 83.7 (C-3'), 52.5 (-SeCH$_2$CO$_2$$\underline{C}H_3$), 27.1 (-C($\underline{C}H_3$)$_2$), 27.0 (C-5'), 25.3 (-C($\underline{C}$H$_3$)$_2$), 22.7 (-Se$\underline{C}$H$_2$CO$_2$CH$_3$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 186.9; IR (film): 1748, 1708, 1668; $[\alpha]^{20}_D$ +1.8 (*c* 0.96, $CHCl_3$); HRMS (ESI): calcd for $C_{22}H_{24}N_2O_8SeNa$ $[M+Na]^+$: 547.0596, found: 547.0596.

***N*-Benzoyl-5'-deoxy-5'-(*tert*-butylacetate)seleno-2',3'-*O*-isopropyridene uridine (8p)**: white foam (43.6 mg, 77% yield)
The reaction was conducted with **7** (55.2 mg, 0.1 mmol), *tert*-butyl bromoacetate (73.8 μL, 0.5 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (300 μL, 0.3 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.93 (m, 2H, Ph), 7.69-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.42 (d, 1H, *J* = 8.7 Hz, H-6), 5.85 (d, 1H, *J* = 8.2 Hz, H-5), 5.66 (d, 1H, *J* = 1.8 Hz, H-1'), 5.04-5.03 (m, 1H, H-2'), 4.75 (dd, 1H, *J* = 6.4, 4.2 Hz, H-3'), 4.38-4.34 (m, 1H, H-4'), 3.15-3.08 (m, 2H, -SeCH$_2$CO$_2$C(C$\underline{H}_3$)$_3$), 3.01-3.00 (m, 2H, H-5'), 1.54 (s, 3H, CH$_3$), 1.45 (s, 9H, -SeCH$_2$CO$_2$C(C$\underline{H}_3$)$_3$), 1.33 (s, 3H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4 (-SeCH$_2$$\underline{C}O_2$C(CH$_3$)$_3$), 168.4 ($\underline{C}$OPh), 162.0 (C-4), 149.1 (C-2), 142.3 (C-6), 135.4, 131.3, 130.6, 129.4 (Ph), 114.8 (-$\underline{C}$(CH$_3$)$_2$), 102.8 (C-5), 95.1 (C-1'), 87.1 (C-4'), 84.6 (C-2'), 83.8 (C-3'), 81.7 (-SeCH$_2$CO$_2$$\underline{C}$(CH$_3$)$_3$), 28.0 (-SeCH$_2CO_2$C($\underline{C}H_3$)$_3$), 27.2 (-C($\underline{C}H_3$)$_2$), 26.7 (C-5'), 25.3 (-C($\underline{C}$H$_3$)$_2$), 24.6 (-Se$\underline{C}$H$_2$CO$_2$C(CH$_3$)$_3$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 179.3; IR (film): 1749, 1709, 1673; $[\alpha]^{20}_D$ +0.82 (*c* 0.55, $CHCl_3$); HRMS (ESI): calcd for $C_{25}H_{30}N_2O_8SeNa$ $[M+Na]^+$: 589.1065, found: 589.1064.

***N*-Benzoyl-5'-deoxy-5'-cyanomethylseleno-2',3'-*O*-isopropyridene uridine (8q)**: white foam (19.8 mg, 67% yield)
The reaction was conducted with **7** (33.1 mg, 0.06 mmol), bromoacetonitrile (12.5 μL, 0.18 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (180 μL, 0.18 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97-7.95 (m, 2H, Ph), 7.70-7.67 (m, 1H, Ph), 7.55-7.51 (m, 2H, Ph), 7.33 (d, 1H, *J* = 8.2 Hz, H-6), 5.87 (d, 1H, *J* = 8.2 Hz, H-5), 5.56 (d, 1H, *J* = 1.8 Hz, H-1'), 5.14-5.12 (m, 1H, H-2'), 4.78 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.37 (ddd, 1H, *J* = 7.8, 7.8, 2.3 Hz, H-4'), 3.25-3.02 (m, 4H, H-5', -SeC$\underline{H}_2$CN), 1.55 (s, 3H, CH$_3$), 1.34 (s, 3H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 ($\underline{C}$OPh), 162.0 (C-4), 149.2 (C-2), 143.0 (C-6), 135.6, 131.2, 130.7, 129.4 (Ph), 117.4 (-SeCH$_2$$\underline{C}$N), 115.0 (-$\underline{C}$(CH$_3$)$_2$), 103.0 (C-5), 96.4 (C-1'), 88.3 (C-4'), 84.5 (C-2'), 84.0 (C-3'), 27.6 (-C($\underline{C}$H$_3$)$_2$), 27.2 (C-5'), 25.4 (-C($\underline{C}$H$_3$)$_2$), 3.4 (-Se$\underline{C}$H$_2$CN); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 234.3; IR (film): 2241 (CN), 1747, 1709, 1668; $[\alpha]^{20}_D$ +6.4 (*c* 0.47, $CHCl_3$); HRMS (ESI): calcd for $C_{21}H_{21}N_3O_6SeNa$ $[M+Na]^+$: 514.0493, found: 514.0502.

***N*-Benzoyl-5'-deoxy-5'-(2-(*tert*-butoxycarbonylamino)butanoate)seleno-2',3'-*O*-isopropyridene uridine (8r)**: white foam (97.2 mg, 73% yield)
The reaction was conducted with **7** (113.1 mg, 0.2 mmol), (*S*)-methyl 2-(*tert*-butoxycarbonylamino)-4-iodobutanoate **16**[26] (137.3 mg, 0.4 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (600 μL, 0.6 mmol).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.92 (m, 2H, Ph), 7.69-7.65 (m, 1H, Ph), 7.53-7.49 (m, 2H, Ph), 7.43 (d, 1H, *J* = 8.3 Hz, H-6), 5.86 (d, 1H, *J* = 8.3 Hz, H-5), 5.65 (s, 1H, H-1'), 5.10-5.02 (m, 2H, H-2', NH), 4.74-4.71 (m, 1H, H-3'), 4.39-4.38 (m, 1H, H-α), 4.30-4.26 (m, 1H, H-4'), 3.73 (s, 3H, CO$_2$C$\underline{H}_3$), 2.83-2.81 (m, 2H, H-5'), 2.61 (t, 2H, *J* = 7.8 Hz, H-γ), 2.17-2.13 (m, 1H, H-βa), 2.01-1.93 (m, 1H, H-βb), 1.55 (s, 3H, CH$_3$), 1.44 (s, 9H, CO$_2$C(C$\underline{H}_3$)$_3$), 1.33 (s, 3H, CH$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7 ($\underline{C}$O$_2$CH$_3$), 168.4 ($\underline{C}$OPh), 162.0 (C-4), 155.5 ($\underline{C}$O$_2$C(CH$_3$)$_3$), 149.2 (C-2), 142.3 (C-6), 135.5, 131.3, 130.7, 129.4 (Ph), 114.9 (-$\underline{C}$(CH$_3$)$_2$), 102.9 (C-5), 95.1 (C-1'), 87.2 (C-4'), 84.6 (C-2'), 83.8 (C-3'), 80.3 (CO$_2$$\underline{C}$(CH$_3$)$_3$), 53.6 (C-α), 52.6 (CO$_2$$\underline{C}H_3$), 33.8 (C-γ), 28.4 (CO$_2$C($\underline{C}H_3$)$_3$), 27.2 (-C($\underline{C}H_3$)$_2$), 26.1 (C-5'), 25.4 (-C($\underline{C}$H$_3$)$_2$), 20.3 (C-β); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 139.0; IR (film): 1748, 1709,

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1672; $[\alpha]^{20}_D$ +17.8 (*c* 0.30, $CHCl_3$); HRMS (ESI): calcd for $C_{29}H_{37}N_3O_{10}SeNa$ $[M+Na]^+$: 690.1542, found: 690.1541.

5′-deoxy-5′-methylseleno-2′,3′-*O*-isopropyridene adenosine (9a): white foam (8.8 mg, 46% yield)

The reaction was conducted with **15** (47.1 mg, 0.1 mmol), methyl iodide (32 μL, 0.5 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (300 μL, 0.3 mmol).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.35 (s, 1H, H-2), 7.94 (s, 1H, H-8), 6.09 (d, 1H, *J* = 2.1 Hz, H-1′), 5.78 (br s, 2H, NH_2), 5.52 (dd, 1H, *J* = 6.2, 2.1 Hz, H-2′), 5.05 (dd, 1H, *J* = 6.2, 3.4 Hz, H-3′), 4.46-4.43 (m, 1H, H-4′), 2.85-2.75 (m, 2H, H-5′), 1.99 (s, 3H, -SeC$\underline{H}_3$), 1.62 (s, 3H, CH_3), 1.40 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 155.7 (C-6), 153.3 (C-2), 149.5 (C-4), 140.2 (C-8), 120.5 (C-5), 114.6 (-$\underline{C}(CH_3)_2$), 90.9 (C-1′), 87.3 (C-4′), 84.4 (C-3′), 84.3 (C-2′), 27.4 (C-5′), 27.2 (-C($\underline{C}H_3)_2$), 25.5 (-C($\underline{C}H_3)_2$), 5.2 (-SeC$\underline{H}_3$); ^{77}Se NMR (113 MHz, $CDCl_3$): δ 53.2; IR (film): 3335, 1647, 1599, 1085; $[\alpha]^{20}_D$ -41.6 (*c* 0.20, $CHCl_3$); HRMS (ESI): calcd for $C_{14}H_{19}N_5O_3SeNa$ $[M+Na]^+$: 408.0551, found: 408.0568.

5′-deoxy-5′-ethylseleno-2′,3′-*O*-isopropyridene adenosine (9b): white foam (28.1 mg, 71% yield)

The reaction was conducted with **15** (47.1 mg, 0.1 mmol), ethyl iodide (24 μL, 0.3 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (300 μL, 0.3 mmol).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H, H-2), 7.99 (s, 1H, H-8), 6.27 (br s, 2H, NH_2), 6.11 (d, 1H, *J* = 2.3 Hz, H-1′), 5.51 (dd, 1H, *J* = 6.4, 2.3 Hz, H-2′), 5.05 (dd, 1H, *J* = 6.4, 3.2 Hz, H-3′), 4.48-4.44 (m, 1H, H-4′), 2.90-2.78 (m, 2H, H-5′), 2.58 (q, 2H, *J* = 7.8 Hz, -SeC$\underline{H}_2$CH$_3$), 1.62 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.35 (t, 3H, *J* = 7.8 Hz, -SeCH$_2$C$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4 (C-6), 152.5 (C-2), 149.3 (C-4), 140.3 (C-8), 120.3 (C-5), 114.7 (-$\underline{C}(CH_3)_2$), 91.0 (C-1′), 87.4 (C-4′), 84.3, 84.3, 27.2 (-C($\underline{C}H_3)_2$), 25.5 (-C($\underline{C}H_3)_2$), 25.4 (C-5′), 18.4 (-Se$\underline{C}$H$_2$CH$_3$), 15.8 (-SeCH$_2\underline{C}$H$_3$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 165.0; IR (film): 3335, 1643, 1599, 1085; $[\alpha]^{20}_D$ -60.7 (*c* 0.13, $CHCl_3$); HRMS (ESI): calcd for $C_{15}H_{21}N_5O_3SeNa$ $[M+Na]^+$: 422.0707, found: 422.0708.

5′-deoxy-5′-isopropylseleno-2′,3′-*O*-isopropyridene adenosine (9c): white foam (10.5 mg, 51% yield)

The reaction was conducted with **15** (23.5 mg, 0.05 mmol), isopropyl iodide (14.9 μL, 0.15 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (s, 1H, H-2), 7.94 (s, 1H, H-8), 6.09 (d, 1H, *J* = 2.3 Hz, H-1′), 5.78 (br s, 2H, NH_2), 5.51 (dd, 1H, *J* = 6.3, 2.3 Hz, H-2′), 5.04 (dd, 1H, *J* = 6.3, 3.5 Hz, H-3′), 4.45 (ddd, 1H, *J* = 6.3, 6.3, 1.8 Hz, H-4′), 3.16-3.09 (m, 1H, -SeC$\underline{H}$(CH$_3)_2$), 2.91-2.85 (m, 1H, H-5′a), 2.81-2.78 (m, 1H, H-5′b), 1.61 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.38-1.32 (m, 6H, -SeCH(C$\underline{H}_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.7 (C-6), 153.3 (C-2), 149.4 (C-4), 140.2 (C-8), 120.5 (C-5), 114.6 (-$\underline{C}(CH_3)_2$), 91.0 (C-1′), 87.5 (C-4′), 84.5 (C-2′), 84.3 (C-3′), 30.1 (C-5′), 27.2 (-C($\underline{C}H_3)_2$), 25.5 (-C($\underline{C}H_3)_2$), 24.9 (-Se$\underline{C}$H(CH$_3)_2$), 24.5 (-SeCH(C$\underline{H}_3)_2$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 259.1; IR (film): 3332, 1647, 1599, 1087; $[\alpha]^{20}_D$ -26.1 (*c* 0.60, $CHCl_3$); HRMS (ESI): calcd for $C_{16}H_{23}N_5O_3SeNa$ $[M+Na]^+$: 436.0864, found: 436.0854.

5′-deoxy-5′-benzylseleno-2′,3′-*O*-isopropyridene adenosine (9d): white foam (32.0 mg, 70% yield)

The reaction was conducted with **15** (47.1 mg, 0.1 mmol), benzyl bromide (23.7 μL, 0.2 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (300 μL, 0.3 mmol).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.33 (s, 1H, H-2), 7.91 (s, 1H, H-8), 7.24-7.23 (m, 2H, Ph), 7.20-7.17 (m, 3H, Ph), 6.06 (d, 1H, *J* = 2.8 Hz, H-1′), 5.59 (br s, 2H, NH_2), 5.44 (dd, 1H, *J* = 6.2, 2.7 Hz, H-2′), 4.91 (dd, 1H, *J* = 6.2, 3.4 Hz, H-3′), 4.37 (ddd, 1H, *J* = 6.2, 6.2, 3.4 Hz, H-4′), 3.78-3.75 (m, 2H, -SeC$\underline{H}_2$Ph), 2.80 (dd, 1H, *J* = 12.4, 7.6 Hz, H-5′a), 2.70 (dd, 1H, *J* = 13.0, 6.2 Hz, H-5′b), 1.60 (s, 3H, CH_3), 1.37 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 155.6 (C-6), 153.4 (C-2), 149.5 (C-4), 140.1 (C-8), 138.9, 129.0, 128.7, 127.1, 120.5 (C-5), 114.7 (-$\underline{C}(CH_3)_2$), 90.8 (C-1′), 87.2 (C-4′), 84.4 (C-2′), 84.3 (C-3′), 27.9 (-Se$\underline{C}$H$_2$Ph), 27.3 (-C($\underline{C}H_3)_2$), 25.7 (C-5′), 25.5 (-C($\underline{C}H_3)_2$); ^{77}Se NMR (113 MHz, $CDCl_3$): δ 227.1; IR (film): 3332, 1647, 1599, 1085; $[\alpha]^{20}_D$ -51.5 (*c* 0.18, $CHCl_3$); HRMS (ESI): calcd for $C_{20}H_{23}N_5O_3SeNa$ $[M+Na]^+$: 484.0864, found: 484.0862.

5′-deoxy-5′-allylseleno-2′,3′-*O*-isopropyridene adenosine (9e): white foam (12.6 mg, 61% yield)

The reaction was conducted with **15** (23.5 mg, 0.05 mmol), allyl bromide (12.7 μL, 0.15 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.34 (s, 1H, H-2), 7.93 (s, 1H, H-8), 6.08 (d, 1H, *J* = 2.8 Hz, H-1′), 5.94 (br s, 2H, NH_2), 5.84-5.77 (m, 1H, -SeCH$_2$C$\underline{H}$CH$_2$), 5.50 (dd, 1H, *J* = 6.9, 2.8 Hz, H-2′), 5.03 (dd, 1H, *J* = 6.9, 2.7 Hz, H-3′), 4.96-4.92 (m, 2H, -SeCH$_2$CHC$\underline{H}_2$), 4.42-4.39 (m, 1H, H-4′), 3.19-3.16 (m, 2H, -SeC$\underline{H}_2$CHCH$_2$), 2.82 (dd, 1H, *J* = 12.4, 7.6 Hz, H-5′a), 2.72 (dd, 1H, *J* = 12.4, 6.2 Hz, H-5′b), 1.61 (s, 3H, CH_3), 1.39 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 155.8 (C-6), 153.3 (C-2), 149.4 (C-4), 140.1 (C-8), 134.6 (Allyl), 120.4 (C-5), 117.0 (Allyl), 114.7 (-$\underline{C}(CH_3)_2$), 90.9 (C-1′), 87.1 (C-4′), 84.4 (C-2′), 84.3 (C-3′), 27.3 (-C($\underline{C}H_3)_2$), 26.8 (C-5′), 25.5 (-C($\underline{C}H_3)_2$), 25.2 (-Se$\underline{C}$H$_2$Allyl); ^{77}Se NMR (113 MHz, $CDCl_3$): δ 161.8; IR (film): 3335, 1643, 1599, 1086; $[\alpha]^{20}_D$ -19.2 (*c* 0.48, $CHCl_3$); HRMS (ESI): calcd for $C_{16}H_{21}N_5O_3SeNa$ $[M+Na]^+$: 434.0707, found: 434.0714.

5′-deoxy-5′-propargylseleno-2′,3′-*O*-isopropyridene adenosine (9f): pale yellow foam (15.3 mg, 75% yield)

The reaction was conducted with **15** (23.5 mg, 0.05 mmol), propargyl bromide (11.3 μL, 0.15 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (150 μL, 0.15 mmol).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.35 (s, 1H, H-2), 7.92 (s, 1H, H-8), 6.09 (d, 1H, *J* = 2.0 Hz, H-1′), 5.79 (br s, 2H, NH_2), 5.51 (dd, 1H, *J* = 6.2, 2.1 Hz, H-2′), 5.10 (dd, 1H, *J* = 6.2, 3.4 Hz, H-3′), 4.51 (ddd, 1H, *J* = 6.9, 6.9, 2.8 Hz, H-4′), 3.21-3.15 (m, 2H, -SeC$\underline{H}_2$CCH), 3.10-3.04 (m, 2H, H-5′), 2.19-2.18 (m, 1H, -SeCH$_2$CC$\underline{H}$), 1.61 (s, 3H, CH_3), 1.40 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 155.7 (C-6), 153.4 (C-2), 149.4 (C-4), 140.2 (C-8), 120.5 (C-5), 114.7 (-$\underline{C}(CH_3)_2$), 90.8 (C-1′), 87.3 (C-4′), 84.4$_4$ (C-2′), 84.3$_8$ (C-3′), 80.5 (-SeCH$_2\underline{C}$CH), 71.7 (-SeCH$_2$C$\underline{C}$H), 27.3 (-C($\underline{C}H_3)_2$), 26.4 (C-5′), 25.5 (-C($\underline{C}H_3)_2$), 7.8 (-Se$\underline{C}$H$_2$CCH); ^{77}Se NMR (113 MHz, $CDCl_3$): δ 225.6; IR (film): 3366, 1643, 1598, 1085; $[\alpha]^{20}_D$ -39.0 (*c* 0.36, $CHCl_3$); HRMS (ESI): calcd for $C_{16}H_{19}N_5O_3SeNa$ $[M+Na]^+$: 432.0551, found: 432.0555.

5′-deoxy-5′-(2-(*tert*-butoxycarbonylamino)butanoate)seleno-2′,3′-*O*-

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isopropyridene adenosine (9g): white foam (154.3 mg, 72% yield)

The reaction was conducted with **15** (173.1 mg, 0.368 mmol), (*S*)-methyl 2-(*tert*-butoxycarbonylamino)-4-iodobutanoate **16**[26] (252.5 mg, 0.736 mmol) and 1M solution of tetrabutyl ammonium fluoride in THF (1.1 mL, 1.1 mmol).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.32 (s, 1H, H-2), 7.92 (s, 1H, H-8), 6.07 (d, 1H, *J* = 2.0 Hz, H-1'), 6.02 (br s, 2H, NH_2), 5.50 (d, 1H, *J* = 6.2 Hz, H-2'), 5.25-5.24 (m, 1H, NH), 5.02 (dd, 1H, *J* = 6.2, 2.8 Hz, H-3'), 4.41-4.35 (m, 2H, H-4', H-α), 3.70 (s, 3H, $CO_2C\underline{H}_3$), 2.84 (dd, 1H, *J* = 12.4, 7.6 Hz, H-5'a), 2.76 (dd, 1H, *J* = 12.4, 6.2 Hz, H-5'b), 2.54 (t, 2H, *J* = 7.6 Hz, H-γ), 2.09-2.08 (m, 1H, H-βa), 1.90-1.87 (m, 1H, H-βb), 1.59 (s, 3H, CH_3), 1.40 (s, 9H, $CO_2C(C\underline{H}_3)_3$), 1.38 (s, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 172.8 ($\underline{C}O_2CH_3$), 155.9 (C-6), 155.5 ($\underline{C}O_2C(CH_3)_3$), 153.3 (C-2), 149.3 (C-4), 140.2 (C-8), 120.4 (C-5), 114.6 (-$\underline{C}(CH_3)_2$), 90.9 (C-1'), 87.4 (C-4'), 84.4, 84.3, 80.2 ($CO_2\underline{C}(CH_3)_3$), 53.6 (C-α), 52.6 ($CO_2\underline{C}H_3$), 33.7 (C-γ), 28.4 ($CO_2C(\underline{C}H_3)_3$), 27.2 (-$C(\underline{C}H_3)_2$), 26.0 (C-5'), 25.5 (-$C(\underline{C}H_3)_2$), 20.0 (C-β); ^{77}Se NMR (113 MHz, $CDCl_3$): δ 143.8; IR (film): 3338, 1740, 1706, 1644, 1599, 1088; $[\alpha]^{20}_D$ +2.0 (*c* 1.00, $CHCl_3$); HRMS (ESI): calcd for $C_{23}H_{34}N_6O_7SeNa$ $[M+Na]^+$: 609.1552, found: 690.1551.

Product derivatization

5'-deoxy-5'-(2-(trimethylsilyl)ethyl)seleno-2',3'-*O*-isopropyridene uridine (6): To a stirred solution of 2-(trimethylsilyl)ethyl 4-methylselenobenzoate (1.98 g, 6.6 mmol) **2**[14] and Cs_2CO_3 (2.15 g, 6.6 mmol) in degassed DMF (4 mL) was added *N*-methylhydrazine (0.35 mL, 6.6 mmol) under an argon atmosphere, and successively a solution of 2',3'-*O*-isopropylidene-2,5'-anhydrouridine **5**[16] (1.46 g, 5.5 mmol) in degassed DMF (4 mL) was added via cannula at rt. The mixture was stirred for 1 h at rt (TLC monitoring; EtOAc:n-hexane = 1:1). The reaction mixture was diluted with EtOAc, and the solution was washed with water and brine, dried over Na_2SO_4, and co-evaporated with toluene in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:n-hexane = 1:5 to 1:2) to afford 6 (2.38 g, 97%) as a white foam. Mp: 115-117 °C (Recrystallized from EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.45 (br s, 1H, NH), 7.35 (d, 1H, *J* = 8.3 Hz, H-6), 5.74 (d, 1H, *J* = 7.6 Hz, H-5), 5.70 (d, 1H, *J* = 2.0 Hz, H-1'), 4.95 (dd, 1H, *J* = 6.2, 2.0 Hz, H-2'), 4.77 (dd, 1H, *J* = 6.2, 4.8 Hz, H-3'), 4.30 (dd, 1H, *J* = 10.3, 5.5 Hz, H-4'), 2.92-2.84 (m, 2H, H-5'), 2.71-2.62 (m, 2H, -Se$\underline{C}H_2CH_2$TMS), 1.56 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 0.95-0.92 (m, 2H, -SeCH$_2\underline{C}H_2$TMS), -0.0098 (s, 9H, -Si($\underline{C}H_3)_3$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 163.5 (C-4), 150.0 (C-2), 142.3 (C-6), 114.9 (-$\underline{C}(CH_3)_2$), 102.8 (C-5), 93.8 (C-1'), 87.0 (C-4'), 84.6 (C-2'), 83.8 (C-3'), 27.3 (-$C(\underline{C}H_3)_2$), 25.7 (C-5'), 25.4 (-$C(\underline{C}H_3)_2$), 20.4 (-Se$\underline{C}H_2CH_2$TMS), 18.7 (-SeCH$_2\underline{C}H_2$TMS), -1.8 (-Si($\underline{C}H_3)_3$); ^{77}Se NMR (113 MHz, $CDCl_3$): δ 181.9; IR (film): 1692, 1631; $[\alpha]^{20}_D$ +28.2 (*c* 1.05, $CHCl_3$); HRMS (ESI): calcd for $C_{17}H_{28}N_2O_5SeSiNa$ $[M+Na]^+$: 471.0830, found: 471.0833.

***N*-Benzoyl-5'-deoxy-5'-(2-(trimethylsilyl)ethyl)seleno-2',3'-*O*-isopropyridene uridine (7)**: To a stirred solution of **6** (447 mg, 1 mmol) and Et_3N (348 μL, 2.5 mmol) in CH_2Cl_2 (9 mL) was added benzoyl chloride (230 μL, 2 mmol) at rt. The mixture was stirred for 3 h at rt (TLC monitoring; EtOAc:n-hexane = 1:1), then the reaction mixture was quenched with H_2O and extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and then concentrated. The residue was purified by column chromatography on silica gel (EtOAc:n-hexane = 1:10 to 1:5) to afford **7** (517.8 mg, 94%) as a white foam.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93-7.91 (m, 2H, Ph), 7.67-7.63 (m, 1H, Ph), 7.52-7.48 (m, 2H, Ph), 7.44 (d, 1H, *J* = 8.2 Hz, H-6), 5.84 (d, 1H, *J* = 8.2 Hz, H-5), 5.68 (d, 1H, *J* = 2.3 Hz, H-1'), 5.00 (dd, 1H, *J* = 6.4, 2.3 Hz, H-2'), 4.73 (dd, 1H, *J* = 6.9, 4.1 Hz, H-3'), 4.31 (ddd, 1H, *J* = 6.4, 6.4, 4.2 Hz, H-4'), 2.82 (d, 2H, *J* = 6.4 Hz, H-5'), 2.67-2.62 (m, 2H, -Se$\underline{C}H_2CH_2$TMS), 1.54 (s, 3H, CH_3), 1.33 (s, 3H, CH_3), 0.95-0.90 (m, 2H, -SeCH$_2\underline{C}H_2$TMS), -0.0046 (s, 9H, -Si($\underline{C}H_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (COPh), 162.0 (C-4), 149.2 (C-2), 142.1 (C-6), 135.4, 131.4, 130.7, 129.4 (Ph), 114.8 (-$\underline{C}(CH_3)_2$), 102.8 (C-5), 94.7 (C-1'), 87.3 (C-4'), 84.6 (C-2'), 83.8 (C-3'), 27.2 (-$C(\underline{C}H_3)_2$), 25.7 (C-5'), 25.4 (-$C(\underline{C}H_3)_2$), 20.3 (-Se$\underline{C}H_2CH_2$TMS), 18.6 (-SeCH$_2\underline{C}H_2$TMS), -1.8 (-Si($\underline{C}H_3)_3$); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 181.6; IR (film): 1750, 1710, 1675; $[\alpha]^{20}_D$ +7.4 (*c* 0.70, $CHCl_3$); HRMS (ESI): calcd for $C_{24}H_{32}N_2O_6SeSiNa$ $[M+Na]^+$: 575.1093, found: 575.1094.

5'-deoxy-5'-(2-(*tert*-butoxycarbonylamino)butanoic acid)seleno-2',3'-*O*-isopropyridene uridine (10): To a stirred solution of **8r** (24 mg, 0.036 mmol) in MeOH was added 1N NaOH aq. (108 μL, 0.108 mmol) at rt. The mixture was stirred for 1 h at 40 °C (TLC monitoring; $CHCl_3$:MeOH = 10:1), then the reaction mixture was diluted with $CHCl_3$, and the solution was acidified with saturated aqueous NH_4Cl, followed by the separation of the organic layer. The aqueous layer was extracted with $CHCl_3$ three times; combined organic layers were dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$:MeOH = 20:1 to 10:1) to afford **10** (17.8 mg, 90%) as a white solid. Mp: 148-150 °C (Recrystallized from $CHCl_3$); ^{1}H NMR (600 MHz, CD_3OD): δ 7.67 (d, 1H, *J* = 7.6 Hz, H-6), 5.79 (s, 1H, H-1'), 5.71 (d, 1H, *J* = 7.6 Hz, H-5), 5.00-4.99 (m, 1H, H-2'), 4.78-4.76 (m, 1H, H-3'), 4.27-4.24 (m, 1H, H-4'), 4.02-3.97 (m, 1H, H-α), 2.91-2.86 (m, 2H, H-5'), 2.65-2.62 (m, 2H, H-γ), 2.16-2.15 (m, 1H, H-βa), 2.01-1.95 (m, 1H, H-βb), 1.54 (s, 3H, CH_3), 1.44 (s, 9H, $CO_2C(CH_3)_3$), 1.34 (s, 3H, CH_3); ^{13}C NMR (150 MHz, CD_3OD): δ 178.7 ($\underline{C}O_2H$), 167.1 (C-4), 157.6 ($\underline{C}O_2C(CH_3)_3$), 152.6 (C-2), 144.0 (C-6), 115.4 (-$\underline{C}(CH_3)_2$), 103.0 (C-5), 94.3 (C-1'), 87.9 (C-4'), 85.7, 85.1, 80.1 ($CO_2\underline{C}(CH_3)_3$), 57.5 (C-α), 36.0 (C-γ), 28.8 ($CO_2C(\underline{C}H_3)_3$), 27.5 (-$C(\underline{C}H_3)_2$), 26.4 (C-5'), 25.5 (-$C(\underline{C}H_3)_2$), 21.4 (C-β); ^{77}Se NMR (113 MHz, CD_3OD): δ 137.4; IR (film): 1690, 1587; $[\alpha]^{20}_D$ -24.7 (*c* 0.10, CH_3OH); HRMS (ESI): calcd for $C_{21}H_{31}N_3O_9SeNa$ $[M+Na]^+$: 572.1123, found: 572.1113.

***Se*-uridyl-L-selenohomocysteine TFA salt (11)**: The compound **10** (12.6 mg, 0.023 mmol) was dissolved in 80% trifluoroacetic acid in distilled water (0.5 mL). The reaction mixture was stirred for 30 min at rt, then concentrated in vacuo. The residue was triturated with Et_2O, the precipitate was collected by filtration and rinsed with Et_2O, then the solid was dried by high vacuum line to afford **11** (10.8 mg, 93%) as a white solid. ^{1}H NMR (600 MHz, D_2O): δ 7.71 (d, 1H, *J* = 7.6 Hz, H-6), 5.88 (d, 1H, *J* = 8.2 Hz, H-5), 5.85 (d, 1H, *J* = 4.1 Hz, H-1'), 4.40-4.39 (m, 1H, H-2'), 4.22-4.19 (m, 1H, H-α), 4.16-4.14 (m,

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1H, H-3'), 3.99-3.97 (m, 1H, H-4'), 3.04 (dd, 1H, *J* = 13.7, 4.9 Hz, H-5'a), 2.95 (dd, 1H, *J* = 13.7, 6.9 Hz, H-5'b), 2.74 (t, 2H, *J* = 7.6 Hz, H-γ), 2.30 (ddd, 1H, *J* = 14.4, 14.4, 7.6 Hz, H-βa), 2.21 (ddd, 1H, *J* = 14.4, 14.4, 7.6 Hz, H-βb); ^{13}C NMR (150 MHz, D_2O): δ 166.2 (C-4), 151.6 (C-2), 142.2 (C-6), 102.5 (C-5), 90.0 (C-1'), 83.1 (C-4'), 73.2, 72.6, 53.9 (C-α), 31.2 (C-γ), 25.2 (C-5'), 19.1 (C-β); ^{77}Se NMR (113 MHz, D_2O): δ 130.2; IR (film): 1682, 1643; $[\alpha]^{20}_D$ +43.7 (*c* 0.10, H_2O); HRMS (ESI): calcd for $C_{13}H_{19}N_3O_7SeNa$ $[M+Na]^+$: 432.0286, found: 432.0295.

5'-deoxy-5'-(2-(trimethylsilyl)ethyl)seleno-2',3'-*O*-isopropyridene adenosine (15): To a stirred solution of bis[2-(trimethylsilyl)ethyl] diselenide **1**[11] (204 mg, 0.566 mmol) and EtOH (82.6 μL, 1.416 mmol) in DMF (1.5 mL), sodium borohydride (21.4 mg, 0.566 mmol) was slowly added at 0 °C. The mixture was stirred for 30 min at 0 °C, after which **14**[25] (153.8 mg, 0.472 mmol) was added to the solution at 0 °C. The mixture was warmed to 60 °C, and stirred for 2 h at 60 °C (TLC monitoring; EtOAc:n-hexane = 2:1), then the reaction mixture was quenched by saturated aqueous NH_4Cl at rt. The solution was extracted with EtOAc, washed with water and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (EtOAc:n-hexane = 1:2 to 2:1) to afford **15** (144.4 mg, 65%) as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (s, 1H, H-2), 7.92 (s, 1H, H-8), 6.47 (br s, 2H, NH_2), 6.08 (d, 1H, *J* = 2.3 Hz, H-1'), 5.50 (dd, 1H, *J* = 6.3, 2.3 Hz, H-2'), 5.01 (dd, 1H, *J* = 6.3, 2.9 Hz, H-3'), 4.43-4.40 (m, 1H, H-4'), 2.86-2.75 (m, 2H, H-5'), 2.62-2.50 (m, 2H, -SeC$\underline{H}_2$CH$_2$TMS), 1.58 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 0.87-0.83 (m, 2H, -SeCH$_2$C$\underline{H}_2$TMS), -0.09 (s, 9H, -Si(C$\underline{H}_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.0 (C-6), 153.1 (C-2), 149.2 (C-4), 139.9 (C-8), 120.3 (C-5), 114.5 (-$\underline{C}$(CH$_3$)$_2$), 90.8 (C-1'), 87.5 (C-4'), 84.4, 84.2, 27.2 (-C(C$\underline{H}_3$)$_2$), 25.6 (C-5'), 25.4 (-C(C$\underline{H}_3$)$_2$), 19.9 (-SeC$\underline{H}_2$CH$_2$TMS), 18.5 (-SeCH$_2$C$\underline{H}_2$TMS), -1.9 (-Si(C$\underline{H}_3$)$_3$); ^{77}Se NMR (94 MHz, $CDCl_3$): δ 188.2; IR (film): 3322, 1650, 1599; $[\alpha]^{20}_D$ -13.9 (*c* 1.00, $CHCl_3$); HRMS (ESI): calcd for $C_{18}H_{29}N_5O_3SeSiNa$ $[M+Na]^+$: 494.1103, found: 494.1114.

5'-deoxy-5'-(2-(*tert*-butoxycarbonylamino)butanoic acid)seleno-2',3'-*O*-isopropyridene adenosine (17): To a stirred solution of **9g** (85 mg, 0.145 mmol) in MeOH (0.85 mL) was added 1N NaOH aq. (436 μL, 0.436 mmol) at rt. The mixture was stirred for 1 h at 40 °C (TLC monitoring; $CHCl_3$:MeOH = 10:1), then the reaction mixture was diluted with $CHCl_3$, and the solution was acidified with saturated aqueous NH_4Cl, then the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ three times, the combined organic layers were dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$:MeOH = 50:1 to 10:1) to afford **17** (75.1 mg, 91%) as a white solid.

Mp: 182-184 °C (Recrystallized from $CHCl_3$); ^{1}H NMR (600 MHz, CD_3OD): δ 8.30 (s, 1H, H-8), 8.23 (s, 1H, H-2), 6.17 (s, 1H, H-1'), 5.50-5.49 (m, 1H, H-2'), 5.03 (m, 1H, H-3'), 4.39 (m, 1H, H-4'), 4.04-3.98 (m, 1H, H-α), 2.86-2.79 (m, 2H, H-5'), 2.59 (m, 2H, H-γ), 2.10 (m, 1H, H-βa), 1.94 (m, 1H, H-βb), 1.58 (s, 3H, CH_3), 1.41 (s, 9H, $CO_2C(CH_3)_3$), 1.38 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CD_3OD): δ 175.9 ($\underline{C}O_2H$), 158.1 (C-6), 157.2 ($\underline{C}O_2C(CH_3)_3$), 153.7 (C-2), 150.2 (C-4), 141.9 (C-8), 120.5 (C-5), 115.5 (-$\underline{C}$(CH$_3$)$_2$), 91.6 (C-1'), 88.4 (C-4'), 85.5 (C-3'), 85.3 (C-2'), 80.5 ($CO_2\underline{C}(CH_3)_3$), 54.7 (C-α), 33.8 (C-γ), 28.7 ($CO_2C(\underline{C}H_3)_3$), 27.4 (-C(C$\underline{H}_3$)$_2$), 26.4 (C-5'), 25.5 (-C(C$\underline{H}_3$)$_2$), 21.2 (C-β); ^{77}Se NMR (113 MHz, CD_3OD): δ 138.3; IR (film): 3349, 1691, 1597; $[\alpha]^{20}_D$ -16.9 (*c* 0.50, CH_3OH); HRMS (ESI): calcd for $C_{22}H_{32}N_6O_7SeNa$ $[M+Na]^+$: 595.1395, found: 595.1392.

SeAH TFA salt (18): The compound **17** (22.4 mg, 0.0392 mmol) was dissolved into a mixture of 80% trifluoroacetic acid in distilled water (0.5 mL). The reaction mixture was stirred for 30 min at rt, then concentrated in vacuo. The residue was triturated with Et_2O, the precipitate was collected by filtration and linsed with Et_2O, then the solid was dried by high vacuum line to afford **18** (21.6 mg, 97%) as a white solid. ^{1}H NMR (600 MHz, D_2O): δ 8.49 (s, 1H, H-2), 8.41 (s, 1H, H-8), 6.11 (d, 1H, *J* = 4.8 Hz, H-1'), 4.86 (dd, 1H, *J* = 5.5, 4.8 Hz, H-2'), 4.40 (dd, 1H, *J* = 5.5, 4.8 Hz, H-3'), 4.35 (dt, 1H, *J* = 6.8, 4.8 Hz, H-4'), 3.90 (t, 1H, *J* = 6.2 Hz, H-α), 3.08-3.00 (m, 2H, H-5'), 2.68 (t, 2H, *J* = 7.9 Hz, H-γ), 2.26-2.12 (m, 2H, H-β); ^{13}C NMR (150 MHz, D_2O): δ 173.0 ($\underline{C}O_2H$), 150.3 (C-6), 148.4 (C-2), 145.0 (C-4), 142.9 (C-8), 119.0 (C-5), 88.4 (C-1'), 84.2 (C-4'), 73.7 (C-2'), 73.0 (C-3'), 53.9 (C-α), 31.2 (C-γ), 25.5 (C-5'), 19.0 (C-β); ^{77}Se NMR (113 MHz, D_2O): δ 130.0; IR (film): 3434, 1686, 1639; $[\alpha]^{20}_D$ +14.3 (*c* 0.50, H_2O); HRMS (ESI): calcd for $C_{14}H_{20}N_6O_5SeNa$ $[M+Na]^+$: 455.0558, found: 455.0556.

SeAM TFA salt (19): SeAH **18** (81.2 mg, 0.143 mmol) was dissolved into a mixture of 1:1 formic acid and acetic acid (0.5 mL). Methyl iodide (445 μL, 7.15 mmol) and silver (I) perchlorate (29.6 mg, 0.143 mmol) was added to the reaction mixture, and stirred for 5 h at rt. The solution was acidified with 10% trifluoroacetic acid in distilled water (1.0 mL), then the aqueous layer was washed with $CHCl_3$ three times. The insoluble materials (AgI) were filtered off, and the aqueous layer was concentrated in vacuo to afford SeAM **19** (56.8 mg, 73%) as a pale yellow waxy solid (47 : 53 mixture of *Se*-epimers as determined by ^{1}H NMR). As previously reported, degradation of the SeAM was observed when stored at room temperature due to this instability.[21b, 23]

^{1}H NMR (600 MHz, D_2O): δ 8.44 (s, 2H, H-2, H-8), 6.12 (d, 1H, *J* = 4.1 Hz, H-1'), 4.85-4.81 (m, 1H, H-2'), 4.60-4.58 (m, 1H, H-3'), 4.53-4.51 (m, 1H, H-4'), 4.05-3.98 (m, 1H, H-α), 3.90-3.82 (m, 2H, H-5'), 3.63-3.36 (m, 2H, H-γ), 2.81/2.77 (s, 3H, 47 : 53, *Se*-epimers, -SeCH$_3$), 2.50-2.31 (m, 2H, H-β); ^{13}C NMR (150 MHz, D_2O): δ 170.8 ($\underline{C}O_2H$), 150.2 (C-6), 148.2 (C-2), 145.0 (C-4), 144.1 (C-8), 119.5 (C-5), 90.3$_5$/90.3$_0$ (C-1'), 79.4 (C-4'), 73.6, 73.5, 73.3, 73.2 (C-2', C-3'), 52.3 (C-α), 42.1/41.7 (C-5'), 35.8/35.5 (C-γ), 25.8/25.7 (C-β), 19.8/19.7 (SeCH$_3$); ^{77}Se NMR (113 MHz, D_2O): δ 325.5/325.0; $[\alpha]^{20}_D$ +13.5 (*c* 0.50, H_2O); HRMS (ESI): calcd for $C_{15}H_{23}N_6O_5Se$ $[M]^+$: 447.0895, found: 447.0892.

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5′-leaving groups such as Br, I, OTs, OMs were caused unwanted cyclisation followed by formation of quaternary ammonium salt.

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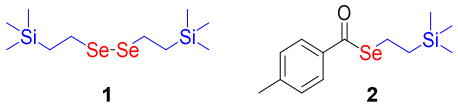

1 2

Fig. 1 The selenating reagents **1** and **2**

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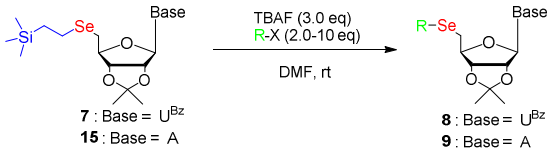
Table 1 Synthesis of 5′-selenium modified nucleosides having various functional group



Entry	Base	Electrophile		Time (h)	R	Yield[a] (%)
		R-X	Equiv.			
1		MeI	5.0	1	Me	80 (**8a**)
2		EtI	5.0	2	Et	74 (**8b**)
3		*i*-PrI	3.0	3	*i*-Pr	64 (**8c**)
4		$PhCH_2Br$	2.0	2	$PhCH_2$	81 (**8d**)
5		4-Me-C_6H_4-CH_2Br	3.0	2	4-Me-C_6H_4-CH_2	93 (**8e**)
6		4-NO_2-C_6H_4-CH_2Br	3.0	3	4-NO_2-C_6H_4-CH_2	61 (**8f**)
7		allyl Br	3.0	2	allyl	85 (**8g**)
8		propargyl Br	3.0	1	propargyl	86 (**8h**)
9		$MeO(CH_2)_2Br$	3.0	2	$MeO(CH_2)_2$	74 (**8i**)
10			10	3		70 (**8j**)
11		1-F-2-NO_2-C_6H_4	2.0	0.5	2-NO_2-C_6H_4	60 (**8k**)
12		1-F-4-NO_2-C_6H_4	2.0	0.5	4-NO_2-C_6H_4	63 (**8l**)
13		$MeC(=O)CH_2Br$	10	5	$MeC(=O)CH_2$	60 (**8m**)
14		$PhC(=O)CH_2Br$	3.0	3	$PhC(=O)CH_2$	80 (**8n**)
15		$MeOC(=O)CH_2Br$	4.0	5	$MeOC(=O)CH_2$	90 (**8o**)
16		*t*-$BuOC(=O)CH_2Br$	5.0	10	*t*-$BuO(C=O)CH_2$	77 (**8p**)
17		$NCCH_2Br$	3.0	3	$NCCH_2$	67 (**8q**)
18			2.0	6		73 (**8r**)
19		MeI	5.0	5	Me	46 (**9a**)
20		EtI	3.0	4	Et	71 (**9b**)
21		*i*-PrI	3.0	10	*i*-Pr	51 (**9c**)
22		$PhCH_2Br$	2.0	4	$PhCH_2$	70 (**9d**)
23		allyl Br	3.0	3	allyl	61 (**9e**)
24		propargyl Br	3.0	4	propargyl	75 (**9f**)
25			2.0	10		72 (**9g**)

[a] Isolated yield

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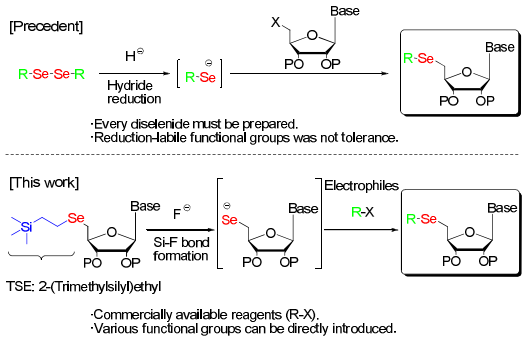
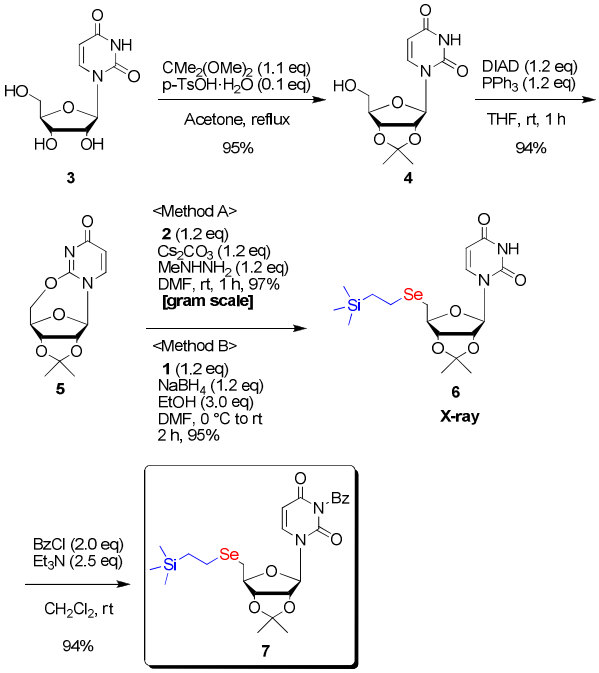
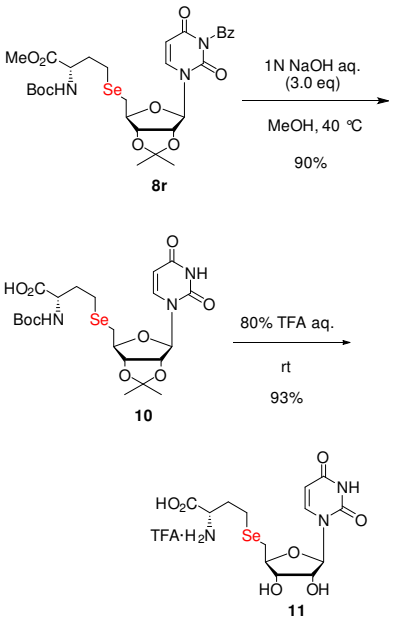


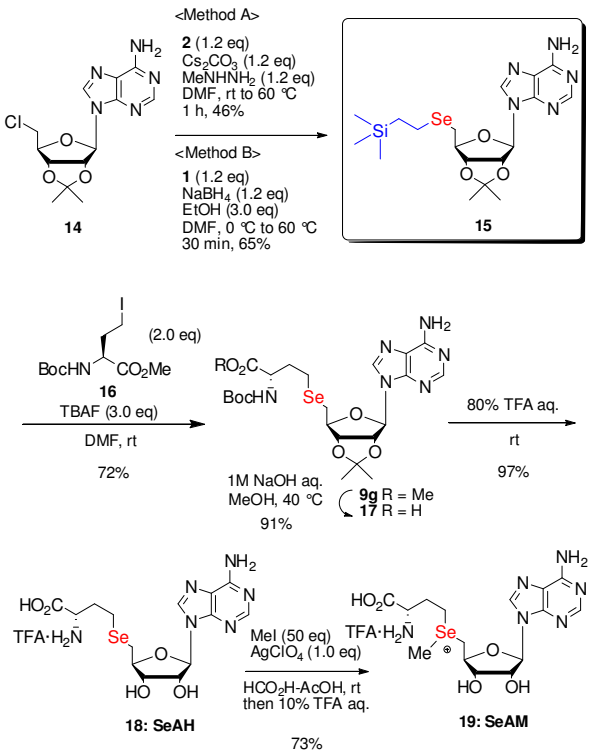
Scheme 1 Synthetic strategy of 5′-selenium modified nucleosides.



Scheme 2 Synthesis of key intermediate **7** using selenating reagent **1** and **2**.



Scheme 3 Synthesis of *Se*-uridyl-L-selenohomocysteine (**11**).



Scheme 4 Synthesis of SeAH (**18**) and SeAM (**19**).

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