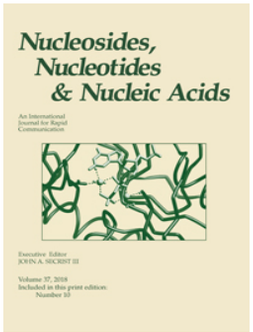

Nucleosides, Nucleotides and Nucleic Acids

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Synthesis of selenomethylene-locked nucleic acids (SeLNA) nucleoside unit bearing an adenine base

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ABSTRACT

Synthesis of selenomethylene-locked nucleic acids nucleoside bearing an adenine base (SeLNA-A) was investigated. We first examined the stereoinversion reaction at 2′-positions of a 5′,3′-*O*-TIPDS-protected 4′-*C*-(hydroxymethyl)ribosyladenine derivative to give the corresponding arabinosyladenine. After triflation, treatment of the arabinosyladenine derivative with a mixture of selenium and sodium borohydride in ethanol managed to construct the desired SeLNA skeleton. Finally, removal of TIPDS by treating with fluoride gave the SeLNA-A nucleoside. In this study, we found the heat-labile property of SeLNA-A. It is necessary to know more precise characteristics of SeLNA to achieve its oligonucleotides synthesis.

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KEYWORDS
Nucleoside; oligonucleotide; LNA; seleno-compound

Introduction

Chemically-modified nucleosides/nucleotides have become important components in oligonucleotide-based drug design and sensor technology because of its nuclease resistance and highly and selectively binding ability to its target nucleic acids.[1–5] Locked nucleic acid (LNA)[6,7]/2′,4′-bridged nucleic acid (2′,4′-BNA)[8] is one of the most impressive nucleoside components that has made recent oligonucleotide-based therapeutic drug development attractive. LNA has a methylene bridge between the 2′-oxygen and 4′-carbon atoms of RNA, which locks its own sugar conformation into the C3′-endo conformation (Figure 1). Since this LNA oligonucleotides show extremely strong binding affinity against complementary DNA and RNA,[9] a number of LNA analogs have been developed.[10–17]

We previously reported selenomethylene-locked nucleic acids (SeLNA) bearing a thymine base (T) (Figure 2).[18] SeLNA-T can be reversibly converted into its oxidized-form (SeOLNA-T), and the hybridization ability and nuclease resistance of oligonucleotides modified with SeLNA were

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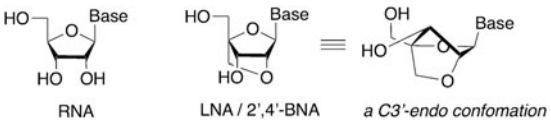


Figure 1. Chemical structures of RNA and LNA/2′,4′-BNA.

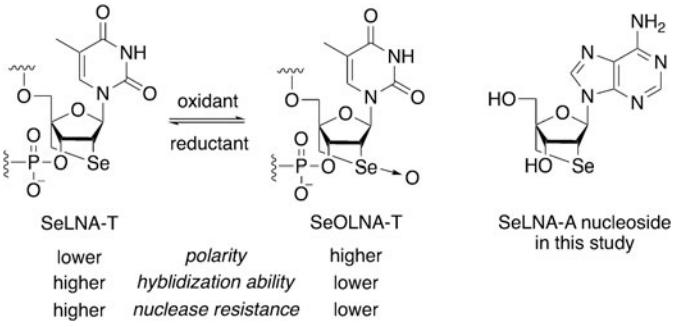


Figure 2. Chemical structures and the properties of SeLNA.

shown to be much higher than those of oligonucleotides modified with SeOLNA. Moreover, it was also found that KOD XL DNA polymerase was an efficient enzyme to extend oligonucleotide strands by reading SeLNA-T nucleotides of the template strand and also by incorporating SeLNA-T triphosphate using DNA templates.[19] These findings suggested that SeLNA-modified oligonucleotides can be developed not only as a sensor module for changes in the redox environment but also as a material for aptamer technology.

Because selenium-modified nucleic acids are important not only for medicinal use but also for structural analysis,[20–23] selenium-modified nucleoside at various positions have been developed so far.[24–26] To enable a wide range of applied research on SeLNA, we also decided to synthesize SeLNA containing a nucleobase other than thymine base, SeLNA bearing adenine (SeLNA-A) in this study, and to elucidate the basic properties thereof.

Herein, the synthesis of SeLNA-A from a branched ribose derivative is described. Seleno bridging reaction between 2′- and 4′-position as a key step was performed by subjecting a bis-sulfonated compound to a selenide solution. Finally, removal of protecting group gave the SeLNA-A nucleoside.

Results and discussion

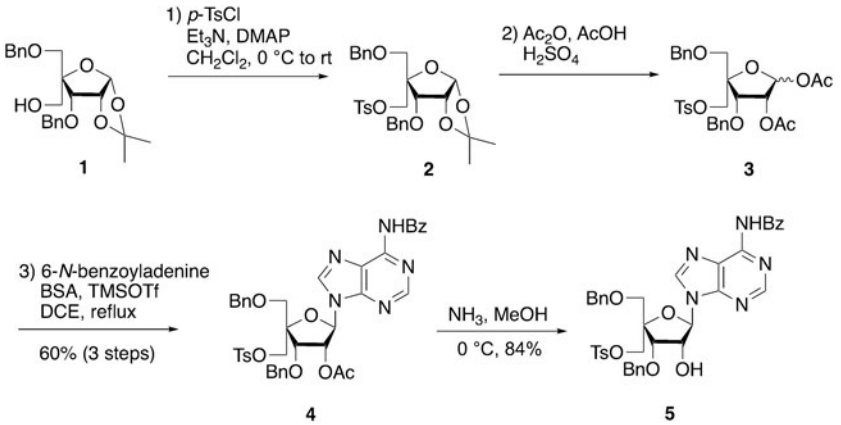
We investigated the synthesis of selenomethylene-locked nucleic acids (SeLNA) nucleoside unit bearing an adenine base. Compound **1**[27] was used as a starting material in this study. After tosylation of the hydroxy group of compound **1**, the obtained **2** was treated with acetic anhydride and acetic acid under sulfuric acid catalytic conditions to afford **3**. Further, acetate group on 1-position of **3** was substituted with 6-*N*-benzoyladenine by modified Vorbrüggen's method,[28] whereby compound **4** was obtained

over three steps in 60% yield. Acetyl group of **4** was removed by ammonia treatment to give compound **5** in 84% yield (Scheme 1).

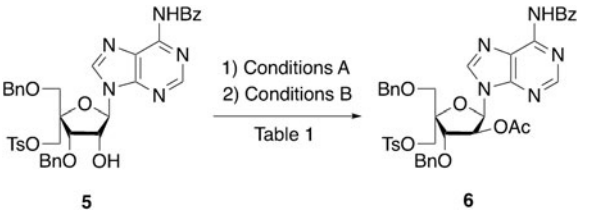
Next, the stereo-inversion reaction at C2′ position of **5** was carried out (Scheme 2 and Table 1). We first attempted to invert the stereochemistry by performing oxidation and reduction in succession, but only a complex mixture was obtained (Table 1, entry 1). So then, S_N2 reaction at 2′-position was examined. Compound **5** was triflated and was subsequently treated with several acetoxylation conditions without purification (entries 2–4). When alkali acetate was used, S_N2 reaction was not efficient because the elimination reaction proceeded (entries 2 and 3). Finally, compound **6** was obtained in moderate yield by treating **5** with acetic acid in the presence of DBU (entry 4).

All protecting groups of **6** was removed by continuously performing hydrogenolysis and aminolysis to afford compound **7** (Scheme 3). Incidentally, it has been confirmed that the benzoyl group was removed prior to the benzyl group under the hydrogenolysis conditions. Compound **7** was subjected to 1,1,3,3-tetraisopropyldisiloxane (TIPDS) protection to obtain compound **8** in 94% yield. This compound **8** was triflated again and treated with sodium hydrogen selenide that was generated by powder selenium and sodium borohydride to afford the TIPDS-protected selenomethylene bridged compound **9**. Subsequently, the silyl group was removed by TBAF treatment, and the desired SeLNA-A nucleoside (**10**) was finally obtained in 16% yield over three steps.

As described, we successfully synthesized SeLNA-A nucleoside from a ribose derivative. In addition, it was found that SeLNA-A nucleoside (**10)** was easily decomposed by heating, and β-methyl glycoside of SeLNA was generated, for example, when recrystallization was carried out in methanol at around its boiling point (data not shown). The reason why SeLNA-A nucleoside (**10)** was obtained only in a low yield is considered to be due to this heat sensitivity. This suggests that in order to synthesize SeLNA-A-containing oligodeoxynucleotides, it is necessary to examine in detail the selection of protecting groups in consideration of its heat-labile property.



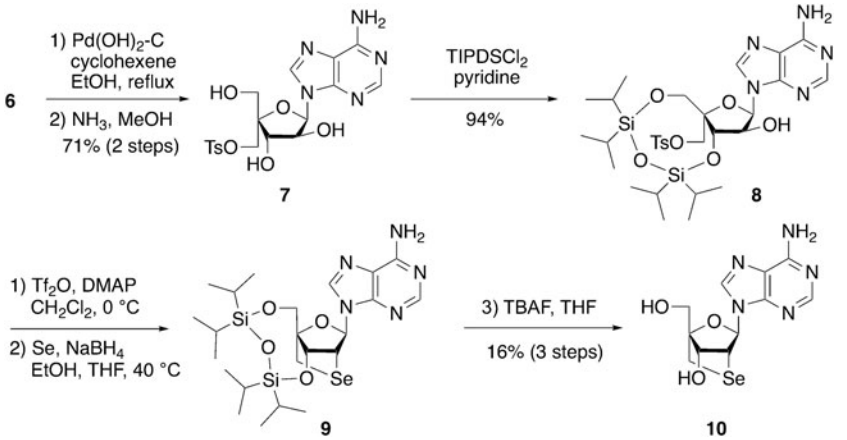
Scheme 1. Synthesis of intermediate **5**.



Scheme 2. Stereo-inversion reaction at 2′-position.

Table 1. Stereo-inversion reaction at C2′ position of compound **5**.

Entry	Conditions A	Conditions B	Yield of **6**
1	IBX, EtOAc, reflux	$NaBH_4$, MeOH	0%
2	Tf_2O, pyridine, CH_2Cl_2, −30 °C	KOAc, 18-crown-6, toluene	32%
3	Tf_2O, pyridine, CH_2Cl_2, −30 °C	CsOAc, DMSO	42%
4	Tf_2O, pyridine, CH_2Cl_2, −30 °C	DBU, AcOH, toluene, 80 °C	56%



Scheme 3. Synthesis of SeLNA-A nucleoside.

Experimental section

All moisture-sensitive reactions were carried out in well-dried glassware under an argon or nitrogen atmosphere. ^{1}H NMR spectra were recorded at 400 MHz. ^{13}C NMR spectra were recorded at 100 MHz. ^{31}P NMR spectra were recorded at 162 MHz. Chemical shifts (δ) are expressed in ppm relative to internal tetramethylsilane (0 ppm), residual $CHCl_3$ (7.26 ppm) or residual DMSO (2.49 ppm) in the ^{1}H NMR spectra, internal chloroform-*d* (77.0 ppm) or dimethyl sulfoxide-d_6 (39.5 ppm) in the ^{13}C NMR spectra. FAB mass spectra of all new compounds were obtained on a LMS-700 instrument. For column chromatography, FL-60B silica gel was used. The progress of the reactions was monitored by analytical thin layer chromatography (TLC) on glass plates (TLC silica gel 60 F254) and the products were visualized by UV light.

6-*N*-benzoyl-9-[2-*O*-acetyl-3,5-di-*O*-benzyl-4-*C*-(*p*-toluenesulfonyloxymethyl)-α-D-ribofuranosyl]adenine (4). Compound **1** (10.4 g, 26.0 mmol) in dichloromethane solution (130 mL) was cooled to 0 °C. Triethylamine (21.7 mL,

156 mmol), 4-dimethylaminopyridine (479 mg, 3.9 mmol) and *p*-toluenesulfonyl chloride (7.42 g, 39.0 mmol) was added and stirred at room temperature for 12 hours. After cold water was added to the reaction solution to stop the reaction, the organic layer was washed with 1 M HCl, sat. $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4 and evaporated. To a solution of the crude product **2** (15.2 g) in acetic acid (29 mL) were added acetic anhydride (15.2 mL, 156 mmol) and concentrated sulfuric acid (0.29 mL, 5.2 mmol) at room temperature. The mixture was stirred at the same temperature for 3 hours. After the reaction solution was cooled to 0 °C, and ice-cooled sat. $NaHCO_3$ was added to the mixture, and was stirred for 5 min. The contents were extracted with ethyl acetate, and the organic layer was washed with saturated sat. $NaHCO_3$ and brine, and dried over Na_2SO_4 to give crude acetate **3** (17.0 g). To a suspension of crude acetate **3** (6.54 g, 10.0 mmol) and *N*-6-benzoyladenine (4.79 g, 20.0 mmol) in 1,2-dichloroethane (100 mL) was added *N*,*O*-bis(trimethylsilyl)acetamide (9.9 mL, 40.0 mmol), and the resulting mixture was refluxed for 2 hours. After cooled to room temperature, and trimethylsilyl trifluoromethanesulfonate (2.7 mL, 15.0 mmol) was added. The mixture was refluxed again for 8 hours. The reaction mixture was diluted with dichloromethane at room temperature, and sat. $NaHCO_3$ was added to the stirring mixture. The organic layer was washed with sat. $NaHCO_3$, water and brine, and dried over Na_2SO_4. The obtained crude product was purified by column chromatography (SiO_2, dichloromethane: acetone = 15:1) to give compound **4** (4.69 g, 6.03 mmol, 60%) as colorless amorphous solid. IR ν_{max} (neat): 3064, 3030, 3007, 2925, 2871, 1748, 1699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 9.05 (s, 1H, 6-NH), 8.71 (s, 1H, H2), 8.14 (s, 1H, H8), 8.01 (d, $J = 7.3$ Hz, 2H), 7.74 (d, $J = 8.2$ Hz, 2H), 7.60 (t, $J = 7.3$ Hz, 1H), 7.51 (t, $J = 7.3$ Hz, 2H), 7.35–7.18 (m, 12H), 6.12 (d, $J = 4.6$ Hz, 1H, H1′), 5.92 (dd, $J = 4.6$, 5.5 Hz, 1H, H2′), 4.73 (d, $J = 5.5$ Hz, 1H, H3′), 4.57 (d, $J = 11.2$ Hz, 1H), 4.49 (d, $J = 11.2$ Hz, 1H), 4.45 (d, $J = 11.9$ Hz, 1H), 4.41 (d, $J = 11.9$ Hz, 1H), 4.32 (d, $J = 10.5$ Hz, 1H), 4.23 (d, $J = 10.5$ Hz, 1H), 3.67 (d, $J = 10.1$ Hz, 1H), 3.56 (d, $J = 10.1$ Hz, 1H), 2.40 (s, 3H, Ts), 2.03 (s, 3H, Ac). ^{13}C NMR (100 MHz, CD_3OD) δ: 169.6, 164.5, 152.7, 151.4, 149.5, 145.0, 141.8, 136.9, 136.9, 133.5, 132.8, 132.5, 129.8, 128.8, 128.5, 128.5, 128.2, 128.1,128.0, 127.8, 127.7, 123.1, 86.4, 85.9, 77.8, 74.7, 74.6, 73.6, 70.1, 68.9, 21.6, 20.5. LRMS (FAB) *m*/*z* 778 $[M+H]^+$. HRMS (FAB): Calcd for $C_{41}H_{40}N_5O_9S$ $[M+H]^+$: 778.2547. Found: 778.2505.

6-*N*-benzoyl-9-[3,5-bi-*O*-benzyl-4-*C*-(*p*-toluenesulfonyloxymethyl)-α-D-ribofuranosyl]adenine (5). Saturated ammonia methanol solution (55 mL) was added to a solution of compound **4** (4.25 g, 5.46 mmol) in methanol (110 mL) at 0 °C and stirred for 19 hours at 0 °C. The reaction mixture was evaporated, and the obtained crude product is purified by column

chromatography (SiO_2, hexane: ethyl acetate = 1:3) to give compound **5** (3.38 g, 4.59 mmol, 84%) as colorless amorphous solid. IR ν_{max} (neat): 3287, 3064, 3031, 2925, 2871, 1699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.99 (s, 1H), 8.68 (s, 1H), 8.08 (s, 1H), 8.02 (d, $J = 7.3$ Hz, 2H), 7.76 (d, $J = 8.2$ Hz, 2H), 7.61 (t, $J = 7.3$ Hz, 1H), 7.53 (t, $J = 7.3$ Hz, 2H), 7.37–7.27 (m, 10 H), 7.20–7.18 (m, 2H), 5.89 (d, $J = 5.0$ Hz, 1H), 4.82 (dd, $J = 6.0$, 11.0 Hz, 1H), 4.71 (d, $J = 11.5$ Hz, 1H), 4.68 (d, $J = 11.5$ Hz, 1H), 4.55 (d, $J = 6.0$ Hz, 1H), 4.46 (s, 1H), 4.33 (d, $J = 10.5$ Hz, 1H), 4.30 (d, $J = 10.5$ Hz, 1H), 3.62 (d, $J = 10.1$ Hz, 1H), 3.59 (d, $J = 10.1$ Hz, 1H), 3.46 (d, $J = 6.9$ Hz, 1H), 2.41 (s, 3H).^{13}C NMR (100 MHz, CD_3OD) δ: 164.6, 152.3, 151.1, 149.3, 145.0, 141.9, 137.0, 136.8, 133.5, 132.8, 132.4, 129.8, 128.8, 128.6, 128.5, 128.4, 128.2,128.0, 127.8, 127.7, 122.9, 89.3, 85.9, 79.3, 74.7, 74.6, 73.6, 70.6, 69.1, 21.6. LRMS (FAB) *m/z* 736 $[M + H]^+$. HRMS (FAB): Calcd for $C_{39}H_{38}N_5O_8S$ $[M + H]^+$: 736.2441. Found: 736.2444.

6-*N*-benzoyl-9-[2-*O*-acetyl-3,5-Di-*O*-benzyl-4-*C*-(*p*-toluenesulfonyloxymethyl)-β-D-arabinofuranosyl]-adenine (6). To a solution of compound **5** (3.14 g, 4.27 mmol) in dichloromethane and pyridine (5:1, 50 mL) was added trifluoromethanesulfonic anhydride (1.4 mL, 8.54 mmol) under at –30 °C and stirred for 3 hours at the same temperature. The reaction mixture was diluted with dichloromethane, and was washed with 1 M HCl, sat. $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. The obtained triflated crude (3.49 g, 4.02 mmol) was used for the next reaction without purification. In another flask, to a solution of DBU (2.40 mL, 16.0 mmol) in toluene (40 mL) was added acetic acid (1.84 mL, 32.0 mmol), and the mixture was stirred at room temperature for 1 hour. This mixed solution (20 mL) was added to a toluene solution (20 mL) of the triflated crude product (3.49 g, 4.02 mmol) and stirred at 80 °C for 7 hours. After cooling to room temperature, reaction mixture was diluted with ethyl acetate, and the organic layer was washed with 1 M HCl, sat. $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. The obtained crude product was purified by column chromatography (SiO_2, hexane: ethyl acetate = 1:1) to give compound **6** (2.02 g, 2.60 mmol, 61%) as colorless amorphous solid. IR ν_{max} (neat): 3064, 3030, 3008, 2926, 2871, 1749, 1698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.98 (s, 1H), 8.71 (s, 1H), 8.03–8.01 (m, 3H), 7.80 (d, $J = 8.2$ Hz, 2H), 7.62 (t, $J = 7.3$ Hz, 1H), 7.53 (t, $J = 7.3$ Hz, 2H), 7.37–7.24 (m, 10 H), 7.18–7.15 (m, 2H), 6.46 (d, $J = 5.7$ Hz, 1H), 5.49 (t, $J = 5.4$ Hz, 1H), 4.70–4.67 (m, 2H), 4.57 (d, $J = 12.1$ Hz, 1H), 4.50 (d, $J = 12.1$ Hz, 1H), 4.40 (d, $J = 12.1$ Hz, 1H), 4.35 (d, $J = 10.8$ Hz, 1H), 4.32 (d, $J = 10.8$ Hz, 1H), 4.23 (d, $J = 10.5$ Hz, 1H), 3.68 (d, $J = 9.6$ Hz, 1H), 3.55 (d, $J = 9.6$ Hz, 1H), 2.36 (s, 3H), 1.56 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ: 169.1, 164.5, 152.6, 151.3, 149.4, 144.9, 142.6, 137.1, 136.8, 133.5, 132.8, 132.7, 129.7, 128.8, 128.4, 128.1, 128.0, 127.9,127.8, 122.6, 83.8, 82.6, 81.4, 76.6, 73.4,

73.1, 69.3, 69.0, 21.5, 20.0. LRMS (FAB) *m/z* 778 $[M+H]^+$. HRMS (FAB): Calcd for $C_{41}H_{40}N_5O_9S$ $[M+H]^+$: 778.2547. Found: 778.2543.

9-[4-*C*-(*p*-toluenesulfonyloxymethyl)-β-D-arabinofuranosyl]adenine (7). To a solution of compound **6** (3.00 g, 3.86 mmol) in ethanol (40 mL) was added 20% $Pd(OH)_2/C$ (2.92 g) and cyclohexene (23.5 mL), and the mixture was refluxed for 15 hours. Since the smarting material did not disappear on TLC, $Pd(OH)_2/C$ was filtered off and the solvent was once removed. The reaction crude was diluted in ethanol (40 mL), 20% $Pd(OH)_2/C$ (2.06 g) and cyclohexene (7.8 mL) were added to the mixture again, and the mixture was refluxed for further 13 hours. The $Pd(OH)_2/C$ was filtered off and the solvent was evaporated to obtain a crude product (1.82 g). Saturated ammonia methanol solution (40 mL) was added to the obtained crude product (1.82 g) at 0 °C, and stirred for 1.5 hours. The crude product removed the solvent was purified by column chromatography (SiO_2, chloroform: methanol = 7:1) to obtain compound **7** (1.20 g, 2.66 mmol, 71%). IR ν_{max} (neat): 3338, 3211, 2746, 1645, 1600, 1356, 1175 cm^{-1}. ^1H NMR (400 MHz, CD_3OD) δ: 8.40 (s, 1H), 8.34 (s, 1H), 7.81 (d, $J = 8.2$ Hz, 2H), 7.37 (d, $J = 8.2$ Hz, 2H), 6.27 (d, $J = 5.0$ Hz, 1H), 4.45–4.39 (m, 2H), 4.29 (d, $J = 10.5$ Hz, 1H), 4.18 (d, $J = 10.5$ Hz, 1H), 3.72 (s, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ: 157.1, 153.7, 150.4, 146.4, 142.3, 134.2, 130.8, 129.2, 119.5, 86.1, 85.5, 77.8, 77.7, 70.4, 62.6, 21.5. LRMS (FAB) *m/z* 452 $[M+H]^+$. HRMS (FAB): Calcd for $C_{18}H_{22}N_5O_7S$ $[M+H]^+$: 452.1240. Found: 452.1210.

9-[4-*C*-(*p*-toluenesulfonyloxymethyl)-3,5-*O*-(1,1,3,3,-tetraisopropyldisiloxane-1,3-diyl)-β-D-arabinofuranosyl]adenine (8). 1,3-Dichloro-1,1,3,3-tetraisopropyldisiloxane (0.97 mL, 3.12 mmol) was added to a pyridine solution (26 mL) of compound **7** (1.17 g, 2.60 mmol) and the mixture was stirred at room temperature for 6.5 hours. The mixture was diluted with ethyl acetate, and washed with 1 M HCl, sat. $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. The obtained crude product was purified by column chromatography (SiO_2, chloroform: methanol = 50:1) to give compound **8** (1.70 g, 2.44 mmol, 94%). IR ν_{max} (neat): 3325, 3175, 2946, 2868, 1645, 1599, 1470, 1362, 1177 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.40 (s, 1H), 8.22 (s, 1H), 7.84–7.82 (m, 3H), 7.35 (d, $J = 8.2$ Hz, 2H), 6.03 (d, $J = 7.3$ Hz, 1H), 5.68 (brs, 2H), 5.23 (d, $J = 8.2$ Hz, 1H), 4.88–4.82 (m, 1H), 4.38 (d, $J = 10.5$ Hz, 1H), 4.18 (d, $J = 10.5$ Hz, 1H), 3.78 (d, $J = 11.5$ Hz, 1H), 3.70 (d, $J = 11.5$ Hz, 1H), 3.72 (s, 2H), 2.45 (s, 3H), 1.16–0.80 (m, 28 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.8, 152.5, 149.1, 144.9, 141.4, 132.8, 129.9, 128.0, 120.3, 83.8, 81.7, 79.6, 78.0, 70.1, 66.4, 21.6, 17.3, 17.3, 17.1, 17.1, 17.0, 17.0, 16.9, 13.3, 12.8, 12.5, 12.4. LRMS (FAB) *m/z* 694 $[M+H]^+$. HRMS (FAB): Calcd for $C_{30}H_{48}N_5O_8SSi_2$ $[M+H]^+$: 694.2762. Found: 694.2764.

9-[2-*Se*,4-*C*-methylene-2-seleno-β-D-ribofuranosyl]adenine (10). To a solution of compound **8** (32 mg, 0.046 mmol) in dichloromethane (0.5 mL) at 0 °C was added 4-dimethylaminopyridine (17 mg, 0.138 mmol) and trifluoromethanesulfonyl chloride (8.8 µL, 0.069 mmol), and the mixture was stirred for 30 min. The reaction mixture was partitioned between ice-cooled CH_2Cl_2 and water. The organic layer was washed with ice-cooled 1% aqueous HCl, ice-cooled water, ice-cooled saturated aqueous $NaHCO_3$, and ice-cooled saturated aqueous NaCl, dried over anhydrous $MgSO_4$, filtered, and evaporated to obtain a crude product of triflate. In another flask, under an argon atmosphere, sodium borohydride (10.9 mg, 0.3 mmol) was added to a stirring suspension of selenium powder (7.9 mg, 0.1 mmol) in absolute ethanol (0.3 mL); black suspension turned to colorless solution. To this solution was added a solution of crude product of triflate in tetrahydrofuran (0.3 mL), and the mixture was stirred at 40 °C for 17 hours. After cooled to room temperature, the mixture was diluted with ethyl acetate, mixed with appropriate amount of SiO_2, and evaporated. The obtained crude product on SiO_2 was roughly purified by column chromatography (SiO_2, chloroform: methanol = 30:1, 20:1, 10:1, 5:1) to give a mixture of **9** and its partially deprotected nucleosides. To the mixture in tetrahydrofuran (0.2 mL) was added tetra-*n*-butylammonium fluoride (1 M in THF, 15 µL, 15 µmol) and stirred at room temperature for 4 hours. The mixture was directly purified by column chromatography (SiO_2, chloroform: methanol = 15:1, 10:1, 7:1, 5:1) to give compound **10** (2.5 mg, 7.3 µmol, 16%) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.38 (s, 1H), 8.13 (s, 1H), 7.28 (s, 2H), 6.34 (s, 1H), 5.73 (d, J = 4.1 Hz, 1H), 5.43 (t, J = 5.5 Hz, 1H), 4.51–4.48 (m, 1H), 3.91 (d, J = 2.8 Hz, 1H), 3.75 (d, J = 5.5 Hz, 2H), 2.91 (d, J = 9.6 Hz, 1H), 2.86 (d, J = 9.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ: 156.0, 152.5, 148.3, 137.8, 119.1, 90.7, 89.4, 71.5, 58.8, 48.2, 39.5, 28.2. LRMS (FAB) m/z 344 $[M+H]^+$. HRMS (FAB): Calcd for $C_{11}H_{14}N_5O_3Se$ $[M+H]^+$: 344.0262. Found: 344.0247.

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