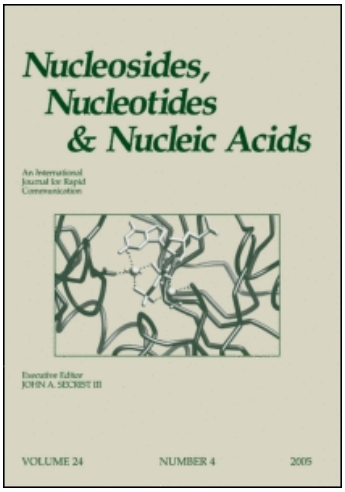


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis and Biological Evaluation of Novel Selenonucleosides

Yao Chen[a]; Yingdan Peng[a]; Jiancun Zhang[a]; Lei Fu[a]
[a] School of Pharmacy, Shanghai Jiaotong University, Shanghai, P. R. China

To cite this Article Chen, Yao , Peng, Yingdan , Zhang, Jiancun and Fu, Lei(2008) 'Synthesis and Biological Evaluation of Novel Selenonucleosides', Nucleosides, Nucleotides and Nucleic Acids, 27: 8, 1001 — 1008
To link to this Article: DOI: 10.1080/15257770802088803
URL: http://dx.doi.org/10.1080/15257770802088803

Nucleosides, Nucleotides and Nucleic Acids, 27:1001–1008, 2008

ISSN: 1525-7770 print / 1532-2335 online
DOI: 10.1080/15257770802088803

Taylor & Francis
Taylor & Francis Group

SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL SELENONUCLEOSIDES

Yao Chen,[1] Yingdan Peng,[1] Jiancun Zhang,[2] and Lei Fu[1]

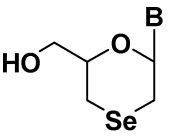
[1]*School of Pharmacy, Shanghai Jiaotong University, Shanghai, P. R. China*
[2]*Guangzhou Institute of Biomedicine and Health, Chinese Academy of Science, Guangzhou, P. R. China*

□ *A series of novel selenonucleoside analogues with 1,4-oxaselenane as the carbohydrate fragment has been synthesized from their corresponding dimesylated seconucleosides treated with NaHSe solution and subsequent deprotection. The synthesized selenonucleoside analogues were evaluated as potential antitumor agents.*

Keywords Synthesis; biological evaluation; selenonucleoside; 1,4-oxaselenane

Nucleoside analogues have played an important role in antitumor and antiviral therapies over the past decades. Today, nucleoside analogues are still one of the most important classes of drugs in these therapeutic areas. For example, the FDA approved another nucleoside analogue, Tyzeka (telbivudine) for the treatment of patients with chronic hepatitis B virus (HBV) in 2006.[1] Structurally, nucleosides consist of a purine or pyrimidine base linked to a carbohydrate moiety usually in the forms of ribose or deoxyribose. Many nucleoside based drugs have their carbohydrate fragments modified or have a heteroatom introduced into the carbohydrate moiety, such as 3′-azido-3′-deoxythymidine (AZT, zidovudine), acyclovir (ACV), lamivudine (3TC). Interestingly, some of them, such as AZT, also showed antitumor activity[2]in addition to its anti-HIV activity.[3] Among the heteroatom substituted carbohydrate fragments, selenium is of great interest to chemists as selenium has a long history of association with human health. At the molecular level, selenium is an essential component of the

Received 6 November 2007; accepted 27 February 2008.
This research was financially supported by an Innovation Grant (08ZZ12) from the Shanghai Municipal Education Commission.
Address correspondence to Lei Fu, School of Pharmacy, Shanghai Jiaotong University, Shanghai 200240, P. R. China; E-mail: leifu@sjtu.edu.cn or Jiancun Zhang, Guangzhou Institute of Biomedicine and Health, Chinese Academy of Science, Guangzhou510663, P. R. China E-mail: zhang_jiancun@gibh.ac.cn.



1a:B=uracil
1b:B=adenine
1c:B=cytosine
1d:B=guanine

FIGURE 1 The title compounds.

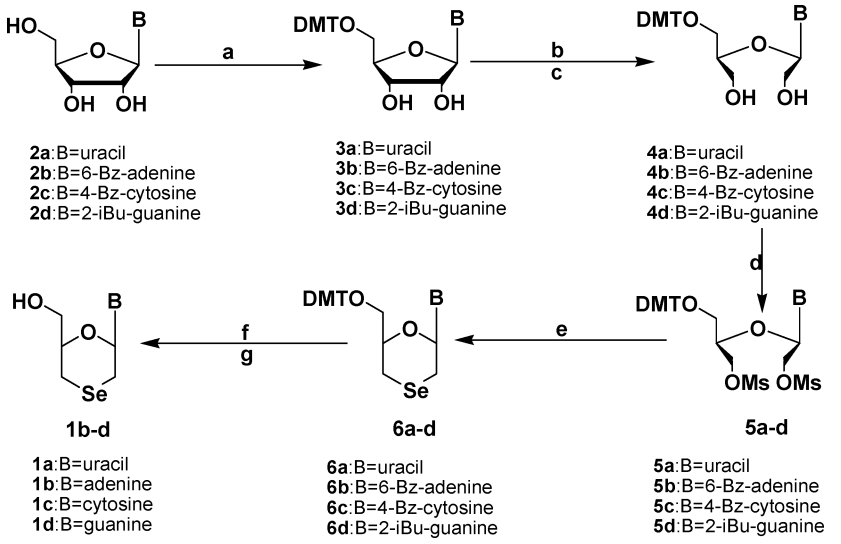
active sites of certain enzymes for the protection of cellular components against oxidative and free radical damage.[4]

Selenonucleosides have been synthesized and studied for their antiviral and antitumor activities. Structure-activity relationship studies on selenazofurin revealed that Se was essential for cytotoxicity and the inhibitory activity against inosine monophosphate dehydrogenase (IMPDH).[5] Selenazofurin and oxaselenolane nucleosides also were reported to exhibit antitumor activities.[6] Furthermore, certain dioxolane and oxathiolane nucleosides have exhibited potent antiviral and anticancer activities. It was reported that 1,4-oxaselenolane derivatives with aromatic groups showed antitumor activities,[7] in which the 1,4-oxaselenolane rings were found to be an essential fragment for their antitumor activities. Among the nucleoside analogues with six-membered carbohydrate fragments, 2,3-dihydro-4*H*-pyrannucleoside and l,5-anhydrohexitol nucleosides exhibited significant antitumor activity.[8],[9] Therefore, it was of interest to synthesize and evaluate isoelectronically substituted oxaselenolane nucleosides.

We are interested in further exploring potential applications of selenium-incorporated nucleosides. We introduced 1,4-oxaselenine ring as the carbohydrate fragment into nucleosides to study their antitumor and antiviral activities. Herein we reported the synthesis of novel selenonucleosides by coupling an 1,4-oxaselenolane ring with uracil, adenine, cytosine and guanine (Figure 1). We also reported our preliminary biological evaluation of these compounds for their in vitro antitumor activities.

RESULTS AND DISCUSSIONS

The title compounds **1a–d** were synthesized according to Scheme 1. The 5′—OH group in compounds **2a–d** was protected with dimethoxytrityl group to yield compounds **3a–d**,[10] which were further oxidized by $NaIO_4$ and subsequently reduced by $NaBH_4$ to give compounds **4a–d**.[11] Compounds **4a–d** were activated by the mesylation of OH groups at 2′ and 3′ positions.[12] The activated **5a–d** were then reacted with a seleniferous nucleophile NaHSe to form the 1,4-oxaselenine ring, and then deprotected sequentially with saturated methanolic ammonia and acetic acid to yield the final products **1a–d**. The yields and characterization data for compounds **2a–d** to **5a–d** were consistent with those reported.



SCHEME 1 Synthetic route for compounds 1a–d. a, DMTCl/Pyr, rt.; b, $NaIO_4/CH_3OH$, rt; c, $NaBH_4/CH_3OH$, rt; d, MsCl/Pyr, rt.; e, NaHSe, dioxane-water, 90°C; f, NH_3/CH_3OH, rt; g, 80%AcOH, rt.

We found that the activation of 2′ and 3′ OH groups in **4a–d** made the 2′ and 3′ carbon atoms more favorable for the seleniferous nucleophilic attack. Sodium hydrogen selenide was selected as the selenium source in the reaction for its ease of preparation and better stability than other selenium reagents. An aqueous solution of NaHSe was prepared according to the literature.[13] The mole ratio of activated seconucleosides and NaHSe was controlled at about 1:5 and a large excess NaHSe caused partial deprotection of the amino group of **5b-d** or **6b-d** by NaHSe, thus, the yields of **6b-d** were slightly lower than that of **6a**. In comparison to the preparation of other 1,4-oxaselenine rings in the literature,[14] a higher yield and more convenient separation were achieved.

Treating compounds **6a–d** sequentially with saturated methanolic ammonia, 80% aqueous acetic acid and then chromatographic separation afforded the titled compounds as white solids in good yield.

The structures of **1a–d** were confirmed by their NMR and HRMS data. The 3′-C and 5′-C of **1a–d** showed a characteristic chemical shift of 15–30 ppm due to the interaction with neighboring selenium atom. Coincidently, the H3 and H5 peaks in **1b** and **1d** were partially overlapped with DMSO and H_2O peaks. However, their presence was confirmed by the H-HCOSY 2D-NMR which indicated a strong correlation between H1 and H3 as well as H5 and H6, respectively.

In conclusion, a selenium atom was successfully introduced into the carbohydrate fragment to form a series of novel selenium-containing nucleoside analogues in good yields.

The synthesized compounds were evaluated in vitro for their activities in various tumor cell lines A549 (human lung tumor cell), LOVO (human colon tumor cell), and HL60 (human leukemia cell). Cytarabine (Ara-C) was chosen as a reference. Preliminary data showed only **1d** weakly inhibited LOVO cells, and the others have no inhibitory activities against these tumor cell lines. The difference in activity among four bases suggests that the inhibitory activity might be base dependent. Further preparation with the 1,4-oxaselenine fragment attached to various modified bases is in progress.

EXPERIMENTAL

Melting points were determined by the use of an electrothermal apparatus (Mel-Temp 1002, Shanghai Wanheng Precision Instruments, Co., Ltd., China). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 spectrometer (Varian, USA; ^{1}H NMR 300 MHz, ^{13}C NMR 75 MHz). Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 glass plates (Merck, Germany), and compound spots were visualized by UV light (254 nm). HRMS spectrometric analyses were confirmed by Micromass LCT (ESI-TOF-MS, Waters, Great Britain) system that utilizes the electro-spray ionization method. All chemical reagents were commercially available.

Sodium borohydride (2.3 g, 61 mmol) in 25ml of water was added dropwise to the flask containing powder of selenium (2.3 g, 29 mmol) suspended in water (25 mL) with vigorous stirring in ice-water bath. After the selenium powder was consumed, the ice-water bath was removed, the solution was kept stirring at room temperature for 30 minutes under nitrogen atmosphere. The resulting colorless solution of NaHSe was ready for use without further treatment.

EXPERIMENTAL

1-(6-((bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-1,4-oxaselenan-2-yl)pyrimidine-2, 4(1H, 3H)-dione (**6a**). Under a nitrogen atmosphere, NaHSe aqueous solution (about 5 mmol, 9 mL) was injected into the solution of **5a** (704 mg, 1 mmol in 50 mL dioxane). The mixture was stirred at 90°C for 12 hours, then the solvent was removed under vacuum, the residue was dissolved in CH_2Cl_2 (70 mL) and washed with 5% sodium bicarbonate solution (2 × 35 mL). The organic layer was separated and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether-ethyl acetate 1:1, v/v) to give compounds **6a** (518 mg, 0.872 mmol) in 87.2% yield as a white solid, m.p. 120–122°C, ^{1}H NMR (CD_3CN, 300 MH_Z), δ 8.96 (s, H-2, CONHCO, 1H), 7.51 (d, J = 6.0 Hz, H-6, 1H), 6.82–7.52 (H of DMT, 13H), 5.84 (dd, J = 1.5Hz and 8.4 Hz, H-5, 1H), 5.65 (dd, J = 1.2 Hz and 6.3 Hz, H-2′, 1H), 4.20 (m, H-6′, 1H), 3.76 (s, $-OCH_3$, 6H) 2.98–3.16 (m, CH_2OH, 2H), 2.93 (t, J

= 8.4 Hz, H-3′a,1H), 2.73 (t, J = 8.7 Hz, H-3′b, 1H), 2.50 (d, J = 13.5 Hz, H5′a, 1H), 2.47 (d, J = 13.8 Hz, H5′a, 1H), HRMS-ESI (m/z): ($M+Na^+$) calcd for$C_{30}H_{30}N_2O_6Se$, 617.1167, found, 617.1176.

N-(9-(6-((Bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-1, 4-oxaselenan-2-yl)-9H-purin-6-yl) ben-zamide (**6b**). Under nitrogen atmosphere, NaHSe aqueous solution (about 5 mmol, 9 mL) was injected into the solution of **5b** (831 mg, 1 mmol in 50 mL dioxane). The mixture was stirred at 90°C and the reaction was monitored by TLC. After 10 h, the solvent was removed under vacuum, the residue was dissolved in CH_2Cl_2 (75 mL) and washed with 5% sodium bicarbonate solution (2 × 35 mL). The organic layer was separated and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether–ethyl acetate 2:3, v/v) to give compounds **6b** (545 mg, 0.756 mmol) in 75.6% yield as a white solid, m.p. 116–118°C, ^{1}H NMR (CD_3CN, 300 MH_Z), δ 9.31 (s, H-6, CONHC=N, 1H), 8.71 (s, H-8, 1H), 8.33 (s, H-2, 1H), 7.45–8.05 (H of PhCO-, 5H), 6.78–7.40 (H of DMT, 13H), 6.17 (dd, J = 1.5 Hz and 8.1 Hz, H-2′, 1H), 4.35 (m, H-6′, 1H), 3.74 (s, $-OCH_3$, 6H), 3.56 (t, J = 9.0 Hz, H-3′a, 1H), 2.97–3.16 (m, CH_2OH, 2H), 2.83(d, J = 8.1 Hz, H-5′a, 1H), 2.80 (t, J = 9.0 Hz, H-3′b, 1H), 2.53 (d, J = 9.3 Hz, H-5′b, 1H), HRMS-ESI (m/z): ($M+H^+$) calcd for: $C_{38}H_{35}N_5O_5Se$, 722.1882, found, 722.1882.

N-(1-(6-((Bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-1,4-oxaselenan-2-yl)-2-oxo-1,2-dihydropyrimidin-4-yl)benzamide (**6c**). Compound **5c** (807 mg, 1 mmol) was treated by the similar procedure as described for **5b**, and purified by column chromatography (petroleum ether–ethyl acetate 1:2, v/v) to give compounds **6c** (504 mg, 0.723 mmol) in 72.3% yield as a white solid, m.p. 208–210°C, ^{1}H NMR (DMSO-d6, 300MH_Z), δ 11.27 (s, H-4, CONHC=N, 1H), 8.15 (d, J = 4.6 Hz, H-6, 1H), 7.47–8.02 (H of PhCO-, 5H), 7.40 (d, J = 5.7 Hz, H-5, 1H), 6.83–7.39 (H of DMT, 13H), 5.95 (dd, J = 1.2 Hz and 7.5Hz, H-2′, 1H), 4.22 (m, H-6′, 1H), 3.73 (s, $-OCH_3$, 6H), 3.08–3.13 (m, $-CH_2OH$ a, 1H), 2.95–3.10 (t, J = 8.4 Hz, H-3′a, 1H), 2.91–2.96 (m, $-CH_2OH$ b, 1H) 2.65 (d, J = 13.2 Hz, H-5′, 2H), 2.65 (t, J = 8.4 Hz, H-3′b, 1H), HRMS-ESI (m/z): ($M+Na^+$) calcd for $C_{37}H_{35}N_3O_6Se$, 720.1589, found, 720.1588.

N-(9-(6-((Bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-1,4-oxaselenan-2-yl)-6-oxo-6,-dihydro-1H-purin-2-yl)isobutyramide (**6d**). Compound **5d** (813 mg, 1 mmol) was treated by the similar procedure as described for **5b**, and purified by column chromatography (petroleum ether-ethyl acetate 1:2, v/v) to give compounds **6d** (482 mg, 0.685 mmol) in 68.5% yield as a white solid, m.p. 141–143°C, ^{1}H NMR (DMSO-d6, 300 MH_Z), δ 12.10 (s, H-2, CONHC=N, 1H), δ 11.70 (s, H-1, CONHC=N, 1H), 8.21 (s, H-8, 1H), 6.75–7.35 (H of DMT, 13H), 5.91 (dd, J = 1.2 Hz and 8.1 Hz, H-2′, 1H), 4.23 (m, H-6′, 1H), 3.69 (s, $-OCH_3$, 6H), 3.55(t, J = 8.7 Hz, H-3′a, 1H), 2.85–3.06 (m, CH_2OH, 2H), 2.79 (d, J = 11.2 Hz, H-5′a, 1H), 2.75

(t, J = 8.4 Hz, H-3′b, 1H), 2.64 (d, J = 11.5 Hz, H-5′b, 1H), 2.59–2.69 [m, $(CH_3)_2CH$-CO, 1H], 1.10 (d, J = 8.4 Hz, CH_3CH-, 3H), 1.09 (d, J = 8.4 Hz, CH_3CH-, 3H), HRMS-ESI (m/z): ($M+Na^+$) calcd for $C_{35}H_{37}N_5O_6Se$, 726.1807, found, 726.1816.

1-(6-(Hydroxymethyl)-1,4-oxaselenan-2-yl)pyrimidine-2,4(1H,3H)-dione **(1a).** Compound **6a** (297 mg, 0.5 mmol) was treated with 80% acetic acid aqueous solution (10 mL) for 1 h at room temperature. After evaporation in vacuum, the residue was chromatographed on a silica column using methylene chloride—methanol (33:1, v/v) to give **1a** (128 mg, 0.438 mmol) in 87.6% yield as a white solid, m.p. 79–81°C, ^{1}H NMR (methanol-d4, 300 MH_Z), δ 7.74 (d, J = 8.1Hz, H-6, 1H), 5.92 (dd, J = 1.8 Hz and 10.5 Hz, H-2′, 1H), 5.90 (d, J = 8.4 Hz, H-5, 1H), 4.07–4.16 (m, H-6′, 1H), 3.58 (t, J = 3.9 Hz, CH_2OH, 2H), 2.98 (t, J = 10.8 Hz, H-3′a, 1H), 2.72 (t, J = 11.4 Hz, H-3′b, 1H), 2.54 (d, J = 12.0 Hz, H-5′a, 1H), 2.42 (d, J = 12.6 Hz, H-5′b, 1H). ^{13}C NMR (Methanol-d4, 75 MH_Z) δ 16.83 and 18.61 (CH_2SeCH_2), 65.14 (CH_2OH), 83.79 (C-6′), 83.81 (C-2′), 101.48 (C-5), 140.92 (C-6), 150.36 (C-2), 164.88 (C-4), HRMS-ESI (m/z): ($M+Na^+$) calcd for $C_9H_{12}N_2O_4Se$, 314.9860, found, 314.9863.

(6-(6-Amino-9H-purin-9-yl)-1,4-oxaselenan-2-yl)methanol **(1b).** The solution of compounds **6b** (361mg, 0.5mmol) in methanolic ammonia (50 mL, saturated at 0°C) was kept stirring for 24 hours at room temperature. The solvent was removed in vacuum, and then treated with 80% acetic acid aqueous solution (10 mL), and purified on silica gel column chromatography with methylene chloride—methanol (15: 1, v/v) as eluent, the title compounds **1b** (133 mg, 0.422 mmol) were obtained in 84.4% yield as a white solid, m.p. 194–196°C, ^{1}H NMR (DMSO-d6, 300 MH_Z), δ 8.34 (s, H-8, 1H), 8.14 (s, H-2, 1H), 7.30 (s, $-NH_2$, 2H), 5.94 (dd, J = 1.5 and 10.8 H_Z, H-2′, 1H), 4.87(br, $-OH$, 1H), 3.99–4.09(m, H-6′, 1H), 3.60 (t, J = 10.8 H_Z, H-3′a,1H), 3.27–3.42 (partially overlapped with H_2O peaks, CH_2OH, 2H), 2.78 (d, J = 12.3 H_Z, H-3′b, 1H), 2.49–2.66 (m, H-5′, 2H). ^{13}C NMR (DMSO-d6, 75 MH_Z) δ: 18.35 and 19.38 (CH_2SeCH_2), 65.20 (CH_2OH), 83.21 (C-6′), 83.43 (C-2′), 119.22 (C-5), 139.18 (C-8), 149.28 (C-4), 153.39 (C-2), 156.73 (C-6). H-H COSY (300 MH_Z): H2′ (δ = 5.94) was associated with H-3′a (δ = 3.60), H-3′b (δ = 2.78), H6′ (δ = 3.99–4.09) was correlated with H-5′a (δ = 2.49–2.66), H6′ (δ = 3.99–4.09) was associated with CH_2OH (δ = 3.27–3.42), OH (δ = 4.87) was correlated with CH_2OH (δ = 3.27–3.42), H-3′a (δ = 3.60) was associated with H-3′b (δ = 2.78). HRMS-ESI (m/z): ($M+Na^+$) calcd for $C_{10}H_{13}N_5O_2Se$, 338.0132, found, 338.0137.

4-Amino-1-(6-(hydroxymethyl)-1,4-oxaselenan-2-yl)pyrimidin-2(1H)-one **(1c).** Compound **6c** (349 mg, 0.5 mmol) was treated by the similar procedure described for **6b**, and purified on silica gel column chromatography with methylene chloride-methanol (12:1, v/v) as eluent. The title compounds **1c** (118 mg, 0.388 mmol) was obtained in 81.1% yield as a white solid, m.p.

320–322°C, ^{1}H NMR(methanol-d4, 300 MH_Z), δ 7.72 (d, J = 7.2 Hz, H-6, 1H), 5.94 (dd, J = 1.5 H_Z and 10.5 H_Z, H-2′, 1H), 5.90 (d, J = 7.8 Hz, H-5, 1H), 4.05–4.16 (m, H-6′, 1H), 3.58 (t, J = 5.4 Hz, CH_2OH, 2H), 2.86 (t, J = 11.4 Hz, H-3′a, 1H), 2.72 (t, J = 11.7 Hz, H-3′b, 1H), 2.58 (d, J = 11.4 Hz, H-5′a, 1H),2.43 (d, J = 12.6 Hz, H-5′b, 1H), ^{13}C NMR (Methanol-d4, 75 MH_Z) δ: 16.95 and 19.30 (CH_2SeCH_2), 65.26 (CH_2OH), 83.60 (C-6′), 84.60 (C-2′), 94.94 (C-5), 141.09 (C-6), 156.16 (C-2), 166.35 (C-4), HRMS-ESI (m/z): ($M+Na^+$) calcd for $C_9H_{13}N_3O_3Se$, 314.0020, found, 314.0016.

2-Amino-9-(6-(hydroxymethyl)-1,4-oxaselenan-2-yl)-1H-purin-6(9H)-one **(1d).** Compound **6d** (352 mg, 0.5 mmol) was treated by the similar procedure described for **1b**, and purified on silica gel column chromatography with methylene chloride-methanol (10:1, v/v). The title compounds **1d** (141 mg, 0.432 mmol) was obtained in in 85.2% yield as a white solid, m.p. 130–133°C, ^{1}H NMR (DMSO-d6, 300 MH_Z), δ 11.01 (s, H-1, 1H), 7.87 (s, H-8, 1H), 6.74 (s, $-NH_2$, 2H), 5.72 (dd, J = 1.2 and 10.5 Hz, H-2′, 1H), 4.91 (br, $-OH$, 1H), 3.89–4.00 (m, H-6′, 1H), 3.28–3.46 (partially overlapped with H_2O peaks, CH_2OH, H-3′a, H-3′b, 4H), 2.51–2.72 (partially overlapped with DMSO-d6 peaks, H5′a, H5′b, 2H), ^{13}C NMR (DMSO-d6, 75 MH_Z) δ 18.33 and 19.62 (CH_2SeCH_2), 65.19 (CH_2OH), 82.73 (C-6′), 83.52 (C-2′), 116.92 (C-5), 135.30 (C-8), 150.87(C-4), 154.77(C-2), 157.74(C-6), HRMS-ESI (m/z): ($M+Na^+$) calcd for $C_{10}H_{13}N_5O_3Se$, 354.0081, found, 354.0087.

REFERENCES

1. Bartholomeusz, A.; Yuen, L.; Locarnini, S.; Kuiper, M. Understanding HBV resistance to Telbivudine: molecular modelling and database mining. *J. Hepatology* **2007**, 46 (Suppl. 1), S185.
2. Jagetia, G.C.; Aruna, R. Correlation of micronuclei-induction with the cell survival in HeLa cells treated with a base analogue, azidothymidine (AZT) before exposure to different doses of –radiation. *Toxicol. Lett.* **2003**, 139, 33–43.
3. Beenhouwer, D.O.; Rankin, J.A.; Mellors, J.W. Anti-HIV-1 activity of 3′- azido-3′—deoxythymidine (AZT) in primary mononuclear phagocytes. *Antiviral Res.* **1992**, 19, 43–54.
4. May, S.W.; May, S.W. Selenium-based pharmacological agents: an update. *Expert Opin. Investig. Drug* **2002**, 11, 1261–1269.
5. Witczak, Z.J. Nucleosides containing selenium. II. *Nucleosides Nucleotides* **1983**, 2, 295–318.
6. Chu, C..; Ma, L.; Olgen, S.; Pierra, C.; Du, J.; Gumina, G.; Gullen, E.; Cheng, Y.-C.; Schinazi, R.F. Synthesis and antiviral activity of oxaselenolane nucleosides. *J. Med. Chem.* **2000**, 43, 3906–3912.
7. Ishihara, H.; Kim, Y.M.; Koketsu, M.; Yang, H.O. KR, 2003026487 A, 2003.
8. Verheggen, I.; Van Aerschot, A.; Toppet, S.; Snoeck, R.; Janssen, G.; Balzarini, J.; DeClercq, E.; Herdewijn, P. Synthesis and antiherpes virus activity of 1,5-anhydrohexitol nucleosides. *J. Med. Chem.* **1993**, 36, 2033–2040.
9. Verheggen, I.; Van Aerschot, A.; Van Meervelt, L.; Rozenski, J.; Wiebe, L.; Snoeck, R.; Andrei, G.; Balzarini, J.; Claes, P.; DeClerq, E.; Herdewijn, P. Synthesis, biological evaluation, and structure analysis of a series of new 1,5-anhydrohexitol nucleosides. *J. Med. Chem.* **1995**, 38, 826–835.
10. Hakimelahi, G.H.; Proba, Z.A.; Ogilvie, K.K.; New catalysts and procedures for the dimethoxytritylation and selective silylation of ribonucleosides. *Can. J. Chem.* **1982**, 60, 1106–1113.
11. Mikhailov, S.N.; Florent′ev, V.L.; Pfleiderer, W. Convenient synthesis of partially blocked oxidized-reduced nucleosides. *Synthesis* **1985**, 399–400.

12. Beaton, G.; Jones, A.S.; Walker, R.T. The chemistry of 2′, 3′-seconucleosides. III. Synthesis and reactions of purine-2′, 3′-secoribonucleosides. *Tetrahedron* **1988**, 44, 6419–6428.
13. Klayman, D.L.; Griffin, T.S. Reaction of selenium with sodium borohydride in protic solvents. A Facile Method for the introduction of selenium into organic molecules. *J. Am. Chem. Soc.* **1973**; 95; 197–199.
14. Kurbanov, S.B.; Mamedov, E.Sh.; Mishiev, R.D.; et al. Reaction of epoxides with hydrogen selenide. *Zhurnal Organicheskoi Khimi* **1991**, 27, 942–946.