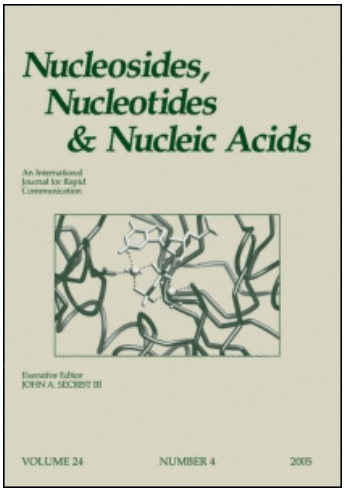

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Synthesis of 6-Sulfur Analogues of Oxanosine and Closely Related Derivatives Thereof

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To cite this Article Hara, Sumiko , Kaneko, Chisato , Matsumoto, Hiroatsu , Nishino, Takeshi , Takeuchi, Tadao , Mori, Takeo , Mizuno, Yoshihisa and Ikeda, Kazuyoshi(1992) 'Synthesis of 6-Sulfur Analogues of Oxanosine and Closely Related Derivatives Thereof', Nucleosides, Nucleotides and Nucleic Acids, 11: 2, 571 — 582
To link to this Article: DOI: 10.1080/07328319208021726
URL: http://dx.doi.org/10.1080/07328319208021726

NUCLEOSIDES & NUCLEOTIDES, 11(2-4), 571-582 (1992)

SYNTHESIS OF 6-SULFUR ANALOGUES OF OXANOSINE AND CLOSELY RELATED DERIVATIVES THEREOF

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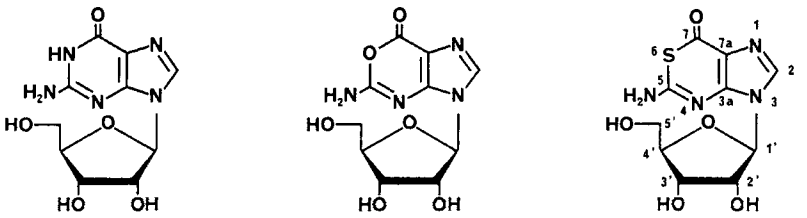
ABSTRACT. Novel β-D-ribofuranosides having a 5-substituted imidazo [4,5-d][1,3]thiazine ring, including the S^6-congener **3** of oxanosine **2**, were synthesized for screening their anticancer and antiviral activities.

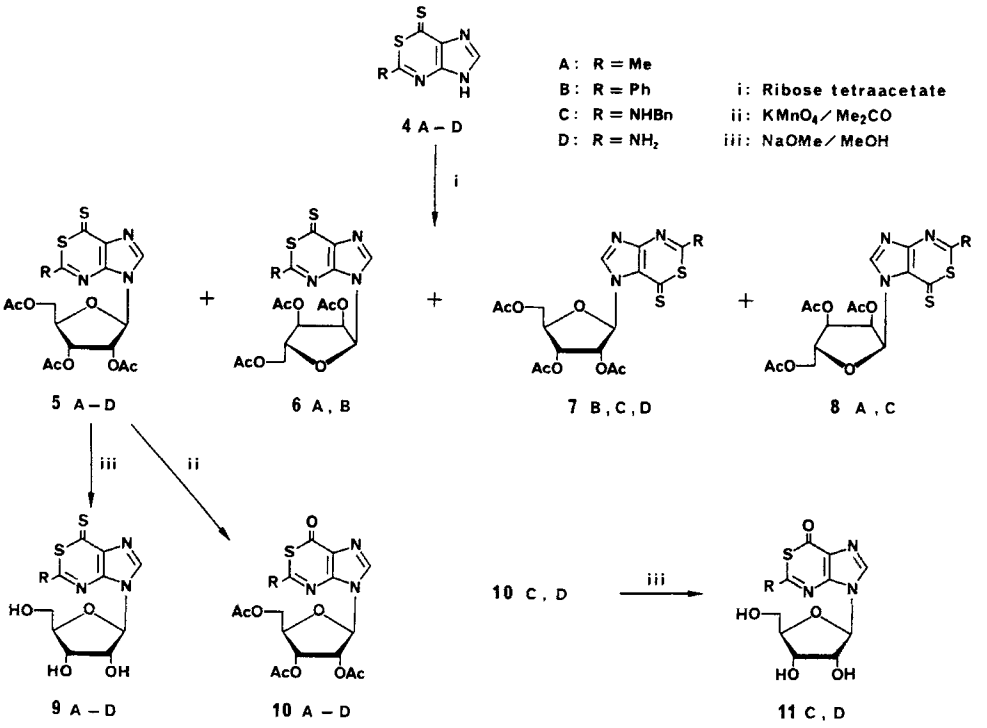
The fact that oxanosine **(2)**, in which N^1 of guanosine **(1)** is replaced by an oxygen atom, exhibits potent antitumor and antiviral activities,[1,2] prompted us to synthesize normal and acyclic nucleosides in which N^1 of purine bases is replaced by O, S, Se, or sp^2 carbon in order to relate structure and antiviral activity. As part of our ongoing program, we recently reported the synthesis of "acyclic oxanosine"[3] and "acyclic thiaoxanosine".[4] It was found that the replacement of N^1 of acyclovir; 9-[(2-hydroxyethoxy)methyl]guanine, with an oxygen or a sulfur atom resulted in a dramatic reduction in antiviral activity against HSV-I and no activity against HIV-I.[3,4]

The present paper is dedicated to the memory of the late Professor Tohru Ueda.



1 2 3

FIG. 1



SCHEME 1

This paper describes the synthesis of 5-amino-3-(β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazin-7(3H)-one, which is referred to hereafter as thiaoxanosine **(3)**, and closely related compounds.

Title compounds were synthesized from the corresponding imidazo-[4,5-d][1,3]thiazine bases[4] and 1,2,3,5-tetra-O-acetyl-β-D-ribofuranose (which, hereafter, is referred to as TAR) by a fusion method in the absence of catalysts.

Thus, a mixture of a imidazo[4,5-d][1,3]thiazin-7-thione bearing a substituent on position 5, **4A-D**[5] (1 equiv.) and TAR (ca. 6 equiv.) was heated at 150 °C in an oil bath for 6 h. The cooled melt was subjected to silica gel chromatography by use of chloroform as solvent. The first fraction containing excess TAR and decomposed sugars of unknown structure was discarded. Further washing of the column with chloroform furnished, after removal of the solvent, 5-substituted 3-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(3H)-thiones **5A-D**, 5-substituted 3-(2,3,5-tri-O-acetyl-α-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(3H)-thiones **6A,B**, 5-substituted 1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(1H)-thiones **7B-D**, and 5-substituted 1-(2,3,5-tri-O-acetyl-α-D-ribofuranosyl)-imidazo[4,5-d][1,3]thiazine-7(1H)-thiones **8A,C**. Nucleosides, **6C,D**, **7A** and **8B,D** could not be isolated from the reaction mixture.

The structural determination including the site of ribosylation and the anomeric configuration rests upon the elemental analysis as well as spectral (UV, ^{1}H-, ^{13}C-NMR and Mass) data.

Thus, it is well known that among a pair of positional (N^1- and N^3-alkyl) isomers in the imidazopyridine and imidazothiazine ring system, the N^3-isomer absorbs UV light at a shorter wavelength than the corresponding N^1-isomer.[4,6] Accordingly **5B** and **6A** were assigned the 3-(D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine structure, whereas **7B** and **8A** were assigned as the N^1-isomer. Nucleosides, **5A**, **5C**, **5D**, and **6B** may be N^3-isomers, because they had almost identical UV spectra with those of the above-mentioned N^3-isomers. By analogy, **7C**, **7D** and **8C** must be N^1-isomers. The fact that **5A** and **6A** are N^3-substituted nucleosides strongly suggests that they are anomers of each other. In keeping with the above conclusion, reached by the UV method, ^{1}H-NMR signals due to the anomeric proton in the N^1-isomers (**7B** and **8A**) were observed at

TABLE 1. Selected spectral (^1H, ^{13}C NMR and UV) data which are pertinent to the discussion in the text.

Compound	Configuration	NMR (ppm) $CDCl_3$ H-1'	C-3a	C-7a		$OCOCH_3$		UV λmax (nm) MeOH or H_2O
5A	3-β	6.13	140.8	135.2	2.12	2.13	2.15	378 [3]
6A	3-α	6.63	141.1	134.2	1.92	2.13	2.16	376
8A	1-α	7.70	152.8	125.0	1.84	2.02	2.17	385
5B	3-β	6.23	141.5	135.1	2.03	2.13	2.17	405 [3]
6B	3-α	6.72	140.8	135.1	1.87	2.13	2.18	405
7B	1-β	7.31	153.9	124.9	2.06	2.19	2.23	417 [3]
5C	3-β	6.28	ND [1]	ND	2.07	2.10	2.11	409 [3]
7C	1-β	---- [2]	ND	ND	2.05	2.10	2.17	422
8C	1-α	7.63	ND	ND	1.90	2.04	2.17	422
5D	3-β	5.80	146.2	130.9	2.09	2.10	2.13	407 [3]
7D	1-β	7.60	156.9	122.9	2.05	2.18	2.20	418

1,ND stands for no determination; 2,We failed to assign the signal due to the anomeric proton of 7C because it was buried in the signals of the aryl protons; 3,H_2O was used as solvent.

lower field than those of the anomeric proton of the corresponding N^3-isomers (**5B** and **6A**), and also in the ^{13}C-NMR chemical shifts of the N^1-isomer, the carbon atom (carbon 7a) which is located at the adjacent position to the ribosylated nitrogen atom is shifted upfield by ca. 10 ppm[7] (see underlined values in TABLE 1), as compared to the chemical shifts of the carbon 7a of the N^3-isomers.

When a pair of anomers could be obtained, the anomeric configuration was determined by the comparison of the chemical shifts in ^1H-NMR of the 2'-O-acetyl group according to the empirical rule which has been originally reported by Montgomery.[8]

The signals due to the 2'-O-acetyl group of 1',2'-cis nucleosides, namely, **6A** and **8C** occur by 0.17-0.22 ppm upfield than the signals of the corresponding 1',2'-trans nucleosides (**5A** and **7C**)(see underlined values in Table 1), demonstrating that the anomeric configuration of **6B**, and **8A** is α-**D**, whereas that of **5B-D**, **7B**, and **7D** is β -**D**.

Treatment of nucleosides **5A-D** with potassium permanganate at room temperature gave rise to 5-substituted 3-(2,3,5-tri-O-acetyl-β-**D**-ribofuranosyl)imidazo[4,5-d][1,3]thiazin-7(3H)-ones **10A** as a viscous oil (72 %), **10B** as crystals (61 %), **10C** as a viscous oil (57 %), and **10D** as a solid (51 %). These products showed the presence of a new carbonyl absorption band at around 1690 cm^{-1} in the IR spectra and hypsochromic shifts of ca. 85 nm in the UV spectra. Both observations are a reflection of the conversion of the 7-thiocarbonyl group to the corresponding carbonyl group.

Deprotection of the acetyl groups in **5A-D** and **10C,D** was achieved by a slight modification of the Zemplen procedure[9] to give 5-substituted 3-(β-**D**-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(3H)-thiones **9A-D** in 44-81 % yield and 5-substituted 3-(β-**D**-ribofuranosyl)imidazo[4,5-d][1,3]thiazin-7(3H)-ones **11C,D** in 34-36 % yield, respectively.

Results on the biological testing will be the subject of a separate paper.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}N-NMR and ^{13}C-NMR spectra were obtained on a JEOL GX-270 and an EX-400 spectrometer using tetramethylsilane as an internal standard, respectively. Chemical shifts are given on the δ scale (ppm). ArH-o,p and ArH-m refer to aromatic protons, located at ortho, para, and meta position, respectively. MS and HR-MS measurements were run on a JEOL JMS-DX303 spectrometer. IR spectra were recorded with a JASCO IRA-1 spectrometer in KBr disks. UV spectra were measured on a Hitachi 200-20 spectrophotometer. Column chromatography was performed on silica gel 60 (Merck, 70-230 mesh).

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-methylimidazo[4,5-d]-[1,3]thiazine-7(3H)-thione (5A), 3-(2,3,5-tri-O-acetyl-1-α-D-ribofuranosyl)-5-methylimidazo[4,5-d][1,3]thiazine-7(3H)-thione (6A), and 1-(2,3,5-tri-O-acetyl-1-α-D-ribofuranosyl)-5-methylimidazo[4,5-d]-[1,3]thiazine-7(1H)-thione (8A) Compound **4A** (194 mg; 1.06 mmol) was fused at 150 °C for 6 h under normal pressure with TAR (2.69 g; 8.43 mmol). The cooled melt was purified by a column chromatography over silica gel (50 g, 2.4 X 32 cm), fraction size being 15 ml, using $CHCl_3$ as solvent. The initial fraction containing decomposed sugar was eluted, discarded and then continued washing of the column with the same solvent gave, after removal of the solvent, **5A** (231 mg, 49 %, viscous oil), **6A** (149 mg, 32 %, viscous oil), and **8A** (42 mg, 9 %, viscous oil). **5A**; MS m/z: 441(M^+). HR-MS calcd for $C_{17}H_{19}N_3O_7S_2$: 441.0664. Found m/z: 441.0661. ^{1}H-NMR ($CDCl_3$): 2.12, 2.13, 2.15 (each 3H, s, $COCH_3$), 2.66 (3H, s, CH_3), 4.38 (2H, m, 5'-CH_2), 4.46, 5.59, 5.80 (1H, m, H-2',3',4'), 6.13 (1H, t, H-1', $J_{1',2'}$ = 4.4 Hz), 8.04 (1H, s, 2-H). ^{13}C-NMR ($CDCl_3$): 87.0 (C-1'), 140.8 (C-3a), 135.2 (C-7a); 139.3 (C-2). UV λmax nm (ε X 10^3) (H_2O): 261 (5.7), 318 (4.0), 380 (5.7). **6A**; MS m/z: 441 (M^+). HR-MS calcd for $C_{17}H_{19}N_3O_7S_2$: 441.0664. Found m/z: 441.0651. ^{1}H-NMR ($CDCl_3$): 1.92, 2.13, 2.16 (each 3H, s, $COCH_3$), 2.63 (3H, s, CH_3), 4.31 (2H, d, 5'-CH_2), 4.66, 5.51, 5.75 (1H, m, H-2',3',4'), 6.63 (1H, d, H-1', $J_{1',2'}$ = 5.4 Hz), 8.17 (1H, s, 2-H). ^{13}C-NMR ($CDCl_3$): 83.1 (C-1'), 141.1 (C-3a), 134.2 (C-7a), 140.2 (C-2). UV λmax nm (MeOH): 261, 320, 376. **8A**; MS m/z: 441 (M^+). HR-MS calcd for $C_{17}H_{19}N_3O_7S_2$: 441.0664. Found m/z: 441.0694. ^{1}H-NMR ($CDCl_3$): 1.84, 2.02, 2.17 (each 3H, s, $COCH_3$), 2.65 (3H, s, CH_3), 4.32 (2H, d, 5'-CH_2), 4.71, 5.47, 5.86 (1H, t, H-2',3',4'), 7.70 (1H, d, H-1', $J_{1',2'}$ = 5.4 Hz), 8.41 (1H, s, 2-H). ^{13}C-NMR ($CDCl_3$): 87.0 (C-1'), 152.8 (C-3a), 125.0 (C-7a), 143.9 (C-2). UV λmax nm (MeOH): 272, 310 (sh), 385.

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-phenylimidazo[4,5-d]-[1,3]thiazine-7(3H)-thione (5B), 3-(2,3,5-tri-O-acetyl-1-α-D-ribofuranosyl)-5-phenylimidazo[4,5-d][1,3]thiazine-7(3H)-thione (6B), and 1-(2,3,5-tri-O-acetyl-1-β-D-ribofuranosyl)-5-phenylimidazo[4,5-d][1,3]-thiazine-7(1H)-thione (7B) Compound **4B** (202 mg; 0.82 mmol) was fused at 150 °C for 6 h under normal pressure with TAR (2.10 g; 6.59

mmol). The reaction mixture was worked up as above to give **5B** (90 mg, 44 %, amorphous), **6B** (84 mg, 41 %, viscous oil) and **7B** (10 mg, 5 %, yellow powder). **5B;** MS m/z; 503 (M^+). HR-MS calcd for $C_{22}H_{21}N_3O_7S_2$: 503.0821. Found m/z: 503.0819. ^{1}H-NMR ($CDCl_3$-20% DMSO-d_6): 2.04, 2.13, 2.17 (each 3H, s, $COCH_3$), 4.35 (2H, m, 5'-CH_2), 4.47, 5.57, 5.90 (1H, m, H-2', 3',4'), 6.23 (1H, d, H-1', $J_{1',2'}$ = 4.4 Hz), 7.49-7.60 (3H, m, ArH-m,p), 8.00-8.08 (2H, m, ArH-o), 8.14 (1H, s, 2-H). ^{13}C-NMR (CD_3OD): 87.3 (C-1'), 141.4 (C-3a), 135.9 (C-7a), 140.0 (C-2). UV λmax nm (ε X 10^3) (H_2O): 264 (31.4), 339 (12.6), 402 (10.7). **6B;** MS m/z: 503 (M^+). ^{1}H-NMR ($CDCl_3$-20% DMSO-d_6): 1.87, 2.13, 2.18 (each 3H, s, $COCH_3$), 4.32 (2H, m, 5'-CH_2), 4.73, 5.50, 5.89 (3H, m, H-2',3',4'), 6.72 (1H, d, H-1', $J_{1',2'}$ = 6.7 Hz), 7.48-7.60 (3H, m, ArH-m,p), 8.00-8.03 (2H, m, ArH-o), 8.20 (1H, s, 2-H). ^{13}C-NMR (CD_3OD): 87.0 (C-1'), 153.2 (C-3a), 125.1 (C-7a), 144.3 (C-2). UV λmax nm (MeOH): 268, 333, 405. **7B;** mp 188-190 °C. MS m/z: 503 (M^+). ^{1}H-NMR ($CDCl_3$-20% DMSO-d_6): 2.06, 2.19, 2.23 (each 3H, s, $COCH_3$), 4.46 (2H, m, 5'-CH_2), 4.50, 5.37, 5.65 (1H, m, H-2',3',4'), 7.31 (1H, d, H-1', $J_{1',2'}$ = 1.8 Hz), 7.49-7.59 (3H, m, ArH-m,p), 8.09-8.12 (2H, m, ArH-o), 8.75 (1H, s, 2-H). ^{13}C-NMR (CD_3OD): 90.2 (C-1'), 153.9 (C-3a), 125.0 (C-7a),143.2 (C-2). UV λmax nm (ε X 10^3) (H_2O): 272 (16.3), 335 (sh) (6.6), 352 (sh) (5.8), 417 (6.9).

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-benzylaminoimidazo[4,5-d][1,3]thiazine-7(3H)-thione (5C), 1-(2,3,5-tri-O-acetyl-1-β-D-ribofuranosyl)-5-benzylaminoimidazo[4,5-d][1,3]thiazine-7(1H)-thione (7C), and 1-(2,3,5-tri-O-acetyl-1-α-D-ribofuranosyl)-5-benzylaminoimidazo[4,5-d][1,3]thiazine-7(1H)-thione (8C) Compound **4C** (100 mg; 0.36 mmol) was fused at 160 °C for 3 h under normal pressure with TAR (0.70 g; 2.19 mmol). The reaction mixture was worked up as above to give **5C** (91 mg, 47 %, yellow powder), **7C** (16 mg, 8 %, viscous oil), and **8C** (27 mg, 14 %, viscous oil). **5C;** mp, 73-74 °C, MS m/z: 532 (M^+), HR-MS calcd for $C_{23}H_{24}N_4O_7S_2$ 532.1086. Found m/z: 532.1089. ^{1}H-NMR ($CDCl_3$): 2.07, 2.10, 2.11 (each 3H, m, $COCH_3$), 4.28 (2H, m, 5'-CH_2), 4.66 (2H, t, CH_2), 5.08, 5.26, 5.36 (1H, q, H-2',3',4'), 6.28 (1H, d, H-1', $J_{1',2'}$ = 4.9 Hz), 7.36 (5H, d, ArH), 7.84 (1H, s, 2-H). UV λmax nm (ε X 10^3)(H_2O): 242 (20.0), 294 (5.3), 410 (19.0). **7C;** MS m/z: 532 (M^+), HR-MS calcd for $C_{23}H_{24}N_4O_7S_2$ 532.1086. Found m/z: 532.1107. ^{1}H-NMR ($CDCl_3$): 2.05, 2.10, 2.17 (each 3H, m, $COCH_3$), 4.23 (2H, m, 5'-

CH_2), 4.70 (2H, t, CH_2), 4.42, 5.08, 5.32 (1H, q, H-2',3',4'), 7.35 (5H, d, ArH), 8.50 (1H, s, 2-H). UV λmax nm (MeOH): 235, 264, 422. **8C;** MS m/z: 532 (M^+), HR-MS calcd for $C_{23}H_{24}N_4O_7S_2$ 532.1086. Found m/z: 532.1060. ^{1}H-NMR ($CDCl_3$): 1.90, 2.04, 2.17 (each 3H, s, $COCH_3$), 4.22 (2H, q, 5'-CH_2), 4.70 (2H, d, CH_2), 4.38, 4.65, 5.46 (1H, q, H-2',3',4'), 7.63 (1H, t, H-1', $J_{1',2'}$ = 4.9 Hz), 7.36 (4H, d, ArH-o,m), 7.63(1H, d, ArH-p), 8.26 (1H, s, 2-H). UV λmax nm (MeOH): 265, 422.

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-aminoimidazo[4,5-d]-[1,3]thiazine-7(3H)-thione (5D) and 1-(2,3,5-tri-O-acetyl-1-β-D-ribofuranosyl)-5-aminoimidazo[4,5-d][1,3]thiazine-7(1H)-thione (7D) Compound **4D** (86 mg; 0.47 mmol) was fused at 150 °C for 3 h under normal pressure with TAR (549 mg; 1.87 mmol). The reaction mixture was worked up as above using 5% MeOH-$CHCl_3$ to give **5D** (94 mg, 46 %, yellow powder) and **7D** (20 mg, 10 %, viscous oil). **5D;** mp, 139-140 °C, MS m/z: 442 (M^+). HR-MS calcd for $C_{16}H_{18}N_4O_7S_2$: 442.0617. Found m/z: 442.0641. ^{1}H-NMR ($CDCl_3$): 2.09, 2.10, 2.13 (each 3H, s, $COCH_3$), 4.10-4.17 (2H, m, 5'-CH_2), 4.21-4.32, 5.56, 5.70 (1H, m, H-2',3',4'), 5.80 (1H, m, H-1', $J_{1',2'}$ = 4.4 Hz), 7.36 (2H, s, NH_2), 7.65 (1H, s, 2-H). ^{13}C-NMR ($CDCl_3$): 85.6 (C-1'), 130.9 (C-7a), 137.6 (C-2), 146.2 (C-3a). UV λmax nm ($\varepsilon \times 10^3$) (H_2O): 233 (17.3), 254 (13.3), 298 (5.5), 405 (18.7). **7D;** MS m/z: 442 (M^+). HR-MS calcd for $C_{16}H_{18}N_4O_7S_2$: 442.0617. Found m/z: 442.0622. ^{1}H-NMR ($CDCl_3$): 2.05, 2.18, 2.20 (each 3H, s, $COCH_3$), 4.43 (2H, d, 5'-CH_2), 4.47, 5.34, 5.64 (1H, d, H-2',3',4'), 7.60 (1H, d, H-1', $J_{1',2'}$ = 4.9 Hz), 6.35 (2H, s, NH_2), 8.50 (1H, s, 2-H). ^{13}C-NMR ($CDCl_3$): 86.7 (C-1'), 122.9 (C-7a), 144.9 (C-2), 156.9 (C-3a). UV λmax nm (MeOH): 229, 264, 418.

5-Methyl-3-(β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(3H)-thione (9A) A catalytic amount of sodium methoxide was added to a solution of **5A** (45 mg, 0.10 mmol) in absolute MeOH (8 ml), and the reaction mixture was kept for 1 h in an ice-bath. After standard work-up including neutralization, **9A** (14 mg, 44 %, yellow powder) was obtained, mp, 110-114 °C. MS m/z: 316 (M^+). ^{1}H-NMR (DMSO-d_6): 2.67 (3H, s, CH_3), 3.62 (2H, m, 5'-CH_2), 3.96, 4.15, 4.45 (1H, m, H-2',3',4'), 5.18, 5.52 (1H, br.m, sugar OH), 5.96 (1H, d, H-1', $J_{1',2'}$ = 5.5 Hz), 8.63 (1H, s, 2-H). UV λmax nm (MeOH): 222, 263, 320, 378.

5-Phenyl-3-(β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(3H)-thione (9B) A catalytic amount of sodium methoxide was added to a solution of **5B** (100 mg, 0.20 mmol) in absolute MeOH (3 ml), and the reaction mixture was worked up as above to give **9B** (57 mg, 76 %, yellow powder), mp, 178-179 °C. FD-MS m/z: 377 (M^+). ^{1}H-NMR (DMSO-d_6): 3.65 (2H, m, 5'-CH_2), 4.00, 4.20, 4.48 (1H, m, H-2',3',4'), 5.19, 5.61 (1H, br.m, sugar OH), 6.10 (1H, d, H-1', $J_{1',2'}$ = 4.9 Hz), 7.59-7.72 (3H, m, ArH-m,p), 8.09-8.12 (2H, m, ArH-o), 8.71 (1H, s, 2-H). UV λmax nm (MeOH): 262, 338, 405.

5-Benzylamino-3-(β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(3H)-thione (9C) Compound **5C** (50 mg; 0.09 mmol) was deacetylated to give **9C** (18 mg, 48%, yellow powder) after working up as above, mp, 180-181 °C, FAB-MS m/z: 407 (M^++1), HR-FAB-MS calcd for $C_{17}H_{18}O_4N_4S_2$: 407.0848. Found m/z: 407.0872. ^{1}H-NMR (DMSO-d_6): 3.53-3.67 (2H, m, CH_2-5'), 3.91, 4.10, 4.22 (1H, m, H-2',3',4'), 4.62 (2H, m, CH_2), 5.79 (1H, d, H-1', $J_{1',2'}$ = 4.9 Hz), 7.33-7.38 (5H, m, ArH), 8.26 (1H, s, 2-H). UV λmax nm (MeOH): 240, 250 (sh), 297, 410.

5-Amino-3-(β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazine-7(3H)-thione (9D) Compound **5D** was deacetylated to give **9D** (54 mg, 81%, yellow powder), mp, 185-186 °C, MS m/z: 317 (M^++1). ^{1}H-NMR (DMSO-d_6): 3.50-3.64 (2H, m, 5'-CH_2), 3.89, 4.10, 4.37 (1H, m, H-2',3',4'), 5.76 (1H, d, H-1', $J_{1',2'}$ = 5.8 Hz), 8.26 (1H, s, 2-H), 8.63 (2H, s, NH_2). UV λmax nm (MeOH): 232, 256, 295, 407.

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-methylimidazo[4,5-d]-[1,3]thiazin-7(3H)-one (10A) To a solution of **5A** (53 mg; 0.12 mmol) in acetone (8 ml), $KMnO_4$ (77 mg) was added gradually at room temperature until the color of the reaction mixture remained violet. The mixture was filtered and the filtrate was evaporated. The residue was purified by a column chromatography on a silica gel (10 g, 11 X 1.2 cm), fraction size being 15 ml, using $CHCl_3$ to give **10A** (37 mg, 72 %, viscous oil), MS m/z: 425 (M^+). ^{1}H-NMR ($CDCl_3$): 2.13, 2.14, 2.15 (each 3H, s, $COCH_3$), 2.72 (3H, s, CH_3), 4.36 (2H, m, 5'-CH_2), 4.45, 5.63, 5.82 (1H, m, H-2',3',4'), 6.16 (1H, d, H-1', $J_{1',2'}$ = 4.4 Hz), 7.97 (1H, s, 2-H). UV λmax nm (MeOH): 228, 265, 290.

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-phenylimidazo[4,5-d]-[1,3]thiazin-7(3H)-one (10B) In a similar manner, **5B** (100 mg; 0.20 mmol) was converted into **10B** (67 mg, 61 %), mp 70-72 °C. MS m/z: 487 (M^+). ^{1}H-NMR ($CDCl_3$): 2.03, 2.13, 2.17 (each 3H, s, $COCH_3$), 4.36 (2H, m, 5'-CH_2), 4.44, 5.59 5.92 (1H, m, H-2',3',4'), 6.26 (1H, d, H-1', $J_{1',2'}$ = 4.0 Hz), 7.50-7.60 (3H, m, ArH-m,p), 8.00-8.04 (2H, m, ArH-o), 8.05 (1H, s, 2-H). UV λmax nm (MeOH): 228, 240 (sh), 267, 338. Anal. Calcd for $C_{22}H_{21}N_3O_8S$: C, 54.20; H, 4.34; N, 8.62; S, 6.58. Found: C, 54.06; H, 4.30; N, 8.53; S, 6.75.

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-benzylaminoimidazo-[4,5-d][1,3]thiazin-7(3H)-one (10C) Similarly, **10C** (65 mg, 57 %, viscous oil) was prepared from **5C** (118 mg; 0.22 mmol), MS m/z: 516 (M^+). HR-MS calcd for $C_{23}H_{24}N_4O_8S$ 516.1314. Found m/z: 516.1334. ^{1}H-NMR ($CDCl_3$): 2.09-2.11 (each 3H, s, $COCH_3$), 4.35-4.39 (2H, m, 5'-CH_2), 4.65 (3H, d, -CH_2- & 4'-H), 5.55 (1H, br.s, 2'-H), 5.89 (1H, t, 2'-H), 5.96 (1H, d, 1'-H), 7.33-7.39 (8H, m, ArH), 7.70 (1H, d, 2-H). UV λmax nm (MeOH): 224, 265, 330.

3-(2,3,5-Tri-O-acetyl-1-β-D-ribofuranosyl)-5-aminoimidazo[4,5-d]-[1,3]thiazin-7(3H)-one (10D) In a similar manner, **5D** (14 mg; 0.03 mmol) was converted into **10D** (7.7 mg, 57 %, colorless powder), mp 85-86 °C, MS m/z: 426 (M^+). HR-MS calcd for $C_{16}H_{18}N_4O_8S$: 426.0845. Found m/z: 426.0839. ^{1}H-NMR ($CDCl_3$): 2.08 (s, 3H, 5'-$COCH_3$), 2.13 (s, 6H, 2' & 3'-$COCH_3$), 4.26-4.30 (1H, q, 5'-CH_2), 4.48-4.51 (1H, q, H-4'), 5.93 (3H, d, H-1',2',3'), 7.66 (1H, s, 2-H). UV λmax nm (MeOH): 263, 321.

5-Benzylamino-3-(β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazin-7(3H)-one (11C) A catalytic amount of sodium methoxide was added to a solution of **10C** (21 mg; 0.04 mmol) in absolute MeOH (10 ml), and the reaction mixture was stirred in an ice-bath for 1 - 1.5 h. After neutralization with dilute AcOH, the mixture was evaporated under reduced pressure. The residue was purified by column chromatography over silica gel (10 g, 11 X 1.2 cm), fraction size being 15 ml, using 2% MeOH-$CHCl_3$ to give **11C** (5.7 mg, 36 %, colorless powder), mp 115-

117 °C, FAB-MS m/z: 391 (M^++1). HR-FAB-MS calcd for $C_{17}H_{18}N_4O_5S$: 391.1076. Found m/z: 391.1082. ^{1}H-NMR (DMSO-d_6): 3.51-3.61 (2H, m, 5'-CH_2), 3.90, 4.08, 4.33 (1H, m, H-2',3',4'), 4.59 (2H, br.s, CH_2), 5.02, 5.16, 5.42 (1H, m, sugar OH), 5.82 (1H, d, 1'-H, $J_{1',2'}$ = 4.9 Hz), 7.27-7.39 (5H, m, ArH), 8.07 (1H, s, 2-H). UV λmax nm (MeOH): 224, 265, 330.

5-Amino-3-(β-D-ribofuranosyl)imidazo[4,5-d][1,3]thiazin-7(3H)-one (11D) A catalytic amount of sodium methoxide was added to a solution of **10D** (24 mg; 0.06 mmol) in absolute MeOH (20 ml), and the reaction mixture was worked up as above to give **11D** (5.8 mg, 34 %, viscous oil), FAB-MS m/z: 301 (M^++1). HR-FAB-MS calcd for $C_{10}H_{12}N_4O_5S$ 301.0606. Found m/z: 301.0613. ^{1}H-NMR (DMSO-d_6): 3.52-3.63 (2H, m, 5'-CH_2), 3.86, 4.10, 4.33 (1H, m, H-2',3',4'), 4.97-5.34 (3H, br.s, sugar OH), 5.80 (1H, d, H-1', $J_{1',2'}$ = 5.86 Hz), 8.05 (1H, d, 2-H), 8.22 (2H, br.s, NH_2). UV λmax nm (MeOH): 265, 324.

ACKNOWLEDGEMENT

The authors are indebted to the staff of the Center for Instrumental Analysis of Hokkaido University for elemental analysis and measurements of MS and NMR spectra.

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Received 9/2/91
Accepted 11/25/91