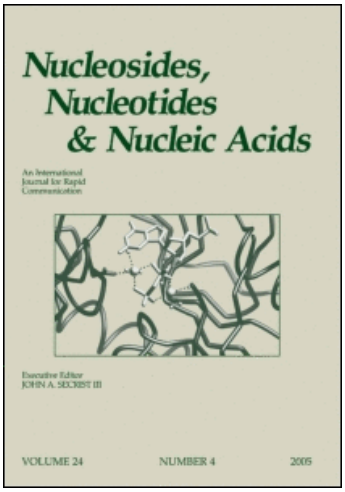

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Syntheses and Antitumor Activities of D-and L-2'-Deoxy-4'-thio Pyrimidine Nucleosides

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To cite this Article Uenishi, Jun'ichi , Takahashi, Keiji , Motoyama, Mitsuhiro , Akashi, Haruo and Sasaki, Takuma(1994) 'Syntheses and Antitumor Activities of D-and L-2'-Deoxy-4'-thio Pyrimidine Nucleosides', Nucleosides, Nucleotides and Nucleic Acids, 13: 6, 1347 — 1361
To link to this Article: DOI: 10.1080/15257779408012157
URL: http://dx.doi.org/10.1080/15257779408012157

NUCLEOSIDES & NUCLEOTIDES, 13(6&7), 1347-1361 (1994)

SYNTHESES AND ANTITUMOR ACTIVITIES OF D- AND L-2'-DEOXY-4'-THIO PYRIMIDINE NUCLEOSIDES§

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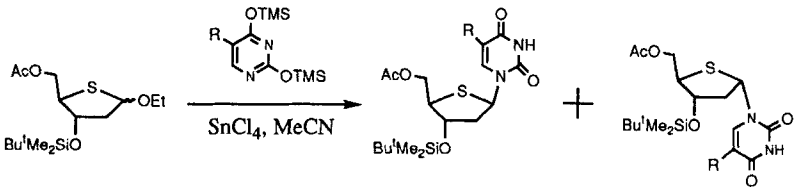
ABSTRACT: Both enantiomers of 2'-deoxy-4'-thiouridine (**9**) and **15**, 4'-thiothymidine (**10**) and **16**, and 2'-deoxy-4'-thiocytidine (**14**) and **17** and 1-(2-deoxy-4-thio-β-D-*erythro*-pentafuranosyl)-5-trifluoromethyluracil (**11**) were synthesized. The key coupling reactions were performed by the reaction of D- or L-enantiomers of ethyl 5-*O*-acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4-thio-α,β-xylofuranoside (**1**) or **18** and 2,4-bis(trimethylsilyloxy)pyrimidine in the presence of $SnCl_4$ in acetonitrile. Cytotoxicities against L-1210 and KB-cells for the compounds **9**, **10**, **11**, **14**, **15**, **16**, and **17** were examined. The compounds **10** and **11** were potentially active.

The search for new nucleosides possessing antitumor or antiviral activities continues actively.[1] Chemical modifications of the sugar moiety have recently received considerable attention.[2] Changing the furanose ring to other saturated heterocycles[3] or to carbocycles[4] has revealed interesting biological activities including potency, selectivity, and low toxicity in the chemotherapeutics. Replacement of a furanose ring oxygen atom by a sulfur atom in nucleosides was made first by Whistler et al.[5] They reported that 4'-thio analogs of purine and pyrimidine nucleosides showed potent antitumor activities but were found to be toxic. More recently D-2'-deoxy-4'-thio nucleosides have been prepared by

§ This article is dedicated to Dr. Morio Ikehara (Emeritus Professor of Osaka University) in the occasion of his 70th birthday.



1 **2β ~ 4β** **2α ~ 4α**

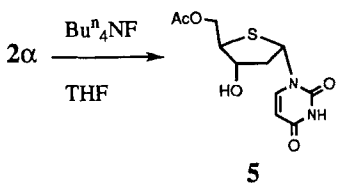
2 R: H
3 R: H_3C
4 R: F_3C

Scheme 1

Walker et al.,[6] and Secrist et al.[7] and these thianucleosides possess remarkable antiviral activities against HSV-1 and VZV and antitumor activities against L-1210 and H-Ep-2. We also have reported syntheses of D-2'-deoxy-4'-thiouridine,[8] and D-4'-thiothymidine,[9] by manipulation of acyclic stereochemistry. However, these thia analogs were found to be toxic.[10] In recent reports, some L-enantiomers of heteroatom nucleosides were found to be active against HIV but with low toxicity.[11] These results prompted us to make L-enantiomers of 4'-thio nucleosides. In this article, we describe the synthetic details and cytotoxicities against L-1210 and KB-cells for D-2'-deoxy-4'-thio nucleosides and their L-enantiomers.

We have reported the preparation of thiafuranose **1**[12] based on the synthesis of asymmetric 2-mercapto-1,3-diols.[13] A coupling reaction of **1** with 2,4-bis(trimethylsilyloxy)pyrimidines was carried out by the Vorbruggen method.[14] The reaction was mediated by $SnCl_4$ in acetonitrile at room temperature in 1-3 hours, as shown in Scheme 1. The reaction with 2,4-bis(trimethylsilyl)uracil gave **2α** and **2β** in 57% and 38% yields. Thymidine derivatives **3α** and **3β** were obtained in 64% and 33% yields respectively. The ratio of the desired β-isomer was decreased as the bulkiness of the nucleophiles increased. In the case of 5-(trifluoromethyl)uracil, the coupling products were obtained in 94% yield but as a 6:1 ratio of α:β isomers.

Assignments of stereochemistries were made based on the coupling constants of the 1'-proton in the NMR spectra. The anomeric proton of **2β** appeared at δ = 6.45 ppm as a double doublets whose coupling constants were 8.1 and 6.2 Hz while that of **2α** was at δ = 6.34 ppm and showed 7.7 and 1.8 Hz as the coupling constants of the double doublets.



5

Scheme 2

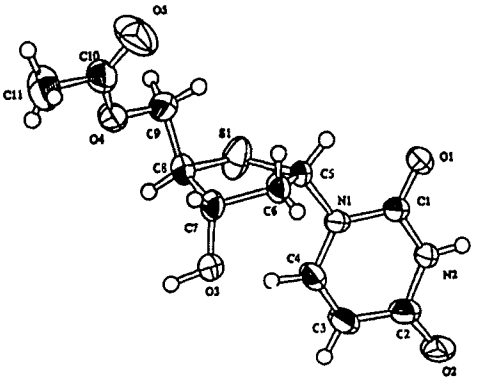
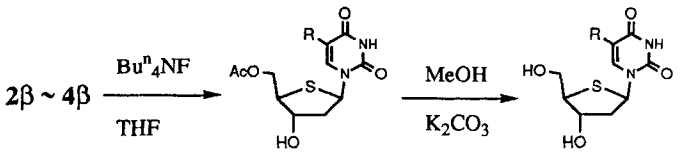


Figure 1 ORTEP view of **5**

The absolute structure was confirmed by X-ray diffraction analysis. Hence good crystals of **5** were obtained after desilylation of **2α**, and it was submitted to X-ray analysis. The ortep view of **5** was shown in Figure 1. It clearly indicates the relative configuration of the α-nucleoside as well as the absolute structure of D-nucleoside. The structure of **3β** had already been determined by X-ray analysis after derivatization to **10**.[9] The anomeric protons of **3α** and **3β** showed a double doublets, at δ = 6.23 ppm for **3α** and at δ = 6.49 ppm for **3β**, with coupling constants of 7.9 and 2.4 Hz for **3α** and 8.4 and 6.2 Hz for **3β**. The anomeric proton of the β-isomers was found to appear at lower field than that of the α-isomers. Two large coupling constants (6.2-8.5 Hz) were observed in the β-isomer between a H-1' proton and two H-2' protons, whereas the α-isomer possessed a pair of large and small coupling constants (7.5-8.0 and 0-2.4 Hz) between them. Thus, the anomeric proton of **4β** showed a 6.9 Hz coupling constant for the triplet-like double doublets at δ = 6.39 ppm, while that of **4α** appeared at δ = 6.22 ppm as a doublet whose coupling constant for the 6.5 Hz. All these data were rational based on the previous studies of nucleoside NMRs.[15]

The β-isomers of the coupling products, **2β**, **3β**, **4β** were transformed into **9**, **10**, and **11**, by two steps, as illustrated in Scheme 3. Desilylation of **2β** was carried out by reaction with tetrabutylammonium fluoride in THF to give **6** in 90% yield. Similarly, **7** and **8** were obtained from **3β** and **4β** in 90% and 88% yields respectively. Potassium carbonate promoted methanolysis of the 5'-*O*-acetate for **6**, **7** and **8** afforded the corresponding nucleosides **9**, **10** and **11** in 98%, 91% and 96% yields, respectively.

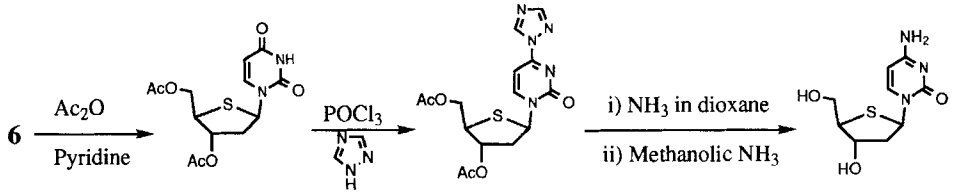
Cytidine derivative **14** was derived from **6** by the standard methods in 3 steps. First, **6** was acetylated with acetic anhydride in pyridine to give **12** in 88% yield. Amination of the C-4 carbonyl group was accomplished by treating of **12** with phosphoryl chloride and 1,2,4-triazole.[16] The triazole derivative **13** was obtained in 99% yield, which was subjected to ammonolysis by aq. ammonia in dioxane followed by treatment with methanolic ammonia to provide **14** in 73% yield.



6, 7, 8 **9, 10, 11**

6, 9 R: H
7, 10 R: H_3C
8, 11 R: F_3C

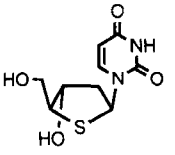
Scheme 3



12 **13** **14**

Scheme 4

We have completed facile syntheses of D-2'-deoxy-4'-thioribopyrimidine nucleosides. Recognition of the structure of nucleoside substrates by enzymes is usually very strict. Particularly mono-phosphorylation by kinases is known to be very specific in recognition for D-β-nucleosides. Therefore, human kinases can distinguish fine structural differences from the proper nucleoside and only supply the correct phosphate for the construction of oligonucleotides. However, a recent report has noted that some viral kinases can catalyze the mono-phosphorylation of L-thymidine.[17] In fact, L-types of synthetic pseudo nucleosides have shown potent antiviral activities but low toxicities.[14] These results might indicate that the specific structure was recognized by a viral kinase but not by a human kinase. Thus in searching for nucleosides with reduced toxicity, L-nucleosides could be good candidate, and hopely, tumor kinases might phosphorylate L-nucleosides. When an L-α-nucleoside is drawn as shown in Chart 1, the relative positions of the 5'-hydroxy group and pyrimidine ring are exactly the same as those of the D-isomer. However, the 2' and 3' carbons then reside at the back side and the heteroatom at the front. These configurational relationships were very interesting relative to biological activities as well as toxicities.



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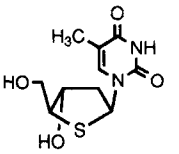

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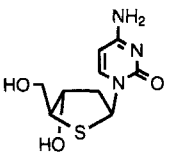
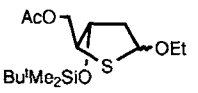
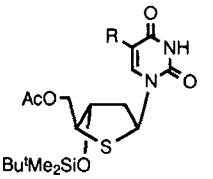


17

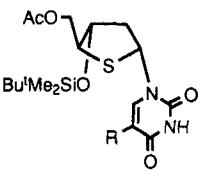
Chart 1



18



19β, 20β



19α, 20α

19 R: H
20 R: H_3C

Chart 2

Based upon these considerations, we have prepared the L-enantiomers of thianucleoside, **15**, **16** and **17**.

These preparations were carried out by the same method employed for the syntheses of the D-series. We have already synthesized the L-enantiomer of ethyl 5-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-4-thio-*erythro*-pentafuranoside (**18**).[12] Coupling reactions and deprotections were carried out exactly in the same manner described for the D-isomers. These coupling products **19β**, and **20β** showed the same spectroscopic data and physical properties as the corresponding D-enantiomers except for optical rotations. L-Nucleosides **15**, **16** and **17** showed almost the same magnitude of their optical rotations but opposite signs to the D-enantiomers.

The in vitro antitumor activity of the nucleosides, **9**, **10**, **11**, **14**, **15**, **16** and **17** against mouse leukemia L1210 and human oral epidermoid carcimona KB cells is summarized in Table 1. Data for 1-β-D-arabinofuranosylcytosine (Ara-C) are also shown for comparison. The compounds **10**, **11**, and **14** were potent inhibitors of the growth of the cells tested. Among these, compound **11** was the most effective inhibitor of the growth of L-1210 cells. On the other hand, none of the L-series nucleosides showed any cytotoxicity toward both cells up to 100 μg/mL except for **16**, which was slightly toxic toward L1210 cells.

Table 1 Inhibitory Effects of D- and L-Thianucleosides on the Growth of L 1210 and KB Cells *a)*

Test compound	IC50 (μg/mL) *b)*	
	L1210	KB
9	> 100	>100
10	0.0087	2.7
11	0.0008	6.6
14	0.15	3.1
15	>100	> 100
16	2.7	> 100
17	>100	> 100
Ara-C *c)*	0.03	0.5

a) Cytotoxic activity assay in vitro was done by the method of Carmichael *et al.* The tumor cells (1 x 10^4 /well) were incubated in the presence or absence of the compounds for 72 h. Then, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide was added and the OD (570 nm) was measured. Percent inhibition was calculated as follows: % inhibition = [1-OD (570 nm) of sample well / OD (570 nm) of control well] x 100. *b)* IC_{50} (μg/mL) was given as the concentration at 50% inhibition of cell growth. *c)* 1-β-D-Arabinofuranosylcytosine as the positive control.

Antiviral activities against HSV-1, HSV-2, and HIV are being examined, and those results will be reported in due course.

Experimental Section

Melting points were taken on a Yanako micromelting apparatus and were uncorrected. ^1H and ^{13}C NMR were recorded on a JEOL GXS and Varian Gemini 300 for ^1H (400 MHz or 300 MHz) and for ^{13}C (100 MHz or 75 MHz). The chemical shifts were shown as δ-value (ppm) using tetramethylsilane (0 ppm) for proton spectra and $CHCl_3$ (77.0 ppm) for carbon spectra as an internal standard. Infrared spectra (IR) were recorded by JASCO IRA-1 spectrometer and were taken as KBr tablets. Low and high resolution mass spectra (LRMS and HRMS) were obtained on a JEOL JMS 303HF spectrometer at the Analytical Center in Okayama University of Science by electron impact (EI) method at 70 eV unless otherwise stated. Only significant peaks are described here for IR and MS. Silica gel (Merck 7734, 70-300 mesh) was used for gravity column chromatography and silica gel (Merck 9385, 230-400 mesh) for flash column chromatography. Precoated silica gel plate

(Merck 5715, 60F254) was used for thin layer chromatography. All air sensitive reactions were conducted in flame dried glass ware under Ar atmosphere. Acetonitrile used for coupling reactions was dried over CaH_2 and distilled.

General Coupling Reaction of 1 and 2,4-Bis(trimethylsilyloxy)pyrimidine. To a stirred solution of 1 (1.5 mmol) and 2,4-bis(trimethylsilyloxy)pyrimidine (3 mmol) in acetonitrile (9 ml) was added anhydrous $SnCl_4$ (2.5 mmol) at room temperature. The mixture was stirred for 1 to 3 hrs at room temperature with monitoring by tlc. After the reaction completed, it was cooled on ice bath and sat. sodium bicarbonate (10 ml) was added into the mixture. The mixture was vigorously stirred for several minutes and diluted with ethyl acetate (100 ml). The organic layer was isolated and washed with water (2 ml x3) and brine (2 ml). The extract was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by column chromatography on silica gel by the following eluents; 60% ethyl acetate in hexane for **2**α and **2**β, and also **4**α and **4**β, 20% ether in methylene chloride for **3**α and **3**β. These chemical yields, physical and spectroscopic data were described below;

1-[5-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4-thio-β-D-*erythro*-pentofuranosyl]uracil (2β). 38% yield, mp 144-146°C recrystallized from ethyl acetate, Rf = 0.30 (40% ethyl acetate in hexane); $[\alpha]_D^{24}$ -30.1° (c 1.0, EtOH); ^1H NMR ($CDCl_3$) 8.40 (1 H, br s, NH), 7.79 (1 H, d, H-6, *J* = 8.2 Hz), 6.45 (1 H, dd, H-1', *J* = 8.1 and 6.2 Hz), 5.80 (1 H, d, H-5, *J* = 8.2 Hz), 4.42 (1 H, m, H-3'), 4.25 (1 H, dd, H-5'a, *J* = 11.7 and 5.5 Hz), 4.14 (1 H, dd, H-5'b, *J* = 11.7 and 8.1 Hz), 3.53 (1 H, ddd, H-4', *J* = 8.1, 5.5 and 2.9 Hz), 2.40 (1 H, ddd, H-2'a, *J* = 13.2, 6.2 and 4.0 Hz), 2.11 (3 H, s, Ac), 2.01 (1 H, ddd, H-2'b, *J* = 13.2, 8.1 and 4.0 Hz), 0.90 (9 H, s, t-Bu), 0.09 (3 H, s, SiMe), 0.08 (3 H, s, SiMe); ^{13}C NMR ($CDCl_3$) 170.3, 162.9, 150.5, 140.5, 103.0, 74.9, 65.0, 61.3, 55.5, 42.8, 25.6, 20.7, 17.9, -4.8, -5.1; IR(KBr) 2900, 1700, 1680 and 1650 cm^{-1}; LRMS *m/z* (rel. intensity, %) 343 (M-57, 20), 283 (6), 256 (5), 234 (15), 209 (9), 189 (64), 97 (base). *Anal.* Calcd for $C_{17}H_{28}N_2O_5SSi$: C, 50.97; H, 7.05; N, 6.99. Found: C, 50.95; H, 7.26; N, 6.77 %.

1-[5-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4-thio-α-D-*erythro*-pentofuranosyl]uracil (2α). 57% yield, mp 50-51°C recrystallized from EtOAc, Rf = 0.36 (40% ethyl acetate in hexane); $[\alpha]_D^{24}$ +40.9° (c 1.0, EtOH); 1H NMR ($CDCl_3$) 8.61 (1 H, br s, NH), 8.23 (1 H, d, H-6, *J* = 8.4 Hz), 6.34 (1 H, dd, H-1', *J* = 7.7 and 1.8 Hz), 5.69 (1 H, d, H-5, *J* = 8.4 Hz), 4.49 (1 H, m, H-3'), 4.10 (1 H, dd, H-5'a, *J* = 11.4 and 5.1 Hz), 3.91 (1 H, dd, H-5'b, *J* = 11.4 and 9.2 Hz), 3.74 (1 H, ddd, H-4', *J* = 9.2, 5.1 and 1.8 Hz), 2.54 (1 H, ddd, H-2'a, *J* = 15.0, 7.7 and 4.0 Hz), 2.16 (1 H, ddd, H-2'b, *J* = 15.0, 1.8 and 1.1 Hz), 2.08 (3 H, s, Ac), 0.87 (9 H, s, t-Bu), 0.11 (3 H, s, SiMe), 0.06 (3 H, s, SiMe); ^{13}C NMR ($CDCl_3$) 170.2, 163.5, 151.0, 143.0, 101.6, 76.7, 64.9, 62.9, 57.3, 44.0, 25.6, 20.6, 17.9, -4.9, -5.1; IR (KBr) 3190, 1700 1680 and 1670 cm^{-1}; LRMS *m/z* (rel. intensity, %) 343 (M-

57), 283 (13), 255 (3), 231 (18), 209 (26), 187 (83), 97 (base). *Anal.* Calcd for $C_{17}H_{28}N_2O_5SSi$: C, 50.97; H, 7.05; N, 6.99. Found: C, 50.86; H, 7.12; N, 6.88.

5'-*O*-Acetyl-3'-*O*-(*tert*-butyldimethylsilyl)-4-thiothymidine (3β). 33% yield, mp 152-153°C recrystallized from EtOAc, Rf = 0.32 (20% Ether in CH_2Cl_2); $[\alpha]_D^{24}$ +2.1° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) 9.33 (1 H, br s, NH), 7.51 (1 H, d, H-6, *J* = 1.1 Hz), 6.49 (1 H, dd, H-1', *J* = 8.4 and 6.2 Hz), 4.41 (1 H, m, H-3'), 4.26 (1 H, dd, H-5'a, *J* = 11.7 and 5.5 Hz), 4.12 (1 H, dd, H-5'b, *J* = 11.7 and 8.1 Hz), 3.51 (1 H, ddd, H-4', *J* = 8.1, 5.5 and 2.5 Hz), 2.33 (1 H, ddd, H-2'a, J = 13.2, 6.2 and 3.3 Hz), 2.10 (3 H, s, Ac), 2.00 (1 H, m, H-2'b), 1.95 (3 H, d, 5-Me, *J* = 1.1 Hz), 0.08 (9 H, s, t-Bu), 0.07 (6 H, s, SiMe); ^{13}C NMR ($CDCl_3$) 170.4, 163.6, 150.6, 136.0, 111.6, 75.0, 65.1, 61.1, 55.6, 42.5, 25.6, 20.7, 17.9, 12.7, -4.8, -5.0; IR (KBr) 2860 1700, 1690, 1680 cm^{-1}; LRMS *m/z* (rel. intensity, %) 414 (M^+, 11), 357 (55), 343 (42), 297 (11), 97 (base). *Anal.* Calcd for $C_{18}H_{30}N_2O_5SSi$: C, 52.15; H, 7.29; N, 6.76. Found: C, 52.36; H, 7.41; N, 6.65.

1-[5-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4-thio-α-D-*erythro*-pentofuranosyl]thymine (3α). 64% yield, mp 91-92°C recrystallized from EtOAc, Rf = 0.24 (20% Ether in CH_2Cl_2); $[\alpha]_D^{24}$ +38.4° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) 8.29 (1 H, br s, NH), 7.95 (1 H, s, H-6), 6.23 (1 H, dd, H-1', *J* = 7.9 and 2.4 Hz), 4.47 (1 H, m, H-3'), 4.11 (1 H, dd, H-5'a, *J* = 11.6 and 5.5 Hz), 3.95 (1 H, dd, H-5'b, *J* = 11.6 and 8.9 Hz), 3.75 (1 H, m, H-4'), 2.54 (1 H, ddd, H-2'a, *J* = 14.7, 7.9 and 4.4 Hz), 2.15 (1 H, m, H-2'b), 2.09 (3 H, s, Ac), 1.93 (3 H, d, 5-Me, *J* = 1.1 Hz), 0.87 (9 H, s, t-Bu), 0.10 (3 H, s, SiMe), 0.06 (3 H, s, SiMe); ^{13}C NMR ($CDCl_3$) 170.3, 164.0, 151.0, 138.4, 110.0, 76.7, 64.9, 62.3, 57.0, 44.1, 25.5, 20.6, 18.0, 12.7, -5.0, -5.1; IR (KBr) 2860, 1720, 1690 and 1660 cm^{-1}; LRMS *m/z* (rel. intensity, %) 414 (M^+, 3), 357 (53), 343 (53), 297 (8), 97 (base). *Anal.* Calcd for $C_{18}H_{30}N_2O_5SSi$: C, 52.15; H, 7.29; N, 6.76. Found: C, 52.08; H, 7.35; N, 6.74.

1-[5-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4-thio-β-D-*erythro*-pentofuranosyl]-5-trifuluoromethyluracil (4β). 13% yield, mp 167-168 °C recrystallized from EtOAc, Rf = 0.40 (30% EtOAc in hexane); $[\alpha]_D^{24}$ +18.6° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) 9.34 (1 H, br s, NH), 8.38 (1 H, s, H-6), 6.39 (1 H, t, *J* = 6.9 Hz), 4.40 (1 H, dd, H-3', *J* = 7.8 and 4.0 Hz), 4.31 (1 H, dd, H-5'a, *J* = 11.9 and 4.7 Hz), 4.16 (1 H, dd, H-5'b, *J* = 11.9 and 6.6 Hz), 3.55 (1 H, m, H-4'), 2.45 (1 H, ddd, H-2'a, *J* = 13.3, 6.4 and 4.7 Hz), 2.10 (3 H, s, Ac), 2.07 (1 H, m, H-2'b), 0.89 (9 H, s, t-Bu), 0.08 (6 H, s, SiMe); ^{13}C NMR ($CDCl_3$) 170.5, 158.1, 149.5, 141.7, 121.6, 105.7, 74.9, 64.2, 62.2, 55.7, 43.4, 25.6, 20.6, 17.9, -4.9, -5.1; IR (KBr) 3410, 1740, 1720 and 1690 cm-1; LRMS m/z (rel. intensity, %) 411 (M-57, 59), 237 (65), 145 (56), 111 (96), 97 (base). *Anal.* Calcd for $C_{18}H_{27}F_3N_2O_5SSi$: C, 46.14; H, 5.81; N, 5.98. Found: C, 46.14; H, 5.60; N, 5.67.

1-[5-*O*-Acetyl-3-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-4-thio-α-D-*erythro*-pentofuranosyl]-5-trifuluoromethyluracil (4α). 81% yield, mp 110-113 °C recrystal-

lized from EtOAc, Rf = 0.20 (30% EtOAc in hexane); $[\alpha]_D^{24}$ +61.5° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) 10.01 (1 H, br s, NH), 8.68 (1 H, s, H-6), 6.22 (1 H, d, H-1', J = 6.5 Hz), 4.51 (1 H, m, H-3'), 4.09 (1 H, dd, H-5'a, J = 11.1 and 4.8 Hz), 3.89~3.75 (2 H, m, H-4', 5'b), 2.48 (1 H, ddd, H-2'a, J = 14.9, 7.2 and 4.0 Hz), 2.25 (1 H, d, H-2'b, J = 14.8 Hz), 2.05 (3 H, s, Ac), 0.80 (9 H, s, t-Bu), 0.05 (3 H, s, SiMe), 0.02 (3 H, s, SiMe); ^{13}C NMR ($CDCl_3$) 158.8, 150.2, 144.1, 127.2, 121.8, 103.9, 77.1, 65.3, 64.7, 57.8, 44.1, 25.5, 20.6, 18.1, -5.2, -5.5; IR (KBr) 3010, 1740, 1730 and 1690 cm-1; LRMS m/z (rel. intensity, %) 411(M-57, 42), 351(6), 237(25), 117(base), 97(95). *Anal.* Calcd for $C_{18}H_{27}F_3N_2O_5SSi$: C, 46.14; H, 5.81; N, 5.98. Found: C, 46.22; H, 5.76; N, 6.02.

Desilyation of 2α, 2β, 3β and 4β. The coupling product (0.5 mmol) was dissolved in a 1:1 mixture of THF and acetonitrile (7 ml). Tetrabutylammonium fluoride (1M THF solution, 1ml) was added and the mixture was stirred for 1-2 hrs at room temperature. Then the mixture was diluted with ethyl acetate (100 ml) and washed with water (2 ml x2) and brine (3 ml). The organic layer was dried over $MgSO_4$ and the solvent was removed. The residue was purified by silica gel chromatography eluted with 80-100% ethyl acetate in hexane. Chemical yields, physical and spectroscopic data were described below;

1-(5-*O*-Acetyl-2-deoxy-4-thio-α-D-*erythro*-pentofuranosyl)uracil (5). 97% yield, mp 170-172°C recrystallized from EtOH, Rf = 0.33 (80% EtOAc in hexane); $[\alpha]_D^{24}$ +95.9° (c 0.5, EtOH); ^1H NMR (DMSO-d_6) 11.01 (1H, br s, NH), 8.24 (1 H, d, H-6, J = 8.2 Hz), 6.31 (1 H, dd, H-1', J = 8.1 and 3.1 Hz), 5.64 (1 H, d, H-5, J = 8.2 Hz), 4.39 (1 H, m, H-3'), 4.10 (1 H, dd, H-5'a, J = 11.4 and 7.7 Hz), 4.03 (1 H, dd, H-5'b, J = 11.4 and 6.6 Hz), 3.80 (1 H, ddd, H-4', J = 7.7, 6.6 and 2.6 Hz), 2.54 (1 H, ddd, H-2'a, J = 14.3, 8.1 and 4.6 Hz), 2.19 (1 H, ddd, H-2'b, J = 14.3, 6.2 and 3.1 Hz), 2.07 (3 H, s, Ac); ^{13}C NMR (DMSO-d_6) 170.7, 163.8, 150.6, 140.8, 102.3, 73.6, 64.9, 60.8, 54.2, 41.8, 20.1; IR (KBr) 3000, 3240, 1720, 1690 and 1660 cm^{-1}; LRMS *m/z* (rel. intensity, %) 286 (M^+, 17), 209 (base), 143 (30), 140 (41). *Anal.* Calcd for $C_{11}H_{14}N_2O_5S$: C, 46.15; H, 4.93; N, 9.78. Found: C, 46.36; H, 5.19; N, 9.98.

1-(5-*O*-Acetyl-2-deoxy-4-thio-β-D-*erythro*-pentofuranosyl)uracil (6). 90% yield, mp 139-140°C recrystallized from EtOH, Rf = 0.12 (80% EtOAc in hexane); $[\alpha]_D^{24}$ -23.5° (c 0.13, EtOH); ^1H NMR (CD_3OD : $CDCl_3$ = 1 : 3) 10.16 (1 H, br s, NH), 7.88 (1 H, d, H-6, J = 8.1 Hz), 6.41 (1 H, t, H-1', J = 7.0 Hz), 5.81 (1 H, d, H-5, J = 8.1 Hz), 4.40 (1 H, q, H-3', J = 4.0 Hz), 4.30 (1 H, dd, H-5'a, J = 11.7 and 6.2 Hz), 4.24 (1 H, dd, H-5'b, J = 11.7 and 6.6 Hz), 3.61 (1 H, ddd, H-4', J = 6.6, 6.2 and 3.7 Hz), 2.74 (1 H, br s, 3'-OH), 2.51 (1 H, ddd, H-2'a, J = 13 5, 6.6 and 4.8 Hz), 2.13 (3 H, s, Ac), 2.11 (1 H, ddd, H-2'b, J = 13.5, 7.2 and 4.0 Hz); ^{13}C NMR (CD_3OD : $CDCl_3$ = 1 : 3) 169.7, 162.8, 150.2, 141.8, 100.8, 74.0, 64.4, 60.6, 55.1, 42.0, 19.8; IR (KBr) 3160, 1710, 1670 and 1650 cm^{-1}; LRMS *m/z* (rel.

intensity, %) 243 (M-57, 6), 223 (18), 209 (19), 201 (34), 187 (55), 97 (base). *Anal.* Calcd for $C_{11}H_{14}N_2O_5S$: C, 46.15; H, 4.93; N, 9.78. Found: C, 45.87; H, 5.11; N, 9.49.

5'-*O*-Acetyl-4'-thiothymidine (**7**). 90% yield, mp 170-172°C recrystallized from EtOH, Rf = 0.12 (70% EtOAc in hexane); $[\alpha]_D^{24}$ -26.7° (c 0.5, EtOH); ^{1}H NMR (DMSO-d_6) 11.37 (1 H, br s, NH), 7.72 (1 H, d, H-6, J = 1.2 Hz), 6.33 (1 H, dd, H-1', J = 9.1 and 6.4 Hz), 5.45 (1 H, d, 3'-OH, J = 3.7 Hz), 4.37 (1 H, m, H-3'), 4.29 (1 H, dd, H-5'a, J = 11.4 and 7.8 Hz), 4.18 (1 H, dd, H-5'b, J = 11.4 and 6.5 Hz), 3.45 (1 H, m, H-4'), 2.29 (1 H, ddd, H-2'a, J = 13.2, 9.3 and 3.9 Hz), 2.18 (1 H, ddd, H-2'b, J = 13.2, 6.4 and 3.2 Hz), 2.06 (3 H, s, Ac), 1.82 (3 H, d, 5-Me, J = 1.0 Hz); ^{13}C NMR (DMSO-d_6) 170.2, 163.5, 150.7, 136.5, 110.3, 73.4, 65.6, 60.2, 55.1, 40.2, 20.7, 12.2; IR (KBr) 3380, 1720, 1650 and 1630 cm^{-1}; LRMS *m/z* (rel. intensity, %) 300 (M+, 12), 240 (14), 222 (18), 175 (20), 127 (18), 115 (58), 97 (base). *Anal.* Calcd for $C_{12}H_{16}N_2O_5S$: C, 47.99; H, 5.37; N, 9.33. Found: C, 47.85; H, 5.30; N; 9.24.

1-(5-*O*-Acetyl-2-deoxy-4-thio-β-D-*erythro*-pentofuranosyl)-5-trifuluoromethyluracil (**8**). 88% yield, mp 172-173°C recrystallized from EtOH, Rf = 0.50 (70% EtOAc in hexane); $[\alpha]_D^{24}$ +10.2° (c 0.26, EtOH); ^{1}H NMR (DMSO-d_6) 11.95 (1 H, br s, NH), 8.33 (1 H, s, H-6), 6.19 (1 H, t, H-1', J = 7.2 Hz), 5.47 (1 H, d, 3'-OH, J = 3.8 Hz), 4.31~4.15 (2 H, m, H-3', 5'a), 4.19 (1 H, dd, H-5'b, J = 11.5 and 6.1 Hz), 3.48 (1 H, m, H-4'), 2.41 (1 H, ddd, H-2'a, J = 13.1, 8.2 and 4.3 Hz), 2.25 (1 H, ddd, H-2'b, J = 13.1, 6.8 and 4.3 Hz), 2.03 (3 H, s, Ac); ^{13}C NMR (DMSO-d_6) 170.2, 158.7, 149.9, 138.3, 122.4, 73.4, 65.0, 62.1, 54.9, 41.0, 20.5, 0.1; IR (KBr) 3410, 1750, 1690 and 1670 cm^{-1}; LRMS (FAB) 355 (M+1). HRMS (FAB) *m/z* *Anal.* Calcd for $C_{12}H_{14}F_3N2O5S$: 355.0576 (M+1). Found: m/z 355.0584.

Preparation of 9, 10 and 11. To a solution of 5'-O-acetyl nucleoside **6**, **7**, or **8** (0.5 mmol) in methanol (6 ml) was added anhydrous K_2CO_3 (138 mg) and it was stirred for 15 min at room temperature. Water (3 ml) was added to the reaction mixture and it was extracted with ethyl acetate (50 ml). The organic layer was washed with brine (3 ml) and dried over $MgSO_4$. The solvent was removed and the residue was purified by column chromatography on silica gel eluted with 80-100% ethyl acetate in hexane to give the nucleosides. These chemical yields, physical and spectroscopic data were shown as following;

2'-Deoxy-4'-thiouridine (**9**). 98% yield, mp 181-182°C recrystallized from EtOAc, mp 186-188°C lit.[7]); Rf = 0.12 (EtOAc); $[\alpha]_D^{24}$ -30.7° (c 0.5, MeOH); ^{1}H NMR (CD_3OD : $CDCl_3$ = 1 : 3) 7.78 (1 H, dd, H-6, J = 8.1 and 4.4 Hz), 5.99 (1 H, dd, H-1', J = 7.3 and 7.7 Hz), 5.34 (1 H, d, H-5, J = 8.1 Hz), 4.05 (1 H, dd, H-3', J = 11.4 and 4.8 Hz), 3.41 (1 H, dd, H-5'a, J = 11.7 and 4.8 Hz), 3.32 (1 H, dd, H-5'b, J = 11.7 and 5.9 Hz), 3.03 (1 H, dt, H-4', J = 8.4 and 4.8 Hz), 2.00 (1 H, ddd, H-2'a, J = 12.8, 7.0 and 5.5 Hz), 1.81 (1 H, ddd, H-2'b, J = 12.8, 7.3 and 4.4 Hz); ^{13}C NMR (CD_3OD : $CDCl_3$ = 1 : 3) 164.4, 151.0,

143.4, 100.9, 74.7, 63.6, 62.1, 59.6, 42.9; IR (KBr) 3360, 1710, and 1670 cm^{-1}; LRMS (FAB) *m/z* 245(M+1). *Anal.* Calcd for $C_9H_{12}NO_4S$: C, 44.25; H, 4.95; N,11.47. Found: C, 43.88; H, 4.90; N, 11.06.

4'-Thiothymidine (10). 91% yield, mp 209-210°C recrystallized from EtOH, mp 208-209 °C lit.[6] and mp 213-215 °C lit.[7] ; Rf = 0.13 (EtOAc); $[\alpha]_D^{24}$ -32.7° (c 1.0, MeOH); ^1H NMR (DMSO-d_6) 11.23 (1 H, br s, NH), 7.79 (1 H, d, H-6, *J* = 1.1 Hz), 6.30 (1 H, t, H-1', *J* = 7.7 Hz), 5.18~5.13 (2 H, br s, 3'-OH, 5'-OH), 4.36 (1 H, m, H-3'), 3.33~3.27 (3 H, m, H-4', 5'a, 5'b), 2.15 (2 H, dd, H-2'a, 2'b, *J* = 7.7 and 3.7 Hz), 1.80 (3 H, s, 5-Me); ^{13}C NMR (DMSO-d_6) 163.4, 150.6, 136.6, 109.9 73.5, 63.4, 60.0, 58.9, 41.3, 12.2; IR (KBr) 3360, 1720 and 1650 cm^{-1}; LRMS *m/z* (rel. intensity, %) 258 (M^+, 19), 240 (6), 222 (9), 133 (base). HRMS m/z *Anal.* Calcd for $C_{10}H_{14}N_2O_4S$: 258.0674 (M^+). Found: 258.0663.

1-(2-Deoxy-4-thio-β-D-*erythro*-pentofuranosyl)-5-trifluoromethyluracil (11). 96% yield, mp 207-208°C recrystallized from EtOH, Rf = 0.26 (80% EtOAc in hexane); $[\alpha]_D^{24}$ +11.2° (c 0.5, Acetone); ^1H NMR (DMSO-d_6) 8.86 (1 H, s, H-6), 6.15 (1 H, t, H-1', *J* = 6.6 Hz), 5.30~5.26 (2 H, m, 3'-OH, 5'-OH), 4.30 (1 H, m, H-3'), 3.68 (1 H, dd, H-5'a, *J* = 11.4 and 3.8 Hz), 3.59 (1 H, dd, H-5'b, *J* = 11.4 and 4.8 Hz), 3.33 (1 H, m, H-4'), 2.25 (2 H, dd, H-2'a, 2'b, *J* = 6.2 and 5.1 Hz); ^{13}C NMR (DMSO-d_6) 158.7, 149.9, 143.4, 123.8, 103.1, 73.7, 61.9, 61.7, 58.4, 42.9; IR (KBr) 3420, 1660 and 1630 cm^{-1}; LRMS *m/z* (rel. intensity, %) 312 (M^+, 16), 186 (69), 181 (62), 164 (69), 144 (7), 139 (base). *Anal.* Calcd for $C_{10}H_{11}F_3N_2O_4S$: C, 38.46; H, 3.55 ; N, 8.97 . Found: C, 38.33; H, 3.65; N, 8.83.

3',5'-Di-*O*-acetyl-2'-deoxy-4'-thiouridine (12). A mixture of **6** (140 mg, 0.49 mmol), acetic anhydride (140 µl, 1.45 mmol) and DMAP (5 mg) in pyridine (0.5 ml) was stirred for 10 min at room temperature. The mixture was diluted with ethyl acetate (50 ml) and washed with 5% hydrochloric acid (1 ml), water (1 ml) and brine (2 ml). The organic layer was dried over MgSO4 and the solvent was removed. The rsidual syrup was purified by silica gel chromatography eluted with 80-100% ethyl acetate in hexane to give diacetate 12 (140 mg) in 88% yield. Oil; Rf = 0.52 (90% EtOAc in hexane); $[\alpha]_D^{24}$ -20.4 ° (c 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) 8.90 (1 H, br s, NH), 7.79 (1 H, d, H-5, *J* = 8.2 Hz), 6.52 (1 H, dd, H-1', *J* = 8.2 and 6.6 Hz), 5.85 (1 H, dd, H-6, *J* = 8.2 and 2.1 Hz), 5.38 (1 H, m, H-3'), 4.33 (1 H, dd, H-5'a, *J* = 11.7 and 5.7 Hz), 4.19 (1 H, dd, H-5'b, J = 11.7 and 7.5 Hz), 3.71 (1 H, ddd, H-4', *J* = 7.7, 5.6 and 2.1 Hz), 2.58 (1 H, ddd, H-2'a, *J* = 14.2, 6.5 and 2.8 Hz), 2.20 (1 H, m, H-2'b), 2.13 (3 H, s, Ac), 2.12 (3 H, s, Ac); ^{13}C NMR ($CDCl_3$) 170.4, 170.1, 163.0, 150.7, 140.0, 103.6, 76.3, 64.8 61.3, 52.4, 39.6, 21.0, 20.7; IR (film) 3020, 1760, 1740 and 1710 cm^{-1}; LRMS *m/z* (rel. intensity, %) 328 (M+, 5), 300 (2), 209 (10), 208 (75), 156 (21), 114 (44), 97 (base). *Anal.* Calcd for $C_{13}H_{16}N_2O_6SSi$: C, 47.56; H, 4.91; N,8.53. Found: C, 47.78; H, 5.12; N, 8.18.

4-(1,2,4-Triazol-1-yl)-1-(3,5-di-*O*-acetyl-2-deoxy-4-thio-β-D-*erythro*-pentofuranosyl)pyrimidin-2(1H)-one (13). Phosphorus oxychloride (38 μl, 0.404 mmol) was added to 1,2,4-triazole (133 mg, 1.92 mmol) in anhydrous acetonitrile (0.5 ml) at room temperature and the mixture was cooled on ice bath. After triethylamine (255 ul, 1.83 mmol) was added, the bath was removed and 12 (0.211 mmol) dissolved in anhydrous acetonitrile (1.3 ml) was added. The whole was stirred for 2 hrs at room temperature then triethylamine (176 μl) and water (46 μl) were succesively added to the mixture and stirred for 10 min. The solvent was removed under reduced pressure and the residue was partitioned with chloroform (50 ml) and sat. sodium bicarbonate (3 ml). The chloroform layer was washed with water (1 ml) and dried over $MgSO_4$. The solvent was removed and the residue was purified by column chromatography on silica gel eluted with 90% ethyl acetate in hexane to give **13** (80 mg) in 99% yield. mp 144-146°C recrystallized from EtOAc, Rf = 0.22 (90% EtOAc in hexane); $[\alpha]_D^{24}$ -30.1° (c 1.0, EtOH); ^{1}H NMR ($CDCl_3$) 9.29 (1 H, s), 8.64 (1 H, d, H-6, *J* = 7.2 Hz), 8.22 (1 H, s), 7.14 (1 H, d, H-5, *J* = 7.2 Hz), 6.58 (1 H, t, H-1', J = 7.0 Hz), 5.37 (1 H, m, H-3'), 4.37 (1 H, dd, H-5'a, *J* = 11.8 and 5.8 Hz), 4.23 (1 H, dd, H-5'b, *J* = 11.8 and 6.8 Hz), 3.78 (1 H, m, H-4'), 2.80 (1 H, ddd, H-2'a, *J* = 14.1, 6.6 and 4.3 Hz), 2.27 (1 H, ddd, H-2'b, *J* = 14.1, 7.4 and 4.5 Hz), 2.13 (3 H, s, Ac), 2.11 (3 H, s, Ac); ^{13}C NMR ($CDCl_3$) 171.1, 170.7, 159.6, 155.6, 154.7, 148.1, 144.0, 96.0, 76.7, 65.1, 64.5, 53.1, 41.3, 21.6, 21.4; IR (KBr) 3400, 1700, 1690 and 1620 cm^{-1}; LRMS *m/z* (rel. intensity, %) 379 (M^+, 60), 259(19), 164(base), 159(62), 114(96). HRMS (FAB) *m/z* *Anal.* Calcd for $C_{15}H_{18}N_5O_5S$: 380.1077 (M+1). Found: 380.1046.

2'-Deoxy-4'-thiocytidine (14). A mixture of **13** (80 mg, 0,211mmol) and ammonium hydroxide (d=0.9, 0.17 ml, 2.52 mmol) in dioxane (0.6 ml) was stirred for 3 hr at room temperature. The solvent was removed under reduced pressure and the residue was treated with methanolic ammonia (saturated in 1 ml of methanol) and then stirred over night at room temperature. Methanol was removed and the crude product was purified by column chromatography on silica gel eluted with 40% methanol in ethyl acetate to give almost pure desired product, which was further purified by sephadex LH-20 column eluted with 30% methanol in chloroform to give pure **14** (37 mg) in 73% yield. mp 208-209°C recrystallized from EtOH, mp 129-132°C lit.[7]; Rf = 0.23 (90% EtOAc in hexane); $[\alpha]_D^{24}$ -23.6° (c 1.0, MeOH); ^{1}H NMR (DMSO-d_6) 7.94 (1 H, d, H-6, *J* = 7.3 Hz), 7.22 (1 H, br s, 4-NH), 7.20 (1 H, br s, 4-NH), 6.36 (1 H, dd, H-1', *J* = 8.4 and 6.6 Hz), 5.79 (1 H, d, H-5, *J* = 7.3 Hz), 5.24 (1 H, d, 3'-OH, *J* = 3.7 Hz), 5.14 (1 H, t, 5'-OH, *J* = 5.3 Hz), 4.34 (1 H, m, H-3'), 3.63~3.50 (2 H, m, H-5'a, 5'b), 3.27 (1 H, m, H-4'), 2.14 (1 H, ddd, H-2'a, *J* = 12.8, 6.2 and 3.7 Hz), 2.06 (1 H, ddd, H-2'b, *J* = 12.8, 8.4 and 4.0 Hz); ^{13}C NMR (DMSO-d_6) 165.4, 155.4, 142.2, 94.8, 73.5, 63.9, 60.5, 58.8, 41.7; IR (KBr) 3400, 3380 and 1640 cm^{-1}; LRMS *m/z* (rel. intensity, %) 208 (M-35, 29), 182 (32), 180 (22). HRMS *m/z* *Anal.* Calcd for

Table 2. Atomic coordinates and Bi_{so}/B_{eq} for **5**

atom	x	y	z	B_{iso}/B_{eq}
S(1)	0.7753(1)	0.0000	0.8101(2)	5.05(3)
O(1)	0.7207(3)	0.2071(2)	0.4914(4)	4.35(8)
O(2)	0.5866(4)	0.4011(2)	0.8447(4)	6.1(1)
O(3)	0.4706(3)	-0.0113(2)	0.8903(4)	5.00(9)
O(4)	0.6343(4)	-0.2456(2)	0.7827(4)	4.59(8)
O(5)	0.6448(6)	-0.3064(3)	0.5471(5)	9.2(2)
N(1)	0.6455(3)	0.1509(2)	0.7155(4)	3.17(8)
N(2)	0.6544(4)	0.3016(3)	0.6749(4)	3.78(9)
C(1)	0.6770(4)	0.2187(3)	0.6199(5)	3.18(10)
C(2)	0.6028(5)	0.3232(3)	0.8130(6)	4.1(1)
C(3)	0.5709(5)	0.2494(4)	0.9036(6)	4.5(1)
C(4)	0.5954(5)	0.1684(3)	0.8563(5)	4.2(1)
C(5)	0.6667(4)	0.0586(3)	0.6635(5)	3.08(10)
C(6)	0.5422(4)	0.0037(3)	0.6352(5)	3.31(9)
C(7)	0.5317(4)	-0.0601(3)	0.7748(5)	3.4(1)
C(8)	0.6644(5)	-0.0910(3)	0.8329(5)	3.6(1)
C(9)	0.7082(5)	-0.1708(3)	0.7385(6)	4.5(1)
C(10)	0.6162(7)	-0.3111(4)	0.6807(6)	5.4(1)
C(11)	0.5538(8)	-0.3883(4)	0.7473(6)	7.4(2)
H(1)	0.6682	0.3397	0.6049	3.8000
H(2)	0.5359	0.2574	0.9997	4.5000
H(3)	0.5621	0.1126	0.9046	4.1000
H(4)	0.7055	0.0666	0.5695	3.0900
H(5)	0.4855	0.0361	0.6221	3.2700
H(6)	0.5502	-0.0303	0.5538	3.2700
H(7)	0.4804	-0.1050	0.7437	3.4000
H(8)	0.4444	-0.0469	0.9750	4.9800
H(9)	0.6606	-0.1070	0.9384	3.6000
H(10)	0.8012	-0.1835	0.7595	4.6000
H(11)	0.6925	-0.1545	0.6191	4.6000
H(12)	0.4709	-0.3934	0.6888	7.4000
H(13)	0.5228	-0.3759	0.8225	7.4000
H(14)	0.6062	-0.4314	0.7175	7.4000

Table 3. Selected bond distances in **5**

S1 - C5	1.833(5)
S1 - C8	1.819(5)
C5 - C6	1.538(7)
C6 - C7	1.538(7)
C7 - C8	1.497(7)
C5 - N1	1.473(6)
C7 - O3	1.420(6)
C8 - C9	1.543(8)

Table 4. Selected bond angles in **5**

C5 - S1 - C8	95.1(2)
S1 - C5 - C6	107.3(3)
S1 - C8 - C7	107.2(3)
C5 - C6 - C7	109.3(3)
C6 - C7 - C8	109.0(3)
S1 - C8 - C9	108.9(3)
C7 - C8 - C9	112.3(4)
C6 - C7 - O3	105.8(3)
C8 - C7 - O3	112.8(4)
S1 - C5 - N1	110.6(3)
C6 - C5 - N1	114.4(4)

$C_9H_{13}N_3O_3S$: 243.0678. Found: 243.0693. *Anal.* Calcd for $C_9H_{13}N_3O_3S$: C, 44.43; H, 5.38; N, 17.27. Found: C, 44.04; H, 5.55; N, 17.08.

L-series of Nucleosides, 19β, 19α, 20β, 20α, 15, 16, and **17**. All the spectroscopic data and physical date were the same as described here D-series of isomers except optical rotaions. Only their optical rotaions were described here; **19β** $[\alpha]_D^{24}$ +30.0° (c 1.0, ethanol); **19α** $[\alpha]_D^{24}$ -40.9° (c 1.0, ethanol); **20β** $[\alpha]_D^{24}$ -2.0° (c 1.0, $CHCl_3$); **20α** $[\alpha]_D^{24}$ -38.6° (c 1.0, $CHCl_3$); **15** $[\alpha]_D^{24}$ +29.7° (c 1.0, MeOH); **16**, $[\alpha]_D^{24}$ +32.5° (c 1.0, MeOH); **17** $[\alpha]_D^{24}$ +23.3° (c 1.0, MeOH).

X-ray Diffraction of 5. Suitable single crystals of **5** ($C_{11}H_{14}N_2O_5S$) were obtained as described in the above experiments. The data were collected on a Rigaku RASA-7R diffractometer. The intensities of three standard reflections did not show any appreciable decay. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. The structure was solved by a direct method and refined by a full-matrix least-squares technique. Anisotropic thermal parameters were used for all non-hydrogen atoms. Computations were perfomed on a Silicon Graphics IRIS Indigo. The programs in the teXsan (Molecular Structure Corporation) were employed. Crystal data for **5**: monoclinic, space group $P2_1$, a=10.330(3) Å, b=15.163(4) Å, c=8.507(2) Å, β=95.22(2)°, V=1327.0(5) $Å^3$, Z=4, Dcalc=1.433 g/cm^3, λ(Mo Kα)=0.71069 Å graphite monochromated, μ=2.62 cm^{-1}, F(000)=600, 2θmax=55°, R(Rw)=0.052(0.051) for 2957 reflections ($I>3.00\sigma(I)$). The unit cell has two independent chemical units, but no significant structural difference can be seen between the two units. One of the molecules is shown in the Figure 1. The atomic coordinates, the selected bond distances and angles are depicted in **Table 2, Table 3, and Table 4**, respectively. Details of the X-ray crystallographic data can be obtained from the author on request.

Biological Activity. Cytotoxicity for seven nucleosides, **9, 10, 11, 14, 15, 16** and **17** against L-1210 and KB Cell were examined in vitro. the experiments were carried out by the same method reported in the literature.[18)]

Acknowledgement: We thank Mr. Motoi Nishiura and Mr. Shigeki Iida for their technical assistance.

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Received 12/1/93
Accepted 1/5/94