Synthesis of Certain 6-Alkylthio-2,2′-anhydro-5-azauridines [1]

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β-D-Arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**7b**) and its *t*-butyldimethylsilyl protected counterpart **7a** were synthesized by treating the appropriate 2-amino-β-D-arabinofurano[1′,2′:4,5]-2-oxazoline with ethoxycarbonyl isothiocyanate. These 2,2′-anhydro-*s*-triazine nucleosides were then subjected to alkylation under similar reaction conditions. Alkylation of 3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:-4,5]oxazolo-*s*-triazin-4-one-6-thione (**7a**) provided the targeted *S*-alkylated nucleosides, *i.e.*, the C6-SCH_3 (**9a**), C6-SCH_2-$CH=CH_2$ (**10a**), and C6-S-CH_2-$C\equiv CH$ (**11a**), in reasonable yields. Attempted deprotection of these nucleosides failed. In order to circumvent this problem, **7b** was alkylated with the same reagents. In each case, instead of the expected *S*-alkylated anhydronucleosides, a mixture of the 5-*N*-alkylanhydro-*s*-triazine-4,6-dione and 5-*N*-alkylanhydro-*s*-triazin-4-one-6-thione derivatives were obtained. The 2,2′-anhydro linkage of **7a** was also found to be more stable than the *s*-triazine ring to mild base. Basic conditions displaced the C6-sulfur substituent and eventually caused ring opening of the *s*-triazine aglycone.

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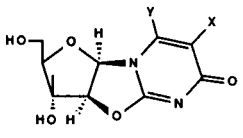
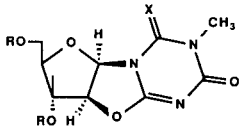
Anhydroazine nucleosides continue to serve as useful synthons in the preparation of novel pyrimidine and pyrimidine-like nucleosides. In addition to their use as chemical intermediates [2], some anhydronucleosides have exhibited marked chemotherapeutic and biological activity. For example, 5-ethyl (**1a**) and 5-propyl-2,2′-anhydrouridine (**1b**) were shown to be selective, competitive inhibitors of uridine phosphorylase [3]. Likewise, the ethyl ester (**2a**) and hydrazide (**2b**) of 2,2′-anhydro-1-(β-D-arabinofuranosyl)orotic acid inhibited multiplication of some DNA-containing viruses and exhibited antitumor activity against Lewis lung carcinoma and sarcoma 298 [4]. A detailed study aimed at the synthesis of dihydro-5-azathymidine (**3**) explored the use of the anhydronucleosides **4b** and **5b** as synthons for this unique nucleoside antibiotic [5,6]. During this study, the anhydronucleoside **4b** was found to exhibit *in vitro* antiviral activity against herpes simplex type 1 as well as to inhibit the induction of a cell-mediated immune response [6]. Such studies coupled with our interests in discovering new, selective inhibitors of pyrimidine enzymes, especially orotidylate decarboxylase (OMPdeCase), prompted us to initiate a synthetic program focused on 6-thiosubstituted anhydronucleosides of the *s*-triazine ring system; nucleosides which could be further elaborated to sulfur isosteres of 5-azaorotidine [7].



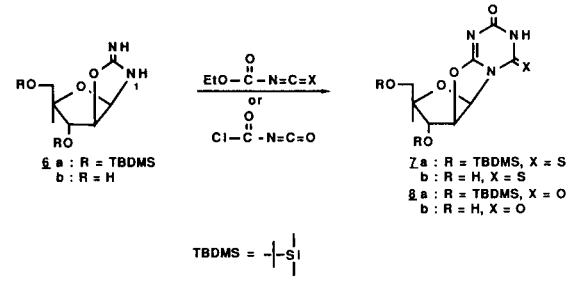
1a : X = C_2H_5; Y = H
b : X = C_3H_7; Y = H
2a : X = H; Y = CO_2Et
b : X = H; Y = $CONHNH_2$



3 : X = H, H; R = H
4a : X = O; R = TBDMS
b : X = O; R = H
5a : X = S; R = TBDMS
b : X = S; R = H

Since 1970, an assortment of pyrimidine [8] and pyrimidine-like nucleosides [5,6,9] have been prepared from 2-aminoglycofuranooxazoline intermediates. This methodology was employed in our preparation of the targeted sulfur 2,2′-anhydronucleosides **7**, **9-11** (Scheme 1 and 2).

Scheme 1

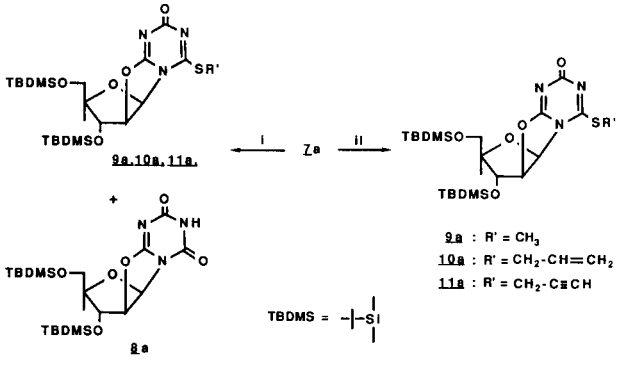


6a : R = TBDMS
b : R = H

7a : R = TBDMS, X = S
b : R = H, X = S
8a : R = TBDMS, X = O
b : R = H, X = O

TBDMS = $-\overset{|}{\underset{|}{Si}}-$

Scheme 2[a]



9a, **10a**, **11a**,

9a : R' = CH_3
10a : R' = CH_2-$CH=CH_2$
11a : R' = CH_2-$C\equiv CH$

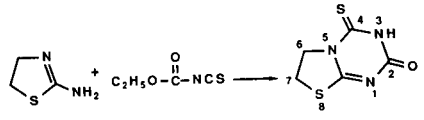
TBDMS = $-\overset{|}{\underset{|}{Si}}-$

8a

[a] I : NaH / THF, R'X, aqueous work-up. II : NaH / THF, R'X, non-aqueous work-up.

Initially we selected as starting materials the protected 2-amino-β-D-arabinofurano[1′,2′:4,5]-2-oxazoline (**6a**) [5] and ethoxycarbonyl isothiocyanate. Wierenga and Woltersom showed that when **6a** was reacted with methyl isothiocyanate in the absence of base the major site of attack was

N1 [5]. Similarly, a study [10] which examined the differing nucleophilic character of the exocyclic (N2) and endocyclic (N1) nitrogen atoms of 2-amino-2-thiazoline, a system resembling **6**, in the presence of ethoxycarbonyl isothiocyanate found that condensation of these reagents lead exclusively to 2,3,6,7-tetrahydrothiazolo[3,2-*a*]-*s*-triazin-2-one-4-thione. Thus, when **6a** was reacted with



ethoxycarbonyl isothiocyanate in benzene at room temperature the anhydronucleoside produced (67%) was tentatively assigned as 3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**7a**). This assignment was confirmed during the methylation of **7a**. Treatment of **7a** with methyl iodide in dry tetrahydrofuran and in the presence of sodium hydride provided a mixture of the *S*-methylated and N5-methylated anhydronucleosides, **9a** and **5a**, respectively, in a 16:1 ratio. The N5-methylated anhydronucleoside **5a** had been prepared earlier using a different synthetic route and its structure firmly established by a rigorous nmr study [5]. Comparison of the pertinent ^{13}C nmr and ^{1}H nmr chemical shifts of **5a** with those values reported in the literature [5] (see Table 1 and 2) showed these anhydronucleosides to be identical and thus, unequivocally established the mode of cyclization of ethoxycarbonyl isothiocyanate with **6a** and the structure of the resulting anhydronucleoside as **7a**.

TABLE 1 : Proton chemical shifts of selected N and S alkylated *s*-Triazine anhydronucleosides [a]

	7a	5a[b]	9a	10a	11a
H-1′	6.57 (d, 1)	6.60 (d, 1)	6.27 (d, 1)	6.23 (d, 1)	6.23 (d, 1)
H-2′	5.17 (d, 1)	5.10 (d, 1)	5.13 (d, 1)	5.06-5.37 (m, 3)	5.07 (d, 1)
H-3′	4.65 (d, 1)	4.63 (d, 1)	4.55 (d, 1)	4.55 (d, 1)	4.60 (d, 1)
H-4′	4.03-4.23 (m, 1)	4.00-4.23 (m, 1)	3.97-4.20 (m, 1)	4.00-4.17 (m, 1)	4.00-4.20 (m, 3)
H-5′	3.37-3.80 (m, 2)	3.40-3.77 (m, 2)	3.27-3.63 (m, 2)	3.30-3.67 (m, 2)	3.33-3.70 (m, 2)
NCH_3		3.64 (s, 3)			
SCH_3			2.57 (s, 3)		
$SCH_2CH=CH_2$				3.87 (d, 2)	
				5.63 (m, 1)	
$S\text{-}CH_2\text{-}C\equiv CH$					2.23 (t, 2)

a : Solvent : Deuteriochloroform; Internal standard : Tetramethylsilane

b : The reported [5] chemical shifts for compound **5a** are as follows : δ 6.65 (d, 1, H′1), 5.15 (d, 1, H′2), 3.66 (s, 3, NCH_3)

TABLE 2 : Carbon chemical shifts of selected N and S alkylated *s*-Triazine anhydronucleosides [a]

	7a	5a[b]	9a	10a	11a
C-2	153.41	153.01	160.69	160.55	160.22
C-4	161.23	159.23	161.18	161.25	161.09
C-6	173.20	174.03	164.58	163.65	162.56
NCH_3		34.89			
SCH_3			13.33		
$SCH_2CH=CH_2$					131.15,119.96, 33.50
$SCH_2CH\equiv CH$					19.66

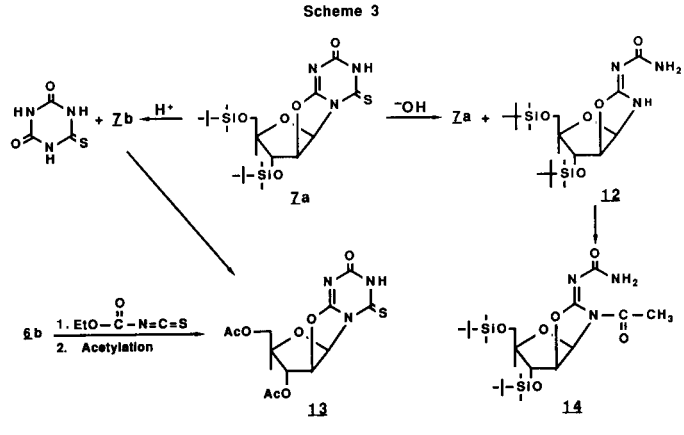
a : Solvent : Deuteriochloroform; Internal standard : Tetramethylsilane

b : The reported [5] chemical shifts for compound **5a** are as follows : δ 153.0 (C-2), 159.3 (C-4), 174.1 (C-6).

The alkylation of **7a** was not as straightforward as anticipated. It was expected that treatment of **7a** with the appropriate alkylating agent using sodium hydride in THF would provide only the desired *S*-alkylated derivatives **9a-11a** as the sole or major product. The alkylations were monitored by tlc and when **7a** was consumed the reactions were worked up. In each case, the desired *S*-alkylated derivative was obtained and "purified" by column chromatography, yet even after this procedure they were always contaminated (^{1}H nmr) with an unknown substance. Although tlc indicated the chromatographed products were single entities, when the plates were visualized with sulfuric acid rather than uv light (254 nm), a second uv inactive product was detected whose Rf was similar to that of the *S*-alkylated anhydronucleosides. Careful chromatographic separation of this mixture then provided the pure *S*-alkylated anhydronucleosides **9a-11a**. The isolated uv inactive material was the same (^{1}H nmr) regardless of the alkylating agent employed during the reaction. This product was subsequently identified as 3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazine-4,6-dione (**8a**, Scheme 2) by comparing the carbon-13 chemical shifts of the heterocyclic ring with those reported for the aglycone of β-cyanuric acid riboside (β-CAR) [11] and by an unambiguous synthesis using **6a** and *N*-chlorocarbonyl isocyanate.

We suspected that the formation of **8a** occurred during the aqueous work-up of the reaction. The C6 sulfur substituent was being displaced by hydroxide ion (see the formation of **8b** depicted in Scheme 6) generated from unreacted sodium hydride. Indeed, this was the case. When a non-aqueous work-up was devised and employed, only the desired *S*-alkylated analogues **9a-11a** were isolated (Scheme 2). It is worth mentioning that treatment of **7a** with 1.25 equivalents of 0.1 *M* sodium hydroxide solution in tetrahydrofuran (THF) at room temperature overnight afforded **8a** along with some unreacted **7a**. When **8a** was subjected to the same conditions, ring opening occurred to give 2-ureido-3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:4,5]-2-oxazoline (**12**, Scheme 3). This material

Scheme 3

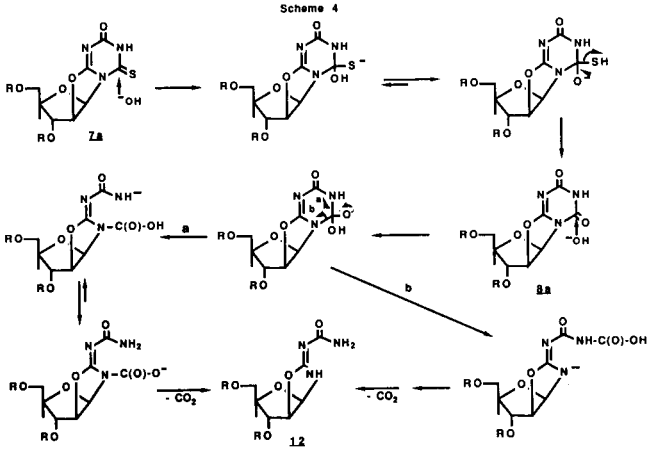


was also accompanied by unreacted starting material **8a**. Compound **12** could be prepared directly from **7a** by using 2.5 equivalents of 0.1 *M* sodium hydroxide solution in THF and allowing the reaction to stir for 36 hours at room temperature. In each case, heating the reaction drove it to completion.

The ring opening mechanism (**7a** → **8a** → **12**) is similar to that proposed for the hydrolytic cleavage of 5-azacytidine [13]. Unlike 5-azacytidine, however, the anhydronucleosides, **7a**, **9a-11a** were stable in aqueous media for extended periods [14]. Evidence for opening of the *s*-triazine ring rather than the 2,2'-anhydro linkage was provided by the ^{13}C- and ^{1}H nmr spectra and elemental analysis of **12**. The ^{1}H nmr spectrum (DMSO-d_6) of **12** exhibited broad resonances for the N(1)H (δ 3.32) and ureido NH_2 (δ 11.43) signals, they integrated for one and two protons, respectively, and were deuterium oxide exchangeable. Acetylation of **12** provided a monoacetate which was tentatively assigned the structure **14** based on its ^{1}H nmr spectrum. If the 2,2'-anhydro link had opened in the presence of hydroxide ion, then the 2'-*O*-acetate so formed would have a definite influence on the carbon-13 and proton chemical shifts of the sugar moiety. Neither the carbon-13 chemical shifts nor the proton chemical shifts experienced any significant change indicating that the anhydro linkage was still intact.

The proposed mechanism (Scheme 4) of the formation of **12** appears to take place in the following manner. The initial attack by hydroxide ion occurs at C6 displacing sulfur (or the sulfur substituent) to furnish **8a**. Once **8a** is formed, then a second nucleophilic attack by hydroxide occurs at this position causing ring opening of the *s*-triazine aglycone and subsequent loss of CO_2 to give **12**. The ring opening of **8a** can be envisaged to follow two possible routes (pathways a and b of Scheme 4). Either pathway would lead to **12**.

Scheme 4



The destruction of the *s*-triazine ring under mild basic conditions was somewhat disturbing because it dampened any future prospects of opening the targeted anhydronucleosides to their respective arabinosides. A common method of opening the 2,2'-linkage of anhydronucleosides is with base [2]. An alternative route involves hydrolysis of this linkage with acid [14]; however, mild acid treatment of **7a** lead only to deprotection and cleavage of the glycosyl bond (Scheme 3).

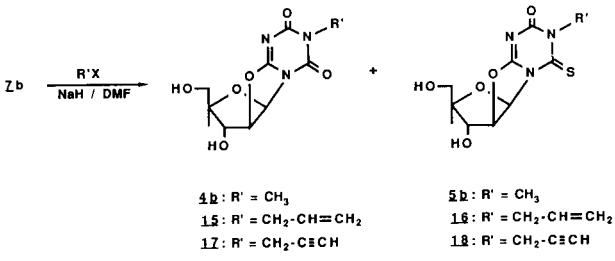
Next the deprotection of the anhydronucleosides **7a** and **9a-11a** were examined. The usual method involving tetra-*n*-butylammonium fluoride in THF met with failure [6]. Likewise, the use of Dowex 50W-X8 (H^+) [15] and boron trifluoride etherate [16] also lead to mixtures. For example, in the latter case boron trifluoride etherate effected removal of the TBDMS groups, but the triethylamine used to hydrolyze the initial complex could not be removed. The ^{1}H nmr spectra of **9b-11b** all exhibited the characteristic triplet and quartet of triethylamine. The total integration of each spectrum suggested that a 1:1 covalent adduct had formed. A similar event had been observed between methanol and 5-azauridine tribenzoate [17]. Methanol formed a 1:1 adduct with this blocked nucleoside at C6 and could be removed by heating under vacuum. In our case, however, repeated co-evaporation of each sample with toluene followed by vacuum drying did not remove the triethylamine. It is worth mentioning that these compounds were uv-active indicating the *s*-triazine ring was still intact.

In order to obtain the titled anhydronucleosides **9b-11b** the original synthetic approach was slightly altered. Instead of employing the silyl protected **6a** as in the initial condensation reaction, the unprotected form **6b** was used. Treatment of **6b** with ethoxycarbonyl isothiocyanate in dry dimethylformamide at room temperature for 16 hours furnished **7b** in moderate yield. That the mode of closure was identical to that of **6a** with ethoxycarbonyl isothiocyanate in THF was confirmed by comparing the carbon chemical shifts of the *s*-triazine moiety of **7b** with those of **7a** and by the preparation of the crystalline diacetate **13**. The anhydronucleoside **13** had been synthesized earlier during our efforts to open the 2,2'-linkage with acid (Scheme 3). Regardless of the procedure, **13** was identical in all respects. Alkylation of **7b** was conducted in the same manner as before with one exception, dimethylformamide was used as solvent.

A completely different pattern of alkylation was observed when **7b** was reacted with either methyl iodide, allyl bromide, or propargyl bromide. Instead of alkylation taking place on sulfur, it occurred on nitrogen. At first, it appeared that only one product was being formed (tlc) during the alkylation reaction, but a ^{13}C- and ^{1}H nmr spectroscopic study conducted on the isolated products proved otherwise. The carbon-13 spectrum of the product obtained from the methylation reaction indicated that the material was an intimate mixture of two compounds neither of which was the desired *S*-alkylated derivative. Examina-

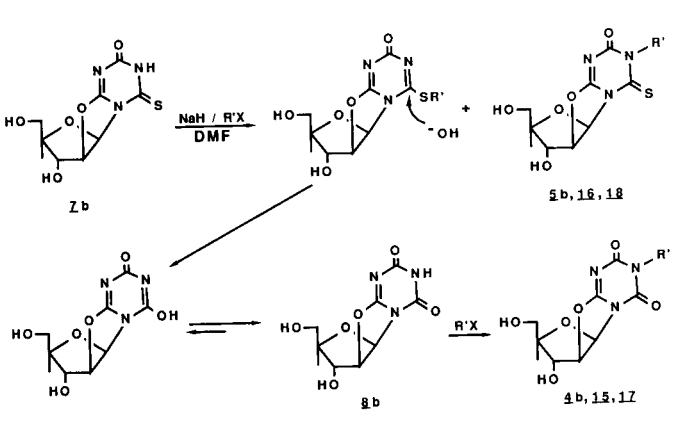
tion of the carbon chemical shift data presented in Table 2 reveals a unique spectral feature associated with sulfur heterocycles. When sulfur is unsubstituted the signal of the ring carbon attached to it resonates between 170 ppm and 180 ppm depending on its environment. Alkylation on sulfur then causes an upfield shift of the carbon signal *ca.* 10-20 ppm [18,19]. Compounds **7a** and **9a** fit this characteristic pattern. The signal of the thione ring carbon (C6)

Scheme 5



of **7a** resides at 173 ppm and conversion to the methylthio shifts this carbon signal 10 ppm upfield. In the spectrum of the methylation product derived from **7b**, eighteen lines were observed. The aromatic region exhibited six signals none of which resonated at 164 ppm. The signal farthest downfield was at 173 ppm. At this point, it was evident that methylation had not taken place on sulfur. The spectrum also displayed two methyl signals at 28.5 and 28.3 ppm which revealed they were attached to nitrogen [19,-20]. If they were attached to sulfur they would be in the 11 to 15 ppm range [19,20]. Further comparision of the carbon chemical shifts of this mixture with those of **5a** and **8a** suggested that the structures of these two anhydronucleosides were **4b** and **5b**. To prove that sulfur was lost during the alkylation procedure, **4b** was unequivocally synthesized (Scheme 7) and its carbon spectrum recorded. This nucleoside was prepared from **8b** which in turn was synthesized from **6b** and ethoxycarbonyl isocyanate. The molecular structure of **4b** was confirmed by an independent X-ray crystallographic study [21]. The ^{13}C nmr spectra of

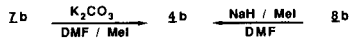
Scheme 6



authentic **4b** and that of the substance found in the mixture from **7b** were identical. The mixture was submitted for high resolution mass spectroscopy and the molecular ion for **5b** confirmed the presence of sulfur.

Similar results were obtained when allyl bromide and propargyl bromide replaced methyl iodide as the alkylating agent. However, in the latter case *N*-alkylated anhydronucleosides **17** and **18** were separable. The ratio of **17**:**18** was 4:6. At this point, it was decided to explore another pathway to **9b-11b**. The only attempt involved treatment of **7b** with methyl iodide in the presence of potassium carbonate in dry dimethylformamide (Scheme 7). Under these conditions, **4b** was obtained exclusively. Although the formation of **4b**, **15** and **17** (Scheme 6) is shown as originating from their respective *S*-alkylated anhydronucleosides an alternate route can be envisaged. This route involves the 5′-hydroxyl group of the sugar moiety. This mechanistic approach is based on the reported cyclic form of 5-azacytidine [17] and our X-ray crystallographic data on **4b** [21]. The use of this data in conjunction with a MM2 molecular modeling study is the topic of the following paper. These calculations indicate that participation by the 5′ oxygen at C6 is indeed feasible and could produce an intermediate which after alkylation at N5 can collapse to either the C6-thione or C6-one analogue. This mechanism would explain the equal amounts of both of these species.

Scheme 7



EXPERIMENTAL

Melting points were determined on a Thomas-Hoover melting apparatus and are uncorrected. The ^1H nmr spectra were obtained with a Varian EM-390 spectrometer and a Bruker AM-300 (7.05 T, 300 MHz) spectrometer interfaced with an ASPECT 3000 computer. The ^{13}C nmr spectra were run on the Bruker AM-300 spectrometer. The chemical shifts are expressed in parts per million with respect to TMS. The high resolution mass spectra were recorded using a MAT 731 mass spectrometer with an Ion Tech 11N FAB ion source operated at 7 keV with Xe. The nucleosides were dissolved in a glycerol matrix at a concentration of approximately 10 μg/ml. Low resolution mass spectra were obtained with a Hewlett Packard 5987A mass spectrometer fitted with a G. C. attachment. Thin layer chromatography was run on precoated (0.2 mm) silica gel 60 F-254 plates manufactured by EM Laboratories, Inc., and short-wave ultraviolet light (254 nm) was used to detect the uv-absorbing spots. Silica gel (Merck, 230-400 mesh, 60A) suitable for chromatographic use was employed for column chromatography. All solvent proportions are by volume unless otherwise stated. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

3′,5′-Bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**7a**).

Ethoxycarbonyl isothiocyanate (1 ml, 8.78 mmoles) in benzene (15 ml) was slowly added, with a syringe, to a stirred solution of 2-amino-3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:4,5]-2-oxazoline (**6a**, 2.53, 6.27 mmoles) in benzene (50 ml). The reaction mixture was allowed to stir overnight at room temperature. Next, the reaction mixture was washed with water, dried over anhydrous sodium sulfate and the solvent removed under diminished pressure. The resulting gum was chromatographed over silica gel and eluted with chloroform-methanol (95/5). The less polar fractions were combined and concentrated to furnish **7a** as a foam (1.92 g, 67%); ^{1}H nmr (deuteriochloroform): δ 3.37-3.8 (m, 2, H5′), 4.03-4.23 (m, 1, H4′), 4.65 (d, 1, H3′), 5.17 (d, 1, H2′), 6.57 (d, 1, H1′), 10.2 (br s, 1, NH, deuterium oxide exchangeable); ^{13}C nmr (deuteriochloroform): δ 173.2 (C-6), 161.2_3 (C-4), 153.4_1 (C-2), 90.0_1 (C2′), 89.2_0 (C4′), 89.0_9 (C1′), 75.4_2 (C3′), 62.0_2 (C5′) [22].

Anal. Calcd. for $C_{20}H_{37}N_3O_5SSi_2$: C, 49.29; H, 7.65; N, 8.61. Found: C, 49.28; H, 7.78; N, 8.62.

6-Methylthio-3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano-[1′,2′:4,5]oxazolo-*s*-triazin-4-one (**9a**).

3′,5′-Bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:4,5]-oxazolo-*s*-triazin-4-one-6-thione (**7a**, 1g, 2.05 mmoles) in tetrahydrofuran (10 ml) was added to a suspension of sodium hydride (50%, 0.12 g, 3.07 mmoles) in dry tetrahydrofuran (15 ml). After salt formation was complete (30 minutes), methyl iodide (0.2 ml, 3.07 mmoles) in dry tetrahydrofuran (3 ml) was slowly added to the mixture and the reaction was stirred overnight at room temperature. The solvent was then removed under diminished pressure and the resulting gum was adsorbed on silcia gel, placed on a sintered glass funnel, and washed with ethyl acetate. The ethyl acetate wash was taken to dryness under diminished pressure and the resulting gum was chromatographed over silica gel and eluted with ethyl acetate-hexane (1/1) to furnish the title compound and **5a**. On standing in the same solvent mixture, the separated nucleosides crystallized from solution. Filtration and drying provided pure **9a** (0.81 g, 79%), mp 169-171° and **5a** (0.06 g, 5.35%); ^{1}H nmr (**9a**, deuteriochloroform): δ 2.57 (s, 3, SCH_3), 3.27-3.63 (m, 2, H5′), 3.97-4.2 (m, 1, H4′), 4.55 (d, 1, H3′), 5.13 (d, 1, H2′), 6.27 (d, 1, H1′); ^{13}C nmr (deuteriochloroform): δ 164.5_8 (C-6), 161.1_8 (C-4), 160.6_9 (C-2), 89.7_0 (C2′), 89.4_9 (C4′), 88.3_5 (C1′), 75.6_7 (C3′), 61.9_7 (C5′), 13.3_3 (SCH_3).

Anal. Calcd. for $C_{21}H_{39}N_3O_5SSi_2$ (**9a**): C, 50.27; H, 7.83; N, 8.37. Found: C, 50.54; H, 7.92; N, 8.23.

Compound **5a** had ^{1}H nmr (deuteriochloroform): δ 3.64 (s, 3, NCH_3), 3.4-3.77 (m, 2, H5′), 4.0-4.23 (m, 1, H4′), 4.63 (d, 1, H3′), 5.1 (d, 1, H2′), 6.66 (d, 1, H1′); ^{13}C nmr (deuteriochloroform): δ 174.0_3 (C-6), 159.2_3 (C-4), 153.0 (C-2), 90.3_7 (C2′), 89.4_6 (C4′), 89.1_7 (C1′), 75.5_5 (C3′), 62.0_9 (C5′), 34.8_9 (NCH_3). The spectra data were identical to that reported [5] for authentic **5a**.

6-Allylthio-3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano-[1′,2′:4,5]oxazolo-*s*-triazin-4-one (**10a**).

A solution of **7a** (0.75 g, 1.54 mmoles) in dry tetrahydrofuran (7 ml) was added to a stirred suspension of sodium hydride (60%, 0.09 g, 2.31 mmoles) in dry tetrahydrofuran (10 ml). After salt formation was complete (30 minutes), allyl bromide (0.2 ml, 2.34 mmoles) in dry tetrahydrofuran (5 ml) was slowly added to the suspension and the reaction mixture was stirred overnight at room temperature. The solvent was then removed under diminished pressure and the resulting gum was adsorbed on silica gel. This material was placed on a sintered glass funnel and washed well with ethyl acetate. The combined wash was taken to dryness under diminished pressure and the resulting gum was chromatographed over silica gel and eluted with ethyl acetate-hexane (1/1) to furnish **10a**. This material was covered with ethyl acetate-hexane (1/1, 10 ml) and on standing crystallized out of solution. The solid was collected by filtration and dried to afford pure **10a** (0.66 g, 81%, mp 129-131°); ^{1}H nmr (deuteriochloroform): δ 3.3-3.67 (m, 2, H5′), 3.87 (d, 2, S-CH_2-CH=CH_2), 4.0-4.17 (m, 1, H4′), 4.55 (d, 1, H3′), 5.06-5.37 (m, 3, S-CH_2-CH=CH_2, H2′), 5.63-6.00 (m, 1, S-CH_2-CH=CH_2), 6.23 (d, 1, H1′); ^{13}C nmr (deuteriochloroform): δ 163.6_5 (C-6), 161.2_5 (C-4), 160.5_5 (C-2), 131.1_5 and 119.9_6 (S-CH_2-CH=CH_2), 89.5_2 (C2′ and C1′), 88.4_0 (C4′), 75.6_9 (C3′), 61.9_4 (C5′), 33.5_0 (S-CH_2-CH=CH_2).

Anal. Calcd. for $C_{23}H_{41}N_3O_5SSi_2$: C, 52.34; H, 7.83; N, 7.96. Found: C, 52.14; H, 7.60; N, 7.84.

6-Propargylthio-3′,5′-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one (**11a**).

Compound **7a** (1 g, 2.05 mmoles) in dry tetrahydrofuran (10 ml) was added to a stirred suspension of sodium hydride (50%, 0.12 g, 3.07 mmoles) in dry tetrahydrofuran (15 ml). After salt formation was complete (30 minutes), propargyl bromide (0.3 ml, 3.07 mmoles) in dry tetrahydrofuran (5 ml) was slowly added and the reaction mixture was allowed to stir overnight at room temperature. The solvent was removed under diminished pressure and the residue was adsorbed on silica gel. This material was placed on a sintered glass funnel and washed with chloroform. The chloroform wash was evaporated to dryness and the resulting gum was triturated with petroleum ether. Solid **11a** (0.58 g, 53%) was removed by filtration and air-dried, mp 197°; ^{1}H nmr (deuteriochloroform): δ 2.23 (t, 1, S-CH_2-C≡CH), 3.33-3.7 (m, 2, H5′), 4.0-4.2 (m, 3, H4′ + S-CH_2-C≡CH), 4.6 (d, 1, H3′), 5.07 (d, 1, H2′), 6.23 (d, 1, H1′); ^{13}C nmr (deuteriochloroform): δ 162.5_6 (C-6), 161.0_9 (C-4), 160.2_2 (C-2), 89.8_7 (C2′), 89.7_0 (C4′) 88.3_3 (C1′), 75.6_5 (C3′) 61.9_3 (C5′), 73.1_4 (C=CH), 19.6_6 (S-CH_2-C=CH).

Anal. Calcd. for $C_{23}H_{39}N_3O_5SSi_2$: C, 52.54; H, 7.48; N, 7.99. Found: C, 52.53; H, 7.32; N, 8.01.

β-D-Arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**7b**).

Method A.

To a solution of compound **7a** (0.78 g, 1.59 mmoles) in absolute ethanol (17 ml) was added a 2*N* ethanolic hydrochloric acid solution (2 ml). The reaction was stirred at room temperature for 2.5 hours and then the solvent was removed under reduced pressure. The resulting solid was recrystallized from chloroform-ethanol (9/1) to furnish **7b** (0.22 g, 53%) mp 224°; ^{1}H nmr (DMSO-d_6): δ 3.23-3.53 (m, 2, H5′), 4.0-4.16 (m, 1, H4′), 4.37 (br s, 1, H3′), 5.02 (t, 1, 5′-OH, deuterium oxide exchangeable), 5.15 (d, 1, H2′), 5.8 (br s, 1, 3′-OH, deuterium oxide exchangeable), 6.33 (d, 1, H1′), 12.53 (br s, 1, NH, deuterium oxide exchangeable).

Anal. Calcd. for $C_8H_9N_3O_5S$: C, 37.07; H, 3.50; N, 16.21. Found: C, 37.53; H, 3.42; N, 15.91.

Method B.

Ethoxycarbonyl isothiocyanate (4.7 ml, 40.2 mmoles) in dry dimethylformamide (15 ml) was slowly added, with a syringe, to a stirred solution of 2-amino-β-D-arabinofurano[1′,2′:4,5]-2-oxazo-

line (**6b**, 5 g, 28.71 mmoles) in dry dimethylformamide (50 ml). The solution was stirred overnight at room temperature and then the solvent was removed under diminished pressure. The residue was co-evaporated with toluene (3 x 30 ml) and the crude oil was chromatographed over silica gel and eluted with methanol-chloroform (15/35) to furnish **7b** as a solid. This material was recrystallized from chloroform-methanol (9/1) to provide analytically pure **7b** (4.06 g, 55%) mp 222-223°; ^{1}H nmr (DMSO-d_6): δ 3.36-3.44 (m, 2, H5'), 4.11 (br s, 1, H4'), 4.44 (s, 1, H3'), 5.16 (br s, 1, 5'-O*H*, deuterium oxide exchangeable), 5.17 (d, 1, H2'), 5.86 (br s, 1, 3'-OH, deuterium oxide exchangeable), 6.39 (d, 1, H1'); ^{13}C nmr (DMSO-d_6): δ 174.3_4 (C-6), 161.5_3 (C-4), 153.6_4 (C-2), 89.7_2 (C2'), 89.5_9 (C4'), 89.1_4 (C1'), 74.5_7 (C3'), 60.9_0 (C5').

Anal. Calcd. for $C_8H_9N_3O_5S$: C, 37.07; H, 3.50; N, 16.21. Found: C, 37.16; H, 3.16; N, 16.13.

3',5'-Di-*O*-acetyl-β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (**13**) from **7b** Which was Derived from the Hydrolysis of **7a**.

Acetic anhydride (1 ml, 10 mmoles) was added to a solution of β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (0.10 g, 0.37 mmoles) in dry pyridine (3 ml). The solution was stirred overnight at room temperature and then it was poured over crushed ice, extracted with chloroform, and washed in succession with a dilute hydrochloric acid solution, a saturated sodium bicarbonate solution, and water. The chloroform layer was dried over anhydrous sodium sulfate. The chloroform was removed under diminished pressure to provide a syrup. The syrup was dissolved in petroleum ether-chloroform (10 ml, 9/1) and let stand overnight. The solid which precipitated was removed by filtration to furnish **13** (0.11 g, 86%), mp 134-136°; m/e, 343.20 (molecular ion); ^{1}H nmr (DMSO-d_6): δ 1.93 (s, 3, OCOC*H*$_3$), 2.1 (s, 3, OCOC*H*$_3$), 3.83-4.33 (m, 2, H5'), 4.43-4.63 (m, 1, H4'), 5.28 (d, 1, H3'), 5.45 (d, 1, H2'), 6.42 (d, 1, H1'), 12.53 (br s, 1, NH, deuterium oxide exchangeable). The one-half mole of chloroform was observed in the ^{1}H nmr spectrum at 8.2 ppm.

Anal. Calcd. for $C_{12}H_{13}N_3O_7S{\cdot}0.5CHCl_3$: C, 37.25; H, 3.38; N, 10.43. Found: C, 37.74; H, 3.40; N, 10.54.

3',5'-Di-*O*-acetyl-β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (**13**) from **7b** Which was Synthesized from **6b**.

Acetic anhydride (1 ml) was added to a stirred solution of β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (0.11 g, 0.43 mmoles) in dry pyridine (2 ml) and the reaction stirred at room temperature overnight. The reaction mixture was then poured over crushed ice, extracted with chloroform, and the chloroform layer washed in succession with a dilute hydrochloric acid solution, a saturated sodium bicarbonate solution and water. The chloroform layer was dried over anhydrous sodium sulfate. The chloroform was removed under diminished pressure and the resulting white solid was triturated with petroleum ether. The solid was removed by filtration and recrystallized from chloroform-ethanol (9/1) to furnish **13** (0.11 g, 73%), mp 134-136°; ^{1}H nmr (DMSO-d_6): δ 1.93 (s, 3, OCOC*H*$_3$), 2.1 (s, 3, OCOC*H*$_3$), 3.83-4.33 (m, 2, H5'), 4.43-4.63 (m, 1, H4'), 5.28 (d, 1, H3'), 5.45 (d, 1, H2'), 6.42 (d, 1, H1'), 12.53 (br s, 1, N*H*, deuterium oxide exchangeable); ^{13}C nmr (DMSO-d_6): δ 174.0_6 (C-6), 169.8_3 (O-*C*=O), 169.6_2 (O-*C*=O), 161.0_6 (C-4), 153.1_6 (C-2), 89.6_3 (C2'), 86.2_5 (C4'), 82.9_3 (C1'), 76.0_2 (C3'), 62.8_8 (C5'), 20.5_0 (CO*C*H$_3$), 20.1_0 (CO*C*H$_3$). This nucleoside was identical in all respects to **13** isolated from the preceding procedure.

2-Ureido-3',5'-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano-1',2':4,5]-2-oxazoline (**12**).

Method A.

To a solution of 3',5'-bis(*O*-*t*-butyldimethylsilyl-β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (**7a**, 1.27 g, 2.60 mmoles) in tetrahydrofuran was added a solution of sodium hydroxide (0.1 *M*, 65 ml) and the mixture stirred at room temperature for 36 hours. At this point, the reaction mixture was extracted with chloroform, and the chloroform layer dried over anhydrous sodium sulfate. After filtration, the excess chloroform was removed under diminished pressure. The resulting gum was chromatographed over silica gel using chloroform-methanol (49/1) as eluant. Concentration of the fractions containing the title compound furnished crystalline **12** (0.32 g, 28%), mp 185-188°; ^{1}H nmr (DMSO-d_6): δ 3.32 (br s, 1, deuterium oxide exchangeable), 3.56-3.85 (m, 3, H4' and H5'), 4.18-4.27 (m, 1, H3'), 5.47 (d, 1, H2'), 6.36 (d, 1, H1'), 11.43 (br s, 2, exchangeable proton); ^{13}C nmr (DMSO-d_6): δ 149.0_4 (C-4), 148.1_6 (C-2), 82.9_1, 81.5_8, 77.2_3, 76.3_5, 64.0_8 (C1'-C5').

Anal. Calcd. for $C_{19}H_{39}N_3O_5Si_2{\cdot}H_2O$: C, 49.21; H, 8.91; N, 9.06. Found: C, 49.53; H, 8.55; N, 8.47.

Method B.

A solution of sodium hydroxide (0.1 *M*, 2 ml) was added to a solution of 3',5'-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano-[1',2':4,5]oxazolo-*s*-triazine-4,6-dione (**8a**, 60 mg, 0.13 mmole) in tetrahydrofuran and the reaction mixture was stirred for 24 hours at room temperature. The reaction mixture was then poured into water, the combined solution extracted with chloroform, and the chloroform layer dried over anhydrous sodium sulfate. After filtration, the chloroform layer was taken to dryness under diminished pressure. The resulting gum was chromatographed over silica gel and the column eluted with hexane-ethyl acetate (1/1) to provide **12** (0.019 g, 33%), mp 183-186°; ^{13}C nmr (DMSO-d_6): δ 149.1_2 (C-4), 148.2_6 (C-2), 82.8_9, 81.5_6, 77.2_4, 76.2_4, 64.1_3 (C1'-C5'). This nucleoside was identical in all respects to **12** prepared from Method A.

3-*N*-Acetyl-2-ureido-3',5'-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1',2':4,5]oxazoline (**14**).

Acetic anhydride (0.4 ml) was added to a solution of 2-ureido-3',5'-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1',2':4,5]-oxazoline (**12**, 0.07 g, 0.16 mmole) in dry pyridine (1 ml) and the reaction was stirred overnight at room temperature. The excess solvent was removed under diminished pressure and the resulting white foam was chromatographed over silica gel using chloroform-methanol (9/1) as the eluant to provide **14** (0.07 g, 87%), mp 185-187°; ^{1}H nmr (deuteriochloroform): δ 2.07 (s, 3, COC*H*$_3$), 3.81-3.98 (m, 3, H4' and H5'), 4.68 (t, 1, H3'), 5.24 (t, 1, H2'), 6.65 (d, 1, H1'), 9.66 (br s, 2, deuterium oxide exchangeable); ^{13}C nmr (deuteriochloroform): δ 170.7_3 (C=O) 148.3_2 (C-2), 147.8_5 (C-4), 83.0_7, 79.8_0, 79.3_2, 74.0_4, 63.9_6 (C1'-C5').

Anal. Calcd. for $C_{21}H_{41}N_3O_6Si_2$: C, 51.71; H, 8.47; N, 8.62. Found: C, 51.83; H, 8.15; N, 8.64.

β-D-Arabinofurano[1',2':4,5]oxazolo-*s*-triazine-4,6-dione (**8b**).

Ethoxycarbonyl isocyanate (95%, 0.6 ml, 5.84 mmoles) in dry dimethylformamide was slowly added to a stirred solution of 2-amino-β-D-arabinofurano[1',2':4,5]-2-oxazoline (**6b**, 0.73 g, 4.17 mmoles) in dry dimethylformamide (10 ml). The reaction mixture

was heated at 100° overnight. After cooling, the solvent was removed *in vacuo*. The resulting gum was co-evaporated with toluene (2 x 20 ml) and then was chromatographed over silica gel using chloroform-methanol (9/1) as the eluant to afford **8b**. This material was recrystallized from chloroform-methanol (9/1) to furnish pure **8b** (0.52 g, 51%), mp 234-236° dec; ^{1}H nmr (DMSO-d_6): δ 3.33 (br d, 1, H5'), 3.9-4.1 (m, 1, H4'), 4.32 (d, 1, H3'), 5.13 (d, 1, H2'), 6.2 (d, 1, H1'); ^{13}C nmr (DMSO-d_6): δ 163.4_0 (C-4), 156.3_6 (C-2), 147.2_7 (C-6), 89.9_6, 89.7_1, 87.0_1, 74.5_6, 60.9_5 (C1'-C5').

Anal. Calcd. for $C_8H_9N_3O_6$: C, 39.51; H, 3.73; N, 17.28. Found: C, 39.44; H, 3.79; N, 17.07.

5-*N*-Methyl-β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazine-4,6-dione (**4b**).

Method A.

β-D-Arabinofurano[1',2':4,5]oxazolo-*s*-triazine-4,6-dione (**8b**, 0.08 g, 0.34 mmole) in dry dimethylformamide (3 ml) was added to a stirred suspension of sodium hydride (60%, 0.02 g, 0.45 mmole) in dry dimethylformamide (7 ml). After salt formation was complete (30 minutes), methyl iodide (0.03 ml, 0.51 mmole) in dry dimethylformamide (1 ml) was added and the reaction mixture stirred for 6 hours. Next, the solvent was removed *in vacuo*. The resulting gum was chromatographed over silica gel and the column eluted with choloroform-methanol (9/1) to give **4b**. An analytical sample was prepared by recrystallization from chloroform-methanol (9/1) (0.06 g, 63%), mp 220-223° dec; ^{1}H nmr (DMSO-d_6): δ 3.13 (s, 3, N-C*H*$_3$), 3.27-3.4 (m, 2, H5'), 4.0-4.13 (m, 1, H4'), 4.37 (d, 1, H3'), 5.0 (t, 1, 5'-O*H*, deuterium oxide exchangeable), 5.17 (d, 1, H2'), 5.83 (d, 1, 3'-O*H*, deuterium oxide exchangeable), 6.27 (d, 1, H1'); ^{13}C nmr (DMSO-d_6): δ 161.7_1 (C-4), 155.4_6 (C-2), 147.4_3 (C-6), 89.9_3 (C2'), 89.7_2 (C4'), 87.5_8 (C1'), 74.4_7 (C3'), 60.7_9 (C5'), 28.0_3 (N-*C*H$_3$).

Anal. Calcd. for $C_9H_{11}N_3O_6$: C, 42.03; H, 4.31; N, 16.34. Found: C, 42.08; H, 4.40; N, 16.19.

Method B.

A mixture of β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (**7b**, 1 g, 3.87 mmoles), methyl iodide (2 ml, 32.13 mmoles), and potassium carbonate (0.54 g) in dry dimethylformamide (10 ml) was stirred at room temperature for 12 hours. After this time, the solvent was removed *in vacuo*. The resulting residue was chromatographed over silica gel using methylene chloride-methanol (95/5) as eluant to furnish **4b**. This was recrystallized from methylene chloride-methanol (9/1) to furnish an analytical sample (0.42 g, 40%), mp 220-223° dec; ^{1}H nmr (DMSO-d_6): δ 3.1 (s, 3, NCH$_3$), 3.3-3.53 (m, 2, H5'), 4.05 (d, 1, H4'), 4.33 (d, 1, H3'), 4.97 (t, 1, 5'-O*H*, deuterium oxide exchangeable), 5.17 (d, 1, H2'), 5.77 (d, 1, 3'-O*H*, deuterium oxide exchangeable), 6.23 (d, 1, H1'); ^{13}C nmr (DMSO-d_6): δ 161.7_4 (C-4), 155.5_3 (C-2), 147.4_5 (C-6), 89.9_3 (C2'), 89.7_9 (C4'), 87.6_2 (C1'), 74.5_0 (C3'), 60.8_0 (C5'), 28.0_5 (N-*C*H$_3$).

Anal. Calcd. for $C_9H_{11}N_3O_6 \cdot H_2O$: C, 39.28; H, 4.76; N, 15.26. Found: C, 39.71; H, 4.77; N, 15.46.

3',5'-Bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1',2':4,5]-oxazolo-*s*-triazine-4,6-dione (**8a**).

Method A.

3',5'-Bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1',2':4,5]-oxazolo-*s*-triazin-4-one-6-thione (**7a**, 0.40 g, 0.82 mmole) was added to a stirred suspension of sodium hydride (0.05 g, 1.23 mmoles) in dry tetrahydrofuran (20 ml). After salt formation was complete (30 minutes), allyl bromide (0.10 ml, 1.23 mmoles) in dry tetrahydrofuran (4 ml) was slowly added, by syringe, and the reaction mixture was allowed to stir at room temperature. After stirring overnight, the reaction was quenched with water, the aqueous extracted with chloroform, and the chloroform layer dried over anhydrous sodium sulfate. The resulting gum was chromatographed over silica gel and the column eluted with ethyl acetate-hexane (1/1). The fractions containing **8a** were pooled and those containing **10a** were combined. The solvent was removed by diminished pressure and the respective solids were covered with a minimal amount of ethyl acetate-hexane (1/1). On standing they crystallized out of solution, were collected by filtration, and air-dried to furnish **8a** (0.07 g, 18%), mp 198-199° and **10a** (0.22 g, 51%); ^{1}H nmr (deuteriochloroform) (**8a**): δ 3.3-3.7 (m, 2, H5'), 3.97-4.13 (m, 1, H4'), 4.55 (d, 1, H3'), 5.13 (d, 1, H2'), 6.33 (d, 1, H1'), 9.52 (br s, 1, NH, deuterium oxide exchangeable); ^{13}C nmr (deuteriochloroform): δ 162.7_6 (C-4), 155.7_6 (C-2), 146.8_9 (C-6), 89.9_0 (C2'), 86.6_9 (C4'), 85.8_6 (C1'), 75.0_3 (C3'), 61.3_3 (C5').

Anal. Calcd. for $C_{20}H_{37}N_3O_6Si_2$ (**8a**): C, 50.93; H, 7.91; N, 8.91. Found: C, 50.84; H, 7.88; N, 9.21 [23].

Method B.

N-Chlorocarbonyl isocyanate (0.10 ml, 0.14 g, 1.29 mmoles) in dry methylene chloride (1 ml) was added to a stirred solution of 2-amino-3',5'-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabino[1',2':4,5]-2-oxazoline (**6a**, 0.5 g, 1.24 mmoles) in dry methylene chloride (10 ml). The clear solution was stirred for 2 hours at room temperature and then triethylamine (0.18 ml, 0.13 g, 1.29 mmoles) was added, and the reaction mixture was allowed to stir for another 30 minutes. At this point water (10 ml) was added, the organic layer separated and washed twice with water, and then dried over anhydrous sodium sulfate. The solvent was removed under diminished pressure to provide a white foam. This material was column chromatographed (silica gel) and the column eluted with ethyl acetate-hexane (1/1) to give **8a** (0.38 g, 64%), mp 199-200°; ^{1}H nmr (deuteriochloroform): δ 3.37-3.77 (m, 2, H5'), 4.0-4.2 (m, 1, H4'), 4.6 (d, 1, H3'), 5.2 (d, 1, H2'), 6.4 (d, 1, H1'), 9.6 (br s, 1, NH, deuterium oxide exchangeable); ^{13}C nmr (deuteriochloroform): δ 163.1_8 (C-4), 156.2_9 (C-2), 146.7_3 (C-6), 90.9_5 (C2'), 88.8_7 (C4'), 86.7_0 (C1'), 75.5_3 (C3'), 62.0_2 (C5').

Anal. Calcd. for $C_{20}H_{37}N_3O_6Si_2$: C, 50.93; H, 7.91; N, 8.91. Found: C, 51.00; H, 8.00; N, 8.71.

Method C.

A solution of sodium hydroxide (0.1 *M*, 10.25 ml) was added to 3',5'-bis(*O*-*t*-butyldimethylsilyl)-β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (**7a**, 0.4 g, 0.82 mmole) in tetrahydrofuran and the reaction mixture stirred for 24 hours at room temperature. The solution was then poured into water, and the aqueous solution extracted with chloroform, the chloroform layer dried over anhydrous sodium sulfate and then the solvent was removed under diminished pressure. The resulting gum was chromatographed over silica gel using hexane-ethyl acetate (1/1) as the eluant to furnish **8a** (0.14 g, 36%), mp 198-200°; ^{13}C nmr (deuteriochloroform): δ 162.9_1 (C-4), 155.4_7 (C-2), 146.2_4 (C-6), 90.9_8 (C2'), 89.0_7 (C4'), 86.4_5 (C1'), 75.4_4 (C3'), 61.9_4 (C5'). This nucleoside was identical in all respects to **8a** prepared from methods A and B.

5-*N*-Methyl-β-D-arabinofurano[1',2':4,5]oxazolo-*s*-triazin-4-one-6-thione (**5b**) and 5-*N*-methyl-β-D-arabinofurano[1',2':4,5]oxazolo-*s*-

triazine-4,6-dione (**4b**).

β-D-Arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**7b**, 0.75 g, 2.89 mmoles) in dry dimethylformamide (10 ml) was added to a stirred suspension of sodium hydride (50%, 0.17 g, 3.54 mmoles) in dry dimethylformamide (7 ml). After salt formation was complete (30 minutes), methyl iodide (0.2 ml, 3.21 mmoles) in dry dimethylformamide (2 ml) was added and the reaction mixture was stirred overnight at room temperature. The solvent was removed *in vacuo*. The resulting gum was chromatographed over silica gel and the column eluted with chloroform-methanol (9/1) to furnish an intimate mixture of **5b** and **4b** (0.55 g) which co-crystallized out of chloroform-methanol (9/1); ^{13}C nmr (DMSO-d_6): δ 172.9$_4$ (C6=S), 161.7$_7$ and 160.1$_4$ (C-4), 155.6$_3$ and 153.3$_5$ (C-2), 147.4$_2$ (C6=O), 93.8$_9$, 89.4$_9$, 90.0$_3$, 86.0$_8$, 89.2$_3$, 87.7$_8$, 75.2$_2$, 74.4$_1$, 61.1$_8$, 60.7$_7$ (C1′-C5′), 28.2$_6$, 28.5$_4$ (N-CH_3).

Mass Calcd. for $C_9H_{11}N_3O_5S$ (**5b**): 273.0419. Found: 273.0432.

5-*N*-Allyl-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazine-4,6-dione (**15**) and 5-*N*-Allyl-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**16**).

β-D-Arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**7b**, 0.75 g, 2.89 mmoles) in dry dimethylformamide (10 ml) was added to a stirred suspension of sodium hydride (50%, 0.17 g, 3.54 mmoles) in dry dimethyl formamide (7 ml). After salt formation was complete (30 minutes), allyl bromide (0.3 ml, 3.46 mmoles) in dry dimethylformamide (5 ml) was slowly added and the reaction mixture was stirred overnight at room temperature. The solvent was removed *in vacuo*. The resulting gum was chromatographed over silica gel and the column eluted with chloroform-methanol (9/1) to afford an intimate mixture of **15** and **16** (0.463 g) which co-crystallized out of chloroform-methanol (9/1); ^{13}C nmr (DMSO-d_6): δ 174.2$_7$ (C6=S), 161.9$_2$, 161.0$_5$ (C-4), 154.8, 152.4$_4$ (C-2), 147.0$_7$ (C6=O), 91.2$_2$, 90.0$_2$, 89.7$_7$, 89.1$_5$, 87.6$_5$, 74.6$_6$, 74.5$_1$, 60.8$_7$ (C1′-C5′), 131.9$_6$, 130.6$_9$, 117.2$_0$, 116.4$_1$ (N-CH_2-CH=CH_2), 48.4$_3$, 43.0$_7$ (N-CH_2-CH=CH_2).

Mass Calcd. $C_{11}H_{13}N_3O_5S$ (**16**): 299.057592. Found: 299.0572.

5-*N*-Propargyl-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazine-4,6-dione (**17**) and 5-*N*-Propargyl-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**18**).

β-D-Arabinofurano[1′,2′:4,5]oxazolo-*s*-triazin-4-one-6-thione (**7b**, 1 g, 3.86 mmoles) in dry dimethylformamide (15 ml) was added to a stirred suspension of sodium hydride (60%, 0.23 g, 5.79 mmoles) in dry dimethylformamide (10 ml). After salt formation was complete (30 minutes), propargyl bromide (0.5 ml, 5.61 mmoles) was added to the cooled solution and the reaction mixture was stirred overnight at room temperature. The solvent was removed *in vacuo* and the dark residue was chromatographed over silica gel and the column eluted with choloroform-methanol (9/1) to furnish **17** (0.22 g, 20%), mp 230° dec and **18** (0.32 g, 27%), mp 262-265°. Each compound was recrystallized from chloroform-methanol (9/1).

The physical constants for **17** are: ^{1}H nmr (DMSO-d_6): δ 3.1 (t, 1, C≡C*H*), 3.23-3.4 (m, 2, H5′), 3.97-4.47 (m, 4, H3′, H4′ and NCH_2-C≡CH), 5.0 (t, 1, 5′-OH, deuterium oxide exchangeable), 5.17 (d, 1, H2′), 5.83 (d, 1, 3′-O*H* deuterium oxide exchangeable), 6.27 (d, 1, H1′); ^{13}C nmr (DMSO-d_6): δ 162.0$_2$ (C-4), 154.2$_4$ (C-2), 146.6$_7$ (C-6), 90.2$_0$ (C2′), 89.7$_5$ (C4′), 87.6$_3$ (C1′), 74.3$_4$ (C3′), 60.7$_3$ (C5′), 78.5$_1$ and 73.5$_7$ (*C*≡*C*), 30.7$_5$ (N*C*H_2-C≡CH).

Anal. Calcd. for $C_{11}H_{11}N_3O_6$ (**17**): C, 46.96; H, 3.94; N, 14.94. Found: C, 46.91; H, 4.27; N, 15.19.

The physical constants for **18** are: ^{1}H nmr (DMSO-d_6): δ 3.13 (t, 1, C≡C*H*), 3.3-3.43 (m, 2, H5′), 4.12-4.17 (m, 1, H4′), 4.4 (d, 1, H3′), 4.9 (d, 2, N-CH_2-C≡CH_2), 5.0 (t, 1, 5′-O*H*, deuterium oxide exchangeable), 5.17 (d, 1, H2′), 5.82 (d, 1, 3′-O*H*, deuterium oxide exchangeable), 6.4 (d, 1, H1′); ^{13}C nmr (DMSO-d_6): δ 173.7$_2$ (C-6), 160.1$_2$ (C-4), 151.9$_4$ (C-2), 91.2$_3$ (C2′), 89.8$_2$ (C4′), 89.3$_6$ (C1′), 74.5$_1$ (C3′), 60.7$_9$ (C5′), 77.7$_3$ and 73.8$_6$ (*C*≡*C*), 36.6$_0$ (N-*C*H_2-C≡C).

Anal. Calcd. for $C_{11}H_{11}N_3O_5S$ (**18**): C, 44.44; H, 3.73; N, 14.13. Found: C, 44.59; H, 3.96; N, 13.86.

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[22] The line sequence for the carbon chemical shifts of the sugar moieties of 2-amino-β-D-arabinofurano[1′,2′:4,5]-2-oxazoline and 5-*N*-methyl-β-D-arabinofurano[1′,2′:4,5]oxazolo-*s*-triazine-4,6-dione were assigned by a Heteronuclear Correlated 2-D (Hetero-COSY) experiment. The carbon chemical shifts for 2-amino-β-D-arabinofurano[1′,2′:4,5]-2-oxazoline (**6b**) are as follows: δ 99.8_2 (C1′), 88.2_5 (C2′), 84.7_0 (C4′), 75.6_4 (C3′), 61.5_7 (C5′). The notation (C1′-C5′) indicates the carbon chemical shifts of the sugar moiety were not assigned.

[23] This nucleoside was analyzed for sulfur and none was detected.