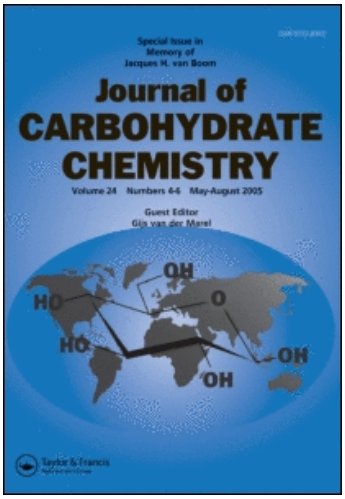

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Novel *C*-Thionucleosides: Synthesis and Reactions of 1,5- and 1,3-Dialkyl Derivatives of (1,5-Dithio-1-thiomethyl-α-D,L-*arabino*pentulo-pyranos-1-yl)-1*H*-1,2,4-triazole Nucleosides

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ABSTRACT

A series of novel *C*-thionucleosides: 1,5- and 1,3-dialkyl derivatives of (2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-α-D,L-*arabino*pentulopyranos-1-yl)-1*H*-1,2,4-triazole nucleosides **10a–d** and **17a–c** were synthesized, after spontaneous rearrangements, from concerted 1,3-cycloaddition of the sugar nitrile **5** with the reactive 1-(chloro-alkyl)-1-aza-2-azoniaallenes **6** and **13** in the presence of a Lewis acid. Deblocking of the acylated nucleosides afforded the free nucleosides **11a–d** and **18a–c**. The structures of the synthesized compounds were confirmed by ^{1}H NMR and mass spectra.

Key Words: Biological activity; Cycloaddition reaction; Cumulenes; Nitriles; 1,2,4-Triazole nucleosides.

INTRODUCTION

Nucleoside analogs play an important role in the field of chemotherapy for cancer and viral diseases[1] because of their ability to interfere with DNA synthesis by inhibiting

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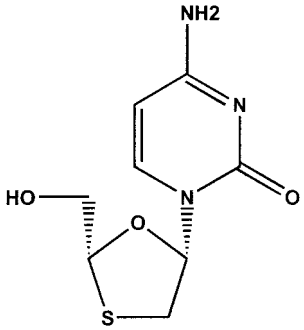
DNA polymerase.[1,2] Chemical modifications of the sugar moiety have recently received considerable attention,[3] especially by changing the furanose ring oxygen atom to sulfur atom which has revealed interesting biological activities including potency, selectivity, and low toxicity in the chemotherapeutics.[4,5] Simon et al.,[6] Walker et al.,[7] Secrist III et al.,[8] Imbach et al.,[9] Uenishi et al.,[10] and recently Voss et al.[11] have described various 4′-thio analogs of purine and pyrimidine nucleosides, since some showed potent activities against HSV-1 and VZV as well as antitumor activities against L-1210 and H-Ep-2, but were found to be toxic. An outstanding candidate which emerged from these compounds is β-L-(−)-2′-deoxy-3′-thiacytidine (limousine, 3TC™) (**1**)[12] that recently approved by FDA for the treatment of AIDS, but showed much lower cytotoxicity than its antipode. Joeng et al.[13] reported recently the synthesis of novel D- and L-2′-azido-2′,3′-dideoxyribofuranosyl-4′-pyrimidines and purines, whereby D-α, and β-N^6-methyladenines analogs were detected with significant anti-HCMV (human cytomegalovirus) activity. In connection with our synthetic program by preparation of various sugars having sulfur in the ring,[14–20] as bioactive molecules and intermediates for synthesis of new nucleosides, we have recently synthesized 1-(5-thio-β-D-xylopyranosyl)-pyrimidine and -lumazine nucleosides,[21] as well as 1-(5-thio-D-β-glucopyranosyl)-6-azauracil nucleosides.[22] A modification in these thiosugars was carried out by introducing the bioactive azide and amino groups, which might lead to potentially active nucleosides. Such thiosugars are 3-acetamido- and azido-3-deoxy-5-thio-D-xylose, 4-acetamido- and azido-4-deoxy-5-thio-L-lyxose, and their arabino- analog,[23] as well as the 3-azido-3-deoxy-5-thio-β-D-ribopyranose[24] and *3*-deoxy-5-thio-β-D-*erythro*-pentopyranose.[25] On the other hand, a few 1,2,4-triazole *C*-glycosides were reported,[26–31] since these compounds were prepared as analog[32] of the potent antiviral *N*-nucleosides ribavirin[33] because of their broad spectrum of action against RNA and DNA viruses. The antiviral activity of some cyclic 1,2,4-triazole *C*-nucleosides[34] against herpes simplex viruses (HSV), and as a part of our program to develop a new anticancer and antiviral agent we have pursued the synthesis of a novel type of *C*-thionucleosides bearing 1,2,4-triazole residues, from non-sugar precursors, as promising antiviral or antitumor candidates.



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RESULTS AND DISCUSSION

We have prepared recently various 1,2,4-triazole *C*-nucleosides[35] such as 1,2,4-triazole-*C*-nucleosides, acyclic *C*-nucleosides, and homo-*C*-nucleosides, (D-*manno*-pentitol-1-yl)-

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1,2,4-triazoles, 3′-1,2,4-triazolo- and 3′-1,3,4-thiadiazoliminothymidines, by cycloaddition of the reactive intermediates 1-(chloroalkyl)-1-aza-2-azoniaallenes with the corresponding nitriles. In the present study, the sugar moiety **5** has been selected for the synthesis of some novel substituted 1,2,4-triazole *C*-nucleosides.

In an earlier study, Vays and Hay[36] had described the synthesis of some unusual sugars having sulfur in the ring by facile Dields–Alder reactions between the reactive dienophiles, methyl cyanodithioformate (MCDF) and 1-methoxy-1,3-butadiene and cyclopentadiene as electrophiles, The sulfur atom here is the most nucleophilic center and it reacts preferentially with most of the electrophilic reagents commonly used to add to carbon–carbon double bonds. Accordingly, compound **3** was prepared (35%) as a racemic mixture of D,L configurations by reaction of MCDF with 1,4-diacetoxybutadiene (**2**).[37] The configuration at the anomeric center was assumed to be α, as discussed by the Vays and Hay,[36] on the basis that cyano group in this open-chain system obeyed the *endo* rule at low temperature and this hypothesis was supported by theoretical studies of Hoffmann and Woodward[38] of **3**, but the most predominant configuration of **3** is the α-D,L as confirmed by the ^{1}H NMR s data. *Cis*-hydroxylation of **3** with OsO_4 in pyridine at 23°C afforded the alcohol **4** (70%), which when treated with acetic anhydride in pyridine gave the tetra-acetate **5** (86%) as a syrup. The structure of **3** was secured by the ^{1}H NMR and mass spectra. Both half conformations of **3**, $^{S}H_2$ and ^2H_S have the same stability since there is no interaction between the *quasi*-axial acetoxy group and lone pairs on the sulfur atom. Te small coupling contants ($J_{3,4}$ 3.9 Hz, $J_{3,4} < 1.0$ Hz, and $J_{5,6}$ 3.8, $J_{5,6} < 1.0$ Hz) might explain the existence of **3** predominately in the ^2H_S conformation. The structure and conformation of **5** were deduced from the ^{1}H NMR spectrum. The doublet at δ 5.20 was assigned to H-3, $J_{3,4} = 3.0$ Hz, a value typical of coupling between vicinal diequatorial protons. The two doublet of doublets centered at δ 5.12 and 5.37 with $J_{4,5} = 4.9$ Hz, $J_{5,6} = 10.0$ Hz were attributed to H-4 and H-5, respectively. H-6 appeared as doublet at δ 4.20. The large coupling constant $J_{5,6} = 10.0$ Hz indicates that **3** and **4** occur exclusively in the $^5C_2$ conformer. The stability of this conformer might be explained also from the fewer 1,3-nonbonded interaction in the $^5C_2$ as compared to the $^2C_5$ conformer, in addition to the "hockey stick effect" resulted from orbital repulsion between a sulfur atom in the ring and a α equatorial SMe group,[39] which in turn would destabilized the $^2C_5$ conformer. Furthermore, the α configuration of **5** was assigned by the *trans*- $^3J_{C\text{-}1,C\text{-}4}$ coupling (4.2 Hz) and these data are in consistence with those of an earlier study by Marschal[40] and Weigert and Roberts[41] on the substituted cyclohexane derivatives, such as **11** and **12** (Sch. 1). Reaction of the sugar nitrile **5** with the chloro compounds **6a–d** proceeded in the presence of $SbCl_5$ in CH_2Cl_2, at −60°C for 1 hr, via the concerted 1,3-cycloaddition of the reactive 1-aza-2-azaoniaallene cations **7a–d** with the cyanide group, to give the inseparable 5-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-D,L-*arabino*-pentulopyranos-1-yl)-3*H*-1,2,4-triazolium hexachloroantimonates **8**. By rising the temperature above −30°C, **7** furnished the protonated triazoles **8** by migration[42] of the alkyl group (R^2) from C-3 to N-2 and elimination of (CO_2Et) group from N-1. Hydrolysis of **8**, in situ, with aqueous $NaHCO_3$ at 23°C afforded **9a–d** in 40–52% yields. Treatment of **9a–d** with NaOMe in MeOH gave the free nucleosides **10a–d** in 65–81% yields (Sch. 1).

The heterocumulenes **14** with *tert*-butyl group was observed to have a better reactivity, and used for synthesis of the electrically neutral 2-unsubstituted 1,2,4-triazoles in the presence of base. Thus, **14** obtained at low temperature (−60°C) from the chloro

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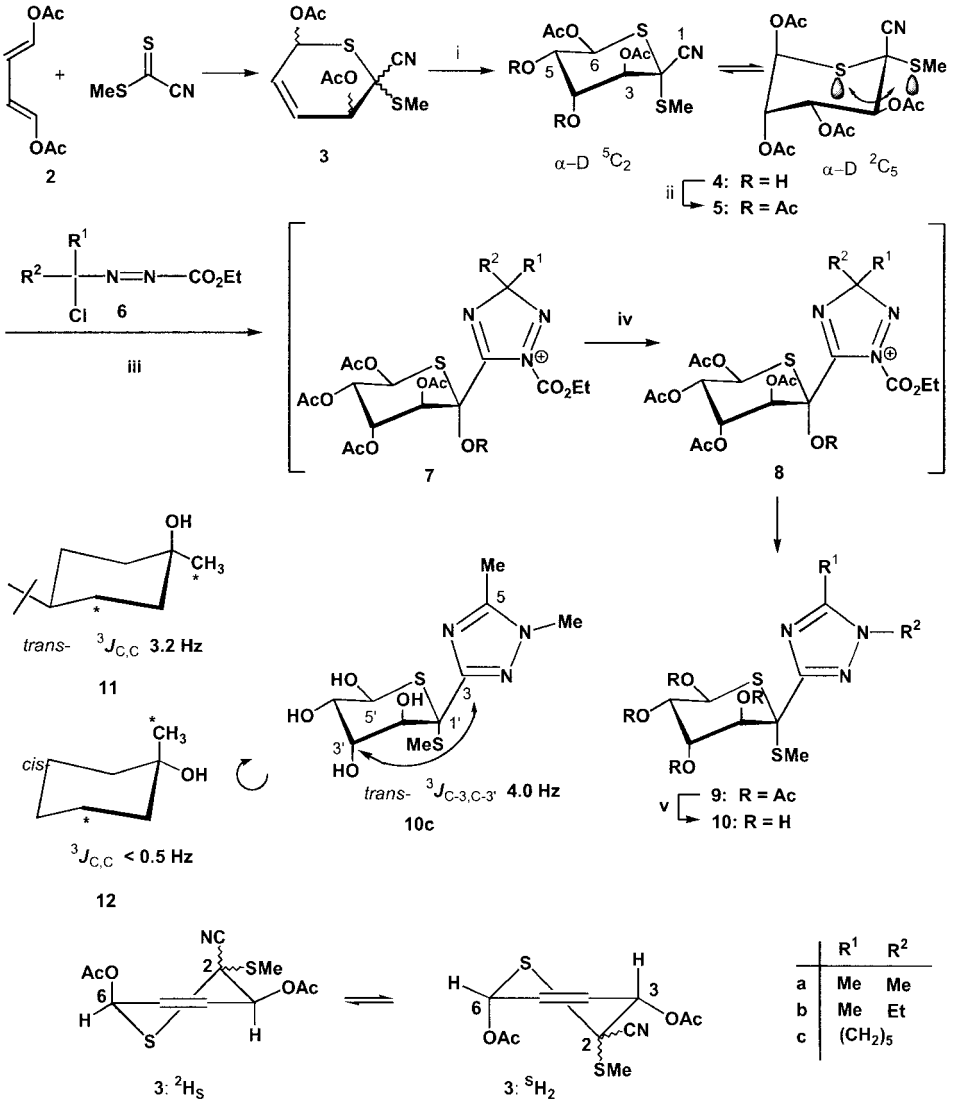

Scheme 1. Reagents and conditions: (i) OsO_4, pyridine, 23°C, 23 hr; (ii) Ac_2O, pyridine; 23°C, 18 hr; (iii) $SbCl_5$, CH_2Cl_2, −60°C to 23°C, 7 hr; (iv) aq. $NaHCO_3$, 23°C; (v) NaOMe, MeOH, 23°C, 4 hr.

compound **13** on treatment with $SbCl_5$, was reacted with the sugar nitrile **5** to give the inseparable hexachloroantimonate salts **15a–c**. The elimination of the bulky *tert*-butyl group as isobutene, and [1,2] H-shift might occur during or after the cycloaddition reaction, leaving back protonated salts **16a–c**, from which the neutral 1,2,4-triazole compounds **17a–c** were obtained in 42%, 41%, and 79% yields, respectively, by hydrolysis, in situ, with aqueous $NaHCO_3$. De-acetylation of **17a–c** with NaOMe in MeOH proceeded smoothly to afford the free nucleosides **18a–c** in 78%, 84%, and 84% yields, respectively (Sch. 2).

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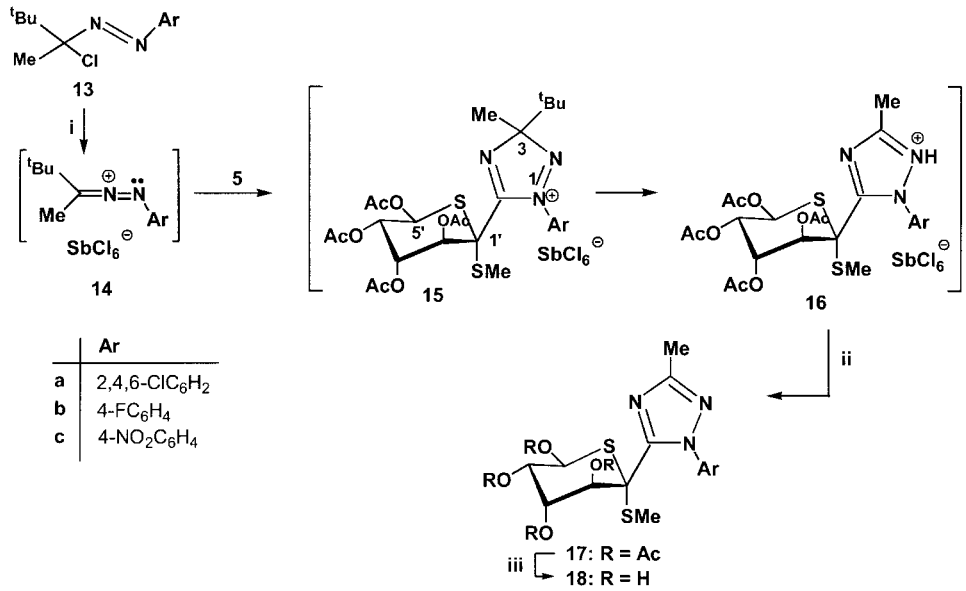

Scheme 2. (i) $SbCl_5$, −60–23°C; (ii) $NaHCO_3$, −30–23°C; (iii) NaOMe/MeOH.

The structures of the newly synthesized compounds were confirmed by the ^{1}H NMR and mass spectra. The ^{1}H NMR spectra of **9a–d** and **17a–c** showed a similar pattern, since H-2′ appeared, mostly, as doublets in the region δ 5.01–5.28. The coupling magnitudes between H-2′ and H-3′ (4.0–4.5 Hz) indicated a pyranosidic ring form with *quasi* equatorial–equatorial OAc groups at C-3′ and C-4′, respectively. H-4′ appeared as doublet of doublets in all compounds in the region δ 5.20–5.34 ($J_{4',5'}$ 9.1–9.5 Hz), while the doublets at lower field δ 4.14–4.28 were attributed to H-5′. The large coupling constant between H-4′ and H-5′ is indicative of the $^4C_1$ conformation, which is still preferred for all the new synthesized nucleosides. When the six-member ring of a sugar moiety is in a chair conformation, the axial–equatorial and equatorial–equatorial vicinal protons generally having coupling magnitudes of 0–5.0 Hz.[43] Therefore, the coupling values between H-3′ and H-4′ ($J_{3',4'}$ 4.5–5.0 Hz), are indicative of an axial OAc group at C-3′ and an equatorial one in C-4′, respectively. The SMe group and the alkyl substituents at the 1,2,4-triazole ring were assigned. The structures of the free nucleosides **10a–d** and **18a–c** were confirmed by the ^{1}H NMR and mass spectra. The ^{1}H NMR spectra (DMSO-d_6/D_2O) showed a close similarity in their coupling constants to those of the acylated analogs, indicative of the pyranose ring with a $^4C_1$ conformation. Compound **10d** was selected for HMQC[44] NMR to confirm the methylene groups CH_2-5–CH_2-9 of the azepine ring at δ 2.82, 1.51, 1.81, 1.65, and 4.14, respectively. Furthermore, these protons were identified by a comparison to those of the analogs bearing the same azepine group.[35] Moreover, compound **10a** was selected for further NMR spectroscopic study to prove the α configuration. Thus, HMQC spectrum of **10a** showed a signal at δ_C 156.2 assigned to C-3 as it has a cross peak to δ_H 2.75 of H-5′, which gives an evidence for the α configuration of the triazole ring. The *trans*- $^3J_{C\text{-}3,C\text{-}4'}$ coupling (4.0 Hz) is an additional proof for the α configuration, as compared to earlier studies.[40,41]

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EXPERIMENTAL

General Method

Melting points are uncorrected. NMR spectra were measured with Bruker AC-250, WM-250 with TMS as internal standard and on a δ scale in ppm. EI and FAB mass spectra were recorded on a MAT 312 mass spectrometer using 3-nitrobenzylalcohol (NBOH) or glycerol as matrix. Some molecular ions were detected by doping the samples with Na^+ ion. The cycloaddition was carried out with exclusion of moisture.

Methyl 3,6-di-*O*-acetyl-4,5-dideoxy-2,6-dithio-α-D,L-*threo*-hex-4-en-2-ulopyranosidononitrile (3). A solution of diene **2** (1.0 g, 5.87 mmol) in toluene (40 mL) was stirred under reflux with MCDF (1.23 g, 11.74 mmol) for 24 hr. The solution was concentrated to approximately 8 mL, and kept overnight at 23°C to give **3** (0.59 g, 35%) as a crystals; m.p. 67–70°C (lit.[37] 68–70°C). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 6.12 (dd, 1H, $J_{4,5}$ 3.3 Hz, H-4), 6.01 (m, 1H, H-5), 5.76 (dd, 1H, $J_{3,4}$ 3.9 Hz, $J_{3,5} < 1.0$ Hz, H-3), 4.13 (dd, 1H, $J_{5,6}$ 3.8, $J_{4,6} < 1.0$ Hz, H-6), 2.46 (s, 3H, SMe), 2.23, 2.16 (2 × s, 6H, 2 × OAc). Anal. Calcd for $C_{11}H_{13}NO_4S_2$ (287.4): C, 45.98; H, 4.56; N, 4.87. Found: C, 45.79; H, 4.48; N, 4.69. MS, m/z (FAB) 288 $[MH]^+$.

Methyl 3,6-di-*O*-acetyl-2,6-dithio-α-D,L-*arabino*-2-hexulopyranosidononitrile (4). To a solution of **3** (0.50 g, 1.74 mmol) in dry pyridine (5 mL) was added a solution OsO_4 (0.71 g, 2.77 mmol) in dry pyridine (4 mL). The reaction mixture was stirred at 23°C for 22 hr, followed by addition of a solution of sodium bisulfate (1.30 g) in a mixture of pyridine (14 mL) and water (21 mL), and the mixture was stirred for an additional 4 hr. The reaction mixture was extracted with CH_2Cl_2 (4 × 30 mL), dried (Na_2SO_4), filtered, and evaporated to dryness to give a syrup. The syrup was dissolved in toluene (4 mL) and poured onto column of SiO_2 (15 g) using, in gradient, ethyl acetate (0–35%) and toluene as eluent. Evaporation of the appropriate fractions and recrystallization from CH_2Cl_2–petroleum ether furnished **4** (0.39 g, 70%) as a crystalline product, m.p. 107–108. ^{1}H NMR ($CDCl_3/D_2O$): δ 5.34 (d, 1H, $J_{3,4}$ 2.5 Hz, H-3), 4.45 (dd, 1H, $J_{5,6}$ 10.0, $J_{4,5}$ 4.8 Hz, H-5), 4.19 (d, 1H, H-6); 3.20 (dd, 1H, H-4), 2.52 (s, 3H, same), 2.20, 2.13 (2 × s, 6H, 2 × OAc). Anal. Calcd for $C_{11}H_{15}NO_6S_2$ (321.4): C, 41.11; H, 4.70; N, 4.36. Found: C, 39.97; H, 4.59; N, 4.18. MS, m/z (FAB) 322 $[MH]^+$, 344 $[MMa]^+$.

Methyl 3,4,5,6-tetra-*O*-acetyl-2,6-dithio-α-D,L-*arabino*-2-hexulopyranosidononitrile (5). A solution of **4** (0.72 g, 2.24 mmol) in dry pyridine (8 mL) was treated with acetic anhydride (5 mL) and the reaction mixture was kept at 23°C for 12 hr. A few drops of water were added and stirred for 1 hr, then the solution was partitioned successively between CH_2Cl_2 (60 mL), 5% H_2SO_4 solution (4 × 25 mL), 5% $NaHCO_3$ solution (35 mL), and finally washed with water (35 mL). The organic layer was dried (Na_2SO_4), filtered, and evaporated to dryness. The residue was purified on short column of SiO_2 (10 g), using toluene–ethyl acetate (4 : 1) as fluent to give **5** (0.78 g, 86%) as a syrup. ^{1}H NMR ($CDCl_3$): δ 5.37 (dd, 1H, $J_{5,6}$ 10.0, $J_{4,5}$ 4.9 Hz, H-5), 5.20 (d, 1H, $J_{3,4}$ 3.0 Hz, H-3), 5.12 (dd, 1H, H-4), 4.20 (d, 1H, H-6), 2.54 (s, 3H, SMe), 2.27, 2.24, 2.21, 2.17 (4 × s, 12H, 4 × OAc). ^{13}C ($CDCl_3$): δ 171.0, 169.8, 168.3 (CO); 111.0 (CN; $J_{CN,C\text{-}4} <$ 1.0 Hz); 73.9 (C-3); 73.0 (C-4); 69.5 (C-2); 59.9 (C-1′); 58.8 (C-5′); 20.6 (CH_3); 12.1 (SMe). MS, m/z (FAB) $C_{15}H_{19}NS_2O_8$ (406) $[MH]^+$, 428 $[MNa]^+$.

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Preparation of Acylated Glycosyl-1*H*-1,2,4-triazole Nucleosides 9 and 17

General Procedure

A solution of $SbCl_5$ (0.60 g, 2.0 mmol) in CH_2Cl_2 (10 mL) was added drop wise to a stirred, cooled (−60°C) solution of the glycosyl cyanide **5** (0.41 g, 1.0 mmol) and the required 1-(chloroalkyl)azo compounds **6** or **13** (2.0 mmol) in CH_2Cl_2 (20 mL). Pentane (200 mL) was added and the resulting precipitate was dissolved in MeCN (47 mL). After cooling of the mixture to 0°C, water (200 mL) and $NaHCO_3$ (30 mL) were added and the mixture was stirred at 23°C for 2 hr. The organic phase was separated and the aqueous phase was extracted with men (3 × 40 mol). The combined organic extracts were dried (Na_2SO_4), filtered, and evaporated to dryness and the residue was dissolved in CH_2Cl_2 (4 mL), and poured onto SiO_2 column. Elution, in gradient, with MeOH (0–10%) and CH_2Cl_2 afforded **9** and **17** as foam.

1,5-Dimethyl-3-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1*H*-1,2,4-triazole (9a). From **6a** (0.36 g). Yield: 0.22 g, 47%. ^{1}H NMR ($CDCl_3$): δ 5.26 (dd, 1H, $J_{4',5'}$ 9.2, $J_{3',4'}$ 4.7 Hz, H-4′), 5.17 (d, 1H, $J_{2',3'}$ 2.7 Hz, H-2′), 5.01 (dd, 1H, H-3′); 4.18 (d, 1H, H-5′), 3.47 (s, 3H, N-Me), 2.54 (s, 3H, SMe), 2.23, 2.21, 2.20, 2.17 (4 × s, 12H, 4 × OAc), 2.15 (s, 3 H, C_5-Me). Anal. Calcd for $C_{18}H_{25}N_3O_8S_2$ (475.5): C, 45.46; H, 5.30; N, 8.84. Found: C, 45.26; H, 5.21; N, 8.66. MS, m/z (FAB) 476 $[MH]^+$.

1-Ethyl-5-methyl-3-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1*H*-1,2,4-triazole (9b). From **6b** (0.38 g). Yield: 0.25 g, 52%. ^{1}H NMR ($CDCl_3$): δ 5.23 (dd, 1H, $J_{4',5'}$ 9.1, $J_{3',4'}$ 4.9 Hz, H-4′), 5.18 (d, 1 H, $J_{2',3'}$ 2.8 Hz, H-2′), 5.04 (dd, 1H, H-3′), 4.14 (d, 1H, H-5′), 3.80 (q, 2H, *J* 7.0 Hz, N*CH*$_2$CH$_3$), 3.47 (s, 3H, N-Me), 2.56 (s, 3H, SMe), 2.21, 2.20, 2.18 (2 ×), 2.16 (4 × s, 15 H, 4 × OAc; C_5-Me), 1.07 (t, 3H, *J* 7.0 Hz, NCH$_2$*CH*$_3$). Anal. Calcd for $C_{19}H_{27}N_3O_8S_2$ (489.7): C, 46.61; H, 5.56; N, 8.58. Found: C, 46.40; H, 5.50; N, 8.39. MS, m/z (FAB) 490 $[MH]^+$.

5,6,7,8-Tetrahydro-2-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1,2,4-triazolo[1,5-*a*]pyridine (9c). From **6c** (0.41 g). Yield: 0.26 g, 52%. ^{1}H NMR ($CDCl_3$): δ 5.20 (dd, 1H, $J_{4',5'}$ 9.4, $J_{3',4'}$ 5.0 Hz, H-4′), 5.18 (d, 1H, $J_{2',3'}$ 2.8 Hz, H-2′), 5.12 (dd, 1H, H-3′), 4.22–418 (m, 3H, CH_2-5, H-5′), 2.85 (m, 2H, CH_2-6), 2.59 (s, 3H, SMe), 2.21, 2.219, 2.17 2.14 (4 × s, 12H, 4 × OAc), 1.78 (m, 2H, CH_2-8), 1.634 (m, 2H, CH_2-9), 1.52 (m, 2H, CH_2-7). Anal. Calcd for $C_{20}H_{27}N_3O_8S_2$ (501.6): C, 47.89; H, 5.43; N, 8.38. Found: C, 47.65; H, 5.37; N, 8.13. MS, m/z (FAB) 524 $[MNa]^+$.

6,7,8,9-Tetrahydro-2-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-5*H*-1,2,4-triazolo[1,5-*a*]azepine (9d). From **6d** (0.44 g). Yield: 0.41 g, 40%. ^{1}H NMR ($CDCl_3$): δ 5.29 (dd, 1H, $J_{4',5'}$ 9.5, $J_{3',4'}$ 5.5 Hz, H-4′), 5.21 (d, 1H, $J_{2',3'}$ 2.7 Hz, H-2′), 5.16 (dd, 1H, H-3′), 4.15 (m, 3H, CH_2-10, H-5′), 2.85 (m, 2H, CH_2-6), 2.60 (s, 3H, SMe), 2.23, 2.21, 2.19 (2 ×) (3 × s, 12H, 4 × OAc), 1.81 (m, 2H, CH_2-8), 1.67 (m, 2H, CH_2-9), 1.55 (m, 2H, CH_2-7). Anal. Calcd for $C_{21}H_{29}N_3O_8S_2$ (515.6): C, 48.92; H, 5.67; N, 8.15. Found: C, 48.73; H, 5.59; N, 7.92. m/z (FAB) 538 $[MNa]^+$.

3-Methyl-5-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1-(2,4,6-trichloro-phenyl)-1*H*-1,2,4-triazole (17a). From **13a** (0.66 g). Yield: 0.21 g, 42%. ^{1}H NMR ($CDCl_3$): δ 7.93, 7.92 (AA′BB′, 2H, ArH), 5.34 (dd, 1H,

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$J_{4',5'}$ 9.4, $J_{3',4'}$ 4.7 Hz, H-4′), 5.28 (d, 1H, $J_{2',3'}$ 2.9 Hz, H-2′), 5.25 (dd, 1H, H-3′), 4.28 (d, 1H, H-5′), 2.59 (s, 3H, SMe), 2.38 (s, 3H, C_5-Me), 2.26, 2.24, 2.22, 2.19 (4 × s, 12H, 4 × OAc). Anal. Calcd for $C_{23}H_{24}Cl_3N_3S_2O_8$ (640.9): C, 43.10; H, 3.77; N, 6.56. Found: C, 42.87; H, 3.68; N, 6.29. MS, m/z (FAB) 641/643 $[MH]^+$.

1-(4-Fluorophenyl)-3-methyl-5-(2,3,4,5-tetra-*O*-acetyl-1,5-dithio-1-methylthio-α-D,L-*arabino*pentulopyranos-1-yl)-1*H*-1,2,4-triazole (17b). From **13b** (0.52 g). Yield: 0.41 g, 73%. ^{1}H NMR ($CDCl_3$): δ 7.96–7.48 (m, 4H, ArH), 5.22 (dd, 1H, $J_{4',5'}$ 9.4, $J_{3',4'}$ 4.8 Hz, H-4′), 5.01 (d, 1H, $J_{2',3'}$ 2.9 Hz, H-2′), 4.97 (dd, 1H, H-3′), 4.14 (d, 1H, H-5′), 2.58 (s, 3H, SMe), 2.34 (s, 3H, C_5-Me), 2.22, 2.20, 2.18, 2.16 (4 × s, 12H, 4 × OAc). Anal. Calcd for $C_{23}H_{26}FN_3O_8S_2$ (555.6): C, 49.72; H, 4.72; N, 7.56. Found: C, 49.52; H, 4.63; N, 7.31. MS, m/z (FAB) 556 $[MH]^+$.

3-Methyl-1-2,3,4,5-tetra-*O*-acetyl-(4-nitrophenyl)-5-(1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1*H*-1,2,4-triazole (17c). From **13c** (0.54 g). Yield: 0.36 g, 79%. ^{1}H NMR ($CDCl_3$): δ 7.98–7.50 (m, 4H, ArH), 5.23 (dd, 1H, $J_{4',5'}$ 9.5 $J_{3',4'}$ 4.9 Hz, H-4′), 5.06 (d, 1H, $J_{2',3'}$ 3.0 Hz, H-2′); 5.01 (dd, 1H, H-3′), 4.16 (d, 1H, H-5′), 2.59 (s, 3H, SMe), 2.36 (s, 3H, C_5-Me), 2.25, 2.22, 2.20, 2.19 (4 × s, 12H, 4 × OAc). Anal. Calcd for $C_{23}H_{26}N_4O_{10}S_2$ (582.6): C, 47.42; H, 4.50; N, 9.62. Found: C, 47.21; H, 4.41; N, 9.41. MS, m/z (FAB) 583 $[MH]^+$.

Preparation of Free Nucleosides (10) and (18)

General Procedure

A solution of acylated nucleosides **9** and **17** (1.3 mmol) in 0.3 M NaOMe (25 mL) was stirred at 23°C for 18 hr. The solution was neutralized with 0.1 M HCl and filtered. The filtrate was evaporated to dryness and the residue was partitioned between water (30 mol) and Et_2O (3 × 20 mL). The aqueous layer was evaporated to dryness and then co-evaporated with EtOH (3 × 20 mL). The residue was purified on SiO_2 column using MeOH, in gradient (0–20%) and CH_2Cl_2 as eluent. Evaporation of the appropriate fractions gave the pure nucleosides **10** and **18**.

1,5-Dimethyl-3-(1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1*H*-1,2,4-triazole (10a). From **9a** (0.62 g). Yield: 0.32 g, 81%; m.p. 145–148°C. ^{1}H NMR (DMSO-d_6/D_2O): δ 3.56 (s, 3H, NMe), 3.26 (dd, 1H, $J_{4',5'}$ 9.5, $J_{3',4'}$ 4.6 Hz, H-4′), 3.20 (d, 1H, $J_{2',3'}$ 3.0 Hz, H-2′), 3.04 (dd, 1H, H-3′), 2.75 (d, 1H, H-5′), 2.61 (s, 3H, SMe), 2.27 (s, 3 H, C_5-Me). ^{13}C NMR (DMSO-d_6): δ 156.2 (C-3; $J_{C\text{-}3,C\text{-}4} < 1.0$ Hz), 151.3 (C-5), 70.6 (C-3′), 69.2 (C-4′), 76.4 (C-2′), 58.8 (C-1′), 56.2 (C-5′), 35.0 (N-Me), 12.6 (SMe); 11.0 (C_5-*Me*). Anal. Calcd for $C_{10}H_{17}N_3O_4S_2$ (307.4): C, 39.07; H, 5.57; N, 13.67. Found: C, 38.82; H, 5.39; N, 13.45. MS, m/z (FAB) 330 $[MNa]^+$.

1-Ethyl-5-methyl-3-(1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1*H*-1,2,4-triazole (10b). From **9b** (0.63 g). Yield: 0.33 g, 79%; m.p. 125–128°C. ^{1}H NMR (DMSO-d_6/D_2O): δ 4.19 (q, 2H, *J* 7.0 Hz, N*CH*$_2$CH$_3$), 3.29 (dd, 1H, $J_{4',5'}$ 9.5, $J_{3',4'}$ 4.7 Hz, H-4′), 3.23 (d, 1H, $J_{2',3'}$ 2.7 Hz, H-2′), 3.12 (dd, 1H, H-3′), 2.79 (d, 1H, H-5′), 2.64 (s, 3H, SMe), 2.27 (s, 3H, C_5-Me), 1.37 (t, 3H, *J* 7.0 Hz, NCH$_2$*CH*$_3$). Anal. Calcd for $C_{11}H_{19}N_3O_4S_2$ (321.4): C, 41.11; H, 5.96; N, 13.07. Found: C, 40.96; H, 5.79; N, 13.27. MS, m/z (FAB) 344 $[MNa]^+$.

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5,6,7,8-Tetrahydro-2-(1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1,2,4-triazolo[1,5-*a*]pyridine (10c). From **9c** (0.65 g). Yield: 0.33 g, 76%; m.p. 88–91°C. ^{1}H NMR (DMSO-d_6/D_2O): δ 3.22 (dd, 1H, $J_{4',5'}$ 9.0 $J_{3',4'}$ 4.8 Hz, H-4′), 3.12 (d, 1H, $J_{2',3'}$ 2.9 Hz, H-2′), 3.05 (dd, 1H, H-3′), 2.79 (pt, 2H, *J* 3.0 Hz, CH_2-6), 2.75 (d, 1H, H-5′), 2.53 (s, 3H, SMe), 1.78 (pt, 2H, *J* 5.5 Hz, CH_2-8), 1.60 (dt, 2H, *J* 5.0 Hz, CH_2-9), 1.49 (dt, 2H, *J* 5.2 Hz, CH_2-7). Anal. Calcd for $C_{12}H_{19}N_3O_4S_2$ (333.4): C, 43.23; H, 5.74; N, 12.60. Found: C, 42.97; H, 5.65; N, 12.45. MS, *m*/*z* (FAB) 334 $[MH]^+$.

6,7,8,9-Tetrahydro-2-(11,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-5*H*-1,2,4-triazolo-[1,5-*a*]azepine (10d). From **9d** (0.67 g). Yield: 0.29 g, 65%; m.p. 85–88°C. ^{1}H NMR (DMSO-d_6/D_2O): δ 4.14 (pt, 2H, *J* 5.0 Hz, CH_2-9), 3.24 (dd, 1H, $J_{4',5'}$ 9.0, $J_{3',4'}$ 4.7 Hz, H-4′), 3.19 (d, 1H, $J_{2',3'}$ 3.0 Hz, H-2′), 3.09 (dd, 1H, H-3′), 2.82 (pt, 2H, *J* 3.0 Hz, CH_2-5), 2.75 (d, 1H, H-5′), 2.61 (s, 3H, SMe), 1.81 (pt, 2H, *J* 5.6 Hz, CH_2-7), 1.65 (dt, 2H, *J* 5.2 Hz, CH_2-8), 1.51 (dt, 2H, *J* 5.4 Hz, CH_2-6). Anal. Calcd for $C_{13}H_{21}N_3O_4S_2$ (347.5): C, 44.94; H, 6.09; N, 12.09. Found: C, 44.60; H, 6.17; N, 11.87. MS, *m*/*z* (FAB) 348 $[MH]^+$.

3-Methyl-5-(1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1-(2,4,6-trichloro-phenyl)-1*H*-1,2,4-triazole (18a). From **17a** (0.83 g). Yield: 0.48 g, 78%; 101–104°C. ^{1}H NMR (DMSO-d_6/D_2O): δ 7.96, 7.94 (AA′BB′, 2H, ArH), 3.28 (dd, 1H, $J_{4',5'}$ 9.3 Hz, $J_{3',4'}$ 5.0 Hz, H-4′), 3.11 (d, 1H, $J_{2',3'}$ 4.1 Hz, H-2′), 3.11 (dd, 1H, H-3′), 2.69 (d, 1H, H-5′); 2.60 (s, 3H, SMe), 2.26 (s, 3H, C_5-Me). Anal. Calcd for $C_{15}H_{16}Cl_3N_3O_4S_2$ (472.8): C, 38.11; H, 3.41; N, 8.89. Found: C, 37.96; H, 3.29; N, 8.71. MS, *m*/*z* (FAB) 473/475 $[MH]^+$.

1-(4-Fluorophenyl)-3-methyl-5-(1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1*H*-1,2,4-triazole (18b). From **17b** (0.72 g). Yield: 0.42 g, 84%; m.p. 154–158°C. ^{1}H NMR (DMSO-d_6/D_2O): δ 7.51, 7.30 (AA′BB′, 4H, ArH), 3.73 (dd, 1H, $J_{4',5'}$ 9.4 Hz, $J_{3',4'}$ 4.8 Hz, H-4′), 3.21 (d, 1H, $J_{2',3'}$ 2.8 Hz, H-2′), 3.12 (dd, 1H, H-3′), 2.76 (d, 1H, H-5′), 2.62 (s, 3H, SMe), 2.27 (s, 3H, C_5-Me). Anal. Calcd for $C_{15}H_{18}FN_3O_4S_2$ (387.5): C, 46.50; H, 4.68; N, 10.85. Found: C, 46.17; H, 4.53; N, 10.53. MS, *m*/*z* (FAB) 410 $[MNa]^+$.

3-Methyl-1-(4-nitrophenyl)-5-(1,5-dithio-1-methylthio-α-D,L-*arabino*-pentulopyranos-1-yl)-1*H*-1,2,4-triazole (18c). From **17c** (0.76 g). Yield: 0.45 g, 84%; m.p. 121–124°C. ^{1}H NMR (DMSO-d_6/D_2O): δ 7.45, 7.32 (AA′BB′, 4H, ArH), 3.76 (dd, 1H, $J_{4',5'}$ 9.6 Hz, $J_{3',4'}$ 4.9 Hz, H-4′), 3.28 (d, 1H, $J_{2',3'}$ 2.9 Hz, H-2′), 3.14 (dd, 1H, H-3′), 2.79 (d, 1H, H-5′), 2.69 (s, 3H, SMe). Anal. Calcd for $C_{15}H_{18}N_4O_6S_2$ (414.5): C, 43.47; H, 4.38; N, 13.52. Found: C, 43.38; H, 4.19; N, 13.36. MS, *m*/*z* (FAB) 415 $[MH]^+$.

REFERENCES

1. Hobbs, J.B. Purine and pyrimidine targets. In *Comprehensive Medicinal Chemistry*; Hansch, C., Sammes, P., Taylor, G.B., Eds.; Pergamon: Oxford, 1990; Vol. 2, 299–332.
2. Gracie, J.C.; Fairy, P.; Camplo, M.; Charvet, A.S.; Mourier, N.; Trabaud, C.; Niddam, V.; Simon, V.; Kraus, J.L. Synthesis of new thiazolidinone nucleoside analogues. Nucleosides Nucleotides **1995**, *14*, 1379–1392.
3. Walker, R.T. 4′-Thio-deoxyribonucleosides, their chemistry and biological properties- R review. Spec. Pub. R. Soc. Chem. **1997**, *198*, 203–237.

MARCEL DEKKER, INC.
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4. Fernández-Bolanós, J.G.; Al-Masoudi, N.A.; Maya, I. Sugar derivatives having sulfur in the ring. Adv. Carbohydr. Chem. **1991**, *57*, 21–98.
5. Tiwari, K.N.; Messine, L.; Montgomery, J.; Secrist III, J.A.. Synthesis and biological activity of 4′-Thio-L-xylofuranosyl nucleosides. Nucleos. Nucleot. Nucleic Acids **2001**, *20*, 743–746, references therein.
6. Inguaggiato, G.; Jasamai, M.; Smith, J.E.; Slater, M.; Simon, C. Novel triazole 2′-deoxy- 4′-thionucleosides: stereoselective synthesis and bilogical evaluation. Nucleosides Nucleotides **1999**, *18*, 457–467.
7. Dyson, M.R.; Coe, P.L.; Walker, R.T. The synthesis and antiviral activity of some 4′-thio-2′-deoxy nucleoside analogues. J. Med. Chem. **1991**, *34*, 2782–2786.
8. Secrist III, J.A.; Tiwari, K.N.; Riodan, J.M. Montgomery, synthesis and biological activity of 2′-deoxy-4′-thio pyrimidine nucleosides J. J. Med. Chem. **1991**, *34*, 2361–2366.
9. Bellon, L.; Barascut, J.-L.; Imbach, J.-L. Effecient synthesis of 4-thio-D-ribofuranose and some 4′-thioribonucleosides. Nucleosides Nucleotides **1992**, *11*, 1467–1479.
10. Uenishi, J.; Takahashi, K.; Motoyama, M.; Akashi, H.; Sasaki, T. Synthesis and anti-tumor activities of D- and L-2′-deoxy-4′-thio pyrimidine nucleotides. Nucleosides Nucleotides **1994**, *13*, 1347–1361.
11. Wirsching, J.; Voss, J.; Adiwidjaja, G.; Balzarini, J.; De Clercq, E. Thiosugars. Part 9: synthesis and biological evaluation of some 4′-thio-L-arabino nucleoside analogues. Bioorg. Med. Chem. **2001**, *11*, 1049–1051, references therein.
12. Chu, C.K.; Beach, J.W.; Jeong, L.S.; Choi, B.G.; Comer, F.I.; Alves, A.J.; Schinazi, R.F. Enantiomeric synthesis of (+)-BCH-189 [(+)-(2*S*,5*R*)-1-[2-(hydroxymethyl)-1,3-oxathiolane-5-yl]cytosine] from D-mannose and its anti-HIV activity. J. Org. Chem. **1991**, *56*, 6503–6505; references therein.
13. Kim, H.O.; Park, Y.H.; Moon, H.R.; Joeng, L.S. Synthesis and biological evaluation of novel D-2′-azido-2′,3′-dideoxyarabinofuranosyl-4′-thiopyrimidines and purines. Bioorg. Med. Chem. Lett. **2002**, *12*, 2403–2406.
14. Al-Masoudi, N.A.; Hughes, N.A. Synthesis of 5-thio-D-altrose and some of its detrivatives. Carbohydr. Res. **1986**, *148*, 39–49.
15. Al-Masoudi, N.A.; Hughes, N.A. Synthesis of 5-thio-D-allose and the methyl 5-thio-α- and β-D-allopyranosides. Carbohydr. Res. **1986**, *148*, 25–37.
16. Al-Masoudi, N.A.; Hughes, N.A. 5-Thiopyranose. Part 11. Isopropylidene acetals of 5-thio-D-glucose, 5-thio-D-allose and 5-thio-D-altrose and some of their methyl glycosides. J. Chem. Soc. Perkin Trans. 1 **1987**, 1413–1420.
17. Al-Masoudi, N.A.; Hughes, N.A. 5-Thiopyranose part 12. Sulfur participation in displacement reactions of sulphonate esters of 5-thio-D-allose, 5-thio-D-altrose and 5-thio-D-glucose derivatives. J. Chem. Soc. Perkin Trans. 1 **1987**, 2061–2067.
18. Al-Masoudi, N.A.; Tooma, N.J. Synthesis of 3-amino-3-deoxy-5-thio-D-allose and 3-amino-3-deoxy-1,2:5,6-*S,O*-diisopropylidene-5-thio-α-D-glucofuranose. Carbohydr. Res. **1993**, *239*, 273–278.
19. Al-Masoudi, N.A.; Pfleiderer, W. The reaction of methyl 3-*O*-toluene-p-sulfonyl-α-D-glucopyranoside and its triacetate with sodium azide. Carbohydr. Res. **1993**, *242*, 287–290.
20. Al-Masoudi, N.A.; Hughes, N.A.; Tooma, N.J. Synthesis of 2-acetamido-2-deoxy-5-thio-D-altrose. Carbohydr. Res. **1995**, *272*, 111–119.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

21. Al-Masoudi, N.A.; Pfleiderer, W. Synthesis and reactions of 1-(5-thio-β-D-xylo-pyranosyl)lumazine and pyrimidine nucleosides. Tetrahedron **1993**, *49*, 7579–7592.
22. Al-Masoudi, N.A.; Pfleiderer, W.; Lazrak, H. Some novel 5-thio-β-D-glucopyranose derivatives of 6-azauracil nucleosides. Nucleosides Nucleotides **1993**, *12*, 687–699.
23. Al-Masoudi, N.A. Synthesis and conformations of 3-acetamido-3-deoxy-5-thio-D-xylose and 4-acetamido-4-deoxy-5-thio-L-lyxose and some of derivatives thereof. Carbohydr. Res. **1992**, *228*, 339–346.
24. Al-Masoudi, N.A. Synthesis of 3-azido-3-deoxy-5-thio-β-D-ribopyranose. Sulfur Lett. **1995**, *19*, 149–156.
25. Al-Masoudi, N.A. Synthesis of 3-deoxy-5-thio-β-D-*erythro*pentopyranose. Sulfur Lett. **1999**, *22*, 179–186.
26. Just, J.; Ramjeesingh, M. C-nucleosides and related compounds, V. The synthesis of D, L-4-(1β-ribofuranosyl)-3-carboxamidopyrazole (V), D, L-5-(1β-ribofuranosyl)-3-amino-1,2,4-triazole (IX). Tetrahedron Lett. **1975**, 985–988.
27. Huynh-Dinh, T.; Igolen, J.; Bisagni, E.; Marquet, J.; Civier, A. Synthesis of *C*-nucleosides part 14. 5(3)-Glycosyl-1,2,4-triazole-3(5)-carboxamides as analogues of ribavirin. J. Chem. Soc. Perkin Trans. 1 **1977**, 761–764.
28. Poonian, M.S.; Nowoswiat, E.F. Novel precursor for the synthesis of *C*-nucleoside analogues. Synthesis the *C*-nucleoside analogues of ribavirin, bredinin, and related compounds. J. Org. Chem. **1980**, *45*, 203–208.
29. Katagiri, N.; Tabei, N.; Atsuumi, S.; Haneda, T.; Kato, T. Synthesis of *C*-nucleosides by ring transformation of 1,3-oxazine derivatives. Chem. Pharm. Bull. **1985**, *33*, 102–109.
30. Sanghvi, Y.S.; Hanna, N.B.; Larson, S.B.; Fujitaka, J.M.; Willis, R.C.; Smith, R.A.; Robins, R.K.; Revankar, G.R. Synthesis and evaluation of 5-amino-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamidine and certain related nucleosides as inhibitors of purine nucleoside phosphorylase. J. Med. Chem. **1988**, *31*, 330–335.
31. Shen, G.-Y.; Robins, R.K.; Revankar, G.R. Synthetic studies on the isomeric *N*-methyl derivatives of C-ribavirin. Nucleosides Nucleotides **1991**, *10*, 1707–1717.
32. Towsend, L.B. *The Chemistry of Nucleosides and Nucleotides*; Plenum Press: New York, 1994; Vol. 3, 47–79.
33. Witkoaski, J.T.; Robins, R.K.; Sidwell, R.W.; Simon, L.N. Design, synthesis and broad spectrum antiviral activity of 1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide and related nucleosides. J. Med. Chem. **1972**, *15*, 1150–1154.
34. Schneller, S.W.; May, J.L.; De Clercq, E. Synthesis and antiviral properties of 8-amino-3-[(2-hydroxyethoxy)methyl]-1,2,4-triazolo[4,3,*a*]pyrazine. Croat. Chem. Acta **1986**, *596*, 307–311, Chem. Abstr. **1987**, *107*, 7490w.
35. (a) Al-Masoudi, N.A.; Hassan, N.A.; Al-Soud, Y.A.; Schmidt, P.; Gaafer, A.E-D M.; Weng, M.; Marino, S.; Schoch, A.; Amer, A.; Jochims, J.C. Synthesis of *C*- and *N*-nucleosides from 1-aza-2-azoniaellene and 1,3-diaza-2-azoniaaallene salts. J. Chem. Soc. Perkin Trans. 1 **1998**, 947–953; (b) Al-Masoudi, N.A.; Al-Soud, Y.A.; Geyer, A. Synthesis and spectroscopic analysis some acyclic *C*-nucleosides and the homo-*C*-analogues from 1-(chloroalkyl)-1-aza-2-azoniaallene salts. Tetrahedron **1999**, *15*, 751–758; (c) Al-Soud, Y.A.; Al-Masoudi, Y.A.; Lagoja, I.M. Synthesis and reactions of 1,5- and 1,3-dialkyl derivatives of (D-*manno*-pentitol-1-yl)-1*H*-1,2,4-triazole nucleosides derived from 1-(chloroalkyl)-1-aza-2-azoniaallene salts. Carbohydr. Res. **1999**, *318*, 67–74; (d) Al-Soud, Y.A.; Al-Masoudi, N.A. Synthesis of 3′-1,2,4-triazolo- and 3′-1,3,4-thiadiazoliminothymidines. Heteroatom Chem. **2003**, *14*, 298–303.

MARCEL DEKKER, INC.
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36. Vays, D.M.; Hay, G.W. Diels-Alder reactions with methyl cyanodithioformate. An approach to the synthesis of novel carbohydrates with sulfur in the ring. Chem. Commun. **1971**, 1411–1412.
37. Vays, D.M.; Hay, G.W. Studies on the synthesis of novel carbohydrates with sulfur in the ring. Part III. The synthesis of derivatives of 2,6-dithio-hex-4-en-2-ulopyranosidono-nitriles. Can. J. Chem. **1975**, *53*, 1362–1366.
38. Hoffmann, R.; Woodward, R.B. Orbital symmetries and *endo*- and *exo*- relationships in concerted cycloaddtion reactions. J. Am. Chem. Soc. **1965**, *87*, 4388–4389.
39. Al-Masoudi, N.A.; Hughes, N.A. 5-thiopyranose part 12. Sulfur participation in displacement reactions of sulphonate esters of 5-thio-D-allose, 5-thio-D-altrose and 5-thio-D-glucose derivatives. J. Chem. Soc. Perkin Trans. 1 **1987**, 2061–2067.
40. Marschal, J.L. *Carbon–Carbon–Proton NMR Couplings: Applications to Organic Stereochemistry and Conformational Analysis*; Verlag Chemie International: Beerfirld Beach, Florida, 1983.
41. Weigert, F.J.; Roberts, J.D. Nuclear magentic resonance spectroscopy. Carbon–carbon coupling. J. Am. Chem. Soc. **1972**, *94*, 6021–6025.
42. Wang, Q.; Amer, A.; Mohr, S.; Ertel, E.; Jochims, J.C. [3 + 2]-Cycloaddition of 1-aza-2-azoniaallene cations to multiple bonds. Tetrahedron **1993**, *49*, 9973–9986, references therein.
43. Lambert, L.B.; Shurvell, H.F.; Lightar, D.; Cooks, R.G. *Introduction to Organic Spectroscopy*; Macmillan Press: New York, 1987; 119–124.
44. Willker, W.; Leibfritz, D.; Kerssebaum, R.; Bermel, W. Gradient selection in inverse heteronuclear correlation spectroscopy. Magn. Reson. Chem. **1993**, *31*, 287–292, references therein.

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