H), 7.37 (s, 1 H, ring A aromatic H), 7.12, 7.68 (AB q, 2 H, J = 8.5 Hz, ring D aromatic H); m/e 339 (M^+, base), 324 (60), 308 (40).

High-resolution mass spectrum: Calcd for $C_{19}H_{17}NO_5$, 339.1102; found 339.1101.

Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.26; H, 5.01. Found: C, 67.26; H, 5.04.

Acknowledgment. This research was supported by NIH research Grant HL-12971, awarded by the National Heart, Lung, and Blood Institute, PHS/DHEW.

Registry No. (±)-**5**, 71700-15-7; (±)-**6**, 71700-16-8; (±)-**9**, 38542-77-7; **10**, 71700-17-9; **11**, 66408-32-0; (±)-**12**, 71733-83-0; (±)-**13**, 71700-18-0; (±)-**14**, 71700-19-1; (±)-**15**, 71700-20-4; (±)-**16**, 71700-21-5; (±)-**17**, 71700-22-6; (±)-**18**, 71700-23-7; (±)-**19**, 38542-77-7; **20**, 66408-31-9; (±)-**21**, 71748-78-2; (±)-**26**, 71700-24-8; (±)-**27**, 71700-25-9; (±)-**30**, 71700-26-0; 13-hydroxyberberine, 66408-27-3; berberine chloride, 633-65-8; oxybis(berberine), 66419-60-1.

Synthesis of Certain β-D-Ribofuranosylthiazole *C*-Nucleosides from a Versatile Precursor[1]

Thomas J. Cousineau and John A. Secrist III*

The Ohio State University, Department of Chemistry, Columbus, Ohio 43210

Received April 6, 1979

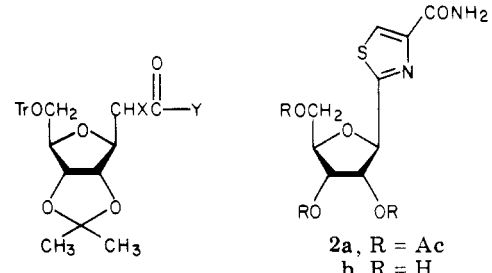
A synthesis of the versatile *C*-nucleoside precursor 3,6-anhydro-2-bromo-2-deoxy-4,5-*O*-isopropylidene-7-*O*-trityl-D-*allo*-heptose (**1c**) is described. Treatment of **1c** with various thiocarbamoyl-containing compounds (**6**) in hexamethylphosphoramide results in the formation of protected 2-substituted-5-*C*-ribosylthiazoles **7–9**. Liberation of the nucleosides **10–12** is accomplished with either methanolic hydrogen chloride or aqueous formic acid. Complete ^{13}C and ^1H NMR data are presented for all compounds.

Since the discoveries that several of the naturally occurring *C*-nucleosides have interesting biological properties,[2,3] considerable effort has been directed toward the synthesis of many structural analogues.[4] One of the principal synthetic methods employed in the *C*-nucleoside area has been the formation of "ribose"-derived intermediates in which a side chain of from one to three carbon atoms, variously functionalized, is attached through a β linkage to the original anomeric carbon. This side chain has then formed the basis for the construction of a multitude of heterocyclic rings.[4]

During the course of our research, we have developed a convenient preparation of the versatile *C*-nucleoside precursor 3,6-anhydro-2-bromo-2-deoxy-4,5-*O*-isopropylidene-7-*O*-trityl-D-*allo*-heptose (**1c**). We present herein the details of the synthesis of **1c** and demonstrate the utility of **1c** through the construction of certain 2-substituted-5-*C*-ribosylthiazoles.

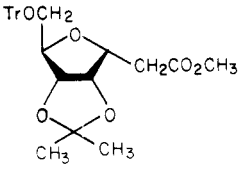
Recently, syntheses of several 2-*C*-ribosylthiazoles have been developed via a thiocarboxamide-substituted carbohydrate.[5-7] Two of these compounds (**2a,b**) have shown useful antiviral activity, a clue to their activity perhaps being that both compounds are active inhibitors of guanine nucleotide biosynthesis.[7] Other thiazole *C*-nucleosides have also been reported, such as those where the thiazole is attached to an acyclic carbohydrate moiety or is attached to the carbohydrate at a site other than the anomeric carbon.[8-12]

The starting point for the preparation of **1c** was the crystalline ester **1a**, readily available from D-ribose in three steps.[13,14] It has been determined that **1a** undergoes a facile base-catalyzed epimerization via an open-chain intermediate to the α anomer **3**, with the equilibrium lying well on the side of **3**.[13] Thus, a synthetic procedure was



1a, X = H; Y = OCH_3
b, X = Y = H
c, X = Br; Y = H

2a, R = Ac
b, R = H



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sought which would avoid this isomerization, since the majority of naturally occurring *C*-nucleosides possess the β configuration.

Treatment of **1a** with 1.1 equiv of diisobutylaluminum hydride in toluene at −78 °C afforded solely the β aldehyde

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(14) Cousineau, T. J.; Secrist, J. A., III. *J. Carbohydr., Nucleosides, Nucleotides* **1976**, *3*, 185–9.

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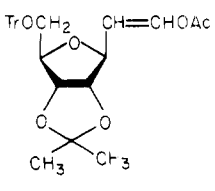
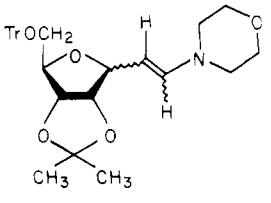
1b in 90% yield. The configurational assignment for **1b** (as well as many other compounds in this research) was made on the basis of ^{13}C NMR data. It is well established that for structures based on 2,3-*O*-isopropylidene-D-ribofuranose, in the β anomer the isopropylidene methyls occur at 25.5 ± 0.2 and 27.5 ± 0.2 ppm, while in the α anomer these signals occur at 24.9 ± 0.3 and 26.3 ± 0.2 ppm.[13] In addition, we have found that in the vast majority of cases, the $\Delta\delta$ for these same two methyl groups is 1.90 ± 0.20 ppm for the β anomer and 1.25 ± 0.20 ppm for the α anomer. The ^{13}C NMR spectrum of **1b** exhibits methyl signals at 25.60 and 27.49 ppm, with a $\Delta\delta$ of 1.89 ppm, clearly indicative of the β configuration. Further support for the configurational assignments comes from an examination of the chemical shift of the central or quaternary isopropylidene carbon. From a study of over 60 examples, we have ascertained that this resonance signal usually appears at 114.5 ± 0.6 ppm for a β anomer and at 112.7 ± 0.6 ppm for an α anomer. Thus, a value of 114.51 ppm for the quaternary carbon of **1b** is consistent with a β configuration.

Conversion of **1b** to **1c** by direct halogenation under a variety of conditions proved unsuccessful.[15] Attention was then turned to the production of **1c** via bromination of a masked aldehyde. Preparation of isomeric enol acetates **4a** and **4b**, both β as judged by ^{13}C NMR data, was accom-



4a, *E* isomer
b, *Z* isomer



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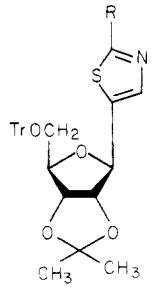
6a, R = CH_3
b, R = CH_2Ph
c, R = H
d, R = $CH_2CO_2CH_3$
e, R = NH_2
f, R = OCH_2CH_3
g, R = $S^-NH_4^+$
h, R = Ph
i, R = $CO_2CH_2CH_3$

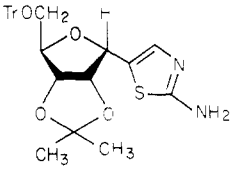
plished by either of two methods. Treatment of **1b** with acetic anhydride and K_2CO_3 in refluxing acetonitrile afforded in 78% yield a 1:1 mixture of **4a**/**4b**. Alternatively, reaction of **1b** with acetic anhydride, triethylamine, and a catalytic amount of 4-(dimethylamino)pyridine in THF at room temperature afforded a 9:1 ratio of **4a**/**4b** in 73% yield.[16] After numerous trials,[17] transformation of **4** into **1c** was realized by adapting a procedure previously employed for the conversion of olefins to bromohydrins.[18] Treatment of **4** with *N*-bromosuccinimide in moist dimethyl sulfoxide produced **1c** in 73% yield after processing. The bromo aldehyde is an inseparable mixture of diastereomers (differing in configuration only at C_2).

As an alternative approach to **1c**, the morpholine enamine **5** was also prepared under mild conditions, but ^{13}C NMR analysis demonstrated that the enamine existed as an α/β mixture. Thus, although the α-bromo aldehyde was available via bromination of **5**, the presence of both anomers of **5** made this approach unsuitable.

Bromo aldehyde **1c** is a highly functionalized intermediate which should have application for the syntheses of many diverse types of *C*-nucleosides. The remainder of this paper is specifically devoted to the conversion of **1c** to a variety of thiazole *C*-nucleosides.

The formation of thiazoles from **1c** by reaction with various thioamides under standard conditions met with little success.[19] Acceptable yields of thiazoles were obtained by using hexamethylphosphoramide (HMPA) as the solvent under carefully defined conditions (see Experimental Section). Thus, condensation of **1c** with **6a** and **6b** afforded thiazoles **7a** and **7b** in yields of 25 and 51%,





7a, R = CH_3
b, R = CH_2Ph
c, R = H
d, R = $CH_2CO_2CH_3$
e, R = CH_2CONH_2
f, R = NH_2
g, R = OCH_2CH_3

8

respectively. The structural assignment for **7a**, for example, is apparent from spectral data. The ^1H NMR exhibited a three-proton singlet at δ 2.59 (thiazole methyl) and a one-proton singlet at δ 7.47 (H_4). The configuration was readily assigned as β from the ^{13}C NMR spectrum, which showed the isopropylidene methyl carbons at 25.64 and 27.59 ppm and the central isopropylidene carbon at 114.85 ppm. By the same procedure, thiazoles **7c** and **7d** were prepared from thioamides **6c** and **6d**. In each case the spectral data indicated the presence of the thiazole ring as well as the β configuration.

Since a number of biologically active nucleosides, including pyrazofurin, sangivamycin, and the thiazoles **2a** and **2b**, possess a carboxamide moiety, we wished to prepare **7e** (as an intermediate leading to **10e**). This was readily accomplished by treatment of **7d** with methanolic ammonia in 81% yield with no loss of configurational integrity.

Unexpectedly, when **1c** was condensed with thiourea (**6e**) under the standard conditions, two isomeric thiazole *C*-nucleosides were formed. These were identified as the β anomer **7f** and the α anomer **8**. The ^{13}C NMR shifts for the three carbons of the isopropylidene group were in the proper position for each isomer (see Table III). In addition, in anomeric pairs of nucleosides,[20] *C*-glycosyl deriva-

(15) Among the methods investigated were the following: Br_2, $CaCO_3$, CH_2Cl_2, 0 °C; *N*-bromosuccinimide (NBS), $CHCl_3$, room temperature; $CuCl_2 \cdot 2H_2O$, LiCl, DMF, 80 °C; NBS, *hν*, $CHCl_3$, 40 °C; phenyltrimethylammonium tribromide, K_2CO_3, THF, room temperature.

(16) Cousineau, T. J.; Cook, S. L.; Secrist, J. A., III. *Synth. Commun.* **1979**, *9*, 157–63.

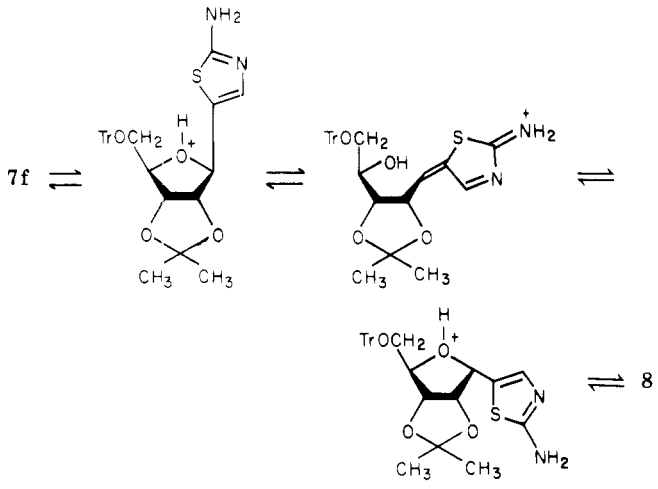
(17) Unsuccessful attempts to brominate the mixture of enol acetates **4a** and **4b** included: Br_2, CH_2Cl_2, 0 °C; NBS, CH_2Cl_2, room temperature; Br_2, K_2CO_3, CH_2Cl_2, 0 °C; NBS, methanol, room temperature.

(18) Dalton, D. R.; Dutta, V. P.; Jones, D. C. *J. Am. Chem. Soc.* **1968**, *90*, 5498–501.

(19) Employing thioacetamide (**6a**) and 2-phenylthioacetamide (**6b**), we explored variations in solvent (ethanol, tetrahydrofuran, pyridine, dimethylformamide, and dimethyl sulfoxide), temperature, concentration, and reactant proportions. Isolated yields of thiazole *C*-nucleosides from these trials varied from 0 to ca. 10% with many side products present.

(20) Townsend, L. B. *Synth. Proced. Nucleic Acid Chem.* **1973**, *2*, 333–9.

Scheme I

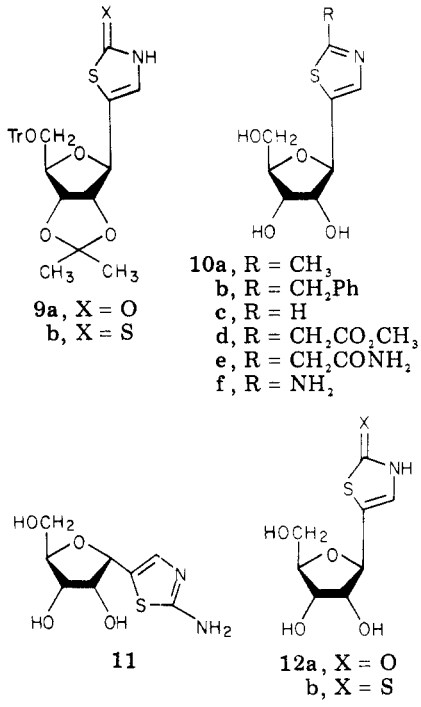


tives, and C-nucleosides[21] the $H_{1'}$ signal of the α anomer always appears at lower field than that of the β anomer. Thus, $H_{1'}$ occurs at δ 5.09 for **7f**, and at δ 5.30 for **8**. Finally, it has been demonstrated that the signal for $H_{4'}$ in anomeric pairs of 2′,3′-*O*-isopropylidene ribonucleoside derivatives appears as an "apparent triplet" for the α anomer and as a more complex multiplet for the β anomer.[22] For **7f**, $H_{4'}$ is a multiplet centered at δ 4.20, while for **8**, $H_{4'}$ appears as a triplet at δ 4.21.

Compounds **7f** and **8** appear to exist as the 2-amino rather than the 2-imino tautomers. From a series of fixed tautomeric compounds, it has been determined that for the 2-amino derivatives, H_4 occurs at ca. δ 7.14, while for the 2-imino compounds H_4 occurs at ca. δ 6.50.[23] The H_4 signals of **7f** and **8** appear at δ 7.02 and 7.04, respectively, both indicative of the 2-amino tautomer.

Since we know that equilibration of **1c** is not a problem under the reaction conditions, it may be that anomerization occurs after the thiazole is formed. When the β isomer **7f** was stirred with thiourea in HMPA, no equilibration occurred. However, when it was stirred in HMPA with thiourea hydrobromide, equilibration did occur. Thus it seems, as shown in Scheme I, that the combination of the 2-amino group and protonation of the furanose ring oxygen by the acid liberated in the reaction allows opening and reclosure to take place. That the α anomer predominates over the β anomer is consistent with other findings for 2,3-*O*-isopropylidene-substituted *C*-glycosides,[13] and a rationalization for this behavior has recently been presented.[24] When reaction times are shortened, production of the α anomer can be virtually eliminated, though yields decrease somewhat.

Treatment of **1c** with *O*-ethyl thiocarbamate (thionourethane, **6f**) produced not the 2-ethoxythiazole **7g** but rather the 2-thiazolone **9a**, which possessed a carbonyl stretch at 1660 cm^{-1} and no hydroxyl absorption in the infrared spectrum. Presumably, under the reaction conditions, **7g** is attacked by bromide ion to produce ethyl bromide and **9a**.[25] Similarly, treatment of **1c** with ammonium dithiocarbamate (**6g**) afforded the thiazolethione **9b**, whose lack of an SH stretch in the IR spectrum indicated a predominance of the thiono tautomer, as expected. Both



9a and **9b** were exclusively of the β configuration.

Not all thioamides examined condensed with **1c** to yield thiazoles. Neither thiobenzamide (**6h**) nor ethyl 2-thiooxamate (**6i**) produced any appreciable amounts of thiazole products, even under forcing conditions.

The free nucleosides **10a–f**, **11**, and **12a** were obtained by deprotecting the corresponding precursors with either methanolic hydrogen chloride or aqueous formic acid. No epimerizations occurred except in the deblocking of the β-2-aminothiazole **7f**, where 3-h reaction times caused significant formation of the α anomer **11** in addition to **10f**. If the acidic treatment was limited to only 10 min, pure **10f** could be isolated. An additional problem occurred in the protecting group removal from amide **7e**, where methanolic hydrogen chloride caused the production of considerable quantities of ester **10d**. A convenient solution to the problem was to prepare **10e** directly from **10d** by treatment with methanolic ammonia. Deprotection of **9b** under a variety of acidic conditions caused considerable decomposition, with no **12b** in evidence. Since thiazolethiones are known to be stable under acidic conditions,[25] participation by the proximate 5′-hydroxyl group may facilitate this decomposition.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are corrected. Infrared spectra were recorded on a Perkin-Elmer 467 grating infrared spectrophotometer, and only selected absorptions are given. ^1H NMR spectra were measured with a Varian EM-360 instrument and ^{13}C NMR spectra with a Bruker WP-80; chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. All ^{13}C NMR assignments are supported by the splittings in off-resonance decoupling experiments. Ultraviolet absorption spectra were recorded on a Cary 15 ultraviolet–visible spectrophotometer. Quantitative measurements were carried out by preparing a stock solution of the compound in water and then diluting it with either 0.1 N HCl, 0.1 N NaOH, or pH 7.0 phosphate buffer. Extinction coefficients (log ε) are listed in parentheses. High-resolution mass spectra were obtained on an AEI-MS9 spectrometer at 70 eV, and only selected fragmentations are given. Optical rotations were measured on a Perkin-Elmer 241 polarimeter in a 1 dm tube; concentrations are in g/100 mL. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, and Mr. William Rond, The Ohio State University. In all cases wherein analyses

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Table I. 60-MHz NMR Chemical Shifts[a]

compd	solvent	H_1	H_2	H_3–H_8 (carbohydrate)	H_7	isopropylidene CH_3	$H_{1'}$	$H_{2'}$, $H_{3'}$	$H_{4'}$	$H_{5'}$,$H_{5''}$	H_4 (thiazole)	OH	aromatic (trityl)	other
1a	C		2.67 (d)	4.04–4.80 (m)	3.11–3.38 (m)	1.31, 1.53 (2 s)							7.05–7.65 (m)	3.63 (s, CH_3)
1b	C	9.81 (t)	2.65–2.90 (d)	4.08–4.78 (m)	3.16–3.37 (m)	1.33, 1.54 (2 s)							7.12–7.65 (m)	
1c	C	9.30–9.42 (m), 9.49 (d)	4.03–4.87 (m)		3.16–3.39 (m)	1.31, 1.36, 1.55 (3 s)							7.02–7.61 (m)	
4a	C	hidden (aromatic)	5.50 (dd)	4.04–4.73 (m)	3.16–3.37 (m)	1.32, 1.53 (2 s)							7.10–7.68 (m)	2.10 (s, $COCH_3$)
4b	C	hidden (aromatic)	4.91–5.08 (m)	4.10–4.75 (m)	3.25 (d)	1.33, 1.57 (2 s)							7.12–7.69 (m)	2.13 (s, $COCH_3$)
5	C	hidden (aromatic)	6.19 (d)	4.02–4.74 (m)	3.11–3.32 (m)	1.33, 1.54 (2 s)							7.10–7.59 (m)	2.70–3.09 (m, CH_2N), 3.50–3.82 (m, CH_2O)
7a	C					1.29, 1.54 (2 s)	5.00 (d)	4.51–4.72 (m)	4.10–4.33 (m)	3.26 (t)	7.47 (s)		6.95–7.55 (m)	2.59 (s, CH_3)
7b	C					1.29, 1.54 (2 s)	4.96–5.12 (m)	4.55–4.70 (m)	4.10–4.35 (m)	3.15–3.35 (m)	7.60 (s)		6.98–7.55 (m)	4.25 (s, CH_2), 7.24 (s, ArH)
7c	C					1.34, 1.60 (2 s)	5.20 (d)	4.65–4.85 (m)	4.15–4.45 (m)	3.30 (t)	7.88 (s)		7.10–7.62 (m)	8.75 (s, H_2)
7d	C					1.29, 1.56 (2 s)	5.02–5.20 (m)	4.58–4.80 (m)	4.12–4.38 (m)	3.30 (t)	7.73 (s)		7.02–7.58 (m)	3.64 (s, OCH_3), 3.95 (s, CH_2)
7e	C					1.32, 1.59 (2 s)	5.09 (d)	4.56–4.77 (m)	4.14–4.41 (m)	3.20–3.41 (m)	7.64 (s)		7.12–7.58 (m)	3.87 (s, CH_2), 6.01 (br s, NH_2)
7f	C					1.32, 1.56 (2 s)	4.94 (d)	4.55–4.70 (m)	4.08–4.32 (m)	3.28 (t)	7.02 (s)		7.10–7.60 (m)	5.03–5.30 (br s, NH_2)
8	C					1.34, 1.58 (2 s)	5.30 (d)	4.70–4.82 (m)	4.21 (t)	3.17–3.37 (m)	7.04 (s)		7.10–7.55 (m)	5.01–5.20 (br s, NH_2)
9a	C					1.31, 1.55 (2 s)	5.50–5.85 (m)		4.10–4.40 (m)	3.15–3.40 (m)	6.59 (s)		7.10–7.60 (m)	10.06 (br s, NH)
9b	C						4.89 (d)	4.52–4.72 (m)	4.15–4.45 (m)	3.18–3.42 (m)	6.87 (s)		7.10–7.65 (m)	
10a	D						4.81 (d)	3.70–3.95 (m)		3.20–3.60 (m)	7.55 (s)	4.60–5.20 (br s)		2.60 (s, CH_3)
10b	D						4.90–5.05 (m)	3.72–3.95 (m)		3.28–3.58 (m)	7.60 (s)	4.70–5.25 (br s)		4.28 (s, CH_2), 7.31 (s, ArH)
10c	D						4.89 (d)	3.65–4.00 (m)		3.35–3.55 (m)	7.82 (s)	4.70–5.20 (br s)		8.96 (s, H_2)
10d	D						5.18 (d)	3.80–4.00 (m)		3.30–3.58 (m)	7.62 (s)	4.70–5.28 (br s)		3.66 (s, OCH_3), 4.12 (s, CH_2)
10e	D						5.20 (d)	3.70–4.10 (m)		3.32–3.65 (m)	7.58 (s)	4.60–5.20 (br s)		3.83 (s, CH_2), 7.10 (br s, NH_2)
10f	D						4.70 (d)	3.65–4.05 (m)		3.35–3.52 (m)	6.80 (s)	4.90–5.50 (br s)		
11	D						5.05 (d)	3.70–3.95 (m)		3.35–3.60 (m)	6.82 (s)	4.60–5.10 (br s)		
12a	D						4.46 (d)	3.60–3.98 (m)		3.31–3.60 (m)	6.87 (s)	4.80–5.30 (br s)		

[a] Chemical shifts are in ppm downfield from internal tetramethylsilane. [b] Solvents: C, $CDCl_3$; D, $(CD_3)_2SO$.

included solvents, the solvent protons were observed in the ^1H NMR spectra.

Toluene was distilled from calcium hydride and stored over 4A molecular sieves. Acetonitrile was predried over 4A molecular sieves, distilled from phosphorus pentoxide, and stored over 4A molecular sieves. Dimethyl sulfoxide was distilled under reduced pressure from sodium hydroxide pellets and stored over 4A molecular sieves. Hexamethylphosphoramide was distilled under reduced pressure from calcium hydride and stored at −10 °C.

Thin-layer chromatography was carried out on precoated glass TLC plates (silica gel F-254, 0.25-mm thickness) from EM Laboratories, Inc. Preparative thick-layer chromatography was performed on glass plates (20 × 20 cm) coated to a 2.0-mm thickness with 30 g of silica gel 60 PF-254 (EM Laboratories, Inc.) with calcium sulfate as binder. Solvent systems used (v/v) were: A, 1:1 benzene–ether; B, 4:1 petroleum ether–ether; C, 2:1 petroleum ether–ether; D, 1:1 petroleum ether–ether; E, 19:1 CH_2Cl_2–CH_3OH; F, 9:1 CH_2Cl_2–CH_3OH; G, 85:15 CH_2Cl_2–CH_3OH; H, 4:1 CH_2Cl_2–CH_3OH.

Methyl 3,6-Anhydro-2-deoxy-4,5-*O*-isopropylidene-7-*O*-trityl-D-*allo*-heptonate (1a). A solution of 20.0 g (0.133 mol) of D-ribose and 5.0 mL of concentrated H_2SO_4 in 400 mL of acetone was stirred for 1 h at room temperature. The reaction mixture was then neutralized with an excess of solid anhydrous sodium carbonate and filtered. Washing of the solids with acetone followed by concentration of the filtrate afforded ca. 25 g of a yellow syrup, consisting mainly of 2,3-*O*-isopropylidene-D-ribofuranose, R_f 0.50 (solvent A).

Without further purification, this material was dissolved in 50 mL of pyridine and treated with 44.5 g (0.160 mol) of triphenylmethyl chloride (trityl chloride) at room temperature for 24 h. The mixture was then poured into 650 mL of water. After the aqueous supernatant layer was decanted, the precipitated syrup was dissolved in 400 mL of dichloromethane and treated with a solution of 50.0 g of cadmium chloride in 500 mL of water. The resulting solids were then filtered and washed with CH_2Cl_2. The organic layer was separated, dried over anhydrous magnesium sulfate, and concentrated to give ca. 60 g of crude 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranose as a colorless foam, R_f 0.48 (solvent D).

This material was then dissolved in 650 mL of acetonitrile and treated with 66.9 g (0.200 mol) of carbomethoxymethylenetriphenylphosphorane at reflux for 8 h. The solvent was removed in vacuo and the residue purified by plug filtration on 250 g of silica gel with solvent D as eluant. Evaporation of the appropriate fractions afforded a sticky solid which was collected by filtration and washed with solvent B to give 26.3 g (41% overall) of **1a** as a free-flowing crystalline solid: mp 121–122 °C; R_f 0.60 (solvent D); IR (KBr) 2860, 1773, 1602, 1390 cm^{-1}; $[\alpha]^{25}_D$ + 5.24° (*c* 1.11, $CHCl_3$); NMR values are in Tables I–III; mass spectrum (calcd *m/e* 488.2199, found *m/e* 488.2207), *m/e* 488 (M^+), 473 (M − CH_3), 458 (M − 2 CH_3), 430 (M − C_3H_6O), 411 (M − C_6H_5), 259 (TrO^+), 243 (Tr^+).

Anal. Calcd for $C_{30}H_{32}O_6$: C, 73.75; H, 6.60. Found: C, 74.05; H, 6.71.

The filtrate contained the α anomer **3** (R_f 0.62, solvent D) and **1a** as the major components in a ratio of ca. 4:1, as indicated by TLC analysis.

3,6-Anhydro-2-deoxy-4,5-*O*-isopropylidene-7-*O*-trityl-D-*allo*-heptose (1b). A solution of 244 mg (0.50 mmol) of **1a** in 2.0 mL of toluene under a N_2 atmosphere was cooled to −78 °C, and 0.60 mL (0.55 mmol) of diisobutylaluminum hydride (19% in hexane) was added via syringe. TLC analysis (solvent D) after 30 min indicated complete disappearance of starting material. The reaction mixture was quenched with 1.0 mL of CH_3OH and allowed to warm to room temperature during 45 min. The resulting gelatinous solid was filtered through a pad of Celite and washed with ether. Concentration of the filtrate and purification by preparative TLC (solvent D) afforded 208 mg (91%) of **1b** as a colorless foam: R_f 0.55 (solvent D); IR (neat) 2920, 2740, 1718, 1595, 1390 cm^{-1}; $[\alpha]^{25}_D$ +6.63° (*c* 0.92, $CHCl_3$); NMR values are in Tables I–III; mass spectrum (calcd *m/e* 458.2093, found *m/e* 458.2102), *m/e* 458 (M^+), 443 (M − CH_3), 400 (M − C_3H_6O), 381 (M − C_6H_5), 243 (Tr^+).

Anal. Calcd for $C_{29}H_{30}O_5$: C, 75.96; H, 6.59. Found: C, 76.34; H, 6.71.

Table II. First-Order Coupling Constants (Hz)

compd	solvent[a]	$J_{1',2'}$ or $J_{1',2}$	$J_{2,3}$	$J_{6,7}$	$J_{4',5'}$
1a	C		6		
1b	C	2			
1c	C	2[b]			
4a	C	13	7		
4b	C			4	
5	C	12			
7a	C	4			3.5
7c	C	4			3.5
7d	C				3.5
7e	C	4			
7f	C	5			4
8	C	2			3.5
9b	C	4			
10a	D	6			
10c	D	6			
10d	D	6			
10e	D	6			
10f	D	6			
11	D	3			
12a	D	6			

[a] Solvents: C, $CDCl_3$; D, $(CD_3)_2SO$. [b] From the δ 9.49 signal.

(*E*)- and (*Z*)-1-*O*-Acetyl-3,6-anhydro-2-deoxy-4,5-*O*-isopropylidene-7-*O*-trityl-D-*allo*-hept-1-enitols (4a and 4b). Method A. A mixture of 215 mg (0.47 mmol) of aldehyde **1b**, 0.18 mL (1.87 mmol) of acetic anhydride, and 259 mg (1.87 mmol) of anhydrous potassium carbonate in 2.35 mL of acetonitrile was heated at reflux for 4 h. After the mixture was cooled, the solids were filtered and washed with chloroform, and the filtrate was evaporated to dryness. Purification by preparative TLC (solvent D) gave 199 mg (85%) of a mixture (ca. 1:1) of the *E* and *Z* isomers (**4a** and **4b**, respectively) as a colorless syrup, R_f 0.65 (solvent D). These two compounds could be separated by preparative TLC by using three developments with solvent B.

Method B. A mixture of 240 mg (0.52 mmol) of aldehyde **1b**, 0.15 mL (1.57 mmol) of acetic anhydride, 0.22 mL (1.57 mmol) of triethylamine, and 6 mg (0.05 mmol) of 4-(dimethylamino)-pyridine in 2.1 mL of dry THF was stirred at room temperature for 5 h. TLC analysis (solvent D) indicated greater than 95% conversion to products. After the reaction mixture was evaporated to dryness, the syrupy residue was dissolved in 25 mL of Et_2O, extracted with 10 mL of aqueous 10% $NaHCO_3$ solution, followed by 10 mL of water, dried over anhydrous magnesium sulfate, and concentrated. Purification by preparative TLC (solvent D) afforded 191 mg (73%) of **4a** and **4b** in a ratio of ca. 9:1.

4a: R_f 0.40 (solvent B); IR (neat) 2932, 1760, 1681, 1601, 1379, 943 cm^{-1}; $[\alpha]^{25}_D$ −20.9° (*c* 1.35, $CHCl_3$); NMR values are in Tables I–III; mass spectrum (calcd for M − CH_3 *m/e* 485.1964, found *m/e* 485.1974), *m/e* 500 (M^+), 485 (M − CH_3), 423 (M − C_6H_5), 243 (Tr^+).

4b: R_f 0.35 (solvent B); IR (neat) 2932, 1762, 1679, 1600, 1380 cm^{-1}; $[\alpha]^{25}_D$ −13.7° (*c* 1.50, $CHCl_3$); NMR values are in Tables I–III; mass spectrum (calcd for M − CH_3 *m/e* 485.1964, found *m/e* 485.1974), *m/e* 500 (M^+), 485 (M − CH_3), 423 (M − C_6H_5), 243 (Tr^+).

Anal. Calcd for $C_{31}H_{32}O_6$ (mixture): C, 74.38; H, 6.74. Found: C, 74.53; H, 6.65.

3,6-Anhydro-2-bromo-2-deoxy-4,5-*O*-isopropylidene-7-*O*-trityl-D-*allo*-heptose (1c). A solution of 136 mg (0.27 mmol) of **4** and 0.01 mL (0.54 mmol) of water in 1.36 mL of Me_2SO cooled in a water bath was treated with 97 mg (0.54 mmol) of *N*-bromosuccinimide. After stirring for 30 min, the reaction mixture was quenched with 2 mL of 10% aqueous $NaHCO_3$ solution, diluted with 5 mL of H_2O, extracted with 2 × 10 mL portions of ether, dried over anhydrous magnesium sulfate, and concentrated. Purification by preparative TLC (solvent D) gave 106 mg (73%) of **1c** as a colorless foam: R_f 0.65 (solvent D), these diastereomers could not be separated; IR (neat) 2935, 2730, 1733, 1598, 1390 cm^{-1}; $[\alpha]^{25}_D$ +9.1° (*c* 0.78, $CHCl_3$); NMR values are in Tables I–III; mass spectrum (calcd for $C_{29}H_{29}{}^{79}BrO_5$ *m/e* 536.1198, found *m/e* 536.1207), *m/e* 538, 536 (M^+), 523, 521 (M − CH_3), 461, 459 (M − C_6H_5), 457 (M − Br), 243 (Tr^+).

Table III. 80-MHz ^{13}C NMR Chemical Shifts[a]

compd	solvent	C_1	C_2	C_3	C_4	C_5	C_6	C_7	isopropylidene CH_3	isopropylidene CH_3	isopropylidene C_{qual}	$C_{1'}$	$C_{2'}$	$C_{3'}$	$C_{4'}$	$C_{5'}$	CPb_3	Ar (trityl)	C_{ipso} (trityl)	other
1a	C	170.92	38.49	80.90	83.55	82.28	84.25	64.26	25.65	27.52	114.19						86.68	127.17 127.79 128.73	143.84	51.74 (CH_3)
1b	C	199.86	47.35	79.61	83.63	82.25	84.49	64.23	25.60	27.49	114.51						86.73	127.08 127.88 128.68	143.78	
1c	C	190.74 192.13	52.86 55.95	81.62 82.23	83.99	82.59 82.90	84.35 84.96	63.90 64.33	25.55	27.37	114.27 114.80						86.84 87.20	127.08 127.26 127.86 128.71	143.46 143.76	
4a	C	138.27	112.44	81.95	83.26	82.63	85.30	64.33	25.63	27.53	114.43						86.80	127.05 127.83 128.80	143.90	20.54 (CH_3) 167.54 (C=O)
4b	C	136.32	112.24	78.65	83.55	82.87	85.93	64.47	25.73	27.57	114.04						86.90	127.15 127.88 128.85	143.90	20.63 (CH_3) 167.44 (C=O)
5(α)	C	143.12	93.60	82.68	82.97	82.97	85.64	64.71	25.20	26.51	112.10						87.14	127.05 127.83 128.75	144.00	46.51 (CH_2N) 68.16 (CH_2O)
5(β)	C	144.00	97.78	83.11	83.79	82.68	86.12	64.71	25.63	27.57	113.94						86.76	127.05 127.83 128.83	144.00	48.69 (CH_2N) 66.37 (CH_2O)
7a	C		166.44		139.43	137.31			25.64	27.59	114.85	80.75	86.76	82.39	83.78	63.94	86.76	127.11 127.84 128.81	143.86	19.87 (CH_3)
7b	C		171.09		139.58	137.88			25.58	27.57	114.91	80.74	86.75	82.34	83.70	63.99	86.75	127.05 127.88 128.80	143.85	40.05 (CH_2) 129.09 (C_{Ar})
7c	C		153.17		140.50	138.12			25.63	27.57	114.96	80.69	87.00	82.44	83.94	63.89	86.85	127.10 127.88 128.80	143.85	
7d	C		169.07		139.33	139.03			25.61	27.55	114.88	80.71	86.78	82.35	83.87	63.96	86.78	127.08 127.86 128.78	143.83	38.90 (CH_2) 52.37 (OCH_3) 161.85 (C=O)
7e	C		169.53		139.43	138.65			25.58	27.53	114.96	80.59	86.76	82.34	83.89	63.89	86.76	127.10 127.88 128.75	143.75	39.95 (CH_2) 163.80 (C=O)
7f	C		168.32		136.42	125.29			25.68	27.62	114.77	80.93	86.17	82.34	83.45	63.94	86.80	127.10 127.88 128.85	143.95	
8	C		170.41		138.95	122.54			25.10	26.41	112.97	78.75	83.65	82.34	83.16	64.81	87.44	127.29 128.02 128.75	143.70	

9a	C	175.21		117.85	119.77									
				25.58	27.53	114.87	81.46	84.96	82.24	83.65	63.89	86.90	127.15	143.80
													127.93	
													128.80	
9b	C	189.97		123.51	131.32								127.25	143.66
				25.54	27.48	115.06	80.49	85.54	82.29	84.04	63.79	86.95	127.93	
													128.75	
10a	D	165.10		139.27	138.64		77.37	77.37	71.40	85.43	61.98			18.77 (CH_3)
10b	D	169.34		139.53	138.12		77.43	77.24	71.37	85.59	61.95		139.09	38.79 (CH_2),
														126.76 (C_{Ar})
														128.56 (C_{Ar})
10c	D	153.61		140.31	139.29		77.63	77.14	71.37	85.64	61.95			128.85 (C_{Ar})
10d	D	169.29		139.29	140.16		77.53	77.24	71.46	85.64	62.00			38.11 (CH_2)
														52.04 (OCH_3)
														161.23 (C=O)
10e	D	169.48		138.85	139.43		77.43	77.29	71.41	85.49	62.00			39.76 (CH_2)
														163.46 (C=O)
10f	D	168.76		136.52	125.21		78.02	76.46	71.37	84.81	62.14			
11	D	170.50		137.64	122.05		76.80	72.87	72.34	81.66	61.70			
12a	D	172.59		119.28	118.65		78.50	75.30	71.22	84.96	61.90			

[a] Chemical shifts are in ppm downfield from internal tetramethylsilane. Assignments may be reversed in cases where chemical shifts are similar and multiplicities are identical by single-frequency decoupling. [b] Solvents: C, $CDCl_3$; D, $(CD_3)_2SO$.

Anal. Calcd for $C_{29}H_{29}BrO_5$: C, 64.81; H, 5.44. Found: C, 64.69; H, 5.55.

3,6-Anhydro-1,2-dideoxy-4,5-*O*-isopropylidene-1-morpholino-7-*O*-trityl-D-*allo*- and -D-*altro*-hept-1-enitol (5). To a solution of 263 mg (0.57 mmol) of aldehyde **1b** in 2.12 mL of benzene protected from moisture was added 75 mg (0.86 mmol, 0.02 mL) of morpholine. After the mixture was stirred 15 min at room temperature, the volatile components were removed by rotary evaporation followed by high-vacuum pumping to afford crude **5** as a colorless foam. This material was used without further purification: IR (neat) 2940, 2860, 1652, 1451, 1370 cm^{-1}; $[\alpha]^{25}_D$ −24.8° (rotation measured immediately after solution preparation), −18.8° (rotation measured seven days after solution preparation) (*c* 1.00, $CHCl_3$); NMR values are in Tables I–III; mass spectrum (calcd *m/e* 527.2671, found *m/e* 527.2684), *m/e* 527 (M^+), 512 ($M - CH_3$), 243 (Tr^+). Product instability precluded satisfactory elemental analysis.

General Condensation Procedure for 1c with Thiocarbamoyl-Containing Compounds. A solution of 645 mg (1.20 mmol) of bromo aldehyde **1c** and 3.00 mmol of the nucleophile in 7.2 mL of HMPA was stirred at 60 °C for 6 h. After being cooled, the reaction mixture was dissolved in 75 mL of Et_2O, extracted with 3 × 10 mL portions of H_2O, dried over anhydrous magnesium sulfate, and concentrated. Purification was accomplished by preparative TLC.

5-*C*-(2,3-*O*-Isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-2-methylthiazole (7a) was prepared from 225 mg of thioacetamide (**6a**): purification, solvent C; colorless foam, 154 mg (25%); R_f 0.35 (solvent C); IR (neat) 2920, 1597, 1388 cm^{-1}; UV λ_{max} (EtOH) 252 nm (acid), 257 (pH 7.0), 254 (base); NMR values are in Tables I–III; mass spectrum, *m/e* 513 (M^+), 498 ($M - CH_3$), 436 ($M - C_6H_5$), 243 (Tr^+).

2-Benzyl-5-*C*-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)thiazole (7b) was prepared from 453 mg of 2-phenylthioacetamide (**6b**): purification, solvent C; colorless foam, 365 mg (52%); R_f 0.28 (solvent C); IR (neat) 2930, 1600, 1389 cm^{-1}; UV λ_{max} (EtOH) 248 nm (acid), 249 (pH 7.0), 247 (base); NMR values are in Tables I–III; mass spectrum, *m/e* 589 (M^+), 574 ($M - CH_3$), 512 ($M - C_6H_5$), 243 (Tr^+).

5-*C*-(2,3-*O*-Isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-thiazole (7c) was prepared from 183 mg of thioformamide (**6c**): purification, solvent D; colorless foam, 276 mg (46%); R_f 0.40 (solvent D); IR (neat) 2920, 1596, 1386 cm^{-1}; UV λ_{max} (EtOH) 266 nm (acid), 261 (pH 7.0), 259 (base); NMR values are in Tables I–III; mass spectrum (calcd *m/e* 499.1817, found *m/e* 499.1830), *m/e* 499 (M^+), 498 ($M - H$), 484 ($M - CH_3$), 422 ($M - C_6H_5$), 243 (Tr^+).

2-(Carbomethoxymethylene)-5-*C*-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)thiazole (7d) was prepared from 400 mg of *O*-methyl 1-thiomalonamate (**6d**): purification, solvent D; colorless foam, 209 mg (31%); R_f 0.35 (solvent D); IR (neat) 2925, 1740, 1595, 1388 cm^{-1}; UV λ_{max} (EtOH) 250 nm (acid), 251 (pH 7.0), 248 (base); NMR values are in Tables I–III; mass spectrum, *m/e* 571 (M^+), 556 ($M - CH_3$), 494 ($M - C_6H_5$), and 243 (Tr^+).

2-(Carbamoylmethylene)-5-*C*-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)thiazole (7e). A solution of 236 mg (0.41 mmol) of **7d** in 10 mL of saturated methanolic ammonia was allowed to stand lightly stoppered at room temperature for 18 h. TLC analysis (solvent E) indicated complete disappearance of starting material. After the volatile materials were removed, the residue was dissolved in 20 mL of $CHCl_3$ and extracted with 25 mL of H_2O. The aqueous layer was back-extracted with 20 mL of $CHCl_3$, and the organic layers were combined, dried over anhydrous magnesium sulfate, and concentrated. Purification by preparative TLC, with solvent E, afforded 186 mg (81%) of **7e** as a colorless foam: R_f 0.20 (solvent E); IR (neat) 3318, 2925, 1681, 1597, 1386 cm^{-1}; UV λ_{max} (EtOH) 255 nm (acid), 261 (pH 7.0), 252 (base); NMR values are in Tables I–III; mass spectrum, *m/e* 556 (M^+), 541 ($M - CH_3$), 479 ($M - C_6H_5$), 243 (Tr^+).

2-Amino-5-*C*-(2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)thiazole (7f) and 2-amino-5-*C*-(2,3-*O*-isopropylidene-5-*O*-trityl-α-D-ribofuranosyl)thiazole (8) were prepared from 228 mg of thiourea (**6e**); purification and anomer separation were accomplished with ether (three elutions). Identical reaction conditions, with the exception of time, were employed

to determine the kinetic and thermodynamic products. Product ratios are those of isolated compounds purified by preparative TLC (reaction time, β/α ratios in parentheses, yield): 15 min (92/8), 34.5%; 30 min (74/26), 37%; 1 h (64/36), 45%; 2 h (42/58), 36%; 6 h or longer (27/73), 42%.

7f: colorless foam, 71 mg (11.5%); R_f 0.40 (ether); IR (neat) 3295, 2935, 1613, 1516, 1370 cm^{-1}; UV λ_{max} (EtOH) 259 nm (acid), 263 (pH 7.0), 263 (base); NMR values are in Tables I–III; mass spectrum (calcd m/e 514.1926, found m/e 514.1936), m/e 514 (M^+), 499 (M – CH_3), 437 (M – C_6H_5), 243 (Tr^+).

8: colorless foam, 190 mg (30.7%); R_f 0.35 (ether); IR (neat) 3316, 2920, 1620, 1509, 1360 cm^{-1}; UV λ_{max} (EtOH) 259 nm (acid), 264 (pH 7.0), 263 (base); NMR values are in Tables I–III; mass spectrum (calcd m/e 514.1926, found m/e 514.1941), m/e 514 (M^+), 499 (M – CH_3), 243 (Tr^+).

Epimerization of 7f. A solution of 206 mg (0.40 mmol) of **7f** and 157 mg (1.00 mmol) of thiourea hydrobromide (prepared by bubbling anhydrous hydrogen bromide into a methanolic solution of thiourea cooled to 0 °C and precipitating the product out with ether; mp 64–67 °C) in 2.4 mL of HMPA was heated at 60 °C for 4 h. Workup as before afforded 52 mg (25%) of **7f** and 109 mg (53%) of **8** (product ratio 32:68). When thiourea was substituted for thiourea hydrobromide in this reaction, **7f** was recovered unchanged.

5-*C*-(2,3-*O*-Isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-2(3*H*)-thiazolone (9a) was prepared from 315 mg of *O*-ethyl thiocarbamate (**6f**): purification, ether; colorless foam, 229 mg (37%); R_f 0.45 (ether); IR (neat) 3188, 2925, 1660, 1385, 1080 cm^{-1}; UV λ_{max} (EtOH) 254 nm (acid), 260 (pH 7.0), 261 (base); NMR values are in Tables I–III; mass spectrum (calcd m/e 515.1766, found m/e 515.1776), m/e 515 (M^+), 500 (M – CH_3), 457 (M – C_3H_6O), 438 (M – C_6H_5), 243 (Tr^+).

5-*C*-(2,3-*O*-Isopropylidene-5-*O*-trityl-β-D-ribofuranosyl)-2(3*H*)-thiazolethione (9b) was prepared from 330 mg of ammonium dithiocarbamate (**6g**): purification, ether; light yellow foam, 243 mg (38%); R_f 0.60 (ether); IR (neat) 3060, 2900, 1596, 1388, 1040 cm^{-1}; UV λ_{max} (EtOH) 321 nm (acid), 322 (pH 7.0), 314 (base); NMR values are in Tables I–III; mass spectrum m/e 531 (M^+), 243 (Tr^+).

General Deprotection Procedure. Method A. A 1.0 M solution of the protected *C*-nucleoside in 10% methanolic hydrogen chloride was allowed to stand at room temperature for 3 h. After evaporation of solvent, the residue was triturated with ether to remove trityl methyl ether. The residue was dissolved in methanol and passed through an Amberlite IR-45 (OH^-) column (3 × 12 cm) with 200 mL of methanol. The solution was concentrated, and the residue was purified by preparative TLC to afford the free *C*-nucleoside.

Method B. A 0.1 M solution of the protected *C*-nucleoside in 9:1 formic acid–water was allowed to stand at room temperature for 18 h. Processing and purification as in method A gave the free *C*-nucleoside.

2-Methyl-5-*C*-(β-D-ribofuranosyl)thiazole (10a). Method B (from 7a): purification, solvent F; white solid, 84%; mp 110–113 °C; R_f 0.25 (solvent F); IR (neat) 3335, 2910 cm^{-1}; UV λ_{max} 247 nm (log ε 3.81; acid), 240 (3.82; pH 7.0), 238 (3.90; base); $[\alpha]^{25}_D$ –60.4° (*c* 2.02, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 231.0565, found m/e 231.0570), m/e 231 (M^+), 213 (M – H_2O), 200 (M – CH_2OH), 128 (B + 30).

Anal. Calcd for $C_9H_{13}NO_4S \cdot 1.1CH_3OH$: C, 45.51; H, 6.58; N, 5.26. Found: C, 45.12; H, 6.30; N, 5.47.

2-Benzyl-5-*C*-(β-D-ribofuranosyl)thiazole (10b). Method A (from 7b): purification, solvent G; white solid, 74%; mp 110–112 °C; R_f 0.45 (solvent G); IR (neat) 3310, 2920 cm^{-1}; UV λ_{max} 254 nm (log ε 3.94; acid), 247 (3.97; pH 7.0), 248 (4.02; base); $[\alpha]^{25}_D$ –57.1° (*c* 3.26, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 307.0878, found m/e 307.0885), m/e 307 (M^+), 289 (M – H_2O), 230 (M – C_6H_5), 216 (M – $CH_2C_6H_5$), and 204 (B + 30).

Anal. Calcd for $C_{15}H_{17}NO_4S$: C, 58.61; H, 5.58; N, 4.56. Found: C, 58.26; H, 5.62; N, 4.51.

5-*C*-(β-D-Ribofuranosyl)thiazole (10c). Method B (from 7c): purification, solvent F; colorless foam, 82%; R_f 0.27 (solvent F); IR (neat) 3340, 2930 cm^{-1}; UV λ_{max} 244 nm (log ε 3.70; acid), 236 (3.73; pH 7.0), 236 (3.83; base); $[\alpha]^{25}_D$ –53.4° (*c* 2.05, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 217.0409, found m/e 217.0413), m/e 217 (M^+), 199 (M – H_2O), 114 (B + 30).

Anal. Calcd for $C_8H_{11}NO_4S \cdot 0.25CH_3OH$: C, 43.99; H, 5.37; N, 6.22. Found: C, 43.62; H, 5.22; N, 6.52.

2-(Carbomethoxymethylene)-5-*C*-(β-D-ribofuranosyl)thiazole (10d). Method A (from 7d): purification, solvent G; colorless foam, 46%; R_f 0.50 (solvent G); IR (neat) 3330, 2910, 1735 cm^{-1}; UV λ_{max} 251 nm (log ε 3.79; acid), 246 (3.80; pH 7.0), 247 (3.87; base); $[\alpha]^{25}_D$ –49.6° (*c* 3.19, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 289.0620, found m/e 289.0627), m/e 289 (M^+), 271 (M – H_2O), 258 (M – CH_2OH), 186 (B + 30).

Anal. Calcd for $C_{11}H_{15}NO_6S \cdot 0.50CH_3OH$: C, 45.23; H, 5.61; N, 4.59. Found: C, 45.19; H, 5.38; N, 4.73.

2-(Carbamoylmethylene)-5-*C*-(β-D-ribofuranosyl)thiazole (10e). Method A (from 7e): purification, solvent H; colorless foam, 46%; 44% of ester **10d** was also isolated from this reaction.

10e: R_f 0.20 (solvent H); IR (neat) 3320, 2915, 1655 cm^{-1}; UV λ_{max} 252 nm (log ε 3.78; acid), 246 (3.81; pH 7.0), 244 (3.86; base); $[\alpha]^{25}_D$ –51.8° (*c* 0.79, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 274.0623, found m/e 274.0632), m/e 274 (M^+), 243 (M – CH_2OH), 171 (B + 30).

Anal. Calcd for $C_{10}H_{14}N_2O_5S$: C, 43.78; H, 5.14; N, 10.22. Found: C, 43.55; H, 5.29; N, 9.88.

Preparation of Amide 10e from Ester 10d. A solution of 175 mg (0.61 mmol) of ester **10d** in 10 mL of saturated methanolic ammonia was allowed to stand lightly stoppered for 24 h. TLC analysis (solvent H) showed the complete disappearance of starting material. Removal of the volatile materials, followed by purification by preparative TLC (solvent H), afforded 129 mg (78%) of **10e**, identical with that prepared from **7e**.

2-Amino-5-*C*-(β-D-ribofuranosyl)thiazole (10f). Method A (10 min Reaction Time from 7f): purification, solvent H; colorless foam, 62%; R_f 0.25 (solvent H); IR (neat) 3310, 2920 cm^{-1}; UV λ_{max} 257 nm (log ε 3.98; acid), 259 (3.93; pH 7.0), 261 (3.94; base); $[\alpha]^{25}_D$ –71.4° (*c* 2.97, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 232.0518, found m/e 232.0523), m/e 232 (M^+), 214 (M – H_2O), 201 (M – CH_2OH), 129 (B + 30).

Anal. Calcd for $C_8H_{12}N_2S \cdot 0.50CH_3OH$: C, 41.11; H, 5.68; N, 11.28. Found: C, 40.90; H, 5.35; N, 10.97.

2-Amino-5-*C*-(α-D-ribofuranosyl)thiazole (11). Method A (10 min Reaction Time from 8): purification, solvent H; colorless foam, 63%; R_f 0.25 (solvent H); IR (neat) 3320, 2935 cm^{-1}; UV λ_{max} 258 nm (log ε 3.98; acid), 261 (3.94; pH 7.0), 261 (3.96; base); $[\alpha]^{25}_D$ –3.64° (*c* 1.10, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 232.0518, found m/e 232.0523), m/e 232 (M^+), 214 (M – H_2O), 201 (M – CH_2OH), 129 (B + 30).

Anal. Calcd for $C_8H_{12}N_2O_4S$: C, 41.37; H, 5.21; N, 12.06. Found: C, 41.52; H, 5.21; N, 11.78.

5-*C*-(β-D-Ribofuranosyl)-2(3*H*)-thiazolone (12a). Method B (from 9a): purification, solvent G; colorless foam, 83%; R_f 0.23 (solvent G); IR (neat) 3310, 2910, 1653 cm^{-1}; UV λ_{max} 245 nm (log ε 3.86; acid), 245 (3.86; pH 7.0), 257 (3.87; base); $[\alpha]^{25}_D$ –32.7° (*c* 1.76, CH_3OH); NMR values are in Tables I–III; mass spectrum (calcd m/e 233.0358, found m/e 233.0366). m/e 233 (M^+), 215 (M – H_2O), 190 (M – CONH), 130 (B + 30).

Anal. Calcd for $C_8H_{11}NO_5S \cdot 0.50CH_3OH$: C, 40.95; H, 5.25; N, 5.62. Found: C, 40.91; H, 5.12; N, 5.28.

Acknowledgment. We wish to acknowledge partial support of this work by The Ohio State University Comprehensive Cancer Center, N.C.I. Grant No. CA16058-05. Assistance with certain details of nomenclature was provided by Dr. Kurt Loening, Chemical Abstracts Service.

Registry No. **1a**, 56752-57-9; **1b**, 70156-48-8; **1c**, 71519-54-5; **4a**, 70156-53-5; **4b**, 71605-90-8; **5**(β), 71519-55-6; **5**α, 71564-40-4; **6a**, 62-55-5; **6b**, 645-54-5; **6c**, 115-08-2; **6d**, 40235-62-9; **6e**, 62-56-6; **6f**, 625-57-0; **6g**, 513-74-6; **7a**, 71537-29-6; **7b**, 71519-56-7; **7c**, 71519-57-8; **7d**, 71519-58-9; **7e**, 71519-59-0; **7f**, 71519-60-3; **8**, 71519-61-4; **9a**, 71519-62-5; **9b**, 71519-63-6; **10a**, 71519-64-7; **10b**, 71519-65-8; **10c**, 71519-66-9; **10d**, 71519-67-0; **10e**, 71519-68-1; **10f**, 71519-69-2; **11**, 71519-70-5; **12a**, 71519-71-6; D-ribose, 50-69-1; 2,3-*O*-isopropylidene-D-ribofuranose, 67814-68-0; 2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranose, 54503-65-0; morpholine, 110-91-8.