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SYNTHESIS OF PURINE AND PYRIMIDINE 2′-DEOXYNUCLEOSIDES FROM A 1,2-DITHIO SUGAR PRECURSOR*†

DEREK HORTON AND MASAKATSU SAKATA
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U. S. A.)
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ABSTRACT

9-(2-*S*-Ethyl-2-thio-α- and β-D-mannofuranosyl)adenine (**8α** and **8β**) were synthesized from ethyl 3,5,6-tri-*O*-acetyl-2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside (**1**) by bromination followed by coupling of the resultant bromide (**2**) with 6-benzamido-(chloromercuri)purine. The 2-chloro analogues (**10α** and **10β**) of **8α** and **8β** were obtained by way of a fusion reaction between 1,3,5,6-tetra-*O*-acetyl-2-*S*-ethyl-2-thio-α-D-mannofuranose (**5**) and 2,6-dichloropurine. Fusion of the bromide **2** with 2,4-bis(trimethylsilyloxy)pyrimidine and its 5-methyl derivative led to 1-(2-*S*-ethyl-2-thio-β-D-mannofuranosyl)uracil (**16**) and its thymine analogue (**15**). The action of Raney nickel led to rapid dechlorination of **10α** and **10β**, and all of the 2′-thionucleosides underwent desulfurization to give the corresponding 2′-deoxynucleosides. Sequential periodate oxidation–borohydride reduction converted the hexofuranosyl nucleosides into their pentofuranosyl analogues. Thus prepared were 9-(2-deoxy-α- and β-D-*arabino*-hexofuranosyl)adenine (**11α** and **11β**) and their 2-deoxy-D-*threo*-pentofuranosyl counterparts (**6α** and 2′-deoxy-3′-epiadenosine, **6β**), and 1-(2-deoxy-β-D-*arabino*-hexofuranosyl)-thymine (**17**) and -uracil (**18**) and their 2-deoxy-D-*threo*-pentofuranosyl counterparts (3′-epithymidine, **21**, and 2′-deoxy-3′-epiuridine, **20**). Detailed n.m.r.-spectral correlations are described for the series, and various derivatives of the nucleosides are reported.

INTRODUCTION

Stereochemical and functional-group modification at the 2′- and 3′-positions of natural nucleosides has been a fruitful source of compounds of interest as antimetabolites, metabolic probes, and antitumor agents[4]. A synthetic program in this laboratory[2,3] has extensively featured the use of sugar dithioacetals[5] as precursors in the synthesis of acyclic-sugar nucleosides[2,3,6,7], of 2′-amino-2′-deoxynucleosides[8],

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and of related systems[9]. There is considerable interest in thionucleosides, such as 2′- (ref. 10) and 3′-thioadenosine[11], both directly as antimetabolites and also as precursors for synthesis of 2′-deoxynucleosides[12].

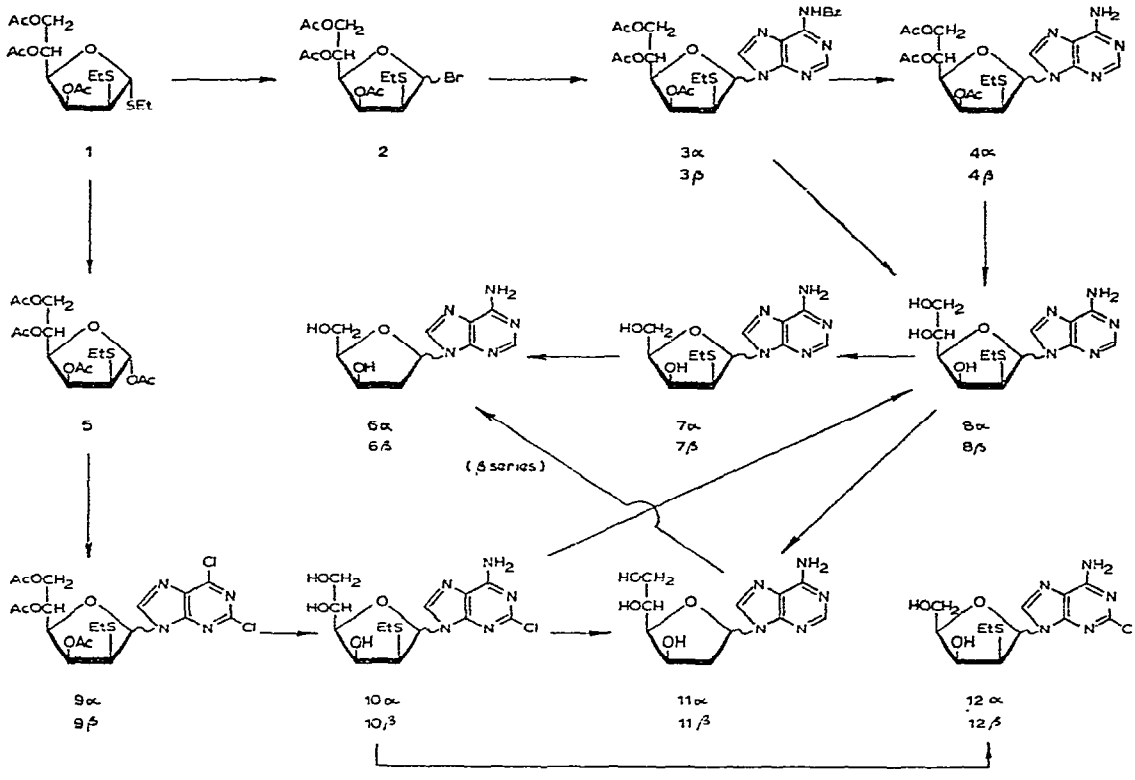
As part of a detailed evaluation of the chemistry of dithioacetals[2,5], it has been shown that a 2-*S*-ethyl-2-thio-D-hexose diethyl dithioacetal first described by Brigl and associates[13] has the D-*manno* stereochemistry[14] and that it is readily transformed into ethyl 2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside[14–16] (**1**), whose structure has been firmly established by various methods[17]. The ready availability[15] of compound **1** makes it a useful synthetic precursor, and its utility in synthesis of 2-thioglycofuranosides has been documented in a preceding report[15]. The present article describes the use of **1** as a precursor for synthesis of 2′-(alkylthio)-2′-deoxynucleosides, together with procedures for desulfurizing these products to the corresponding 2′-deoxynucleosides.

RESULTS AND DISCUSSION

The starting material, ethyl 3,5,6-tri-*O*-acetyl-2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside (**1**), was obtained[15] in good net-yield in five steps[13–15] from D-glucose diethyl dithioacetal. Bromination of **1** in carbon tetrachloride led to replacement of the 1-ethylthio group by bromine, and the unstable bromide[15] **2** was condensed at once in toluene solution with 6-benzamido(chloromercuri)purine[18]. The anomeric mixture of protected nucleosides **3** resulting was resolved by preparative t.l.c. or column chromatography, to give the α anomer (**3α**) as a dextrorotatory glass in 40% yield and the β anomer (**3β**) in 20% yield as a levorotatory glass. When the isolation was performed with an intermediate stage of treatment with picric acid in boiling ethanol[19], the corresponding *N*-debenzoylated products (**4**) were obtained as picrates; these were depicrated with Dowex-1 (CO_3^{2-}) ion-exchange resin, and then separated into the pure anomers by preparative t.l.c. Both anomers were obtained crystalline and analytically pure; the faster-migrating, dextrorotatory product was assigned as the α anomer, and the levorotatory, slower-migrating one as the β anomer.

Saponification of the fully protected α-nucleoside (**3α**) with hot, methanolic sodium methoxide gave in 82% yield the crystalline, deprotected nucleoside **8α** having $[\alpha]_D$ +29.5° in water; the same product was obtained by the action of methanolic ammonia on the *N*-debenzoylated, *O*-acetylated nucleoside **4α**. Likewise, saponification of the fully protected β-nucleoside (**3β**) or *O*-deacetylation of the *N*-debenzoylated analogue **4β** gave, in each instance, a high yield of crystalline 9-(2-*S*-ethyl-2-thio-β-D-mannofuranosyl)adenine (**8β**), $[\alpha]_D$ −77° in water. The mass spectra of **8α** and **8β** showed three principal, high-mass ions, corresponding to the molecular ion and the two fragments resulting from glycosyl–base cleavage. The invariance of the u.v.-spectral absorption (260 nm) of **8α** over the pH range 2–12 is characteristic[20] of 9-substituted purines, and the 9-substitution mode in all purine derivatives in this report has received independent and unequivocal confirmation from subsequent transformations of **8β** into a known nucleoside, namely, **6β**; the latter also provided

definitive corroboration of the anomeric assignments made on the basis of polarimetric and n.m.r.-spectral data.



Detailed, proton n.m.r.-spectral analyses of all products were made; Table I records chemical-shift data, and Table II gives first-order, spin-coupling values. As may be seen from Table II, the $J_{1,2}$ spin-couplings for the α and β anomers are almost identical (8–9 Hz), so that anomeric differentiation on the basis of $J_{1,2}$ values is not feasible. This near-identity of $J_{1,2}$ values for anomeric 2-*S*-ethyl-2-thio-D-mannofuranose derivatives has already been noted with 1-*O*-acetyl and 1-*O*-methyl derivatives[15], and contrasts with the behavior of 2′-thioribonucleosides, which exhibit $J_{1,2}$ 7.0–7.5 Hz for the α anomers, and $J_{1,2}$ 9.0–9.5 Hz for the β anomers[10]. However, the relative chemical-shifts of H-1 showed a clear correlation with anomeric configuration throughout the series of 2′-thionucleoside derivatives reported here; the α anomers showed their H-1 resonances at higher field (δ 6.01–5.90 for the acylated derivatives in chloroform) than those of the β anomers (δ 6.85–6.52). This behavior for these 2-thio-D-mannofuranosyl (and the homomorphous 2-thio-D-lyxofuranosyl) derivatives is opposite to that displayed by the ribose analogues[10,21], in accord with the principle[21] that H-1 *cis* to a sulfur atom at C-2 resonates at lower field than a corresponding *trans*-disposed proton at C-1.

Although the behavior of thio sugar derivatives with periodate may be complex[22], the exocyclic diol group in **8α** and **8β** was successfully cleaved by treatment with slightly more than one molar equivalent of sodium metaperiodate in water, and subsequent reduction of the products with borohydride gave the corresponding 9-(2-*S*-ethyl-2-thio-α- and β-D-lyxofuranosyl)adenines (**7α** and **7β**) in 87–88% yield; **7α** was obtained crystalline, but **7β** was a glass.

Attempted desulfurization of compounds **8α** and **8β** with Raney nickel in *N*,*N*-dimethylformamide for 12 h at 90–100°, by the general procedure of Goodman and coworkers[23], failed to effect the desired conversion. When the mixture was boiled under reflux for several hours, there was evidence (t.l.c.) that desulfurization had occurred, but that it was accompanied by considerable decomposition through base–sugar cleavage. However, inclusion of 10% of water in the reaction medium hindered the latter mode of decomposition, and the desired desulfurization was successfully achieved. The most satisfactory conditions were found with a reaction time of 5–7 h under reflux; although conversion was not complete, the separation of product from unreacted starting-material was readily accomplished by preparative t.l.c. Thorough extraction of the Raney nickel (Soxhlet apparatus) after the reaction was essential, as the product was adsorbed very tenaciously by the catalyst. The desulfurized products (**11α** and **11β**) were both obtained crystalline in yields of 48 and 36%, respectively, based on the amounts of unrecovered starting-materials **8α** and **8β**.

The 9-(2-deoxy-α- and β-D-*arabino*-hexofuranosyl)adenines (**11α** and **11β**) display characteristic differences in their n.m.r. spectra (Fig. 1), most notably in the signals for H-1 and the two protons at C-2. For the α anomer (**11α**), the H-1 signal appears as a triplet, and the C-2 protons give rise to a high-field multiplet because of a very small, chemical-shift difference between them. The appearance of the H-1 signal may result from equal coupling of H-1 with H-2 and H-2′ ($J_{1,2} \approx J_{1,2'} \approx 5$ Hz), although the small separation of the H-2 and H-2′ signals may also cause these first-order spacings to deviate somewhat from the true coupling-constants. In contrast, the H-1 resonance of the β anomer (**11β**) appears as a doublet of doublets showing a wide ($J_{1,2} = 8.5$ Hz) and a narrow ($J_{1,2'} = 2.5$ Hz) spacing, and the signals for H-2 and H-2′ are widely separated and amenable to direct, first-order analysis. These n.m.r. patterns for H-1, H-2, and H-2′ of **11α** and **11β** are exactly the reverse of the situation observed with the anomeric 2′-deoxyribonucleosides[24,25], wherein the β anomers show a triplet for H-1 and little separation of the signals for H-2 and H-2′, and the α anomers display a doublet of doublets for H-1 and wide separation of the H-2 and H-2′ signals. This difference is to be expected, as compounds **11α** and **11β** have at C-3 the opposite stereochemistry from that for the 2′-deoxyribonucleosides; the net arrangement of H-1, H-2, H-2′, and H-3 in **11α** (1,3-*trans* substituents) is the same as in the 2-deoxy-β-D-*erythro* nucleosides, and the arrangement in **11β** (1,3-*cis* substituents) corresponds to that in the 2-deoxy-α-D-*erythro* nucleosides.

Desulfurization of the ethylthiopentose nucleosides **7α** and **7β** with Raney nickel gave rise to the dextrorotatory 9-(2-deoxy-α-D-*threo*-pentofuranosyl)adenine (**6α**) and its (levorotatory) β anomer (2′-deoxy-3′-epiadenosine, **6β**), and the latter

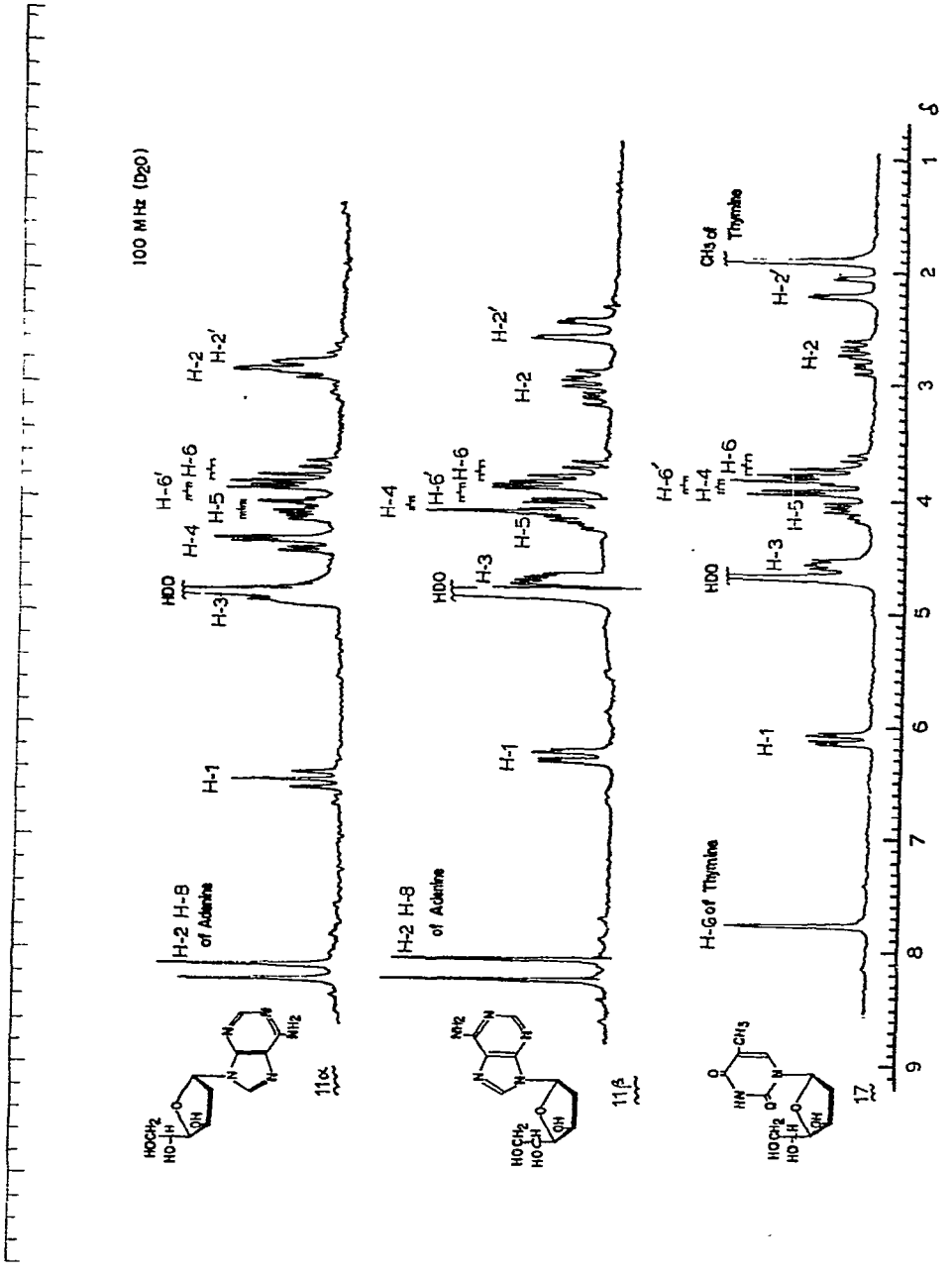


Fig. 1. The 100-MHz n.m.r. spectra in deuterium oxide of 9-(2-deoxy-α-D-*arabino*-hexofuranosyl)adenine (**11α**), 9-(2-deoxy-β-D-*arabino*-hexofuranosyl)adenine (**11β**), and 1-(2-deoxy-β-D-*arabino*-hexofuranosyl)thymine (**17**).

was found to be identical with an authentic sample[26]; this correlation provides firm, independent proof of the structures and anomeric attribution of all purine nucleoside derivatives reported here. Compound **6β** could also be obtained in 81% yield from the corresponding deoxyhexose nucleoside **11β** by sequential periodate oxidation–borohydride reduction.

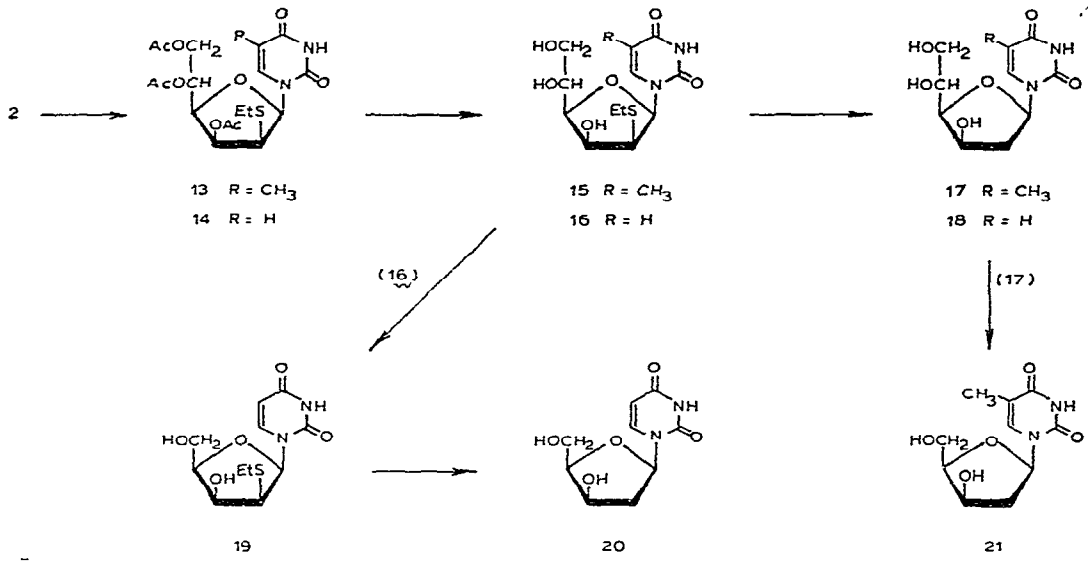
In an alternative route, based on the fusion method[27], to the foregoing nucleosides, the dithioglycoside **1** was first converted, in almost quantitative yield, into the corresponding 1-acetate (**5**) by treatment[17] with mercuric chloride to remove the glycosidic ethylthio group, followed by acetylation[15,17] of the resultant aldofuranose. Fusion of **5** with 2,6-dichloropurine plus a trace of *p*-toluenesulfonic acid as catalyst gave an anomeric mixture (**9**) of protected nucleosides from which the α anomer (**9α**) was obtained crystalline in 31% yield; it was strongly dextrorotatory ($[\alpha]_D$ +99° in chloroform). Column chromatography of the remaining product afforded the β anomer (**9β**) as a levorotatory ($[\alpha]_D$ −6° in chloroform) syrup in 16% yield. The anomeric assignments for **9α** and **9β** were based on the polarimetric data, the relative chemical-shifts of the H-1 signals (Table I), and subsequent transformations into the deoxynucleosides **11α** and **11β** already identified.

Treatment of **9α** and **9β** with methanolic ammonia in a sealed tube at 60–70° led to *O*-deacetylation and concurrent replacement of the chlorine at C-6, to give the crystalline 6-amino-2-chloro-9-(2-*S*-ethyl-2-thio-α- and β-D-mannofuranosyl)purines (**10α** and **10β**, respectively) in high yield. Selective replacement of the chlorine atom at C-6 is anticipated in view of the lower reactivity at C-2 toward nucleophilic displacement, and proof was secured from the identity of the subsequent transformation-products **11α** and **11β**. Compounds **10α** and **10β** were readily degraded by sequential periodate oxidation and borohydride reduction, to give the corresponding 6-amino-2-chloro-9-(2-*S*-ethyl-2-thio-α- and β-D-lyxofuranosyl)purines (**12α** and **12β**), both obtained crystalline in high yield.

When compound **10α** was treated with Raney nickel in *N*,*N*-dimethylformamide, initial dechlorination to give compound **8α** was observed, and more-vigorous conditions led to desulfurization to afford the deoxynucleoside **11α**, obtained in 51% yield (based on material not recovered as the dechlorination product **8α**). Similar results were observed in the β series. This overall sequence from the acetate **5** thus constitutes a valid alternative route to the 2′-thio- and 2′-deoxy-nucleosides, but overall yields were somewhat lower than those realized in the sequence from the bromide **2**.

The bromide **2** was also used as the starting point for synthesis of pyrimidine 2′-thio- and 2′-deoxy-nucleosides. Fusion[28] of **2** with 5-methyl-2,4-bis(trimethylsilyloxy)pyrimidine[28,29], followed by treatment with aqueous methanol, gave the crystalline 1-(3,5,6-tri-*O*-acetyl-2-*S*-ethyl-2-thio-β-D-mannofuranosyl)thymine (**13**) in 59% yield; there was no evidence for the presence of any significant proportion of the other anomer in the mother liquors. *O*-Deacetylation of **13** with methanolic ammonia gave the crystalline, deprotected nucleoside **15** in 83% yield. The same sequence conducted with 2,4-bis(trimethylsilyloxy)pyrimidine[28,29] gave the cor-

responding, acetylated uracil nucleoside **14**, which was deacetylated directly to give the crystalline 1-(2-*S*-ethyl-2-thio-β-D-mannofuranosyl)uracil (**16**) in 52% net yield; again, there was no evidence for the production of a significant proportion of the other anomer.



Desulfurization of **15** and **16** with Raney nickel by the same general procedure used with the purine nucleosides gave the corresponding, crystalline 2′-deoxynucleosides **17** and **18** in 55 and 27% yields, respectively. Periodate oxidation of **17** followed by borohydride reduction gave an 80% yield of crystalline 1-(2-deoxy-β-D-*threo*-pentofuranosyl)thymine (3′-epithymidine, **21**), whose m.p. and specific rotation were in excellent agreement with those reported by Horwitz *et al.*[30] for this compound. The corresponding uracil derivative (**20**) was obtained from compound **16** by periodate oxidation–borohydride reduction to the thiopentose nucleoside (**19**) followed by desulfurization to the 2′-deoxynucleoside **20**.

The direct correlation of product **21** with the known compound[30] provided firm evidence for the structural and anomeric configurational assignments for the thymine derivatives **13**, **15**, **17**, and **21**, and strong indication that the uracil derivatives **14**, **16**, **19**, and **20** were similarly constituted. Independent evidence for the β configuration in all of these products was afforded by n.m.r. spectroscopy and by optical rotatory dispersion. The $J_{1,2}$ values of the 2′-thionucleoside derivatives **13**–**16** were 8.0–8.5 Hz, but these values cannot be used for assigning anomeric configuration because, from the results with the purine nucleoside analogues (Table II), the α anomers would be expected to show values almost identical to those for the β anomers. However, for compounds **13** and **14**, the chemical shifts of H-1 were δ 6.75 and 6.52,

respectively, and for H-4, the values were δ 4.30 and 4.15. By comparison with values for comparable purine derivatives (Table I) these shifts support the β configuration. Furthermore, the optical rotatory dispersion spectra of **15** and **16** in water showed a positive Cotton effect, a behavior that thas been shown[31] characteristic of pyrimidine nucleosides having the β configuration.

All four of the pyrimidine 2′-deoxynucleosides (**17**, **18**, **20**, and **21**) gave well-separated signals for the two protons on C-2, and, for H-1, a doublet of doublets pattern arising from a large ($J_{1,2}$ 8–8.5 Hz) and a small ($J_{1,2'}$ 2–3 Hz) coupling with the C-2 methylene group (Tables I and II). For the reasons already advanced with the purine derivatives, such a pattern for the H-1 and H-2 signals is considered characteristic of the *cis*-arrangement of 1,3-substituents and, hence, of the β configuration in this homomorphous family of nucleosides.

TABLE I

N.M.R. CHEMICAL-SHIFT DATA[a] FOR COMPOUNDS 3, 4, 6–13, AND 15–24

Compound	*Solvent*	*H-1*	*H-2*	*H-2′*	*H-3*	*H-4*	*H-5*	*H-5′*
3α	$CDCl_3$	5.92 d	4.81 dd		5.87 dd	5.18 dd	5.30 o	
3β	$CDCl_3$	6.69 d	4.01 dd		5.83 dd	4.45 dd	5.43 o	
4α	$CDCl_3$	5.90 d	4.90 dd		5.88 dd	5.08 dd	5.32 o	
4β	$CDCl_3$	6.83 d	4.01 dd		5.81 dd	4.41 dd	5.48 o	
6α	D_2O	6.42 t	3.03———2.54 m		———4.48 m———		4.12———3.76 m	
6β	D_2O	6.09 dd	2.94 o	2.39 dq	4.51 o	4.13 m	4.05———3.73 m	
7α	C_5D_5N[b]	6.86 d	——5.15———4.96 m———			5.43 m	4.62 q	4.47 q
7β	D_2O	6.53 d	[c]		4.52 dd	4.34 m	4.20———3.90 m	
8α	C_5D_5N[b]	6.69 d	4.89 dd		—5.30—5.11 m—		4.73 m	
8β	C_5D_5N[b]	7.02 d	4.23 dd		4.99 dd	4.55 dd	4.73 o	
9α	$CDCl_3$	6.01 d	4.59 dd		5.95 dd	5.11 dd	5.36 o	
9β	$CDCl_3$	6.85 d	4.05 dd		5.89 dd	4.50 dd	5.50 o	
10α	C_5D_5N	6.69 d	4.75 m		—5.53—5.10 m—		4.75 m	
10β	C_5D_5N	6.89 d	[d]		5.00 dd	4.80———4.50 m		
11α	D_2O	6.48 t	3.05———2.60 m		4.90 m	4.40 dd	4.12 m	
11β	D_2O	6.26 dd	3.01[e]	2.50 dd	4.69 dd	4.04 dd	4.17[e]	
12α	C_5D_5N	6.76 d	4.88 dd		5.01 dd	5.33 m	4.59 q	4.42 q
13	$CDCl_3$	6.75 d	3.92 dd		5.76 dd	4.30 dd	5.45 o	
15	C_5D_5N[b]	6.99 d	4.08 dd		4.96 dd	[d]	4.76 o	
16	D_2O	6.39 d	3.93 dd		4.42 dd	3.93 dd	4.06[e]	
17	D_2O	6.11 dd	2.75 o	2.13 dd	4.57 dd	3.91 dd	4.12[e]	
18	D_2O	6.06 dd	2.71 o	2.14 dd	4.51 dd	3.89 dd	4.07 o	
19	D_2O	6.29 d	[c]		4.29 dd	[c]	4.20———3.60 m	
20	D_2O	5.94 dd	2.66 o	2.07 dq	4.38 o	———4.08——3.67 m———		
21	D_2O	6.09 dd	2.75 o	2.10 dq	4.50 o	———4.16——3.76 m———		
22	$CDCl_3$	6.62 d	3.87 dd		5.71 dd	[d]	5.34 o	
23	$CDCl_3$	6.75 d	3.88 dd		5.73 dd	4.20 dd	4.93 m	
24	$CDCl_3$	6.60 d	3.83 dd		5.63 dd	4.11 dd	5.34[e]	

[a]Signal multiplicities: d, doublet; m, multiplet; o, octet; q, quartet; s, singlet; t, triplet. [b]Containing D_2O. [c]Included in the H-5,5′ multiplet. [d]Included in the H-6,6′ multiplet. [e]Septet. [f]Including CH_3 group of thymine. [g]CH_3 group of thymine.

K. V. Bhat and Zorbach[32] prepared 2-deoxy-D-*arabino*-hexofuranosyl nucleosides of thymine and uracil. Their thymine derivative had m.p. 166–168°, $[\alpha]_D$ −10.5° in water, in good agreement with values (m.p. 168.5–169.5°, $[\alpha]_D$ −8° in water) found for compound **17**, thus establishing the β configuration for their product. For the uracil derivative, Bhat and Zorbach[32] reported m.p. 180–182°, $[\alpha]_D^{24}$ −16.5°, which does not accord with the values (m.p. 201°, $[\alpha]_D^{22}$ +16.7° in water) found here for 1-(2-deoxy-β-D-*arabino*-hexofuranosyl)uracil (**18**). The tentative assignment of anomeric configuration for their product was based on observation of a triplet pattern for H-1 and a supposed analogy with the n.m.r.-spectral behavior of thymidine and its α anomer. In the light of the arguments presented here, an H-1 triplet would be expected for the *trans* arrangement of the base and the 3-hydroxyl group, and hence, it would appear that the uracil nucleoside of Bhat and Zorbach

H-6	*H-6′*	SCH_2CH_3	*Purine or pyrimidine CH*	*OAc (s)*	*Other (assignments)*
4.52 q	4.04 q	2.40 q, 1.00 t	8.76 s, 8.11 s	2.15, 2.03, 1.98	9.37 s (NH), 8.04–7.45 m (Bz)
4.60 q	4.14 q	2.50 q, 1.08 t	8.77 s, 8.36 s	2.17, 2.07, 2.05	9.38 s (NH), 8.04–7.38 m (Bz)
4.52 q	4.09 q	2.40 q, 1.00 t	8.37 s, 7.91 s	2.14, 2.12, 1.98	6.53 s (NH_2)
4.63 q	4.15 q	2.51 q, 1.09 t	8.40 s, 8.22 s	2.22, 2.09, 2.06	6.70 s (NH_2)
			8.18 s, 8.04 s		
			2.04 s, 7.84 s		
		2.44 q, 0.94 t	8.87 s, 8.84 s		
		2.47 q, 1.08 t	8.33 s, 8.18 s		
4.31 q	4.13 q	2.35 q, 0.90 t	8.68 s, 8.63 s		
4.34 q	4.15 q	2.54 q, 1.02 t	8.99 s, 8.66 s		
4.57 q	4.11 q	2.47 q, 1.08 t	8.38 s	2.20, 2.08, 2.08	
4.63 q	4.20 q	2.60 q, 1.07 t	8.57 s	2.22, 2.11, 2.07	
4.32 q	4.14 q	2.44 q, 0.98 t	8.75 s		
4.50——	4.04 m	2.56 q, 1.04 t	9.01 s		
3.97 q	3.79 q		8.26 s, 8.11 s		
3.94 q	3.75 q		8.24 s, 8.06 s		
		2.49 q, 1.02 t	8.83 s		
4.63 q	4.19 q	2.60 q, 1.20 t	8.45 s	2.16, 2.10, 2.06	
				2.01[f]	9.92 s (NH)
4.48——	4.18 m	2.65 q, 1.14 t	8.38 s, 1.38 s[g]		8.73 s (NH)
3.80 q	3.62 q	2.58 q, 1.88 t	7.86 d, 5.76 d		
3.89 q	3.71 q		7.80 s, 1.89 s[g]		
3.84 q	3.66 q		7.92 d, 5.79 d		
		2.53 q, 1.12 t	7.72 d, 5.68 d		
			7.78 d, 5.68 d		
			7.80 d, 1.90 d[g]		
4.53——	4.20 m	2.58 q, 1.18 t	7.37 s	2.14, 2.03, 1.98[f]	7.90, 7.47, 2.48 (Ts)
3.63 q	3.46 q	2.59 q, 1.19 t	7.43 s	2.15, 2.10, 2.00[f]	8.07 (NH)
3.59 q	3.00 q	2.56 q, 1.18 t	7.38 s	2.11, 1.99[f]	9.76 (NH), 2.35 (SAc)

TABLE II

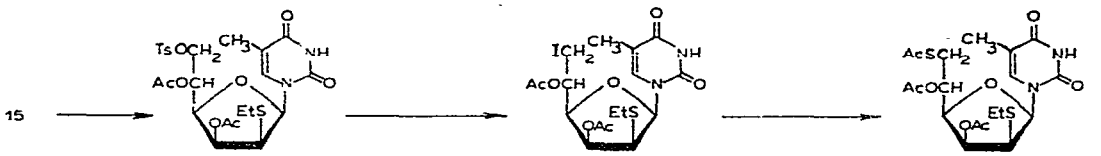
FIRST-ORDER COUPLING-CONSTANTS (Hz) FOR COMPOUNDS 3, 4, 6–13, AND 15–24

Compound	*Solvent*	$J_{1,2}$	$J_{1,2'}$	$J_{2,2'}$	$J_{2,3}$	$J_{2',3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
3α	$CDCl_3$	9.0			4.0		3.0	9.0			2.5	6.0	12.0
3β	$CDCl_3$	8.0			5.0		3.5	9.0			3.5	5.0	12.5
4α	$CDCl_3$	8.0			4.0		2.5	9.0			2.0	5.0	12.0
4β	$CDCl_3$	8.0			4.5		3.0	10.0			2.5	5.0	12.0
6α[a]	D_2O	7.0	7.0										
6β[a]	D_2O	8.0	3.0	15.0	5.5	1.2	3.0						
7α[a]	C_5D_5N[b]	8.0						6.0	6.5	13.0			
7β[a]	D_2O	8.5			4.0		3.0						
8α[a]	C_5D_5N[b]	8.5			4.0						3.0	5.0	12.5
8β	C_5D_5N[b]	8.0			4.5		3.0	8.5			3.0	5.0	12.0
9α	$CDCl_3$	9.0			4.5		3.0	10.0			2.0	5.0	12.0
9β	$CDCl_3$	8.0			5.0		3.0	10.0			3.0	5.0	12.0
10α[a]	C_5D_5N	9.0									3.0	5.0	11.0
10β[a]	C_5D_5N	8.0			4.0		3.0						
11α[a]	D_2O	7.0	7.0				3.5	8.5			3.0	5.5	12.5
11β	D_2O	8.5	2.5	15.5	5.5	<1	3.0	8.5			3.0	5.0	12.0
12α	C_5D_5N	8.5			4.5		3.0	5.0	6.0	12.0			
13	$CDCl_3$	8.5			5.0		3.0	10.0			2.0	5.0	12.5
15	C_5D_5N[a,b]	8.0			5.0		3.0				3.0	5.5	
16[c]	D_2O	8.0			4.5		2.5	9.0			3.0	5.0	12.0
17	D_2O	8.5	2.5	15.0	5.0	<1	3.0	8.5			3.0	5.0	12.0
18[d]	D_2O	8.0	2.0	15.0	5.0	<1	2.5	8.5			3.0	5.0	12.0
19[a,d]	D_2O	8.0			5.0		3.0						
20[a,c]	D_2O	8.0	3.0	15.0	5.5	1.0	3.0						
21[a,e]	D_2O	8.0	3.0	15.0	5.5	1.0	3.0						
22[a]	$CDCl_3$	8.0			5.0		3.0	10.0					
23	$CDCl_3$	8.0			5.0		3.0	10.0			3.0	4.0	12.0
24	$CDCl_3$	8.0			5.0		3.0	9.5			3.0	6.5	12.0

[a]Other couplings not determined because of second-order effects. [b]Containing D_2O. [c]$J_{5,6}$ of uracil = 11 Hz. [d]$J_{5,6}$ of uracil = 10.0 Hz. [e]J_{5,CH_3} of thymine = 1.0 Hz.

(and also the cytosine analogue reported by them[32]) was, in fact, the α anomer. The specific rotations of 2′-deoxynucleosides do not provide a reliable basis for attribution of anomeric configuration, because such compounds may exhibit behavior in violation of Hudson's rules[33].

An attempt was made to prepare a 2,6′-anhydronucleoside from **15**. Unimolecular *p*-toluenesulfonylation of **15** followed by acetylation gave an almost quantitative yield of the 6′-*p*-toluenesulfonate **22**. The sulfonate group was readily replaced by iodine by treatment of **22** with sodium iodide in hot butanone[34] to give the crystalline iodide **23**. However, attempts to cyclize **23**, by treatment with silver acetate according to the procedure of West[35], failed, and the starting material was recovered. Evidently attack at C-6′ by O-2 (to generate a bicyclo[5.2.1] ring-system) is sterically much less favorable than the well-documented mode of attack at C-5′ in a pentose analogue (to generate a bicyclo[4.2.1] ring-system), which leads to the 2,5′-anhydronucleoside system. Compound **23** underwent simple replacement at C-6′ by



22 23 24

the action of external nucleophiles, as demonstrated in the reaction with potassium thiolacetate in ethanol, which afforded the acetylated dithio nucleoside derivative **24**.

The results of *in vivo* biological screening against murine L-1210 leukemia cells for various nucleoside derivatives described in this report are given in Table III. The Table also includes data on the *in vitro* inhibition of various bacterial cell-lines. The behavior of 9-(2-*S*-ethyl-2-thio-α-D-mannofuranosyl)adenine (**8α**) is noteworthy; it shows appreciable activity (T/C 132) in the *in vivo* screen at a dose level of 400 mg/kg, and it shows moderate growth-inhibition of the K_{12} strain of *Escherichia coli*, a strain

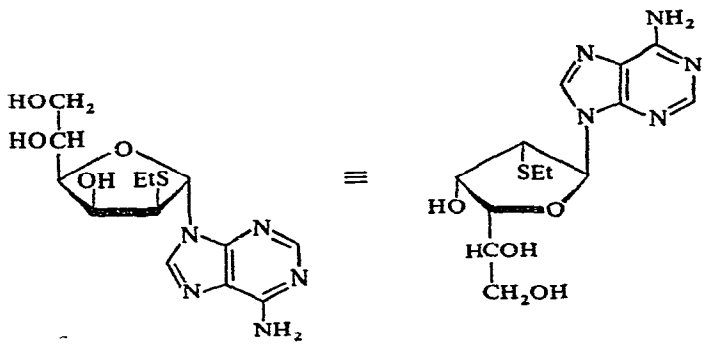
TABLE III

BIOLOGICAL TESTING DATA

Compound	*NSC Number*[a]	*Molar concentration for 50% inhibition of*			In vivo *activity against L-1210 leukemia in the mouse*[b]
		Streptococcus faecalis	*Leukemia L-1210 cells*	Escherichia coli K_{12}	
1	152761				[g]
3α		[d]	6×10^{-4}[e]	[e,f]	
4α		[d]	[d]	[f]	
4β		[d]	5×10^{-4}	[f]	
5	152762				[g]
7α		[d]	5×10^{-4}	[f]	
8α	157062	1×10^{-3}	5×10^{-4}	1×10^{-4}[e]	T/C132[h]
8β	157063	[d]	5×10^{-4}	[f]	[g]
9α	152760	[d]	[d]	[f]	T/C 109[i]
10α		[d]	[d]	[f]	
10β		[d]	[e,d]	[f]	
11α		[d]	5×10^{-4}	[f]	
12α		[d]	[d]	[f]	
13	157061				[g]
15	152759	[d]	[d]	[f]	[g]
16	177987				T/C 113
17		[d]	[d]	[f]	
19	177986				[g]
23	157064				[g]
24	157065	[d]	[d]	[f]	[g]

[a]Serial number of the U.S.P.H.S. Division of Cancer Treatment. [b]At doses up to 400 mg/kg. [c]Partially precipitated from solution at this concentration. [d]Greater than 10^{-3}. [e]Inhibition of 40% at this concentration. [f] Greater than 10^{-4}. [g]Inactive, nontoxic. [h]At 400 mg/kg; at 200 mg/kg, T/C = 113. [i]At 100 mg/kg.

whose sensitivity to antimetabolites correlates well with the *in vivo* antitumor activity of such antimetabolites. Although the α-nucleosides may superficially appear to be very dissimilar from the normal nucleosides, examination of molecular models from a different viewpoint reveals that a compound such as **8α** is, in fact, largely isosteric with 2′-deoxyadenosine, so that intact incorporation into DNA may be possible. The alternative depiction shown for **8α** illustrates how the ring systems may be oriented as in a β-nucleoside and how O-4′ might provide an isosteric replacement for the methylene group of 2′-deoxyadenosine. It may be noted that certain other examples of α-nucleosides, such as α-2′-deoxy-6-thioguanosine[36], effectively inhibit rodent neoplasms[37] and have been shown[38] to undergo incorporation at the terminus of DNA chains.



8α

EXPERIMENTAL

General methods. — Unless otherwise indicated, solutions were evaporated under diminished pressure at 40°. Melting points were determined with a Thomas–Hoover "Unimelt" apparatus. I.r. and u.v. spectra were recorded with a Perkin–Elmer Model 137 and a Cary Model 14 spectrophotometer, respectively. N.m.r. spectra were recorded by using Varian A-60A, HA-100, and Jeol MH-100 instruments, with either tetramethylsilane or sodium 4,4-dimethyl-4-silapentane-1-sulfonate as the internal standard. Spectra were recorded at 1000- and 500-Hz sweep-widths, and coupling constants are given to the nearest 0.5 Hz. Specific rotations were measured with a Perkin–Elmer Model 141 recording polarimeter. Mass spectra were obtained with an AEI MS-9 double-focusing, high-resolution spectrometer. Microanalyses were performed by W. N. Rond. T.l.c. was effected with 250-μm layers of Silica Gel G containing a fluorescent indicator (E. Merck, Darmstadt, Germany), activated at 110°, and indication was effected by u.v. light and by sulfuric acid. Column chromatography was performed with Silica Gel No. 7734 (Merck). X-Ray powder diffraction data give interplanar spacings (Å) for CuKα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The three strongest lines are numbered (1, strongest).

3,5,6-Tri-O-acetyl-2-S-ethyl-2-thio-D-mannofuranosyl bromide (**2**). — This compound was prepared from ethyl 3,5,6-tri-*O*-acetyl-2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside (**1**, 2.00 g, 5.08 mmol) and bromine (0.90 g, 5.62 mmol) exactly according to the procedure previously described[15]. The resulting, unstable syrup was used immediately in the following step.

6-Benzamido-9-(3,5,6-tri-O-acetyl-2-S-ethyl-2-thio-α-D-mannofuranosyl)purine (**3α**) *and its β anomer* (**3β**). — A suspension of finely ground 6-benzamido(chloromercuri)purine[18] (4.00 g, 8.45 mmol) and Celite (2.00 g) in dry toluene (50 ml) was dried by distilling off 10 ml of toluene. The stirred mixture was cooled to 40–50°, and a solution of **2** freshly prepared from **1** (3.00 g, 7.62 mmol) in dry toluene (15 ml) was added. The stirred mixture was boiled for 1 h under reflux, and filtered while hot. The filter cake was washed with hot chloroform (50 ml), and the filtrate and washings were combined and evaporated. The residue was stirred with chloroform (50 ml), and the mixture filtered. The filtrate was successively washed with 30% aqueous potassium iodide and water, dried (sodium sulfate), and concentrated to 5 ml. T.l.c. showed two major components having strong u.v.-absorption, and the mixture was resolved by preparative t.l.c. with 19:1 ether–methanol as eluant. The faster-moving component was isolated as a glass and identified as the α anomer **3α**; yield 1.75 g (40%), $[\alpha]_D^{25}$ +72° (*c* 1.3, chloroform). The slower-moving component was identified as the β anomer **3β**, and was also isolated as a glass; yield 0.884 g (20%), $[\alpha]_D^{25}$ −70° (*c* 1.1, chloroform).

9-(3,5,6-Tri-O-acetyl-2-S-ethyl-2-thio-α-D-mannofuranosyl)adenine (**4α**) *and its β anomer* (**4β**). — Compound **2** [derived from 3.00 g (7.62 mmol) of **1**], 6-benzamido-(chloromercuri)purine[18] (4.00 g, 8.45 mmol), and Celite (2.00 g) were treated in toluene as in the foregoing experiment. The resultant syrup was dissolved in ethanol (50 ml), picric acid (1.80 g, 7.86 mmoles) was added, and the mixture was boiled for 2 h under reflux[19]. Refrigeration of the resultant solution for several hours gave a yellow, crystalline precipitate that was filtered off, washed with cold ethanol, and dried; yield 2.55 g (48%). A solution of the picrate in warm, 50% aqueous acetone (200 ml) was stirred with an excess (50 ml) of moist Dowex-1 (CO_3^{2-}) anion-exchange resin, and the resultant, faintly yellow solution was concentrated to 30 ml. The gummy suspension was extracted with two 30-ml portions of chloroform, and the extracts were combined, dried (sodium sulfate), and evaporated; yield of mixed anomers **4α** and **4β**, 1.58 g (44%).

T.l.c. showed two strongly u.v.-absorbing components that were resolved by preparative t.l.c. (9:1 ether–methanol, double development), and the components were extracted from the bands with acetone. The solutions were evaporated and a small amount of ether was added to the residues, whereupon each product crystallized.

The faster-moving component was identified as the α anomer **4α**, yield 0.84 g (24%), which was recrystallized from ether; m.p. 131–132°, $[\alpha]_D^{24}$ +91° (*c* 1.45, chloroform); λ_{max}^{EtOH} 260 nm (ε 14,500); X-ray powder diffraction data: 8.94 s (3),

7.69 m, 7.19 w, 6.76 s, 5.93 vs (1), 5.49 s, 5.15 w, 4.90 w, 4.55 s, 4.27 m, 4.05 vw, 3.82 s (2), 3.72 w, and 3.60 w.

Anal. Calc. for $C_{19}H_{25}N_5O_7S$: C, 48.81; H, 5.39; N, 14.98; S, 6.86. Found: C, 48.96; H, 5.28; N, 14.69; S, 6.96.

The slower-moving component was identified as the β anomer **4β**, yield 0.50 g (14%), which was recrystallized from ethanol to afford the analytical sample; m.p. 193–194°, $[\alpha]_D^{23}$ −62° (*c* 1.6, chloroform); λ_{max}^{EtOH} 260 nm (ε 14,800); X-ray powder diffraction data: 9.48 w, 7.84 w, 7.02 vs (1), 6.21 m, 5.83 vw, 5.30 s (3), 5.09 vw, 4.93 w, 4.75 m, 4.45 m, 4.24 m, 3.91 m, 3.80 m, 3.69 m, 3.52 s (2), 3.36 vw, and 3.32 vw.

Anal. Calc. for $C_{19}H_{25}N_5O_7S$: C, 48.81; H, 5.39; N, 14.98; S, 6.86. Found: C, 49.03; H, 5.53; N, 14.79; S, 6.64.

*9-(2-S-Ethyl-2-thio-α-*D*-mannofuranosyl)adenine* (**8α**). — *A. From compound* **3α**. Sodium (200 mg) was dissolved in dry methanol (40 ml), and compound **3α** (1.75 g, 3.07 mmol) was added. The solution was boiled under reflux for 1.5 h, and then brought to pH 8 by adding 10% sulfuric acid. The precipitated salts were filtered off, and the filtrate was evaporated to a thick oil. The residue was dissolved in water (30 ml), and the solution extracted with two 15-ml portions of chloroform. The organic layer was extracted with two 15-ml portions of water, and the aqueous extracts were combined and evaporated to dryness. The yellow residue was dissolved in a little water, and the solution was kept for 2 days at ~25°, whereupon crystalline **8α** (0.463 g) separated. The mother liquors were evaporated, and the residue purified by preparative t.l.c. (7:3 chloroform–methanol) to afford a further 0.374 g of **8α**; total yield 0.837 g (80%). Recrystallization from water gave the analytical sample, m.p. 132°, $[\alpha]_D^{25}$ +29.5° (*c* 1.5, water); $\lambda_{max}^{H_2O}$ 260 (ε 14,500) at pH 7, 259 at pH 2, and 260 nm at pH 12; *m/e* 341 (M^+), 206 (M^+ − adenine), and 135 (adenine); X-ray powder diffraction data: 9.82 w, 6.69 vs (1), 5.19 m, 4.87 s (2), 4.65 w, 4.47 w, 4.29 m, 4.00 m, 3.60 w, 3.49 s (3), 3.29 vw, and 3.06 w.

Anal. Calc. for $C_{13}H_{19}N_5O_4S$: C, 45.74; H, 5.61; N, 20.51; S, 9.39. Found: C, 45.41; H, 5.75; N, 20.26; S, 9.55.

B. From compound **4α**. Ammonia was passed through a solution of compound **4α** (0.50 g) in methanol (30 ml) at 0–5°. After 18 h at ~25°, the mixture was evaporated and the residue recrystallized from a small amount of water to give **8α**; yield 0.30 g (82%), m.p. 132°, identical with the product from the preceding experiment.

*9-(2-S-Ethyl-2-thio-β-*D*-mannofuranosyl)adenine* (**8β**). — *A. From compound* **3β**. Compound **3β** (0.884 g, 1.55 mmol) was treated with methanolic sodium methoxide as in the preceding experiment, to give **8β**; total yield 0.410 g (78%). Recrystallization from a little water gave the analytical sample, m.p. 156–157°, $[\alpha]_D^{24}$ −77° (*c* 1.3, water), λ_{max}^{EtOH} 260 nm (ε 15,000); *m/e* 341 (M^+), 206 (M^+ − adenine), and 135 (adenine); X-ray powder diffraction data: 13.97 w, 11.55 vw, 10.23 vs (1), 7.51 s, 6.96 m, 6.28 w, 5.77 w, 5.39 vw, 4.85 s (3), 4.41 vs (2), 4.16 m, 3.96 w, 3.74 w, and 3.53 m.

Anal. Calc. for $C_{13}H_{19}N_5O_4S$: C, 45.74; H, 5.61; N, 20.51; S, 9.39. Found: C, 45.63; H, 5.53; N, 20.39; S, 9.30.

B. From compound **4β**. Compound **4β** (0.30 g) was treated with methanolic ammonia by the procedure used with **4α**, to give **8β**; yield 0.18 g (81%), m.p. 156–157°.

9-(2-S-Ethyl-2-thio-α-D-lyxofuranosyl)adenine (**7α**). — A solution of sodium metaperiodate (312 mg, 1.46 mmol) in water (6 ml) was added to a stirred solution of **8α** (500 mg, 1.46 mmol) in methanol at 0–5°. After 1 h, the precipitated sodium iodate was filtered off. To the filtrate was added 30–50 mg of sodium borohydride, and the solution was stirred for 5 min. The base was neutralized with 0.5M sulfuric acid, and the precipitated inorganic salts were filtered off. The filtrate was evaporated, and the residue extracted with methanol. Inorganic salts were filtered off, and the filtrate was evaporated. The residue was dissolved in a small volume of ethanol–water, and the solution was kept for 2 h at ~25° and for 1 h at 0°, whereupon crystalline **7α** separated; yield 380 mg (83%). Pure **7α** was obtained by recrystallization from ethanol; m.p. 124.5–125.5°, $[\alpha]_D^{24}$ +42° (*c* 1.0, methanol); λ_{max}^{EtOH} 260 nm (ε 14,000); *m/e* 311 (M^+), 176 (M^+ − adenine), and 135 (adenine); X-ray powder diffraction data: 12.84 m (3), 10.80 w, 9.25 s (2), 8.09 w, 6.99 vw, 6.24 vs (1), 5.44 vw, 4.88 m, 4.52 w, 4.23 m, 4.00 m, 3.77 m, and 3.64 w.

Anal. Calc. for $C_{12}H_{17}N_5O_3S$: C, 46.27; H, 5.50; N, 22.49; S, 10.29. Found: C, 46.13; H, 5.42; N, 22.63; S, 10.05.

9-(2-S-Ethyl-2-thio-β-D-lyxofuranosyl)adenine (**7β**). — Compound **8β** (200 mg, 587 μmol) was treated with sodium metaperiodate (127 mg, 593 μmol), and then with sodium borohydride by the procedure used for the α anomer. The syrupy product was purified by preparative t.l.c. to afford **7β** as a glass; yield 160 mg (88%); $[\alpha]_D^{25}$ −58° (*c* 1.26, water); λ_{max}^{EtOH} 261 nm (ε 14,000); *m/e* 311 (M^+), 176 (M^+ − adenine), and 135 (adenine).

2,6-Dichloro-9-(3,5,6-tri-O-acetyl-2-S-ethyl-2-thio-α-D-mannofuranosyl)purine (**9α**) *and its β anomer* (**9β**). — A mixture of 1,3,5,6-tetra-*O*-acetyl-2-*S*-ethyl-2-thio-α-D-mannofuranose (**5**, 10.6 g, 27.0 mmol, prepared from **1** by the method already described[15,17]) and 2,6-dichloropurine (5.2 g, 27.5 mmol), in a round-bottomed flask fitted with a vacuum aspirator and stirrer, was heated with stirring at 110° *in vacuo* until vigorous evolution of gas ceased (~3 min). The mixture was cooled to 50–70°, finely powdered *p*-toluenesulfonic acid (25 mg) was added with stirring, and the mixture was heated *in vacuo* for 15 min at 120° and for a further 10 min at 140°, until the vigorous evolution of acetic acid had ceased. The cooled mixture was dissolved in chloroform, and the solution was washed successively with aqueous sodium hydrogen carbonate and water, dried (sodium sulfate), and evaporated. Ether (50 ml) was added to the residue, and the mixture was refluxed gently until all of the syrup had dissolved. A solid that remained undissolved was filtered off; it was crude **9α** (yield 4.4 g, 31%). Recrystallization from ethanol gave pure **9α**, m.p. 198–199°, $[\alpha]_D^{22}$ +99° (*c* 1, chloroform); λ_{max}^{EtOH} 274 (ε 9,400) and 255 nm (5,800); *m/e* 522 (M^+), 333 (M^+ − purine); X-ray powder diffraction data: 8.60 s, 7.82 w, 6.64 m, 5.93 s (3), 5.33 m, 4.84 vs (1), 4.54 vs (2), 4.00 s, 3.82 vw, 3.63 s, 3.47 s, 3.32 w, 3.14 vw, 3.02 w, and 2.85 w.

Anal. Calc. for $C_{19}H_{22}Cl_2N_4O_7S$: C, 43.77; H, 4.25; Cl, 13.60; N, 10.75; S, 6.16. Found: C, 43.97; H, 4.37; Cl, 13.72; N, 11.06; S, 6.14.

The ethereal filtrate contained a second, strongly u.v.-absorbing component (fluorescent t.l.c. plate), which was separated from the mixture by chromatography on a column (3.5 × 50 cm) of silica gel with 3:7 ether–benzene as the eluant, to afford syrupy **9β**; yield 2.3 g (16%), $[\alpha]_D^{22}$ −6° (*c* 1.1, chloroform); *m/e* 522 (M^+).

6-Amino-2-chloro-9-(2-S-ethyl-2-thio-α-D-mannofuranosyl)purine (**10α**). — A suspension of compound **9α** (3.00 g, 5.76 mmol) in methanol (50 ml) in a tube (2 × 70 cm) was saturated with ammonia at 0–5°. The tube was sealed, and shaken gently to dissolve the solid. After 18 h, the tube was heated for 3 h in a bath at 60–70°, and then cooled in an ice bath, opened, and the contents evaporated to dryness. The residue was dissolved in water (30 ml), and the solution was kept for 3 h at ~25° and 18 h at 5°, whereupon crude compound **10α** crystallized out; yield 2.10 g (97%). Recrystallization from ethanol gave pure **10α**; m.p. 185–186°, $[\alpha]_D^{22}$ +83° (*c* 1.1, pyridine); λ_{max}^{EtOH} 265 nm (ε 13,500); *m/e* 375 (M^+), 206 (M^+ − base), and 169 (base); X-ray powder diffraction data: 12.65 w, 9.55 s (2), 7.38 m, 6.58 m, 4.77 s (3), 4.33 s, 4.09 vs (1), 3.88 m, 3.71 vw, 3.54 w, 3.40 vw, and 3.29 w.

Anal. Calc. for $C_{13}H_{18}ClN_5O_4S$: C, 41.55; H, 4.83; Cl, 9.44; N, 18.64; S, 8.53. Found: C, 41.84; H, 5.26; Cl, 9.69; N, 18.53; S, 8.72.

6-Amino-2-chloro-9-(2-S-ethyl-2-thio-β-D-mannofuranosyl)purine (**10β**).—Compound **9β** was treated with methanolic ammonia by the procedure used in the preceding experiment. The crude **10β** contained a minor contaminant that was not removed by several recrystallizations, and an analytical sample was obtained by preparative t.l.c. Pure **10β** had m.p. 218–220° (dec.), $[\alpha]_D^{24}$ −90° (*c* 1.3, pyridine); *m/e* 375 (M^+), 206 (M^+ − base), and 169 (base); X-ray powder diffraction data: 10.42 w, 7.74 vw, 6.37 m, 4.90 s (2), 4.45 vs (1), 4.30 m (3), 3.79 w, 3.59 w, 3.25 vw, and 3.00 vw.

Anal. Calc. for $C_{13}H_{18}ClN_5O_4S$: C, 41.55; H, 4.83; Cl, 9.44; N, 18.64; S, 8.53. Found: C, 41.42; H, 5.19; Cl, 9.83; N, 18.44; S, 8.42.

6-Amino-2-chloro-9-(2-S-ethyl-2-thio-α-D-lyxofuranosyl)purine (**12α**). — Sodium metaperiodate (300 mg, 1.40 mmol) in water (10 ml) was added with stirring at 0–5° to a solution of compound **10α** (500 mg, 1.33 mmol) in methanol, and the mixture was stirred for 45 min. The precipitated salt was filtered off, and washed with ethanol (20 ml). The filtrate and washings were combined, and evaporated to a white solid that was triturated with ethanol (25 ml). The mixture was filtered, the filtrate was stirred at ~25°, and a solution of sodium borohydride (100 mg) in water (10 ml) was added dropwise during 5 min. After 15 min, the mixture was made neutral with 0.5M sulfuric acid, filtered, and the filtrate evaporated to dryness. The resulting, white crystals of **12α** were washed with water (30 ml), and dried; yield 373 mg (81%). Recrystallization from ethanol gave pure **12α**, m.p. 217–218°, $[\alpha]_D^{24}$ +64° (*c* 1, pyridine); λ_{max}^{EtOH} 265 nm (ε 15,000); *m/e* 345 (M^+), 176 (M^+ − base), and 169 (base); X-ray powder diffraction data: 12.70 s, 8.34 vs (1), 6.37 vw, 5.09 m, 4.88 vw, 4.63 w, 4.38 w, 4.12 vw, 3.97 s (2), 3.79 s (3), 3.53 m, and 3.38 w.

Anal. Calc. for $C_{12}H_{16}ClN_5O_3S$: C, 41.68; H, 4.66; Cl, 10.25; N, 20.25; S, 9.27. Found: C, 41.62; H, 4.74; Cl, 10.46; N, 20.46; S, 9.23.

6-Amino-2-chloro-9-(2-S-ethyl-2-thio-β-D-lyxofuranosyl)purine (**12β**). — The foregoing oxidation–reduction sequence was performed with compound **10β** (500 mg, 1.33 mmol) in methanol with sodium metaperiodate (300 mg, 1.40 mmol) in water. The yield of **12β** was 347 mg (75%). Recrystallization from water gave pure **12β**, m.p. 130–131°, $[\alpha]_D^{24}$ −79° (*c* 1, methanol); λ_{max}^{EtOH} 265 nm (ε 15,500); *m/e* 345 (M^+), 176 (M^+ − base), and 169 (base); X-ray powder diffraction data: 10.71 m, 7.76 m (3), 6.32 w, 5.47 vw, 4.90 s (2), 4.49 vs (1), 3.80 w, 3.58 w, 3.35 vw, 3.18 vw, and 3.05 w.

Anal. Calc. for $C_{12}H_{16}ClN_5O_3S$: C, 41.68; H, 4.66; N, 20.25. Found: C, 41.64; H, 4.87; N, 19.93.

9-(2-Deoxy-α-D-arabino-hexofuranosyl)adenine (**11α**). — *A. From compound* **8α**. Active Raney nickel catalyst (No. 28, W. R. Grace Co., 3.0 g wet wt) was added to a solution of compound **8α** (300 mg, 0.88 mmol) in *N,N*-dimethylformamide (30 ml) containing 10% of water, and the mixture was boiled under reflux for 5 h, with stirring by means of a paddle-type stirrer. The catalyst was filtered off, and washed with hot water (50 ml), and the filtrate and washings were combined and evaporated, final traces of *N,N*-dimethylformamide being removed by repeated evaporation of water and then ethanol from the residue. The resulting syrup was dissolved in a little ethanol, and the solution was refrigerated for 18 h. The crude **11α** (33 mg) that precipitated was filtered off. The filtrate was evaporated, and the residue resolved by preparative t.l.c. (4:1 chloroform–methanol) to give an additional 16 mg of **11α** together with 89 mg of unchanged starting-material **8α**. The nickel catalyst was extracted with *N,N*-dimethylformamide for 7 h in a Soxhlet apparatus, and the extract was resolved by preparative t.l.c. to give an additional 25 mg of **11α** and 26 mg of **8α**. The total recovery of starting material (**8α**) was 115 mg (38%), and the total yield of **11α** was 74 mg (48%, based on the amount of unrecovered **8α**). Recrystallization from water gave pure **11α**, m.p. 207–208° (air-dried sample), $[\alpha]_D^{24}$ +40° (*c* 1.5, water); λ_{max}^{EtOH} 260 nm (ε 14,000); *m/e* 281 (M^+), 147 (glycosyl$^+$), and 134 (adenyl$^+$); X-ray powder diffraction data: 7.96 w, 7.24 vw, 6.85 vs (1), 6.05 vw, 5.67 s (2), 5.31 vw, 4.74 s (3), 4.38 s, 4.09 vw, 3.95 s, 3.81 m, 3.67 s, 3.54 m, and 3.41 vw.

Anal. Calc. for $C_{11}H_{15}N_5O_4 \cdot 0.5H_2O$: C, 45.51; H, 5.56; N, 24.13. Found: C, 45.67; H, 5.76; N, 23.90.

B. From compound **10α**. The foregoing procedure was repeated with compound **10α** (300 mg) and active Raney nickel (4 g, wet wt). With isolation after 7 h of reaction, the yield of **11α** was 71 mg (51%, based on the proportion of starting material not recovered as the dechlorination product **8α**), m.p. 207–208°.

When the reaction was conducted for only 1 h, t.l.c. showed a single component present; it was found to be compound **8α**.

9-(2-Deoxy-β-D-arabino-hexofuranosyl)adenine (**11β**). — Compound **8β** (200 mg) and active Raney nickel (2.0 g) were refluxed for 5 h in *N,N*-dimethylformamide (30 ml) containing 10% of water, as described for the α analogue. The

nickel was extracted for 12 h in a Soxhlet apparatus with *N,N*-dimethylformamide containing 10% of water. The filtrate and extract were combined, and resolved by preparative t.l.c. (4:1 chloroform–methanol) to give unchanged **8β** (74 mg, 37%) and the deoxy nucleoside **11β**; yield 38 mg (36%). Recrystallization of the latter from ethanol gave pure **11β**, m.p. 176–177°, $[\alpha]_D^{23}$ −55° (*c* 1, water); λ_{max}^{EtOH} 260 nm (ε 14,000); *m/e* 281 (M^+), 147 (glycosyl$^+$), and 134 (adenyl$^+$); X-ray powder diffraction data: 7.32 w, 6.12 vw, 5.47 m, 5.17 m, 4.62 s (2), 4.08 m, 3.82 s (3), 3.47 w, and 1.91 vs (1).

Anal. Calc. for $C_{11}H_{15}N_5O_4$: C, 46.96; H, 5.38; N, 24.90. Found: C, 47.05; H, 5.73; N, 24.78.

This compound was also obtained in similar yield, accompanied by **8β**, when compound **10β** was used as the starting material.

*9-(2-Deoxy-α-*D*-threo-pentofuranosyl)adenine* (**6α**). — A mixture of compound **7α** (300 mg) and active Raney nickel (3.0 g wet wt) was refluxed for 5 h in *N,N*-dimethylformamide (40 ml) containing 10% of water, and the product was isolated and resolved by preparative t.l.c. (4:1 chloroform–methanol) as already described. The recovery of starting material (**7α**) was 90 mg (30%), and the yield of **6α** was 80 mg (47%). Attempted crystallization from ethanol gave **6α** as a powdery product having no sharp m.p.; $[\alpha]_D^{25}$ +41° (*c* 0.5, water); λ_{max}^{EtOH} 260 nm (ε 15,000); *m/e* 251 (M^+) and 135 (adenine). The homogeneity and identity of the product were verified by its clearly resolved n.m.r. spectrum (Tables I and II).

Anal. Calc. for $C_{10}H_{13}N_5O_3 \cdot 0.5H_2O$: C, 46.15; H, 5.42; N, 26.91. Found: C, 45.70; H, 5.58; N, 27.04.

*9-(2-Deoxy-β-*D*-threo-pentofuranosyl)adenine* (**6β**). — Sodium metaperiodate (80 mg, 374 μmol) in water (3 ml) was added to a solution of compound **11β** (100 mg, 356 μmol) in methanol, and the product was subsequently treated with sodium borohydride (10–20 mg), all by the procedure used for the degradation of compound **8α**. The syrupy product was purified by preparative t.l.c. (4:1 chloroform–methanol) to afford 72 mg (81%) of **7β**. Recrystallization from ethanol gave the pure deoxynucleoside **6β**, m.p. 191–192° (lit.[26] m.p. 191–192°), $[\alpha]_D^{24}$ −29° (*c* 1.3, water); $\lambda_{max}^{H_2O}$ 259 (pH 2), 260 (pH 7), and 260 nm (pH 12); *m/e* 251 (M^+) and 135 (adenine); X-ray powder diffraction data: 6.99 vs (1), 5.23 s (3,3), 5.03 vw, 4.72 w, 4.32 s (3,3), 4.06 vs (2), 3.91 vw, 3.64 s, 3.37 m, 3.11 m, 3.02 m, 2.87 m, and 2.68 m.

Anal. Calc. for $C_{10}H_{13}N_5O_3$: C, 47.81; H, 5.21; N, 27.87. Found: C, 47.52; H, 4.97; N, 27.75.

Desulfurization of compound **7β**, essentially as described for **7α**, gave compound **6β** in similar yield.

*1-(3,5,6-Tri-*O*-acetyl-2-*S*-ethyl-2-thio-β-*D*-mannofuranosyl)thymine* (**13**). — 5-Methyl-2,4-bis(trimethylsilyloxy)pyrimidine[28,29] (3.00 g, 11.1 mmol) was added to a solution of the bromide **2** [prepared from the thioglycoside **1** (3.00 g, 7.62 mmol)] in carbon tetrachloride (30 ml). The mixture was stirred until homogeneous, and then evaporated, and the residue was heated for 1 h at 90–100°. The cooled, dark residue was dissolved in 4:1 methanol–water (40 ml), and the solution was boiled for 15 min under reflux and then evaporated. The residue was triturated with

chloroform (50 ml), and the solid thymine that separated was filtered off. The filtrate was washed successively with aqueous sodium hydrogen carbonate and water, dried (sodium sulfate), and evaporated to a thick syrup that crystallized on trituration with ether, to give compound **13**; yield 2.06 g (59%). Recrystallization from ethanol gave the analytical sample, m.p. 190–191°, $[\alpha]_D^{25}$ +15° (*c* 1.3, chloroform); λ_{max}^{EtOH} 265 nm (ε 9,000); *m/e* 458 (M^+) and 333 (glycosyl$^+$); X-ray powder diffraction data: 9.19 w, 8.42 vw, 7.51 s, 7.05 vs (1), 6.51 s (2), 5.87 m, 5.38 vw, 5.12 w, 4.79 s (3), 4.60 m, 4.38 vw, 4.21 vw, 4.02 m, 3.86 s, 3.76 m, 3.64 w, 3.53 vw, 3.25 s, and 3.05 m.

Anal. Calc. for $C_{19}H_{26}N_2O_9S$: C, 49.77; H, 5.72; N, 6.11; S, 6.99. Found: C, 49.96; H, 5.73; N, 6.27; S, 7.15.

*1-(2-S-Ethyl-2-thio-β-*D*-mannofuranosyl)thymine* (**15**). — A suspension of compound **13** (1.80 g, 3.93 mmol) in methanol (40 ml) was saturated with ammonia at 0–5°. After 18 h at ~25°, the solution was evaporated, and the residue was crystallized from ethanol to give **15**, yield 1.1 g (84%), m.p. 174–175°, $[\alpha]_D$ +22° (*c* 1.5, water); positive Cotton effect; λ_{max}^{EtOH} 268 nm (ε 9,800); *m/e* 332 (M^+), 207 (glycosyl$^+$), and 126 (base); X-ray powder diffraction data: 9.94 w, 6.70 vs (1), 5.19 m, 4.87 s (2), 4.66 vw, 4.48 vw, 4.31 w, 4.00 m, 3.62 vw, and 3.50 m (3).

Anal. Calc. for $C_{13}H_{20}N_2O_6S$: C, 46.98; H, 6.07; N, 8.43; S, 9.65. Found: C, 47.28; H, 6.15; N, 8.62; S, 9.49.

*1-(2-S-Ethyl-2-thio-β-*D*-mannofuranosyl)uracil* (**16**). — 2,4-Bis(trimethylsilyloxy)pyrimidine (4.0 g, 15.6 mmol) and the bromide **2** [freshly prepared from **1** (5.00 g, 12.7 mmol)] were treated as described for preparation of the thymine derivative **13**. The resultant syrup was dissolved in methanol (40 ml), and the solution was saturated with ammonia at 0–5°. After 18 h at ~25°, the solution was evaporated to a dark, crystalline solid which was dissolved in a little ethanol, whereupon crude compound **16** crystallized out; yield 2.1 g (52%). Recrystallization from ethanol with use of activated charcoal gave pure **16**; m.p. 210°, $[\alpha]_D^{22}$ +58.5° (*c* 1.4, water); positive Cotton effect; λ_{max}^{EtOH} 263 nm; *m/e* 318 (M^+) and 207 (glycosyl$^+$); X-ray powder diffraction data: 11.18 s, 9.19 m, 7.72 m, 7.10 w, 6.59 s, 5.60 w, 5.22 vs (2), 4.69 s, 4.46 w, 4.32 w, 4.18 vs (1), 3.91 w, 3.53 vs (3), and 3.33 s.

Anal. Calc. for $C_{12}H_{18}N_2O_6S$: C, 45.28; H, 5.70; N, 8.80; S, 10.07. Found: C, 45.51; H, 5.71; N, 8.95; S, 10.21.

A sample of the initial, syrupy, acetylated product (**14**) showed the following n.m.r. data (chloroform-*d*): δ 6.52 d ($J_{1,2}$ 8.0 Hz, H-1), 3.74 dd ($J_{2,3}$ 4.5 Hz, H-2), 5.57 dd ($J_{3,4}$ 3.0 Hz, H-3), 4.15 dd ($J_{4,5}$ 10.0 Hz, H-4), and 5.26 o (H-5).

*1-(2-Deoxy-β-*D*-*arabino*-hexofuranosyl)thymine* (**17**). — A mixture of compound **15** (300 mg) and active Raney nickel (No. 28, W. R. Grace Co., 3.0 g wet wt) in *N,N*-dimethylformamide (30 ml) containing 10% of water was boiled under reflux for 4 h. The nickel was filtered off, and washed with hot water (3 × 30 ml). The filtrate and washings were combined and evaporated, and the residue was resolved by preparative t.l.c. (9:1 chloroform–methanol) to give starting material **15** (34 mg) and compound **17** (93 mg). The nickel was then extracted with boiling water for 15 h in a Soxhlet apparatus, and preparative t.l.c. of the extract gave a further 10 mg of **15** and 22 mg

of **17**; the total recovery of **15** was 44 mg (15%), and the total yield of **17** was 115 mg (55% on the basis of unrecovered **15**). Recrystallization from ethanol gave pure **17**; m.p. 168.5–169.5°, $[\alpha]_D^{22}$ −8° (*c* 1, water); λ_{max}^{EtOH} 267 nm (ε 9,400); *m/e* 272 (M^+); X-ray powder diffraction data: 9.38 m, 6.50 w, 5.45 vs (1), 5.03 vw, 4.65 w, 4.43 s (2), 4.02 w, 3.97 s (3), 3.73 vw, 3.53 w, 3.26 m, 3.06 vw, and 2.78 s.

Anal. Calc. for $C_{11}H_{16}N_2O_6$: C, 48.53; H, 5.92; N, 10.29. Found: C, 48.40; H, 6.12; N, 10.15.

For a compound tentatively identified as the β anomer of 1-(2-deoxy-D-*arabino*-hexofuranosyl)thymine, K. V. Bhat and Zorbach[32] reported m.p. 166–168°, $[\alpha]_D^{24}$ −10.5° in water.

*1-(2-Deoxy-β-*D-arabino-*hexofuranosyl)uracil* (**18**). — Compound **16** (300 mg) and active Raney nickel (3.0 g, wet wt) were refluxed for 7 h in *N,N*-dimethylformamide (30 ml) containing 10% of water. The nickel was filtered off, and washed with hot water (5 × 30 ml). The filtrate and washings were combined, and evaporated to a thick oil that was resolved by preparative t.l.c. with 4:1 chloroform–methanol. The recovery of starting material (**16**) was 70 mg (23%), and the yield of product **18** was 55 mg (29%). Recrystallization of the latter from ethanol gave pure **18**, m.p. 201°, $[\alpha]_D^{22}$ +16.7° (*c* 1, water); λ_{max}^{EtOH} 263 nm; *m/e* 258 (M^+), 147 (glycosyl$^+$), and 112 (base); X-ray powder diffraction data: 6.94 w, 6.18 s, 5.50 vs (3), 4.79 w, 4.41 vs (1), 4.10 vs (2), 3.79 s, 3.59 vw, 3.48 vw, 3.38 w, 3.01 vs, 2.90 w, 2.74 m, 2.63 m, 2.48 m, 2.39 vw, and 2.30 m.

Anal. Calc. for $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.46; N, 10.85. Found: C, 46.55; H, 5.57; N, 10.93.

For a compound described as 1-(2-deoxy-β-D-*arabino*-hexopyranosyl)uracil, K. V. Bhat and Zorbach[32] reported m.p. 180–182°, $[\alpha]^{24}$ −16.8° in water.

*1-(2-*S*-Ethyl-2-thio-β-*D*-lyxofuranosyl)uracil* (**19**). — Sodium metaperiodate (340 mg, 1.59 mmol) in water (20 ml) was added to a solution of compound **16** (500 mg, 1.57 mmol) in methanol (75 ml), and the mixture was stirred for 1 h at 0–5°. The precipitated salt was filtered off, and sodium borohydride (20–30 mg) was added to the filtrate. The solution was stirred for 5 min, and then made neutral with 0.5M sulfuric acid. The mixture was filtered, the filtrate evaporated, and the residue purified by preparative t.l.c. (4:1 chloroform–methanol), to give compound **19**; yield 390 mg (86%). Recrystallization from ethanol gave pure **19**; m.p. 158–159°, $[\alpha]_D^{24}$ +86.5° (*c* 1.5, water); λ_{max}^{EtOH} 263 nm; *m/e* 288 (M^+), 176 (M^+ − base), and 112 (base); X-ray powder diffraction data: 8.70 vw, 7.16 m, 6.44 s, 5.99 s, 5.54 s, 5.30 vw, 5.13 vw, 4.82 w, 4.53 w, 4.31 s, 4.16 m, 3.87 vs (1), 3.46 m, 3.35 m, 3.21 w, 3.05 m, 2.97 vw, 2.87 w, 2.82 w, 2.76 w, 2.67 m, and 2.53 m.

Anal. Calc. for $C_{11}H_{16}N_2O_5S$: C, 45.81; H, 5.59; N, 9.72; S, 11.12. Found: C, 46.05; H, 5.87; N, 9.57; S, 11.08.

*1-(2-Deoxy-β-*D-threo-*pentofuranosyl)uracil* (**20**). — A mixture of compound **19** (500 mg) and Raney nickel (5.0 g) was refluxed in *N,N*-dimethylformamide containing 10% of water for 7 h, and the product was isolated by the general procedure described for the other desulfurization reactions. The recovery of **19** was 150 mg, and the yield

of **20** was 70 mg (25%, based on unrecovered **19**). Recrystallization of the latter from ethanol gave pure **20**; m.p. 165–166°, $[\alpha]_D^{22}$ +40° (*c* 1.4, water); λ_{max}^{EtOH} 263 nm,; *m/e* 228 (M^+) and 116 (M^+ − base).

Anal. Calc. for $C_9H_{12}N_2O_5$: C, 47.37; H, 5.30; N, 12.27. Found: C, 47.75; H, 5.52; N, 12.22.

*1-(2-Deoxy-β-*D-threo-*pentofuranosyl)thymine* (**21**). — Compound **17** (300 mg, 1.10 mmol) and sodium metaperiodate (240 mg, 1.12 mmol) were treated according to the procedure described for compound **19**, and the residue was purified by preparative t.l.c.; yield 215 mg (80%). Recrystallization from ethanol gave pure **21**; m.p. 170–171°, $[\alpha]_D^{22}$ +13.4° (*c* 1.1, water) (lit.[30] m.p. 170–171°, $[\alpha]_D$ +12° in water); λ_{max}^{EtOH} 266 nm; *m/e* 242 (M^+), 126 (base), and 117 (glycosyl$^+$); X-ray powder diffraction data: 9.84 m, 8.68 m, 6.80 w, 6.05 vw, 5.78 s, 5.50 vs (1), 4.89 w, 4.58 s (3), 4.33 m, 4.11 m, 4.02 vs (2), 3.91 vw, 3.77 m, 3.68 w, 3.57 w, 3.42 m, 3.37 w, 3.23 vw, 3.15 w, 3.05 w, and 2.91 m.

Anal. Calc. for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.82; N, 11.57. Found: C, 49.49; H, 5.76; N, 11.77.

*1-(3,5-Di-*O*-acetyl-2-*S*-ethyl-2-thio-6-*O*-p-tolylsulfonyl-β-*D*-mannofuranosyl)-thymine* (**22**). — *p*-Toluenesulfonyl chloride (1.90 g, 10.0 mmol) was stirred with a solution of compound **15** (3.00 g, 9.04 mmol) in anhydrous pyridine (12 ml) at 0° in an ice bath. After 30 min at 0° and 4 h at ~25°, acetic anhydride (20 ml) was added, and the mixture was kept for 18 h at ~25°. The solution was then triturated with ice–water, to give **22** as a fine powder, yield 5.10 g (98%), suitable for the next step. A small portion was purified by preparative t.l.c. (19:1 ether–methanol), and recrystallized from ethanol to give pure **22**; m.p. 129.5–130.5°, $[\alpha]_D^{24}$ −5° (*c* 1.9, chloroform); λ_{max}^{EtOH} 266 (ε 10,000) and 273 nm (shoulder, 9,000); X-ray powder diffraction data: 14.29 w, 11.65 vs (3), 9.98 vw, 8.97 vs (2), 7.79 m, 6.79 s, 6.37 vw, 5.77 m, 5.00 vs (1), 4.76 w, 4.72 vw, 4.32 m, 4.03 s, 3.86 w, 3.64 s, and 3.44 m.

Anal. Calc. for $C_{24}H_{30}N_2O_{10}S_2$: C, 50.52; H, 5.30; N, 4.91; S, 11.24. Found: C, 50.53; H, 5.12; N, 4.88; S, 11.23.

*1-(3,5-Di-*O*-acetyl-6-deoxy-2-*S*-ethyl-6-iodo-2-thio-β-*D*-mannofuranosyl)thymine* (**23**). — To a solution of crude **22** (2.42 g, 4.25 mmol) in butanone[34] (50 ml) was added sodium iodide (0.80 g, 5.33 mmol). The mixture was boiled for 3.5 h under reflux, and then evaporated to dryness. A solution of the residue in chloroform (30 ml) was washed successively with aqueous sodium thiosulfate and water, dried (sodium sulfate), and evaporated; the residue crystallized from ethanol to give the iodo derivative **23**, suitable for further reaction; yield 1.82 g (81%). A small portion was further purified by preparative t.l.c. (3:2 ether–benzene), and recrystallized from ethanol to give pure **23**; m.p. 133–134°, $[\alpha]_D^{24}$ −6° (*c* 1.75, chloroform); λ_{max}^{EtOH} 266 nm (ε 10,000); *m/e* 526 (M^+), 400 (M^+ − thymine); X-ray powder diffraction data: 12.18 vw, 10.37 vs (1), 8.58 w, 8.48 vw, 7.57 vw, 7.02 s, 5.89 w, 5.65 w, 5.16 m, 4.83 m, 4.29 s, 4.02 s, 3.77 vs (2), 3.67 vs (3), 3.50 m, 3.41 w, 3.25 vw, 3.07 m, and 2.93 m.

Anal. Calc. for $C_{17}H_{23}IN_2O_7S$: C, 38.80; H, 4.40; N, 5.32. Found: C, 38.57; H, 4.65; N, 5.53.

A methanolic solution of compound **23** was refluxed with silver acetate by the procedure described by West[35]. Isolation as described gave back starting-material.

1-(3,5-Di-O-acetyl-6-S-acetyl-2-S-ethyl-2,6-dithio-β-D-mannofuranosyl)thymine (**24**). — A mixture of crude compound **23** (3.30 g, 6.28 mmol) and potassium thiolacetate (1.07 g, 9.39 mmol) in ethanol (50 ml) was boiled for 1.5 h under reflux. The mixture was concentrated to 10 ml and poured into water (100 ml). The precipitated crystalline mass was filtered off, washed with water, dried, and recrystallized from ethanol to give pure **24**; yield 2.23 g (75%); m.p. 181°, $[\alpha]_D^{25}$ +44° (*c* 1.25, chloroform); λ_{max}^{EtOH} 266 nm (ε 9,800); *m/e* 474 (M^+), 348 (M^+ − thymine); X-ray powder diffraction data: 7.34 vs (1), 6.68 w, 5.92 s (2), 5.12 vw, 4.72 s (3), 4.05 s, 3.74 w, 3.38 m, 3.17 w, 3.03 vw, and 2.84 w.

Anal. Calc. for $C_{19}H_{26}N_2O_8S_2$: C, 48.08; H, 5.52; N, 5.90; S, 13.51. Found: C, 47.94; H, 5.47; N, 5.71; S, 13.57.

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