133°; λ_{max}^{MeOH} 266 mμ (ε 11,750); λ_{max}^{chf} br, bonded absorption 3.0–4.5, 5.92, 6.2–6.3 (br), 7.2, and 7.4 μ; nmr in deuterioacetone τ 5.04 (s) $-CH_2$, τ 8.28 (s) $-CH_3$; positive ferric chloride test.

Anal. Calcd for $C_6H_6O_2Br_2$: C, 26.69; H, 2.24; Br, 59.21. Found: C, 27.45; H, 2.55; Br, 58.79.

Registry No.—**3**, 899-79-6; **5**, 13865-85-5; **6**, 13865-86-6; **7**, 13765-87-7; **8**, 13865-88-8; **8a**, 517-06-6; **9** (X = Br), 13865-90-2; **9** (X = Cl), 13865-91-3; **9** (X = FSO_3), 13865-92-4; **10**, 13865-93-5.

Nuclear Magnetic Resonance Studies on Acetylated 1-Thioaldopyranose Derivatives[1,2]

CHARLES V. HOLLAND, DEREK HORTON,[3] MARTHA J. MILLER,[4]

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

AND NORMAN S. BHACCA

Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803

Received April 10, 1967

The nmr spectra of the fully acetylated 1-thioaldopyranoses having the configurations β-D-*xylo* (**1**), α-L-*arabino* (**2**), β-D-*ribo* (**4**), β-D-*gluco* (**5**), and β-D-*galacto* (**6**) were determined in chloroform-*d*, acetone-d_6, and benzene-d_6. The H-1 signal in these derivatives appears ~0.35 ppm to higher field than its position in the 1-oxygenated analogs. The relative chemical shifts of the various ring protons were sufficiently different in the three solvents to permit useful conformational and configurational information to be derived by partial first-order analysis of spectra measured at 60 MHz. Spectral measurements at 100 MHz were required for first-order analysis of the spectra of the hexose derivatives **5** and **6**. First-order analysis of the signals of the methine protons, in the α-L-*arabino* derivative **2** (or its D enantiomorph, **3**), was not possible at 100 MHz with any of the three solvents; complete first-order analysis was, however, possible when the spectrum was measured at 220 MHz in chloroform-*d*. Comparative spectral data are recorded for a series of *S*-substituted analogs (**7**–**10**) of substance **6**, and 4,6-di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyranose (**11**) is shown to adopt the *H1* conformation.

Investigations in this laboratory on the reactions of thio sugar derivatives with halogens have shown[2] that the progress of the reactions can be followed conveniently by nmr spectroscopy. Acetylated 1-thioaldose derivatives react with bromine to give acetylated glycosylsulfenyl bromides,[2b,5] acetylated glycosyl bromides, and other products, according to the conditions. The nmr spectra of a range of acetylated aldopyranosyl bromides have been analyzed[6] in terms of configurational and conformational factors, and it has been shown[2] that these products are readily detected in the mixtures of substances formed when 1-thioaldose derivatives are treated with bromine under various conditions.

The present report describes a comparative analysis of the nmr spectra of a series of acetylated 1-thioaldopyranoses and some related derivatives, at 60, 100, and, in some cases, at 220 MHz. The results illustrate the use of solvent effects as an aid in spectral analysis, for reducing the signals of methine and methylene protons to patterns that are amenable to first-order interpretation. Such interpretation is particularly facile for a proton (or protons) attached to C-5 of the pyranoid ring, and the derived coupling constants are especially useful for providing information on conformation and configuration.

Materials

1-Thio-β-D-glucopyranose pentaacetate (**5**) was prepared from tetra-*O*-acetyl-α-D-glucopyranosyl bromide and potassium thiolacetate.[7,8] 1-Thio-β-D-galactopyranose pentaacetate (**6**), 1-thio-β-D-xylopyranose tetraacetate[9] (**1**), 1-thio-α-L-arabinopyranose tetraacetate (**2**), and the α-D analog (**3**) of **2** were prepared similarly. Low yields of product were obtained when this procedure was used to prepare 1-thio-β-D-ribopyranose tetraacetate (**4**) from tri-*O*-acetyl-β-D-ribopyranosyl bromide, and it was difficult to remove an accompanying side product. Condensation of tri-*O*-acetyl-β-D-ribopyranosyl bromide with thiourea, to give 2-(2,3,4-tri-*O*-acetyl-β-D-ribopyranosyl)-2-thiopseudourea hydrobromide, followed by cleavage of the *S*-amidino group by the general procedure of Černý, Vrkoč, and Staněk,[10] with subsequent reacetylation, gave pure **4**. The same route was also used to prepare **2** (an **3**[10]) by way of 2-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl)-2-thiopseudourea (and its D enantiomorph[10]). The enantiomorphs **2** and **3** had the anticipated opposite signs of rotation, and were each obtained in two dimorphous forms, one melting at 39° and the other at 81.5–82°. Melting points of 79°[9] and 80–81°[10] have been reported for substance **3**. The anomeric configurations assigned to the products are those anticipated to result from attack by the sulfur nucleophile on an intermediate, 1,2 cyclic acetoxonium ion during the condensation step. Nmr and optical rotatory data provide firm support for the anomeric assignments. Each of the products **1**–**6** showed absorption at 5.85–5.90 μm in its infrared spectrum, characteristic[8] of the

(1) Supported in part by the Agricultural Research Service, U. S. Department of Agriculture, Grant No. 12-14-100-7208 (71) (The Ohio State University Research Foundation Project 1827) administered by the Northern Utilization Research and Development Division, Peoria, Ill. The 60-MHz nmr spectrometer was provided through a grant from the National Science Foundation.

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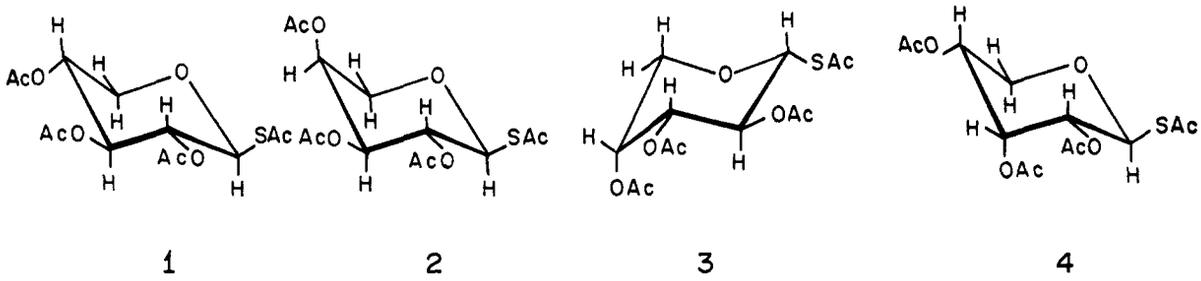
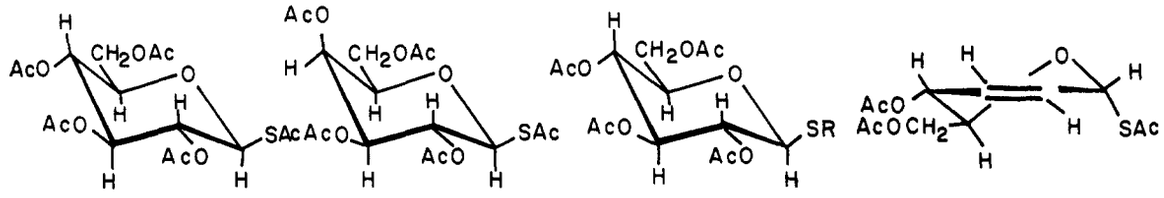


1 2 3 4



5 6 11

7 R = CH_2Ph
8 R = Bz
9 R = CSOEt
10 R = tert-Bu

S-acetyl group, in addition to the *O*-acetyl absorption near 5.75 μm.

Benzyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside[11] (**7**) was obtained in high yield by treatment of tetra-*O*-acetyl-α-D-glucopyranosyl bromide with potassium α-toluenethioxide in ethanol, followed by reacetylation of the product, which was partially saponified during the condensation. This general procedure, satisfactory for preparation of 2,3,4,6-tetra-*O*-acetyl-1-*S*-benzoyl-1-thio-β-D-glucopyranose[12,13] (**8**) and tetra-*O*-acetyl-β-D-glucopyranosyl ethylxanthate[14] (**9**) without the acetylation step, was unsatisfactory as a preparative route to *t*-butyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**10**) when sodium 2-methyl-2-propanethioxide was used even when the product was reacetylated. Mercaptolysis of β-D-glucopyranose pentaacetate with 2-methyl-2-propanethiol and zinc chloride, by the procedure of Fletcher and co-workers[15] gave **10** in good yield. 4,6-Di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyranose (**11**) was prepared from D-glucal triacetate and thiolacetic acid, as described by Tejima and co-workers.[16]

Results and Discussion

The nmr spectra of the acetylated 1-thioaldopyranoses **1**–**6** were measured at room temperature in chloroform-*d*, acetone-d_6, and benzene-d_6. Substances **2** and **3** gave, as anticipated, identical spectra. All spectra were determined at 60 and also at 100 MHz. The low-field portion of the 100-MHz spectrum for each of the three solvents, is shown for **1** (Figure 1), **3** (Figure 3), **4** (Figure 4), **5** (Figure 5), and **6** (Figure 6). The spectrum of **2** in chloroform-*d* was also measured at 220 MHz, and the low-field portion of this spectrum is shown in Figure 2. The lowest field portions of the 220-MHz spectra of **1** and **5**, in acetone-d_6, are shown in Figure 7, and Figure 8 shows the 220-MHz spectrum

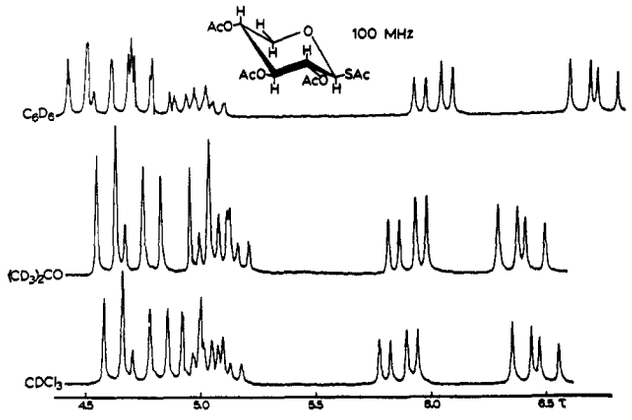


Figure 1.—The low-field portion of the 100-MHz spectra of 1-thio-β-D-xylopyranose tetraacetate (**1**) in chloroform-*d*, acetone-d_6, and benzene-d_6.

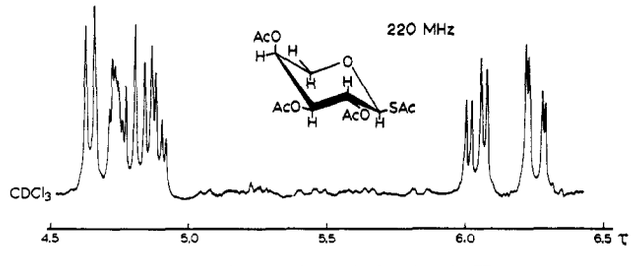


Figure 2.—The low-field portion of the 220-MHz spectrum of 1-thio-α-L-arabinopyranose tetraacetate (**2**) in chloroform-*d*.

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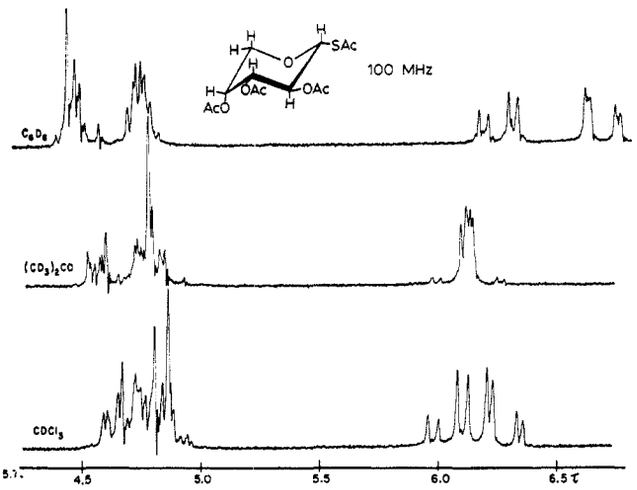

Figure 3.—The low-field portion of the 100-MHz spectrum of 1-thio-α-D-arabinopyranose tetraacetate (**3**) in chlorororm-*d*, acetone-d_6, and benzene-d_6.

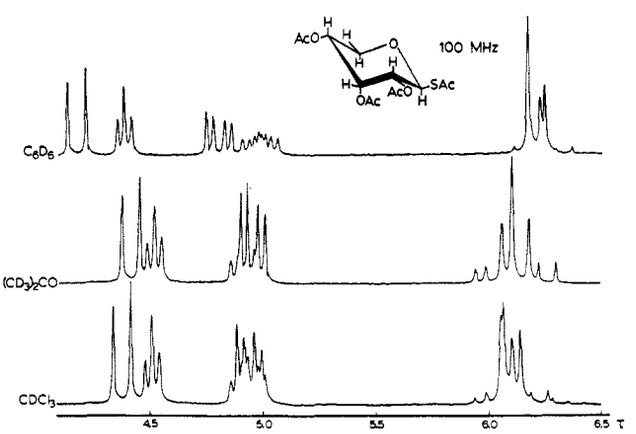

Figure 4.—The low-field portion of the 100-MHz spectrum of 1-thio-β-D-ribopyranose tetraacetate (**4**) in chlorororm-*d*, acetone-d_6, and benzene-d_6.

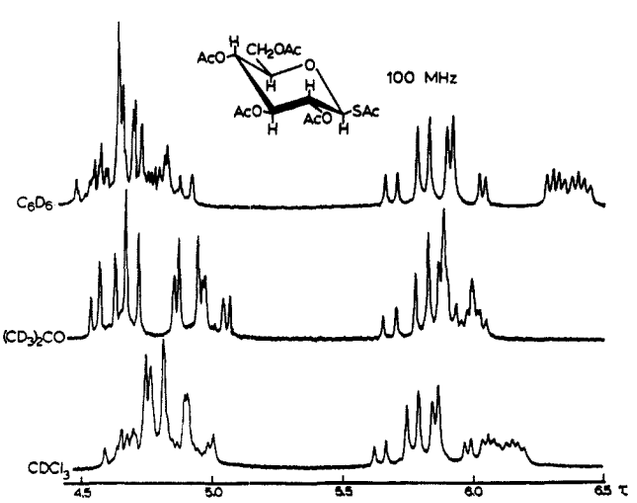

Figure 5.—The low-field portion of the 100-MHz spectrum of 1-thio-β-D-glucopyranose pentaacetate (**5**) in chlorororm-*d*, acetone-d_6, and benzene-d_6.

of the unsaturated derivative **11**, in acetone-d_6. Chemical shift data for the methine and methylene protons, taken from the 100- and 220-MHz spectra, are given in Table I. First-order coupling constants are given in Table II, and chemical-shift data for the acetyl methyl protons are given in Table III.

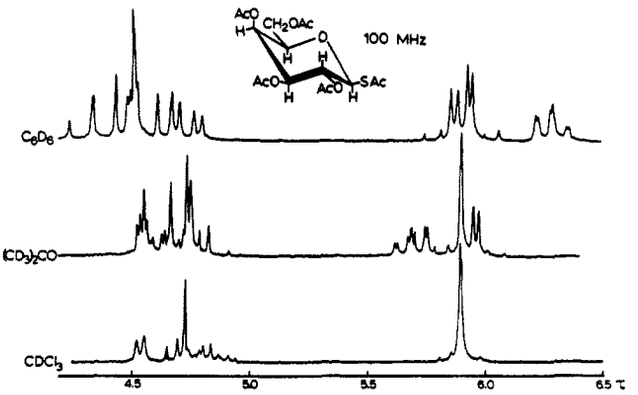

Figure 6.—The low-field portion of the 100-MHz spectrum of 1-thio-β-D-galactopyranose pentaacetate (**6**) in chloroform-*d*, acetone-d_6, and benzene-d_6.

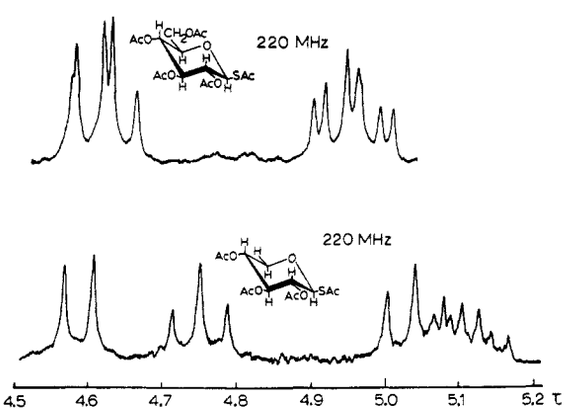

Figure 7.—The signals of H-1, 2, 3, and 4 of 1-thio-β-D-xylopyranose tetraacetate (**1**) and 1-thio-β-D-glucopyranose pentaacetate (**5**) in acetone-d_6 at 220 MHz.

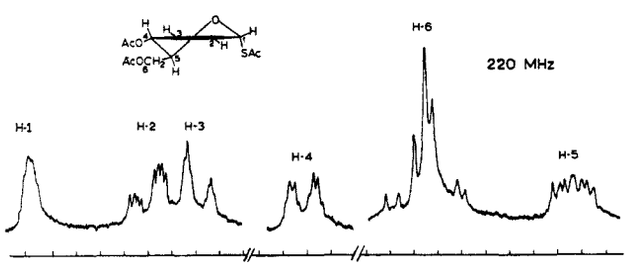

Figure 8.—The low-field portion of the 220-MHz spectrum of 4,6-di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyranose (**11**) in acetone-d_6. The scale divisions correspond to 10 Hz.

Signals of the Acetyl Methyl Groups.—In all of the spectra measured in chloroform-*d* or acetone-d_6 a characteristic[2] three-proton singlet, assigned to the (equatorial) *S*-acetyl group, is observed near τ 7.65. Signals of the acetoxy groups, in these two solvents, showed resonances in the τ 7.93–8.11 range; in the case of substances **2** (in chloroform-*d*), **4**, and **6**, a three-proton singlet at somewhat lower field was also observed. The latter signal may be attributed to an axial acetoxy group,[17–19] although such an assignment can be regarded as tentative only[19] and does not constitute unambiguous evidence, such as would be provided by synthesis of specifically trideuterioacetylated

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TABLE I

CHEMICAL SHIFTS OF METHINE AND METHYLENE PROTONS OF PERACETYLATED 1-THIOALDOPYRANOSES[a]

			Chemical shifts, τ									
			H-1	H-2	H-3		H-4		H-5		H-6	H-6′
Compd	Confign	Solvent	a	a	e	a	e	a	e	a		
1	β-D-*xylo*	$CDCl_3$	4.62	5.00		4.78		5.08	5.84 (5.86)[b]	6.46 (6.45)[b]		
		$(CD_3)_2CO$	4.60	5.04		4.75		5.11	5.90 (5.91)[b]	6.40 (6.39)[b]		
		C_6D_6	4.49	4.81		4.63		5.02	6.03 (6.03)[b]	6.73 (6.72)[b]		
2 (or 3)	α-L-*arabino* (or α-D-*arabino*)	$CDCl_3$	4.57–4.95[c]						6.04[d] (6.05)[b]	6.26[d] (6.25)[b]		
		$CDCl_3$	4.65[e]	4.81[e]		4.89[e]		4.74[e]	6.04[d]	6.26[d]		
		$(CD_3)_2CO$	4.46–4.98[c]						6.05[d]	6.19[d]		
		C_6D_6	4.40–4.78[c]						6.22[d] (6.24)[b]	6.60[d] (6.59)[b]		
4	β-D-*ribo*	$CDCl_3$	4.38	4.94	4.51			4.93	6.02 (6.06)[b]	6.17 (6.13)[b]		
		$(CD_3)_2CO$	4.41	4.96	4.52			4.93	6.03 (6.05)[b]	6.20 (6.18)[b]		
		C_6D_6	4.18	4.80	4.39			4.99	6.15 (6.19)[b]	6.28 (6.23)[b]		
5	β-D-*gluco*	$CDCl_3$	4.59–5.00[c]							6.12	5.71 (5.73)[b]	5.92 (5.90)[b]
		$(CD_3)_2CO$	4.62	4.97		4.63		4.94		~5.98	5.74 (5.76)[b]	5.95 (5.92)[b]
		C_6D_6	4.48–4.93[c]							6.37	5.75 (5.77)[b]	5.98 (5.96)[b]
6	β-D-*galacto*	$CDCl_3$	4.52–4.94[c]								~5.89[c]	
		$(CD_3)_2CO$	4.55–4.76[c]			~4.76	~4.54			5.68	5.87 (5.91)[b]	5.99 (5.95)[b]
		C_6D_6	4.55	4.33		4.73	4.50			6.28	5.83 (5.84)[b]	5.97 (5.95)[b]

[a] Data taken, unless otherwise noted, from spectra measured at 100 MHz. [b] Shifts given in parentheses were calculated by ABX analysis; see ref 22. [c] Complex multiplet, not analyzed on a first-order basis. [d] The two H-5 signals are not unambiguously differentiated. [e] From spectrum measured at 220 MHz.

TABLE II

FIRST-ORDER COUPLING CONSTANTS FOR PERACETYLATED 1-THIOALDOPYRANOSES[a]

			Coupling constants, Hz								
Compd	Confign	Solvent	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5e}$	$J_{4,5a}$	$J_{5a,5e}$	$J_{5a,6}$[b]	$J_{5,6'}$[b]	$J_{6,6'}$
1	β-D-*xylo*	$CDCl_3$	8.1	7.5	7.5	4.7 (4.7)[c]	8.3 (8.2)[c]	11.8			
		$(CD_3)_2CO$	8.2	7.8	7.7	4.8 (4.9)[c]	8.4 (8.5)[c]	11.8			
		$(CD_3)_2CO$	8.6[d]	8.2[d]	8.0[d]	4.9[d]	8.6[d]	11.9[d]			
		C_6D_6	8.1	7.9	7.3	4.9 (5.0)[c]	8.8 (8.8)[c]	11.8			
2 (or 3)	α-L-*arabino* (or α-D-*arabino*)	$CDCl_3$	*e*	*e*	*e*	4.5[f] (4.6)[c]	2.4[f] (2.0)[c]	12.2			
		$CDCl_3$	7.0[d]	8.0[d]	3.3[d]	4.7[d,f] (4.6)[c,d]	2.3[d,f] (2.4)[c,d]	12.5[d]			
		$(CD_3)_2CO$	*e*	*e*	*e*	3.6[f]	3.0[f]	12.6			
		C_6D_6	*e*	*e*	*e*	3.9 (4.1)[c]	2.0 (1.7)[c]	12.4			
4	β-D-*ribo*	$CDCl_3$[g]	7.7	3.0	3.0	4.7 (3.1)[c]	7.5 (9.0)[c]	11.8			
		$(CD_3)_2CO$[g]	7.6	3.1	3.0	4.6 (4.4)[c]	7.7 (8.4)[c]	12.0			
		C_6D_6[g]	7.9	3.1	3.0	5.2 (2.5)[c]	7.5 (10.1)[c]	11.7			
5	β-D-*gluco*	$CDCl_3$	*e*	*e*	*e*		9.4		4.4 (4.9)[c]	2.2 (2.2)[c]	12.4
		$(CD_3)_2CO$	10.0	9.1	9.1		9.3		5.0 (5.6)[c]	~2 (1.7)[c]	12.4
		$(CD_3)_2CO$	10.6[d]	9.5[d]	9.5[d]		10.1[d]		5.4[d]		13.2[d]
		C_6D_6	*e*	*e*	*e*		9.9		4.5 (4.8)[c]	2.3 (2.2)[c]	12.4
6	β-D-*galacto*	$CDCl_3$	*e*	*e*	*e*		*e*		*e*	*e*	*e*
		$(CD_3)_2CO$	*e*	*e*	~3.0		1.1		5.7 (2.8)[c]	7.0 (10.2)[c]	11.0
		C_6D_6	10.0	9.4	3.4		1.2		6.7 (9.3)[c]	6.0 (3.6)[c]	11.2

[a] Data taken, unless otherwise noted, from spectra measured at 100 MHz. [b] The proton on C-6 giving the higher field signal is designated H-6′. [c] Coupling constants given in parentheses were calculated by ABX analysis; see ref 22. [d] Data from spectrum measured at 220 MHz. [e] First-order couplings not observed. [f] $J_{4,5e}$ and $J_{4,5a}$ refer to coupling of H-4 with lowest field and highest field H-5 signals, respectively. [g] $J_{3,5e}$ = ~0.6 Hz.

TABLE III

CHEMICAL SHIFTS OF ACETYL METHYL PROTONS[a]

			Chemical shifts, τ (integral, protons)				
Compd	Confign	Solvent					
1	β-D-*xylo*	$CDCl_3$	7.65 (3)	7.97 (9)			
		$(CD_3)_2CO$	7.66 (3)	8.02 (6)	8.03 (3)		
		C_6D_6		8.25 (3)	8.31 (3)	8.33 (3)	8.41 (3)
2 (or 3)	α-L-*arabino* (or α-D-*arabino*)	$CDCl_3$	7.65 (3)	7.92 (3)	7.96 (6)		
		$(CD_3)_2CO$	7.66 (3)	7.97 (3)	8.01 (3)	8.04 (3)	
		C_6D_6		8.14 (3)	8.22 (3)	8.28 (3)	8.32 (3)
4	β-D-*ribo*	$CDCl_3$	7.58 (3)	7.85 (3)	7.93 (6)		
		$(CD_3)_2CO$	7.60 (3)	7.90 (3)	7.99 (6)		
		C_6D_6		8.18 (3)	8.26 (3)	8.28 (3)	8.35 (3)
5	β-D-*gluco*	$CDCl_3$	7.65 (3)	7.96 (3)	8.01 (6)	8.03 (3)	
		$(CD_3)_2CO$	7.66 (3)	8.05 (6)	8.07 (3)	8.10 (3)	
		C_6D_6		8.25 (3)	8.31 (6)	8.32 (6)	
6	β-D-*galacto*	$CDCl_3$	7.64 (3)	7.87 (3)	8.00 (6)	8.04 (3)	
		$(CD_3)_2CO$	7.65 (3)	7.92 (3)	8.05 (6)	8.11 (3)	
		C_6D_6		8.26 (6)	8.28 (3)	8.35 (3)	8.38 (3)
		CCl_4[b]	7.65 (3)	7.87 (3)	8.01 (6)	8.06 (3)	

[a] Data taken, unless otherwise noted, from spectra measured at 100 MHz. [b] Data taken from 60-MHz spectrum.

derivatives.[20,21] The spectrum of **2** in acetone-d_6 indeed does not show a signal below τ 7.93, although at least one axial acetoxy group clearly must be present. In benzene-d_6 solution, all of the acetyl-group signals are observed at high field[20,21] (τ 8.2–8.4), and differences of shift characteristic of the environment of the acetyl groups were not readily rationalized.

Signals of the Methine and Methylene Protons. General.—The low-field portion of the spectra of substances **1–6** resembles the spectra of other acetylated aldopyranoses in that it can be subdivided into two nonoverlapping regions. Signals of H-5 and H-6 methylene groups (pentopyranoses and hexopyranoses, respectively) and the proton of the C_2CHOR group (H-5 of hexopyranoses) appear in the region τ 5.65–6.75. Signals of the remaining methine protons, on H-1, 2, 3, and 4, appear at lower field, below τ 5.25.

Signals in the upper (H-5, 6) group constitute three- (pentopyranoses) or four- (hexopyranoses) spin systems, in which the H-5 proton(s) also interact with the proton on H-4, whose signal appears at lower field. The H-5 signals of pentopyranoses constitute the AB[22] portion of an ABX system, where X is H-4, unless the H-5 protons have the same chemical shift, in which case an A_2X system is observed. In the ABX case the J_{AB} coupling can be measured directly and approximate values of J_{AX} and J_{BX} can be obtained by direct measurement (first-order analysis), or the values of J_{AX} and J_{BX} can be determined more exactly by calculation[22] from the observed spectral lines. The magnitudes of the couplings between H-4 and the H-5 protons (J_{AX} and J_{BX}) thereby obtained are especially useful for configurational and conformational studies, as they indicate whether the relationship of H-4 with each of the H-5 protons is antiparallel or *gauche*. In the case of the hexopyranoses, the C-6 methylene group and H-5 interact with H-4 as a four-spin system, commonly of the ABXY or ABCY type, where A and B are the C-6 protons, X(or C) is H-5, and Y is H-4; the difference in chemical shift between X and Y is normally large. For configurational and conformational studies, a spectrum of the ABXY type is the most informative because it enables $J_{X,Y}$, the coupling between H-4 and H-5, to be determined; this indicates whether H-4 and H-5 are antiparallel or *gauche*. The $J_{X,Y}$ value is readily determined in the ABXY system because $J_{A,X} + J_{B,X}$ can be measured from the spacings of the AB octet, and the total width between outer peaks of the H-5 multiplet is $J_{A,X} + J_{B,X} + J_{X,Y}$. The examples studied in the present article illustrate how specific solvent shielding, especially the use of benzene to cause upfield shift of the signal of an axial proton at C-5, can be used to reduce a complex ABCY multiplet to the ABXY case, amenable to simple analysis.

In addition to the first-order chemical shift and coupling data given in Tables I and II, calculated[22] values are given in parentheses for the ABX systems. It can be seen that, in those instances where the A and B quartets are fully separated, the first-order splittings are very close to the calculated J_{AX} and J_{BX} values. Substantial differences between the first-order splittings and the calculated couplings are evident when overlap of the A and B quartets occurs, as in **4** and **6**.

Signals in the lower (H-1, 2, 3, 4) group constitute a mutually coupled spin system in which H-4 is also coupled with H-5. This portion of the spectrum may be very complex unless the differences in chemical shift between strongly coupled protons are large compared to the coupling constants. In the acetylated aldopyranoses, and many other aldopyranose derivatives, analysis of this group of signals is facilitated by the fact that the H-1 signal [CH(OR)(OR′) group] appears at considerably lower field than the H-2, 3, and 4 signals (CHOR groups), so that the H-1 signal can be treated as the X portion of an AX system, where A is H-2 (or as the X portion of an AA′X system[23] when H-2 and H-3 are strongly coupled and differ little in chemical shift). The observed coupling, J_{AX}, between H-1 and H-2 is useful for determining anomeric configuration and favored ring conformation. In the case of the acetylated 1-thioaldopyranoses **1**, **4**, **5**, and **6**, the H-1 signals [of the CH(OR)(SR) group] appear 0.35–0.4 ppm to higher field than the H-1 signals for the corresponding 1-oxygenated analogs,[19] while the chemical shifts of the H-5 signals are approximately the same (within 0.1 ppm), for spectra measured in chloroform-*d* (Table I). The shift to higher field of the H-1 signal causes it to appear close to, or within, the "envelope" of signals for H-2, 3, and 4 in the spectra of **1–6**, so that first-order interpretations of this region of the spectra of the acetylated 1-thioaldopyranoses are more difficult than with the 1-oxygenated analogs. The use of solvent effects for obtaining first-order analyses in this region is illustrated herein.

Coupling Constants, Configuration, and Conformational Inversion.—For protons on adjacent carbon atoms in a six-membered ring system, the generalization, based on the Karplus relationship,[24] that antiparallel protons give rise to large (7.5–10 Hz) first-order couplings and *gauche* protons give small (<5.5 Hz) couplings, is valid,[18] although precise calculations of bond angles from coupling constants may not be meaningful. In particular, configurational factors may influence the magnitudes of *gauche* couplings;[25] adjacent diequatorial protons show couplings (~1–2 Hz) considerably smaller than the usual coupling (~3–4 Hz) of adjacent, axial–equatorial protons.[26] It is unlikely that molecular distortion is entirely responsible for these differences.

Assuming that the energy barrier for ring inversion is sufficiently low that conformational inversion is fast on the nmr time scale, the observed spectra will represent a time average of the various conformers present. The measured coupling constants will be averaged values of those of the various conformers, weighted according to the proportion of each present. The proportion of each conformer will depend on its free energy in the system, and forms of presumed high

(20) D. Horton, J. B. Hughes, J. S. Jewell, Kerstin D. Philips, and W. N. Turner, *J. Org. Chem.*, **32**, 1073 (1967).

(21) D. Horton, W. E. Mast, and Kerstin D. Philips, *ibid.*, **32**, 1471 (1967).

(22) For details of the ABX notation and calculation of J_{AX} and J_{BX} couplings, see J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 132; J. D. Roberts, "An Introduction to the Analysis of Spin–Spin Splitting in Nuclear Magnetic Resonance," W. A. Benjamin, Inc., New York, N. Y., 1962, p 71.

(23) J. I. Musher and E. J. Corey, *Tetrahedron*, **18**, 791 (1961).

(24) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Am. Chem. Soc.*, **85**, 2870 (1963).

(25) D. H. Williams and N. S. Bhacca, *ibid.*, **86**, 2742 (1964).

(26) B. Coxon, *Tetrahedron*, **21**, 3481 (1965).

energy such as the nonchair conformations will make a negligible contribution to the total conformational population. Considering only the two possible chair conformations for substances **1–6**, it is evident from the interaction energies[27] between various ring substituents that, in the case of the D-glucose and D-galactose derivatives (**5** and **6**), the *C1* (D) conformation shown is overwhelmingly favored, and the very small proportion of the *1C* (D) conformation statistically present will have a negligible effect on the appearance of the nmr spectrum. With the pentose derivatives **1–4** the possibility cannot be discounted, especially with **2–4**, that the alternative chair form may exist in appreciable proportion in equilibrium with the (apparently favored) forms shown. It cannot be assumed that the forms having the most substituents equatorial are necessarily the most stable, because of possible unfavorable polar interactions between the ring-oxygen atom and the C-1 substituent (anomeric effect).[6,27-29]

1-Thio-β-D-glucopyranose Pentaacetate (5).—Complete first-order analysis of the spectra was possible by use of acetone-d_6 and benzene-d_6 as solvents (Figure 5). The H-5, 6 multiplet for **5** in benzene-d_6 could be analyzed as a simple ABXY system at either 60 or 100 MHz. The H-5 signal is observed at high field (τ 6.37) as a symmetrical eight-peak multiplet. The width of this multiplet is expected to be $J_{4,5} + J_{5,6} + J_{5,6'}$, and, since $J_{5,6'}$ and $J_{5,6}$ are readily measured from the H-6 and H-6′ signals (AB portion), the value of $J_{4,5}$ (9.9 Hz) is determined by difference. A similar analysis could be made of the H-5, 6 multiplet for the spectrum of **5** in chloroform-*d*, but only at 100 MHz. First-order analysis of this multiplet was not possible when acetone-d_6 was used as solvent, because the H-5 signal overlapped the high-field H-6 signal (H-6′), although it was still possible to observe the lower field H-6 signal as a quartet.

The low field envelope of signals (H-1, 2, 3, 4) was not amenable to simple analysis when benzene-d_6 or chloroform-*d* was used as solvent, in contrast to the spectrum of the 1-oxygenated analog[19] of **5**, where the H-1 signal appears at substantially lower field than the signals of the other methine hydrogens. However, in acetone-d_6 at 100 MHz it was possible to assign signals of all four protons on a first-order basis despite overlap of multiplets, because the overlaps involved the signals of the noncoupled pairs of protons H-1 and H-3, and H-2 and H-4. After identification of the H-1 doublet in the group of five peaks centered near τ 4.63, it was evident that the remaining three peaks were the H-3 triplet, because any other assignment would have given a second-order spectrum in this or the τ τ 4.95 region. The H-2 and H-4 signals could then be assigned straightforwardly in the multiplet near τ 4.95. The same pattern of signals for H-1, 2, 3, and 4 was observed when the spectrum was measured at 220 MHz in acetone-d_6 (Figure 7), and the first-order couplings were slightly greater (by ~0.5 Hz) than those measured from the 100-MHz spectrum. The first-order vicinal couplings of all methine protons were large (9.1–10.0 Hz from the 100-MHz spectrum), as anticipated for the all-axial arrangement of protons in **5**. The splittings measured from the 220-MHz spectrum are, presumably, closer to the absolute coupling constants than those measured from the 100-MHz spectrum.

The conformations that the acetoxymethyl group (C-5 substituent) can adopt by rotation about the C-5–C-6 bond undoubtedly give rise to a time-averaged spectrum, with contributions from the three staggered rotomers.[19,30] The magnitudes of the observed $J_{5,6}$ and $J_{5,6'}$ couplings indicate a major contribution from the rotomer having the C-4 and C-6 acetoxy groups antiparallel, and a smaller contribution from the rotomer having H-5 bisecting the angle of the C-6 methylene group (H-5 and 6-OAc antiparallel). The rotomer having the 4,6-acetoxy groups opposed (*syn*) probably makes no significant contribution.

1-Thio-β-D-xylopyranose Tetraacetate (1).—In each of the three solvents, at 100 MHz (Figure 1) and at 60 MHz, it was possible to analyze the signals of the C-5 methylene group as the AB portion of an ABXY system, and the higher field quartet in each spectrum is clearly assignable to the axial H-5 in the *C1* conformation on the basis of the large (8.3–8.8 Hz) coupling with H-4. The $J_{4,5e}$ coupling (4.7–4.9 Hz) is larger than that normally observed for vicinal protons in a *gauche* relationship, but it is relevant to note that relatively large $J_{4,5e}$ couplings have been observed with tetra-*O*-acetyl-α-D-xylopyranosyl chloride[29] and α-D-xylopyranose tetraacetate.[19]

The signals of the methine protons yielded readily to first-order analysis in the spectrum measured in acetone-d_6 at 100 MHz and also at 60 MHz. The wide doublet at τ 4.60 is assigned to H-1. The line intensities of the triplet at τ 4.75 and the absence of second-order effects indicate that this is the signal of H-3 rather than H-2. From the remaining signals the H-2 triplet (τ 5.04) can be distinguished. The remaining multiplet, at τ 5.11, has a width of 21 Hz between the outer peaks, in agreement with the value determined independently for the H-4 signal from the sum of $J_{3,4} + J_{4,5e} + J_{4,5a}$. Similar assignments of the methine signals can be made for the spectra in chloroform-*d* and benzene-d_6 at 100 MHz, although some deviation from strict first-order character is observed. The spectrum of **1** in acetone-d_6 at 220 MHz showed the H-1 doublet and H-3 triplet well separated with little intensity buildup toward higher field (Figure 7). The highest field peak of the H-2 triplet overlapped one peak of the H-4 multiplet, and the latter was observed as a six-line multiplet, width 21.7 Hz. The first-order coupling constants measured from the 220-MHz spectrum are slightly greater than those measured at 100 MHz, and are probably very close to the absolute $|J|$ values.

In comparison with its hexose homomorph **5**, the pentose derivative **1** shows somewhat smaller vicinal coupling constants (~7.5–8.5 Hz) between axial protons. The possibility that a small proportion of the alternative, all-axial *1C* conformer of **1** is present

(27) R. U. Lemieux in "Molecular Rearrangements," Part 2, P. de Mayo, Ed., Interscience Division, John Wiley and Sons, Inc., New York, N. Y., 1964, pp 735–743.

(28) B. Coxon, *Tetrahedron*, **22**, 2281 (1966); C. V. Holland, D. Horton, and J. S. Jewell, *J. Org. Chem.*, **32**, 1818 (1967).

(29) The anomeric effect of the acetylthio group appears to be less than that of the acetoxy group, because in the 1-oxygenated analog of **4** the *1C* (D) conformation preponderates over the *C1* (D) conformation by about 2:1, as revealed directly by low-temperature nmr spectroscopy in acetone-d_6 (N. S. Bhacca and D. Horton, to be published).

(30) D. Horton and M. J. Miller, *J. Org. Chem.*, **30**, 2457 (1965).

in equilibrium with the favored *C1* (all-equatorial) conformation cannot be excluded.

1-Thio-β-D-galactopyranose Pentaacetate (6).—As in the case of the D-*gluco* analog (**5**), the H-5, 6 multiplet was most readily analyzed when benzene-d_6 was used as the solvent (Figure 6), and again the H-5 signal is observed in this solvent at considerably higher field than the H-6 signals. Full analysis at 60 MHz was not possible, but at 100 MHz the $J_{5,6}$ and $J_{5,6'}$ couplings could be determined from the AB portion (H-6 and H-6′) of the ABXY system. The H-6 and H-6′ signals overlapped, and the calculated[22] couplings with H-5 were substantially different from the observed line splittings. The H-5 signal was observed as a triplet of narrow multiplets, in sharp contrast to its appearance in the D-*gluco* analog **5** where it was observed as an octet. The difference between $J_{5,6} + J_{5,6'}$ and the separation of the outer peaks of the H-5 signal in **6** indicates that $J_{4,5e}$ is 1.1 Hz. In acetone-d_6 the H-5 signal was observed at lower field than the H-6 signals. In chloroform-*d* H-5 and H-6 had almost identical chemical shifts, and analysis was not attempted.

The H-1, 2, 3, and 4 signals were observed as a complex multiplet in chloroform-*d*, even at 100 MHz, and no analysis was attempted. Partial analysis was possible when acetone-d_6 was the solvent. In benzene-d_6 a full first-order analysis was possible. The wide triplet at τ 4.33 and the quartet at τ 4.73 can clearly be assigned to H-2 and H-3, respectively, and the H-1 doublet, occurring at higher field (τ 4.55) than the H-2 signal, can be observed. The remaining signal, a multiplet at τ 4.50 assigned to H-4 has a line width of 4.5 Hz, in good agreement with that determined as $J_{3,4} + J_{4,5}$.

The values observed for $J_{5,6}$ and $J_{5,6'}$ indicate that the two C-5–C-6 rotomers having H-5 antiparallel to one of the C-6 protons are both involved, with the rotomer having the 6-acetoxy group antiparallel to C-4 presumably being the most highly populated state; it is probable that the contribution of the rotomer having the 4- and 6-acetoxy groups opposed (H-5 *gauche* to both C-6 protons) is negligible. One C-6 proton shows a larger coupling with H-5 than the other. In acetone-d_6, the relative positions of the H-6 signals in the field appears to be the reverse of that observed in benzene-d_6.

1-Thio-α-L-arabinopyranose Tetraacetate (2).—The spectrum of this compound, or that of its α-D enantiomorph (**3**), proved to be extremely difficult to analyze. The methine protons gave complex multiplets in chloroform-*d*, acetone-d_6, and benzene-d_6, when measured at 100 MHz (Figure 3). The methylene protons gave a pattern recognizable as the AB portion of an ABXY system in the spectrum measured in chloroform-*d*. A similar pattern was also observed with the spectrum in benzene-d_6, although second-order effects were apparent, probably because of a small difference in the chemical shift between X and Y (H-4 and H-3). In acetone-d_6 the two H-5 protons were almost equivalent, so that the H-5 signals overlapped; the first-order splittings of the H-5 protons with H-4 were approximately equal (~3 Hz).

The spectrum could be reduced to first-order analysis by measurement, in chloroform-*d*, at 220 MHz (Figure 2). In this spectrum, the multiplet of the methine protons was completely resolved. At lowest field a wide doublet (H-1) was observed. The quartet at highest field in this group of signals was readily assigned to H-3. The wide triplet, 0.08 ppm to lower field than the H-3 signal, was assigned to H-2. The five-peak multiplet observed between the H-1 and H-2 signals was assigned to H-4; the separation of the outer peaks of this signal (10.3 Hz) is in excellent agreement with the value calculated ($J_{3,4} + J_{4,5e} + J_{4,5a}$ from coupling constants measured elsewhere in the spectrum. It was not possible to differentiate the H-5e and H-5a signals unambiguously from the $J_{4,5}$ couplings since both of these are for vicinal-*gauche* protons, and the chemical shifts (Table I) and couplings (Table II) given for the H-5 signals are not specifically identified as those of H-5e and H-5a.

The nmr data clearly support the *C1* (L) conformation of **2** (and the corresponding *1C* (D) conformation of **3**) as the favored conformation. The fact that the diaxial couplings ($J_{1,2}$ and $J_{2,3}$) are appreciably smaller than those observed in the hexose structures suggests that there may be an appreciable contribution from the less favored, alternative chair conformation. No direct evidence was obtained to support this possibility; the low field portion of the spectrum of **3** at 220 MHz showed no detectable change to indicate "freezing-out" of the conformational equilibrium at −30°.

The first-order analysis of the methine multiplet of **3** that is possible by nmr measurements at 220 MHz effectively illustrates the use of the high-field strengths achieved with a superconducting solenoid. The relative chemical shifts involved are very small, $\delta_{1,2}$ = 0.16 ppm, $\delta_{2,3}$ = 0.08 ppm, $\delta_{3,4}$ = 0.15 ppm, and because the vicinal couplings are comparatively large (~3–8 Hz) the spectra measured at lower field strengths are very complex owing to second-order effects.

1-Thio-β-D-ribopyranose Tetraacetate (4).—A complete analysis of the spectrum of this compound could be achieved by measurements at 60 MHz; more accurate parameters were obtained by measurements at 100 MHz (Figure 4). The methylene signals were readily analyzed in the spectrum measured in acetone-d_6 and the signals of each of the methine protons were clearly observed as nonoverlapping multiplets when benzene-d_6 was the solvent. The H-1 signal was observed at lowest field as a wide doublet, and a narrow triplet at somewhat higher field was assigned to H-3. Further upfield, a quartet and an eight-peak multiplet were assigned to H-2 and H-4, respectively. The signals of H-2 and H-4 overlapped in spectra measured in acetone-d_6 and chloroform-*d*. In each case the width of the H-4 multiplet (~15.5 Hz) was in good agreement with that calculated as the sum ($J_{3,4} + J_{4,5e} + J_{4,5a}$).

The separation of the H-5e and H-5a signals was small in each of the solvents, but was greatest with acetone-d_6. In all cases there was overlap of the H-5e and H-5a signals, and the calculated $J_{4,5e}$ and $J_{4,5a}$ values are appreciably different from the directly measured splittings. The observed coupling constants indicate the *C1* (D) form as the favored conformation, and the signals of the axial and equatorial protons at C-5 are clearly differentiated. The lower

field H-5 quartet (H-5e) was slightly broadened, as were the peaks in the H-3 triplet, indicating a long-range coupling between H-5e and H-3 ($J_{3,5e}$ = 0.6 Hz). Long-range couplings of this magnitude are well established[19,29,31] for diequatorial protons in the "W" arrangement.

4,6-Di-*O*-acetyl-1-*S*-acetyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyranose (11).—Details of spectral measurements on this substance are recorded in the Experimental Section. At 60 MHz in chloroform-*d* the two olefinic protons were almost equivalent and the $J_{1,2}$ and $J_{3,4}$ couplings were very small. The H-1 signal was observed as a narrow multiplet, and a wide doublet of narrow doublets was assigned to H-4; the narrow splitting indicated homoallylic coupling of H-1 with H-4. The appearance of the H-4 signal and that of H-5 indicated a large $J_{4,5}$ coupling (~9 Hz), clearly supporting formulation of **11** in the *H1* conformation, with the ring oxygen atom above, and C-5 below, the plane of C-1, C-2, C-3, and C-4. Measurements in acetone-d_6 at 100 and at 220 MHz (Figure 8) fully supported this assignment, and these spectra indicated more subtle features of the couplings involved. The H-1 signal remained an incompletely resolved multiplet, even at 220 MHz, presumably because of virtual coupling[23] with H-3, and long-range coupling with H-3 and H-4. The lowest field olefinic hydrogen signal is observed as a doublet of narrow quartets; this signal is assigned to H-2, coupled to H-3, to H-1, and also to H-4. The H-3 signal is observed as a doublet of narrow multiplets by strong coupling with H-2, virtual coupling with H-1, and small coupling with H-4. The H-4 signal shows the large coupling with H-5, and the multiplicity of the peaks is ascribed to homoallylic, long-range coupling with H-1, and couplings with H-2 and H-3. Addition of benzene-d_6 to the solution caused the H-2 and H-3 signals to collapse to a single peak, and the spectrum then resembled closely the 60-MHz spectrum in chloroform-*d;* the H-4 signal became a sharper quartet and the H-1 multiplet became narrower.

Derivatives of 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranose.—A detailed spectral analysis was made only for the 1-*S*-acetyl derivative (**5**). Spectral data, recorded at 60 MHz, are given in the Experimental Section for the benzyl and *t*-butyl glycosides (**7** and **10**), the 1-*S*-benzoyl derivative **8**, and the ethylxanthate derivative **9**. In none of the spectra of these compounds was it possible to observe the H-1 signal independently of the envelope of signals for the methine protons at C-2, 3, and 4. In each case, however, it was possible to observe the characteristic H-5 multiplet, when the spectra were measured in benzene-d_6.

Experimental Section[32]

1-Thio-β-D-galactopyranose Pentaacetate (6).—A mixture of tetra-*O*-acetyl-α-D-galactopyranoyl bromide[33] (mp 84–86°, 41.6 g), potassium thiolacetate (11.6 g, 1.01 molar equiv), and dry acetone (250 ml) was shaken for 18 hr at room temperature. The mixture was filtered, the solution was evaporated, and the residue was crystallized from ethanol. The crude product was decolorized with activated carbon[34] and recrystallized from ethanol, yield 35.9 g (88%), mp 115–116°, $[\alpha]^{26}D$ +31.3 ±0.5° (*c* 1.9, chloroform); R_f 0.51; λ_{max}^{KBr} 5.78 (OAc), 5.87 (SAc), 11.15 μm (axial H-1);[35] λ_{max}^{EtOH} 226 nm (ε 3500); nmr data, see Figure 6 and Tables I, II, and III; X-ray powder diffraction data: 12.57 vw, 9.09 vs (1), 7.80 vw, 5.61 m, 5.28 m, 4.91 w, 4.60 s (2), 4.29 w, 4.10 m, 3.68 s (3), 3.41 m.

Anal. Calcd for $C_{16}H_{22}O_{10}S$: C, 47.30; H, 5.43; S, 7.90. Found: C, 47.44; H, 5.53; S, 8.08.

Preparation of 1-Thio-β-D-xylopyranose Tetraacetate (1).—This substance was prepared from tri-*O*-acetyl-α-D-xylopyranosyl bromide[36] (mp 100–103°, 0.100 mole) and potassium thiolacetate (0.101 mole) in acetone, essentially by the procedure used for the D-galactose analog, yield 82%, mp 103°, $[\alpha]^{20}D$ −7.7 ±0.5° (*c* 1.4, chloroform) [lit.[9] mp 99°, $[\alpha]^{24}D$ −6.88° (chloroform)]; R_f 0.70; λ_{max}^{KBr} 5.72 (OAc), 5.88 μm (SAc); λ_{max}^{EtOH} 225 nm (ε 3000); nmr data, see Figure 1 and Tables I, II, and III; X-ray powder diffraction data: 9.02 vs (1), 7.41 m, 7.09 m, 6.12 w, 4.89 vs (2), 4.20 s (3,3) 3.91 s (3,3), 3.64 vw, 3.17 w.

Anal. Calcd for $C_{13}H_{18}O_8S$: C, 46.80; H, 5.38; S, 9.58. Found: C, 46.99; H, 5.66; S, 9.31.

2-(2,3,4-Tri-*O*-acetyl-β-D-ribopyranosyl)-2-thiopseudourea Hydrobromide.—A mixture of tri-*O*-acetyl-β-D-ribopyranosyl bromide[37] (mp 96°, 3.7 g) and thiourea (0.83 g 1 molar equiv) in dry acetone (25 ml) was refluxed for 15 min, and the resultant clear solution was refrigerated overnight. The crystalline product was filtered and washed with cold acetone, yield 1.50 g (33%), mp 173–174°, $[\alpha]^{20}D$ −85.4 ±1.0° (*c* 0.8, water); λ_{max}^{KBr} 5.70 (OAc), ~3.2 (broad), 6.01, 6.10 μm (amidinium); X-ray powder diffraction data: 11.59 s (2), 7.15 m, 6.52 w, 6.16 s (3,3), 5.31 m, 4.90 m, 4.58 s (3,3), 4.19 m, 3.80 m, 3.55 vs (1), 3.39 vw, 3.08 w, 2.85 s, 2.78 s, 2.66 vw, 2.60 vw.

A sample recrystallized from acetone had mp 173–174°.

Anal. Calcd for $C_{12}H_{19}BrN_2O_7S$: C, 34.70; H, 4.58; Br, 19.20; N, 6.75; S, 7.73. Found: C, 34.72; H, 4.48; Br, 20.00; N, 7.19; S, 7.93.

When the preparation was repeated, starting with syrupy tri-*O*-acetyl-β-D-ribopyranosyl bromide (26.1 g), the yield of the product was 15.5 g (49%), mp 172–174°.

1-Thio-β-D-ribopyranose Tetraacetate (4). A. From 2-(2,3,4-Tri-*O*-acetyl-β-D-ribopyranosyl)-2-thiopseudourea Hydrobromide.—The general procedure of Černý and co-workers[10] was followed. A solution of sodium pyrosulfite ($Na_2S_2O_5 \cdot 7H_2O$, 1.75 g) in water (9 ml) was stirred for 10 min at 85° with 2-(2,3,4-tri-*O*-acetyl-β-D-ribopyranosyl)-2-thiopseudourea hydrobromide (5.0 g) and carbon tetrachloride (20 ml). The mixture was cooled, the organic phase was separated, and the aqueous layer was extracted twice with 10-ml portions of carbon tetrachloride. The combined organic phase was dried (magnesium sulfate), evaporated, and to the resultant syrupy 2,3,4-tri-*O*-acetyl-1-thio-β-D-ribopyranose was added pyridine (15 ml) and acetic anhydride (10 ml). After 18 hr at room temperature, the mixture was poured onto ice (100 g), and after 3 hr the oily product was extracted with three 50-ml portions of dichloromethane. The extract was washed successively at 0° with 1 *N* sulfuric acid, water, aqueous sodium hydrogen carbonate, and water, and the dried (magnesium sulfate) extract was evaporated. The

(31) L. D. Hall and L. Hough, *Proc. Chem. Soc.* (London), 382 (1962).

(32) Melting points were determined with a Thomas–Hoover "Unimelt" apparatus (Arthur H. Thomas Co., Philadelphia, Pa.) and are uncorrected. Optical rotations were determined in a 2-dm polarimeter tube. Infrared spectra were measured by the potassium bromide disk technique with Perkin–Elmer Model 137 or 237 infrared spectrophotometers. Ultraviolet spectra were measured with a Perkin-Elmer Model 202 recording spectrophotometer. Nuclear magnetic resonance spectra were measured with Varian A-60 or HA-100 nmr spectrometers, with tetramethylsilane (τ = 10.00) as the internal standard. Nmr spectra at 220 MHz were measured with a Varian spectrometer equipped with a superconducting solenoid (*cf.* F. A. Nelson and H. E. Weaver, "High Resolution Superconducting Spectrometer," presented at the International Conference on Magnetic Resonance and Relaxation, XIVth Colloque Ampère, Ljubljana, Yugoslavia, Sept 1966). Microanalyses were determined by W. N. Rond. X-Ray powder diffraction data give interplanar spacings, A, for Cu Kα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually: s, strong; m, moderate; w, weak; v, very. The strongest lines are numbered in order (1, strongest); double numbers indicate approximately equal intensities. Thin layer chromatography was perofmred with Desaga equipment by the ascending technique, with silica gel G (E. Merck, Darmstadt, Germany), activated for 2 hr at 110°, as the adsorbent. Unless otherwise stated, 4:1 chloroform–ether was used as the developing solvent, and indication was effected with sulfuric acid.

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(35) H. Spedding, *Methods Carbohydrate Chem.*, **1**, 539 (1962).

(36) L. C. Kreider and W. L. Evans, *J. Am. Chem. Soc.*, **58**, 797 (1936).

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resultant syrup was dissolved in ethanol (5 ml), and the solution was refrigerated to give **4**, yield 1.5 g (38%), mp 88–89°. Recrystallization from ethanol gave pure **4**, mp 88–89°, $[\alpha]^{22}D$ +9.1 ±0.2° (*c* 0.8, chloroform); R_f 0.60; λ_{max}^{KBr} 5.70 (OAc), 5.86 μm (SAc); λ_{max}^{EtOH} 229 nm (ε 4560); nmr data, see Figure 4 and Tables I, II, and III; X-ray powder diffraction data: 12.36 vw, 7.91 vs (2), 6.89 vw, 6.28 vs (1), 5.68 s (3), 5.00 vw, 4.66 w, 4.51 vw, 4.27 m, 4.02 m, 3.79 w, 3.56 s.

Anal. Calcd for $C_{13}H_{18}O_5S$: C, 46.80; H, 5.38; S, 9.58. Found: C, 46.61; H, 5.26; S, 9.56.

For this product, prepared by way of tri-*O*-acetyl-β-D-ribopyranosyl ethylxanthate, Tejima and co-workers[38] reported mp 85–87°, $[\alpha]^{17}D$ +10.7° (*c* 1.97, chloroform).

B. From Tri-*O*-acetyl-β-D-ribopyranosyl Bromide.—A mixture of tri-*O*-acetyl-β-D-ribopyranosyl bromide[37] (mp 96°, 2.17 g), potassium thiolacetate (0.74 g, 1 molar equiv), and dry acetone (25 ml) was shaken for 10 hr at room temperature. The mixture was filtered, the filtrate was evaporated, and the residue was crystallized from ethanol, yield 0.58 g (27%), mp 94–94.5°, $[\alpha]^{22}D$ +8.9 ±0.2° (*c* 2.3, chloroform). The product, in admixture with **4** prepared by method A, had mp 88°, and the tlc mobilities, infrared spectra, and X-ray powder diffraction patterns of the two samples were indistinguishable. The nmr spectrum of the product prepared by method B showed the presence of impurities giving rise to weak signals at τ 4.96 (doublet, J = 5 Hz), and 7.39 (chloroform-*d*), which were not completely removed, even after six recrystallizations.

2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-2-thiopseudourea Hydrobromide.—A mixture of tri-*O*-acetyl-β-L-arabinopyranosyl bromide[39] (mp 138–140°, 18.7 g) and thiourea (6.2 g, ~1.5 molar equiv) in dry acetone (75 ml) was refluxed for 15 min, and the resultant clear solution was refrigerated overnight. The crystalline product was filtered and washed with cold acetone, yield 18.5 g (81%), mp 169–171°, $[\alpha]^{21}D$ +8.8° (*c* 1.3, water), λ_{max}^{KBr} 5.70 (OAc), ~3.2 (broad), 6.03 μm (amidinium).

Anal. Calcd for $C_{12}H_{19}BrN_2O_7S$: C, 34.70; H, 4.58; Br, 19.20; N, 6.75; S, 7.73. Found: C, 34.93; H, 4.61; Br, 18.72; N, 7.05; S, 7.64.

The same procedure was used to convert tri-*O*-acetyl-β-D-arabinopyranosyl bromide (39 g) into 2-(2,3,4-tri-*O*-acetyl-α-D-arabinopyranosyl)-2-thiopseudourea hydrobromide, yield 33.65 g (71%), mp 170–171°, $[\alpha]^{20}D$ −6.1° (*c* 2.5, water), λ_{max}^{KBr} 5.72 (OAc), ~3.2 (broad), 6.03 μm (amidinium).

For the latter product, prepared by a similar route, Černý and co-workers[10] reported mp 172°, $[\alpha]D$ −26.5° (*c* 2.1, ethanol).

1-Thio-α-L-arabinopyranose Tetraacetate (2). A. From 2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-2-thiopseudourea Hydrobromide.—The general procedure of Černý and co-workers,[10] as used for preparation of **4**, was followed. The product **2** was obtained from ethanol as large prisms, mp 39°, and subsequently as small needles, mp 81.5–82°, $[\alpha]^{20}D$ +39.4° (*c* 2.2, chloroform); R_f 0.65; λ_{max}^{KBr} 5.73 (OAc), 5.89 μm (SAc); nmr data, see Figure 2 and Tables I, II, and III; X-ray powder diffraction data (high-melting point form): 9.46 w, 7.97 s (3), 7.22 w, 5.81 w, 5.43 vs (1,1), 5.23 vs (1,1), 4.94 m, 4.70 s (2), 4.52 m, 4.08 m, 3.74 m, 3.58 s.

Anal. Calcd for $C_{13}H_{18}O_8S$: C, 46.80; H, 5.38; S, 9.58. Found: C, 46.73; H, 5.38; S, 9.41.

B.—The same product **2**, mp 38° (high-melting dimorph, mp 80°), $[\alpha]^{21}D$ +41.3° (*c* 3, chloroform), was obtained in 72% yield by treatment of tri-*O*-acetyl-β-L-arabinopyranosyl bromide with potassium thiolacetate, by the general procedure of Gehrke and Kohler.[9] The products from A and B were homogeneous by thin layer chromatography, and had superposable infrared and nmr spectra, and the high-melting point dimorphs had identical X-ray powder diffraction patterns. The product from method B was slightly yellow, and the color was not removed by repeated recrystallization.

1-Thio-α-D-arabinopyranose Tetraacetate (3).—This product was prepared from 2-(2,3,4-tri-*O*-acetyl-α-D-arabinopyranosyl)-2-thiopseudourea hydrobromide by the method of Černý and co-workers,[10] and also from tri-*O*-acetyl-β-D-arabinopyranosyl bromide by the method of Gehrke and Kohler.[9] The product from each preparation had mp 39° $[\alpha]D$ −37.4° (*c* 1.6, chloroform). The products were homogeneous by tlc, and gave infrared and nmr spectra (Figure 3) superposable on those of the L enantiomorph **2**. Nucleation of an ethanolic solution of **3** with a sample furnished by Dr. M. Černý gave a high-melting dimorph, mp 81.5–82°. The X-ray powder diffraction pattern was superposable on that of the high-melting-point dimorph of the L enantiomorph **2**.

For 1-thioarabinose tetraacetate of unspecified configuration at C-1 and C-5, Gehrke and Kohler[9] reported mp 79°, $[\alpha]^{20}D$ +41.8°, indicating that their product was the α-L pyranose form. For **3**, Černý and co-workers[10] reported mp 80–81°, $[\alpha]D$ −44.2° (*c* 1.2, chloroform).[40]

Preparation of Benzyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (7).—To a solution of α-toluenethiol (3 ml, 0.024 mole) in 3 *N* ethanolic potassium hydroxide (8 ml) was added tetra-*O*-acetyl-α-D-glucopyranosyl bromide (10.00 g, 0.024 mole) that had just been dissolved in warm ethanol (25 ml). The mixture was shaken for 5 hr at room temperature, and then concentrated to a syrup. The latter was refluxed briefly with anhydrous sodium acetate (1 g) in acetic anhydride (17 g), the cooled solution was poured onto ice (500 g), and the mixture was stirred for 2 hr. The gum that separated was extracted with carbon tetrachloride (100 ml); the extract was washed with saturated aqueous sodium hydrogen carbonate, dried (magnesium sulfate), and evaporated to a syrup, yield 9.71 g (88%). Crystallization from methanol gave **7** as needles, yield 8.3 g (75%), mp 100–101°, $[\alpha]^{20}D$ −94 ±1° (*c* 0.6, chloroform); λ_{max}^{KBr} 5.72 (OAc), 6.70, 6.89 (aryl C=C), 14.0 μm (substituted benzene); λ_{max}^{EtOH} 208 nm (ε 10,500); nmr data (60 MHz, chloroform-*d*): τ 2.63 (five-proton singlet, Ph), 4.61–5.12 and 5.50–5.88 (multiplets, three and three protons, H-1, 2, 3, 4, 6, 6′), τ 6.08 two protons, benzylic CH_2), 6.37 (one-proton multiplet, width ~20 Hz, H-5), 7.88, 7.98, 8.00 (three-, six-, and three-proton singlets, OAc); X-ray powder diffraction data: 10.65 w, 9.72 w, 8.84 w, 7.08 vw, 5.28 s (1,1), 4.85 s (1,1), 4.62 vw, 4.19 s (2), 3.97 m (3), 3.80 vw.

Anal. Calcd for $C_{21}H_{26}O_9S$: C, 55.48; H, 5.72; S, 7.05. Found: C, 55.65; H, 5.91; S, 7.07.

When the experiment was performed with omission of the acetylation stage, a crystalline product, yield 53%, was obtained. This product was found by tlc to contain **7** together with a series of slower moving components, presumably products of partial *O*-deacetylation. Acetylation of this product gave chromatographically homogeneous **7**.

For this compound, prepared by a related procedure, Schneider and co-workers[11] reported mp 98°, $[\alpha]^{24}D$ −93.1° (1,1,2,2-tetrachloroethane), and a yield of 15%.

Preparation of 2,3,4,6-Tetra-*O*-acetyl-1-S-benzoyl-1-thio-β-D-glucopyranose (8).—A solution of thiolbenzoic acid (10.9 g) in ethanol (50 ml) was neutralized with 3 *N* ethanolic potassium hydroxide (50 ml), and to this was added tetra-*O*-acetyl-α-D-glucopyranosyl bromide (27.5 g) which had just been dissolved in warm ethanol (50 ml). The mixture was shaken for 18 hr at room temperature, and poured onto ice (1 kg). The gum that separated crystallized on trituration, and after 3 hr the product was filtered and washed with water, yield 29.9 g (94%). Recrystallization from methanol gave pure product, mp 130–131°, $[\alpha]^{20}D$ −12.5 ±0.5° (*c* 1, chloroform); λ_{max}^{KBr} 5.70 (OAc), 5.95 (SBz), 6.20, 6.30, 6.89 (aryl C=C), 13.0 μm (aryl); λ_{max}^{EtOH} 206 nm (ε 13,500), 240 nm (ε 12,500); nmr data (60 MHz, chloroform-*d*): τ 1.98–2.70 (five-proton multiplet, Ph), 4.33–4.91 (four-proton multiplet, H-1,2,3,4), 5.65 (one-proton quartet, $J_{5,6}$ ~5 Hz, $J_{6,6'}$ ~12 Hz, H-6), 5.92 (one-proton quartet, $J_{5,6'}$ ~2 Hz, H-6′), ~6.07 (one-proton multiplet, width ~20 Hz, H-5), τ 7.95, 7.97, 7.99, 8.01 (three-proton singlets, OAc); X-ray powder diffraction data: 10.0 w, 8.43 w, 7.65 s (1), 6.37 s (3), 5.37 m, 4.80 m, 4.25 m, 4.11 w, 3.90 w, 3.72 vw, 3.52 s (2).

Anal. Calcd for $C_{21}H_{24}O_{10}S$: C, 53.84; H, 5.12; S, 6.83. Found: C, 54.16; H, 5.05; S, 6.88.

The following constants have been reported for this compound, prepared by a related procedure,[12] mp 127–128°, $[\alpha]^{20}D$ −13.2° (chloroform), and by a different procedure,[13] mp 126°, $[\alpha]^{20}D$ −12.44° (1,1,2,2-tetrachloroethane).

Preparation of *t*-Butyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (10).—An adaptation of the procedure used for the benzyl analog **7** gave low yields, but treatment of penta-*O*-acetyl-β-D-glucopyranose with *t*-butyl mercaptan and zinc chloride, according to the procedure of Fletcher and co-workers[15] gave **10** in 65% yield, mp 142° (lit.[15] mp 145–146°); λ_{max}^{KBr} 5.72 mμ (OAc); nmr data (60 MHz, chloroform-*d*): τ 4.62–5.48 (four-

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(39) M. Gehrke and F. X. Aichner, *Ber.*, **60**, 918 (1927).

(40) In the original paper of Černý and co-workers[10] the rotation of **3** was given incorrectly as +44.2° (personal communication from Dr. M. Černý).

proton multiplet, H-1,2,3,4), 5.71, 6.00 (two protons, H-6, H-6'), 6.20 (one-proton multiplet, H-5), 7.95, 7.98, 8.01 (three-, six-, and three-proton singlets, OAc), 8.62 (nine-proton singlet, CMe_3).

Nmr Data for 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl Ethylxanthate (9).—Substance **9**, prepared by the method of Schneider, *et al.*,[14] gave nmr data (60 MHz, chloroform-*d*): τ 4.42–5.05 (four-proton multiplet, H-1,2,3,4), 5.33 (two-proton quartet, J = 7 Hz, CH_2 of ethyl), ~5.83 (two-proton multiplet, H-6,6'), 6.29 (one-proton multiplet, H-5), 7.95, 7.98, 8.00 (three-, six-, and three-proton singlets, OAc), 8.59 (three-proton triplet, CH_3 of ethyl).

Nmr Data for 4,6-Di-*O*-acetyl-1-S-acetyl-2,3-dideoxy-1-thio-α-D-*erythro*-hex-2-enopyranose (11).—D-Glucal triacetate was treated with thiolacetic acid and sulfuric acid[41] according to the procedure of Tejima, *et al.*[16] to give **11**, mp 102–105° (lit.[16] mp 104–105°). In chloroform-*d*, the 60-MHz spectrum of **11** gave τ 3.70 (one-proton multiplet, W_h = 4.8 Hz, H-1), 4.08 [two-proton singlet with satellites, $J_{2,3}$ = ~10 Hz, H-2, 3 (lit.[16] τ 4.10 singlet)], 4.59 (one-proton quartet, $J_{4,5}$ = 9 Hz, H-4), 5.68 (one-proton quartet, $J_{5,6}$ = 5 Hz, $J_{6,6'}$ = 12.5 Hz, H-6), 5.90 (one-proton quartet, $J_{5,6'}$ = 2.5 Hz, H-6'), 6.10 (one-proton multiplet, width = 16.5 Hz, H-5), 7.58 (three-proton singlet, SAc), 7.90, 7.93 (three-proton singlets, OAc). Large values of $J_{4,5}$, indicative of the axial–quasi axial disposition of H-4 and H-5, have been observed[42] for related 2,3-unsaturated pyranose derivatives.

(41) This experiment was performed by J. S. Jewell and P. Durette.

(42) R. J. Ferrier, W. G. Overend, and G. H. Sankey, *J. Chem. Soc.*, 2380 (1965).

The spectrum of **11** in acetone-d_6 was measured at 100 and at 220 MHz (Figure 8) and gave the following data: τ 3.78 (one-proton triplet, width 6.6 Hz, H-1), 4.01 (one-proton doublet of narrow quartets, $J_{2,3}$ = 10.3 Hz, width of quartets 4.7 Hz, H-2), 4.15 (one-proton doublet of narrow multiplets, H-2), 4.68 (one-proton doublet of narrow multiplets, $J_{4,5}$ = 9.3 Hz, width of multiplets 4.5 Hz, H-4), 5.77 (one-proton quartet, $J_{5,6}$ = 5.0 Hz, $J_{6,6'}$ = 11.7 Hz, H-6), 5.92 (one-proton quartet, $J_{5,6'}$ = 2.8 Hz, H-6'), 6.12 (one-proton multiplet, width 17.0 Hz, H-5). Addition of benzene-d_6 to the solution caused the H-2 and H-3 signals to collapse to a singlet, and H-5 signal to shift to higher field. At the same time the H-1 signal collapsed to W_h = 4.5 Hz and the H-4 signal collapsed to a doublet of narrow doublets, $J_{1,4}$ = ~2 Hz.

Registry No.—**1**, 6739-54-4; **2**, 13639-47-9; **3**, 13639-48-0; **4**, 13639-49-1; **5**, 13639-50-4; **6**, 6806-56-0; **7**, 6612-63-1; **8**, 6767-60-8; **9**, 13639-54-8; **10**, 13639-55-9; **11**, 4631-35-0; 2-(2,3,4-tri-*O*-acetyl-β-D-ribopyranosyl)-2-thiopseudourea hydrobromide, 13639-57-1; 2-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl)-2-thiopseudourea hydrobromide, 13639-58-2.

Acknowledgments.—The authors thank W. N. Turner and J. B. Hughes for some of the 60-MHz nmr measurements and R. H. Bell for assistance in measurement of some of the data.

Amino Derivatives of Starches. Amination of 6-*O*-Tritylamylose

M. L. WOLFROM, H. KATO, M. I. TAHA, A. SATO, G. U. YUEN, T. KINOSHITA, AND E. J. SOLTES

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

Received January 17, 1967

Amylose aminated at the secondary hydroxyl groups was prepared by (a) tritylation, *p*-tolylsulfonylation, reaction with sodium azide, reduction, and detritylation, or by (b) the same method except for replacement of sodium azide with hydrazine. The product of route a, DS 0.45, was *N*-acetylated and hydrolyzed to give mainly 3-amino-1,6-anhydro-3-deoxy-D-altrose. The product of route b, DS 0.8, gave on hydrolysis in low yield 3-amino-1,6-anhydro-3-deoxy-D-altrose and 2-amino-2-deoxy-D-glucose. Apparently both amination routes proceed through the 2,3-D-*manno*-epoxide derivative, the modified units of product (a) having mainly the D-*altro* configuration. Attempts to apply the Guthrie amination reaction (successive periodate oxidation, controlled reaction with phenylhydrazine, and reduction) failed at the reduction stage with both starch and 6-*O*-tritylamylose, although evidence was obtained that the phenylazo group was present in the latter.

Amylose has been aminated to a degree of substitution (DS) of 1.4 by successive *p*-tolylsulfonylation, hydrazinolysis, and reduction.[1] The product obtained contained 3,6-anhydro units and subsequent model studies[2-4] showed that the main modified unit present very probably possessed the 3,6-diamino-3,6-dideoxy-D-altrose structure.[2,3] We then decided to block C-6 hydroxyl participation by the use of 6-*O*-tritylamylose[5,6] and to replace the secondary *p*-tolylsulfonyloxy group by reaction with azide ion rather than by reaction with the more basic hydrazine molecule. Accordingly, 6-*O*-tritylamylose was *p*-tolylsulfonylated to a DS of 0.8. It has been pointed out previously[1] that evidence exists to show that this product had been sulfonated mainly, if not exclusively, at the C-2 hydroxyl group. This amylose derivative was then treated with sodium azide, under the conditions used previously[7] for monosaccharide derivatives, to produce a product, with the trityl group intact, containing an azide function (DS 0.45). The azide entity was transformed readily to the amino group by reduction with lithium aluminum hydride[8] and the product was detritylated with methanolic hydrochloric acid.[5,6] The final, aminated amylose (DS 0.45) was purified by dialysis and was isolated by lyophilization as a white, nonhygroscopic powder of high dextrorotation that was readily soluble in water and dimethyl sulfoxide. The *N*-acetyl derivative was prepared and showed similar properties.

The amino sugar fraction of the acid hydrolysate of the *N*-acetylaminated amylose showed two components by paper chromatography in an approximate 5:1 ratio. The main component crystallized and was identified as 3-amino-1,6-anhydro-3-deoxy-D-altropy-

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