Nitrous Acid Deamination of Acyclic, Polyfunctional Systems. Part 3.[1,2] Vicinal Participation in the Nitrous Acid Deamination of Chiral 1-Thio-2-aminoalkanepolyols: the Deamination of 2-Amino-2-deoxy-D-glucose Ethylene and Propan-1,3-diyl Dithioacetals, and the Crystal and Molecular Structure of 1,2-*SS'*-Ethylene-5,6-*O*-isopropylidene-1,2-dithio-α-D-mannofuranoside

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Deamination of 2-amino-2-deoxy-D-glucose ethylene dithioacetal (1) at pH 5.6, followed by acetylation of the product, gave an 8 : 40 : 3 mixture of 3,5,6-tri-*O*-acetyl-1,2-*SS'*-ethylene-1,2-dithio-α-D-mannofuranoside (5b), 3,4,6-tri-*O*-acetyl-1,2-*SS'*-ethylene-1,2-dithio-α-D-mannopyranoside (4b), and 3,5,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexono-1,4-lactone (2b). Deamination of (1) at pH <1 by use of dinitrogen trioxide followed by acetylation gave the lactone (2b) essentially exclusively. Similar treatment of the propan-1,3-diyl analogue (3) of (1) at pH <1 also gave the lactone (2b); at pH 5.6 the main product was 3,5,6-tri-*O*-acetyl-1,2-*SS'*-(propan-1,3-diyl)-1,2-dithio-α-D-mannofuranoside (7b). Structural assignments were based on formation of the 5,6-isopropylidene acetals [(8) and (10)] from the non-acetylated precursors of (5b) and (7b), by ^{1}H n.m.r. spectroscopy at 250 MHz for compounds (2b), (4b), (5b), (7b), (8), and (10), and by electron-impact mass spectrometry. An *X*-ray crystal structure-determination conducted on 1,2-*SS'*-ethylene-5,6-*O*-isopropylidene-1,2-dithio-α-D-mannofuranoside (8) permitted unambiguous assignment of the ring size, relative stereochemistry, and favoured conformation of this strained molecule. The reaction course and product distribution in the deamination were monitored and quantitated by g.l.c.–mass spectrometry of the corresponding per-trimethylsilylated derivatives and are discussed from preparative and mechanistic standpoints.

NITROUS acid deamination of polyfunctional amines is generally a complex reaction that is controlled, at least in six-membered cyclic systems, by the ground-state conformational disposition.[3] When the conformation is relatively homogeneous [as in 2-amino-2-deoxy-D-gluco-[4] and -D-galacto-pyranose [5]], the outcome of the reaction is dominated by participation of the oxygen atom (O-5) antiperiplanar (*trans*-antiparallel) to the amino-group in the favoured conformation [6,7] (leading, in the examples cited, to the corresponding 2,5-anhydroaldohexoses having the configuration at C-2 inverted). Similar treatment of systems that are conformationally more rigid, such as aminodeoxy-1,6-anhydroaldohexopyranoses, generally gives a higher level of specificity.[8] In contrast, the reaction course upon nitrous acid deamination of related systems that are acyclic, and thus conformationally more mobile,[9] is more susceptible to subtle factors controlling the reaction and the outcome is not easy to predict; vicinal participation-reactions appear to play a preponderant role.

Thus, the nitrous acid deamination of 2-amino-2-deoxyhexonic acids leads to 2,5-anhydrohexonic acids with net retention [10] of configuration at C-2, whereas the same reaction performed on 2-amino-2-deoxy-D-glucitol leads to a complex mixture of products, mainly those resulting from migration to C-2 of either a carbon or a hydrogen atom.[11] The nitrous acid deamination of 1-amino-1-deoxypentitols is somewhat simpler in that it leads [12] exlucisvely to a mixture of 1,4- and 2,5-anhydrides plus the corresponding alditol, in proportions that can be related to the relative stabilities of the conformations of these molecules in their initial and their transition states for reaction.[1] The presence of a sulphur-containing group vicinal to the amino-group greatly modifies the course of this reaction; although products of intermediary alkylthio-group participation might be expected to result by a course analogous to that occurring with the 2-amino-2-deoxyaldonic acids, the actual products encountered are those resulting from migration of the RS group.[13,14] Interestingly, the structure and stereochemistry of the products formed depend markedly on the pH utilised in the deamination reaction. Thus, deamination of 2-amino-2-deoxy-D-glucose diethyl dithioacetal at pH *ca.* 0 leads mainly to 2-*S*-ethyl-2-thio-D-glucose,[13] whereas at pH 5.6 the principal product [14] is ethyl 2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside. Participation reactions implicating 1,2-episulphonium-ion intermediates have been proposed [6,13-15] to account for the outcome of these reactions. In consequence, it might be expected that hindrance to the migration of sulphur, by using a substituent bridging the two sulphur atoms, could substantially modify the outcome of the deamination reaction, possibly opening routes to useful new products and also providing further insight into mechanistic factors controlling the reaction of 2-amino-2-deoxyhexose dialkyl dithioacetals upon diazotisation.[14,15]

RESULTS

The bridged dithioacetals used in this study, 2-amino-2-deoxy-D-glucose ethylene and propan-1,3-diyl dithioacetals, were readily prepared in high yield as their hydrochloride salts [(1) and (3)] by treating 2-amino-2-deoxy-D-glucose hydrochloride in aqueous hydrochloric acid (saturated at

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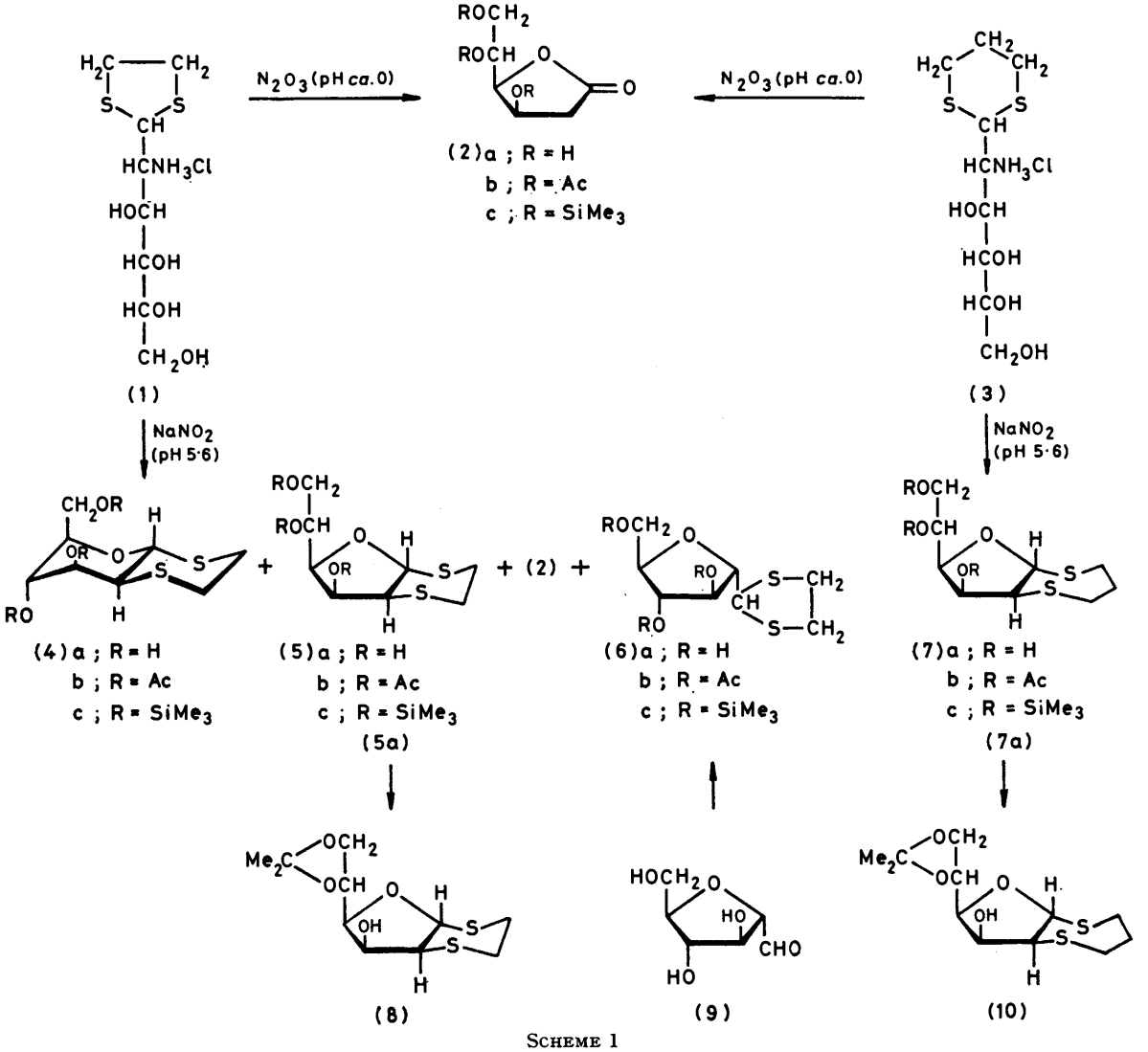


SCHEME 1

0 °C with hydrogen chloride) with ethane-1,2-dithiol and propane-1,3-dithiol, respectively (Scheme 1).

Nitrous acid deamination of the dithioacetals (1) and (3) in aqueous solution was conducted under two different sets of conditions; (*a*) at pH *ca.* 0 by passage of a current of dinitrogen trioxide at *ca.* 20 °C followed by neutralisation of the acid generated (by shaking the solution with a chloroform solution of *NN*-dimethyloctylamine);[4] and (*b*) at pH 5.6, in a solution buffered with sodium acetate, by addition of sodium nitrite. The reactions were terminated as soon as all the starting material had disappeared from the solution.

The product obtained under acid conditions (N_2O_3) from either (1) or (3) showed i.r. absorption at 1 770 cm^{-1} (5-membered lactone). It was acetylated by use of acetic anhydride–pyridine to give a chromatographically homogeneous oil that crystallized with some difficulty, affording a solid of molecular formula $C_{12}H_{16}O_8$ whose i.r. spectrum displayed absorption at 1 780 cm^{-1} typical of a lactone group; this compound was assigned the structure 3,5,6-tri-*O*-acetyl-D-*arabino*-hexono-1,4-lactone (2b). The ^1H n.m.r. spectrum (Table 1) indicated the presence of three acetoxy groups, one of these being manifestly at C-5 as indicated by the low-field octet observed for H-5; this evidence provides strong support for the 1,4-lactone structure assigned. This attribution is further confirmed by the mass spectrum (Table 2), where the abundant ion at *m/e* 145 is characteristic of the side-chain fragment formed by C-4–C-5 rupture with charge-retention on this fragment, the counter ion (*m/e* 143) formed through charge-retention on the other part of the molecule accords with an *O*-acetylmonodeoxy-1,4-lactone structure. The high-field AB portion of an ABX system observed in the ^1H n.m.r. spectrum (Table 1) was in full concordance with expectations for a C-2 methylene group adjacent to a proton at C-3 that is deshielded by an acetoxy group. The structure (2b) assigned was further proved by direct comparison with a sample prepared independently by acetylation of the known [16] 2-deoxy-D-*arabino*-hexono-1,4-lactone; similar difficulties were encountered in the recovery of this product upon crystallisation.

The preponderance of lactone (2b) in the product of deamination–acetylation of (1) or (3) at low pH was further supported by per-trimethylsilylation of the crude deamination product, followed by g.l.c.–mass spectrometry; the authentic [16] non-acetylated lactone (2a) provided [as its tris(trimethylsilyl) ether (2c)] a reference sample (Table 3).

The principal peak in the chromatogram of the product from deamination (see Table 4), amounting to 75% of the total products from compound (1) and compound (3), had an identical retention time and mass spectrum (Tables 3 and 4) as the reference sample; this major product was accompanied by several minor, unidentified products.

Deamination of the propan-1,3-diyl dithioacetal (3) at pH 5.6 led to essentially one single product, isolated as before

TABLE 1

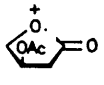
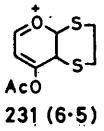
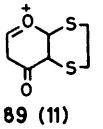
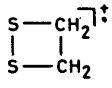
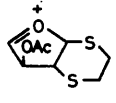
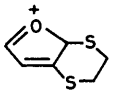
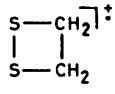
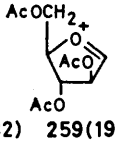
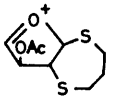
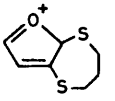
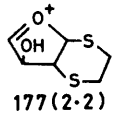
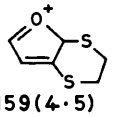
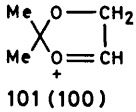
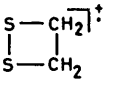
250 MHz ^{1}H n.m.r. spectral data; chemical shifts (δ); first-order couplings (Hz) in parentheses; s = singlet, d = doublet, t = triplet, sept = septuplet, oct = octuplet, app = apparent, m = multiplet, br = broad

Compound (solvent)	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5}$)	H-5 ($J_{5,6a}$)	H-6a ($J_{6a,6b}$)	H-6b ($J_{5,6b}$)	Other protons
(2b)	2.58d [a]	2.90dd [b]	5.62dd	4.68dd	35.5oct	4.15dd	4.64dd	2.03, 2.06, 2.03 (3 s, each 3 H, OAc)
($CDCl_3$)	(18.5)	(5.5) [c]	(4)	(9.5)	(4.5)		(2.5)	
(4a)	5.84d	4.12dd	4.42t	4.46t	4.58m	4.33dd	4.58m	3.30—2.64br m
(C_5D_5N)	(10)	(3)	(3)	(2)	(7)	(14)		($S[CH_2]_2S$)
(4b)	5.20d	3.58dd	5.08t	4.83t	*ca.* 4.20m	4.20dd	4.66dd	3.36—2.72br m
($CDCl_3$)	(10)	(3)	(3)	(2)	(5)	(13)	(10)	($S[CH_2]_2S$)
								2.14s (6 H, OAc), 2.10s (3 H, CH_2OAc)
(5a)	5.60d	3.43dd	5.02m	4.64dd	4.77sept	4.40dd	4.26dd	3.20—2.77br m
(C_5D_5N)	(9.5)	(3.9)	(3)	(8.5)	(3)	(11)	(5)	($S[CH_2]_2S$)
(5b)	4.94d	3.26dd	5.70t	4.42dd	5.20oct	4.60dd	4.12dd	3.18—2.78br m
($CDCl_3$)	(9.5)	(4)	(4.00)	(9.5)	(2.5)	(12)	(5)	($S[CH_2]_2S$)
(6b)	4.78d	4.24m	5.69dd	5.32t	←	4.24m →		2.63—2.37br m
(C_6D_6)	(7)	(1)	(4)	(4)				($S[CH_2]_2S$)
(7a)	5.73d	3.57dd	5.01	←	4.73m →	4.41dd	4.26dd	3.10—2.76br m
(C_5D_5N)	(9.6)	(4)	(app. t)		(2.5)		(4.5)	($S[CH_2]_3S$)
(7b)	5.10d	3.36dd	5.76t	4.50dd	5.16oct	4.08dd	4.60dd	3.04—2.56br m
($CDCl_3$)	(10)	(4)	(4)	(10)	(5)	(12)	(2.5)	($S[CH_2]_3S$)
(8)	4.82d	3.10dd	*ca.* 4.29m	4.10dd	*ca.* 4.24m	3.98	3.78	3.14—2.69 br m
[$(CD_3)_2SO$]	(9.5)	(3.9)	(3.5)	(6.0)	(6.9)	(8.5)	(6.0)	($S[CH_2]_2S$) 1.33 and 1.27 (2s, 6 H, CMe_2)

[a] H-2a; $J_{2a,2b}$ = 18.5 Hz. [b] *H*-2b. [c] $J_{2b,3}$.

TABLE 2

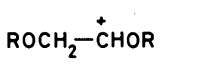
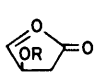
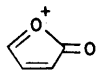
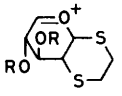
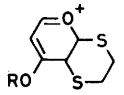
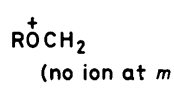
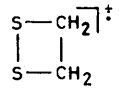
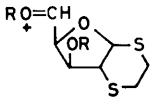
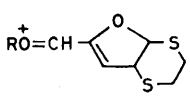
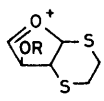
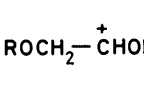
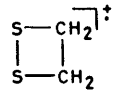
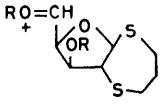
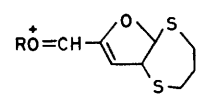
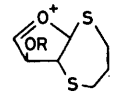
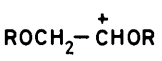
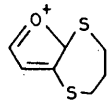
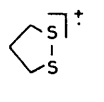
Mass-spectral data for peracetylated derivatives

Compound	Source temp. (°C)	Ionisation energy (eV)	Electron current (μA)	$M^{+\cdot}$	Assignments [a] (*m/e* values, with percentage of base peak in parentheses). Most characteristic fragments
					$M^+ - \dot{C}H_2OAc$
(2b)	110	70	100		215(10·5) 145(11·5) AcOCH—$\overset{+}{C}$HOAc 143(6·9) 
					  
(4b) [b]	110	70	500	364(10)	231 (6·5) 189 (11) 92 (100)
					  
(5b) [b]	160	70	100	364 (24)	219(0·6) 159(13·5) 145(2·2) AcOCH$_2$—$\overset{+}{C}$HOAc 92 (100)
					 
(6 b) [b]	110	70	20	364 (0·32)	259(19) 105(100)
					  
(7b)	150	70.	330	378 (1)	233(<0·5) 173(7·2) 145(2·8) AcOCH$_2$—$\overset{+}{C}$HOAc 106(88)
					   
(8)	190	70	100	278 (27)	177(2·2) 159(4·5) 101 (100) 92 (55)

[a] Most probable assignments; isomeric formulations are not excluded. [b] These compounds also display a series of ions at $M^{+\cdot}$ − 60, $M^{+\cdot}$ − 60 − 42, $M^{+\cdot}$ − (2 × 60), and $M^{+\cdot}$ − (2 × 60) − 42.

TABLE 3

Mass-spectral data for per-trimethylsilylated derivatives and apparent isomer [a] of (5c)

Compound	$M^{+\cdot}$	Assignments [a] (m/e values, with intensities as percentages of base peak in parentheses). Most characteristic fragments [c]				
						
(2c)		205 (12·5)	173 (<0·5)	83 (0·7)		
						
(4c)	454 (1·2)	351 (<0·5)	261 (4·6)	103 (15·4)	92 (36·5)	
						
(5c)	454 (<0·5)	351 (0·6)	261 (7)	249 (0·7)	205 (35·8)	92 (9·4)
		$M^{+\cdot} - ROH$	$M^{+\cdot} - 2\,ROH$	$\overset{+}{R}OCH_2$		
(6c)	454 (<0·5)	364 (0·5)	274 (<0·5)	103 (26·6) (no ion at m/e 205)		
						
(7c)	468 (<0·5)	365 (<0·5)	275 (4)	263 (<0·5)		
						
	205 (17·6)		173 (2·7)	106 (95)		
a	454 (<0·5)	351 (3·4)	205 (16·8)	261 (3·5)	92 (6)	

Apparent isomer of (5c), especially as indicated by the ions listed

R = Me_3Si

[a] See text. [b] Most probable structures; isomeric assignments are not excluded. [c] These compounds also exhibit a series of ions corresponding to $M^{+\cdot} - CH_3$, $M^{+\cdot} - CH_3 - Me_3SiOH$, and $M^{+\cdot} - CH_3 - 2(Me_3SiOH)$.

after acetylation of the product mixture; it was a crystalline solid having the molecular formula $C_{15}H_{22}O_7S_2$, which was established to be 3,5,6-tri-*O*-acetyl-1,2-*SS'*-(propan-1,3-diyl)-1,2-dithio-α-D-mannofuranoside (7b) by a combination of chemical and physical methods. The mass spectrum (Table 2) showed the molecular ion (m/e 378) and also the fragment $AcO\overset{+}{C}H_2CHOAc$ (m/e 145), and a counter-ion at m/e 233, suggesting a type of C-4–C-5 cleavage observed in (2b), with a 3-*O*-acetyl-1,2-*SS'*-(propan-1,3-diyl)-1,2-dithioglycofuranoside system being detached. An intense ion at m/e 106 (Table 2) attributed to the 1,2-dithiolane molecular ion, provided further evidence for the $-S-[CH_2]_3-S-$ fragment in (7b). The ^1H n.m.r. spectrum of (7b) confirmed these results (Table 1) and showed resonances for those acetoxy groups and an ABX system for H-6,6',5 closely comparable with the corresponding signals for (2b). The fact that the H-1 and H-2 signals showed no appreciable change in chemical shift after conversion into the *O*-deacetylated analogue (7a) indicated that C-1 and C-2 were substituted by alkylthio-groups corresponding to an annelation reaction at C-1 and C-2 by the $-S-[CH_2]_3-S-$ group. The overall structure of a 3,5,6-tri-*O*-acetyl-1,2-*SS'*-(propan-1,3-diyl)-1,2-dithiohexofuranoside for (7b) was confirmed by acetonation of its *O*-deacetylated analogue (7a) with acetone–copper(II) sulphate, which led to the 5,6-isopropylidene acetal (10).

The stereochemistry of (7) at C-1 and C-2 was indicated to be *trans* by the large $J_{1,2}$ coupling (*ca.* 9.5 Hz) observed for (7a) and (7b). This value is even larger (by 1.5 Hz) than the value of $J_{1,2}$ observed for ethyl 2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside,[14] whose configuration has been established unambiguously by crystallographic and other methods;[17] the $J_{2,3}$ value for the latter is very close to the value (4 Hz) observed for (7b) and thus is consistent with

TABLE 4

Analysis of the products of deamination of compounds (1) and (3) by g.l.c. as their per-trimethylsilated derivatives [a]

Product (as Me_3Si derivative)	Retention time/min	Relative proportion (%) Reaction at pH 5.6	Reaction at pH *ca.* 0
Reaction with dithioacetal (1)			
(5c)	59	12	
(4c)	49	52	
(2c)	17	7	75 [b]
(6c)	45	22	
c	57	7	
Reaction with dithioacetal (3)			
(7c)	71	80 [b]	
(2c)	17		75 [b]

[a] See Experimental section for procedural details. [b] The remainder was composed of a series of minor, unidentified products. [c] Unidentified product, apparent isomer of (5c); see text.

the *cis*-disposition of H-2 and H-3 in (7b) and, accordingly. the overall α-D-*manno*-stereochemistry. The specific rotation (+10°) of (7a) is significantly lower than that (+74°) of ethyl 3,5,6-tri-*O*-acetyl-2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside, probably because of the torsional effect of the bridging group between the sulphur atoms. Further support for the α-D-*manno*-configuration assigned to (7b) is afforded by the fact that the corresponding 1,2-ethylene analogue (see later), which is more strained, has been proved by crystallography to have the α-D-*manno*-configuration.

Examination by g.l.c.–mass spectrometry of the trimethylsilylated product from the nitrous acid deamination of (3) at pH 5.6 showed that compound (7c) constituted *ca.* 80% of the reaction product, with only small proportions of other, unidentified products.

In contrast to the preceding results, the nitrous acid deamination of the more-constrained ethylene dithioacetal (1) at pH 5.6 gave a mixture of some complexity, containing five products, as detected by per-trimethylsilylation of the crude product and subsequent examination by g.l.c.–mass spectrometry (see Table 4). Three major products were isolated after acetylation of the deamination product followed by chromatographic separation on silica gel. The principal one, obtained crystalline in 40% yield, was readily identified as 3,4,6-tri-*O*-acetyl-1,2-*SS'*-ethylene-1,2-dithio-α-D-mannopyranoside (4b). Its mass spectrum (Table 3) showed the molecular ion (*m/e* 364), together with a fragment (*m/e* 231) corresponding to loss of the C-6 fragment and a molecule of acetic acid, and the base peak at *m/e* 92 corresponding to the 1,2-dithietan radical-ion; these data suggest an annelated structure involving the ethane-1,2-dithio-group. The ^1H n.m.r. spectrum of this compound was fully first-order except for the H-5,6,6′ portion. Three acetoxy groups are present, and the substituents at C-3, C-4, and C-6 are in mutually *trans*-diaxial disposition; the vicinal couplings of equatorially disposed protons ($J_{3,4}$ and $J_{4,5}$) are small, as expected. The equatorial–axial coupling of H-2 with H-3 leads to the observed coupling of 3 Hz, and the *trans*-diaxial protons at C-1 and C-2 give rise to the observed, large $J_{1,2}$ coupling (10 Hz). These data allow unambiguous formulation of the product as (4b) in the $^1C_4$ (D) conformation.

The second product from the deamination of (1) at pH 5.6, obtained from the acetylated product in 8% yield, was identified as 3,4,6-tri-*O*-acetyl-1,2-*SS'*-ethylene-1,2-dithio-α-D-mannofuranoside (5b), whose general structure was attributed by n.m.r. and mass spectrometry and whose configuration at C-1 and C-2 was specified definitively by *X*-ray structure determination of a transformation product. The mass spectrum of (5b) showed (Table 3) the molecular-ion peak (*m/e* 364) together with fragment-ions closely analogous to those observed for the propan-1,3-diyl analogue (7b). Similarly, the ^1H n.m.r. spectrum (Table 1) of (5b) was very similar to that of (7b) except for the signals of an additional methylene group in the spectrum of (7b) and small differences in chemical shift and coupling constants of certain protons; H-1 and H-4 in (5b) are, respectively, shielded and deshielded by comparison with their positions in the spectrum of (7b). These differences may be attributed to additional strain effects in compound (5b).

Although the ^1H n.m.r. data for (5b) lent good support for the α-D-*manno*-configuration, the low specific rotation (−43°) for this compound gave cause for concern, even though torsional effects of bridging between the sulphur atoms may very reasonably be expected to provoke a major change in optical rotation in comparison with the corresponding 1,2-di-*S*-ethyl analogue [14] ($[\alpha]_D$ +74°) and the 1,2-*SS'*-(propan-1,3-diyl) analogue (7b), which has $[\alpha]_D$ +10°. As these specific-rotational variations were not amenable to firm interpretation, a proof of structure by *X*-ray diffraction was sought. Compound (5b) did not prove satisfactory for this purpose, but a suitable derivative was obtained by *O*-deacetylation to give (5a) and subsequent acetonation with acetone–copper(II) sulphate to the 5,6-isopropylidene acetal (8). Compound (8) was even more laevorotatory ($[\alpha]_D$ −66°) than (5b) and showed ^1H n.m.r. coupling constants (Table 1) for protons in the ring that were very close to those of the precursor (5b), indicating that no significant stereochemical changes had occurred during the transformation of (5b) into (8). The crystallographic study that confirmed structure (8) is presented later.

A third, minor product (3%), isolated from the deamination mixture (pH 5.6) from (1) after acetylation, was shown to be the lactone (2b) already described. In the parallel deamination study of (1) at pH 5.6, with per-trimethylsilylation of the products and analysis by g.l.c.–mass spectrometry, the three *O*-trimethylsilylated products (4c), (5c), and (2c) were found to be present (Table 4) in the mixture in 52, 12, and 7% proportion, the remaining fraction being composed of two minor, additional products, constituting 22 and 7% of the total mixture. The former one was identified tentatively as the per-trimethylsilyl ether (6b) of 2,5-anhydro-D-mannose ethylene dithioacetal (6a) on the basis that it had the same mass spectrum and retention time in g.l.c. as that of the per-trimethylsilyl derivative of a sample of (6a) that had been prepared by synthesis from 2,5-anhydro-D-mannose (9).[4] The minor (7% in g.l.c.) of the two additional products, only slightly separated from (5c) in g.l.c., gave a mass spectrum similar or identical to that of (5c), but difficulties attending its preparative separation precluded firm characterization of this product.

Details of procedures used in the crystal-structure determination performed in 1,2-*SS'*-ethylene-5,6-*O*-isopropylidene-1,2-dithio-α-D-mannofuranoside (8) are given in the Experimental section. The interatomic distances and bond angles are given in Figure 1, and Figure 2 shows a projection of the molecule on the C(1)–C(2)–S(2) plane with the torsional angles in each ring. The sulphur atoms are indeed in *trans*-disposition with the following dihedral

angles: S(2)–C(2)–C(1)–S(1) = 75° and S(2)–C(2)–C(3)–O(4) = 46°. A comparison of these and other dihedral angles for this compound and various related glycofuranosides is presented in Table 5.

TABLE 5

Comparison of crystallographically determined torsional angles in the furanoid ring in 1,2-*SS'*-ethylene-5,6-isopropylidene-1,2-dithio-α-D-mannofuranoside [a] (8) with those in ethyl 2-*S*-ethyl-1,2-dithio-α-D-mannofuranoside [b] (11), ethyl 1-thio-α-D-glucofuranoside [c] (12), and methyl α-D-galactofuranoside [d] (13)

	Value of angle (°) for compounds			
Torsional angles	(8)	(11)	(12)	(13)
S(1)–C(1)–C(2)–S(2)	75.3	111		
S(1)–C(1)–C(2)–C(3)	−160.4	−130		
S(2)–C(2)–C(1)–O(4)	−166.1	−129		
S(2)–C(2)–C(3)–O(3)	45.8	33		
C(1)–C(2)–C(3)–C(4)	40.7	30	33.8	31.2
C(2)–C(3)–C(4)–O(4)	−27.2	−41	−28.4	−12.8
C(3)–C(4)–O(4)–C(1)	2.0	37	12.7	−12.3
C(4)–O(4)–C(1)–C(2)	25.1	−18	11.2	32.2
O(4)–C(1)–C(2)–C(3)	−41.8	−9	−27.7	−39.0
O(4)–C(4)–C(5)–C(6)	66.1	72	58.2	
O(4)–C(4)–C(5)–O(5)	179.9	−171	179.3	
C(3)–C(4)–C(5)–C(6)	−173.3	−176	177.6	
C(3)–C(4)–C(5)–O(3)	−59.5	−60	−61.2	
O(3)–C(3)–C(4)–O(4)	88.0	80	82.3	

[a] This work. [b] See ref. 17. [c] See ref. 18. [d] See ref. 19.

The data in Table 5 show that the furanoid ring is similar to that observed in related furanoid derivatives; the ring adopts the E_2 (D) conformation with C(2) being located 0.65 Å from the approximate plane ($-0.884X + 0.340Y - 0.321Z + 5.254 = 0$) passing through C(1), C(3), C(4), and O(4). Short C–C bonds (1.43—1.52 Å) are observed in the furanose ring, as has been noted [18,19] with other furanose derivatives.

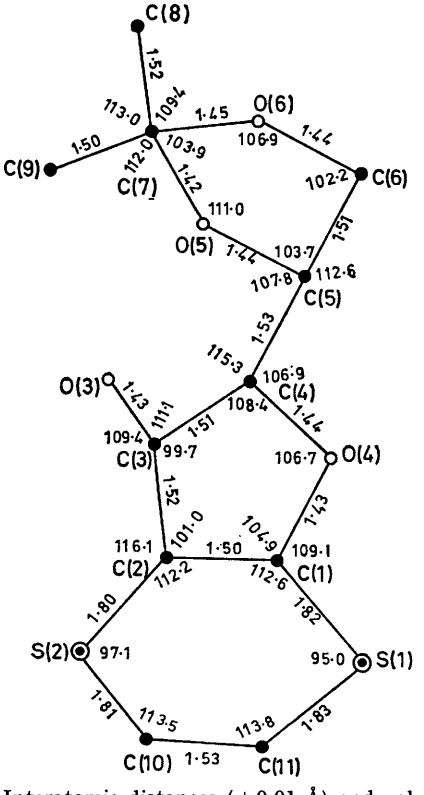


FIGURE 1 Interatomic distances (±0.01 Å) and valence angles (±0.5°) for 1,2,-*SS'*-ethylene-5,6-*O*-isopropylidene-1,2-dithio-α-D-mannofuranoside (8)

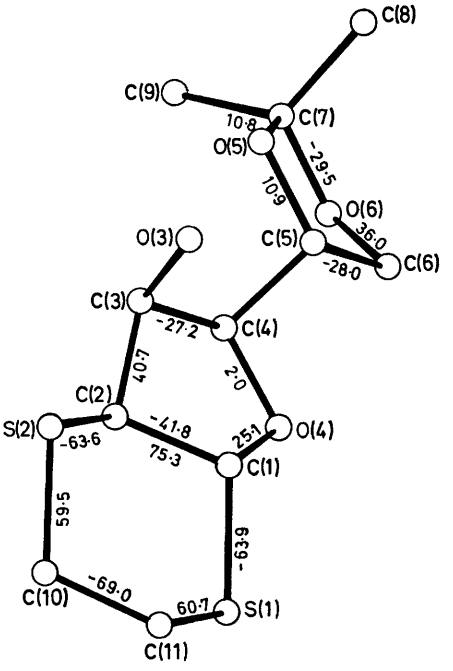


FIGURE 2 ORTEP projection of the molecule of compound (8) in the C(1)–C(2)–S(2) plane

Compound (8) forms intermolecular hydrogen-bonds: O(3) (x,y,z)–O(6) $(1-x, \frac{1}{2}+y, \frac{1}{2}-z)$ of 2.74 Å. The vicinal proton–proton torsional angles (Table 6) determined from the crystallographic data for (8) are in good general agreement with those estimated from vicinal spin-coupling data from the ^{1}H n.m.r. spectrum of (8) in [$^2H_6$]dimethyl sulphoxide solution.

TABLE 6

Crystallographically determined vicinal proton–proton dihedral angles for compound (8) and comparison with n.m.r. spin couplings for compounds (5b) and (8)

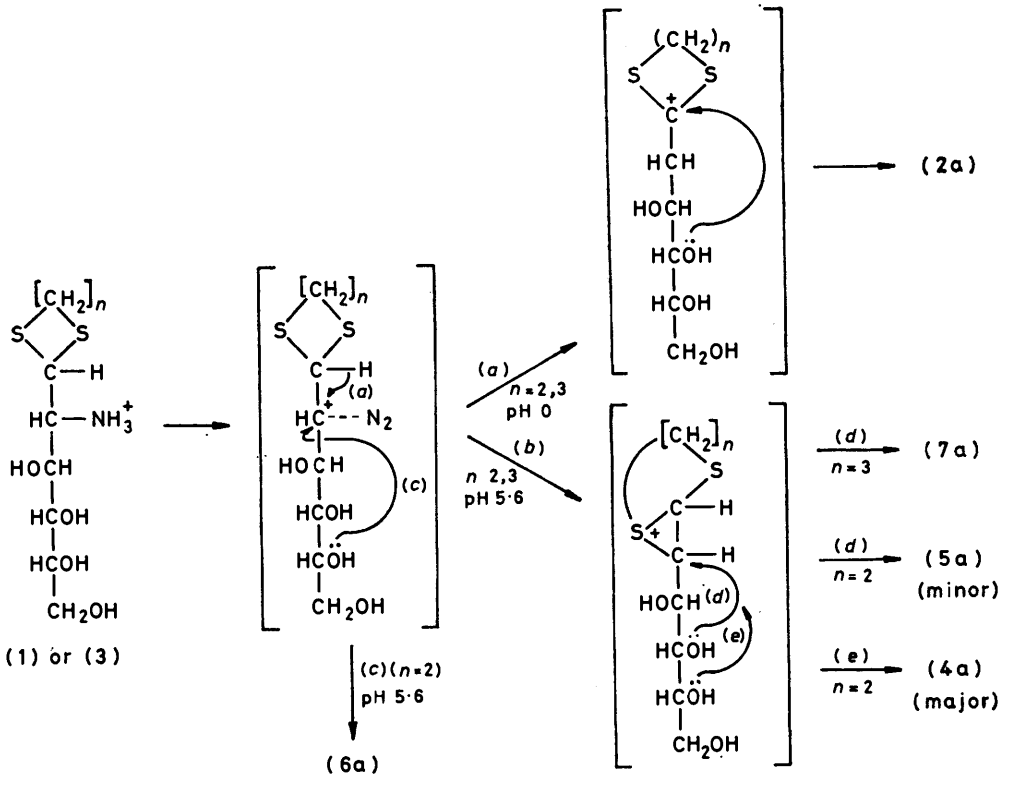
		N.m.r. spin couplings/Hz	
Dihedral angle	Angle (°) from crystal structure	(5b) [a]	(8) [b]
H(1)–C(1)–C(2)–H(2)	−168	9.5	9.5
H(2)–C(2)–C(3)–H(3)	47	4.0	3.9
H(3)–C(3)–C(4)–H(4)	−27	4.0	4.5
H(4)–C(4)–C(5)–H(5)	−175	9.5	6.0
H(5)–C(5)–C(6)–H-(6)	−32	2.5	6.9
H(5)–C(5)–C(6)–H'-(6)	95	5	6.0

[a] In [^{2}H]chloroform. [b] In [$^2H_6$]dimethyl sulphoxide.

DISCUSSION

These results confirm, as previously proposed,[6,13,14,20] that the result of nitrous acid deamination of chiral 2-amino-1-alkylthioalkanols is determined essentially by the participatory aptitude of the sulphur atom vicinal to the incipent carbo-cation at C-2 (see Scheme 2). In strongly acid media, the nucleophilicity of the sulphur atom is attenuated, and the sole observed deamination product from either the ethylene (1) or propan-1,3-diyl

dithioacetal (3) in each instance is the lactone (2a), isolated as its triacetate (2b); no significant proportion of sulphur-migration product is observed. The incipient carbo-cation at C-2, presumably formed initially in all these reactions, evidently undergoes hydride migration from C-1 [pathway (*a*)] to give the 1,3-dithiolanium (or 1,3-dithianium) cation. The route from this stabilised cation to the lactone (2a) could involve either attack by water at C-1, hydrolysis to the corresponding 2-deoxy-aldonic acid, and subsequent lactonisation, or alternatively occur by kinetically controlled attack by O-4 on C-1, with hydrolytic conversion directly into the 1,4-lactone. As the reaction gives the 1,4-lactone, rather subject to steric control by the relative energies of possible transition-states for conversion into stable products. Thus the propan-1,3-diyl derivative (3) can be presumed to react *via* the D-*manno*-episulphonium ion by kinetically controlled attack by O-4 at C-1 [pathway (*d*)], with net inversion at C-1 to give the observed α-D-mannofuranoside (7a), whereas the ethylene analogue (1) cannot so readily achieve the same transition-state for formation of the furanoid ring because of the additional strain involved; in consequence the favoured reaction-pathway [Figure 2, pathway (*e*)] involves attack at C-1 by O-5, again giving a product (4a) having the α-D-*manno*-stereochemistry, but having a



SCHEME 2 Possible mechanistic pathways in the deamination of (1) and (3)

than a mixture of tautomers, the latter pathway is considered to be the more probable.

This result contrasts with the behaviour [13] of 2-amino-2-deoxy-D-glucose diethyl dithioacetal on deamination in acid medium, where no major formation of the lactone is observed, and the product isolated results from migration of an ethylthio-group to C-2. In this instance, the unbridged alkylthio-group is more free to migrate, and the C-1 cation resulting from hydride migration would not have the stabilizing ring-structure.

When the deamination of (1) or (3) is conducted under conditions closer to neutrality (pH 5.6), the augmented nucleophilicity of sulphur favours the migration pathway [Scheme 2, (*b*)], despite the element of strain introduced by bridging between the two sulphur atoms. The D-*manno*-episulphonium ion is presumably formed at the outset, and the further course of the reaction is pyranoid ring in a product whose conformation has the stable *trans*-decalin type of system. The furanoside analogue (5a) is also formed [*via* pathway 2 (*d*)], but in considerably lower yield. Also formed in this reaction are minor proportions of two products that evidently arise without episulphonium-ion participation; these are the 2,5-anhydro-dithioacetal (6a) and the lactone (2a); the former presumably arises by kinetically controlled attack by O-5 on the C-2 carbo-cation [Figure 2, pathway (*c*)] and the latter by the process already discussed [pathway 2 (*a*)]. As in the case of the deamination of 2-amino-2-deoxy-D-glucose diethyl dithioacetal, and in contrast to some proposed generalisations,[21] the reaction from (1) to the anhydride (6a) is indeed only a minor pathway.

Exclusive cyclisation [Figure 2, pathways (*d*) and (*e*)] to the α-anomeric product may be attributed to the

diastereotopic relation of the two sulphur atoms in the chiral environment and the fact that the deamination reaction involves negligible activation energy,[1] so that ground-state conformational control is in effect; the sulphur atom not implicated in attack at C-2 may be expected to favour an initial conformational orientation where it is *not* in parallel, β-disposition to the C-3–O-3 bond in (1) or (3).

Furthermore, this series of studies on bridged dithioacetals, in which steric restraints would preclude any type of double inversion at C-2 by sulphur, showed no evidence for the formation of 2-alkylthio-products having the D-*gluco*-configuration, such as have been encountered [13] in the deamination of 2-amino-2-deoxy-D-glucose diethyl dithioacetal at acid pH. Alternative hypotheses [6,13,15] for the course of the latter reaction require additional experimental verification before a clear decision can be made.

The results of this work provide compounds of considerable synthetic utility, as in the preparation of nucleoside analogues and 2-deoxynucleosides,[22] and, in a more general sense, provide a new method for annelation leading to 1,3-dithiolans and 1,3-dithians in carbocyclic systems.[23]

EXPERIMENTAL

General Methods.—Solutions were dried with anhydrous sodium sulphate and were evaporated under reduced pressure at temperatures not exceeding 45 °C. Thin-layer chromatography (t.l.c.) was performed on silica gel plates (Merck F-254, Merck, Darmstadt, Germany) with 4 : 1 (v/v) ether–hexane (*A*) or 3 : 1 (v/v) dichloromethane–ether (*B*) as eluants. Preparative chromatography was performed on columns of silica gel (Merck, no, 60, 70—230 mesh) with the eluants indicated. Gas–liquid chromatography (g.l.c.) was performed on a Girdel model 3000 chromatograph with flame-ionisation detection and a column with no dead volume. Melting points were measured on a Leitz block apparatus under a microscope, and are corrected. Optical rotations were measured at *ca.* 20 °C with a Quick polarimeter (Roussel et Jouan). Elemental analyses were determined by the CNRS Central Microanalytical Service (Thiais). Hydrogen n.m.r. spectra at 250 MHz were recorded with a Cameca spectrometer (Thomson-CSF, Paris) operating in the frequency-sweep mode with tetramethylsilane as the field-frequency lock signal; spectra were recorded by MM. H. Reutenauer and A. Rousseau of the Groupe Grenoblois de Resonance Magnétique à Haute Résolution. Chemical shifts are recorded on the δ scale (p.p.m.) from the internal reference. Assignments were routinely verified by double irradiation or INDOR. Mass spectra were recorded with an AEI MS-30 double-beam, high-resolution spectrometer, either by direct introduction (ionization energy 70 eV) or by g.l.c. coupling with a membrane interface (30 eV ionization energy). The acceleration potential was 4 kV and the electron current was 330 μA. Relative abundances of ions with respect to the base peak are given in parentheses.

X-*Ray Crystal-structure Determination for* 1,2-SS′-*Ethylene*-5,6-O-*isopropylidene*-1,2-*dithio*-α-D-*mannofuranoside* (8).—Colourless, single crystals of (8) were grown from an ether–hexane solution. The space group is orthorhombic, $P2_12_12_1$, and had the following parameters: a = 9.766(6), b = 10.635(6), c = 13.278(6) Å; Z = 4; D_c = 1.33 g cm^{-3}. A total of 975 significant reflections were collected on a four-circle Siemens diffractometer by using Mo-K_α radiation with the five-point method.[24] The structure was solved by using the multi-solution method with the MULTAN program.[25] It was refined by a full-matrix, least-squares method [26] with anisotropic thermal parameters for the heavy atoms (ORFLS program). Angles and distances were calculated by using the ORFFE program.[27] Positions of the hydrogen atoms (except for those, not located, of the methyl groups) are included in the calculations, but were not refined; for these atoms, isotropic temperature-factors (*B*-value of the bonded carbon atom) were introduced. A final R' of 6.7% was obtained, with a weighting scheme as defined by [28] $R' = (\Sigma w(F_o - F_c)^2 / \Sigma w F_o^2)^{1/2}$. Atomic co-ordinates, anisotropic thermal parameters and final calculated structure factors are listed in Supplementary Publication No. SUP 22449.*

2-*Amino*-2-*deoxy*-D-*glucose ethylene dithioacetal hydrochloride* (1).—To a solution of 2-amino-2-deoxy-D-glucose hydrochloride (23 g) in fuming hydrochloric acid (concentrated hydrochloric acid subsequently saturated with hydrogen chloride at 0 °C) was added 1,2-ethanedithiol (20 g) at 0 °C with vigorous agitation. The mixture was kept for 3 d at room temperature with magnetic stirring and the clear solution obtained was diluted with ethanol, made neutral by addition of an excess of lead carbonate and, after removal of lead salts by filtration, was evaporated to dryness to give a powdery, hygroscopic solid (29 g, *ca.* 100%) which was not recrystallized; $[\alpha]_D^{20}$ −16° (*c* 2.4, water) (Found: C, 33.15; H, 6.15; Cl, 12.30; N, 4.75; S, 21.85. Calc. for $C_8H_{18}ClNO_4S_2$: C, 32.93; H, 6.17; Cl, 12.18; N, 4.80; S, 21.96).

2-*Amino*-2-*deoxy*-D-*glucose Propan*-1,3-*diyl Dithioacetal Hydrochloride* (3).—The general procedure used for preparation of (1) was repeated, with use of 2-amino-2-deoxy-D-glucose hydrochloride (15 g), hydrochloric acid (120 ml), and propane-1,3-dithiol (18 g) to give the crystalline dithioacetal (3), yield 18 g (84%); m.p. 204—206 °C (ethanol, water, ether), $[\alpha]_D^{16}$ −8.9° (*c* 1.45, water) (Found: C, 35.35; H, 6.35; Cl, 11.90; N, 4.35; S, 21.85. Calc. for $C_9H_{20}ClNO_4S_2$: C, 35.25; H, 6.53; Cl, 11.60; N, 4.60; S, 21.0).

Nitrous Acid Deamination of the Dithioacetals (1) *and* (3).—*General Procedure.*—(*a*) *At* pH 5.6. The dithioacetal (1) or (3) (15 mmol), dissolved in a buffer solution [1 : 1 (v/v) 1M acetic acid–1M sodium hydroxide (100 ml)], was treated at *ca.* 20 °C with an aqueous solution of sodium nitrite (100 mmol, 50 ml). The mixture was magnetically stirred for 20 h at *ca.* 20 °C and then degassed for 1 h at *ca.* 15 mmHg with passage of a slow current of nitrogen. The solution was then concentrated under reduced pressure with final lyophilization of the product. An aliquot sample (15—20 mg) of the amorphous powder thus obtained was used for g.l.c. analysis after conversion into the trimethylsilylated analogue. The remainder was dissolved in dry pyridine (80 ml) and acetic anhydride (100 ml) was added. After being set aside for 24 h at *ca.* 20 °C, the mixture was poured into water and the aqueous solution was extracted with chloroform. The organic extract was washed successively with aqueous solutions of sodium hydrogensulphate (10%), sodium hydrogencarbonate (saturated), and water, and

* For details see Notice to Authors No. 7, *J.C.S. Perkin I*, 1978, Index issue.

dried. The resultant oil was examined by t.l.c. [solvent (A)] and separation of the components was effected by column chromatography with the same solvent.

(*b*) *At* pH <1. A stream of dinitrogen trioxide (2 bubbles per s) was passed through a solution of dithioacetal (1) or (3) (15 mmol) in water (100 ml) during 2 h at *ca.* 20 °C, with magnetic stirring. The solution was then degassed as described in the preceding experiment and subsequently made neutral by washing with a 10% (v/v) solution of *NN*-dimethyloctylamine in chloroform. The solution was then washed with ether (2 × 100 ml). Concentration and subsequent lyophilisation of the aqueous solution gave an amorphous residue of which a 10-mg aliquot was withdrawn for g.l.c. analysis. The principal fraction was acetylated as just described (*A*) and the components were separated by column chromatography.

Study of the reaction products by g.l.c.–mass spectrometry. The mixtures obtained by methods (*A*) or (*B*) (15 mg) were treated with *NO*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) (1 ml) and set aside for 18 h at room temperature or for 2 h at 60 °C. After this time, an aliquot of the solution was injected into a g.l.c. column (3 m × 2.17 mm packed with Chromosorb WHMDS charged with OV-1 (3%) as stationary phase, with helium as carrier gas, flow-rate 15 ml min^{-1}, and inlet pressure 1.5 bar. The temperature was programmed from 155 to 200 °C at a rate of 0.5 °C min^{-1} and the injector and detector temperatures were 230 °C. The relative percentages of the components were determined by use of a numerical integrator (LTT 2100, Paris). Identification of the components was achieved by comparison of their retention times and mass spectra with data from authentic samples of (2c), (4c), (5c), (6c), and (7c). The membrane separator of the g.l.c.–mass spectrometry system was operated at 150 °C. Table 3 records the characteristic fragmentations of the trimethylsilyl derivatives, and qualitative and quantitative data on the composition of the deamination mixtures are reported in Table 4.

Nitrous acid deamination of 2-amino-2-deoxy-D-glucose ethylene dithioacetal hydrochloride (1); *isolation and characterization of the products formed.* (*a*) *At* pH 5.6. Deamination of the dithioacetal (1) (4.36 g) and acetylation of the crude mixture gave an oil (4.1 g) that by t.l.c. [eluant *A* elution for 4 h on a 100-mm plate) showed the presence of at least three major components, which were separated on a column of silica gel (150 g)]. The products were eluted in the order described next, and their n.m.r. and mass spectra are recorded in Tables 1 and 2, respectively. 3,5,6-*Tri*-O-*acetyl*-1,2-S′-*ethylene*-1,2-*dithio*-α-D-*mannofuranoside* (5b); yield 0.420 g (7.7%), m.p. 154—156 °C (ether–hexane), $[\alpha]_D$ −43° (*c* 1.5, chloroform); R_F 0.75 (Found: C, 46.00; H, 5.50; S, 17.60. Calc. for $C_{14}H_{20}O_7S_2$: C, 46.18; H, 5.53; S, 17.61). 3,4,6-*Tri*-O-*acetyl*-1,2-S′-*ethylene*-1,2-*dithio*-α-D-*mannopyranoside* (4b); yield 2.2 g (40%), m.p. 98—100 °C (ether), $[\alpha]_D^{25}$ +5.8° (*c* 1.2, chloroform); R_F 0.61 (Found: C, 46.25; H, 5.50; S, 17.80. Calc. for $C_{14}H_{20}O_7S_2$: C, 46.18; H, 5.53; S, 17.61). 3,5,6-*Tri*-O-*acetyl*-2-*deoxy*-D-arabino-*hexono*-1,4-*lactone* (2b); yield 0.15 g (3%), m.p. 103—105 °C (ether), $[\alpha]_D^{20}$ +34° (*c* 1.3, chloroform); $\nu_{max.}$(KBr) 1 740 (OAc) and 1 780 cm^{-1} (lactone) (Found: C, 49.90; H, 5.60. Calc. for $C_{12}H_{16}O_8$: C, 49.92; H, 5.46). The latter compound was likewise obtained by acetylation of 2-deoxy-D-*arabino*-hexono-1,4-lactone [16] (2a) (500 mg) by use of pyridine–acetic anhydride (1 : 1 v/v, 20 ml).

Conventional extraction afforded an oil (600 mg) that was purified by column chromatography (eluant *B*). The acetylated lactone (2b) was obtained crystalline; yield 220 mg.

(*b*) *At* pH <1. Deamination of the dithioacetal (1) (6 g), with acetylation of the crude product-mixture, gave an oil (5.6 g) that in t.l.c. (eluant *A*) showed essentially one component; it was isolated pure by column chromatography with the same solvent and the product was crystallized; yield 2.8 g (48%) identical with the 3,5,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexono-1,4-lactone (2b) already described.

Nitrous acid deamination of 2-amino-2-deoxy-D-glucose propan-1,3-diyl dithioacetal hydrochloride (3): *isolation and characterisation of the products formed.* (*a*) *At* pH 5.6. Deamination of the dithioacetal (3) (6 g), followed by acetylation, gave an oil (5.9 g) that by t.l.c. (eluant *B*) showed the presence of essentially a sole component (R_F 0.73) accompanied by several minor components. Column chromatography (eluant *A*) afforded the major component, 3,5,6-tri-*O*-acetyl-1,2-*SS*′-(propan-1,3-diyl)-1,2-dithio-α-D-mannofuranoside (7b) (4 g, 66%); m.p. 96—98 °C (ether), $[\alpha]_D^{22}$ +10° (*c* 1.1, chloroform) (Found: C, 47.35; H, 5.60; S, 16.80. Calc. for $C_{15}H_{22}O_7S_2$: C, 47.62; H, 5.86; S, 16.84).

(*b*) *At* pH <1. Starting from the dithioacetal (3) (2 g), acetylation of the mixture gave an oil (1.2 g) that by t.l.c. (eluant *A*) showed essentially a single component that was purified by column chromatography; yield 0.7 g (37%); it was identified as the 3,5,6-*tri*-O-*acetyl*-2-*deoxy*-D-arabino-*hexono*-1,4-*lactone* (2b) already described.

1,2-SS′-*Ethylene*-1,2-*dithio*-α-D-*mannofuranoside* (5a).—The peracetylated derivative (5b) (250 mg) was dissolved in methanol saturated with ammonia at 0 °C (15 ml). After 2 h of agitation, the alcoholic solution was evaporated to dryness to give a crystalline residue (98 mg, 59%), m.p. 153—156 °C (methanol–ether), $[\alpha]_D$ −41° (*c* 0.9, methanol) (Found: C, 39.15; H, 6.20; S, 23.70. Calc. for $C_8H_{14}O_4S_2 \cdot CH_3OH$: C, 39.90; H, 6.66; S, 23.68). Drying *in vacuo* at 100 °C gave the product free from methanol of crystallization; m.p. 165—166 °C, $[\alpha]_D^{20}$ −41.5° (*c* 1.2, methanol) (Found: C, 40.20; H, 6.0; S, 26.65. Calc. for $C_8H_{14}O_4S_2$: C, 40.34; H, 59.20; S, 26.87).

1,2-SS′-*Ethylene*-5,6-O-*isopropylidene*-1,2-*dithio*-α-D-*mannofuranoside* (8).—The thioglycoside (5b) (85 mg) was dissolved in acetone (15 ml), anhydrous copper(II) sulphate was added, and the mixture was stirred magnetically for 48 h. The mineral salts were then removed and the acetone solution was evaporated under reduced pressure to give an oil (120 mg) which crystallized from ether–hexane; yield 80 mg (*ca.* 80%), m.p. 139—142 °C, $[\alpha]_D^{22}$ −66° (*c* 1.45, chloroform) (Found: C, 47.05; H, 6.25; S, 22.70. Calc. for $C_{11}H_{18}O_4S_2$: C, 47.48; H, 6.52; S, 23.00).

1,2-SS′-*Ethylene*-1,2-*dithio*-α-D-*mannopyranoside* (4a).—The peracetylated derivative (5b) (160 mg) was dissolved in dry methanol (5 ml) and added at 0 °C to methanol (15 ml) saturated at 0 °C with ammonia. After 2 h at 0 °C, the alcoholic solution was evaporated to give a crystalline residue (95 mg, 90%); m.p. 200—201 °C (methanol–ether), $[\alpha]_D$ +23° (*c* 1.1, methanol) (Found: C, 40.95; H, 5.90; S, 27.0. Calc. for $C_8H_{14}O_4S_2$: C, 40.34; H, 5.92; S, 26.87).

1,2-SS′-*Propane*-1,3-*diyl*-1,2-*dithio*-α-D-*mannofuranoside* (7a).—The peracetylated derivative (7b) (190 mg) was dissolved in dry methanol (5 ml) and added at 0 °C to a methanolic solution saturated at 0 °C with ammonia. After 3 h at room temperature, the alcoholic solution was evaporated to furnish a crystalline residue (110 mg, 85%) which was recrystallised from the minimum amount of

methanol; m.p. 138—140 °C, $[\alpha]_D^{25}$ +1° (*c* 1.1, methanol) (Found: C, 42.7; H, 6.3; S, 25.3. Calc. for $C_9H_{16}O_4S_2$: C, 42.86; H, 6.39; S, 25.37).

1,2-SS'-*Propane*-1,3-*diyl*-5,6-O-*isopropylidene*-1,2-*dithio*-α-D-*mannofuranoside* (10).—To a solution of the thioglycoside (7a) (35 mg) in acetone (5 ml) was added anhydrous copper(II) sulphate. The mixture was stirred magnetically for 48 h at *ca.* 20 °C, filtered, and the filtrate was evaporated to an oil (40 mg, *ca.* 100%) which crystallised from chloroform–ether; m.p. 113—117 °C, $[\alpha]_D^{22}$ −25° (*c* 1.8, chloroform) (Found: C, 49.15; H, 6.75; S, 21.25. Calc. for $C_{12}H_{20}O_4S_2$: C, 49.31; H, 6.90; S, 21.89).

3,4,6-*Tri*-O-*acetyl*-2,5-*anhydro*-D-*mannose Ethylene Dithioacetal* (6b).—A magnetically stirred solution of 2-amino-2-deoxy-D-glucose hydrochloride (5 g) in water (100 ml) was submitted to a stream of dinitrogen trioxide (2 bubbles per s) during 2 h at room temperature. The solution was then degassed at *ca.* 15 mmHg with passage of a stream of nitrogen and subsequently rendered neutral by washing with a 10% (v/v) solution of *NN*-dimethyloctylamine in chloroform and then washing with ether (2 × 100 ml). Lyophilisation of the aqueous solution gave a colourless, glassy residue (3.1 g) to which was added ethane-1,2-dithiol (2.5 ml) and hydrochloric acid (*d* 1.19, 30 ml) at 0 °C. The mixture was shaken vigorously for 45 min at *ca.* 20 °C and then made neutral by addition of lead carbonate. The salts were filtered off and washed with ethanol, and the filtrate and washings were evaporated to give (6a) as an amorphous residue (5.9 g), a sample of which was used for preparation of the pertrimethylsilyl derivative (6c). The main portion of (6a) was dissolved in pyridine (30 ml) and acetic anhydride (15 ml), and the solution was set aside for 24 h at room temperature. The mixture was poured into water and the product extracted conventionally with chloroform. Evaporation of the chloroform extract gave an oil which by t.l.c. (eluant *B*) showed one major component accompanied by minor side-products. Purification on a column of silica gel (180 g) gave (5) as a chromatographically homogeneous oil (4.1 g, 48%); $[\alpha]_D^{20}$ +34° (*c* 1.3, chloroform) (Found: C, 46.15; H, 5.50; S, 17.45. Calc. for $C_{14}H_{20}O_7S_2$: C, 46.18; H, 5.53; S, 17.61).

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