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DIPHENYL DITHIOACETALS OF D-RIBOSE, D-XYLOSE, AND D- AND L-ARABINOSE. CONFORMATIONAL STUDIES AND FORMATION OF A KETENE DIPHENYL DITHIOACETAL*†

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ABSTRACT

D-Ribose, D-xylose, D-arabinose, and L-arabinose have been converted in good yield into their respective diphenyl dithioacetals, **1**, **5**, **8**, and **3**. The tetraacetate **4** of **3** adopts a planar, zigzag conformation in chloroform solution, but the D-*xylo* analog **6** and D-*ribo* analog **2** adopt conformations that have no parallel 1,3-interactions of acetoxyl groups. A crystalline diisopropylidene acetal **7** was obtained from **1**. On treatment with a strong base, the corresponding acetal **9** from the D-*arabino* derivative **8** underwent elimination of acetone to give the ketene diphenyl dithioacetal **10**, characterized as its crystalline 3-*p*-nitrobenzoate **11** and its remarkably stable 3-methyl ether **12**.

INTRODUCTION

The uncatalyzed addition of benzenethiol to chloral was reported[3] in 1870, although the product was neither characterized nor identified. In 1885, Baumann demonstrated the formation of diphenyl dithioacetals from pyruvic acid, acetone, benzaldehyde, and chloral[4], and the use of this reaction in natural-product chemistry was demonstrated in 1887 with the preparation of the 3-(diphenyl dithioacetal) of 3,7,11-trioxocholanic acid[5]. Seven years later, Emil Fischer[6] reported the preparation of dialkyl dithioacetals of sugars, and stated that benzenethiol does not react with aldoses. This assertion was repeated[7] in 1909.

In 1958, El-Hewehi[8] challenged Fischer's dictum, and reported the isolation of the crystalline diphenyl dithioacetal of D-galactose by mercaptolysis of lactose. Treatment of D-ribose with benzenethiol in the presence of zinc chloride and hydrochloric acid, followed by acetylation and distillation of the product, gave an unspecified yield of an oil that was identified as tetra-*O*-acetyl-D-ribose diphenyl dithioacetal on the basis of carbon and hydrogen analyses. In 1965, Horton and Wander[2] briefly noted the preparation of crystalline diphenyl dithioacetals of D-ribose and L-arabinose,

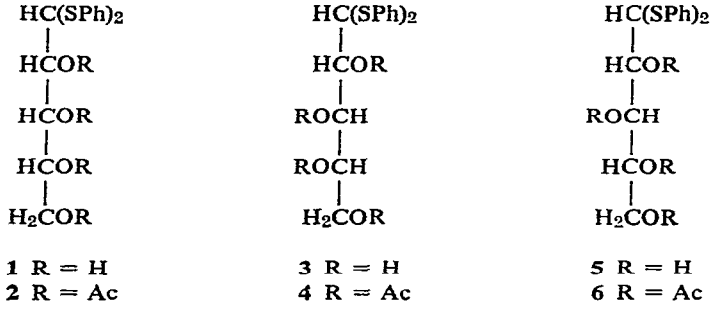
*Dedicated to the memory of Professor M. L. Wolfrom.
†This paper is part 4 of a series entitled "Conformation of Acyclic Derivatives of Sugars". For part 3, see ref. 1. For a preliminary report of part of this work, see ref. 2.

and, in the following year, Zissis, Clingman, and Richtmyer[9] described the diphenyl dithioacetals of D-glucose and D-mannose.

This report describes in detail the preparation of diphenyl dithioacetals of D-ribose, D-xylose, and D- and L-arabinose, together with three *O*-acetyl and two *O*-isopropylidene derivatives, and also describes a 1,2-elimination reaction to give a ketene dithioacetal derivative that was noted briefly in the preliminary report[2].

DISCUSSION

Preparation of diphenyl dithioacetals. — Conversion of D- and L-arabinose into their crystalline diphenyl dithioacetals **8** and **3**, respectively, proceeded satisfactorily with benzenethiol and concentrated hydrochloric acid within ~1 h at room temperature, to give the products in 70% yield. The D-xylose analog **5** was obtained similarly; a crystalline sample was first obtained by saponification of the tetraacetate **6** of **5**. Richtmyer *et al.*[9] reported that an extended time of reaction was required for preparation of the diphenyl dithioacetals of D-glucose, D-mannose, and D-galactose. The crystalline diphenyl dithioacetal of D-ribose (**1**) was obtained by the general procedure used for **3**, **5**, and **8**, but careful recrystallization was necessary for removal of a second component (a mixture of thioglycosides) from the reaction product.



1 R = H
2 R = Ac

3 R = H
4 R = Ac

5 R = H
6 R = Ac

Acetylation of **1**, **3**, and **5** with acetic anhydride in pyridine gave the corresponding tetraacetates **2**, **4**, and **6** in excellent yield; the L-*arabino* and D-*xylo* products **4** and **6** were crystalline, but the D-*ribo* analog **2** was obtained after distillation as an extremely viscous, colorless oil.

Conformational analysis of acetylated diphenyl dithioacetals. — The conformations of the three acetates in solution were examined by n.m.r. spectroscopy. In previous reports from this laboratory[1,10,11], it has been shown that acyclic sugar chains in solution tend to adopt a planar, zigzag arrangement[10] of carbon atoms, unless such a conformation would lead to a 1,3-eclipsed interaction of polar substituents[1,11]. The latter interaction, which resembles the *syn*-diaxial arrangement in a disubstituted, 6-membered ring-system, has been shown to be a powerful destabilizing factor, forcing the molecule to adopt a "sickle" conformation, resulting from rotation about a carbon–carbon bond, in order to relieve the 1,3-interaction.

Such a situation has also been observed in the solid state for the ribitol chain in riboflavin[12], and recently, in the crystallographic work of Jeffrey and coworkers, for ribitol[13] and xylitol[14].

The acetates **2**, **4**, and **6** in chloroform-*d* gave n.m.r. spectra that were readily analyzed by the methods already reported[1], and the observed chemical-shift and spin-coupling data for protons on the backbone chain are recorded in Table I, together

TABLE I

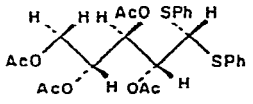
CHEMICAL SHIFTS AND COUPLING CONSTANTS FROM 100-MHz P.M.R. SPECTRA, IN CHLOROFORM-*d*, OF TETRA-*O*-ACETYL-D-RIBOSE DIPHENYL DITHIOACETAL (**2**), TETRA-*O*-ACETYL-L-ARABINOSE DIPHENYL DITHIOACETAL (**4**), TETRA-*O*-ACETYL-D-XYLOSE DIPHENYL DITHIOACETAL (**6**), AND THEIR DIETHYL ANALOGS

	Tetra-O-acetylpentose dithioacetal					
	D-ribo		D-xylo		L-arabino	
	Diethyl[a]	*Diphenyl*	*Diethyl*[a]	*Diphenyl*	*Diethyl*[a]	*Diphenyl*
Couplings						
$J_{1,2}$	6.2	3.6	5.2	3.0	8.3	5.4
$J_{2,3}$	5.7	7.2	5.9	7.0	2.8	3.1
$J_{3,4}$	3.6	3.7	4.2	3.1	7.9	8.5
$J_{4,5}$	3.1	3.8	4.3	5.1	2.9	3.8
$J_{4,5'}$	7.7	7.3	6.6	7.2	6.0	5.2
$J_{5,5'}$	12.0	12.2	11.8	11.9	12.3	12.8
Chemical shifts						
H-1	6.01	5.51	6.02	5.59	6.09	5.46
H-2	4.67	4.53	4.65	4.58	4.70	4.61
H-3	4.37	4.26	4.26	4.22	4.28	4.19
H-4	4.62	4.67	4.62	4.62	4.87	4.91
H-5	5.55	5.70	5.67	5.77	5.70	5.81[b]
H-5'	5.89	5.93	5.99	6.13	5.98	5.92[b]
Acetate[c]	7.89	8.06	7.96 (6)	7.95	7.92	7.93
	7.95	8.09	7.98	7.99	7.93	7.99
	7.97	8.12 (6)	8.02	8.02	7.99	8.06
	8.00			8.09	8.00	8.38

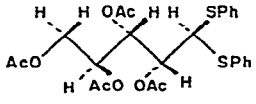
[a]Data from ref. 1. [b]By ABX analysis. [c]Three-proton singlets, unless otherwise noted in parentheses.

with corresponding data[1] for the diethyl dithioacetal analogs. By comparison of the spin couplings in the three acetates **2**, **4**, and **6**, and of those in the diethyl analogs, it may be seen that there is very little difference in the magnitudes of corresponding couplings, except for the value of $J_{1,2}$. By the arguments already presented[1] for the diethyl analogs, the favored conformation of tetra-*O*-acetyl-L-arabinose diphenyl dithioacetal (**4**) may be formulated as the planar, zigzag arrangement **4a**, corresponding to maximum relief of steric interactions between small–medium–large sets of groups along each carbon–carbon bond without the generation of parallel 1,3-interactions of substituents.

The spin-coupling data for tetra-*O*-acetyl-D-ribose diphenyl dithioacetal (**2**) clearly do not accord with the planar, zigzag arrangement **2a**; such a conformation would require large values for $J_{2,3}$ and $J_{3,4}$, as H-2, H-3, and H-4 would be mutually



2a
not favored



4a
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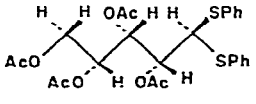
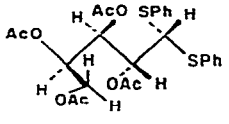


6a
not favored



2b
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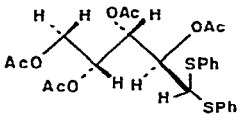

6b
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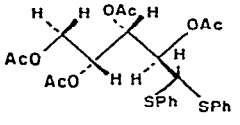


6c

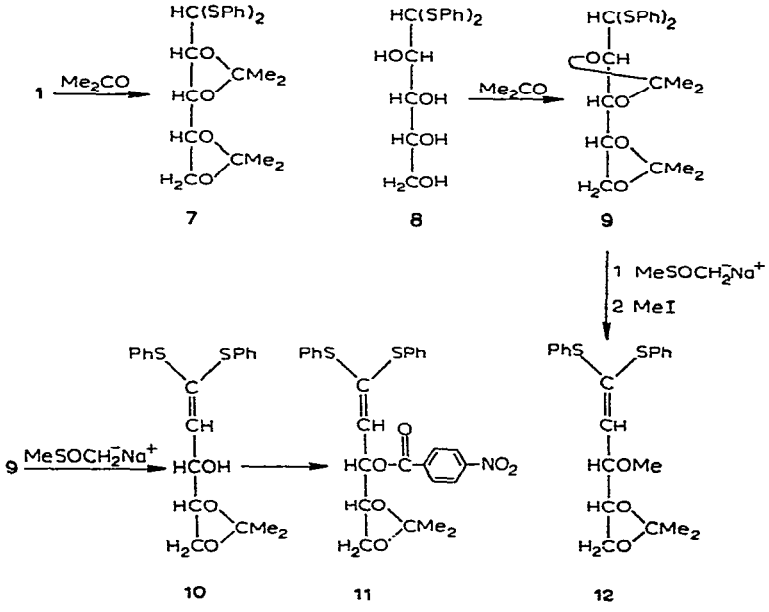
antiparallel. The value of 7.2 Hz observed for $J_{2,3}$ accords with an antiparallel disposition of H-2 and H-3, but the low value (3.7 Hz) of $J_{3,4}$ requires that H-3 and H-4 be gauche-disposed. The observed data are accommodated by the "sickle" conformation (**2b**) derived from the planar, zigzag arrangement **2a** by rotation along C-3–C-4 in order to remove the parallel interaction with the 2-acetoxyl group. The representation **2b** depicts the C-1–C-2 rotamer state that has H-1 and H-2 gauche-disposed (to accommodate the observed $J_{1,2}$ value of 3.6 Hz) and that has no parallel interaction between the 3-acetoxyl group and one phenylthio group. Such a parallel interaction would destabilize the other two C-1–C-2 rotamers, even though the one having H-1 and H-2 antiparallel would have the maximum staggering of small–medium–large sets of groups along C-1–C-2.

In the case of tetra-*O*-acetyl-D-xylose diphenyl dithioacetal (**6**), the observed spin-couplings again do not support the planar, zigzag formulation **6a**, because such a conformation would require small values for $J_{2,3}$ and $J_{3,4}$. Although $J_{3,4}$ is small (3.1 Hz), the value of $J_{2,3}$ (7.0 Hz) indicates that H-2 and H-3 are antiparallel in the favored rotamer state. The coupling data indicate that the molecule exists principally in the sickle conformation **6b**, derived from **6a** by rotation along C-2–C-3 in order to remove the 1,3-parallel interaction between the acetoxyl groups at C-2 and C-4, and to bring H-2 and H-3 into an antiparallel disposition. The C-1–C-2 rotamer state depicted in **6b** has H-1 and H-2 gauche-disposed, in order to accord with the observed small value (3.0 Hz) of $J_{1,2}$. That C-1–C-2 rotamer having maximum staggering of bulky groups, namely, **6c**, would have H-1 and H-2 antiparallel, giving a large value of $J_{1,2}$. It is probable that steric interference between the 4-acetoxyl group and the (bulky) phenylthio group causes **6c** to be less stable than **6b**, because the latter conformer is free from such interaction.

For the diphenyl derivatives **2**, **4**, and **6**, the H-1 signal appears ~0.5 p.p.m.

to lower field than its position for the diethyl analogs (see Table I), indicating a substantial difference in the electronic environment of H-1 in the two series of derivatives. In the light of the demonstrated[15] dependence of coupling constants on substituent character, it is possible that this factor may also make some contribution to the differences in $J_{1,2}$ values observed between the diphenyl derivatives and their diethyl analogs.

Formation of ketene dithioacetals. — Acetonation of D-arabinose diphenyl dithioacetal **8** in the presence of copper(II) sulfate and a trace of sulfuric acid gave, in good yield, a distillable, liquid diisopropylidene acetal that was identified as the 2,3:4,5 isomer **9** by analogy with the corresponding diethyl dithioacetal[16], and on the basis of mass-spectral data (see Experimental section and Table III) and subsequent reactions. Similar acetonation of the D-ribose analog **1** gave, in good yield, a crystalline diisopropylidene acetal presumed also to be the 2,3:4,5 isomer, namely, **7**, by analogy with the corresponding diethyl dithioacetal[17] and by analysis of its mass-spectral fragmentation pattern (see Experimental section and Table III).



The fully protected diphenyl dithioacetals **7** and **9** had been prepared with a view to generating a carbanion at C-1 by abstracting H-1, as a proton, with a strong base. The formation of alkoxide anions was to be prevented by the use of the *O*-isopropylidene group, normally alkali-stable, and it was supposed that the arylthio groups could stabilize the C-1 carbanion by resonance. Alkylation of such a carbanion might afford a route to higher ketoses. The D-*arabino* derivative **9** was therefore treated at room temperature with sodium methylsulfinylcarbanion in methyl sulfoxide, and an exothermic reaction ensued. Treatment of the product with methyl iodide caused a second exothermic reaction. Removal of the solvents and the excess of

reagents gave a syrupy product, $C_{21}H_{24}O_3S_2$, that was remarkably stable to alkali and to oxidizing agents; it could be recovered unchanged after treatment with concentrated permanganate (alkaline). The same product could be obtained by use of potassium *tert*-butoxide or butyllithium as the base, or of methyl sulfate as the methylating reagent.

TABLE II

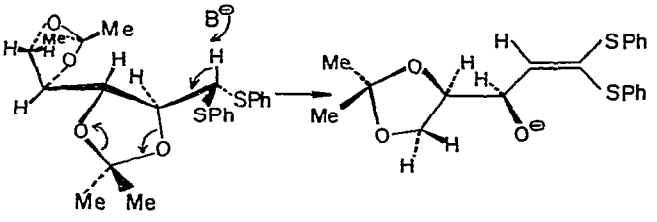
N.M.R. SPECTRAL DATA (100 MHz) FOR COMPOUNDS **7, 9, 10, 11, 12,** AND THE DIETHYL ANALOG OF **12,** IN CHLOROFORM-*d*

Spectral parameter	**7**	**9**	**10**[a]	**11**	**12**	*Diethyl analog of* **12**[a,b]
First-order couplings, Hz						
$J_{1,2}$	1.2	0.9				
$J_{2,3}$	[c]	4.3	9	8.6	8.8	8
$J_{3,4}$	[c]	[c]	5	4.0	5.6	[c]
$J_{4,5}$	[c]	[c]	[c]	7.0	[c]	[c]
$J_{4,5'}$	[c]	[c]	[c]	6.7	[c]	[c]
$J_{5,5'}$	[c]	[c]	[c]	8.5	[c]	[c]
Chemical shifts, τ						
H-1	5.30	5.17				
H-2	5.76[d]	5.64	3.78	4.03	4.08	4.00
H-3	6.02	5.75[d]	5.04	3.75	5.70	5.35[d]
H-4	6.16[d]	|	5.64[d]	5.60	5.97[d]	|
H-5	|	|	|	5.90	|	|
H-5′	6.31	6.20	6.14	6.14	6.32	6.14
Ph_2	2.45–2.80	2.50–2.86	2.50–2.78	2.74, 1.76[e]	2.84	7.08[f] 8.60[f]
CMe_2	8.56, 8.60 (2) 8.67	8.51, 8.63 8.73, 8.77	8.60 (2), 8.63 (2)	8.66 (2)	8.74 8.81	8.60 (2)
OMe					6.82	6.61
OH			6.60[g]			

[a]Measured at 60 MHz. [b]1,2-Dideoxy-1,1-bis(ethylthio)-3-*O*-methyl-D-*erythro*-pent-1-enitol. [c]Not determined. [d]Unresolved multiplet. [e]Four protons of the *p*-nitrobenzoyl group. [f]Protons of two EtS groups. [g]Exchanged by deuterium oxide.

The n.m.r. spectrum of the product $C_{21}H_{24}O_3S_2$ (see Table II) showed that two phenyl groups were still present, but that only one *O*-isopropylidene group remained. A 3-proton signal was observed in the region characteristic of methoxyl-group resonances. A 3-proton group of signals appeared in the spectral region where the starting acetal **9** showed resonances for H-4, H-5, and H-5′. A one-proton doublet showing a spacing of 8.8 Hz was observed at τ 4.08, and a one-proton quartet that also showed this spacing, together with a spacing of 5.6 Hz, was observed at τ 5.70. These data indicate that the product is formed by 1,2-elimination from **9**, loss of a molecule of acetone, and methylation of an alkoxide anion. The structure 1,2-dideoxy-4,5-*O*-isopropylidene-3-*O*-methyl-1,1-bis(phenylthio)-D-*erythro*-pent-1-enitol (**12**) is,

therefore, proposed for this compound; the doublet signal at τ 4.08 was assigned to the vinylic proton (H-2), and the quartet at τ 5.70 was assigned to H-3. Evidently, the base abstracts H-1 from **9**, but a synchronous or subsequent process leads to displacement of O-2 as an anion, and loss of acetone; and the resultant oxyanion is methylated in the subsequent step, as shown in the following scheme.



Treatment of **9** with base, without subsequent *O*-alkylation but with the addition of water, leads to the 3-hydroxy analog **10** of **12**, as a syrup. The n.m.r. spectrum of **10** (see Table II) closely resembles that of **12**, except that the methoxyl-group signal is absent and an additional signal is observed, namely, that of a proton that was labile to exchange with deuterium oxide. A crystalline *p*-nitrobenzoate **11** was prepared from **10**, and its n.m.r. spectrum (see Fig. 1 and Table II) could be completely analyzed on a first-order basis. The spectrum of **11** resembled that of the

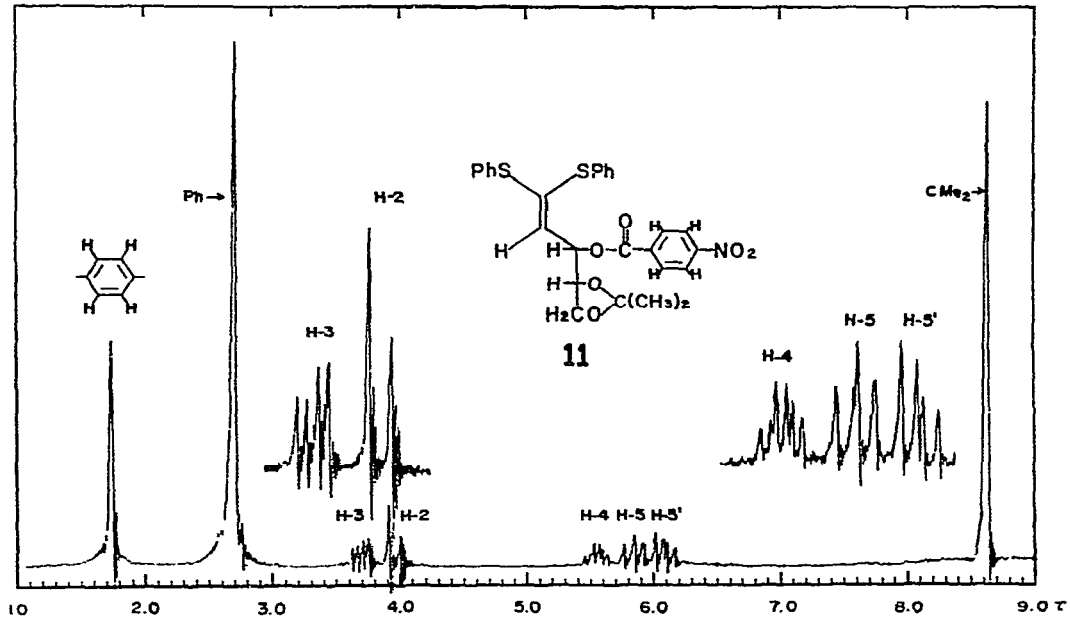


Fig. 1. The 100-MHz n.m.r. spectrum of 1,2-dideoxy-4,5-*O*-isopropylidene-3-*O*-(*p*-nitrobenzoyl)-1,1-bis(phenylthio)-D-*erythro*-pent-1-enitol (**11**) in chloroform-*d*. The main spectrum to which the scale refers was measured at a sweep-width of 1000 Hz; insets measured at a sweep-width of 500 Hz show fine structure of the signals of H-2, 3, 4, 5, and 5'.

3-methyl ether **12**, except that H-3 in **11** resonated at considerably lower field than H-3 in **12**, the result of the greater deshielding effect of the *p*-nitrobenzoyloxy group.

The mass spectrum of the unsaturated ether **12** showed a major ion having *m/e* 123 that was present to a considerably smaller extent in the spectrum of the precursor **9** (see Table III). The ion having *m/e* 123 is, presumably, that of $C_7H_7S^+$, and it can be expected to have arisen from **12** by the process shown in the following scheme.

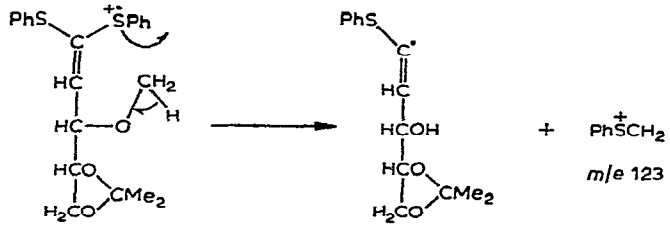


TABLE III

PRINCIPAL IONS FROM MASS-SPECTRAL DECOMPOSITION AT 70 eV (BASE PEAK = 100.0)

m/e	*Compound*			*Assignment*
	7	**9**	**12**	
43	78.0	100.0	28.5	CH_3CO^+
77	14.4	8.0	28.0	$C_6H_5^+$, phenyl
78	9.3	4.1	55.2	$C_6H_6^+$
91	14.9	14.4	48.9	$C_7H_7^+$, tropylium
101	10.0	33.3	0.2	[a]$C_5H_9O_2^+$
109	33.7	25.0	65.8	$C_6H_5S^+$, probably thiatropylium
110	43.5	11.1	10.3	$C_6H_6S^+$
123	69.0	32.2	100.0	$C_7H_7S^+$ ($PhSCH_2^+$)
135	50.0	41.8	0.2	unidentified
207	65.2	33.3	>0.1	unidentified
264	100.0	58.3	0.1	unidentified
388	—	—	>0.1	M^+
417	3.5	2.1	—	M^+–CH_3
432	5.0	9.5	—	M^+

[a]See Experimental.

In the case of **9**, a pathway involving scission of a $-CH_2-$ group from the 2,3-*O*-isopropylidene group would be unfavored on steric and electronic grounds.

Treatment of the diethyl analog[16] of **9** with strong base, followed by methylation, gave a product identified by its n.m.r. spectrum as the diethyl analog of **12**. It is evident, therefore, that aryl groups attached to sulfur are not essential to occurrence of the elimination reaction.

The base-induced elimination **9**→**10** resembles the 1,2-eliminations observed with certain α-substituted acetals of aldehydes[18] and with α-substituted thioethers[19];

α-haloaldehyde dialkyl dithioacetals eliminate hydrogen halide spontaneously upon formation[20]. For cyclic acetal groups, alkaline displacements bearing a formal resemblance to the behavior observed with **9** include the alkaline removal of the 3,5-*O*-isopropylidene group of 6-deoxy-1,2:3,5-di-*O*-isopropylidene-6-nitro-α-D-galactofuranose[21], and the debenzylidenation of methyl 4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-glucopyranoside[22].

Although some dialkyl dithioacetals of simple ketenes have been reported[18–20,23], the products **10**, **11**, and **12**, and their dialkyl analogs, represent a new class of unsaturated sugar. Studies on the reactivity of these ketene dithioacetals of sugars will be reported at a later date.

EXPERIMENTAL

General methods. — Melting points were measured with a Thomas–Hoover "Unimelt" oil-bath apparatus. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter and a 1-dm tube. T.l.c. was performed with Silica Gel G, and column chromatography with Silica Gel 7734 (E. Merck, Darmstadt, Germany); plates were activated at 110°. Indication was effected with sulfuric acid. U.v. spectra were recorded with a Cary Model 14 spectrophotometer, and i.r. spectra were recorded with a Perkin–Elmer Model 137 i.r. spectrophotometer. N.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer in the frequency-sweep mode, with 5% of tetramethylsilane as a lock signal and internal standard, according to the general procedures reported earlier[1]. X-Ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. Relative intensities were estimated visually: m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities. Elemental analyses were performed by W. N. Rond, by Galbraith Laboratories, and by Huffman Laboratories. Mass spectra were recorded by C. R. Weisenberger under the supervision of Dr. R. C. Dougherty; an AEI MS-902 instrument was used with a direct-insertion probe, at an inlet temperature of 250°, an ionizing potential of 70 eV, and an accelerating potential of 8 kV.

D-*Ribose diphenyl dithioacetal* (**1**). — A mixture of D-ribose (3.0 g), benzenethiol (5.6 ml), and 9.0 ml of concentrated hydrochloric acid pre-saturated at 0° with hydrogen chloride gas was shaken for 2 h at 0° and then for 20 min at room temperature. The resultant, homogeneous solution was poured into cold water (100 ml), and the syrupy product that formed was separated by decantation of the water layer. The syrup was dissolved in ethyl acetate (50 ml), and the solution was dried (sodium carbonate) and evaporated. A solution of the product in benzene (100 ml) was kept for 2 days at 0° to give the crude dithioacetal **1**; yield 3.0 g (42%) in two crops, m.p. 96–98°. Recrystallization from ethanol–ether and then from ethanol–water gave pure **1** as fluffy, white clusters of very fine needles, m.p. 101.5–102.0°, $[\alpha]_D^{27}$ +42.3 ±0.6° (*c* 1, pyridine); λ_{max}^{KBr} 6.35, 6.75, 6.95 (aryl C=C), 13.60, 14.20, and 14.55 μm (aryl); λ_{max}^{EtOH} 256 (ε 12,000) and 217 (sh) nm (15,000); X-ray powder

diffraction data: 13.69 m (3), 10.84 m, 9.16 m, 5.31 vs (1), 4.74 s (2,2), 4.54 m, 4.04 s (2,2), 3.77 m, 3.07 m, 2.93 m, 2.45 w, 2.11 w, and 1.96 w.

Anal. Calc. for $C_{17}H_{20}O_4S_2$: C, 57.95; H, 5.68; S, 18.18. Found: C, 58.25; H, 5.98; S, 17.99.

A second component from the reaction product, less soluble than **1** in ethanol, was isolated; yield ~0.1 g, m.p. 178–180°, $[\alpha]_D^{27}$ −48 ±1° (*c* 1.1, pyridine).

Anal. Calc. for $C_{11}H_{14}O_4S$: C, 54.54; H, 5.78; S, 13.22. Found: C, 54.30; H, 6.04; S, 13.09.

From the data, the side product appears to be a phenyl 1-thio-D-riboside; its ring size and anomeric configuration have not yet been established. After acetylation with acetic anhydride in pyridine, a syrup was obtained (R_F 0.6 in dichloromethane) whose n.m.r. spectrum in chloroform-*d* showed signals for one phenyl group and a total of three acetyl groups; the n.m.r. spectrum indicated that the product was a mixture of isomeric forms.

D-*Arabinose diphenyl dithioacetal* (**8**). — A solution of D-arabinose (50 g) in concentrated hydrochloric acid (125 ml) was shaken with benzenethiol (85 ml) at room temperature until the mixture had become solid (30–45 min). The off-white solid was dispersed in 1 liter of water in a blender, and the slurry was filtered. The resultant solid was dissolved in boiling, abs. ethanol (3 liters), and the solution was allowed to cool slowly overnight. After an additional 24 h at 0°, the mixture was filtered to give **6** as matted, white needles; yield 80 g (70%) in two crops, m.p. 186.5–187.0°, $[\alpha]_D^{29}$ +24.0 ±0.6° (*c* 1, pyridine); λ_{max}^{KBr} 6.35, 6.80, 6.95, 7.20 (aryl C=C), 13.50, 14.20, and 14.55 μm (aryl); λ_{max}^{EtOH} 256 (ε 9,000) and 216 (sh) nm (17,000); X-ray powder diffraction data: 12.99 s (2), 11.70 m, 9.35 s (3,3), 8.30 m, 5.38 m, 5.16 vw, 4.70 s, 4.33 s (3,3), 4.12 vs (1), 4.00 vw, 3.89 w, 3.61 vw, 3.47 vw, and 2.67 w.

Anal. Calc. for $C_{17}H_{20}O_4S_2$: C, 57.95; H, 5.68; S, 18.18. Found: C, 57.94; H, 5.95; S, 18.24.

L-*Arabinose diphenyl dithioacetal* (**3**). — The previous experiment was repeated, but with L-arabinose as the starting material. The product (**3**) had m.p. 186–186.8°, $[\alpha]_D^{29}$ −25.9 ±0.6° (*c* 1.2, pyridine); the i.r. and u.v. spectra and X-ray powder diffraction pattern were superposable on those of **8**.

Anal. Calc. for $C_{17}H_{20}O_4S_2$: C, 57.95; H, 5.68; S, 18.18. Found: C, 57.81; H, 5.90; S, 18.24.

D-*Xylose diphenyl dithioacetal* (**5**). — A solution of D-xylose (10 g) in 15 ml of concentrated hydrochloric acid was shaken with 17 ml of benzenethiol for 1 h at room temperature. The homogeneous mixture was poured into ice–water (400 ml), and the mixture was extracted with two 100-ml portions of ethyl acetate. The extracts were combined, dried (magnesium sulfate), and evaporated, to give crude **5** as a clear, pale-yellow syrup, yield 11.5 g (50%).

Crystalline **5** was obtained by saponification of the tetraacetate **6**. To a solution of **6** (1.0 g) in methanol (50 ml) was added sodium (~10 mg); after 6 h, Dry Ice (~2 g) was added, and the mixture was filtered. The filtrate was evaporated, and

the residue was dried at 150°/0.04 torr; trituration of the residue with ethanol caused it to crystallize. Recrystallization from ethanol gave **5** as white granules, m.p. 98–100°, yield 475 mg (77%); after being dried at 150° and further recrystallized, it had m.p. 100–101.5°, $[\alpha]_D^{26}$ −8 ±1° (*c* 0.5, ethanol); λ_{max}^{KBr} 2.95 (OH), 6.20, 8.85, 9.35, 11.60, 13.45, and 14.60 μm (aryl); λ_{max}^{EtOH} 256 (ε 9,000) and 217 (sh) nm (16,000); X-ray powder diffraction data: 8.20 s (2), 5.82 m, 4.77 vs (1), 4.44 m, 4.21 s (3), and 2.21 m.

Anal. Calc. for $C_{17}H_{20}O_4S_2$: C, 57.95; H, 5.68; S, 18.18. Found: C, 57.95; H, 5.91; S, 18.05.

Tetra-O-acetyl-D-xylose diphenyl dithioacetal (**6**). — A solution of crude, syrupy **5** (10.5 g) in pyridine (60 ml) and acetic anhydride (20 ml) was kept overnight at room temperature, and then poured into ice–water (750 ml). After 15 min, the mixture was extracted with two 250-ml portions of dichloromethane, and the extracts were combined, dried (magnesium sulfate), and evaporated. A solution of the product in dichloromethane was passed through a short column (2.5 × 1 cm) of silica gel. Evaporation of the effluent, and crystallization of the product from ether (40 ml) and petroleum ether (b.p. 30–60°, ~10 ml) at 0° gave **6** as a white solid; yield 10.6 g (67%), m.p. 81–90°. Recrystallization from hot ethanol gave 9.1 g of **6** as broad needles, m.p. 90–91°, $[\alpha]_D^{25}$ +54.5° (*c* 1, ethanol); λ_{max}^{KBr} 5.65 (OAc), 6.35, 7.25, 11.20, 11.95, 13.50, and 14.55 μm (aryl); λ_{max}^{EtOH} 256 (ε 9,000) and 216 (sh) nm (18,700); for n.m.r. data, see Table I; X-ray powder diffraction data: 9.02 s (2,2), 8.34 vs (1), 6.47 m, 6.03 s (2,2), 5.58 s (2,2), 4.39 m, 4.01 s (2,2), 3.85 s (2,2), 3.65 s (2,2), and 2.82 w.

Anal. Calc. for $C_{25}H_{28}O_8S_2$: C, 57.69; H, 5.38; S, 12.30. Found: C, 57.40; H, 5.41; S, 12.13.

Tetra-O-acetyl-D-ribose diphenyl dithioacetal (**2**). — A solution of **1** (5 g) in dry pyridine (25 ml) and acetic anhydride (10 ml) was kept for 18 h at room temperature, and then poured into ice–water (500 ml). The mixture was extracted with dichloromethane, and the extract was dried (magnesium sulfate) and evaporated, to give **2** as a pale-yellow syrup, yield 6.3 g (84%). The analytical sample was obtained by distillation at 205° (bath)/5 torr; $[\alpha]_D^{26}$ +79.8 ±0.5° (*c* 1.18, chloroform); R_F 0.4 (dichloromethane); λ_{max}^{Film} 5.60, (OAc), 6.35, 6.80, 6.85 (aryl C=C), 7.20, 13.45, and 14.55 μm (aryl); λ_{max}^{EtOH} 252 (ε 7,200) and 217 (sh) nm (14,500); for n.m.r. data see Table I.

Anal. Calc. for $C_{25}H_{28}O_8S_2$: C, 57.69; H, 5.38; S, 12.30. Found: C, 57.71, H, 5.64; S, 12.10.

El-Hewehi[8] described **2** as a yellowish oil boiling at 140–150° under "high vacuum".

Tetra-O-acetyl-L-arabinose diphenyl dithioacetal (**4**). — A solution of **3** (5.0 g) in pyridine (25 ml) and acetic anhydride (25 ml) was kept for 18 h at room temperature, and then poured into ice–water (500 ml). The resultant solid was filtered off, and recrystallized from ether–petroleum ether (b.p. 30–60°) to give **4** as dense prisms; yield 6.4 g (80%), m.p. 80–81°. A small sample was freed of minor impurities by

passing a solution in dichloromethane through a short column (2.5 × 1 cm) of silica gel; recrystallization, as before, gave pure **4**, m.p. 82–83°; $[\alpha]_D^{27}$ −60.3 ±0.6° (*c* 1, pyridine); λ_{max}^{KBr} 5.65 (OAc), 6.30, 6.70, 6.95 (aryl C=C), 12.95, 13.10, 13.35, 14.40, and 14.55 μm (aryl); λ_{max}^{EtOH} 257; (ε 10,000) and 217 (sh) nm (20,000); for n.m.r. data, see Table I; X-ray powder diffraction data: 9.35 s (2,2), 8.28 vs (1), 7.35 m, 6.56 m, 5.60 m, 4.64 s (2,2), 4.14 m, 3.95 w, and 3.69 w.

Anal. Calc. for $C_{25}H_{28}O_8S_2$: C, 57.69; H, 5.38; S, 12.30. Found: C, 57.53; H, 5.54; S, 12.06.

2,3:4,5-Di-O-isopropylidene-D-ribose diphenyl dithioacetal (**7**). — D-Ribose diphenyl dithioacetal (**1**, 1.0 g) was shaken for 24 h at room temperature with acetone (50 ml), anhydrous copper(II) sulfate (5 g), and 1 drop of concentrated sulfuric acid. The acid was neutralized with solid sodium carbonate (~1 g), and the mixture was filtered. Evaporation of the filtrate gave a syrup that began to crystallize after 12 h. Trituration with chloroform (0.3 ml) and ethanol (2 ml) gave white platelets of **5** that were filtered off and washed twice with 1.5-ml portions of ethanol; yield 1.0 g (80%), m.p. 124.5–126°, $[\alpha]_D^{26}$ +17.7 ±0.9° (*c* 0.78, chloroform): λ_{max}^{KBr} 6.95 (aryl C=C), 7.25 (CMe_2), 9.35, 11.10, 13.40, 14.00, and 14.55 μm (aryl); λ_{max}^{EtOH} 260 (ε 14,000) and 218 (sh) nm (21,000); for n.m.r. data, see Table II; X-ray powder diffraction data: 11.51 m, 7.74 m, 6.90 s (2,2), 4.94 s (2,2), 4.47 vs (1), 3.84 s (3), 3.47 w, 3.25 w, and 2.27 m; for mass-spectral data, see Table III.

Anal. Calc. for $C_{23}H_{28}O_4S_2$: C, 63.88; H, 6.46; S, 14.81. Found: C, 63.97; H, 6.71; S, 14.59.

The presence in the mass spectrum of **7** (see Table III) of a fragment having *m/e* 101 is diagnostic for a 4-monosubstituted 2,2-dimethyl-1,3-dioxolane residue, such as is seen for the exocyclic 5,6-acetal grouping of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[24], and indicates that the substitution pattern in **7** is 2,3:4,5.

2,3:4,5-Di-O-isopropylidene-D-arabinose diphenyl dithioacetal (**9**). — A mixture of **8** (40 g) and anhydrous copper(II) sulfate (40 g) in acetone (500 ml) containing concentrated sulfuric acid (4 drops) was shaken for 72 h at room temperature. The acid was neutralized by stirring with anhydrous sodium carbonate (2 g), the mixture was filtered, and the filtrate was evaporated, to give **7** sufficiently pure for further conversions; yield 32.2 g (55%). An analytical sample was prepared by passing a solution of the product in dichloromethane through a short column of silica gel, evaporating off the solvent, and distilling the syrup at 210° (bath)/5 torr. The product **9** had $[\alpha]_D^{27}$ −35.7 ±0.6° (*c* 1, chloroform); R_F 0.5 (dichloromethane); λ_{max}^{Film} 6.35, 6.70, 6.95 (aryl C=C), 7.20 (CMe_2), 13.50, and 14.50 μm (aryl); λ_{max}^{EtOH} 257 (ε 13,000) and 225 (sh) nm (25,000); for n.m.r. data, see Table II; for mass-spectral data, see Table III.

Anal. Calc. for $C_{23}H_{28}O_4S_2$: C, 63.88; H, 6.46; S, 14.81. Found: C, 63.63; H, 6.51; S, 15.03.

As with **7**, the ion at *m/e* 101 in the mass spectrum of **9** results[24] from cleavage of the C-3–C-4 bond with retention of the charge at C-4, and indicates that the order of attachment of the isopropylidene groups is 2,3 and 4,5.

The product **9** decomposed on being stored, even when it had been carefully purified, to give acetone and the starting dithioacetal **8**. This decomposition was greatly accelerated by traces of acid. The unchanged acetal **9** could be extracted from the partially decomposed product by use of ether.

*1,2-Dideoxy-4,5-*O*-isopropylidene-3-*O*-methyl-1,1-bis(phenylthio)*-D-erythro-*pent-1-enitol* (**12**). — To a solution of sodium methylsulfinylcarbanion prepared by dissolving sodium (5 g) in freshly distilled methyl sulfoxide (80 ml) was added 2,3:4,5-di-*O*-isopropylidene-D-arabinose diphenyl dithioacetal (**9**, 23.4 g, 50 mmoles), with cooling during the ensuing exothermic reaction to keep the temperature below 40°. When the reaction had subsided, methyl iodide was added dropwise to the dark-red solution, with cooling (30°) to control the exothermic reaction. When addition of methyl iodide no longer elicited liberation of heat (~10–15 ml added), a final 2 ml was added. After a few minutes, the resultant sludge was transferred to a 1-liter separatory funnel with ice and water (500 ml) and ether (250 ml), and the mixture was shaken. The layers were separated, and the aqueous layer was extracted with 300 ml of ether. The extracts were combined, washed with cold water (500 ml), dried (magnesium sulfate), and evaporated, to give **10** as a reddish orange syrup; yield 14.2 g (68%), R_F 0.5 (dichloromethane). The product was chromatographically homogeneous, and its n.m.r. spectrum indicated that substantial proportions of contaminants were absent. Some of the colored contaminants could be removed by passing a solution of the product in dichloromethane through a column (5×2 cm) of silica gel, but attempts to distil the product at 250° (bath)/3 torr led to extensive charring and decomposition, and the yield of distillate was insignificant. Treatment of the crude product (2 g) with water (5 ml), potassium hydroxide (3 g), and potassium permanganate (3 g) at room temperature led to an initially exothermic reaction. After 24 h, an excess of 40% formaldehyde solution was added to the dark-green solution, inorganic solids were filtered off, and the filtrate was extracted with chloroform. The extract was passed through a short column of silica gel and then evaporated, to give pure **10** as a red-orange syrup, with little net loss; $[\alpha]_D^{27}$ +35.7 ±0.5° (*c* 1.2, chloroform); λ_{max}^{Film} 6.30, 6.70, 6.95 (aryl C=C), 7.20 (CMe_2), 13.45, and 14.55 μm (aryl); λ_{max}^{EtOH} 246 (ε 17,500) and 212 (sh) nm (45,000); for n.m.r. data, see Table II; for mass-spectral data, see Table III.

Anal. Calc. for $C_{21}H_{24}O_3S_2$: C, 64.96; H, 6.18; S, 16.49; OCH_3, 7.99. Found: C, 64.72; H, 6.27; S, 16.20; OCH_3, 8.11.

Essentially the same results were obtained when potassium *tert*-butoxide in *tert*-butyl alcohol, or butyllithium in ether or methyl sulfoxide, was used as the base, or when methyl sulfate was used instead of methyl iodide.

When 2,3:4,5-di-*O*-isopropylidene-D-arabinose diethyl dithioacetal[16] was used instead of the diphenyl analog, a syrupy product was obtained whose n.m.r. spectrum (see Table II) indicated that it was the diethyl analog of **12**.

*1,2-Dideoxy-4,5-*O*-isopropylidene-1,1-bis(phenylthio)*-D-erythro-*pent-1-enitol* (**10**). — To a solution prepared by dissolving sodium (0.6 g) in methyl sulfoxide (30 ml) was added **9** (3.0 g, 6.9 mmoles). After the ensuing, exothermic reaction had subsided,

the mixture was shaken in a separatory funnel containing ice and water (400 ml) and ether (250 ml). The layers were separated, and the aqueous phase was extracted with 100 ml of ether. The extracts were combined, washed successively with water and saturated aqueous sodium chloride, dried (magnesium sulfate), and evaporated, to give **10** as a yellow-orange syrup, yield 1.2 g (44%); for n.m.r. data, see Table II. The crude product was used directly in the next experiment.

1,2-Dideoxy-4,5-O-isopropylidene-3-O-(p-nitrobenzoyl)-1,1-bis(phenylthio)-D-erythro-pent-1-enitol (**11**). — The syrupy **10** from the preceding experiment was dissolved in 20 ml of pyridine, *p*-nitrobenzoyl chloride (6.0 g) was added, and the mixture was kept overnight at room temperature. The mixture was poured into 600 ml of ice–water, and the resultant solid was filtered off, washed with 500 ml of water, and dried. The solid was leached with ether (25 ml), to dissolve the product and leave most of the contaminating *p*-nitrobenzoic acid undissolved. The extract was evaporated, the resultant, crude product was dissolved in dichloromethane (400 ml), and the solution was passed through a column (20 × 1 cm) of silica gel to remove the remaining *p*-nitrobenzoic acid. Evaporation of the eluate and crystallization of the residue from ether–petroleum ether (b.p. 30–60°) gave **12** as a yellowish solid; yield 1.15 g (74%), m.p. 100–102°. Recrystallization from the same solvents gave **12** as a microcrystalline, off-white powder, m.p. 102–103°, $[\alpha]_D^{28}$ +37.9 ±0.5° (*c* 1.2, chloroform); λ_{max}^{KBr} 5.80 (C=O), 6.30, 6.55 (aryl), 7.45 (doublet, CMe_2), 13.50, 13.90, and 14.55 μm (aryl); λ_{max}^{EtOH} 257 (ε 22,000) and 206 nm (26,500); for n.m.r. data, see Table II; X-ray powder diffraction data: 10.67 s (2,2), 8.64 m, 7.37 m, 5.37 m, 5.10 vs (1), 4.88 w, 4.34 m, 4.15 m, 3.80 s (2,2), 3.46 s (2,2), 3.35 w, and 3.19 s (3).

Anal. Calc. for $C_{27}H_{25}NO_6S_2$: C, 61.95; H, 4.78; N, 2.68; S, 12.24. Found: C, 61.79; H, 4.83; N, 2.70; S, 12.24.

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