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Formation and Reactions of Ketene Diphenyl Dithioacetals Derived from Aldoses[1,2]

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Acetonation of D-xylose diphenyl dithioacetal (**4**) gives the 2,3:4,5-diisopropylidene acetal (**5**), which suffers elimination of acetone by action of methylsulfinyl carbanion to yield 2-deoxy-4,5-*O*-isopropylidene-D-*threo*-pent-1-enose diphenyl dithioacetal (**6**). This product, its 3-methyl ether (**7**), its 3-*p*-nitrobenzoate (**8**), and the corresponding D-erythro analogs (**1–3**), on treatment with concentrated hydrochloric acid and subsequent acetylation, gave mixtures from which 5-*O*-acetyl-2-deoxy-3-*S*-phenyl-3-thio-D-*erythro*- and -D-*threo*-pentono-1,4-lactones (**10** and **11**) were isolated. Extended heating of compound **2** in 1 *M* aqueous ethanolic hydrochloric acid gave a low yield of a crystalline compound, tentatively identified as either 2,5-bis(phenylthio)-6*H*-pyran (**9**) or 2-phenylthio-5-(phenylthiomethyl)furan (**14**). *p*-Nitrobenzoylation of compound **1** gave, in addition to the 3-*p*-nitrobenzoate (**3**) having the same stereochemistry at C-3, some of the 3 epimer (**8**). An improved preparation of compound **4** is recorded.

Despite Fischer's statements[4,5] that diphenyl dithioacetals of aldoses could not be made, several examples have been reported in recent years.[2,6–9] These derivatives appear to be formed more slowly and are less labile to hydrolysis than the dialkyl analogs,[2,9] but their conformational behavior and the reactions of the polyhydroxyalkyl chain appear essentially the same.[2,7–9]

The action of any one of several powerful bases on the 2,3:4,5-diisopropylidene acetal of D-arabinose diphenyl dithioacetal was found to cause elimination of acetone to give 2-deoxy-4,5-*O*-isopropylidene-D-*erythro*-pent-1-enose diphenyl dithioacetal[10] (**1**), characterized as its 3-methyl ether (**2**) and 3-*p*-nitrobenzoate (**3**). These products are formally derivatives of a carbohydrate ketene, the unknown 2-deoxy-D-*erythro*-pent-1-enose. It was found[2,11] that compound **2** is exceptionally inert to common reactions of alkenes or of dithioacetals, although it was decomposed by aqueous acid. A formally related compound, tetrakis(phenylthio)ethylene, has been reported[12] to be inert toward singlet oxygen, whereas a number of simple ketene dithioacetals are highly susceptible to electrophiles.[13]

Uncertainty about the stereochemistry of the products of acid-catalyzed degradation of **2** prompted a parallel study on reactions of the 3 epimer of **2**. This report describes an improved preparation of D-xylose diphenyl dithioacetal (**4**) and its conversion, by way of the 2,3:4,5-diisopropylidene acetal (**5**), into the D-threo analogs (**6–8**, respectively) of **1–3** (Scheme I). Also reported are the isolation and spectroscopic identification of two lactones (**10** and **11**) and other products, resulting from acid hydrolysis of both stereochemical series of ketene dithioacetal derivatives.

Discussion

Preparation of Compounds 4–8.—An improved direct preparation of crystalline D-xylose diphenyl dithioacetal[2] (**4**) involved treatment of D-xylose with benzenethiol and saturated aqueous hydrogen chloride for 4 hr at 0°, and shaking the cold, diluted mixture with ether; a 53% of crystalline **4** was obtained in reactions on a 50-g scale. Acetonation of **4** in the presence of copper(II) sulfate and sulfuric acid gave, in good yield, a distillable diisopropylidene acetal considered to be the 2,3:4,5 isomer (**5**) by analogy with the corresponding diethyl dithioacetal,[14] and by

(1) Supported, in part, by Grant No. GM-11976 from the National Institutes of Health, U. S. Public Health Service, Bethesda, Md. 20014 (The Ohio State University Research Foundation, Project 1820).

(2) Previous paper in this series: D. Horton and J. D. Wander, *Carbohyd. Res.*, **13**, 33 (1970).

(3) To whom correspondence should be addressed.

(4) E. Fischer, *Ber.*, **27**, 673 (1894).

(5) E. Fischer, "Untersuchungen über Kohlenhydrate und Fermente (1884–1908)," Julius Springer Verlag, Berlin, 1909, p 89.

(6) Z. El-Hewehi, *Chem. Ber.*, **91**, 2039 (1958).

(7) D. Horton, J. B. Hughes, J. M. J. Tronchet, W. N. Turner, and J. D. Wander, Abstracts, 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 12–17, 1965, p 21D.

(8) E. Zissis, A. L. Clingman, and N. K. Richtmyer, *Carbohyd. Res.*, **2**, 461 (1966).

(9) D. Horton and J. D. Wander, *ibid.*, **15**, 271 (1970).

(10) So named by inserting the unsaturation locant and infix "1-en" into the name of the saturated analog. The name used previously,[2] 1,2-dideoxy-4,5-*O*-isopropylidene-1,1-bis(phenylthio)-D-*erythro*-pent-1-enitol, although not incorrect, renders less obvious the direct relationship of **1** to the aldose dithioacetals.

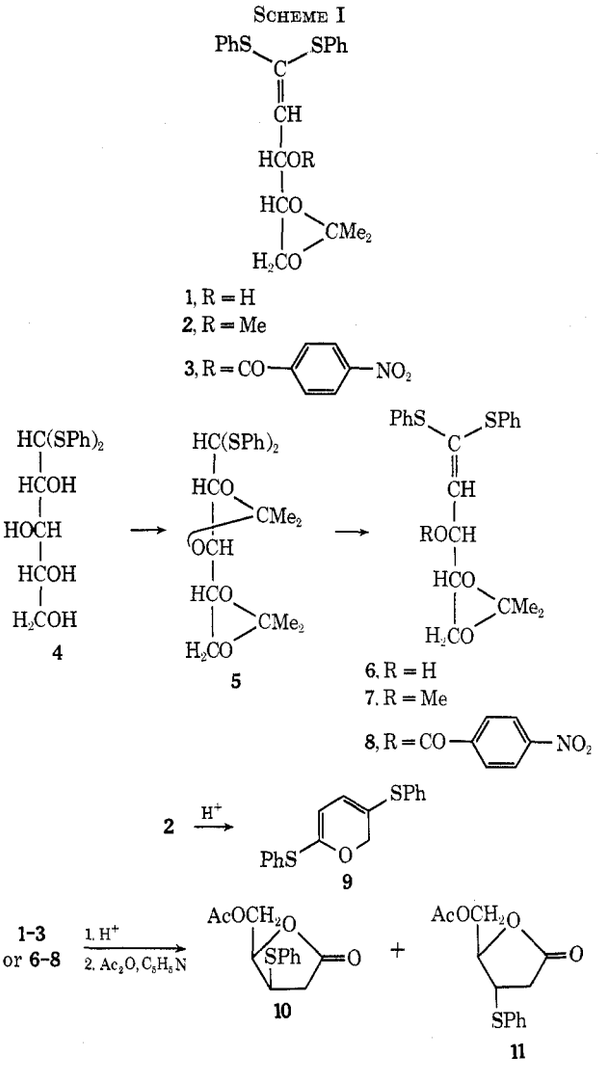
(11) J. D. Wander, Ph.D. Dissertation, The Ohio State University, 1970, pp 206–213, 238–258; *Diss. Abstr.*, Order No. 70-26,384.

(12) W. Adam and J.-C. Liu, *J. Amer. Chem. Soc.*, **94**, 1206 (1972).

(13) F. A. Carey and J. R. Neergaard, *J. Org. Chem.*, **36**, 2731 (1971).

(14) H. Zinner and J. Milbradt, *Carbohyd. Res.*, **3**, 389 (1967).

SCHEME I



the fact that the conversion product **6**, formed from **5** under basic conditions, has an *O*-isopropylidene group at positions 4 and 5. The mass spectrum of **5** (see Experimental Section) showed a major ion at *m/e* 101, presumably a 2,2-dimethyl-1,3-dioxolanium ion resulting from C-3–C-4 bond cleavage in **5**; a similar fragmentation (between C-4 and C-5) has been observed[15] with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.

Treatment of compound **5** with methylsulfinyl carbanion in methyl sulfoxide leads, as with the D-arabino analog,[2,7] to abstraction of H-1 with synchronous or subsequent elimination of the 2,3-*O*-isopropylidene group as acetone; the resultant anion, on treatment with water, gives the syrupy, chromatographically homogeneous 2-deoxy-4,5-*O*-isopropylidene-D-*threo*-pent-1-enose diphenyl dithioacetal (**6**) in 62% yield. Treatment of the anion of **6** with methyl iodide gave the corresponding 3-methyl ether (**7**), also a liquid. A crystalline, levorotatory *p*-nitrobenzoate (**8**) (mp 90–92°) was prepared from **6** by the conventional procedure,[2] and its nmr spectrum (Table I) permitted detailed assignments. The site of acylation was identified as O-3 by the low-field appearance of a doublet of doublets assignable only to H-3 (τ 3.70; $J_{2,3}$ = 8.5, $J_{3,4}$ = 5.6 Hz); the pattern shifted

(15) D. C. DeJongh and K. Biemann, *J. Amer. Chem. Soc.*, **86**, 67 (1964).

TABLE I

NMR SPECTRAL DATA (60 MHz, $CDCl_3$) FOR KETENE DITHIOACETAL DERIVATIVES **6**, **7**, AND **8**

	Chemical shifts, ppm							
Compd	H-2	H-3	H-4	H-5	H-5′	Ph	CMe_2	Other
6	3.85	5.17	5.72	—	6.26	2.73	8.57, 8.65	7.30[a]
7	4.16	5.43	5.67	—	6.32	2.74	8.56, 8.65	6.66[b]
8	4.01	3.70	5.42	—	6.26	2.66–2.85	8.52, 8.63	1.78[c]

[a] OH resonance: $J_{2,3}$ = 8.8, $J_{3,4}$ = 5.8 Hz. [b] OMe resonance $J_{2,3}$ = 8.9, $J_{3,4}$ = 6.0 Hz. [c] *p*-Nitrophenylene resonances: $J_{2,3}$ = 8.5, $J_{3,4}$ = 5.6 Hz.

to lower field by acylation would have been more complex had the acyl group been located at O-4 or O-5. This evidence therefore establishes the structure formulated for compound **8**, and thus also for compounds **5**, **6**, and **7**.

A very minor, dextrorotatory side product (mp 100–102°) from the *p*-nitrobenzoylation of **6** was found to be identical with the 3 epimer of **8** (**3**) previously prepared,[2] by *p*-nitrobenzoylation of 2-deoxy-4,5-*O*-isopropylidene-D-*erythro*-pent-1-enose diphenyl dithioacetal[2] (**1**). The *p*-nitrobenzoylation of **1** was repeated and it was found that, in addition to the dextrorotatory D-erythro derivative **3** (mp 102–103°) already reported[2] there was formed a lesser proportion of the levorotatory D-threo derivative **8** (mp 91–92°). As the nmr spectra of compounds **1**, **2**, **6**, and **7** showed no evidence whatsoever of epimeric contamination, it must be concluded that epimerization of the *p*-nitrobenzoates **3** and **8** occurs either in pyridine solution or on the silicic acid column, possibly by a process involving brief separation and internal return of the *p*-nitrobenzoate anion; further work would be necessary to clarify this point.

Reactivity of the Ketene Dithioacetal 2.—Compound **2** was remarkably stable toward reagents that normally react with alkenes or with dithioacetals. It was recovered unchanged upon attempted cleavage of the dithioacetal group by Raney nickel[16] or by mercuric chloride,[17] even in the presence of an overwhelming excess of the reagent. It was not appreciably hydrolyzed by the action of 1 equiv of bromine in acetic acid,[18] although a substantial excess of bromine led to decomposition of **2** with formation of diphenyl disulfide[19] and other, unidentified products. Diphenyl disulfide was also produced in fair yield from **2** by ozonolysis at ~25° or by dissolution in acetic anhydride–sulfuric acid; complex mixtures again accompanied this product.

Extended oxidation of **2** with peroxypropionic acid[20] led to methyl phenyl sulfone,[21] whereas extended exposure of **2** to alkaline hydrogen peroxide in acetone gave benzenesulfonic acid. The product of oxidation with peroxyacetic acid detonated spontaneously during isolation.

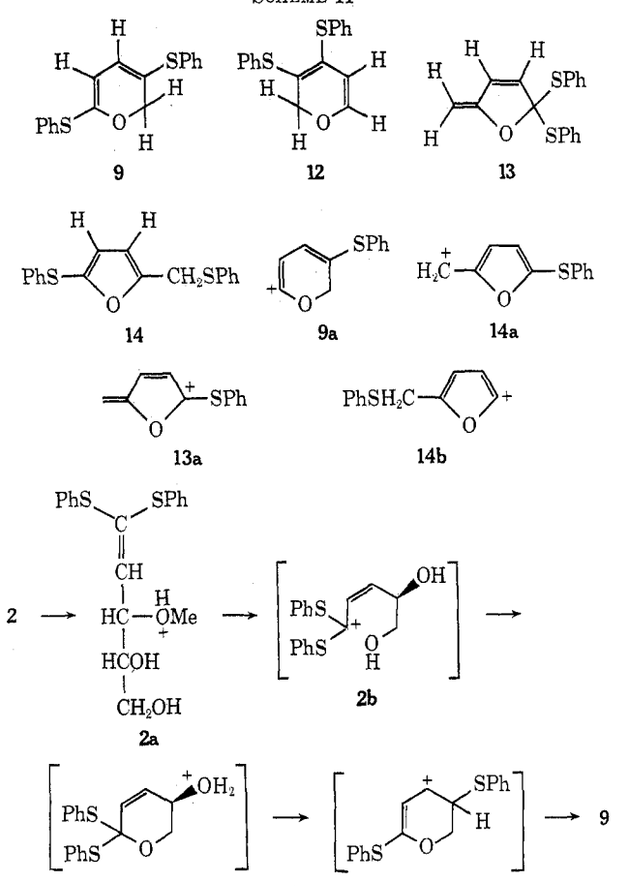
Hydrolysis of **2** in 1 *M* aqueous ethanolic hydrochloric acid for 24 hr at reflux gave a dark mixture of products from which a crystalline, optically inactive solid (mp

(16) M. L. Wolfrom and J. V. Karabinos, *ibid.*, **66**, 909 (1944).
(17) M. L. Wolfrom, *ibid.*, **51**, 2188 (1929).
(18) F. Weygand, H. J. Bestmann, and H. Ziemann, *Chem. Ber.*, **91**, 1040 (1958).
(19) E. Dreher and R. Otto, *Justus Liebigs Ann. Chem.*, **154**, 178 (1870).
(20) D. L. MacDonald and H. O. L. Fischer, *J. Amer. Chem. Soc.*, **74**, 2087 (1952).
(21) A. Michael and G. M. Palmer, *Amer. Chem. J.*, **6**, 254 (1884).

53°) was isolated in low yield; its analysis and mass spectrum indicated the molecular formula $C_{17}H_{14}OS_2$, and detailed inspection of the mass spectral and nmr data led to tentative[11] formulation of this product as 2,5-bis(phenylthio)-6*H*-pyran (**9**). The partial structure $C_5H_4O(SPh)_2$ was readily recognized from three mass spectral ions: *m/e* 298 ($M\cdot^+$), 189 (base peak, $M\cdot^+ - \cdot SPh$), and 109 (PhS^+), and from the nmr spectrum, which shows a ten-proton multiplet for two phenyl groups, a two-proton singlet at τ 6.08 ($-CH_2O-$), and an AB system (τ 3.75, 3.96; J_{AB} = 3.1 Hz) indicative of two vicinal, vinyl protons. Assuming conventional hydrolytic cleavage of the acetal group from **2**, followed by protonation at O-3 and loss of methanol to give an allylic carbonium ion stabilized by the thio groups, cyclization to give furan or pyran derivatives could take place by attack of either O-4 or O-5 at C-1. Bearing in mind the proclivity of RS groups to migrate *via* episulfonium ions under acidic conditions,[22] it is possible to formulate numerous plausible isomers of the structure $C_5H_4O(SPh)_2$, although the nmr data appear to exclude all but four of these, namely structures **9**, **12**, **13**, and **14**. Structure **12** is not attractive because the ions formed by loss of PhS· from **12** would not be expected to possess the extreme stability manifested by *m/e* 189, and furthermore the separation of the vinyl proton resonances is not so large as would be anticipated from the effect of the oxygen atom in structure **12**. The mass spectral fragment $PhSCH_2^+$ (*m/e* 123) was shown[2] earlier to exhibit considerable stability, so that the absence of this fragment from the observed mass spectrum appears to militate against structure **14**; it is observed, however, that the benzyl cation (*m/e* 91, $PhCH_2^+$) dominates the mass spectrum of benzylthiobenzene,[23] whereas the phenylthiomethyl cation (*m/e* 123) is exceedingly minor. As the benzyl cation and the furylmethyl cation (**14a**) could be expected to exhibit generally similar stabilities, structure **14** cannot be excluded at the present. Whereas structures **9** and **14** accord with all experimental data, the magnetic equivalence of the methylene protons in **13** would be an improbable but not impossible circumstance. Strong support for structure **9** or **14** and against structure **13** is provided by the mass spectral peak at *m/e* 161, identified as the transition *m/e* 189 → 28 by the metastable peak at *m/e* 137.5. Loss of C_2H_4 from *m/e* 189 is out of the question for either structure, and no mechanism can be drawn for loss of CO from **13a**; in contrast the ions **9a** and **14b** can readily extrude this fragment. The route from **2** to 2,5-bis(phenylthio)-6*H*-pyran (**9**) can be supposed to follow the process shown in Scheme II, whereas a similar process with the roles of the hydroxyl groups reversed would lead to 2-phenylthio-5-(phenylthiomethyl)furan (**14**). Unambiguous assignment of the structure of $C_5H_4O(SPh)_2$ will require studies on suitable reference compounds.

Conversion of Compounds 1, 2, 3, 6, 7, and 8 into the Lactones 10 and 11.—Dissolution of compound **7** in concentrated hydrochloric acid at ~25°, isolation of the organic product after 20 min, and subsequent acetylation with acetic anhydride–pyridine gave a mixture that was resolved by chromatography to give

SCHEME II



22% of crystalline 2-deoxy-3-*S*-phenyl-3-thio-D-*threo*-pentono-1,4-lactone (**10**) and 13% of the syrupy D-erythro isomer (**11**) of **10**. Essentially similar results were obtained when compounds **1**, **2**, **3**, **6**, or **8** were substituted for **7** as starting material, with compounds **10** and **11** being isolated in about 3:2 proportion in an overall yield of 25–35% (appreciable manipulative losses probably occurred during chromatographic separation).

The structures of the lactones **10** and **11** were assigned from various lines of evidence. The empirical formula $C_{13}H_{14}O_4S$ of the crystalline isomer **10** was also the molecular formula, as the mass spectrum showed a molecular ion at *m/e* 266. The liquid product **11** had a mass spectrum identical with that of **10** except for relative peak intensities, indicating that **11** is a diastereoisomer of **10**; the nonidentical, nonzero specific rotations observed for the two products supported this diastereoisomeric relationship. The nmr spectrum of each product showed a five-proton multiplet for the phenyl group, a three-proton singlet for an acetoxyl group, and separated multiplets accounting for six proton resonances having couplings appropriate only for the saturated, four-carbon-atom sequence $WCH_2C(H,X)C(H,Y)CH_2Z$, in which W, X, Y, and Z are not magnetically active nuclei. The ir spectra of the products show, in addition to typical acetate C=O absorption at 5.72 μm, a second carbonyl band at 5.62 μm, typical[24] of 1,4-lactones. Accordingly, the two products were formulated as diastereoisomeric 3,5-disubstituted 4-hydroxypentanoic 1,4-lactones hav-

(22) B. Berrang and D. Horton, *Chem. Commun.*, 1038 (1970).
(23) F. Taboury, *Bull. Soc. Chim. Fr.*, **31**, 1183 (1904).
(24) K. Nakanishi, "Infrared Absorption Spectroscopy—Practical," Holden-Day, San Francisco, Calif., 1962, p 44.

TABLE II

COMPARATIVE NMR SPECTRAL DATA (100 MHz, $CDCl_3$) FOR 10, 11, AND SEVERAL RACEMIC 4-HYDROXY-3-THIOPENTANOIC 1,4-LACTONE DERIVATIVES

	Chemical shifts, ppm						Coupling constants, Hz						
Compd	H-2	H-2′	H-3	H-4	H-5	H-5′	$J_{2,2'}$	$J_{2,3}$	$J_{2',3}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$
15	6.94	7.47	6.14	5.54	8.57		17.9	8.9	8.6	6.7	6.5		
16	6.84	7.38	5.89	5.34	8.54		17.7	8.8	7.9	6.3	6.3		
17	6.98	7.44	6.70	5.63	8.51		17.1	8.1	8.8	7.0	6.3		
18	6.87	7.42	6.53	5.53	8.55		17.9	8.0	8.1	6.4	6.4		
19	7.04	7.50	6.75	5.65	8.59		17.0	7.8	9.6	7.4	6.2		
11	7.08	7.31	5.83	5.14	5.55	5.55	17.7	8.4	8.4	6.9	4.3	4.3	*a*
10	7.19	7.65	6.20	5.44	5.66	5.90	17.0	8.0	6.9	5.6	2.9	4.4	11.8
20	6.93	7.52	6.19	5.25	8.59		17.5	7.5	4.1	5.3	6.4		
21	*b*	*b*	*b*	*b*	*b*		17.4[c]	8.0[c]	5.0[c]	*b*	*b*		

[a] Not available owing to the fortuitous magnetic equivalence of H-5 and H-5′. [b] Not reported. [c] Data from ref 25; measured at 56.4 MHz.

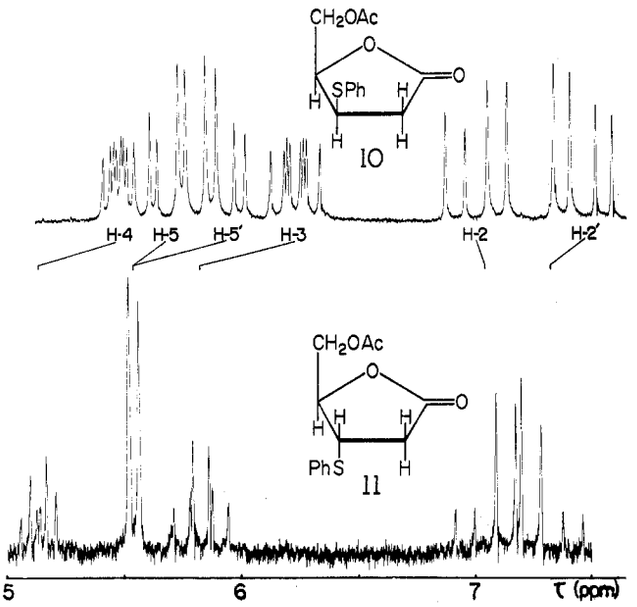


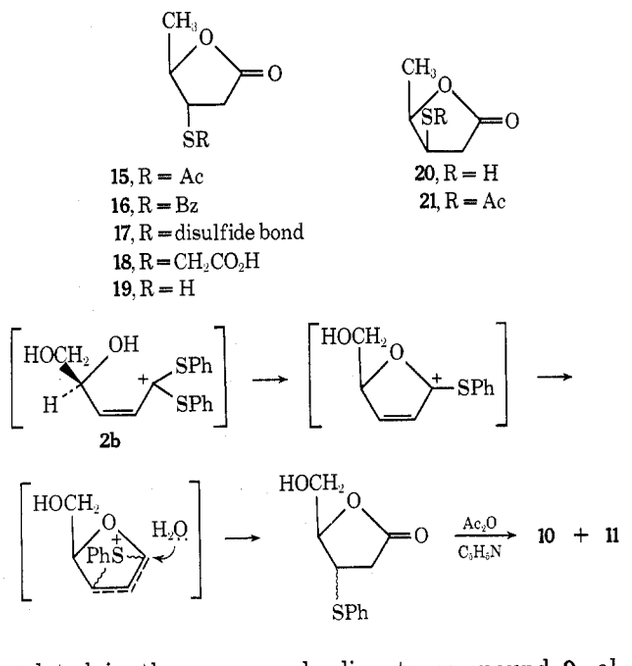
Figure 1.—Central portion of the nmr spectra (100 MHz, $CDCl_3$) of (a) 5-*O*-acetyl-2-deoxy-3-*S*-phenyl-3-thio-D-*threo*-pentono-1,4-lactone (**10**) and (b) the D-erythro analog (**11**).

ing one acetoxyl and one arylthio group. As the mass spectra exhibit peaks at *m/e* 73 ($AcOCH_2^+$) but not at *m/e* 123 ($PhSCH_2^+$) (see ref 2) there is good evidence to assign the 5-*O*-acetyl-2-deoxy-3-*S*-phenyl-3-thiopentono-1,4-lactone skeleton structure to the two products. Support for this assignment is found in the nmr spectra (Figure 1) of the diastereoisomers; the H-3 signals are observed at fields that are atypically high for acetoxymethylene protons [but are within the range observed (Table II) for substituted thiomethylene groups], whereas H-5 and H-5′ resonate within the range of chemical shift (τ 5–6) characteristic of acetoxymethyl groups in carbohydrate derivatives. As the products (a) are optically active, (b) are not enantiomorphs, and (c) are formed in a ratio not influenced by the stereochemistry at C-3 of the starting material, it may be inferred that the stereochemistry at C-4 of the two lactones is the same as that in the precursors. Thus it remains only to differentiate specifically the two isomers as D-erythro (trans) and D-threo (cis).

Although attempts at direct determination of relative stereochemistry in **10** and **11** [as by comparing relative intensities of the *m/e* 84 ($M\cdot^+ - PhSCH_2OAc$) fragment] proved indecisive, the assignment was assisted by nmr spectral comparison with several 4-hydroxy-3-thiopentanoic-1,4-lactones (**15–21**) that have been described in the literature[25,26] (see Table II). Although the values of $J_{2,2}$ and $J_{2,3}$ remain essentially constant for both the cis and trans numbers of the series, the other coupling values vary characteristically between the two series; $J_{2',3}$ in the known (racemic) derivatives exceeds 8 Hz in the trans isomers whereas it is several hertz smaller in the cis isomers, and $J_{3,4}$ (trans isomers) surpasses $J_{3,4}$ (cis isomers). The crystalline lactone ($J_{2',3}$ = 6.9, $J_{3,4}$ = 5.6 Hz) is thus presumed to be the cis isomer (5-*O*-acetyl-2-deoxy-3-*S*-phenyl-3-thio-D-*threo*-pentono-1,4-lactone, **10**) and the liquid one ($J_{2',3}$ = 8.4, $J_{3,4}$ = 6.9 Hz) the trans isomer (5-*O*-acetyl-2-deoxy-3-*S*-phenyl-3-thio-D-*erythro*-pentono-1,4-lactone, **11**). These structures await confirmation by classical degradative methods.

The sequence of steps leading to compounds **10** and **11** could possibly follow a route such as that shown in Scheme III, from an intermediate **2b** already formulated in the sequence leading to compound **9**, although experimental evidence for the steps is not available. The formation of these products probably

SCHEME III



(25) G. Fuchs, *Ark. Kemi*, **29**, 379 (1968).
(26) G. Fuchs, *Acta Chem. Scand.*, **22**, 1052 (1968).

depends on competing processes that are influenced by the reaction conditions.

Examination of molecular models indicates that, in compound **10**, the phenyl group is sterically constrained away from C-5; this conformational restriction and the shielding effect of the π-electron cloud of the phenyl group may be the reason for the higher field position observed for H-2′ and certain other resonances in **10** as compared with **11**.

Experimental Section[27]

Improved Preparation of D-Xylose Diphenyl Dithioacetal (4).—D-Xylose (50 g) was dissolved in concentrated hydrochloric acid (100 ml) that had previously been saturated at 10° with hydrogen chloride. The solution was cooled to 0° and stirred with benzenethiol (85 g) for 4 hr at 0°. The homogeneous solution was poured into ice–water (1 l.) and shaken with ether (~100 ml) to promote crystallization. The mixture was kept overnight at 0° and the white, crystalline product was filtered off and recrystallized from ethanol–water to give pure **4**, yield 55 g (53%), mp 100–101°, $[\alpha]^{22}D$ −8° (*c* 0.4, ethanol) (lit.[2] mp 101–101.5°, $[\alpha]D$ −8° in ethanol).

2,3:4,5-Di-*O*-isopropylidene-D-xylose Diphenyl Dithioacetal (5).—A mixture of compound **4** (40 g), anhydrous copper(II) sulfate, dry acetone (500 ml), and sulfuric acid (0.2 ml) was stoppered securely and shaken vigorously for 70 hr at ~25°. The mixture was filtered and the filtrate was stirred for 20 min with anhydrous sodium carbonate (8 g). Filtration and evaporation of the filtrate gave **5** as a chromatographically homogeneous syrup that could be kept without decomposition for several weeks at 0°: yield 30 g (51%); R_f 0.83 [1:9:10 isopropyl alcohol–benzene–petroleum ether (bp 30–60°)]; bp (bath) 140° (0.1 mm); $[\alpha]^{24}D$ −33° (*c* 1.2, chloroform); mass spectrum *m/e* 432 (0.3, $M\cdot^+$), 417 (0.05, $M^+ - \cdot CH_3$), 323 (4.5, $M^+ - PhS\cdot$), 265 (6.5), 244 [6.0, $(PhSCH{=}CHSPh)\cdot^+$], 207 (12.5), 135 (24.5, $PhSC^+{=}CH_2$), 123 (17, $PhSCH_2^+$), 110 (100, $PhSH\cdot^+$), 109 (36, PhS^+), 101 (13, $C_5H_9O_2^+$), 91 (17, $C_7H_7^+$), 78 (17, PhH^+), 77 (16, Ph^+), 43 (67, Ac^+).

Anal. Calcd for $C_{23}H_{28}O_4S_2$: C, 63.88; H, 6.46; S, 14.82. Found: C, 64.06; H, 6.70; S, 15.13.

2-Deoxy-4,5-*O*-isopropylidene-D-*threo*-pent-1-enose Diphenyl Dithioacetal (6).—The acetal **5** (14 g) was dissolved (with external cooling to maintain the temperature below 40°) in dry dimethyl sulfoxide (120 ml) in which sodium (5 g) had previously been dissolved. After 10 min, the red-brown solution was agitated vigorously with a mixture of cold water (1 l.) and benzene (300 ml). The organic phase was washed twice with water, dried (sodium sulfate), and evaporated to an orange-yellow, chromatographically homogeneous syrup: yield 7.5 g (62%); R_f 0.30 (1:9:10 isopropyl alcohol–benzene–petroleum ether). A sample was further purified on a 20 × 1 cm column of silica gel (1:1 ether–petroleum ether) to give **6** as a pale yellow syrup, $[\alpha]^{24}D$ −61° (*c* 1.1, chloroform); for nmr, see Table I.

2-Deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-D-*threo*-pent-1-enose Diphenyl Dithioacetal (7).—Sodium (5 g) was dissolved in dry dimethyl sulfoxide (150 ml), and compound **6** (10 g) was added with stirring and external cooling to 25°; after a few minutes methyl iodide (30 g) was added dropwise with continued cooling. After 3 min the resulting slurry was poured into a well-agitated mixture of water (1.5 l.) and benzene (300 ml). The benzene extract was washed with water, dried (sodium sulfate), and evaporated to a yellow-orange syrup, yield 6 g (65%). Purification of 1 g of the product on a 25 × 1 cm column of silica gel (1:2 ether–petroleum ether) gave **7** as a pale-yellow syrup, R_f 0.45 (1:9:10 isopropyl alcohol–benzene–petroleum ether), $[\alpha]^{25}D$ −66° (*c* 1.4, chloroform); for nmr, see Table I.

2-Deoxy-4,5-*O*-isopropylidene-3-*O*-(*p*-nitrobenzoyl)-D-*threo*-pent-1-enose Diphenyl Dithioacetal (8).—A solution of **6** (700 mg) and *p*-nitrobenzoyl chloride (3 g) in freshly distilled pyridine (20 ml) was stirred overnight at ~25° and then poured into water (500 ml) at 0°. The crude **8** that precipitated was dissolved in benzene and purified on a column of silica gel (dichloromethane as eluent). The product crystallized slowly from methanol to give pure **8**: yield 380 mg (40%); mp 90–92°; $[\alpha]^{22}D$ −47° (*c* 1.2, chloroform); R_f 0.43 [1:9:10 isopropyl alcohol–benzene–petroleum ether); nmr, see Table I; X-ray powder diffraction data 9.76 (vs) (1), 9.00 (w), 8.20 (w), 6.88 (m), 6.60 (w), 5.65 (m), 5.33 (m), 4.82 (s) (2), 4.41 (m), 4.28 (m), 3.75 (s) (3), 3.56 (m), 3.30 (m), 3.03 (m), 2.76 (w).

Anal. Calcd for $C_{27}H_{25}NO_6S_2$: C, 61.95; H, 4.78; N, 2.68; S, 12.24. Found: C, 61.73; H, 4.88; N, 2.80; S, 12.33.

In another preparation, the methanolic mother liquors were concentrated to give additional **8** and, in later fractions, a low yield (~3%) of a different, dextrorotatory product crystallizing as white needles, mp 100–102°; the physical constants of this second product were the same as those of the 3 epimer **3**.

2-Deoxy-4,5-*O*-isopropylidene-3-*O*-*p*-nitrobenzoyl-D-*erythro*-pent-1-enose Diphenyl Dithioacetal (3).—The conditions previously described[2] for *p*-nitrobenzoylation of 2-deoxy-4,5-*O*-isopropylidene-D-*erythro*-pent-1-enose diphenyl dithioacetal (**1**) were essentially followed, but the crude product remained in contact with aqueous pyridine and with silica gel for a longer period. A solution of **1** (700 mg) and *p*-nitrobenzoyl chloride (3 g) in dry pyridine was stirred overnight at ~25° and the resultant slurry was poured into ice–water (300 ml). The precipitate that formed was filtered off, dried, and extracted with benzene at 10°. The orange-colored extract was purified on a 20 × 1 cm column of silica gel with dichloromethane as eluent to give a pure *p*-nitrobenzoate fraction, which was fractionally recrystallized from ethanol by cooling very slowly to 0°. The early fractions were fine, white needles of the D-erythro ester **3**, yield 250 mg (26%), mp 102–103°, $[\alpha]^{23}D$ +38° (*c* 1, chloroform), identical with **3** previously reported[2] by melting point, $[\alpha]D$, nmr spectrum, and X-ray diffractogram.

Later fractions yielded clusters of white prisms of the D-threo ester **8**, yield 120 mg (12%), mp 91–92°, identical with authentic **8** by mixture melting point, $[\alpha]D$, nmr spectrum, and X-ray diffractogram.

Additional crystalline fractions obtained behaved as mixtures of **3** and **8**.

Reactions of 2-Deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-D-*erythro*-pent-1-enose Diphenyl Dithioacetal (2). A. Raney Nickel.—A solution of **2** (2 g) in 80% aqueous ethanol (40 ml) was refluxed for 48 hr with 4 tablespoonfuls of neutral, W-4 Raney nickel. The reaction solution was found (tlc and nmr) to contain mainly starting material, contaminated with several minor products.

B. Mercuric Chloride.—Compound **2** (3 g) in acetone (65 ml) was stirred vigorously for 24 hr at 40° with mercuric chloride (25 g) and cadmium carbonate (15 g), and the mixture was filtered. Evaporation of the filtrate, extraction of the residue with dichloromethane, and washing the extract with aqueous potassium iodide gave a solution that contained (tlc and nmr) several components but mainly **2**; no free aldehyde was formed and little loss of phenyl groups had occurred (nmr).

C. Bromine.—Treatment of **2** (2 g) with bromine (1.5 g) in 70% aqueous acetic acid for 5 min at ~25° by the general procedure of Weygand and coworkers[18] gave an almost quantitative return of **2**. When a large excess (15 g) of bromine was used there was obtained, as the only product soluble in organic solvents, diphenyl disulfide, yield 500 mg (55%), mp 59–60° (undepressed on admixture with an authentic sample[19]). Treatment of **2** (1 g) with bromine (3 ml) in methanol (15 ml) gave a black, apparently polymeric material.

D. Ozone.—A stream of ozonized oxygen was passed for ~30 min at −78° through a solution of **1** (2 g) in methanol (25 ml). Evaporation of the solution gave a product that by tlc and nmr appeared to be mainly starting material.

E. Acetolysis.—To a mixture of acetic anhydride (20 ml) and sulfuric acid (4 ml) kept below 10° was added **2** (2 g), and after 5 min the mixture was poured onto ice and treated with

(27) Solutions were evaporated under diminished pressure below 50°. Melting points were determined with a Thomas-Hoover "Unimelt" apparatus and are uncorrected. Tlc was effected with 250-μm layers of silica gel G (Merck) activated at 110°, and column chromatography with silica gel 7734 (Merck). Ir spectra were recorded with a Perkin-Elmer Model 137 or a Perkin-Elmer Model 457 spectrophotometer. Nmr spectra were recorded at 60 or 100 MHz with Varian A-60 or HA-100 nmr spectrometers, respectively, tetramethylsilane (τ 10.00) being used as the internal standard. Mass spectra were recorded with an AEI MS-9 instrument at a source temperature of 250°, an ionizing potential of 70 eV, and an accelerating potential of 8 kV. X-Ray powder diffraction data give interplanar spacings in angstroms for Cu Kα 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. The camera diameter was 114.59 mm. Microanalyses were performed by W. N. Rond.

sodium hydrogen carbonate. Extraction of the mixture with ether gave diphenyl disulfide, yield 0.5 g (55%), mp and mmp 59–60°.

F. Peroxy Acids.—A solution of **2** (2 g) in ~2 *M* peroxypropionic acid in propionic acid (20 ml) was kept for 4 hr at ~25°, the excess peroxy acid was decomposed with manganese dioxide, and the dichloromethane-soluble product was purified by column chromatography on silica gel to give methyl phenyl sulfone: yield 0.3 g (35%); mp 85–86° (lit.[21] mp 88°); nmr $CDCl_3$) τ 2.55–2.00 (5 protons, Ph), 6.98 (3-proton singlet, Me).

Hydrogen peroxide (30%, 5 ml) was added to a solution of **2** (1 g) in acetic acid (20 ml), and after 1 hr at ~25° the mixture was treated with manganese dioxide. After cessation of effervescence the solid was filtered off. Evaporation of the solution in a rotary evaporator left a residue that detonated spontaneously.

When a solution of **2** (2 g) in acetone (10 ml) was treated with hydrogen peroxide (30%, 5 ml) for 3 months at 5°, a precipitate was formed that was identified as benzenesulfonic acid, mp and mmp 42–43°.

Acid Degradation of 2 to an Unsaturated Bis(phenyl thioether) $C_4H_5O(SPh)_2$ (9 or 14).—A solution of **2** (2 g) in 2 *M* hydrochloric acid (50 ml) and ethanol (50 ml) was heated for 24 hr under reflux on a steam bath. The malodorous mixture was concentrated to ~50 ml and then extracted with dichloromethane. The extract was washed with water, dried (magnesium sulfate), and evaporated, and the resultant syrup was kept overnight at ~25° with acetic anhydride (5 ml) and pyridine (5 ml). The mixture was evaporated at ~25° and two 2-ml portions of toluene were evaporated from the residue. A solution of the residue in methanol (5 ml) was kept for 30 min at −80° to give a solid that was filtered at 0° and recrystallized from cold methanol (2 ml) to give a white solid: yield 50 mg (5%); mp 50–52° [52.3–53.2° after sublimation at 150° (bath) (4 Torr)]; $[\alpha]^{26}D$ 0° (*c* 1.6, chloroform); λ_{max}^{EtOH} 246 nm (ϵ 44,000) and 211 (sh, 23,000); λ_{max}^{KBr} 3.3 (CH), 6.3, 6.8, 7.0, 8.1, 8.2, 8.4, 8.8, 8.9, 9.3, 9.9, 10.4, 10.6, 12.6, 13.6, 14.5 μm (aryl); nmr (100 MHz, $CDCl_3$) τ 2.85–3.00 (10-proton multiplet, 2 Ph), 3.75 and 3.96 (1-proton doublets, $J_{3,4}$ = 3.1 Hz, H-3, H-4), 6.08 (2-proton singlet, CH_2); X-ray powder diffraction data 7.91 (m), 5.75 (w), 5.48 (w), 4.72 (m), 4.55 (vs), (1), 4.33 (w), 4.00 (s) (2), 3.62 (w), 3.43 (s) (3), 3.07 (m); mass spectrum *m/e* 298 (0.9, $M\cdot^+$), 189 [100, $M\cdot^+$ − PhS· (m* 119.8, calcd 119.9)], 161 [5.0, 189 − CO (m* 137.5, calcd 137.2)], and 109 [4.4, $M\cdot^+$ − 189 (m* 39.6, calcd 39.3)].

Anal. Calcd for $C_{17}H_{14}OS_2$: C, 68.46; H, 4.70; S, 21.47. Found: C, 68.23; H, 4.57; S, 21.17.

A slightly better yield (90 mg, 9%) of this product was obtained by passing the initial dichloromethane extract through a column (2.5 × 10 cm) of silica gel. Diphenyl disulfide (0.2 g) was eluted first by dichloromethane, followed by $C_5H_4O(SPh)_2$; slower-moving components from the column were poorly defined, apparently polymeric products.

Degradation of 2-Deoxy-4,5-*O*-isopropylidene-3-*O*-methyl-D-*threo*-pent-1-enose Diphenyl Dithioacetal (7) and Analogs (1, 2, 3, 6, and 8) to the Lactones 10 and 11.—A solution of **7** (800 mg) in concentrated hydrochloric acid (10 ml) was kept for 20 min at ~25° and then diluted with water and extracted with dichloromethane. The extract was washed with water, dried (sodium sulfate), and evaporated to a yellow syrup that by tlc contained many components. Acetic anhydride (5 ml) and dry pyridine (5 ml) were added and after 18 hr at ~25° the solvent and reagents were evaporated off at 40°. The residual syrup was purified by elution with dichloromethane through a 50 × 1 cm column of silica gel to give a fraction having R_f 0.33 (1:9:10 isopropyl alcohol–benzene–petroleum ether). This fraction was repeatedly rechromatographed on a similar column, with ether–petroleum ether as eluent, to give two chromatographically homogeneous products having R_f 0.49 and 0.60 (1:2 ether–petroleum ether).

The faster migrating compound (R_f 0.60), assigned the structure 5-*O*-acetyl-2-deoxy-3-*S*-phenyl-3-thio-D-*threo*-pentono-1,4-lactone (**10**), recrystallized as white needles: yield 120 mg (22% based on **7**); mp 61–62°; $[\alpha]^{21}D$ +53° (*c* 1, chloroform); λ_{max}^{EtOH} 253 nm (ϵ 5200), 215 (sh, 21,000); λ_{max}^{KBr} (Perkin–Elmer 457 ir spectrophotometer) 3.23 (ArH), 3.33 (CH), 5.62 (C=O, 1,4-lactone), 5.72 (AcO), 6.31 (aryl), 7.10 (-CH_2CO-), 7.20, 7.30 (Ac), 8.18 (asymmetric Ac–O stretch), 8.50 (symmetric Ac–O stretch), 9.25, 9.60, 10.45, 11.50, 12.05, 13.35, and 14.45 μm (aryl); nmr, see Table II; mass spectrum *m/e* 266 (6, $M\cdot^+$), 193 (0.8, $M\cdot^+$ − ·CH_2OAc), 157 (2.5, $M\cdot^+$ − ·SPh), 137 (0.7, $PhSCHCH_3^+$), 136 (3.1), 135 (3.5), 110 (100, $PhSH\cdot^+$), 109 (23, PhS^+), 84 (14, $M\cdot^+$ − $PhSCH_2OAc$), 78 (8, $PhH\cdot^+$), 77 (12, Ph^+), 73 (5, $AcOCH_2^+$), 43 (86, Ac^+); X-ray powder diffraction data 10.10 (s) (2, 2), 5.71 (w), 5.20 (m), 5.06 (s) (2, 2), 4.75 (s) (3, 3), 4.23 (vs) (1, 1), 3.96 (vs) (1, 1), 3.81 (w), 3.70 (m), 3.40 (s) (3, 3), 3.06 (m), 2.57 (w), 2.34 (vw).

Anal. Calcd for $C_{13}H_{14}O_4S$: C, 58.63; H, 5.30; S, 12.04. Found: C, 58.76; H, 5.37; S, 11.90.

The slower migrating component, R_f 0.49, assigned the structure 5-*O*-acetyl-2-deoxy-3-*S*-phenyl-3-thio-D-*erythro*-pentono-1,4-lactone (**11**), was obtained as a colorless syrup: yield 70 mg (13% based on **7**); $[\alpha]^{22}D$ +35° (*c* 1.2, chloroform); λ_{max}^{film} 3.22 (CH), 3.39 (CH_2), 5.60 (C=O of 1,4-lactone), 5.74 (AcO), 6.32, 6.90 (aryl), 7.10, 7.28, 8.11 (asymmetric Ac–O stretch), 8.53 (symmetric Ac–O stretch), 9.52, 10.58, 13.43, 14.46 μm (aryl); nmr, see Table II; mass spectrum *m/e* 266 (16), 193 (2), 157 (1.2), 137 (3), 136 (22, $M\cdot^+$ − CH_2=CHPh), 135 (12, $M\cdot^+$ − ·CHCHSPh), 110 (90), 109 (26), 84 (15), 78 (8), 77 (15), 73 (6), 43 (100).

The following relative yields were obtained when other ketene dithioacetal derivatives were used as starting materials [starting material, yield of **10** (%), yield of **11** (%)]: **1**, 15, 6; **2**, 8, 5; **3**, 15, 6; **6**, 21, 13; **8**, 16, 12.5.

Registry No.—**3**, 28697-90-7; **5**, 37107-87-2; **6**, 37107-88-3; **7**, 37107-89-4; **8**, 37107-90-7; **9**, 37107-91-8; **10**, 37112-32-6; **11**, 37112-33-7; **14**, 37157-02-1.

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