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2-DEOXY-D-*arabino*-HEXOSE, 2-DEOXY-D-*lyxo*-HEXOSE, AND THEIR (2*R*)-2-DEUTERIO ANALOGS*

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ABSTRACT

A general method for the synthesis of 2-deoxyhexoses is described. 2-Deoxy-D-*arabino*-hexose and 2-deoxy-D-*lyxo*-hexose were prepared from D-glucose and D-galactose, respectively, by a route involving reduction of the respective 4,5-*O*-isopropylidene ketene diethyl dithioacetals with lithium aluminum hydride, followed by removal of the protecting groups. In agreement with the results of earlier studies with ketene dithioacetals of pentose analogs, reduction of the hexose ketene dithioacetals was found to occur both regio- and stereo-specifically. Reduction with lithium aluminum deuteride gave the (2*R*)-2-deoxy-2-deuterio-hexoses exclusively.

INTRODUCTION

In a recent communication[1], we described a potentially general method for the synthesis of 2-deoxyaldoses and, in a later report, the application of that method to the synthesis of 2-deoxypentoses[2]. This method is based on selective deoxygenation of the parent aldoses at C-2, *via* a reaction sequence involving the formation and reduction of ketene dithioacetal intermediates. This report describes the extension of this method to the synthesis of 2-deoxyhexoses, which requires modification of the reaction sequences used to generate the requisite ketene dithioacetal and remove the protecting groups. The synthetic strategy is illustrated by the preparation of 2-deoxy-D-*arabino*-hexose and 2-deoxy-D-*lyxo*-hexose because of the ready availability of the respective parent hexoses.

RESULTS AND DISCUSSION

The accompanying scheme gives the reactions involved in the conversion of D-

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glucose (**1a**) and D-galactose (**1b**) into 2-deoxy-D-*arabino*-hexose (**9a**) and 2-deoxy-D-*lyxo*-hexose (**9b**), respectively. The key reaction in this synthesis, the reduction of ketene diethyl dithioacetals **5a** and **5b** with lithium aluminum hydride, has previously been demonstrated to proceed *via* the intermediacy of an alkoxyaluminum hydride salt formed by participation of the free 3-hydroxyl group[1,2]. The requirement for the free allylic hydroxyl group in **5a** and **5b** necessitates their derivation by elimination of a 2,3-acetal function. In the pentose series, this conversion is straightforward as the diethyl dithioacetals are readily acetonated to give the 2,3:4,5-di-*O*-isopropylidene derivatives. Acetonation of hexose dithioacetals, however, can result in the formation of three different di-*O*-isopropylidene derivatives, only two of which will undergo elimination to give the appropriate ketene dithioacetal. Although acetonation of

Scheme A

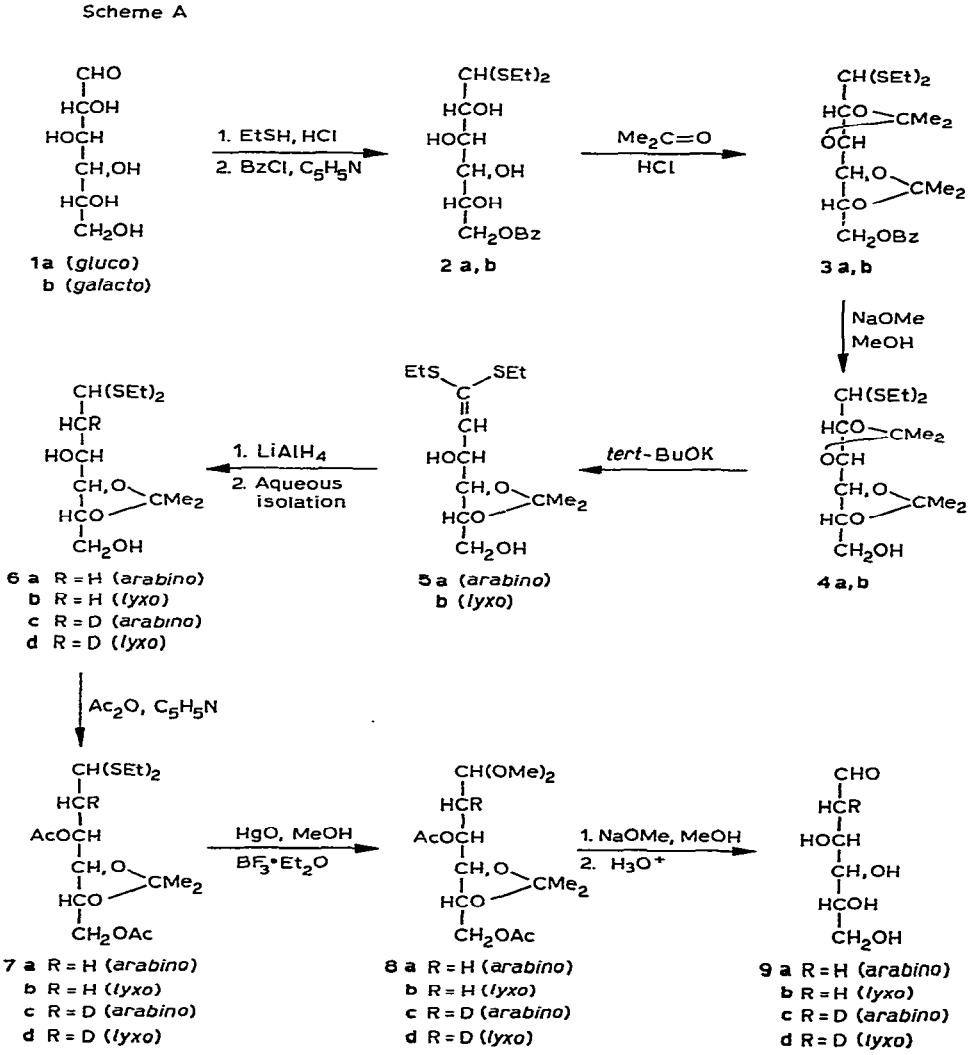

TABLE I

PROTON-NOISE-DECOUPLED ^{13}C-N.M.R. SPECTRA OF DI-*O*-ISOPROPYLIDENE DIETHYL DITHIOACETALS **4a, b**, KETENE DIETHYL DITHIOACETALS **5a, b**, AND REDUCTION PRODUCTS **6a, b**, AND THEIR (2*R*)-2-DEUTERIO ANALOGS (**6c, d**)

Compound	*C-1*	*C-2*	*C-3,4*	*C-5*	*C-6*	*Isopropylidene*		*Ethyl*	
						C	*CH$_3$*[a]	*CH$_2$*[a]	*CH$_3$*
4a	52.75	(75.40)[b]	(77.28, 77.88)[b]	(80.27)[b]	61.86	110.33, 108.69	(26.65, 26.94)	(27.38)	14.44
4b	51.92	(78.84)[b]	(79.22, 81.24)[b]	(84.96)[b]	62.26	110.56, 109.63	(26.88, 27.00)	(27.19)	14.34, 14.47
5a	135.57	134.08	(67.86, 77.73)[c]	(79.76)[c]	61.26	108.73	(25.10, 27.13)	(27.28, 27.67)	13.93, 15.16
5b	135.45	133.48	(69.81, 78.95)[c]	(80.20)[c]	62.70	109.19	(26.87, 27.03)	(27.57)	13.95, 15.05
6a	48.02	41.62	(67.02, 77.58)[c]	(79.52)[c]	61.01	108.54	(25.06, 27.23)	(24.34)	14.52
6b	48.25	39.92	(71.12, 80.24)[c]	(81.20)[c]	63.34	109.32	(23.70, 27.04)	(24.39)	14.49
6c	47.88	41.13 (t, J = 19.3)	(66.79, 77.49)[c]	(79.43)[c]	60.79	108.45	(25.02, 27.15)	(24.28)	14.50
6d	48.02	39.88 (t, J = 19.4)	(70.67, 80.51)[c]	(81.26)[c]	63.25	109.35	(23.46, 27.10)	(24.41)	14.51

[a]The isopropylidene CH_3 and ethyl CH_2 resonances were not assigned and are shown in parentheses. [b]The C-2,3,4,5 resonances were not assigned. [c]The C-3,4,5 resonances were not assigned.

D-galactose diethyl dithioacetal gave the 2,3:4,5-diisopropylidene acetal (**4b**) in good yield[3], direct acetonation of D-glucose diethyl dithioacetal gave a mixture of the two di-*O*-isopropylidene derivatives with substitution at positions 3,4:5,6 and 2,3:5,6, in addition to mono-*O*-isopropylidene derivatives[4]. 2,3:4,5-Di-*O*-isopropylidene-D-glucose diethyl dithioacetal (**4a**) was formed in much better yield (90%) from 6-*O*-benzoyl-D-glucose diethyl dithioacetal[5] (**2a**), the latter being obtained from D-glucose diethyl dithioacetal in 70% yield.

Treatment of the respective 2,3:4,5-di-*O*-isopropylidene diethyl dithioacetal of D-glucose (**4a**) and D-galactose (**4b**) with 2.1 equivalents of potassium *tert*-butoxide in 1:15 (v/v) dimethyl sulfoxide–oxolane gave 2-deoxy-4,5-*O*-isopropylidene-D-*arabino*-hex-1-enose diethyl dithioacetal (**5a**) in 67% yield and 2-deoxy-4,5-*O*-isopropylidene-D-*lyxo*-hex-1-enose diethyl dithioacetal (**5b**) in 78% yield. Ketene diethyl dithioacetal **5a** was also obtained directly from 6-*O*-benzoyl-2,3:4,5-di-*O*-isopropylidene-D-glucose diethyl dithioacetal (**3a**) on treatment with 2.1 equivalents of potassium *tert*-butoxide. These conditions were found to give higher yields of ketene dithioacetals than those used to generate these derivatives in the pentose series[1,2]. The ketene diethyl dithioacetal intermediates were characterized by ^{1}H- and ^{13}C-n.m.r. spectroscopy. The ^{1}H-n.m.r. spectra of these derivatives showed a characteristic doublet for H-2 at δ 6.0 ($J \sim 8$ Hz), well downfield of other resonances. In addition, integration of these spectra demonstrated the presence of a single *O*-isopropylidene group instead of the two acetal groups present in the starting materials. The ^{13}C-n.m.r. spectra of these derivatives also gave the expected resonances (Table I). The C-1 resonances were observed at $\delta \sim 135$, well downfield from the C-1 resonances of the starting di-*O*-isopropylidene diethyl dithioacetals (δ 52), and the C-2 resonances were observed at δ 134. The latter resonances gave the expected doublet when off-resonance decoupled, whereas the C-1 resonances remained as singlets.

Reduction of ketene diethyl dithioacetals **5a** and **5b** was accomplished with lithium aluminum hydride in dry oxolane (tetrahydrofuran) under the same conditions previously reported for analogs of the pentose series. In the ^{13}C spectra of the reduction products, the C-1 and C-2 resonances were observed at $\delta \sim 48$ and ~ 40, respectively, and gave doublets and triplets, respectively, when off-resonance decoupled. When the reduction of **5a** and **5b** was accomplished with lithium aluminum deuteride, the 2-deuterio analogs (**6c** and **6d**, respectively) were formed, as expected[1,2]. In the proton-decoupled, ^{13}C spectra of the deuterated derivatives (Table I), the C-2 resonances were present as triplets (J 19 Hz), and the other resonances in these spectra had chemical shifts identical to those of the undeuterated compounds, **6a** and **6b**.

Removal of the protecting groups from the reduction products (**6a–d**) to generate the free 2-deoxyhexoses (**9a–d**) could not be accomplished in high yield by the same procedure used for deprotection of the pentose analogs[2]. For the hexose analogs, removal of the protecting groups was accomplished by a four-step procedure involving acetylation of the 3- and 6-hydroxyl groups, conversion of the diethyl dithioacetal into the dimethyl acetal, and finally, sequential alkaline and mild, aqueous-acid hydrolysis. For example, acetylation of **6a** with pyridine and acetic

anhydride followed by treatment with 2 equiv. of mercuric oxide and 2 equiv. of boron trifluoride etherate in dry methanol gave the dimethyl acetal (**8a**). Saponification of **8a**, followed by hydrolysis for 24 h in 0.01M trifluoroacetic acid at 4°, gave 2-deoxy-D-*arabino*-hexose (**9a**) in 50% overall yield. Treatment of **6b** under identical conditions gave 2-deoxy-D-*lyxo*-hexose (**9b**) in 53% overall yield. Final purification of the 2-deoxyhexoses and their 2-deuterio analogs was accomplished by gel-permeation chromatography on Bio-Gel P-2 as previously described[2].

The free 2-deoxyaldoses and their 2-deuterio analogs were characterized by ^{1}H-n.m.r. spectroscopy. In the ^{1}H-n.m.r. spectrum of 2-deoxy-D-*arabino*-hexose (**9a**) (Fig. 1, lower spectrum), the H-1 resonance of the β-pyranose form (δ 4.94) is a doublet of doublets showing $J_{1a,2a} = 9.7$ and $J_{1a,2e} = 1.1$ Hz, and the H-1 resonance of the α-pyranose form (δ 5.39) is an unresolved doublet of doublets having $J_{1e,2e} = <1$ and $J_{1e,2a} = 3.6$ Hz. These values are in close agreement with those previously reported[6]. In the ^{1}H-n.m.r. spectrum of the 2-deuterio analog, (**9c**) (Fig. 1, upper

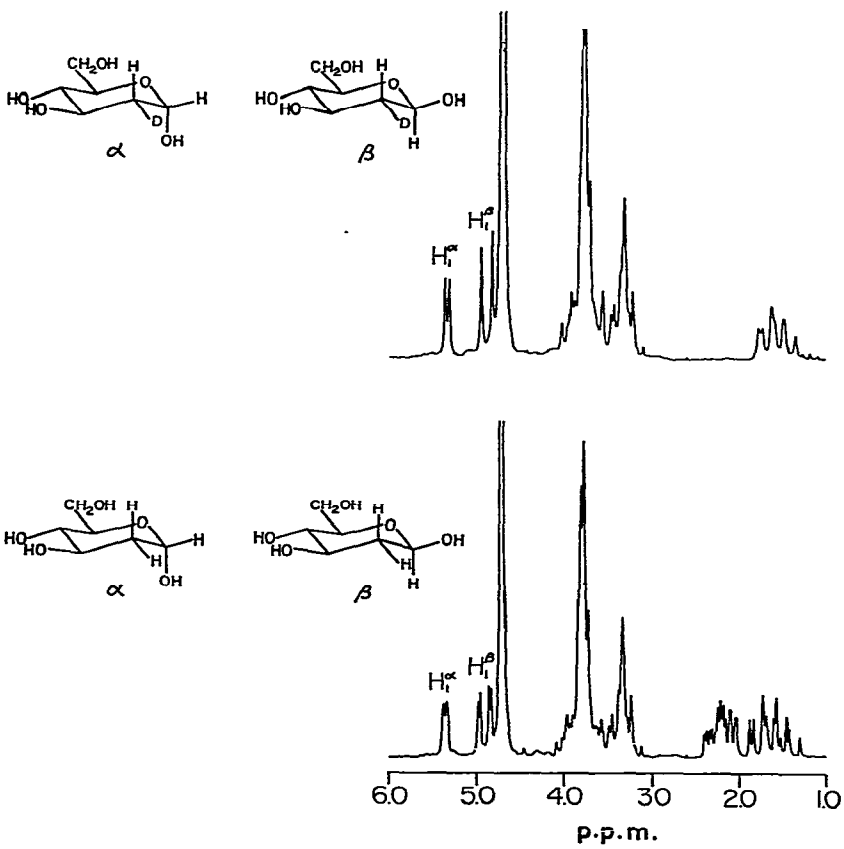

Fig. 1. The 80-MHz proton magnetic resonance spectra of 2-deoxy-D-*arabino*-hexose (**9a**) (lower spectrum) and (2*R*)-2-deoxy-2-deuterio-D-*arabino*-hexose (**9c**) (upper spectrum) in D_2O at 27° with sodium 2,2,3,3-tetradeuterio-4,4-dimethyl-4-silapentanoate as external standard (coaxial capillary).

spectrum), the H-1 resonance of the β-pyranose form is a doublet having a large coupling-constant (9.8 Hz), reflecting *trans*-diaxial coupling with H-2a, and the H-1 resonance of the α-pyranose form is a doublet having a smaller coupling-constant (J = 3.6 Hz), reflecting gauche coupling with H-2a. These results demonstrate that deuterium substitution at C-2 is equatorial, and therefore that **9c** is the (2*R*)-2-deuterio analog exclusively.

Similar analysis of the anomeric-proton resonances in the spectra of 2-deoxy-D-*lyxo*-hexose (**9b**) and its 2-deuterio analog reveals that **9d** is exclusively the (2*R*)-2-deuterio analog. In agreement with previous findings[6], the H-1 resonance of the β-pyranose form of **9b** occurs at δ 4.84 as a doublet of doublets (J = 9.5 and 2.5 Hz), and the H-1 resonance of the α-pyranose form at δ 5.43 is a poorly resolved triplet (J 2.3 Hz). In the spectrum of **9d** (not shown), the H-1 resonances of both pyranose forms are doublets as expected, however, the H-1 resonance of the β-pyranose form is a doublet showing a large coupling-constant (J 9.8 Hz), reflecting *trans*-diaxial coupling with H-2a. Anomeric-proton resonances of furanose forms were evident in the spectrum of **9b**, as previously reported[6], but, they were not resolved sufficiently to allow assignment.

With respect to the synthesis of the two other 2-deoxyhexoses, it should be mentioned that an important feature of this synthetic strategy is that a mixture of aldoses epimeric at C-2 can be utilized. This is an especial advantage where either the parent aldoses are not commercially available or are difficult to prepare in quantity. 2-Deoxy-D-*ribo*-hexose, for example, could be prepared from D-ribose, utilizing the mixture of epimeric aldoses formed in the cyanohydrin synthesis. As allose and altrose give rise to the same ketene dithioacetal, separation of the epimeric sugars and concomitant loss in yield could be avoided. In a similar manner, 2-deoxy-D-*xylo*-hexose could be prepared from D-xylose.

The preparation of the (2*R*)-2-deuterio analogs of 2-deoxy-D-*arabino*-hexose and 2-deoxy-D-*lyxo*-hexose as described herein provides further examples of the regiospecificity and stereospecificity of the reduction of allylic ketene dithioacetal alcohols by lithium aluminum hydride. Mechanistically, these were the expected products of reduction by lithium aluminum deuteride, as deuteride (hydride) transfer in pentose analogs has been demonstrated to occur intramolecularly *via* the C-3 alkoxyaluminum salt having the s-*trans* configuration about the C-2–C-3 bond[2]. Verification of this mechanism for analogs of the hexose series leads to the prediction that the (2*S*)-2-deuterio analogs of 2-deoxy-D-*ribo*-hexose and 2-deoxy-D-*xylo*-hexose could be obtained similarly.

EXPERIMENTAL

General. — With the exception of aqueous hydrolyses, acetylations, and deacetylations, all syntheses were conducted under an atmosphere of dry nitrogen. Elemental analyses were obtained on samples purified by high-performance liquid chromatography by elution on Porasil A (Waters Associates) in chloroform. High-

resolution mass spectra were recorded on an AEI MS-30 mass spectrometer. Specific rotations were measured with a Perkin–Elmer Model 241 polarimeter. ^{1}H-N.m.r. spectra were recorded at 27° (except where noted) with a Varian HFT-80 spectrometer, and ^{13}C spectra at 27° with a Varian XL-100-15 n.m.r. spectrometer. Spectra recorded with $CDCl_3$ as solvent are referenced to internal tetramethylsilane and those with D_2O as solvent are referenced to sodium 2,2,3,3-tetradeuterio-4,4-dimethyl-4-silapentanoate, contained in an internal capillary as a solution in D_2O. Coupling constants in ^{13}C spectra are recorded ±1 Hz and, in ^{1}H spectra, ±0.5 Hz. ^{13}C Spectra were recorded with proton-noise decoupling, but off-resonance decoupling was performed to identify methyl, methylene, methine, and quaternary carbon atoms.

*2,3:4,5-Di-*O*-isopropylidene-*D*-galactose diethyl dithioacetal* (**4b**). — D-Galactose diethyl dithioacetal[7] (10 g, 34.97 mmol) was converted into its 2,3:4,5-diisopropylidene acetal (**4b**) as previously described[3]. The crude product was purified by column chromatography on silica gel and the major fraction was eluted with 1:6 (v/v) ethyl acetate–hexane and identified as **4b** (9.8 g, 76.6%); $[\alpha]_D^{23}$ −68.3° (*c* 3.9, chloroform) (lit.[3] −67.7°); ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.26 (t, 6 H, *J* 7.2 Hz, ethyl CH_3), 1.38, 1.45 (2 s, 12 H, isopropylidene CH_3), 2.74 (q, 4 H, *J* 7.4 Hz, ethyl CH_2), and 3.67–4.42 (complex, 7 H, H-1,2,3,4,5,6); M^+ *m/e* 366.1523 ($C_{16}H_{30}O_5S_2$ requires 366.1534).

Anal. Calc. for $C_{16}H_{30}O_5S_2$: C, 52.46; H, 8.20; S, 17.49. Found: C, 52.34; H, 8.30; S, 17.66.

*2-Deoxy-4,5-*O*-isopropylidene-*D*-lyxo-hex-1-enose diethyl dithioacetal* (**5b**). — To a solution of 1.38 g (12.30 mmol) of potassium *tert*-butoxide in 150 mL of freshly distilled oxolane and 10 mL of dry dimethyl sulfoxide at 23° was added dropwise during 15 min a solution of 2,3:4,5-di-*O*-isopropylidene-D-galactose diethyl dithioacetal (2.15 g, 5.87 mmol) in 20 mL of oxolane. After stirring for 45 min at 23°, the mixture was poured over 400 g of ice, the aqueous layer was extracted 3 times with 150-mL portions of chloroform, and the combined extracts were washed with cold water, dried (sodium sulfate), and evaporated under vacuum to give 1.73 g (5.62 mmol) of **5b** as a yellow oil. Chromatography on silica gel (2.5 × 30 cm) in 1:2 (v/v) ethyl acetate–hexane gave 1.42 g (78%) of pure **5b**; $[\alpha]_D^{23}$ −23.8° (*c* 3.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.24 (t, 3 H, *J* 7.3 Hz, ethyl CH_3), 1.26 (t, 3 H, *J* 7.4 Hz, ethyl CH_3), 1.40 (s, 6 H, isopropylidene CH_3), 2.68–2.97 (complex, 4 H, ethyl CH_2), 3.69–4.08 (complex, 4 H, H-4,5,6), 4.86 (dd, 1 H, *J* 5.3 Hz, 8.2 Hz, H-3), and 6.00 (d, 1 H, *J* 8.2 Hz, H-2); M^+ *m/e* 308.1088 ($C_{13}H_{24}O_4S_2$ requires 308.1115).

Anal. Calc. for $C_{13}H_{24}O_4S_2$: C, 50.65; H, 7.79; S, 20.78. Found: C, 50.44; H, 7.89; S, 20.88.

*2-Deoxy-4,5-*O*-isopropylidene-*D*-lyxo-hexose diethyl dithioacetal* (**6b**). — To a stirred mixture of lithium aluminum hydride (0.38 g, 10.03 mmol) in 30 mL of oxolane was added, during 5 min at 23°, a solution of 0.39 g of **5b** in 10 mL of oxolane. After stirring for 3 h, the mixture was processed conventionally[8] to give 0.3 g (77%) of **6b** which was purified by elution through a column of silica gel with 1:3 (v/v) ethyl

acetate–hexane; $[\alpha]_D^{23}$ +19.4° (*c* 2.9, chloroform); ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.26 (t, 6 H, *J* 7.3 Hz, ethyl CH_3), 1.39 (s, 6 H, isopropylidene CH_3), 1.89–2.18 (complex, 2 H, H-2), 2.54–2.81 (complex, 4 H, ethyl CH_2), and 3.65–4.18 (complex, 6 H, H-1,3,4,5,6); M^+ *m/e* 310.1283 ($C_{13}H_{26}O_4S_2$ requires 310.1271).

Anal. Calc. for $C_{13}H_{26}O_4S_2$: C, 50.32; H, 8.39; S, 20.65. Found: C, 50.40; H, 8.42; S, 20.75.

(2R)-*2-Deoxy-2-deuterio-4,5-*O*-isopropylidene-*D*-lyxo-hexose diethyl dithioacetal* (**6d**). — Reduction of **5b** (0.12 g, 0.39 mmol) was accomplished with lithium aluminum deuteride (0.089 g, 2.13 mmol) in oxolane. After stirring for 8.5 h, the mixture was processed as before to give 0.1 g (83%) of **6d**; $[\alpha]_D^{23}$ +20.3° (*c* 5.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.26 (t, 6 H, *J* 7.4 Hz, ethyl CH_3), 1.39 (s, 6 H, isopropylidene CH_3), 2.13 (broad d, 1 H, *J* 8 Hz, H-2), 2.67–2.83 (complex, 4 H, ethyl CH_2), and 3.43–4.15 (complex, 6 H, H-1,3,4,5,6); M^+ *m/e* 311.1315 ($C_{13}H_{25}DO_4S_2$ requires 311.1335).

*3,6-Di-*O*-acetyl-2-deoxy-4,5-*O*-isopropylidene-*D*-lyxo-hexose diethyl dithioacetal* (**7b**). — A solution of **6b** (0.11 g, 0.35 mmol) in dry pyridine (distilled over phosphorus pentaoxide and stored over 3-Å molecular sieves) was added to a solution of 0.17 mL (1.81 mmol) of acetic anhydride in 2 mL of dry pyridine, cooled in an ice bath. The solution was kept overnight at 4°, and was then poured over 100 g of ice and extracted twice with chloroform. The combined extracts were evaporated under vacuum, and then three times from 25-mL portions of water to remove residual pyridine. The colorless syrup was purified by elution through a column (2.5 × 30 cm) of silica gel in 1:6 (v/v) ethyl acetate–hexane to give 0.12 g (84%) of pure **7b**; $[\alpha]_D^{23}$ +39.7° (*c* 3.4, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.25 (t, 6 H, *J* 7.4 Hz, ethyl CH_3), 1.41 (s, 6 H, isopropylidene CH_3), 2.10 (s, 6 H, acetyl CH_3), 2.01–2.23 (complex, 2 H, H-2), 2.51–2.85 (complex, 4 H, ethyl CH_2), 3.75–4.40 (complex, 5 H, H-1,4,5,6), and 5.34 (q, 1 H, *J* 6 Hz, H-3); ^{13}C-n.m.r. ($CDCl_3$): δ 14.39 (ethyl CH_3), 20.75, 21.06 (isopropylidene CH_3), 23.86, 24.30 (ethyl CH_2), 26.96 (acetyl CH_3), 37.71 (C-2), 47.46 (C-1), 64.70 (C-6), 71.77, 76.64, 78.83 (C-3,4,5), 110.31 (isopropylidene C), 170.03, and 170.31 (acetyl C); M^+ *m/e* 394.1493 ($C_{17}H_{30}O_6S_2$ requires 394.1483).

Anal. Calc. for $C_{17}H_{30}O_6S_2$: C, 51.78; H, 7.61; S, 16.24. Found: C, 51.92; H, 7.77; S, 16.39.

(2R)-*3,6-Di-*O*-acetyl-2-deoxy-2-deuterio-4,5-*O*-isopropylidene-*D*-lyxo-hexose diethyl dithioacetal* (**7d**). — Acetylation of **6d** with acetic anhydride–pyridine as just described gave **7d** as a syrup; $[\alpha]_D^{23}$ +40.5° (*c* 3.3, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.25 (t, 6 H, *J* 7.4 Hz, ethyl CH_3), 1.40 (s, 6 H, isopropylidene CH_3), 2.10 (s, 6 H, acetyl CH_3), 1.95–2.25 (complex, 1 H, H-2), 2.51–2.79 (complex, 4 H, ethyl CH_2), 3.77–4.41 (complex, 5 H, H-1,4,5,6), and 5.36 (dd, 1 H, *J* 3.2 Hz, 5.6 Hz, H-3); ^{13}C-n.m.r. ($CDCl_3$): δ 14.41 (ethyl CH_3), 20.81, 21.11 (isopropylidene CH_3), 23.94, 24.38 (ethyl CH_2), 27.02 (acetyl CH_3), 37.45 (t, *J* 20 Hz, C-2), 47.55 (C-1), 64.89 (C-6), 71.94, 76.85, 79.04 (C-3,4,5), 110.66 (isopropylidene C), 170.53, and 170.84 (acetyl C); M^+ *m/e* 395.1565 ($C_{17}H_{29}DO_6S_2$ requires 395.1545).

2-Deoxy-D-lyxo-*hexose* (**9b**). — Red mercuric oxide (0.303 g, 1.40 mmol), boron trifluoride etherate (0.172 mL, 1.40 mmol), and 2 mL of dry methanol (distilled over magnesium) were stirred vigorously in a 3-necked flask equipped with a serum cap and a nitrogen inlet-tube. Compound **7b** (0.28 g, 0.71 mmol) was dissolved in the minimum amount of methanol and added by syringe during 5 min, and stirring was continued for 30 min. Ethyl ether (20 mL) was then added, and a white precipitate formed immediately. The salts were removed by filtration and the ether solution was washed with saturated sodium carbonate and water until neutral, dried (magnesium sulfate), and evaporated to yield the crude dimethyl acetal **8b** (0.18 g, 77%). ^{1}H-N.m.r. spectroscopy indicated complete consumption of starting material and formation of **8b**. The product was slightly contaminated with a trace of white, crystalline material, but no further purification was carried out at this stage; ^{1}H-n.m.r. ($CDCl_3$): δ 1.41 (s, 6 H, isopropylidene CH_3), 2.01 (s, 6 H, acetyl CH_3), 1.86–2.03 (complex, 2 H, H-2), 3.22, 3.24 (2 s, 6 H, OCH_3), 3.74–4.53 (complex, 5 H, H-1,4,5,6), and 4.96–5.18 (complex, 1 H, H-3).

To a solution of 0.05 g (0.15 mmol) of **8b** in 50 mL of methanol was added a solution of 0.2M sodium methoxide in methanol until the pH was 9–10. The mixture was kept for 16 h at 4°, neutralized with Dowex-50 (H^+) resin, and then filtered and evaporated under vacuum to give a white solid (0.035 g, 94%), which was used without further purification; ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.38 (s, 6 H, isopropylidene CH_3), 1.74–2.07 (complex, 2 H, H-2), 3.33, 3.36 (2 s, 6 H, OCH_3), 3.50–4.07 (complex, 5 H, H-3,4,5,6), and 4.63 (t, 1 H, J 5.1 Hz, H-1). 2-Deoxy-4,5-*O*-isopropylidene-D-*lyxo*-hexose dimethyl acetal (0.035 g, 0.14 mmol) was converted into **9b** by hydrolysis for 24 h in 15 mL of 0.01M trifluoroacetic acid at 4°. After dilution with 2 volumes of water, the mixture was evaporated to dryness under vacuum, and then again diluted with water and evaporated to dryness twice to remove acid. The product was purified by gel filtration[2] on Bio-Gel P-2 to give **9b** (0.019 g, 83%); $[\alpha]_D^{23}$ +60.0° (*c* 0.17, water) (lit.[9] +57°); ^{1}H-n.m.r. (equilibrated in D_2O): δ 1.40–2.17 (complex, H-2), 3.40–4.20 (complex, H-3,4,5,6), 4.84 (dd, J 9.5 Hz, 2.5 Hz, H-1 of β-pyranose), and 5.43 (unresolved t, J ~2 Hz, H-1 of α-pyranose); ^{13}C-n.m.r. (equilibrated in D_2O): δ 34.18, 37.01 (C-2), 63.65, 63.94, 66.87, 69.00, 70.04, 70.19, 72.97, 77.58 (C-3,4,5,6), 93.80, and 96.18 (C-1).

(2R)-*2-Deoxy-2-deuterio*-D-lyxo-*hexose* (**9d**). — Compound **7d** was converted into **8d** (0.2 g) in an overall yield of 75% as already described for the preparation of **8b**; ^{1}H-n.m.r. ($CDCl_3$): δ 1.41 (s, 6 H, isopropylidene CH_3), 1.96–2.10 (complex, 1 H, H-2), 2.09, 2.10 (2 s, 6 H, acetyl CH_3), 3.31, 3.32 (2 s, 6 H, OCH_3), 3.74–4.50 (complex, 5 H, H-1,4,5,6), and 5.10–5.20 (unresolved multiplet, 1 H, H-3). Deacetylation of **8d** (0.4 g, 1.20 mmol) was performed as described for the deacetylation of **8b** to give (2*R*)-2-deoxy-2-deuterio-4,5-*O*-isopropylidene-D-*lyxo*-hexose dimethyl acetal in 96% yield; ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.39 (s, 6 H, isopropylidene CH_3), 2.03–2.10 (m, 1 H, H-2), 3.37, 3.39 (2 s, 6 H, OCH_3), 3.44–4.11 (complex, 5 H, H-3,4,5,6), and 4.64 (d, J 5.1 Hz, H-1). (2*R*)-2-Deoxy-2-deuterio-D-*lyxo*-hexose (**9d**, 0.14 g) was prepared in 74% yield from (2*R*)-2-deoxy-2-deuterio-

4,5-*O*-isopropylidene-D-*lyxo*-hexose dimethyl acetal (0.27 g, 1.15 mmol) as described for the preparation of **9b**; $[\alpha]_D^{23}$ +48.8° (*c* 0.37, water); ^{1}H-n.m.r. (equilibrated in D_2O): δ 1.45–2.0 (complex, H-2), 3.58–4.56 (complex, H-3,4,5,6), 4.85 (d, *J* 9.8 Hz, H-1 of β-pyranose), and 5.41 (d, *J* 3.9 Hz, H-1 of α-pyranose); ^{13}C-n.m.r. (equilibrated in D_2O): C-2 resonances, δ 33.83 (t, *J* 20 Hz) and 36.70 (t, *J* 20 Hz). The other resonances were identical with those of the parent sugar, 2-deoxy-D-*lyxo*-hexose (**9b**).

*2,3:4,5-Di-*O*-isopropylidene-*D*-glucose diethyl dithioacetal* (**4a**). — A solution of 6-*O*-benzoyl-2,3:4,5-di-*O*-isopropylidene-D-glucose diethyl dithioacetal[5] (**3a**, 4.2 g, 11.23 mmol) in 100 mL of methanol was adjusted to pH 9–10 with 0.2M sodium methoxide. After 3 days at ~25°, the mixture was made neutral with Dowex-50 (H^+) resin, filtered, and the filtrate evaporated to dryness under vacuum. Chromatography on silica gel (2.5 × 30 cm) in 1:6 (v/v) ethyl acetate–hexane gave **4a** (3.27 g, 100%); $[\alpha]_D^{23}$ −52.8° (*c* 4.1, chloroform) (lit.[5] −51.5°); ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.27 (t, 6 H, *J* 7.4 Hz, ethyl CH_3), 1.46, 1.50 (2 s, 6 H, isopropylidene CH_3), 2.75 (q, 4 H, *J* 7.4 Hz, ethyl CH_2), and 3.76–4.54 (complex, 7 H, H-1,2,3,4,5,6); M^+ *m/e* 366.1557 ($C_{16}H_{30}O_5S_2$ requires 366.1534).

Anal. Calc. for $C_{16}H_{30}O_5S_2$: C, 52.46; H, 8.20; S, 17.49. Found: C, 52.36; H, 8.32; S, 17.61.

*2-Deoxy-4,5-*O*-isopropylidene-*D*-*arabino*-hex-1-enose diethyl dithioacetal* (**5a**).— Compound **5a** (0.68 g, 2.21 mmol) was prepared in 67% yield from **4a** (1.2 g, 3.28 mmol) as already described for the preparation of **5b**; $[\alpha]_D^{23}$ −33.2° (*c* 2.2, chloroform); ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.25 (t, 6 H, *J* 7.4 Hz, ethyl CH_3), 1.37, 1.53 (2 s, 6 H, isopropylidene CH_3), 2.63–2.98 (complex, 4 H, ethyl CH_2), 3.76–4.30 (complex, 4 H, H-4,5,6), 4.89 (dd, 1 H, *J* 8.4 Hz, 3.4 Hz, H-3), and 6.04 (d, 1 H, *J* 8.3 Hz, H-2); M^+ *m/e* 308.1157 ($C_{13}H_{24}O_4S_2$ requires 308.1115).

Anal. Calc. for $C_{13}H_{24}O_4S_2$: C, 50.65; H, 7.79; S, 20.78. Found: C, 50.62; H, 8.00; S, 20.73.

*2-Deoxy-4,5-*O*-isopropylidene-*D*-arabino-hexose diethyl dithioacetal* (**6a**). — Compound **6a** (1.25 g, 4.03 mmol) was prepared in 87% yield from **5a** (1.43 g, 4.62 mmol) as already described for the preparation of **6b**; $[\alpha]_D^{23}$ +22.5° (*c* 2.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.26 (t, 6 H, *J* 7.3 Hz, ethyl CH_3), 1.37, 1.51 (2 s, 6 H, isopropylidene CH_3), 1.83–2.19 (complex, 2 H, H-2), 2.53–2.82 (complex, 4 H, ethyl CH_2), 3.29 (broad s, 2 H, OH), and 3.78–4.28 (complex, 6 H, H-1,3,4,5,6); M^+ *m/e* 310.1285 ($C_{13}H_{26}O_4S_2$ requires 310.1271).

Anal. Calc. for $C_{13}H_{26}O_4S_2$: C, 50.32; H, 8.39; S, 20.65. Found: C, 50.21; H, 8.42; S, 20.52.

*(2R)-2-Deoxy-2-deuterio-4,5-*O*-isopropylidene-*D*-arabino-hexose diethyl dithioacetal* (**6c**). — Reduction of **5a** (0.64 g, 2.08 mmol) with lithium aluminum deuteride and aqueous processing as already described for the preparation of **6d** gave **6c** (0.6 g, 94%); $[\alpha]_D^{23}$ +23.7° (*c* 1.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.26 (t, 6 H, *J* 7.4 Hz, ethyl CH_3), 1.37, 1.51 (2 s, 6 H, isopropylidene CH_3), 1.82 (broad d, 1 H, *J* 10 Hz, H-2), 2.52–2.82 (m, 4 H, ethyl CH_2), and 3.77–4.28 (complex, 6 H, H-1,3,4,5,6); M^+ *m/e* 311.1342 ($C_{13}H_{25}DO_4S_2$ requires 311.1335).

*3,6-Di-*O*-acetyl-2-deoxy-4,5-*O*-isopropylidene-*D*-arabino-hexose diethyl dithioacetal* (**7a**). — Acetylation of **6a** was conducted as described for the formation of **7b** to give **7a** in 86% yield; $[\alpha]_D^{23}$ +15.8° (*c* 3.6, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.25 (t, 6 H, *J* 7.5 Hz, ethyl CH_3), 1.35, 1.50 (2 s, 6 H, isopropylidene CH_3), 2.08 (s, 6 H, acetyl CH_3), 2.05–2.22 (complex, 2 H, H-2), 2.65 (q, 4 H, *J* 7.5 Hz, ethyl CH_2), 3.83 (t, 1 H, *J* 7.4 Hz, H-1), 4.08–4.41 (complex, 4 H, H-4,5,6), and 5.19–5.34 (m, 1 H, H-3); ^{13}C-n.m.r. ($CDCl_3$): δ 14.31 (ethyl CH_3), 20.84, 21.26 (acetyl CH_3), 23.61, 24.60, 25.43, 27.18 (isopropylidene CH_3, ethyl CH_2), 38.20 (C-2), 47.52 (C-1), 63.00 (C-6), 69.79, 74.95, 76.89 (C-3,4,5), 109.38 (isopropylidene C), 170.27, and 170.74 (acetyl C); M^+ *m/e* 394.1511 ($C_{17}H_{30}O_6S_2$ requires 394.1483).

Anal. Calc. for $C_{17}H_{30}O_6S_2$: C, 51.78; H, 7.61; S, 16.24. Found: C, 51.50; H, 7.76; S, 16.46.

(2R)-*3,6-Di-*O*-acetyl-2-deoxy-2-deuterio-4,5-*O*-isopropylidene-*D*-arabino-hexose diethyl dithioacetal* (**7c**). — Acetylation of **6c** was performed as described for the preparation of **7b** to give **7c** in 98% yield; $[\alpha]_D^{23}$ +16.2° (*c* 1.8, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.25 (t, 6 H, *J* 7.4 Hz, ethyl CH_3), 1.36, 1.50 (2 s, 6 H, isopropylidene CH_3), 2.09 (s, 6 H, acetyl CH_3), 2.02–2.20 (complex, 1 H, H-2), 2.61 (q, 4 H, *J* 7.4 Hz, ethyl CH_2), 3.83 (d, 1 H, *J* 8.1 Hz, H-1), 4.08–4.36 (complex, 4 H, H-4,5,6), and 5.28 (dd, 1 H, *J* 3.5, 5.2 Hz, H-3); ^{13}C-n.m.r. ($CDCl_3$): δ 14.29, 14.38 (ethyl CH_3), 20.83, 21.27 (acetyl CH_3), 23.62, 24.62, 25.45, 27.22 (ethyl CH_2, isopropylidene CH_3), 37.89 (t, *J* 20 Hz, C-2), 47.55 (C-1), 63.05 (C-6), 69.84, 75.05, 76.94 (C-3,4,5), 109.43 (isopropylidene C), 170.29, and 170.74 (acetyl C); M^+ *m/e* 395.1557 ($C_{17}H_{29}DO_6S_2$ requires 395.1545).

*2-Deoxy-*D*-arabino-hexose* (**9a**). — Compound **8a** (0.4 g) was prepared in 65% yield from **7a** as described for the preparation of **8b**; ^{1}H-n.m.r. ($CDCl_3$): δ 1.36, 1.51 (2 s, 6 H, isopropylidene CH_3), 1.88–2.05 (complex, 2 H, H-2), 2.08 (s, 6 H, acetyl CH_3), 3.30, 3.34 (2 s, 6 H, OCH_3), 4.06–4.53 (complex, 5 H, H-1,4,5,6), and 4.9–5.2 (multiplet, 1 H, H-3). The conversion of **8a** (0.28 g, 0.84 mmol) into 2-deoxy-4,5-*O*-isopropylidene-D-*arabino*-hexose dimethyl acetal (0.2 g, 0.80 mmol) was accomplished in 95% yield as already described for the preparation of 2-deoxy-4,5-*O*-isopropylidene-D-*lyxo*-hexose dimethyl acetal; ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.37, 1.51 (2 s, 6 H, isopropylidene CH_3), 1.80–1.99 (m, 2 H, H-2), 3.36, 3.39 (2 s, 6 H, OCH_3), 3.75–4.18 (complex, 5 H, H-3,4,5,6), and 4.64 (dd, 1 H, *J* 4.7, 6.2 Hz, H-1). 2-Deoxy-4,5-*O*-isopropylidene-D-*arabino*-hexose dimethyl acetal (0.2 g, 0.8 mmol) was converted into **9a** as already described for the preparation of **9b**, and the product was purified by gel filtration to give **9a** (0.096 g, 73%); $[\alpha]_D^{23}$ +48.8° (*c* 0.13, water) (lit.[10] +46.6°); ^{1}H-n.m.r. (equilibrated in D_2O): δ 1.29–1.87 (complex, H-2a), 2.03–2.40 (complex, H-2e), 3.26–4.12 (complex, H-3,4,5,6), 4.94 (dd, *J* 9.7 Hz, 1.1 Hz, H-1 of β-pyranose), and 5.39 (broad d, *J* 3.6 Hz, H-1 of α-pyranose); ^{13}C-n.m.r. (equilibrated in D_2O): δ 39.53, 41.77 (C-2), 63.02, 63.27, 70.26, 72.77, 73.17, 73.50, 74.31, 78.31 (C-3,4,5,6), 93.61, and 95.73 (C-1).

(2R)-*2-Deoxy-2-deuterio-*D*-arabino-hexose* (**9c**). — Compound **7c** was converted into **8c** (0.24 g, 69%) as described for the preparation of **8b**; ^{1}H-n.m.r. ($CDCl_3$):

δ 1.36, 1.50 (2 s, 6 H, isopropylidene CH_3), 2.08, (s, 6 H, acetyl CH_3), 1.90–2.15 (complex, 1 H, H-2), 3.30, 3.34 (2 s, 6 H, OCH_3), 4.15–4.49 (complex, 5 H, H-1,4,5,6), and 5.11 (t, 1 H, J 4 Hz, H-3). Saponification of **8c** gave (2*R*)-2-deoxy-2-deuterio-4,5-*O*-isopropylidene-D-*arabino*-hexose dimethyl acetal in 93% yield; ^{1}H-n.m.r. ($CDCl_3$, exchanged with D_2O): δ 1.38, 1.51 (2 s, 6 H, isopropylidene CH_3), 1.82 (broad d, 1 H, J 8 Hz, H-2), 3.36, 3.39 (2 s, 6 H, OCH_3), 3.75–4.26 (complex, 5 H, H-3,4,5,6), and 4.63 (d, 1 H, J 6.6 Hz, H-1). Hydrolysis of the latter with mild acid, as described for the preparation of **9b**, gave **9c** (0.11 g) in 67% yield; $[\alpha]_D^{23}$ +34.9° (c 1.0, water); ^{1}H-n.m.r. (equilibrated in D_2O): δ 1.49 (t, J 10.3 Hz, H-2a of β-pyranose), 1.68 (dd, J 12 Hz, 3.3 Hz, H-2a of α-pyranose), 3.14–4.12 (H-3,4,5,6), 4.93 (d, J 9.8 Hz, H-1 of β-pyranose), and 5.38 (d, J 3.6 Hz, H-1 of α-pyranose); ^{13}C-n.m.r. (equilibrated in D_2O): C-2 resonances, δ 39.19 (t, J 20 Hz) and 41.43 (t, J 19.8 Hz). The other resonances were identical to those of 2-deoxy-D-*arabino*-hexose (**9a**).

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