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METHYLENE-INSERTION REACTIONS WITH UNSATURATED SUGARS. SYNTHESIS OF 4-*C*-CYCLOPROPYL-D-*ribo*-TETROFURANOSE DERIVATIVES*†

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ABSTRACT

3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (**1**) was converted by the Simmons–Smith reaction into the cyclopropyl derivative **2**, which was debenzylated to the known[2] 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (**3**). Oxidation of **3** with ruthenium tetraoxide gave the corresponding 3-ketone **4**, which underwent stereospecific reduction by borohydride to give 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranose (**6**). In an alternative route to **6**, 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-allofuranose (**10**) was prepared by a high-yielding procedure and converted into 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**12**), either by way of an orthoformate (**11**) or thionocarbonate (**14**) intermediate; the alkene **12** was then converted into the cyclopropyl derivative **15**, and **15** was subsequently debenzylated to give **6**. 1,2-*O*-Isopropylidene-α-D-allofuranose (**7**) was converted, either by way of the 5,6-thionocarbonate **8** or an orthoformic ester, into 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**9**). High yields were achieved in all steps, and n.m.r. spectral data are given for the products. Mass-spectral data are given for the ketone **4**, the cyclopropyl derivative **6**, the thionocarbonate **8**, and the alkenes **9** and **12**; o.r.d. and c.d. data are also given for the thionocarbonates **8** and **14**.

INTRODUCTION

The Simmons–Smith reaction was first applied in the carbohydrate field[3] for the preparation of a cyclopropyl derivative from methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranose, a cyclic, nonterminal alkene. With a chain-terminal alkene, 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose, the reaction provides an excellent preparative route[2], under extremely mild conditions, to 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (**3**), and

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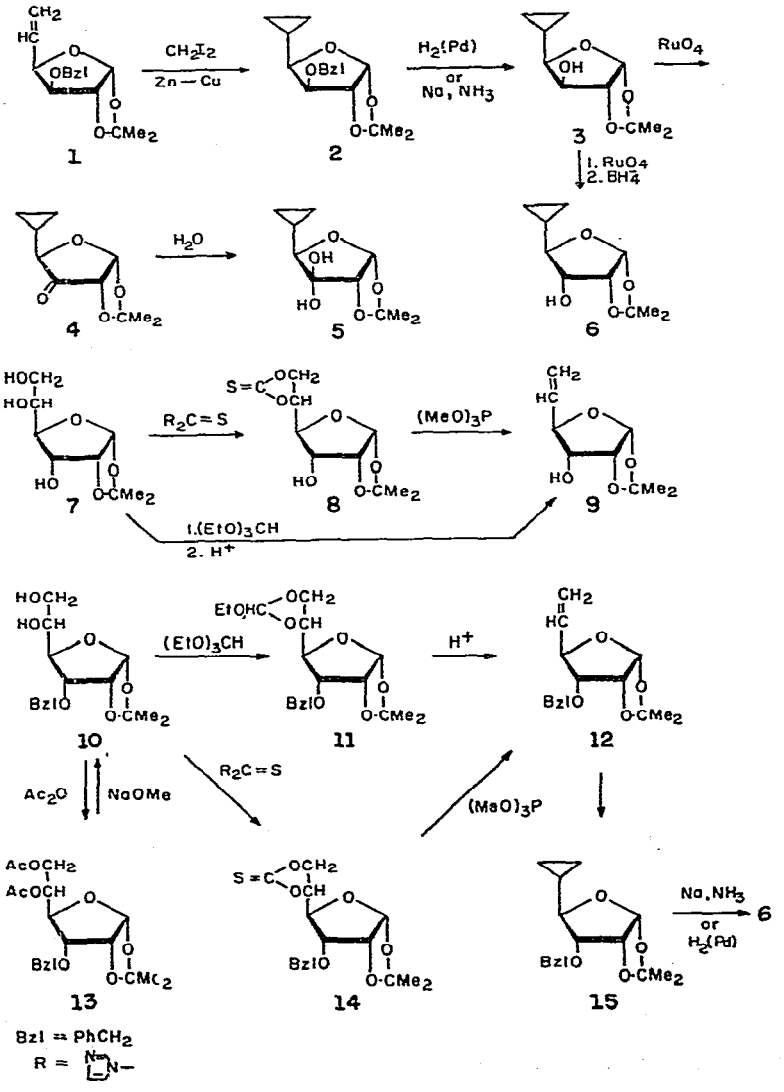
this product has been used in a detailed evaluation of the behavior of the cyclopropyl group as part of the carbon chain of a sugar under the conditions of various synthetic transformations commonly employed with carbohydrates[2].

The present work describes the synthesis of the 3-epimer (**6**) of **3** from **3** by an oxidation–reduction sequence and also by application of the Simmons–Smith reaction to 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**12**); the 3-epimer (**1**) of **12** was also converted into a cyclopropyl derivative (**2**). The terminal alkene **12** could be obtained either by way of a 5,6-orthoester (**11**) or a 5,6-thionocarbonate (**14**). Conversion of 1,2-*O*-isopropylidene-α-D-allofuranose (**7**) into the corresponding 5,6-alkene (**9**) has also been achieved by way of the 5,6-thionocarbonate (**8**) or an orthoester intermediate.



DISCUSSION

3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose was converted in 96% yield into the corresponding 5,6-alkene **1** by a large-scale adaptation[4] of the method of Josan and Eastwood[5] by way of an intermediate 5,6-*O*-(ethoxymethylene) derivative. Treatment of the alkene **1** with diiodomethane and zinc–copper couple (Simmons–Smith reagents) under the conditions previously described[2] gave the crystalline cyclopropyl derivative **2** in ~70% yield. Compound **2** gave a satisfactory elemental analysis, and its n.m.r. spectrum (see Tables I and II) was entirely consistent with the structure assigned. The structure of **2** was verified directly by debenzylation to give the known[2] 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (**3**). Quantitative debenzylation of **2** could be achieved by catalytic hydrogenation over palladium or by use of sodium in liquid ammonia; the latter procedure was somewhat more convenient than the former when the reaction was performed on a large scale. The high yield observed in the conversion of the alkene **1** into the cyclopropyl derivative **2** indicates that the presence of a free hydroxyl group in the alkene substrate is not a requirement for the reaction to proceed satisfactorily. The conversion of **2** into **3** demonstrates directly that reductive debenzylation can be accomplished in a cyclopropyl sugar derivative without involvement of the cyclopropyl group. The sequence from **1** to **3** provides a route from D-glucose to the cyclopropyl derivative **3** that is higher-yielding than the route[2] by way of the non-benzylated analog of the alkene **1**, because of the higher yields obtained in preparation of the benzylated alkene **1** and in the cyclopropane-forming step to give **2**.

Oxidation of 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (**3**) in alcohol-free chloroform with ruthenium tetraoxide gave a near-quantitative yield of the corresponding 3-ketone (**4**), which could be isolated crystalline in 75% yield and be purified by sublimation. The volatility of **4** caused some difficulty in obtaining exact elemental analyses, but the mass spectrum of **4** (see Table III) showed a minor peak for the molecular ion (*m/e* 198) and a stronger peak at *m/e* 183 corresponding to $M^+ - CH_3$. The i.r. spectrum of **4** showed strong carbonyl absorption at 5.68 μm and no absorption for an O–H stretching mode. The n.m.r. spectrum of the ketone **4** in chloroform-*d* (see Tables I and II) showed, in addition to signals for the cyclopropyl group and the 1,2-substituent, a doublet at τ 4.09 for H-1 that exhibited a coupling of 5.0 Hz with H-2. The H-4 signal appeared at τ 6.11, and showed strong coupling ($J_{4,5}$ 7.0 Hz) with H-5; a very small (<1 Hz) long-range coupling with H-2 was also observed, so that the H-2 signal (at τ 5.73) appeared as a doublet of very narrow doublets. Moist ether converted the ketone **4** into a crystalline hydrate (**5**) that was characterized by elemental analysis and by i.r. (see Experimental section) and n.m.r. spectroscopy. In deuterium oxide, **5** showed the H-1, H-2, and H-4 resonances as doublets (see Tables I and II); no $J_{2,4}$ coupling was observed.

Reduction of the crude ketone **4** (or its hydrate **5**) by sodium borohydride in aqueous ethanol gave 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranose (**6**), isolated crystalline in 90% yield (based on the *xylo* derivative **3**). The reaction is

stereospecific, and the *ribo* derivative **6** is the sole product of reaction. The structure of **6** is indicated by the elemental analysis, by the mass spectrum (see Table III), which showed a peak at *m/e* 185 for $M^+ - CH_3$, and by the n.m.r. spectrum in chloroform-*d* (see Tables I and II). The n.m.r. spectrum of **6** is clearly differentiated from that[2] of its 3-epimer **3** by the fact that H-2 is coupled to H-3 ($J_{2,3}$ 5.0 Hz) in **6**, so that the H-2 signal appears as a quartet. An octet is observed for H-3, collapsing to a quartet when the sample is deuterated, because H-3 is coupled to H-2, H-4, and also to the hydroxyl proton at C-3. The fact that spin-coupling involving the 3-OH proton is readily observed in **6**, in contrast to the behavior observed with **3**, suggests that the hydroxyl proton in **6** undergoes exchange more slowly than is the case with **3**.

Two alternative synthetic routes to the cyclopropyl derivative **6** were also evaluated, in which the requisite stereochemistry on the furanose ring was to be generated before introduction of the cyclopropyl ring. One approach involved 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**9**) as an intermediate, but the synthesis failed at the cyclopropane-forming step. The other approach, which was successful, involved the 3-benzyl ether (**12**) of the alkene **9**. Both routes allow comparative evaluation of the thionocarbonate[6] and orthoester[5] methods for generating alkenes from terminal glycol groups of sugars, and provide satisfactory preparative methods for the new 5,6-alkenes **9** and **12**.

A scaled-up adaptation of the oxidation–reduction sequence[7] with 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose was devised, to give 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[8] crystalline in 85% yield on a 50–100-g scale. In the oxidation step, a catalytic amount of ruthenium dioxide[9] was used in the presence of an excess of periodate. The *allo* product was subjected to partial hydrolysis with acidic ion-exchange resin to give the known[10], crystalline 1,2-*O*-isopropylidene-α-D-allofuranose (**7**) in 80% yield. Treatment of **7** with bis(imidazol-1-yl)thione in refluxing acetone by the general procedure described earlier[4,6] gave the 5,6-thionocarbonate **8** in high yield, although it was somewhat difficult to crystallize; the maximum yield of crystalline material obtained was 68%. The thionocarbonate **8** gave an acceptable elemental analysis, and in its mass spectrum (see Table III), showed peaks for the molecular ion at *m/e* 262 and for $M^+ - CH_3$ at *m/e* 247. The n.m.r. spectrum of **8** (see Tables I and II) was consistent with the structure assigned, and an absorption at 2.90 μm for the OH group was observed in the i.r. spectrum. The compound showed a positive Cotton effect in its o.r.d. spectrum (see Fig. 1), with an inflection near 315 nm, and a positive circular-dichroism (c.d.) maximum at 318 nm, close to a weak u.v. band at 310 nm; strong u.v. absorption was observed at 234 nm.

When the thionocarbonate **8** (the crude, syrupy reaction-product from **7**) was refluxed for 48 h in trimethyl phosphite, it was converted into 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**9**), isolated crystalline in 68% overall yield (based on 1,2-*O*-isopropylidene-α-D-allofuranose, **7**) after purification and subsequent recrystallization. The elemental analysis of **9** was satisfactory, and its mass spectrum showed a weak molecular-ion peak (*m/e* 186) and a stronger peak for $M^+ - CH_3$ at *m/e* 171 (see Table III). The n.m.r. spectrum of **9** in chloroform-*d* (see

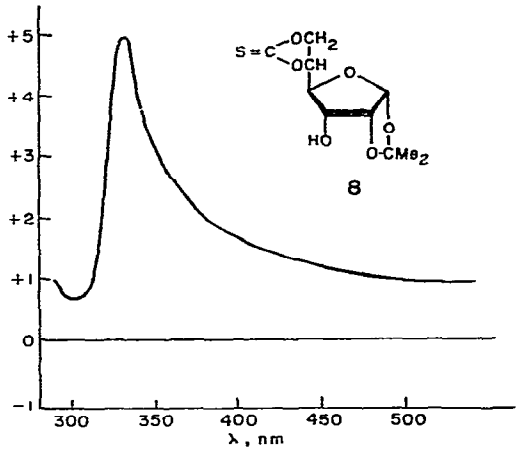


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Fig. 1. The o.r.d. spectrum of 1,2-*O*-isopropylidene-α-D-allofuranose 5,6-thionocarbonate (**8**) in ethanol (*c* 0.2, at 25°).

Tables I and II) showed a typical ABX pattern in the region expected for a vinylic system, and the X-portion (H-5) appeared as an octet, because of the additional coupling of H-5 with H-4. The H-4 signal appeared as a quartet through coupling with H-3 and H-5, and some line-broadening was evident due to allylic coupling of H-4 with H-6. The hydroxyl proton resonated as a sharp doublet, and the H-3 signal appeared as an octet; deuteration of the sample caused the OH signal to disappear and the H-3 signal to collapse to a quartet.

In an alternative route to the alkene **9**, 1,2-*O*-isopropylidene-α-D-allofuranose (**7**) was treated with triethyl orthoformate, and the resulting mixture of orthoformates was pyrolyzed in the presence of triphenylacetic acid, under the general conditions of Josan and Eastwood[5]. The alkene **9** was obtained, but the yield (55%) was lower than that achieved by way of the thionocarbonate **8**. The intermediate orthoester is probably a mixture containing, in addition to the diastereoisomeric 5,6-*O*-(ethoxymethylene) derivatives of **7**, a component also derivatized at C-3. Interestingly, the D-*gluco* analog of **7** reacts[1] with triethyl orthoformate to give a quantitative yield of 1,2-*O*-isopropylidene-α-D-glucofuranose 3,5,6-orthoformate[11], a stable product that does not give a 5,6-alkene when pyrolyzed in the presence of an acidic catalyst[1].

The alkene **9** was treated with diiodomethane and zinc–copper couple under the conditions of the Simmons–Smith reaction. The starting material **9** was decomposed completely during 48 h, but none of the cyclopropyl derivative **6** was detectable by t.l.c., although its presence in the reaction product would have been clearly evident. In t.l.c., the reaction product migrated much more rapidly than **9** or **6**, and the reaction was not further investigated.

In the second, successful synthesis of the cyclopropyl derivative **6**, the hydroxyl group at C-3 was protected as the benzyl ether. 1,2:5,6-Di-*O*-isopropylidene-α-D-allofuranose was converted into the 3-benzyl ether[12], obtained crystalline in 89% yield without need for chromatographic purification; graded hydrolysis of this ether

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TABLE I

CHEMICAL SHIFTS[a] MEASURED AT 100 MHz

Compound	*Solvent*	*Chemical shifts[a] (τ) from 100-MHz spectra*								
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*CMe_2*	*Other*
3-*O*-Benzyl-4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (2)	$CDCl_3$	4.12d	5.46d	6.22d	6.65q	9.17	——	9.90[b]	8.58, 8.73	5.29d[c], 5.45d[c], 2.72s[d]
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*erythro*-tetrofuranos-3-ulose (4)	$CDCl_3$	4.09d	5.73d		6.11d	9.08m[b]	—— 9.56m[b] ——		8.53, 8.61	
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*erythro*-tetrofuranos-3-ulose hydrate (5)	D_2O[e]	4.10d	5.55d		6.80d	8.84	——	9.76[b]	8.47, 8.62	
4-*C*-Cyclopropyl-1,2-*O*-*isopropylidene*-α-D-*ribo*-tetrofuranose (6)	$CDCl_3$	4.20d	5.41q	6.23q[f]	6.75q	9.05m	9.25 ——	9.75[b]	8.45, 8.63	7.45d[g]
1,2-*O*-Isopropylidene-α-D-allofuranose 5,6-thionocarbonate (8)	$(CD_3)_2CO$	4.16d	5.35t	6.10q[f]	5.78q	4.65m	—— 5.2m ——		8.52, 8.70	7.19s[g]
5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (9)	$CDCl_3$	4.11d	5.38q	6.27o[f]	5.80q	4.03o	4.55m	4.71m	8.40, 8.65	7.48d[g]

3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**12**)	$CDCl_3$	4.34d	~5.6m	6.65q	~5.6m	4.17o	4.66m	4.87m	8.47, 8.71	5.35d[c], 5.59d[c], 2.73s[d]
	C_6D_6	4.35d	5.77t	6.73q	~5.3m	4.05o	4.55m	4.85m	8.50, 8.71	5.35d[c], 5.64d[c], 2.54–2.80m[d]
5,6-Di-*O*-acetyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-allofuranose (**13**)	$CDCl_3$	4.34d	5.49m[h]	6.22q	5.93q	4.72o	5.72q	5.98q	8.50, 8.74	8.08[j], 8.13[j], 5.33d[c], 5.67d[c], 2.68s[d]
3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-allofuranose 5,6-thionocarbonate (**14**)	$CDCl_3$	4.20d	5.38t	6.27q	5.70q	4.87m	5.4q	5.5q	8.40, 8.63	5.20d[c], 5.45d[c], 2.60s[d]
3-*O*-Benzyl-4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranose (**15**)	$CDCl_3$	4.44d	5.6m	6.41—6.64		8.5————		9.6[b]	8.55, 8.73	5.40d[c], 5.54d[c], 2.72m[d]
	C_6D_6	4.38d	5.73t	6.65q	6.28q	8.6————		9.8[b]	8.51, 8.78	5.28d[c], 5.57d[c], 2.5–2.9[d]

[a]First-order values are given; peak multiplicities: d, doublet; m, multiplet; o, octet; q, quartet; s, singlet; t, triplet. [b]From 60-MHz spectrum. [c]Benzylic protons. [d]Phenyl protons. [e]Sodium 4,4-dimethyl-4-silapentane-1-sulfonate (τ = 10.00) as the internal standard. [f]In the presence of D_2O. [g]OH proton. [h]Verified by spin decoupling. [i]Becomes a quartet on addition of D_2O. [j]Acetyl groups.

TABLE II

FIRST-ORDER COUPLING CONSTANTS (Hz) FROM 100-MHz SPECTRA

Compound	*Solvent*	*Coupling constants (Hz)*							
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{a,b}$ benzylic	J, *other*
3-*O*-Benzyl-4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (2)	$CDCl_3$	3.9	<0.5	3.0	9.0			12.0	
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*erythro*-tetrofuranos-3-ulose (4)	$CDCl_3$	5.0			7.0				$J_{2,4}$ <1
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*erythro*-tetrofuranos-3-ulose hydrate (5)	D_2O	4.3			10.0				$J_{2,4}$ 0
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranose (6)	$CDCl_3$	4.0	5.0	8.9	7.3				$J_{3,OH}$ 10.0
1,2-*O*-Isopropylidene-α-D-allofuranose 5,6-thionocarbonate (8)	$(CD_3)_2CO$	3.5	4.5	8.5	2.0	[a]	[a]		
5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (9)	$CDCl_3$	4.0	5.0	9.0	6.2	~18	~11		$J_{3,OH}$ 10.5 $J_{4,6}$ <1 *J* 1.1[b], *J* 2.0[b]
3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (12)	$CDCl_3$	3.8	4.1	9.0	5.8	~17	~10	12.0	*J* 2[b], *J* 1[b]
	C_6D_6	3.6	4.3	9.8	5.8	~17	~10	12.0	*J* 2[b], *J* 1[b]
5,6-Di-*O*-acetyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-allofuranose (13)	$CDCl_3$	3.8	4.3	8.7	5.0	3.5	7.5	11.1	$J_{6,6'}$ 12.2
3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-allofuranose 5,6-thionocarbonate (14)	$CDCl_3$	3.7	4.4	9.1	2.0	~6	~9	11.5	$J_{6,6'}$ ~9
3-*O*-Benzyl-4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranose (15)	$CDCl_3$	4.0						12.0	
	C_6D_6	4.0	4.5	8.8	7.0			12.4	

[a] $J_{5,6} + J_{5,6'} = 15$ Hz. [b] $J_{geminal}$ or $J_{allylic}$.

TABLE III

MASS-SPECTRAL DATA FOR COMPOUNDS **4**, **6**, **8**, **9**, AND **12**

Compound	*Mass-spectral peaks (relative intensities in parentheses)*
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*erythro*-tetrofuranos-3-ulose (**4**)	198 (≪1), 183 (1.0), 141 (7.0), 113 (1.0), 112 (2.0), 111 (2.0), 101 (7.0), 100 (100), 95 (1.0), 87 (1.0), 86 (5.5), 85 (100), 84 (1.0), 83 (4.0), 82 (4.0), 81 (4.0), 71 (18), 70 (1.5), 69 (6.0), 68 (4.0), 67 (2.0), 60 (15), 59 (11), 58 (10), 57 (4.0), 55 (9.0), 54 (10), 53 (8.0), 51 (1.5), 43 (50)
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranose (**6**)	185 (3.0), 173 (1.0), 167 (0.5), 159 (0.3), 143 (1.0), 142 (0.9), 129 (18), 125 (2.0), 117 (1.5), 113 (2.0), 101 (1.0), 100 (0.5), 97 (1.0), 95 (1.0), 85 (2.5), 84 (2.0), 83 (8.5), 81 (1.5), 79 (1.5), 73 (3.0), 72 (4.0), 71 (80), 70 (1.5), 69 (3.0), 68 (3.0), 67 (2.0), 66 (1.5), 60 (3.0), 59 (100), 55 (17), 43 (50)
1,2-*O*-Isopropylidene-α-D-allofuranose 5,6-thionocarbonate (**8**)	262 (27), 247 (10), 187 (2.0), 185 (2.0), 159 (5.5), 133 (3.5), 132 (1.5), 129 (10), 127 (22), 113 (3.0), 109 (5.0), 103 (5.5), 101 (5.0), 100 (4.0), 99 (6.0), 98 (3.5), 97 (5.0), 89 (1.0), 88 (1.0), 87 (1.5), 86 (3.5), 85 (12), 76 (1.0), 75 (1.0), 74 (1.5), 73 (15), 72 (2.5), 71 (18), 70 (5.0), 69 (16), 68 (3.0), 60 (30), 59 (100), 58 (5.0), 57 (22), 56 (1.5), 55 (17), 54 (1.0), 53 (3.0), 43 (87)
5,6-Dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**9**)	187 (≪1), 186 (≪1), 171 (5.0), 130 (1.0), 129 (3.5), 128 (1.0), 115 (12), 111 (3.0), 101 (2.5), 100 (1.5), 99 (1.6), 85 (1.0), 83 (2.5), 82 (1.5), 81 (1.0), 73 (2.0), 72 (1.5), 71 (10), 70 (8.0), 69 (10), 60 (3.5), 59 (100), 58 (3.5), 57 (17), 56 (1.0), 55 (10), 53 (1.0), 43 (50)
3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**12**)	261 (0.8), 218 (0.8), 162 (1.8), 161 (3.0), 159 (1.0), 149 (3.5), 147 (1.2), 134 (1.0), 133 (2.5), 129 (11), 127 (1.5), 114 (1.0), 112 (2.5), 111 (1.5), 109 (2.5), 108 (25), 107 (20), 106 (5.0), 105 (8.5), 100 (0.8), 92 (23), 91 (100), 90 (4.0), 89 (2.5), 85 (2.5) 82 (2.0), 79 (2.5), 78 (25), 77 (3.0), 76 (16), 74 (1.5), 73 (1.5), 71 (2.5), 69 (1.5), 66 (1.5) 65 (8.5), 63 (2.5), 62 (1.0), 59 (5.0), 57 (1.5), 55 (5.0), 53 (2.0), 52(4.0), 51 (8.5), 50 (3.5), 43 (7.0)

gave 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-allofuranose (**10**), obtained as an oil in 96% yield. The crystalline 5,6-diacetate (**13**) of **10** was prepared, and characterized (see Experimental section and Tables I and II); it could be reconverted into **10** by Zemplén deacetylation. The diol **10** was converted by the action of bis(imidazol-1-yl)-thione into the 5,6-thionocarbonate (**14**), obtained crystalline in 51% yield. The product was characterized by elemental analysis and by its n.m.r. spectrum (see Tables I and II); it showed u.v. absorption maxima at 234 and 310 nm. The band at 310 nm is evidently an optically active transition of the thionocarbonate group, as a negative maximum is observed in the circular-dichroism curve at this wavelength.

When a solution of the thionocarbonate **14** in trimethyl phosphite was boiled under reflux, **14** was converted into 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**12**), obtained in 82% yield and purified by distillation. The structure of **12** was evident from the microanalytical data, from the mass-spectral

data (see Table III), which showed a fragment having *m/e* 261 ($M^+ - CH_3$), and from the n.m.r. spectral data (see Tables I and II). The n.m.r. spectrum in chloroform-*d* was not readily amenable to complete interpretation, but that in benzene-d_6 showed, in addition to signals for the benzyl and isopropylidene groups, an ABX pattern for the vinyl group, with a well-resolved octet for H-5. The $J_{2,3}$ coupling (4.3 Hz) provided clear indication of the *cis*-disposition of H-2 and H-3, and the signals for these two protons appear as a triplet and a quartet, respectively.

In an alternative route from the diol **10** to the alkene **12**, compound **10** was treated with triethyl orthoformate to give a diastereoisomeric mixture of orthoformates (**11**), isolated as a distilled oil in quantitative yield. The n.m.r. spectrum of **11** (see Experimental section) indicated that the product contained approximately equal quantities of the two diastereoisomers. Pyrolysis of **11** in the presence of triphenylacetic acid gave the alkene **12** in 94% yield after purification by distillation. This procedure is clearly the one of choice for converting the diol **10** into the alkene **12**, in contrast to the situation where the hydroxyl group at C-3 is free; in the latter, the thionocarbonate route is the preferred procedure for the conversion of **7** into **9**, and is the only one (of the two) effective for a similar conversion with the D-*gluco* analog of **7**.

Treatment of the alkene **12** with diiodomethane and zinc–copper couple gave 3-*O*-benzyl-4-*C*-cyclopropyl-α-D-*ribo*-tetrofuranose (**15**) as an extremely mobile, distillable oil, obtained in 83% yield. The compound gave a correct elemental analysis, and gross assignments of the n.m.r. spectrum in chloroform-*d* (see Tables I and II) could be made, although the circumstance that the H-3 and H-4 signals were almost superposed and the H-2 signal was obscured by the benzylic-proton resonances made detailed ring-proton assignments difficult with this solvent. In benzene-d_6, the ring-proton signals were well resolved, and the anticipated patterns were observed, namely, a doublet for H-1, a triplet for H-2, and quartets for H-3 and H-4. The structure of **15** was firmly established by debenzylation to give the known, crystalline 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranose (**6**), obtained in almost quantitative yield either by hydrogenolysis over palladium or by the action of sodium in liquid ammonia.

The foregoing results provide good, preparative methods for the new terminal-alkene derivatives **9** and **12**, and for the cyclopropyl derivatives **6** and **15** that are, formally, D-ribofuranose analogs having a cyclopropyl group in place of the hydroxymethyl group. The preparation of nucleoside analogs containing this moiety will be described in a forthcoming report.

EXPERIMENTAL

General methods. — Solutions were evaporated below 50° under diminished pressure. Melting points were determined with a Thomas–Hoover "Unimelt" apparatus and are uncorrected. I.r. spectra were recorded with a Perkin–Elmer Model 137 i.r. spectrophotometer. U.v. spectra were recorded with a Cary Model 14 u.v. spectrophotometer. Optical rotations were measured in 1-dm tubes with a Perkin–Elmer

Model 141 polarimeter. O.r.d. and c.d. measurements were made with a Jasco UV5 recording spectropolarimeter. Mass spectra were measured with an AEI MS-9 double-focusing, high-resolution spectrometer with an accelerating potential of 8 kV, an ionizing potential of 70 eV, and a direct-insertion probe with an inlet temperature of 250°. N.m.r. spectra were measured at 60 and 100 MHz with Varian A-60 and HA-100 n.m.r. spectrometers, respectively. Spin-decoupling experiments were performed with the HA-100 instrument. Chemical shifts are given on the τ scale. Unless otherwise stated, n.m.r. spectra were measured at ~30° with solutions (~10%) in chloroform-*d*, with tetramethylsilane (τ = 10.00) as the internal standard. Spectra were analyzed on a first-order basis. Microanalyses were performed by W. N. Rond. 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), and double numbers indicate approximately equal intensities. The camera diameter was 114.59 mm. T.l.c. was performed with 250-μm layers of Silica Gel G (E. Merck, Darmstadt, Germany), activated at 110°, as the adsorbent, and indication was effected with sulfuric acid and iodine vapor.

Preparation of 3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene-α-D-xylo-hex-5-enofuranose (**1**). — The following procedure is a larger -scale adaptation of the method of Josan and Eastwood[5]. A magnetically stirred mixture of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose[13] (33.8 g, 109 mmoles), ethyl orthoformate (40 ml, 36 g, 240 mmoles), and acetic acid (2 ml) was refluxed for 6 h, and the excess reagents were then removed by evaporation under diminished pressure at 80–100°. Toluene (three 100-ml portions) was added to and evaporated from the product to remove traces of reagents, and the resultant mixture of diastereoisomeric orthoformic esters was used in the next step without further purification. Triphenylacetic acid (0.5 g) was added to the product, and the flask was fitted with a take-off condenser. The mixture was stirred and heated for 6 h at 170°, during which time, ethanol distilled from the mixture. The resultant product was dissolved in ether (300 ml), solid potassium carbonate was added, and the mixture was kept overnight. The mixture was filtered, and the filtrate was washed twice with saturated aqueous potassium carbonate, dried (magnesium sulfate), and evaporated. The product was distilled to give the pure alkene **1**; yield 29.1 g (105 mmoles, 96%), b.p. 124–128°/0.2 torr, 111–115°/50 mtorr, $[\alpha]_D^{20}$ −66 ±0.5° (*c* 3, ethanol); R_F 0.4 (3:1 cyclohexane–ether). [Lit.[14] b.p. 124–129°/0.2 torr, $[\alpha]_D^{21}$ −55.5° (ethanol[5]); $[\alpha]_D^{28}$ −56.4° (chloroform[14]); and $[\alpha]_D^{28}$ −63.2° (chloroform[14]).]

3-O-Benzyl-4-C-cyclopropyl-1,2-O-isopropylidene-α-D-xylo-tetrofuranose (**2**). — A solution of the alkene **1** (32 g, 115 mmoles) and diiodomethane (64 g, 239 mmoles) in anhydrous ether (150 ml) was added dropwise to a stirred suspension of zinc–copper couple[15] (128 g) in anhydrous ether (200 ml), and the mixture was stirred for 48 h under reflux. The mixture was filtered, and the residue was washed with ether (300 ml). The filtrate and washings were mixed carefully with saturated, aqueous ammonium chloride, and the mixture was stirred for 1 h. The organic layer was separated, washed successively with saturated, aqueous potassium carbonate and saturated, aqueous

sodium chloride, dried (magnesium sulfate), and evaporated to give crystalline **2**. Recrystallization from 3:7 water–ethanol gave **2** as white needles; yield 22.5 g (78 mmoles, 68%), m.p. 78–81°, $[\alpha]_D^{21}$ −67.4 ±0.5° (*c* 2, chloroform); R_F 0.8 (3:1 chloroform–ether); λ_{max}^{KBr} 3.35, 3.42, and 3.48 μm (cyclopropyl CH); X-ray powder diffraction data: 13.70 s (3), 10.16 m, 8.34 m, 6.99 m, 6.10 w, 5.24 s, 5.01 s (1), 4.78 s, 4.55 m, 4.23 m, 3.99 m, 3.62 s (2), and 3.43 w.

Anal. Calc. for $C_{17}H_{22}O_4$: C, 70.31; H, 7.64. Found: C, 70.01; H, 7.99.

4-C-Cyclopropyl-1,2-O-isopropylidene-α-D-xylo-tetrofuranose (**3**). — *A. By catalytic hydrogenolysis of* **2**. A solution of cyclopropyl derivative **2** (200 mg, 725 μmoles) in abs. ethanol (20 ml) was stirred with a catalytic amount of palladium black under hydrogen at 1 atm pressure for 16 h at room temperature. The mixture was filtered, and petroleum ether (b.p. 90–97°, 20 ml) was added to the filtrate. Evaporation of the solution to 20 ml gave crystalline **3**, yield 145 mg (725 μmoles, 100%), m.p. 147–148°, $[\alpha]_D^{20}$ −26 ±1° (*c* 4, chloroform), identical with an authentic sample[2] by t.l.c., i.r. and n.m.r. spectra, and X-ray powder diffraction pattern.

B. By treatment of **2** *with sodium in liquid ammonia.* To a stirred mixture of the cyclopropyl derivative **2** (11.5 g, 40 mmoles) in liquid ammonia (600 ml) was added sodium (3.6 g, 156 mmoles) portionwise during 1 h. To the resultant, dark-blue solution was added solid ammonium chloride until the color had been discharged. The ammonia was evaporated by means of a stream of nitrogen, and the resultant solid was partitioned between water (200 ml) and chloroform (200 ml). The organic layer was separated, and the aqueous layer was extracted with two 100-ml portions of chloroform. The organic extracts were combined and evaporated to a solid that was recrystallized from ether–petroleum ether (b.p. 90–97°) to give pure **3**; yield 7.7 g (38 mmoles, 95%), m.p. 147–148°; identical with an authentic sample[2].

4-C-Cyclopropyl-1,2-O-isopropylidene-α-D-erythro-tetrofuranos-3-ulose (**4**). — To a suspension of 51% ruthenium dioxide (10 g, Engelhard Industries, Newark, New Jersey) in carbon tetrachloride (250 ml) was added 10% aqueous sodium metaperiodate (200 ml), and the mixture was stirred vigorously for 1 h at 0°. The organic layer (containing 38 mmoles of ruthenium tetraoxide) was separated and added to a solution of compound **3** (2.8 g, 14 mmoles) in alcohol-free chloroform (25 ml). The mixture was stirred for 2 h at 0° and then for 3 h at room temperature. Isopropyl alcohol (10 ml) was added, and the mixture was filtered. Evaporation of the filtrate gave a crystalline solid that was recrystallized from cold petroleum ether (b.p. 90–97°) to give **4** as colorless needles; yield 2.1 g (11 mmoles, 75%), m.p. 70.0–71.5°, sublimes at 30°/0.5 torr, $[\alpha]_D^{22}$ +181.3 ±1.0° (*c* 0.7, chloroform); R_F 0.9 (3:1 chloroform–ether); λ_{max}^{KBr} 3.32 (cyclopropyl CH) and 5.68 μm (C = O); X-ray powder diffraction data: 7.56 s (1), 7.14 m, 6.45 w, 5.82 vw, 5.44 s (2), 5.04 vw, 4.91 m, 4.53 m, 4.22 m, and 3.97 w.

Anal. Calc. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.06; H, 7.05.

4-C-Cyclopropyl-1,2-O-isopropylidene-α-D-erythro-tetrofuranos-3-ulose hydrate (**5**). — The crystalline ketone **4** (200 mg, 1.01 mmoles) was dissolved in water-saturated ether (6 ml), and hexane (6 ml) was added. The solution was refrigerated for 24 h,

and the resulting, crystalline hydrate **5** was filtered off; yield 130 mg (0.54 mmole, 54%). Evaporation of the filtrate gave the starting ketone **4**; yield 91 mg (0.46 mmole, 46%). Recrystallization of the crude hydrate **5** from ether (1 ml) and hexane (5 ml) gave pure **5**, m.p. 103–104.5°, $[\alpha]_D^{22}$ +15.2 ±0.5° (*c* 0.4, water); λ_{max}^{KBr} 2.88 (OH), 3.20, 3.30, and 3.35 μm (cyclopropyl CH); X-ray powder diffraction data: 17.24 s, 9.75 vs (1), 8.70 vw, 7.46 w, 6.32 w, 5.85 vw, 5.40 s, 5.16 s, 4.92 s, and 4.53 s (2).

Anal. Calc. for $C_{10}H_{16}O_5$: C, 55.57; H, 7.46. Found: C, 55.45; H, 7.71.

4-C-Cyclopropyl-1,2-O-isopropylidene-α-D-ribo-tetrofuranose (**6**). — A solution of ruthenium tetraoxide, prepared as already described from 5 g of 61% ruthenium dioxide, in carbon tetrachloride (350 ml) was added to a solution of 5 g (25 mmoles) of compound **3** in alcohol-free chloroform (35 ml). The mixture was stirred for 1 h at 0° and for 3 h at room temperature. Isopropyl alcohol (20 ml) was added, and the mixture was filtered. Evaporation of the filtrate gave the crystalline ketone **4**, which was dissolved in 3:7 water–ethanol (100 ml), and sodium borohydride (3 g) was added. After 2 h, the ethanol was evaporated off, and the residual, aqueous solution was extracted with four 150-ml portions of dichloromethane. Evaporation of the extracts gave **6** as a white solid, obtained pure after recrystallization from petroleum ether (b.p. 90–97°); yield 4.5 g (22.5 mmoles, 90%), m.p. 84.5–87.0°, $[\alpha]_D^{25}$ +41.4 ±0.5° (*c* 2, chloroform); R_F 0.52 (3:1 chloroform–ether); λ_{max}^{KBr} 2.88 μm (OH); X-ray powder diffraction data: 9.02 vs (1), 5.20 vs (2), 4.86 s (3), 4.57 vw, 4.29 m, 4.13 m, 3.89 w, 3.67 vw, 3.35 m, 3.21 w, 3.11 w, 3.64 vw, and 2.56 vs.

Anal. Calc. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.91; H, 8.23.

Large-scale preparation of 1,2:5,6-di-O-isopropylidene-α-D-allofuranose. — A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (80 g, 0.31 mole) in alcohol-free chloroform (350 ml) was added to a mixture of water (350 ml), potassium metaperiodate (115 g, 0.5 mole), potassium carbonate (12 g), and 51% ruthenium dioxide (2 g). The mixture was stirred rapidly for 24 h at room temperature. An additional 115 g of potassium metaperiodate and 12 g of potassium carbonate were then added, and the mixture was stirred for a further 24 h. Isopropyl alcohol (150 ml) was added, and, after 10 min, the mixture was filtered. The organic layer was separated and the aqueous phase was extracted with two 150-ml portions of chloroform. The organic layer and the extracts were combined, and evaporated, to give the hydrate of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexopyranos-3-ulose as a yellow, crystalline mass. To a solution of the latter in 3:7 water–ethanol (750 ml) was added sodium borohydride (24 g, 0.65 mole). The solution was stirred for 3 h at room temperature, and then concentrated to 500 ml. Water (250 ml) was added, and the solution was concentrated to 500 ml, and extracted with four 250-ml portions of dichloromethane. The extracts were combined, dried (magnesium sulfate), and evaporated to a white solid, which was recrystallized from 3:1 benzene–hexane to give 68 g (85%) of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose, m.p. 74.5–75.5°, $[\alpha]_D^{20}$ +38° (*c* 3, chloroform) [lit.[8] m.p. 76–77°, $[\alpha]_D^{20}$ +38° (chloroform)[16]]. From the mother liquors there was obtained 1.5 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.

Preparation of 1,2-O-isopropylidene-α-D-allofuranose (**7**). — To a solution of

1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (10 g, 38.5 mmoles) in water (400 ml) was added Amberlite IR-120 (H^+) ion-exchange resin (12 g), and the mixture was stirred for 3.5 h at 25°. The resin was filtered off and washed with water (200 ml); the filtrate and washings were combined and evaporated to give a crystalline solid. Recrystallization from hot chloroform gave pure **7**; yield 6.7 g (80%), m.p. 133–134°, $[\alpha]_D^{20}$ +44° (*c* 1, water) [lit.[10] m.p. 133–134°, $[\alpha]_D^{25}$ +44° (water)].

1,2-O-Isopropylidene-α-D-allofuranose 5,6-thionocarbonate (**8**). — A suspension of **7** (5.0 g, 23 mmoles) and bis(imidazol-1-yl)thione (5.0 g, 28 mmoles) in anhydrous acetone (200 ml) was boiled for 18 h under reflux. The resultant solution was decolorized with 0.5 g of activated charcoal and evaporated to a syrup. A solution of the syrup in dichloromethane (100 ml) was washed with two 100-ml portions of water, dried (magnesium sulfate), and evaporated to give a light-brown, crystalline mass. The solid was dissolved in methanol (50 ml), and the solution was refrigerated, to give 1.6 g of **8** as white crystals. Concentration of the mother liquor to 25 ml followed by refrigeration gave an additional 2.5 g of **8**; total yield 4.1 g (15.6 mmoles, 68%), m.p. 176–178°. Recrystallization from methanol gave an analytical sample of **8**, m.p. 177–178°, $[\alpha]_D^{25}$ +23.0 ±0.5°(*c* 1, tetrahydrofuran); R_F 0.29 (3:1 chloroform–ether); λ_{max}^{KBr} 2.90 μm (OH); λ_{max}^{EtOH} 234 (ε 16,600) and 310 nm (20); o.r.d. data (see also Fig. 1) at 25° (*c* 0.20, ethanol): $[M]_{589}$ +7,000°, $[M]_{334}$ +49,250°, $[M]_{300}$ +6,550°, $[M]_{290}$ +10,000°; c.d. data at 25° (*c* 0.20, ethanol); $\Delta\varepsilon_{295}$ 0, $\Delta\varepsilon_{315}$ +0.44, $\Delta\varepsilon_{329}$ 0; X-ray powder diffraction data: 11.81 s, 9.00 w, 7.44 s, 5.17 s, 4.86 vs (1), 4.61 s (2), 4.32 vw, 4.13 vw, 3.90 m, 3.64 s (3,3), 3.51 s (3,3), 3.37 s, and 3.26 vw.

Anal. Calc. for $C_{10}H_{14}O_6S$: C, 45.78; H, 5.34; S, 12.22. Found: C, 45.79; H, 5.48; S, 12.10.

5,6-Dideoxy-1,2-O-isopropylidene-α-D-ribo-hex-5-enofuranose (**9**). — *A. From thionocarbonate* **8**. A solution of the crude, syrupy thionocarbonate **8** from the foregoing experiment [prepared from 2.5 g (11 mmoles) of compound **7**] in trimethyl phosphite (25 ml) was boiled for 72 h under reflux. To the cooled solution was added 6M aqueous sodium hydroxide (50 ml), and the mixture was stirred until a permanently basic, homogeneous solution was obtained (~1 h). The solution was extracted with chloroform (three 100-ml portions) and the extracts were combined, dried (magnesium sulfate), and evaporated to give a crystalline mass. Sublimation of the product at 22°/10 mtorr, followed by recrystallization from petroleum ether (b.p. 90–97°) gave pure **9**; yield 1.4 g (7.5 mmoles, 68% based on **7**), m.p. 67.0–68.5°, $[\alpha]_D^{22}$ +40.5 ±0.5° (*c* 1, chloroform); λ_{max}^{KBr} 2.89 (OH), 3.32 (CH of alkene), and 6.08 μm (C=C); R_F 0.58 (3:1 chloroform–ether); X-ray powder diffraction data: 8.73 vs (1), 6.55 m, 5.08 m, 4.65 s (2,2), 4.43 m, 4.24 m, 4.02 s (2,2), 3.73 vw, 3.46 vw, 3.25 w, and 3.17 w.

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.57. Found: C, 57.76; H, 7.41.

B. From 1,2-O-isopropylidene-α-D-allofuranose (**7**) *by way of orthoformic esters.* A mixture of **7** (0.5 g, 2.3 mmoles), triethyl orthoformate (0.15 g, 2.6 mmoles), and acetic acid (1 drop) was stirred for 5 h at 120°. T.l.c. of the product (3:1 chloroform–ether) showed the presence of 4 components, having R_F 0.42, 0.50, 0.78, and 0.85. Triphenylacetic acid (50 mg) was added, and the mixture was heated in an atmosphere

of nitrogen for 3 h at 180°. The product **9** was sublimed from the mixture at 45°/0.1 torr, and recrystallized from petroleum ether (b.p. 90–97°) to give pure **9**; yield 0.234 g (1.25 mmoles, 55%), m.p. 67.0–68.5°.

Reaction of 5,6-dideoxy-1,2-O-isopropylidene-α-D-ribo-hex-5-enofuranose (**9**) *with the Simmons–Smith reagents.* — A solution of **9** (100 mg, 0.54 mmole) in anhydrous ether (7 ml) was stirred with a mixture of diiodomethane (1.3 g, 0.4 ml, 4.8 mmoles) and zinc–copper couple (0.7 g) in 15 ml of anhydrous ether. After 48 h, t.l.c. showed that the starting sugar had reacted completely to give a mixture of fast-moving components, but that none of the desired cyclopropyl derivative (**6**) was present.

Preparation of 3-O-benzyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranose. — A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (20 g, 77 mmoles) in *N,N*-dimethylformamide (75 ml) was added dropwise to a stirred suspension of sodium hydride (61% oil dispersion, 4.3 g, 110 mmoles) in *N,N*-dimethylformamide (250 ml). After 0.5 h, a solution of benzyl chloride (13 g, 100 mmoles) in *N,N*-dimethylformamide (50 ml) was added dropwise during 15 min. The mixture was stirred for 12 h, and then poured onto ice (500 g). Stirring was continued until the ice had melted, and the resulting crystalline solid was filtered off, washed with water, and dried. The product was dissolved in hot hexane, and the solution was cooled slowly, eventually at 0° (with seeding), to give the crystalline ether (20.7 g). A further 3.0 g was obtained from the mother liquors; total yield 23.7 g (89%), m.p. 66.0–66.5°, $[\alpha]_D^{25}$ +106 ±1° (*c* 1, chloroform); R_F 0.75 (3:1 chloroform–ether); X-ray powder diffraction data: 13.22 vs (2), 9.11 w, 8.02 s, 6.39 vw, 5.75 m, 5.35 s, 5.04 s (3), 4.78 vw, 4.56 vs (1), 4.21 w, 3.99 s, and 3.75 m.

For this compound, prepared in about 30% yield by a procedure involving isolation by column chromatography, Brimacombe and Ching[12] reported m.p. 64–65°, $[\alpha]_D$ +110° (*c* 1, methanol, temperature not specified).

Preparation of 3-O-benzyl-1,2-O-isopropylidene-α-D-allofuranose (**10**). — A solution of 3-*O*-benzyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (20.0 g, 29 mmoles) in 4:1 acetic acid–water (120 ml) was stirred at 40° until the starting material was absent, as shown by t.l.c. (4.5 h). The acid was neutralized by addition of 6M aqueous sodium hydroxide, and the solution was extracted with four 100-ml portions of dichloromethane. The extracts were combined, washed once with water (100 ml), and dried (magnesium sulfate). Evaporation of the solution gave **10** as a colorless oil that was homogeneous by t.l.c.; yield 17.0 g (96%), $[\alpha]_D^{20}$ +104° (*c* 2, methanol) [lit.[12] $[\alpha]_D$ +103° (*c* 0.6, methanol)]; R_F 0.1 (3:1 chloroform–ether), 0.85 (4:1 ethyl acetate–ethanol).

5,6-Di-O-acetyl-3-O-benzyl-1,2-O-isopropylidene-α-D-allofuranose (**13**). — To a solution of **10** (6.5 g, 21 mmoles) in pyridine (100 ml) was added acetic anhydride (20 ml), and the solution was kept for 12 h at room temperature. Ice and water (350 ml) were added, and the mixture was stirred for 2 h. The product was extracted with two 150-ml portions of dichloromethane, and the extracts were combined, washed with five 100-ml portions of water, and evaporated to a syrup; toluene

(2 × 100 ml) and carbon tetrachloride (2 × 100 ml) were successively added and evaporated off. The resultant, pale-yellow syrup was dissolved in ether (60 ml), hexane (60 ml) was added, and the solution was cooled slowly to 0°, to give **13** as white prisms; yield 7.6 g (92%) in two crops. Recrystallization from hexane gave pure **13**; yield 7.3 g (89%), m.p. 66.5–67.0° $[\alpha]_D^{20}$ +98.0 ±1.0° (*c* 2, chloroform); R_F 0.75 (3:1 chloroform–ether); λ_{max}^{KBr} 5.73 μm (OAc); X-ray powder diffraction data: 9.76 m, 8.66 s (2), 6.64 m, 5.73 w, 5.00 vs (1), 4.75 w, 4.57 m, 4.41 w, 4.26 m, 3.94 m, 3.79 m, 3.61 m, 3.31 w, 3.07 m, 2.96 w, and 2.89 w.

Anal. Calc. for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64. Found: C, 60.60; H, 6.59.

Deacetylation of **13** (3.0 g, 7.6 mmoles) with 0.1 mmole of sodium methoxide in anhydrous methanol (30 ml) for 24 h at 0°, followed by neutralization with Amberlite IR-120 (H^+) and evaporation of the solvent, gave **10** (2.4 g, 100%) as a chromatographically homogeneous syrup.

Diastereoisomeric mixture of 3-O-benzyl-5,6-O-(ethoxymethylene)-1,2-O-isopropylidene-α-D-allofuranose (**11**). — A mixture of the diol **10** (17.0 g, 55 mmoles), triethyl orthoformate (20 ml, 120 mmoles), and acetic acid (2 ml) was boiled for 6 h under reflux. Excess reagents were removed by evaporation at 45° under diminished pressure, and then by addition and evaporation of toluene (2 × 100 ml) and carbon tetrachloride (2 × 100 ml) from the residual syrup. The resulting, yellow syrup was distilled from 0.1 g of sodium, to give **11** as a colorless oil; yield 20.0 g (54 mmoles, 98%), b.p. 150–155°/100 mtorr; no hydroxyl absorption in the i.r. spectrum; n.m.r. data (100 MHz, chloroform-*d*): τ 4.10, 4.16 (singlets, total integral 1 proton, ratio 1:1, orthoformyl C*H*), τ 4.2 (1 proton total integral, overlapping doublets for H-1 of the two diastereoisomers, $J_{1,2}$ ~3.5 Hz).

3-O-Benzyl-1,2-O-isopropylidene-α-D-allofuranose 5,6-thionocarbonate (**14**). — A solution of the diol **10** (7.0 g, 22.5 mmoles) and bis(imidazol-1-yl)thione (7 g, 39 mmoles) in acetone (250 ml) was boiled for 4 h under reflux. Charcoal (1 g) was added, and the cooled suspension was filtered, and the filtrate evaporated. A solution of the resultant, dark syrup in dichloromethane (100 ml) was washed with water (3 × 100 ml), and then evaporated to a dark syrup that was crystallized from methanol (75 ml) to give the thionocarbonate **14** as white needles. Recrystallization from methanol gave pure **14**; yield 4.1 g (11.5 mmoles, 51%), m.p. 115.5–116.5°, $[\alpha]_D^{21}$ +123 ±1° (*c* 2, chloroform); $[\alpha]_{400}^{25}$ +360°, $[\alpha]_{350}^{25}$ +520°, $[\alpha]_{310}^{25}$ +840°, $[\alpha]_{300}^{25}$ +1,000°, and $[\alpha]_{280}^{25}$ +1,510° (*c* 0.2, ethanol); R_F 0.89 (3:1 chloroform–ether); λ_{max}^{KBr} 3.40, 3.48, 3.52 (CH), and 5.60 μm (C=S); λ_{max}^{EtOH} 234 (ε 14,100), 310 nm (26); c.d. data at 25° (*c* 0.20, ethanol): $\Delta\varepsilon_{280}$ 0, $\Delta\varepsilon_{310}$ −0.84, $\Delta\varepsilon_{337}$ 0; X-ray powder diffraction data: 13.85 vs (1), 7.22 s, 6.72 w, 6.38 w, 5.98 w, 5.63 w, 5.22 s (3), 4.80 s (2), 4.49 s, 4.41 s, 3.94 w, and 3.76 m.

Anal. Calc. for $C_{17}H_{20}O_6S$: C, 57.93; H, 5.70; S, 9.10. Found: C, 57.79; H, 5.58; S, 9.29.

3-O-Benzyl-5,6-dideoxy-1,2-O-isopropylidene-α-D-ribo-hex-5-enofuranose (**12**). — *A. From the orthoesters* **11**. To the diastereoisomeric mixture of orthoesters **11** (17 g, 46 mmoles) was added triphenylacetic acid (1 g), and the mixture was heated with

stirring for 6 h at 200°. Potassium carbonate (1 g) was added to the cooled mixture, and stirring was continued for 12 h. Ether (100 ml) was added, the mixture was filtered, and the filtrate was evaporated to give a dark syrup which, on distillation, gave the pure alkene **12**; yield 12.0 g (43 mmoles, 94%), b.p. 123–125°/0.1 torr; $[\alpha]_D^{20}$ +64 ±0.5° (*c* 1.0, chloroform); R_F 0.6 (3:1 cyclohexane–ether); λ_{max}^{film} 3.32 (CH) and 6.08 μm (C=C).

Anal. Calc. for $C_{16}H_{20}O_4$: C, : 69.59; H, 7.23. Found: C, 69.50; H, 7.31.

B. From the thionocarbonate **14**. A solution of **14** (4.0 g, 11.4 mmoles) in trimethyl phosphite (25 ml) was boiled for 28 h under reflux in an atmosphere of nitrogen. The solution was cooled to 25° and poured into a mixture of 6M sodium hydroxide (200 ml) and ice (200 g). The resulting mixture was stirred for 2 h and then extracted with three 100-ml portions of ether. The extracts were combined, dried (magnesium sulfate), and evaporated, to give **12** as a colorless, chromatographically homogeneous syrup; yield 2.6 g (82%). Distillation gave pure **12**; yield 2.3 g (8.3 mmoles, 73%), b.p. 123–125°/0.1 torr, identical with the product obtained by route *A*.

*3-O-Benzyl-4-C-cyclopropyl-1,2-O-isopropylidene-α-*D-ribo-*tetrofuranose* (**15**). — To a stirred mixture of zinc–copper couple[15] (20 g) and diiodomethane (9.9 g, 37 mmoles) in anhydrous ether (50 ml) was added a solution of the alkene **12** (5.42 g, 19.5 mmoles) in anhydrous ether (10 ml), and the mixture was boiled for 48 h under reflux. The mixture was filtered, and the zinc was washed with two 50-ml portions of ether. The ethereal solutions were combined, and successively washed with saturated aqueous ammonium chloride (2 × 100 ml), saturated aqueous potassium carbonate (2 × 50 ml), and saturated aqueous sodium chloride (50 ml). The ethereal solution was evaporated, and the resultant oil was dissolved in benzene (50 ml). The solution was evaporated to give **15** as a very mobile oil (4.7 g, 83%), which was homogeneous by t.l.c. Distillation gave pure **15**; yield 4.25 g (75%), b.p. 125–130°/0.1 torr, $[\alpha]_D^{22}$ +81° (*c* 1, ethanol); R_F 0.70 (3:1 cyclohexane–ether); λ_{max}^{film} 3.36, 3.42, and 3.50 μm (CH).

Anal. Calc. for $C_{17}H_{22}O_4$: C, 70.31; H, 7.46. Found: C, 70.43; H, 7.62.

The preparation was repeated with quantities of 3 to 15 g of **12**, and yields of **15** in the range of 67–75% were obtained.

*Conversion of 3-*O*-benzyl-4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-*D-ribo-*tetrofuranose* (**15**) *into 4-*C*-cyclopropyl-1,2-*O*-isopropylidene-α-*D-ribo-*tetrofuranose* (**6**). — *A. By catalytic hydrogenolysis.* A solution of **15** (0.33 g, 1.1 mmoles) in abs. ethanol was shaken with 0.25 g of 5% palladium-on-charcoal under hydrogen at 1 atm pressure until uptake of hydrogen ceased (12 h). The mixture was filtered, and the filtrate was evaporated to give pure, crystalline **6**; yield 0.22 g (99%), m.p. 84–87°, identical with an authentic specimen.

B. By use of sodium in liquid ammonia. A solution of **15** (10.5 g, 36 mmoles) in dry tetrahydrofuran (50 ml) was added dropwise to liquid ammonia (600 ml), and then sodium (3.5 g, 150 mmoles) was added portionwise to the stirred solution during 1 h. The color of the resultant, dark-blue solution was discharged by careful addition of solid ammonium chloride, and the ammonia was evaporated by use of a stream

of nitrogen. The residue was partitioned between dichloromethane (200 ml) and water (100 ml). The aqueous phase was extracted with two 100-ml portions of dichloromethane, and the extracts were combined, and evaporated, to give crystalline **6**. Recrystallization from 1:5 ether–petroleum ether (b.p. 90–97°) gave pure **6**; yield 6.8 g (93%), m.p. 84–87°, identical with an authentic sample.

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