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A FURTHER INVESTIGATION OF THE STANNIC CHLORIDE-CATALYZED CONDENSATION REACTION OF 1-HEXENE AND 1,2,3,5-TETRA-*O*-ACYL-β-D-RIBOFURANOSES*

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ABSTRACT

The reaction of 1-hexene with either 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**5b**) or 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (**5a**) in the presence of stannic chloride leads to the formation of a complex mixture of products. By a combination of ^{1}H-n.m.r. and mass spectroscopy, the products were shown to be anomeric and diastereomeric mixtures of the 8,9,11-tri-*O*-acyl-protected derivatives of 7,10-anhydro-1,2,3,4,5,6-hexadeoxy-D-*allo*(*altro*)-undec-4-enitol (**1**) and 7,10-anhydro-5-chloro-1,2,3,4,5,6-hexadeoxy-D-*allo*(*altro*)-undecitol (**2**). The α anomer of **1** was the predominant anomer, whereas the α and β anomers of **2** were present in approximately equal amounts. It was found that **2** was not formed when trimethylsilyl trifluoromethanesulfonate was used as the catalyst instead of stannic chloride. The acyl-protected sugar 3,6-anhydro-2-deoxy-D-*allo*(*altro*)-heptose (**3**), prepared by ozonolysis of **1**, reacted with *tert*-butoxycarbonylmethyltriphenylphosphorane to give *tert*-butyl *trans*-5,8-anhydro-6,7,9-tri-*O*-acetyl-2,3,4-trideoxy-D-*allo*(*altro*)-non-2-enanate (**4**). The basicity of the ylide was sufficient to cause anomerization and resulted in an α,β ratio of 5:1 in the product, **4**.

INTRODUCTION

A number of procedures[2] have been developed for the condensation of carbon nucleophiles with the anomeric carbon atom of suitable sugars. Thus[3], 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**5a**), treated with 1-hexene in the presence of stannic chloride afforded a good yield (75%) of 1-(2,3,5-tri-*O*-benzoyl-D-ribofuranosyl)-2-hexenitol** [**1a(b)**, unspecified anomeric configuration]. Oxidation of the double bond could lead to a potentially useful *C*-nucleoside precursor. Indeed, when the authors[3] treated compound **1a(b)** with permanganate–periodate, 2-(2,3,5-tri-*O*-

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*For a preliminary report, see ref. 1.

**Systematically this compound should be referred to as 7,10-anhydro-1,2,3,4,5,6-hexadeoxy-8,9,11-tri-*O*-benzoyl-D-*allo*(*altro*)-undec-4-enitol but, for ease of discussion, it and other structurally related compounds will be referred to by more immediately obvious trivial names. The term anomeric is not strictly applicable to *C*-glycosyl compounds, but is used for convenience.

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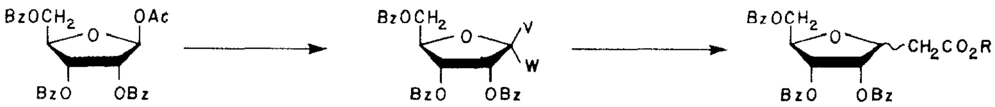


5a

1a V = H, W = $CH_2CH{=}CHC_3H_7$

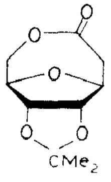
1b V = $CH_2CH{=}CHC_3H_7$, W = H

6a R = H

6b R = Et

benzoyl-D-ribofuranosyl)acetic acid (**6a**) was formed in 32% yield. This compound (**6a**) was subsequently converted into the ethyl ester **6b**.

Other compounds, structurally similar to **6b**, containing an active methylene group attached to the anomeric carbon atom, have been shown to be good intermediates for synthesis of several important *C*-nucleosides, as in the successful synthesis[4] of several pyrimidine *C*-nucleosides from the intermediate **7**. Also, syntheses of oxazinomycin[5], 9-deazaadenosine[6], 9-deazainosine[7], and several analogs of pseudouridine[8] have recently been accomplished, starting from the protected sugars **8a**



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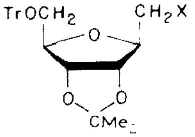
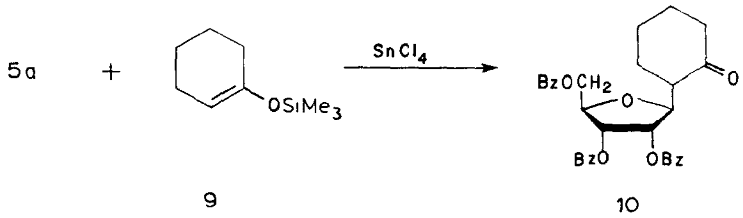
and **8b**. We therefore felt that the condensation of a peracylglycoside with 1-hexene warranted a closer investigation to determine its feasibility as an economical route for the formation of an important intermediate in *C*-nucleoside synthesis.



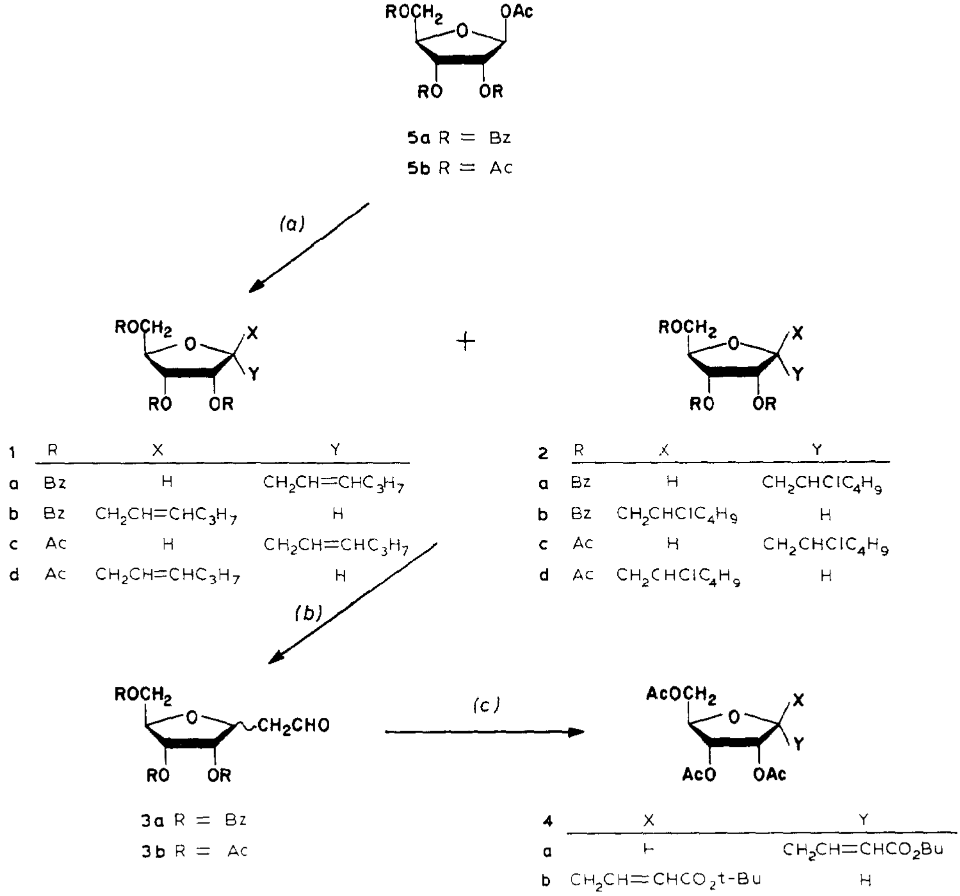
8a X = CN

8b X = CO_2Et

This reinvestigation was (*a*) to optimize the yield by making systematic changes in the experimental conditions of the reported[3] method, and (*b*) to determine which conditions, if any, would favor the predominant or exclusive formation of the desired β anomer. Although there was no mention of the absolute configuration[3] at the anomeric carbon atoms of compounds **1**, **6a**, and **6b**, a subsequent publication[9] implies that, in each case, the α anomer predominated. This was of considerable interest, as the trimethylsilyl enol ether **9** was shown to react[3] with **5a** in the presence of stannic chloride to produce only the β-D *C*-nucleoside, 2-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)cyclohexanone (**10**) in high yield.


5a
+
SnCl4
OSiMe3
BzOCH2
O
O
BzO
OBz
9
10

1,2,3,5-Tetra-*O*-acetyl-*β*-D-ribofuranose (**5b**) was used in the initial condensation reactions as well as the previously used sugar (**5a**). This change in protecting groups was expected to have little effect on the course of the condensation reaction, but would permit ozonolysis rather than periodate–permanganate oxidation, while avoiding possible oxidative reactions with the benzoyl protecting groups.


ROCH2
OAc
O
RO
OR
5a R = Bz
5b R = Ac
(a)
+
X
Y
(b)
CH2CHO
3a R = Bz
3b R = Ac
(c)
AcOCH2
AcO
OAc

1	R	X	Y
a	Bz	H	$CH_2CH{=}CHC_3H_7$
b	Bz	$CH_2CH{=}CHC_3H_7$	H
c	Ac	H	$CH_2CH{=}CHC_3H_7$
d	Ac	$CH_2CH{=}CHC_3H_7$	H

2	R	X	Y
a	Bz	H	$CH_2CHClC_4H_9$
b	Bz	$CH_2CHClC_4H_9$	H
c	Ac	H	$CH_2CHClC_4H_9$
d	Ac	$CH_2CHClC_4H_9$	H

4	X	Y
a	H	$CH_2CH{=}CHCO_2Bu$
b	$CH_2CH{=}CHCO_2t\text{-}Bu$	H

Scheme 1. (*a*) 1-Hexene, $SnCl_4$, CH_3CN, room temperature; (*b*) O_3, methanol, −78°, dimethyl sulfide; (*c*) *tert*-Butoxycarbonylmethyltriphenylphosphorane, CH_3CN, room temperature.

Condensation of **5b** with 1-hexane proceeded readily (Scheme I) to afford a mixture that appeared (t.l.c.) to contain two sugar components. The total yield and ratio of products seemed to be unaffected by the nature of the reaction solvent (1,2-dichloroethane, dichloromethane, acetonitrile, or nitromethane). The time required for complete reaction (t.l.c.) was increased when the temperature was lowered from 25 to 0°, but gave no apparent advantage; all subsequent reactions were routinely conducted at 25°. Our initial assumption was that the two observed sugar components were the α and β anomers (**1c** and **1d**), but closer examination cast some doubt on the actual identity or at least the purity of these products. First, this mixture of products contained chlorine according to Beilstein's ignition test. Trace contamination by stannic chloride was doubtful as the isolation procedure involved initial hydrolysis of this catalyst by sodium hydrogencarbonate and methanol. This procedure was followed by evaporation of the mixture to afford an oil that was subsequently subjected to column chromatography on silica gel. It could thus be assumed that chlorine was most probably present in the product mixture itself. Furthermore, although the n.m.r. spectrum of the mixture showed signals (5.9 p.p.m.) for alkenic protons, their integrated area was ~0.5 of that expected for pure **1c** and **1d** in relation to the integrated area assigned to the acetyl protons. In addition, several attempts to purify the mixture by repeated chromatography on silica failed to provide compounds giving acceptable analyses. Despite these indications that the product was not pure, we performed oxidative cleavage of the double bond. Because low yields were previously obtained[3] with periodate-permanganate, ozonolysis was investigated for this oxidative cleavage.

The crude mixture was subjected to conventional ozonolysis (ozone in methanol at −78°), followed by a reductive isolation with methylsulfide[10], to afford an acetaldehyde derivative. The mixture of products obtained was chromatographed on silica and two fractions were collected. The first fraction had the same R_f value as the starting material, and was isolated in 33% yield based on **5b**. This material contained halogen (Beilstein's ignition test) and elemental analysis indicated the empirical formula $C_{17}H_{27}ClO$. When this material was rechromatographed by low-pressure chromatography, two compounds were isolated whose structures were subsequently confirmed as **2c** and **2d** by ^{1}H-n.m.r. and mass-spectral analysis. In the ^{1}H-n.m.r. spectra, signals were observed at δ 4.41 (4.46) and 4.12, respectively, and assigned as the anomeric protons **2c** and **2d**. This assignment was made on the basis of the general trend observed for α and β anomers of various protected, 1-substituted ribofuranoses[11] in which the β anomeric-proton signal lies upfield of that of the α anomer because of the shielding effect of the *cis* O-8 (O-2′ if the trivial nomenclature is used). In both anomers, it was demonstrated unequivocally that the chlorine atom is located at C-5. This assignment was confirmed by 360-MHz ^{1}H-n.m.r. spectra through sequential proton spin-decoupling of H-7 and H-5, which showed that these protons were coupled to a common set of protons, the 6-CH$_2$ protons.

The structural similarity of **2c** and **2d** was also observed in their electron-ionization mass spectra, which showed virtually identical fragmentation-patterns.

except for slight variations in relative fragment-intensities. Fragments of considerable interest in both spectra were *m/z* 343 ($M^*H^+ - Cl$) and *m/z* 259 ($M^*H^+ - C_6H_{13}Cl$), which confirmed the presence of a chlorine atom situated on the alkyl side-chain. The fragment at *m/z* 259 is also diagnostic[12] for many, if not all, tri-*O*-acetylribofuranosyl nucleosides.

As halogenation at C-5 to form compounds **2c** and **2d** would most probably arise from an addition to an intermediate carbonium ion, both diastereomers would be expected. Indeed, the ^{1}H-n.m.r. spectra of both **2c** and **2d** demonstrate that diastereomeric mixtures are present in ~1 : 1 ratios. This point was particularly evident in the spectrum of **2c**, where two distinct H-5 multiplets were observed at δ 4.02 and 3.83 as well as two distinct H-7 doublets of triplets at δ 4.46 and 4.41. In the case of **2d**, the evidence for a diastereomeric mixture was less clear but still present. Subtle complexities in the ^{1}H-n.m.r. spectrum of **2d** are best explained by a mixture of almost identical compounds, such as diastereomers. Five distinct, acetyl-methyl signals were

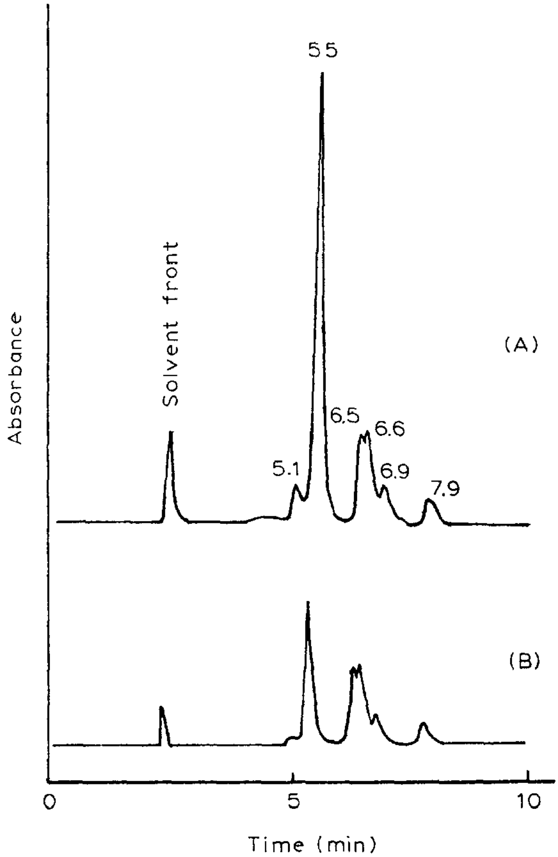


Fig. 1. Liquid chromatograms of (A) the reaction between **5a** and 1-hexene, and (B) the ozonolysis product from the mixture (A). Column, Micropak Si-5; liquid phase, 17:3, v/v, hexane–ethyl acetate; u.v. detector; 254 nm. The ozonide product of the ozonolysis is eluted only after 30 min.

observed in the δ 2.1–2.0 region and were apparently contributed by two compounds in which the acetyl groups were in very similar but not identical environments. Similarly, the spectrum for the α anomer (**2c**) showed six acetyl signals. Examination of the proton signals for the terminal methyl group revealed two distinct, overlapping triplets at δ 0.88. This same complexity was observed for the α anomer (δ 0.88 and 0.87).

The second fraction from the ozonolysis product-mixture contained 2-(2,3,5-tri-*O*-acetylribofuranosyl)acetaldehyde (**3b**), isolated in 22% yield (based on **5b**). This compound gave a positive aldehyde test in a t.l.c. spray-test with 2,4-dinitrophenylhydrazine reagent, and was confirmed to be a ~2:1 α,β mixture by ^{1}H-n.m.r. spectrometry.

To evaluate the role of protecting groups in the starting sugar[3], the reaction was repeated with the benzoylated sugar **5a**. Condensation of **5a** and 1-hexene in dichloromethane appeared to proceed according to the previous report[3] and furnished a 2-component mixture (t.l.c., solvent A). Different reaction solvents, such as acetonitrile, nitromethane, or 1,2-dichloroethane, afforded virtually identical product-mixtures. However, l.c. analysis of the mixture revealed it to be more complex than indicated by t.l.c. Six significant peaks were observed in the chromatogram (Fig. 1A) ^{1}H-N.m.r. spectra were recorded for the compounds corresponding to the largest peak (R_t 5.5 min) and for the compounds constituting a mixture of the next two peaks (R_T 6.5, 6.6) (Fig. 1A). Structural assignments were made by performing spin-decoupling experiments on selected signals and by comparing the chemical shift-data from these spectra with the ^{1}H-n.m.r. spectral data of compounds **1c** and **2c**.

The first fraction (R_t 5.5) (assumed to be a single component, see later) was actually a mixture of two compounds in 3:1 ratio. The minor component, 2-chloro-1-(2,3,5-tri-*O*-benzoyl-α-D-ribofuranosyl)hexane (**2a**) was a 1:1 mixture of diastereomers. Signals for the anomeric proton (H-1) were observed at δ 4.78 (dt) and at δ 4.71 (dt), whereas signals for H-2 were located at δ 4.26 and 3.96 (see Table I for 360-MHz ^{1}H-n.m.r. chemical-shift data and Table II for ^{1}H-n.m.r. coupling constants). The major component [**1a**(**b**)] of the first fraction was an *E*/*Z* isomeric mixture (~2:1) of a single anomer; the signal for the anomeric proton was observed at δ 4.42. Absolute anomeric assignment was not possible as an ^{1}H-n.m.r. spectrum for the other anomer could not be obtained. Spin decoupling of the H-1 signals (δ 2.50, *trans*; δ 2.56, *cis*) resulted in collapse of the H-2 signal (apparent dt) to two doublets (J_{trans} 15.5 and J_{cis} 6.8 Hz), which confirmed the alkenic assignments. The second fraction (R_T 6.5, 6.6 min) contained a diastereomeric mixture of 2-chloro-1-(2,3,4-tri-*O*-benzoyl-β-D-ribofuranosyl)hexanes (**2b**). The anomeric-proton signal (δ 4.43) lay upfield from the anomeric-proton signal of the α anomer.

In order to further illustrate the complexity of the mixture obtained by condensation of 1-hexene and **5a**, a portion of the crude mixture was subjected to ozonolysis in methanol at −78°. After completion of the reaction, the solution was purged with nitrogen and the solvent removed *in vacuo*. A small amount (~5 mg) of the remaining residue was dissolved in ethyl acetate (1 mL) and a 10-μL aliquot

TABLE I

360-MHz PROTON MAGNETIC RESONANCE SPECTRA[a]

Compound	*Solvent*	*H-6*	*H-5*	*H-4*	*H-3*	*H-2*	*H-1a*	*H-1b*
1a (1b)[b]	$CDCl_3$	0.78m, 0.75m	1.26m	1.90m	5.45dt	5.36dt	2.50q (*trans*)	2.56dt (*cis*)
2a[c]	$CDCl_3$	0.88t, 0.89t	[d]	[d]	[d]	3.96m 4.26m	[d]	[d]
2b	$CDCl_3$	0.85t	1.53–1.31m	1.70–1.62m	2.11–1.62m	3.90m	2.11–1.62	2.11–1.62
2c[c]	$CDCl_3$	0.87t, 0.88t	1.22m	1.51m	[f]	3.93m, 4.02m	2.04–1.98m, 1.96m	2.04–1.98m, 1.76m
2d[c]	$CDCl_3$	0.88t, 0.88t		1.8–1.3m	1.8–1.3m	3.87m	1.9–1.7m	1.9–1.7m
4a	$CDCl_3$				5.79dt	6.77dt	2.50m	2.50m
4b	$CDCl_3$				5.85dt	6.81dt	2.49m	2.49m
		H-1′	*H-2′*	*H-3′*	*H-4′*	*H-5a′*	*H-5b′*	*Others*
1a (1b)		4.42dt	5.86dd	5.77m	4.67		4.52m	7.24–8.04m aromatics
2a[c]		4.78dt, 4.71dt	5.93dd, 5.90dd	[d]	[d]	[d]	[d]	[d]
2b		4.43m	5.86dd	5.77dd[e]	4.60m	4.53dd	4.64dd	7.24–8.03m aromatics
2c[c]		4.41dt, 4.46dt	5.42dd, 5.46dd	5.32dd, 5.29dd	4.15m	4.06dt	4.31dd, 4.27dd	2.00s, 2.01s, 2.06s, 2.06s, 2.09s, 2.10s $C(O)CH_3$
2d		4.12m	5.40t	5.22dd	4.15m	4.06dd	4.06dd	2.00s, 2.00s, 2.05s, 2.10s, 2.10s, $C(O)CH_3$
4a		4.29dt	5.43t	5.26dd	4.10dd	4.20m	4.20m	1.46s, $C(CH_3)$; 2.04s, 2.10s, 2.21s, $C(O)CH_3$
4b		4.08dt	4.29t	5.14dd	4.29dd	4.14m	4.14m	1.47s, $C(CH_3)$; 2.06s, 2.08s, 2.10s, $C(O)CH_3$

[a] Chemical shifts are in p.p.m. from Me_4Si ($\delta = 0$). For convenience, the carbon atoms in compounds listed have been numbered in either direction starting at the bond between the anomeric carbon atom and the alkyl side-chain. Those carbon atoms that make up the traditional sugar moiety are assigned primed values whereas the other carbon atoms are given nonprimed values. [b] Values are for one anomer, the identity of which was not determined. [c] Double values denote chemical shifts for the pair of diastereomers. [d] Signals obscured by those of compound **1a**. [e] Additional complexity present. [f] Signals obscured by acetyl signals.

TABLE II

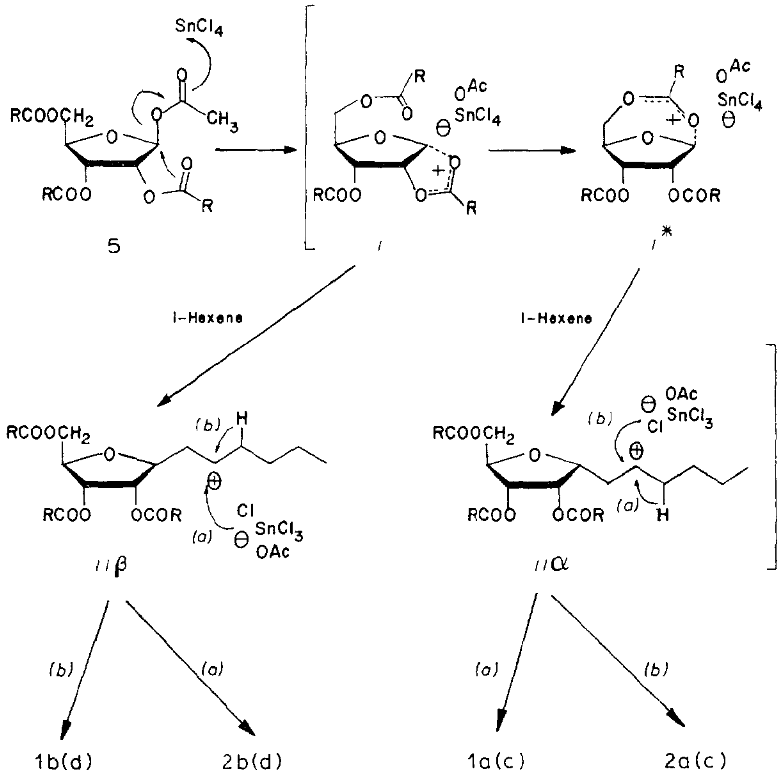
^{1}H COUPLING CONSTANTS[a]

Compound	$J_{2,3}$	$J_{1,3}$	$J_{1,2}$	$J_{1,1'}$	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'a}$	$J_{4',5'b}$	$J_{5'a,5'b}$
1a (1b)	15.5 (trans) 6.8 (cis)		[b]	7.1 (trans) [b] (cis)	3.3	4.9	[b]	[b]	[b]	[b]
2a	[b]	[b]	[b]	9.4, 6.8	3.4, 3.7	4.6, 4.6	[c]	[c]	[c]	[c]
2b	[b]	[b]	[b]	[b]	3.9	4.7	6.6	4.2	3.4	11.0
2c	[b]	[b]	[b]	9.7, 6.9	3.5, 3.5	4.3, 4.6	[b]	8.7, 8.8	4.5	11.7
2d	[b]	[b]	[b]	[b]	4.0	4.0	7.6	3.0	4.7, 4.9	11.7
4a	15.6	1.3	7.3	2.5	4.5	4.5	7.4	11.8	[b]	[b]
4b	15.7	1.5	7.1	5.5	6.0	6.0	4.7	13.5	[b]	[b]

[a] See footnote [c] of Table I [b] Unresolved [c] Either obscured by compound **1a (1b)** or unresolved

of this solution was analyzed by l.c. Comparison of the resulting chromatogram (Fig. 1B) with A (Fig. 1) showed that only the two peaks having retention times of 5.1 and 5.5 min were affected by ozone treatment. Besides noting the fact that **2a** and **2b** are present in almost equal quantities, it may also be concluded from these chromatograms that two unsaturated products result from the initial condensation, and that they are probably the α and β anomers, **1a** and **1b**.

A possible mechanism for the formation of compounds **1** and **2** is shown in Scheme 2. The first step is probably acetoxyl-group abstraction by the Lewis acid to generate the classical, stabilized acyloxonium ion *i*. The exact nature of this intermediate was not proved, but its presence was inferred with both sugars, because a very slowly migrating component became apparent while monitoring the reaction in t.l.c. as stannic chloride was added to the mixture. Formation of this slowly migrating material was independent of 1-hexene, as in a control experiment in which **5b** and stannic chloride were combined in dichloromethane containing no 1-hexene, the concentration of the intermediate seemed to reach equilibrium with **5b**. Addition of 1-hexene to this control caused simultaneous decrease of the concentration of both the assumed intermediate *i* and **5b** until both finally disappeared as the reaction



Scheme 2

proceeded to completion. The formation of the β anomers of **1** and **2** may be considered to occur by addition of the alkene to the β face of *i* to form intermediate *ii β*, which gives rise to either **1**, after elimination of H-3, or **2** by simple addition of a chloride ion at C-2. However, the α anomer could arise only if another intermediate in addition to *i* were involved. One such mechanism is illustrated in which the acyloxy group attached to C-5′ attacks the anomeric carbon atom, leading to an alternative oxonium ion *i**. 1-Hexene can then add to the α face of the sugar, causing formation of the α anomer of **1** and **2** following proton elimination or chloride addition. Other intermediates and/or reaction mechanisms can undoubtedly be drawn that would also explain the preponderance of the α anomer.

In an attempt to circumvent the problem of chlorine addition, the use of several Lewis acids other than stannic chloride was investigated. Table III lists these catalysts and the major problems associated with their use in this reaction. Of the four Lewis acids, trimethylsilyl trifluoromethanesulfonate showed the most promise, as uncontaminated alkene could be obtained. However, in three different solvents (acetonitrile, nitromethane, and dichloromethane), the best yield achieved of a 5:1 mixture of **1a** and **1b** was only ~20%. This anomeric mixture was converted by ozonolysis, followed by reductive step (methylsulfide), into the aldehyde **3a** in 95% yield. The α/β ratio as determined by ^{1}H-n.m.r. was unaffected by these chemical transformations.

Even though the initial condensation gives at best only a 5:1 α,β mixture, we were also interested in chemical conversion of the oxidation product **3a** into its β anomer exclusively. It has recently been shown[2a,9] that the α anomer of **6b** may be converted into the β anomer by first deacylating with sodium ethoxide and then reprotecting with the same acyl groups for comparative purposes. The authors hypothesized that the basic conditions used for protection not only removed the acyl groups, but also abstracted a proton from the active methylene group, which allowed the 5-membered ether ring to open and reannulate to the favored, β configuration. Whether or not the anomerization occurred before, after, or concomitantly with the debenzoylation was not explored. If the acyl protecting-groups played some role in forming the β anomer prior to their removal, then it is also possible that a non-nucleophilic base might cause anomerization without effecting deprotection. If this

TABLE III

LEWIS-ACID CATALYSIS FOR THE CONDENSATION OF 1-HEXENE AND TETRA-*O*-ACYLRIBOFURANOSES

Catalyst	*Yield*	*Problem*
$SnCl_4$	≃50%	Chloro substitution
$TiCl_4$	20%	Chloro substitution
BF_3 · etherate	Trace	Low yield
Me_3Si-triflate[a]	≃20%	Low yield

[a] $Me_3SiSO_2CF_3$.

were possible, then anomerization of the aldehyde **3b** might be accomplished without removing the acetyl groups. In this connection, when the carbon chain of **3b** was extended with the Wittig reagent *tert*-butoxymethyltriphenylphosphorane[13], compounds **4a** and **4b** were obtained in 70% combined yield. Of interest was the fact that, in the presence of this base, the α,β ratio changed from 5:1 to 1:3.

Contrary to a previous report[3], our investigations demonstrate that the stannic chloride-catalyzed condensation of 1-hexane and a tetra-*O*-acyl-D-ribofuranose affords a complex mixture of products containing the desired alkenic product as a minor component that proved difficult to isolate. Formation of the major component in the product-mixture, the chlorine adduct is circumvented by the use of trimethylsilyl triflate as a catalyst, although its use did not improve the yield. In general, the low yields are attributed to the low nucleophilicity of 1-hexene in this reaction. Therefore, it seems that this condensation is an inadequate method for the preparation of such *C*-nucleoside precursors as compounds **9** and **8**. Although the α anomer preponderates in the initial condensation, it has been reported[11] that the α anomer of **6b** is readily anomerized under basic conditions. Similarly, we found that treatment of the aldehyde **3** with a suitable phosphorane (basic conditions) affords not only the desired product **4**, but also partially epimerized the anomeric center to afford mainly the desired β anomer.

EXPERIMENTAL

General methods. — Low pressure column chromatography was performed by using Merck Lobar (Silica gel-60) prepacked columns (sized B and C) with typical flow rates of 5–10 mL/min. Fractions (15 mL) were collected with an ISCO Retriever III automatic fraction-collector. U.v.-absorbing compounds were detected by using an Altex Model 152 dual-wavelength u.v. detector (254 nm) with a preparative flow-cell. Gravity column chromatography was performed with 70–230 mesh Merck silica gel. Thin-layer chromatography (t.l.c.) was accomplished with SilicAR 7GF (250 μm layer) on prescored glass plates (2.5 × 8 cm) from Analtech, Inc., Newark, Delaware. Solvent systems used were: (*a*) 3:1 (v/v) hexane–ethyl acetate, (*b*) 20:1 (v/v) dichloromethane–acetone, (*c*) 3:1 (v/v) chloroform–ethyl acetate, (*d*) 17:3 (v/v) benzene–ethyl acetate, (*e*) 6:1 (v/v) dichloromethane–ethyl acetate, (*f*) 2:1 (v/v) hexane–ethyl acetate, (*g*) 40:1 (v/v) dichloromethane–ethyl acetate, (*h*) 9:1 (v/v) hexane–ethyl acetate. Evaporations were performed with a Buchler flash evaporator, a water aspirator, and a water bath at room temperature, unless otherwise noted. Proton n.m.r. spectra were obtained with a Varian EM-360 spectrometer, JEOL FX-90A spectrometer, JEOL PFT 100 spectrometer, or a Bruker WM 360 spectrometer. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter. High-performance liquid chromatography (l.c.) was conducted with a Varian Vista 54 chromatograph, a Micropak (10- or 5-μm particle size) silica column (0.4 × 30 cm), Brownlee 10-μm particle-size guard column, and a Varian UV-50 variablewavelength u.v. detector or Waters model 401 refractive-index detector. Retention times (R_T) were measured from time of injection, and flow rates of 1 mL min were maintained except where noted. Mass-spectral data were obtained with a Finnigan Model g.l.c.–m.s. instrument and electron ionization. Elemental analyses were obtained from M-H-W Laboratories, P.O. Box 15853, Phoenix, Arizona 85018

*7,10-Anhydro-1,2,3,4,5,6-hexadeoxy-8,9,11-tri-O-benzoyl-*D-allo(altro)*-undec-4-enitol* [**1a**(**b**)]; and *7,10-anhydro-5-chloro-1,2,3,4,5,6-hexadeoxy-8,9,11-tri-O-benzoyl-*D-altro(allo)*-undecitol* [**2a**(**b**)]. — (*A*) Literature method. Following are the experimental details for the previously reported[3] reaction of 1-hexene with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**5a**). Care was taken to duplicate the original procedure as closely as possible.

Stannic chloride (0.2 mL, 2 mmol), was added to a solution of **5a** (1.01 g, 2 mmol) in dichloromethane (10 mL, dried over 4-Å sieves). After 5 min, 1-hexene (1 mL) was added and the solution was stirred at 20° until **5a** was no longer detectable (~6 h) by t.l.c. (solvent *a*). The solution was poured into a well-stirred mixture of dichloromethane (100 mL), sodium hydrogencarbonate (2 g), and methanol (2.3 mL). After stirring for 16 h, Celite (3 g) was added and the resulting suspension was filtered through a thin bed of Celite on a sintered-glass funnel. The Celite was washed with dichloromethane (3 × 25 mL) and the filtrate and washings were combined and then evaporated to afford a yellow syrup (1.1 g). This syrup was a complex mixture of compounds **1a**, **1b**, **2a**, and **2b**, even though t.l.c. indicated only two major components having R_F 0.60 and 0.63 (solvent *a*), with minor components having R_F 0.15 and 0.13 (solvent system *b*). The syrup was chromatographed on a Lobar column (size B), eluted with solvent system *b*. Fractions (15 mL) were collected and each was analyzed by l.c. This procedure permitted selection of two specific fractions, each containing one of the major constituents of the mixture as indicated by a single spot in t.l.c. The liquid chromatogram of the product-mixture is shown in Fig. 2 (chromatogram A). Fraction 1 contained the peak having R_T 5.5 min, and was a mixture of compounds **1a**(**b**) and **2a** in 3:1 ratio, as estimated from its 360 MHz ^{1}H-n.m.r. spectrum (Table I). Fraction 2 contained the peaks having R_T 6.5 and 6.6 min, and was a diastereomeric mixture of **2b** (see Table I). Because of the complexity of the product-mixture, isolation and analysis of individual components was not accomplished.

(*B*) *7,10-Anhydro-1,2,3,4,5,6-hexadeoxy-8,9,11-tri-O-benzoyl-*D-allo(altro)*-undec-4-enitol*, [**1a**(**b**)]. — A solution of **5a** (1.01 g, 2 mmol) in acetonitrile (10 mL, dried over 4A molecular sieves) was treated with trimethylsilyl triflate (0.35 mL, ~1 eq.) and stirred for 1 h at room temperature under nitrogen. 1-Hexene (1.0 mL) was then added in one portion and the resulting dark mixture was stirred for 3 h. An additional portion of trimethylsilyl triflate (0.35 mL) was then added and the solution stirred overnight. Evaporation gave a dark residue that was dissolved in dichloromethane (10 mL) and added to the surface of a bed of silica gel (~20 g) contained in a fritted-glass filter funnel (65-mm diameter). The bed was eluted with dichloromethane (200 mL) and the eluate was collected as one fraction and then evaporated to a yellow syrup (~0.6 g). The syrup was dissolved in ethyl acetate (2 mL), added via loop injection to a Lobar (size B) silica gel column and chromatographed under low pressure [eluent: 5:1 (v/v) petroleum ether, (b.p. 60–90°)–ethyl acetate. Evaporation of the appropriate fractions (R_F 0.63, 0.60, solvent *a*) yielded a colorless syrup, **1a(b)** (0.20 g, 19%) as an α,β mixture; ^{1}H-n.m.r. (60 MHz, $CDCl_3$): δ 0.8–2.2 (m, 7 H, 3 H-1, 2 H-2, 2 H-3), 2.6 (m, 2 H, 2 H-6), 4.6 (m, 4 H, H-7, H-10, H-11a, H-11b), 5.5 (m, 2 H, H-4, H-5), 5.9 (m, 2 H, H-8, H-9), 8.2–7.4 (m, 15 aromatic).

Anal. Calc. for $C_{32}H_{32}O_7$: C, 72.71; H, 6.10. Found: C, 72.91; H, 6.14.

*7,10-Anhydro-5-chloro-1,2,3,4,5,6-hexadeoxy-8,9,11-tri-*O*-acetyl-*D-altro-*undecitol* (**2c**) and -D-allo-*undecitol* (**2d**), and *3,6-anhydro-2-deoxy-4,5,7-tri-*O*-acetyl-*D-allo(altro)-*heptose* (**3b**). — A solution of **5b** (8.0 g, 25 mmol) in 1,2-dichloroethane (35 mL) was treated at room temperature with stannic chloride (2.95 mL, 1.01 eq. based on **5b**) under nitrogen. After 30 min, the solution was cooled to −10° and treated dropwise with a solution of 1-hexene (2.7 g, 33 mmol) in 1,2-dichloroethane (10 mL) over a period of 30 min. The mixture was then stirred for an additional 16 h. Treatment of the dark mixture with solid sodium hydrogencarbonate (19 g), methanol (20 mL), and Celite (10 g) afforded a light-yellow suspension which was stirred mechanically for 8 h. The mixture was filtered and the collected Celite pad was washed with dichloromethane (3 × 100 mL). The combined filtrates were evaporated to a golden syrup that was purified by rapid, open-bed chromatography (silica, 100 g) in a sintered-glass funnel (14-cm diameter) with benzene as the eluent. The desired 50-mL fractions, as indicated by t.l.c. (R_F 0.27–0.38, solvent *d*), were pooled and evaporated to give a mixture of **1c(d)** and **2c(d)**; yield 8.4 g.

A portion of the mixture (1.50 g) was dissolved in abs. methanol (50 mL) and then treated with ozone at −78° until the blue color became permanent. The solution was purged with dry nitrogen for 30 min at −78°, dimethyl sulfide (~10 mL) was added, and the resulting solution was allowed to warm during 3 h to room temperature. The solution was then stirred for 12 h at room temperature and evaporated to a colorless syrup. The syrup was dissolved in dichloromethane (30 mL) and washed with saturated sodium hydrogen carbonate solution (2 × 10 mL), with water (2 × 10 mL), and then dried (magnesium sulfate). Filtration, and evaporation of the dichloromethane, afforded a colorless syrup that was chromatographed on a column (30-mm diameter) of silica gel (60 g) eluted with 6:1 (v/v) dichloromethane–ethyl acetate. The desired 15-mL fractions, as indicated by t.l.c. (solvent *c*) were pooled and evaporated to afford syrupy **2c(d)**, 0.56 g (33% yield based on **5b**), and **3b**, 0.30 g (22% yield based on **5b**).

Anal [for compound **2c(d)**] Calc. for $C_{17}H_{27}ClO$: C, 53.90; H, 7.18; O, 29.56. Found: C, 53.88; H, 7.40; O, 29.36.

The anomeric mixture of **2c** and **2d** was chromatographed on a Lobar silica gel column (size C) under low pressure with 40:1 (v/v) dichloromethane–acetone. Again, the desired (t.l.c., solvent *c*), 15-mL fractions were pooled and evaporated to yield ~0.25 g each of **2c** and **2d**.

Compound **2c** had R_F 0.63 (solvent *c*); l.c. R_T 7.4 min (Micropak Si-5, 30 cm;

solvent *f*): $[\alpha]_D^{26}$ +52.6° (*c* 1.0, chloroform); *m/z* 379 ($M*H^+$) 343 ($M*H^+ - HCl$), 319 ($M*H^+ - CH_3CO_2H$), 305 ($M*H^+ - CH_3CO_2CH_3$), 259 ($M*H^+ - C_6H_{13}Cl$), 139 (*m/z* 259 − 2 CH_3CO_2H), 216, and 203 (parent).

Compound **2d** had R_F 0.60 (solvent *c*); l.c. R_t 8.4 min (Micropak S-5, 30 cm; solvent *f*): $[\alpha]_D^{26}$ +48.7° (*c* 1.0, chloroform); *m/z* 379 (parent), 343, 319, 305, 259, 139, 216, and 203.

Compound **3b** had R_F 0.2 (solvent *e*); ^{1}H-n.m.r. (100 MHz, $CDCl_3$): δ 2.03 (s, 3 H), 2.06 (s, 3 H), 2.08 (s, 3 H), 2.76 (dd, 2 H, $J_{2,3}$ 6.7, $J_{1,2}$ 1 Hz, 2 H-2), 4.05–5.44 (m, 6 H, H-3,4,5,6, 2 H-7), and 9.75 (t, 1 H, $J_{1,2}$ 1 Hz).

Anal. Calc. for $C_{13}H_{18}O_8$: C, 51.66; H, 6.00; O, 42.34. Found: C, 51.88; H, 6.04; O, 42.04.

*3,6-Anhydro-2-deoxy-4,5,7-tri-*O*-benzoyl-*D-altro-(allo)-*heptose* [**3a**(**b**)]. — A solution of the mixture of compounds **1a** and **1b** (100 mg, 0.20 mmol) in methanol (15 mL) was stirred at −70°, purged with oxygen (10 min), and then treated with ozone until a persistent blue color remained (~1 min). Nitrogen was then passed through the solution for 30 min while maintaining the temperature at −70°. Methyl sulfide (0.07 mL, 5 eq.) was added and the solution allowed to warm to room temperature during 90 min, and then stirred for an additional 16 h. After removing the solvent, the residue was chromatographed under low pressure on silica gel (Lobar column, size B, eluent: 5:1 ligroin–ethyl acetate). Evaporation of the proper fractions, as indicated by t.l.c. (solvent *a*), yielded a mixture of **3a** and **3b**, 88 mg (95%) in 2:1 ratio (estimated from ^{1}H-n.m.r.); R_F 0.52 and 0.41 (solvent *g*), and 0.23 and 0.19 (solvent *a*). The mixture was not separated. ^{1}H-n.m.r. (100 MHz, $CDCl_3$), signals are reported for α and β anomers and assignments for H-1'α and β are based on homospin decoupling of the adjacent C-2 methylene protons: δ 2.93 (m, 4 H, α and β H-2), 4.64–4.58 (m, 7 H, 2 H-7α, 2 H-7β, H-6α, H-6β, H-3β), 5.02 (d of t, *J* 7.0, $J_{3,4}$ 4.3 Hz, H-3α), 5.44 (t, 1 H, H-5β), 5.87–5.66 (m, 2 H, H-5α, H-4β), 5.98 (t, 1 H, $J_{3,4}$ 4.3 Hz, H-4α), 8.06–7.26 (m, 30 H, aromatic), and 9.83 (pseudo triplet, 2 H, H-1α, H-1β).

Anal. Calc. for $C_{28}H_{24}O_8$: C, 68.85; H, 4.95. Found: C, 68.67; H, 5.00.

tert-*Butyl* trans-*5,8-anhydro-6,7,9-tri-*O*-acetyl-2,3,4-trideoxy-*D-altro-*non-2-enanate* (**4a**) and trans-D-allo-*non-2-enanate* (**4b**). — A solution of the α,β mixture **3b** (6.75 g, 20 mmol) and *tert*-butoxycarbonylmethyltriphenylphosphorane (8.4 g, 20 mmol) in acetonitrile (200 mL) was stirred for 4.5 h at room temperature. The solvent was evaporated and the residue suspended in ether (50 mL). The suspension was refrigerated at 8° (4 h) and the precipitated triphenylphosphine oxide was collected by filtration. Evaporation of the filtrate gave a residue that was again suspended in ether (100 mL). This suspension was chilled at 8° (4 h) and a second crop of triphenylphosphine oxide collected by filtration. Evaporation of this second filtrate resulted in a syrupy residue that was chromatographed on a column (6.5-cm diameter) of silica gel (500 g) with 40:1 (v/v) dichloromethane–acetone. Fractions (15 mL) were collected and the fractions containing the product, as determined by t.l.c. (solvent *a*) were pooled and evaporated to provide compound **4a** (0.24 g), compound **4b** (0.83 g), and a mixture of **4a** and **4b** (5.18 g) as colorless oils. The total combined yield was 6.25 g (70%). The estimated (from t.l.c.) ratio of **4b**:**4a** was 5:1.

Compound **4a** had: R_F 0.13 (solvent *a*) 0.40 (solvent *b*); $[\alpha]_D^{24}$ +48.4° (*c* 1.0, chloroform); *m/z* 401 (M*H$^+$), 327 (M*H$^+$ − OCMe$_3$), 259 (M*H$^+$ − CH$_2$CH=CHCO$_2$ *tert*-butyl), and 139 (parent).

Anal. Calc. for $C_{19}H_{28}O_9$: C, 56.99; H, 7.05. Found: C, 56.87; H, 7.02.

Compound **4b** had R_F 0.17 (solvent *a*), 0.47 (solvent *b*); $[\alpha]_D^{24}$ −0.7° (*c* 1.0, chloroform); *m/z* 401, 327, 259, and 139 (parent).

Anal. Calc. for $C_{19}H_{28}O_9$: C, 56.99; H, 7.05. Found: C, 56.87; H, 7.02.

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