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PREPARATION OF DERIVATIVES OF L-IDOSE AND L-IDURONIC ACID FROM 1,2-*O*-ISOPROPYLIDENE-α-D-GLUCOFURANOSE BY WAY OF ACETYLENIC INTERMEDIATES*

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ABSTRACT

The products (**1**) from the periodate oxidation of 1,2-*O*-isopropylidene-α-D-glucofuranose were converted by ethynylmagnesium bromide into a separable, 14:11 mixture of 6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-hept-6-ynofuranose (**2**) and its α-D-*gluco* analog **3**. These crystalline products were further characterized as their respective 3,5-diacetates (**5** and **7**) and 3,5-dibenzoates (**4** and **6**). Ozonolysis of **2** and **3** led to 1,2-*O*-isopropylidene-β-L-idofuranurono-6,3-lactone (**8**) and its α-D-*gluco* analog **9**, respectively; similar ozonolysis of the dibenzoates **4** and **6**, followed by treatment with diazomethane, gave methyl 3,5-di-*O*-benzoyl-1,2-*O*-isopropylidene-α-L-idofuranuronate (**10**) and its α-D-*gluco* analog **11**, respectively. Diborane reduction of the ozonolysis products from **4** gave 1,2-*O*-isopropylidene-β-L-idofuranose (**13**) as its 3,5-dibenzoate (**12**), and a similar sequence was performed with **6**. The propargylic alcohols **2** and **3** were reduced by lithium aluminum hydride, in high yield, to the allylic alcohol analogs **15** and **16**, further characterized as their 3,5-dibenzoates **17** and **18**; compounds **15** and **16** were also obtainable by vinylation of compounds **1**. The two series of derivatives in this work, epimeric at C-5, were examined comparatively by polarimetry and p.m.r. spectroscopy.

INTRODUCTION

The reaction of ethynylmagnesium bromide with periodate-oxidized 1,2-*O*-isopropylidene-α-D-glucofuranose gives a C-5 epimeric mixture of C_7 acetylenic derivatives[2], from which the syrupy β-L-*ido* derivative has been obtained by fractional distillation and converted, in low (15%) yield, by ozonolysis into 1,2-*O*-isopropylidene-β-L-idofuranurono-6,3-lactone[3]. This reaction has been re-examined in detail; both C-5 epimeric products have been separated pure, and characterized further by means of various derivatives, and the ozonolysis procedure has been

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improved to provide a preparatively useful reaction for L-iduronic and D-glucuronic acid derivatives. A subsequent diborane reduction-step has also been performed that furnishes a route to the corresponding aldose derivatives. This sequence thus provides access to the biologically important L-iduronic acid, and also furnishes a potentially general method for chain-ascent at the ω-position of a sugar derivative.

DISCUSSION

Following the procedure already described[3], 1,2-*O*-isopropylidene-α-D-glucofuranose, dissolved in 37% aqueous formaldehyde, was oxidized with sodium metaperiodate to give 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose as a mixture[4] of the formaldehyde adduct **1a** of its hydrate plus a small proportion of the "dimer" **1b**. These components were readily differentiated by t.l.c.

The mixture of **1a** and **1b** was treated with an excess of ethynylmagnesium bromide in tetrahydrofuran, according to the earlier procedure[3]. A syrup, subsequently shown to be a mixture of epimeric, acetylenic alcohols, namely, 6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*(and α-D-*gluco*)-hept-6-ynofuranose (**2** and **3**), was obtained in 74% overall yield. In the previous study[3], the product was fractionally distilled, and the L-*ido* epimer (**2**) was obtained as a syrup in 34% yield. In the present work, both 5-epimers were isolated crystalline by chromatography on a column of silica gel with 1:1 ether–petroleum ether as eluant. The D-*gluco* epimer (**3**) was eluted first, and was subsequently purified by vacuum distillation. The pure, crystalline compound had m.p. 87–89°. The slower-migrating component (the L-*ido* epimer, **2**) was purified by recrystallization, whereupon it had m.p. 126–128°. A mixture of the two isomers showed a marked depression in the melting points.

The configurations of the C-5 epimeric propargyl alcohols **2** and **3** were established by chemical degradation to known derivatives; supporting evidence was provided from physical studies. By using *O*-trimethylsilyl derivatives of the pure compounds **2** and **3** as standards, the ratio of **2** to **3** in the mixture resulting from the Grignard reaction was determined by g.l.c. to be 14.11.

The i.r. spectra of the epimers **2** and **3** showed absorptions (3.03 and 4.68 μm) characteristic of the C–H and C≡C bonds of a terminal, acetylenic group (C≡C–H), together with absorption at 7.25 μm indicative of a CMe_2 group, and broad absorption (2.81–2.90 μm) for a hydrogen-bonded hydroxyl group. Both products were levorotatory in chloroform solution; the L-*ido* epimer had $[\alpha]_D^{25}$ −23°, and the D-*gluco* epimer, $[\alpha]_D^{25}$ −7°.

Both epimers gave readily interpretable, 100-MHz, p.m.r. spectra (see Figs. 1 and 2). Assignments were confirmed by decoupling and by proton–deuterium exchange at the hydroxyl group. Full details are recorded in Tables I and II. The acetylenic proton resonated as the anticipated, narrow doublet (L-*ido*, δ 2.55; D-*gluco*, δ 2.62), showing a $J_{5,7}$ coupling of 2.5 Hz. The signal of H-5 appeared (after deuterium exchange) as a well-resolved doublet of doublets showing a small spin-coupling (2.5 Hz) with H-7, and a larger spin-coupling with H-4. The $J_{4,5}$ value for the

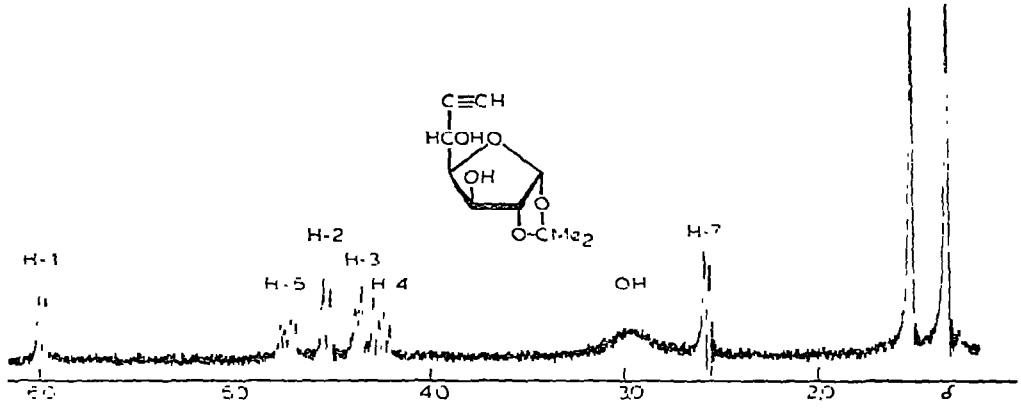


Fig 1. The partial p.m.r. spectrum of 6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-hept-6-ynofuranose (**2**) at 100 MHz in chloroform-*d*.

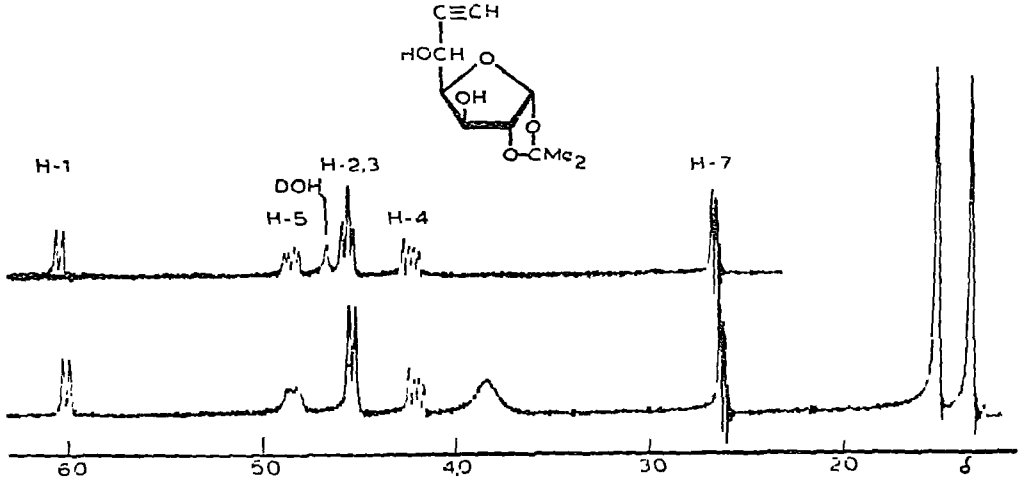


Fig 2. The partial p.m r. spectrum of 6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*gluco*-hept-6-ynofuranose (**3**) at 100 MHz in chloroform-*d*. The upper trace was recorded after addition of one drop of D_2O.

L-*ido* epimer **2** was 5.5 Hz, and for the D-*gluco* epimer **3**, 5.0 Hz. The H-4 resonance was manifested as another doublet of doublets that showed the $J_{4,5}$ spin-coupling, and a second spacing (3.5 Hz) that was taken as the magnitude of $J_{3,4}$. As the magnitude of $J_{2,3}$ is approximately zero, the closely proximal H-3 and H-2 signals did not show second-order perturbation. The H-1 signal was observed as a doublet ($J_{1,2}$ 3.5 Hz) at δ 5.97 for **2**, and at δ 5.99 for **3**. These assignments for H-1, 2, and 3 follow well-established precedents[3,5] for this general fused-ring system.

TABLE I

CHEMICAL SHIFTS OF PROTONS

Compd	*Solvent*	*Chemical shifts (δ) from 100-MHz spectra*[a]											
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-7*	*H-7'*	*Ar*	*CMe_2*	*OAc*	*OMe*	*OH*
2	$CDCl_3$	5.97d	4.52d	4.35d	4.24dd	4.71dd		2.56d			1.32, 1.51			
3	$CDCl_3$[b]	5.99d	4.53d	4.36d	4.17dd	4.80dd		2.62d			1.35, 1.52			
4	$CDCl_3$	6.00d	4.65d	5.68d	4.77dd	5.93dd		2.43d		7.74–7.26, 8.04–8.02	1.32, 1.51			
5	$CDCl_3$	5.93d	4.49d	5.39d	4.54dd	5.57dd		2.43d			1.31, 1.53	2.11, 2.09		
6	$CDCl_3$	6.05d	4.67d	5.58d	4.78dd	5.89d		2.53d		7.63–7.25, 7.87–8.07	1.35, 1.60			
7	$CDCl_3$	5.98d	4.50d	5.36d	4.48dd	5.55dd		2.50d			1.31, 1.52	2.02		
	O ‖													
8	CD_3CCD_3[b]	6.01d	4.91d	5.06	4.75d	4.24s					1.32, 1.47			
	O ‖													
9	CD_3CCD_3[b]	5.96d	4.90d	— 4.71m —		4.63d					1.38, 1.47			
	$CDCl_3$	5.98d	4.80d	4.82d	4.94dd	4.55d					1.35, 1.52			
10	$CDCl_3$	6.08d	4.69d	5.65d	4.93dd	5.71d				7.26–7.58, 7.90–8.12	1.34, 1.58		3.68	
11	$CDCl_3$	6.07d	4.70d	5.71d	4.88dd	5.45				7.27–7.59, 7.90–8.02	1.34, 1.58		3.83s	
12	$CDCl_3$	6.03d	4.65d	5.61d	4.81dd	5.52m	3.94dd[d] 3.81dd			7.26–8.10	1.58, 1.32			2.36
14	$CDCl_3$	6.01d	4.66d	5.56d	4.80dd	5.47m	4.12dd[d] 4.01dd			7.26–8.01	1.59, 1.32			2.37
15	$CDCl_3$[b]	6.00d	4.53d	4.26d	4.08dd	4.54dd	6.03oct	5.42sxt	5.25sxt		1.28, 1.48			
16	$CDCl_3$[b]	5.99d	4.51d	4.31d	4.01dd	4.65dd	6.02oct	5.46sxt	5.28sxt		1.34, 1.51			
17	$CDCl_3$	6.04d	4.64d	5.49d	4.63dd	5.72–6.05m		5.36sxt	5.25sxt	7.65–7.39, 8.18–8.03	1.33, 1.60			
18	$CDCl_3$	6.03d	4.65d	5.58d	4.61dd	5.82dd	6.12oct	5.45sxt	5.33sxt	7.51–7.33, 8.01–7.85	1.32, 1.57			

[a]First-order values are given. Observed multiplicities: d, doublet; dd, doublet of doublets; oct, octet; s, singlet; sxt, sextet. [b]Under proton-deuterium exchange, OH signal disappears. [c]Prime refers to the *cis*-proton of alkenes. [d]AB portion of an ABX system.

TABLE II

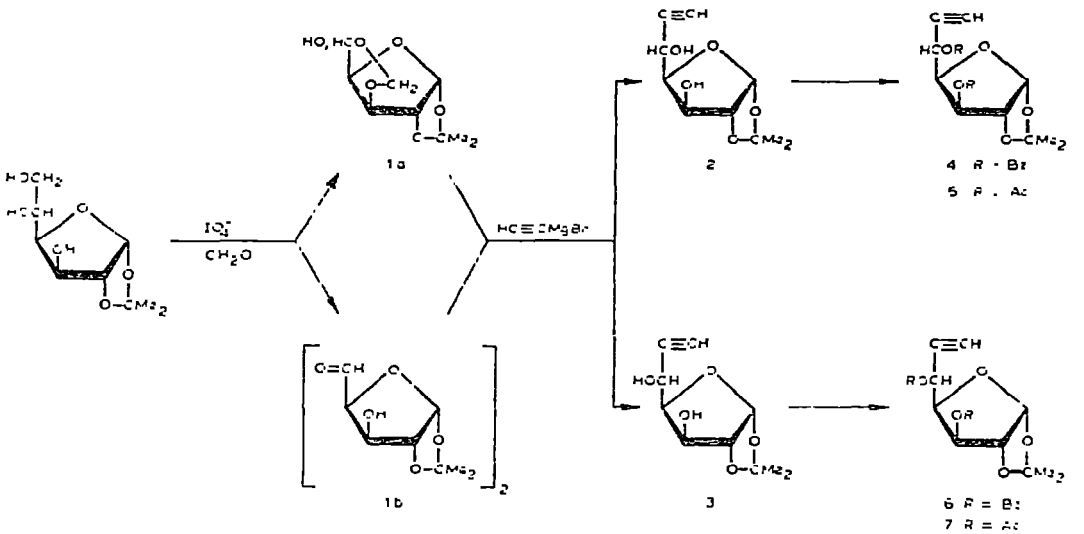
FIRST-ORDER, PROTON–PROTON COUPLING-CONSTANTS

Compd.	Solvent	Coupling constants (Hz) from 100-MHz spectra										
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,7}$	$J_{4,7}$[b]	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$	Other
2	$CDCl_3$	3.5	0	3.0	5.5		2.5					
3	$CDCl_3$[a]	3.5	0	2.5	5.0		2.0					
4	$CDCl_3$	4.0	0	3.5	9.0		2.5					
5	$CDCl_3$	3.5	0	3.5	9.0		2.0					
6	$CDCl_3$	3.5	0	3.5	8.0		2.5					
7	$CDCl_3$	3.5	0	3.0	8.5		2.0					
8	$CD_3\overset{O}{\overset{\|}{C}}CD_3$[a]	3.0	0	4.0	0							
9	$CD_3\overset{O}{\overset{\|}{C}}CD_3$[a]	3.5	0		4.5							
	$CDCl_3$	3.5	0	3.0	4.0							
10	$CDCl_3$	4.0	0	3.5	7.0							
11	$CDCl_3$	4.0	0	3.5	9.0							
12	$CDCl_3$	4.0	0	3.5	7.5	3.3 4.7[c]						12.5 ($J_{6,6'}$)
14	$CDCl_3$	4.0		3.0	9.0	3.0[c] 4.0						12.5 ($J_{6,6'}$)
15	$CDCl_3$[a]	3.5	0	3.0	4.0	5.5	1.2	1.0	17.0	10.0	1.5	
16	$CDCl_3$[a]	3.5	0	3.0	5.0	5.0	1.7	1.5	15.0	10.5	1.7	
17	$CDCl_3$	4.0	0	3.0	8.0	5.5	3.0	1.7	13.0	8.0	2.5	
18	$CDCl_3$	3.5	0	3.0	9.0	5.5	2.0	1.0	17.5	10.5	2.0	

[a]Spectra were simplified by proton–deuterium exchange. [b]Prime refers to the *cis*-proton of alkenes. [c]AB portion of an ABX system.

Benzoylation of the mixture of **2** and **3** gave a brown syrup which, after fractional recrystallization, afforded 3,5-di-*O*-benzoyl-6,7-dideoxy-1,2-*O*-isopropylidene-*β*-L-*ido*-hept-6-ynofuranose (**4**) in 34% yield. This product was identical with that obtained by benzoylation of the pure L-*ido* epimer **2** and with the product previously obtained[3] by benzoylation of a noncrystalline preparation of **4**. Unknown impurities impeded the isolation of the D-*gluco* epimer from the mixture. The benzoylated derivative (**6**) of the D-*gluco* epimer was obtained by benzoylation of pure compound **3**. Both compounds **2** and **3** were also characterized as their crystalline 3,5-diacetates (**5** and **7**, respectively).

The p.m.r. spectra of the benzoates (**4** and **6**) and acetates (**5** and **7**) showed the signal for the acetylenic proton as a narrow, high-field doublet. The magnitude of $J_{4,5}$ for each of the two epimers increased with the conversion of **2** and **3** into their respective benzoates (**4** and **6**) and acetates (**5** and **7**). However, the difference between $J_{4,5}$ for the epimers remained small (9.0 Hz for **4** and **5**, 8.0 Hz for **6**, and 8.5 Hz for



7), and it is thus not feasible to use p.m.r. data as a basis for reliable, stereochemical assignments at C-5 in this series of derivatives (see later discussion).

In the previous study[3], a syrup containing mainly the L-*ido* epimer **2** was treated in carbon tetrachloride with an excess of ozone, to afford 1,2-*O*-isopropylidene-β-L-idofuranurono-6,3-lactone (**8**) in 15% yield. As it has been shown[6] that the ozonolysis of simple α-hydroxyacetylenes to α-hydroxy acids may be effected in quantitative yield if a small proportion of protic solvent is present, the effect of adding acetic acid was examined, and a significant improvement in yield was observed.

Each of the pure acetylenic compounds **2** and **3**, in 17:3 (v/v) carbon tetrachloride–acetic acid, was treated at 0° with an excess of ozone. The acetylenic group was cleaved, to generate the respective carboxylic acids, which lactonized readily with the 3-hydroxyl group, to give the known 1,2-*O*-isopropylidene-β-L-idofuranurono-6,3-lactone[7] (**8**) and 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone[8] (**9**), isolated in 42 and 41% yields, respectively. These conversions provided firm chemical proof of the stereochemistry at C-5 of the precursors, and afford a useful preparative route to the important L-iduronic acid derivative **12**. When the crude D-*gluco* isomer was used, an ill-defined, syrupy mixture was obtained. It is important that the acetylenic precursors be pure if complication in the ozonolysis reaction is to be avoided.

As the free uronic acids[7,8] may be obtained by hydrolysis of the lactone derivatives **12** and **13** with acid, this route appears to be a convenient method for preparing L-iduronic acid.

The D-*gluco* lactone (**9**) and the L-*ido* lactone (**8**) exhibited a significant difference in their n.m.r. spectra in acetone-d_6. The L-*ido* epimer (**8**) showed a 1-proton singlet for H-5. In contrast, the D-*gluco* epimer showed a doublet for H-5, displaying a coupling with H-4 of 4.5 Hz. The absence of spin coupling between H-4 and H-5 of

the L-*ido* epimer suggests, on the basis of the Karplus equation[9], that the H-4–H-5 dihedral angle is ~90°. Overlapped multiplets are observed for H-2, H-3, and H-4 in the n.m.r. spectrum of the D-*gluco* epimer. Changes in spectral dispersion, affording simplification of the n.m.r. spectra, were achieved by adding the lanthanide shift-reagent, tris(2,2,6,6-tetramethylheptanedionato)europium(III). This reagent was described by Hinckley[10], who showed that it induces an isotropic shift of certain signals that is linearly related to the mole ratio of shift reagent to substrate[10]. Use of this shift reagent has been described for several sugar derivatives[11]. The $Eu(dpm)_3$ associates with the substrate at the hydroxyl group, and the induced shifts decrease

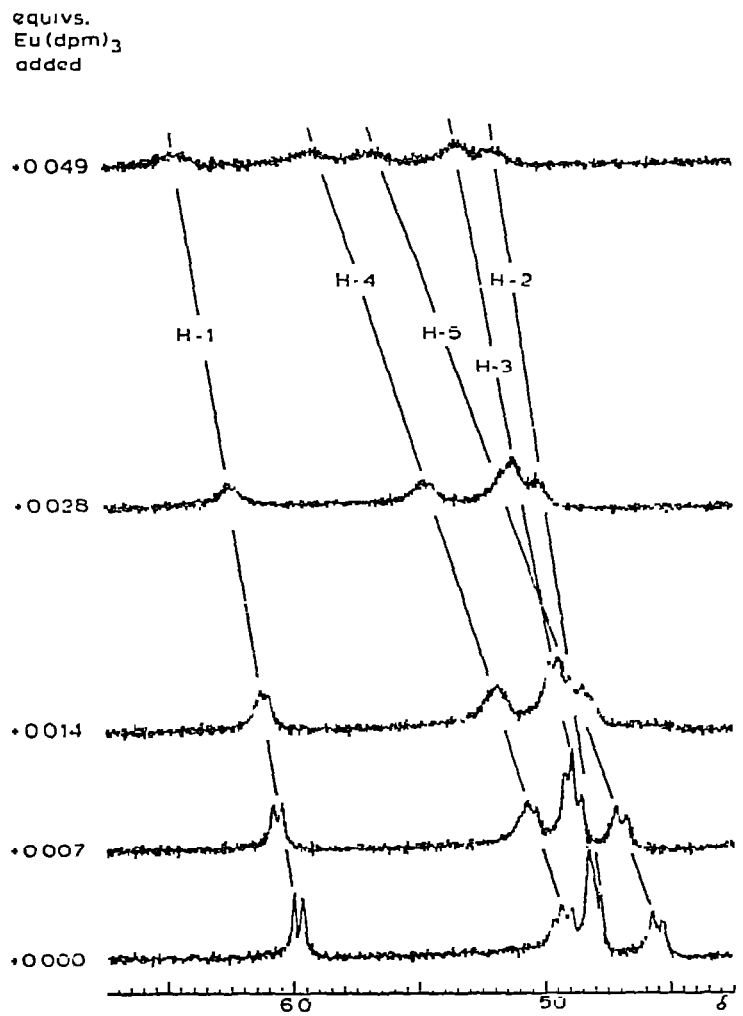
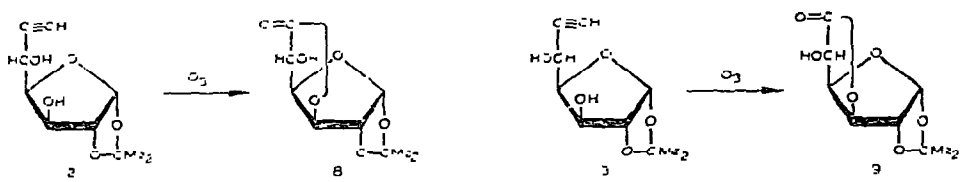
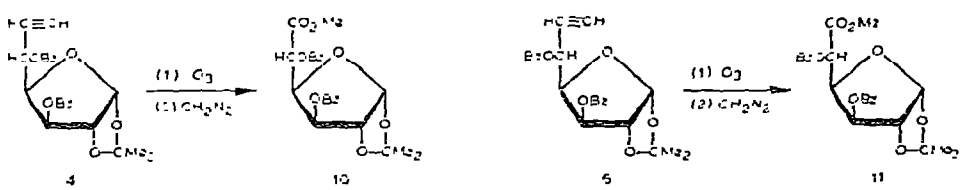


Fig. 3. The 100-MHz spectrum of 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (**8**) in chloroform-*d*, with progressive addition of $Eu(dpm)_3$ [tris(2,2,6,6-tetramethylheptanedionato)-europium(III)] in the proportions (moles per mole of **8**) indicated.

rapidly with increasing distance of the protons from the hydroxyl group. By extrapolation to zero concentration of the shift reagent, the chemical shifts in the absence of shift reagent may be estimated. In the present study, a linear relationship is observed (see Fig. 3), with H-5 showing the largest paramagnetic shift-gradient. The original chemical-shifts of H-2 (δ 4.80) and H-3 (δ 4.82) for compound **13** may be obtained by extrapolation.

The 3,5-di-*O*-benzoyl-6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*(and α-D-*gluco*)-hept-6-ynofuranoses (**4** and **6**) were also ozonized, producing 3,5-di-*O*-benzoyl-1,2-*O*-*O*-isopropylidene-β-L-ido(and α-D-gluco)furanuronic acids. These acids were not readily isolated pure from the mixture, and the crude products were treated with diazomethane, and characterized as their methyl esters **10** and **11**, respectively.



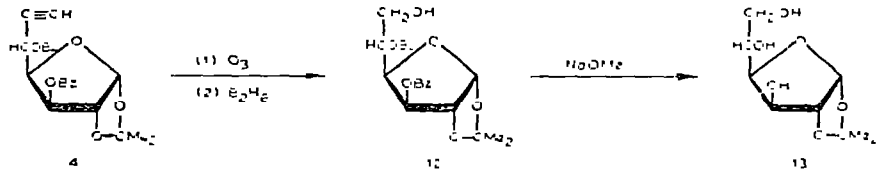


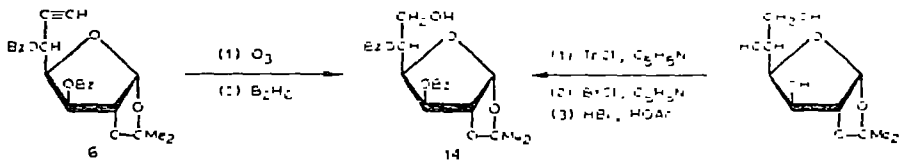
Saponification and subsequent acid hydrolysis of the methyl esters **10** and **11** would be an unsatisfactory route to the free uronic acids, as the base used for saponification can be expected to cause epimerization at the α-carbon atom (C-5), by analogy with results in similar systems[3].

Additional studies were undertaken to examine the stereochemical integrity of the α-carbon atom of uronic acids during reduction with diborane. The uronic acids obtained by ozonolysis of 3,5-di-*O*-benzoyl-6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*(and α-D-*gluco*)-hept-6-ynofuranose (**4** and **6**) were treated with an excess (of at least three equivalents) of diborane, yielding 3,5-di-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-ido(and α-D-gluco)furanose (**12** and **14**), respectively. The L-*ido* derivative **12** was crystalline, whereas the D-*gluco* derivative was a syrup.

The presumed retention of configuration at the α-carbon atom adjacent to the reaction site was proved by saponification of the L-*ido* derivative **12** to give 1,2-*O*-isopropylidene-β-L-idofuranose (**13**). This product was identical with that previously obtained by reduction of 1,2-*O*-isopropylidene-β-L-idofuranurono-6,3-lactone with

lithium aluminum hydride[7]. The D-*gluco* 3,5-dibenzoate derivative **18** was synthesized independently from 1,2-*O*-isopropylidene-α-D-glucofuranose through sequential tritylation, benzoylation, and detritylation, and the two samples were found identical. These reactions thus establish that there is retention of configuration at C-5 of the uronic acid during reduction by diborane.





Both epimeric dibenzoates **12** and **14** gave interpretable, 100-MHz, p.m.r. spectra. The spectra showed the anticipated ABX system for H-5, H-6, and H-6′. The H-6 and H-6′ signals of each compound appeared as two closely spaced, but resolvable, four-line patterns, and H-5 gave rise to a multiplet. ABX analysis of the p.m.r. data yielded, for the D-*gluco* derivative, $J_{5,6}$ 3.0 Hz and $J_{5,6'}$ 4.0 Hz; and for the L-*ido* derivative, $J_{5,6}$ 3.3 Hz and $J_{5,6'}$ 4.7 Hz. Both compounds displayed geminal coupling-constants ($J_{6,6'}$) of 12.5 Hz. The difference between the $J_{5,6}$ and $J_{5,6'}$ couplings is smaller than that obtained from a related system studied previously[12], but the latter example had a pyranoid ring, and H-5 was consequently attached to a ring-carbon atom. Assignment of favored conformations was not made, because of the complexity inherent in a system where free rotation about C-5–C-6, and 1,3-dipolar interaction between O-6 and the oxygen atom of the furanose ring, may be involved.

Reduction of the propargyl alcohols **2** and **3** was performed with lithium aluminum hydride[13], to give the respective allylic alcohols (**15** and **16**) in essentially quantitative yield.

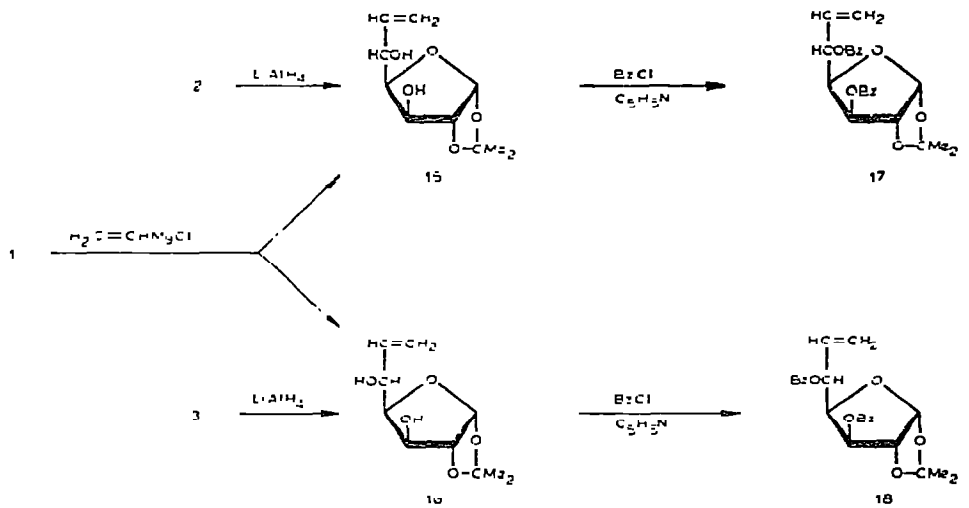
The i.r. spectra of the alkenes **15** and **16** were consistent with the disappearance of the acetylenic group and the appearance of a vinyl group. The 100-MHz, p.m.r. spectra of the alkenes **15** and **16** showed the anticipated ABX system for the vinyl protons[14]. The H-7 and H-7′ signals appeared as resolved, four-line patterns, and H-6 gave a multiplet. The ABX system showed a *trans* coupling of 17.0 Hz, a *cis* coupling of 10.0 Hz, a geminal coupling of 1.5 Hz, and a long-range coupling of

1.5 Hz between H-5 and H-7; these values accord with general literature values for vinyl derivatives[15]. In the p.m.r. spectrum of the L-*ido* epimer, the H-2 and H-5 signals resonated as an overlapped multiplet at 4.49–4.59 p.p.m., whereas the D-*gluco* epimer showed the H-2 and H-5 signals as a well-resolved doublet and quartet, respectively.

This reduction procedure[13] for converting propargyl alcohols into allylic alcohols is procedurally superior to hemihydrogenation[16] in the presence of Lindlar catalyst, because yields are excellent and there is no evidence for incomplete reduction, or over-reduction to the saturated derivative.

The alkenes **15** and **16** were alternatively prepared by vinylation of the crude aldehyde (**1a** plus **1b**) with vinylmagnesium chloride. The reaction gave a syrupy mixture of **15** and **16** in an overall yield of 76%. The two isomers were separated by column chromatography on silica gel with 1:1 ether–petroleum ether as eluant, to give crystalline **15** and **16** in the relative yields of 3:2. The physical data for the two epimers were identical with those of those prepared by reduction of the alkynes **2** and **3** with lithium aluminum hydride.

Preparation of the alkenes **15** and **16** by reduction of their respective alkynes **2** and **3** with lithium aluminum hydride offered a procedural advantage, in that the acetylenic Grignard reagent was found less difficult to prepare than the vinylic Grignard reagent. This advantage, together with the ease of separation of the acetylenic compounds, in contrast to their alkenic counterparts in other systems[17], demonstrates that the route to alkenic sugar derivatives, by reduction of acetylenic intermediates, is generally more effective than the direct approach through vinylation.



Both epimeric alkenes **15** and **16** were further characterized as their crystalline 3,5-dibenzoates (**17** and **18**). The L-*ido* isomer **17** was identical to a product obtained by hemihydrogenation of an acetylenic dibenzoate derivative and originally suggested[2]

to be the D-*gluco* isomer. As assignment of the L-*ido* configuration to **17** is based upon firm evidence, the ozonolysis of the parent compound to the known 1,2-*O*-isopropylidene-β-L-idurono-6,3-lactone (**8**), the previous, tentative, configurational assignment[2] must be corrected.

This investigation has furnished eight compounds (**2**, **4**, **5**, **8**, **10**, **12**, **15**, and **17**) having the β-L-*ido* stereochemistry, and eight (**3**, **6**, **7**, **9**, **11**, **14**, **16**, and **18**) having the α-D-*gluco* stereochemistry, all having the same general structure. It was of interest to compare the specific rotations and $J_{4,5}$ values of these eight pairs of derivatives, and these are recorded in Table III.

TABLE III

CORRELATION OF SPECIFIC ROTATION AND $J_{4,5}$ VALUES FOR 4-*C*-SUBSTITUTED 1,2-*O*-ISOPROPYLIDENE-α-D-TETROFURANOSES HAVING THE α-D-*gluco* AND β-L-*ido* STEREOCHEMISTRY[a]

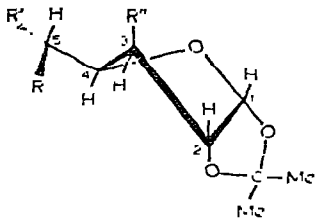
4-Substituent (*3-substituent*)	L-ido			D-gluco		
	Compd.	$J_{4,5}$ (*Hz*)	$[\alpha]_D^{25}$ (*degrees*)	*Compd*	$J_{4,5}$ (*Hz*)	$[\alpha]_D^{25}$ (*degrees*)
HC≡C-CHOH-(3-OH)	**2**	5.5	−23	**3**	5.0	−7.0
HC≡C-CHOBz-(3-OBz)	**4**	9.0	−15.4	**6**	8.0	−97.0
HC≡C-CHOAc-(3-OAc)	**5**	9.0	+15.9	**7**	8.5	−27.0
H_2C=CH-CHOH-(3-OH)	**15**	4.0	−20	**16**	5.0	−5.0
H_2C=CH-CHOBz-(3-OBz)	**17**	8.0	−49	**18**	9.0	−61.0
-(C=O)CHOH-(6,3-lactone)	**8**	0[b]	+101.8[b] +109.4	**9**	4.5[b]	+73.3[b] +50.5
MeO_2C-CHOBz-(3-OBz)	**10**	7.0	+8.0	**11**	9.0	−51.0
HOH_2C-CHOBz-(3-OBz)	**12**	7.5	+8.5	**14**	9.0	−84.5

[a]Measured in chloroform-*d*, except where indicated. [b]Measured in acetone-d_6.

Several studies concerned with p.m.r.-spectral comparisons of epimeric propargylic alcohols have been reported from this laboratory[2,3,16–19]. A substantial, configurationally dependent difference in coupling constant between the propargylic (-C≡C-C*H*) proton and the vicinal proton has been generally observed for the ethynylation products of various aldehydo sugars, except for the products from 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose, where the epimers had almost identical couplings[13]. The latter system resembles the present examples, in that the proton vicinal to the propargylic proton is attached to a carbon atom in the sugar ring.

In the present study, the spectra showed a large spin-coupling of ~9 Hz between H-4 and H-5 for all of the derivatives except the 3,5-dihydroxy acetylenic compounds (**2** and **3**), whose $J_{4,5}$ values were ~5 Hz. These observations indicate a

favored, antiparallel disposition of H-4 and H-5 in the ester derivatives. Evidently, the two bulkier groups R and R' always favor an orientation away from the furanoid ring, so that H-5, the smallest substituent at C-5, lies over the ring and is approximately antiparallel to H-4.



4 R = -C≡CH, R' = R" = -OBz
5 R = -C≡CH, R' = R" = -OAc
6 R = R" = -OBz, R' = -C≡CH
7 R = R" = -OAc, R' = -C≡CH
17 R = -CH=CH$_2$, R' = R" = -OBz
18 R = R" = -OBz, R' = -CH=CH$_2$

The alkenes **15** and **16** (and their benzoates **17** and **18**) showed $J_{4,5}$ values similar to those of the corresponding alkynes.

All of the derivatives exhibited very small, or zero, coupling between H-2 and H-3 ($J_{2,3}$ <0.3 Hz). This result is consistent with related work on various 3-*O*-benzyl analogs[3], and is in line with data in other published reports on this fused-ring system[5].

EXPERIMENTAL

General methods. — Evaporations were performed in a rotary evaporator under diminished pressure (~15 mm) at 45°. Specific rotations were measured in a 1-dm tube with a Perkin–Elmer Model 141 photoelectric polarimeter. Melting points were determined with a Thomas–Hoover "Unimelt" apparatus. I.r. spectra were recorded with a Perkin–Elmer Model 137 spectrophotometer. N.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer; for routine monitoring of reactions, a Varian A-60 60-MHz spectrometer was used. Chemical shifts refer to an internal standard of tetramethylsilane ($\delta = 0.00$) for organic solutions. Microanalyses were performed by W. N. Rond. X-Ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually: m, moderate; s, strong; v, very, and w, weak. The strongest lines are numbered (1, strongest), multiple numbers indicate approximately equal intensities. Thin-layer chromatography (t.l.c.) was performed on Silica Gel G (E. Merck, Darmstadt, Germany), activated at 110°, as the adsorbent. Unless otherwise indicated, the developers used were *A*, 1:1 ether–petroleum ether (b.p. 30–60°), and *B*,

3:1 chloroform–ether. Detection was effected by spraying with sulfuric acid, unless otherwise specified. Column chromatography was performed with Silica Gel No. 7734 (0.05–0.2 mm mesh size, E. Merck AG), with 1 g of the mixture to be separated per 30 g of adsorbent. The petroleum ether used was a fraction having b.p. 30–60°. G.l.c. was performed in a Beckman model GC-5 gas chromatograph by using a stainless-steel column (152.4 cm × 3.17 mm) with 10% (w/w) of neopentyl glycol sebacate polyester on Chromosorb W (80–100 mesh) (Analabs, Inc., Hamden, Connecticut). Helium was used as the carrier gas at a flow-rate of 45 ml.min^{-1}, and the column temperature was maintained at 145°. Ozone was generated by using a Welsbach ozonator, model T-408 (The Welsbach Company, Philadelphia, Pennsylvania).

Preparation of 1,2-O-isopropylidene-α-D-xylo-pentodialdo-1,4-furanose "dimer" (**1b**) *and 1,2-O-isopropylidene-3,5-O-methylene-α-D-xylo-pentodialdo-1,4-furanose 5-aldehydrol* (**1a**). — The original procedure[4], as later modified[3], was used, on 5 times the scale and with minor modifications. To a solution of 1,2-*O*-isopropylidene-α-D-glucofuranose[20] (30 g, 13.7 mmol) in 37% aqueous formaldehyde (350 ml) cooled in an ice bath was slowly added a solution of sodium metaperiodate (30 g, 14 mmol) in water (250 ml), with stirring. After 3 h, ethylene glycol (1.5 ml) was added to decompose any unreacted periodate. The solution was concentrated to half the original volume, and the sodium iodate that precipitated was filtered off. The solution was extracted with five 100-ml portions of chloroform. The dried (magnesium sulfate) extract was evaporated to a syrup (yield 20.65 g, 69.5%) which contained mainly **1a** (R_f 0.75, ether; Schiff positive), together with a small proportion of **1b** (R_F 0.40, ether; Schiff negative).

For these products, Schaffer and Isbell[4(a)] recorded a yield of 64% (hydrated form); Inch[4(b)], 62%; and Horton and Swanson[3], 59%.

*Preparation of 6,7-dideoxy-1,2-O-isopropylidene-β-*L*-ido(and-α-*D*-gluco)-hept-6-ynofuranose* (**2** *and* **3**) — The initial mixture of **2** and **3** was prepared essentially as previously described[3]. A solution of ethyl bromide (48 g) in dry tetrahydrofuran (300 ml) was slowly added to magnesium dust (10 g) that was covered with dry tetrahydrofuran (50 ml). The mixture was vigorously stirred, to initiate the exothermic reaction, which was allowed to continue until it subsided. Acetylene was then passed slowly through dry tetrahydrofuran (500 ml) in a 2-liter flask by means of a gas-dispersion tube, and the liquid was stirred magnetically. After 1 h, the solution of ethylmagnesium bromide was added dropwise to the tetrahydrofuran through an addition funnel. The resultant solution was stirred for 1 h while the stream of acetylene gas was maintained. To the dark-brown solution, a solution of the mixture of **1a** and **1b** (20 g, 101 mmoles; from the preceding experiment) in dry tetrahydrofuran (100 ml) was added dropwise, with stirring, at room temperature, a slow stream of acetylene being passed through the solution throughout the reaction. Stirring, and passage of acetylene gas, were continued for an additional 2 h. The solution was evaporated, and ethyl ether (200 ml) was added to the residual syrup. The mixture was shaken with cold, aqueous, saturated ammonium chloride, and the aqueous phase was extracted with ether (4 × 200 ml). The extracts were combined,

washed, dried (magnesium sulfate), and evaporated, to give a dark-brown syrup that was a mixture of the epimers **2** and **3**; yield 14.4 g (73.5%). The epimers had R_F 0.20 (**3**) and 0.10 (**2**), respectively (1:1 ether–petroleum ether).

Separation of the epimers **2** *and* **3** — A suspension of silica gel (450 g) in 1:1 petroleum ether–ether was poured into a column (1.25 m × 5 cm), and allowed to settle. The syrupy mixture of **2** and **3**, dissolved in 1:1 petroleum ether–ether (20 ml), was placed on the top of the column. Elution with the same solvent-mixture gave two components, resolved completely from each other. The first product to be eluted, the D-*gluco* epimer (**3**) was a solid; yield 2.58 g (18%); R_F 0.20 (solvent *A*), 0.25 (solvent *B*). This epimer was purified by distillation at 140°/0.05 torr, whereupon it had m.p. 87–89°, $[\alpha]_D^{25}$ −7° (*c* 1.0, chloroform); λ_{max}^{KBr} 3.03 (C≡C–H), 4.65 (C≡C), and 7.25 μm (doublet, CMe_2); X-ray powder diffraction data: 9.93 s (2,2), 7.46 w, 6.23 s (2,2), 4.95 vs (1), 4.57 m, 4.26 m, 4.05 w, 3.56 w, 3.30 vw, 2.92 w, and 2.72 m.

Anal. Calc. for $C_{10}H_{14}O_5$: C, 56.01; H, 6.58. Found: C, 56.00; H, 6.72.

The second component to be eluted, the L-*ido* epimer (**2**), was also obtained as a solid; yield 3.80 g (26%), R_F 0.10 (solvent *A*), 0.15 (solvent *B*). Recrystallization from ether–petroleum ether gave pure **2**, m.p. 126–128°, $[\alpha]_D^{25}$ −23 (*c* 0.7, chloroform); λ_{max}^{KBr} 3.03 (C≡C–H), 4.68 (C≡C), and 7.25 μm (doublet, CMe_2); X-ray powder diffraction data: 8.93 vs (2), 6.91 m, 5.43 s, 4.85 vs (1), 4.43 m, 3.91 m, 3.74 m, 3.45 s (3,3), 3.24 s (3,3), 2.93 m, 2.85 w, and 2.77 w.

Anal. Calc. for $C_{10}H_{14}O_5$: C, 56.01; H, 6.58. Found: C, 55.97; H, 6.59.

The latter compound had been isolated[3] as a syrup, b.p. 125–135° (75 mtorr, bath temp. 175–185°) in 34% yield.

A 1:1 mixture of the epimers melted over the range 64–75°.

O-Trimethylsilyl derivatives of **2** *and* **3**. — The di-*O*-trimethylsilyl derivatives of the acetylenic compounds **2** and **3** were prepared by shaking each sample (10 mg) with 1 ml of a mixture of chlorotrimethylsilane and hexamethyldisilazane in pyridine (Tri-Sil, Pierce Chemical Company, Rockford, Illinois). The prepared samples were kept for 20 min before injection into a g.l.c. column (see General methods). The bis(trimethylsilyl) ether of the D-*gluco* epimer (**3**) had a retention time of 17.5 min, and that of the L-*ido* epimer, 11 min. Each product was epimerically pure. By using a calibration curve obtained with the pure bis(trimethylsilyl) ethers of **2** and **3**, it was determined that the ratio of **2** to **3** in the crude mixture was 14:11.

*Preparation of 3,6-di-O-benzoyl-6,7-dideoxy-1,2-O-isopropylidene-β-*L*-ido-hept-6-ynofuranose* (**4**). — To a solution of pure, crystalline **2** (600 mg, 2.8 mmol) in dry pyridine (5 ml) at 0° was slowly added benzoyl chloride (1 ml) dissolved in dichloromethane (3 ml), and the solution was stirred overnight. The mixture was poured into cold, aqueous sodium hydrogencarbonate solution (30 ml), and the product was extracted with two 30-ml portions of dichloromethane. The extract was evaporated, and toluene was several times added to, and evaporated from, the residue to remove pyridine. The product was recrystallized from abs. ethanol; yield 1.30 g (87%), m.p. 195–196°, $[\alpha]_D^{25}$ −15.4° (*c* 1, chloroform); R_F 0.90 (solvent *A*), 0.96 (solvent *B*).

Compound **4** had been prepared[3] in 49% yield by benzoylation of syrupy **2**

obtained by distillation of a mixture of **2** and **3**; constants reported were[3] m.p. 195–196°, $[\alpha]_D^{18}$ $-16 \pm 3°$ (*c* 1.04, chloroform). The X-ray powder diffraction patterns[3] and i.r. spectra of the two samples were identical.

Benzoylation of the crude, unseparated mixture of **2** and **3**, followed by recrystallization of the product from abs. ethanol, gave **4** in 34% yield; further treatment of the mother liquors did not lead to isolation of the D-*gluco* dibenzoate **6**.

3,5-Di-O-acetyl-6,7-dideoxy-1,2-O-isopropylidene-β-L-ido-*hept-6-ynofuranose* (**5**). — To a solution of the acetylenic alcohol **2** (200 mg) in acetic anhydride (3 ml) was added anhydrous sodium acetate (100 mg), and the mixture was heated for 30 min at 90° and then boiled for 1 min. The solution was cooled, poured into ice–water (30 ml), and kept for 1 h; the solution was extracted with three 30-ml portions of dichloromethane, and the extract was successively washed with water (30 ml) and saturated, aqueous sodium hydrogencarbonate (30 ml), dried (magnesium sulfate), and evaporated, to give **5**, which was recrystallized from abs. ethanol; yield 232 mg (83%), m.p. 89–90°, $[\alpha]_D^{25}$ +15.9° (*c* 0.9, chloroform); R_F 0.70 (solvent *A*), 0.88 (solvent *B*); λ_{max}^{KBr} 3.03 (C≡C–H), 4.68 (C≡C), 5.70 (C=O), and 7.30 μm (doublet, CMe_2); X-ray powder diffraction data: 11.63 s (2,2), 8.58 w, 6.55 s (2,2), 6.00 w, 5.36 vs (1), 5.01 s, 4.52 s (3,3,3), 4.06 s (3,3,3), 3.64 s (3,3,3), 3.45 m, and 3.23 m.

Anal. Calc. for $C_{14}H_{18}O_7$: C, 56.37; H, 6.04. Found: C, 56.27; H, 6.18.

3,5-Di-O-benzoyl-6,7-dideoxy-1,2-O-isopropylidene-α-D-gluco-*hept-6-ynofuranose* (**6**). — The crude α-D-*gluco* epimer **3** (444 mg) was benzoylated by the procedure used for conversion of **2** into **4**, to give the dibenzoate **6** as a solid; yield 557.5 mg (63.5%); m.p. 73–75°, $[\alpha]_D^{25}$ $-97°$ (*c* 1.6, chloroform); R_F 0.85 (solvent *A*), 0.96 (solvent *B*); λ_{max}^{KBr} 3.03 (C≡C–H), 4.68 (C≡C), 5.78 (C=O), 7.25 μm (doublet, CMe_2), and 14.10 μm (aryl); X-ray powder diffraction data: 10.65 s (2,2,2), 9.50 vs (1), 7.73 vw, 7.19 w, 6.41 m, 5.59 vs (2,2,2), 5.27 m, 4.79 s (2,2,2), 4.29 m, 4.16 w, and 3.93 m.

Anal. Calc. for $C_{24}H_{22}O_7$: C, 68.23; H, 5.24. Found: C, 68.34; H, 5.50.

3,5-Di-O-acetyl-6,7-dideoxy-1,2-O-isopropylidene-α-D-gluco-*hept-6-ynofuranose* (**7**). — Prepared from the D-*gluco* acetylene **3** (200 mg) by the method used for the 5-epimer **5**, and recrystallized from ethanol, the product **7**, yield 203 mg (73%), had m.p. 79–81°, $[\alpha]_D^{25}$ $-27°$ (*c* 0.54, chloroform); R_F 0.70 (solvent *A*), 0.88 (solvent *B*); λ_{max}^{KBr} 3.04 (C≡C–H), 4.68 (C≡C), 5.70 (C=O), and 7.30 μm (doublet, CMe_2). X-ray powder diffraction data: 10.04 m, 9.17 s (2,2), 6.93 s (2,2), 6.80 vw, 5.79 vs (1,1), 5.15 m, 4.55 vs (1,1), and 4.31 m.

Anal. Calc. for $C_{14}H_{18}O_7$: C, 56.37; H, 6.04. Found: C, 56.49; H, 6.24.

Preparation of 1,2-O-isopropylidene-β-L-*idofuranurono-6,3-lactone* (**8**). — The crystalline, epimerically pure alkyne **2** (500 mg) was dissolved in a mixture of carbon tetrachloride (85 ml) and acetic acid (15 ml) at 0. The temperature was maintained at 0° while ozone was passed through the solution for 40 min, and then pure oxygen was passed through until the blue color had been discharged, the solution was evaporated to a syrup, and several portions of toluene were added to, and evaporated from, the residual syrup. The latter was dissolved in ether, and the solution was passed through a small column of silica gel. Crystallization from the effluent gave pure **8**; yield 210 mg

(42%); m.p. 134–135°, $[\alpha]_D^{25}$ +101.8° (*c* 0.5, acetone), +109.4° (*c* 0.8, chloroform); R_F 0.90 (solvent *A*). For this compound, Wolfrom and co-workers[7] reported m.p. 137–138°, $[\alpha]_D^{26}$ +100° (*c* 2, acetone). The X-ray powder diffraction patterns of these two samples were identical; data: 6.37 s (2,2), 5.57 m (4,4,4,4), 4.84 vs (1), 4.37 s (3,3), 4.17 s (2,2), 3.98 m (4,4,4,4), 3.83 m, 3.57 m (4,4,4,4), 3.83 m, 3.57 m (4,4,4,4), 3.40 s (3,3), 3.22 w, 3.13 vw (5,5), 2.98 vw (5,5), 2.79 w, and 2.32 m.

Starting from a syrupy preparation of **2**, compound **8** has been obtained[3] in 15% yield; m.p. 135–136°.

*1,2-O-Isopropylidene-α-*D*-glucofuranurono-6,3-lactone* (**9**). — Ozonolysis of the pure, distilled, crystalline D-*gluco* alkyne **3** (571 mg), as just described for the L-*ido* epimer **8**, gave the D-*gluco* lactone **9**; yield 234 mg (41%); m.p. 118–119°, $[\alpha]_D^{25}$ +73.3° (*c* 0.85, acetone), +50.5° (*c* 0.9, chloroform); R_F 0.46 (solvent *A*). The product was identical with an authentic sample by X-ray powder diffraction pattern: data: 10.65 m, 6.86 w, 5.32 vs (1), 4.58 s, 4.07 w (2,2), 3.89 w (2,2), and 3.47 vw. For this compound, Owen and co-workers[21] and Sowden[8] reported m.p. 119–120°, $[\alpha]_D^{26}$ +70° (*c* 1.0, acetone).

*Methyl 3,5-di-O-benzoyl-1,2-O-isopropylidene-β-*L*-idofuranuronate* (**10**). — To an ice-cold solution of the alkyne **4** (200 mg, 0.48 mmol) in carbon tetrachloride (85 ml) was added acetic acid (15 ml). Ozone was passed through the solution for 40 min at 0°, and then pure oxygen was passed through until the blue color of ozone had been discharged. The solution was evaporated to a syrup, and several small portions of toluene were added to, and evaporated from, the residue to remove acetic acid. The residue was dissolved in ethyl ether (50 ml), and an excess of diazomethane[22] in ether was added to the solution. The solution was stirred for 30 min, and then aqueous acetic acid was added slowly until the yellow color disappeared and evolution of nitrogen ceased. The solution was evaporated, and the product, dissolved in 1:1 petroleum ether–ether, was passed through a small column packed with silica gel, to give the ester **10** as a solid; yield 102 mg (48%); m.p. 93–94°, $[\alpha]_D^{25}$ +8° (*c* 0.35, chloroform); R_F 0.80 (solvent *A*), 0.96 (solvent *B*); λ_{max}^{KBr} 5.70, 5.80 (C=O), 7.25 (CMe_2), 8.25, 8.60 (CO_2Me), and 14.15 μm (aryl); X-ray powder diffraction data: 11.95 vs, 6.15 m, 4.80 m, 4.51 m, 4.26 s, 3.79 w, and 3.43 vw.

Anal. Calc. for $C_{24}H_{26}O_8$: C, 63.16; H, 5.26. Found: C, 63.45; H, 5.5.

*Methyl 3,5-di-O-benzoyl-1,2-O-isopropylidene-α-*D*-glucofuranuronate* (**11**). — Prepared from the alkyne **6** (250 mg, 0.59 mmol) in the same way as for the L-*ido* derivative, the D-*gluco* ester **11** was obtained as a syrup; yield 106 mg (39%); $[\alpha]_D^{25}$ −51° (*c* 0.4, chloroform); R_F 0.75 (solvent *A*), 0.96 (solvent *B*); λ_{max}^{film} 5.70, 5.80 (C=O), 7.25 (CMe_2), 8.22, 8.60 (CO_2Me), and 14.15 μm (aryl).

Anal. Calc. for $C_{24}H_{26}O_9$: C, 63.16; H, 5.26. Found: C, 63.39; H, 5.52.

*3,5-Di-O-benzoyl-1,2-O-isopropylidene-β-*L*-idofuranose* (**12**). — To tetrahydrofuran (15 ml) containing diborane (15 mmol), under nitrogen, was added a solution of 500 mg (1.19 mmol) of the crude product prepared by ozonolysis of compound **4** in tetrahydrofuran (15 ml); the mixture was kept under nitrogen for 3 h at 0°, and water (1.5 ml) was slowly added dropwise. The solvent was evaporated off under

diminished pressure, and several portions of methanol were added to, and evaporated from, the syrupy residue to remove residual boric acid. The syrup was dissolved in 1:1 ether–petroleum ether, and the solution passed through a small column packed with silica gel. Recrystallization of the eluted product from ether–petroleum ether gave pure **12**; yield 193 mg (38%); m.p. 75–77°, $[\alpha]_D^{25}$ +8.5° (*c* 0.3, chloroform); R_F 0.45 (solvent *A*), 0.75 (solvent *B*); λ_{max}^{KBr} 2.85 (OH), 5.79 (C=O) 7.25 (CMe_2), and 14.15 μm (aryl); X-ray powder diffraction data: 11.91 vs (1), 9.83 w (2,2), 8.50 w (2,2), 5.57 m, 4.92 s, 4.62 w (3,3,3), 4.37 w (3,3,3), and 4.18 w (3,3,3).

Anal. Calc. for $C_{23}H_{24}O_8$: C, 64.48; H, 5.61. Found: C, 64.18; H, 5.69.

1,2-O-*Isopropylidene-β*-L-*idofuranose* (**13**). — To a solution of the 3,5-dibenzoate **12** (113 mg) in methanol (10 ml) was added 3 ml of M methanolic sodium methoxide. The solution was stirred for 3 h at ~25°, and then made neutral by treatment with Amberlite IR-120 (H^+) ion-exchange resin (20 ml) for 10 min. The resin was filtered off, and the filtrate evaporated to give compound **13** as a solid which was recrystallized from methanol–ether, giving pure product; yield 50 mg (87%), m.p. 112–113° (lit.[7] m.p. 113–114°). The product and an authentic sample gave identical X-ray powder diffraction data: 17.60 m, 9.30 s (2), 5.18 w, 4.88 vs (1), 4.48 m, 4.00 vw, 3.75 m, and 3.50 m.

L-*Idose*. — Hydrolysis of compound **13** with 0.05M sulfuric acid for 8 h at 50° by the procedure described by Shafizadeh and Wolfrom[7,23] gave L-idose as a syrup in essentially quantitative yield.

3,5-Di-O-benzoyl-1,2-O-isopropylidene-α-D-glucofuranose (**14**). — Compound **14** was obtained as a syrup when prepared from the D-*gluco* acetylenic derivative **6** (300 mg, 0.71 mmol) by the method used for the L-*ido* epimer **12**, yield 94.5 mg (31%); $[\alpha]_D^{25}$ −84.5° (*c* 0.4, chloroform); R_F 0.40 (solvent *A*), 0.75 (solvent *B*); λ_{max}^{film} 2.85 (OH), 5.82 (C=O), 7.30 (CMe_2), and 14.18 μm (aryl).

Anal. Calc. for $C_{23}H_{24}O_8$: C, 64.48; H, 5.61. Found: C, 64.52; H, 5.36.

3,5-Di-O-benzoyl-1,2-O-isopropylidene-α-D-glucofuranose (**14**), *prepared by an independent route*. — Compound **14** was prepared from 1,2-*O*-isopropylidene-α-D-glucofuranose by successive tritylation, benzoylation, and detritylation[24]. A mixture of 1,2-*O*-isopropylidene-α-D-glucofuranose (2.2 g, 10 mmol), dry pyridine (16 ml), and chlorotriphenylmethane (2.8 g) was stirred vigorously for 3 days at ~25°. The pyridine was removed under diminished pressure, and the residual solid was extracted with ether (two 30-ml portions). The ethereal extract was evaporated to give the crude 6-trityl ether. Without further purification, the ether was benzoylated by the procedure described for conversion of **2** into **4**, to give a syrupy mixture containing 3,5-di-*O*-benzoyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-glucofuranose as the major product.

A solution of this fully protected derivative (2 g) in acetic acid (10 ml) was cooled to 20°, and a solution of hydrogen bromide in acetic acid (2 ml) that had been saturated at 0° was added. The mixture was shaken for 60 seconds and then filtered, the filtrate passing directly into 60 ml of a mixture of ice and water. The bromotriphenylmethane that remained on the filter was washed with cold water, and the combined filtrate and washings were extracted with three 40-ml portions of

chloroform. The extracts were combined, dried (magnesium sulfate), and evaporated to a syrup. Several portions of toluene were evaporated from the residue to remove acetic acid. The residue, dissolved in 1:1 ether–petroleum ether, was passed through a column of silica gel to give compound **14** as a syrup, identical by n.m.r. spectra, i.r. spectra, and specific optical rotations, with the compound prepared by diborane reduction of the ozonolysis product obtained from the acetylenic derivative **6**.

*6,7-Dideoxy-1,2-O-isopropylidene-β-*L*-ido-hept-6-enofuranose* (**15**) *by reduction of the alkyne* **2** *with lithium aluminum hydride.* — A solution of the alkyne **2** (428 mg) in dry ether was added to a suspension of lithium aluminum hydride (300 mg) in ether (50 ml), and the mixture was stirred for 2 h. The following general procedure[25] was used for isolation of the product. Water (0.3 ml) was added very slowly, followed by 15% aqueous sodium hydroxide (0.3 ml), and more water (1 ml). The mixture was filtered, and the filtrate was evaporated, to give **15** as a solid. Recrystallized from ether–petroleum ether, the product (yield 418 mg, 95%), had m.p. 96–98°, $[\alpha]_D^{25}$ −20° (*c* 1.3, chloroform); R_F 0.10 (solvent *A*), 0.17 (solvent *B*); λ_{max}^{KBr} 3.38 (C≡C–H), 6.05 (C=C), and 7.28 μm (doublet CMe_2); X-ray powder diffraction data: 9.45 vs (1,1), 5.47 m, 4.84 vs (1,1), 4.48 m, 3.53 w, 3.27 w, 2.48 vw, and 1.95 m.

Anal. Calc. for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.26; H, 7.80.

*6,7-Dideoxy-1,2-O-isopropylidene-α-*D*-gluco-hept-6-enofuranose* (**16**) *by reduction of the alkyne* **3** *with lithium aluminum hydride.* — A solution of the alkyne **3** (444 mg) in dry ether was added to a suspension of lithium aluminum hydride (300 mg) in ether (50 ml), and the mixture was stirred for 2 h. Use of the same isolation procedure as given in the preceding experiment gave **16** as a solid. Recrystallized from ether–petroleum ether, the product (yield 302 mg, 67.5%) had m.p. 76–78°, $[\alpha]_D^{25}$ −5.0° (*c* 1.13, chloroform); R_f 0.20 (solvent *A*), 0.30 (solvent *B*); λ_{max}^{KBr} 3.38 (C≡C–H), 6.05 (C=C), and 7.28 μm (doublet, CMe_2); X-ray powder diffraction data: 9.71 s (2,2), 7.76 m, 6.86 w, 6.04 s (2,2), 5.60 vw, 4.64 vs (1), 4.28 m, 4.09 m, 3.88 w, and 3.66 w.

Anal. Calc. for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.36; H, 7.43.

*6,7-Dideoxy-1,2-O-isopropylidene-α-*D*-gluco(and β-*L*-ido)-hept-6-enofuranose* (**15** *and* **16**) *by simulation of* **1**. — Fresh vinylmagnesium chloride was prepared by the method of Ramsden and co-workers[26], or was obtained from Alfa Inorganic Ventron (Beverly, Massachusetts). A solution of mixture **1** (15 g) in dry tetrahydrofuran (100 ml) was added dropwise to the vinylmagnesium chloride solution, and the mixture was stirred for 2 h. The solution was evaporated, and the residue was shaken with ice-cold, saturated, aqueous ammonium chloride. The aqueous phase was extracted with four 100-ml portions of ether, and the extracts were combined, dried (magnesium sulfate), and evaporated. The resulting syrup showed two spots in t.l.c.: R_F 0.20 and 0.10 (1:1 petroleum ether–ether) as major products. Separation of the mixture by column chromatography on silica gel 7734 with 1:1 petroleum ether–ether as eluant gave **15** (yield 3.2 g, 28%) and **16** (yield 2.4 g, 21%) as homogeneous compounds, respectively identical by n.m.r. spectra, i.r. spectra, and X-ray powder diffraction patterns with **15** and **16** prepared by reduction of the acetylenes **2** and **3** with lithium aluminum hydride.

*3,5-Di-O-benzoyl-6,7-dideoxy-1,2-O-isopropylidene-β-*L-ido*-hept-6-enofuranose* (**17**). — Prepared from crude **15** (150 mg) by the method used for **2**, the dibenzoate **17** was recrystallized from abs. ethanol; yield 190 mg (65%); m.p. 139–140°, $[\alpha]_D^{25}$ −49° (*c* 0.7, chloroform); R_F 0.90 (solvent *A*), 0.96 (solvent *B*); λ_{max}^{KBr} 3.30 (C=C–H, Ar–H), 5.75 (C=C), and 7.20 μm (doublet, CMe_2); X-ray powder diffraction data: 12.10 s (2,2), 7.02 w, 6.04 s (2,2), 5.37 w, 4.93 m, 4.67 m, 4.36 m, 4.12 vs (1), 3.66 m, 3.42 w, and 3.29 w.

Anal. Calc. for $C_{24}H_{24}O_7$: C, 67.92; H, 5.66. Found: C, 67.67; H, 5.46.

A product having m.p. 143–145°, purported to be the D-*gluco* derivative **18**, obtained[2] by hemihydrogenation of an acetylenic dibenzoate precursor shown[3] to have the L-*ido* configuration, appeared to be identical with compound **17**.

*3,5-Di-O-benzoyl-6,7-dideoxy-1,2-O-isopropylidene-α-*D-gluco*-hept-6-enofuranose* (**18**). — Prepared in the same way as the L-*ido* analog **17**, and recrystallized from abs. ethanol, the dibenzoate **18** was obtained in a yield of 183 mg (62%); m.p. 99–101°, $[\alpha]_D^{25}$ −61° (*c* 0.6, chloroform); R_F 0.90 (solvent *A*), 0.96 (solvent *B*); λ_{max}^{KBr} 3.32 (C=C–H, Ar–H), 5.78 (C=O), and 7.25 μm (doublet, CMe_2); X-ray powder diffraction data: 10.65 w, 9.45 m, 7.62 vs (1,1), 6.69 m, 5.47 s, 4.71 vs (1,1), 4.31 vw, 3.85 vw, 3.64 s, and 3.04 w.

Anal. Calc. for $C_{24}H_{24}O_7$: C, 67.92; H, 5.66. Found: C, 67.66; H, 5.85.

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