Carbohydrate Research, 28 (1973) 201–212

SYNTHESIS OF UNSATURATED ALDEHYDES BY HYDROBORATION OF PROPARGYL ALCOHOLS AND FROM ALDEHYDO SUGAR PRECURSORS*†

DEREK HORTON, AVRAHAM LIAV, AND STEVEN E. WALKER
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U. S. A.)
(Received November 8th, 1972; accepted for publication, December 7th, 1972)

ABSTRACT

Propargyl acetates obtained by ethynylation of aldehydo sugar derivatives, followed by acetylation, can be converted by hydroboration with bis(isoamyl)borane and subsequent treatment with hydrogen peroxide into α,β-unsaturated aldehydes; the latter may also be obtained by treating the original aldehydo sugar derivative with formylmethylenetriphenylphosphorane. By these two routes the aldehydo sugars 2,3-*O*-isopropylidene-*aldehydo*-D-glyceraldehyde (**1**), 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose (**5**), and 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose (**9**) have been converted with 2-carbon chain-extension into the corresponding *trans*-unsaturated aldehydes **3**, **7**, and **11**, respectively. Likewise, by the acetylene route, 1,2:3,4-di-*O*-isopropylidene-6-*aldehydo*-α-D-*galacto*-hexodialdo-1,5-pyranose (**13**) was converted into the C_8 unsaturated aldehyde **15**, although the Wittig route was unsuccessful in this instance, as it was with methyl 2,3-di-*O*-acetyl-4-deoxy-6-*aldehydo*-β-L-*threo*-hex-4-enodialdo-1,5-pyranoside (**16**).

INTRODUCTION

Earlier reports from this laboratory have detailed various applications of the ethynyl functional group for synthetically useful transformations of carbohydrate derivatives[4]. It was of interest to evaluate the hydroboration–oxidation reaction employing a hindered borane, shown by Brown and Zweifel[5] to convert simple terminal alkynes into primary aldehydes, for its potential in the carbohydrate field. It is shown here that the propargylic acetates obtained from protected aldehydo sugars by ethynylation and subsequent acetylation react with bis(isoamyl)borane followed by peroxide to give *trans*-2,3-unsaturated aldehydes in about 30% yield; these products can also be obtained in some, but not all, instances by treating the original aldehydo derivative with formylmethylenetriphenylphosphorane[6], a Wittig

*Dedicated to Dr. Louis Long, Jr., in honor of his 70th birthday.

†Part XI of the series "Extension of Sugar Chains Through Acetylenic Intermediates". For Part X, see Ref. 1. This investigation was supported by the National Institute of General Medical Sciences, National Institutes of Health, U. S. Public Health Service, Grant No. GM-11976 (The Ohio State University Research Foundation Project 1820). For preliminary reports of parts of this work see Refs. 2 and 3.

reagent earlier used in the sugar field by Zhdanov and coworkers[7]. The 2,3-unsaturated aldehydo sugars obtained by this route are of synthetic interest as they offer the possibility, through nucleophilic additions at C-3, to 3-substituted 2-deoxyaldoses having RO-, R_2N-, or other groups at C-3; such structures are present in numerous unusual sugars encountered in antibiotics[8] and cardiac glycosides[9]. The products described here are functionally distinct from the 2-oxygenated 2,3-unsaturated aldehyde structure evaluated in an earlier report[10]; as expected on electronic grounds, the latter type of unsaturated aldehyde suffers attack by nucleophiles exclusively at the aldehyde group.

DISCUSSION

2,3-*O*-Isopropylidene-*aldehydo*-D-glyceraldehyde (**1**) was ethynylated and then acetylated as described by Horton and Thomson[11]; the resultant 3-epimeric 1-pentyne derivatives **2** were not separated but were treated, in admixture at 25° in tetrahydrofuran, with a 1.5-molar excess of bis(isoamyl)borane that had been prepared *in situ* from 2-methyl-1-butene and diborane. Reaction was rapid and the product presumably the R_2B–CH=CH– adduct, was not isolated but was decomposed by cold 30% aqueous hydrogen peroxide in the presence of sodium hydrogen carbonate. Isolation and chromatographic purification of the product gave syrupy *trans*-2,3-dideoxy-4,5-*O*-isopropylidene-*aldehydo*-D-*glycero*-pent-2-enose (**3**) in about 30% overall yield from **2**; it was identified by n.m.r. and mass-spectral data and was further characterized as its crystalline *p*-nitrophenylhydrazone **4**.

The n.m.r. spectrum of the aldehyde **3** in chloroform-*d* was completely first-order, even at 60 MHz, and showed the H-1 signal as a wide doublet ($J_{1,2}$ 7 Hz) at low field (τ 0.44). The H-2 signal at τ 3.70 showed large (16 Hz) coupling with H-3 indicative of the *trans*-alkene structure[12] (J_{trans} 16–18 Hz, J_{cis} 10–12 Hz) together with a small (1 Hz) long-range coupling with H-4; the H-3 signal resonated at somewhat lower field (τ 3.26) than H-2 and showed moderate (5.5 Hz) coupling to H-4. The anticipated ABX system was observed for H-5,5′ and H-4. Full details of the spectrum are recorded in Tables I and II. The n.m.r. spectrum of the unpurified reaction-product showed additional lines for alkenic-type protons, suggesting that a small proportion of the *cis* isomer may have been present before purification.

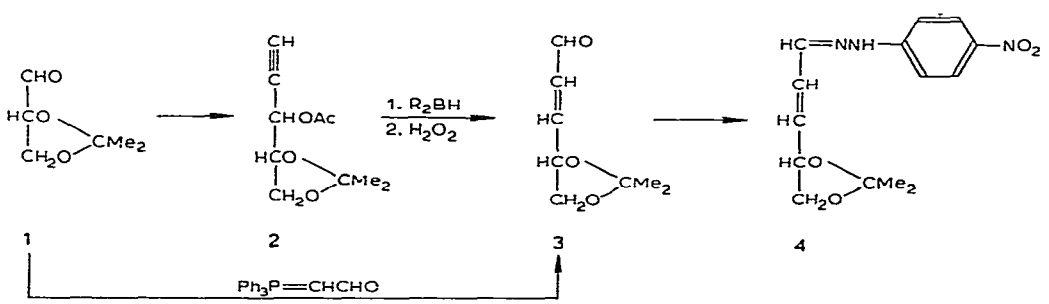


TABLE I

CHEMICAL-SHIFT DATA[a]

Compound	*Chemical shifts (first-order, τ values)*[b]										
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-5′*	*H-6*	*H-7*	*H-8*	*CMe_2*	*Other*
3[c]	0.44 d	3.70 ddd	3.26 dd	5.23 m	5.77 q	6.39 q				8.56, 8.60	
4[d]	2.51 d	3.48 dd	4.06 dd	5.35 m	5.87 q	6.37 q				8.53, 8.61	1.62[e], 1.87, 2.98 (aryl)
7	0.40 d	3.82 ddd	3.23 dd	——4.05–4.80 m——				5.5–6.0 m			7.85, 7.92, 7.94 (2) (Ac)
11[c]	0.32 d	3.55 ddd	3.00 dd	5.30 m	——5.70–6.40 m——					8.56 (2), 8.58, 8.64	
15[d,f]	4.54 d	5.84 dd	5.44 dd	6.15 dd	5.59 m		3.55——3.63 m		0.62 m	8.43 (2), 8.86, 8.92	
15	4.42 d	5.68 dd	~5.3	~5.7	5.45 dd		3.25 dd	3.65 ddd	0.47 d	8.48, 8.59 8.64 (2),	
[g]	4.40 d	~5.64	5.34 dd	~5.7	~6.2					8.46, 8.54, 8.65 (2)	

[a]At 60 MHz, in chloroform-*d* unless otherwise specified, relative to internal standards of Me_4Si (τ 10.00) and $CHCl_3$ (τ 2.75) or C_6D_6 (τ 2.80). [b]Multiplicities: d, doublet; q, quartet; s, singlet; m, multiplet. [c]Data supersede those of Ref. 2. [d]At 100 MHz. [e]NH proton, disappears on deuteration. [f]In benzene-d_6. [g]Data for 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, from Ref. 21.

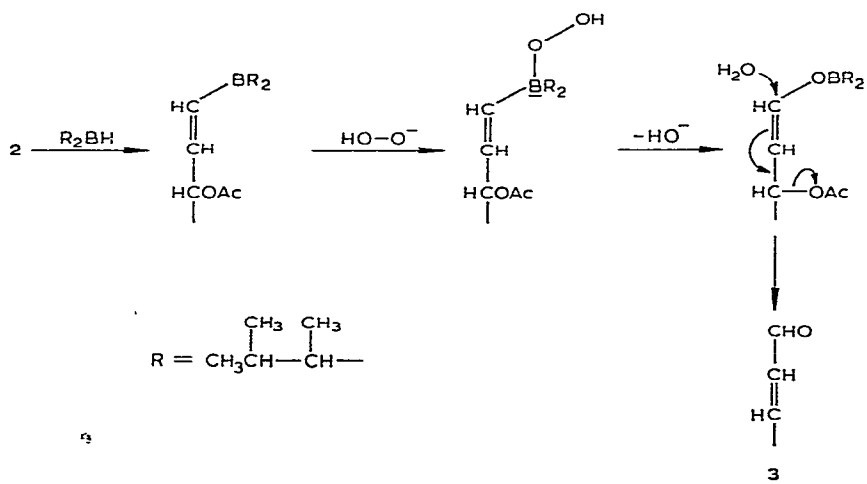
TABLE II

FIRST-ORDER COUPLING CONSTANTS[a]

Compound	*Couplings (Hz)*							
	$J_{1,2}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$	$J_{4,5}$	$J_{4,5'}$	$J_{5,5'}$	*Other*
3	7.0	16.0	1.0	5.5	7	7	9	
4[b]	9.0	16.0		7.0	6.5	7.5	8	
7	7	16	1.5	4				
11	7	16	1.5	4	8			
15[b,c]	5.4	2.6		8.4	2.4			[d]
15	4.8	2.2		8.0	2.4			$J_{5,6}$ 4.0, $J_{5,7}$ 1.5, $J_{6,7}$ 16.0, $J_{7,8}$ 7.6
[e]	5.0	2.4		8.0	~1.4			

[a]In chloroform-*d* at 60 MHz, unless otherwise stated. [b]At 100 MHz. [c]In benzene-d_6. [d]Not determined owing to second-order effects. [e]Data for 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose from Ref. 21.

The mass spectrum of **3** showed a molecular-ion peak, the anticipated $M^{+\cdot} - \cdot CH_3$ peak, an ion for $M^{+\cdot} - \cdot CH{=}CHCHO$, and various related peaks (see Experimental). The *p*-nitrophenylhydrazone **4** gave an acceptable analysis, a strong molecular-ion in its mass spectrum together with other anticipated ions (see Experimental section), and gave n.m.r. data fully concordant with the assigned structure (see Tables I and II).

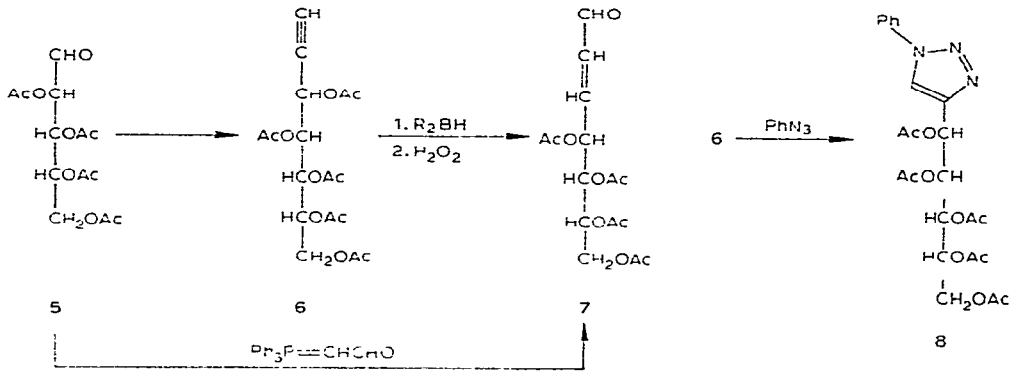


The reaction sequence from **2** to **3** contrasts with the behavior observed[5] with simple alkynes, which give saturated aldehydes. Presumably an alkylborane is formed from **2**, which suffers nucleophilic attack by peroxide anion followed by loss of hydroxide ion and rearrangement to the boric ester. The presence of the

good leaving group at C-3 renders the elimination and bond-migration process shown a more-effective pathway than simple hydrolysis of the enol ester.

As a preparative route to the unsaturated aldehyde **3**, reaction of the precursor aldehyde **1** with formylmethylenetriphenylphosphorane was the superior method as it gave **3** in high yield in a single step; the product and its derivative **4** were identical in all respects with the products obtained by way of the acetylenes **2**.

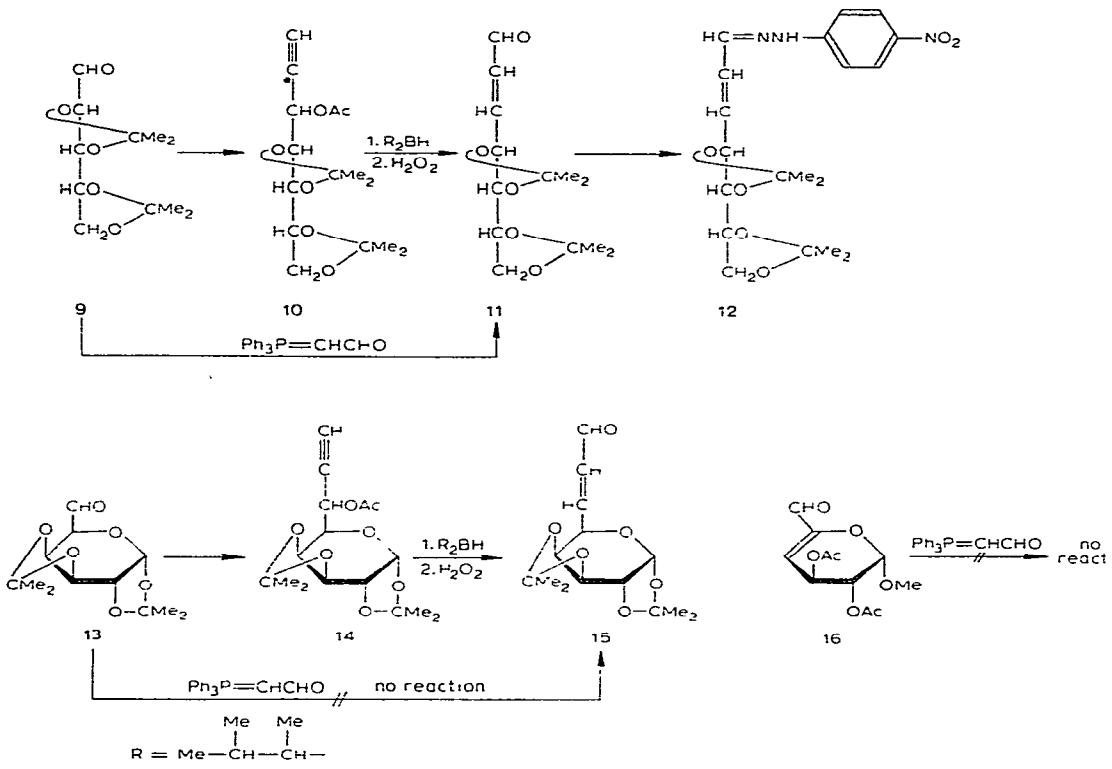
Ethynylation of 2,3,4,5-tetra-*O*-acetyl-*aldehydo*-D-arabinose[13] (**5**) and acetylation of the product gave a syrupy 3-epimeric mixture of alkynes (**6**) that was characterized by reaction with phenyl azide to give a crystalline triazole derivative; this product was formulated tentatively as the 1-*N*-phenyl-4-substituted derivative (**8**) on the basis of steric considerations favoring the less-hindered product[14]. The reaction **5**→**6** further illustrates the feasibility of Grignard additions to aldehydes even when acyl groups are present; an example involving use of a benzoylated aldehydo sugar has already been discussed[15].



Hydroboration–oxidation of the acetylenes **6** by the procedure used for **2** gave a 35% yield of the crystalline *trans*-2,3-unsaturated aldehyde **7**, whose assigned structure was fully supported by the evidence of microanalysis, mass spectrum (see Experimental section), and n.m.r. spectrum (see Tables I and II) along lines closely analogous to those presented for compound **3**. The same unsaturated aldehyde **7** could also be obtained in 85% yield by the Wittig route from the C_5 aldehyde **5**.

By a similar sequence, 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-D-arabinose[16] (**9**) was ethynylated and the product acetylated to give the 3-epimeric mixture **10**; similar reactions in the L series have previously been reported[17]. Successive treatment with bis(isoamyl)borane and hydrogen peroxide gave in 30% yield the corresponding *trans*-2,3-unsaturated aldehyde **11** as a syrup, characterized by physical data and by conversion into a crystalline *p*-nitrophenylhydrazone **12**. The alternative Wittig route from the C_5 aldehyde **9** again proved a superior route to **11** from the standpoint of yield (76%).

When the hydroboration–oxidation sequence was applied to the C_8 acetylenic



derivatives **14** obtained[1] from 1,2:3,4-di-*O*-isopropylidene-6-*aldehydo*-α-D-*galacto*-hexodialdo-1,5-pyranose[18] (**13**) by ethynylation and acetylation, there resulted the crystalline, unsaturated aldehyde **15**, isolated in 35% yield. The usefulness of the route in this instance is demonstrated by the fact that the Wittig route failed to yield the unsaturated aldehyde **15** from the precursor aldehyde **13**. Another aldehyde having the aldehyde group attached to a ring system, namely methyl 2,3-di-*O*-acetyl-4-deoxy-6-*aldehydo*-β-L-*threo*-hex-4-enodialdo-1,5-pyranoside[10,19] (**16**) also failed to react with formylmethylenetriphenylphosphorane under the conditions that gave high yields of unsaturated aldehydes from acyclic aldehydo sugar precursors.

The C_8 unsaturated aldehyde derivative **15** gave an acceptable analysis, showed the anticipated[20] strong u.v. absorption near 240 nm, and its n.m.r. spectrum showed signals typical of the *trans*-2,3-unsaturated aldehyde system, as observed with compounds **3**, **7**, and **11** (Tables I and II). The H-8 signal resonated at low field as a wide doublet ($J_{7,8}$ 7.6 Hz), and the H-7 signal showed *trans*-alkenic coupling (16.0 Hz) and appreciable (1.5 Hz) long-range coupling with H-5; the H-6 signal resonated somewhat downfield of H-6. In chloroform-*d*, the spectrum of **15** for the ring protons resembles closely the general pattern reported by Cone and Hough[21] for this type of ring system and interpreted by them in terms of a pyranoid skew-conformation. Second-order effects render the pattern for H-2,3,4, and 5 difficult to analyze, but

in benzene-d_6, these resonances were well separated, so that the appropriate couplings could readily be extracted (see Tables I and II). In contrast, in the latter solvent the H-6 and H-7 signals were scarcely resolved, and extra multiplicity in the H-8 signal through "virtual coupling"[22] was clearly evident. Compound **15** showed a strong $M^{+} - \cdot CH_3$ peak in its mass spectrum, and other fragmentations (see Experimental section) interpretable in terms of the schemes proposed[23] for 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose.

In aqueous acetone solution, the unsaturated aldehyde **15** did not undergo hydration of the aldehyde group to any appreciable extent; the n.m.r. spectrum showed a 1:1 intensity ratio between the aldehydic proton (H-8) and H-1 signals. This behavior contrasts with that of saturated aldehydo sugars, which undergo extensive hydration under similar conditions[24]. Evidently, the stabilization of the aldehyde by conjugation with the double bond is sufficient to counteract the driving force for hydration of the aldehyde group.

The reactions described provide useful general methods of access to *trans*-2,3-unsaturated aldehydo sugars, even for those systems in which the Wittig method is not effective.

EXPERIMENTAL

General methods. — Melting points were recorded with a Thomas–Hoover apparatus, specific rotations with a Perkin–Elmer Model 141 polarimeter, u.v. spectra with a Bauch and Lomb Model 505 spectrometer, i.r. spectra with a Perkin–Elmer Model 137 spectrometer, mass spectra with an A.E.I. MS-9 high-resolution mass spectrometer (ionizing potential 70 eV, source temperature, 250°), and n.m.r. spectra with Varian A-60, A-60A, and HA-100 spectrometers; tetramethylsilane ($\tau = 10.00$) was used as the internal standard and signal assignments were verified by spin decoupling. Gas chromatography was performed with an Aerograph "Autoprep" Model 705 gas chromatograph with a 9 mm × 3 m column of 10% Carbowax 20M on Chromosorb W (type AW-DMCS, 70–80 mesh, Varian Aerograph Co.). Adsorption column chromatography was effected with silica gel No. 7734 (0.05–0.2 mm, E. Merck, Darmstadt, Germany) and t.l.c. with 0.25 mm layers of Silica Gel G (Merck) activated at 110° with the developers *A* 3:1 chloroform–ether, *B* 1:1 ether–petroleum ether, or *C* 2:1 ether–petroleum ether; indication was effected with Schiff reagent or by sulfuric acid and heat. Petroleum ether refers to a fraction having b.p. 30–60°. Elemental analyses were determined by W. N. Rond. X-Ray powder diffraction data give interplanar spacings, Å, for CuKα radiation with a camera diameter of 114.59 mm. Relative intensities were estimated visually: s, strong; m, moderate; w, weak; v, very. The strongest lines are numbered (1, strongest).

Preparation of starting aldehydes. — 2,3-*O*-Isopropylidene-*aldehydo*-D-glyceraldehyde (**1**) was prepared from D-mannitol (340 g) by a modification[11] of the original procedure[25]: yield of distilled product 110 g (30%), homogeneous by t.l.c., R_F 0.50 (5:1 dichloromethane–ether).

Tetra-*O*-acetyl-*aldehydo*-D-arabinose (**5**) was prepared from tetra-*O*-acetyl-D-arabinose diethyl dithioacetal by the procedure of Wolfrom *et al.*[13]; yield 60%, m.p. 110–112°, $[\alpha]_D^{24}$ +63° (*c* 1, chloroform); lit.[13] m.p. 112–114°, $[\alpha]_D$ +65° (chloroform).

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-D-arabinose (**9**) was prepared from the corresponding diethyl dithioacetal, as described by Zinner *et al.*[16], as a yellow oil, $[\alpha]_D^{23}$ −13° (*c* 1.4, chloroform); lit.[16] $[\alpha]_D$ −16.1° (chloroform).

1,2:3,4-Di-*O*-isopropylidene-6-*aldehydo*-α-D-*galacto*-hexodialdo-1,5-pyranose (**13**) was obtained as previously described[18] in 51% yield, b.p. 112–120° (bath, 20 mtorr).

Methyl 2,3-di-*O*-acetyl-4,5-dideoxy-β-L-*threo*-hex-4-enodialdo-1,5-pyranoside (**16**) was prepared from methyl 2,3,4-tri-*O*-acetyl-6-azido-6-deoxy-α-D-glucopyranoside by sequential photolysis, mild hydrolysis, and treatment with triethylamine[19]; b.p. 160–170° (bath, 0.3 torr); the product was homogeneous by t.l.c.: R_F 0.85 (5:1 dichloromethane–ether).

Preparation of acetylenic derivatives. — *A. 3-*O*-Acetyl-1,2-dideoxy-4,5-*O*-isopropylidene-*D-erythro(*and* D-threo)-pent-1-ynitol* (**2**). Ethynylation of the aldehyde **1** by the procedure previously described[11] and distillation of the resultant product gave the 3-epimeric propargyl alcohol derivatives, homogeneous by t.l.c. (R_F 0.48 in solvent A) and by g.l.c. (T_R 7.2 min at a column temperature of 170° and nitrogen flowrate 2 ml/sec). Acetylation[11] gave the mixed acetates **2** migrating as one spot on t.l.c. (R_F 0.72 in solvent A and 0.70 in solvent C) and barely separable by g.l.c. (T_R 4.8 and 5.2 min).

*B. 3,4,5,6,7-Penta-*O*-acetyl-1,2-dideoxy-*D-gluco(*and* D-manno)-hept-1-ynitol* (**6**). The aldehyde **5** (1.6 g) was ethynylated by the general procedure previously described[11] to afford a syrup that was acetylated[11]. The pure product **6** was isolated in 65% yield after purification by column chromatography on silica gel with 17:1 benzene–ether as eluant. This product was characterized as the crystalline triazole derivative **8** described later, and was used directly in the preparation of the unsaturated aldehyde **7**.

*C. 3-*O*-Acetyl-1,2-dideoxy-4,5:6,7-di-*O*-isopropylidene-*D-gluco(*and* D-manno)-hept-1-ynitol* (**10**). Ethynylation[11] of the aldehyde **9** (0.73 g) gave the enantiomorphs of the products already reported[17]; acetylation of these in admixture, with acetic anhydride and pyridine, gave **10** as a syrup (0.72 g) that was used directly in the preparation of the unsaturated aldehyde **11**.

*D. 6-*O*-Acetyl-7,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-*D(*and* L)-glycero-α-D-galacto-oct-7-ynopyranose* (**14**). Ethynylation of the aldehyde **13** as already described[1] but without separation of the 6-epimers, followed by acetylation of the product with acetic anhydride—sodium acetate gave, in 94% yield for the acetylation step, a crystalline mixture of acetates **14**. These could be readily separated by recrystallization from ethanol—benzene to give the pure epimers already described[1], but were used directly as a mixture in the present work.

4-(D-manno-*1,2,3,4,5-pentaacetoxypentyl)-1-phenyltriazole* (**8**). — To the syrupy ethynylation product **6** (0.34 g) from the aldehyde **5** was added phenyl azide (1 ml) and the mixture was heated for 5 h at 90–95°. The excess volatile reagent was

evaporated off and the residue was recrystallized from acetone–petroleum ether to give the triazole **8** as a single compound; yield 0.23 g (50%), m.p. 151–152°, $[\alpha]_D^{21}$ +11.5° (*c* 1, chloroform); n.m.r. (chloroform-*d*, 60 MHz): τ 1.87 (H-5 of triazole), 2.1–2.6 (5-proton multiplet, Ph), 3.71–4.42 (multiplets, H-1,2,3 of chain), ~4.78 (multiplet, H-4 of chain), ~5.78 (multiplet, H-5,5′ of chain), 7.88, 7.89, 7.92, 8.02 (singlets, acetyl groups).

Anal. Calc. for $C_{23}H_{27}N_3O_{10}$: C, 54.65; H, 5.34; N, 8.31. Found: C, 54.92; H, 5.04; N, 8.39.

The D-*manno* stereochemistry is assigned on the basis of an independent[3], stereochemically definitive synthesis of **8**.

trans-*2,3-Dideoxy-4,5*-O-*isopropylidene*-aldehydo-D-glycero-*pent-2-enose* (**3**). — *A. From the acetylenes* **2**. To 2-methyl-1-butene (1.1 g, 15 mmoles) in a flask equipped with a stirrer, provision for exclusion of moisture, and an atmosphere of nitrogen, was added M diborane in tetrahydrofuran (Alfa Inorganics, Ventron Products, Beverly, Mass. 01915, 7.5 ml) at −10°. After 4 h at −10° the mixture was warmed briefly to 20° and then cooled again to −10°. The acetylenic derivative **2** (1.0 g, 5 mmoles) was added dropwise, and the mixture was stirred for 2 h at 25° under nitrogen. T.l.c. indicated that the starting acetylene had reacted within 15 min of the addition. The solution was then cooled to −10° and added slowly to a stirred mixture of 30% hydrogen peroxide (~7 ml), saturated sodium hydrogen carbonate (~7 ml), and an excess of ice. The mixture was extracted with five 20-ml portions of dichloromethane and the extract was washed with water (20 ml) and 5% aqueous ferrous sulfate (20 ml) .The extract was passed rapidly through a bed of silica gel (5 g), with ether as eluant, and the effluent was evaporated. The resultant syrup was purified by chromatography on silica gel (75 g) with 8:1 dichloromethane–ether as eluant to give **3** as a chromatographically homogeneous syrup (230 mg, 30%): t.l.c.: R_F 0.55 (solvent A), 0.50 (solvent C); Schiff positive; n.m.r. data: see Tables I and II: m.s.: *m/e* 312 (2, $2M^+$), 311 (10, $2M^+ - 1$), 156 (3, M^+), 155 (8, $M^+ - 1$), 141 (14, $M^+ - \cdot CH_3$), 111 (12, $M^+ - \cdot CH_3 - CH_2O$), 101 (77, $\overline{OH_2\overset{+}{C}CH{=}OCMe_2}$) (for complete tabulation of mass-spectral peaks see Ref. 26).

The initial rapid filtration through silica gel was essential if major loss of product was to be avoided, presumably by the action of excess peroxide. Yields under a variety of experimental conditions were determined[26] by adding a calculated quantity of *N,N*-dimethylformamide to the product after evaporation of the dichloromethane and then determining by n.m.r.-spectral integration the ratio of the H-1 signal of **3** and the signal of the aldehyde proton of *N,N*-dimethylformamide. It was found that the pH in the hydrolytic step was not critical over the range 5–9, but higher values led to decreased yields. Little effect on the yield was observed by varying the amount of excess oxidant, the temperature of the hydrolytic step between 0 and 25°, or the solvent (water, methanol, or tetrahydrofuran) present.

B. From the aldehyde **1**. A solution of **1** (1.00 g) and formylmethylenetriphenylphosphorane[6] (2.30 g) in benzene (50 ml) was boiled for 1 min under reflux. The

mixture was cooled to 25°. The product **3** was not isolated directly but was characterized as the *p*-nitrophenylhydrazone, as described in the following experiment.

trans-*2,3-Dideoxy-4,5*-O-*isopropylidene*-D-glycero-*pent-2-enose* (p-*nitrophenyl*)-*hydrazone* (**4**). — To a solution of *p*-nitrophenylhydrazine (1 g) in methanol (30 ml) was added compound **3** obtained from 1.0 g of the acetylenes **2**. Reaction was rapid, as judged by disappearance of the Schiff-positive spot on t.l.c. (solvent A), but it could be further accelerated by addition of a drop of acetic acid. Evaporation of the solution followed by chromatographic purification of the product on silica gel (100 g) with 8:1 dichloromethane–ether as eluant gave **4** (0.44 g, 31%), m.p. 173–175°. Recrystallization from ethanol gave an analytical sample, m.p. 175–176°, $[\alpha]_D^{26}$ +26° (*c* 1, chloroform); t.l.c.: R_F 0.50 (A), 0.35 (C); u.v. data: $\lambda_{max}^{95\%\ EtOH}$ 398.5 (ε 30,000), 322.5 (4,000), 293.5 (7,000), 249 (6,000), 215 nm (10,000); n.m.r. data: see Tables I and II; m.s.: *m/e* 291 (30, M^+), 261 (30, $M^+ - NO$), 233 (46, $M^+ - NO - CO$ or $M^+ - Me_2CO$) (for further details, see Ref. 26); X-ray powder diffraction data: 10.73 w, 9.11 m, 7.86 w, 7.09 m, 6.20 w, 5.51 vs (1), 4.89 m, 5.55 m, 4.30 m, 4.00 s, 3.71 s, 3.44 m, 3.22 w, 3.05 m.

Anal. Calc. for $C_{14}H_{17}N_3O_4$: C, 57.72; H, 5.88; N, 14.43. Found: C, 57.84; H, 5.99; N, 14.63.

In a separate route to **4**, the aldehyde **3**, prepared by the Wittig route from aldehyde **1** as described in the preceding experiment, was used without isolation. To the solution in benzene was added *p*-nitrophenylhydrazine (1.25 g), and product **4** was isolated as previously described with use of a column of silica gel (50 g) with dichloromethane as eluant. Compound **4** was obtained in a yield of 1.62 g (73%), identical with authentic **4** by n.m.r. spectroscopy, mixed m.p., elemental analysis, and t.l.c.

trans-*4,5,6,7-Tetra*-O-*acetyl-2,3-dideoxy*-aldehydo-D-arabino-*hept-2-enose* (**7**). — *A. From the acetylenes* **6**. The acetylene derivative **6** (0.9 g) was treated successively with bis(isoamyl)borane and then hydrogen peroxide by the procedure described for conversion of **2** into **3**, and the product was purified by chromatography on a column of silica gel with 8:1 benzene–ether as eluant to give **7** (0.3 g, 35%). Recrystallization (twice) from benzene–petroleum ether gave an analytical sample, m.p. 81–83°, $[\alpha]_D^{21}$ +51° (*c* 1, chloroform); n.m.r. data: see Tables I and II; m.s.: *m/e* 314 (0.1, $M^+ - CH_2O$), 285 (0.6, $M^+ - \cdot OAc$), 255 (0.3, $M^+ - \cdot OAc - HOAc$).

Anal. Calc. for $C_{15}H_{20}O_9$: C, 52.32; H, 5.81. Found: C, 52.28; H, 5.95.

B. From the aldehyde **5**. A solution of the aldehyde **5** (0.41 g) and formylmethylenetriphenylphosphorane (0.7 g) in benzene (50 ml) was boiled for 1 h under reflux. The mixture was evaporated and the residue was chromatographed on a column of silica gel. Elution with 8:1 benzene–ether gave syrupy **7** (0.33 g, 85%). Crystallization from benzene–petroleum ether gave **7** identical with product obtained by method *A*.

trans-*2,3-Dideoxy-4,5:6,7-di*-O-*isopropylidene*-aldehydo-D-arabino-*hept-2-enose* (**11**). — *A. From the acetylenes* **10**. By the general hydroboration–oxidation method used for preparing **3** and **7**, compound **10** was converted into **11**, obtained as a

Schiff-positive oil that was purified on a column of silica gel with 14:1 benzene–ether as eluant, yield 30%, $[\alpha]_D^{24}$ +10° (*c* 1, chloroform); n.m.r. data: see Tables I and II; m.s.: *m/e* 256 (0.12, $M^{\ddagger}$), 241 (24, $M^{\ddagger} - \cdot CH_3$), 101 (60), 43 (100).

The product was identical, except for the sign of optical rotation, with the compound prepared[2] in the L series starting from the L enantiomorph of **9** and proceeding by way of the L enantiomorph of **10**.

B. From the aldehyde **9**. A solution of the aldehyde **9** (0.68 g) and formylmethylenetriphenylphosphorane (1 g) in benzene (40 ml) was boiled for 1 h under reflux. The mixture was evaporated and the residue was chromatographed on a column of silica gel with 14:1 benzene–ether as eluent to afford pure **11** as an oil (0.52 g, 76%), identical with the product obtained by the preceding procedure by t.l.c. and n.m.r. spectrum.

trans-*2,3-Dideoxy-4,5:6,7-di*-O-*isopropylidene*-D-arabino-*hept-2-enose* p-*nitrophenylhydrazone* (**12**). — To a solution of the aldehyde **11** (130 mg) in methanol (2 ml) were added *p*-nitrophenylhydrazine (200 mg) in pyridine (1 ml) and water (3 ml) containing 2 drops of 0.1M hydrochloric acid. After 5 h at ~25° the mixture was evaporated and the residue was extracted with chloroform. The extract was washed successively with cold water, M hydrochloric acid, and aqueous sodium hydrogen carbonate. The extract was evaporated and the residue was crystallized from acetone–petroleum ether to give **12** (yield 75 mg, 38%), m.p. 148–149°, $[\alpha]_D^{24}$ +41° (*c* 1.2, chloroform).

Anal. Calc. for $C_{19}H_{25}N_3O_6$: C, 58.30; H, 6.43; N, 10.73. Found: C, 58.60; H, 6.69; N, 10.77.

trans-*6,7-Dideoxy-1,2:3,4-di*-O-*isopropylidene-8*-aldehydo-α-D-galacto-*oct-6-enodialdo-1,5-pyranose* (**15**). — The 7-epimeric mixture of acetylenes **14** (1.6 g) was subjected to the hydroboration–oxidation procedure applied for preparation of compound **3**, and the product was purified on a column of silica gel. Crystallization of the product from benzene–ligroin gave 0.49 g (35%) of **15**, m.p. 93–95°. Further recrystallization afforded an analytical sample, m.p. 97.5–99.5°, $[\alpha]_D^{26}$ −135° (*c* 1, chloroform): t.l.c.: R_F 0.63 (A), 0.50 (B), 0.70 (C); u.v. datum: $\lambda_{max}^{95\%\ EtOH}$ 241 nm (ε 17,000), i.r. data: λ_{max}^{KBr} 3.36–3.50 (CHO), 5.86 μm (C=O); n.m.r. data: see Tables I and II; m.s.: *m/e* 284 (0.02, $M^{\ddagger}$), 269 (12, $M^{\ddagger} - \cdot CH_3$), 211 ($M^{\ddagger} - \cdot CH_3 - Me_2CO$), 209 (0.9, $M^{\ddagger} - \cdot CH_3 - HOAc$); X-ray powder diffraction data: 13.28 m, 9.37 s, 6.69 m, 5.47 vs (2), 5.10 w, 4.80 vs (1), 4.59 w, 4.38 m, 4.08 vw, 3.61 w.

Anal. Calc. for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found. C, 58.89; H, 6.96.

Treatment of the aldehyde **13** with formylmethylenetriphenylphosphorane, under conditions successfully employed in preparing the unsaturated aldehydes **3**, **7**, and **11**, or by refluxing in methanol, failed to afford compound **15**. Similarly, the unsaturated aldehyde **16** failed to react with the Wittig reagent.

Hydration equilibrium of aldehyde **15**. — A solution of **15** (30 mg) in acetone-d_6 (0.35 ml) and deuterium oxide (0.15 ml) was kept for 35 h at 25°. The n.m.r. spectrum of the solution showed a 1:1 ratio of the signals for H-1 and H-8, and no signal attributable to a proton of an aldehydrol group could be detected.

ACKNOWLEDGMENTS

The authors thank Dr. R. Hems for assistance and useful suggestions in part of this work, and C. R. Weisenberger for recording the mass spectra.

REFERENCES

1 R. HEMS, D. HORTON, AND M. NAKADATE, *Carbohyd. Res.*, 25 (1972) 205.
2 D. HORTON, J. B. HUGHES, AND J. M. J. TRONCHET, *Chem. Commun.*, (1965) 481.
3 D. HORTON, *Abstr. Papers 5th Intern. Symp. Carbohyd. Chem.*, Paris, France, August 17–22, 1970; D. HORTON AND A. LIAV, *Abstr. Papers Amer. Chem. Soc. Meeting*, 162 (1971) CARB-9.
4 See Ref. 1 and earlier papers in this series, cited therein.
5 H. C. BROWN AND G. ZWEIFEL, *J. Amer. Chem. Soc.*, 83 (1961) 3834.
6 S. TRIPPETT AND D. M. WALKER, *J. Chem. Soc.*, (1961) 1266.
7 YU. A. ZHDANOV, YU. E. ALEXEEV, AND G. N. DOROFEENKO, *Zh. Obshch. Khim.*, 37 (1967) 98; compare YU. A. ZHDANOV, YU. E. ALEXEEV, AND V. G. ALEXEEVA, *Advan. Carbohyd. Chem. Biochem.*, 27 (1972) 227.
8 D. HORTON, in R. W. JEANLOZ (Ed.), *The Amino Sugars*, Vol. IA, Academic Press, New York, 1969, pp. 1–209; S. HANESSIAN AND T. H. HASKELL, in W. PIGMAN AND D. HORTON (Eds.), *The Carbohydrates: Chemistry and Biochemistry*, Vol. IIA, Academic Press, New York, 1970, chap. 31.
9 J. E. COURTOIS AND F. PERCHERON, in W. PIGMAN AND D. HORTON (Eds.), *The Carbohydrates: Chemistry and Biochemistry*, Vol. IIA, Academic Press, New York, 1970, chap. 32.
10 D. HORTON AND A. LIAV, *Carbohyd. Res.*, 24 (1972) 105.
11 D. HORTON AND J. K. THOMPSON, *J. Org. Chem.*, 33 (1968) 728.
12 H. S. GUTOWSKY, M. KARPLUS, AND D. M. GRANT, *J. Chem. Phys.*, 31 (1959) 1278; T. SCHAEFER, *Can. J. Chem.*, 40 (1962) 1.
13 M. L. WOLFROM, D. I. WEISBLAT, W. H. ZOPHY, AND S. W. WAISBROT, *J. Amer. Chem. Soc.*, 63 (1941) 201.
14 H. EL KHADEM, D. HORTON, AND M. H. MESHREKI, *Carbohyd. Res.*, 16 (1971) 409.
15 J. L. GODMAN, D. HORTON, AND J. M. J. TRONCHET, *Carbohyd. Res.*, 4 (1967) 392.
16 H. ZINNER, E. WITTENBERG, AND G. REMBARZ, *Chem. Ber.*, 92 (1959) 1614.
17 D. HORTON AND J. M. J. TRONCHET, *Carbohyd. Res.*, 2 (1966) 315.
18 D. HORTON, M. NAKADATE, AND J. M. J. TRONCHET, *Carbohyd. Res.*, 7 (1968) 56.
19 D. HORTON, A. E. LUETZOW, AND J. C. WEASE, *Carbohyd. Res.*, 8 (1968) 366; A. E. LUETZOW, Ph. D. Dissertation, The Ohio State University, 1970; D. M. CLODE, R. HEMS, D. HORTON, A. E. LUETZOW, AND H. SHOJI, *Abstr. Papers Amer. Chem. Soc. Meeting*, 157 (1969) CARB-5.
20 W. F. FORBES AND R. SHILTON, *J. Amer. Chem. Soc.*, 81 (1959) 786.
21 C. CONE AND L. HOUGH, *Carbohyd. Res.*, 1 (1965) 1.
22 J. MUSHER AND E. J. COREY, *Tetrahedron*, 18 (1962) 791.
23 D. C. DEJONGH AND K. BIEMANN, *J. Amer. Chem. Soc.*, 86 (1964) 67.
24 D. HORTON AND J. D. WANDER, *Carbohyd. Res.*, 16 (1971) 477.
25 E. BAER AND H. O. L. FISCHER, *J. Biol. Chem.*, 128 (1939) 463.
26 S. E. WALKER, M. S. Thesis, The Ohio State University, 1971; D. HORTON AND S. E. WALKER, unpublished data.