SYNTHESIS OF D-*glycero*-D-*galacto*-HEPTITOL (PERSEITOL), L-*glycero*-D-*galacto*-HEPTITOL, AND AN ALLENIC SUGAR DERIVATIVE, FROM ACETYLENIC PRECURSORS*†

ROGER HEMS, DEREK HORTON‡, AND MASAHIRO NAKADATE
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U. S. A.)
(Received June 7th, 1972; accepted for publication, June 15th, 1972)

ABSTRACT

Ethynylation of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**1**) gave, in 73% yield, a 3:2 mixture of 7,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-oct-7-ynopyranose (**2**) and its L-*glycero* 6-epimer (**6**), both isolated crystalline and further characterized as the corresponding crystalline 6-*p*-toluenesulfonates (**3** and **7**) and 6-acetates (**4** and **8**). Reduction of the acetylenes **2** and **6** with lithium aluminum hydride gave the corresponding, crystalline 7-alkenes (**5** and **9**) in 75–80% yield; the 6-methanesulfonate (**10**) of **9** was also prepared. A minor product from the reaction of **2** or **6** with lithium aluminum hydride was isolated crystalline and characterized as the allenic sugar derivative **11** by n.m.r. and mass spectrometry, by reduction to the 6,7,8-trideoxyoctose derivative **16**, and by ozonolysis to give the aldehyde **1**. Ozonolysis of the alkene **5** followed by borohydride reduction gave the 1,2:3,4-diisopropylidene acetal (**12**) of D-*glycero*-α-D-*galacto*-heptopyranose, which was deacetonated, and the product reduced with borohydride to give crystalline D-*glycero*-D-*galacto*-heptitol (perseitol, **13**) in 62% yield from **5**. Similar degradation of the L-*glycero* alkene **9** gave the L-*glycero*-D-*galacto*-heptose derivative **14** and, subsequently, the crystalline L-*glycero*-D-*galacto*-heptitol (**15**) in 55% yield from **9**; these degradative reactions served to establish the configurations assigned to the original acetylenes **2** and **6** and to the related intermediates.

INTRODUCTION

A program of synthesis in this laboratory has been concerned with the reactions of carbonyl sugars with unsaturated Grignard reagents[2–4]. Terminal acetylene functions formed by addition of ethynylmagnesium bromide to aldehydo sugars have proved to be of wide versatility in synthesis[4]. The present report describes the ethynyl-

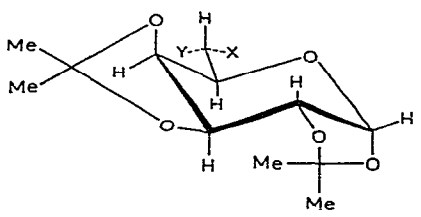
*Part X of the series "Extension of Sugar Chains Through Acetylenic Intermediates". For part IX, see ref. 1. For preliminary reports on parts of this work, see refs. 2 and 3.
†This work was supported by the National Institute of General Medical Sciences, National Institutes of Health, U. S. Public Health Service Grant No. GM-11976 (The Ohio State University Research Foundation Project 1820).
‡To whom inquiries should be addressed.

ation of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose[2,5] (**1**), and characterization of the resultant 8-carbon sugar derivatives by a route that provides a convenient preparation of the natural heptitol D-*glycero*-D-*galacto*-heptitol[6,7] (perseitol, **13**) together with L-*glycero*-D-*galacto*-heptitol[8,9] (**15**). The acetylenic intermediates, which are of interest in the synthesis of lincomycin analogs, are conveniently reduced to the alkene analogs by lithium aluminum hydride, and a side-product formed in this reaction has been characterized as an allene derivative (**11**).

RESULTS AND DISCUSSION

1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose[2] (**1**) was prepared and purified as already described[5]; an alternative route involved photolysis of 6-azido-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose. The ethynylation step, for which proper purification of the aldehyde **1** as described[5] was essential for maximum yields, was performed with ethynylmagnesium bromide by the general route already utilized[4], to give a 73% yield of the mixed, epimeric acetylenes **2** and **6** in 3:2 ratio. The products were barely separable by t.l.c., but fractional recrystallization or column chromatography of the product gave the two 6-epimers in pure form. Their specific optical rotations differed by only 6 degrees, and their melting points were only 5 degrees apart, but, on admixture, the melting point was sharply depressed. With this epimeric pair, as with other such pairs in this work, the epimers were clearly identified by their totally different X-ray powder diffraction patterns. Polarimetry was not a sensitive tool, as three of the pairs of epimers showed only small differences in specific rotation, presumably because configurational change in the acyclic part of the molecule gives rotational contributions that are of small magnitude in comparison with the rotational contribution of the polycyclic part.

The 6-epimeric propargyl alcohols **2** and **6** were converted into their respective 6-*p*-toluenesulfonates (**3** and **7**) and 6-acetates (**4** and **8**). Examination of the p.m.r. spectra (see Tables I and II for full details on the p.m.r. spectra of all compounds in this study) of the three D-*glycero*-D-*galacto* derivatives **2**, **3**, and **4**, and of the L-*glycero*-D-*galacto* analogs **6**, **7**, and **8**, showed that, in each example, the $J_{5,6}$ spin-coupling was large (~9 Hz), indicating a favored antiparallel disposition of H-5 and H-6 throughout the series. This behavior no doubt arises as a result of the reluctance of either of the larger C-6 substituents (HC≡C– and OH, OTs, or OAc) to become aligned parallel to O-4.



	X	Y
2	HC≡C–	HO–
3	HC≡C–	TsO–
4	HC≡C–	AcO–
6	HO–	HC≡C–
7	TsO–	HC≡C–
8	AcO–	HC≡C–

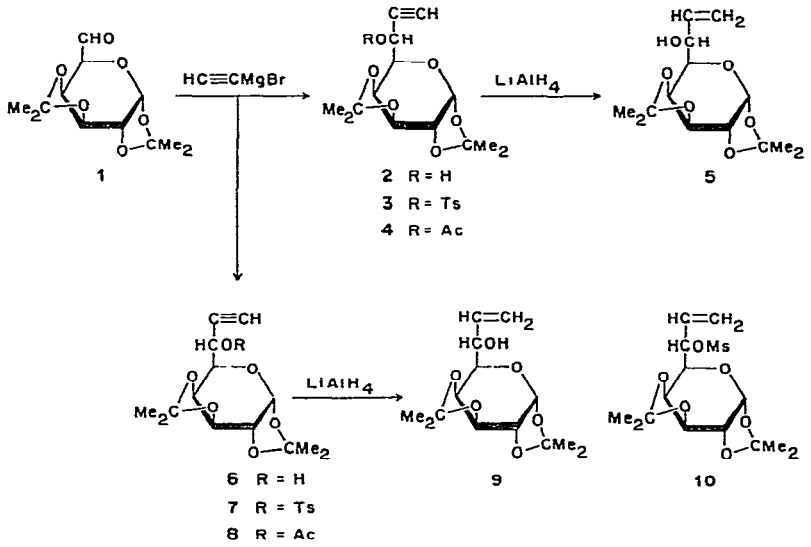
TABLE I

CHEMICAL-SHIFT DATA

Compound	*Chemical shifts*[a] (τ)								CMe_2	*Others*
	H-1	*H-2*	*H-3*	*H-4*	*H-6*	*H-5*	*H-7*	*H-8*		
2	4.40d	← 5.25–5.78m →				6.17dd	—	7.47d	8.46, 8.52, 8.64, 8.66	6.61 (d, OH)[b]
6	4.42d	← 5.20–5.80m →				6.2dd	—	7.46d	8.44, 8.55, 8.65 (2)	7.21 (s, OH)[b]
3	4.48d	5.71dd	5.43dd	5.82dd	4.79dd	6.04dd	—	7.47d	8.48, 8.67 (2), 8.80	2.0–2.8 (m, aryl), 7.56 (s, aryl C-Me)
7	4.72d	5.77dd	5.42dd	5.64dd	4.87dd	6.10dd	—	7.40d	8.53, 8.68, 8.71 (2)	2.1–2.9 (m, aryl), 7.62 (s, aryl C-Me)
4[c]	4.40d	5.61dd	5.32dd	5.70dd	4.54dd	5.96dd	—	7.43d	8.42, 8.56 (2), 8.65	7.90 (s, OAc)
8[c]	4.48d	5.68dd	5.35dd	5.52dd	4.42dd	6.04dd	—	7.46d	8.41, 8.51, 8.62 (2)	7.87 (s, OAc)
5	4.44d	← 5.24–5.83m →				6.36dd	3.91o	4.42–5.06[d]	8.50 (2), 8.64, 8.67	7.17 (s, OH)[b]
9	4.46d	← 5.31–5.82m →				6.49dd	4.07o	4.36–4.94[d]	8.50, 8.55, 8.68 (2)	6.90 (s, OH)[b]
10[c]	4.42d	5.63dd	5.35dd	5.78dd	4.80dd	6.16dd	3.92o	4.24–4.64[d]	8.47, 8.53, 8.66 (2)	6.88 (s, OSO_2CH_3)
11[c]	4.37d	5.63dd	5.31dd	5.73dd	4.56o	5.58dd	—	4.90–5.20[d]	8.44, 8.51, 8.63 (2)	
16	4.42d	5.67dd	5.39dd	5.84dd		6.19td	—			7.8–9.4 (19H, CMe_2, and H-6, 7, 8)

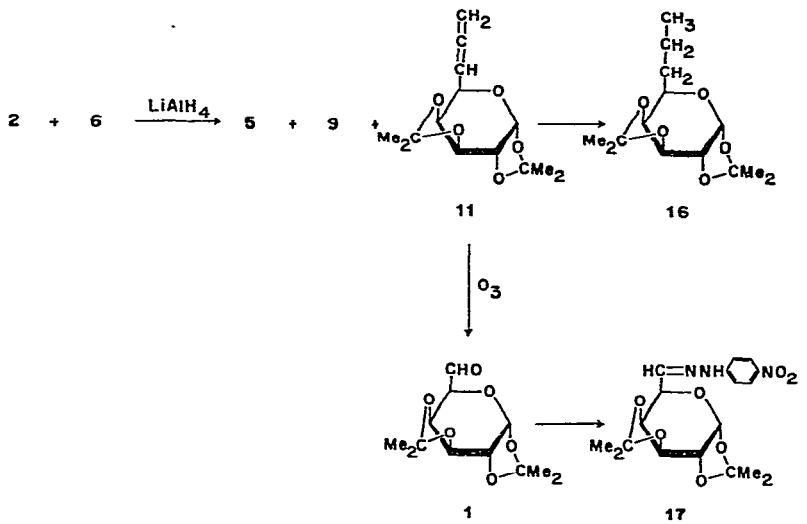
[a]At 60 MHz in chloroform-*d*, unless noted otherwise. Peak multiplicity in parentheses: d, doublet; dd, doublet of doublets; m, multiplet; o, octet; td, triplet of doublets; s, singlet. Ring-proton assignments were verified, where necessary, by spin-decoupling. [b]Disappears on deuteration. [c]At 100 MHz. [d]Second-order, two-proton multiplet for H-8,8′.

The possibility of employing, in the assignment of stereochemistry, p.m.r. spin-coupling data as an adjunct to chemical degradation, as used in previous studies[10,11], was not, therefore, available in the present work; consequently, the configurations were assigned strictly on the basis of chemical transformations.



Although the preponderant acetylenic epimer (**2**) had been reduced to the corresponding alkene **5** in this laboratory[2] by hydrogenation over Lindlar catalyst, the somewhat capricious nature of this catalyst led to the search for a more satisfactory method for reducing the acetylenes to the corresponding alkenes. Reduction with lithium aluminum hydride[12] was found to be effective[3], and the alkene **5** was obtained from the acetylene **2**; similarly, acetylene **6** gave the alkene **9**; yields were 75–82%. Compound **5** was identical with the product formed[2] from the acetylene **2** by hemi-hydrogenation over Lindlar catalyst; this product was subsequently prepared[13] by vinylation of the aldehyde **1**. As with the other derivatives already mentioned, the $J_{5,6}$ values of alkenes **5** and **9** were large (7.5–8.0 Hz), indicating that H-5 and H-6 favored the antiparallel orientation, and precluding stereochemical assignment from coupling data alone.

A side-product in the reduction[12] of either acetylene (**2** or **6**) was isolated crystalline, and found to be the same product in each instance. This compound was characterized as the allene derivative **11** on the basis of physical and chemical evidence. In g.l.c., it migrated much more rapidly than the vinylic sugar derivatives **5** and **9**. Its i.r. spectrum showed allenic absorption[14] at 5.09 μm, and the anticipated[15] n.m.r. spectral integral for the C-5 substituent confirmed the presence of this type of unsaturated system. The molecular-ion peak was absent from the mass spectrum, but a peak at *m/e* 253 was observed, corresponding to $M^{+} - \cdot CH_3$. Chemical proof for the structure of **11** was afforded by ozonolysis, which gave the aldehyde **1** [characterized



as its crystalline (*p*-nitrophenyl)hydrazone[5], **17**], and by reduction to the saturated derivative **16**, whose n.m.r. spectrum showed the anticipated multiplet for the propyl substituent at C-5. Compound **11** appears to be the first example recorded of an unsaturated carbohydrate derivative having an allene function present; presumably, it arises through attack by AlH_4^- at C-8 of the acetylene, with removal of the 6-OH group in coordination with Li^+. It is noteworthy that, in the series studied here, this compound is the sole example where H-5 and H-6 appear not to be maintained almost exclusively in the antiparallel disposition ($J_{5,6}$ 6 Hz; see Table II). Analogs of **11**

TABLE II

FIRST-ORDER COUPLING-CONSTANTS

Compound	*First-order couplings*[a] *(Hz)*						
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,8}$	*Others*
2	5.0			2.0	7.0	2.5	
6	5.0			2.0	9.0	2.5	
3	5.0	2.5	8.0	2.0	9.0	2.5	
7	5.0	2.0	7.5	2.0	9.0	2.5	
4[b]	5.0	3.0	8.0	2.0	9.5	2.5	
8[b]	5.0	2.5	8.0	2.0	9.5	2.5	
5	5.0			2.0	7.5	—	$J_{6,7}$ 5.0; $J_{7,8trans}$ 17.0; $J_{7,8cis}$ 10.0
9	5.0			2.0	8.0	—	$J_{6,7}$ 5.0; $J_{7,8trans}$ 17.0; $J_{7,8cis}$ 9.5
10[b]	5.0	2.5	8.0	2.0	9.0	—	$J_{6,7}$ 6.0; $J_{7,8trans}$ 17.0; $J_{7,8cis}$ 10.5
11	5.0	3.0	5.0	3.0	10	8.7, 7.5	
16	5.0	2.0	7.7	2.0	~6		

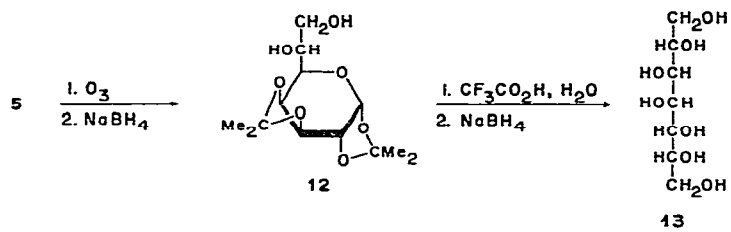
[a]Measured at 60 MHz in chloroform-*d*, unless noted otherwise. [b]At 100 MHz.

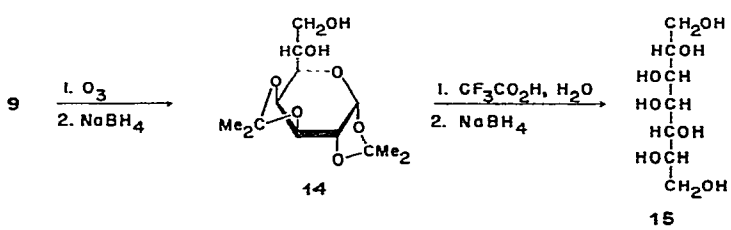
substituted at C-8, obtained from substituted acetylenic Grignard reagents through reaction with aldehydo sugars, would be of interest as a route to optically active allenes, as the allenic sugar derivatives could be resolved as diastereoisomers, and the sugar chain could subsequently be degraded.

The alkenes **5** and **9** were conveniently obtained on a preparative scale by reduction of the mixed acetylenes **2** and **6** with lithium aluminum hydride, followed by direct crystallization of the D-*glycero* alkene **5**, and recovery of the L-*glycero* alkene **9** as its 6-methanesulfonate **10**; overall yields were excellent.

Ozonolysis of the D-*glycero*-D-*galacto* alkene **5**, followed by borohydride reduction, gave the diisopropylidene acetal (**12**) of the corresponding heptose, which was deacetonated, and the resultant heptose[16] reduced with borohydride, to give the known[6] D-*glycero*-D-*galacto*-heptitol (perseitol, **13**) in 62% overall yield from the alkene **5**. This sequence serves to establish the stereochemistry of the acetylene **2**, and of its derivatives **3**, **4**, and **5**; the configuration of compound **5** (refs. 2 and 3) has also been established[13] by another degradative route. The sequence **1**→**2**→**5**→**13** provides a preparative route from D-galactose to perseitol (**13**).

Degradation of the L-*glycero*-D-*galacto* alkene **9** by ozonolysis–reduction gave the corresponding protected heptose (**14**) which, after conversion into the corresponding free heptose[9], was reduced to give the known[8] L-*glycero*-D-*galacto*-heptitol (**15**) in 55% overall yield from **9**. This sequence provides independent proof of the configuration of the series of derivatives **6**, **7**, **8**, and **9**.





EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover "Unimelt" apparatus and are uncorrected. Specific rotations were determined in a

2-dm, polarimeter tube. N.m.r. spectra were determined at 60 or 100 MHz with a Varian A-60 or HA-100 spectrometer, respectively. Spectra were recorded for solutions (15–20%) in chloroform-*d*, with tetramethylsilane ($\tau = 10.00$) as the internal standard. Elemental analyses 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; w, weak. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities. G.l.c. was performed with a Wilkens "Autoprep" Model 705 gas chromatograph (Varian Aerograph, Walnut Creek, California) equipped with a flame-ionization detector and a stainless-steel column (10 ft × 0.25 in.) packed with 5% STAP on Chromosorb W-AW DMSC (Steroid Analysis Phase on acid-washed, dichlorodimethylsilane-treated, diatomaceous earth, Varian Aerograph). Nitrogen was used as the carrier gas at a flow rate of ~80 ml/min. The R_F values for t.l.c. refer to precoated, abrasion-resistant, Silica Gel plates (20 × 20 cm; E. Merck, Darmstadt, Germany). The developers used were *A*, 1:1 ether–petroleum ether; *B*, 9:1 chloroform–ether; *C*, 9:1 benzene–ether; and *D*, chloroform. Indication was effected with sulfuric acid, iodine vapor, or Schiff reagent. Petroleum ether refers to a fraction having b.p. 60–110°.

*7,8-Dideoxy-1,2:3,4-di-*O*-isopropylidene-*D-glycero-α-D-galacto-*oct-7-ynopyranose* (2) *and its* L-glycero-α-D-galacto *epimer* (6). — A solution of ethylmagnesium bromide prepared from magnesium (3.0 g) and ethyl bromide (30 ml) in dry tetrahydrofuran (150 ml) was added dropwise to tetrahydrofuran (150 ml) through which a stream of acetylene was passed before, during, and after the addition. To the resultant solution, a solution of freshly distilled 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose[2,5] (**1**, 10.0 g) in tetrahydrofuran (100 ml) was added dropwise, with stirring, at room temperature. A steady stream of acetylene was passed through the solution throughout the addition, and for a further 3 h. The solution was concentrated to half its volume, ether (500 ml) was added, and the solution was successively washed at 0° with 10% aqueous ammonium chloride (3 × 300 ml) and water (3 × 300 ml), and dried (magnesium sulfate). Evaporation of the solution gave the product (**2**+**6**) as a brown syrup (8.0 g, 73%) that crystallized slowly upon refrigeration and trituration with hexane. T.l.c. of the product established that the starting aldehyde **1** was absent, and two scarcely separated zones, in the intensity ratio of 3:2, were observed.

Two recrystallizations of the product from benzene–petroleum ether gave the pure, faster-moving, major product **2** as white needles; yield 2.4 g (22%), m.p. 131.0–131.5°, $[\alpha]_D^{20}$ −63° (*c* 2.5, chloroform); R_F^* 0.4 (solvent *A*), 0.2 (solvent *C*), and 0.15 (solvent *D*); λ_{max}^{KBr} 2.87 (OH), 3.08 (C≡CH), and 4.72 μm (C≡C); X-ray powder diffraction data: 12.02 m, 7.44 m, 6.55 vs (1), 5.81 s (3), 5.47 m, 4.64 vs (2), 4.49 s (4), 4.25 m, 3.88 m, 3.70 w, 3.55 w, 3.44 vw, 3.34 w, 3.17 vw, 3.11 vw, and 3.01 w.

Anal. Calc. for $C_{14}H_{20}O_6$: C, 59.13; H, 7.09. Found: C, 59.21; H, 6.95.

Recrystallization (twice), from ether–petroleum ether, of the residue from the second recrystallization of **2** gave pale-yellow plates which were separated manually from **2** and recrystallized once more, to give pure 7,8-dideoxy-1,2:3,4-di-*O*-isopro-

pylidene-L-*glycero*-α-D-*galacto*-oct-7-ynopyranose (**6**), m.p. 136–137° (depressed markedly in admixture with **2**), $[\alpha]_D$ −57° (*c* 1.2, chloroform); R_F 0.4 (solvent *A*), 0.15 (solvent *C*), and 0.1 (solvent *D*); λ_{max}^{KBr} 2.89 (OH), 3.08 (C≡CH), and 4.70 μm (C≡C); X-ray powder diffraction data: 8.75 s (2,2), 7.67 s (2,2), 6.65 w, 6.13 s (2,2), 5.16 s (2,2), 4.86 m, 4.27 vs (1), 3.96 vw, 3.62 m, 3.52 m, 3.29 m, 3.10 m, 2.90 m, 2.79 vw, and 2.71 m.

Anal. Calc. for $C_{14}H_{20}O_6$: C, 59.13; H, 7.09. Found: C, 58.99; H, 6.98.

Column chromatography of a 3.0-g portion of the crude reaction-product from a similar ethynylation was performed on a column of Kieselgel (No. 7734, Merck; 140 g). Elution with 3:1 petroleum ether–ether gave first the D-*glycero* derivative **2** (0.7 g), followed by a mixture of **2** and **6** (1.1 g), and, finally, the pure L-*glycero* derivative **6** (1.0 g).

7,8-Dideoxy-1,2:3,4-di-O-*isopropylidene-6*-O-p-*tolylsulfonyl*-D-glycero-α-D-galacto-*oct-7-ynopyranose* (**3**). — A solution containing **2** (2.97 g) and *p*-toluenesulfonyl chloride (2.33 g, 1.1 molar equivs.) in pyridine (30 ml) was stirred for 48 h at ~25°. Water (1 ml) was added and, after 1 h, the mixture was poured into ice–water (300 ml). The precipitated product, which slowly solidified, was filtered off, washed with water, and dried. Recrystallization from benzene–hexane gave the pure D-*glycero* derivative **3**; yield 2.70 g (56%), m.p. 119–120°, $[\alpha]_D^{21}$ −142° (*c* 1.1, chloroform); R_F 0.5 (solvent *A*), 0.93 (solvent *B*), and 0.5 (solvent *D*); λ_{max}^{KBr} 3.1 (C≡CH), 4.7 (C≡C), and 6.25 μm (aryl); X-ray powder diffraction data: 9.82 vw, 8.38 vs (1,1), 7.82 vw, 7.08 s (3), 6.48 vs (1,1), 6.12 s (2), 5.26 s (4), 4.99 vs (1,1), 4.80 vw, 4.66 s (4), 4.19 s (2), 3.97 w, 3.75 w, 3.59 s (3), and 3.42 m.

Anal. Calc. for $C_{21}H_{26}O_8S$: C, 57.51; H, 5.98; S, 7.31. Found: C, 57.37; H, 5.94; S, 7.45.

7,8-Dideoxy-1,2:3,4-di-O-*isopropylidene-6*-O-p-*tolylsulfonyl*-L-glycero-α-D-galacto-*oct-7-ynopyranose* (**7**). — Prepared in the same way as the D-*glycero* derivative **3**, and recrystallized from ethanol–hexane, the L-*glycero* derivative **7** had m.p. 120–121°, $[\alpha]_D$ −151° (*c* 1.1, chloroform); R_F 0.5 (solvent *A*), 0.91 (solvent *B*), and 0.4 (solvent *D*); λ_{max}^{KBr} 3.07 (C≡CH), 4.7 (C≡C), and 6.25 μm (aryl); X-ray powder diffraction data: 11.20 vw, 9.40 m, 7.64 m, 6.01 m, 5.66 m, 5.42 s (2,2), 5.16 m, 4.68 vs (1), 4.35 s (2,2), 4.22 s (2,2), 3.78 w, 3.42 m, and 3.09 s (2,2).

Anal. Calc. for $C_{21}H_{26}O_8S$: C, 57.51; H, 5.98; S, 7.31. Found: C, 57.27; H, 5.85; S, 7.66.

6-O-*Acetyl-7,8-dideoxy-1,2:3,4-di*-O-*isopropylidene*-D-glycero-α-D-galacto-*oct-7-ynopyranose* (**4**). — Prepared conventionally from **2** with acetic anhydride and sodium acetate, and recrystallized from ethanol, the acetate **4** had m.p. 143.5–144.5°, $[\alpha]_D^{22}$ −129° (*c* 1.2, chloroform); R_F 0.55 (solvent *A*), 0.85 (solvent *B*), and 0.25 (solvent *D*); λ_{max}^{KBr} 3.07 (C≡CH), 4.7 (C≡C), and 5.62 μm (C=O); X-ray powder diffraction data: 12.22 m, 7.70 vs (1,1), 6.30 m, 5.46 vs (1,1), 4.88 s (2,2), 4.46 (2,2), 4.09 m, and 3.89 m.

Anal. Calc. for $C_{16}H_{22}O_7$: C, 58.89; H, 6.80. Found: C, 58.63; H, 6.62.

6-O-*Acetyl-7,8-dideoxy-1,2:3,4-di*-O-*isopropylidene*-L-glycero-α-D-galacto-*oct-7-ynopyranose* (**8**). — Prepared from **6** by the method used for **4**, the product **8** was

recrystallized from ethanol–petroleum ether, and had m.p. 122°, $[\alpha]_D^{22}$ −29° (*c* 1, chloroform); R_F 0.55 (solvent *A*), 0.8 (solvent *B*), and 0.25 (solvent *D*); λ_{max}^{KBr} 3.07 (C≡CH), 4.7 (C≡C), and 5.7 μm (C=O); X-ray powder diffraction data: 7.73 vs (1,1), 6.37 w, 5.46 vs (1,1), 4.91 m, 4.48 vs (1,1), 4.07 m, 3.91 m, 3.72 vw, 3.48 w, 3.16 vw, and 2.93 vw.

Anal. Calc. for $C_{16}H_{22}O_7$: C, 58.89; H, 6.80. Found: C, 58.83; H, 6.84.

7,8-Dideoxy-1,2:3,4-di-O-*isopropylidene*-D-glycero-α-D-galacto-*oct-7-enopyranose* (**5**) *by reduction of* **2** *with lithium aluminum hydride.* — A solution of the acetylene **2** (7.0 g) in dry ether (40 ml) was added dropwise to a stirred suspension of lithium aluminum hydride (1.0 g) in ether (130 ml) during ~30 min. The solution was heated gently for 3 h under reflux, and then cooled in ice. The excess of the reductant was decomposed by cautious, dropwise addition, to the stirred solution at 0°, of wet ether (~100 ml) and then water (~10 ml). The precipitate was filtered off, and the filtrate was dried (magnesium sulfate) and evaporated, to give a crystalline residue (6.8 g) that was recrystallized from petroleum ether to afford the alkene **5**; yield 5.76 g (82%), m.p. 107–108°, $[\alpha]_D^{20}$ −50° (*c* 1, chloroform); R_F 0.45 (solvent *A*), 0.2 (solvent *C*), and 0.2 (solvent *D*); λ_{max}^{KBr} 2.9 μm (OH); X-ray powder diffraction data: 12.10 m, 7.82 w, 7.46 m, 6.65 vs (1), 5.92 s (2,2), 5.58 w, 4.73 s (2,2), 4.50 s (3), 4.29 m, 3.92 m, 3.74 w, 3.59 w, 3.36 vw, 3.19 w, 3.04 w, 2.82 w, and 2.52 w.

Anal. Calc. for $C_{14}H_{22}O_6$: C, 58.72; H, 7.69. Found: C, 59.00; H, 7.63.

This compound (**5**) was first obtained[2] by reduction of **2** (whose configuration at C-6 was not at that time established) with hydrogen over Lindlar catalyst, according to the general conditions already described[10]; the product **5** was identical with that just described, by mixed m.p., t.l.c., and i.r. and n.m.r. spectra. It has also been prepared[13] by vinylation of the aldehyde **1**.

7,8-Dideoxy-1,2:3,4-di-O-*isopropylidene*-L-glycero-α-D-galacto-*oct-7-enopyranose* (**9**) *by reduction of* **6** *with lithium aluminum hydride.* — Reduction of **6** (310 mg) with lithium aluminum hydride, as just described for the D-*glycero* epimer (**2**), gave the L-*glycero* alkene **9**; yield 235 mg (75%), b.p. 110–120° (bath)/0.1 torr. The distilled product slowly solidified, and was recrystallized from petroleum ether; m.p. 64–66°, $[\alpha]_D^{20}$ −61° (*c* 1, chloroform); R_F 0.45 (solvent *A*), 0.2 (solvent *B*), and 0.2 (solvent *D*); λ_{max}^{film} 2.87 μm (OH); X-ray powder diffraction data: 11.18 w, 9.06 vs (1,1), 7.59 vw, 6.58 m, 5.28 vs (1,1), 4.44 m, 4.14, 3.69 m, and 3.44 m.

Anal. Calc. for $C_{14}H_{22}O_6$: C, 58.72; H, 7.69. Found: C, 58.92; H, 7.64.

6,7,8-Trideoxy-1,2:3,4-di-O-*isopropylidene*-α-D-galacto-*octo-6,7-dienopyranose* (**11**). — A mixture (~1:1) of the acetylenes **2** and **6** (7.0 g) was subjected to reduction with lithium aluminum hydride as described for the conversion of **2** into **5**. Crystallization of the syrupy product from petroleum ether gave the D-*glycero* alkene **5** (3.81 g) which, after recrystallization from the same solvent, gave pure **5** (3.03 g, 43%; m.p. 107–108°). G.l.c. of the mother liquors (at 170°) showed the presence of the following components; the D-*glycero* alkene **5** (retention time 27 min) and the L-*glycero* alkene **9** (retention time 19 min) in the ratio of ~1:12, together with a minor proportion of a product (retention time 10 min) that was identified as the allene **11**.

The combined mother liquors were fractionated on a column of Kieselgel (Merck, 7734) with 9:1 benzene–ether as eluant. Fractions eluted first contained the allene **11**, obtained as crystals; yield 180 mg (3%). Sublimation at 70–80°/0.2 torr gave pure **11**, m.p. 68–70°, $[\alpha]_D^{22}$ −163° (*c* 1, chloroform); R_F 0.8 (solvent *A*), 0.7 (solvent *C*), and 0.4 (solvent *D*); λ_{max}^{KBr} 5.09 μm (C=C=C); X-ray powder diffraction data: 12.70 w, 8.42 s (3,3), 7.33 s, 6.39 s (2,2), 5.85 s (3,3), 5.22 vs (1), 4.91 s (2,2), 4.70 m, 4.25 m, 4.09 m, 3.69 s (4), 3.57 w, 3.39 m, 3.20 m, 3.08 w, 3.00 m, and 2.71 m; *m/e* 253 ($M^+ - \cdot CH_3$).

Anal. Calc. for $C_{14}H_{20}O_5$: C, 62.67; H, 7.52. Found: C, 62.75; H, 7.48.

Further elution of the column gave the alkene **9** containing a small proportion of **5**; this product was used in the preparation of the 6-*O*-(methylsulfonyl) derivative (**10**) of **9**.

Ozonolysis of the allene **11** *to give the aldehyde* **1**. — Ozonized oxygen was passed for 15 min through a solution of **11** (70 mg) in ethanol at 0°. After passage of oxygen for a further 5 min, the solution was evaporated under diminished pressure. T.l.c. indicated that the product contained a principal, Schiff-positive component having the same migration characteristics as the aldehyde[5] **1**. To a solution of this material in methanol (3 ml) was added a solution of (*p*-nitrophenyl)hydrazine hydrochloride (70 mg) in a mixture of water (1 ml) and pyridine (0.2 ml). After 1 h, water (50 ml) was added to the solution, and the mixture was shaken with benzene (50 ml). The benzene extract was washed twice with water (25 ml), dried (magnesium sulfate), and evaporated. Recrystallization of the residue from benzene–ethanol gave 1,2,3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose 6-(*p*-nitrophenyl)hydrazone (**17**); yield 39 mg (28% from **11**), m.p. 214–215°. The product was identical with an authentic specimen[5] by mixed m.p., i.r. spectrum, and X-ray diffraction pattern.

6,7,8-Trideoxy-1,2:3,4-di-O-*isopropylidene*-α-D-galacto-*octopyranose* (**16**) *by reduction of the allene* **11**. — A solution of **11** (100 mg) in ethanol (20 ml) was stirred under hydrogen at 1 atm. pressure in the presence of 5% palladium-on-carbon (50 mg). After 4 h, the catalyst was filtered off, and the filtrate was evaporated to give **16** as a syrup; yield 85 mg (84%), b.p. 90–120° (bath)/0.05 torr.

Anal. Calc. for $C_{14}H_{24}O_5$: C, 61.75; H, 8.88. Found: C, 62.27; H, 8.94.

7,8-Dideoxy-1,2:3,4-di-O-*isopropylidene-6*-O-(*methylsulfonyl*)-L-glycero-α-D-galacto-*oct-7-enopyranose* (**10**). — The fractions containing mostly the L-*glycero* alkene **9**, from the experiment leading to the allene **11**, were evaporated. The dried residue (3.07 g) was dissolved in pyridine (30 ml) at 0°, and a solution of methanesulfonyl chloride (0.92 ml) in pyridine (10 ml) was added dropwise during 30 min. After 16 h at ~25°, water (1 ml) was added and, after 1 h, the solution was poured into ice–water (800 ml). The resultant precipitate was filtered off, and recrystallized from ethanol–petroleum ether to give pure **10**; yield 2.52 g (62%), m.p. 121.5–122.5°, $[\alpha]_D^{21}$ −61° (*c* 1.3, chloroform); R_F 0.8 (solvent *B*), 0.4 (solvent *C*), and 0.2 (solvent *D*); X-ray powder diffraction data: 7.82 s (3,3), 7.31 m, 6.77 m, 6.12 m, 5.54 s (2,2), 5.00 s (2,2), 4.55 vs (1), 4.14 vw, 3.93 w, 3.77 s (3,3), 3.51 vw, and 3.27 vw.

Anal. Calc. for $C_{15}H_{24}O_8S$: C, 49.43; H, 6.64; S, 8.79. Found: C, 49.71; H, 6.63; S, 8.83.

*Conversion of 7,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-*D-glycero-α-D-galacto-*oct-7-enopyranose* (**5**) *into* D-glycero-D-galacto-*heptitol* (*perseitol*) (**13**). — Ozonized oxygen was passed for 40 min through a solution of **5** (390 mg) in ethanol (100 ml) maintained at −70°. After subsequent passage of oxygen for 10 min, the solution was diluted with water (20 ml), and sodium borohydride (200 mg) was added. The solution was kept for 1 h at ~25°, and then Amberlite IR-120 (H^+) ion-exchange resin (30 ml) was added, and the mixture was stirred for 10 min. The resin was filtered off and washed with ethanol, and the filtrate was evaporated; boric acid was removed by repeated addition of methanol to, and evaporation from, the residue.

The resultant syrupy, chromatographically homogeneous 1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-heptose (**12**; yield 310 mg) was dissolved in 9:1 trifluoroacetic acid–water (5 ml), and the solution was kept for 10 min at ~25°. The solvent was then evaporated off, water (20 ml) was added, and the resultant solution was cooled to 0°. Sodium borohydride (200 mg) was added, and the solution was stirred for 2 h at 0°, and then with Amberlite IR-120 (H^+) ion-exchange resin (20 ml) for 10 min. The resin was filtered off, the filtrate was evaporated, and the residue was freed from boric acid as before by use of methanol, to give perseitol (**13**) as a white, microcrystalline solid; yield 180 mg (62% from **5**). The material was recrystallized from 80% aqueous methanol to yield pure **13**, m.p. 186–187°; X-ray powder diffraction data: 9.96 vs (2), 4.69 vs (1), 4.33 w, 4.07 s (3,3), 3.88 s (3,3), 3.44 w, 3.09 w, 2.97 w, 2.83 w, 2.72 w, 2.61 w, 2.52 w, 2.44 m, 2.38 vw, and 2.23 m.

The product was identical with an authentic sample[6] of perseitol (m.p. 187–188°) by mixed m.p., i.r. spectrum, and X-ray powder diffraction patten.

*Conversion of 7,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-*L-glycero-α-D-galacto-*oct-7-enopyranose* (**9**) *into* L-glycero-D-galacto-*heptitol* (**15**). — By the route used for converting **5** into **13**, the alkene **9** (326 mg) was converted, by way of 1,2:3,4-di-*O*-isopropylidene-L-*glycero*-α-D-*galacto*-heptose (**14**), into L-*glycero*-D-*galacto*-heptitol (**15**); yield 130 mg (55% from **9**), m.p. 140.5–142°; X-ray powder diffraction data: 6.80 m, 5.75 vs (1,1), 4.73 m, 4.41 vs (1,1), 4.17 w, 3.95 s (2), 3.84 vw, 3.49 m, 3.37 m, 3.31 m, 3.13 m, 3.03 m, 2.85 s (3), 2.76 m, 2.35 m, and 2.25 m.

The product was identical, by mixed m.p., i.r. spectrum, and X-ray powder diffraction pattern, with an authentic sample[8] of **15** having m.p. 141–142°.

ACKNOWLEDGMENTS

The authors thank Dr. Nelson K. Richtmyer for authentic samples of D-*glycero*-D-*galacto*-heptitol (perseitol, **13**) and L-*glycero*-D-*galacto*-heptitol (**15**), and Dr. J. M. J. Tronchet for preliminary studies on the ethynylation of compound **1**.

REFERENCES

1 H. EL KHADEM, D. HORTON, AND M. H. MESHREKI, *Carbohyd. Res.*, 16 (1971) 409.
2 D. HORTON, J. B. HUGHES, J. M. J. TRONCHET, W. N. TURNER, AND J. D. WANDER, *Abstr. Papers Amer. Chem. Soc. Meeting*, 150 (1965) 21D; D. HORTON, J. B. HUGHES, AND J. M. J. TRONCHET, *Chem. Commun.*, (1965) 481.
3 R. HEMS, D. HORTON, AND M. NAKADATE, *Abstr. Papers Amer. Chem. Soc. Meeting*, 158 (1969) CARB-7.
4 See D. HORTON AND FRANCES O. SWANSON, *Carbohyd. Res.*, 14 (1970) 159, and papers referred to therein.
5 J. L. GODMAN, D. HORTON, AND M. NAKADATE, *Carbohyd. Res.*, 7 (1968) 56.
6 R. M. HANN AND C. S. HUDSON, *J. Amer. Chem. Soc.*, 61 (1939) 33.
7 J. S. BRIMACOMBE AND J. M. WEBBER, in W. PIGMAN AND D. HORTON (Eds.), *The Carbohydrates, Chemistry and Biochemistry*, 2nd edition, Vol. IA, Academic Press, New York, 1972, p. 490.
8 L. C. STEWART, N. K. RICHTMYER, AND C. S. HUDSON, *J. Amer. Chem. Soc.*, 74 (1952) 2206.
9 S. DAVID AND M.-O. POPOT, *Carbohyd. Res.*, 8 (1968) 350.
10 D. HORTON AND J. M. J. TRONCHET, *Carbohyd. Res.*, 2 (1966) 315.
11 D. HORTON, J. B. HUGHES, AND J. K. THOMSON, *J. Org. Chem.*, 33 (1968) 728.
12 R. A. RAPHAEL, *Acetylenic Compounds in Organic Synthesis*, Butterworths, London, 1955; J. D. CHANLEY AND H. SOBOTKA, *J. Amer. Chem. Soc.*, 71 (1949) 4140.
13 G. B. HOWARTH, D. G. LANCE, W. A. SZAREK, AND J. K. N. JONES, *Can. J. Chem.*, 47 (1969) 75; D. G. LANCE, W. A. SZAREK, J. K. N. JONES, AND G. B. HOWARTH, *ibid.*, 47 (1969) 2871.
14 J. W. WOTIZ AND D. E. MANCUSO, *J. Org. Chem.*, 22 (1957) 207.
15 E. B. WHIPPLE, J. H. GOLDSTEIN, AND L. MANDELL, *J. Chem. Phys.*, 30 (1959) 1109.
16 E. M. MONTGOMERY AND C. S. HUDSON, *J. Amer. Chem. Soc.*, 64 (1942) 247.