Carbohydrate Research
Elsevier Publishing Company, Amsterdam
Printed in Belgium

EXTENSION OF SUGAR CHAINS THROUGH ACETYLENIC INTERMEDIATES

III. 1-HEPTYNE-L-*gluco*- AND L-*manno*-3,4,5,6,7-PENTOL FROM 2,3,4,5-TETRA-*O*-BENZOYL-*aldehydo*-L-ARABINOSE*

J. L. GODMAN, D. HORTON**, AND J. M. J. TRONCHET
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U. S. A.)

(Received February 20th, 1967)

Previous reports in this series[1,2] described the ethynylation of 2,3:4,5-di-*O*-isopropylidene-*aldehydo*-L-arabinose to give a mixture of 4,5:6,7-di-*O*-isopropylidene-1-heptyne-L-*gluco*-3,4,5,6,7-pentol and the L-*manno* epimer, separable by preparative g.l.c.[1,2] or by fractional recrystallization[2] of the derived 3-(3,5-dinitrobenzoates) (**5** and **8**, respectively). This method of chain extension, by ethynylation of *aldehydo* sugars, has been applied[1] with other substituted *aldehydo* sugars. In each case, cyclic acetal substituents were employed as protecting groups to prevent the aldehyde group from undergoing intramolecular cyclization.

The purpose of the present investigation was to determine if ethynylation of a fully acylated *aldehydo* sugar could be used as a practical method for chain extension. Fully acylated *aldehydo* sugars are generally more accessible than are *aldehydo* sugars having cyclic acetal substituents as protecting groups. However, since acyloxy groups are susceptible to attack by organometallic reagents, it was not known if selective attack at the aldehyde group could be effected.

In this report, it is shown that ethynylation of an aldehyde group in the presence of benzoyloxy substituents is feasible as a preparative procedure for extension of a sugar chain. Ethynylation of *aldehydo*-L-arabinose tetrabenzoate (**1**) gave a mixture of 3-epimeric pentol derivatives (**2**), separated as the perbenzoates (**3** and **6**). The latter, and the derived pentols (**4** and **7**) were characterized on a crystalline basis. Preparation of the pentols **4** and **7**, and of the pentabenzoates **3** and **6**, by an alternative, stereochemically definitive route, provided independent confirmation of structures assigned to the products prepared from **1**, and served to identify the epimers specifically.

3-*O*-(3,5-Dinitrobenzoyl)-4,5:6,7-di-*O*-isopropylidene-1-heptyne-L-*gluco*-3,4,5,6,7-pentol (**5**) and its L-*manno* epimer (**8**), whose configurations have been determined unequivocally by degradation to known, crystalline derivatives[2], were used to prepare

*Supported by the National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare, Bethesda, Maryland 20014; Grant No. GM-11976-03 (The Ohio State University Research Foundation Project 1820). Funds for purchase of the n.m.r. spectrometer were provided by the National Science Foundation, Washington, D. C.
**To whom inquiries should be addressed.

authentic samples of 1-heptyne-L-*gluco*-3,4,5,6,7-pentol* (**4**) and its L-*manno* epimer* (**7**), and also the corresponding pentabenzoates **3** and **6**. The substituted derivatives **5** and **8** were treated with aqueous acetic acid for 1.5 h at 100° to remove the *O*-isopropylidene groups, and subsequent removal of the 3,5-dinitrobenzoyl group with a catalytic amount of sodium methoxide in methanol (Zemplén deacylation) gave the free pentols **4** and **7**. Benzoylation of **4** and **7** gave the corresponding pentabenzoates **3** and **6**. The pentabenzoates **3** and **6** could be reconverted into the respective pentols by Zemplén deacylation.

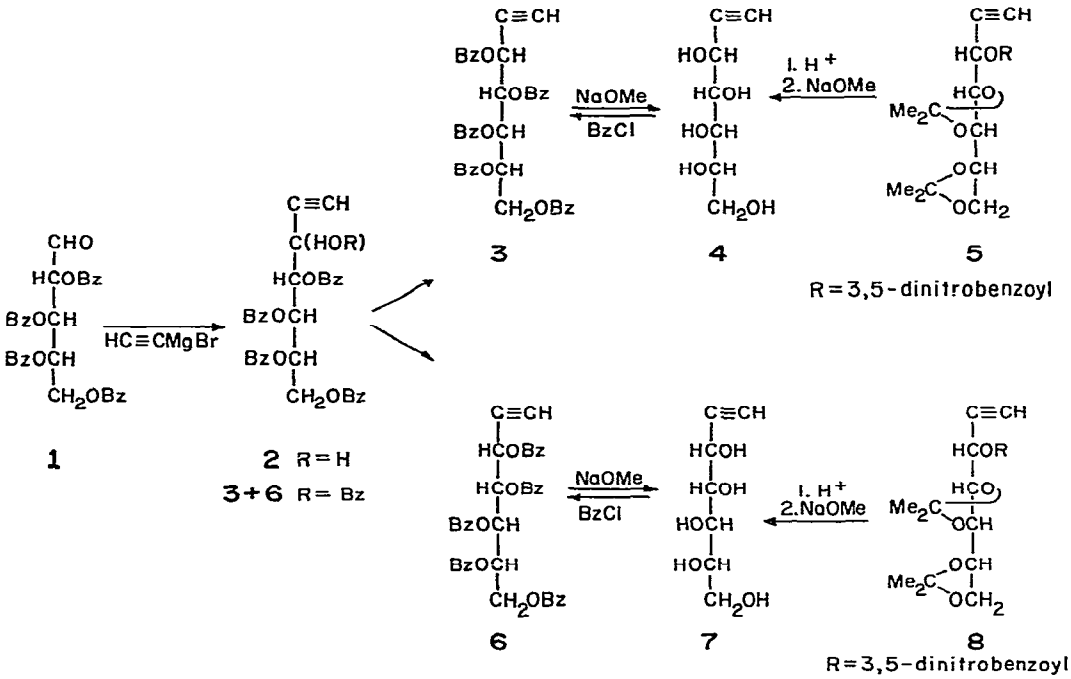
Spectroscopic evidence provided full support for the gross structures assigned to the perbenzoates **3** and **6**. A terminal acetylene function was indicated by the i.r. spectra, and the n.m.r. spectra showed a 1-proton, narrow doublet at τ 7.40 in **3** and at τ 7.51 in **6**, characteristic[2] of an acetylenic hydrogen, long-range coupled to a hydrogen atom four bonds distant ($J_{1,3} \sim 1.2$ Hz). Integration of the signals in the aryl region showed the presence of 5 benzoyl groups. A 2-proton, 8-peak multiplet, the AB portion of an ABX system, was observed near τ 5.3, and was assigned to the C-7 methylene group. The remaining signals, total integral 4 protons, observed in the region τ 3.4–4.3, were assigned to H-3, 4, 5, and 6, but the complexity of the multiplets observed made analysis in detailed stereochemical terms difficult. The two pentabenzoates had sharp melting points, gave different X-ray powder diffraction patterns, and showed different fine-structure in their n.m.r. and i.r. spectra. There was no evidence to indicate any interconversion of **3** and **6**, or other configurational change, during their preparation from **5** and **8**. A chromatographic method for effecting a clear separation of **3** and **6** was not found.

The free pentols (**4** and **7**) were both obtained crystalline. They showed absorptions characteristic of the acetylene group in their i.r. spectra, and both gave satisfactory elemental analyses. The pure L-*gluco* epimer (**4**) melted sharply at 114–116°, and the pure L-*manno* epimer (**7**) melted sharply at 122–123°. The two pentols were not separable by paper chromatography or electrophoresis in a number of different systems, but sharp separations were readily achieved by g.l.c. of the trimethylsilyl ethers, and it was possible to detect as little as 1% of the one 3-epimer in admixture with the other. Substances **4** and **7** were found to be completely homogeneous by this procedure. This result indicates that the starting materials for their preparation (**3** and **6**, or **5** and **8**) were epimerically pure and that no epimerization had occurred during their conversion into the respective pentols

Since it could be argued that the pentols **4** and **7** might undergo epimerization at C-3 under acid hydrolytic conditions, by allylic-type assistance in the generation of a carbonium ion at C-3, an experiment was performed to determine the configurational stability and gross structural stability of the pentols to aqueous acid. The separate pentols **4** and **7** were heated in N sulfuric acid for 1 h at 100°. The recovered

*Compounds **4** and **7** are strictly named as 6-heptyne-D-*gulo*- and L-*manno*-1,2,3,4,5-pentol, respectively. In this paper, and in the preceding one[2], the alkyne terminus is considered to be C-1, so that configurational relationships are readily apparent between the acetylenic derivatives, their precursors, and their degradation products.

products, analyzed by g.l.c. of their trimethylsilyl ethers, were epimerically pure and essentially unchanged. No epimerization at C-3 was noted, even after longer times of treatment. These observations, together with the conversions used in the preparation of **4** and **7** from **5** and **8**, are of consequence in connection with the use of acetylenic sugar



derivatives in synthesis; they indicate that the acetylenic alcohol system in such structures as **4** and **7** is stable to conditions of glycoside hydrolysis, hydrolysis of *O*-isopropylidene groups, and the Zemplén deacylation procedure.

2,3,4,5-Tetra-*O*-benzoyl-*aldehydo*-L-arabinose (**1**) was prepared from 2,3,4,5-tetra-*O*-benzoyl-L-arabinose diethyl dithioacetal by way of 1,1-di-*O*-acetyl-2,3,4,5-tetra-*O*-benzoyl-*aldehydo*-L-arabinose aldehydrol, essentially by the procedure of Zinner and coworkers[3,4] for the D-enantiomorph. N.m.r. spectral data for **1** and its precursors are recorded in the Experimental section. Ethynylation of the *aldehydo* sugar derivative **1** gave, in high yield, the mixed, 3-epimeric, ethynylated products (**2**). Benzoylation of this mixture gave a high yield of a mixture of the pentabenzoates **3** and **6**, in a ratio of about 1:2. Separation of this mixture was difficult, and isolation of pure samples of the 3-epimeric pentabenzoates **3** and **6** was achieved only at the expense of yield. Preliminary fractionation by silicate extrusion-chromatography, followed by fractional recrystallization, gave pure samples of the pentabenzoates **3** and **6** that were identical in all respects with the corresponding samples prepared for **5** and **8**, and saponification of the products gave the respective pentols **4** and **7**, identical with the authentic products.

Since fully acylated *aldehydo* sugars are readily prepared from aldose dialkyl

dithioacetals, the results of the present study increase the potential of the ethynylation reaction for synthesis in the carbohydrate field.

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover melting-point apparatus (Arthur H. Thomas Co., Philadelphia, Pennsylvania) and are uncorrected. Specific rotations were determined in a 2-dm polarimeter tube. I.r. spectra were measured with a Perkin–Elmer Model 137 "Infracord" infrared spectrometer. N.m.r. spectra were measured at 60 MHz with a Varian A-60 n.m.r. spectrometer. Chemical shifts are given on the τ scale, and spectra were measured at *ca.* 40° with solutions (5–15%) in chloroform-*d*, with tetramethylsilane (τ 10.00) as the internal standard. Microanalyses were determined 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: s, strong; m, moderate; w, weak; v, very. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities. Paper chromatography was performed on Whatman No. 1 paper by downward irrigation with either (A) 3:1:1 butyl alcohol–ethanol–water, or (B) 5:5:3:1 pyridine–ethyl acetate–water–acetic acid. Paper electrophoresis was performed on Whatman No. 3 paper by the enclosed-strip technique[5] with either borate buffer[6] (pH 9.2) or molybdate buffer[7](pH 5). Components were detected with alkaline silver nitrate[8]. T.l.c. was performed with Silica Gel G (E. Merck, Darmstadt, Germany) activated at 110° as the adsorbent, 99:1 benzene–methanol as the developer, and sulfuric acid as the indicator. G.l.c. analyses were made with an Aerograph Autoprep Model 705 gas chromatograph (Wilkens Instrument and Research, Inc., Walnut Creek, California) equipped with a flame-ionization detector. Nitrogen was used as the carrier gas.

1-Heptyne-L-gluco-*3,4,5,6,7-pentol* (**4**). — A solution of 3-*O*-(3,5-dinitrobenzoyl)-4,5:6,7-di-*O*-isopropylidene-1-heptyne-L-*gluco*-3,4,5,6,7-pentol[2] (**5**, 163 mg) in 60% aqueous acetic acid (7 ml) was heated for 1.5 h at 100°. The solution was evaporated, and toluene was twice added to and evaporated from the residue, to yield 3-*O*-(3,5-dinitrobenzoyl)-1-heptyne-L-*gluco*-3,4,5,6,7-pentol as a white solid. To a suspension of the latter in dry methanol (5 ml) was added a catalytic amount of sodium methoxide in dry methanol (5 ml). Complete dissolution was achieved rapidly. The solution was kept for 2.5 h at room temperature, neutralized with solid carbon dioxide, and evaporated to dryness, and the residue was stirred with water (15 ml) for 15 min at room temperature. The resultant suspension was washed with two 25-ml portions of chloroform, and the combined chloroform solutions were extracted once with water (10 ml). The aqueous layers were combined, and stirred with a large excess of Amberlite IRC-50 (H^+) cation-exchange resin for 15 min. Evaporation of the solution gave a colorless, chromatographically homogeneous syrup (papergram), in essentially quantitative yield, which solidified on trituration with acetone. Recrystallization from acetone–ethanol gave the pentol **3** as fine granules, yield 33 mg (49%), m.p. 114–116°; R_F 0.30, R_G 1.59

(solvent A), R_G 1.49 (solvent B), M_G 0.85 (borate), $M_{Mannitol}$ 1.07 (molybdate); X-ray powder diffraction data : 7.95 m, 5.27 w, 4.96 m, 4.80 s (2,2), 4,26 s (3,3), 3.98 w, 3.66 s (3,3), 3.58 w, 3.46 w, 3.24 s, (2,2), 2.96 m, 2.66 w, 2.54 vw, 2.46 w, 2.36 s (1), 2.24 vw, and 2.13 w.

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.75; H, 7.11.

1-Heptyne-L-manno-*3,4,5,6,7-pentol* (7). — 3-*O*-(3,5-Dinitrobenzoyl)-4,5,6,7-di-*O*-isopropylidene-1-heptyne-L-*manno*-3,4,5,6,7-pentol (8, 367 mg) was heated with aqueous acetic acid to give 3-*O*-(3,5-dinitrobenzoyl)-1-heptyne-L-*manno*-3,4,5,6,7-pentol, and the latter was saponified by the general procedure described for the L-*gluco* epimer. The resultant pentol (7), obtained as a chromatographically homogeneous syrup (papergram), yield 140 mg (97%), solidified on trituration with acetone. Recrystallization from acetone gave 7 as fine granules, yield 50 mg (35%). A second recrystallization from acetone gave 38 mg of 7, m.p. 122–123°; R_F 0.32, R_G 1.67 (solvent A), R_G 1.58 (solvent B), M_G 0.85 (borate), $M_{Mannitol}$ 1.07 (molybdate); λ_{max}^{KBr} ~2.9 (OH), 3.07 (C≡CH), 4.74 μ (C≡C); X-ray powder diffraction data: 8.78 m (4), 6.61 vs (1), 5.04 w, 4.83 w, 4.65 m, 4.40 s (2,2), 4.32 s (2,2), 4.03 m, 3.73 w, 3.49 w, 3.41 m, 3.23 w, 3.10 m, 2.99 vw, 2.88 w, 2.73 s (3), 2.62 w, 2.49 m, 2.40 w, 2.33 vw, and 2.21 m.

Anal. Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found : C, 47.41; H, 6.87.

The L-*manno* pentol 7 and the L-*gluco* pentol 4 in admixture were not clearly distinguishable by paper chromatography, either in solvent A or in solvent B. No separation was effected by electrophoresis in borate or molybdate buffers. The homogeneity and epimeric purity of the pentols 4 and 7 was verified by g.l.c. of their trimethylsilyl ethers, in which system a clear separation was achieved.

Gas–liquid chromatography of the trimethylsilyl ethers of 1-heptyne-L-gluco (*and* L-manno)-*3,4,5,6,7-pentol* (4 *and* 7). — Trimethylsilyl ethers were prepared by shaking the sample with 10–20 times its weight of a mixture of chlorotrimethylsilane and hexamethyldisilazane in pyridine (TRI-SIL, Pierce Chemical Company, Rockford, Illinois). The prepared samples were kept for at least 5 min before injection onto the column. A stainless-steel column (10 ft × 1/4 in) packed with 5% STAP stationary phase (Varian Aerograph, Walnut Creek, California) on Chromosorb W (AW-DMCS) (Varian Aerograph, Walnut Creek, California) was used, with nitrogen as the carrier gas. At temperatures in the range of 140–150°, with a carrier-gas flowrate in the range of 90–120 ml/min, the trimethylsilyl ether of the L-*manno* pentol 7 emerged as a single, sharp peak having a retention time in the range of 6.3–9.6 min. Under identical conditions, the trimethylsilyl ether of the L-*gluco* pentol 4 emerged approximately 1 min later than the L-*manno* derivative, and likewise gave a sharp, single peak. Analysis of prepared mixtures of 4 and 7, with integration of g.l.c. peak areas, indicated that quantitative determination of 4 and 7 in admixture could be achieved with a precision of ±1% or less.

Action of dilute acid on the pentols 4 *and* 7. — A solution of the L-*manno* pentol 7 (1 mg) was heated with N sulfuric acid (1 ml) for 1 h at 100°. The solution was neutralized with barium carbonate, and evaporated, and the product was trimethylsilylated.

G.l.c. revealed the presence of a single component having the retention time of the trimethylsilyl ether of **7**, and no component corresponding to the trimethylsilyl ether of **4** was detected.

The L-*gluco* pentol **4** was treated similarly with sulfuric acid. G.l.c. of the trimethylsilylated product revealed a major component having the same retention time as the trimethylsilyl ether of **4**, together with a minor component (~5%) having approximately twice the retention time. No component having the retention time of the trimethylsilyl derivative of **7** was detected.

No interconversion of the pentols **4** and **7** was observed, even after treatment with N sulfuric acid for 12 h at 100°.

3,4,5,6,7-Penta-O-*benzoyl-1-heptyne*-L-gluco-*3,4,5,6,7-pentol* (**3**). — To a solution of **4** (21.4 mg) in dry pyridine (3 ml) was added benzoyl chloride (0.10 ml), and the solution was stirred for 9 h at room temperature. A few drops of water were added, and after 15 min, the solution was poured into saturated aqueous sodium hydrogen carbonate (50 ml). The oily solution was extracted portionwise with a total of 80 ml of chloroform, and the combined extracts were washed with water (30 ml). The dried (magnesium sulfate) organic layer was evaporated to dryness, and toluene was twice added to, and evaporated from, the residue. The resulting syrup crystallized on trituration with ethanol, yield 52 mg (61%). Recrystallization from ethanol gave pure **3** as spherical clusters, yield 39 mg (46%), m.p. 122.5–123.5°, $[\alpha]_D^{18}$ −47.4 ±3° (*c* 0.56, chloroform); R_F 0.71 (t.l.c.); λ_{max}^{KBr} 3.15 (C≡CH), 4.78 (C≡C), 5.81 μ (benzoate); n.m.r. data: τ 1.69–2.25 (broad double peak) and 2.25–2.94 (broad multiplet) (25 protons, aryl), τ 3.43–3.63 (1-proton multiplet) and 3.72–4.23 (3-proton multiplet) (H-3, 4,5,6), τ 5.06 (1-proton quartet, $J_{6,7}$ 3.5 Hz, $J_{7,7'}$ 12.5 Hz, H-7), τ 5.40 (1-proton, quartet, $J_{6,7'}$ 5.5 Hz, H-7'), τ 7.40 (1-proton doublet, $J_{1,3}$ 1.2 Hz, H-1); X-ray powder diffraction data: 10.26 m, 9.32 w, 8.36 m, 7.36 vw, 6.62 m, 6.33 w, 6.03 w, 5.44 w, 5.19 m, 4.85 m, 4.39 vs (1), 4.22 s (2), 4.09 w, 3.93 s (3,3), 3.82 vvw, 3.71 vw, 3.58 w, 3.44 w, 3.28 s (3,3), and 3.18 s (3,3).

Anal. Calc. for $C_{42}H_{32}O_{10}$: C, 72.40; H, 4.62. Found: C, 72.42; H, 4.41.

3,4,5,6,7-Penta-O-*benzoyl-1-heptyne*-L-manno-*3,4,5,6,7-pentol* (**6**). — The L-*manno* pentol **7** (29 mg) was benzoylated by the procedure described for the L-*gluco* epimer **4**. The product **6** was obtained as a syrup that, on trituration with ethanol, crystallized as spherical clusters. Recrystallization from ethanol gave pure **6**, yield 52 mg (46%), m.p. 131–132.5°, $[\alpha]_D^{18}$ −8 ±4° (*c* 0.8, chloroform); R_F 0.72 (t.l.c.); λ_{max}^{KBr} 3.07 (C≡CH), 4.72 (C≡C), 5.80 μ (benzoate); n.m.r. data: τ 1.67–2.32 (broad single peak) and τ 2.32–3.00 (broad multiplet) (25 protons, aryl), τ 3.60–3.78 (1-proton multiplet) and 3.80–4.30 (3-proton multiplet) (H-3,4,5,6), τ 5.10 (1-proton quartet, $J_{6,7}$ 3.5 Hz, $J_{7,7'}$ 12.0 Hz, H-7), τ 5.47 (1-proton quartet, $J_{6,7'}$ 5.5 Hz, H-7'), τ 7.51 (1-proton doublet, $J_{1,3}$ ~1 Hz, H-1); X-ray powder diffraction data: 14.67 w, 9.19 s (2), 7.58 m, 6.78 vw, 5.81 m, 5.34 w, 4.90 vs (1), 4.71 s (3,3), 4.38 w, 4.09 m, 3.93 vw, 3.77 s (3,3), 3.45 vw, 3.29 vw, and 3.13 m.

Anal. Calc. for $C_{42}H_{32}O_{10}$: C, 72.40; H, 4.62. Found: C, 71.97; H, 4.64.

The n.m.r. spectra of **3** and **6** showed differences in the shape of the H-3,4,5,6

multiplets, in addition to the difference in appearance of the lower-field group of aryl-proton signals, but first-order analysis of the H-3,4,5,6 multiplets was not possible at 60 MHz.

2,3,4,5-Tetra-O-benzoyl-L-arabinose diethyl dithioacetal. — L-Arabinose diethyl dithioacetal[9] (30 g) in pyridine (300 ml) was treated with benzoyl chloride (80 ml) in pyridine (100 ml) at −10 to 0°. After 13 h at 0°, the solution was poured into 3.5 l of ice and water. After 14 h, the syrupy product was purified, and crystallized from methanol, as described[3] for the D enantiomorph, yield 65 g (83%), m.p. 67–69° (lit.[3] m.p. 69.5° for the D enantiomorph); λ_{max}^{KBr} 5.81 (OBz), 6.23, 6.32, 6.73, 6.92 μ (aryl); n.m.r. data: τ 1.80–2.10, 2.45–2.75 (multiplets, 20 protons, Ph), τ 3.51 (1-proton quartet, $J_{2,3}$ 3.8 Hz, $J_{3,4}$ 6.0 Hz, H-3), τ 3.92–4.20 (2-proton multiplet, H-2, H-4), τ 5.03 (1-proton quartet, $J_{4,5}$ 3.5 Hz, $J_{5,5'}$ 12 Hz, H-5), τ 5.38 (1-proton quartet, $J_{4,5'}$ 6.5 Hz, H-5'), τ 5.68 (1-proton doublet, $J_{1,2}$ 6.9 Hz, H-1), τ 3.28 (4-proton quartet, J 7.5 Hz, CH_2 of Et), τ 8.81 (6-proton triplet, CH_3 of Et).

Anal. Calc. for $C_{37}H_{36}O_8S_2$: C, 66.05; H, 5.39; S, 9.53. Found: C, 65.95; H, 5.25; S, 9.27.

The first-order $J_{1,2}$, $J_{4,5}$, and $J_{4,5'}$ couplings derived from the n.m.r. spectrum indicated that the quartet at τ 3.51 was not the H-2 or the H-4 signal. The observed couplings of hydrogen atoms on the chain were in agreement with a planar, zig-zag backbone of carbon atoms (largest groups antiparallel) as the favored conformation (most populated rotamer state), as has been noted[10] with other acyclic sugar derivatives. The occurrence of the H-1 signal at higher field than the signals of all other hydrogen atoms on the carbon chain is noteworthy.

1,1-Di-O-acetyl-2,3,4,5-tetra-O-benzoyl-aldehydo-L-*arabinose aldehydrol.* — 2,3,4,5-Tetra-*O*-benzoyl-L-arabinose diethyl dithioacetal (35 g) was dissolved in a mixture of acetic anhydride (400 ml) and sulfuric acid (20 ml) that had been cooled to −10°. The reaction mixture was treated as described by Zinner and co-workers[4] for the D enantiomorph. Crystallization from methanol gave the product, yield 22.1 g (63%), m.p. 128.5–129.5° (lit.[4] m.p. 130° for the D enantiomorph); λ_{max}^{KBr} 5.65 (OAc), 5.77 (OBz), 6.23, 6.32, 6.72, 6.91 μ (aryl); n.m.r. data: τ 1.81–2.15, 2.31–2.67 (20 protons, aryl), τ 2.80 (1-proton doublet, $J_{1,2}$ 7 Hz, H-1), τ 3.73–4.30 (3-proton multiplet, H-2,3,4), τ 5.10 (1-proton quartet, $J_{4,5}$ 3Hz, $J_{5,5'}$ 12.5 Hz, H-5) τ 5.47 (1-proton quartet, $J_{4,5'}$ 6 Hz, H-5'), τ 7.97, 8.09 (3-proton singlets, OAc).

Anal. Calc. for $C_{37}H_{32}O_{12}$: C, 66.46; H, 4.82. Found: C, 66.67; H, 4.89.

2,3,4,5-Tetra-O-benzoyl-aldehydo-L-*arabinose* (**1**). — A solution of 1,1-di-*O*-acetyl-2,3,4,5-tetra-*O*-benzoyl-*aldehydo*-L-arabinose aldehydrol (22.1 g) in a mixture of *p*-dioxane (600 ml) and 15% perchloric acid (150 ml) was heated for 2 h at 100°, according to the general procedure of Zinner and co-workers[4]. The solution was poured into ice and water (1.5 l), and the product was extracted with dichloromethane. The extract was washed 3 times with water, dried (magnesium sulfate), and evaporated. The product was dried under vacuum for 24 h at 78° to give **1** as an amorphous solid, yield 13.65 g (73%), λ_{max}^{KBr} 5.82 (CHO, OBz), 6.29, 6.77, 6.95 μ (aryl); n.m.r. data: τ 0.30 (1-proton singlet, H-1), τ 1.82–2.12, 2.38–2.72 (20 protons, aryl), τ 3.78–4.23

(3-proton multiplet, H-2,3,4), τ 5.03 (1-proton quartet, $J_{4,5}$ ~3 Hz, $J_{5,5'}$ 12 Hz, H-5), τ 5.38 (1-proton quartet, $J_{4,5'}$ ~5 Hz).

Anal. Calc. for $C_{32}H_{26}O_9$: C, 69.96; H, 4.63. Found: C, 69.39; H, 4.76.

The product gave a positive Schiff test. In common with other (saturated) *aldehydo* sugars that have been examined[1,11], the signal of the aldehyde proton is observed as a singlet, indicating that $J_{1,2}$ is ~0 Hz.

*3,4,5,6,7-Penta-*O*-benzoyl-1-heptyne-*L-gluco *(and* L-manno*)-3,4,5,6,7-pentol* (**3** *and* **6**) *by ethynylation of 2,3,4,5-tetra-*O*-benzoyl-*aldehydo-L-*arabinose* (**1**). — The freshly prepared *aldehydo* sugar **1** (12.85 g) was treated with ethynylmagnesium bromide (prepared from 1 g of magnesium), essentially by the procedure described previously[2], except that addition of **1** (in 200 ml of tetrahydrofuran) was rapid, to give syrupy 4,5,6,7-tetra-*O*-benzoyl-1-heptyne-L-*gluco* (and L-*manno*)-3,4,5,6,7-pentol (**2**), yield 11.2 g (83%), λ_{max}^{film} 2.92 (OH), 3.07 (C≡CH), 4.72 (C≡C), ~5.8 μ (benzoate). This product (2.1 g) was treated with benzoyl chloride (2.1 ml) and pyridine, according to the general procedure used for the benzoylation of the pentols **4** and **7**. The product (**3** and **6**) was obtained as a dark syrup, yield 2.1 g (85%); λ_{max}^{film} 3.09 (C≡CH), 4.73 (C≡C), ~5.8 μ (benzoate), OH absent. The n.m.r. spectrum of the crude product indicated that it contained **3** and **6** in the ratio of approximately 1:2. T.l.c. indicated a principal component having R_F ~0.7 (**3** and **6**), together with 7 minor or trace components.

Separation of the mixed, benzoylated pentols **3** *and* **6**. — A sample (2.35 g) of the crude mixture from the preceding experiment was dissolved in benzene, and applied to a column (25 × 7.5 cm) of 1:1 Magnesol–Celite*. The column was developed with 1:100 *tert*-butyl alcohol–benzene (850 ml), and extruded by the procedure of Thompson[12], and zones were detected by streaking with 1% potassium permanganate in 10% aqueous sodium hydroxide. A major zone, centered 13 cm from the origin of the chromatogram, was detected. The portion of the column that was 12–14 cm from the origin was excised, and extracted with acetone, and the extract was evaporated, to give a colorless syrup, yield 1.15 g. A solution of the latter in ethanol (~20 ml) crystallized after 2 days at room temperature, yield 465 mg, m.p. 129–138°. Recrystallization of this product from ethanol gave the pure L-*manno* derivative **6**, m.p. 132–133°. This product was indistinguishable from **6**, prepared through the route **8**→**7**→**6**, by mixed m.p., X-ray powder diffraction pattern, elemental analysis, specific rotation, and comparative i.r. and n.m.r. spectra.

The mother liquors from the crystallization of **6** were refrigerated for 3 weeks. A second crop of crystals, yield 311 mg, m.p. 114–122°, was obtained. This product was recrystallized three times from ethanol, to give 133 mg of the pure L-*gluco* derivative **3**, m.p. 122.5–123.5°. The product was indistinguishable from **3**, prepared by the route **5**→**4**→**3**, by mixed m.p., X-ray powder diffraction pattern, elemental analysis, specific rotation, and comparative i.r. and n.m.r. spectra.

*Magnesol was obtained from the Westvaco Chemical Division of the Food, Machinery, and Chemical Corporation, South Charleston, West Virginia; Celite 545 was obtained from the Johns-Manville Co., New York, N. Y.

Conversion of the benzoylated pentols **3** *and* **6** *into the free pentols* **4** *and* **7**. — The benzoylated, L-*manno* pentol **6** (150 mg), obtained by separation of the mixture of **3** and **6**, was dissolved in dry methanol (5 ml), and a catalytic amount of sodium methoxide in dry methanol (5 ml) was added. After 2.5 h, the saponified product was isolated as described in the preparation of **7** from **8**. The syrupy, chromatographically homogeneous product **6**, yield 43 mg (80%), was crystallized from acetone to give **6** as fine granules, m.p. 122–122.5°. The product was indistinguishable, by X-ray powder diffraction pattern, from **6** prepared from **7**, and g.l.c. of the trimethylsilyl ether of the product showed a single peak having the same retention time as that of a reference sample.

Saponification of the benzoylated L-*gluco* pentol **3** (10 mg) from the epimeric mixture, by the procedure used for **6**, gave the L-*gluco* pentol **4**, indistinguishable by papergram, and by g.l.c. of the trimethylsilyl ether, from an authentic sample of **4** prepared from **5**.

SUMMARY

Ethynylation of 2,3,4,5-tetra-*O*-benzoyl-*aldehydo*-L-arabinose (**1**) gave a product (**2**), which was converted by benzoylation into a separable mixture of 3,4,5,6,7-penta-*O*-benzoyl-1-heptyne-L-*gluco*-3,4,5,6,7-pentol (**3**) and the L-*manno* epimer (**6**). Saponification of **3** and **6** gave 1-heptyne-L-*gluco*-3,4,5,6,7-pentol (**4**) and the L-*manno* epimer (**7**). The structures assigned to **3** and **4**, and to **6** and **7**, were verified by conversion of the known 3-*O*-(3,5-dinitrobenzoyl)-4,5:6,7-di-*O*-isopropylidene-1-heptyne-L-*gluco*-3,4,5,6,7-pentol (**5**) into **4** and thence into **3**, and by conversion of **8**, the known L-*manno* epimer of **5**, into **7** and thence into **6**. The 1-heptyne-3,4,5,6,7-pentols **4** and **7**, obtained crystalline, were separable by g.l.c. as their trimethylsilyl ethers, and were not decomposed or epimerized by treatment with N sulfuric acid for 1 h at 100°. The conversions demonstrate that ethynylation of a free aldehyde group in the presence of benzoyloxy groups is a feasible synthetic procedure for chain-extension reactions with carbohydrate derivatives. The terminal acetylene function on a polyhydroxyalkyl chain is shown to be stable under normal conditions of catalytic transesterification (Zemplén deacylation) and acid hydrolysis of acetals or glycosides.

REFERENCES

1 D. HORTON, J. B. HUGHES, AND J. M. J. TRONCHET, *Chem. Commun.* (London), (1965) 481.
2 D. HORTON AND J. M. J. TRONCHET, *Carbohyd. Res.*, 2 (1966) 315.
3 H. ZINNER, H. BRANDNER, AND G. REMBARZ, *Ber.*, 89 (1956) 800.
4 H. ZINNER, K. WESSELY, W. BOCK, K. RIECKHOFF, F. STRANDT, AND W. NIMMICH, *Ber.*, 90 (1957) 500.
5 A. B. FOSTER, *Chem. Ind.* (London), (1952) 1050.
6 D. GROSS, *Nature*, 172 (1953) 908.
7 E. J. BOURNE, D. H. HUTSON, AND H. WEIGEL, *J. Chem. Soc.*, (1960) 4252.
8 W. E. TREVELYAN, D. P. PROCTER, AND J. S. HARRISON, *Nature*, 166 (1950) 444.
9 E. FISCHER, *Ber.*, 27 (1894) 673.
10 D. HORTON AND MARTHA J. MILLER, *J. Org. Chem.*, 30 (1965) 2457.
11 A. E. EL-ASHMAWY AND D. HORTON, *Carbohyd. Res.*, 1 (1965) 164.
12 A. THOMPSON, *Methods Carbohydrate Chem.*, 1 (1962) 36.