Carbohydrate Research, 176 (1988) 59–72
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

ANALOGS OF CELL SURFACE CARBOHYDRATES. SYNTHESIS OF D-GALACTOSE DERIVATIVES HAVING AN ETHYNYL, VINYL OR EPOXY RESIDUE AT C-5*

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(Received December 1st, 1986; accepted for publication in revised form, May 15th, 1987)

ABSTRACT

Compounds derived from D-galactose having an ethynyl, vinyl, or epoxide residue at C-5, as well as 7,7-dibromo olefinic, isomeric 7,7-*gem*-bromofluoro olefinic, and 6,6-*gem*-difluoro derivatives were obtained from 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose.

INTRODUCTION

The occurrence of significant changes in plasma membrane and function associated with malignant transformation are evident from the studies[1] on the properties and composition of the cell surface of normal and malignant cells. Many of these differences are associated with the carbohydrate[2] portion of the cell surface glycoproteins and glycolipids, which are implicated in antigenicity, degree of differentiation[3], behavior of cells in cell-to-cell contact, and metastasis[4]. It has been suggested that the carbohydrate units distally located on the cell surface, mainly the D-galactose[5] and sialic acid units, are involved in receptor function and density-dependent growth inhibition[6].

Modification of the terminal cell-surface carbohydrates is one approach that may lead to the development of anticancer chemotherapeutic agents[3,7]. The carbohydrate analogs may become incorporated as components into the cell-surface glycoconjugates, or interfere as antimetabolites with its cellular biosynthesis[7–9]. We are interested in modifying the D-galactose unit that is located in penultimate position relative to sialic acid in glycoconjugates and in the biological effects of this modification. In the biosynthetic processes preceding macromolecular incorporation, D-galactose is activated by phosphorylation at O-1 prior to the formation of

*This study was supported by grants CA-13038, CA-24538, and CA-08793 from the National Cancer Institute, National Institutes of Health.
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0008-6215/88/$ 03.50

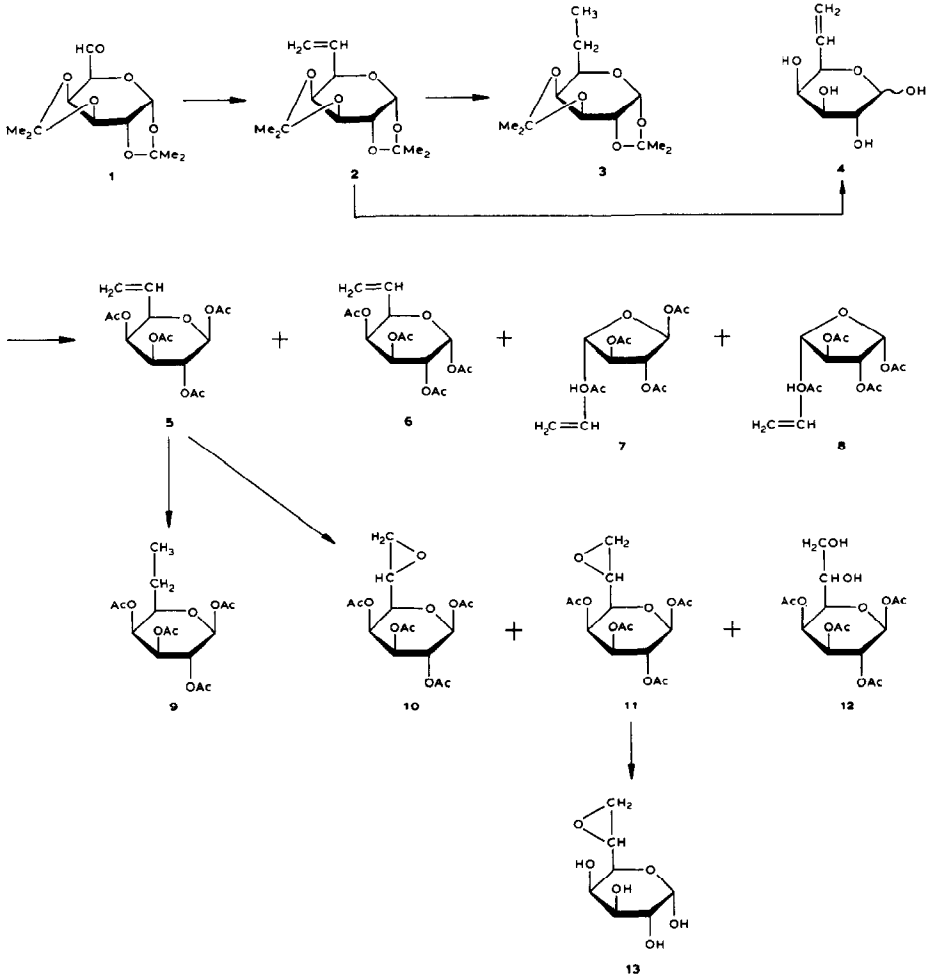
the nucleotide sugar, UDP-D-galactose. Therefore, the present report describes the modifications of this carbohydrate unit at C-6.

RESULTS AND DISCUSSION

1,2:3,4-Di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (**1**) was the key intermediate in the preparation of several D-galactose analogs modified at C-6. The yield of **1**, obtained by treatment[10] of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose with dimethyl sulfoxide and dicyclohexyl carbodiimide in the presence of anhydrous pyridine hydrochloride, was improved. The Wittig reaction of **1** with methyltriphenylphosphonium bromide in the presence of butyllithium gave the vinyl derivative[11] **2**. The ^{1}H-n.m.r. spectrum of **2** indicated the disappearance of the aldehydic proton and the signal for H-6 appeared as a multiplet with an upfield shift. Hydrolysis of **2** with aqueous acid afforded the 5-vinyl derivative **4** in 87% yield in crystalline form. Compound **4** anomerized rapidly in solution, as shown by optical rotation and the isolation of four acetylated derivatives after subsequent acetylation. Two of the isomers were heptopyranoses (**5** and **6**) and two heptofuranoses (**7** and **8**). In the ^{1}H-n.m.r. spectra of **5** and **6**, the vinylic protons appeared in the region of δ 5–5.6, along with H-2,3,4. However, the peaks could be assigned by double irradiation. The olefinic compound **5** was converted very smoothly into the epimeric epoxides **10** and **11**. A third product, a vicinal diol **12**, was also isolated in minor proportion as a mixture of L-*glycero*- and D-*glycero*-D-galactose derivatives which could not be resolved. These were most likely formed by the opening of a small proportion of the epoxide ring during the reaction with 3-chloroperbenzoic acid or the workup. As a result of epoxide formation, the signals of H-6 and H-7 were shifted markedly upfield in the ^{1}H-n.m.r.-spectra of **10** and **11**. The two epoxides were separated and characterized, and hydrolysis of **11** gave **13** for biological testing. Catalytic hydrogenation of **5** with palladium-on-charcoal in ethyl acetate afforded 1,2,3,4-tetra-*O*-acetyl-6,7-dideoxy-β-D-*galacto*-heptopyranose (**9**) in excellent yield.

The acetylenic derivative **17** was synthesized *via* the 7,7-dibromovinylic compound **14** by a simplification of earlier procedures[11–13]. Thus, the aldehyde **1** was added to the reagent prepared from triphenylphosphine, zinc dust, and carbon tetrabromide. After the reaction, the crude product was treated with butyllithium to afford the acetylenic compound **15** as a clear oil in 55% yield. In the ^{1}H-n.m.r. spectrum of **14**, the olefinic H-6 appeared as a doublet. Due to diamagnetic anisotropy, the acetylenic proton in **15** shifted significantly upfield to δ 2.2. In the ^{13}C-n.m.r. spectrum, C-7 appeared markedly upfield at δ 74.4, as compared with olefinic C-7 of compound **14**. 6,7-Dideoxy-D-*galacto*-heptopyranose (**16**) was obtained in crystalline form by hydrolysis of **15** with aqueous acetic acid. Subsequently **16** was acetylated to afford the acetylated derivative as an anomeric mixture (90% yield), from which the α-D anomer **17** could be isolated by crystallization.

In an attempt to prepare a 7-fluoroethynyl derivative, **1** was treated with tri-



phenyl phosphine, zinc dust, and tribromofluoromethane in anhydrous dichloromethane to afford the *gem*-bromofluoroolefin, in 71% yield, as a chromatographically homogeneous, syrupy 2:1 mixture of the *Z* (**18**) and *E* (**19**) isomers, which could not be separated. Many attempts at dehydrobromination of these olefins to lead to the corresponding 7-fluoroethynyl derivative were not successful.

Since 6-deoxy-6-fluoro-D-galactose[14] was found to possess antitumor activity[15], we were interested in the synthesis of 6-deoxy-6-difluoro-D-galactose. The 6-*aldehydo* derivative **1** was treated with *N,N*-diethylaminosulfur trifluoride[16] in dichloromethane to give **20** as a crystalline solid. In the ^{1}H-n.m.r. spectrum, H-6 appeared as an octet centered at δ 5.86 owing to the geminal difluoro groups and vicinal H-5 with coupling constants of $J_{H\text{-}6,F\text{-}6'} = J_{H\text{-}6,F\text{-}6}$ 57 Hz, and $J_{H\text{-}5,F\text{-}6}$ 6.8 Hz, In the ^{13}C-n.m.r. spectrum, C-6 appeared as quartet at δ 115.6 ($J_{C,F} = J_{C,F'}$ 241.9 Hz). Hydrolysis of **20** with aqueous acetic acid afforded 6-deoxy-6-difluoro-D-galactose (**21**) in 95% yield.

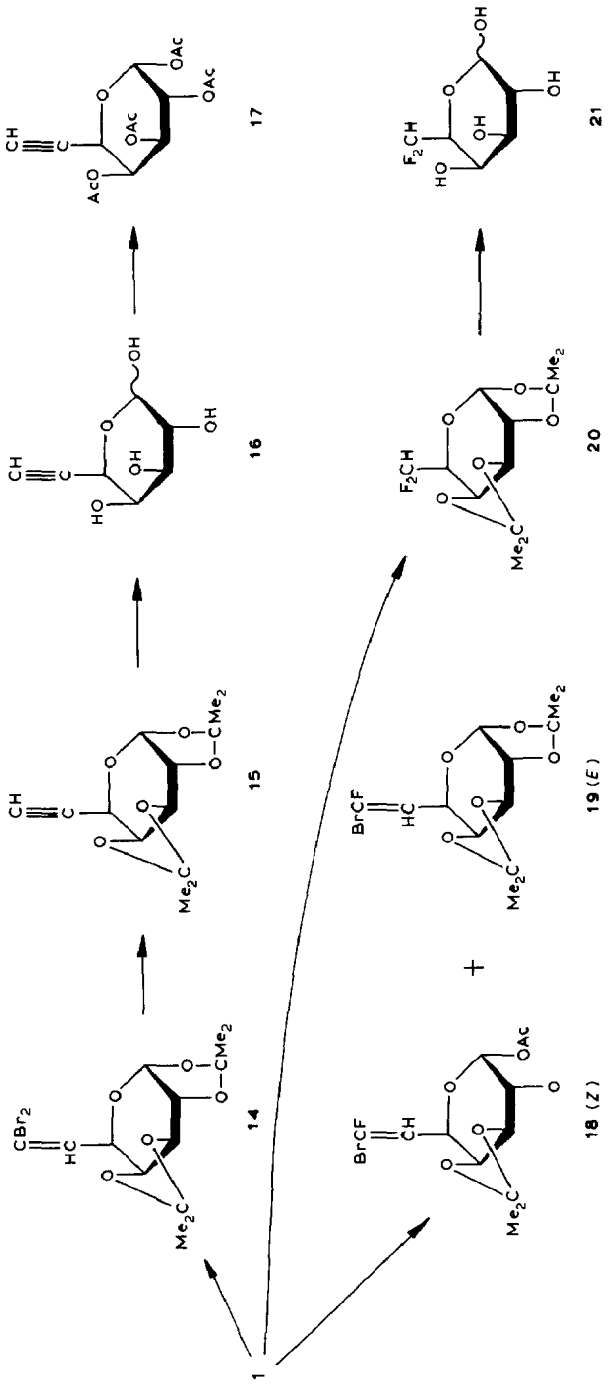


TABLE I

EFFECTS OF COMPOUNDS **1, 4, 6–11, 16, 17,** AND **21** ON CELL GROWTH (L1210) AND ON PERCENTAGE OF INCREASED LIFE SPAN OF DBA/2J MICE BEARING LEUKEMIA-L1210

Compound	*ID_{50} (M)[a] (L1210 Cell line)*	*Drug dosage (mg/kg/day)*	*Survival[b] (% ILS)*
1	1.8×10^{-4}	25	14
4	~35% at 10^{-3}		[c]
6	$>10^{-3}$	25	11
7	~20 at 10^{-3}	25	0
8	~20 at 10^{-3}	25	15
9	~40% at 10^{-3}		[c]
10	5.3×10^{-5}	25	9
11	5.4×10^{-5}	25	15
16	$>10^{-3}$	40	15
17	4.5×10^{-4}	100	28
21	$>10^{-3}$		[c]

[a]L1210 leukemia cells were grown in RPMI 1640 medium containing 10% fetal bovine serum. Compounds were added at various concentrations (up to 1mM) at time zero; 48 h later, cell-growth inhibition was measured and the concentration of agent which caused 50% growth inhibition (IC_{50}) was determined. [b]Female DBA/2 mice were implanted i.p. with 10^6 L1210 leukemia cells on day zero. On days 1–5, drugs were administered i.p. once daily. Survival was monitored daily and percent increase in life span (% ILS) over the control group was calculated[15]. Optimal therapeutic drug dosages are listed. [c]Not determined.

Growth inhibition of L1210 leukemia cells by D-*galactose analogs.* — At the highest concentration tested (1mM) most of the D-galactose analogs inhibited L1210 leukemia cell growth *in vitro* (Table I) to some extent. However, only the epoxides **10** and **11** demonstrated a significant cytotoxicity, causing 50% cell-growth inhibition (IC_{50}) at the lower concentration of 53μM. Compounds **16** and **21** demonstrated little or no cell-growth inhibition at the highest concentration (1mM) tested, and compounds **1** and **13** showed IC_{50} values of 0.18 and 0.45mM, respectively. Compounds **6, 7, 8, 10, 11, 16,** and **17** were also evaluated for their antitumor activity in mice implanted i.p. with 10^6 L1210 leukemia cells on day zero. The compounds dissolved in vehicle (normally saline solution), and various drug dosages (1–500 mg/kg/day) were administered i.p. once daily for five consecutive days (day 1–5), starting one day after tumor implantation. Small increases in life span (% ILS) were noted for most of the compounds tested (10–15%), with the exception of **7**, which was completely ineffective, and **17** which caused a 28% ILS at the optimum dosage of 100 mg/kg/day for 5 days (Table I). These data demonstrate marginal therapeutic activity for these D-galactose analogs, and therefore drug development was not pursued further.

EXPERIMENTAL

General methods. — Unless otherwise stated, the following general methods

were employed. Melting points (m.p.) were determined with a Fisher Model 355 Digital Melting Point analyzer and were corrected. Specific rotations were measured with a Perkin–Elmer 141 automatic polarimeter. I.r. spectra were recorded with a Perkin–Elmer 457 Grating Infrared Spectrophotometer on a thin film (for a liquid) between NaCl plates or as a KBr disc (for a solid sample). ^{1}H-N.m.r. spectra were recorded with Varian 390 and XL 100 instruments, and ^{13}C- and ^{19}F-n.m.r. spectra with a Varian XL 100-NMR Spectrometer, operating in the F.t. mode. Chemical shifts (δ) are expressed relative to the signals of tetramethylsilane (for ^{1}H and ^{13}C), and trichlorofluoromethane (for ^{19}F) as external or internal reference. T.l.c. was performed on Analtech Uniplate 2.5 cm × 10 cm glass plates coated with Silica Gel GF, 250-microns in thickness, and column chromatography on Silica Gel H (EM Reagent, Art. 7736) under a pressure of 30–120 kPa or on Bio-Rad Bio-Sil A (100–200 mesh) silicic acid without any applied pressure.

*1,2:3,4-Di-O-isopropylidene-α-*D-galacto-*hexodialdo-1,5-pyranose*[10] (**1**). — 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (1.94 g, 7.5 mmol) in anhydrous dimethyl sulfoxide (35 mL) was added to anhydrous pyridine hydrochloride, obtained by saturating anhydrous pyridine (0.5 mL) in anhydrous ether (100 mL) with anhydrous HCl, followed by evaporation of solvent and drying *in vacuo*. Dicyclohexylcarbodiimide (4.75 g, 19 mmol) was added and the solution stirred for 4 days at 25° under an atmosphere of N_2. A solution of oxalic acid (1.56 g, 17 mmol, 2.2 g of dihydrate) in methanol (5 mL) was added and the mixture stirred for 0.5 h. It was then poured into saturated aqueous NaCl (100 mL), the precipitate removed, and the clear filtrate extracted with chloroform (5 × 25 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (30 mL) and water (6 × 30 mL). The aqueous washings were extracted with chloroform (3 × 50 mL) and the combined organic phases dried ($MgSO_4$). Evaporation of solvent gave a colorless liquid which was dissolved in warm anhydrous acetone (30 mL) and filtered. Evaporation of solvent gave a colorless liquid which was taken up into anhydrous toluene (10 mL) and the mixture re-evaporated on the Rotavapor at 50°. This process was repeated twice to give **1** as a colorless, chromatographically pure oil (1.69 g, 87%). It was distilled *in vacuo* in the Kugelrohr to give **1** as a colorless liquid (1.44 g, 74%), b.p. 104–105° (24 Pa) (bath), $[\alpha]_D^{23}$ −99° (*c* 0.8, chloroform); lit.[10] b.p. 104–105° (70 Pa), $[\alpha]_D^{28}$ −111° (*c* 2.3, chloroform); R_F (1:1 benzene–ether) 0.56; ν_{max}^{film} 2980 (C–H), 1735 (C=O), and 1380 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.33, 1.36, 1.45, and 1.52 (4 s, 12 H, 4 Me), 4.21 (d, 1 H, *J* 1.8 Hz, H-5), 4.33–4.75 (m, 3 H, H-2,3,4), 5.67 (d, 1 H, *J* 5.0 Hz, H-1), and 9.67 (s, 1 H, CHO); ^{13}C-n.m.r. ($CDCl_3$): δ 24.3, 24.8, 25.8, and 26.0 (4 Me), 70.4 and 70.5 (C-2,3), 71.7 (C-4), 73.2 (C-5), 96.2 (C-1), 109.1 and 109.9 (2 CMe_2), and 199.9 (CHO).

*6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-α-*D-galacto-*hept-6-enopyranose*[11] (**2**). — Methyltriphenylphosphonium bromide (25 g, 70 mmol) was added in five portions to a solution of butyllithium (90 mmol; 58 mL of a 1.55M solution in hexane) in anhydrous ether (300 mL) with stirring under an N_2 atmosphere. The mixture was stirred for 4 h after the addition of **1** (13.4 g, 52 mmol) in anhydrous

oxolane (100 mL) then added dropwise, and the mixture stirred for 16.5 h at room temperature under an N_2 atmosphere. Anhydrous ether (500 mL) was added to the mixture which was filtered, and the solid washed thoroughly with anhydrous ether. The filtrate was washed with 0.25M H_2SO_4 (20 mL) and water (3 × 200 mL). Solvent was evaporated to give a yellow oil which was taken up into chloroform (250 mL), the aqueous layer separated, and the organic layer dried (Na_2SO_4). Evaporation gave a yellow oil which was purified by column chromatography on a silica gel column (100 g) with benzene as eluent to give **2** (6.4 g, 48%), colorless liquid, $[\alpha]_D^{26}$ −93° (*c* 3.95, chloroform); lit.[11] $[\alpha]_{578}^{21}$ −200.2° (*c* 3.17, chloroform); R_F (4:1 ether–benzene) 0.67; ν_{max}^{film} 2985 (C–H stretch), 1650 (C=C stretch), 1385, and 1064 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.34, 1.46, and 1.54 (3 s, 12 H, 4 Me), 4.19–4.37 (m, 3 H, H-2,4,5), 4.63 (q, 1 H, *J* 7.8, 2.6 Hz, H-3), 5.25 (sext., 1 H, *J* 5.5, 1.8, 1.2 Hz, H-7), 5.38 (sext., 1 H, *J* 12.2, 2.0, 1.4 Hz, H-8), 5.59 (d, 1 H, *J* 5.1 Hz, H-1), and 5.96 (oct., 1 H, H-6); ^{13}C-n.m.r. ($CDCl_3$): δ 24.4, 24.9, 26.0, and 26.1 (4 Me), 68.9 (C-5), 70.4 and 70.9 (C-2,3), 73.4 (C-4), 96.4 (C-1), 108.3 and 109.2 (2 C), 117.1 (C-7), and 133.8 (C-6).

6,7-Dideoxy-1,2,3,4-di-O-*isopropylidene*-α-D-galacto-*heptopyranose* (**3**). — Compound **2** (150 mg, 0.6 mmol) in ethyl acetate (25 mL) was hydrogenated in the presence of 10% Pd–C (95 mg) under a slight positive pressure of H_2. After 23 h, the mixture was filtered through sintered glass and the filtrate evaporated to give **3** (120 mg, 80%), yellow oil, $[\alpha]_D^{25}$ −60° (*c* 0.87 chloroform), R_F (4:1 benzene–ether) 0.70; ^{1}H-n.m.r. ($CDCl_3$): δ 0.97 (t, 3 H, *J* 7.2 Hz, H-7), 1.36, 1.45, and 1.52 (3 s, 12 H, 4 CH_3), 1.56 (quint., 2 H, *J* 7.2 Hz, H-6), 3.62 (d, 1 H, *J* 6.7, 1.6 Hz, H-5), 4.16 (q, 1 H, *J* 7.9, 1.6 Hz, H-4), 4.29 (q, 1 H, *J* 5.1, 2.2 Hz, H-2), 4.58 (q, 1 H, *J* 7.7, 2.2 Hz, H-3), and 5.54 (d, 1 H, *J* 5.0 Hz, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 10.2 (C-7), 23.3 (C-6), 24.4, 25.0, and 26.0 (4 CH_3), 69.0 (C-5), 70.6 and 70.9 (C-2,3), 72.4 (C-4), 96.5 (C-1), 108.1 and 108.8 (2 C).

Anal. Calc. for $C_{13}H_{22}O_5$: C, 60.46; H, 8.53. Found: C, 60.68; H, 8.64.

6,7-Dideoxy-α,β-D-galacto-*hept-6-enopyranose* (**4**). — Compound **2** (6.4 g, 25 mmol) was heated for 6 h at 90° in 70% aqueous acetic acid (150 mL). Evaporation on the Rotavapor at 40° gave a pale brown oil. Water (100 mL) was added and the mixture re-evaporated. Water (100 mL) was added to the oily residue, the solution extracted with ether (3 × 75 mL), and the aqueous phase evaporated to give a yellow oil. Water (200 mL) was added and the yellow solution was stirred with activated charcoal for 0.5 h, filtered, and the colorless solution evaporated to give **4** as a pale yellow viscous oil (3.82 g, 87%). The oil solidified at 0° and a sample crystallized slowly from ether–methanol, m.p. 97–97°, $[\alpha]_D^{24}$ +67° (equil., *c* 0.95, water), R_F (1:1 benzene–methanol) 0.70; ν_{max}^{KBr} 3600–3200 (O–H stretch), 2920 (C–H stretch), and 1638 (C=C stretch) cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 3.69–4.17 (m, 4 H, H-2,3,4,5), 4.83 (d, 1 H, *J* 7.9 Hz, H-1), 5.47–5.66 (m, 2 H, $C=CH_2$), and 6.15 (oct., 1 H, H-6); ^{13}C-n.m.r. (D_2O): δ 72.6 (C-2), 73.8 (C-3), 72.0 and 76.5 (C-4,5), 97.3 (C-1), 118.9 (C-7), and 134.4 (C-6).

Anal. Calc. for $C_7H_{12}O_5$: C, 47.73; H, 6.87. Found: C, 47.55; H, 6.68.

Acetylation of **4**. — Acetic anhydride (29 mL) was added dropwise to a solution of **4** (1.01 g, 5.74 mmol) in anhydrous pyridine (42 mL) with stirring at room temperature. After 24 h, the mixture was poured onto ice and extracted with chloroform, and the extract dried (Na_2SO_4) and evaporated. The residue was freed from pyridine by co-evaporating with toluene to give a brown syrup (2.3 g), which was chromatographed on a column of silica gel (300 g). Elution with 5:1 carbon tetrachloride–ether gave *1,2,3,4-tetra-*O*-acetyl-6,7-dideoxy-α-*D-galacto-*hept-6-enopyranose* (**6**), which crystallized from dichloromethane–ether as colorless plates (893 mg, 45%), m.p. 108–109°, $[\alpha]_D^{22}$ +142° (*c* 0.56, chloroform), R_F (5:1 carbon tetrachloride–ether) 0.43; ν_{max}^{KBr} 3095 (w), 3020 (w) (olefinic C–H), 1745 (s) (OAc), and 1648 (m) (C=C) cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.02, 2.13, 2.15 (3 s, 12 H, 4 $COCH_3$), 4.57–4.77 (m, 1 H, H-5), 5.10–6.05 (m, 6 H, H-2,3,4,6,7), and 6.46 (m, 1 H, $J_{1,2}$ 2.1 Hz, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 20.50 (3 $COCH_3$), 20.84 ($COCH_3$), 66.47 (C-2), 67.57 (C-4), 69.80 (C-3), 71.64 (C-5), 89.74 (C-1), 118.17 (C-7), 131.64 (C-6), and 168.66, 169.59, 169.80, 169.95 (4 C=O).

Anal. Calc. for $C_{15}H_{20}O_9$: C, 52.32; H, 5.86. Found: C, 52.13; H, 6.05.

Further elution of the column afforded a mixture of **5** and **8** (740 mg, 38%). Final elution of the column with 5:1 carbon tetrachloride–ether afforded *1,2,3,4-tetra-*O*-acetyl-6,7-dideoxy-β-*D-galacto-*hept-6-enofuranose* (**7**) (89 mg, 5%) which crystallized from ether as colorless needles, m.p. 83–84°, $[\alpha]_D^{22}$ −52° (*c* 0.52, chloroform), R_F (5:1 carbon tetrachloride–ether) 0.30; ν_{max}^{KBr} 3025 (w), 3010 (w) (olefinic C–H), 1746 (s) (OAc), and 1640 (w) (C=C) cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.13 (s, 12 H, 4 $COCH_3$), 4.36 (br. t, 1 H, $J_{3,4} = J_{4,5}$ 4.9 Hz, H-4), 4.97–5.93 (m, 6 H, H-2,3,5,6, H_2-7), and 6.23 (br. s, 1 H, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 20.63, 20.94 (2 s, 4 $COCH_3$), 72.80 (C-5), 76.23 (C-2), 80.74 (C-2), 80.74 (C-3), 84.06 (C-4), 99.14 (C-1), 119.63 (C-7), 131.49 (C-6), 168.79, 169.12, 169.35 (3 s, 4 C=O).

Anal. Calc. for $C_{15}H_{20}O_9$: 52.32; H, 5.86. Found: C, 52.08; H, 5.93.

The mixture of **5** and **8** was rechromatographed on a column of silica gel (80 g) and eluted with 10:1 benzene–ether to afford pure *1,2,3,4-tetra-*O*-acetyl-6,7-dideoxy-β-*D-galacto-*hept-6-enopyranose* (**5**), which crystallized from ether–hexane, m.p. 82–83°, $[\alpha]_D^{25}$ +52° (*c* 1.17, chloroform), R_F (10:1 benzene–ether) 0.33; ν_{max}^{KBr} 1744 (C=O), 1226, and 1062 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.00, 2.05, 2.13, and 2.14 (4 s, 12 H, 4 CH_3), 4.36 (br. d, 1 H, *J* 4.6 Hz, H-5), 5.07–5.45 (m, 5 H, H-2,3,4,7,8), 5.77 (d, 1 H, *J* 7.8 Hz, H-1), and 5.60–5.91 (m, 1 H, H-6); ^{13}C-n.m.r. ($CDCl_3$): δ 20.6 and 20.8 (4 CH_3), 67.8 (C-2), 69.2 (C-4), 71.0 (C-3), 74.5 (C-5), 92.1 (C-1), 118.7 (C-7), 131.0 (C-6), and 168.8, 169.1, 169.7, and 170.0 (4 C).

Anal. Calc. for $C_{15}H_{20}O_9$: C, 52.33; H, 5.85. Found: C, 52.53; H, 5.84.

Further elution of the column gave *1,2,3,4-tetra-*O*-acetyl-6,7-dideoxy-α-*D-galacto-*hept-6-enofuranose* (**8**), which crystallized from ether (198 mg, 10%), m.p. 88–89°, $[\alpha]_D^{22}$ +64° (*c* 0.64, chloroform), R_F (10:1 benzene–ether) 0.25; ν_{max}^{KBr} 3032 (m), 3018 (m) (olefinic C–H), 1744 (s) (OAc), and 1647 cm^{-1} (w) (C=C); ^{1}H-n.m.r. ($CDCl_3$): δ 2.12, 2.07 (2 s, 12 H, 4 $COCH_3$), 4.11 (d, 1 H, $J_{4,5}$ 7.0, $J_{3,4}$ 5.5 Hz, H-4), 5.16–5.86 (m, 6 H, H-2,3,5,6, H_2-7), and 6.35 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1); ^{13}C-n.m.r.

($CDCl_3$): δ 20.41, 20.71, 20.91, 20.00 (4 s, $COCH_3$), 73.74 (C-2), 74.53 (C-5), 75.49 (C-3), 81.19 (C-4), 93.30 (C-1), 120.33 (C-7), 131.04 (C-6), 169.03, 169.33, and 169.54 (4 C=O).

Anal. Calc. for $C_{15}H_{20}O_9$: C, 52.32; H, 5.86. Found: C, 52.56; H, 6.06.

*1,2,3,4-Tetra-*O*-acetyl-6,7-dideoxy-β-*D-galacto-*heptopyranose* (**9**). — Compound **5** (150 mg, 0.44 mmol) in ethyl acetate (25 mL) was hydrogenated in the presence of 10% Pd–C (90 mg) at room temperature under a slight positive pressure of H_2. After 23 h, the mixture was filtered through sintered glass to give a colorless solution. Evaporation gave a colorless oil which crystallized at 0° (150 mg, 99%), and was recrystallized from hexane–ether to give **9** as white needles, m.p. 77–78°, $[\alpha]_D^{25}$ +32° (*c* 0.45, chloroform), R_F 0.40 (4:1 benzene–ether); ν_{max}^{KBr} 2969 (C–H stretch), 1739 (C=O), 1369, 1214, and 1043 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 0.82 (t, *J* 6.8 Hz, CH_3CH_2), 1.56 (m, *J* 7.0 Hz, CH_3CH_2), 2.00, 2.05, 2.12, and 2.18 (4 s, 12 H, CH_2), 3.66 (q, 1 H, *J* 7.0, 0.5 Hz, H-5), 5.08 (q, 1 H, *J* 10.3, 3.4 Hz, H-3), 5.35 (q, 1 H, *J* 10.3, 8.2 Hz, H-2), and 5.38 (q, 1 H, *J* 7.9 Hz, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 9.7 (C-7), 20.6 and 20.8 (CH_3), 23.3 (C-6), 68.2 (C-2), 68.5 (C-4), 71.3 (C-3), 75.7 (C-5), 92.3 (C-1), and 169.2, 169.8, and 170.1 (4 C=O).

Anal. Calc. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.40. Found: C, 52.14; H, 6.69.

Epoxidation of **5**. — Anhydrous dichloromethane (12 mL) was added to a mixture of **5** (271 mg, 0.788 mmol) and 3-chloroperoxybenzoic acid (1.62 mL, 85%, 7.88 mmol), and the homogeneous solution was stirred at room temperature for 58 h. It was then washed with cold (0°) saturated aqueous $NaHCO_3$ (15 mL), and the products were extracted into dichloromethane (60 mL). The extract was washed successively with aqueous NaS_2O_3, saturated aqueous $NaHCO_3$ (30 mL), and water (60 mL), and dried ($MgSO_4$). The solvent was evaporated *in vacuo* to give a pale-yellow syrup (386 mg) which was chromatographed on a column of silica gel (80 g) and eluted with 1:1 carbon tetrachloride–ether to afford *1,2,3,4-tetra-*O*-acetyl-5,6-anhydro-*L-glycero-β-D-galacto-*heptopyranose* (**11**) (137 mg, 48%) which crystallized from diethyl ether as colorless fine needles, m.p. 97–98°, $[\alpha]_D^{22}$ +25° (*c* 0.54, chloroform), R_F (1:1 carbon tetrachloride–ether) 0.26; ν_{max}^{KBr} 3062 (w, terminal epoxy C–H), 3002 (w, substituted epoxy C–H), 1756 (s), 1742 (s, OAc), and 1248 cm^{-1} (s, epoxy C–O); ^{1}H-n.m.r. ($CDCl_3$): δ 2.00, 2.04, 2.12, 2.19 (12 H, 4 $COCH_3$), 2.76 (dd, 1 H, $J_{7a,7b}$ 5.1, $J_{6,7b}$ 2.5 Hz, H-7b), 2.84 (dd, 1 H, $J_{7a,7b}$ 5.1, $J_{6,7a}$ 3.8 Hz, H-7a), 3.06 (dd, 1 H, $J_{5,6}$ 5.4, $J_{6,7b}$ 2.5, $J_{6,7a}$ 3.8 Hz, H-6), 3.57 (dd, 1 H, $J_{5,6}$ 5.5 $J_{4,5}$ 1.2 Hz), 5.09 (dd, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 3.3 Hz, H-3), 5.38 (dd, 1 H, $J_{1,2}$ 8.1, $J_{2,3}$ 10.2 Hz, H-2), 5.56 (dd, 1 H, $J_{4,5}$ 1.2 Hz, H-4), and 5.70 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1).

Anal. Calc. for $C_{15}H_{20}O_{10}$: C, 50.00; H, 5.60. Found: C, 50.12; H, 5.72.

Further elution of the column gave *1,2,3,4-tetra-*O*-acetyl-6,7-anhydro-*D-glycero-β-D-galacto-*heptopyranose* (**10**) (31 mg, 25%), which crystallized from diethyl ether as colorless plates, m.p. 134.5–135.5°, $[\alpha]_D^{22}$ +40° (*c* 0.56, chloroform); R_F (1:1 carbon tetrachloride–ether) 0.20; ν_{max}^{KBr} 3004 (w, epoxy C–H), 1746 (s, OAc), and 1240 cm^{-1} (s, epoxy C–O); ^{1}H-n.m.r. ($CDCl_3$): δ 2.02, 2.06, 2.14, 2.22 (4 s, 12 H, 4 $COCH_3$), 2.69 (dd, 1 H, $J_{7a,7b}$ 4.8, $J_{6,7b}$ 2.7 Hz, H-7b), 2.78

(dd, 1 H, $J_{7a,7b}$ 4.8, $J_{6,7}$ 4.3 Hz, H-7a), 3.15 (ddd, 1 H, $J_{5,6}$ 4.8, $J_{6,7}$ 4.2, $J_{6,7b}$ 2.7 Hz, H-6), 3.64 (dd, 1 H, $J_{5,6}$ 4.9, $J_{4,5}$ 1.2 Hz, H-5), 5.10 (dd, 1 H, $J_{2,3}$ 10.2, $J_{3,4}$ 3.3 Hz, H-3), 5.42 (dd, 1 H, $J_{2,3}$ 10.2, $J_{1,2}$ 8.1 Hz, H-2), 5.55 (dd, 1 H, $J_{3,4}$ 3.2, $J_{4,5}$ 1.2 Hz, H-4), and 5.74 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1).

Anal. Calc. for $C_{15}H_{20}O_{10}$: C, 50.00; H, 5.60. Found: C, 49.91; H, 5.71.

The latter fractions of elution of the column gave a mixture of a diastereoisomers, **12** (66 mg, 35%) as a colorless solid in chloroform–ether, m.p. 181–185°, $[\alpha]_D^{22}$ +25° (*c* 0.19, chloroform), R_F (1:1 carbon tetrachloride–ether) 0.16; ν_{max}^{KBr} 3475 (s, OH), and 1748 cm^{-1} (s, OAc); ^{1}H-n.m.r. ($CDCl_3$): δ 2.03, 2.07, 2.13, 2.15, 2.20 (12 H, 4 $COCH_3$), 3.50–4.32 (m, 5 H), and 4.95–5.92 (m, 4 H, H-1,2,3,4).

6,7-Anhydro-L-glycero-α-D-galacto-*heptopyranose* (**13**). — Compound **11** (113 mg, 0.314 mmol) was added to 1:6:2 triethylamino–methanol–water (9 mL), and the mixture was stirred for 1 h at room temperature, in the dark. It was evaporated *in vacuo* to give a brown syrup which was purified by chromatography on a silica gel column (10 g; 1:1 ether–methanol) to afford pure **13** as a colorless, thick syrup (61 mg, 100%) which crystallized from methanol and was recrystallized from ether–methanol, m.p. 142.5–145.5°, $[\alpha]_D^{22}$ +76.8° (initial)→+84° (equil., *c* 0.17, methanol), R_F (1:1 ether–methanol) 0.56; ν_{max}^{KBr} 3540, 3320 (OH), 3090, 3006 (epoxy C–H), 1255, 1224, 942, 864, and 778 cm^{-1} (epoxy ring); ^{1}H-N.m.r. (D_2O): δ 2.98 (m, 2 H, H-7), 3.31 (m, 1 H, H-6), 3.43–3.73 (m, 2 H, H-2,5), 3.87 (m, 1 H, H-4), 4.07 (m, 1 H, H-3), 4.58 and 5.30 (2 m, 1 H, H-1).

Anal. Calc. for $C_7H_{12}O_6$: C, 43.75; H, 6.29. Found: C, 43.49; H, 6.42.

7,7-Dibromo-6,7-dideoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-*hept-6-enopyranose*[13] (**14**). — A mixture of 1,2:3,4 di-*O*-isopropylidene-α-D-galactohexodialdo-1,5-pyranose (444 mg, 1.72 mmol), Zn dust (225 mg, 3.44 mmol), carbon tetrabromide (1.14 g, 3.44 mmol), and triphenylphosphine (902 mg, 3.44 mmol) in anhydrous 1:1 oxolane–dichloromethane (20 mL) was stirred for 2.5 h at room temperature under a N_2 atmosphere. Petroleum ether (108 mL) was added and the suspension filtered. The brown solid was taken up into dichloromethane (20 mL), and petroleum ether (80 mL) was again added and the mixture filtered. The combined filtrates were evaporated *in vacuo* to give a yellow syrup (2.15 g), which was purified on a silica gel column (100 g) and eluted with 20:1 carbon tetrachloride–diethyl ether. Pure **14** (715 mg, 75%) was obtained as a pale-yellow solid which crystallized from petroleum ether to give colorless plates, m.p. 84–85°, $[\alpha]_D^{22}$ −105° (*c* 0.50, chloroform), R_F (5:1 carbon tetrachloride–ether) 0.50; ν_{max}^{KBr} 3055 (vinyl C–H), and 1629 cm^{-1} (C=C); ^{1}H-n.m.r. ($CDCl_3$): δ 1.33, 1.47, and 1.60 (3 s, 12 H, 4 CH_3), 4.16–4.78 (m, 4 H, H-2,3,4,5), 5.53 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), and 6.66 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-6); ^{13}C-n.m.r. ($CDCl_3$): δ 24.34, 24.94, 25.93, and 26.14 (4 CH_3), 69.24 (C-5), 70.13 (C-3), 70.72 (C-2), 71.81 (C-4), 92.45 (C-7), 96.27 (C-1), 108.82, and 109.47 [2 C (CH_3)], and 134.52 (C-6); lit.[13] m.p. 81.5–83.6°; $[\alpha]_D$ −109.4° (*c* 1, chloroform).

6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-*hept-6-enopyranose*[13] (**15**). — Triphenylphosphine (11.79 g, 45 mmol) in anhydrous dichloromethane

(100 mL) was added dropwise to a mixture of carbon tetrabromide (14.94 g, 45 mmol) and Zn dust (2.94 g, 45 mmol) in anhydrous dichloromethane, stirred at 0° under a N_2 atmosphere. After the addition had been completed, the mixture was stirred for 23 h at room temperature. 1,2:3,4-Di-*O*-isopropylidene-α-D-galacto-hexodialdo-1,5-pyranose (**1**) (5.89 g, 22.5 mmol) in anhydrous dichloromethane (100 mL) was then added dropwise, and the mixture stirred for 2 h at room temperature. The purple solution was poured into anhydrous pentane (1.5l), and the supernatant solution was decanted from the colored oil and filtered. The oil was taken up into anhydrous dichloromethane (100 mL), pentane (400 mL) was added, and the mixture filtered. The combined filtrates were evaporated to give a yellow oil containing some white solid, which was dissolved in anhydrous oxolane (100 mL). The solution was cooled to −78° under N_2 atmosphere, and butyllithium (55 mmol, 35.5 mL of a 1.55M solution in hexane) added slowly to the stirred solution. The red solution was stirred for 1 h at −78°, followed by 2 h at room temperature. Water (100 mL) was added slowly, followed by ether (200 mL). The organic layer was separated and the aqueous layer extracted with ether (3 × 50 mL). The combined organic fractions were dried (Na_2SO_4) and evaporated to give a red oil (6.2 g). This was purified by chromatography on a silica gel column (250 g) with benzene as initial eluent, followed by gradient elution with ether, to give **15** as a chromatographically pure yellow oil (105–110°, 3.2 g, 55%); b.p.$_{0.1\ kPa}$, $[\alpha]_D^{25}$ −122° (*c* 0.57, chloroform), R_F (4:1 benzene–ether) 0.63; ν_{max}^{KBr} 3275 (C–H stretch), 2130 (C=C stretch), 1382, and 1077 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.35, 1.40 and 1.55 (3 s, 12 H, 4 CH_3), 2.55 (d, 1 H, *J* 2.2 Hz, H-7), 4.26–4.38 and 4.61–4.71 (m, 4 H, H-2,3,4,5), and 5.58 (d, 1 H, *J* 4.9 Hz, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 24.4, 24.8 and 26.0 (4 CH_3), 60.0 (C-5), 70.1 and 70.6 (C-2,3), 72.6 (C-4), 74.4 (C-7), 78.7 (C-6), 96.3 (C-1), 108.7 and 109.8 [2 $C(CH_3)$]; lit.[13] $[\alpha]_D$ −125.9° (*c* 1.4, chloroform).

6,7-Dideoxy-D-galacto-*hept-6-ynopyranose* (**16**). — Compound **15** (2.7 g, 10.6 mmol) was heated with 80% aqueous acetic acid (100 mL) for 6.5 h at 90°. After being cooled, the yellow solution was evaporated on the Rotavapor at 70° to give a yellow oil. Water (100 mL) was added and the evaporation repeated. After dilution with water (100 mL), the aqueous solution was extracted with ether (3 × 50 mL). Evaporation of the aqueous layer gave **16** as a yellow oil (2.03 g, 100%). This was taken up into hot ether–methanol and kept at 0° to give fine white needles (0.87 g, 43%), m.p. 142–143°, $[\alpha]_D^{23}$ +45° (equil., *c* 1.09, water); R_F (1:1 benzene–methanol) 0.77; ν_{max}^{KBr} 3330–3250 (O–H), 1072, 1016, and 783 cm^{-1}; ^{1}H-n.m.r. (D_2O): δ 3.10 (d, 1 H, *J* 2.0 Hz, C=CH), 4.02 and 4.23 (2 m, 3 H, H-2,3,4), 5.08 (m, 1 H, H-5), and 5.47 (d, 1 H, *J* 2.9 Hz, H-1).

Anal. Calc. for $C_7H_{10}O_5$: C, 48.28; H, 5.79. Found: C, 48.05; H, 5.87.

6,7-Dideoxy-1,2,3,4-tetra-O-*acetyl*-α-D-galacto-*hept-6-ynopyranose* (**17**). — A mixture of acetic anhydride (50 mL) and anhydrous pyridine (65 mL) at 0° was added to amorphous **16** (1.0 g, 5.7 mmol) at 0°, and the mixture stirred for 1 h at this temperature, and then for 22 h at room temperature under N_2. It was then poured into ice–water (250 mL) and stirred. The resultant yellow solution was ex-

tracted with chloroform (4 × 50 mL), and the combined organic extracts were washed with M HCl (2 × 100 mL) and water (2 × 100 mL), and dried (Na_2SO_4). Evaporation of the solvent gave an oil (1.14 g, 90%) which was chromatographically pure. Crystallization from ether–hexane gave **17** (0.38 g, 20%) as white needles, m.p. 122–123°, $[\alpha]_D^{25}$ +146° (*c* 0.43, chloroform); R_F (4:1 benzene–ether) 0.38; ν_{max}^{KBr} 1737 (C=O), 1370, and 1205 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 2.02, 2.17, and 2.22 (3 s, 12 H, 4 CH_3), 2.51 (d, 1 H, *J* 2.4 Hz, H-7), 4.92 (m, 1 H, H-5), 5.37 (m, 2 H, H-2,3), 5.60 (m, 1 H, H-4), and 6.42 (d, 1 H, *J* 2.0 Hz, H-1); ^{13}C-n.m.r. ($CDCl_3$): δ 20.5 and 20.8 (4 CH_3), 63.1 (C-5), 66.0, 66.8, and 69.3 (C-2,3,4), 75.5 (C-6), 76.4 (C-7), 89.5 (C-1), 168.3, and 169.8 (4 C).

Anal. Calc. for $C_{15}H_{18}O_9$: C, 52.63; H, 5.30. Found: C, 52.45; H, 5.30.

(Z)- (**18**) *and* (E)-*7-Bromo-6,7-dideoxy-7-fluoro-1,2,3,4-di-*O*-isopropylidene-α-*D*-galacto-hept-6-enopyranose* (**19**). — Triphenylphosphine (323 mg, 1.23 mmol) and Zn dust (81 mg, 1.23 mmol) were added successively to a solution of tribromofluoromethane (334 g, 1.23 mmol) in anhydrous dichloromethane (10 mL) with stirring for 5 min at room temperature. A solution of **1** (159 mg, 0.616 mmol) in anhydrous dichloromethane (1 mL) was added, and the mixture stirred for 67 h at room temperature, at which time t.l.c. indicated that some starting aldehyde **1** was still left. Another portion of tribromofluoromethane, triphenylphosphine, and Zn dust were added and after stirring for another 1.5 h, the starting material **1** was almost consumed. After a total reaction time of 70 h the mixture was diluted with petroleum ether (45 mL) and filtered. The solid was taken up into dichloromethane (10 mL) and precipitated again with petroleum ether (40 mL) and filtered. The combined filtrates were evaporated *in vacuo* to give a syrup (731 mg) which was purified by silica gel column (70 g; 5:1 carbon tetrachloride–diethyl ether) to afford a nonseparable mixture of **18** and **19** (~2:1 by ^{1}H-n.m.r.) as a colorless syrup (154 mg, 71%), b.p.$_{10\ Pa}$ 54–58°, $[\alpha]_D^{22}$ −91° (*c* 1.03, chloroform); R_F (5:1 carbon tetrachloride–diethyl ether) 0.34; ν_{max}^{KBr} 3105 (w) and 3070 (m) (vinyl C–H), 2998, 2948, 2917 (C–H), 1675 (s) (C=C), 1384 (s), 1258, 1216, 1170, 1102, 1073, and 1003 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$): δ 1.33, 1.46, 1.57, and 1.62 (4 s, 12 H, 4 CH_3), 4.08–4.85 (m, 4 H, H-2,3,4,5), 5.50 (d, 1 H, $J_{1,2}$ 5.3 Hz, H-1), 5.46 (dd, $J_{6,F(trans)}$ 30.6, $J_{5,6}$ 9.0 Hz, H-6 of **18**), and 5.85 (dd, $J_{6,F(cis)}$ 12.0, $J_{5,6}$ 8.8 Hz, H-6 of **17**); ^{13}C-n.m.r. ($CDCl_3$): δ 24.37, 24.94, 25.93, and 26.13 (CH_3), 62.88 (C-5 of **18**), 66.66 ($J_{C\text{-}5,F}$ 7.9 Hz, C-5 of **17**), 70.15 (C-3), 70.74 (C-2), 72.43 (C-4), 96.28 (C-1), 107.56 ($J_{C\text{-}6,F}$ 18.7 Hz, C-6 of **17**), 109.23 ($J_{C\text{-}6,F}$ 8.2 Hz, C-6 of **18**), 108.73, 109.06, and 109.39 (*C*Me$_2$), 135.02 ($J_{C\text{-}7,F}$ 323 Hz, C-7 of **18**), and 137.45 ($J_{C\text{-}7,F}$ 320 Hz, C-7 of **17**); ^{19}F-n.m.r. ($CDCl_3$–$CFCl_3$; **18**, *E*-isomer: δ −69.11 (dd, $J_{H\text{-}6,F(trans)}$ 30.6, $J_{H\text{-}5,F}$ 1.5 Hz), *Z*-isomer: δ −66.52 (dd, 2.2, $J_{H\text{-}6,F(cis)}$ 12.0, $J_{H\text{-}5,F}$ 2.4 Hz).

Anal. Calc. for $C_{13}H_{18}BrFO_5$: C, 44.21; H, 5.14; Br, 22.62; F, 5.38. Found: C, 44.03; H, 5.18; Br, 22.72; F, 5.51.

*6-Deoxy-6,6-difluoro-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**20**). — A solution of **1** (282 mg, 1.09 mmol) in dry dichloromethane (1 mL) was added to diethylaminosulfur trifluoride (0.14 mL, 1.09 mmol) in the same solvent (0.6

mL) at room temperature. After being stirred for 18 h, the mixture was shaken with water (20 mL) and the product extracted with dichloromethane (2 × 20 mL). The extract was washed with water (2 × 20 mL), dried ($MgSO_4$), and the solvent removed *in vacuo* to give crude **20** (258 mg), which was purified by chromatography on a column of silica gel (25 g). Elution with 5:1 petroleum ether–ether afforded **19** (129 mg, 42.3%) which crystallized from ether–petroleum ether, m.p. 51.5–52.5°, $[\alpha]_D^{22}$ −48.5° (*c* 1, chloroform); R_F (5:1 petroleum ether–ether) 0.46; ^{1}H-n.m.r. [(^{2}H)Me_2CO]: δ 1.33 (s, 6 H, 2 CH_3), 1.40 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.70–4.17 (m, 1 H, H-5), 4.41 (br. d, 1 H, $J_{3,4}$ 8.0, $J_{4,5}$ 1.4 Hz, H-4), 4.43 (dd, 1 H, $J_{1,2}$ 5.0 Hz, H-2), 4.73 (br. dd, 1 H, $J_{3,4}$ 8.0, $J_{2,3}$ 2.5 Hz, H-3), 5.56 (br. d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), and 5.86 (dd, 1 H, $J_{H\text{-}6,F}$ 57, 55, $J_{5,6}$ 6.8 Hz, H-6); ^{13}C-n.m.r. [(^{2}H)Me_2CO]: δ 24.43, 24.98, and 26.16 (3 s, 4 CH_3), 68.74 (dd, $J_{C\text{-}5,F}$ 30.1, 25.6 Hz, C-5), 70.47 (br. d, $J_{C\text{-}4,F}$ 6.8 Hz, C-4), 71.15 (C-2,3), 96.76 (C-1), 109.41 and 110.21 (2 CMe_2), and 115.66 (dd, $J_{C\text{-}6,F}$ 241.9, 238.2 Hz, C-6); m.s.: (relative intensity): *m/z* 280 (M^+; 0.03), 264 (0.79), 206 (0.21), 147 (0.14), 119 (0.23), 100 (0.20), 85 (0.14), 59 (0.25), and 43 (1.00).

Anal. Calc. for $C_{12}H_{18}F_2O_5$: C, 51.43; H, 6.47; F, 13.56. Found: C, 51.24; H, 6.41; F, 13.30.

6-Deoxy-6,6-difluoro-D-*galactose* (**21**). — A solution of **20** (126 mg, 0.450 mmol) in 80% aqueous acetic acid (15 mL) was heated for 6 h at 90–100°. The mixture was cooled to room temperature, filtered, concentrated *in vacuo*, and the remaining solvent coevaporated with water (3 × 25 mL) to give **21** (88 mg, 98%) as a light-yellow syrup which crystallized at room temperature overnight. Recrystallization from methanol–ether gave colorless needles, m.p. 143.5–144.5°, $[\alpha]_D^{22}$ +135° (*c* 1, water); ^{1}H-n.m.r. [($^2H_6$)acetone]: δ 3.20–4.68 (m, 4 H, H-2,3,4,5), 5.25 (m, H-1), 4.78–5.12, 5.66–6.14, and 6.60–7.05 (m, H-6); ^{19}F-n.m.r. [($^2H_6$)Me_2CO–$CFCl_3$]: δ −126.37 (β, oct. $J_{Fa,Fb}$ 291.0, $J_{H\text{-}6,Fa}$ 56.0, $J_{H\text{-}5,Fa}$ 15.6, $J_{H\text{-}4,Fa}$ 7.4 Hz); and −130.0 (oct. $J_{Fa,Fb}$ 291.0, $J_{H\text{-}6,Fb}$ 56.6, $J_{H\text{-}5,Fb}$ 43.0, $J_{H\text{-}4,Fa}$ 11.2 Hz), −127.73 (α, closed oct., $J_{Fa,Fb}$ 302.0, $J_{H\text{-}6,Fa}$ 58.0, $J_{H\text{-}5,Fa}$ 9.6 Hz), and −131.09 (closed oct., $J_{Fa,Fb}$ 302.0, $J_{H\text{-}6,Fb}$ 56.0, $J_{H\text{-}5,Fb} = J_{H\text{-}4,Fb}$ 7.2 Hz).

Anal. Calc. for $C_6H_{10}F_2O_5$: C, 36.01; H, 4.93; F, 18.98. Found: C, 35.77; H, 4.93; F, 18.77.

ACKNOWLEDGMENTS

The authors thank Dr. E. Mihich for his active encouragement throughout the program, Ms. Onda Simmons for determining the n.m.r. spectra, and Ms. Alice Atwood, Ms. Prudy Wohlheutter, and Ms. Patricia McKernan for the biological evaluation of the compounds.

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