Formic Acid. A solution of **4c** (50 mg) in 5 ml of trimethylammonium formate [bp 92° (18 mm)] was stirred for 2 hr at room temperature and left overnight. This solution was gently refluxed in an oil bath for 3 hr until the reaction mixture was colored dark brown. When cooled, the separated crystals were collected and recrystallized from hexane–chloroform to colorless needles, mp 195–196°. This was treated with 1 *N* sodium hydroxide form 1-benzylbenzimidazole, mp and mmp with authentic sample 115°.

B. With Phosphoryl Chloride or Thionyl Chloride in Pyridine. To a solution of **4c** (400 mg) in pyridine or pyridine–chloroform, phosphoryl chloride (5 ml) or thionyl chloride (4 ml) was added at 0–5°. After the reaction mixture was stirred for 1 hr at room temperature, it was poured into ice–water. Extraction of the reaction mixture with benzene afforded 1-benzylbenzimidazole.

C. With Lithium Aluminum Hydride–Aluminum Chloride. To an ether solution of **4c** (450 mg), lithium aluminum hydride (50 mg) and aluminum chloride (25 mg) were added under stirring at 0–5°. After stirring overnight at room temperature, the reaction mixture was treated with ethyl acetate and then with 0.1 *N* hydrochloric acid. Evaporation of the dried ether solution left a brownish syrup, which showed four spots on tlc (R_f 0.79, 0.45, 0.30, and 0.14), and the main spot (R_f 0.45) was found to be 1-benzylbenzimidazole.

Acknowledgment. This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education (801589), Japan.

Registry No.—**1**, 32257-18-4; **3**, 7306-64-1; **4a**, 51057-41-1; **4b**, 51057-42-2; **4c**, 51057-43-3; **4d**, 51057-44-4; **4e**, 51057-45-5; **4f**, 51057-46-6; **4g**, 51108-10-2; **5a**, 51057-47-7; **5b**, 51057-48-8; **5c**, 51057-49-9; **8b**, 51057-50-2; **8c**, 51057-51-3; **8d**, 51057-52-4; **9b**, 51057-53-5; **11a**, 51057-54-6; **11b**, 51057-55-7; **11b** acetate, 51057-56-8; **11c**, 51057-57-9; **11g**, 51057-58-0; **12b**, 51057-59-1; **12b** acetate, 51057-60-4; **12c**, 51057-61-5; benzylsydnone, 16844-42-1; α-bromopyridine, 109-04-6; 3-benzyl-4-bromosydnone, 4918-27-8.

References and Notes

(1) This paper constitutes part XV of a series entitled "Studies on Heterocyclic Compounds."
(2) J. M. J. Tronchet and M. F. Perret, *Helv. Chim. Acta*, **54**, 683 (1971).
(3) R. P. Panzica and L. B. Townsend, *J. Org. Chem.*, **36**, 1594 (1971).
(4) G. H. Milne and L. B. Townsend, *J. Chem. Soc., Perkin Trans.* **1**, 2677 (1972).
(5) H. Ohrui and J. J. Fox, *Tetrahedron Lett.*, 1951 (1973).
(6) H. Ogura, H. Takahashi, and T. Itoh, *J. Org. Chem.*, **37**, 72 (1972).
(7) H. Ogura and M. Ogiwara, *Chem. Pharm. Bull.*, **20**, 848 (1972); H. Ogura, M. Ogiwara, T. Itoh, and H. Takahashi, *ibid.*, **21**, 2051 (1973).
(8) H. Gilman and J. W. Morton, Jr., *Org. React.*, **8**, 258 (1954).
(9) R. G. Micetich, *Can. J. Chem.*, **48**, 2006 (1970).
(10) P. W. Alley and D. A. Shirley, *J. Org. Chem.*, **23**, 1791 (1958).
(11) D. A. Shirley and P. W. Alley, *J. Amer. Chem. Soc.*, **79**, 4922 (1957).
(12) H. Ogura and H. Takahashi, *Syn. Commun.*, **3**, 135 (1973).
(13) W. S. Chilton and R. C. Krahn, *J. Amer. Chem. Soc.*, **89**, 4129 (1967); **90**, 1318 (1968).
(14) U. Lerch, M. G. Burdon, and J. G. Moffatt, *J. Org. Chem.*, **36**, 1507 (1971).
(15) C. Satoh, A. Kiyomoto, and T. Okuda, *Carbohyd. Res.*, **5**, 140 (1967); C. Satoh and A. Kiyomoto, *ibid.*, **7**, 138 (1968).
(16) G. Snatzke, F. Werner-Zamojska, L. Szilágyi, R. Bognár, and I. Farkas, *Tetrahedron*, **28**, 4197 (1972).
(17) All melting points were measured on a Mettler FP-1 melting point apparatus and are uncorrected. Gas chromatography was performed with a JGC-810 gas chromatograph and an OV-1 column was used at 180°. CD and ORD curves were obtained on a Japan Spectroscopic Model J-20 recording polarimeter. Test solutions were prepared by dissolving about 2 mg of the sample in 1.5 ml of methanol, and quartz cells with an optical path of 1, 0.2, and 0.1 mm were used. Nmr spectra were measured with a Varian T-60 spectrometer and tetramethylsilane was used as an internal reference. Mass spectra were determined with a JEOL-01S spectrometer by a direct inlet system at 75 eV.

Synthesis of Macrolide Antibiotics. I.[1] Stereospecific Addition of Methyllithium and Methylmagnesium Iodide to Methyl α-D-*xylo*-Hexopyranosid-4-ulose Derivatives. Determination of the Configuration at the Branching Carbon Atom by Carbon-13 Nuclear Magnetic Resonance Spectroscopy

Momčilo Miljković,* Miodrag Gligorijević, Toshio Satoh, and Dušan Miljković

Department of Biological Chemistry, The Milton S. Hershey Medical Center, The Pennsylvania State University, Hershey, Pennsylvania 17033

Received November 8, 1973

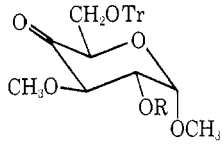
Methyllithium (LiBr-free) adds stereospecifically to methyl 2,3-di-*O*-methyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (**1**) and methyl 3-*O*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (**2**) in an ethereal solution at −80° to give methyl 2,3-di-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**9**) and methyl 3-*O*-methyl-4-*C*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**11**), respectively. Methylmagnesium iodide adds to the oxo sugars **1** and **2** in an ethereal solution at −80° again stereospecifically, giving methyl 2,3-di-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (**8**) and methyl 3-*O*-methyl-4-*C*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (**10**), which are, however, the C-4 epimers of the branched-chain sugars **9** and **11**. The stereochemistry of the addition of Grignard reagent to the oxo sugars **1** and **2** depended upon the reaction temperature, the solvent, and the nature of the halogen atom. Carbon-13 nmr spectroscopy was used for unequivocal configurational assignments at the branching-carbon atom in branched-chain sugars **8**–**11**. A rationalization of the observed stereospecificity was proposed.

In the course of our studies directed toward the stereoselective synthesis of the 14-membered lactone ring of erythromycins A and B from appropriate sugar derivatives, it was necessary to introduce an axial methyl group at the C-4 carbon atom of a methyl D-*xylo*-hexopyranosid-4-ulose derivative and to develop a simple but reliable method for configurational assignment of the thus obtained branching carbon atom.[2]

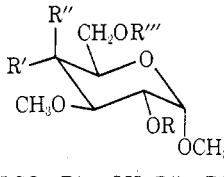
It is well known that the addition of Grignard reagents and organolithium compounds to carbonyl groups in carbohydrates is highly stereoselective[4] yielding in certain cases products epimeric at the quaternary carbon atom,[5,6] whereas in other instances branched-chain sugars with the same configuration at the branching carbon atom[7] are obtained. Since a clear rationalization of these findings[8] does not exist, many stereochemical "anomalies"[4] re-

ported in the literature have led to the conclusion that the steric course of the addition of Grignard reagents and/or alkyl- (or aryl-) lithium to oxo sugars cannot be reliably predicted.[9]

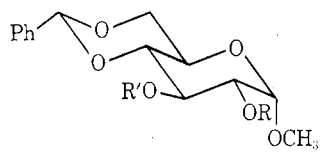
We now wish to report the results of our studies on the addition of methylmagnesium halides and methyllithium to the methyl α-D-*xylo*-hexopyranosid-4-uloses **1** and **2**, and on the application of the carbon-13 nmr spectroscopy for configurational assignments at the thus created branching carbon atom.



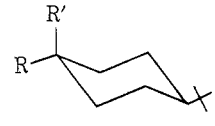
1, R = CH_3
2, R = CH_3SO_2



3, R = CH_3SO_2; R′ = OH; R″ = R‴ = H
4, R = CH_3; R′ = OH; R″ = H; R‴ = Tr
5, R = CH_3SO_2; R′ = OH; R″ = H; R‴ = Tr
6, R = H; R′ = CH_3; R″ = OH; R‴ = Tr
7, R = H; R′ = OH; R″ = CH_3; R‴ = Tr
8, R = R′ = CH_3; R″ = OH; R‴ = Tr
9, R = R″ = CH_3; R′ = OH; R‴ = Tr
10, R = CH_3SO_2; R′ = CH_3; R″ = OH; R‴ = Tr
11, R = CH_3SO_2; R′ = OH; R″ = CH_3; R‴ = Tr



12, R = CH_3SO_2; R′ = H
13, R = CH_3SO_2; R′ = CH_3



14, R = H; R′ = OH
15, R = OH; R′ = H
16, R = CH_3; R′ = OH
17, R = OH; R′ = CH_3

Methyl 2,3-di-*O*-methyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (**1**) and methyl 3-*O*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (**2**) were synthesized by the oxidation of methyl 2,3-di-*O*-methyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**4**) and methyl 3-*O*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**5**) with dimethyl sulfoxide–acetic anhydride at 50–60°.

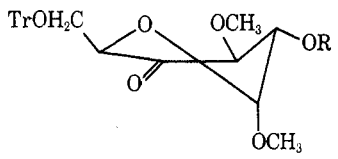
Reaction of the oxo sugars **1** and **2** with an ethereal solution of methyllithium (LiBr-free) at −80° afforded, in each case, only one product: methyl 2,3-di-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**9**, from **1**) and methyl 3-*O*-methyl-4-*C*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**11**, from **2**).

Reaction of the oxo sugars **1** and **2** with an ethereal solution of methylmagnesium iodide at −80° again proceeded stereospecifically, but the products obtained were the C-4 epimers of the branched-chain sugars **9** and **11**. Thus, **1** gave methyl 2,3-di-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (**8**), whereas **2** gave methyl 3-*O*-methyl-4-*C*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (**10**).

In contrast to the above results, methylmagnesium iodide and methyllithium added nonstereospecifically and at a considerably slower rate to 4-*tert*-butylcyclohexanone at −80°, yielding in each case a mixture of both C-1 epimers: *cis*-4-*tert*-butyl-1-methylcyclohexan-*r*-1-ol (**16**) and *trans*-4-*tert*-butyl-1-methylcyclohexan-*r*-1-ol (**17**). The isomer with the equatorial methyl group (**16**) was the predominant product in both reactions.

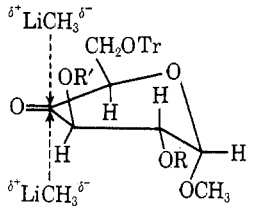
The stereochemistry of the addition of Grignard reagent to the oxo sugars **1** and **2** depended upon the reaction temperature, the solvent,[15] and the nature of the halogen atom. Thus, treating an ethereal solution of **1** and/or **2** with methylmagnesium iodide at −80° afforded **8** and/or **10** as the only isolable products. At reflux, both C-4 epimers, **8** and **9** (from **1**) and **6**, **7**, and **10** (from **2**),[16] were obtained, but the isomers having the methyl group in the equatorial orientation (**6**, **7** and **10**) predominated in *ca.* 6:1 ratio. The dependence of the stereochemistry of the addition reaction upon the nature of the halogen atom and of the solvent was demonstrated in the following way: refluxing a 10:1 ether–tetrahydrofuran solution of **2** with methylmagnesium chloride gave a 1:1 mixture of C-4 epimers **6** and **7**,[17] whereas methylmagnesium iodide under the same experimental conditions gave a mixture of C-4 epimers **6** and **7**, in which the axial isomer predominated by a ratio of 2.3:1.

The stereospecificity of the addition reaction of methyllithium to the C-4 carbonyl carbon atom in the oxo sugars **1** and **2** at −80° can be rationalized in the following way. It is well known from studies of the conformational equilibrium of α-halocyclohexanones[18-21] that conformations in which the halogen atom is axially oriented are strongly favored in solvents of low dielectric constant. This tendency of halogen atoms to assume the axial rather than equatorial orientation was attributed to the strong electrostatic repulsions of the nearly coplanar and equally oriented C=O and C–halogen dipoles in conformations in which the halogen atom is equatorially oriented. A similar situation probably exists in the case of the oxo sugars **1** and **2**. If so, then the C1 conformation of **1** and **2** wherein the C-3 methoxy group is equatorially oriented should be destabilized in solvents of low dielectric constant (*e.g.*, ether), owing to an electrostatic repulsion of the nearly coplanar and equally oriented C=O and C–O dipoles. Consequently, the oxo sugars **1** and **2**, will, at −80°, most likely adopt either a half-chair conformation **18** or a conformation which is between the C1 and a half-chair conformation (**18**). The adoption of any conformation other than C1 by **1** and/or **2** prior to the reaction with methyllithium will then be responsible for pure axial addition of methyllithium to the C-4 carbonyl carbon atom, since the severe electrostatic and nonbonding steric interactions between an electronegative methyl group (from CH_3Li) approaching the C-4 carbonyl carbon atom from the "equatorial" direction and the C-1 methoxy group will impede the equatorial addition of methyllithium. Furthermore, in case of an axial attack of methyllithium to the C-4 carbonyl carbon atom, not only will the severe "1,4-diaxial" interactions in the transition state **19** be avoided, but also the two relatively strong nonbonding steric interactions between the two axial hydrogens at C-3 and C-5 with an equatorially approaching methyl group will be replaced by one weaker 1,3-nonbonding interaction between the axially incoming methyl group and the C-2 axial hydrogen atom. This rationalization is strongly supported by the fact that methyl 2,3-di-*O*-methyl-6-*O*-triphenylmethyl-β-D-*xylo*-hexopyranosid-4-ulose (**20**), *i.e.*, a D-hexopyranosid-4-ulose of the *β series*, where such "1,4-diaxial" electrostatic and nonbonding steric interactions do not exist, reacts with an ethereal solution of methyllithium at −80°, yielding both C-4 epimers, **23** and **24**. It is interesting to



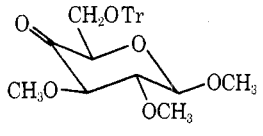
18, R = CH_3, CH_3SO_2

axial approach

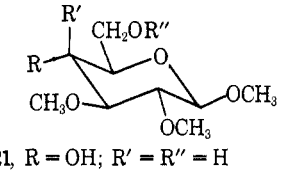


equatorial approach

19, R = CH_3, CH_3SO_2; R′ = CH_3



20

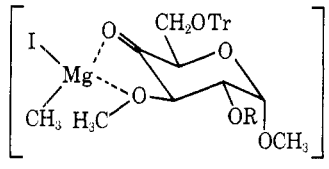


21, R = OH; R′ = R″ = H

22, R = OH; R′ = H; R″ = Tr

23, R = CH_3; R′ = OH; R″ = Tr

24, R = OH; R′ = CH_3; R″ = Tr



25, R = CH_3; CH_3SO_2

note that a similar explanation was proposed[22] for the observation[23,24] that 4-chlorocyclohexanone and cyclohexanones with other electronegative substituents at C-4 give unusually high proportions of axial (cis) alcohols on reduction with complex hydrides.

The reversal of stereochemistry of the addition of the Grignard reagent to the oxo sugars 1 and 2 can be rationalized as a consequence of "chelation" of the magnesium atom of the Grignard reagent with the C-4 carbonyl oxygen and the C-3 oxygen atom.[15b,25,26] Thus, the formation of the cyclic five-membered ring intermediate 25 forces the oxo sugars 1 and 2 to adopt the C1 conformation prior to the addition of the methyl group to the C-4 carbonyl carbon. The solvent dependence of stereochemistry of the addition of Grignard reagent to the oxo sugars 1 and 2 strongly supports this view.

Various methods have been used thus far in carbohydrate chemistry for making unequivocal configurational assignments to a branching-carbon atom in branched-chain sugars,[27] and the conclusions often had to be supported by chemical evidence.

Table I

Branched-chain sugar	Chemical shift, ppm[a]	Methyl group at C-4
6	21.9	e
7	15.4	a
8	21.8	e
9	15.5	a
10	21.8	e
11	15.3	a

[a] Downfield from TMS.

The observations on methylcyclohexanes[28,29] that the carbon-13 chemical shift of an axial methyl group is 6 ppm toward a higher field than that of an equatorial methyl group prompted us to investigate the possibility of utilizing the carbon-13 resonance of the C-4 methyl group for determination of the configuration at the branching carbon atom in sugars 6–11.[2]

Table I lists carbon-13 chemical shifts of the C-4 methyl groups in the branched-chain sugars 6–11.

The identification of the C-4 methyl group in carbon-13 nmr spectra of the branched-chain sugars 6–11 was straightforward, since it was the only sp^3 carbon atom not attached to an oxygen atom. This was in accord with a previous finding[30] that the carbon-13 resonance of the C-6 methyl group of methyl α-L-rhamnopyranoside is shifted strongly upfield relative to the carbon-13 resonances of the other carbon atoms.

The carbon-13 chemical shift of the equatorial and axial methyl group in the branched-chain sugars 6–11 had a fairly constant value: 21.8 ppm for the equatorial and 15.4 ppm for the axial methyl group (average values). The upfield shift of the axial methyl group in 7, 9, and 11, relative to the carbon-13 chemical shifts of the equatorial methyl group in 6, 8 and 10, is 6.4 ppm. This was in good agreement with the chemical-shift difference of an axial and equatorial methyl group found in the 4-*tert*-butyl-1-methylcyclohexanols (6.0 ppm). Table II lists the carbon-13 chemical shifts of the two isomeric 4-*tert*-butyl-1-methylcyclohexanols (16 and 17). Our spectral assignments are compared with reported spectral assignments made for carbon-13 resonances of *cis*- and *trans*-4-*tert*-butylcyclohexanols (14 and 15).[31] [The conversion $\delta_C(TMS) = 192.8 - \delta_C(CS_2)$ was used in order to express the carbon-13 resonances for 14 and 15 in parts per million downfield from TMS.]

Experimental Section

General. The silica gel used for all column chromatography was E. Merck (Darmstadt, Germany) silica gel, grain size <0.08 mm. The melting points are uncorrected. Optical rotations were determined with a Cary 60 spectropolarimeter in a 1.0-cm cell. The ir spectra were recorded with a Perkin-Elmer infrared spectrophotometer, Model 267. The proton nmr spectra were recorded

Table II

Substituted cyclohexanol	Chemical shift, ppm C-1	C-2, C-6	C-4	C-3, C-5	(e)CH_3	(a)CH_3
cis-4-*tert*-Butyl-1-methylcyclohexan-*r*-1-ol (**16**)[a]	68.9	39.4	47.7	22.7	31.4	
trans-4-*tert*-Butyl-1-methylcyclohexan-*r*-1-ol (**17**)[b]	71.0	41.0	47.9	25.0		25.4
cis-4-*tert*-Butylcyclohexanol (**14**)[c]	65.0	33.3	48.2	21.0		
trans-4-*tert*-Butylcyclohexanol (**15**)[d]	70.4	35.7	47.3	25.7		

[a] Quaternary carbon atom from *tert*-butyl group, 32.4 ppm; methyl groups from *tert*-butyl group, 27.7 ppm. [b] Quaternary carbon atom from *tert*-butyl group, 32.3 ppm; methyl groups from *tert*-butyl group, 27.7 ppm. [c] Quaternary carbon atom from *tert*-butyl group, 32.4 ppm; methyl groups from *tert*-butyl group. 27.4 ppm. [d] Quaternary carbon atom from *tert*-butyl group, 32.1 ppm; methyl groups from *tert*-butyl group, 27.5 ppm.

with Varian T-60 and HR-220 spectrometers using tetramethylsilane as an internal standard. Chemical shifts (δ) are expressed in parts per million. The proton noise decoupled carbon-13 nmr spectra were recorded with a TNM PS-100 FT spectrometer. The spectra were obtained using 5000-Hz sweep with 8K data points. The pulse width was 7.0 μsec and pulse repetition rate was 1.5 sec.

Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (1). Methyl 2,3-di-*O*-methyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (4,[32] 1.000 g, 2.16 mmol) was dissolved in 10:7 dimethyl sulfoxide–acetic anhydride (17 ml) and heated at 65° for 2 hr. The residual syrup, obtained after evaporation of solvents *in vacuo*, was dissolved in ether (50 ml) and washed with saturated aqueous NaCl solution. The ether extract was dried over anhydrous Na_2SO_4 and evaporated *in vacuo*, yielding a white, amorphous solid (830 mg, yield 83%). An analytical sample was obtained by chromatographing crude 1 (250 mg) on silica gel (30 g). Elution with 120:60:1 hexane–acetone–water gave pure 1 (212 mg) as an amorphous solid, $[\alpha]^{27}D$ +123° (*c* 0.6, $CHCl_3$), ir ($CHCl_3$) 1735 cm^{-1} (C=O stretch). *Anal.* Calcd for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.45; H, 6.23.

Reaction of Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (1) with Methyllithium (LiBr-Free) in an Ethereal Solution at −80°. To an ethereal solution (10 ml) of 1 (76 mg, 0.16 mmol), cooled to −80°, an ethereal solution (0.5 ml, 2 *M*) of methyllithium (LiBr-free) was added and the reaction mixture was stirred for 1.5 hr at −80°. Water was then added (10 ml), the ethereal layer was separated, and the water solution was extracted with three 30-ml portions of ether. The combined ethereal extracts were washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. The white, amorphous crude product (77 mg) was chromatographed on silica gel (15 g). Elution with 95:5 benzene–2-propanol afforded pure methyl 2,3-di-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**9**, 53 mg, 70%), which after recrystallization from isopropyl ether showed mp 119°: $[\alpha]^{27}D$ +51° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 3580 and 3520 cm^{-1} (broad peaks, OH); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 4.80 (d, $J_{1,2}$ = 4.2 Hz, 1, H-1), 0.99 (s, 3, C-4-methyl group). *Anal.* Calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 73.00; H, 7.27.

Reaction of Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (1) with Methylmagnesium Iodide in an Ethereal Solution at −80°. An ethereal solution (5 ml) of methylmagnesium iodide (50 mg of Mg + 0.3 ml of MeI) cooled to −80° was added to an ethereal solution (10 ml) of pure 1 (50 mg, 0.11 mmol) precooled to −80°. The reaction was monitored by tlc using the solvent system 95:5 benzene–2-propanol. After the reaction mixture was stirred for 2.5 hr at −80°, a few milliliters of methanol was added and then 1 *N* H_2SO_4 (30 ml). After extraction with three 30-ml portions of ether, the combined ethereal extracts were washed with saturated aqueous NaCl solution until neutral and dried over anhydrous Na_2SO_4. A syrup (74 mg) obtained after removal of ether *in vacuo* was chromatographed on silica gel (20 g). Elution with 95:5 benzene–2-propanol gave 49 mg (94%) of pure methyl 2,3-di-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (**8**), which after recrystallization from isopropyl ether showed mp 149–149.5°: $[\alpha]^{27}D$ +73° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 3570 and 3510 cm^{-1} (broad peaks, OH); nmr ($CDCl_3$) δ 7.7–7.1 (m, 15, triphenylmethyl), 5.00 (d, $J_{1,2}$ = 3.8 Hz, 1, H-1), 1.03 (s, 3, C-4 methyl group). *Anal.* Calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 72.58; H, 6.99.

Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (13). A benzene solution (50 ml) containing methyl 4,6-*O*-benzylidene-2-*O*-methylsulfonyl-α-D-glucopyranoside (**12**,[33] 1.30 g, 3.61 mmol), methyl iodide (6.0 ml, 96.3 mmol), and Ag_2CO_3 (1.3 g, 4.71 mmol) was refluxed for 5 hr. At the end of every hour an additional amount of Ag_2CO_3 (1.3 g, 4.71 mmol) was added. The solid was then filtered off through Celite, and the filtrate was evaporated *in vacuo*. The crude product (1.55 g) was chromatographed on silica gel (85 g). Elution with 155:45 benzene–ethyl acetate afforded pure **13** (1.22 g, 90%). After recrystallization from ether, compound **13** had mp 110–111°; $[\alpha]^{27}D$ +70° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 1367 and 1175 cm^{-1} (asymmetric and symmetric SO_2 stretch); nmr ($CDCl_3$) δ 7.5–7.2 (m, 5, phenyl), 5.53 (s, 1, methine H from benzylidene group), 4.91 (d, $J_{1,2}$ = 3.8 Hz, 1, H-1), 3.57 (s, 3, Me from C-3 methoxy group), 3.41 (s, 3, Me from C-1 methoxy group), 3.23 (s, 3, Me from methylsulfonyl group). *Anal.* Calcd for $C_{16}H_{22}O_8S$: C, 51.33; H, 5.92; S, 8.57. Found: C, 51.43; H, 6.01; S, 8.68.

Methyl 3-*O*-Methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (3). A 50% aqueous acetic acid solution (50 ml) containing methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (**13**, 1.984 g, 5.3 mmol) was heated at 100° for 1 hr. The solvent was evaporated *in vacuo*, and the crude product (1.864 g) was chromatographed on silica gel (70 g). Elution with 1:1 acetone–hexane afforded 1.410 g (91%) or pure **25** as an oil: $[\alpha]^{27}D$ +95° (*c* 1.5, $CHCl_3$); ir ($CHCl_3$) 3580 (shoulder) and 3420 cm^{-1} (broad peak, OH); nmr ($CDCl_3$) δ 4.93 (d, $J_{1,2}$ = 3.9 Hz, 1, H-1), 3.60 (s, 3, Me from C-3 methoxy group), 3.42 (s, 3, Me from C-1 methoxy group), 3.08 (s, 3, Me from methylsulfonyl group). *Anal.* Calcd for $C_9H_{18}O_8S$: C, 37.76; H, 6.34; S, 11.18. Found: C, 37.63; H, 6.42; S, 11.31.

Methyl 3-*O*-Methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (5). To a pyridine solution (20 ml) of methyl 3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (**13**, 1.410 g, 5.18 mmol), triphenylmethyl chloride (1.90 g, 6.83 mmol) was added. After standing at room temperature overnight, the solvent was evaporated *in vacuo*. The residue was dissolved in benzene (it does not dissolve completely), and water was added. The benzene layer was separated, and, after drying over anhydrous Na_2SO_4, the benzene was evaporated *in vacuo*. The crude product was chromatographed on silica gel (160 g). Elution with 2:1 hexane–acetone afforded 2.500 g (94%) of pure **5**, in amorphous state: $[\alpha]^{27}D$ +47° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 3580 and 3500 (two broad peaks, OH), 1597, 1490, and 1449 (benzene ring stretching frequencies), 1365 and 1175 cm^{-1} (asymmetric and symmetric SO_2 stretch); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 4.91 (d, $J_{1,2}$ = 3.9 Hz, 1, H-1), 3.57 (s, 3, Me from C-3 methoxy group), 3.40 (s, 3, Me from C-1 methoxy group), 3.04 (s, 3, methyl from methylsulfonyl group). *Anal.* Calcd for $C_{28}H_{32}O_8S$: C, 63.62; H, 6.10; S, 6.07. Found: C, 63.86; H, 6.06; S, 6.00.

Methyl 3-*O*-Methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (2). Methyl 3-*O*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**5**, 578 mg, 1.1 mmol) was dissolved in a 2:1 mixture of dimethyl sulfoxide–acetic anhydride (4.5 ml). After the reaction mixture was kept at 60° for 2 hr, the solvents were removed *in vacuo* and the crude product (**2**), because it is very unstable, was not purified, but directly used for reaction with methyllithium.

Reaction of Methyl 3-*O*-Methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (2) with Methyllithium in an Ethereal Solution at −80°. An ethereal solution (20 ml) containing crude **2** (580 mg) was cooled to −80°, whereby the solution became very turbid, and *ca.* 2 *M* ethereal solution (2 ml) of methyllithium was added. After stirring for 1.5 hr at −80°, methanol was added, whereby the solution became clear. After removal of solvents *in vacuo*, the crude product (630 mg) was purified by several chromatographies, on silica gel, using 95:5 benzene–2-propanol and 3:1 hexane–acetone for elution, whereby the pure 3-*O*-methyl-4-*C*-methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**11**, 320 mg, 53%) was obtained as an oil: $[\alpha]^{27}D$ +92° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 3580 (shoulder) and 3520 (broad peak) (OH), 1360 and 1175 cm^{-1} (asymmetric and symmetric SO_2 stretch); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 4.83 (d, $J_{1,2}$ = 4.0 Hz, 1, H-1), 4.22 (q, $J_{1,2}$ = 4.0 and $J_{2,3}$ = 10.0 Hz, 1, H-2), 3.87 (broad t, $J_{5,6}$ = 6.4 Hz, 1, H-5), 3.55 (s, 3, Me from C-3 methoxy group), 3.40 (s, 3, Me from C-1 methoxy group), 3.00 (s, 3, Me from methylsulfonyl group), 1.01 (s, 3, C-4 methyl group). *Anal.* Calcd for $C_{29}H_{34}O_8S$: C, 64.19; H, 6.32; S, 5.91. Found: C, 63.99; H, 6.21; S, 5.85.

Reaction of Methyl 3-*O*-Methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (2) with Methylmagnesium Iodide in an Ethereal Solution at −80°. To an ethereal solution (20 ml) of methylmagnesium iodide (200 mg of Mg + 0.5 ml of CH_3I) cooled to −80°, an ethereal solution (15 ml) of **2** (300 mg, 0.57 mmol) was added with stirring. After the reaction mixture had been stirred for 1 hr at −80°, aqueous methanol was added and the reaction product was extracted with ether. The crude product (300 mg), obtained after removal of ether *in vacuo*, was chromatographed on silica gel. Elution with 95:5 benzene–2-propanol afforded pure **10** (166 mg; 53%), which after recrystallization from ether–isopropyl ether showed mp 117.5°: $[\alpha]^{27}D$ +75° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 3570 (shoulder) and 3490 (broad peak) (OH), 1365 and 1178 cm^{-1} (asymmetric and symmetric SO_2 stretch); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 5.13 (d, $J_{1,2}$ = 4.0 Hz, 1, H-1), 4.86 (q, $J_{1,2}$ = 4.0 and $J_{2,3}$ = 10.0 Hz, 1, H-2), 3.57 (s, 3, Me from C-3 methoxy group), 3.48 (s, 3, Me from C-1 methoxy group), 3.07 (s, 3, Me from methylsulfonyl group), 1.05 (s, 3, C-4 methyl group). *Anal.* Calcd for $C_{29}H_{34}O_8S$: C, 64.19; H, 6.32; S, 5.91. Found: C, 63.98; H, 6.44; S, 5.81.

Reaction of Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (1) with Methylmagnesium Io-

dide in an Ethereal Solution at Reflux. To a refluxing ethereal solution (10 ml) of methylmagnesium iodide (50 mg of Mg + 0.5 ml of CH_3I), an ethereal solution (10 ml) of **1** (116 mg, 0.25 mmol) was added dropwise during 7 min. After refluxing for 20 min the reaction mixture was diluted with ether, and the ethereal solution was washed with saturated aqueous NaCl solution, aqueous K_2CO_3–$NaHSO_3$ solution, and again with saturated aqueous NaCl solution. The ethereal phase was dried over anhydrous Na_2SO_4, and ether was evaporated *in vacuo*. The semicrystalline residue (117 mg) was chromatographed on silica gel (15 g). Elution with 95:5 benzene–2-propanol gave tlc-homogenous product (83 mg) which according to the nmr spectrum was a *ca.* 6:1 mixture of **8** and **9**, **8** being the predominant product.

Reaction of Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (1) with Methylmagnesium Chloride in a 40:1 Ether–Tetrahydrofuran Solution at Reflux. To an ethereal solution (20 ml) of **1** (200 mg, 0.43 mmol) a 3 *M* solution of methylmagnesium chloride in tetrahydrofuran (0.5 ml, *ca.* 2 mmol) was added, whereby a white precipitate appeared. After the reaction mixture was refluxed for 2 hr, it was kept at room temperature overnight. Methanol (10 ml) was then added (the white precipitate dissolved) and the solvents were evaporated *in vacuo*. The residue was dissolved in ether–1 *N* HCl mixture, and the ethereal layer was separated. The aqueous phase was extracted three times with ether, the combined ethereal extracts were washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4, and the ether was removed *in vacuo*. The crude product (203 mg) was a 1.3:1 mixture of **8** and **9**, **8** being the predominant product.

Reaction of Methyl-3-*O*-Methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (2) with Methylmagnesium Chloride in Refluxing 10:1 Ether–Tetrahydrofuran Solution. To an ethereal solution (20 ml) of **2** (346 mg, 0.66 mmol) a 3 *M* solution of methylmagnesium chloride (2.00 ml, 6 mmol) in tetrahydrofuran was added and the reaction mixture was refluxed for 4 hr. The excess of methylmagnesium chloride was destroyed by addition of ethyl acetate and the reaction mixture was poured into water (80 ml) containing 2 ml of concentrated HCl. The aqueous layer was extracted with ether, the combined ethereal extracts were washed with water and dried over anhydrous Na_2SO_4, and ether was removed *in vacuo*. The residue (280 mg) was chromatographed on silica gel. Elution with 95:5 benzene–2-propanol gave a product (140 mg) homogenous on tlc, but which, according to the nmr spectrum, was a 1:1 mixture of **6** and **7**.

Reaction of Methyl 3-*O*-Methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (2) with Methylmagnesium Iodide in an Ethereal Solution at Reflux. To an ethereal solution (20 ml) of methylmagnesium iodide (200 mg of Mg + 0.5 ml of CH_3I), an ethereal solution (20 ml) of **2** (600 mg, 1.14 mmol) was added at reflux. After refluxing for 1.5 hr, water was added until no undissolved material remained. The ethereal layer was separated and the aqueous phase was extracted with ether, the combined ethereal extracts were dried over anhydrous Na_2SO_4, and ether was evaporated *in vacuo*. The residue (470 mg) was chromatographed on silica gel. The elution with 95:5 benzene–2-propanol afforded two fractions. The first fraction (159 mg, 25%), after rechromatography on silica gel (25 g) and recrystallization from isopropyl ether, was identified (mixture melting point, ir and nmr spectra) as **10**, whereas from the second fraction (155 mg, 29%), which was according to the nmr spectrum a 2.8:1 mixture of C-4 epimers **6** and **7**, after rechromatography on silica gel (25 g) and recrystallization from isopropyl ether was isolated pure methyl 3-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (**6**): mp 125–126°; $[\alpha]^{27}D$ +30° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 3570 and 3510 cm^{-1} (broad peak) (OH); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 4.90 (d, $J_{1,2}$ = 4.0 Hz, 1, H-1), 3.60 (s, 3, Me from C-3 methoxy group), 3.51 (s, 3, Me from C-1 methoxy group), 1.02 (s, 3, C-4 methyl group). *Anal.* Calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.44; H, 7.05.

Reaction of Methyl 3-*O*-Methyl-2-*O*-methylsulfonyl-6-*O*-triphenylmethyl-α-D-*xylo*-hexopyranosid-4-ulose (2) with Methylmagnesium Iodide in 10:1 Ether–Tetrahydrofuran Solution at Reflux. To a 5:1 ether–tetrahydrofuran solution (22 ml) of methylmagnesium iodide (200 mg of Mg + 0.5 ml of CH_3I), an ethereal solution (10 ml) of **2** (350 mg, 0.66 mmol) was added. After the reaction mixture was heated under reflux for 1 hr, water was added and the water phase was extracted with ether. The combined ethereal extracts were dried over anhydrous Na_2SO_4 and ether was evaporated *in vacuo*. The crude product (300 mg) was chromatographed on silica gel. Elution with 95:5 benzene–2-propanol afforded a tlc-homogenous product (148 mg) which was, according to the nmr spectrum, a mixture of **6** and **7** in the ratio 1:2.3.

Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-β-D-glucopyranoside (22). A pyridine solution (60 ml) containing methyl 2,3-di-*O*-methyl-β-D-glucopyranoside (**21**,[36] 3.778 g, 17 mmol) and triphenylmethyl chloride (6.000 g, 21.5 mmol) was kept at room temperature for 2 days. The residue obtained after removal of pyridine *in vacuo* was dissolved in water, the solution was extracted three times with benzene (50 ml), the combined benzene extracts were washed successively with water, 1 *N* sulfuric acid, and again with water and dried over anhydrous Na_2SO_4, and benzene was evaporated *in vacuo*. The residue (9.778 g) was chromatographed twice on silica gel (250 g). Elution with 3:1 hexane–acetone afforded pure **22** (6.621 g, 83%) as a white, amorphous substance: $[\alpha]^{27}D$ −39° (*c* 1.0, $CHCl_3$); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 4.23 (m, 1, H-1), 3.63, 3.56, and 3.55 (three s, 9, Me from C-1, C-2, and C-3 methoxy groups). *Anal.* Calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.59; H, 7.03.

Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-β-D-*xylo*-hexopyranosid-4-ulose (20). To a dimethyl sulfoxide solution (17 ml) of methyl 2,3-di-*O*-methyl-6-*O*-triphenylmethyl-β-D-glucopyranoside (**22**, 1.750 g, 3.8 mmol), acetic anhydride (10 ml) was added with stirring and the reaction mixture was kept at 55–60° for 2 hr. The solvents were then evaporated *in vacuo* to a syrup (maintaining the bath temperature below 40°). The syrup was dissolved in ether (50 ml) and the ethereal solution was washed with saturated aqueous NaCl solution. The ethereal phase was dried over anhydrous Na_2SO_4 and ether was removed *in vacuo*. The crude product (1.746 g) was chromatographed on silica gel (150 g). Elution with 120:60:1 hexane–acetone–water gave pure **20** (1.260 g, 70%), which was recrystallized from isopropyl ether as needles: mp 100–102°; ir ($CHCl_3$) 1740 cm^{-1} (C=O stretch); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 4.63 (d, $J_{1,2}$ = 6.0 Hz, 1, H-1), 3.53 and 3.51 (two s, 9, Me from C-1, C-2, and C-3 methoxy group).

Reaction of Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-β-D-*xylo*-hexopyranosid-4-ulose (20) with Methylmagnesium Iodide in an Ethereal Solution at −80°. To an ethereal solution (15 ml) of methylmagnesium iodide (100 mg of Mg + 1 ml of CH_3I) cooled to −80° an ethereal solution (5 ml) of **20** (190 mg, 0.41 mmol), precooled to −80°, was added, whereby a white precipitate separated. After stirring for 3 hr at −80°, water was added, the ethereal layer was separated, the aqueous phase was extracted with ether, the combined ethereal extracts were dried over anhydrous Na_2SO_4, and ether was evaporated *in vacuo*. The crude product (155 mg, 76%) was according to the nmr spectrum only one isomer. After chromatography on silica gel (50 g) and elution with 2:1 benzene–ether, pure methyl 2,3-di-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-β-D-galactopyranoside (**23**) was obtained as an amorphous solid: $[\alpha]^{27}D$ −13° (*c* 1.0, $CHCl_3$); nmr ($CDCl_3$) δ 7.6–7.1 (m, 15, triphenylmethyl), 4.16 (d, $J_{1,2}$ = 8.0 Hz, 1, H-1), 3.60 and 3.55 (two s, 9, Me from C-1, C-2, and C-3 methoxy group), 1.01 (s, 3, C-4 methyl group). *Anal.* Calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 73.04; H, 7.40.

Reaction of Methyl 2,3-Di-*O*-methyl-6-*O*-triphenylmethyl-β-D-*xylo*-hexopyranosid-4-ulose (20) with Methyllithium (LiBr-Free) in an Ethereal Solution at −80°. To an ethereal solution (10 ml) of **20** (243 mg, 0.53 mmol) cooled to −80° a 2 *M* ethereal solution (1 ml) of methyllithium was added. After the reaction mixture was stirred at −80° for 4.5 hr, water was added, the ethereal layer was separated, and the aqueous layer was extracted with three 30-ml portions of ether. The combined ethereal extracts were washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. The crude product (236 mg) obtained after removal of ether *in vacuo* was according to the nmr spectrum at 3:1 mixture of **23** and **24**, **24** being the predominant product. *Anal.* Calcd for $C_{29}H_{34}O_6$: C, 72.78; H, 7.16. Found: C, 72.67; H, 7.16.

Reaction of 4-*tert*-Butylcyclohexanone with Methylmagnesium Iodide in an Ethereal Solution at −80°. To an ethereal solution (15 ml) of methylmagnesium iodide (144 mg of Mg + 0.5 ml of CH_3I) cooled to −80° an ethereal solution (5 ml) of 4-*tert*-butylcyclohexanone (460 mg, 3 mmol) precooled to −80° was added (during cooling of the ethereal solution of ketone to −80°, the ketone crystallized out so that the suspension was added). After stirring for 6 hr at −80°, water was added, the undissolved solid was dissolved by adding 1 *N* HCl, and the aqueous phase was extracted with three 70-ml portions of ether. Combined ethereal extracts were successively washed with saturated aqueous NaCl solution, saturated aqueous NaCl solution which contained

K_2CO_3 and $NaHSO_3$, and again with saturated aqueous NaCl solution. The ethereal extract was dried over anhydrous Na_2SO_4, and the ether was evaporated *in vacuo*. The crystalline residue (447 mg) was chromatographed on silica gel (40 g). Elution with 7:3 benzene–ethyl acetate gave three fractions; the first fraction (110 mg) was starting material, the second fraction (170 mg, 33%) was pure **16**, whereas the third fraction (103 mg, 20%) was pure **17**. The ratio of **16**:**17** was hence 1.7:1.

Reaction of 4-*tert*-Butylcyclohexanone with Methyllithium in an Ethereal Solution at −80°. To an ethereal solution (20 ml) of 4-*tert*-butylcyclohexanone (308 mg, 2 mmol) cooled to −80°, a 2 *M* ethereal solution (1.4 ml, 2.8 mmol) of methyllithium was added. After stirring for 2 hr at −80°, water was added, the ethereal layer was separated, and the aqueous phase was extracted with ether. The combined ethereal extracts were washed with water and dried over anhydrous Na_2SO_4. The crude crystalline product (274 mg) was chromatographed on silica gel (15 g). Elution with 17:3 benzene–ethyl acetate gave three fractions; the first fraction (66 mg) was the unreacted starting material, the second fraction (132 mg, 40%) was pure **16**, whereas the third fraction (37 mg, 11%) was pure **17**. The ratio **16**:**17** was therefore 3.6:1.

Acknowledgment. We are greatly indebted to Professor L. M. Jackman for recording carbon-13 nmr spectra.

Registry No.—**1**, 51016-07-0; **2**, 51016-08-1; **3**, 51016-09-2; **4**, 51016-10-5; **5**, 51016-11-6; **6**, 51016-12-7; **7**, 51016-13-8; **8**, 51016-14-9; **9**, 51016-15-0; **10**, 51016-16-1; **11**, 51016-17-2; **12**, 51016-18-3; **13**, 51016-19-4; **14**, 937-05-3; **15**, 21862-63-5; **16**, 16980-55-5; **17**, 16980-56-6; **20**, 51016-20-7; **21**, 10227-29-9; **22**, 51016-21-8; **23**, 51016-22-9; **24**, 51016-23-0; methyllithium, 917-54-4; methylmagnesium iodide, 917-64-6; methylmagnesium chloride, 676-58-4; 4-*tert*-butylcyclohexanone, 98-53-3.

References and Notes

(1) This work was supported, in part, by Grant CA 15483 from the National Institutes of Health.

(2) After the preparation of this manuscript, a paper was published dealing with the configurational assignment by carbon-13 nmr spectroscopy of quaternary centers in carbohydrates containing C-1,3 dithianyl branched chains: G. Lukacs, A. M. Sepulchre, A. Gateau-Olesker, G. Vass, S. D. Gero, R. D. Guthrie, W. Voelter, and E. Breitmaier, *Tetrahedron Lett.*, 5163 (1972). In an earlier paper Sepulchre, *et al.*,[3] made a configurational assignment at the branching carbon atom of branched-chain sugars based on carbon-13 nmr spectroscopy together with circular dichroism studies, but without disclosing any details; the data were listed as unpublished results.

(3) A. M. Sepulchre, A. Gateau-Olesker, G. Lukacs, G. Vass, S. D. Gero, and W. Voelter, *Tetrahedron Lett.*, 3945 (1972).

(4) T. D. Inch, *Advan. Carbohyd. Chem. Biochem.*, **27**, 204 (1972).

(5) J. S. Burton, W. G. Overend, and N. R. Williams, *J. Chem. Soc.*, 3433 (1965).

(6) A. A. J. Feast, W. G. Overend, and N. R. Williams, *J. Chem. Soc. C*, 303 (1966).

(7) B. Flaherty, W. G. Overend, and N. R. Williams, *J. Chem. Soc. C*, 398 (1966).

(8) It should be noted that all reported studies thus far have been done with conformationally rigid bicyclic systems, *i.e.*, 4,6-*O*-benzylidene,[9-11] 2,3-*O*-isopropylidene,[12-14] or 3,4-*O*-isopropylidene[5,6] oxo sugar derivatives.

(9) T. D. Inch, G. J. Lewis, and N. E. Williams, *Carbohyd. Res.*, **19**, 17 (1971).

(10) F. A. Carey and K. O. Hodgson, *Carbohyd. Res.*, **12**, 463 (1970).

(11) G. B. Howarth, W. A. Szarek, and J. K. N. Jones, *Carbohyd. Res.*, **7**, 284 (1968).

(12) B. M. Gough, S. W. Gunner, W. G. Overend, and N. R. Williams, *Carbohyd. Res.*, **14**, 173 (1970).

(13) W. G. Overend, A. C. White, and N. R. Williams, *Carbohyd. Res.*, **15**, 185 (1970).

(14) D. Horton and E. K. Just, *Carbohyd. Res.*, **18**, 81 (1971).

(15) (a) T. D. Inch, *Carbohyd. Res.*, **5**, 45 (1967); (b) D. Guillerm-Dron, M.-L. Capman, and W. Chodkiewicz, *Tetrahedron Lett.*, 37 (1972).

(16) In addition to **10**, methyl 3-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-galactopyranoside (**6**) and methyl 3-*O*-methyl-4-*C*-methyl-6-*O*-triphenylmethyl-α-D-glucopyranoside (**7**) were obtained as hydrolysis products of **10** and **11**.

(17) The branched-chain sugars **10** and **11** could not be isolated.

(18) E. J. Corey, *J. Amer. Chem. Soc.*, **75**, 2301 (1953); *Experientia*, **9**, 329 (1953).

(19) C. Djerassi, L. E. Geller, and E. J. Eisenbraun, *J. Org. Chem.*, **25**, 1 (1960).

(20) N. L. Allinger, J. Allinger, L. E. Geller, and C. Djerassi, *J. Org. Chem.*, **25**, 6 (1960).

(21) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, p 460.

(22) D. N. Kirk, *Tetrahedron Lett.*, 1727 (1969).

(23) M. G. Combe and H. B. Henbest, *Tetrahedron Lett.*, 404 (1961).

(24) H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.*, **84**, 2833 (1962).

(25) D. J. Cram and K. R. Kopecky, *J. Amer. Chem. Soc.*, **81**, 2748 (1959); for a discussion of the relationship between chelated and nonchelated coordination transition states and the stereospecificity of the reaction between Grignard reagent and α-alkoxy carbonyl derivatives see ref 15b and 26.

(26) J. Yoshimura, Y. Ohgo, K. Ajisaka, and Y. Konda, *Bull. Chem. Soc. Jap.*, **45**, 916 (1972).

(27) H. Grisebach and R. Schmidt, *Angew. Chem., Int. Ed. Engl.*, **11**, 159 (1972).

(28) D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.*, **89**, 6612 (1967).

(29) F. A. L. Anet, C. H. Bradley, and G. W. Buchanan, *J. Amer. Chem. Soc.*, **93**, 258 (1971); see also J. B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, N. Y., 1972, pp 404, 426.

(30) E. Breitmaier, W. Voelter, G. Jung, and C. Tänzer, *Chem. Ber.*, **104**, 1147 (1971); D. E. Dorman and J. D. Roberts, *J. Amer. Chem. Soc.*, **92**, 1355 (1970).

(31) J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, and H. J. Riech, *J. Amer. Chem. Soc.*, **92**, 1338 (1970).

(32) G. J. Robertson, *J. Chem. Soc.*, 737 (1933); J. W. H. Oldham and G. J. Robertson, *ibid.*, 685 (1935); F. L. Fowler, I. K. Buckland, F. Brauns, and H. Hibbert, *Can. J. Res., Sect. B*, **15**, 486 (1937).

(33) Methyl 4,6-*O*-benzylidene-2-*O*-methylsulfonyl-α-D-glucopyranoside (**13**)[34] was synthesized according to the procedure given by Jeanloz and Jeanloz.[35]

(34) J. Honeyman and J. W. W. Morgan, *J. Chem. Soc.*, 3660 (1955).

(35) R. W. Jeanloz and D. Jeanloz, *J. Amer. Chem. Soc.*, **79**, 2579 (1957).

(36) D. S. Mathers and G. J. Robertson, *J. Chem. Soc.*, 696 (1933); J. W. H. Oldham, *J. Amer. Chem. Soc.*, **56**, 1360 (1934); T. H. Evans, I. Levi, W. L. Hawkins, and H. Hibbert, *Can. J. Res., Sect. B*, **20**, 175 (1942).