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SYNTHESIS OF 2,3-ANHYDRO- AND 3,4-ANHYDRO-HEXOPYRANOSIDES HAVING A METHYL BRANCH ON THE OXIRANE RING, AND THEIR REACTIONS WITH SOME LITHIUM METHYLCUPRATE REAGENTS*

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ABSTRACT

Three 2,3-anhydroaldohexopyranosides having a 2-*C*-methyl or 3-*C*-methyl branch, as well as three 3,4-anhydroaldohexopyranosides having a 3-*C*-methyl (**7**) or 4-*C*-methyl branch, were newly synthesized. The reactions of these, together with those of a known 3-*C*-methyl epoxide (**2**), with three kinds of lithium methylcuprate were investigated. Except for **2** and **7**, the vicinal monodeoxy di-*C*-methyl derivatives were obtained by attack of the cuprates at the sterically less-hindered site of the oxirane ring, irrespective of the stereoelectronic effect. Formation of a unique, acyclic 1-enitol derivative from **2**, and of a 4-enolone derivative from **7**, was ascertained. Differences in the reactivity among the cuprates was also observed.

INTRODUCTION

Recently, carbohydrates have been widely used as chiral synthons[2,3]. Branched-chain sugars obtained by the reaction of anhydro sugars with alkylmetal reagents have often been used for the total synthesis of such natural products as multistriatin[4], blastmycinon[5], erythronolide[6], and tylosin[7]. The reactions of branched-chain, anhydro sugars that have a methyl branch on the oxirane ring with various nucleophiles can provide new types of chiral synthons. In the present study, the reactions of the branched-chain anhydrohexopyranosides **1, 2, 4, 5, 7, 8,** and **9** newly synthesized, except for **2**, with lithium methylcuprate reagents were investigated in the expectation that a vicinal, monodeoxy di-*C*-methyl grouping or, albeit challenging, a quarternary dimethyl function could be constructed stereoselectively.

Regioselectivity in the ring-opening reaction of anhydroglucopyranosides should be greatly influenced by their conformations; that is, the stereoelectronic effect plays an important or predominant role, as represented by the Fürst–Plattner

*Branched-chain Sugars, Part XXXVII. For Part XXXVI, see ref. 1.

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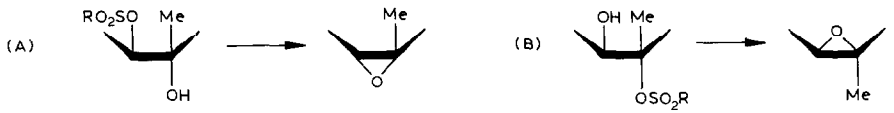
rule, especially in the case of such conformationally rigid glycopyranosides as 4,6-*O*-benzylidene derivatives[8]. In order to be able to evaluate the conformational factor, we planned to synthesize, as much as possible, stereoisomeric pairs having reverse configurations only at the oxirane ring, or branched-chain anhydrohexopyranosides. Such isomeric pairs can principally be prepared from a common *trans*-diol derivative *via* two kinds of mono-*O*-sulfonyl derivative thereof. In the present case, a difficulty arises because of the situation that one isomer should be formed *via* an SN2 reaction of a tertiary sulfonyloxy group, as depicted in Type B of Scheme 1.



Scheme 1

RESULTS AND DISCUSSION

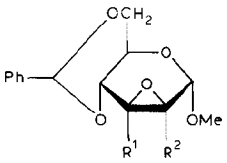
The strategy just described was substantiated by the synthesis of methyl 2,3-anhydro-4,6-*O*-benzylidene-2-*C*-methyl-α-D-mannopyranoside (**1**) and its α-D-*allo* isomer (**4**), which were derived from a common 2-*C*-methyl-α-D-glucopyranoside, namely, **10**; the 3-tosylate (**11**) of **10**, readily obtained by selective tosylation of the secondary hydroxyl group, was treated with sodium methoxide in methanol under reflux, to give **1** in 88% yield. Furthermore, the same treatment of the 3-*O*-benzoyl-2-*O*-(methylsulfonyl) derivative (**13**), which was obtained by mesylation of the tertiary hydroxyl group of the 3-benzoate (**12**) with methanesulfonyl chloride in the presence of 4-(dimethylamino)pyridine, afforded **4** in 59% yield. Preparation of **12** by the reaction of methyl 4,6-*O*-benzylidene-3-*O*-benzoyl-α-D-*arabino*-hexopyranosid-2-ulose with methylmagnesium iodide was reported previously[9]. Re-

TABLE I

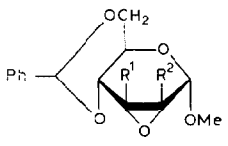
REACTION OF METHYL 3-*O*-BENZOYL-4,6-*O*-BENZYLIDENE-α-D-*arabino*-HEXOPYRANOSID-2-ULOSE WITH METHYLMAGNESIUM IODIDE

Solvents	*MeMgI (equiv.)*	*Temperature (degrees) and time (h)*	*Products (%)*		
			12	**10**	*2-Epimer of* **10**
Ether	3	−78, 2	quant.	—	—
	3	−78, 4 → r.t.[a], 2	84.5	12	—
	3	−78, 4 + r.t., 6	33	66	—
Ether–benzene (2:1)	3	r.t., 1.5	—	56	11
(3:1)	3	reflux, 1.5	—	64	34
(1:1)	1	reflux, 1.5	49[b]	—	—

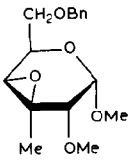
[a]r.t. = room temperature. [b]Ref. 9.



1 $R^1 = H, R^2 = Me$
2 $R^1 = Me, R^2 = H$
3 $R^1 = R^2 = H$



4 $R^1 = H, R^2 = Me$
5 $R^1 = Me, R^2 = H$
6 $R^1 = R^2 = H$



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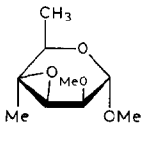

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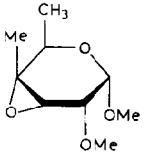

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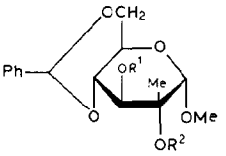


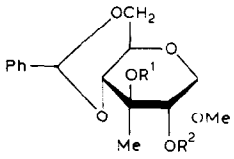
10 $R^1 = R^2 = H$
11 $R^1 = Ts, R^2 = H$
12 $R^1 = Bz, R^2 = H$
13 $R^1 = Bz, R^2 = Ms$

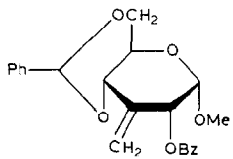
Bz = PhCO
Ms = SO_2Me
Ts = $SO_2C_6H_4Me$-*p*

examination of this reaction (in order to improve the yield) revealed that the reaction with a 2-molar excess of the Grignard reagent in ether at −78° gave **12** quantitatively, whereas, at higher temperatures, its *O*-debenzoylated derivative **10** was preponderant, as shown in Table I. Similar reaction with an excess of the Grignard reagent in ether–benzene gave a mixture of **10** and its 2-epimer in ratios of 5–2:1.

On the other hand, the same strategy could not be applied to the synthesis of a stereoisomeric pair of branched-chain 2,3-anhydropyranosides having a methyl branch on C-3. Whereas the α-D-*manno* isomer **2** has been prepared[10] from methyl 4,6-*O*-benzylidene-3-*C*-methyl-α-D-glucopyranoside (**14**) *via* its 2-tosylate (**15**), principally as described for **1**, an attempt to synthesize the α-D-*allo* isomer (**5**) *via* the 3-sulfonates (**17** or **18**) was unsuccessful. On mesylation of the tertiary hydroxyl group in the 3-benzoate **16** in the same way as just mentioned, only the *exo*-methylene compound **20** was obtained, instead of the expected 3-mesylate **17**. Although the corresponding 3-tosylate (**18**) could be prepared by bilayer sulfonylation[11] with *p*-toluenesulfonyl chloride in dichloromethane–aqueous sodium hydroxide in the presence of tetrabutylammonium hydrogensulfate, treatment of **18** with sodium methoxide again gave **20** exclusively. These results may be explained by 1,3-diaxial repulsion between the 3-*C*-methyl and the 1-methoxyl group which should force the elimination reaction to proceed.

Therefore, the epoxide **5** was prepared by starting from methyl 4,6-*O*-ben-



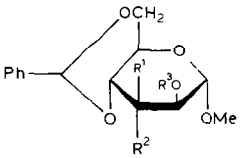


14 $R^1 = R^2 = H$
15 $R^1 = H, R^2 = Ts$
16 $R^1 = H, R^2 = Bz$
17 $R^1 = Ms, R^2 = Bz$
18 $R^1 = Ts, R^2 = Bz$
19 $R^1 = H, R^2 = Me$

20

zylidene-α-D-altropyranoside (**21**). Its 2-*O*-allyl derivative (**22**) was obtained in 76% yield by treatment of **21** with allyl bromide in dichloromethane–aqueous sodium hydroxide in the presence of tetrabutylammonium bromide[12], and **22** was oxidized with dimethyl sulfoxide (Me_2SO) and trifluoroacetic anhydride (TFAA)[13], to give the glycosid-3-ulose **23** in 98% yield. The nucleophilic addition of a methyl group to **23** by use of methyllithium gave better stereoselectivity than that with methylmagnesium iodide, where the ratios of the D-*altro* (**24**) to the D-*manno* (**25**) isomer were proved by ^{1}H-n.m.r. to be 5:1 and 2:1, respectively. These results differ from the stereoselectivity observed[14] for the corresponding 2-*O*-methyl derivative of **23**, presumably due to slightly different bulkiness of the substituents. The D-*altro* isomer (**24**), obtained in 60% yield by using methyllithium as the nucleophile, was *O*-deallylated with potassium *tert*-butoxide in *N,N*-dimethylformamide followed by treatment with mercuric chloride–mercuric oxide, or iodine–pyridine[15], to give **26** in 53 or 50% yield, respectively. Treatment of the 2-tosylate (**27**) of **26** with potassium hydroxide in methanol gave **5** in 83% yield.

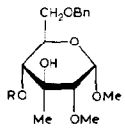
In accordance with the results of the aforementioned experiments, the synthetic routes for all model, branched-chain 3,4-anhydro sugars were planned to



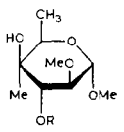
21 $R^1 = R^3 = H, R^2 = OH$
22 $R^1 = H, R^2 = OH, R^3 = All$
23 $R^1, R^2 = O, R^3 = All$
24 $R^1 = Me, R^2 = OH, R^3 = All$
25 $R^1 = OH, R^2 = Me, R^3 = All$
26 $R^1 = Me, R^2 = OH, R^3 = H$
27 $R^1 = Me, R^2 = OH, R^3 = Ts$

All = $-CH_2CH{=}CH_2$

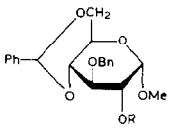
form the oxirane ring by substitution of the secondary sulfonyloxy group (Type A). Methyl 3,4-anhydro-6-*O*-benzyl-3-*C*,2-*O*-dimethyl-α-D-galactopyranoside (**7**) was prepared from methyl 6-*O*-benzyl-3-*C*,2-*O*-dimethyl-α-D-glucopyranoside (**28**) *via* its 4-tosylate (**29**) in 82% yield by the conversion just described for preparing **5** from **26**. The intermediate **28** was obtained quantitatively by reductive and regioselective cleavage of the 4,6-*O*-benzylidene derivative (**19**) with sodium cyanoborohydride in the presence of hydrochloric acid in ether[16]. The same conversion was also used for synthesis of 3,4-anhydro-4-*C*-methylhexopyranoside derivatives, having the D-*talo* (**8**) and D-*allo* (**9**) configuration, from methyl 6-deoxy-4-*C*,2-*O*-dimethyl-α-D-idopyranoside (**30**) and -α-D-glucopyranoside (**38**), respectively, *via* their 3-tosylates (**31** and **39**), both in 70% yield (in two steps).



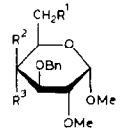
28 R = H
29 R = Ts
Bn = $PhCH_2$



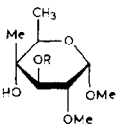
30 R = H
31 R = Ts



32 R = H
33 R = Me



34 R^1 = OTs, R^2 = H, R^3 = OH
35 $R^1 = R^2$ = H, R^3 = OH
36 R^1 = H, R^2, R^3 = =O



37 R = Bn
38 R = H
39 R = Ts

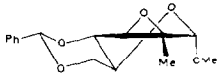
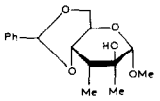
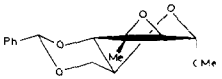
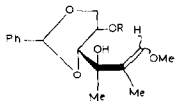
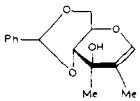
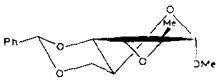
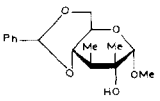
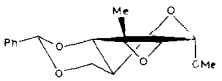
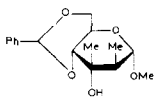
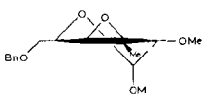
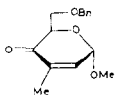
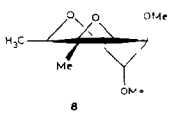
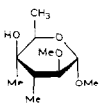
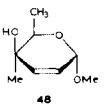
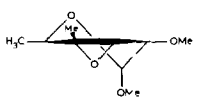
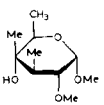
The intermediate glycosidulose (**36**) for preparation of the latter was derived from methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**32**). *O*-Debenzylidenation of its 2-methyl ether (**33**) with 70% aqueous acetic acid, followed by selective tosylation, gave the 6-tosylate (**34**) in 50% yield from **32**. The corresponding 6-deoxy compound (**35**), obtained by reduction with sodium borohydride in Me_2SO[17], was oxidized with Me_2SO–TFAA, to give the glycosid-4-ulose (**36**) quantitatively. The nucleophilic reaction of **36** with methyllithium gave the D-*gluco* isomer (**37**) almost exclusively, in ~65% yield. As the minor component could not be separated therefrom, further conversions, *i.e.*, *O*-debenzylation, tosylation, and epoxidation, were conducted without complete purification of the intermediates **37, 38,** and **39**.

The reaction of anhydrohexopyranosides with organometallic reagents were relatively well investigated for methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-manno- (**3**) and -D-allopyranoside (**6**). As reported for ring-opening reactions with other nucleophiles[18], reactions of **3** with such organometallic reagents as Grignard reagents[19] and methyllithium[20] gave, in moderate yields, 3-*C*-alkyl derivatives having the *altro* configuration; both the electrostatic effect of the anomeric center and the stereoelectronic effect (Fürst–Plattner rule) favor attack of the nucleophile at C-3.

On the other hand, for **6**, these two effects function in opposite directions, to favor attack at C-3 and C-2, respectively, giving complex reaction-products. Only the 2-*C*-alkyl compound (Fürst–Plattner product) could be obtained, albeit in low yield[19], by the reaction with methylmagnesium chloride. Other Grignard reagents, and methyllithium, gave only such byproducts as 2-deoxy-D-altropyranosides[19], 2-

TABLE II

THE REACTIONS OF BRANCHED-CHAIN ANHYDRO SUGARS WITH LITHIUM METHYLCUPRATES

Anhydro sugars and conformations	*Products*	*Yields (%)*		
		Me_2CuLi	*$MeCu(CN)Li$*	*$Me_2Cu(CN)Li_2$*
 1	 40	69	n.r.[a]	54
 2	 41 R = H 42 E R = Ac[b]			
	 43	n.r.[a,c]	60 17 (15)[d]	48.5 32 (18)[d]
 4	 44	65	64	84
 5	 45	82.5	80	79
 7	 46	56	15 (55)[d]	55
 8	 47	39	40	41
	 48	55	25 (10)[d]	58.5
 9	 49	63.5	n.r.[a] (64)[d]	44

[a]No reaction. [b]Obtained by acetylation of **41***E*. [c]When methyllithium and cuprous iodide were used in the molar ratios of 5:1 and 8:1, compounds **43** and **41**, respectively, were mainly obtained, each in 70% yield. A reaction with methyllithium gave **43** in only 15% yield. [d]Anhydro sugars recovered.

deoxy-2-halogeno-D-altropyranosides[19], and D-allal derivatives[19,20]. The last two byproducts were formed owing to the presence of halide ion and the basicity of the reagents, which promote the elimination of halohydrin from alkoxy halides. To circumvent these difficulties, lithium dimethylcuprate was successfully introduced for the ring-opening of **6**, to give the expected 2-*C*-methyl derivative in good yield[21].

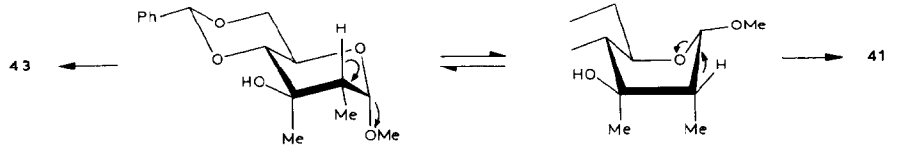
The reaction of the synthetic, branched-chain, anhydro sugars **1, 2, 4, 5, 7, 8,** and **9** was studied by using three kinds of lithium methylcuprate: lithium dimethylcuprate, Me_2CuLi; a mixed methylcuprate[22] MeCu(CN)Li; and a recently reported[23], higher-order, mixed methylcuprate, $Me_2Cu(CN)Li_2$. The results are summarized in Table II.

As a general consequence of the highly regioselective attack of the cuprates (irrespective of their kind) on the secondary carbon atom, vicinal di-*C*-methyl derivatives were obtained, except in the case of **7**. The bulkiness of these nucleophiles seems to be responsible for the attack at the less sterically hindered site of the oxirane ring, because the smaller nucleophiles, such as hydride and azide, can attack at the more sterically hindered, tertiary carbon atom, in accord with the Fürst–Plattner rule[24]. The reactions with the cuprates exhibited completely stereospecific, *anti*-opening of the oxirane ring; this was confirmed, clearly, by the coupling constants of the ring protons in the cases of **40, 44,** and **49**. Besides the reasonable products, some unsaturated sugars were obtained in the reactions of **2, 7,** and **8**.

Two unsaturated sugars (**41** and **43**) were obtained in the reaction of **2** with MeCu(CN)Li and $Me_2Cu(CN)Li_2$ [instead of methyl 4,6-*O*-benzylidene-2,3-di-*C*-methyl-α-D-glucopyranoside (**50**)], and no reaction occurred with Me_2CuLi. It is, however, noteworthy that, when methyllithium, cuprous iodide, and **2** were mixed in the molar ratios of 20:4:1 and 32:8:1, the unsaturated compounds **43** and **41**, respectively, were obtained, each as the major product in >70% yield. In these reactions, the reactive species is considered[25] to be the same cuprate, *viz.*, Me_3CuLi, although the proportion of methyllithium clearly affects the reaction course, presumably owing to its basicity.

On the one hand, the reaction of **2** with methyl lithium gave **43** in a yield of only ~15%. It seems reasonable to presume that **41** and **43** were formed *via* the common intermediate **50**, followed by elimination between the relatively acidic hydrogen atom on C-2 and the ring-oxygen or anomeric oxygen atom as shown in Scheme 2. The 1,3-diaxial interaction between the 1-methoxyl and the 3-*C*-methyl groups in **50** may promote this elimination.

In contrast, for **45**, which is a stereoisomer of **50**, the same interaction bet-



50

Scheme 2

TABLE III

^{1}H-N M R DATA FOR BRANCHED-CHAIN ANHYDRO SUGARS AND THEIR SYNTHETIC INTERMEDIATES[a,b]

Compound	*H-1* $J_{1,2}$	*H-2* $J_{2,3}$	*H-3* $J_{3,4}$	*H-4* $J_{4,5}$	*H-5* $J_{5,6}$	*H-6* $J_{5,6}$	$J_{6,6'}$	*C-CH$_3$*	*O-CH$_3$*	*Ph-CH*	*Ph*	*Others*
1[c]	4.61s	—	3.27s	3 66–3 96m(2H)		3.53t	4.14dd	1.25s	3.11s	5.32s	7.20–7.74m	
	—	—	<0 5	†[d]	3.8	9.6	9.6					
4[e]	4.57s	—	3 19bs	3.73dd	4.07dt	3.59t	4.22dd	1.02s	3.41s	5.42s	7.20–7 58m	
	—	—	1.6	7.8	4.0	7.8	7.8					
5	4.67s	2.83s	—	3 58–3.90m(2H)		3.48t	4.11dd	1.32s	3.45s	5.53s	7.30–7.62m	
	<0.5	—	—	†	3.8	9.6	9 6					
7	4.72d	3.36d	—	3.09d	4.22bdt	3.67bd(2H)		1.43s	3.47s	—	7.33bs	4.62s (CH_2 in Bn)
	3.2	—	—	1.8	$J_{5,6}$ 6.2				3.53s			
8	4.52bs	3.49dd	3 30d	—	3.96q	1.34d(3H)		1.35s	3.40s	—	—	
	2.0	4.2	—	—	$J_{5,6}$ 6.2				3 55s			
9	4.76d	3.77dd	3.22d	—	4.14q	1.35d(3H)		1 38s	4.42s	—	—	
	4.2	2.8	—	—	$J_{5,6}$ 7 8				4.55s			
11	4.45s	—	4 96d	3.4–4.0m(3H)			4.39dd	1.35s	3.44s	5.36s	7.20–7.40m	2.28s (CH_3 in Ts)
	—	—	8.8	†	3 0	†	8.6					
13	5.28s	—	5 90d	3.81t	~4 1m	3.80dd	4.35dd	2.01s	3.52s	5.50s	7.3–7.65m	3.03s (CH_3 in Ms)
	—	—	9.6	9.6	4.0	8.4	10.8				8.0–8.2m	
18	5.10d[f]	5.04d[f]	—	3.6–3.9m(3H9			4.32dd	1.63s	3.36s	5.54s	7.3–7.6m	2 42s (CH_3 in Ts)
	3.8	—	—	†	3.2	†	8.8				7 7–7 8m	
											8.05–8.15m	
20	5.03d	5 61bd	—	4.36d	3.80–4.2m(3H)			5.2–5.4m	3.42s	5.63s	7.3–7.6m	
	4.0	—	—	5.6	†	†	†	(2H, CH_2=C)			8.0–8.2m	
22	4 52bd	3 68dd		3 80–4.2m(3H)	5 2–5 4m			—	3 42s	5.60s	7.3–7.7m	5.2–5.4m (CH_2=)
	1.2	3.8	†	†	†	†	†					5.7–6.1m (=CH-)
23	5.01d	3.83d	—	4.85d	4.0–4.2m(4H)[g]		4.38dd	—	3.42s	5.62s	7.3–7.6m	5.2–5.5m (CH_2=)
	1.8	—	—	9.6	2.4	†	8.0					5 6–6.1m (=CH-)

24	4.76d	3 35d	—	3.72d	4.0–4 2m(3H)[g]	3.83t	4.35dd	1.39s	3.47s	5.59s	7.3–7.6m	5.2–5.5m (CH_2=)
	1.4	—	—	9.8	4.2	8.2	8.2					5 7–6 1m (=CH-)
26	4.74d	3.65d	—	3.72d	4.08dt	3.82t	4.35dd	1.40s	3.47s	5.60s	7.3–7.58m	
	1.4	—	—	10.0	4.0	9.8	9.8					
28	4.88d	3 30d	—		3 6–3 8bd(4H)			1.37s	3.40s	—	7.36bs	4.62s (CH_2 in Bn)
	4.0	—	—	†	†	†	†		3.49s			
29	4 85d	3.39d	—	4.75d	3.88m	3.66bd(2H)		1.31s	3.40s	—	7.28d, 7.78d	4.54ABq (J 12.0, CH_2 in Bn)
	3.8	—	—	10.2	†	†	†		3.56s		(J 8.4)	
											7.32bs	2.42s (CH_3 in Ts)
31	4.65t	~3.50	4.39dd	—	3.95q	1.15d(3H)		0.91s	3.38s	—	7.37d, 7.88d	2.48s (CH_3 in Ts)
	1.2	2.8	$J_{1,3}$ 1.2	—					3.44s		(J 7.8)	
						$J_{5,6}$ 6.0						
33	4.86d	3.38dd		3.6–4.1m(4H)			4.28dd	—	3.44s	5.55s	7.28–7.56m	4 84ABq (J 10.8, CH_2 in Bn)
	4.0	9.4	†	†	2.6	†	8.0		3.57s			
34	4.77d	3.25dd		3.4–3.8m(4H)		4.25bd(2H)		—	3.37s	—	7.32d, 7 78d	4.89ABq (J 11.8, CH_2 in Bn)
	4.0	9.6	†	†	$J_{5,6}$ 4.4				3.48s		(J 8.0)	2.43s (CH_3 in Ts)
											7.37bs	
35	4.82d			3.0–4.0m(4H)		1.16(3H)		—	3.44s	—	7.35bs	4 81ABq (J 11.2, CH_2 in Bn)
	3.8	†	†	†	$J_{5,6}$ 7.0				3.52s			
36	4.95d	3.19dd	4.38d	—	4.23q	1.31d(3H)		—	3.58s	—	7.3–7.5m	4.78ABq (J 10.8, CH_2 in Bn)
	3.8	10.0	—	—	$J_{5,6}$ 6.6				3.68s			
37	4.83d	3.27dd	3.5–3.9m(2H)	—	3.5–3.9m(2H)	1.24d(3H)		1.18s	3.45s	—	7.36bs	4.81ABq (J 11.6, CH_2 in Bn)
	3.6	9.8	—	—	$J_{5,6}$ 6.4				3.62s			
38	4.83d	3.15dd	3.84d	—	3.67q	1.19d(3H)		1.16s	3.42s	—	—	
	3 8	10.0	—	—	$J_{5,6}$ 7.0				3.50s			
39	4.82d	3 50dd	4.73d	—	3.78q	1.16d(3H)		1.31s	2.95s	—	7.38d, 7.86d	2.45s (CH_3 in Ts)
	3.6	7.8	—	—	$J_{5,6}$ 6.8				3.40s		(J 8.2)	

[a]Measured in $CDCl_3$, unless otherwise stated. [b]The following abbreviations are used: b, broad; d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet [c]Measured in C_6D_6. [d]Could not be analyzed. [e]Measured in 1:1 $CDCl_3$–C_6D_6. [f]These signals are interchangeable. [g]Including CH_2 in allyl group.

TABLE IV

N M R DATA FOR REACTION PRODUCTS[a,b]

Compound		*1*	*2*	*3*	*4*	*5*	*6*		*2-CH$_3$*	*3-CH$_3$*	*4-CH$_3$*	*O-CH$_3$*	Ph=*CH*	*Ph*	*Others*
40	^{1}H	4 26s	—	2 17dq ($J_{3,4}$ 2 2)	4 08dd ($J_{4,5}$ 5 4)	4 26m	3.75t ($J_{5,6e}$ 3 9)	3 88dd ($J_{5,6i}$ 9 3)	1.27s	1 16d	—	3.36s	5 55s	7 2–7 5m	2 35bs(OH)
	^{13}C	101.45[c]	72.47	40 35	80.92	64 50	69 18		18.87	8.84	—	55 09	101 38[d]	[e]	
41E	^{1}H	5.88d ($J_{1,2Me}$ 2 0)	—	—	3.47d ($J_{4,5}$ 9 0)	3 96dt ($J_{5,6i}$ 9 6,	3 58dd $J_{5,6e}$ 4 5,	4 26dd $J_{6i,6e}$ 10 2)	1 63d	1 48s	—	3 60s	5 42s	7 2–7 5m	
	^{13}C	143 34	116.73	78 86	86.17	63.75	70 86		17 06	26.17	—	60.24	101 33	[f]	
42E[d]	^{1}H	5 86bs	—	—	3.94d ($J_{4,5}$ 9 8)	5 10d	3 58dd ($J_{5,6e}$ 5 3)	4 42dd ($J_{5,6i}$ 10 3)	1 62s	1.41s	—	3.55s	5 50s	7 2–7 6m	2 07s(CH_3CO) 4 46s(OH)
	^{13}C	142.85	116.24	76.71	83 39	64.92	67 40		16 72	23 88	—	60.04	100.94	[g]	21.05(CH_3CO) 169.61(CO)
43	^{1}H	6.04bs	—	—		3 7–4 0m(3H)	($J_{5,6e}$ 2 7,	4 38dd $J_{6a,6e}$ 9 0)	1 64d	1.48s	—	—	5.60s	7 26–7.58m	
	^{13}C	137.60	113 58	70 63	83 24	67.29	68.85		11.03	22 13	—	—	101.66	[h]	
44	^{1}H	4.30s	—	2 10dq ($J_{3,4}$ 10 8, $J_{3,Me}$ 6 3)	3 23dd	4 24m ($J_{4,5}$ 9 6)	~3 70m(2H)		1 18s	1 08d	—	3 42s	5 46s	7 2–7 5m	2 38bs(OH)
	^{13}C	101.32	72 38	40 22	75 75	64 42	69 06		18.89	8 78	—	54 96	104.06	[i]	
45	^{1}H	4 58bs	2 09q ($J_{2,Me}$ 7 4)	—	3.58d ($J_{4,5}$ 9.8)		←3 65–4 36m(3H)→		1 17d	1.30s	—	3.46s	5 61s	7 3–7 62m	2 08b(OH)
	^{13}C	102 20	44 80	71 16	80.24	60 38	69.36		14.74	22 89	—	55 30	104.54	[j]	
46	^{1}H	4.81d	6 76m	—	—	~4 68m	3 63dd	3.72dd	—	1.85d	—	3 57s	—	7 35bs	4 64s(2H, CH_2 in Bn)

		($J_{1,2}$ 1 2)	($J_{2,3Me}$ 2 8)			($J_{5,6a}$ 7.8,	$J_{5,6e}$ 2.2,	$J_{6a,6e}$ 10.2)								
	^{13}C	98.78	143.29	132.41	189.56	68.28	71.50[c]		—	14 84	—	56.66	—	[k]		73 70[c](CH_2 in Bn)
47	^{1}H	4.76t	3.17t	2 06tq	—	3.88t	1 19d(3H)		—	1 05d	10 3s	3 42s	—	—		
		($J_{1,2}$ = $J_{3,4}$ = 1.4)	($J_{2,3}$ 1 4)	($J_{3,Me}$ 7 6)		($J_{5,6}$ 6.4)						3 45s	—	—		
	^{13}C	99 47	82 14	39 97	70.92	66.04	23 17		—	14 15	13.86	54.95	—	—		
												57 49	—	—		
48	^{1}H	4.86d	5.77dd	5 98d	—	3 98q	1.26d(3H)		—	—	1 18s	3.46s	—	—		
		($J_{1,2}$ 2 4)	($J_{2,3}$ 10 2)			($J_{5,6}$ 7 0)										
	^{13}C	95 22	136.14	125.67	65 99	70.48	23 04		—	—	13.76	55 54	—	—		
49	^{1}H	4.82d	2.97dd	1.96dq	—	3.75q	1.06d(3H)		—	1 16d	1.05s	3.45s	—	—		
		($J_{1,2}$ 3 8)	($J_{2,3}$ 11 0)	($J_{3,Me}$ 6.8)		($J_{5,6}$ 7.2)						3.49s	—	—		
	^{13}C	96.39	81 26	42.32	72 82	70 82	13.72			10 05	13 85	54.86	—	—		
												57.88				
51	^{1}H	4.61bs	—			←3 7–4.0m(3H)→		–4 27	1.68bs	1 74s	—	3 44s	5.54s	7.2–7 7m		
		($J_{1,2\text{-}Me}$ 1 6)														
	^{13}C	100.01	139.8	126.1	77.84	64 30	69 45		11 76[c]	14 59[c]		55.93	101.91	[l]		
52	^{1}H	5.10bd	—	—		←3 7–4 0m(3H)→	4	4 28dd	1.74d	1.76s	—	—	5 56s	7.2–7 6m		3.19d(OH) ($J_{1\ OH}$ 5.0)
							($J_{5,6e}$ 3.8,	$J_{6a,6e}$ 9 6)								
	^{13}C	93 02	137.56	127 58	77.50	63.89	69 21		11 57[c]	14 59[c]	—	—	101.71	[m]		
53	^{1}H	10 13s	—	—	4 72bd	~4.0m	3.70t	4 34dd	1.89s	2 25bs	—	—	5.56s	7.2–7.6m		3.04bs(OH)
					($J_{4,5}$ 8.2)	($J_{5,6a}$ 9 8,	$J_{5,6e}$ 4 0,	$J_{6a,6e}$ 9 8)								
	^{13}C	192.39	151.54	137 49	82.09	63.30	71.26		11.66[c]	12 10[c]	—	—	100 88	[n]		

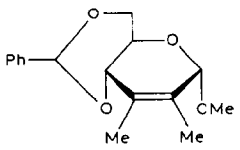
[a]Measured in $CDCl_3$ [b]The same abbreviations as in Table III are used [c]These signals are interchangeable. [d]Obtained by acetylation of **41E** [e]125 92, 128.00, 128.65, and 137 57 [f]128.13, 128 76, 129.20, and 134 88 [g]126 83, 128.16 128 86, and 137 68 [h]126 24, 128 23, 129.10, and 137.38. [i]125 92, 127 87, 128 55, and 137 63 [j]126 26, 128 11, and 128 79 [k]127.77, 127 78, 128 07, and 128.46. [l]126 26, 128 16, 128.90, and 130 70 [m]126 06, 128 07, 128 75, and 130 65 [n]126.26, 128 36, 129.24, and 135.29

ween the 1-methoxyl group and the 3-hydroxyl group favors stabilization by hydrogen bonding.

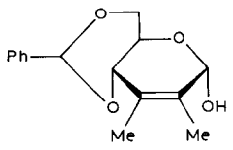
The structures of **41** and **43** coincide well with the ^{1}H- and ^{13}C-n.m.r. data, shown in Table III. Compound **41** was proved to be a mixture of two geometrical isomers, and only the *E*-isomer (**41*E***), whose geometrical structure was deduced from the reaction mechanism shown in Scheme 2, was first obtained in the pure state after decomposition of the contaminated *Z*-isomer (**41*Z***) during storage, as will be mentioned later. The signals of the alkenic protons, at δ 5.98 (major component) and δ 6.28 (minor one) for **41**, and δ 6.04 for **43**, are together indicative of signals for two sp^2 carbon atoms, at ~140 and 115 p.p.m.

The acyclic structure of the main chain in **41** was confirmed by its conversion into the monoacetate **42**, whose ^{1}H-n.m.r. spectrum showed a downfield shift of the H-5 signal. Further evidence for the structure of **41** was obtained from examination of its decomposition products. The mixture (**41**) of geometrical isomers gave three new compounds during storage for a few weeks at room temperature, whereas part of **41*E*** still remained unchanged. A compound formed in the early stages proved to be methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-di-*C*-methyl-α-D-*erythro*-hex-2-enopyranoside (**51**), contaminated with a small proportion of its β anomer.

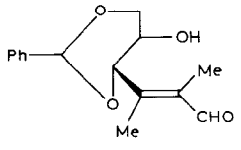
A recyclization may occur *via* an SN2′-like mechanism initiated by attack of the hydroxyl group on C-1. The other two compounds were a pair of geometrical isomers of 4,6-*O*-benzylidene-2,3-dideoxy-2,3-di-*C*-methyl-D-*erythro*-hex-2-enose, where the *Z*-isomer (**52**) exists in a pyranose form and the *E*-isomer (**53**) in an acyclic one. ^{1}H- and ^{13}C-N.m.r. data for **53** indicated the presence of an aldehyde group (see Table IV).



51



52

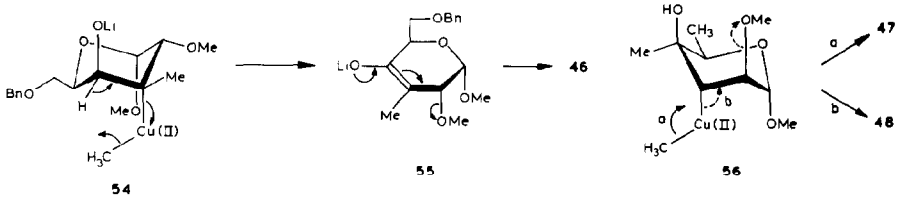


53

In the case of **7** only, instead of introduction of a methyl group, an unexpected reaction occurred, to give the enolone derivative **46**, whose structure was confirmed by comparison of its n.m.r. data with those of structurally analogous sugar enolones[26]. The formation of **46** can be reasonably explained as occurring *via* a glycosid-4-ulose, followed by β-elimination of the 2-methoxyl group, because the rearrangement of an epoxide to a carbonyl compound in the presence of organocopper reagents[27] is well known. However, this rearrangement requires the attack of the copper atom on the tertiary carbon atom. The stereoelectronic effect and a chelate-like interaction of the cuprate with an appropriately situated oxygen atom, such as the methoxyl and the 6-benzyloxy group in **7**, seem to stabilize the

transition state, to afford the oxidative addition product (**51**), which can readily rearrange into the glycos-4-ulose enolate (**52**).

For an explanation of its formation, the side product **48** seems to require a new mechanism. As in the reaction with the halogen-free cuprates used in our experiments, the formation of an unsaturated sugar *via* a halohydrin derivative, which is often observed in the reaction of anhydro sugars with alkylmagnesium iodides[19], cannot be considered; an oxidative elimination of the intermediate **53** may be a possible mechanism for the formation of **48** (see Scheme 3). The axially oriented 2-methoxyl group may assist this energetically disfavored change of Cu(II) into Cu(III), provided that existence of the cuprates in the dimeric form is assumed. The difference in the yields of **48** (as between use of Me_2CuLi and the mixed cuprates) may reflect the effect of the ligand on this step[28]. However, the mechanism (see Scheme 3) is only speculative.



Scheme 3

Furthermore, the differences in the reactivities of the cuprates deserve comment. In general, the higher reactivity of Me_2CuLi_2 was also observed here. The difference between Me_2CuLi_2 and MeCu(CN)Li as shown for compounds **1, 2, 7,** and **9** cannot be readily explained, but it is presumed to depend on the difference in the association state[25] or the structure of the copper cluster, or both, which has a direct effect on the oxidative-addition and reductive-elimination steps of the reaction.

In conclusion, the branched-chain 2,3- and 3,4-anhydroaldohexopyranosides react with the lithium methylcuprates to give, except in a few cases, the vicinal di-*C*-methyl derivatives exclusively, under the influence of steric factors. The α-D-*manno* isomer (**2**) of methyl 2,3-anhydro-3-*C*-methylhexopyranoside gave an acyclic (**41**) and a cyclic (**43**) 1-enitol derivative by further intermolecular and intramolecular eliminations, respectively, of the normal, ring-opening product (**50**). The reactions of the α-D-*galacto* isomer (**7**) of methyl 3,4-anhydro-3-*C*-methylhexopyranoside and the α-D-*talo* isomer (**8**) of methyl 3,4-anhydro-4-*C*-methylhexopyranoside proceed in different ways, completely, and partially, respectively, after the first step of the reaction, *i.e.*, the oxidative addition of the copper atom, to give the 4-enolone (**46**) and the methyl 2-enopyranoside (**48**) by different types of reductive elimination.

EXPERIMENTAL

General methods. — Melting points were determined with a Mel-Temp ap-

paratus, or with a Yanagimoto micro melting-point apparatus, and not corrected. Optical rotations were measured in chloroform, by using a 0.5-dm tube in a Carl Zeiss LEP-AL polarimeter. I.r. spectra were recorded with a Hitachi EPI-G2 grating spectrometer. ^{1}H- and ^{13}C-N.m.r. spectra were recorded at 100 MHz with a JEOL JMN PS-100 spectrometer, and at 22.5 MHz, with a JEOL FX-90Q spectrometer, respectively, with tetramethylsilane as the internal standard. Column chromatography was performed on Wakogel C-200 or C-300 (Wako Pure Chemical Industries, Ltd.). ^{1}H-N.m.r. data for compounds **1** to **39** (except for reported ones), and ^{1}H- and ^{13}C-n.m.r. data for compounds **40** to **53** are summarized in Tables III and IV, respectively.

*Methyl 2,3-anhydro-4,6-*O*-benzylidene-2-C-methyl-α-*D*-mannopyranoside* (**1**). — A solution of **11** (1.9 g, 5 mmol) in methanol (100 mL) containing sodium (200 mg, 9.5 mmol) was boiled under reflux for 6 h. The compound that precipitated on cooling, as long needles, was filtered off, washed with water, and recrystallized from ethanol (**1**; 1.0 g, 87%), and a further crop of **1** was obtained from the mother liquor (0.13 g, 11%); m.p. 228–230°, $[\alpha]_D$ +113° (*c* 0.20).

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.79; H, 6.53.

*Methyl 2,3-anhydro-4,6-*O*-benzylidene-2-C-methyl-α-*D*-allopyranoside* (**4**). — Treatment of **13** (3.58 g, 7.6 mmol) with methanol (120 mL) containing sodium (500 mg, 23.8 mmol) as just described gave **4** (1.27 g, 59%); m.p. 139–140°, $[\alpha]_D$ +68.1° (*c* 0.44).

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.52; H, 6.43.

*Methyl 2,3-anhydro-4,6-*O*-benzylidene-3-C-methyl-α-*D*-allopyranoside* (**5**). — To a solution of **26** (256.5 mg, 0.87 mmol) in dry pyridine (5 mL) was added *p*-toluenesulfonyl chloride (1 g, 4.3 mmol). The solution was kept for 5 days at room temperature, shaken with dichloromethane (10 mL) and water (10 mL), and the dichloromethane layer evaporated to dryness. The crude 2-tosylate was treated with methanol (10 mL) containing KOH (0.3 g, 5.3 mmol) for 1 h at 0°, and the solution poured into water, and extracted with dichloromethane. The extract was evaporated to dryness, and the residue was purified on a column of silica gel (C-300) with 7:2:1 benzene–hexane–acetone, to give **5** (200.4 mg, 83.2%); m.p. 209–212° (dec.), $[\alpha]_D$ +47.3° (*c* 0.69).

Anal. Calc. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.64; H, 6.34.

*Methyl 3,4-anhydro-6-*O*-benzyl-3-C-methyl-2-*O*-methyl-α-*D*-galactopyranoside* (**7**). — Treatment of **28** (1.06 g, 3.4 mmol) with *p*-toluenesulfonyl chloride (2 g, 8.6 mmol) in pyridine (5 mL) for 2 days at room temperature gave crude 4-tosylate **29**, a small portion of which was purified by preparative t.l.c. with 8:1 $CHCl_3$–ethanol; its n.m.r. data are given in Table III.

Tosylate **29** was treated with KOH (0.3 g, 5.3 mmol) in methanol (10 mL) for 1 h at room temperature, and the residue that was obtained as described for **5** was purified on a column of silica gel with 7:3 hexane–acetone, to afford **7** as a syrup (0.82 g, 82%); $[\alpha]_D$ +8° (*c* 2.4).

Anal. Calc. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.36; H, 7.34.

Methyl 3,4-anhydro-6-deoxy-4-C-methyl-2-O-methyl-α-D-talopyranoside (**8**). — Treatment of **30** (1.61 g, 7.8 mmol) with *p*-toluenesulfonyl chloride (2 g, 8.6 mmol) in pyridine (15 mL) for 4 days at room temperature gave crude **31**, which was characterized only by its n.m.r. data (see Table III).

Compound **31** was treated with KOH (0.3 g, 5.3 mmol) in methanol (5 mL) for 1 h at 0°, and the residue, obtained as described for **5**, was purified on a column of silica gel with 5:1 hexane–ethyl acetate to afford **8** (1.02 g, 69.5%); $[\alpha]_D$ +163.2° (*c* 0.19).

Anal. Calc. for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.14; H, 8.36.

Methyl 3,4-anhydro-6-deoxy-4-C-methyl-2-O-methyl-α-D-allopyranoside (**9**). — To a solution of **36** (3.36 g, 11.9 mmol) in ether (150 mL) was added dropwise, during 15 min, a solution of MeLi (1.2 M, 60 mL) in ether, with stirring and cooling (−78°). After 4 h, the solution was poured into saturated, aqueous NH_4Cl solution, and the mixture extracted with dichloromethane. Evaporation of the extract gave crude **37**, contaminated with a small amount of 4-epimer which could not be separated well, and further reactions were conducted without separation of the epimers. Formation of **37** was confirmed by the n.m.r. data (see Table III).

A solution of crude **37** (2.06 g, 7.3 mmol) in methanol (30 mL) was shaken for 20 h at room temperature under hydrogen at 1 atm. in the presence of 5% Pd–C (0.5 g). The catalyst was filtered off, and the filtrate was evaporated, to give crude **38**; for n.m.r. data, see Table II.

Treatment of crude **38** (1.63 g, 7.9 mmol) with *p*-toluenesulfonyl chloride (3 g, 12.9 mmol) in pyridine (10 mL) for 4 days at room temperature gave crude 3-tosylate (**39**) as a syrup (for n.m.r. data, see Table II). Then, conversion of **39** into **9** was conducted, as described for **5**, with KOH (0.5 g, 8.8 mmol) in methanol (15 mL) for 1 h at room temperature. Crystallization and recrystallization from ether–hexane gave white needles of **9** (851 mg, 57.2% from **36**); m.p. 108–110°, $[\alpha]_D$ +87° (*c* 0.93).

Anal. Calc. for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.67; H, 8.39.

Reaction of methyl 3-O-benzoyl-4,6-O-benzylidene-α-D-arabino-hexopyranosid-2-ulose with methylmagnesium iodide. — (i) In ether at −78° and then at room temperature: simultaneous preparation of methyl 4,6-O-benzylidene-2-C-methyl-α-D-glucopyranoside (**10**) *and methyl 3-O-benzoyl-4,6-O-benzylidene-2-C-methyl-α-D-glucopyranoside* (**12**). To a solution of methylmagnesium iodide, prepared from methyl iodide (40 mL, 256 mmol) and magnesium (9.24 g, 256 mmol) in ether (500 mL), was added, at −78° with stirring, a solution of the glycosid-2-ulose (33.1 g, 85.4 mmol) in ether (500 mL). The mixture was stirred for 4 h at −78°, and then for 6 h at room temperature, poured into saturated, aqueous ammonium chloride, and extracted with dichloromethane. Conventional processing of the extract gave a syrupy residue that was fractionated on a column of silica gel with 3:1 toluene–acetone to give **10** (8.1 g, 33%) and **12** (17 g, 66%). The physical constants and n.m.r. data for **10** and **12** were consistent with those reported[9].

(ii) In ether at −78°. To a solution of methylmagnesium iodide, prepared

from methyl iodide (7.7 g, 38.8 mmol) and magnesium (1.05 g, 38.0 mmol), was added at −78°, with stirring, a solution of the glycosid-2-ulose (5.0 g, 12.9 mmol) in ether (100 mL), and the temperature was maintained for 4 h. Processing similar to that just described gave crystalline **12** (5.18 g, quantitative).

(iii) In 3:1 ether–benzene under reflux. To a solution of methylmagnesium iodide, prepared from methyl iodide (1.7 g, 11 mmol) and magnesium (0.26 g, 11 mmol), in ether (21 mL) was added a solution of the glycosid-2-ulose (1.38 g, 36 mmol) in benzene (6.9 mL), and the mixture was boiled under reflux for 1.5 h. Conventional processing, and separation on a column of silica gel with 9:1 hexane–ethanol gave **10** (0.71 g, 64%) and its 2-epimer (0.39 g, 34%).

Methyl 4,6-O-benzylidene-2-C-methyl-3-O-tosyl-α-D-glucopyranoside (**11**). — Compound **10** (1 g, 3.38 mmol) was tosylated in the usual way with *p*-toluenesulfonyl chloride (1.5 g, 5.7 mmol) in pyridine (10 mL) for 3 days at room temperature. Purification was conducted on a column of silica gel with 5:2 hexane–ethyl acetate, to give **11** (1.1 g, 66%); $[\alpha]_D$ +35.4° (*c* 3.3); ν_{max}^{NaCl} 3500 (OH), 1360, and 1180 cm^{-1} (SO_3). Compound **10** was recovered in 23% yield (0.23 g).

Anal. Calc for $C_{22}H_{26}O_8S$: C, 53.60; H, 5.81; S, 7.20. Found: C, 53.81; H, 5.92; S, 7.33.

Methyl 3-O-benzoyl-4,6-O-benzylidene-2-O-mesyl-2-C-methyl-α-D-glucopyranoside (**13**). — Compound **12** (3 g, 7.68 mmol) was treated with methanesulfonyl chloride (2.4 mL, 30.7 mmol) and 4-(dimethylamino)pyridine (50 mg, 0.41 mmol) in pyridine (20 mL) for 5 days at room temperature. The crude product obtained by the usual processing was purified on a column of silica gel with toluene, to give **13** (1.52 g, 42%); m.p. 70–75° (dec.), $[\alpha]_D$ +115° (*c* 0.67); ν_{max}^{KBr} 1710 (C=O), 1370, and 1170 cm^{-1} (SO_3).

Anal. Calc. for $C_{23}H_{26}O_9S$: C, 57.73; H, 5.48; S, 6.70. Found: C, 57.60; H, 5.32; S, 6.70.

Methyl 2-O-benzyl-4,6-O-benzylidene-3-C-methyl-3-O-tosyl-α-D-glucopyranoside (**18**). — To a solution of **16** (280.9 mg, 0.70 mmol) in dichloromethane (25 mL) were added tetrabutylammonium hydrogensulfate (50 mg), *p*-toluenesulfonyl chloride (601 mg, 2.38 mmol), and 5% aqueous NaOH solution (2 mL). The mixture was stirred vigorously overnight at room temperature, and then the dichloromethane layer was separated, dried (Na_2SO_4), and evaporated to dryness. The residue was purified on a column of silica gel with 5:1 hexane–ethyl acetate, to afford **18** as a syrup (105.6 mg, 39%); $[\alpha]_D$ +20.1° (*c* 0.92); ν_{max}^{NaCl} 1720 (C=O), 1365, and 1180 cm^{-1} (SO_3).

Anal. Calc. for $C_{29}H_{30}O_9S$: C, 62.76; H, 5.45; S, 5.85. Found: C, 62.58; H, 5.55; S, 6.11.

Methyl 2-O-benzyl-4,6-O-benzylidene-3-C-methylene-α-D-ribo-hexopyranoside (**20**). — To a solution of **16** (4.80 g, 12 mmol) in pyridine (15 mL) were added methanesulfonyl chloride (3.84 mL, 48.0 mmol) and 4-(dimethylamino)pyridine (100 mg); the solution was kept for 4 days at room temperature, and processed as described for **5**. Fractionation on a column of silica gel with 3:1 hexane–ethyl ace-

tate afforded **20** (1.41 g, 31.2%); m.p. 131–132°, $[\alpha]_D$ +171.2° (*c* 0.76); ν_{max}^{KBr} 1720 (C=O) and 1660 cm^{-1} (C=C). [Unreacted **10** (2.80 g, 58.4%) was recovered.]

Anal. Calc. for $C_{21}H_{20}O_6$: C, 68.48; H, 5.47. Found: C, 68.69; H, 5.49.

*Methyl 2-O-allyl-4,6-O-benzylidene-α-*D*-altropyranoside* (**22**). — To a solution of **21** (200 mg, 0.71 mmol) in dichloromethane (7 mL) were added allyl bromide (113.1 mg, 0.85 mmol), tetrabutylammonium bromide (59.8 mg, 0.18 mmol), and 10% aqueous NaOH solution (0.7 mL), with stirring, and stirring was continued for 2 days at room temperature. The mixture was processed as described for **18**, followed by chromatography on a column of silica gel with 7:2:1 benzene–hexane–acetone to give **22** as a syrup (174.8 mg, 76%); $[\alpha]_D$ +45.8° (*c* 2.2).

Anal. Calc. for $C_{17}H_{22}O_6$: C, 63.34; H, 6.78. Found: C, 63.59; H, 6.77.

Treatment of **22** with acetic anhydride in dry pyridine overnight at room temperature gave the corresponding 3-acetate, which was characterized only by n.m.r. data: δ 4.56 (d, $J_{1,2}$ 1.2 Hz, H-1), 3.74 (dd, $J_{2,3}$ 3.2 Hz, H-2), 5.25 (dd, $J_{3,4}$ 4.0 Hz, H-3), and 2.11 (s, 3 H, OAc).

*Methyl 2-O-allyl-4,6-O-benzylidene-α-*D*-arabino-hexopyranosid-3-ulose* (**23**). — To a solution of dimethyl sulfoxide (1.47 mL, 14.5 mmol) in dichloromethane (25 mL) was added dropwise with stirring, at −78°, a solution of trifluoroacetic anhydride (1.35 mL, 9.66 mmol) in dichloromethane (15 mL). After 20 min, a solution of **22** (1.61 g, 4.83 mmol) in dichloromethane (10 mL) was added, the mixture kept for 1 h at −78°, triethylamine carefully added to neutralize the acid, and the mixture poured into dilute acetic acid. The organic layer was separated, washed with water, dried, and evaporated, to give **23** as a syrup (1.48 g, 92.5%); $[\alpha]_D$ +28.9° (*c* 0.99); ν_{max}^{NaCl} 1730 cm^{-1} (C=O).

Anal. Calc. for $C_{17}H_{20}O_6$: C, 63.74; H, 6.24. Found: C, 64.01; H, 6.38.

*Methyl 4,6-O-benzylidene-3-C-methyl-α-*D*-altropyranoside* (**26**). — To a solution of **23** (1.48 g, 4.54 mmol) in ether (50 mL) was added dropwise, at −78°, a 1.2M solution of MeLi in ether (30.3 mL). After 6 h, the mixture was poured into saturated, aqueous NH_4Cl solution, and extracted with dichloromethane. Evaporation of the dried extract, followed by separation on a column of silica gel with 4:1 hexane–ethyl acetate, afforded **24** (0.81 g, 61%) and **25** (0.22 g, 17%). Compound **24**: a syrup, $[\alpha]_D$ +31.4° (*c* 0.42); ^{1}H-n.m.r. data in Table III. Compound **25**: a syrup; ^{1}H-n.m.r. data: δ 4.92 (d, $J_{1,2}$ 1.2 Hz, H-1), 3.38 (d, H-2), 4.28 (dd, $J_{5,6e}$ 4.2, $J_{6a,6e}$ 8.0 Hz, H-6*e*), 3.40 (s, 3 H, OCH_3) and 1.26 (s, 3 H, CCH_3). The ratio of **24** to **25**, estimated from the methyl signals of the crude mixture, was ~5:1.

To a solution of **24** (0.81 g, 2.1 mmol) in *N,N*-dimethylformamide (15 mL) was added potassium *tert*-butoxide (1.0 g, 8.9 mmol). The solution was heated for 4 h at 80°, cooled, poured into saturated, aqueous NH_4Cl solution, and extracted with dichloromethane. The crude 2-propenyl ether obtained by evaporation of the dried extract, $HgCl_2$ (1.99 g, 7.3 mmol), and HgO (1.35 g, 6.2 mmol) were suspended in 10:1 acetone–water (45 mL) and stirred overnight. The undissolved materials were filtered off, and the filtrate was extracted with dichloromethane. The extract was washed with aqueous NaI solution and evaporated to dryness.

Purification on a column of silica gel with 3:1 hexane–acetone afforded **26** (0.31 g, 53.1%); m.p. 146–149°, $[\alpha]_D$ +30.9° (*c* 0.87).

Anal. Calc. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.68; H, 6.51.

*Methyl 6-O-benzyl-3-C-methyl-2-O-methyl-α-*D*-glucopyranoside* (**28**). — To a solution of **19** (4.4 g, 14.2 mmol) and sodium cyanoborohydride (8.5 g, 127.8 mmol) in dry ether (350 mL) containing finely powdered, 3A molecular sieves was added saturated hydrogen chloride–ether, at 0°, until the solution became acidic. After being kept for 4 h at 0°, the mixture was poured into saturated $NaHCO_3$ solution, and extracted with dichloromethane. The extract was washed with water, dried, and evaporated *in vacuo,* to give **28** as a colorless syrup (4.4 g, quantitative); $[\alpha]_D$ +89.1° (*c* 1.1).

Anal. Calc. for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74. Found: C, 61.78; H, 7.70.

*Methyl 3-O-benzyl-2-O-methyl-6-O-*p*-tolylsulfonyl-α-*D*-glucopyranoside* (**34**). — To a solution of **32** (12.1 g, 32.5 mmol) in *N,N*-dimethylformamide (300 mL) were added sodium hydride (20 g, 260 mmol) and then methyl iodide (43 g, 260 mmol) at 0°. The mixture was kept overnight at room temperature, poured into ice–water, and extracted with ether. The extract was washed with water, dried, and evaporated, to give **33** (12.5 g, quantitative); $[\alpha]_D$ +19.1° (*c* 0.56).

Anal. Calc. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78. Found: C, 68.14; H, 6.55.

Compound **33** was *O*-debenzylidenated with 70% acetic acid (150 mL) under reflux for 8 h. The mixture was cooled, evaporated to dryness, and the residue dissolved in dry pyridine (300 mL). To the solution was added a solution of *p*-toluenesulfonyl chloride (7.2 g, 32.5 mmol) in dry dichloromethane (30 mL) at 0°, and the mixture kept overnight at the same temperature, poured into ice–water, and extracted with dichloromethane. Evaporation of the extract, followed by purification on a column of silica gel with 9:1 benzene–acetone afforded **34** as a syrup (5.54 g, 50%); $[\alpha]_D$ +3.5° (*c* 2.54); ν_{max}^{NaCl} 3480 (OH), 1355, and 1180 cm^{-1} (SO_3).

Anal. Calc. for $C_{22}H_{28}O_8S$: C, 58.39; H, 6.24; S, 7.08. Found: C, 58.15; H, 6.30; S, 6.86.

*Methyl 3-O-benzyl-6-deoxy-2-O-methyl-*D*-*arabino*-hexopyranosid-4-ulose* (**36**). — To a solution of **34** (5.5 g, 12.2 mmol) in dimethyl sulfoxide (50 mL) was added sodium borohydride (2.5 g, 68 mmol), and the mixture was heated for 8 h at 80°, cooled, poured into ice–water, and extracted with ether. Evaporation of the extract gave **35** as a syrup (3.36 g, quantitative); $[\alpha]_D$ +46.4° (*c* 0.54).

Anal. Calc. for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.96; H, 7.57.

To a solution of dimethyl sulfoxide (3.62 mL, 35.7 mmol) in dichloromethane (50 mL) was added a solution of trifluoroacetic anhydride (3.32 mL, 23.8 mmol) in dichloromethane (10 mL) at −78°. After 15 min, a solution of **35** (3.36 g, 12 mmol) in dichloromethane (10 mL) was added. The mixture was kept for 45 min at −78°, and processed as described for **23**, to give **36** as a syrup (3.32 g, quantitative); $[\alpha]_D$ +12.8° (*c* 1.41); ν_{max}^{NaCl} 1730 cm^{-1} (C=O).

Anal. Calc. for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.55; H, 7.37.

Reaction of the branched-chain anhydrohexopyranosides with dimethyllithium

cuprate. — To a suspension of CuI (4 equiv.) in ether was added a 1.2M ethereal solution of MeLi (8 equiv.) at 0°, and then, after 5 min, a solution of an epoxide (1 equiv.) in ether. The mixture was stirred for 2 days, poured into saturated, aqueous NH_4Cl solution, and extracted with dichloromethane. The extract was evaporated, and the residue was purified on a column of silica gel.

Reaction of the branched-chain anhydrohexopyranosides with mixed cuprate. — To a suspension of CuCN (4 equiv.) in ether was added a 1.2M ethereal solution of MeLi (4 equiv.) at −78°. After the solid had dissolved, a solution of epoxide (1 equiv.) in ether was added. The mixture was kept for 4 days at room temperature, and then poured into saturated, aqueous NH_4Cl solution. After addition of M NH_4OH, to dissolve the precipitate, the solution was processed as just described.

Reaction of the branched-chain anhydrohexopyranosides with higher-order, mixed 1.2M ethereal cuprate. — To a suspension of CuCN (4 equiv.) in ether was added a solution of MeLi (8 equiv.) in ether at −78°. After the solid had dissolved, a solution of epoxide (1 equiv.) in ether was added. Reactions were processed as described for the reaction with mixed cuprate.

Methyl 4,6-O-benzylidene-3-deoxy-2,3-di-C-methyl-α-D-altropyranoside (**40**). — This was purified on a column with 7:2:1 benzene–hexane–acetone, to give a syrup; $[\alpha]_D$ +62.4° (*c* 0.49); ν_{max}^{NaCl} 3490 cm^{-1} (OH).

Anal. Calc. for $C_{16}H_{22}O_5$: C, 65.30; H, 7.51. Found: C, 65.25; H, 7.41.

4,6-O-Benzylidene-2-deoxy-2,3-di-C-methyl-1-O-methyl-D-arabino-hex-2-enitol (**41**) *and 1,5-anhydro-4,6-O-benzylidene-2-deoxy-2,3-di-C-methyl-D-arabino-hex-2-enitol* (**43**). — A mixture of **41** and **43** was separated on a column with 4:1 hexane–ethyl acetate. Compound **41**: syrup; ν_{max}^{NaCl} 3440 (OH) and 1600 cm^{-1} (C=C). Because of its instability, the elemental analysis could not be done. Compound **43**: syrup; $[\alpha]_D$ +38.4° (*c* 0.78); ν_{max}^{NaCl} 3450 (OH) and 1670 cm^{-1} (C=C).

Anal. Calc. for $C_{15}H_{16}O_4$: C, 65.38; H, 6.20. Found: C, 65.16; H, 6.37.

Decomposition products of **41**. — After storage of **41** (297 mg, 1.11 mmol; ratio of *E* to *Z* isomer, 3:2) for two weeks at room temperature, there were four components in t.l.c.; these were separated on a column of silica gel with 3:1 hexane–ethyl acetate, to give methyl 4,6-*O*-benzylidene-2,3-di-*C*-methyl-α-D-*erythro*-hex-2-enopyranoside (**51**; 47.7 mg, 0.18 mmol, 17%), 4,6-*O*-benzylidene-2,3-dideoxy-2,3-di-*C*-methyl-α-D-*erythro*-hex-2-enopyranose (**52**; 50.7 mg, 0.20 mmol, 19%), its *E* isomer (**53**; 35.4 mg, 0.14 mmol, 13%), and **41*E*** (104.6 mg, 0.39 mmol, 36%). These compounds were characterized only by their ^1H- and ^{13}C-n.m.r. data (see Table IV).

Methyl 4,6-O-benzylidene-3-deoxy-2,3-di-C-methyl-α-D-glucopyranoside (**44**). — This was purified on a column with 7:2:1 benzene–hexane–acetone, giving a syrup; $[\alpha]_D$ +45.0° (*c* 0.42); ν_{max}^{NaCl} 3440 cm^{-1} (OH).

Anal. Calc. for $C_{16}H_{22}O_5$: C, 65.30; H, 7.51. Found: C, 65.30; H, 7.76.

Methyl 4,6-O-benzylidene-2-deoxy-2,3-di-C-methyl-α-D-altropyranoside (**45**). — Purified on a column with 5:1 hexane–acetone, it was a syrup; $[\alpha]_D$ +13.8° (*c* 0.45); ν_{max}^{NaCl} 3500 cm^{-1} (OH).

Anal. Calc. for $C_{16}H_{22}O_5$: C, 65.30; H, 7.51. Found: C, 65.34; H, 7.33.

*Methyl 6-O-benzyl-2,3-dideoxy-3-C-methyl-α-*D-glycero-*hex-2-enopyranosid-4-ulose* (**46**). — Purified on a column with 8:1 toluene–acetone, it was a syrup; $[\alpha]_D$ +7.7° (*c* 0.84); ν_{max}^{NaCl} 1690 (C=O) and 1670 cm^{-1} (C=C).

Anal. Calc. for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.42; H, 6.63.

*Methyl 3,6-dideoxy-3,4-di-C-methyl-2-O-methyl-α-*D-*idopyranoside* (**47**) *and methyl 2,3,6-trideoxy-4-C-methyl-α-*D-threo-*hex-2-enopyranoside* (**48**). — A mixture of **47** and **48** was separated on a column with 20:1 toluene–acetone. Compound **47**: a syrup; $[\alpha]_D$ +27.4° (*c* 0.91); ν_{max}^{NaCl} 3500 cm^{-1} (OH).

Anal. Calc. for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87. Found: C, 58.67; H, 9.76.

Compound **48**: a syrup; $[\alpha]_D$ +93.3° (*c* 1.3); ν_{max}^{NaCl} 3460 (OH) and 1680 cm^{-1} (C=C).

Anal. Calc. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.93; H, 9.22.

*Methyl 3,6-dideoxy-3,4-di-C-methyl-2-O-methyl-α-*D-*glucopyranoside* (**49**). — Purified on a column with 5:1 hexane–ethyl acetate, it was a syrup; $[\alpha]_D$ +101.4° (*c* 0.98); ν_{max}^{NaCl} 3450 cm^{-1} (OH).

Anal. Calc. for $C_{10}H_{20}O_4$: C, 58.80; H, 9.87. Found: C, 58.60; H, 9.54.

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