A STEREOCHEMICAL COMPARISON OF SOME ADDITION REACTIONS TO METHYL 4,6-*O*-BENZYLIDENE-3-DEOXY-3-*C*-ETHYL-α-D-HEXOPYRANOSID-2-ULOSES

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ABSTRACT

Methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*ribo*-hexopyranosid-2-ulose (**2**) reacts with lithium aluminium hydride, methylmagnesium iodide, and phenylmagnesium bromide to give products having only the *allo* configuration. The C-3 epimer of **2**, methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*arabino*-hexopyranosid-2-ulose (**7**), reacts with lithium aluminium hydride to give only a product having a *gluco* configuration. With methylmagnesium iodide and phenylmagnesium bromide, **7** gives products having *gluco* and *manno* configurations. The 2-*C*-methyl-glucopyranoside preponderates in the former reaction, and the 2-*C*-phenyl-mannopyranoside is the major product in the latter reaction. The reaction between **2** and diazomethane gives a spiro-epoxide having the *allo* configuration as the major product (*i.e.*, the same configuration as the **2**–MeMgI reaction product), whereas the **7**–diazomethane reaction gives a spiro-epoxide having the *manno* configuration (*i.e.*, the same configuration as the minor product from the **7**–MeMgI reaction) as the major product. With the thionyl chloride–pyridine reagent, 3-deoxy-3-*C*-ethyl-2-*C*-methyl-α-D-hexopyranosides are dehydrated endocyclically when H-3 and HO-2 are antiparallel and exocyclically when H-3 and HO-2 have a gauche relationship.

INTRODUCTION

The steric course of reactions between keto sugars and Grignard reagents or alkyl(or aryl)-lithiums cannot reliably be predicted. In some instances, keto sugar–Grignard reagent reactions and keto sugar–alkyl-lithium reactions give the same preponderant product, whereas, in other instances, epimeric products are formed preponderantly[1]. However, in the examples that have been reported, keto sugar–methylmagnesium halide reactions all give preponderant products that are epimeric with the major products formed by lithium aluminium hydride reduction of the spiro-epoxides from keto sugar–diazomethane reactions[2]. Conversely, the action of metal hydride reducing-agents has been found to follow the same steric course as Grignard addition reactions, and, in some instances, this observation has been used to provide evidence for the configuration of a branched-chain sugar derivative[3]. In this paper, from a consideration of the reactions of lithium aluminium hydride,

methylmagnesium iodide, and phenylmagnesium bromide with methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*ribo*- and -*arabino*-hexopyranosid-2-uloses (**2** and **7**, respectively), it will be demonstrated that the configurations of the preponderant products formed by reaction of a keto sugar with different Grignard reagents are not necessarily the same and thus may differ from the configuration of the product of metal hydride reduction. It will also be demonstrated that keto sugar–diazomethane reactions and keto sugar–methylmagnesium halide reactions do not necessarily give preponderant products of different configuration.

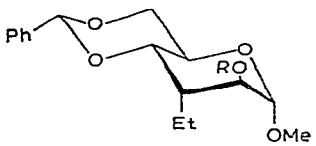
DISCUSSION

Methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*ribo*-hexopyranosid-2-ulose (**2**) was prepared as a chromatographically homogeneous syrup by prolonged oxidation of methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-altropyranoside[4] (**1**) with an excess of the ruthenium dioxide–sodium (or potassium) metaperiodate reagent. Although this procedure was satisfactory for small-scale preparations, it was usually more convenient to effect the oxidation of compound **1** on a larger scale with acetic anhydride–methyl sulphoxide. In the latter procedure, small proportions of the 2-acetate (**1a**) and 2-methylthiomethyl ether (**1b**) were also formed. It was not possible to separate **2** from **1a** and **1b** by chromatographic resolution over silica gel, since **2** was thereby converted, entirely or in part, into the crystalline C-3 epimer, methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-*arabino*-hexopyranosid-2-ulose (**7**). The conversion of **2** into **7** was most easily achieved by storing **2** in a solution of triethylamine in *N*,*N*-dimethylformamide for 48 h. A similar epimerisation has been reported previously[5], and, presumably, the non-bonded 1,3-diaxial interaction in **2** favours the complete conversion into **7**. The pyranosid-2-uloses **2** and **7** were distinguished by different chromatographic mobilities and different n.m.r. spectra. However, the n.m.r. spectra did not permit configurational assignments to be made at C-3.

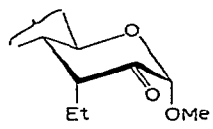
That **2** had the assigned structure was established when lithium aluminium hydride reduction afforded the allopyranoside derivative **3**. The acetate (**3a**) from **3** showed coupling constants ($J_{1,2}$ 3.8 and $J_{2,3}$ 5.2 Hz) which are fully consistent with the α-D-allopyranoside structure. The absence of an electronegative substituent at C-3 causes the $J_{2,3}$ coupling constant to be larger than that normally found in α-D-allopyranoside derivatives[6].

Similarly, lithium aluminium hydride reduction of **7** gave a product having a *gluco* configuration. The n.m.r. spectrum of the acetate **8a** showed coupling constants ($J_{1,2}$ 3.6, $J_{2,3}$ 9.2 Hz) which were consistent with the α-D-glucopyranoside structure. Careful examination of the crude reduction products of both **2** and **7** by t.l.c. and n.m.r. failed to reveal the presence of the *altro* derivative (**1**) corresponding to **3**, or of the *manno* derivative corresponding to **8**, indicating that both reductions were essentially stereospecific.

The reactions of **2** with methylmagnesium iodide and phenylmagnesium bromide were also stereospecific, the allopyranoside derivatives **4** and **6** being formed in good yield. However, the reaction of **7** with methylmagnesium iodide afforded the



1 R = H
1a R = Ac
1b R = CH_2SMe



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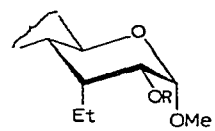
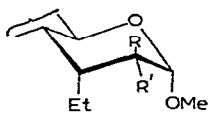
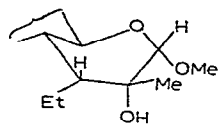


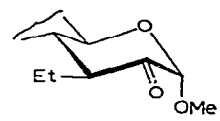
3 R = H
3a R = Ac



4 R = Me, R' = OH
5 R = OH, R' = Me
6 R = Ph, R' = OH



4b



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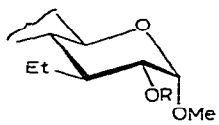
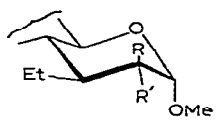


8 R = H
8a R = Ac

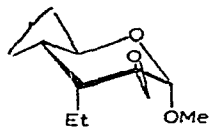


9 R = Me, R' = OH
10 R = Ph, R' = OH
11 R = OH, R' = Me
12 R = OH, R' = Ph

glucopyranoside derivative **9** (72%) and the mannopyranoside derivative **11** (22%). Similarly, the reaction between **7** and phenylmagnesium bromide afforded two products, but in this reaction the mannopyranoside derivative **12** (62%) was in excess of the glucopyranoside derivative **10** (30%). When **7** was treated with phenyl-lithium, however, the glucopyranoside derivative **10** was the major product.

From the reaction of diazomethane and **2**, three products were obtained; methyl 2,2′-anhydro-4,6-*O*-benzylidene-3-deoxy-3-*C*-hydroxymethyl-α-D-altropyranoside (**13**, 25%), the corresponding allopyranoside derivative (**14**, 40%), and the ring-expansion product **15**. Reduction of the major epoxide **14** with lithium aluminium hydride afforded the 2-*C*-methyl derivative **4** which was also the only product from the **2**–MeMgI reaction. Similar reduction of the minor epoxide **13** gave methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-methyl-α-D-altropyranoside (**5**), a product that was not obtained by the **2**–MeMgI reaction. Thus, in reactions between **2** and methylmagnesium iodide and diazomethane, the stereochemistry of the major product is the same, unlike previously reported examples[2]. Conversely, reduction of the major epoxide **16** (65%) from the diazomethane–**7** reaction with lithium aluminium hydride afforded the 2-*C*-methyl derivative **11** which was the minor product from the **7**-MeMgI reaction. The diazomethane–**7** reaction also afforded the minor glucopyranoside derivative **17** and the ring-expansion product **18**. The structure and stereochemistry of both seven-membered ring ketones (**15** and **18**) and the mechanism

of the reactions between diazomethane and **2** and **7** will be discussed in detail in the following paper[7].



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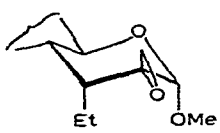

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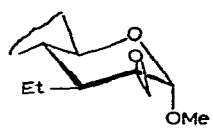

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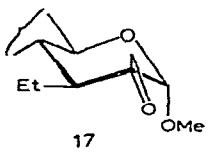

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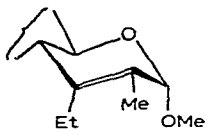

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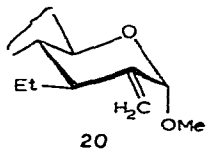

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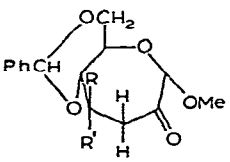
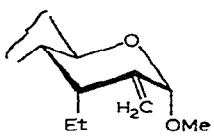


15 R = H, R' = Et
18 R = Et, R' = H



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The configurations of the 2-*C*-methyl derivatives (and thus of the corresponding epoxides) and of the 2-*C*-phenyl derivatives were first assigned on the basis of the n.m.r. parameters listed in Table I and by comparison products of reduction with lithium aluminium hydride.

Comparison of the chemical shifts for H-1, H-3, and the benzylic proton in

TABLE I

ASSIGNMENTS[a] IN THE N.M.R. SPECTRA OF SOME METHYL 4,6-*O*-BENZYLIDENE-3-DEOXY-3-*C*-ETHYL-α-D-HEXOPYRANOSIDES

Compound	*H-1*	*H-2*	*H-3*	*benzylic H*	$J_{1,2}$	$J_{2,3}$
1	4.57	3.95		5.51	~1	~1
1a	4.55	5.03		5.57	~1	~1
3	4.63		2.35	5.51	3.5	—
3a	4.73	4.98	2.35	5.52	3.8	5.2
4	4.20		1.95	5.45	—	—
5	4.25		1.95	5.48	—	—
6	4.87		2.25	5.35	—	—
8a	4.82	4.78		5.51	3.6	9.2
9	4.23		1.85	5.45	—	—
10	4.55			5.50	—	—
11	4.19		1.65	5.35	—	—
12	4.26			5.61	—	—

[a]Chemical shifts are expressed as δ values in p.p.m.; coupling constants are in Hz; the spectra at 100 MHz were measured in chloroform-*d* with tetramethylsilane as internal standard.

compounds **3** and **6** shows that the phenyl substituent in **6** shields H-3 and the benzylic proton, but deshields H-1. Calculations based on the Bovey–Johnson model[8] show that such shielding values are consistent with an axially situated phenyl group orientated so that its plane approximately bisects the HO-2–C-3 bond angle. For a compound in which the 2-phenyl substituent is equatorially situated, only deshielding of the benzylic proton would be expected, and in **6** the benzylic proton resonates at higher field than in **1**. Thus, **6** has the *allo* configuration.

Similar comparisons of the chemical shifts for H-1 and the benzylic proton of the 2-*C*-phenyl derivatives **10** and **12** with those for **8a** show deshielding of the benzylic proton in **12** compared with **8**, but shielding of the benzylic proton in **10** compared with **8**. This result immediately indicates that **10** has the *gluco* configuration, in which the phenyl substituent is axially orientated, and that **12** has the *manno* configuration where the phenyl group is orientated equatorially. It will be noted that, whereas H-1 was deshielded in **6**, shielding of H-1 was observed in **8**. Calculations show that a small change in the conformation of the axial 2-phenyl substituent (probably caused by the presence of the equatorial 3-*C*-ethyl substituent in **8**) can account for this change in the sign of H-1 shielding. If the *gluco* and *manno* configurations assigned to the minor and major products **10** and **12**, respectively, are correct, the PhMgBr–**7** reaction represents an example of a difference in the steric course of reactions between keto sugars and Grignard reagents and metal hydrides, since it was shown previously that the **7**–$LiAlH_4$ reaction afforded only the product having the *gluco* configuration.

Methylmagnesium iodide, like lithium aluminium hydride and phenylmagnesium bromide, reacted stereospecifically with **2** to give only one product (**4**), which was assigned the *allo* configuration by comparison with the configuration assigned to the products from the **2**–PhMgBr and **2**–$LiAlH_4$ reactions. The n.m.r. spectra of **4** and its C-2 epimer **5** were very similar and showed no differences that were indicative of the C-2 configuration in these compounds.

The first indication that the major products from the MeMgI–**7** and PhMgBr–**7** reactions had different configurations was provided by the observation that, whereas the major 2-*C*-methyl derivative **9** had a higher R_F value on silica gel than its C-2 epimer **11**, the major 2-*C*-phenyl derivative **12** had a lower R_F value than its C-2 epimer **10**. A further indication that the preponderant products from the two Grignard reactions had different configurations at C-2 was provided when it was shown that the steric course of the PhMgBr–**7** reaction was different than for the **7**–$LiAlH_4$ reaction. In the latter case, the reaction was stereospecific in favour of a product having a *gluco* configuration, whereas, in the former instance, a product having a *manno* configuration was strongly favoured. It thus appeared possible that the MeMgI–**7** reaction demonstrated a gradual change in the steric course of addition reactions of **7** if the major product had a *gluco* configuration and the minor product a *manno* configuration. More direct evidence to show that the major 2-*C*-methyl derivative **9** had a *gluco* configuration was provided by a comparison of the n.m.r. spectra of **9** and the minor 2-*C*-methyl derivative **11**. Comparison of the H-1 and H-3

chemical shifts in **9** and **11** (Table I) shows that, whereas the H-1 shifts are very similar and thus essentially independent of the configuration at C-2, the H-3 shifts at 1.85 and 1.65 p.p.m. respectively show appreciable dependence on the C-2 configuration. Since the H-1 shift in **9** and **11** is at much higher field than in **8a**, both axial and equatorial 2-*C*-methyl substituents obviously shield vicinal, gauche protons. Also, since H-1 in methyl 4,6-*O*-benzylidene-α-D-mannopyranoside[6b] is at 0.2 p.p.m. to lower field than in the corresponding 2-*C*-methyl-2-deoxy derivative[9], 2-*C*-methyl groups also show a stronger shielding effect than hydroxyl groups on vicinal, gauche protons. Thus, it is reasonable to assign compound **11**, in which H-3 is 0.2 p.p.m. to higher field than in **9**, a *manno* configuration, since, in this configuration, there is a vicinal, gauche 2-methyl–H-3 interaction. In the epimeric *gluco* configuration, 2-*C*-methyl and H-3 have an antiparallel relationship, and H-3 is not shielded by the 2-methyl substituent.

It was essential to our subsequent research programme that an unequivocal proof of configuration of the 2-*C*-methyl derivatives **4**, **5**, **9**, and **11** (and thus of the related spiro-epoxides) be obtained. Such an unequivocal proof was obtained in the following manner. By analogy with related reactions in the steroid field[10], it was expected that compound **11**, where there is a *trans* relationship between H-3 and the C-2 hydroxyl group, would undergo rapid dehydration with phosphorus oxychloride in pyridine to yield **19**. On the other hand, compound **9**, where the *gauche* relationship between H-3 and the C-2 hydroxyl group is unfavourable to endocylic elimination, would be dehydrated exocyclically to yield **20**. The $POCl_3$–pyridine reagent is usually preferred to the $SOCl_2$–pyridine reagent as being more stereoselective[11]. However, the $POCl_3$–pyridine reagent reacted very slowly with compounds **9** and **11** and was not investigated further, whereas the $SOCl_2$–pyridine reagent reacted immediately with **11** and more slowly with **9** to give the endocyclic olefin **19** and the exocylic olefin **20**, respectively. It has been suggested that the proportions of exo- and endocyclic olefins obtained when a tertiary alcohol is dehydrated with $SOCl_2$–pyridine is independent of the configuration of the molecule[12]. The above results do not bear out this suggestion and provide clear evidence for the structures of **9** and **11**.

In the chair forms illustrated, both **4** and **5** would be expected to react with $SOCl_2$–pyridine to yield the exocyclic olefin **21**. However, **4** can easily adopt the non-chair conformation illustrated (**4b**), in which H-3 and HO-2 have an antiparallel relationship. Such a relationship cannot be achieved for **5**. Thus, **4** affords the endocyclic olefin **19** when treated with $SOCl_2$–pyridine, whereas, under similar conditions, **5** slowly affords the exocyclic olefin **21**.

The structure of methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-ethyl-2-*C*-methylene-α-D-*arabino*-hexopyranoside (**20**) and the corresponding α-D-*ribo*-hexopyranoside (**21**) followed from their n.m.r. spectra; in each case, low-field doublets (*e.g.*, at 5.16 and 5.03 p.p.m. with J_{gem} 1.5 Hz for **12** and at 5.00 and 4.89 p.p.m. with J_{gem} 1.5 Hz for **20**) were only consistent with a $=CH_2$ group at C-2. Also, **20** and **21** were the products of Wittig reactions of methylenetriphenylphosphorane and the pyranosid-2-uloses **7** and **2**, respectively[13].

The structure of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2-*C*-methyl-3-*C*-ethyl-α-D-*erythro*-hex-2-enopyranoside was assigned to **19** on the basis that it was a common dehydration product of both **11** and **4**. The n.m.r. parameters of **19** were also consistent with this assignment. A long-range coupling of 1.5 Hz was observed between H-1 and the protons of the 2-methyl substituent. This type of coupling has been observed previously for HC–C(=C)CH systems[14].

EXPERIMENTAL

Thin-layer chromatography was performed by upward irrigation (with multiple development, where necessary) on microscope slides coated with Merck Silica Gel G, and column chromatography was performed with Merck Silica Gel of particle size 0.05–0.2 mm. The chromatoplates were developed with 50% sulphuric acid and/or iodine vapour. P.m.r. spectra were measured with a JEOL, JNM-4-H-100 n.m.r. spectrometer at 100 MHz. Solvents were dried over $MgSO_4$ and, unless stated otherwise, light petroleum refers to the fraction b.p. 60–80°. Acetylations were carried out with acetic anhydride in pyridine at room temperature, and Grignard reactions were performed in ether with an approximately ten-fold excess of Grignard reagent. Identification of compounds was based on comparisons of n.m.r. and infrared spectra and on chromatographic properties.

*Methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-*D*-ribo-hexopyranosid-2-ulose* (**2**). — (*a*) A mixture of **1** (1 g), potassium metaperiodate, and ruthenium dioxide (0.08 g) in ethanol-free chloroform (15 ml) and water (15 ml) was stirred at room temperature. The reaction was monitored by t.l.c. (triple development; ether–light petroleum, 4:1; **7** had a slightly higher R_F value than **2**). It was found necessary to add more ruthenium dioxide and potassium (or sodium) metaperiodate to complete the oxidation. After 48 h, the reaction mixture was filtered, diluted with water, and extracted with chloroform. The chloroform extract was dried and concentrated to yield a chromatographically homogeneous syrup having n.m.r. and i.r. spectral data consistent with those of the final product. N.m.r. data: δ 5.48 (benzylic H), 4.55 (H-1), 3.40 (OCH_3), 2.8 (H–C–Et), 1.98 (HC–CH_2–CH_3), 0.9 (HC–CH_2–CH_3) p.p.m. The resonance pattern for H-4, H-5, H-6, and H-6′ between 3.4 and 4.5 p.p.m. was quite different from the pattern obtained for compound **7**.

(*b*) The ruthenium dioxide oxidation procedure was unsatisfactory for larger scale preparations of **2** and so the more-convenient procedure using acetic anhydride in methyl sulphoxide was employed. This procedure is described for **7**. Attempts to purify **2**, formed in this way, from some methylthiomethyl ether (**1b**) and some 2-acetate (**1a**) by chromatography over silica gel were unsuccessful, since isomerisation of **2** into **7** occurred. However, for subsequent experiments, the crude **2** was used directly.

*Methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-*D*-arabino-hexopyranosid-2-ulose* (**7**). — A solution of **1** (14 g) and acetic anhydride (42 ml) in methyl sulphoxide (250 ml) was stored overnight at room temperature, poured into water, and extracted

with ether. The ether extract, which was shown by t.l.c. [ether–light petroleum (1:4)] to be mainly **2**, was dried ($MgSO_4$), concentrated, and dissolved in *N,N*-dimethylformamide containing triethylamine (3 ml). The solution was stored at room temperature for 48 h, poured into water, and extracted with ether. The extract was dried and concentrated, and the product was crystallised from light petroleum to yield **7** (9 g, 65%), m.p. 108°, $[\alpha]_D$ +57.5° (*c* 2, chloroform) (Found: C, 65.9; H, 6.8. $C_{16}H_{20}O_5$ calc.: C, 65.7; H, 6.9%). In some experiments, **7** was purified over silica gel in ether–light petroleum (1:1) prior to crystallisation. N.m.r. data: δ 5.49 (benzylic H), 4.53 (H-1), 3.45 (OCH_3), 2.9 (H–C–Et), 1.75 (HC–CH_2–CH_3), 0.95 (HC–CH_2–CH_3) p.p.m.

*Methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-*D*-allopyranoside* (**3**). — The crude oxidation product **1** (1 g) in ether was reduced with lithium aluminium hydride, in the usual way, to yield, after chromatographic purification over silica gel in ether–light petroleum (1:1), the title compound **3** (0.75 g, 75%), m.p. 74° (from light petroleum), $[\alpha]_D$ +110° (*c* 1, chloroform) (Found: C, 65.0; H, 7.4. $C_{16}H_{22}O_5$ calc.: C, 65.3; H, 7.5%). Compound **3** was acetylated with acetic anhydride in pyridine to yield a chromatographically homogeneous syrup [R_F 0.4, ether–light petroleum (1:1)].

*Methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-*D*-glucopyranoside* (**8a**). — A solution of ketone **7** (0.3 g) and excess of lithium aluminium hydride in ether was stirred at room temperature for 30 min. Excess of reductant and alkoxides was decomposed with ethyl acetate and water, and the solution was dried ($MgSO_4$) and concentrated. The solid residue was acetylated directly and recrystallised from light petroleum to yield **8a** (0.2 g, 60%), m.p. 94–95°, $[\alpha]_D$ +64° (*c* 1, chloroform) (Found: C, 64.3; H, 7.2. $C_{18}H_{24}O_6$ calc.: C, 64.3; H, 7.2%). The mother liquors from **8** were concentrated and examined by n.m.r., and shown to be essentially devoid of the corresponding mannopyranoside derivative.

*Methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-methyl(and 2-*C*-phenyl)-α-*D*-allopyranoside* (**4**) [and (**6**)]. — The product from the oxidation of **1** (7 g) with acetic anhydride and methyl sulphoxide was divided into two equal portions and treated separately with (*a*) methylmagnesium iodide and (*b*) phenylmagnesium bromide. Chromatographic resolution [over silica gel in ether–light petroleum (1:2)] of the product from (*a*) yielded methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*O*-methylthiomethyl-α-D-altropyranoside (0.4 g) and methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-methyl-α-D-allopyranoside (**4**, 2.7 g, 74% from **1**), $[\alpha]_D$ +41° (*c* 1, chloroform), as chromatographically homogeneous syrups. No C-2 epimer of **4** was detected.

Chromatographic resolution over silica gel in ether–light petroleum (1:4) of the product from (*b*) yielded methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-phenyl-α-D-allopyranoside (**6**, 1.8 g, 40% from **1**), m.p. 118° (from ethanol or light petroleum), $[\alpha]_D$ +47° (*c* 2, chloroform) (Found: C, 71.0; H, 7.0. $C_{22}H_{26}O_5$ calc.: C, 71.3; H, 6.9%). No C-2 epimer of **6** was detected.

*Reaction of methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-*D*-arabino-hexopyranosid-2-ulose* (**7**) *with methylmagnesium iodide.* — The product from the reaction between methylmagnesium iodide and the hexopyranosid-2-ulose (**7**, 1.7 g) was resolved chromatographically over silica gel in ether–light petroleum (1:2) to yield

methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-methyl-α-D-glucopyranoside (**9**, 1.3 g, 72%), $[\alpha]_D$ +72° (*c* 1.4, chloroform), as a colourless syrup, and methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-methyl-α-D-mannopyranoside (**11**, 0.4 g, 22%), m.p. 105–106° (from ethanol), $[\alpha]_D$ +62° (*c* 1, chloroform) (Found: C, 66.2; H, 7.8. $C_{17}H_{24}O_5$ calc.: C, 66.2; H, 7.8%).

*Reaction of methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-α-D-arabino-hexopyranosid-2-ulose* (**7**) *with phenylmagnesium bromide.* — The product from the reaction between phenylmagnesium bromide and the keto sugar (**7**, 2 g) was separated over silica gel in ether–light petroleum (1:1) to yield methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-phenyl-α-D-glucopyranoside (**10**, 0.75 g, 30%), $[\alpha]_D$ +16.5° (*c* 1.5, chloroform), as a homogeneous syrup, and methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-phenyl-α-D-mannopyranoside (**12**, 1.6 g, 62%), m.p. 120° (from light petroleum), $[\alpha]_D$ +66.6° (*c* 1, chloroform) (Found: C, 71.4; H, 7.2. $C_{22}H_{26}O_5$ calc.: C, 71.3; H, 7.1%).

Reaction of **2** *with diazomethane**. — A solution of the crude product **2** [from the oxidation of **1** (7 g) with acetic anhydride–methyl sulphoxide] in methanol was treated directly with an ethereal solution of diazomethane. After storage overnight at room temperature, the solution was concentrated and the residue was resolved chromatographically over silica gel in ether–light petroleum (1:4). In order of elution, the four crystalline products isolated were (*a*) the keto sugar **6** (1 g); (*b*) methyl 2,2′-anhydro-4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-hydroxymethyl-α-D-altropyranoside (**13**) (1 g, 25%), m.p. 119–122° (from light petroleum), $[\alpha]_D$ +86.5° (*c* 1.5, chloroform); compound **13** was separated by crystallisation from an unidentified syrup (Found: C, 66.2; H, 7.3. $C_{17}H_{22}O_5$ calc.: C, 66.7; H, 7.2%); n.m.r. data: δ 5.60 (benzylic H), 3.99 (H-1), 3.38 (OMe), and 2.85 (2 × H-2′) p.p.m.; (*c*) methyl 2,2′-anhydro-4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-hydroxymethyl-α-D-allopyranoside (**14**) (1.6 g, 40%), m.p. 70° (from light petroleum), $[\alpha]_D$ +90° (*c* 2, chloroform) (Found: C, 66.5; H, 7.3. $C_{17}H_{22}O_5$ calc.: C, 66.7; H, 7.2%); n.m.r. data: δ, 5.54 (benzylic H), 4.06 (H-1), 3.40 (OMe), 2.72 and 2.63 (H-2′) p.p.m., $J_{2',2'}$ 4.9 Hz; reduction of **14** with lithium aluminium hydride afforded a product having chromatographic and spectroscopic properties indistinguishable from those of **4**; (*d*) methyl 5,7-*O*-benzylidene-3,4-dideoxy-4-*C*-ethyl-α-D-*ribo*-heptoseptanosid-2-ulose (**15**) (0.5 g, 12%), m.p. 125–130° (from light petroleum), $[\alpha]_D$ −20° (*c* 2, chloroform) (Found: C, 66.0; H, 7.3. $C_{17}H_{22}O_5$ calc.: C, 66.7; H, 7.2%); n.m.r. data: δ 5.55 (benzylic H), 4.68 (H-1), 3.50 (OMe), 2.98 and 2.68 (H-3 and H-3′) p.p.m., $J_{3,3'}$ 12.5; $J_{3,4}$ 2.8; $J_{3',4}$ 6 Hz.

Reaction of diazomethane and **7**. — A solution of diazomethane in ether was added to an ice-cold solution of ketone **7** (0.4 g) in methanol, and the reaction was monitored by t.l.c. in ether–light petroleum (1:4). When no starting material remained, three products were detected. The solution was concentrated, and the products were separated over silica gel to give, in order of elution, (*a*) methyl 2,2′-anhydro-4,6-*O*-

*In this experiment, percentage yields were calculated by assuming 70% conversion of **1** into **2**.

benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-hydroxymethyl-α-D-mannopyranoside (**16**, 0.27 g, 65%), $[\alpha]_D$ +37° (*c* 1.6, chloroform); n.m.r. data: δ 5.50 (benzylic H), 4.23 (H-6e), 3.93 (H-1), 3.35 (OCH_3), 2.88 and 2.25 (H-2'), 2.35 (H-3) p.p.m., $J_{2',2'}$ 3.8, $J_{3,4}$ 10.5 Hz; reduction of **16** with lithium aluminium hydride afforded the crystalline 2-*C*-methyl-α-D-mannopyranoside derivative **11**; (*b*) methyl 2,2'-anhydro-4,6-*O*-benzylidene-3-deoxy-3-*C*-ethyl-2-*C*-hydroxymethyl-α-D-glucopyranoside (**17**, 34 mg, 8%), m.p. 62–64° (from light petroleum), $[\alpha]_D$ +63° (*c* 0.5, chloroform) (Found: C, 66.8; H, 7.27. $C_{17}H_{22}O_5$ calc.: C, 66.7; H, 7.24%); n.m.r. data: δ 5.50 (benzylic H), 4.28 (H-6e), 4.05 (H-1), 3.41 (OCH_3), 2.87 and 2.57 (H-2'), 2.55 (H-3) p.p.m., $J_{2',2'}$ 3.8, $J_{3,4}$ 10.5, $J_{6a,6e}$ 9.2, $J_{5,6a}$ 9.4, $J_{5,6e}$ 4 Hz; reduction of **17** with lithium aluminium hydride afforded the 2-*C*-methyl-α-D-glucopyranoside derivative **9**. (*c*) methyl 5,7-*O*-benzylidene-3,4-dideoxy-4-*C*-ethyl-α-D-*arabino*-heptoseptanosid-2-ulose (**18**, 75 mg, 18%), m.p. 174° (from ethanol), $[\alpha]_D$ +0.2° (*c* 1, chloroform) (Found: C, 67.0; H, 7.2; $C_{17}H_{22}O_5$ calc.: C, 66.7; H, 7.2%); δ 5.47 (benzylic H), 4.76 (H-1), 3.45 (OCH_3), 2.73 (H-3), 2.42 (H-3') p.p.m., $J_{3,3'}$ 11.0, $J_{3,4}$ 11.8, $J_{3',4}$ 2.5 Hz; in benzene, δ values were 5.26 (benzylic H), 4.30 (H-1), 4.13 (H-6e), 3.75 (H-5), 3.49 and 3.25 (H-4 and H-6a), 3.02 (OCH_3) p.p.m., $J_{7a,7e}$ 9.5, $J_{7e,6}$ 4.5, $J_{5,6}$ ~9; $J_{7a,6}$ ~9 Hz.

Formation of methyl 4,6-O-benzylidene-2-C-methyl-3-C-ethyl-α-D-erythro-hex-2-enopyranoside (**19**). — (*a*) Thionyl chloride (1 ml) was added dropwise to a solution of **11** (0.25 g) in pyridine (5 ml), and the mixture was stored at room temperature for 30 min. The solution was poured into water and extracted with ether, and the ether extract was dried and concentrated. The product was purified over silica gel in ether–light petroleum (1:3) to yield the title product **19** (0.2 g, 85%), m.p. 88–89° (from light petroleum), $[\alpha]_D$ +56° (*c* 1.5, chloroform) (Found: C, 70.4; H, 7.6; $C_{17}H_{22}O_4$ calc.: C, 70.3; H. 7.6%).

(*b*) Similar reaction of **4** (1 g) with thionyl chloride (3 ml) and pyridine (10 ml) afforded **19** (0.45 g, 48%). N.m.r. data: δ 5.46 (benzylic H), 4.50 (H-1), 1.65 (CH_3) p.p.m., J_{1,CH_3} 1.5 Hz.

Reaction of **9** *and* **5** *with thionyl chloride in pyridine.* — A solution of thionyl chloride (5 ml) in pyridine (20 ml) was added dropwise to a cooled solution of **8** (1.5 g) in pyridine. After the addition was complete, the mixture was stored at room temperature for 1 h, poured into water, and extracted with ether, and the ether extract was dried and concentrated. The product was chromatographed over silica gel to give methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-ethyl-2-*C*-methylene-α-D-*arabino*-hexopyranoside (**20**) (1 g, 70%), m.p. 47° (from aqueous ethanol), $[\alpha]_D$ +16.4° (*c* 1.5, chloroform) (Found: C, 70.1; H, 7.6. $C_{17}H_{22}O_4$ calc.: C, 70.3; H, 7.6%).

Compound **5** (0.1 g), obtained by reduction of the altropyranoside derivative **13** with lithium aluminium hydride, was treated with thionyl chloride in pyridine, in similar fashion to compound **9**. The preponderant product in the reaction mixture was methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-ethyl-2-*C*-methylene-α-D-*ribo*-hexopyranoside (**21**), which had an n.m.r. spectrum indistinguishable from that of the product from the reaction between **2** and methylenetriphenylphosphorane.

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