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SYNTHESIS AND STEREOCHEMISTRY OF SOME DERIVATIVES OF D-PSICOSE

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ABSTRACT

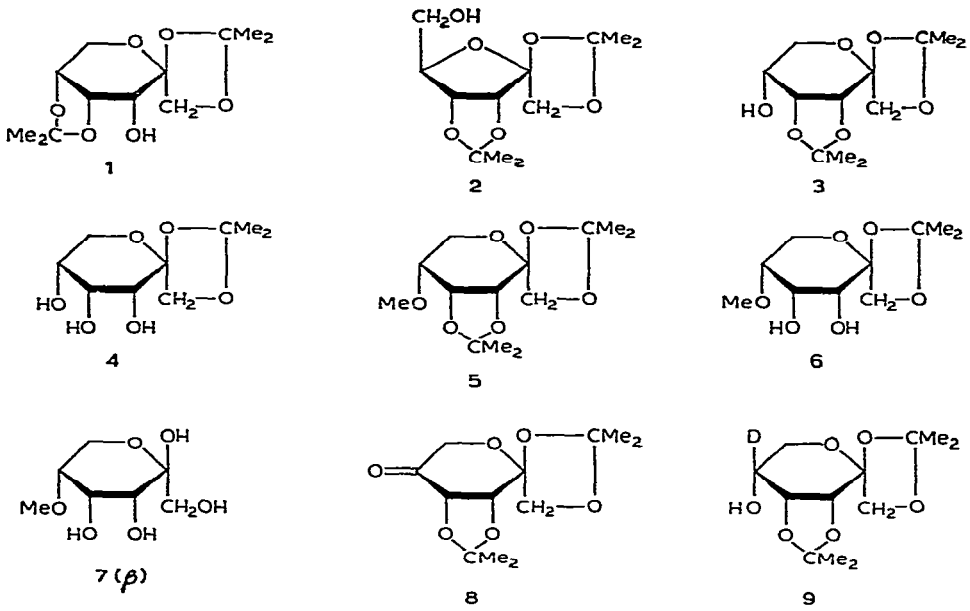
A number of derivatives of the ketohexose D-psicose have been synthesized, comprising examples of acetals, esters, ethers, and glycosides Among them are precursors of 1-, 3-, 5-, and 6-mono-*O*-methyl-D-psicose, including 3-*O*-methyl-β-D-psicopyranose 4,5-carbonate, the first crystalline representative of the reducing form of the ketose A synthesis of D-psicofuranose 6-phosphate is also described At least three types of conformation are encountered among the pyranose derivatives, according to n m r -spectroscopic data, they appear to be $^2C_5$, $^3S_0$, and $^5S_0$, the last two being characteristic of 3,4- and 4,5-*O*-isopropylidene or cyclic carbonate derivatives, respectively Some conformational features of the furanose derivatives are also described

INTRODUCTION

In order to study tautomeric equilibria of D-psicose, and conformations of its ring forms[1,2], various reference compounds were needed, and obtaining them involved the synthesis of a substantial number of new derivatives of the ketose, based on the readily available[2–6] 1,2 4,5-di-*O*-isopropylidene-β-D-psicopyranose (**1**) as the starting material The preparation of these derivatives, and some of their stereochemical characteristics, are reported here

RESULTS AND DISCUSSION

(*A*) *1,2 3,4-Di-O-Isopropylidene-β-D-psicopyranose* — It has been shown earlier[5] that, when **1** is treated with acetone in the presence of an acid catalyst, it is rapidly converted into 1,2 3,4-di-*O*-isopropylidene-β-D-psicofuranose (**2**) For many years, the latter has been known[7] as a crystalline derivative of the sugar, suitable for its isolation and characterization During the present study, the isomerization of **1**→**2** has been re-examined At equilibrium, the ratio of **2** to **1** was ~5 1 (according to t l c and ^{1}H-n m r -spectral observations), although a third component detected was isolated in 10% yield by column chromatography. This third product was also



crystalline, and proved to be the previously unknown 1,2 3,4-di-*O*-isopropylidene-β-D-psicopyranose (**3**)

Evidence supporting structure **3** was obtained as follows Selective hydrolysis with 80% acetic acid for 3 h at room temperature yielded 1,2-*O*-isopropylidene-β-D-psicopyranose (**4**), which had previously been obtained[5] analogously from **1** Barring a rearrangement, this showed that **3** is pyranoid and contains a 1,2-acetal group Methylation of **3** afforded a crystalline monomethyl ether (**5**), partial, acid hydrolysis of **5** (as for **3**) gave **6**, and complete hydrolysis yielded syrupy 5-*O*-methyl-α,β-D-psicopyranose (**7**)*, characterized[2] by ^{13}C-n m r spectroscopy. Thus, O-3 and O-4 of **3** must be the sites of the second *O*-isopropylidene group

On oxidation with ruthenium tetraoxide, **3** gave crystalline 1,2 3,4-di-*O*-isopropylidene-β-D-*erythro*-2,5-hexodiulo-2,6-pyranose (**8**) in 90% yield The D-*ribo* configuration was regenerated when **8** was reduced with lithium aluminum deuteride, that is, **9**, the 5-deutero analog of **3**, was obtained (70% yield)** Differences observed in the ^{1}H-n m r spectrum of **9**, as compared with that of **3**, were as expected, the signal ascribed to H-5 of **3** was missing and that of OH-5, formerly a doublet, was a singlet, H-4 now produced a doublet, rather than a triplet, and the H-6 and H-6′ signals were changed to a simple AB pattern All of these findings aided in confirming the structure of **3**

*Another route to **7**, and also **6**, involving the preparation of a cyclic carbonate intermediate, is described in sect C

D-Psicose-5-*d*, prepared by acid hydrolysis of **9, has been used[2] in an analysis of the ^{13}C-n m r spectrum of D-psicose The high degree of stereoselectivity observed in the formation of **9** parallels that for the preparation of **1** from the corresponding 3-keto precursor[3-6]

^{1}H-N m r spectroscopy was used to monitor the acid-catalyzed isomerization of **1** to **2**, using acetone-d_6 as the medium the CH_3 signals of the 4,5-*O*-isopropylidene group decreased markedly within 0 5 h, followed by those of the 1,2-acetal substituent during the next 3 5 h, when the observable spectrum corresponded to that of **2** (neglecting minor signals) This suggests that the isomerization does not entail intramolecular rearrangement of the *O*-isopropylidene groups of **1** but, rather, a continuous exchange with acetone molecules in the medium Under the same conditions, the spectrum of **2** remained essentially unchanged, aside from the expected disappearance of the CH_3 signals*

(*B*) *3-O-Methyl derivatives* — In order to obtain 3-*O*-methyl-D-psicose (**10**) for use in the ^{13}C-n m r studies cited[1 2], **1** was treated with methyl iodide and silver oxide, giving **11**, following which, the acetal substituents were removed by hydrolysis with a cation-exchange resin By selective hydrolysis with 80% acetic acid, **11** was converted into syrupy monoacetal **12** which, by reaction with phosgene in pyridine, yielded the 4,5-carbonate **13** When the *O*-isopropylidene group of **13** was removed by hydrolysis, 3-*O*-methyl-β-D-psicopyranose 4,5-carbonate (**14**) was obtained It appears that this is the first example of a crystalline form of D-psicose containing a free, anomeric hydroxyl group

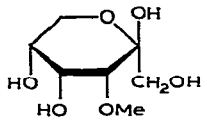
Ketose **14** was strongly levorotatory ($[\alpha]_D$ −97°), indicative of the β configuration assigned, and it exhibited no mutarotation in water However, its ^{1}H-n m r spectrum in dimethyl sulfoxide-d_6 contained a weak singlet, in addition to the prominent OH-2 singlet[8], suggesting that perhaps 5% of the α anomer was present The presence of a triplet ascribable[1] to OH-1 confirmed that this group in **14** is also unsubstituted

An alternative synthesis of **13** is described in the succeeding section

(*C*) *Cyclic and acyclic carbonate derivatives of 1,2-O-isopropylidene-β-D-psicopyranose* (**4**) — The *cis-cis*-3,4,5-triol grouping in D-psicopyranose allows[9] the possibility of two different, cyclic carbonate derivatives Indeed, the reaction of 1,2-*O*-isopropylidene-β-D-psicopyranose (**4**) with phosgene was found to yield a mixture of the 3,4- and 4,5-carbonates (**15** and **16**), together with some products assumed to be dimeric (t l c evidence) As one objective of this experiment had been to prepare 1,2-*O*-isopropylidene-5-*O*-methyl-β-D-psicopyranose 4,5-carbonate (**17**), *en route* to 5-*O*-methyl-D-psicose (**7**), the mixture of compounds was treated directly with methyl iodide and silver oxide Column chromatography of the methylation product on silica gel then afforded 10% of crystalline **17**, as well as 40% of the 3-*O*-methyl derivative **13**, this large difference in yields showed that the 4,5-diol grouping of **4** is much more reactive than the 3,4-diol** towards phosgene The identity of **17** was established by its conversion into **6** by de-esterification with sodium methoxide

*The use of **2** for the synthesis of various furanose derivatives, including D-psicose 6-phosphate, is described herein

A branched analog of **4 bearing a 3-C-(pyridin-2-yl) substituent exhibits an even greater disparity, under the same conditions, it gave a 1 9 ratio of the 3,4- and 4,5-carbonates[10]



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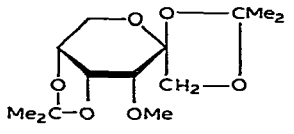

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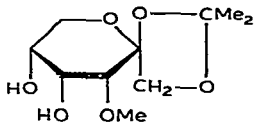

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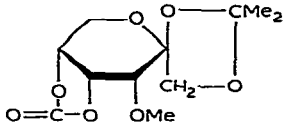

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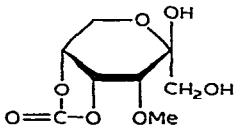

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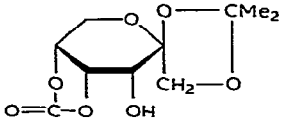

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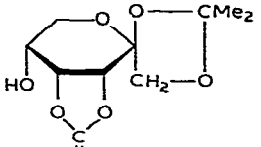

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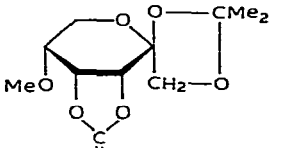

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Two additional products were eluted from the column, in yields of 15–20% Each exhibited a strong i r. absorption band (1770 cm^{-1}) characteristic of an acyclic carbonate[9], as well as one (1820 cm^{-1}) for a cyclic carbonate[9], each product also showed a methoxyl ^1H singlet which was not, however, that of an ether substituent, as shown by the fact that, in sodium methoxide solution, both products yielded the original triol (**4**) Taken together with elemental analyses, these characteristics indicated that the compounds are 1,2-*O*-isopropylidene-3-*O*-(methoxycarbonyl)-β-D-psicopyranose 4,5-carbonate (**18**) and 1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-β-D-psicopyranose 3,4-carbonate (**19**) A fuller characterization of **18** and **19** was afforded by their ^1H-n m r spectra (see sect *E*)

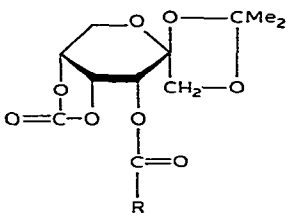
In one experiment, another pair of crystalline products (**20** and **21**) was isolated As shown by elemental analysis, i r spectroscopy, and the fact that each yielded **4** when treated with methoxide, these products are dicarbonates similar to **18** and **19** Moreover, **20** appeared to be closely akin to **18**, and **21** to **19**, judging from a comparison of their ^1H-n m r spectra Surprisingly, however, **20** and **21** exhibited signals attributable to an OCH_2CH_3 group (rather than the OCH_3 of **18** and **19**), which was consistent with the elemental analyses Hence, the products are formulated as 3-*O*-(ethoxycarbonyl)-1,2-*O*-isopropylidene-β-D-psicopyranose 4,5-carbonate (**20**) and its isomeric 5-*O*-(ethoxycarbonyl) 3,4-carbonate (**21**) The occurrence of an ethoxyl group in these compounds was unexpected, and its source was found to be ethanol, present as a stabilizer in the chloroform used during processing, that is, following the reaction of **4** with phosgene, this impure chloroform had been introduced as an

extractant, but **20** and **21** were not detected when ethanol-free chloroform was used for the purpose

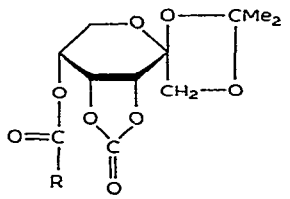
It is probable that compounds **18–21** are derived from the unidentified products accompanying **14** and **15** An intermolecular carbonate (*e g* , **22**) is one possibility[9], as already noted, and its carbonate bridge would be expected[11] to be much more liable to solvolysis in neutral or basic media than the cyclic carbonate group Hence, in the basic medium generated by silver oxide during methylation, **22** would be converted into a mixture of **18** (or **19**) and **13** (or **17**) Similarly, ethanolysis[11] of **22** could account for product **20** (or **21**) An alternative source of the *O*-(alkoxycarbonyl) derivatives, particularly **20** and **21**, may be 3- and 5-chloroformates (**23** and **24**), although the relatively unstable 3-*O*-(chloroformyl)-1,2 4,5-di-*O*-isopropylidene-α-D-glucofuranose has been prepared[12]

Compound **19** was utilized to synthesize a precursor of 1-*O*-methyl-D-psicose (compound **18**, **20**, or **21** might have served equally well) Removal of the 1,2-*O*-isopropylidene group with a cation-exchange resin, followed by methylation, afforded crystalline methyl 5-*O*-(methoxycarbonyl)-1-*O*-methyl-β-D-psicopyranoside (**25**) The structure of **25** was given by the results of elemental analysis, ^{1}H-n m r. and i r spectroscopy, and its strong, negative, specific rotation (—84°) No trace of the α anomer was detected in its preparation

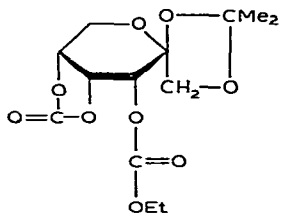
(*D*) *Glycosides of* D-*psicose* — D-Psicose, prepared by acid hydrolysis of **1**, was heated under reflux in methanolic hydrogen chloride, chromatographic examination of the reaction mixture at intervals indicated that equilibrium was approached in 5 h The products were isolated by successive chromatography on cellulose and an anion-exchange resin, or, as peracetates, by chromatography on silica gel These



18 (R = OMe)
23 (R = Cl)



19 (R = OMe)
24 (R = Cl)



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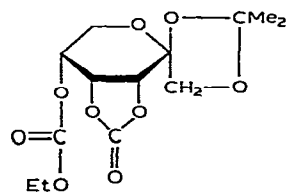

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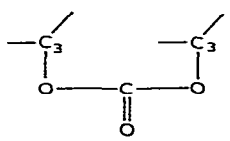

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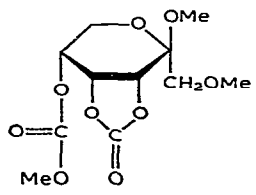

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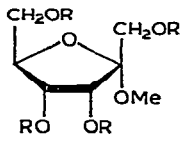
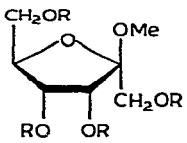
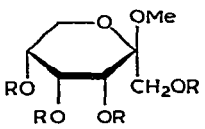


26 (R = H)
29 (R = Ac)



27 (R = H)
30 (R = Ac)



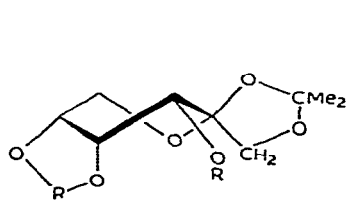
28 (R = H)
31 (R = Ac)

TABLE I

^{1}H–^{1}H COUPLING[a] AND OPTICAL ROTATORY DATA FOR PYRANOSE DERIVATIVES CONTAINING 1,2- OR 4,5-CYCLIC SUBSTITUENTS, OR BOTH

Compound	$J_{1,1}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6}$	$J_{6,6}$	M_D[b] *(degrees)*
1[c]	9 0	2 7	7 5	2 0	1 0	13 5	−315
1(OAc)[d]	9 5	2 8	7 5	1 8	1 2	14 0	−350
11[d]	9 0	2 8	7 5	1 5	1 5	[e]	−420
13[d]	9 2	3 5	7 5	1 9	1 4	[e]	−345
18[f]	9 5	3 5	7 5	1 6	0 6	14 0	−365
20[f]	9 5	3 5	7 5	1 2	2 2	14 0	−372
14[c]	11 5	4 1	7 0	2 5	1 0	14 5	−213

[a]Observed spacings (Hz) [b]In chloroform [c]In acetone-d_6 [d]In $CDCl_3$ [e]H-6 and H-6′ signals almost coincide [f]In 1 1 chloroform-*d*–benzene-d_6



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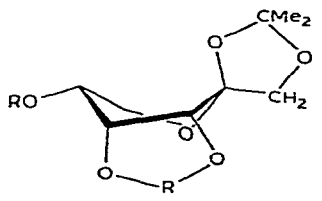

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procedures afforded methyl α- and β-D-psicofuranoside (**26** and **27**) and methyl β-D-psicopyranoside (**28**), in the ratios of 1 1 1 2, as well as their respective tetra-acetates (**29–31**), compounds **28**, **30**, and **31** were crystalline The glycosides have been differentiated by ^{13}C-n m r spectroscopy[2,13], as well as by their ^{1}H-n m r spectra, and by polarimetry

It is noteworthy that the α-pyranoside was not detected in either group of products However, its formation has been observed[13] when calcium ion is present during the methanolysis

(*E*) *Conformation of pyranose derivatives containing a fused, 4,5-ring substituent* — ^{1}H–^{1}H coupling and optical rotatory data are presented in Table I for derivatives related to **1**, *i.e.*, those bearing either a 4,5-*O*-isopropylidene or a 4,5-carbonate group and also a substituent on O-3 Clearly, all of them exhibit similar

patterns of vicinal coupling, and are strongly levorotatory. The fact that $J_{4,5}$ (consistently 7 5 Hz) is large, and $J_{5,6}$ and $J_{5,6}$ are small (2 5 Hz, or less) implies that the C-4–H and C-5–H bonds are substantially eclipsed, and that the 5,6 and C-6′–H bonds are *gauche* Similarly, $J_{3,4}$, the value of which is uniformly close to ~3 Hz, indicates staggering of the corresponding C–H bonds From an inspection of molecular models, these coupling data are in accord with the $^3S_0$ conformation (**32**) for each of these derivatives of D-psicopyranose

The data in Table I have been utilized to differentiate between the dicarbonate derivatives (see sect *D*) That is, **18** and **20** have been assigned a 4,5-ring substituent because their characteristics readily place them in this group, rather than in the 3,4 category (see sect *F*) Accordingly, the alkoxycarbonyl groups are situated on O-3

Included in Table I are data for 3-*O*-methyl-β-D-psicopyranose 4,5-carbonate (**14**), they are closely similar to those for the other compounds, aside from a somewhat larger value of $J_{1,1}$ This analogy suggests that the *spiro*-dioxolane ring at C-2 is not of substantial importance in determining the conformation of these molecules

Another basis for comparison is offered by the coupling data for methyl 1,3,4,5-tetra-*O*-acetyl-β-D-psicopyranoside (**31**) All of the vicinal couplings for this compound are relatively small (<4 Hz) and, also, there is long-range coupling between H-3 and H-5 (the sole example of long-range ^{1}H–^{1}H coupling encountered in the study) These characteristics, which are distinctive from those for all of the other derivatives, indicate that, in the absence of the fused 4,5-ring, the β-D-psicopyranoside **31** adopts the $^5C_2$ conformation

(*F*) *Conformation of pyranose derivatives having a fused, 3,4-ring substituent* — Derivatives related to **3**, *i e*, those containing a ring fused at C-3 and C-4 and a substituent on O-5, are compared in Table II Their ^{1}H–^{1}H coupling characteristics differ in several respects from those in Table I values of $J_{5,6}$ and $J_{5,6}$ are much larger ($7\,5 < J_{5,6} + J_{5,6} < 15$), indicating that H-5 is *axial* (in **3**) or *quasi-axial*, the large value of $J_{3,4}$ implies near-eclipsing of the C-3–H and C-4–H bonds, and a

TABLE II

^{1}H–^{1}H COUPLING[a] AND OPTICAL ROTATORY DATA FOR PYRANOSE DERIVATIVES CONTAINING 1,2- OR 3,4-CYCLIC SUBSTITUENTS, OR BOTH

Compound	$J_{1,1}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6}$	$J_{6,6}$	M_D[b] *(degrees)*
3[c]	8 5	7 5	3 2	6 4	9 5	9 2	−182
5[c]	9 0	7 5	2 5	~6	[d]	[d]	−203
17[e]	[f]	7 5	3 6	6 0	5 0	[f]	−255
19[g]	[f]	7 5	4 0	2 5	3 8	[f]	−188
21[g]	[f]	7 5	4 0	4 0	6 5	[f]	−193
25[g]	11 0	7 0	4 5	4 5	4 5	[f]	−245

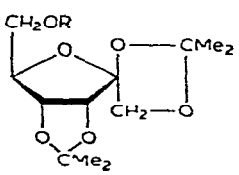
[a]Observed spacings (Hz) [b]In chloroform [c]In acetone-d_6 [d]Signals overlapped [e]In benzene-d_6 [f]H-1 and H-1′ signals, and H-6 and H-6′ signals almost coincide [g]In 1 1 chloroform-*d*–benzene-d_6

relatively small value for $J_{4,5}$, indicates a staggered arrangement of the bonds at C-4 and C-5 In general, these coupling data suggest the $^5S_0$ conformation (33) for all of these compounds Alkoxycarbonyl derivatives **19** and **21** exhibit coupling and rotatory data consistent with their inclusion in this group of derivatives, re-inforcing the structural designations given

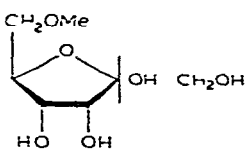
As with the 4,5-series, one compound listed in Table II does not have a 1,2-*O*-isopropylidene group, namely, methyl 5-*O*-(methoxycarbonyl)-1-*O*-methyl-β-D-psicopyranoside 3,4-carbonate (**25**) The close similarities between it and the other derivatives is an indication that, in this series also, the conformation of the pyranose derivatives is not materially affected by a *spiro*-dioxolane ring appended to C-2

(*G*) *Derivatives of 6-O-methyl- and 6-O-benzyl-D-psicofuranose* — 1,2 3,4-Di-*O*-isopropylidene-β-D-psicofuranose (**2**)* was methylated to give the 6-*O*-methyl derivative (**34**) On acid hydrolysis the latter gave 6-*O*-methyl-α,β-D-psicofuranose (**35**), methanolysis of which provided a 2 3 mixture of α-(**36**) and β-(**37**) glycosides ($[\alpha]_D$ +90° and −40°, respectively), these were separated by column chromatography on an anion-exchange resin Compounds **35–37** have been studied further by ^{13}C-n m r spectroscopy[2]

The 6-*O*-benzyl derivative (**38**) was also prepared from **2** Removal of the *O*-isopropylidene groups of **38** with acid, and acetylation of the liberated sugar, gave two tetraacetates, separable by column chromatography on silica gel Although these products must be the anomers **39** and **40**, they showed an unusually small difference in optical rotation ($[\alpha]_D$ +40° and +17° respectively) Undoubtedly, the value for **40** is "anomalous" both the optical activity and the ^{1}H–^{1}H coupling characteristics of **39** are closely similar to those of methyl 1,3,4 6-tetra-*O*-acetyl-α-D-psicofuranoside (**29**), whereas **40** and the β-furanoside **30** are configurationally analogous, according to their coupling patterns, but not according to their rotations (see Table III) A



34 (R = Me)
38 (R = CH_2Ph)



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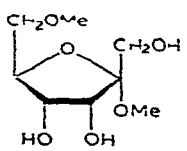

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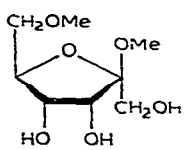

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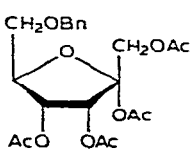

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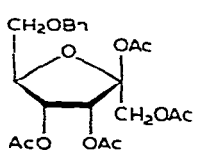


40

*When isolated by direct crystallization from the reaction mixture, following the isomerization of **1** (see sect A), **2** was contaminated with **3**, it was purified by column chromatography

TABLE III

^1H–^1H COUPLING[a] AND OPTICAL ROTATORY DATA FOR FURANOSE DERIVATIVES

Compound	$J_{1,1}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6}$	$J_{6,6}$	M_D[b] *(degrees)*
29[c]	12.2	7.0	3.5	~3	~3	[d]	+159
39[e]	11.2	6.4	3.0	3.0	3.0	[d]	+162
30[c]	12.5	5.0	7.0	3.4	6.5	12.0	−112
40[e]	12.0	4.7	7.5	3.2	3.2	11.0	+74

[a]Observed spacings (Hz) [b]In chloroform [c]In benzene-d_6 [d]H-6 and H-6 signals almost coincide [e]In chloroform-*d*

TABLE IV

^1H–^1H COUPLING[a] AND OPTICAL ROTATORY DATA FOR FURANOSE DERIVATIVES CONTAINING 1,2- AND 3,4-CYCLIC SUBSTITUENTS

Compound	$J_{1,1}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6}$	$J_{6,6}$	M_D[b] *(degrees)*
2[c]	9.5	6.0	0.5	2.7	3.7	13.0	−211
34[e]	10.0	6.0	1.0	7.0	8.0	[d]	−227
38[e]	9.5	6.0	1.0	7.5	8.5	[d]	−231
45[c]	9.5	5.9	0.2	5.5	5.5	[d]	−169
46[c]	11.0	6.0	0.1	~5	~5	[d]	
47[f]	10.0	5.5	0.5	5.5	5.8	[d]	−201[g]

[a]Observed spacings (Hz) [b]In chloroform [c]In chloroform-*d* [d]H-6 and H-6′ signals almost coincide [e]In chloroform-*d*–benzene-d_6 (1:1) [f]In D_2O [g]In water

feasible cause of this apparent discrepancy is the 6-*O*-benzyl group of **40**, because there are a number of examples[14–16] of "anomalous" rotations that are attributable to aryl substituents. As reflected in their contrasting values of $J_{4,5}$ (see Table III), the conformations of **39** and **40** (as well as of **29** and **30**) are different, whereas the fact that $J_{5,6} = J_{5,6} = \sim 3$ Hz indicates that the C-6–O-6 bond in each is oriented approximately as in rotamer **41**. Hence, the spatial relationship of the 6-*O*-benzyl group of **40** with respect to chiral centers of the ring differs from that in **39**. Presumably, its orientation is such as to influence the rotation of the molecule materially.

Ethers **34** and **38** differ notably from the parent diacetal **2** in the arrangement of substituents relative to the C-5–C-6 bond. Their large values of $J_{5,6}$ and $J_{5,6'}$ (see Table IV) indicate population by rotamers (**42** and **43**) in which H-5 is *anti* with respect to H-6 and H-6′ whereas the *gauche, gauche* rotamer **41** agrees well with smaller values exhibited by **2**. For all three compounds, $J_{3,4}$ is 1 Hz or less, showing that the corresponding dihedral angle is close to 90°. Inspection of a molecular model of **2** in the E_o conformation incorporating rotamer **41** suggested that hydrogen

TABLE V

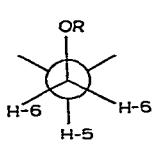
^{1}H CHEMICAL-SHIFTS (δ)[a] FOR DERIVATIVES OF D-PSICOSE

Compound	*H-1*	*H-1′*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6′*	*IpCH$_3$*[b]	*Other protons*	*Solvent*[c]
Pyranoses having a 1,2 or 4,5 ring-substituent, or both										
1	4.35(d)	3.77(d)	3.93(q)	4.46(q)	4.27(o)	3.83(q)	3.59(q)	1.42, 1.42 1.34, 1.29	4.14(d, OH-3)	A
1(OAc)	4.34(d)	3.92(d)	5.20(d)	4.50(q)	4.30(o)	3.75(q)	3.93(q)	1.50, 1.46 1.34, 1.34	2.17(s, OAc-3)	C
11	4.34(d)	3.86(d)	3.49(d)	4.54(q)	4.23(m)	~3.7(m)	~3.7(m)	1.49, 1.49 1.43, 1.33	3.55(s, OMe-3)	A
13	4.24(d)	4.02(d)	3.55(d)	4.99(q)	4.70(m)	~4.1(m)	~4.1(m)	1.49, 1.43	3.60(s, OMe-3)	C
18	4.23(d)	3.94(d)	4.96(d)	4.60(q)	4.12(o)	~3.7(m)	~3.7(m)	1.41, 1.33	3.60(s, CO_2Me-3)	C + B
20	4.31(d)	3.93(d)	4.98(d)	4.15(q)	3.45(o)	3.43(q)	3.21(q)	1.32, 1.26	3.88(q, CH_2) 0.94(t, Me)	B
14	3.84(d)	3.54(d)	3.65(d)	5.10(q)	4.83(o)	4.20(q)	3.90(q)	—	5.10(br, OH) 3.60(s, OMe-3)	A
Pyranoses having a 1,2 or 3,4 ring-substituent, or both										
3	4.04(d)	3.81(d)	4.19(d)	4.51(q)	4.15(m)	3.76(q)	3.64(q)	1.44, 1.44 1.34, 1.34	3.20(d, OH-5)	A
5	4.03(d)	3.80(d)	4.15(d)	4.75(q)		3.96–3.64(m)		1.42, 1.40 1.33, 1.33	3.38(s, OMe-5)	A
17	~4.0	~4.0	3.98(d)	4.38(q)	3.34(o)	~3.7(m)	~3.7(m)	1.37, 1.27	3.06(s, OMe-5)	B
19	~4.0	~4.0	4.17(d)	4.72(q)	5.10(o)	~3.7(m)	~3.7(m)	1.43, 1.33	3.65(s, CO_2Me-5)	C + B
21	~4.0	~4.0	4.00(d)	4.17(q)	5.04(o)	~3.8(m)	~3.8(m)	1.38, 1.28	4.03(q, CH_2) 1.13(t, Me)	C + B
25	3.64(d)	3.48(d)	4.62(d)	4.97(q)	5.13(q)	~3.9(m)	~3.9(m)	—	3.79, 3.39, 3.33 (3s, OMe-1,2,5)	C

TABLE V *(continued)*

Furanoses having 1,2 and 3,4 ring-substituents									
2	4 17(d)	4 06(d)	4 64(d)	4 91(q)	4 27(m)	3 89(q)	3 60(q)	1 52, 1 46 1 42, 1 34	3 60(OH-6)	C
34	4 27(d)	4 02(d)	4 59(d)	4 73(q)	4 22(m)	~3 4(m)	~3 4(m)	1 44, 1 44 1 38, 1 32	3 39(OMe-6)	C
38	4 28(d)	4 02(d)	4 56	4 74(q)	4 39	~3 5(m)	~3 5(m)	1 43, 1 43 1 36, 1 31	7 28 (Ph) 4 54 (Me)	C + B
45	4 29(d)	4 03(d)	4 54(d)	4 70(q)	4 28	~4 3(m)	~4 3(m)	1 44, 1 42 1 36, 1 29	7 27 (Ph)	C
46[d]	4 34(d)	4 10(d)	4 76(d)	4 95(d)		4 4–3 8(m)		1 67 1 50	7 28 (Ph)	D
47[d]	4 78(d)	4 56(d)	5 37(d)	5 53(d)		4 9–4 1		2 00, 2 00 1 91, 1 89	—	D
Other furanose derivatives										
29	4 5–4 1		5 28(d)	5 19(q)		4 5–4 1		—	2 14, 2 12(×2)2 08 (OAc), 3 42(OMe)	C
30	4 5–4 1		5 36(d)	5.51(q)		4 5–4 1		—	2 10, 2 08, 2 04, 2 02(OAc), 3 12 (OMe)	C
39	4 71(d)	4 55(d)	5 52(d)	5 40(q)	4 39(q)	~3 7(m)	~3 7(m)	—	2 06(×2)2 05, 209 (OAc), 7 3(Ph) 4 5(CH_2)	C
40	4 85(d)	4 57(d)	5 51(d)	5.70(q)	4 34(m)	3 74(q)	3 52(q)	—	2 12, 2 04, 2 01, 1 77(OAc), 7 31(Ph) 4 54(CH_2)	C

[a]Multiplicities are indicated in parentheses d, doublet, m, multiplet, o, octet, q, quartet [b]Methyl signals of *O*-isopropylidene (Ip) substituents [c]A, acetone-d_6, B, benzene-d_6, C, chloroform-*d*, D, D_2O [d]Cyclohexylammonium salt, cyclohexyl protons are not listed



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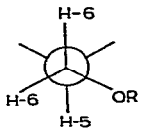

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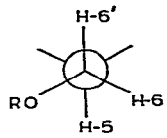

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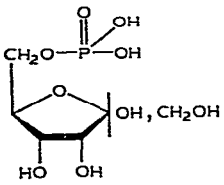

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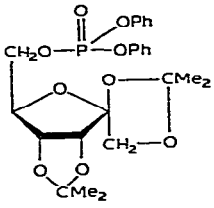

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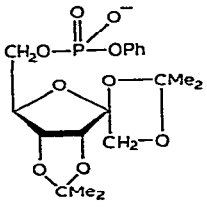

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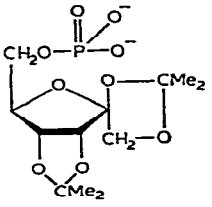

47

bonding between OH-6 and O-2 is feasible, this may account for the differences noted Other data in Table IV are for the 6-(diphenylphosphate) derivative (**45**) of **2** (see sect *H*), the rotameric population of its C-6 exocyclic moiety appears to be intermediate between that of the parent alcohol and those of the two ether derivatives

(*H*) D-*Psicofuranose 6-phosphate* — D-Psicose occurs free in Nature[17–19], and also as a component of some nucleosides[20–22] As has been pointed out[17 23], the biochemistry of the ketose would be expected to involve such metabolites as D-psicofuranose 6-phosphate (**44**) Although the latter has yet to be found in living systems, its synthesis was undertaken by analogy with the ether syntheses just described (see sect *G*)

Phosphorylation of **2** with diphenylphosphorochloridate afforded the crystalline 6-(diphenylphosphate) (**45**). When **45** was hydrogenolyzed over a platinum catalyst, a mixture of 1,2 3,4-di-*O*-isopropylidene-β-D-psicofuranose 6-phosphate (**47**) and 6-(monophenylphosphate) (**46**) was obtained, each being isolated as the dicyclohexylammonium salt through fractional recrystallization Acid hydrolysis of **47** with a cation-exchange resin then gave D-psicofuranose 6-phosphate (**44**)

As it appeared possible that migration, or partial hydrolysis, of the phosphate group might have occurred during removal of the acetal groups of **47**, the final product was characterized more rigorously A comparison of its ^{13}C-n m r spectrum with those[2] of 5-*O*-methyl-D-psicopyranose (**7**) and 6-*O*-methyl-D-psicofuranose (**35**) showed clearly that the only species produced in the reaction sequence were α- and β-furanose derivatives For example, no signals were found near 100–98 p p m or 60 p p m , regions characteristic[1,2,13 24] of C-1 and C-6, respectively, of α- and β-psicopyranose Rather, the chemical shifts and relative intensities of most of the signals in the spectrum of the product were closely analogous to those of 6-*O*-methyl-α,β-D-psicofuranose (**35**), as expected, the main differences involved the C-6 signals [66 3 p p m (**44**,β) and 64 5 p p m (**44**,α), as compared with 75 5 p p m (**35**,β) and 72 5 p p m (**35**,α)] Additional evidence that the phosphate group was situated at C-6 came from the fact that the C-6α and C-6β signals were doublets, due to

coupling (of ~6 Hz) with ^{31}P, and there was also coupling with C-5 (although this was partly obscured by signal overlap)

(*I*). *^{1}H-N m r chemical shifts* — Spin–spin coupling-parameters have already been presented for most of the compounds (in the discussion of structural and conformational features). For convenience, Table V lists the corresponding, chemical-shift data under the structural classifications used in Tables I–IV

EXPERIMENTAL

General methods. — Proton magnetic resonance spectra were recorded with a Varian HA-100 spectrometer ^{13}C-N m r spectra were recorded at 25 1 MHz with a Varian XL-100 FT spectrometer Chemical shifts (δ) are reported with reference to tetramethylsilane I r spectra were recorded for KBr discs with a Unicam SP-200 G grating spectrophotometer Optical rotations were determined, for solutions in 1-dm tubes, with a Carl Zeiss polarimeter (Model 367732) Microanalyses were performed by C Daessle, Montreal Plates of Silica Gel G were used for t l c , and the developing solvents were ethyl acetate or 2 1 benzene–ethyl acetate Silica Gel for column chromatography (0 08-mm particle size) was obtained from Macherey Nagel and Co Solutions were usually evaporated below 40° under diminished pressure.

*1,2 3,4-Di-*O*-isopropylidene-β-*D*-psicofuranose* (**2**) and *1,2 3,4-di-*O*-isopropylidene-β-*D*-psicopyranose* (**3**) — To a stirred solution of 1,2 4,5-di-*O*-isopropylidene-β-D-psicopyranose[3–6] (**1**) (10 g) in dry acetone (400 ml) was slowly added conc sulfuric acid (3 ml) After 5 h, an excess of calcium carbonate was introduced, and the filtrate and washings were combined and evaporated, giving a partly crystalline residue (9 2 g) By chromatography on a column (1 5 × 80 cm) of silica gel with 2 1 benzene–ethyl acetate as the eluant, compound **2** was isolated, after recrystallization from hexane (yield, 6 5 g), **2** had m p 56–56 5° (lit [5] m p 55–56°), $[\alpha]_D$ −80° (*c* 1 72, chloroform) Eluted soon after **2** was a second product (**3**) which, after recrystallization from hexane (yield*, 0 14 g) had m p 120–121°, $[\alpha]_D$ −70° (*c* 0 93, chloroform) ^{1}H-N m r data for **2** are presented in Tables IV and V, and for **3** in Tables II and V

Anal Calc for $C_{12}H_{20}O_6$ C, 55 4, H, 7 7 Found (for **3**) C, 55 3, H, 7 7

*1,2-*O*-Isopropylidene-β-*D*-psicopyranose* (**4**) — Diacetal **1** (15 g), dissolved in 80% acetic acid (1 liter), was found (t l.c.) to undergo selective hydrolysis in 5 h at room temperature Evaporation of the solvent left a solid to which ethanol and ethyl acetate were successively added, followed by evaporation. The residue was recrystallized from ethyl acetate (yield, 9.7 g, 76%), m p 175–177°, $[\alpha]_D$ −113 5° (*c* 1 0, ethanol) (lit [5] m p 175–176°, $[\alpha]_D$ −114°). Crystalline **4** was also obtained from **3** by selective hydrolysis under the same conditions

*1,2 3,4-Di-*O*-isopropylidene-5-*O*-methyl-β-*D*-psicopyranose* (**5**) — A solution

*Compound **3** was found to sublime under vacuum at room temperature, resulting in a diminished yield Analysis by t l c suggested that the ratios of **1** **2** **3** in the crude mixture were ~2 10 1

of **3** (60 mg) in methyl iodide (5 ml) containing suspended silver oxide (1 g) and molecular sieves was boiled under reflux for 18 h Chloroform was added, the solids were filtered off and washed with chloroform, and the filtrate and washings were combined and evaporated The solid residue (54 mg) was recrystallized from hexane, m p 74 5–75 5°, $[\alpha]_D$ —74 3° (*c* 1 4, chloroform), ^{1}H-n m r data are presented in Tables II and V

1,2-O-*Isopropylidene-5*-O-*methyl-β*-D-*psicopyranose* (**6**) — Selective hydrolysis of **5** (40 mg) with 80% acetic acid, as for **4**, gave a crystalline product which, recrystallized from ethanol–hexane, had m p 98 5–99°, $[\alpha]_D$ —98 3° (*c* 0 94, chloroform), ^{1}H-n m r data (acetone-d_6) δ 4.09 (d, 1 H, H-1), 3 93 (d, 1 H, H-1′), 3.88 (m, 1 H, H-6), 3 76 (q, 1 H, H-6′), 3 46 (s, 3 H, OCH_3), 1.22 and 1 13 (s, 2 × 3 H, Ip-CH_3)

1,2 3,4-Di-O-*isopropylidene-β*-D-erythro-*2,5-hexodiulo-2,6-pyranose* (**8**) — Ruthenium dioxide hydrate (60 mg) and sodium hypochlorite (5%, 10 ml) were added to a vigorously stirred solution of **3** (100 mg) in chloroform (5 ml) After 4 h, the suspension was filtered, the solids washed with chloroform, and the filtrate and washings were combined, and treated with a few drops of isopropyl alcohol (to reduce the ruthenium tetraoxide remaining) The chloroform layer was washed with small portions of water, dried (sodium sulfate), and evaporated, affording a solid (90 mg, 91%) Recrystallized from hexane, it had m p. 111–111.5°, $[\alpha]_D$ —93 3° (*c* 0 82, chloroform), and exhibited a negative Cotton-effect, ν_{max}^{KBr} 1750 cm^{-1} (strong), ^{1}H-n.m.r data are presented in Tables I and V, calc for $C_{12}H_{18}O_6$ M^+, 258, found M^+, 258.

1,2·3,4-Di-O-*isopropylidene-β*-D-*psicopyranose*-5-d (**9**). — Reduction of **8** (30 mg) in diethyl ether with lithium aluminum deuteride afforded crystalline **9** (21 mg, 70%), m p 120–121° Its ^{1}H-n m r spectrum is compared with that of **3** in sect A

1,2 4,5-Di-O-*isopropylidene-3*-O-*methyl-β*-D-*psicopyranose* (**11**). — Methylation of **1** (2 g), as described for the preparation of **5**, afforded a clear syrup (1 9 g, 90%), $[\alpha]_D$ —201° (*c* 0 91, chloroform), ^{1}H-n m r data are given in Tables I and V

1,2-O-*Isopropylidene-3*-O-*methyl-β*-D-*psicopyranose 4,5-carbonate* (**13**) — Selective hydrolysis of **11** (1 5 g) with 80% acetic acid gave 1 15 g (90%) of an oil To a solution thereof in pyridine (6 ml) and benzene (20 ml) at 0° was added phosgene in benzene (12% w/w) during 5 min After 1 h at room temperature, the solution was diluted with ethanol-free chloroform, washed successively with cold 10% hydrochloric acid and satd sodium hydrogencarbonate, dried (sodium sulfate), and evaporated, giving a solid residue which was recrystallized from ethyl acetate–hexane, yield 0 82 g (62%), m p 114 5–115 5°, $[\alpha]_D$ —124 8° (*c* 0 94, chloroform), ν_{max}^{KBr} 1790 cm^{-1} (br, strong), ^{1}H-n m r data are presented in Tables I and V.

Anal Calc. for $C_{11}H_{16}O_7$. C, 50.8, H, 6 2 Found C, 50 7, H, 6 4.

3-O-*Methyl-β*-D-*psicopyranose 4,5-carbonate* (**14**). — Amberlite IR-120 (H^+) ion-exchange resin was added to a solution of **13** (0 4 g) in water (200 ml), the suspension was heated for 2 h on a steam bath with stirring, the resin was filtered

off, and the filtrate was evaporated to yield a solid residue After recrystallization from ethanol–hexane [yield, 0 22 g (64%)], the product had m p 125–126°, $[\alpha]_D$ −97° (initial, constant, *c* 1 05, water), ^{1}H-n m r. data are presented in Tables I and V

1,2-O-Isopropylidene-3-O-methyl-β-D-psicopyranose 4,5-carbonate (**13**), *-3-O-(methoxycarbonyl)-β-D-psicopyranose 4,5-carbonate* (**18**), *-3-O-(ethoxycarbonyl)-β-D-psicopyranose 4,5-carbonate* (**20**), *-5-O-methyl-β-D-psicopyranose 3,4-carbonate* (**17**), *-5-O-(methoxycarbonyl)-β-D-psicopyranose 3,4-carbonate* (**19**), *and -5-O-(ethoxycarbonyl)-β-D-psicopyranose 3,4-carbonate* (**21**) — 1,2-O-Isopropylidene-β-D-psicopyranose (**4**) (9 0 g) was treated with phosgene in pyridine as described for the preparation of **13** from **11**, except that the processing involved extraction with chloroform (500 ml) stabilized with 2% of ethanol The syrupy product was then methylated as described for the preparation of **5**, yielding 8 6 g of a syrup consisting of at least six components (t l c in 1 1 benzene–ether) Chromatographic separation of the mixture on a column of silica gel (4 5 × 80 cm), with 1 1 benzene–ether as the eluant, afforded the six title compounds in crystalline form Each was recrystallized from ethyl acetate–hexane or ethanol–hexane Physical constants, elemental analyses, and other data are presented in Table VI, and ^{1}H-n m r data in Tables I, II, and V.

TABLE VI

CARBONATE DERIVATIVES PREPARED FROM 1,2-*O*-ISOPROPYLIDENE-β-D-PSICOPYRANOSE (**4**)

Compound	*M p (degrees)*	$[\alpha]_D$[a] *(degrees)*	R_F[b]	%[c]	ν_{max}	*Formula*	*Calc* *C*	*H*	*Found* *C*	*H*
13	114 5–115 5	−125	0 15	40	1790	$C_{11}H_{16}O_7$	50 77	6 2	50 7	6 4
17	71– 74	−98	0 41	10	1800	$C_{11}H_{16}O_7$	50 77	6 2	50 5	6 4
18	169–170	−120	0 30	20	1810, 1765	$C_{12}H_{16}O_9$	47 37	5 3	47 9	5 1
19	174–175	−62	0 46	15	1815, 1750	$C_{12}H_{16}O_9$	47 37	5 3	47 7	5 2
20	132–132 5	−117	0 35	10	1805, 1765	$C_{13}H_{18}O_9$	49 06	5 7	49 6	5 7
21	116–117	−63	0 51	5	1811, 1747	$C_{13}H_{18}O_9$	49 06	5 7	49 4	6 0

[a]In chloroform [b]T l c in 1 1 benzene–ether [c]Percent of total recovered

Methyl 5-O-(methoxycarbonyl)-1-O-methyl-β-D-psicopyranose 3,4-carbonate (**25**) — Compound **19** (0 5 g) was hydrolyzed with cation-exchange resin as described for **14** A syrupy product (0 39 g) was obtained which, on methylation, yielded partly crystalline material (0 39 g), after 4 recrystallizations from ethyl acetate–hexane, the product had m p 127–128°, $[\alpha]_D$ −84 2° (*c* 0 98, chloroform), ν_{max}^{KBr} 1800 (br, strong) and 1750 cm^{-1} (strong), ^{1}H-n m r data are presented in Tables II and V

Anal Calc for $C_{11}H_{16}O_9$ C, 45 2, H, 5 5 Found C, 45 4, H, 5 4

Methyl glycosidation of D-*psicose* — A solution of D-psicose (8 0 g, prepared as described in ref 2) in anhydrous methanol (500 ml) containing acetyl chloride (0 2 ml) was boiled under reflux for 5 h and then made neutral with silver carbonate

Paper chromatography indicated that three glycosides were present, in addition to 10–20% of unreacted sugar. ^{13}C-N m r spectroscopy suggested[1,2] that two furanosides and one pyranoside had been produced in about equal proportions.

Methyl β-D-psicofuranoside (**27**) *and methyl 1,3,4,6-tetra-O-acetyl-β-D-psicofuranoside* (**30**) — The syrupy glycoside mixture (8 0 g) obtained by evaporating the solution just described was partially separated by chromatography on a column (4 × 60 cm) of Rexyn 201 (OH^-) ion exchange resin (200–400 mesh) using CO_2-free water as the eluant[26]. The first fraction is discussed in the next experiment The second fraction (2 2 g), consisting primarily of **27**, was acetylated with acetic anhydride–pyridine, affording crystalline material, after recrystallization from ethanol, m.p 44 5–45°, $[\alpha]_D$ −31° (*c* 1 0, chloroform)

Anal Calc for $C_{15}H_{22}O_{10}$ C, 49 7, H, 6 1 Found (for **30**) C, 49 6, H, 6 3

Chromatographically pure, syrupy **27** was obtained by deacetylation of **30** in methanol containing sodium methoxide, followed by a brief treatment with mixed ion-exchange resins $[\alpha]_D$ −39° (*c* 1 1, water) Compound **27** has been characterized[2] further by ^{13}C-n m r spectroscopy

Methyl β-D-psicopyranoside (**28**), *methyl α-D-psicofuranoside* (**26**), *methyl 1,3,4,5-tetra-O-acetyl-β-D-psicopyranoside* (**31**), *and methyl 1,3,4,6-tetra-O-acetyl-α-D-psicofuranoside* (**29**) — The first fraction (4 5 g) obtained from the chromatogram (preceding section) was rechromatographed on a column (4 5 × 80 cm) of cellulose with 14·3 3 2-butanone–isopropyl alcohol–water as the developing solvent The first product eluted was **28**, which, after recrystallization from tetrahydrofuran (yield 0 9 g), had m p 78–79°, $[\alpha]_D$ −109° (*c* 1 45, water), it was characterized further by ^{13}C-n m r spectroscopy[2]

Anal Calc for $C_7H_8O_6$ C, 43 3, H, 7 3 Found (for **28**) C, 43 0, H, 7 3

Material eluted subsequently was a mixture of **28** and **26** Acetylation of this mixture with acetic anhydride–pyridine, followed by column chromatography on silica gel (eluant, 1 1 benzene–ether), afforded crystalline **31** (2 6 g), recrystallized from ethanol, it had m p 112–112 5°, $[\alpha]_D$ −83 6° (*c* 1 78, chloroform), ^{1}H-n m r data ($CDCl_3$–C_6D_6) δ 4 37 (d, 1 H, H-1), 4 04 (d, 1 H, H-1'), 5 30 (q, 1 H, H-3), 5 37 (t, 1 H, H-4), 5 10 (m, 1 H, H-5), 3 70 (m, 2 H, H-6,6'), 3 12 (s, 3 H, OCH_3), and 1 99, 1 97, 1 87, and 1 85 [4 s, 4 × 3 H, $(COCH_3)_4$], $J_{1,1}$ 12 5, $J_{3,4}$ 3 9, $J_{4,5}$ 3 9, $J_{5,6}$ 1 9, and $J_{5,6}$ 1 9 Hz

A second fraction obtained from the column consisted of syrupy **29** (2 2 g), $[\alpha]_D$ +43 6° (*c* 1 62, chloroform), ^{1}H-n m r data are presented in Tables III and V

Anal Calc for $C_{15}H_{22}O_{10}$ C, 49 7, H, 6 1 Found C, 49 3, H, 6 1

Deacetylation of **29** gave syrupy **26**, $[\alpha]_D$ +70° (*c* 1 08, water), characterized further by ^{13}C-n m r spectroscopy[2]

1,2 3,4-Di-O-isopropylidene-6-O-methyl-β-D-psicofuranose (**34**) — Prepared by methylation of **2** (3.09 g) with methyl iodide–silver oxide, ether **34** (3 06 g, 94%) was a clear, chromatographically pure syrup, $[\alpha]_D$ −82 6° (*c* 2 36, chloroform), ^{1}H-n m r data are presented in Tables IV and V

6-O-Methyl-D-psicofuranose (**25**) — Diacetal **24** (2 g) was hydrolyzed in

aqueous solution at 95° in the presence of Amberlite IR-120 (H^+) resin, yielding syrupy **25** (1 2 g, 87%), $[\alpha]_D$ +29° (*c* 1 15, water) N m r spectroscopy indicated[2] that **25** consists of an ~2 1 mixture of the α and β anomers

Methyl 6-O-methyl-α-D-psicofuranoside (**36**) *and -β-D-psicofuranoside* (**37**) — A solution of **25** (1 2 g) in methanol (100 ml) containing acetyl chloride (0 2 ml) was boiled under reflux for 9 h, made neutral with silver carbonate, and evaporated to a syrup (1 09 g, 83%), $[\alpha]_D$ 0° (*c* 1 0, water) By chromatography of the syrup on an anion-exchange resin, as for **27**, two crystalline products were isolated, both were recrystallized from isopropyl alcohol Glycoside **36** (0 25 g), eluted from the column first, had m p 62 5–63 5°, $[\alpha]_D$ +90° (*c* 1 10, water), for **37** (yield, 0 51 g), the m p was 68 5–69 5°, and $[\alpha]_D$ −40° (*c* 1 21, water) These products were characterized further by ^{13}C-n m r spectroscopy[2]

Anal Calc for $C_8H_{16}O_6$ C, 46 2, H, 7 8 Found (for **36**) C, 46 2, H, 7 9, (for **37**) C, 46 2, H, 7 9.

6-O-Benzyl-1,2 3,4-di-O-isopropylidene-β-D-psicofuranose (**38**) *and 6-O-benzyl-D-psicofuranose* — Diacetal **2** (20 g) was dissolved in tetrahydrofuran (300 ml, distilled over $LiAlH_4$), and sodium wire was introduced, 4 h later, the residual sodium was removed, and α-bromotoluene (10 ml) was added during 30 min After 6 h, when t l c showed that ~30% of **2** remained, the solution was evaporated to a syrup, this was chromatographed on silica gel, using 2 1 benzene–ethyl acetate as the eluant A product (17 g), assumed to be **38**, was obtained as a yellow oil, $[\alpha]_D$ −66° (*c* 1 54, chloroform) This oil (14 g) was subjected to hydrolysis in 0 1M oxalic acid[27] for 3 h at 80°, the hydrolyzate was made neutral with calcium carbonate, de-ionized with mixed-bed ion-exchange resins, and evaporated, yielding a pale-yellow syrup (10 1 g, 94%), $[\alpha]_D$ +24° (*c* 1 17, water) The ^{1}H-n m r spectrum in[1] Me_2SO-d_6 showed the presence of two singlets, at δ 5 98 [OH-2(β)] and 5 70 [OH-2(α)], in the ratio of 1 2

1,2,3,4-Tetra-O-acetyl-6-O-benzyl-α-D-psicofuranose (**39**) *and -β-D-psicofuranose* (**40**) — 6-*O*-Benzyl-D-psicose (10 g) was added to a mixture of pyridine (200 ml) and acetic anhydride (150 ml), and, after 24 h at room temperature, the solution was evaporated Chloroform was added, and the solution was washed successively with cold, M hydrochloric acid, saturated sodium hydrogencarbonate solution, and water, dried (anhyd sodium sulfate), and evaporated, the residue (14 g) was applied to a column (4 5 × 80 cm) of silica gel Development of the chromatogram with 2 1 benzene–ethyl acetate afforded **40** as a syrup (6 7 g), $[\alpha]_D$ +17 2° (*c* 1 35, chloroform), this was followed by **39**, also a syrup (4 3 g), $[\alpha]_D$ +40° (*c* 1 5, chloroform) ^{1}H-N m r data for **39** and **40** are presented in Tables III and V

1,2 3,4-Di-O-isopropylidene-β-D-psicofuranose 6-(diphenylphosphate) (**45**) — Compound **2** (2 6 g) was dissolved in dry pyridine (10 ml), diphenylphosphorochloridate (3 1 g) in pyridine (5 ml) was added with stirring at 0° during 0 5 h, and the mixture was kept for 18 h at 5° Chloroform (200 ml) was added, and the solution was washed successively with cold 1% sodium sulfate (3 times), cold M sulfuric acid, satd sodium hydrogencarbonate, and 1% sodium sulfate (twice) Each aqueous

wash was back-extracted with chloroform. The extracts were combined, dried (anhyd sodium sulfate), and evaporated, yielding a solid (4 6 g, 93%) Recrystallized from hexane, it had m p. 53.5–54°, $[\alpha]_D$ −38 5° (*c* 1 58, chloroform) ^{1}H-N m r data are presented in Tables IV and V

Anal. Calc for $C_{24}H_{29}O_9P$ C, 58 5, H, 5 9; P, 6 3 Found· C, 58 3; H, 5 7: P, 6 3

1,2 3,4-Di-O-isopropylidene-β-D-psicofuranose 6-(dicyclohexylammonium phosphate) (**47**) *and 6-(monocyclohexylammonium phenylphosphate)* (**46**). — Hydrogen was bubbled into a vigorously stirred solution of **45** (4 1 g) in absolute ethanol (100 ml) containing platinum oxide monohydrate (0.38 g) in suspension Following the rapid, initial uptake of the gas, an additional 0 2 g of the catalyst was introduced; this procedure was repeated When **45** had reacted completely (t l c. evidence), the catalyst was filtered off, and sufficient cyclohexylamine was added to the filtrate to bring the pH to ~9–10 On evaporation of the solvent, a crystalline residue (4 5 g) was obtained, this was dissolved in boiling isopropyl alcohol, and the solution was cooled slowly in a Dewar flask. Crystalline material was deposited (1 63 g) that had m p 180° (dec) and $[\alpha]_D$ −38° (*c* 1 0, water), and was identified as **47** ^{1}H-N m r data are presented in Tables IV and V

Anal Calc for $C_{24}H_{38}NO_9P$ C, 56 9, H, 7 3 Found C, 57 2, H, 7 4

The mother liquor was concentrated, water was added, and the aqueous layer was washed successively with chloroform and dichloromethane (to remove residual **47**), and then evaporated to dryness By repeated recrystallization of the resulting solid from water–acetone, pure **46** was isolated (yield, 1 51 g), the compound decomposed above 180°, and had $[\alpha]_D$ −41° (*c* 1 09, water) ^{1}H-N m r data are presented in Tables IV and V

Anal. Calc for $C_{24}H_{47}N_2O_9P$ C, 53 5, H, 8 6 Found C, 53 3, H, 8 5

D-*Psicofuranose 6-(disodium phosphate)* (**44**) — A solution of **46** (1 5 g) in water (100 ml) was stirred with Amberlite 1R-120 (H^+) ion-exchange resin (30 ml) for 10 min, the resin was filtered off, and replaced with fresh resin, and the suspension was heated for 2 h at 80°, with stirring (periodic monitoring of the optical rotation showed that no further change occurred after that time) The suspension was filtered, and the pH of the filtrate was adjusted to 6 8 with sodium hydrogencarbonate For ^{13}C-n m r analysis, the product was "exchanged" with D_2O, and acidified, as this made for better resolution than was obtained with the neutral solution; ^{13}C-n m r data (D_3O^+) δ 106 5 (C-2β), 104 0 (C-2α), 82 0 (d, C-5α), 81 9 (C-5β), 75 0, 71 3, 71 1 (C-3α,β and C-4α,β), 66 3 (C-6β), 64 5 (C-6α), 63 2 (C-1α), and 62 7 (C-1β)

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