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NUCLEOPHILIC ADDITION-REACTIONS OF 1,2 4,5-DI-*O*-ISOPROPYLIDENE-*β*-D-*erythro*-2,3-HEXODIULO-2,6-PYRANOSE, AND THE STEREOCHEMISTRY OF THE PRODUCTS

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ABSTRACT

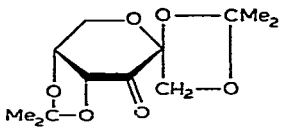
The addition of pyridin-2-yl-, (pyridin-2-ylmethyl)-lithium or lithium acetylide to 1,2 4,5-di-*O*-isopropylidene-*β*-D-*erythro*-2,3-hexodiulo-2,6-pyranose (**1**) affords the corresponding tertiary alcohol derivative in good yield with high stereoselectivity Some elimination of the 4,5-*O*-isopropylidene group of **1** occurs in the reaction with lithium acetylide, as well as with butyllithium, as shown by the formation of a 3-*C*-(2-oxopropyl) adduct and 5-deoxy-3-*C*-ethynyl-1,2-*O*-isopropylidene-*β*-D-*glycero*-2,4-hexodiulo-2,6-pyranose Butyllithium and the Grignard reagents tested do not serve effectively as nucleophiles, but cause proton abstraction and resultant decomposition Chemical and n m r -spectroscopic evidence shows that the addition products possess the *β*-D-*ribo* configuration and, probably, a slightly flattened $^{1}C_{4}$(D) conformation According to n m r -spectral and rotatory data, 3-*O*-methyl derivatives of the branched alcohols exhibit a conformation more highly skewed, possibly $^{3}S_{o}$, than that of the parent compounds Among the compounds synthesized in establishing the configuration at the site of addition (C-3) were the 3,4- and 4,5-cyclic carbonates of 1,2-*O*-isopropylidene-3-*C*-(pyridin-2-yl)-*β*-D-psicopyranose

INTRODUCTION

1,2 4,5-Di-*O*-isopropylidene-*β*-D-*erythro*-2,3-hexodiulo-2,6-pyranose (**1**), readily obtainable by oxidation of 1,2 4,5-di-*O*-isopropylidene-*β*-D-fructopyranose, is a useful intermediate for the synthesis of D psicose[1–5] That is, reduction of **1** with hydride affords the D-*ribo* product (**2**) exclusively, from which the free ketose is obtained by hydrolysis with acid We now describe other nucleophilic addition-reactions of **1** using organometallic reagents, these afforded several novel, branched, ketose derivatives

RESULTS AND DISCUSSION

Reactions of ketone **1** *with organometallic compounds* — Addition reactions



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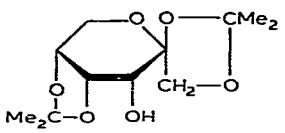

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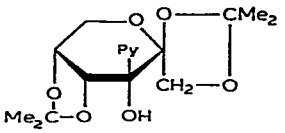

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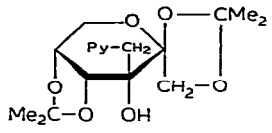
(Py = pyridin-2-yl)



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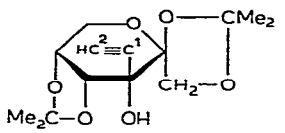

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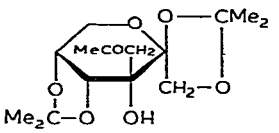

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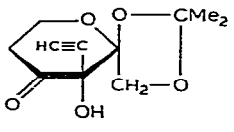

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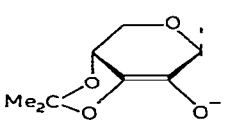

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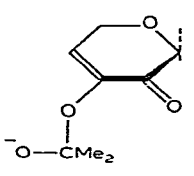

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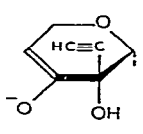

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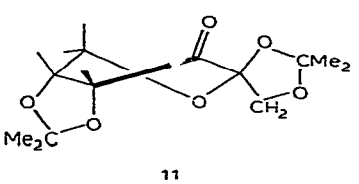


11

of **1** with several organometallic compounds have been examined One involved the use of pyridin-2-yl-lithium* The product of this reaction, which crystallized readily in yields of 60 to 75%, was 1,2 4,5-di-*O*-isopropylidene-3-*C*-(pyridin-2-yl)-*β*-D-psicopyranose (**3**), structural evidence for which is presented Addition to **1** also proceeded readily with (pyridin-2-ylmethyl)lithium, giving an 80% yield of crystalline **4**, which is also assigned the D-*ribo* configuration From the reaction of **1** with lithium acetylide, the crystalline 3-*C*-ethynyl adduct (**5**) was obtained in 50% yield

Several secondary products were formed in the last reaction Two of these were isolated in crystalline form, and characterized by analysis and spectroscopy

*The kind collaboration of Dr A R Vinutha in preliminary experiments is gratefully acknowledged

as 1,2 4,5-di-*O*-isopropylidene-3-*C*-(2-oxopropyl)-β-D-psicopyranose (**6**) and 5-deoxy-3-*C*-ethynyl-1,2-*O*-isopropylidene-β-D-*glycero*-2,4-hexodiulo-2,6-pyranose (**7**) Evidence for the presence of the 2-oxopropyl group of **6** was provided by the strong C=O absorption in the infrared region, as well as by CH_3 and CH_2 singlets in the p m r spectrum at 2 32 and 2 52 p p m , respectively Other p m r data in support of structure **6** were signals for the two *O*-isopropylidene groups, a hydroxylic proton singlet, and a typical AB pattern accounting for the 1-protons Product **7** also exhibited C=O absorption in the infrared region, as well as O–H and acetylenic C–H stretching bands Its p m r spectrum contained four 8-line signals comprising an ABMX pattern, when **7** was heated briefly in D_2O–pyridine[3 5], two of these signals (H-5,5′) no longer appeared, and the other two (H-6,6′) collapsed to a broad AB pattern One-proton singlets at 2 59 and 4 07 p p m were ascribable to the acetylenic and tertiary protons, respectively, only two *O*-isopropylidene methyl singlets were detectable, and protons H-1 and H-1′ were accounted for as an AB pair. The configuration proposed for C-3 of these compounds is made by analogy with that for adducts **3–5**

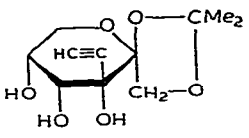
The concomitant occurrence of **6** and **7** indicates a partial loss of the 4,5-*O*-isopropylidene group of **1** The acetone liberated can add, as a carbanion in the strongly basic medium, to liberated **1**, to yield **6** Elimination of the *O*-isopropylidene group probably involves such enolic intermediates as **8–10**, the fact that H-4 undergoes a facile, base-catalyzed deuterium-exchange[3 5] supports the formulation of **8** as an early intermediate

The reaction of **1** with butyllithium gave a complex mixture of products, of which the 3-(2-oxopropyl) derivative **6**, isolated in 10% yield, was the only one identified Its formation again showed that acetone is liberated under basic conditions when an *O*-isopropylidene group is adjacent to a carbonyl group, and is in accord with an earlier report[3] of such instability Furthermore, based on chromatographic evidence, compound **6** was produced when **1** was treated in acetone with potassium hydroxide or tritylsodium Two Grignard reagents, methylmagnesium iodide and benzylmagnesium bromide, were also used, but gave rise to mixtures of at least eight, unidentified products

In all of these reactions, competition between addition and proton-abstraction (the latter leading to such products as **6** and **7**) was to be expected Clearly, the anions generated with lithium are the more effective nucleophiles, this is particularly true of those anions, *e g* , pyridin-2-yl, capable of effective charge delocalization By contrast, the aliphatic member of the group, butyllithium, appeared to act much more selectively in abstracting the α-proton and promoting subsequent, base-catalyzed, degradation products, as also did the Grignard reagents

Conformation of ketone **1** — A knowledge of the conformation of **1** may be of value for rationalizing the characteristics of its addition reactions One proposal[1] favored the $^{0}S_{3}$ conformation, whereas a second possibility considered[4] was the $^{3}S_{0}$ conformation Inspection of molecular models suggested that the 5- and 6,6′-protons of the former would be spatially related by dihedral angles of ~160° and ~40°, and hence, associated[6] with ^{3}J values of ~8 Hz and ~5 Hz, respectively

In the $^3S_0$ conformation, by contrast, both dihedral angles (~70° and ~50°) should give rise to couplings of <5 Hz As the values observed are 2 0 and 0 7 Hz, the $^3S_0$ conformation **11** is the more probable Other information given by the p m r spectrum of **1** also supports this likelihood, and confirms the formulation of Tipson and co-workers[4] That is, a comparison of the chemical shifts of H-1 and H-1′ with those of structurally related *O*-isopropylidene compounds derived from D-psicose and D-fructose (11 compounds in all[7]), showed that H-1 of **1** is unusually strongly deshielded for compound **1**, δ 4 60 (H-1), 3 97 (H-1′), $\delta\Delta$ (0 63), for related compounds[7], δ 4 14–4 46 (H-1), 3 88–4 10 (H-1′), $\Delta\delta$ (0 19–0 47) This may be attributed



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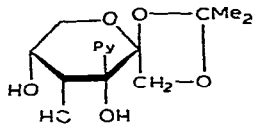

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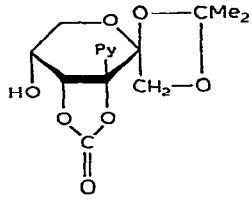

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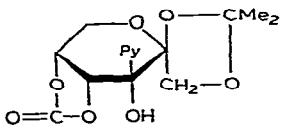

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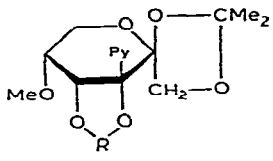
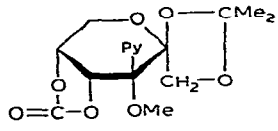


16 (R = C=O)
20(R = H , H)



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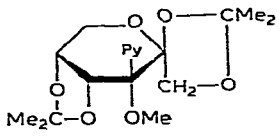

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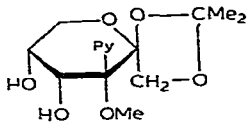

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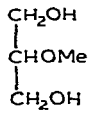

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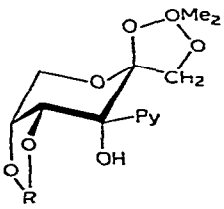
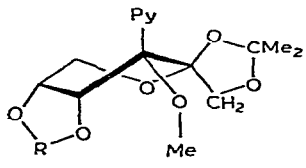


22
(R = CMe2 or C=O)



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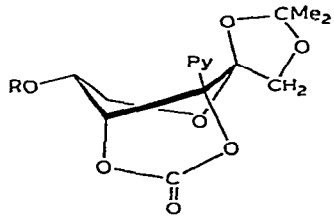
(R = CMe2 or C=O)



24
(R = H or Me)

to a diamagnetic anisotropy contribution by the carbonyl group, because inspection of molecular models suggested that, in conformation **11**, H-1 is positioned relatively close to the deshielding region[8] of the C=O bond

Configuration of tertiary alcohols **4**, **5**, *and* **6** — As already noted, reduction of ketone **1** with hydride exclusively affords[4] the D-*ribo* derivative (**2**) For this reason, the $^{o}S_3$ conformation was proposed[1] for **1**, because it appears to be consistent with a facile approach of hydride towards C-3 from "*above*" the plane of the ring However, inspection of a molecular model suggested that, for the $^{3}S_0$ conformation **11**, an incoming nucleophile could have access to C-3 about equally as well from below (*quasi*-equatorially) as from above (*quasi*-axially) Hence, the configuration of the adducts in these various reactions may be determined more by a "product-development control" than by the ease of approach of the nucleophiles Whichever the reason, the experimental evidence available shows that addition products **3**–**5** are configurationally related to **2**

Information about the configuration of C-3 of the *C*-ethynyl derivative **5** was obtained by ^{13}C-n m r spectroscopy, measurements of ^{13}C–^{1}H coupling in the product obtained by selective hydrolysis of the 4,5-*O*-isopropylidene group of **5** indicated[10] that this product is 3-*C*-ethynyl-1,2-*O*-isopropylidene-β-D-psicopyranose (**12**) The coupling between C-6 and H-4 of **12** is <2 Hz, consistent with a *gauche* relationship between the nuclei, and hence, with the $^{1}C_4$(D) conformation shown, these nuclei would be *antiperiplanar* in the alternative conformation, giving rise to a $^{3}J_{C-H}$ value of, perhaps, >5 Hz Analogously, the absence of appreciable coupling[10] between C-3′ and H-4 places these nuclei in a *gauche* relationship as well, requiring that the ethynyl group be equatorially attached, as in **12** On this basis, the parent diacetal derivative **5** may be designated a D-*ribo*, rather than a D-*arabino*, epimer

Largely because of signal overlap, comparable ^{13}C–^{1}H data were not obtained for the *C*-(pyridin-2-yl) derivative **3**, nor for its selective-hydrolysis product corresponding to **12**, *i e* , **13** However, the chemical shifts of most of the carbon atoms

TABLE I

^{13}C CHEMICAL-SHIFTS FOR TERTIARY ALCOHOLS **3**, **4**, AND **5**[a]

	Aryl-C	*1,2-IpC*[b]	*4,5-IpC*	*C-2*	*C-4*	*C-3*	*C-1*	*C-5*	*C-6*	*Ip-CH*$_3$
3	157 8, 147 3, 136 5 123 0, 122 9	113 0	109 2	106 8	76 0	73 3	72 5	71 6	60 0	26 5, 26 0 25 8(2)
4	158 7, 148 0, 136 6 124 8, 121 5	111 9	108 8	107 0	75 9	72 5	72 1	71 5	60 0[c]	26 5, 25 9 25 7(2)
5	—	113 7	110 0	105 8[d]	76 7	73 6	71 3	69 7	60 4	27 2, 26 6 26 4, 25 8

[a]In p p m from tetramethylsilane (solvent, $CDCl_3$) Signal assignments are based on reference to appropriate, model compounds, and on signal multiplicities in ^{1}H-coupled spectra [b]Ip = isopropylidene [c]α-CH_2, 41 6 [d]C-3^{1}, 83 4, C-3^{2}, 73 8

of **3** are closely similar to those of **5**, as well as those of **4** (see Table I), which implies a strong stereochemical kinship between all three adducts Furthermore, definitive information in support of a D-*ribo* assignment for **3** was obtained from chemical evidence involving the preparation of cyclic carbonate derivatives of triol **13**

Treatment of **13** with phosgene in pyridine (in dilute solution, to minimize dimer formation), afforded a mixture of the 3,4- and 4,5-cyclic carbonates (**14** and **15**) as the main products These proved to be difficult to purify by chromatography, although their methyl ethers (**16** and **17**) were cleanly separated by fractional recrystallization, in the ratio of 1 9 The great preponderance of the 4,5-carbonate (**15** or **17**) may be attributed only partially to a relatively low reactivity of the tertiary 3-hydroxyl group in **13**, because, in the reaction of phosgene with 1,2-*O*-isopropylidene-*β*-D-psicopyranose (in which H replaces the pyridin-2-yl group of **13**), a 1 4 ratio of 3,4- 4,5-carbonate is obtained[7] Ether **17** was characterized as being a 3-*O*-methyl derivative through its synthesis by an unambiguous route· methylation of di-*O*-isopropylidene derivative **3** gave **18**, converted into **19** by acid hydrolysis of the 4,5-*O*-isopropylidene group, and then **19** was allowed to react with phosgene The location of the *O*-methyl group in **16** was checked in the following way removal of the carbonate group with sodium methoxide gave a diol (**20**) that was oxidizable with periodate*, borohydride reduction of the resulting dialdehyde, followed by hydrolysis, afforded 2-*O*-methylglycerol (**21**) This result showed that **16** is a 5-*O*-methyl derivative, and hence, that the cyclic carbonate structure is located** at O-3 and O-4 The structure of **16** revealed by p m r spectroscopy is also consistent with this formulation Therefore, these findings establish that OH-3 and OH-4 of triol **13** are[1] *cis*, and that **3** and the other *C*-(pyridin-2-yl) derivatives belong to the D-*ribo* series

Conformations of the tertiary alcohol derivatives — According to the ^{13}C–^{1}H coupling evidence cited, 3-*C*-ethynyl-1,2-*O*-isopropylidene-*β*-D-psicopyranose (**12**) assumes the $^{1}C_{4}$(D) conformation Comparable information was not accessible for the parent derivative (**5**) bearing a 4,5-*O*-isopropylidene group, nor for the analogous pyridin-2-yl diacetal (**3**) However, some n m r.-spectral characteristics of **4** suggest that derivatives of this type adopt a conformation (**22**) that approximates $^{1}C_{4}$(D) For example, the 5- and 6,6′-protons of **3** are weakly coupled, exhibiting spacings of 3 2 and 0 8 Hz, the same couplings hold for the 4,5-carbonate analog **15** (see Table II) This is consistent with the *gauche* relationship between H-5, H-6, and H-6′ required by structure **22**, whereas the alternative conformation should entail a coupling of >5–6 Hz, because H-5 would then be *antiperiplanar* to one H-6 Nevertheless, $J_{4,5}$ is relatively large (6 0 Hz, the value for **15** is 6 5 Hz), implying[6] that the angle between the C-4–H-4 and C-5–H-5 bonds is <60°, and hence, that the ring

*As expected for a reaction involving a tertiary hydroxyl group, the periodate cleavage of **21** was slow, requiring 4 days for completion

Attempts to isomerize **3 in acetone–HCl in order to obtain a 3,4-*O*-isopropylidene derivative, under conditions that rapidly isomerize[7] **2** into 1,2 3,4-di-*O*-isopropylidene-*β*-D-psicofuranose, were unsuccessful

TABLE II

^{1}H-N M R AND ROTATORY DATA[a] FOR TERTIARY ALCOHOLS **4**, **15**, AND RELATED COMPOUNDS

Compound	*Spacings (Hz)*					*Chemical shifts (δ)*			M_D
	1,1′	*4,5*	*5,6*	*5,6′*	*6,6′*	*H-1*	*H-1′*	*Ip-CH$_3$*	
3	9 3	6 0	3 2	0 8	13 5	4 03	3 64	1 62, 1 49	−634
								1 35, 1 12	
15	9 5	6 5	0 8	3 2	14 5	3 99	3 54	1 40, 1 14	−610
13	9 5	~2	~2	~2	11 0	3 85	3 62	1 42 1 04	−502[b]
4	9 4	—	—[c]	—	—	4 37	4 05	1 57, 1 41	−165
								1 49, 1 20	
5	9 2	—	—[c]	—	—	4 47	4 09	1 64, 1 54	−497
								1 49, 1 44	
6	9 5	—	—[c]	—	—	4 31	3 95	1 57, 1 48	−404
								1 42, 1 35	
2	9 2	6 5	2 0	1 1	13 2	4 25	4 05	1 56, 1 50	−328
								1 41, 1 38	
18	9 5	~7	3 6	3 6	13 0	4 82	4 15	1 58, 1 46	+66
								1 44, 1 44	
17	9 7	8 0	1 7	1 0	13 5	4 90	3 98	1 39 1 39	+8
14	9 8	3 0	6 5	8 2	11 0	4 41	4 15	1 44, 0 60	−362
16	9 7	2 5	6 7	9 0	10 0	4 35	4 09	1 43, 0 60	−452

[a]$CDCl_3$ was the solvent for the measurement of chemical shifts and optical rotations, in some instances, spacings were measured with acetone-d_6 or $CDCl_3$–C_6D_6 as the solvent [b]Solvent, acetone [c]Signals for H-4 to H-6′ overlapped heavily

is somewhat more flattened in this region than is indicated by formula **22** The coupling-constant data for 1,2 4,5 di-*O*-isopropylidene-β-D-psicopyranose (**2**) (see Table II) are close to those for **3** and **15**, which led to similar conclusions[3] about the conformation of **2** Consistent with these possibilities is the fact that **13**, which does not bear a fused 4,5-ring, exhibits a small value of $J_{4,5}$, as well as other small, vicinal couplings (see Table II), an indication that the C–H bonds at C-4, 5, and 6 are all staggered, and hence, that the conformation of **13** is closer to the ideal $^1C_4$(D) than is that of the tricyclic compounds

In helping to define the shape of that moiety of the ring constituted of O-5, C-2, and C-3, reference is made to "anomalies" in the chemical shifts of some protons of **3** and related compounds On comparing the values of δ for the pyridin-2-yl derivatives **3**, **15**, and **13** with those of **2** and the ethynyl and 2-oxopropyl derivatives **5** and **6** (see Table II), it was found that the protons of one CH_3 of each of the former group of compounds are particularly strongly shielded (δ 1 04, 1 12, and 1 14 *vs* δ 1 38, 1 35, and 1 44), the data for **15** and **13** show that this "atypical" CH_3 is located on the 1,2-acetal ring Similarly, one proton (H-1′) of the 1-methylene group of **3**, **15**, or **13** resonated[5] well upfield of the 1-methylene protons of **2**, **5**, and **6**

(see Table II)* According to a molecular model of **22**, the *endo* (1,2) CH_3 group is located one (or two) bond length(s) from the shielding, anisotropic zone of the aromatic ring, and the *endo* H-1 is also directed towards this region (Indeed, free rotation of the aryl substituent appears to be restrained by this CH_3 and the 1-methylene group) Hence, the large, upfield shift experienced by the protons of one CH_3 group and H-1′ is consistent with the orientations of the 1-, 2-, and 3-substituents depicted for **3** and **15** in conformational formula **22****.

Other data, for methyl ethers **17** and **18**, reinforce the foregoing proposals. That is, the introduction of the ether substituent removes the evidence of enhanced shielding, so that all of the *O*-isopropylidene ^1H signals are now more closely grouped together in the spectrum, as for compounds **2**, **5**, and **6** (see Table II) This is taken to indicate that **17** and **18** adopt a conformation differing from that of **3** and **15**, such that the pyridin-2-yl ring in the former compounds no longer shields an *O*-isopropylidene CH_3 group Additionally, small differences are observed (see Table II) for the C-4, C-5, and C-6 segments of the molecules spacings for the 5, 6, and 6′ protons are small, which again corresponds to two *gauche* relationships between these protons, whereas the large magnitude of $J_{4,5}$ indicates that the C–H bonds of C-4 and C-5 are almost eclipsed Overall, these effects suggest a more skewed conformation, possibly the $^3S_0$ (**23**), for **17** and **18** than for **3** and **15**

There are other striking differences between the tertiary alcohols and their *O*-methyl derivatives The alcohols (**3** and **15**) have large, negative specific rotations, whereas the values for the corresponding ethers are slightly positive (see Table II) These drastic differences in optical properties must be due to conformational changes introduced on methylation This step would, for example, cause interference with any intramolecular hydrogen-bonding by the hydroxyl group of **3** (or **15**), and could thereby lead to a change in conformation However, no analogous effects are observed[7] when the hydroxyl group is secondary, *i e*, on comparing 1,2 4,5-di-*O*-isopropylidene-β-D-psicopyranose (**2**) with its 3-methyl ether A more probable cause of conformational change is relief of steric compression inspection of molecular models suggested that, were **17** and **18** in the $^1C_4$(D) conformation **22**, the OCH_3 group would be highly crowded, and that this crowding could be relieved by a slight twisting of the ring into, *e g*., the $^3S_0$ conformation

Data for the 3,4-carbonate derivative **14** and its methyl ether (**16**) (see Table II) show that the conformation of these compounds is distinctly different from those of 4,5-substituted derivatives The large H-5,H-6 and H-5,H-6′ couplings indicate that the C-4, C-5, C-6 segment of the ring is inverted with respect to **22** and **23**.

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*Examination of the chemical shifts of all of the 1-methylene protons listed in Table II suggested that the *exo*-H has a chemical shift of ~4 0 p p m (designated H-1 for **3**, **15**, and **13**, and H-1′ for the other compounds) This implies that the *endo*-H of **3**, **15**, and **13** may experience "extra" shielding of >0 6–0 7 p p m

Data for the 3-*C*-(pyridin-2-ylmethyl) derivative **4 (see Table II), suggest that the aromatic ring in this compound is so positioned as to induce shielding of the *endo* (1,2) CH_3 protons (δ 1 20), but is remote from the 1-methylene group, because the chemical shifts of H-1 and H-1′ are not atypical

Furthermore, one of the *O*-isopropylidene CH_3 groups exhibits even stronger shielding than in the examples (**3**, etc.) already cited, which suggests that this group and the pyridin-2-yl ring are correspondingly closer in space. According to molecular models, these characteristics are consistent in general with a conformation such as $^5S_0$ (**24**). It is also worth noting that, in this instance, the OCH_3 substituent (of **16**), being remote from possible centers of crowding, has no effect on the conformation of the compound, as evidenced by the close similarities in the p.m.r. and rotatory data for **14** and **16**.

EXPERIMENTAL

General methods — ^{1}H-N.m.r. spectra were recorded with a Varian HA-100 spectrometer. ^{13}C-N.m.r. spectra were recorded at 22.63 MHz with a Bruker WH-90 FT spectrometer. Chemical shifts (δ) are given with reference to tetramethylsilane. I.r. spectra were recorded with a Unicam SP-200G 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 1:1 benzene–ether. G.l.c. was performed with a Hewlett–Packard 402 instrument, using a column of 4% of silicone gum rubber UCW 98 on Chromosorb W. Solutions were usually evaporated below 40° under diminished pressure.

*1,2:4,5-Di-O-isopropylidene-β-*D-erythro-*2,3-hexodiulo-2,6-pyranose* (**1**) — This compound was prepared by oxidation of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose, as previously described[5], m.p. 101–102°, $[\alpha]_D$ −108° (*c* 1, ethanol), lit.[4] m.p. 102–103°, $[\alpha]_D^{25}$ −113.5° (*c* 1.0, ethanol).

*1,2:4,5-Di-O-isopropylidene-3-*C-*(pyridin-2-yl)-β-*D-*psicopyranose* (**3**) — (*In this and all subsequent addition-reactions, all glassware was dried at 120°, and anhydrous solvents were used.*) Following the procedure of Gilman and Spatz[12], a solution of 2-bromopyridine (1 ml, 10 mmol) in ether (5 ml) was slowly added, with stirring, to a 2.35M solution of butyllithium (4.25 ml, 10 mmol) in ether (20 ml) cooled in a Dry Ice–acetone bath, a deep brown-red color developed. Twenty minutes later, a solution of diketone **1** (2.6 g, 10 mmol) in ether (20 ml) was introduced slowly, and after an additional 1 h, the temperature was raised to room temperature. Water-saturated ether (50 ml) was added, the solution was poured onto ice, and the aqueous layer was extracted 4 times with ether. The extracts were combined, washed with water, dried (anhydrous sodium sulfate), and evaporated, affording a crystalline residue (2.5 g, 75%) which was recrystallized from hexane, m.p. 157–159°, $[\alpha]_D$ −188° (*c* 0.8 chloroform), ν_{max} 3290, 1590, and 755 cm^{-1} (s), 1590, 1150, and 1112 cm^{-1} (w), ^{1}H-n.m.r. data ($CDCl_3$) δ 8.57, 7.74, 7.28 (m, 4 H, aryl-H), 5.43 (s, 1 H, OH), 4.91 (d, 1 H, H-4), 4.36 (m, 1 H, H-5), 4.29 (q, 1 H, H-6), 4.10 (q, 1 H, H-6'), 4.03 (d, 1 H, H-1), 3.64 (d, 1 H, H-1'), and 1.6–1.1 (4 s, 12 H, 4 CH_3). (acetone-d_6) $J_{1,1'}$ 9.2, $J_{4,5}$ 6.0, $J_{5,6}$ 3.2, $J_{5,6'}$ 0.8, and $J_{6,6'}$ 13.5 Hz. ^{13}C-N.m.r. data are given in Table II.

Anal Calc for $C_{17}H_{23}NO_6$ C, 60 5, H, 6 9. Found C, 60 4; H, 6 9

1,2 4,5-Di-O-isopropylidene-3-C-(pyridin-2-ylmethyl)-β-D-psicopyranose (**4**) — Bromobenzene (3 14 g, 20 mmol) was added to a stirred suspension of lithium turnings (0 28 g, 40 mmol) in ether (20 ml) at such a rate that the ether refluxed gently, followed, after 1 h, by the addition of 2-picoline (1 86 g, 20 mmol) (procedure of Woodward and Kornfeld[13]) The deep red-brown solution formed was cooled to 0°, a solution of diketone **1** (2 6 g, 10 mmol) in ether (20 ml) was introduced slowly, the temperature was raised to room temperature and the mixture was poured onto ice Ether extraction followed by evaporation afforded a brown syrup (2 9 g, 82%) that crystallized slowly in the cold The product was decolorized with charcoal–Celite and, after successive recrystallization from hexane and ethanol, had m p 101 5–102 0°, $[\alpha]_D$ −47° (*c* 0 94, chloroform), ^{1}H-n m r data ($CDCl_3$) δ 8 43, 7 61, 7 18 (m, 4 H, aryl-H), 4 31 (d, 1 H, H-1), 4 05 (d, 1 H, H-1′), 4 3–4 1 (m, 6 H, H-4,5,6,6′, CH_2), and 1 57–1 20 (4 s, 12 H, 4 CH_3) ^{13}C-N m r data are presented in Table II

Anal Calc for $C_{18}H_{25}NO_6$ C, 61 5, H, 7 2 Found C, 61 8, H, 7 0

3-C-Ethynyl-1,2 4,5-di-O-isopropylidene-β-D-psicopyranose (**5**) — A solution of diketone **1** (5 16 g, 20 mmol) in ether (40 ml) was added dropwise to a stirred slurry of 1 1 lithium acetylide–ethylenediamine complex[14] in ether (25 ml) at 0°, accompanied by a slow stream of acetylene led into the mixture After 1 h, the brown mixture was poured onto ice, additional ether was added, and the organic layer was evaporated The residual syrup (4 49 g, 79%) was found by t l c to contain a major component, four minor ones, and traces of others A portion of the syrup (4 20 g) was chromatographed on a column (3 cm × 60 cm) of Silica Gel G with 1 1 benzene–ether as the eluant, to afford crystalline **5** (2 99 g, 52%), m p , after recrystallization from hexane, 132 5–133°, $[\alpha]_D$ −175° (*c* 1 23, chloroform), ν_{max} 3510 (broad), 3270 (sharp, s), and 2110 (sharp, m) cm^{-1}, ^{1}H-n m r data ($CDCl_3$) δ 4 47 (d, 1 H, H-1), 4 09 (d, 1 H, H-1′), 4 5–4 1 (broad m, 4 H, H-4,5,6,6′), 2 35 (s, 1 H, ethynyl-H), and 1 64–1 44 (4 s, 12 H, 4 CH_3) ^{13}C-N m r data are given in Table II

Anal Calc for $C_{14}H_{20}O_6$ C, 59 1, H, 7 1 Found C, 59 0, H, 7 5

*5-Deoxy-3-C-ethynyl-1,2-O-isopropylidene-β-*D-glycero*-2,4-heptodiulo-2,6-pyranose* (**7**) — The title compound was eluted from the column (preceding paragraph) as a second fraction of crystalline material (0 2 g, 4 3%, this yield may have been low, because the compound was observed to sublime at an appreciable rate *in vacuo* at room temperature), m p , after recrystallization from 2-propanol, 108 5–109°, $[\alpha]_D$ +41 5° (*c* 0 70, chloroform), ν_{max} 3230 (s), 2110 (m, sharp), and 1730 (s) cm^{-1}, ^{1}H-n m r data ($CDCl_3$) δ 4 42 (d, 1 H, H-1′), 4 22 (d, 1 H, H-1′), 4 07 (s, 1 H, OH), 3.93 (o, 1 H, H-6′), 3 78 (o, 1 H, H-6), 3 14 (o, 1 H, H-5), 2 20 (o, 1 H, H-5′), and 2 59 (s, 1 H, ethynyl-H)

Anal Calc for $C_{11}H_{14}O_5$ C, 58 4, H, 6 2 Found C, 58 8, H, 6 5

1,2 4,5-Di-O-isopropylidene-3-C-(2-propyl)-β-D-psicopyranose (**6**) — To butyllithium (2 4 ml of a 2 35M solution in hexane, 5 6 mmol) in ether (15 ml) cooled with Dry Ice–acetone, was added a solution of diketone **1** (1 3 g, 5 mmol) in ether (10 ml) during 1 h. The temperature was brought to room temperature, water-

saturated ether (25 ml) was introduced, followed by ice, and the organic layer was separated, and evaporated The syrupy residue, shown by t l c to be a complex mixture of products, was chromatographed on a column of Silica Gel G with 1 1 benzene–ether as the eluant One fraction crystallized (yield, 0 09 g, 5%), and this material, after recrystallization from hexane, had m p 111 5–112°, $[\alpha]_D$ −128° (*c* 1 0, chloroform), ν_{max} 3485 (broad) and 1705 (s) cm^{-1}, ^{1}H-n m r data ($CDCl_3$) δ 4 31 (d, 1 H, H-1), 3 95 (d, 1 H, H-1′), 4 2–4 0 (m, 4 H, H-4,5,6,6′), 2 56 (s, 2 H, CH_2), 2 32 (s, 3 H, CH_3), and 1 57–1 35 (4 s, 12 H, 4 CH_3)

Anal Calc for $C_{15}H_{24}O_7$ C, 57 0, H, 7 7 Found C, 56 5, H, 7 4

1,2 4,5-Di-O-isopropylidene-3-O-methyl-3-C-(pyridin-2-yl)-β-D-psicopyranose (**18**) — A mixture of **3** (1 5 g), methyl iodide (15 ml), silver oxide (4 g), and molecular sieves (1 g) was shaken in the dark for 10 days The solids were filtered off, and washed with chloroform, and the filtrate and washings were combined, and evaporated to a syrup (1.4 g, 90%), $[\alpha]_D$ +19 3° (*c* 0 86, chloroform), ^{1}H-n m r data ($CDCl_3$) δ 8 44, 7 66, 7 18 (m, 4 H, aryl H), 5 0 (m, 2 H, H-4,5), 4 82 (d, 1 H, H-1), 4 15 (d, 1 H, H-1′), 3 90 (q, 1 H, H-6), 3 59 (q, 1 H, H-6′), 3 15 (s, 3 H, OCH_3), and 1 58–1 44 (4 s, 12 H, 4 CH_3), (acetone-d_6) $J_{1,1}$ 9 5, $J_{4,5}$ ~7, $J_{5,6}$ 3 6, $J_{5,6}$ 3 6, and $J_{6,6}$ 13 0 Hz, ^{13}C-n m r data δ 25 6, 26 2, 26 4, 26 7 (4 C, 4 CH_3), 63 8 (C-6), 72 2 (C-5), 73 5 (C-1), 74 0 (C-4), 80 0 (C-3), 106 2 (C-2), 108 5 (4,5-isopropylidene C), 109 8 (1,2-isopropylidene C), and 158–122 (5 C, aryl)

1,2-O-Isopropylidene-3-O-methyl-3-C-(pyridin-2-yl)-β-D-psicopyranose (**19**) — A solution of compound **18** (1 g) in 80% acetic acid (100 ml) was kept for 5 h at room temperature, and evaporated, affording a solid residue, to which ethanol and ethyl acetate were successively added and evaporated off On recrystallization from ethanol, the product (0 62 g, 70%) had m p 136–137 5°, $[\alpha]_D$ −98° (*c* 1 43, acetone), ^{1}H-n m r data (acetone-d_6) δ 8 61, 7 74, 7 28 (m 4 H, aryl-H), 4 98 (d, 1 H, H-4), 4 67 (d, 1 H, H-1), 4 09 (q, 1 H, H-6), 3 92 (m, 1 H, H-5), 3 88 (d, 1 H, H-1′), 3 75 (q, 1 H, H-6′), 3 54 (s, 3 H, OCH_3), 1 30 (s, 3 H, CH_3), and 0 60 (s, 3 H, CH_3) $J_{1,1}$ 9 2, $J_{4,5}$ 3 0, $J_{5,6}$ 1 8, $J_{5,6}$ 2 3, and $J_{6,6}$ 11 5 Hz

Anal Calc for $C_{15}H_{21}NO_6$ C, 57 9. H, 6 8. N, 4 5 Found C, 58 0, H, 6 9, N, 4 4

4,5-O-Carbonyl-1,2 4,5-di-O-isopropylidene-3-O-methyl-3-C-(pyridin-2-yl)-β-D-psicopyranose (**17**) — To a stirred solution of **19** (0 5 g) in pyridine (3 ml) and benzene (10 ml) at 0° was added phosgene in benzene (12%, w/w) during 5 min After 15 min at room temperature, chloroform was introduced, and the solution was washed successively with cold 10% HCl, saturated sodium hydrogencarbonate, and water, dried (anhydrous sodium sulfate), and evaporated, affording crystals (4 2 g, 78%) which were recrystallized from ethyl acetate–hexane, m p 177–182° (dec), $[\alpha]_D$ +1 7° (*c* 0 85, chloroform), ν_{max} 1815 cm^{-1} (s, broad), ^{1}H-n m r data ($CDCl_3$) δ 8 44, 7 64, 7 26 (m, 4 H, aryl-H), 5 62 (d, 1 H, H-4), 5 33 (o, 1 H, H-5), 4 90 (d, 1 H, H-1), 3 98 (d, 1 H, H-1′), 3 95 (q, 1 H, H-6′), 3 15 (s, 3 H, OCH_3), and 1 39 (s, 6 H, 2 CH_3), (acetone-d_6) $J_{1,1}$ 9 7, $J_{4,5}$ 8 0, $J_{5,6}$ 1 7, $J_{5,6}$ 1 0, and $J_{6,6}$ 13 5 Hz

Anal. Calc for $C_{16}H_{19}NO_7$ C, 57 0, H, 5 7, N, 4 2 Found C, 56 7, H, 5 9, N, 3 9.

1,2-O-Isopropylidene-3-C-(pyridin-2-yl)-β-D-psicopyranose (**13**) — Partial hydrolysis of **4** in 80% acetic acid for 5 h at room temperature, as for **19**, afforded a solid that was recrystallized from ethanol (yield, 1 41 g, 80%), m p 130–131°, $[\alpha]_D$ −169° (*c* 1 08, acetone), ^{1}H-n m r data (acetone-d_6), δ 8 52, 7 78, 7 32 (m, 4 H, aryl-H), 4 24 (m, 1 H, H-5), 4 11 (m, 1 H, H-4), 3 95 (m, 1 H, H-6), 3 85 (d, 1 H, H-1), 3 75 (m, 1 H, H-6′), 3 62 (d, 1 H, H-1′), 1 42 (s, 3 H, CH_3), and 1 04 (s, 3 H, CH_3); $J_{1\ 1}$ 9 5, $J_{4\ 5}$ ~2, $J_{5\ 6}$ ~2, $J_{5\ 6}$ ~2, and $J_{6\ 6}$ 11 0 Hz

Anal Calc for $C_{14}H_{19}NO_6$ N, 4 7 Found N, 4 3 Calc for tri-*O*-(trimethylsilyl) derivative ($C_{23}H_{46}NO_6Si_3$) mol wt, 513 Found· M^+, 513

4,5-O-Carbonyl-1,2-O-isopropylidene-3-C-(pyridin-2-yl)-β-D-psicopyranose (**15**) — The monoacetal **13** (3 g) was treated with 1 2 molar proportions of phosgene as described for **17**, yielding a syrupy product (2 75 g) T l c analysis (solvent, 1 1 benzene–ether) showed the presence of a major product (R_F 0 25), a minor product (R_F 0 32), and several slower-moving, minor components Chromatography of the mixture on a column of Silica Gel G (eluant, 1 1 benzene–ether) afforded crystalline **15** (2 09 g) from one fraction M p, after several recrystallizations from ethyl acetate–hexane, 176 5–177°, $[\alpha]_D$ −189° (*c* 1 13, chloroform), ν_{max} 3480 (br) and 1850 cm^{-1} (s, br), ^{1}H-n m r data ($CDCl_3$–benzene-d_6) δ 8 6–7 3 (m, 4 H, aryl H), 4 87 (d, 1 H, H-4), 4 35 (o, 1 H, H-5), 4 21 (q, 1 H, H-6), 3 99 (d, 1 H, H-1), 3 90 (q, 1 H, H-6′), 3 54 (d, 1 H, H-1′), 1 40 (s, 3 H, CH_3), 1 14 (s, 3 H, CH_3), $CDCl_3$–C_6D_6)· $J_{1\ 1'}$ 9 5, $J_{4\ 5}$ 6 5, $J_{5,6}$ 0 8, $J_{5,6}$ 3 0, and $J_{6,6}$ 14 5 Hz

Anal * Calc for $C_{15}H_{17}NO_7$ C, 55 7, H, 5 3, N, 4 3 Found C, 55 0, H, 4 8, N, 4 0 Calc for *O*-trimethylsilyl derivative ($C_{18}H_{26}NO_7Si$) mol wt, 395 Found M^+, 395

3,4-O-Carbonyl-1,2-O-isopropylidene-3-C-(pyridin-2-yl)-β-D-psicopyranose (**14**) — The other fractions eluted (previous paragraph) were combined, and rechromatographed, yielding a second crop of **15** (0 69 g), and a fraction (0 19 g) consisting of crystalline **14**, after several recrystallizations from ethyl acetate–hexane, the latter had m p 244–257° (dec), $[\alpha]_D$ −112° (*c* 0 62, chloroform), ν_{max} 3450 (s, br) and 1830 cm^{-1} (s, br), ^{1}H-n m r data ($CDCl_3$) δ 8 67, 7 76, 7 36 (m, 4 H, aryl-H), 5 81 (o, 1 H, H-5), 5 69 (d, 1 H, H-4), 4 41 (d, 1 H, H-1), 4 41 (q, 1 H, H-6), 4 15 (d, 1 H, H-1′), 4 06 (q, 1 H, H-6′), 1 44 (s, 3 H, CH_3), and 0 60 (s, 3 H, CH_3), $J_{1\ 1'}$ 9 8, $J_{4\ 5}$ 3 0, $J_{5\ 6}$ 6 5, $J_{5\ 6}$ 8 2, and $J_{6\ 6}$ 11 0 Hz

Anal * Calc for $C_{15}H_{17}NO_7$ C, 55 7, H, 5 3, N, 4 3. Found C, 54 9, H, 5 2, N, 4 3 Calc for *O*-trimethylsilyl derivative ($C_{18}H_{26}NO_7Si$) mol wt, 395 Found M^+, 395

4,5-O-Carbonyl-1,2-O-isopropylidene-3-O-methyl-3-C-(pyridin-2-yl)-β-D-psico-

*The values of %C for **15** and **14** were unsatisfactory, despite repeated recrystallization However, the compounds were pure according to t l c and ^{1}H-n m r spectroscopy, and their *O*-methyl derivatives (**17** and **16**, respectively) gave satisfactory elemental analyses (see later)

pyranose (**17**) — Methylation of **15** (0 46 g), as for **18**, afforded a crystalline product (0 43 g, 90%), indistinguishable from methyl ether **17** obtained from **19**

3,4-O-Carbonyl-1,2-O-isopropylidene-5-O-methyl-3-C-(pyridin-2-yl)-β-D-psico-pyranose (**16**) — Carbonate **14** (0 1 g) was methylated as described for **18**, giving 0 09 g (87%) of crystalline **16**, recrystallized from ethyl acetate–hexane, it had m p 111.5–112 5°, $[\alpha]_D$ −133 7° (*c* 0 89, chloroform), ν_{max} 1815 cm^{-1} (s, br), ^{1}H-n m r data ($CDCl_3$) δ 8 64, 7 78, 7 32 (m, 4 H, aryl-H), 5 57 (d, 1 H, H-4), 4 43 (o, 1 H, H-5), 4 35 (d, 1 H, H-1), 4 22 (q, 1 H, H-6), 4 09 (d, 1 H, H-1′), 3 89 (q, 1 H, H-6′), 3 55 (s, 3 H, OCH_3), 1 43 (s, 3 H, CH_3), and 0 60 (s, 3 H, CH_3); $J_{1\,1}$ 9.7, $J_{4\,5}$ 2 5, $J_{5,6}$ 6 7, $J_{5,6}$ 9 0, and $J_{6\,6}$ 10 0 Hz

Anal Calc for $C_{16}H_{19}NO_7$ C, 57 0, H, 5 7, N, 4 2 Found C, 57 1, H, 5 9, N, 4 0

Preparation of **16** *and* **17** *from* **14** — Compounds **16** and **17** were obtained more readily by methylation of the crude mixture of carbonates prepared from **14** When the mixture (1 g) was methylated with methyl iodide–silver oxide, 0 95 g (91%) of a syrup was obtained that crystallized on standing Recrystallized from ethyl acetate–hexane, the product (0 67 g, 64%) was indistinguishable from **17** The mother liquors were evaporated, affording a second solid product that, on recrystallization from ethyl acetate–hexane, proved to be **16** (yield, 0 07 g, 6 6%)

2-O-Methylglycerol from **17** — A solution of **17** (10 mg) in methanol (2 ml) was treated with an excess of sodium methoxide, followed after 15 min by a mixed-bed, ion-exchange resin, and then evaporated to dryness The crystalline residue was dissolved in 0 1M sodium periodate (1 5 ml), and the solution was kept in the dark for 4 days (oxidation was then almost complete, according to t l c), de-ionized with a mixed-bed, ion-exchange resin, and evaporated Ethanol was introduced, followed by aqueous sodium borohydride, and the solution was diluted with water, acidified with Amberlite IR-120 (H^+) ion-exchange resin, and evaporated A portion of the syrupy residue was acetylated with acetic anhydride–pyridine, and another portion was per(trimethylsilyl)ated, the products of both treatments were analyzed by g l c comparative g l c analysis with the corresponding derivatives prepared from authentic 2-*O*-methylglycerol showed that the latter was present in the degradation products obtained from **17**

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REFERENCES

1 E J McDonald, *Carbohydr Res*, 5 (1967) 106–108
2 K James, A R Tatchell, and P K Ray, *J Chem Soc*, *C*, (1967) 2681–2686

3 G M CREE AND A S PERLIN, *Can J Biochem*, 46 (1968) 765–770.
4 R S TIPSON, R F BRADY, JR, AND B F WEST, *Carbohydr Res*, 16 (1971) 383–393.
5 P. C M HERVE DU PENHOAT AND A S PERLIN, *Carbohydr Res*, 36 (1974) 111–120
6 M KARPLUS, *J Am Chem Soc*, 85 (1963) 2870–2871
7 P C M HERVE DU PENHOAT AND A S PERLIN, *Carbohydr Res*. 71 (1979) 149–167.
8 J A POPLE, *J. Chem Phys*, 37 (1962) 53–59, 60–66
9 W G DAUBEN, G J FONKEN, AND D S NOYCE, *J Am Chem Soc*, 78 (1956) 2579–2582, E L ELIEL, N L ALLINGER, S J. ANGYAL, AND G A MORRISON, *Conformational Analysis*, Interscience, New York, 1967, pp 115–120
10 A S PERLIN, N CYR, R G S RITCHIE, AND A PARFONDRY, *Carbohydr Res*, 37 (1974) c1–c4
11 L HOUGH, J E PRIDDLE, AND R S THEOBALD, *Adv Carbohydr Chem*, 15 (1960) 91–151.
12 H GILMAN AND S M SPATZ, *J Org Chem*, 16 (1951) 1485–1494
13 R B WOODWARD AND E C KORNFELD, *Org Synth Coll Vol*, 3 (1955) 413–415
14 O F BEUMEL, JR, AND R F HARRIS, *J Org Chem*, 28 (1963) 2775–2779