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REACTION OF TETRA-*O*-ACETYL-α-D-HEXOPYRANOSYL BROMIDES WITH SODIUM *p*-NITROPHENOXIDE IN *N,N*-DIMETHYLFORMAMIDE. FORMATION OF *p*-NITROPHENYL 2,3,4,6-TETRA-*O*-ACETYL-β-D-HEXOPYRANOSIDES VERSUS 2,3,4,6-TETRA-*O*-ACETYL-1,5-ANHYDRO-D-HEX-1-ENITOLS

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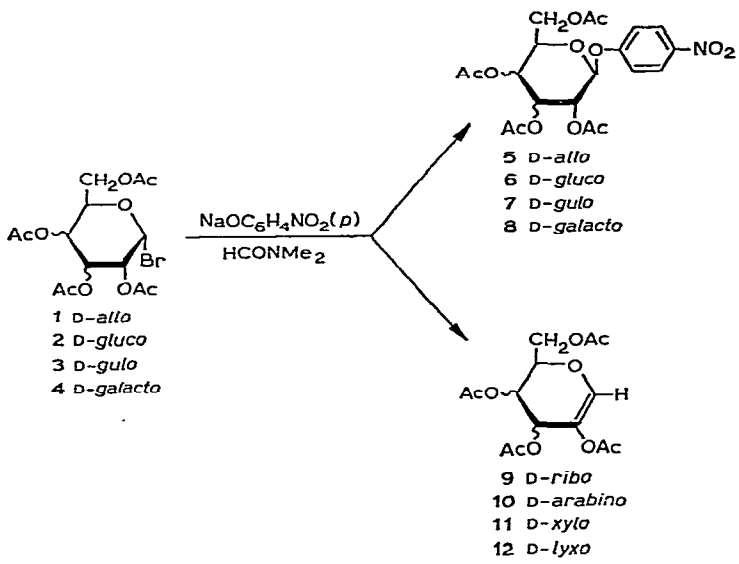
ABSTRACT

The reaction of the four acetylated hexopyranosyl bromides (D-*allo*, D-*gluco*, D-*gulo*, and D-*galacto*) with sodium *p*-nitrophenoxide in *N,N*-dimethylformamide was investigated in order to determine their tendency for displacement at C-1 (to form the *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-hexopyranoside) or β-elimination (to give the 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-hex-1-enitol). The tendency for the formation of tetra-*O*-acetyl-1,5-anhydro-D-hex-1-enitols decreased in the following order: D-*allo* > D-*gulo* ≳ D-*gluco* > D-*galacto*, whereas the preference for the formation of *p*-nitrophenyl tetra-*O*-acetyl-β-D-hexopyranosides was in the reverse order (D-*allo* < D-*gulo* ≲ D-*gluco* < D-*galacto*). The conformations of the four tetra-*O*-acetyl-1,5-anhydro-D-hex-1-enitols (D-*ribo*, D-*arabino*, D-*xylo*, and D-*lyxo*) were determined from their 250-MHz ^{1}H-n.m.r. data; the D-*lyxo* derivative was determined to exist in the H_4^5(D) conformation, whereas the H_5^4(D) conformation was demonstrated for the other three isomers. The yields of the four tetra-*O*-acetyl-1,5-anhydro-D-hex-1-enitols were found to be directly related to factors governing the stability of their conformations.

INTRODUCTION

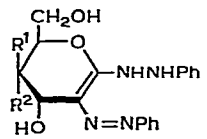
Aryl glycosides are useful for the assay of glycosidases, and hence methods for their synthesis are of considerable interest. Literature methods[1] for stereospecific synthesis of a single one of the two possible anomeric aryl glycopyranosides are limited and they generally lead to 1,2-*trans* glycosides. The *O*-acetylglycosyl halides are usually condensed with phenols in the presence of alkali in aqueous acetone[2–7], or with the salt of the phenol in ethanol[7]. Low yields of the desired acetylated aryl glycosides are frequently encountered[4,6,7] by this procedure, and hence, there is a need for an alternative method for preparation of these derivatives.

When 2,3,4,6-tetra-*O*-acetyl-α-D-allopyranosyl bromide (**1**) was condensed with *p*-nitrophenol in the presence of sodium hydroxide in aqueous acetone, the yield of



p-nitrophenyl tetra-*O*-acetyl-β-D-allopyranoside (**5**) was negligible; furthermore, glycosidation of **1** with *p*-nitrophenol in chloroform–methanol as solvent gave **5** in only 5% yield, the major product (~25% yield) being 3,4,6-tri-*O*-acetyl-D-allopyranose 1,2-(*exo*-methyl orthoacetate)[8]. In the light of these difficulties in the preparation of **5**, the reaction of tetra-*O*-acetyl-D-allopyranosyl bromide (**1**) with sodium *p*-nitrophenoxide in *N*,*N*-dimethylformamide (DMF) appeared to be a possible alternative. In 1968, Zurabyan *et al.* first reported[9] the reaction of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride with potassium or sodium *p*-nitrophenoxide in DMF for the preparation of *p*-nitrophenyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside, isolated in 76% overall yield in two steps from 2-acetamido-2-deoxy-D-glucose; a yield of 50% was reported by Petitou and Sinaÿ[10] for the same conversion. Vafina and coworkers have extended this reaction to the condensation of several other 3,4,6-tri-*O*-acetyl-2-acylamino-[11] and -2-aroylamino-2-deoxy-α-D-glucopyranosyl chlorides[12] with sodium *p*-nitrophenoxide in DMF.

The reaction of acetylated glycosyl halides with sodium *p*-nitrophenoxide in DMF was also of interest because of the possibility of dehydrohalogenation by β-elimination, in view of the reported[13,14] β-elimination from *p*-substituted 2-phenylethyl bromides by this reagent. Although the formation of 3,4,6-tri-*O*-acetyl-2-acyl(aroyl)amino-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitols [2-acyl(aroyl)amino-2-deoxy analogs of **10**] was not noted[9–12] in the reaction of various 3,4,6-tri-*O*-acetyl-2-acyl(aroyl)amino-2-deoxy-α-D-glucopyranosyl chlorides with sodium *p*-nitrophenoxide in DMF, it was considered possible that an acetylated glycosyl bromide might undergo dehydrohalogenation with greater facility than the chloro analog.



17 R^1 = H R^2 = OH
18 R^1 = OH R^2 = H

RESULTS AND DISCUSSION

With the foregoing considerations in mind, 2,3,4,6-tetra-*O*-acetyl-α-D-allopyranosyl bromide[8,15] (**1**) was treated with sodium *p*-nitrophenoxide in DMF at room temperature. T.l.c. indicated 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*ribo*-hex-1-enitol (**9**) as a predominant product; after processing of the mixture, crystalline **9** was isolated in 49.6% yield. The mother liquor was estimated by t.l.c. to contain an additional 11% of **9** and 8% of *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-allopyranoside (**5**). The presence of **5** in the mother liquor was established by comparison (t.l.c.) with authentic[8] **5**.

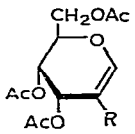
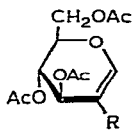
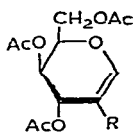
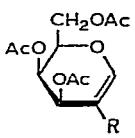
Although the m.p. (105–106°) of **9** prepared in this study was close to that (108–110°) of **9** prepared by Haga and Tejima[15] by reaction of **1** with diethylamine in benzene, there was a large disparity in the specific rotations of **9** prepared by the two methods: Haga and Tejima[15] reported for **9** a specific rotation of −21.8° (chloroform), as compared with our value of +246.9° (chloroform). The latter value is regarded as correct, as the magnitudes of the optical rotations of **9** ($[\alpha]_D$ +246.9°) and its C-3 epimer[16] (**10**, $[\alpha]_D$ −32.0°) accord with the observation[15] made by Haga and Tejima concerning the specific rotations of 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-hex-1-enitols (**13**–**16**), namely, that D-*ribo*-(**13**) and D-*xylo*-hex-1-enitols (**15**) are strongly dextrorotatory as compared with their respective 3-epimers **14** and **16** (Table I). The optical rotations of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*xylo*-hex-1-enitol (**11**) and its 3-epimer[17] (**12**) also conform with this correlation (Table I), as do those[18] of 4,6-*O*-benzylidene-D-glucal (−19°) and -D-allal (+195°) in chloroform. Similarly, the rotations of "dehydro-D-allosazone" (**17**) and "dehydro-D-gulosazone" (**18**) are reported[19] to be +346 and +300° (both in 1:1 pyridine–ethanol), respectively.

While this work was in progress, the preparation of *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**8**) in 43.5% yield by the reaction of **4** with sodium *p*-nitrophenoxide in DMF was reported[22]; no mention was made of the formation of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**12**). In view of the formation of a large amount of **9** *vis-à-vis* the glycoside **5** from the reaction of tetra-*O*-acetyl-D-allopyranosyl bromide (**1**) with sodium *p*-nitrophenoxide in DMF, a closer examination of the reaction with the D-galactose analog (**4**) seemed warranted. Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**2**) and the D-gulose analog (**3**) were also included in the study to determine their preference for β-elimination or substitution at C-1.

The reaction of **4** with sodium *p*-nitrophenoxide in DMF gave a 47.1% yield of crystalline **8**. Chromatography of the mother liquor gave an additional 9.1% of crystalline **8**, and a 7.6% yield of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**12**); the overall yield of **8** was 56.2%. Similarly, 2,3,4,6-tetra-*O*-acetyl-α-D-

TABLE I

OPTICAL ROTATIONS OF 3,4,6-TRI-*O*-ACETYL-1,5-ANHYDRO-2-DEOXY- AND 2,3,4,6-TETRA-*O*-ACETYL-1,5-ANHYDRO-D-HEX-1-ENITOLS

Compound		$[\alpha]_D$ *(Chloroform)*		*Reference*
		R = OAc	*R = H*	
	9	+ 246.9°		*a*
	13	− 21.8°		15
			+ 310.3°	15
	10	− 32.0°		16
	14		− 12.0°	15
	11	+ 191.1°		*a*
	15		+ 248.0°	20
	12	− 3.8°		17
	16		− 16.5°	21

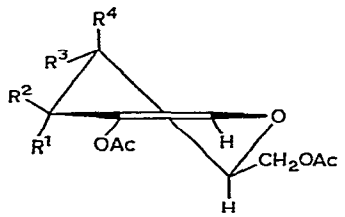
[a]This work.

glucopyranosyl bromide (**2**) gave the crystalline glycoside **6** in 16.7% yield, and the syrupy 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (**10**) in 34.2% yield. *p*-Nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-gulopyranoside (**7**) and 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*xylo*-hex-1-enitol (**11**) were obtained from **3** in 13.8 and 42.4% yields, respectively.

The 250-MHz ^{1}H-n.m.r. data for the four 2-hydroxyglycal peracetates (**9**–**12**) are given in Tables II and III. The chemical shifts and coupling constants of tetra-*O*-acetyl-2-hydroxy-D-glucal (**10**) determined at 250 MHz were similar to those obtained at[23] 60 MHz and[24] 100 MHz, and are consistent with the H_5^4(D) conformation (**20**). The main difference between the spectra of **10** determined here at 250 MHz and those determined at[23] 60 MHz and[24] 100 MHz was the observation here of the H-3 resonance as a sextet (compared to a doublet[23,24]) due to long-range coupling ($J_{1,5}$ 0.5, $J_{3,5}$ 0.9 Hz) with both H-1 and H-5; accordingly, the H-1 signal appeared as a doublet ($J_{1,3}$ 0.5 Hz). The large chemical shift (0.88 p.p.m.) between H-4 and H-5 precludes the possibility of extra splitting of the H-3 resonance of **10** due[25a] to "virtual coupling".

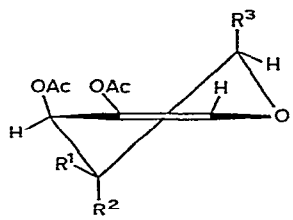
D-Glucal triacetate (**14**), which lacks the vinylic acetoxyl group of **10**, has also been determined[26] to exist in the H_5^4(D) conformation, and in acetone-d_6 shows[27] the long-range coupling of H-3 with H-5 ($J_{3,5}$ 0.7 Hz) and with H-1 ($J_{1,3}$ 1.3 Hz).

The $J_{4,5}$ value of 11.0 Hz for 2-hydroxy-D-allal tetraacetate (**9**) established the diaxial orientation of H-4 and H-5, and hence the H_5^4(D) conformation (**19**) for this derivative; the H-3–H-4 coupling of 4.1 Hz is also commensurate with this conformation. These coupling constants compare favorably with those ($J_{3,4}$ 3, $J_{4,5}$ 10 Hz) of the 3,4,6-tri-*O*-acetyl derivative of "dehydro-D-allosazone" (**17**), which was determined[19] also to exist in the H_5^4(D) conformation.



19 $R^1 = R^3 = OAc$ $R^2 = R^4 = H$
20 $R^1 = R^4 = H$ $R^2 = R^3 = OAc$
21 $R^1 = R^4 = OAc$ $R^2 = R^3 = H$
22 $R^1 = R^3 = H$ $R^2 = R^4 = OAc$

H_5^4 (D) Conformation



23 $R^1 = R^3 = H$ $R^2 = OAc$
24 $R^1 = OAc$ $R^2 = H$ $R^3 = CH_2OAc$

H_4^5 (D) Conformation

The $J_{3,4}$ value of 2.4 Hz is indicative of the *quasi*-equatorial–equatorial orientation of H-3 and H-4 in 2-hydroxygulal peracetate (**11**), and supports assignment of the H_5^4(D) conformation (**21**) to this derivative. In the alternative H_4^5(D) conformation, the allylic proton at C-3 and H-4 of **12** would occupy *quasi*-axial and axial positions, respectively, subtending a dihedral angle of ~150°, which should result in a coupling[28] (~7 Hz) much larger than that observed (2.4 Hz). The disposition of H-3 and H-4 in the H_5^4(D) conformation (**21**) of 2-hydroxygulal tetraacetate (**11**) is identical to that found for 2-hydroxy-D-xylal triacetate (**25**), for which the H_4^5(D) conformation (**23**) has been established[29]; the observed[29] $J_{3,4}$ value of 2.2 Hz for **25** agrees well with the $J_{3,4}$ value of 2.4 Hz for 2-hydroxygulal tetraacetate (**11**), and supports assignment of the H_5^4(D) conformation (**21**) for the latter. Whereas the H-4–axial H-5 coupling in the H_4^5(D) conformation (**23**) of tri-*O*-acetyl-2-hydroxy-D-xylal (**25**) is observed[29] to be 2.2 Hz, the analogous coupling in 2-hydroxygulal tetraacetate (**11**, conformation **21**) is found to be zero. This difference between equatorial H-4–axial H-5 couplings for **11** (conformation **21**) and **25** (conformation **23**) is accounted for by the fact that in the former the rotation about the C-4–C-5 bond, prompted by the *gauche* relationship of the axial 4-acetoxyl group with both the ring-oxygen atom and the equatorial 5-acetoxymethyl group, increases the H-4–H-5 dihedral angle by ~15° (to ~75°), resulting in a decrease in the H-4–axial H-5 coupling constant from[29] 2.2 Hz (for **25**, conformation **23**) to 0 Hz (for **11**, conformation **21**).

The 250-MHz ^{1}H-n.m.r. spectrum of 2-hydroxygalactal tetraacetate (**12**) was

TABLE II

CHEMICAL SHIFTS (τ VALUES) OF 2,3,4,6-TETRA-*O*-ACETYL-1,5-ANHYDRO-D-HEX-1-ENITOLS (**9–12**) AT 250 MHz IN CHLOROFORM-*d* SOLUTION[a]

Compound	*Chemical shifts (τ values)*						
	H-1	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*Acetoxyl*[b]
D-*ribo* (**9**)	3.27(s)	4.28(d)	4.72(q)	5.76(o)	5.62———	5.67(um)	7.87, 7.89, 7.91, 7.97
D-*arabino* (**10**)	3.36(d)	4.42(sx)	4.74(q)	5.62(m)	5.55(q)	5.76(q)	7.90[c], 7.91, 7.94
D-*xylo* (**11**)	3.25(s)	4.66(d)	4.96(d)	5.67———		5.79(um)	7.86, 7.89[d], 7.91
D-*lyxo* (**12**)	3.37(d)	4.15(o)[e]	4.51(q)	5.60(m)	5.68(q) (5.71)[f]	5.76(q) (5.78)[f]	7.86, 7.88, 7.91, 7.95

[a]Abbreviations: d, doublet; m, multiplet; o, octet; q. quartet; s. singlet; sx, sextet; um, unresolved multiplet. [b]Unless stated otherwise, each signal represents 3 protons. [c]Six protons. [d]Two acetoxyl singlets separated by a small chemical shift (0.005 p.p.m.). [e]Doublet of triplets (each triplet with a broad, middle peak). [f]Calculated by ABX analysis (see ref. 25b).

TABLE III

COUPLING CONSTANTS[a] (Hz) FOR 2,3,4,6-TETRA-*O*-ACETYL-1,5-ANHYDRO-D-HEX-1-ENITOLS (**7–12**) MEASURED AT 250 MHz IN CHLOROFORM-*d* SOLUTION

Compound	*Coupling constants (Hz)*						
	$J_{1,3}$	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
D-*ribo* (**9**)	0	4.1	0	11.0	2.4	3.7	–
D-*arabino* (**10**)	0.5	4.4	0.9	6.4	6.6	2.8	11.2
D-*xylo* (**11**)	0	2.4	0	0	–	–	–
D-*lyxo* (**12**)	1.2	4.8	1.0	2.1	7.0 (7.2)[b]	5.2 (5.0)[b]	11.2

[a]Unless mentioned otherwise, the coupling constants given are first-order values. [b]Calculated by ABX analysis (see ref. 25b).

similar to that[26,27] of **10** and **11**, but differed from those[15] of **9**, **11**, and **13**, in respect of the presence of the long-range coupling of H-3 with both H-1 and H-5. Whereas the H-1 resonance of[15] **9**, **11**, and **13** appeared as a singlet, that of **12** was a doublet having $J_{1,3}$ 1.2 Hz. This spacing was also present in the signal for H-3, which appeared as an octet (doublet of triplets, each triplet having a broad, middle peak); the $J_{3,4}$ and $J_{3,5}$ values were calculated to be 4.8 and 1.0 Hz, respectively (see Table III). These assignments were confirmed by double-resonance experiments, whereby irradiation of the H-5 signal at τ 5.68 caused the collapse of the H-3 octet at τ 4.15 to a quartet, and of the H-4 quartet at τ 4.51 to a doublet, and the irradiation of the H-1 resonance at τ 3.37 converted the H-3 signal at τ 4.15 to a quartet without affecting other resonances.

The coupling (~1 Hz) of H-3 with H-5 in the spectra of **10** and **12** denotes a "1,3-diequatorial" relationship of these two protons, an arrangement only possible in the H_4^5(D) conformation. This conformation could be ruled out for tetra-*O*-acetyl-2-hydroxy-D-glucal (**10**), however, on the basis of the large value of $J_{4,5}$, and conforma-

tion **20** [H_5^4(D)] has been assigned[23] to this derivative. This criterion is not suitable to distinguish between the H_5^4(D) (**22**) and H_4^5(D) (**24**) conformations of **12**, as the expected H-4–H-5 coupling in either of the two conformations will be small and of the same order of magnitude. The assignment of the H_4^5(D) conformation (**24**) to **12** is possible, however, on the basis of the H-3–H-4 coupling constants; the $J_{3,4}$ value of 4.8 Hz corresponds to a dihedral angle between H-3 and H-4 of ~40°, which is attained in the H_4^5(D) conformation (**24**). In the alternative H_5^4(D) conformation (**22**), a coupling of less than 2 Hz, far less than the observed value of 4.8 Hz, would be required to justify a dihedral angle of 60–65°. Thus, it is certain that tetra-*O*-acetyl-2-hydroxygalactal (**12**) exists in the H_4^5(D) conformation (**24**) (in chloroform solution), in contrast to the H_5^4(D) conformation (**19–21**) favored by the other three, isomeric 2-hydroxyglycal peracetates (**9–11**).

It is possible to correlate the favored conformations (**19–21, 24**) of the four 2-hydroxyglycal tetraacetates (**9–12**) with the configurational preferences of various substituents on the 2,3-dihydropyran ring, namely, that the allylic substituent tends to occupy the *quasi*-axial position as against the *quasi*-equatorial, whereas in the nonallylic position an equatorial orientation is favored over an axial one[29]. According to these criteria, tetra-*O*-acetyl-1,5-anhydro-D-*ribo*-hex-1-enitol (**9**) in its favored H_5^4(D) conformation (**19**) has all of its substituents on the 2,3-dihydropyran ring in the favored orientations, whereas the D-*arabino* (**10**) and D-*xylo* (**11**) analogs in the H_5^4 conformation (**20** and **21**) each have one substituent in unfavorable geometry; the allylic 3-acetoxyl group in the former is *quasi*-equatorial and the nonallylic 4-acetoxyl group in the latter is axial.

Both the C-3 and C-4 substituents of tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**12**) would be oriented unfavorably in the H_5^4(D) conformation (**22**). For 2-hydroxyglucal tetraacetate (**10**), it has been determined[23] that the repulsion caused by the near-eclipsing of the vinylic 2- and the *quasi*-equatorial 3-acetoxyl groups in the H_5^4(D) conformation (**20**) is somewhat relieved by rotation about the C-3–C-4 and C-4–C-5 bonds, which results in a decrease of the H-3–H-4 and H-4–H-5 dihedral angles by about 10°. This avenue for the relief of strain is apparently not open to 2-hydroxygalactal tetraacetate (**12**) in the H_5^4(D) conformation (**22**), as rotation about the C-3–C-4 and C-4–C-5 bonds brings the *quasi*-equatorial 3-acetoxyl group nearer to an eclipsed relationship with the axial 4-acetoxyl group. The favorable orientation of both the 3- (*quasi*-axial) and the 4- (equatorial) acetoxyl groups of **12** is attained simultaneously, however, by inversion to the H_4^5(D) conformation (**24**); although this results in the introduction of non-bonded interaction between the *quasi*-axial 3-acetoxyl and axial 5-acetoxymethyl groups, such interaction is not regarded[29] to be so severe as that between *syn*-diaxial substituents.

The relative yields of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-hex-1-enitols (**9–12**) and *p*-nitrophenyl β-D-glycopyranoside tetraacetates (**5–8**) are given in Table IV. The *trans*-disposition of the leaving groups at C-1 and C-2 of acetylated glycosyl bromides is essential[30] for β-elimination to occur, as treatment[31] of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide with sodium *p*-nitrophenoxide in DMF failed to reveal any

TABLE IV

RELATIVE YIELDS OF ACELYTATED *p*-NITROPHENYL β-D-HEXOPYRANOSIDES AND 2,3,4,6-TETRA-*O*-ACETYL-1,5-ANHYDRO-D-HEX-1-ENITOLS

Tetra-O-acetyl-α-D-hexopyranosyl bromide	*p-Nitrophenyl tetra-O-acetyl-β-D-hexopyranoside*	*Yield (%)*	*Tetra-O-acetyl-1,5-anhydro-D-hex-1-enitol*	*Yield (%)*
D-*allo* (**1**)	D-*allo* (**5**)	8.0	*D-ribo* (**9**)	60.9
D-*gluco* (**2**)	D-*gluco* (**6**)	16.7	D-*arabino* (**10**)	34.2
D-*gulo* (**3**)	D-*gulo* (**7**)	13.8	D-*xylo* (**11**)	42.4
D-*galacto* (**4**)	D-*galacto* (**8**)	56.2	D-*lyxo* (**12**)	7.6

trace of **10** in the mixture (t.l.c.). It is noteworthy (see Table IV) that the hex-1-enitol (D-*ribo*, **9**) having the most stable features in its favored conformation (**19**) is formed the most readily, whereas the one (D-*lyxo*, **12**) having the fewest favorable features in either of its conformations [H_5^4(D) (**22**) or H_4^5(D) (**24**)] is formed the fewest readily. The remaining two D-hex-1-enitols [*arabino* (**10**) and *xylo* (**11**)] possess one instability factor each, namely, the 3-*quasi*-equatorial acetoxyl group in **10** (conformation **20**) and 4-axial acetoxyl group in **11** (conformation **21**), and are formed in comparable amounts (Table IV), intermediate between those of **9** and **12**. Thus, it is understandable that the yield of tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**12**, 12.5%) has never matched that of the D-*arabino* isomer (**10**, 51%), and even under improved conditions barely exceeds one-half (32%) of that of **10** (60%)[32]. The high yield (Table IV) of *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**8**) as compared to the yields of the other three *p*-nitrophenyl glycosides (**5**–**7**) is explicable by the fact that the lesser tendency of **4** for β-elimination makes more of it available for displacement at C-1 by the *p*-nitrophenoxylate anion. On the other hand, for the acetylated glycosyl bromides **1**–**3**, considerable β-elimination occurs at the expense of substitution at C-1.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured at room temperature in a 1-dm cell with a Perkin–Elmer Model 241 automatic polarimeter. I.r. spectra were recorded with a Perkin–Elmer Model 257 spectrophotometer. The 250-MHz ^{1}H-n.m.r. spectra were recorded, in chloroform-*d* with tetramethylsilane as internal reference, at the N.M.R. Facility for Biomedical Studies, Mellon Institute, Pittsburgh, Pennsylvania. Unless mentioned otherwise, the chemical shifts represent mid-points of multiplets, and the coupling constants are first-order values. The R_F values were determined on silica gel G t.l.c. plates (layer thickness, ~0.25 mm) in the following solvents: (*A*) 5:2 benzene–ethyl acetate and (*B*) 3:1 light petroleum–acetone; two developments of the plate were made in solvent *B*. The spots on t.l.c. plates were made visible by exposure to iodine vapor and/or by charring with 5% (v/v) methanolic

sulfuric acid. Silica gel G was purchased from Sigma Chemical Company, St. Louis, Missouri. Column chromatography was performed on Hi-Flosil, 60–200 mesh (Applied Science Laboratories, State College, Pennsylvania). Prior to use, sodium *p*-nitrophenoxide dihydrate (Eastman Kodak Company, Rochester, N.Y.) was dried overnight at 100° under high vacuum over phosphorus pentaoxide, and then stored over this drying reagent. DMF was dried over Davison No. 4A molecular sieves. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee and Atlantic Microlab, Inc., Atlanta, Georgia.

*Reaction of 2,3,4,6-tetra-*O*-acetyl-α-*D*-hexopyranosyl bromides with sodium* p*-nitrophenoxide in* N,N*-dimethylformamide. — A. Reaction with 2,3,4,6-tetra-*O*-acetyl-α-*D*-allopyranosyl bromide* (**1**). To a solution of compound[8,15] **1** (0.440 g, 1.07 mmol) in dry *N,N*-dimethylformamide (1.8 mL) was added sodium *p*-nitrophenoxide (0.233 g, 1.45 mmol). After 18 h at room temperature, the clear, yellow solution was evaporated to dryness under diminished pressure at 50–55° (traces of DMF being removed by repeated evaporations of xylene from the product), and the residue was dissolved in chloroform (10 mL). The chloroform solution was washed successively with 4 × 5mL each of cold water, cold M sodium hydroxide, and cold water, dried (sodium sulfate), and evaporated to dryness. The residual syrup crystallized from ethanol to afford 0.175 g (49.6%) of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*ribo*-hex-1-enitol (**9**), m.p. 104.5–106.5°, which was homogeneous by t.l.c. in solvents *A* and *B*.

An analytical sample of **9** from another preparation had m.p. 105–106°, $[\alpha]_D$ +246.9° (*c* 0.2, chloroform) [lit.[15] m.p. 108–110°, $[\alpha]_D^{25}$ −21.8° (*c* 2.6, chloroform)]: R_F 0.65 (solvent *A*), 0.93 (solvent *B*); ν_{max}^{KBr} 1750 and 1735 (C=O), and 1688 cm^{-1} (C=C); n.m.r. data: see Tables II and III.

Anal. Calc. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49. Found: C, 51.10; H, 5.60.

Evaporation of the filtrate from the removal of **9** left a syrup (99 mg) that was estimated by visual t.l.c. inspection (solvents *A* and *B*) to consist of ~40 mg (11%) of **9**, ~40 mg (8%) of **5** [R_F 0.58 (solvent *A*), 0.84 (solvent *B*)], and ~19 mg of two unidentified components; **5** was identified by comparison (t.l.c., solvents *A* and *B*) with authentic[8] **5**.

*B. Reaction with 2,3,4,6-tetra-*O*-acetyl-α-*D*-glucopyranosyl bromide* (**2**). The reaction of **2** (ref. 4) (2.0 g, 4.87 mmol) with sodium *p*-nitrophenoxide (1.14 g, 7.08 mmol) in dry *N,N*-dimethylformamide (8.0 mL), and processing as described for **1**, afforded a syrup that crystallized from ethanol to give 0.382 g (16.7%) of *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**6**), m.p. 176–178°, $[\alpha]_D$ −38.0° (*c* 0.19 chloroform) [lit.[33] m.p. 174–175°, $[\alpha]_D$ −41.0° (*c* 2.0, chloroform)]; t.l.c. in solvents *A* (R_F 0.54) and *B* (R_F 0.84) showed the presence of a trace of **10** in this product.

The syrup (1.29 g) obtained by evaporation of the filtrate (from the removal of **6**) was chromatographed on silica gel, the column being eluted with benzene, followed by 10:1 benzene–ethyl acetate. Pooling of appropriate fractions (monitored by t.l.c. in solvent *B*), and removal of solvent afforded chromatographically homogeneous, syrupy 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (**10**); yield, 0.551 g (34.2%), $[\alpha]_D$ −26.6° (*c* 0.45, chloroform) [lit.[16] $[\alpha]^{18}$ −32.0° (chloroform)]; R_F 0.63 (solvent

A), 0.95 (solvent *B*); ν_{max}^{film} 1780–1735 (broad, C=O), and 1686 cm^{-1} (C=C); n.m.r. data: see Tables II and III.

*C. Reaction with 2,3,4,6-tetra-*O*-acetyl-α-*D*-gulopyranosyl bromide* (**3**). Treatment of **3** (ref. 34) (0.450 g, 1.09 mmol) with sodium *p*-nitrophenoxide (0.250 g, 1.55 mmol) in dry *N,N*-dimethylformamide (1.8 mL), and processing as described for **1**, yielded a colorless syrup (0.267 g) that consisted of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*xylo*-hex-1-enitol (**11**) as the major product and *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-gulopyranoside (**7**) as the minor component, according to t.l.c. in solvents *A* and *B*. The crude syrup was chromatographed on a column of silica gel, using successively benzene and 10:1 benzene–ethyl acetate as solvents. The 2-hydroxygulal tetraacetate (**11**) was eluted first, and was isolated as a pale-yellow syrup; yield, 0.153 g (42.4%); $[\alpha]_D$ +191.1° (*c* 0.25, chloroform); R_F 0.62 (solvent *A*), 0.94 (solvent *B*); ν_{max}^{film} 1780–1725 (broad, C=O), and 1680 cm^{-1} (C=C); n.m.r. data: see Tables II and III.

Anal. Calc. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49. Found: C, 51.19; H, 5.49.

The *p*-nitrophenyl β-D-gulopyranoside tetraacetate (**7**) was obtained as a chromatographically homogeneous syrup (71 mg, 13.8%) by pooling and evaporation of the appropriate, subsequent fractions; R_F 0.52 (solvent *A*), 0.85 (solvent *B*); ν_{max}^{film} 1735 (C=O), 1610 and 1590 (aromatic), and 1515 and 1340 cm^{-1} (nitro).

*D. Reaction with 2,3,4,6-tetra-*O*-acetyl-α-*D*-galactopyranosyl bromide* (**4**). The reaction of **4** (ref. 35) (2.4 g, 5.11 mmol) with sodium *p*-nitrophenoxide (1.19 g, 7.39 mmol) in dry *N,N*-dimethylformamide (8.0 mL) and processing as for **1**, gave a syrup that crystallized from ethanol to give 1.50 g of crude **8**, m.p. 130–136°, $[\alpha]_D$ −7.2° (*c* 0.21, chloroform); t.l.c. (solvent *B*) indicated the presence of a small amount of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**12**). One recrystallization of the crude product from ethanol afforded pure *p*-nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**8**); yield 1.13 g (47.1% from **4**), m.p. 144.5–146°, $[\alpha]_D$ −11.6° (*c* 0.16, chloroform) [lit.[36] m.p. 144–145°, lit.[22,36] $[\alpha]_D$ −11.3° (chloroform) and −8.3° (chloroform), respectively]; R_F 0.60 (solvent *A*), 0.82 (solvent *B*).

The mother liquors from the crystallization and recrystallization of **8** were combined and evaporated. The residual syrup was dissolved in benzene and applied to a column of silica gel packed in 1:1 benzene–heptane. The column was successively eluted with 1:1 benzene–heptane (100 mL) and 5:5:1 benzene–heptane–acetone. The appropriate fractions containing 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**12**) were pooled and evaporated. Crystallization of the residue from a small amount of ethanol gave 0.128 g (7.6% from **4**) of **12**, m.p. 108–109°, $[\alpha]_D$ −3.7° (*c* 0.19, chloroform) [lit.[17] m.p. 110°, $[\alpha]_D$ −3.8° (chloroform)]; R_F 0.63 (solvent *A*), 0.92 (solvent *B*); ν_{max}^{KBr} 1740 (C=O), and 1685 $cm^{-}{}_{F}$ (C=C); n.m.r. data: see Tables II and III.

Evaporation of subsequent fractions and crystallization of the residue afforded 0.218 g (9.1% from **4**) of chromatographically homogeneous **8**; m.p. 144–145°; R_F 0.60 (solvent *A*), 0.82 (solvent *B*). The overall yield of **8** was 56.2%.

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