Arylazo-glycenosides. Part 7.[1] Syntheses of Amino-sugars from Methyl Arylazo-hexenopyranosides

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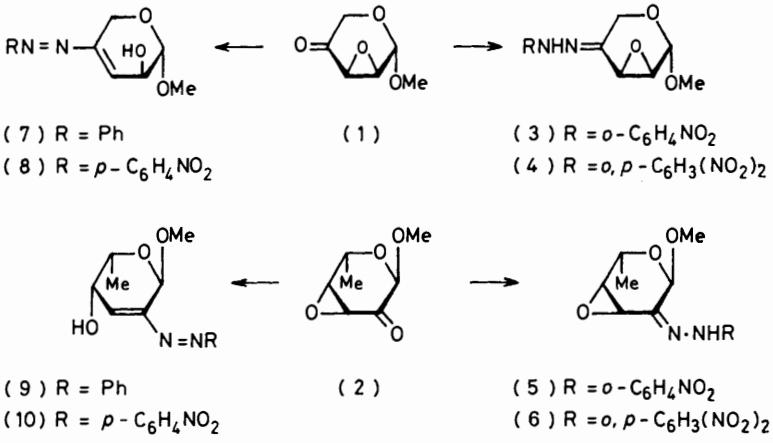
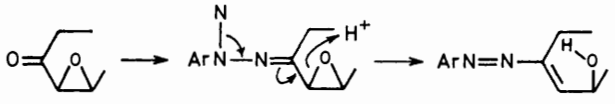
Reaction of the anhydro-glycopyranosiduloses (1) and (2) with *o*-nitro- and *o,p*-dinitro-phenylhydrazine yielded the hydrazones (3)—(6), whereas phenyl- or *p*-nitrophenyl-hydrazine yielded the phenylazoalkenes (7)—(10), formed by rearrangement of intermediate hydrazones. Reaction of the azoalkanes (8) and (9) with a range of nuceophiles yielded the α-substituted phenylhydrazones (11)—(19) and (24)—(28), respectively, by 1,4-addition. It has been shown that the α-amino-hydrazones (20), (25), and (28) can be reduced to vicinal diamino-sugars, thereby providing a new route to these compounds. Reduction of the azoalkene (9) yielded the 2-amino-2,3,6-trideoxy-hexopyranoside, isolated as the *ON*-diacetyl derivative (31).

In a previous paper [2] we have reported on the synthesis and some reactions of α-epoxyketones derived from sugars, which constitute a class of carbohydrate derivatives with promising potential as intermediates for the synthesis of a range of modified sugars. Illustrative of this potential we described their use in syntheses of colitose and an amino-deoxysugar.[2] Paulsen and Sinnwell have also described the use of such compounds in synthesis and have reported recently a synthesis of the naturally occurring branched-chain sugar, γ-octose, derived from isoquinocycline antibiotics.[3] Now, we report on the reaction of epoxyketones of this type with phenylhydrazine or nitrophenylhydrazines to give either phenylhydrazones or arylazoalkene derivatives which can subsequently be transformed into a variety of substituted amino-sugars. The formation and reactions of azo-alkenes derived from glycosiduloses have been reported previously from these laboratories [4] and the reactions now described provide an alternative route to these useful intermediates.

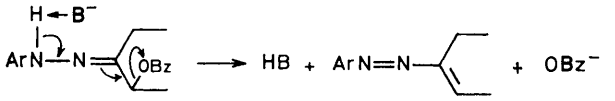


Formation of Arylhydrazones and Arylazo-alkenes.—Treatment of methyl 2,3-anhydro-β-L-*erythro*-pentopyranosid-4-ulose (1) [2] or methyl 3,4-anhydro-6-deoxy-α-L-*lyxo*-hexopyranosid-2-ulose (2) [2] with *o*-nitrophenylhydrazine or *o,p*-dinitrophenylhydrazine in ethanol containing acetic acid at room temperature yielded the corresponding arylhydrazones (3)—(6) as yellow, crystalline compounds in 65—75% yields. On the other hand, treatment of either epoxyketone with phenylhydrazine or *p*-nitrophenylhydrazine under similar conditions yielded the azoalkenes (7)—(10), which were obtained as orange crystals in *ca.* 70% yield. Examination of these reaction mixtures in weakly alkaline solution (pH 8) indicated that the arylhydrazone is first formed and, subsequently, gives rise to the azoalkene which has a lower R_F value; the same sequence of reactions occurs much more rapidly in acidic solution (pH 4.0) with the initial faster-moving component (t.l.c.) appearing within 2 min and disappearing within a further 30 s. For the various arylhydrazines used, kinetic studies on both epoxyketones indicated the expected sequence of reactivity of phenyl > *p*-nitrophenyl ≈ *o*-nitrophenyl > *o,p*-dinitrophenyl with the reaction being 10—20 times faster at pH 4.0 than at pH 8.0. These results suggest that the hydrazone derivative of the ketone is first-formed, which then undergoes rearrangement involving acid-catalysed opening of the epoxide ring (Scheme 1).



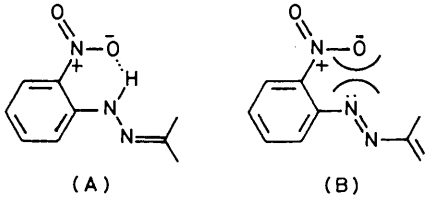
Scheme 1

By contrast, formation of azoalkenes from glycosidulose arylhydrazones has hitherto involved base-catalysed (B) elimination of an α-ester or halogeno-leaving group (Scheme 2).[4]



SCHEME 2

Of particular interest is the fact that the phenylhydrazines with an *ortho*-nitro-group present in the aromatic ring yield the hydrazones as stable products whereas those lacking such a group rapidly rearrange to azoalkenes. The fact that both *o*- and *p*-nitrophenylhydrazine conform to this pattern, yet react at similar rates at pH 8.0 with the epoxyketones (1) and (2), suggests that the nitrophenylhydrazones are formed similarly in both cases, but that, for some reason, the rearrangement of the *ortho*-nitro-substituted hydrazone is then inhibited. This, possibly, could be ascribed to the formation of a strong, intramolecular hydrogen bond between the imino-hydrogen and a nitro-oxygen, as in (A) (which is only feasible for the *ortho*-isomer), thereby rendering the imino-hydrogen less sensitive to attack by base; this does not, however, explain the stability in acidic solution. More plausibly, the *ortho*-nitro-group may inhibit the rearrangement by making the resultant azoalkene less stable than it is when there is no *ortho*-nitro-group present. This may be ascribed to a direct through-space electronic interaction between the oxygen and nitrogen lone pairs as in (B).

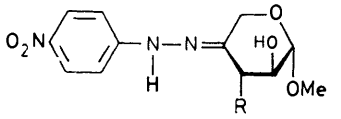


(A) (B)

The hydrazones could be distinguished readily from the azoalkene derivatives since they differed both in colour and in their i.r. spectra in the ν 1 600 cm^{-1} region. All the compounds in this and previous work [4] which have been assigned hydrazone structures exhibit strong absorption at or close to ν 1 600 cm^{-1}, which we ascribe to the C=N stretching vibration in these derivatives; in contrast, the azoalkenes either lack an absorption band in this region or show only relatively weak absorptions. In addition, the *o*,*p*-dinitrophenylhydrazones exhibit a second, strong band at ν 1 580 cm^{-1}, and the *o*-nitrophenylhydrazones a further band at ν 1 560 cm^{-1}. The rearrangement of a hydrazone to an azoalkene structure also causes a bathochromic shift in the u.v. spectrum; $\lambda_{max.}$ for the *o*-nitrophenylhydrazones (3) and (5) occurs at 300 nm whereas the *p*-nitrophenylazoalkenes (8) and (10) have $\lambda_{max.}$ at 320 and 314 nm, respectively.

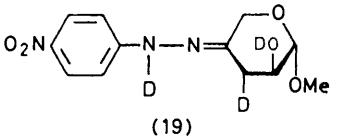
In confirmation of the assignments, the ^1H n.m.r. spectra of the compounds with an azoalkene structure lacked signals for an imino-proton, but showed doublets in the region δ 6.8—7.2 which could be assigned to the alkenyl proton at C-3, coupled to either 2-H or 4-H. By contrast, the signal for 3-H in the *o*-nitrophenylhydrazones (3) and (5) appeared at δ 3.97 and 3.82, respectively, being somewhat deshielded for an epoxide proton by the adjacent hydrazone group and exhibiting coupling to the adjacent epoxide proton of 3—4 Hz, as expected. Compound (5) was obtained as a mixture of *syn*- and *anti*-stereoisomers in *ca.* 1 : 1 ratio as indicated by its n.m.r. spectrum which shows duplicate signals for 1-H, 3-H, 5-H, CMe, and OMe. Unfortunately, it was not possible to obtain interpretable spectra for the *o*,*p*-dinitrophenylhydrazone derivatives.

Reactions of the Arylazoalkenes.—Treatment of the *p*-nitrophenylazoalkene (8) with a range of nucleophilic reagents yielded the series of compounds (11)—(19) which are formed by 1,4-addition in a manner analogous to the reactions of azoalkenes previously described.[4] The



(11) R = NMe_2
(12) R = NHMe
(13) R = NHEt
(14) R = NH_2
(15) R = NHNHPh
(16) R = N_3
(17) R = OMe
(18) R = H

reactions occurred readily at room temperature: they could be monitored easily by t.l.c. and in most cases there was a change of colour from orange to yellow. The



(19)

addition products could be isolated readily in good yield as stable, yellow crystalline solids. Optical rotations and n.m.r. spectral information for these derivatives are summarised in Table 1. All these compounds exhibited a strong absorption band at or close to ν 1 600 cm^{-1} which we assign to the C=N double bond in an arylhydrazone, indicating the formation of a 1,4-addition compound.

The α-D-*threo*-configuration assigned to these compounds is based on the configuration of the starting material, which determines the configuration at C-1 and C-2, and also by relation to the configuration of the derived diamino-sugars, described below [prepared from the benzylamino-adduct (20) of the phenylazoalkene (7)], which determined the configuration at C-3. As is indicated in Table 1, the close similarity of the n.m.r. data, especially the coupling constants for compound (20) with those of the related amine adducts (11)—(14), strongly suggests that a similar conformation and configuration are involved for these compounds. Further, the large value of the coupling constant between 2-H and 3-H (*J* 7.2—8.0 Hz) would suggest that these protons

TABLE 1

Optical rotations and n.m.r. spectral data for compounds (11)—(20)

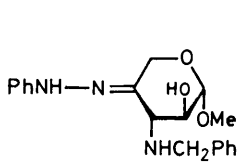
Compound	C-3 substituent	$[\alpha]_D$ [a]	N.m.r. spectral data (δ and Hz) 1-H	2-H	3-H	5-H 5′-H	OMe	N*H*Ar		$J_{1.2}$	$J_{2.3}$	Solvent [b]
(11)	NMe_2	+407	d, 4.86	q, 4.12	d, 3.74	q, 4.74 (J_{gem}16)	s, 3.34	s, 10.48	2.65 (NMe_2)	4.0	8.0	Y
(12)	NHMe	+202	d, 4.80	q, 3.79	d, 3.46	s, 4.60	s, 3.30	s, 10.08	2.93 (NMe)	3.0	7.2	Z
(13)	NHEt	+142	d, 4.76	q, 3.77	d, 3.57	s, 4.58	s, 3.28	s, 10.04	1.03 and 2.64 (EtN)	2.5	7.0	Z
(14)	NH_2		d, 4.83	q, 3.86	d, 4.10	q, 4.66 (J_{gem}14)	s, 3.36	s, 10.06		3.0	8.0	Z
(15)	NHNHPh	−146	d, 4.94	q, 4.25	d, 4.14	q, 4.68 (J_{gem}16)	s, 3.32			3.0	7.0	Y
(16) [c]	N_3	−364	d, 4.85	q, 5.22	d, 4.40	dd, 4.80 and 4.32 (J_{gem}15.5)	s, 3.46		2.15 (OAc)	2.7	4.0	Y
(17)	OMe	−178	d, 4.82	m, 4.10	d, 4.23	s, 4.75	s, 3.35	s, 10.35	3.52 (OMe)	3.0	6.0	Z
(18)	H	−55	d, 4.78	m, 4.04	q + q, 3.0 and 2.76	q, 4.60 (J_{gem}16)	s, 3.40	s, 10.12		3.0	4.5 and 5.5	Z
(19)	D	−34.5	d, 4.76	q, 4.04	d, 2.96	q, 4.60 (J_{gem}16)	s, 3.35			3.0	4.0	Z
(20)	CH_2Ph	+85 [d]	d, 5.0	q, 4.06	d, 3.83	q, 4.81 (J_{gem}16)	s, 3.40	s, 9.59	t, 6.95 (NH); q, 4.23 (CH_2Ph)	3.0	8.0	Z

[a] Rotations in MeOH, *c* 0.1—0.2. [b] Y, [$^2H_5$]pyridine; Z, [$^2H_5$]pyridine + $(CD_3)_2SO$. [c] N.m.r. data for the 2-*O*-acetyl derivative. [d] *c* 0.07 In EtOH.

are *trans*, diaxially oriented, and not *cis*-related. However, the difficulty with this interpretation is that the sugars would need to adopt the $^1C_4$ chair conformation (21) to make this arrangement possible, whereas the low value of the coupling constant between 1-H and 2-H (J 2.5—4.0 Hz) clearly indicates that these protons are not diaxially oriented as this conformation would require. In fact, neither chair conformation accommodates the coupling data. We propose that the results might be accommodated if these derivatives adopt the twist-boat conformation (22) in which 2-H and 3-H approach an anti-periplanar orientation, whereas 1-H and 2-H are closer to an anti-clinal relationship which could be compatible with the observed $J_{1.2}$ values. In this conformation the compound avoids the marked syn-diaxial non-bonded interaction between the C-1 and C-3 substituents which would be present in the $^4C_1$ chair form, whilst the marked anomeric effect, which would otherwise stabilise this chair form, may still operate effectively in the twist form. In addition, an intramolecular hydrogen bond can operate in the twist form, involving a six-membered ring between the hydrazone proton and the C-3 amine group, or a five-membered ring between the proton of the hydroxy-group at C-2 and the amino-group at C-3, which is not possible in the $^4C_1$ conformation. Although both these hydrogen bonds could also equally form in the alternative $^1C_4$ chair form, in this case the anomeric effect would be a destabilising force. In addition, it may be noted that the presence of an sp^2-hybridised atom in a cyclohexane ring reduces the energy difference between chair and twist-boat forms from >5 to *ca.* 3 kcal mol^{-1} (1 cal = 4.184 J).[5] On this basis, we conclude that the methoxy-derivative (17) adopts a rather similar conformation, whereas the acetate derived from the azido-adduct (16), and the 3-deoxy sugars (18) and (19) appear to adopt the $^4C_1$ conformation. This is not surprising since there is no marked syn-diaxial interaction to destabilise this chair form and the anomeric effect would be expected to control the preferred form in this case.

It is interesting to note the wide range of optical rotations observed for these adducts; whereas the amino-adducts, for which we suggest a twist-boat conformation, have a marked positive rotation except for the phenylhydrazino-compound (15), those derivatives with the $^4C_1$ chair conformation have negative rotations.

With the exception of the benzylamino-derivative (20), attempts to prepare similar adducts from the phenylazoalkene (7) were unsuccessful, leading either to recovery of starting material, with the addition step apparently being reversible under the conditions used during work-up, or to complex mixtures of products which could not be satisfactorily separated for identification. The benzylamino-adduct (20) was obtained as colourless crystals from compound (7) with benzylamine under conditions similar to those used for the *p*-nitrophenyl adducts (11)—(19). The fact that compound (20) alone crystallises directly from the reaction solution could explain why it could be readily isolated, in contrast to the other adducts. However, when the product obtained by reaction of compound (7) with sodium methoxide was hydrogenated directly over Raney nickel without prior isolation, a product could be isolated which, after purification by column chromatography and acetylation, yielded crystalline methyl 4-acetamido-



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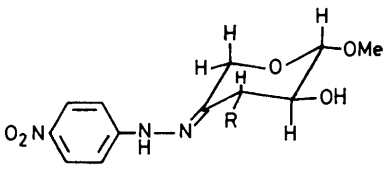

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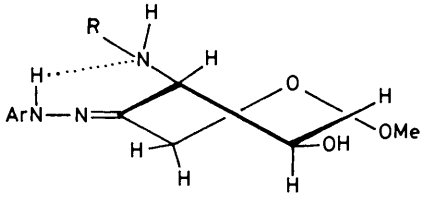

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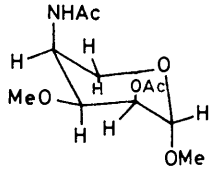

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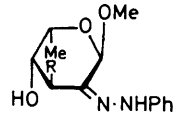
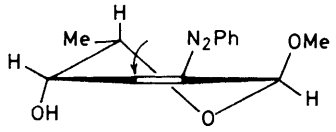


(24) R = NMe_2
(25) R = NHMe
(26) R = NHEt
(27) R = NH_2
(28) R = $NHCH_2Ph$



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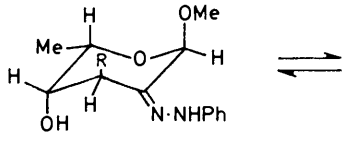
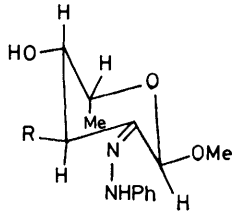


(29a)



(29b)

2-*O*-acetyl-3-*O*-methyl-4-deoxy- β-L-ribopyranoside (23). The *ribo*-configuration assigned to the compound was deduced from n.m.r. spectral data (Experimental section) which shows $J_{1,2}$ 1.5 Hz, establishing 1-H and 2-H as *trans*-diequatorial and not *trans*-diaxial, and $J_{4,5ax} = J_{4,5eq} = 3.0$ Hz, establishing 4-H as equatorial also. The configuration at C-3 is much less certain; the coupling $J_{2,3} = J_{3,4} = 4.0$ Hz is compatible with 3-H being either equatorial or, perhaps, more likely, axial. The apparent absence of long-range coupling between 3-H and 5-H_{eq}, which could be detected (*J ca.* 0.5 Hz) for the 5-H_{eq} signal in the 3-deoxy-analogue of this sugar (35), which adopts the same conformation,[2] tends to support an axial assignment for 3-H. Finally, the chair form suggested by the coupling data would not be expected to be preferred if the methoxy-group at C-3 was axial, since a marked syn-axial interaction between the C-1 and C-3 methoxy-groups would then occur, and indeed the L-*xylo*-diamino-sugar (34), described below, does adopt the alternative $^1C_4$ conformation.

Treatment of the phenylazoalkene (9) with a number of amine reagents yielded the corresponding phenylhydrazones (24)—(28) by 1,4-addition, which were obtained as pale yellow or colourless crystalline solids, except for the benzylamine adduct (28) which could be obtained only as a syrup. In this case, the n.m.r. spectral evidence suggested the presence of a mixture of stereoisomers in *ca.* 8 : 1 ratio. Optical rotations and n.m.r. spectral data for these compounds are summarised in Table 2. All the substances exhibited the strong absorption band between ν 1 590—1 610 cm^{-1} for the hydrazone group. Compound (9) also underwent ready reaction with phenylhydrazine, sodium methoxide, sodium azide, and sodium borohydride, but in each case

TABLE 2

Optical rotations and n.m.r. spectral data for compounds (24)—(28)

Compound	C-3 substituent	$[\alpha]_D$ [a]	N.m.r. spectral data (δ and Hz) [b] 1-H	3-H	4-H	5-H	CMe	OMe	other	NH	$J_{3,4}$	$J_{4,5}$
(24)	NMe_2	−270	s, 5.26	d, 3.19	q, 3.83	oct, 4.43	d, 1.32	s, 3.50	2.46 (NMe_2)	s, 8.0	5.5	3.0
(25)	NHMe	−397	s, 5.16	d, 3.17	*ca.* 3.45 [c]	oct, 4.14	d, 1.38	s, 3.43	2.44 (NMe)	s, 8.2	5.0	3.5
(26)	NHEt	−259	s, 5.16	d, 3.26	*ca.* 3.45 [c]	oct, 4.15	d, 1.28	s, 3.43	2.7 (CH_2Me), 1.12 (CH_2*Me*)	s, 8.2	5.5	3.5
(27) [d]	NH_2	−184	s, 4.76	d, 3.26	q, 3.32	m, 4.0	d, 2.32	s, 2.96			5.5	(4.0)
(28)	$NHCH_2Ph$		s, 5.17; s, 4.88 [e]	d, 3.28		oct, 4.10	d, 1.2; d, 1.03 [e]	s, 3.35; s, 3.31 [e]	q, 3.78	8.3	5.0	3.0

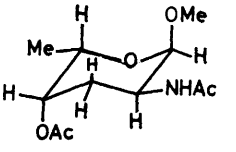
[a] *c* 0.1 In $CHCl_3$. [b] Spectra measured in $CDCl_3$. [c] Signal for 4-H masked under OMe signal. [d] Spectrum measured in C_6D_6. [e] Data for minor component.

a mixture of products resulted from which no pure compounds could be isolated.

The *xylo*-configuration assigned to compounds (24)—(28) was deduced from the structures of the *ido*- and *gulo*-diamino-sugars, described below, and derived from compounds (25) and (28). These require a *trans*-configuration for the substituents at C-3 and C-4, the *cis*-relationship of the C-4 and C-5 substituents following from the configuration of the initial azoalkene. The n.m.r. spectral results for these compounds are more equivocal. In the $^1C_4$ conformation (29a) which has the C-5 alkyl group equatorial as is normally found for L-hexopyranoses, the low value of the 4-H—5-H coupling (J 3.0—4.0 Hz) is expected for gauche-related protons, with 5-H axial and 4-H equatorial. The value of $J_{3,4}$ (5.0—5.5 Hz) is most naturally interpreted also as a gauche coupling, but this is excluded by the evidence from the diamino-sugars. The 3-H—4-H coupling seems too large for diequatorially related protons. One explanation could be that the alternative $^4C_1$ chair form (29b) is also present and is, perhaps, the major form. It may be that, like the phenylhydrazones derived from compound (8), a twist-boat conformation is preferred. In either event the change from the $^1C_4$ conformation allows the syn-diaxial interaction between the C-1 and C-3 substituents to be relieved and, on the other hand, an intramolecular hydrogen bond involving the C-3 amino-substituent and either the C-2 phenylhydrazono-group or the C-4 hydroxy-group, becomes possible in the alternative forms. It may be noted that these results were consistent with axial attack at C-3 on the more stable half-chair conformation (30).

Reduction of compound (9) with sodium borohydride followed by hydrogenation over Raney nickel and subsequent acetylation yielded crystalline methyl 2-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-L-*xylo*-hexopyranoside (31). The *xylo*-configuration was assigned from n.m.r. data; a value of $J_{2,3ax}$ 11.0 Hz established that 2-H and 3-H_{ax} were diaxially related, whereas $J_{1,2}$ 2.5, $J_{2,3eq}$ 5.0, and $J_{5,4}$ 1.5 Hz suggested that these are gauche relationships, as required by the $^1C_4$ conformation.

Synthesis of Diamino-sugars.—Methyl 3-benzylamino-3-deoxy-α-D-*threo*-pentopyranosid-4-ulose phenylhydrazone (20) was hydrogenated over Raney nickel and the product mixture purified by column chromatography to give methyl 4-amino-3-benzylamino-3,4-dideoxy-β-L-xylopyranoside (32). This was then hydrogenolysed over 10% palladium-on-charcoal to give a quantitative yield of crystalline methyl 3,4-diamino-3,4-dideoxy-β-L-xylopyranoside (33), characterised as its tri-*NNO*-benzoyl derivative, methyl 3,4-dibenzamido-2-*O*-benzoyl-3,4-dideoxy-β-L-xylopyranoside (34). Although



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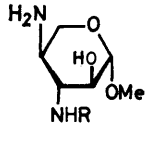
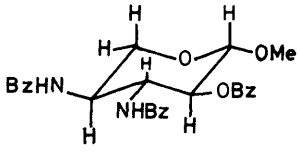


(32) R = CH_2Ph
(33) R = H



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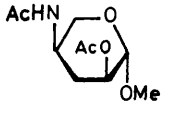

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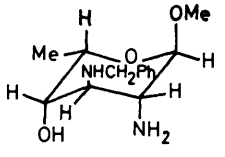

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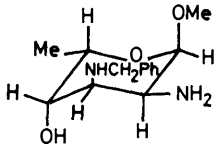
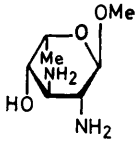
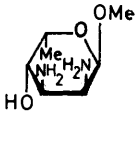


(37)



(38)



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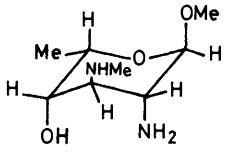

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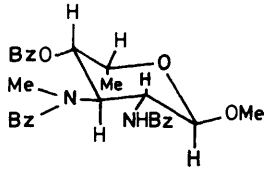
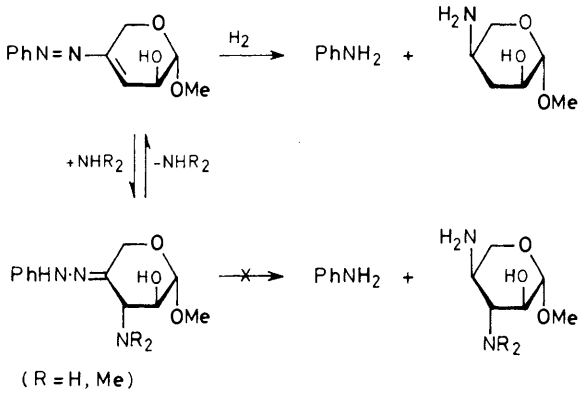


(41)

this compound was not adequately soluble in the usual solvents for n.m.r. spectral analysis, an adequate solution could be obtained in trifluoroacetic acid, which allowed n.m.r. signal assignments to be made. A doublet at δ 5.2 ($J_{1,2}$ 8.0 Hz), was assigned to 1-H, and a quartet at δ 5.61 ($J_{1,2}$ 8.0 and $J_{2,3}$ 10.0 Hz) was assigned to 2-H, establishing the conformation as a $^1C_4$ chair form (34) with 1-H and 2-H diaxially oriented. The further 2-H—3-H coupling of J 10 Hz then establishes the *trans*-configuration of the substituents at C-2 and C-3. Whereas the signals for 3-H and 4-H could not be clearly resolved from each other, $J_{4,5}$ values could be obtained from the signals for 5-H_{eq} and 5-H_{ax}, which appeared as quartets at δ 4.6 (J_{gem} 12.0 and $J_{5eq,4}$ 4.5 Hz) and at δ 4.12 ($J_{5ax,4}$ 8.0 Hz), respectively. The latter clearly suggests that 4-H and one of the 5-H protons are diaxially oriented, which leads, therefore, to the L-*xylo*-configuration for the product. This establishment of the L-*xylo*-configuration of compound (34) serves to confirm the D-*threo*-configuration of the phenylhydrazone precursor (20) and, by analogy, the configurations of compounds (11)—(19).

In an attempt to convert other amine adducts of the phenylazoalkene (7) into diamino-sugars, the reaction solution obtained with either dimethylamine, methylamine, or ammonia was directly hydrogenated over Raney nickel, without any attempt to isolate the phenylhydrazone intermediate (which the colour change from orange to pale yellow and t.l.c. monitoring indicated had been formed). However, in each case, the product obtained after acetylation was found to be methyl 4-acetamido-2-*O*-acetyl-3,4-dideoxy-β-L-*erythro*-pentopyranoside (35) which had been obtained previously by another route.[2] This was the product expected from direct hydrogenation of the azoalkene (7), which suggests that the amine adduct is in dynamic equilibrium with the azoalkene and free amine and that the azoalkene is reduced more readily than the adduct (see Scheme 3).



SCHEME 3

In a similar way, methyl 3-benzylamino-3,6-dideoxy-α-L-*lyxo*-hexopyranosid-2-ulose phenylhydrazone (28), prepared *in situ* by the reaction of benzylamine with amine adduct is sufficiently stable to be reduced whereas the adducts with simple aliphatic amines are not.

compound (9), was hydrogenated over Raney nickel. T.l.c. examination of the reaction solution indicated that, besides a small amount of starting material, four products were present; these were considered to be two sets of stereoisomers in a ratio of *ca.* 10 : 1. The major pair of products had the higher R_F value. Column chromatography of the mixture allowed partial separation of the components and this was completed by fractional crystallisation. In this way the major pair of isomers were separated to give methyl 2-amino-3-benzylamino-2,3,6-trideoxy-α-L-idopyranoside (36) as a syrup, and methyl 2-amino-3-benzylamino-2,3,6-trideoxy-α-L-gulopyranoside (37) as a crystalline solid, obtained in a 3 : 2 ratio. The configurations assigned to these compounds followed from their n.m.r. spectra (see Table 3).

For the idoside (36), all the vicinal couplings between the ring protons were J 2.5 Hz or less, and further

TABLE 3

N.m.r. spectral data for diamino-sugar derivatives

Compd.	Solvent[a]	N.m.r. spectral data (δ and Hz) 1-H	2-H	3-H	4-H	5-H	CMe	OMe	other	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
(34)	K	d, 5.2	t, 5.61			q, 4.6 q, 4.12	12.0			8.0	10.0		4.5 8.0
(36)	L	s, 4.35 br	q, 3.04	sex, 2.70	q, 3.40	oct, 3.95	d, 1.22 (J 6.5)	3.25	3.70 (CH_2Ph), 2.54 (NH_2, NH, OH)	1.5	2.5	2.5 ($J_{2,4}$1.5, $J_{1,3}$1.0)	1.5
(37)	L	d, 4.21	t, 3.10	t, 2.74	m, 3.56	oct, 3.96	d, 1.19 (J 6.5)	3.26	3.74 (CH_2Ph), 2.24 (NH_2, NH, OH)	3.0	4.0	3.0	1.5
(40)	L	s, 4.38 br	m, 2.96	m, 2.59	m, 3.42	oct, 3.88	d, 1.22 (J 6.5)	s, 3.26	s, 2.34 (NMe)	1.5	2.5	3.0 ($J_{2,4}$2.0, $J_{1,3}$1.5)	1.5
(41)	M	d, 5.3	m, 5.1	m, 5.6—6.0		m, 4.48	d, 1.36	3.18	d, 8.58 (NH), ($J_{NH,2}$8.0), 2.96 (NMe)	7.0	9.0	>8.0	—

[a] K, CF_3CO_2H; L, $CDCl_3$; M, C_6D_6.

Other evidence for an adduct being in equilibrium with a phenylazoalkene and addition reagent has been obtained in our laboratory.[6,7] In the case of the reaction with ammonia, a trace of another product was obtained, as indicated by t.l.c., which had an R_F value similar to that of the diamino-sugar (33). It is not clear why the benzyl-

splitting of the proton signals of J *ca.* 1 Hz for 1- to 4-H could be assigned to long-range coupling between 1-H and 3-H and between 2-H and 4-H. This was confirmed by double irradiation experiments which clearly suggests that all these protons are equatorially disposed, as required for an α-L-idose derivative in the $^1C_4$ con-

formation shown in structure (36). In the case of the gulose isomer (37), somewhat larger vicinal coupling constants for 2-H were observed ($J_{1,2}$ 3.0, $J_{2,3}$ 4.0 Hz) (compared with the idoside), compatible with gauche-related protons, whereas the values for $J_{3,4}$ and $J_{4,5}$ were similar to those for compound (36) (J 3.0 and 1.5 Hz respectively); further, no long-range coupling between 2-H and 4-H was detected. These results fit with the *gulo*-configuration assigned to compound (37). Hence, the two major stereoisomers are epimeric at C-2, with the C-3 substituent axial. It may be surmised that the two minor products, which were not individually characterised, were the corresponding isomers having the C-3 substituent equatorial, *i.e.* the *talo*- and *galacto*-isomers. The *ido*- and *gulo*-configurations assigned to compounds (36) and (37), respectively, serve to establish the *xylo*-configuration of compound (28).

Catalytic hydrogenation of compound (36) over palladium-on-charcoal yielded methyl 2,3-diamino-2,3,6-trideoxy-α-L-idopyranoside (38) as a crystalline solid and, similarly, compound (37) gave methyl 2,3-diamino-2,3,6-trideoxy-α-L-gulopyranoside (39).

The methylamino-adduct (25) was also hydrogenated over Raney nickel *in situ* to yield a mixture of two products (ratio *ca.* 10 : 1) which could be separated by column chromatography to give the major product as a syrup in 67% yield. It was identified as methyl 2-amino-3-methylamino-2,3,6-trideoxy-α-L-idopyranoside (40), with values for the vicinal coupling constants similar to those for compound (36) and, again, long-range coupling was apparent between the W-related ring protons, 2-H, 4-H, and 1-H, 3-H. The assignment of the *ido*-configuration for compound (40) confirms the *xylo*-configuration of compound (25). By analogy, compounds (24), (26), and (27) are also considered to have the L-*xylo*-configuration.

Compound (40) was characterised by preparation of its *NNO*-tribenzoyl derivative (41), obtained as a syrup. In this case the vicinal ring-proton coupling constants which could be determined indicated that the compound had switched to the alternative $^4C_1$ chair conformation. Values of $J_{1,2}$ 7.0, $J_{2,3}$ 9.0, and $J_{3,4} > 8.0$ Hz clearly suggest that the relevant protons are all now diaxially related, in contrast with the correspondingly low coupling constants found for compound (40) where they are all di-equatorially related.

This work provides a route for the synthesis of glycopyranosides of diamino-sugars and of mono-*N*-alkylated diamino-sugars in which the amino-groups are located on adjacent carbon atoms in the pyranoid ring. It is noteworthy that in each example cited the major diamino-sugar derivative produced by reduction of the phenylhydrazone is that in which the amino-groups are *trans*-located.

EXPERIMENTAL

Methods.—U.v. spectra were measured on a Perkin-Elmer 402 Ultraviolet and Visible spectrometer, in 96% ethanol unless stated otherwise. I.r. spectra were measured for solids dispersed in potassium bromide discs, and for syrups as smears on potassium bromide discs. N.m.r. spectra were determined with a Varian A-60D instrument or with a JEOL JNM-MH-100 spectrometer: unless otherwise stated measurements were made on solutions in deuteriochloroform relative to the internal standard tetramethylsilane. Coupling constants were obtained by first-order analysis of the spectra. The operating frequency for partially second-order spectra was 100 MHz. It is recognised that in the first-order analysis errors will be greater from a 60 MHz spectrum than from a 100 MHz spectrum. Also it is recognised that due consideration must be given to the deviation of line spacings from the coupling constants in second-order spectra, but this is not critical to our determinations. The J values quoted are used only to distinguish possible chair forms and not to deduce detailed conformational structures. Optical rotations were measured with a Perkin-Elmer 141 polarimeter, on chloroform solutions unless stated otherwise. T.l.c. was performed on microscope slides coated with either Kieselgel G or G_{254} nach Stahl with one of the following solvent systems: *A*, dichloromethane; *B*, dichloromethane–ethyl acetate, 4 : 1; *C*, ethyl acetate; or *D*, ethyl acetate–methanol, 10 : 1. Spots were located with an anisaldehyde–sulphuric acid–ethanol spray at elevated temperatures, or under u.v. light. In the addition reactions the mother liquors from the isolation of the major product were not examined by t.l.c. for trace or minor products.

Preparation of Arylhydrazones or Arylazoalkenes.—General procedure. The anhydroglycosidulose (1) or (2) (0.15—0.5 g) in ethanol (3—15 ml) was treated with a slight excess (1.1 mol equiv.) of the relevant arylhydrazine dissolved in ethanol (4—6 ml) containing acetic acid (0.2 ml). The mixture was stirred at room temperature for 1—2 h and, after cooling the solution in an ice-bath, crystals were filtered off and recrystallised from ethanol to give the stated yields of product. The following compounds were obtained by this general procedure: *methyl* 2,3-*anhydro*-β-L-erythro-*pentopyranosid*-4-*ulose* o-*nitrophenylhydrazone* (3) [from compound (1) (0.3 g) and *o*-nitrophenylhydrazine (0.35 g)] as yellow needles (0.43 g, 74%), m.p. 153—154 °C; $[\alpha]_D$ +144° (*c* 0.14); $\lambda_{max.}$ 300 nm (ε 12 800); $\nu_{max.}$ 1 610 cm^{-1} (C=N); δ 5.06 (s, 1-H), 4.30 (q, J_{gem} 14.5 Hz, 5- and 5′-H), 3.97 (d, $J_{2,3}$ 4.0 Hz, 3-H), 3.56 (s, OMe), and 3.47 (d, 2-H) (Found: C, 51.7; H, 4.5; N, 15.0. $C_{12}H_{13}N_3O_5$ requires C, 51.6; H, 4.7; N, 15.05%).

With *o*,*p*-dinitrophenylhydrazine (0.6 g), compound (1) (0.45 g) gave *methyl* 2,3-*anhydro*-β-L-erythro-*pentopyranosid*-4-*ulose* o,p-*dinitrophenylhydrazone* (4) as bright yellow crystals (0.75 g, 76%), m.p. 166—167 °C; $[\alpha]_D$ +22° (*c* 0.1); $\lambda_{max.}$ 317 nm (ε 14 800); $\nu_{max.}$ 3 260 (NH) and 1 600 cm^{-1} (C=N) (Found: C, 44.45; H, 3.9; N, 16.85. $C_{12}H_{12}N_4O_7$ requires C, 44.4; H, 3.7; N, 17.3%).

Compound (2) (0.3 g) with *o*-nitrophenylhydrazine (0.31 g) gave *methyl* 3,4-*anhydro*-6-*deoxy*-α-L-lyxo-*hexopyranosid*-2-*ulose* o-*nitrophenylhydrazone* (5) as pale yellow crystals (0.39 g, 69%), m.p. 138—139 °C, $[\alpha]_D$ −395° (*c* 0.1); $\lambda_{max.}$ 300 nm (ε 15 900); $\nu_{max.}$ 3 350 (NH) and 1 600 cm^{-1} (C=N); δ 5.21 and 4.97 (2 × s, 1-H), 4.32 and 4.24 (2 × q, $J_{5,4}$ 1.5 Hz, 5-H), 3.88 and 3.82 (2 × d, $J_{3,4}$ 3.0 Hz, 3-H), 3.61 and 3.47 (2 × s, OMe), *ca.* 3.42 [*m*, 4-H (overlapped by OMe)], and 1.41 and 1.44 (2 × d, $J_{Me,5}$ 6.5 Hz, CMe) (Found: C, 52.8; H, 5.0; N, 14.4. $C_{13}H_{15}N_3O_5$ requires C, 53.2; H, 5.2; N, 14.3%).

With *o*,*p*-dinitrophenylhydrazine (0.21 g), compound (2)

(0.16 g) gave *methyl* 3,4-*anhydro*-6-*deoxy*-α-L-lyxo-*hexopyranosid*-2-*ulose* o,p-*dinitrophenylhydrazone* (6) as bright yellow needles (0.32 g, 67%), m.p. 163—164 °C; $[\alpha]_D$ −284° (*c* 0.1); $\lambda_{max.}$ 352 nm (ε 21 600); $\nu_{max.}$ 3 400 (NH) and 1 600 cm^{-1} (C=N) (Found: C, 46.7; H, 4.2; N, 16.9. $C_{13}H_{14}N_4O_7$ requires C, 46.2; H, 4.2; N, 16.6%).

Compound (1) (0.5 g) with phenylhydrazine (0.4 g) gave *methyl* 4-*phenylazo*-3,4-*dideoxy*-β-L-glycero-*pent*-3-*enopyranoside* (7) as bright orange crystals (0.56 g, 70%), m.p. 130—131 °C (from ethanol); $[\alpha]_D$ +87.8° (*c* 0.2); $\lambda_{max.}$ 308 nm (ε 13 500); $\nu_{max.}$ 3 300 (OH) and 1 640 cm^{-1} (C=C); δ 6.91 (m, 3-H), 4.72 (d, $J_{1.2}$ 2.5 Hz, 1-H), 4.53 (t, 5- and 5′-H), 4.31 (m, 2-H), 3.50 (s, OMe), and 2.51br (s, OH) (Found: C, 61.3; H, 6.1; N, 11.5. $C_{12}H_{14}N_2O_3$ requires C, 61.5; H, 6.0; N, 12.0%).

From *p*-nitrophenylhydrazine (0.76 g) and compound (1) (0.7 g) *methyl* 4-(p-*nitrophenyl*)*azo*-3,4-*dideoxy*-β-L-glycero-*pent*-3-*enopyranoside* (8) was isolated as orange needles (0.79 g, 68%), m.p. 171—172 °C; $[\alpha]_D$ −45° (*c* 0.1 in MeOH); $\lambda_{max.}$ 320 nm (ε 19 900); $\nu_{max.}$ 3 300 (OH) and 1 600 cm^{-1} (C=C); δ 7.07 (m, 3-H), 4.73 (d, $J_{1.2}$ 3.0 Hz, 1-H), 4.55 (t, 5- and 5′-H), 4.39 (m, 2-H), 3.53 (s, OMe), and 2.26br (s, OH) (Found: C, 51.65; H, 4.7; N, 14.8. $C_{12}H_{13}N_3O_5$ requires C, 51.6; H, 4.7; N, 15.05%).

Compound (2) (0.32 g) with phenylhydrazine (0.23 g) gave *methyl*-2-*phenylazo*-2,3,6-*trideoxy*-α-L-threo-*hex*-2-*enopyranoside* (9) as pale orange crystals (0.30 g, 60%), m.p. 144—145 °C; $[\alpha]_D$ +1 074° (*c* 0.1 in MeOH); $\lambda_{max.}$ 305 nm (ε 14 400); $\nu_{max.}$ 3 300 (OH) and 1 650 cm^{-1} (C=C); δ 6.79 (d, $J_{3.4}$ 5.0 Hz, 3-H), 5.26 (s, 1-H), 4.2 (oct, 5-H), 3.91 (m, $J_{4.5}$ 2.0 Hz, 4-H), 3.36 (s, OMe), 2.22br (s, OH), and 1.35 (d, $J_{Me.5}$ 6.0 Hz, CMe) (Found: C, 62.6; H, 6.5; N, 11.4. $C_{13}H_{16}N_2O_3$ requires C, 62.9; H, 6.5; N, 11.3%).

Compound (2) (0.24 g) with *p*-nitrophenylhydrazine (0.24 g) gave *methyl* 2-(p-*nitrophenyl*)*azo*-2,3,6-*trideoxy*-α-L-threo-*hex*-2-*enopyranoside* (10) as dark orange needles (0.32 g, 72%), m.p. 140—141 °C; $[\alpha]_D$ +898° (*c* 0.1); $\lambda_{max.}$ 314 nm (ε 18 200); $\nu_{max.}$ 3 400 (OH) and 1 600 cm^{-1} (C=C); δ 7.15 (d, $J_{3.4}$ 6.5 Hz, 3-H), 5.4 (s, 1-H), 4.34 (q, $J_{4.5}$ 2.5 Hz, 4-H), 4.09 (m, 5-H), 3.47 (s, OMe), 2.26br (s, OH), and 1.38 (d, CMe) (Found: C, 52.7; H, 5.2; N, 13.8. $C_{13}H_{15}N_3O_5$ requires C, 53.2; H, 5.2; N, 14.3%).

Addition Reactions with Compound (8).—*Methyl* 3-*dimethylamino*-3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (11). The *p*-nitrophenylazoalkene (8) (0.4 g) in ethanol (5 ml) was added to a solution of dimethylamine in ethanol (33%, w/v, 2 ml). The solution darkened immediately and t.l.c. analysis indicated that the reaction was complete after 10 min, then water (5 ml) was added, and the solution was concentrated under reduced pressure. The residue was extracted with dichloromethane, the extract was dried ($MgSO_4$), and concentrated to yield a crystalline residue which was recrystallised from dichloromethane–light petroleum (b.p. 40—60 °C) as yellow crystals of the p-*nitrophenylhydrazone* (11) (0.2 g, 63%), m.p. 139—140 °C (decomp.); $\lambda_{max.}$ 367 nm (ε 22 800) (Found: C, 51.6; H, 6.2, N, 17.0. $C_{14}H_{20}N_4O_5$ requires C, 51.8; H, 6.2; N, 17.3%).

By the same procedure with methylamine in ethanol (33%, w/v) compound (8) (0.56 g) gave *methyl* 3-*methylamino*-3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (12) as yellow needles (0.41 g, 70%), m.p. 153—154 °C; $\lambda_{max.}$ 368 nm (ε 21 400) (Found C, 50.3; H, 5.85. $C_{13}H_{18}N_4O_5$ requires C, 50.4; H, 5.8%).

Similarly, aqueous ethylamine (70%) with compound (8) (0.56 g) gave *methyl* 3-*ethylamino*-3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (13) (0.45 g, 73%), m.p. 154—155 °C; $\lambda_{max.}$ 368 (ε 25 400) (Found: C, 52.3; H, 6.05; N, 16.6. $C_{14}H_{20}N_4O_5$ requires C, 51.85; H, 6.2; N, 17.2%).

With ammonia solution (*d* 0.88) (1.0 ml) in ethanol (5 ml), compound (8) (0.3 g) gave *methyl* 3-*amino*-3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (14) (0.24 g, 76%) as bright yellow crystals, m.p. 212 °C (decomp); $\lambda_{max.}$ 371 nm (ε 13 400) Found: C, 48.4; H, 5.6; N, 18.1. $C_{12}H_{16}N_4O_5$ requires C, 48.6; H, 5.4; N, 18.8%).

Compound (8) (0.29 g) with phenylhydrazine (0.13 g) in ethanol (2 ml) containing acetic acid (0.1 g) gave *methyl* 3-*phenylhydrazino*-3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (15) (0.20 g, 51%) as yellow needles, m.p. 183—184 °C; $\lambda_{max.}$ 367 nm (ε 18 700) (Found: C, 55.5; H, 5.55; N, 18.15. $C_{18}H_{21}N_5O_5$ requires C, 55.8; H, 5.5; N, 18.1%).

A mixture of compound (8) (0.2 g), sodium azide (0.1 g), and ammonium chloride (0.05 g) in aqueous acetone (75%) (13 ml) was stirred for 30 min at room temperature and then concentrated to half-volume to yield, after recrystallisation from ethanol, yellow crystals of *methyl* 3-*azido*-3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (16) (0.15 g, 66%), m.p. 150—151 °C (decomp.); $\lambda_{max.}$ 365 nm (ε 19 700); $\nu_{max.}$ 2 100 cm^{-1} (N_3) (Found: C, 45.3; H, 4.65; N, 25.85. $C_{12}H_{14}N_6O_5$ requires C, 44.7; H, 4.4; N, 26.1%).

Compound (8) (0.2 g) in methanol (6 ml) was stirred with sodium methoxide, prepared from methanol (4 ml) with sodium hydride (0.35 g), at room temperature until the reaction was complete (10 min, by t.l.c.). The solution was then neutralised (solid CO_2), treated with water (5 ml), and the product extracted with dichloromethane (3 × 50 ml). The combined extracts were dried ($MgSO_4$), and concentrated, and the residue was recrystallised from dichloromethane–light petroleum (b.p. 40—60 °C) to give orange–yellow crystals of *methyl* 3-O-*methyl*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (17) (0.13 g, 57%), m.p. 202 °C (decomp.); $\lambda_{max.}$ 367 nm (ε 25 400) (Found: C, 49.8; H, 5.7; N, 13.6. $C_{13}H_{17}N_3O_6$ requires C, 50.2; H, 5.5; N, 13.5%).

Compound (8) (0.28 g) was stirred in methanol (10 ml) with sodium borohydride (0.05 g) at room temperature for 20 min, by which time the orange colour faded and no starting material remained (t.l.c.). On cooling the solution in an ice-bath, the product crystallised directly and was recrystallised from ethanol to give *methyl* 3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (18) (0.18 g, 65%) as bright yellow needles, m.p. 185—186 °C; $\lambda_{max.}$ 369 nm (ε 21 100) (Found: C, 51.7; H, 5.3; N, 14.7. $C_{12}H_{15}N_3O_5$ requires C, 51.25; H, 5.3; N, 14.9%).

The same procedure on compound (8) with sodium borodeuteride (0.05 g) in [$^2H_1$]methanol (4 ml), with addition of deuterium oxide (0.5 ml) after 25 min to encourage crystallisation, and recrystallisation from [$^2H_1$]methanol afforded *methyl* 3-*deoxy*-2-O,3-C,N-*trideuterio*-α-D-threo-*pentopyranosid*-4-*ulose* p-*nitrophenylhydrazone* (19) (0.18 g, 72%) as yellow needles, m.p. 188—189 °C; $\lambda_{max.}$ 369 nm (ε 20 900) (Found: C, 51.2; H, 5.4; N, 14.5. $C_{12}H_{12}D_3N_3O_5$ requires C, 50.7; H, 5.65; N, 14.8%).

Addition Reactions with Compound (7).—*Methyl* 3-*benzylamino*-3-*deoxy*-α-D-threo-*pentopyranosid*-4-*ulose* *phenylhydrazone* (20). The phenylazoalkene (7) (5.5 g) in ethanol (30 ml) was treated with benzylamine (3 ml) and the mixture was stirred for 2 h at 35—40 °C until the reaction was

complete (t.l.c.), the colour fading from orange to pale yellow. Crystals were obtained on cooling the solution in an ice-bath and were collected and recrystallised from ethanol to give needles of the *benzylamino-adduct* (20), (6.75 g, 85%), m.p. 156—157 °C; $\lambda_{max.}$ 277 nm (ε 13 039) (Found: C, 66.7; H, 6.65; N, 12.3. $C_{19}H_{23}N_3O_3$ requires C, 66.8; H, 6.8; N, 12.3%).

Methyl 4-acetamido-2-O-acetyl-3-O-methyl-4-deoxy-β-L-ribopyranoside (23). Sodium methoxide (0.1 g) in methanol (25 ml) was added to compound (7) and the mixture was stirred for 12 h at room temperature. The colour of the solution changed from orange to pale yellow and examination by t.l.c. indicated a single product and no residual starting material. The solution was transferred to a hydrogenation flask containing Raney nickel (1 g) and methanol (25 ml) and hydrogenation was carried out for 6 h (at room temperature and atmospheric pressure) after which time uptake of hydrogen ceased. The crude, syrupy product was isolated conventionally and was purified by chromatography on a silica-gel column [solvents: (i) *B*, (ii) *D*]. The aminoglycoside (1.14 g) obtained was acetylated [pyridine (15 ml)–acetic anhydride (15 ml)] to afford the *title compound* (23) (1.1 g), m.p. 95—96 °C [from diethyl ether–light petroleum (b.p. 40—60 °C)]; $[\alpha]_D$ +91.2° (*c* 0.6), $\nu_{max.}$ 3 350 (NH) and 1 720 (C=O) cm^{-1}; δ [($^2H_6$]benzene) (see text) 6.32—6.10br (1 H, s, NH), 5.18 (1 H, q, 2-H), 4.55 (1 H, d, $J_{1,2}$ 1.5 Hz, 1-H), 4.50—4.25 (1 H, m, 4-H), 3.55 (2 H, oct, $J_{5ax,5eq}$ 12.0, $J_{5ax,4}$ and $J_{5eq,4}$ 3.0 Hz, 5-H_{ax} and 5-H_{eq}), 3.38 (1 H, t, $J_{3,4}$ and $J_{3,2}$ 4.0 Hz, 3-H), 3.02 (3 H, s, OMe), 2.93 (3 H, s, OMe), 1.69 (3 H, s, NAc), and 1.63 (3 H, s, OAc) (Found: C, 50.5; H, 7.3; N, 5.2. $C_{11}H_{19}NO_6$ requires C, 50.6; H, 7.3; N, 5.4%).

Addition Reactions with Compound (9).—*Methyl 3-dimethylamino-3,6-dideoxy-α-L-xylo-hexopyranosid-2-ulose phenylhydrazone* (24). Compound (9) (0.4 g) in ethanol (6 ml) was treated with a solution of dimethylamine in ethanol (33%, w/v, 2 ml) at room temperature. After 15 min, when reaction was complete (t.l.c.), the solution was concentrated under reduced pressure and the residue was crystallised from diethyl ether–light petroleum (b.p. 40—60 °C) to give the dimethylamino-adduct (24) (0.31 g, 66%) as cream coloured crystals, m.p. 122—123 °C; $\lambda_{max.}$ 282 nm (ε 19 500) (Found: C, 61.1; H, 7.8; N, 14.4. $C_{15}H_{23}N_3O_3$ requires C, 61.4; H, 7.9; N, 14.3%).

By a similar procedure, compound (9) (0.25 g) with methylamine in ethanol yielded *methyl 3-methylamino-3,6-dideoxy-α-L-xylo-hexopyranosid-2-ulose phenylhydrazone* (25) as plates (0.2 g, 71%), m.p. 85—86 °C; $\lambda_{max.}$ 282 nm (ε 18 400) (Found: C, 60.3; H, 7.6; N, 14.6. $C_{14}H_{21}N_3O_3$ requires C, 60.2; H, 7.6; N, 15.0%).

Compound (9) (0.2 g) with aqueous ethylamine (70%) similarly gave *methyl 3-ethylamino-3,6-dideoxy-α-L-xylo-hexopyranosid-2-ulose phenylhydrazone* (26) as fibrous crystals (0.16 g, 67%), m.p. 118—119 °C; $\lambda_{max.}$ 281 nm (ε 18 500) (Found: C, 61.1; H, 7.7; N, 14.8. $C_{15}H_{23}N_3O_3$ requires C, 61.4; H, 7.9; N, 14.3%).

Compound (9) (0.25 g) with aqueous ammonia (*d* 0.880) (2 ml) in ethanol (5 ml) likewise yielded *methyl 3-amino-3,6-dideoxy-α-L-xylo-hexopyranosid-2-ulose phenylhydrazone* (27) as pale yellow crystals (0.21 g, 79%), m.p. 130—131 °C; $\lambda_{max.}$ 281 nm (ε 14 900) (Found: C, 58.85; H, 7.1; N, 15.2. $C_{13}H_{19}N_3O_3$ requires C, 58.85; H, 7.2; N, 15.8%).

Treatment of compound (9) (3.2 g) with benzylamine according to the above procedure yielded a pale yellow syrup, purified by preparative t.l.c., which could not be obtained crystalline. The ^1H n.m.r. spectrum of this material suggested that the syrup was a mixture of the stereoisomers of *methyl 3-benzylamino-3,6-dideoxy-α-L-xylo-hexapyranosid-2-ulose phenylhydrazine* (28) in *ca.* 8 : 1 ratio (see Table 2 for spectral data).

Compound (9) (1.2 g) in methanol (20 ml) was reduced with sodium borohydride (0.2 g). Reaction was complete in 0.5 h and then the reaction mixture was diluted with more methanol (20 ml) and further reduced with hydrogen at atmospheric pressure and room temperature in the presence of Raney nickel (1 g). Uptake of hydrogen ceased after 4 h and t.l.c. revealed two components which were separated by chromatography on silica gel, solvents *B* and *D* being used successively as eluants. The major component (0.7 g) was obtained as a syrup and was acetylated in pyridine (15 ml) with acetic anhydride (2 ml). The product, *methyl 2-acetamido-4-O-acetyl-2,3,6-trideoxy-α-L-xylo-hexopyranoside* (31) (0.65 g, 55%), was recrystallised from ethyl acetate–light petroleum (b.p. 40—60 °C) as white, chunky crystals, m.p. 137—138 °C; $[\alpha]_D$ −100° (*c* 0.2); $\nu_{max.}$ 3 350 (NH) and 1 730 cm^{-1} (C=O); δ ($CDCl_3$), 5.6—5.4br (1 H, d, NH), 4.80 (1 H, m, 4-H), 4.50 (1 H, d, $J_{1,2}$ 2.5 Hz, 1-H), 4.40—4.10 (1 H, m, 2-H), 3.82 (1 H, oct, $J_{4,5}$ 1.5 Hz, 5-H), 3.30 (3 H, s, OMe), 2.08 (3 H, s, OAc), 1.90br (s, NAc, 3- and 3′-H), and 1.08 (3 H, d, Me) (Found: C, 53.9; H, 7.8; N, 5.8. $C_{11}H_{19}NO_5$ requires C, 53.9; H, 7.75; N, 5.7%).

Methyl 4-Amino-3-benzylamino-3,4-dideoxy-β-L-xylo-pyranoside (32).—The benzylamino-phenylhydrazone (20) (5 g) in ethanol (100 ml) was shaken with hydrogen over Raney nickel (1.5 g) at room temperature for 6 h until hydrogen uptake ceased. T.l.c. examination of the filtered solution showed that the reaction was incomplete, but a repeat treatment with more reagents and then evaporation of the solvent and column chromatography on silica gel with ethyl acetate–methanol (4 : 1, v/v) yielded compound (32) as a glass (2.95 g, 78%).

When compound (32) (2.5 g) in methanol (50 ml) was shaken in hydrogen over 10% palladium-on-charcoal (2 g) uptake of gas ceased after 7 h. The solution was filtered and its volume reduced to one-fifth when *methyl 3,4-diamino-3,4-dideoxy-β-L-xylopyranoside* (33) (1.52 g, 95%) separated as needles, m.p. 190—192 °C (decomp.) (Found: C, 44.4; H, 8.7; N, 17.2. $C_6H_{14}N_2O_3$ requires C, 44.4; H, 8.7; N, 17.3%). Benzoylation (BzCl–C_5H_5N) of compound (33) by standard procedure yielded *methyl 3,4-dibenzamido-2-O-benzoyl-3,4-dideoxy-β-L-xylopyranoside* (34) (3.1 g, 78%) as crystals, m.p. 269 °C (from ethanol); $\nu_{max.}$ 1 730 cm^{-1} (C=O) (see Table 3 for n.m.r. spectral data) (Found: C, 67.9; H, 5.45; N, 5.7. $C_{27}H_{26}N_2O_6$ requires C, 68.3; H, 5.5; N, 5.9%).

Methyl 2-Amino-3-benzylamino-2,3,6-trideoxy-α-L-idopyranoside (36) *and -gulopyranoside* (37).—Compound (9) (6.5 g) in ethanol (50 ml) was treated with benzylamine (4 ml) and the mixture was stirred at 40 °C for 1.5 h. It was added to a suspension of Raney nickel (15 g) in ethanol (50 ml) and shaken with hydrogen (4 atm) at room temperature. Uptake of hydrogen ceased within 24 h, at which stage the reaction was incomplete, so the treatment was repeated with a fresh quantity of Raney nickel for a further 36 h, when only a trace of starting material remained. T.l.c. examination of the solution then indicated the presence of four products: the two with the higher R_F values were the major components. The solvent was evaporated to afford a viscous syrup which was subjected to column chromatography on silica gel (solvent *B*) to yield the α-L-

idopyranoside (36) as a syrup, $[\alpha]_D$ −87° (*c* 1.15, $CHCl_3$) (Found: C, 61.9; H, 8.4; N, 10.0. $C_{14}H_{22}N_2O_3$ requires C, 63.1; H, 8.3; N, 10.5%) and the α-L-*gulopyranoside* (37) as needles after recrystallisation from ethyl acetate–light petroleum (b.p. 40—60 °C), m.p. 130—131 °C; $[\alpha]_D$ −93° (*c* 1.75, $CHCl_3$) (Found: C, 62.9; H, 8.1; N, 10.5. $C_{14}H_{22}N_2O_3$ requires C, 63.1; H, 8.3; N, 10.5%). The total yields of compounds (36) and (37) were 2.4 g (58%) and 1.5 g (36%), respectively.

Methyl 2,3-*Diamino*-2,3,6-*trideoxy*-α-L-*idopyranoside* (38) *and* -*gulopyranoside* (39).—Compound (36) (1.0 g) in methanol (40 ml) was shaken with hydrogen (4 atm) at room temperature over 10% palladium-on-charcoal (0.5 g) for 12 h. Filtration and concentration of the solution to one third volume yielded the α-L-*idopyranoside* (38) (0.6 g; 92%) as needles, m.p. 199—200 °C; $[\alpha]_D$ −96° (*c* 0.9, MeOH) (Found: C, 46.9; H, 9.0; N, 15.7. $C_7H_{16}N_2O_3$ requires C, 47.7; H, 9.15; N, 15.9%).

By a similar procedure compound (37) (1.5 g) yielded *methyl* 2,3-*diamino*-2,3,6-*trideoxy*-α-L-*gulopyranoside* (39) (0.90 g, 92%) as crystals, m.p. 221—222 °C; $[\alpha]_D$ −97° (*c* 1.2, MeOH) (Found: C, 47.0; H, 9.0; N, 15.8. $C_7H_{16}N_2O_3$ requires C, 47.7; H, 9.15; N, 15.9%).

Methyl 2-*Amino*-3-*methylamino*-2,3,6-*trideoxy*-α-L-*idopyranoside* (40).—Compound (9) (3.75 g) in ethanol (30 ml) was treated with methylamine in ethanol (3 ml, 33%, w/v), and the solution was stirred for 1 h at room temperature. It was then added to a suspension of Raney nickel (10 g) in ethanol (50 ml), and this mixture was shaken with hydrogen (4 atm) at room temperature for 12 h; the procedure was repeated with a fresh quantity of nickel to complete the reaction. T.l.c. analysis indicated that two products were present in *ca.* 10 : 1 ratio. Filtration and concentration of the solution afforded a pale yellow syrup which was subjected to column chromatography on silica gel (solvent *B*) to give the partially pure major product, identified as the α-L-idopyranoside (40), (1.6 g, 67%) as a syrup, $[\alpha]_D$ −100° (*c* 1.5, $CHCl_3$) (Found: N, 12.7. $C_8H_{18}N_2O_3$ requires N, 14.7%). Benzoylation of this compound (0.2 g) by standard procedure ($BzCl–C_5H_5N$) yielded a product which was purified by column chromatography on silica gel using solvent *B* to afford *methyl* 2-*benzamido*-4-O-*benzoyl*-3-N-*methylbenzamido*-2,3,6-*trideoxy*-α-L-*idopyranoside* (41) (0.37 g, 72%) as a viscous syrup, $[\alpha]_D$ −97° (*c* 1.05, $CHCl_3$) (Found: C, 68.8; H, 6.0; N, 5.4. $C_{29}H_{30}N_2O_6$ requires C, 69.3; H, 6.0; N, 5.6%).

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