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REACTIONS OF ACETYLATED SUGAR OSAZONES WITH N OR O NUCLEOPHILES: SYNTHESIS OF 3-SUBSTITUTED AND 3,6-ANHYDRO DERIVATIVES*

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ABSTRACT

3,4,5-Tri-*O*-acetyl-D-*erythro*-pentosulose 1,2-bis(phenylhydrazone), its 1-*N*-acetyl derivative (D-*erythro*-**4**), 3,4,5,6-tetra-*O*-acetyl-L-*xylo*-hexosulose 1,2-bis-(phenylhydrazone), and its 1-*N*-acetyl derivative have been treated with nucleophiles. Reaction of 3,4,5,6-tetra-*O*-acetyl-D-*lyxo*-hexosulose 1-acetylphenylhydrazone 2-phenylhydrazone with sodium azide–acetic acid afforded a diastereoisomeric mixture of 4,5,6-tri-*O*-acetyl-3-azido-3-deoxy-D-*lyxo*- and -D-*xylo*-hexosulose 1-acetylphenylhydrazone 2-phenylhydrazones. Treatment of L-*erythro*-**4** with methanolic sodium methoxide gave 3-*O*-methyl-L-*erythro*- and -L-*threo*-pentosulose 1,2-bis(phenylhydrazone). By treatment with methanolic ammonia, diastereoisomerically pure 3-acetamido-3-deoxyaldosulose 1,2-bis-(phenylhydrazones) with unidentified chirality at C-3 were obtained starting from *O*-acetylaldosulose 1,2-bis(phenylhydrazones) or 1-acetylphenylhydrazone 2-phenylhydrazones. Treatment of the 3,4,5,6-tetra-*O*-acetyl-D-*lyxo*-hexosulose 1,2-bis(acetylphenylhydrazone) with methanolic ammonia afforded D-*lyxo*-hexosulose 1,2-bis(phenylhydrazone).

INTRODUCTION

Many of the reactions of sugar osazones[1] with nucleophiles can be explained by the transitory formation of a reactive 2-phenylazo-2-ene[2–6]. Thus, in acidic media, hexosulose and heptosulose 1,2-bis(arylhydrazones) give 3,6-anhydro-osazones[1,7] with high stereoselectivity, whereas similar treatment of pentosulose 1,2-bis(phenylhydrazones) in the presence of alcohols yields diastereoisomeric 3-*O*-alkyl derivatives[3].

Alkaline deacetylation of *O*-acetylosazones effects the above-mentioned transformation of the 2-arylhydrazono moiety and yields products of various types. *O*-Acetylated hexose osazones bearing monosubstituted hydrazono moieties give

*Dedicated to Professor Rezső Bognár in the year of his 75th birthday.

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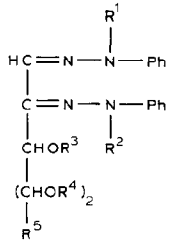
Percival's dianhydro-osazones (*e.g.*, **14**, R = H)[1,8,9] in alkaline aqueous acetone, because of the presence of nucleophile NH groups. As *O*-acetyl-3,6-anhydro-hexosazones (*e.g.*, **16** and **20**) fail to give dianhydrohexosazones, the formation of a tetrahydrodiazine ring is postulated to precede[9] that of the 3,6-anhydro ring. Thus, (even temporary) acetylation of the NH group of the 1-phenylhydrazono moiety [*e.g.*, 3,4,5,6-tetra-*O*-acetyl-D-*lyxo*-hexosulose 1-acetylphenylhydrazone 2-phenylhydrazone, (D-*lyxo*-**6**)] results in the formation of 3,6-anhydro-D-*lyxo*-hexosulose 1,2-bis(phenylhydrazone) (**15**) upon deacetylation in aqueous alkaline acetone[10]. Protection of HO-4 of an osazone with an alkali-stable substituent prevents the formation of dianhydro-osazones. Thus, lactose[11], maltose[11], and cellobiose[12] phenylosazone hepta-acetates give 3,6-anhydro derivatives. The mechanism of the formation of 3,6-anhydro derivatives from *O*-acetylated osazones proved that the mixed osazone A reported by Votoček and Vondraček[13,14] was D-*arabino*-hexosulose 1-methylphenylhydrazone 2-phenylhydrazone[15] and not 2-methylphenylhydrazone 1-phenylhydrazone as claimed[16,17]. Similarly, the product of the sodium hydroxide-mediated deacetylation of tetra-*O*-acetyl-D-*lyxo*-hexosulose 1-methylphenylhydrazone 2-phenylhydrazone is 3,6-anhydro-D-*lyxo*-hexosulose 1-methylphenylhydrazone 2-phenylhydrazone[18] (**18**) and not the bicyclic pyrazolidine derivative[16].

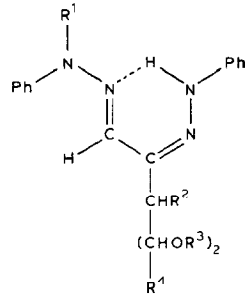
Findings on the deacetylation of various acetylated sugar osazones, the effect of the basicity of the reaction medium, and intra- and inter-molecular nucleophilic reactions are now reported.

RESULTS AND DISCUSSION

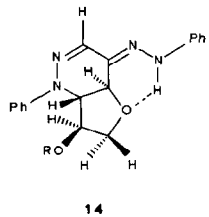
The reaction of 3,4,5,6-tetra-*O*-acetyl-D-*lyxo*-hexosulose 1,2-bis(phenylhydrazone) (D-*lyxo*-**5**), 1-acetylphenylhydrazone 2-phenylhydrazone (D-*lyxo*-**6**), or 1,2-bis(acetylphenylhydrazone) (D-*lyxo*-**7**) with methanolic sodium methoxide or that of D-*lyxo*-**6** in aqueous sodium hydroxide–acetone gave 3,6-anhydro-D-*lyxo*-hexosulose 1,2-bis(phenylhydrazone) (**15**) with high stereoselectivity. Similar treatment of 3,4,5,6-tetra-*O*-acetyl-L-*xylo*-hexosulose 1,2-bis(phenylhydrazone) (L-*xylo*-**5**) with methanolic sodium methoxide afforded 3,6-anhydro-L-*lyxo*-hexosulose 1,2-bis(phenylhydrazone) (**19**, the enantiomer of **15**)[10]. These findings show that the rules of stereochemistry[5,19], found for the formation of 3,6-anhydro derivatives from osazones in acidic media (the configuration is identical on C-3 and C-4 in the favoured product, *i.e.*, the two hydrazone groups assume a position opposite to that of the HO-4), are also valid for the transformation of acetylated osazones in alkaline medium. The presence of an acetyl group on the 1-hydrazono moiety of the starting osazones facilitates the formation of the anhydro-osazones with smaller amounts of impurities, which eases the isolation of the pure product. The finding that the use of a small excess (~1.1 mol/mol of substrate) of sodium methoxide in methanol results in the transformation of D-*lyxo*-**6** into 3,6-anhydro-D-*lyxo*-hexosulose 1-acetylphenylhydrazone 2-phenylhydrazone (**17**) indicates that the



	R^1	R^2	R^3	R^4	R^5
1	H	H	H	H	H
2	H	H	H	H	CH_2OH
3	H	H	Ac	Ac	H
4	Ac	H	Ac	Ac	H
5	H	H	Ac	Ac	CH_2OAc
6	Ac	H	Ac	Ac	CH_2OAc
7	Ac	Ac	Ac	Ac	CH_2OAc
8	H	H	Me	H	H



	R^1	R^2	R^3	R^4
9	H	NHAc	H	H
10	Ac	NHAc	H	CH_2OH
11	H	NHAc	H	CH_2OH
12	Ac	NHAc	Ac	CH_2OAc
13	Ac	N_3	Ac	CH_2OAc



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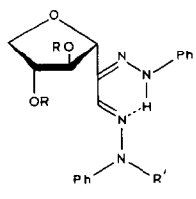
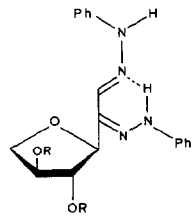
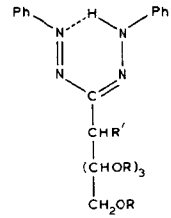


	R	R′
15	H	H
16	Ac	H
17	H	Ac
18	H	Me



19 R = H
20 R = Ac



	R	R′
21	Ac	OAc
22	H	NHAc

elimination of AcO-3 and cleavage of AcO groups precede that of the N-Ac bond.

Acetylated pentosazones cannot form 3,6-anhydro rings in the deacetylation reaction, which explains why treatment of 3,4,5-tri-*O*-acetyl-L-*erythro*-pentosulose 1-acetylphenylhydrazone 2-phenylhydrazone (L-*erythro*-**4**) with methanolic sodium methoxide gave L-*erythro*- (L-*erythro*-**8**) and L-*threo*-3-*O*-methylpentosulose 1,2-bis(phenylhydrazone) (L-*threo*-**8**) in about the same yield. The physical and micro-analytical data (Table I) of the products accorded with those of the known enantiomers (L- and D-*erythro*-**8** and D-*threo*-**8**), obtained either by osazone formation[20,21] or from D-*erythro*- or D-*threo*-pentosulose 1,2-bis(phenylhydrazone) by treatment with sulphuric acid in methanol[3]. Although the stereoselectivity of the 1,4-addition of methanol to the cyclic phenylazo-ene system is high[22,23], it was not observed in the deacetylation of the acyclic acetylated pentosazones in alkaline

TABLE I

PREPARATION AND PHYSICAL DATA FOR **2–6** AND **8**

Product	*Starting material (mmol)*	*Solvent (mL)*	*Agent (mL)*	*Reaction time (h) (temp.)*[a]	*Yield (%) [crude (pure)]*	*M.p. (degrees) (solvent of recrystn.)*	$[\alpha]_D^{23}$ *(degrees) (c, solvent)*	*Formula Anal.: Found (Calc.)*
D-*lyxo*-**2**	D-*lyxo*-**7**[27] (3)		NH_3–MeOH[b–d] (60)	66 (0–4[e]), then 6	92 (45)	180–182[e] ($MeOCH_2CH_2OH$)		$C_{18}H_{22}N_4O_4$[f]
D-*erythro*-**3**	D-*erythro*-**1** (9)	Pyridine[b] (15)	Ac_2O[g] (15)	15	94 (67)	136–137[h] ($EtOH–H_2O$)		$C_{23}H_{26}N_4O_6$
D-*erythro*-**4**	D-*erythro*-**3** (6.6)	Me_2NPh[b] (11.5)	AcCl (11.5)	19[i]	78 (70)	121[j] ($EtOH–H_2O$)	+17.5[j] (1, $CHCl_3$)	$C_{25}H_{28}N_4O_7$
L-*xylo*-**5**	L-*xylo*-**2** (67)	Pyridine[b] (128)	Ac_2O[k] (48)	18	87 (82)	142[l,m] (EtOH–heptane)	−82[m] (1.1, $CHCl_3$)	$C_{26}H_{30}N_4O_8$
L-*xylo*-**6**	L-*xylo*-**5** (7.6)	Me_2NPh[b] (2.4)	AcCl (1.5)	18[i]	100 (62)[n]	Amorphous	−145 (1, $CHCl_3$)	$C_{28}H_{32}N_4O_9$; C, 59.17 (59.14); H, 5.56 (5.67); N, 9.87 (9.85); *m/z* 569 (M^+), 135 (AcNHPh)
L-*erythro*-**8**	L-*erythro*-**4**[30] (9)	$CHCl_3$[b] (15)	0.5M NaOMe–MeOH[b] (40)	19	95[o] (13)[p]	167[q] (MeCN)	−11[q] (0.9, MeOH)	$C_{18}H_{22}N_4O_3$; MeO, 8.91 (9.06); *m/z* 343 ($M^+ + 1$), 281 [$M^+ - CH(OH)CH_2OH$], 188[r]
L-*threo*-**8**	L-*erythro*-**4**[30] (9)	$CHCl_3$[b] (15)	0.5M NaOMe–MeOH[b] (40)	19	95[o] (16)[s]	177–178[t] (^{i}PrOH)	+36.5[t] (1, MeOH)	$C_{18}H_{22}N_4O_3$; MeO, 9.07 (9.06); *m/z* 342 (M^+), 281[u], 188[u]

[a]Room temperature unless noted otherwise. [b]Anhydrous. [c]Saturated at 0°. [d]The same product was obtained [yields, 92 (51)%] by a more laborious procedure[10] involving treatment of D-*lyxo*-**7** in methanol with traces of conc. ammonium hydroxide added at intervals. [e]Lit.[28] m.p. 185–187° (from 2-methoxyethanol). [f]The product was also identified by treatment with acetic anhydride–pyridine to give D-*lyxo*-**5**. [g]According to the known method[8]. [h]Lit.[29] amorphous; lit.[30] L enantiomer, m.p. 137°. [i]See ref. 27. [j]L Enantiomer: lit.[30] m.p. 121°, $[\alpha]_D^{23}$ −17° (*c* 1, chloroform). [k]The pyridine was added to an ice-cold suspension of L-*xylo*-**2** in acetic anhydride. The cooling was continued until dissolution was complete. [l]Heptane was added to a heated ethanolic solution. [m]Lit.[30] m.p. 80–82°, $[\alpha]_D^{23}$ −80° (*c* 1, chloroform). [n]After column chromatography (3:1 benzene–ethyl acetate). [o]After acidification with acetic acid, the reaction mixture was concentrated and the residue was triturated with water. The crude product was mainly a 1:1 mixture of L-*erythro*-**8** and L-*threo*-**8** together with five minor components (t.l.c., 8:2 chloroform–methanol). [p]After purification by column chromatography (1:1 butyl acetate–ethyl acetate); R_F 0.33 (t.l.c.). [q]Lit.[20] m.p. 163° (from aqueous ethanol); D enantiomer[3], m.p. 167° (from acetonitrile), $[\alpha]_D^{20}$ +10° (*c* 0.9, methanol). [r]MeO-C$^+$H-(2-phenyl-1,2,3-triazol-4-yl). [s]After purification as described above for L-*erythro*-**8**, R_F 0.23 (t.l.c., 1:1 butyl acetate–ethyl acetae). [t]D Enantiomer[3], m.p. 177° (from 2-propanol), $[\alpha]_D^{20}$ −36° (*c* 1, methanol). [u]As that of L-*erythro*-**8**.

media described here or in the transformation of pentosazones in an acid–alcohol solution[3].

When a 2-phenylazo-2-ene structure cannot be formed during the cleavage of OAc groups, addition or anhydro products are not formed. Thus, treatment of the 1,2-bis(acetylphenylhydrazone) derivative D-*lyxo*-**7** in chloroform–methanol with traces of conc. ammonium hydroxide, added at intervals of 1–2 h, afforded[10] the deacetylated osazone D-*lyxo*-**2**. Moreover, the same result was obtained using a large excess of anhydrous, saturated methanolic ammonia at 0° (see Table I).

Treatment of pentosazone and hexosazone derivatives containing 2-phenylhydrazone moieties and suitable C-3 leaving-groups with conc. ammonium hydroxide or anhydrous methanolic ammonia yields 3-acetamido-3-deoxyaldosulose 1,2-bis(phenylhydrazones) as a consequence of 1,4-addition of ammonia to the 2-phenylazo-2-ene system, followed by $O \rightarrow N$ acetyl migration. Thus, 70% of 3-acetamido-3-deoxy-L-pentosulose 1,2-bis(phenylhydrazone) (L-**9**) was obtained from 3,4,5-tri-*O*-acetyl-L-*erythro*-pentosulose 1,2-bis(phenylhydrazone) (L-*erythro*-**3**), or, more conveniently, from the corresponding 1-acetylphenylhydrazone 2-phenylhydrazone derivative (L-*erythro*-**4**) on treatment with methanolic ammonia. In a similar reaction, D-*erythro*-**4** gave 77% of the 3-acetamido derivative D-**9** (Table II). Whereas the addition of methanol to the 2-phenylazo-2-ene system of the osazone gives a 1:1 mixture of C-3 diastereoisomeric methyl ethers, the addition of ammonia is highly stereoselective, probably because of the chirality control exerted by C-4. This effect is even more evident with hexose derivatives. The reaction of 3,4,5,6-tetra-*O*-acetyl-D-*lyxo*-hexosulose 1-acetylphenylhydrazone 2-phenylhydrazone (D-*lyxo*-**6**) yielded 3-acetamido-3-deoxy-D-4,5-*threo*-hexosulose 1,2-bis(phenylhydrazone) (D-4,5-*threo*-**11**). The same reaction of 3,4,5,6-tetra-*O*-acetyl-L-*xylo*-hexosulose 1,2-bis(phenylhydrazone) (L-*xylo*-**5**) or the 1-acetylphenylhydrazone 2-phenylhydrazone derivative (L-*xylo*-**6**) gave 3-acetamido-3-deoxy-L-4,5-*threo*-hexosulose 1,2-bis(phenylhydrazone) (L-4,5-*threo*-**11**), the enantiomer of the former product, clearly by change of the configuration at C-3 in the *lyxo* or *xylo* starting compounds. When the reaction was interrupted or carried out at a lower temperature, the intermediate 3-acetamido-3-deoxyhexosulose 1-acetylphenylhydrazone 2-phenylhydrazones (D- and L-4,5-*threo*-**10**) could be isolated.

Treatment of the penta-acetate D-*lyxo*-**6** with hydrazoic acid resulted in exchange of the AcO-3 group (Table II). The ^{1}H-n.m.r. data (Table III) revealed the purified amorphous product to be a ~2:1 mixture of the corresponding *xylo* and *lyxo* diastereoisomers (D-4,5-*threo*-**13**). Treatment of this with methanolic sodium methoxide gave (t.l.c.) the 3,6-anhydrohexosazone, whereas reaction with methanolic ammonia afforded 35% of the 3-acetamido-3-deoxy derivative, D-4,5-*threo*-**11**. Since NHAc is not as good a leaving group as OAc, treatment of D-4,5-*threo*-**11** with hot acetic anhydride gave the penta-acetate D-4,5-*threo*-**12**. Similar treatment of *O*-acetylaldosulose 1,2-bis(phenylhydrazone)[24] or 1-acetylphenylhydrazone 2-phenylhydrazones[6] yielded acetylated dianhydroarylosazones (**25**) with a pyrazole structure.

TABLE II

PREPARATION AND PHYSICAL DATA FOR **9–13**

Product	*Starting material (mmol)*	*Solvent (mL)*	*Agent (mL)*	*Reaction time (h) (temp.)*[a]	*Yield (%) [crude (pure)]*	*M.p. (degrees) (solvent of recrystn.)*	$[\alpha]_D^{25}$ *(degrees) (c, solvent)*	*Formula Anal.: Found (Calc.)*
D-**9**[b]	D-*erythro*-**4** (80)		NH_3–MeOH[c,d] (1200)	42	97 (77)	199 (aq. EtOH)	−192 (0.7, $MeOCH_2CH_2OH$)	$C_{19}H_{23}N_5O_3$
L-**9**[b]	L-*erythro*-**3**[30] (4)		NH_3–MeOH[c,d] (60)	48	89 (42)	199.5–200 (aq. EtOH)		$C_{19}H_{23}N_5O_3$; *m/z* 369 (M^+; 369.41), 351 ($M^+ - H_2O$), 333 ($M^+ - 2\,H_2O$),
	L-*erythro*-**4**[30] (2)	MeOH (30)	25% NH_4OH (30)	70	95 (47)	198–199 (aq. EtOH)		308 [M^+ − $CH(OH)CH_2OH$]
	L-*erythro*-**4**[30] (4)		NH_3–MeOH[c,d] (60)	42 (0–4°), then 24	98 (70)	199.5–200 (aq. EtOH)	+193.5 (0.76, $MeOCH_2CH_2OH$)	C, 61.73 (61.77); H, 6.28 (6.27); N, 18.96 (18.96)
D-4,5-*threo*-**10**	D-*lyxo*-**6**[6] (20)		NH_3–MeOH[c,d] (300)	66 (0–4°)	(27)[e]	232–233 ($MeOCH_2CH_2OH$–H_2O)		$C_{22}H_{27}N_5O_5$; N, 15.86 (15.86); *m/z* 441 (M^+; 441.48), 350 [M^+ − $(CHOH)_2CH_2OH$]
L-4,5-*threo*-**10**[f]	L-*xylo*-**6** (9.3)	$CHCl_3$[c] (15)	NH_3–MeOH[c,d] (150)	45	(7)[g]	232–233 ($MeOCH_2CH_2OH$–H_2O)		[f]
D-4,5-*threo*-**11**[h]	D-*lyxo*-**6**[6] (4)		NH_3–MeOH[c,d] (60)	72	95 (78)	209–210 ($MeOCH_2CH_2OH$–H_2O)	+161.5 (0.7, $MeOCH_2CH_2OH$)	$C_{20}H_{25}N_5O_4$; C, 60.26 (60.13); H, 6.33 (6.31); N, 17.50 (17.53)
	D-*lyxo*-**6**[6] (10)	MeOH (150)	25% NH_4OH (150)	60	95 (63)	204–205 ($MeOCH_2CH_2OH$–H_2O)		*m/z* 399 (M^+), 381 ($M^+ - H_2O$) 364 ($M^+ - H_2O - NH_3$),
	D-4,5-*threo*-**10** (0.9)		NH_3–MeOH[c,d] (15)	44	(95)	208 ($MeOCH_2CH_2OH$–H_2O)		322 ($M^+ - H_2O - NH_3 - CH_2CO$) 308 [$M^+$ − $(CHOH)_2CH_2OH$]
	D-4,5-*threo*-**13** (4.5)		NH_3–MeOH[c,d] (180)	66	61 (35)	205–206 ($MeOCH_2CH_2OH$–H_2O)	+162 (0.7, $MeOCH_2CH_2OH$)	N, 17.56 (17.53)
L-4,5-*threo*-**11**[h]	L-*xylo*-**6** (9.3)	$CHCl_3$[c] (15)	NH_3–MeOH[c,d] (150)	45	(50)	205–206 ($MeOCH_2CH_2OH$–H_2O)		$C_{20}H_{25}N_5O_4$; C, 59.96 (60.13); H, 6.52 (6.31); N, 17.33 (17.53)
	L-*xylo*-**5** (12)		NH_3–MeOH[c,d] (180)	67	(51)	205–206 ($MeOCH_2CH_2OH$–H_2O)	−161.5 (0.7, $MeOCH_2CH_2OH$)	*m/z* 399 (M^+; 399.44)
D-4,5-*threo*-**12**	D-4,5-*threo*-**11** (2.5)		Ac_2O (10)	1.5 (b.p.)	(25)[i]	amorphous		$C_{28}H_{33}N_5O_8$; N, 12.17 (12.34); *m/z*[i] 568 (M^+; 567.58); 508 (M^+ − AcOH)
D-4,5-*threo*-**13**[k]	D-*lyxo*-**6** (10)	AcOH (25)	NaN_3 (100 mmol)	70 (50°)	95 (47)[k]	amorphous	+164 (1, chloroform)	$C_{26}H_{29}N_7O_7$; N, 17.52 (17.78); *m/z* 552 (M^+; 551.55)

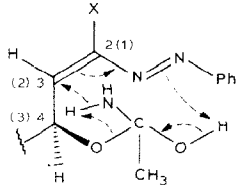
[a]Room temperature unless noted otherwise. [b]T.l.c. (9:1 ethyl acetate–methanol, or 8:2 chloroform–methanol) properties and i.r. spectra of D-**9** and L-**9** (obtained from L-*erythro*-**3**, D- or L-*erythro*-**4**) are identical. [c]Anhydrous. [d]Saturated at 0°. [e]From the mother liquor, 49% of pure D-4,5-*threo*-**11** could be isolated. [f]T.l.c. properties and i.r. and ^{1}H-n.m.r. spectra are identical with those of D-4,5-*threo*-**10**. [g]From the mother liquor, 50% of pure L-4,5-*threo*-**11** could be isolated. [h]The i.r. and ^{1}H-n.m.r. spectral data and t.l.c. properties of the product prepared in different ways were the same, and identical with those of the other enantiomer. [i]After column chromatography (8:2 chloroform–acetone). [j]At −15 eV. [k]See Experimental.

TABLE III

I.R. AND ^{1}H-N.M.R. DATA FOR **4–6** AND **8–13**

Compound	ν_{max}^{KBr} *(cm^{-1})*	*δ (p.p.m.)*
D-*erythro*-**4**	1736 (OAc), 1691 (PhNAc), 1598 (Ar), 1565 and 1525 (NH)	
L-*xylo*-**5**	3297 (NH), 1751, 1744, 1734, 1720[a] (OAc), 1600 (Ar), 1558 and 1521 (NH)	
L-*xylo*-**6**	1747 (OAc), 1691 (PhNAc), 1599 (Ar), 1575 and 1530 (NH)	($CDCl_3$): 7.62–7.00 (10 H, H–Ar), 6.88 (s, 1 H, CH=N), 5.70 (dd, 1 H, *J* 3 and 8.5 Hz, H-4), 5.30–5.22 (m, 2 H, H-3,5), 4.25-3.94 (m, 2 H, CH_2), 2.64 (bs, 2 H, 2/3 NAc), 2.17 (s, 1 H, 1/3 NAc), 2.04, 2.00, 1.96, and 1.95 (4 s, each 3 H, 4 AcO)
L-*erythro*-**8**	3400 (OH), 3298 and 3250 (NH), 2819 (MeO), 1600 (Ar)	[$(CD_3)_2CO$]: 12.46 (12.53[b]) (s, 1 H, NH[c]), 9.74 (10.27[b]) (s, 1 H, NH[d]), 7.79 (s, 1 H, CH=N), 3.32 (s, 3 H, MeO)
L-*threo*-**8**	3540 and 3400 (OH), 3245 (NH), 2819 (MeO), 1599 (Ar)	[$(CD_3)_2CO$]: 12.45 (12.51[b]) (s, 1 H, NH[c]), 9.78 (10.32[b]) (s, 1 H, NH[d]), 7.78 (s, 1 H, CH=N), 3.31 (s, 3 H, MeO)
L-**9**	3362 (OH), 3295 and 3240 (NH), 1638 (NHAc[e]), 1599 (Ar), 1564 (NH), 1513 (Amide II[f]), 1369 (CH_3)	[$(CD_3)_2SO$]: 12.01 (s, 1 H, NH[c]), 10.70 (s, 1 H, NH[d]), 7.88 (d, 1 H, $J_{3,NH}$ 8.5 Hz, N*H*Ac[d]), 7.67 (s, 1 H, CH=N), 7.38–6.83 (m, 10 H, 2 Ph), 4.87 (d, 1 H, $J_{4,OH}$ 5.5 Hz, HO-4[g]), 4.74 (dd, 1 H, $J_{3,4}$ 4 Hz, $J_{3,NH}$ 8.5 Hz, H-3), 4.62 (t, 1 H, $J_{5,OH}$ 5.5 Hz, HO-5[g]), 3.84 (m, 1 H, H-4), 3.39 (m, 2 H, $J_{4,5}$ 5.5 Hz, CH_2), 1.95 (s, 3 H, Ac)
D-4,5-*threo*-**10**	3425 (OH), 3340 (NH), 1673 (PhNAc), 1639 (NHAc[e]), 1597 (Ar) 1558 and 1546 (NH), 1525 (Amide II[f]), 1369 (CH_3)	[$(CD_3)_2SO$]: 11.92 (s, NH[c]), 7.88 (d, 1 H, *J* 8 Hz, N*H*Ac[d]), 7.00 (s, 1 H, CH=N), 1.75 (s, 3 H, NH*Ac*[h]) (pyridine-d_5)[i]: 11.37 (s, PhN*H*[c]), 9.28 (d, ~1/2 H, *J* ~8.5 Hz, ~1/2 N*H*Ac[d]), 8.85 (d, ~1/2 H, *J* ~8 Hz, ~1/2 N*H*Ac[d]), 2.54 (bs, 3 H, PhNAc[j]), 2.13 (s, ~0.45 NH*Ac*), 2.06 (s, ~0.55 NH*Ac*)
L-4,5-*threo*-**10**	3410 (OH), 3338 (NH), 1674 (PhNAc), 1640 (NHAc[e]), 1598 (Ar), 1560 (NH), 1527 (Amide II[f]), 1368 (CH_3)	(pyridine-d_5)[i]: 11.39 (s, PhN*H*[c]), 9.29 (d, ~1/2 H, *J* ~8.5 Hz, ~1/2 N*H*Ac[d]), 8.85 (d, ~1/2 H, *J* ~8 Hz, ~1/2 N*H*Ac[d]), 2.53 (bs, 3 H, PhN*Ac*), 2.11 (s, ~0.43 NH*Ac*), 2.05 (s, ~0.57 NH*Ac*)
D-4,5-*threo*-**11**	3375 (OH), 3350[a] and 3250 (NH), 1638 (NHAc[e]), 1599 (Ar), 1561 (NH), 1516 (Amide II[f]), 1370 (CH_3)	[$(CD_3)_2SO$][i]: 12.08 (s, 1 H, NH[c]), 10.71 (s, 1 H, NH[d]), 7.95 (d, 1 H, *J* 8.5 Hz, N*H*Ac[d]), 7.66 (s, 1 H, CH=N), 1.88 (s, 3 H, NH*Ac*)
L-4,5-*threo*-**11**	3375 (OH), 3300 and 3250 (NH), 1639 (NHAc[e]), 1599 (Ar), 1561 (NH), 1517 (Amide II[f]), 1370 (CH_3)	[$(CD_3)_2SO$][i]: 12.08 (s, 1 H, NH[c]), 10.71 (s, 1 H, NH[d]), 7.98 (d, 1 H, *J* 9 Hz, N*H*Ac[d]), 7.66 (s, 1 H, CH=N), 1.90 (s, 3 H, NH*Ac*)
D-4,5-*threo*-**12**	1745 (OAc), 1689 (PhNAc), 1675[a] and 1655[a] (NHAc[e]) 1600 (Ar), 1588 (NH), 1529 (Amide II[f])	($CDCl_3$): 7.64–6.98 (m, 10 H, 2 Ph), 6.85 (s, 1 H, CH=N), 6.19 (d, 1 H, $J_{3,NH}$ 9 Hz, N*H*Ac[g]), 5.41 (dd, 1 H, $J_{4,5}$ 5 Hz, H-4), 5.18 (m, 1 H, H-5), 4.80 (dd, 1 H, $J_{3,4}$ 6.5 Hz, H-3), 4.20 (m, 2 H, $J_{5,6}$ 4.5, $J_{5,6'}$ 5.5, $J_{6,6'}$ 12 Hz, CH_2), 2.72–2.36 (bs, 2 H, 2/3 PhN*Ac*) and 2.17 (s, 1 H, 1/3 PhN*Ac*), 2.00, 1.98, 1.96, and 1.94 (4 s, each 3 H, NH*Ac* and 3 AcO)
D-4,5-*threo*-**13**[k]	2099 (N_3), 1749 (OAc), 1694 (PhNAc), 1600 (Ar), 1576 and 1530 (NH)	($CDCl_3$): 13.84 and 12.27 (bs, NH), 7.62–7.27 (m, 9 H, H–Ar), 7.03 (m, ~4/3 H, H–Ar and 1/3 CH=N), 6.80 (s, 2/3 H, 2/3 CH=N[l]), 5.42 (dd, ~2/3 H, *J* 3 and 9 Hz, H-4[l]), 5.35–5.11 (m, ~4/3 H), 4.32–3.95 (m, 3 H, 1 H + CH_2), 2.64 (bs, 3 H, NAc), 2.10[l,m], 2.08, 2.02, 2.00[l,m], 1.98, and 1.83[l,m] (6 s, 9 H, 3 AcO)

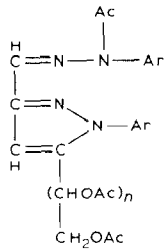
[a]Shoulder. [b]After the addition of D_2O. [c]Exchangeable with deuterium (slowly, chelated intramolecularly). [d]Exchangeable with deuterium. [e]The Amide I bands of the NHAc groups have low intensities. [f]As the spectra of D-*erythro*-**4**, L-*xylo*-**5**, L-*xylo*-**6**, and D-4,5-*threo*-**13** contain bands at 1560–1570 and 1520–1530 cm^{-1}, the bending NH vibrations of PhNH and NHAc groups (Amide II) are uncertain. A relative increase in the intensity of the band at ~1520 cm^{-1} and the presence of bands at ~1639 (Amide I) and ~1369 cm^{-1} (O=C–CH_3) corroborates the assignment. [g]Exchangeable with deuterium. [h]The signal of PhNAc is covered by those of the solvent. [i]Identical with the spectrum of the enantiomer. [j]After addition of D_2O, split into 2.65 and 2.53 p.p.m. [k]Presumably a ~2:1 mixture of the *xylo* and *lyxo* diastereoisomers. [l]Probably that of the D-*xylo* diastereoisomer. [m]2 H.



23 X = N=N—Ph

24 X = CH=N—NR—Ph

(R = H, Ac)



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The 1,4-addition of nucleophiles (NH_3, HN_3, *etc.*) to phenylazohexopyranoenosides takes place[22,23] with high stereoselectivity. Similar stereoselectivity was observed in the reactions of *O*-acetyl sugar formazans with ammonium hydroxide in ethanol. This reaction takes place *via* an intermediate having a 1,1-bis(phenylazo)-1-ene moiety[25]. Thus, 2,3,4,5,6-penta-*O*-acetyl-D-galactose (D-*galacto*-**21**) and -glucose diphenylformazans (D-*gluco*-**21**) react with retention of configuration at C-2, whereas the corresponding D-*manno* derivative (D-*manno*-**21**) reacts with inversion of configuration to give 2-acetamido-2-deoxy-D-2,3-*threo*-hexose diphenylformazans (D-*galacto*-**22** and D-*gluco*-**22**)[25] with high stereoselectivity. Presumably, the products with the preferred 2,3-*threo* configuration are formed in such a way that the 1,1-bis(phenylazo)-1-ene intermediates, produced by the elimination of AcO-3, have a planar zigzag conformation, and the addition of NH_3 to the AcO-3 carbonyl group would form a tetrahedral intermediate responsible for the transfer of ammonia to the preferred side of the 1-ene bond (**23**) and $O \rightarrow N$ acetyl migration would also take place. If this assumption is correct, then **9–11** would be expected to have the 3,4-*threo* configuration. The favoured role of AcO-3 in the formation of the 2-phenylazo-2-ene moiety renders the 3-acetamido-3-deoxyosazone structures of the products probable. ^{1}H-N.m.r. and mass-spectral data {*m/z* 308 [M^+ − $CH(OH)CH_2OH$] for L-**9**, or 350 [M^+ − $(CHOH)_2CH_2OH$] for D-4,5-*threo*-**10**, see Tables II and III} prove these structures.

There was a direct connection for the 3-acetamido-3-deoxy derivatives (D- and L-**9**, D- and L-4,5-*threo*-**11**, D-4,5-*threo*-**13**) and also for one (L-*threo*-**8**) of the 3-*O*-methyl compounds between the chirality of C-4 of the osazones and the $[\alpha]_D$ values (similar to that found[26] for unsubstituted sugar osazones). C.d. spectra give information[19,26] on the chirality of C-3 of sugar osazones. Because of the intermediate J values observed in the ^{1}H-n.m.r. spectra, c.d. studies are in progress in order to determine the chirality of C-3 of the products obtained from acetylated osazones with nucleophiles.

EXPERIMENTAL

General methods. — Melting points are uncorrected and were determined on a Kofler block. Solutions were concentrated at ⩽40° (bath)/~17 mmHg. T.l.c. was performed on Alurolle-Kieselgel $60F_{254}$ (Merck). Optical rotations were measured with a Schmidt–Haensch visual polarimeter (1-dm pathlength). I.r. spectra (KBr discs) were recorded with a Perkin–Elmer 283B spectrophotometer and 200-MHz ^{1}H-n.m.r. spectra (internal Me_4Si) with a Bruker WP 200 SY spectrometer. Mass spectra (70 eV) were obtained by using a VG-7035 GC/MS/DS instrument (ion current, 0.1 mA; direct insertion technique).

Preparation of 3-acetamido-3-deoxyhexosulose 1,2-bis(phenylhydrazones) (**9–11**) (*cf.* Table II). — (*a*) The acetylated osazone (or its solution in anhydrous chloroform) was added with ice-cooling to anhydrous methanol saturated with gaseous NH_3 at 0°. When dissolution was complete, the solution was kept at the temperature stated, and then concentrated. The residue was triturated with ice-cold water, and the crude product was collected and crystallised.

(*b*) The acetylated osazone was stirred with a mixture of concentrated, aqueous ammonium hydroxide and methanol until dissolution was complete. The solution was kept for the time stated at room temperature, and then processed as in (*a*).

*4,5,6-Tri-*O*-acetyl-3-azido-3-deoxy-*D-lyxo- *and* -D-xylo-*hexosulose 1-acetylphenylhydrazone 2-phenylhydrazones* (D-*4,5*-threo-**13**) (*cf.* Table II). — Powdered sodium azide was added to a solution of the penta-acetate D-*lyxo*-**6** in acetic acid at 40–42°. The mixture was kept for 70 h at 50–52° and then concentrated, and the residue was triturated with water. A solution of the crude product in benzene was washed with aqueous $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. Column chromatography (silica gel, 2:1 benzene–ethyl acetate) of the residue gave (^{1}H-n.m.r. data) a product suggested to be a ~1:2 mixture of the D-*lyxo* and D-*xylo* diastereoisomers (see Tables II and III).

*3,6-Anhydro-*D-lyxo-*hexosulose 1-acetylphenylhydrazone 2-phenylhydrazone* (**17**). — Methanolic 0.5M NaOMe (6.5 mL, 3.25 mmol) was added to a solution of the penta-acetate D-*lyxo*-**6** (1.706 g, 3 mmol) in anhydrous chloroform. The solution was kept for 24 h at room temperature (by this time, it was not alkaline to phenolphthalein paper). The crude **17** (0.415 g, m.p. 199–200°) was collected, and the mother liquor was treated with Amberlite IR-105 (H^+) resin, and then concentrated. The residue was crystallised from methanol to give more **17**. Recrystallisation of the combined products from methanol yielded material (0.645 g, 56%) having m.p. 202°; ν_{max}^{KBr} 3409 (OH), 3223 (NH), 1668 (NAc), 1582 and 1530 cm^{-1} (Ar). Mass spectrum: *m/z* 382 (M^+), 364 ($M^+ - H_2O$), 322 ($M^+ - H_2O - CH_2CO$), 135 (AcHNPh).

Anal. Calc. for $C_{20}H_{22}N_4O_4$: C, 62.81; H, 5.80; N, 14.65. Found: C, 62.84; H, 5.91; N, 14.80.

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