687. *Nitrogen-containing Carbohydrate Derivatives. Part III. Some Methyl 3-Arylazo-4,6-O-benzylidene-3-deoxy-α-D-glucosides.*

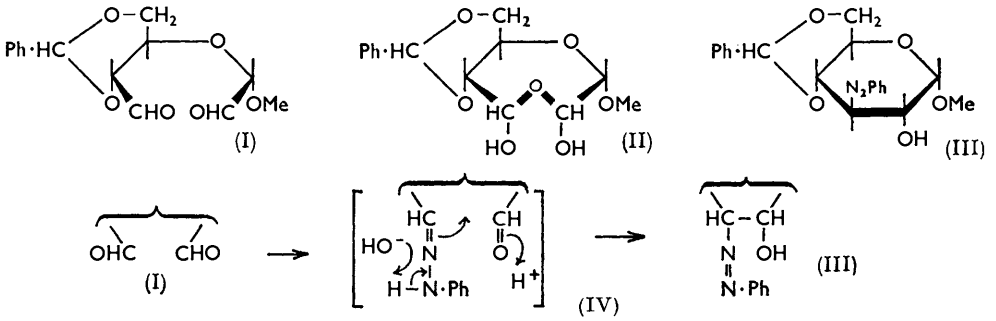
By G. J. F. Chittenden and R. D. Guthrie.

Periodate-oxidised methyl 4,6-*O*-benzylidene-α-D-glucoside has been treated with a number of arylhydrazines. Unless these contained strongly deactivating groups the product was the 3-arylazo-D-glucose derivative. Several of the crude products have been chromatographed and shown to contain no other arylazo-sugars than the 3-arylazoglucosides. The mechanistic and other implications of these findings are discussed.

Reaction of aqueous phenylhydrazine with periodate-oxidised methyl 4,6-*O*-benzylidene-α-D-glucoside [in the dialdehyde form (I) [2,3]] yields methyl 4,6-*O*-benzylidene-3-deoxy-3-phenylazo-α-D-glucoside (III) in 60% yield,[1,4] although the mechanism proposed did not preclude formation of 2- and 3-phenylazo-derivatives of D-glucose, D-mannose, D-allose, and D-altrose, through the dialdehyde monophenylhydrazone (IV). The crude product has now been subjected to chromatography on alumina. It was initially dissolved in ether to give a yellow solution and an insoluble residue (16%) which was shown to be the hemialdal (II) (characterised as its diacetate). Chromatography of the ether solution gave the 3-phenylazoglucoside (III) (68%) and five brown, oily components (total 7%). Comparison of the ultraviolet and infrared spectra of these other components with those expected for the 3-phenylazo-derivative (III) or any phenylazoalkane failed to reveal any similarity. $E_{1\,cm.}^{1\%}$ values (in EtOH) were used for ultraviolet spectral comparison; those for compound (III) were 278 and 6·9 at 266 and 390 mμ, respectively. The five minor

[1] Part II, Chittenden and Guthrie, *J.*, 1963, 2358.
[2] Guthrie and Honeyman, *J.*, 1959, 2441.
[3] Guthrie, Honeyman, and Parsons, *J.*, 1959, 2449.
[4] Guthrie and Johnson, *J.*, 1961, 4166.

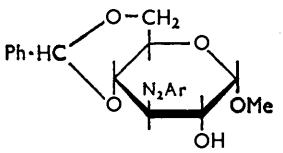
fractions had single absorptions with $E^{1\%}_{1\,cm.}$ values between 513 and 2000. These values indicated that these fractions were probably phenylhydrazones of the dialdehyde (I) or its hydrolysis products, and this was supported by a strong absorption band at 1610 cm.$^{-1}$ characteristic of the Ph·NH·N=C group. Thus it appears that the 3-phenylazoglucoside



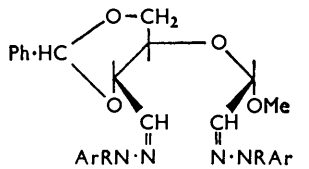
(III) is the only phenylazo-sugar formed on condensation of aqueous phenylhydrazine with the dialdehyde (I).

The above mechanism has also been supported by the non-formation of an arylazo-derivative from *p*-nitrophenylhydrazine;[5] here the *p*-nitro-group lessens the availability of electrons necessary for the rearrangement. The mechanism has now been further investigated by examining the effect of a range of substituents in the arylhydrazine.

The reaction has been carried out in the same way as for phenylhydrazine, to give the corresponding methyl 3-arylazo-4,6-*O*-benzylidene-3-deoxy-α-D-glucosides (V—XI). Each of these compounds gave a monoacetate, the correct elementary analyses, and the expected ultraviolet spectra and had no infrared absorption bands characteristic of arylhydrazones; none of the compounds yielded a formazan derivative. They were, therefore, all considered to be arylazo-derivatives. (The ultraviolet, infrared, and proton magnetic resonance spectra of these products will be discussed later.)



(V) Ar = *p*-Me·C_6H_4
(VI) Ar = *o*-Me·C_6H_4
(VII) Ar = *p*-MeO·C_6H_4
(VIII) Ar = *p*-Cl·C_6H_4
(IX) Ar = *p*-F·C_6H_4
(X) Ar = *p*-$NaO_2C·C_6H_4$
(XI) Ar = *p*-$NH_2SO_2·C_6H_4$



(XII) R = H, Ar = *m*-$NO_2·C_6H_4$
(XIII) R = Me, Ar = Ph

These results show that the arylhydrazine must be deactivated by electron-withdrawing groups more powerful than *p*-sulphonamido in order to prevent rearrangement of the proposed intermediate. When Hammett σ constants [6,7] are used as a measure of reactivity, the substituents studied decreased in effectiveness of electron-withdrawal over the range *p*-sulphonamido (σ 0·621) to *p*-methoxy (σ −0·268). It was known that the *p*-nitro-derivative (σ 0·758) prevented the rearrangement [5] and it has now been shown that the *m*-nitro-group (σ 0·710), which is intermediate in deactivation between the *p*-nitro- and the *p*-sulphonamido-group, also leads to a bisarylhydrazone (XII), and not an arylazo-derivative. Thus it is probable that the *p*-sulphonamido-group is approaching the limiting value of electron-withdrawal beyond which the rearrangement will not occur.

[5] Colbran, Guthrie, and Parsons, *J.*, 1960, 3532.
[6] Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 96; *Trans. Faraday Soc.*, 1938, **34**, 156.
[7] Jaffé, *Chem. Rev.*, 1953, **53**, 222.

The mechanism was also supported when it was shown that *N*-methyl-*N*-phenylhydrazine gave the bisarylhydrazone (XIII); rearrangement is prevented here by the *N*-methyl group.

During the course of this work O'Connor [8] showed that the phenylhydrazones of aliphatic aldehydes and ketones rapidly tautomerise to the corresponding phenylazoalkanes in neutral solution, that the process is either an irreversible reaction, or that any equilibrium that may be involved must be heavily in favour of the azo-tautomer. It was then shown [9] that powerful electron-withdrawing groups, such as *p*-nitro, prevented tautomerisation and that activating groups such as *p*-methyl favoured it. This was consistent with earlier work,[10,11] and with the results described above.

The crude 3-*p*-tolylazo- and 3-*p*-chlorophenylazo-glucosides (V and VIII) were chromatographed to see if the substituents on the arylhydrazine caused formation of any other arylazo-sugars. The crude *p*-tolyazo-compound (V), when dissolved in ether, gave the hemialdal (II) hydrate (5%) as an insoluble residue. Chromatography of the solution gave the 3-*p*-tolylazoglucoside (68%) together with two oily components (25% total). Their $E^{1\%}_{1\,cm.}$ values showed they were not arylazo-sugars and both had an infrared band at 1660 cm.$^{-1}$, probably due to the CH=N·NHAr group. Chromatography of the crude 3-*p*-chlorophenylazoglucoside gave, in addition to the pure compound (65%), two other solid components (total 7%). The behaviour of these solids again suggested that they were arylhydrazones.

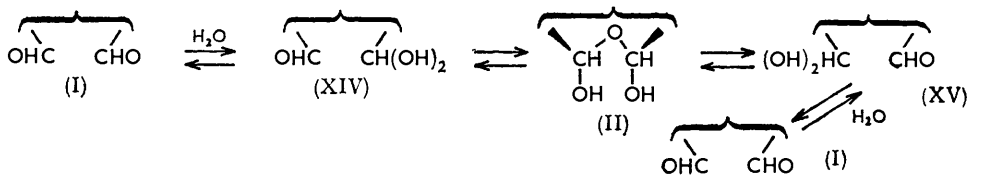
Catalytic hydrogenation of the 3-arylazoglucosides in the presence of Raney nickel, as previously described,[4] gave in each case methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (characterised as the acetamido-compound). The compounds that contained the most strongly deactivating groups in the aryl nucleus, that is, *p*-sulphonamido and *p*-carboxy, required a longer time for reduction than the less deactivated derivatives. These results are consistant with those of Khalifa *et al.*,[12] who observed that substituents in aromatic azo-compounds which increase the electron-density of the azo-group favour reductive fission; compounds with strongly electron-withdrawing substituents were much more resistant to fission and were reduced only to the hydrazo-stage.

In view of Khalifa's findings,[12] we examined the effect, on the 3-*p*-methoxyphenylazo-derivative (VII), of some of the reducing agents previously reported for conversion of the 3-phenylazoglucoside (III) into the 3-phenylhydrazino-derivative; [1] it was hoped that the electron-repelling methoxyl group would lead to reductive fission. Sodium dithionite and hydrazine hydrate–palladised charcoal, however, both gave methyl 4,6-*O*-benzylidene-3-deoxy-3-*p*-methoxyphenylhydrazino-α-D-glucoside. This was reduced with a Raney nickel catalyst to the 3-aminoglucoside; oxidation with yellow mercuric oxide [1] gave back the original 3-*p*-methoxyphenylazoglucoside. These reactions are further proof of configuration of the latter compound (cf. ref. 1). Attention is drawn to the reductive conditions described for the 3-phenylazo-compound. It has been found that at temperatures above 90°,[13] or in the described conditions but with a very active catalyst [14] (such as Nishimura's T-4 catalyst [15]), removal of the benzylidene group occurs by hydrogenolysis.

No reasons have yet been suggested for the preferential attack by the arylhydrazine on the 3-aldehyde group (original sugar ring numbering) of the dialdehyde (I). Molecular models indicate that approach to both aldehyde groups is unhindered, so the cause is not steric. Preferential hydration of the 2-aldehyde group may be the controlling factor.

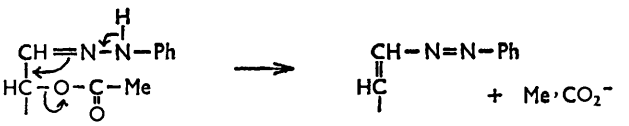
[8] O'Connor, *J. Org. Chem.*, 1961, **26**, 4375.
[9] O'Connor and Rosenbrook, *J. Org. Chem.*, 1961, **26**, 5208.
[10] Baly and Tuck, *J.*, 1906, 982.
[11] Shingu, *Sci. Papers Inst. Phys. Chem. Res., Tokyo*, 1938, **35**, 78.
[12] Khalifa and Linnell, *J. Org. Chem.*, 1959, **24**, 853; Khalifa, *J.*, 1960, 1854.
[13] Guthrie and Mutter, unpublished results.
[14] Richardson, personal communication.
[15] Nishimura, *Bull. Chem. Soc. Japan*, 1959, **32**, 61.

It has been suggested [2,16] that in the formation of the hemialdal (II) one of the aldehyde groups was first hydrated (XIV) or (XV), this being followed by normal lactol ring closure with the other aldehyde group. Such a system allows an equilibrium between the dialdehyde and the hemialdal in aqueous solution.



It is considered that the acetal group (O·CH·OMe) joined to the 2-aldehyde group would have a greater inductive effect than the 4-O group joined to the 3-aldehyde group. This would cause the 2-group to become preferentially hydrated in the above equilibrium (XIV), leaving the 3-aldehyde group more open to attack by phenylhydrazine. The final product has the *gluco*-configuration because this is conformationally the most stable of those possible.

Two other examples of compounds containing an arylazo-group attached directly to a sugar residue have recently been recorded. Mester and Moczar [17] showed that Diels's anhydro-D-glucose phenylosazone has a structure containing the Ph·N:N·C:C group. The same group has been shown [18] to be present in the products formed on acetylation of acylic sugar phenylhydrazones with, in some cases, additional treatment with ethanol or ethanol–pyridine. No reference to O'Connor's results [8,9] was given, although the mechanism postulated was an extended phenylhydrazone ⟶ phenylazo rearrangement.



References occur in the literature to the " mutarotation " of acyclic sugar phenylhydrazones in solvents such as pyridine and ethanol–pyridine.[19,20] We have observed that the final solutions from such " mutarotations " are yellow and predict that a phenylhydrazone ⟶ phenylazo rearrangement is involved and not, as Mester and Major suggest,[20] a change from an acylic to a cyclic form.

Experimental

Alumina was of type " H," 100—200 mesh, supplied by Peter Spence Ltd. The identity of compounds was proved where necessary by mixed m. p.s and infrared spectrometry. Optical rotations were measured for chloroform solutions, unless otherwise stated.

Reaction of Periodate-oxidised Methyl 4,6-O-*Benzylidene*-α-D-*glucoside* [2] *with Arylhydrazines.* —(*a*) *With phenylhydrazine.* Reaction with phenylhydrazine was carried out as described previously,[2,4] except that the hot aqueous solution of the hemialdal (II) hydrate was cooled until crystallisation had just begun before the solution of phenylhydrazine hydrochloride and sodium acetate was added. Dissolution of the hemialdal (II) hydrate in hot *NN*-dimethylformamide (10 ml./g.) before it is added to the hot water [14] removes the necessity of

[16] Guthrie and Honeyman, *Chem. and Ind.*, 1958, 388.
[17] Mester and Moczar, *Chem. and Ind.*, 1962, 554.
[18] Wolfrom, Thompson, and Lineback, *J. Org. Chem.*, 1962, **27**, 2563.
[19] Butler and Cretcher, *J. Amer. Chem. Soc.*, 1931, **53**, 4358.
[20] Mester and Major, *J. Amer. Chem. Soc.*, 1955, **77**, 4297.

filtering off any undissolved solid before adding the phenylhydrazine solution. The reaction mixture was rapidly cooled in ice and by portionwise addition of ice, the crude product crystallising; recrystallisation from a small volume of propan-1-ol or butan-1-ol gave methyl 4,6-*O*-benzylidene-3-deoxy-3-phenylazo-α-D-glucoside (III) (60%), m. p. 182—183° (lit.,[2] m. p. 182—183°) $\lambda_{max.}$ 266 ($E^{1\%}_{1\,cm.}$ 278) and 390 mμ ($E^{1\%}_{1\,cm.}$ 6·9).

Reaction of the hemialdal (II) hydrate under the same conditions, but with phenylhydrazine hydrochloride (2·2 mol.), gave the same product in the same yield (61%).

The crude phenylazo-compound (III) (2·564 g.) was extracted in ether (200 ml.), to give a yellow solution and a white solid (0·42 g.), m. p. 138—152°, whose infrared spectrum was similar to that of the hemialdal (II) hydrate. With acetic anhydride–pyridine for 16 hr. at 0° this solid gave, after two recrystallisations from ethyl acetate–light petroleum, the hemialdal diacetate (70%) m. p. 177—179° (lit.,[2] m. p. 177—179°).

The yellow solution was chromatographed to give, with cyclohexane–ethyl acetate (10 : 1) as eluent, a brown-orange fraction (A). Elution with ethyl acetate–benzene (4 : 1) gave a yellow fraction (B). Fractions (A) and (B) were concentrated and re-chromatographed. With (A), elution with ethyl acetate–benzene (3 : 97) gave three fractions: (i) a brown oily semi-solid (4·8 mg.) with an acrid odour, $\lambda_{max.}$ 245 mμ ($E^{1\%}_{1\,cm.}$ 2000), $\nu_{max.}$ 3010, 1950w, and 1610 cm.$^{-1}$; (ii) a brown oil (64 mg.) with an acrid odour, $\lambda_{max.}$ 270 mμ ($E^{1\%}_{1\,cm.}$ 1506), $\nu_{max.}$ 3320w and 1610 cm.$^{-1}$; and (iii) a brown oil (41 mg.) with sweet odour, $\lambda_{max.}$ 270 mμ ($E^{1\%}_{1\,cm.}$ 740), $\nu_{max.}$ 3550—3350vs and 1610ms cm.$^{-1}$. Elution with ethyl acetate–benzene (1 : 1) gave an oil (iv) (47 mg.), $\lambda_{max.}$ 270 mμ ($E^{1\%}_{1\,cm.}$ 1007), $\nu_{max.}$ 3650, 3380, and 1610ms cm.$^{-1}$. Elution with ethyl acetate–methanol (1 : 1) gave a brown oil (v) (16 mg.), $\lambda_{max.}$ 282 mμ ($E^{1\%}_{1\,cm.}$ 513).

Development of fraction (B) with ethyl acetate–benzene (1 : 9), followed by elution with ethyl acetate–benzene (4 : 1), gave the 3-phenylazoglucoside (III) (1·741 g., 68%), $\lambda_{max.}$ 266 ($E^{1\%}_{1\,cm.}$ 278) and 390 mμ ($E^{1\%}_{1\,cm.}$ 6·9). The total recovery (1·957 g.) represented 91% of ether-soluble material.

(*b*) *With* p-*chlorophenylhydrazine*. Reaction with *p*-chlorophenylhydrazine hydrochloride in the same way as for phenylhydrazine hydrochloride gave, on recrystallisation from butan-1-ol, *methyl* 4,6-O-*benzylidene*-3-p-*chlorophenylazo*-3-*deoxy*-α-D-*glucoside* (63%), m. p. 220—221° (decomp.), $[\alpha]_D^{21}$ −6·8° (*c* 1·108) (Found: C, 59·6; H, 5·3. $C_{20}H_{21}ClN_2O_5$ requires C, 59·3; H, 5·2%). With acetic anhydride–pyridine it gave, after two recrystallisations from ethyl acetate–light petroleum, a 2-*acetate*, m. p. 198—199°, $[\alpha]_D^{21}$ +64·2° (*c* 1·34) (Found: C, 59·6; H, 5·3. $C_{22}H_{23}ClN_2O_6$ requires C, 59·1; H, 5·1%).

The crude 3-*p*-chlorophenylazo-compound (1·10 g.) was extracted with ether (250 ml.), to give a yellow solution and a white solid (0·16 g.), m. p. 143—162°, whose infrared spectrum was similar to that of the hemialdal (II) hydrate. The solid with acetic anhydride–pyridine for 16 hr. at 0° gave, after two recrystallisations from ethyl acetate–light petroleum the hemialdal diacetate, m. p. 177—179°.

Chromatography of the yellow ether solution with chloroform as eluent gave 3 fractions: (i) a cream solid (8 mg.), m. p. 192°, $\lambda_{max.}$ 281 mμ ($E^{1\%}_{1\,cm.}$ 804), $\nu_{max.}$ 3420—3400, 1660w, and 1610 cm.$^{-1}$; (ii) a yellow-orange solid (71 mg.), m. p. 194°, $\lambda_{max.}$ 279 mμ ($E^{1\%}_{1\,cm.}$ 484), $\nu_{max.}$ 3450, 1670ms, and 1610s cm.$^{-1}$ (Found: N, 6·6%); and (iii) 3-p-chlorophenylazoglucoside (0·72 g., 65%) m. p. 220—221°, $\lambda_{max.}$ 273 and 388 mμ (the glucoside was not sufficiently soluble in absolute ethanol for accurate intensity values to be determined). The total recovery was 72%, based on ether-soluble material.

No formazan was formed from the azo-sugar or its acetate or from the analogues described below.

(*c*) *With* p-*carboxyphenylhydrazine*. Reaction with *p*-carboxyphenylhydrazine hydrochloride as above gave, on recrystallisation from butan-1-ol, *methyl* 4,6-O-*benzylidene*-3-p-*carboxyphenylazo*-3-*deoxy*-α-D-*glucoside sodium salt* (70%), m. p. 193—194° $[\alpha]_D^{21}$ −16·7° (*c* 0·6 in 1 : 1 acetone–chloroform) (Found: C, 58·0; H, 5·2. $C_{21}H_{21}N_2NaO_7$ requires C, 57·8; H, 5·0%). The presence of sodium was confirmed by ignition to a grey powder, which gave a yellow precipitate with zinc uranyl acetate reagent and a sodium flame test. The sodium ions were not removed when a solution of the product in methanol was treated with Amberlite IR-120(H^+) ion-exchange resin.

The product with acetic anhydride–pyridine gave, after three recrystallisations from ethyl acetate–ethanol–light petroleum, a 2-*acetate* (68%), m. p. 253°, $[\alpha]_D^{21}$ +83·0° (*c* 1·048) (Found: C, 60·6; H, 5·5. $C_{23}H_{24}N_2O_8$ requires C, 60·5; H, 5·3%).

(*d*) *With* p-*fluorophenylhydrazine*. Reaction with *p*-fluorophenylhydrazine hydrochloride as above gave, on recrystallisation from aqueous ethanol or ethanol–light petroleum, *methyl* 4,6-O-*benzylidene*-3-*deoxy*-3-p-*fluorophenylazo*-α-D-*glucoside* (62%), m. p. 214—215°, $[\alpha]_D^{21}$ +15·8° (*c* 1·01) (Found: C, 61·9; H, 5·6. $C_{20}H_{21}FN_2O_5$ requires C, 61·9; H, 5·4%).

(*e*) *With* o-*tolylhydrazine*. Reaction with *o*-tolylhydrazine hydrochloride in the same way gave, on recrystallisation from butan-1-ol, *methyl* 4,6-O-*benzylidene*-3-*deoxy*-3-o-*tolylazo*-α-D-*glucoside* (68%), m. p. 178—179°, $[\alpha]_D^{21}$ +55·9° (*c* 0·96) (Found: C, 65·9; H, 6·3. $C_{21}H_{24}N_2O_5$ requires C, 65·6; H, 6·3%).

The product with acetic anhydride–pyridine gave, after two recrystallisations from ethanol–light petroleum, a 2-*acetate* m. p. 118—119°, $[\alpha]_D^{21}$ +109°, (*c* 0·93) (Found: C, 64·7; H, 6·9. $C_{23}H_{26}N_2O_6$ requires C, 64·8; H, 6·2%).

(*f*) *With* p-*tolylhydrazine*. Reaction with *p*-tolylhydrazine hydrochloride in the same way gave, on recrystallisation from butan-1-ol, *methyl* 4,6-O-*benzylidene*-3-*deoxy*-3-*p-tolylazo*-α-D-*glucoside* (70%), m. p. 195°, $[\alpha]_D^{22}$ +1·65° (*c* 1·335) (Found: C, 65·4; H, 6·2. $C_{21}H_{24}N_2O_5$ requires C, 65·6; H, 6·3%). Acetylation and two recrystallisations of the product from ethanol–light petroleum gave the 2-*acetate*, m. p. 174°, $[\alpha]_D^{21}$ +71·4° (*c* 1·099) (Found: C, 65·3; H, 6·3. $C_{23}H_{26}N_2O_6$ requires C, 64·8; H, 6·2%).

The crude 3-*p*-tolylazo-compound (1·40 g.) was extracted in ether (100 ml.) and gave a yellow solution and a white solid (60 mg.), m. p. 135—178°, whose infrared spectrum was similar to that of the hemialdal (II) hydrate. The solid gave, as usual, the hemialdal (II) diacetate, m. p. 176—178°.

The yellow solution was chromatographed to give, with ether as eluent, (i) a brown oil (87·5 mg.), $\lambda_{max.}$ 250 mμ ($E^{1\%}_{1\,cm.}$ 3004), $\nu_{max.}$ 3340 and 1660 cm.$^{-1}$, and (ii) a brown oil (0·15 g.), $\lambda_{max.}$ 385 mμ ($E^{1\%}_{1\,cm.}$ 2410), $\nu_{max.}$ 3550 and 1660 cm.$^{-1}$. Elution with ethyl acetate–cyclohexane (5 : 95) gave a sticky brown solid (iii) (98 mg.), $\lambda_{max.}$ 323 mμ ($E^{1\%}_{1\,cm.}$ 1134), $\nu_{max.}$ 1660 cm.$^{-1}$. Elution with ethyl acetate–cyclohexane (1 : 1) gave (iv) the 3-*p*-tolylazo-compound (0·904 g., 68%), m. p. 195°, $\lambda_{max.}$ 274 ($E^{1\%}_{1\,cm.}$ 315) and 394 mμ ($E^{1\%}_{1\,cm.}$ 6·54). The total recovery was 93%, based on ether-soluble material.

(*g*) *With* p-*methoxyphenylhydrazine*. *p*-Methoxyphenylhydrazine (1·2 mol) was added to a solution of the hemialdal (II) hydrate (1 mol.) in aqueous *NN*-dimethylformamide–water (10 : 1) (25 ml./g.) [13] and left at room temperature for 24 hr. Pouring on ice and storage in the dark for 8 hr. gave a yellow precipitate which was collected, washed with water, and dried *in vacuo* (P_2O_5) at room temperature then having m. p. 184—186° (86%). Recrystallisation from butan-1-ol gave *methyl* 4,6-O-*benzylidene*-3-*deoxy*-3-p-*methoxyphenylazo*-α-D-*glucoside* (67%), m. p. 189°, $[\alpha]_D^{21}$ −22° (*c* 0·725) (Found: C, 62·9; H, 6·0. $C_{21}H_{24}N_2O_6$ requires C, 63·0; H, 6·0%). This gave a 2-*acetate* (from ethanol–light petroleum), m. p. 203—204°, $[\alpha]_D^{22}$ +54·5° (*c* 0·954) (Found: C, 62·6; H, 6·0. $C_{23}H_{26}N_2O_7$ requires C, 62·4; H, 5·9%).

(*h*) *With p-sulphamoylphenylhydrazine*. Reaction with *p*-sulphamoylphenylhydrazine hydrochloride in the same way yielded, after two recrystallisations from methanol, *methyl* 4,6-O-*benzylidene*-3-*deoxy*-3-*p-sulphamoylphenylazo*-α-D-*glucoside* (80%), m. p. 220—222°, $[\alpha]_D^{21}$ +2·1° (*c* 0·93) (Found: C, 53·5; H, 5·3. $C_{20}H_{23}N_3O_7S$ requires C, 53·5; H, 5·1%).

The same product was obtained by heating a solution of the hemialdal hydrate in ethanol with *p*-sulphamoylphenylhydrazine for 30 min. under reflux. Cooling the solution gave the product (64%), m. p. 219°.

The product gave a 2-*acetate* (from ethanol–light petroleum), m. p. 178—181°, $[\alpha]_D^{21}$ +53·2° (*c* 1·016) (Found: C, 53·7; H, 5·4. $C_{22}H_{25}N_3O_8S$ requires C, 53·8; H, 5·1%).

(*i*) *With* N-*methyl*-N-*phenylhydrazine*. A solution of the hemialdal hydrate (1·0 g.) in methanol (10 ml.) was boiled under reflux for 3 hr. with *N*-methyl-*N*-phenylhydrazine (1·5 g.). Addition of water gave a sticky solid which, after 14 days, gave colourless crystals, m. p. 110—112°. Four recrystallisations from ethanol–light petroleum gave needles of 2,4-O-*benzylidene*-3-O-(1-*methoxy*-2-*oxoethyl*)-D-*erythrose bis*-N-*methyl*-N-*phenylhydrazone* (71%), m. p. 112—115°, $[\alpha]_D^{21}$ +57° (*c* 1·009) (Found: C, 69·0; H, 6·9. $C_{28}H_{32}N_4O_4$ requires C, 68·9; H, 6·6%).

(*j*) *With* m-*nitrophenylhydrazine*. This reaction in the same way as for phenylhydrazine gave an orange solid (94%), m. p. 178—179°, raised by recrystallisation from ethanol–chloroform to 185—187°. Two further recrystallisations from butan-1-ol–acetone–light petroleum gave yellow-orange needles of 2,4-O-*benzylidene*-3-O-(1-*methoxy*-2-*oxoethyl*)-D-*erythrose bis*-m-*nitrophenylhydrazone* (90%), m. p. 188—189° $[\alpha]_D^{21}$ −21·1° (*c* 1·042 in acetone) (Found: C, 56·9; H, 4·3; N, 15·2. $C_{26}H_{26}N_6O_8$ requires C, 56·7; H, 4·8; N, 15·3%).

Reduction of Methyl 3-*Arylazo*-4,6-O-*benzylidene*-3-*deoxy*-α-D-*glucosides*.—Reduction was carried out in ethanol solution in the presence of Raney nickel [21] for 8 hr. at 60—90°/40—60 atm. The colourless solution was evaporated *in vacuo* to a gel, which, when crystallised from light petroleum–ethanol or –chloroform, gave methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (60—75%), m. p. 184—186° (decomp.; sublimed) [lit.,[4] m. p. 184·5—186° (decomp.; sublimed)].

With acetic anhydride–pyridine the product gave in 5 min. methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (*ca.* 70%), m. p. 294—296° (decomp.; sublimed); this is a correction on the figure previously given.[4] The yields and conditions for individual compounds are tabulated.

Me 3-arylazo-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside	Time (hr.)	Yield (%) of 3-amino-3-deoxy-α-D-glucoside
3-*p*-Tolylazo	8	66
3-*o*-Tolylazo	8	66
3-*p*-Methoxyphenylazo	8	59
3-*p*-Chlorophenylazo	8	60
3-*p*-Carboxyphenylazo	17	59
3-*p*-Sulphonamidophenylazo	18	60

Reduction of Methyl 4,6-O-*Benzylidene*-3-*deoxy*-3-p-*methoxyphenylazo*-α-D-*glucoside*.–(*a*) *With sodium dithionite*. Sodium dithionite (4 g.) and sodium hydroxide (0·25 g.) were added with stirring to a solution of the 3-*p*-methoxyphenylazoglucoside (1 g.) in ethanol (50 ml.) and water (20 ml.) at 70—80°. The mixture was kept at this temperature for 3 hr. during which sodium dithionite (5 g.) was added portionwise (1 g.). Pouring the colourless mixture into ice–water (250 ml.) precipitated a solid (0·85 g.), m. p. 142—144°, which was collected, washed with water, and dried *in vacuo* (P_2O_5). Recrystallisation from propan-1-ol containing hydrazine hydrate (*ca.* 1%) gave *methyl* 4,6-O-*benzylidene*-3-*deoxy*-3-p-*methoxyphenylhydrazino*-α-D-*glucoside* (82%), m. p. 144°, $[\alpha]_D$ +62·6° (*c* 0·83 in ethanol) (Found: C, 62·6; H, 6·7. $C_{21}H_{25}N_2O_6$ requires C, 62·7; H, 6·5%).

(*b*) *With hydrazine hydrate–palladised charcoal* (10%). A solution of the 3-*p*-methoxyphenylazoglucoside (0·5 g.) in methanol (30 ml.) was boiled under reflux with hydrazine hydrate (1 g.) in the presence of 10% palladised charcoal until the yellow colour of the azo-compound had disappeared (1 hr.). The solution was filtered through Celite and poured into ice–water, to give a white solid which, when recrystallised as above, gave methyl 4,6-*O*-benzylidene-3-deoxy-3-*p*-methoxyphenylhydrazino-α-D-glucoside (78%), m. p. 142—144°, $[\alpha]_D^{22}$ +62·7° (*c* 0·96, in ethanol).

Reduction of the 3-*p*-methoxyphenylhydrazino-compound as described [4] for the phenylazoglucoside (III) gave, after recrystallisation from ethanol–light petroleum, methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside (62%), m. p. 183—185° (decomp.; sublimed), $[\alpha]_D^{21}$ +102° (*c* 0·74) {lit.,[4] m. p. 184·5—186° (decomp.; sublimed); $[\alpha]_D^{20}$ +102° (*c* 1·5)}.

Treatment of the product with acetic anhydride–pyridine for 5 min.[4] gave methyl 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucoside, m. p. 292—295° (decomp.; sublimed).

Oxidation of the 3-*p*-methoxyphenylhydrazino-compound with yellow mercuric oxide as described earlier,[1] but for 74 hr., gave methyl 4,6-*O*-benzylidene-3-deoxy-3-*p*-methoxyphenylazo-α-D-glucoside (98%), m. p. 189°.

Preparation of Various Arylhydrazine Hydrochlorides.—To the amine (0·25 mol.), suspended in water (62·5 ml.), was added concentrated hydrochloric acid (62·5 ml.), and the mixture was cooled to −5°. Diazotisation with a solution of sodium nitrite (0·25 mol.) in water (63 ml.) at −5° to 0° gave a solution of the arenediazonium chloride. This was filtered rapidly into a solution of sodium sulphite (1·1 mol) in water (400 ml.) at 70° to give a bright yellow-orange solution which was heated at 65—70° for 1 hr. The solution was acidified to litmus with 6N-hydrochloric acid and then heated a further 6 hr. at 70° to give, on cooling, the crude arylhydrazine hydrochloride. Recrystallisation by boiling with hydrochloric acid and charcoal, followed by filtration, gave, on cooling, the pure arylhydrazine hydrochloride, which was dried *in vacuo* (P_2O_5) and stored in the dark. The yields and m. p. of the hydrochlorides prepared are tabulated.

[21] Dominguez, Lopez, and France, *J. Org. Chem.*, 1961, **26**, 1625.

Arylhydrazine hydrochloride	Yield (%)	M. p.	Reported yield (%)	Reported m. p.
o-Tolyl	93	194—195°	56 [22]	195°
p-Tolyl	76	155—157	63 [22]	155—160
p-Chlorophenyl	93	222—224	67 [22]	221·5—223
p-Carboxyphenyl	79	248—250	76 [23]	252—253
p-Sulphonamido	82	206—208	77 [24] *	204 [25]

* Yield quoted for free base.

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