Carbohydrate Research
Elsevier Publishing Company, Amsterdam
Printed in Belgium

NUCLEOPHILIC DISPLACEMENT REACTIONS IN CARBOHYDRATES

PART XVI[1]. SYNTHESES OF 3,5-DIACETAMIDO-3,5-DIDEOXY-D-RIBOSE AND 3,5-DIACETAMIDO-3,5-DIDEOXY-D-XYLOSE DERIVATIVES

J. S. BRIMACOMBE* AND A. M. MOFTI*

Chemistry Department, The University, P.O. Box 363, Birmingham 15 (Great Britain)

(Received May 27th, 1970; accepted for publication, June 16th, 1970)

ABSTRACT

3,5-Diacetamido-3,5-dideoxy-D-ribose has been prepared from 3-acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**1**). This was achieved by selective removal of the 5,6-*O*-isopropylidene group, followed by a conventional chain-shortening reaction on the resulting diol **2** to give 3-acetamido-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**3**). The derived methanesulphonate **4** underwent a smooth displacement reaction with azide ion to yield, after reduction and acetylation, 3,5-diacetamido-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**7**). Acid hydrolysis then gave the free sugar, which was shown to exist mainly in the furanoid ring-form (**8**) at equilibrium in aqueous solution.

3,5-Diacetamido-3,5-dideoxy-D-xylose was synthesised by way of an azide-exchange reaction on 1,2-*O*-isopropylidene-3,5-di-*O*-toluene-*p*-sulphonyl-α-D-ribofuranose (**20**), for which a convenient preparation is described. The diazide **21** resulting from this reaction was transformed by reduction, acetylation, and acid hydrolysis into the free sugar. The six-membered ring-form (**23**) of 3,5-diacetamido-3,5-dideoxy-D-xylose is favoured in aqueous solution at equilibrium. An attempt to prepare this sugar by means of an azide-exchange reaction on 3-acetamido-3-deoxy-1,2-*O*-isopropylidene-5-*O*-toluene-*p*-sulphonyl-α-D-xylofuranose (**15**) was unsuccessful due to a competing solvolytic displacement of the sulphonate group, involving acetamido-group participation.

INTRODUCTION

The chemistry of diamino sugars has attracted a good deal of attention since the discovery of 2,6-diamino-2,6-dideoxy-D-glucose and -L-idose as components of the neomycin and paromycin antibiotics[2]. A number of stereoisomers of these 2,6-diamino sugars have been synthesised[3], and considerable efforts have been made to prepare isomeric 2,3-[4] and 3,6-diaminohexoses[5]. The present paper describes syntheses of two 3,5-diaminopentose derivatives, which were undertaken as part of a programme

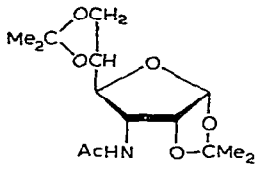
*Present address: Chemistry Department, The University, Dundee DD1 4HN, Great Britain.

aimed at the synthesis of analogues of 3-amino-3-deoxy-D-ribose, a component of the nucleoside-like antibiotics puromycin[6] and 3′-amino-3′-deoxyadenosine[7]. Both antibiotics possess antitumour activity[7,8], and it was hoped that analogues containing functional groups other than the hydroxyl group at position-5 of the sugar residue might be biologically active. We sought, therefore, to prepare a number of 3,5-diacetamido-3,5-dideoxypentose derivatives which could subsequently be condensed with a purine base to form the nucleoside. In general, the methods selected for the synthesis of these sugars could also be adapted to allow such substituents as halogen and thiol to be introduced at position-5 of a 3-acetamido-3-deoxypentose.

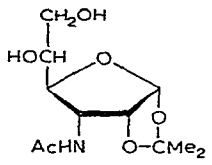
The 3,5-diacetamido-3,5-dideoxypentoses are also of chemical interest since the six-membered ring-form can be regarded as a 3-amino sugar derivative in which the ring-oxygen atom has been replaced by an acetamido group[9]. Not only is the ratio of five- to six-membered rings at equilibrium of interest, but the 3,5-diamino sugars should exhibit interesting behaviour in acid media[9]. We now report syntheses of 3,5-diacetamido-3,5-dideoxy-D-ribose and -D-xylose; a subsequent paper will describe syntheses of 3,5-diacetamido-3,5-dideoxy-L-arabinose and -L-lyxose. A salt of 3,5-diamino-3,5-dideoxy-1,2-*O*-isopropylidene-D-ribose has been reported previously by Wolfrom and his co-workers[10], but the properties of this compound were not investigated.

DISCUSSION

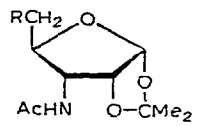
3-Acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[11] (**1**) served as a convenient starting material for the synthesis of 3,5-diacetamido-3,5-dideoxy-D-ribose, and it was converted into the diol **2** on partial hydrolysis with 75% aqueous acetic acid at room temperature. Successive treatments of **2** with aqueous sodium periodate and ethanolic sodium borohydride gave 3-acetamido-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**3**). Esterification of the latter compound with methanesulphonyl chloride in pyridine afforded 3-acetamido-3-deoxy-1,2-*O*-isopropylidene-5-*O*-methanesulphonyl-α-D-ribofuranose (**4**), which reacted smoothly with sodium azide in *N*,*N*-dimethylformamide at 80° to yield 3-acetamido-5-azido-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**5**). Hydrogenation of the azide **5** over palladised charcoal, with acetylation of the resulting amine **6**, gave 3,5-diacetamido-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (**7**). Finally, removal of the acetal group, in the presence of Amberlite IR-120(H^+) resin, afforded the free sugar which was indicated (t.l.c.) to exist in neutral solution as a mixture of the furanoid **8** and six-membered **9** ring-forms. Separation of the two forms was not achieved satisfactorily, but their presence was clearly indicated by the isolation of the peracetates **10** and **11** following acetylation of the concentrated solution and chromatography of the products on silica gel. The peracetates **10** and **11** were isolated in a ratio of approximately 4.5:1, respectively; it is assumed that the proportion of free sugars at equilibrium is not seriously disturbed during acetylation, and this seems reasonable in view of other results[9,12].



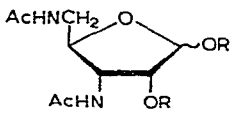
1



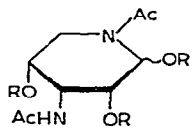
2



3 R = OH 6 R = NH_2
4 R = OMs 7 R = NHAc
5 R = N_3



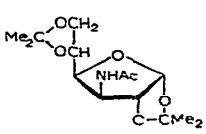
8 R = H
10 R = Ac

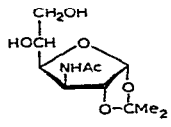


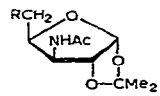
9 R = H
11 R = Ac

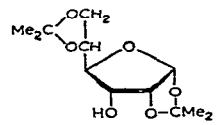
The structures of the peracetates **10** and **11** were based on elemental analyses and n.m.r. spectroscopy. The n.m.r. spectrum (D_2O) of the major peracetate **10** ($C_{13}H_{20}N_2O_7$) exhibited three singlets, integrating for twelve protons, at τ 7.85, 7.88, and 8.02 (intensity ratios, 1:1:2) which demonstrated the presence of two *O*-acetyl and two *N*-acetyl groups. A singlet appearing at τ 3.94 was assigned to the anomeric proton of the β-D-acetate, whereas a much smaller doublet observed at τ 3.65 (J 4 Hz) was attributed to the presence of a small proportion of the α-D-acetate. The minor peracetate **11** ($C_{15}H_{22}N_2O_8$) was obtained in crystalline form, and its n.m.r. spectrum ($CDCl_3$) contained four resonances at τ *ca.* 8.00 (see Experimental) which integrated for a total of fifteen protons. Hemiacetal formation involving the 5-acetamido group cannot, of course, be revealed by infrared spectroscopy[9,13] due to the presence of the amide II band of the 3-acetamido group. The β-D configuration for **11** was suggested by comparison of its molecular rotation (−36°) with those calculated for 1,2,3,4-tetra-*O*-acetyl-5-benzyloxycarbonylamino-5-deoxy-β-D-ribopyranose ($[M]_D$ −79.5°) and the isomeric α-D-acetate ($[M]_D$ +62°)[12].

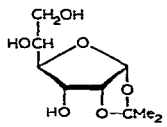
Our first attempt to synthesise 3,5-diacetamido-3,5-dideoxy-D-xylose was based on a route similar to that described above. 3-Acetamido-3-deoxy-1,2-*O*-isopropylidene-5-*O*-toluene-*p*-sulphonyl-α-D-xylofuranose (**15**) was obtained from the diacetal[14] **12**, but attempts to displace the 5-sulphonate group with sodium azide in boiling *N*,*N*-dimethylformamide gave only a low yield of the desired azide **16**, and the major product was identified as the alcohol **14**. The formation of **14** can reasonably be ascribed to neighbouring acetamido-group participation in the solvolysis of the sulphonate *via* a six-membered dihydro-oxazine derivative. Other examples of such participation have been reported[15,16], and evidence supporting this mechanism was provided by the rapid solvolysis of the sulphonate **15** in 95% 2-methoxyethanol–sodium acetate to afford the alcohol **14** as the only product. Although solvolysis of sulphonic ester groups has been noted[16] under these conditions, it did not occur at a rate comparable to that observed in the present case. The evidence thus points to an anchimerically assisted solvolysis of the sulphonate **15**.

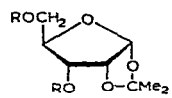

12

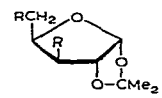

13

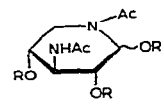

14 R = OH
15 R = OTs
16 R = N_3

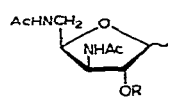

17


18


19 R = H
20 R = Ts


21 R = N_3
22 R = NHAc


23 R = H
25 R = Ac


24 R = H
26 R = Ac

In view of the complication arising from neighbouring acetamido-group participation in the foregoing procedure, it was necessary to introduce both nitrogen groups (as azide) in the same reaction step. Partial hydrolysis of the D-allose diacetal[14,17] **17** in 70% aqueous acetic acid at room temperature yielded the triol **18**, which, when subjected to the usual chain-shortening procedure, gave 1,2-*O*-isopropylidene-α-D-ribofuranose (**19**). The latter compound is a minor product of the acetonation of D-ribose[18], but it is more conveniently prepared by the method described above. Toluene-*p*-sulphonylation of **19** gave the disulphonate **20**, which smoothly exchanged both ester groups on being heated with sodium azide in *N*,*N*-dimethylformamide to form 3,5-diazido-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**21**). Hughes and Speakman[19] have already shown that the primary ester group of disulphonate **20** is rapidly displaced with benzoate ion, and this is followed by a slower displacement of the *endo*-sulphonate group. Moreover, *endo*-sulphonates attached to trioxabicyclo-[3.3.0]octane ring-systems in carbohydrates are known[14,20] to be fairly reactive towards bimolecular nucleophilic displacement.

The diazide **21** was converted into 3,5-diacetamido-3,5-dideoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**22**) following reduction with lithium aluminium hydride and acetylation of the resulting diamine. Hydrolysis of **22**, in the presence of Amberlite IR-120(H^+) resin, gave the free sugar which t.l.c. indicated to exist as a mixture of the six-membered (**23**) and the furanoid (**24**) ring-forms. Peracetylation gave crystalline 3,5-diacetamido-1,2,4-tri-*O*-acetyl-3,5-dideoxy-D-xylopyranose (**25**) as the main product, together with a second, syrupy product presumed to be the furanoid diacetate **26**; the latter diacetate was not obtained in an analytically pure form and it was not examined further. The peracetates **25** and **26** were recovered in the ratio of *ca.* 2:1, respectively.

The structure of the triacetate **25** was assigned on the basis of elemental analyses and n.m.r. data. The n.m.r. spectrum of **25** ($C_{15}H_{22}N_2O_8$) exhibited three sharp singlets, each integrating for three protons, at τ 7.95, 7.97, and 8.08. Two other singlets (integrating for six protons) were observed at τ 7.78 and 7.85, in an intensity ratio of 1:3. This difference in intensity is presumably the result of rotational iso-

merism[9,21] exhibited by the acetamido group incorporated into the six-membered ring. This would cause a doubling of the methyl signal of the ring *N*-acetyl group; in this case, the other part of the signal must lie under that of one of the acetoxyl groups if it is assumed, by analogy with assignments made[26] for other amino sugar derivatives, that the resonance at τ 8.08 is due to the equatorial acetamido group at C-3. The lower region of the spectrum was not sufficiently clear to permit a definitive assignment of configuration at the anomeric centre. However, the triacetate **25** was tentatively assigned the α-D configuration in view of the pronounced anomeric effect shown by other 5-acylamino-5-deoxy-D-xylopyranoses[9,12], which are acetylated under similar conditions without change of the anomeric configuration. The molecular rotation (+143°) of **25**, when compared with that (+111°) calculated for 5-acetamido-1,2,3,4-tetra-*O*-acetyl-5-deoxy-α-D-xylopyranose[22], supports this assignment.

Although our results are not likely to be as precise as those[9] relating to the equilibrium behaviour of the corresponding 5-acetamido-5-deoxypentoses, nevertheless, the proportions of six-membered and furanoid forms at equilibrium show much the same trend. It would be more pertinent, however, to comment on this point when our other results are made known.

EXPERIMENTAL

General methods. — Thin-layer chromatography (t.l.c.) was performed on microscope slides (2.5 × 7.5 cm) coated with Kieselgel G (Merck), and the components were detected by spraying the dried chromatogram with ethanolic vanillin–sulphuric acid reagent[23] and heating at 120° for a few minutes. Infrared spectra were recorded on a Perkin–Elmer 125 or Infracord spectrometer. Nuclear magnetic resonance (n.m.r.) spectra were usually measured on deuteriochloroform solutions, with tetramethylsilane as internal reference, using a Perkin–Elmer R-10 spectrometer at 60 MHz and a Perkin–Elmer R-14 spectrometer at 100 MHz. Tetramethylsilane was generally used as external reference for spectra recorded on solutions in deuterium oxide. Solvents were generally removed by evaporation at *ca.* 40°.

SYNTHESIS OF 3,5-DIACETAMIDO-3,5-DIDEOXY-D-RIBOSE

*3-Acetamido-3-deoxy-1,2-*O*-isopropylidene-α-*D*-allofuranose* (**2**). — Graded acid hydrolysis of diacetal **1** was best performed in the following manner. A solution of the diacetal (1.3 g) in 75% aqueous acetic acid was kept for 24 h at room temperature, the solvents were then evaporated with repeated additions of toluene, and the residue was recrystallised from ethanol–ether to give the 1,2-acetal **2** (1 g), m.p. 156–157°; lit.[11,24] m.p. 158–159° and 154–156°.

*3-Acetamido-3-deoxy-1,2-*O*-isopropylidene-α-*D*-ribofuranose* (**3**). — A solution of the preceding diol (8 g) in methanol (200 ml) was treated with sodium periodate (7 g) in the minimum amount of water for 30 min, after which time t.l.c. (ethyl acetate–methanol, 9:1) showed that all of the starting material had reacted. Insoluble material

was filtered off and washed with acetone, the filtrate and washings were concentrated, and the residue was extracted with dry acetone (3 × 100 ml). Removal of the solvent yielded a syrupy residue which was taken up in dry ethanol (200 ml) and treated with sodium borohydride (2.4 g) for 2 h at room temperature. Ethyl acetate (100 ml) and water (100 ml) were then added, the solution was shaken with Amberlite IR-120 (H^+) resin for 15 min, and the resin was filtered off. Removal of the solvents and crystallisation of the residue from acetone–light petroleum (b.p. 40–60°) gave compound **3** (6 g, 81%), m.p. 151–152°, $[\alpha]_D$ +18.5° (*c* 1, chloroform) (Found: C, 52.0; H, 7.5; N, 5.6. $C_{10}H_{17}NO_5$ calc.: C, 51.9; H, 7.4; N, 6.1%). N.m.r. data: τ 4.21 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1), 5.42 (1-proton triplet, $J_{2,3}$ 4 Hz, H-2); 7.97 (3-proton singlet, NAc), and 8.46, 8.65 (3-proton singlets, CMe_2).

*3-Acetamido-3-deoxy-1,2-*O*-isopropylidene-5-*O*-methanesulphonyl-α-*D*-ribofuranose* (**4**). — Methanesulphonyl chloride (0.3 ml) was gradually added to a solution of compound **3** (0.5 g) in dry pyridine (10 ml) and, after 1.5 h, the reaction mixture was processed in the usual way. The methanesulphonate **4** (0.55 g, 82%) had m.p. 132–133° (from methanol), $[\alpha]_D$ +44° (*c* 1, chloroform) (Found: C, 42.7; H, 5.9; N, 4.3; S, 10.6. $C_{11}H_{19}NO_7S$ calc.: C, 42.7; H, 6.2; N, 4.5; S, 10.35%). N.m.r. data: τ 4.20 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1), 6.98 (3-proton singlet, $MeSO_2$), 8.01 (3-proton singlet, N-Ac), and 8.46, 8.65 (3-proton singlets, CMe_2).

*3-Acetamido-5-amino-3,5-dideoxy-1,2-*O*-isopropylidene-α-*D*-ribofuranose* (**6**). — A stirred solution of methanesulphonate **4** (0.82 g) in *N,N*-dimethylformamide (40 ml) containing sodium azide (2 g) was heated at 80–90° for 4 h when t.l.c. (carbon tetrachloride–methanol, 5:1) showed that the displacement was complete. The solution was filtered, the solvents were removed, the residue was dissolved in chloroform, and insoluble material was filtered off. Removal of the solvents gave the azide **5** (ν_{max} 2100 cm^{-1}), which was dissolved immediately in methanol (50 ml) and reduced with a slight overpressure of hydrogen for 2 h at room temperature in the presence of 10% palladised charcoal (1 g). Removal of the catalyst and solvents afforded a solid residue which was recrystallised from chloroform–light petroleum (b.p. 40–60°) to give the amine **6** (0.55 g, 90%), m.p. 149–150°, $[\alpha]_D$ +64° (*c* 0.6, chloroform) (Found: C, 51.9; H, 7.6; N, 12.3. $C_{10}H_{18}N_2O_4$ calc.: C, 52.2; H, 7.9; N, 12.2%). N.m.r. data: τ 4.23 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1), 8.01 (3-proton singlet, N-Ac), and 8.46, 8.66 (3-proton singlets, CMe_2).

*3,5-Diacetamido-3,5-dideoxy-1,2-*O*-isopropylidene-α-*D*-ribofuranose* (**7**). — A solution of the amine **6** (0.93 g) in dry pyridine (10 ml) containing acetic anhydride (10 ml) was set aside at room temperature for 2.5 h, after which time the solvents were removed, and the residue was recrystallised from chloroform–light petroleum (b.p. 80–100°) to give the diamide **7** (1.1 g), m.p. 152–153.5°, $[\alpha]_D$ +112° (*c* 1, methanol), in nearly quantitative yield (Found: C, 52.7; H, 7.4; N, 10.6. $C_{12}H_{20}N_2O_5$ calc.: C, 52.9; H, 7.4; N, 10.3%). N.m.r. data (Me_2SO-d_6): τ 4.27 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1), 5.45 (1-proton triplet, $J_{2,3}$ 4 Hz, H-2), 8.14, 8.20 (3-proton singlets, 2 × NAc), 8.55 and 8.74 (3-proton singlets, CMe_2).

*3,5-Diacetamido-1,2,4-tri-*O*-acetyl-3,5-dideoxy-β-*D*-ribopyranose* (**11**) *and 3,5-*

diacetamido-1,2-di-O-acetyl-3,5-dideoxy-D-ribofuranose (**10**). — A solution of the acetal **7** (0.5 g) in water (7 ml) containing a suspension of Amberlite IR-120(H^+) resin (0.4 g) was stirred at 60–65° for 5 h, during which time complete hydrolysis had occurred; t.l.c. (chloroform–methanol, 9:1) revealed the formation of a major component together with a small proportion of a slightly faster-moving component. The cooled solution was filtered, the resin was washed thoroughly with water, and the filtrate and washings were concentrated to yield a mixture (0.31 g, 73%) which presumably contained the six-membered (**9**) and furanoid (**8**) ring-forms of the free sugar. The mixture was treated in dry pyridine (4 ml) with acetic anhydride (3 ml) for 3 h at room temperature. Removal of the solvents and chromatography on silica gel (ethyl acetate–methanol, 9:1) gave firstly the triacetate **11** (65 mg), m.p. 170–171° (from ethanol), $[\alpha]_D$ −10 ±1° (*c* 1, chloroform) (Found: C, 50.45; H, 6.2; N, 7.4. $C_{15}H_{22}N_2O_8$ calc.: C, 50.3; H, 6.2; N, 7.8%). The n.m.r. spectrum of **11** showed signals at τ 7.78, 7.85, 7.95, and 8.02 (intensities, 1:2:1:1), integrating for a total of fifteen protons, which indicated the presence of two acetamido groups and three acetoxyl groups. Continued elution gave the diacetate **10** (0.31 g), $[\alpha]_D$ +34 ±3° (*c* 0.45, water), as an amorphous solid (Found: C, 49.0; H, 6.7; N, 8.6 $C_{13}H_{20}N_2O_7$ calc.: C, 49.3; H, 6.4; N, 8.9%). N.m.r. data (D_2O): τ 3.65 (doublet, $J_{1,2}$ 4 Hz, H-1 α-form), 3.94 (singlet, H-1 β-form), 4.78 (doublet, $J_{2,3}$ 4 Hz, H-2), and 7.85, 7.88, 8.02 (singlets, 12 protons, intensities 1:1:2, 2 × OAc and 2 × NAc).

SYNTHESIS OF 3,5-DIACETAMIDO-3,5-DIDEOXY-D-XYLOSE

1,2-O-Isopropylidene-3,5-di-O-toluene-p-sulphonyl-α-D-ribofuranose (**20**). — To a solution of 1,2-*O*-isopropylidene-α-D-allofuranose[25] (**18**) (5 g) in water (25 ml) was added sodium periodate (5.5 g) in water (50 ml), and the reaction mixture was kept at room temperature for 2 h; t.l.c. (chloroform–methanol, 9:1) then showed that all of the starting material had reacted. Methanol (200 ml) was added, and the solution was left at −10° for 3 h, whereupon insoluble material was filtered off, and the solvents were removed. The residue was dissolved in chloroform–methanol (9:1, 60 ml), insoluble material was filtered off, and the filtrate was concentrated to yield the syrupy aldehyde (*ca.* 5 g), which was probably contaminated with some inorganic material. The aldehyde in 70% aqueous ethanol (50 ml) was reduced with sodium borohydride (2 g) at room temperature for 2 h, and cations were removed by stirring the solution with an excess of Amberlite IR-120(H^+) resin. The resin was filtered off and washed thoroughly with methanol, and the filtrate and washings were concentrated, with repeated additions of methanol, to afford a syrupy product (4.1 g) presumed to be 1,2-*O*-isopropylidene-α-D-ribofuranose[18] (**19**). No attempt was made to crystallise this acetal which was treated in pyridine solution (10 ml) with toluene-*p*-sulphonyl chloride (8 g) in dry pyridine (10 ml) for 24 h at room temperature. Work up in the usual manner gave the disulphonate **20** (7.7 g, 62%), m.p. 123–124°, $[\alpha]_D$ +72° (*c* 1, chloroform); Hughes and Speakman[19] recorded m.p. 123°, $[\alpha]_D$ +71° (*c* 1.1, chloroform), for this compound prepared by acetonation of D-ribose[18] (Found: C, 52.8;

H, 4.9; S, 12.9. $C_{22}H_{26}O_9S_2$ calc.: C, 53.0; H, 5.2; S, 12.85%). N.m.r. data: τ *ca.* 2.5 (8-proton multiplet, aromatic protons), 7.57, 7.61 (3-proton singlets, ArMe), and 8.55, 8.74 (3-proton singlets, CMe_2).

*3,5-Diazido-3,5-dideoxy-1,2-*O*-isopropylidene-α-*D*-xylofuranose* (**21**). — The disulphonate **20** (3 g) in *N,N*-dimethylformamide (70 ml) containing sodium azide (8 g) was heated gently under reflux for 4 h; t.l.c. (acetone–toluene, 3:10) then revealed the formation of a single product. The cooled solution was filtered, insoluble material was washed thoroughly with acetone, and the filtrate and washings were concentrated. The residue was taken up in chloroform (100 ml), the solution was washed with water (3 × 50 ml), and dried ($MgSO_4$). Removal of the solvents and distillation of the residue gave the diazide **21** (0.875 g, 61%), b.p. 83°/0.2 mmHg, $[\alpha]_D$ −60° (*c* 1, chloroform), ν_{max} 2100 cm^{-1} (N_3) (Found: C, 40.4; H, 5.2; N, 36.0. $C_8H_{12}N_6O_3$ calc.: C, 40.0; H, 5.0; N, 35.0%).

*3,5-Diacetamido-3,5-dideoxy-1,2-*O*-isopropylidene-α-*D*-xylofuranose* (**22**). — A solution of the diazide **21** (0.66 g) in dry ether (100 ml) containing lithium aluminium hydride (0.8 g) was heated under reflux for 1 h after which time the excess of reagent was destroyed by the addition of ethyl acetate (15 ml) and water (1 ml), and heating for 10 min at reflux temperature. Insoluble material was filtered off and washed thoroughly with ether, the combined filtrate and washings were dried ($MgSO_4$), and the solvents were removed. The syrupy residue was dissolved in methanol (2 ml) and treated with acetic anhydride (2 ml) for 1 h at room temperature. Removal of the solvents, with repeated additions of toluene, gave the diamide **22** (0.7 g, 94%), $[\alpha]_D$ +30° (*c* 1, water), as an amorphous solid (Found: C, 52.9; H, 7.2; N, 10.0. $C_{12}H_{20}N_2O_5$ calc.: C, 52.9; H, 7.4; N, 10.3%). N.m.r. data (D_2O); τ 4.03 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1), 8.02, 8.06 (3-proton singlets, 2 × NAc), 8.50 and 8.68 (3-proton singlets, CMe_2).

*3,5-Diacetamido-1,2,4-tri-*O*-acetyl-3,5-dideoxy-α-*D*-xylopyranose* (**25**). — A solution of the acetal **22** (0.1 g) in water (3 ml) containing Amberlite IR-120(H^+) resin (0.15 g) was stirred for 3 h at 60°, after which time t.l.c. (ethyl acetate–ethanol, 9:1) revealed the formation of two products presumed to be the six-membered (**23**) and furanoid (**24**) ring-forms of the free sugar. After processing, as described previously, the mixture was treated with acetic anhydride (0.5 ml) in pyridine (0.5 ml) and the peracetates were chromatographed on silica gel (ethyl acetate–ethanol, 9:1) to give the triacetate **25** (50 mg), m.p. 201–202.5° (from acetone–ether), $[\alpha]_D$ +40° (*c* 0.25, chloroform) (Found: C, 50.7; H, 6.0; N, 8.1. $C_{15}H_{22}N_2O_8$ calc.: C, 50.3; H, 6.2; N, 7.8%). The n.m.r. spectrum of **25** showed the following signals at *ca.* τ 8.00 which integrated for a total of fifteen protons and for which the following tentative assignments were made: τ 7.95. 7.97 (3-proton singlets, 2 × OAc), 7.78, 7.85 (singlets, 6 protons, intensity ratio *ca.* 1:3, OAc and ring NAc), and 8.08 (3-proton singlet, equatorial NAc[26]). Continued elution gave a second, impure, syrupy product (*ca.* 23 mg), which was presumably the furanoid diacetate **26**; this compound was not examined further.

*3-Acetamido-3-deoxy-1,2-*O*-isopropylidene-5-*O*-toluene-*p*-sulphonyl-α-*D*-xylofur-*

anose (**15**). — The title sulphonate, m.p. 116-117° (from acetone–light petroleum, b.p. 40–60°), $[\alpha]_D$ +3 ±1° (*c* 0.7, chloroform), was obtained in 80% yield on treatment of 3-acetamido-3-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose[14] **14** with toluene-*p*-sulphonyl chloride in pyridine (Found: C, 52.7; H, 6.0; N, 3.5; S, 8.4. $C_{17}H_{23}NO_7S$ calc.: C, 53.0; H, 6.0; N, 3.6; S, 8.3%). N.m.r. data (Me_2SO-d_6): τ *ca.* 2.40 (4-proton multiplet, aromatic protons), 4.21 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1), 5.65 (1-proton doublet, $J_{1,2}$ 4 Hz, H-2), 7.60 (3-proton singlet, ArMe), 8.23 (3-proton singlet, NAc), 8.65 and 8.79 (3-proton singlets, CMe_2).

Attempted azide-exchange reaction on the toluene-p-*sulphonate* **15**. — The sulphonate (0.5 g) in *N*,*N*-dimethylformamide (25 ml) containing sodium azide (1 g) was heated for 4 h at 80°; t.l.c. then demonstrated that all of the starting material had reacted to form several products. The cooled solution was filtered, and the filtrate was concentrated to a syrup, the i.r. spectrum of which showed only weak absorption at *ca.* 2100 cm^{-1} attributable to an azide group. Chromatography on silica gel (ethyl acetate–isopropyl alcohol, 6:1) gave, firstly, a small amount of syrupy material (28 mg), which was presumably the azide **16** since its infrared spectrum contained an absorption band at 2100 cm^{-1}. Continued elution gave a small amount (*ca.* 10 mg) of an unidentified component, followed by the alcohol[14] **14** (0.1 g), which was obtained as a clear syrup. The alcohol **14** was identified by re-conversion into the 5-sulphonate **15**, m.p. and mixed m.p. 116–117°; the infrared spectrum of the sulphonate was identical with that of an authentic sample.

Solvolysis of the toluene-p-*sulphonate* **15** *in 95% 2-methoxyethanol.* — The sulphonate (0.1 g) in 95% 2-methoxyethanol (10 ml) containing sodium acetate (0.2 g) was heated at reflux temperature for 1.5 h, during which time all of the starting material had reacted; t.l.c. (ethyl acetate–isopropyl alcohol, 6:1) showed the formation of a single product with chromatographic properties indistinguishable from those of **14**. The solution was concentrated, the residue was extracted with hot ethyl acetate (3 × 20 ml), and the extract was filtered and dried ($MgSO_4$). Removal of the solvent and toluene-*p*-sulphonylation of the residue gave the sulphonate **15** (60 mg, 60%), m.p. and mixed m.p. 116–117°.

ACKNOWLEDGMENTS

We thank Professor M. Stacey, C.B.E., F.R.S., for his interest, Dr. E F. Mooney for n.m.r. spectral measurements, and the Saudi Arabian Government for financial support.

REFERENCES

1 Part XV :J. S. BRIMACOMBE, P. A. GENT, AND J. H. WESTWOOD, *J. Chem. Soc.* (*C*), (1970) 1632.
2 K. L. RINEHART, *The Neomycins and Related Antibiotics*, Wiley, New York, 1964.
3 H. WEIDMANN AND H. K. ZIMMERMAN, *Ann.*, 641 (1961) 138; *ibid.*, 644 (1961) 127; K. L. RINEHART, M. HICHENS, K. STREIGLER, K. R. ROVER, T. P. CULBERTSON, S. TATSUOKA, S. HORII, T. YAMAGUCHI, H. HITOMI, AND A. MIYAKE, *J. Amer. Chem. Soc.*, 83 (1961) 2964; W. MEYER ZU RECKENDORF, *Ber.*, 96 (1963) 2017; *ibid.*, 97 (1964) 1275; *ibid.*, 98 (1965) 93; *Tetrahedron*, 19

(1963) 2033; P. H. GROSS, K. BRENDEL, AND H. K. ZIMMERMAN, *Ann.*, 681 (1965) 225; *ibid.*, 683 (1965) 179; L. V. SMITH, P. G. GROSS, K. BRENDEL, AND H. K. ZIMMERMAN, *Ann.*, 681 (1965) 228; A. ZOBAČOVA AND J. JARÝ, *Collection Czech. Commun.*, 31 (1966) 1848; P. H. GROSS, K. BRENDEL, AND H. K. ZIMMERMAN, *Naturwiss.*, 52 (1965) 185; M. L. WOLFORM, P. CHAKRAVARTY, AND D. HORTON, *J. Org. Chem.*, 30 (1965) 2728.

4 H. H. BAER AND T. NEILSON, *J. Org. Chem.*, 32 (1967) 1068; H. H. BAER AND F. RAJABALEE, *Carbohyd. Res*, 12 (1970) 241, and references therein.
5 J. KOVÁR AND J. JARÝ, *Coll. Czech. Chem. Commun.*, 34 (1969) 2619, and references cited therein.
6 A. B. FOSTER AND D. HORTON, *Advan. Carbohyd. Chem.*, 14 (1959) 214.
7 N. N. GERBER AND H. A. LECHEVALIER, *J. Org. Chem.*, 27 (1962) 1731.
8 J. D. DUTCHER, *Advan. Carbohyd. Chem.*, 18 (1963) 259.
9 H. PAULSEN AND K. TODT, *Advan. Carbohyd. Chem.*, 23 (1968) 115.
10 M. L. WOLFROM, F. SHAFIZADEH, R. K. ARMSTRONG, AND T. M. SHEN HAN, *J. Amer. Chem. Soc.*, 81 (1959) 3716.
11 B. COXON AND L. HOUGH, *J. Chem. Soc.*, (1961) 1643.
12 H. PAULSEN AND F. LEUPOLD, *Ber.*, 102 (1969) 2804.
13 J. K. N. JONES AND W. A. SZAREK, *Can. J. Chem.*, 41 (1963) 636.
14 J. S. BRIMACOMBE, J. G. H. BRYAN, A. HUSAIN, M. STACEY, AND M. S. TOLLEY, *Carbohyd. Res.*, 3 (1967) 318.
15 W. MEYER ZU RECKENDORF, *Ber.*, 96 (1963) 2019.
16 S. HANESSIAN, *J. Org. Chem.*, 32 (1967) 163.
17 W. SOWA AND G. H. S. THOMAS, *Can. J. Chem.*, 44 (1966) 836.
18 N. A. HUGHES AND P. R. H. SPEAKMAN, *Carbohyd Res.*, 1 (1965) 171.
19 N. A. HUGHES AND P. R. H. SPEAKMAN, *Carbohyd Res.*, 1 (1966) 341.
20 D. T. WILLIAMS AND J. K. N. JONES, *Can. J. Chem.*, 45 (1967) 8; J. S. BRIMACOMBE, P. A. GENT, AND M. STACEY, *J. Chem. Soc. (C)*, (1968) 567; J. M. HEAP AND L. N. OWEN, *ibid.*, (1970) 712.
21 W. A. SZAREK, S. WOLFE, AND J. K. N. JONES, *Tetrahedron Lett.*, (1964) 2745.
22 H. PAULSEN, *Ann.*, 670 (1963) 121.
23 E. MERCK A. G., *Chromatography*, Darmstadt, 2nd edn, p. 30.
24 R. U. LEMIEUX AND P. CHU, *J. Amer. Chem. Soc.*, 80 (1958) 4745.
25 P. M. COLLINS, *Tetrahedron*, 21 (1965) 1809.
26 D. HORTON, J. B. HUGHES, J. S. JEWELL, K. D. PHILLIPS, AND W. N. TURNER, *J. Org. Chem.*, 32 (1967) 1073.