*Carbohydrate Research*, 51 (1976) 195–206


# OLEFINIC INTERMEDIATES IN THE SYNTHESIS OF BRANCHED-CHAIN PYRANOSIDES BY THE NITROMETHANE ROUTE*

JOHANNES H. JORDAAN, JACOBUS J. NIEUWENHUIS, AND GERHARDUS J. LOURENS†
*Division of Life Sciences, Atomic Energy Board, Pretoria (South Africa)*
(Received February 10th, 1976; accepted for publication, April 12th, 1976)

ABSTRACT

Addition of the sodium salt of nitromethane to methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranosid-3-ulose (**1**), methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose (**2**), and benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose (**3**) gave the corresponding 3-*C*-nitromethyl-3-hydroxy derivatives, **10**, **4**, **6**, and **12**. *p*-Toluenesulfonic acid-catalyzed acetylation in acetic anhydride gave the *O*-acetyl derivatives, **11**, **5**, **7**, and **13**, which were reduced with sodium borohydride in acetonitrile to the nitroalkane-branched derivatives **23**, **25**, and **24**, without isolation of nitro-olefin intermediates. Treatment of the 3-*O*-acetyl-3-*C*-nitromethyl-glucopyranoside **11** with methanolic ammonia gave three products, namely, the exocyclic nitroalkene **16**, the endocyclic olefin **19**, and the addition product **22** of ammonia to **16**. Equilibration of a solution of **16** in boiling pyridine gave **19**. The exocyclic nitromethylene compound **16** could be reduced to the nitroalkane **23** with sodium borohydride, whereas the endo-olefin **19** could not. Treatment of **7** with potassium *tert*-butoxide in tetrahydrofuran gave only the endocyclic olefin **20**. Similar olefinic intermediates were obtained, and similar interconversions performed, for the 3-*C*-nitromethyl-3-*O*-acetyl branched derivatives **5**, **7**, and **13**.

## INTRODUCTION

Condensation of nitromethane with suitably protected glycosiduloses in alkaline medium presents a facile route for the synthesis of branched-chain sugar derivatives[1–6]. This approach is also applicable to the synthesis of nitromethyl and aminomethyl branched-chain nucleosides[7,8]. Generally, the condensation is performed in a suitable solvent with sodium alkoxide as base[2–6], or with a suspension of preformed sodium nitromethanide[1] in nitromethane. The procedure therefore requires protecting groups on the ketose that are reasonably stable to base. The

*Taken in part from the Ph.D. dissertation of J.J.N. submitted to the University of South Africa.
†Present address: Adcock-Ingram Research, Johannesburg, South Africa.

*C*-nitromethyl-*C*-hydroxy branched-chain condensation products lend themselves to further modification.

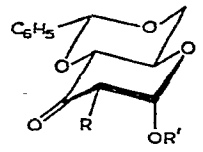
Removal of the β-hydroxyl group at the branching point in the nitroalkyl products is often desirable, in order to obtain deoxy sugars with functionalized branched-chains. Acetic acid is readily eliminated from β-acetoxynitroalkanes under basic catalysis[9,10]. Acetylation of the tertiary hydroxyl group at the branching point, followed by mild treatment with base, gives an exocyclic α-nitro-olefin that is reducible with borohydrides to the corresponding nitro-alkane[1,2,10]. Precise conditions for the conversion of sugar β-acetoxynitroalkanes into α-nitro-olefins depend on the configuration of substituents at the branching point, and on the ease with which a trans-alignment of leaving groups can be attained[5].

The nitromethane route to branched-chain sugars has not been studied extensively on fully substituted glycopyranosiduloses, and not at all on those bearing acylamino substituents. This report describes some examples of nitromethane condensation with 2-acylamino-2-deoxy- and 2-tosyloxy-glucopyranosid-3-uloses, as well as conditions for the conversion of the resulting *C*-acetoxy-*C*-nitromethyl derivatives into α-nitro-olefins and *C*-deoxy-nitroalkanes. Some interesting side-reactions and double-bond migrations of the intermediate, exocyclic, conjugated nitro-alkenes are reported.

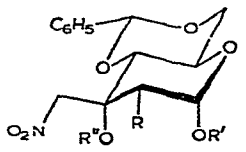
## RESULTS AND DISCUSSION

Treatment of methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranosid-3-ulose[11] (**1**) with a suspension of sodium nitromethanide in nitromethane gave the branched-chain *C*-nitromethyl derivative **10** in 82% yield. Nucleophilic attack on a pyranosid-3-ulose would be expected[6] to occur from the least-hindered equatorial side. Thus, **10** should be the *C*-nitromethyl-alloside. Surprisingly, however, comparison[12] of lanthanide-induced shift gradients of identifiable signals in the n.m.r. spectrum of **10** with those of related compounds of known configuration showed **10** to have the *gluco* configuration. Acetylation of **10** in acetic anhydride with *p*-toluenesulfonic acid as catalyst gave **11** in 81% yield. The n.m.r. spectrum of **11** showed an acetoxyl-resonance signal at τ 8.00, which suggests[15] an axial orientation for the acetoxyl group. Although this result disagrees with the configurational assignment based on comparison of shift gradients, the latter is considered more reliable, since shielding effects[13] by the 2-tosyl group may perturb the resonance signal of a neighbouring acetoxyl group. The expected *allo* epimer of **10** could not be isolated from the reaction mixture of **1** with nitromethane.

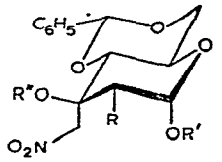
Condensation of nitromethane with methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose[14] (**2**) gave the expected 3-*C*-nitromethyl-allopyranoside **4** in 67% yield. The configurational assignment of the branching point was based on lanthanide-induced shift gradients[12]. Acetylation of **4** with acetic anhydride and *p*-toluenesulfonic acid produced **5**. The n.m.r. spectrum of **5** showed a 3-proton acetyl singlet at τ 7.80, which is in agreement with that expected[15] for an



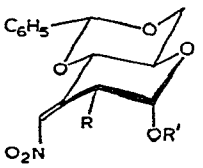
1 R = OTs ; R′ = $CH_3$
2 R = NHBz ; R′ = $CH_3$
3 R = NHAc ; R′ = Bn



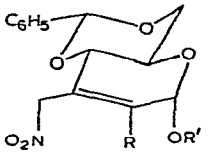
4 R = NHBz ; R′ = $CH_3$ ; R″ = H
5 R = NHBz ; R′ = $CH_3$ ; R″ = Ac
6 R = NHAc ; R′ = Bn ; R″ = H
7 R = NHAc ; R′ = Bn ; R″ = Ac
8 R = H ; R′ = $CH_3$ ; R″ = H
9 R = H ; R′ = $CH_3$ ; R″ = Ac



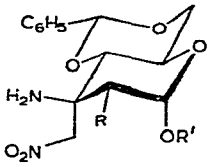
10 R = OTs ; R′ = $CH_3$ ; R″ = H
11 R = OTs ; R′ = $CH_3$ ; R″ = Ac
12 R = NHAc ; R′ = Bn ; R″ = H
13 R = NHAc ; R′ = Bn ; R″ = Ac
14 R = H ; R′ = $CH_3$ ; R″ = H
15 R = H ; R′ = $CH_3$ ; R″ = Ac



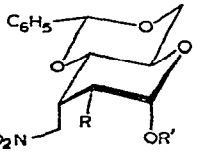
16 R = OTs ; R′ = $CH_3$
17 R = NHBz ; R′ = $CH_3$
18 R = H ; R′ = $CH_3$



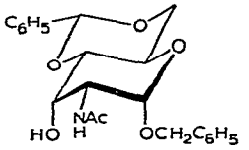
19 R = OTs ; R′ = $CH_3$
20 R = NHAc ; R′ = Bn
21 R = H ; R′ = $CH_3$



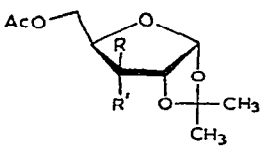
22 R = OTs ; R′ = $CH_3$



23 R = OTs ; R′ = $CH_3$
24 R = NHAc ; R′ = Bn
25 R = NHBz ; R′ = $CH_3$
26 R = H ; R′ = $CH_3$



27



28 R = $CH_2NO_2$ ; R′ = OAc
29 R = H ; R′ = $CH_2NO_2$

axial acetoxyl group; the assignment of the *allo* configuration to **4** was corroborated in this case.

Oxidation of benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-gluco-pyranoside[16] with methyl sulfoxide and phosphorus pentaoxide afforded the pyranosid-3-ulose **3** in 72% yield. Reaction of **3** with the sodium salt of nitromethane gave a mixture of 3-*C*-nitromethyl branched-chain derivatives which could be separated, by fractional crystallization, into 52% of the allopyranoside **6**, and 33% of a product considered to be the *gluco* epimer **12** by virtue of its n.m.r. behaviour in the presence of a europium shift-reagent[12]. Acetylation of **6** and **12** gave the corresponding acetyl derivatives **7** and **13** in yields of 97 and 93%, respectively. The n.m.r. spectra of both **7** and **13** showed acetyl-singlets at τ 8.15. These spectra could

therefore not be used for unambiguous configurational assignments of the branching points, or for corroboration of the assignments[1,2] based on comparisons of lanthanide-induced shift gradients. A similar mixture of epimers, **8** and **14**, was obtained[5] in the nitromethane addition to methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose in basic medium. The addition of the nitromethanide carbanion to the keto group of pyranosid-3-uloses seems somewhat unpredictable, and of low stereo-specificity. The ratio of isomers obtained may be influenced by the choice of solvent and reaction temperature[3,5].

Several authors have reported[1–5] on the base-catalyzed elimination of the elements of acetic acid from 3-*C*-nitromethyl-3-acetoxy branched-glycosides to produce exocyclic nitromethylene derivatives. These nitro-olefins could be reduced to the 3-deoxy-3-*C*-nitromethyl derivatives with sodium borohydride. Remarkable differences in the reactivity of epimeric 3-acetoxy-3-*C*-nitromethyl-pyranosides towards carbonate-catalyzed eliminations have been demonstrated[5]. The nitromethyl-branched acetyl derivative **11** was totally unreactive towards anhydrous potassium carbonate in boiling benzene; only unreacted starting-material could be detected after 6 h.

Treatment of methyl 3-*O*-acetyl-4,6-*O*-benzylidene-3-*C*-nitromethyl-2-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside (**11**) with saturated, methanolic ammonia at ambient temperature gave the exocyclic 3-nitromethylene elimination-product **16** as a precipitate in the reaction mixture. The 60-MHz n.m.r. spectrum of **16** (42% yield) showed a 1-proton quartet for H-2 at τ 4.95 ($J_{2,1}$ 4.0; $J_{2,3'}$ 1.8 Hz, allylic coupling), and a 1-proton triplet for the exocyclic vinylic proton at τ 3.24 ($J_{3',2} = J_{3',4} = 1.8$ Hz; allylic coupling), indicating the exocyclic 3-nitromethylene group. After separation of **16**, the reaction mixture was evaporated, and the residue chromatographed on silica gel with chloroform as eluent. The component eluted first, which crystallized from ethyl acetate in 20% yield, gave a 100-MHz n.m.r. spectrum that was compatible with the structure **19**; a 1-proton singlet at τ 4.99 for H-1 and a 1-proton doublet at τ 5.52 ($J_{4,5}$ 8.4 Hz) for H-4 suggested a 2,3-double bond, and a 2-proton singlet at τ 4.92 indicated the unsplit exocyclic 3-nitromethyl substituent. A second, pure component (10% yield) was the addition product (**22**) of ammonia to the nitro-olefin **16**. The i.r. spectrum of **22** showed absorption maxima at 3380 and 3320 $cm^{-1}$ for a primary amino group, which was confirmed by the presence of a broad 2-proton singlet at τ 8.94, that was lost on addition of deuterium oxide, in its 100-MHz n.m.r. spectrum. This spectrum also had a 1-proton doublet at τ 5.17 ($J_{1,2}$ 4.0 Hz) for H-1, a 1-proton doublet at τ 6.48 ($J_{2,1}$ 4.0 Hz) for H-2, and two 1-proton doublets at τ 5.34 and 4.82 ($J_{gem}$ 12.2 Hz) for the exocyclic nitromethyl group. The configuration at the branching point of **22** was not proved. Assuming that attack on the nitromethylene group of **16** by ammonia would occur from the least-hindered, equatorial side, the *gluco* configuration is suggested for **22**.

The reaction sequence for the formation of isomeric nitro-olefins **16** and **19** from **11** is probably as follows. Attack by base on a proton α to the nitro-group would lead to elimination of acetic acid, with formation of the exocyclic olefin **16** by kinetic

control. Exposure of **16** to ammonia could lead to the $NH_3$-addition product **22**, or could lead to further proton abstraction at C-2, and equilibration to the more-stable[17] endocyclic olefin. The endocyclic preference of the double bond was demonstrated by the conversion of **16** into **19** (60% yield) by treatment with boiling pyridine.

Treatment of the 3-*C*-nitromethyl-3-*O*-acetyl derivatives with potassium *tert*-butoxide in anhydrous tetrahydrofuran at 0–5° gave nitro-olefins. In the case of the 2-*O*-tosyl derivative **11**, the exocyclic nitro-olefin **16** was obtained in 39% yield. Similar treatment of the 2-acetamido-2-deoxy-alloside **7** gave the endocyclic olefin **20** in 75% yield. In the reported[5] base-catalyzed elimination of acetic acid from the 2-deoxy derivatives **9** and **15**, the main product was the nitromethylene derivative **18**. An uncharacterized nitro-olefin encountered[5] in this sequence might have been the endocyclic nitro-olefin **21**. Treatment of the 3-*O*-acetyl-2-deoxy-3-*C*-nitromethyl-pyranoside **9** with potassium *tert*-butoxide in tetrahydrofuran gave **21**.

Attempts to reduce the endocyclic olefins **19**, **20**, and **21** to the corresponding branched-chain nitroalkanes (**23**, **24**, and **26**) in a variety of solvents with sodium borohydride were unsuccessful; only unchanged starting materials were recovered. Reduction of the exocyclic nitro-olefin **18** has been reported[5] to proceed readily to **26**. Similarly, the reduction of **16** and **17** with sodium borohydride in acetonitrile gave the nitroalkanes **23** and **25**, respectively. Conversion of 3-*C*-nitromethyl-3-acetoxy branched-derivatives into 3-*C*-nitromethylene derivatives, and isolation of these olefinic intermediates, prior[5] to reduction with sodium borohydride proved unnecessary. Direct reduction of the 3-*O*-acetyl-3-*C*-nitromethyl-pyranosides **5**, **7**, **9**, **11**, **13**, and **15** with sodium borohydride in acetonitrile at room temperature gave the branched-chain nitroalkanes **23**, **24**, **25**, and **26** in excellent yields. The reduction probably proceeded *via* exocyclic nitroalkene intermediates formed in the basic reduction medium. In the reduction of **5** at 0°, the presence of the intermediate olefin **17** could be demonstrated by t.l.c. and by the presence of a 1-proton multiplet at $\tau$ 3.0 for the olefinic proton. The configuration of the final nitroalkanes would be expected to be *allo*, if it is assumed that hydride ion approaches the olefinic carbon at the branching point from the least-hindered, equatorial side. The 60-MHz n.m.r. spectra of **23** and **24** were compatible with the *allo* configuration; in the case of **25**, the *allo* configuration is suggested, but corroborative evidence could not be obtained from its n.m.r. spectrum. Direct reduction of 3,5-di-*O*-acetyl-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-D-ribofuranose[1] (**28**), under similar conditions, proceeded smoothly to give 5-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-D-ribofuranose[1] (**29**) in 77% yield. The direct-reduction procedure therefore seems generally applicable. The solvent is important, as **7** was reduced readily in acetonitrile, whereas, in ethanol, only benzyl 2-acetamido-4,6-*O*-benzylidene-α-D-allopyranoside (**27**) could be isolated. The latter was identical with the alloside obtained by reduction of the 3-keto derivative **3** with sodium borohydride in acetonitrile, and was clearly different from benzyl 2-acetamido-4,6-*O*-benzylidene-α-D-glucopyranoside, used for the preparation of **3**, as demonstrated by t.l.c. behaviour and n.m.r. spectroscopy, including europium-induced chemical shifts[12]. In the protic solvent, cleavage of the

3-*C*-nitromethyl-3-acetoxy derivative **7**, to liberate the original ketone **3**, is preferred to an elimination to form the nitromethylene intermediate; subsequent reduction of the intermediate **3** yielded **27**.

## EXPERIMENTAL

*General.* — Melting points were taken in capillary tubes in a Büchi silicone oil-bath apparatus and are uncorrected. I.r. spectra of solids were determined for KBr disks with a Perkin–Elmer 257 grating spectrophotometer; for liquids, films on KBr disks were used. N.m.r. spectra were recorded on Varian EM-360, or HA-100 spectrometers, with tetramethylsilane as internal standard. Optical rotations were determined with a Perkin–Elmer 141 polarimeter. T.l.c. was performed on Silica Gel F (precoated-plates, Merck), and spots were detected by visual examination under 254-nm u.v. light, or by spraying with 0.5% of $KMnO_4$ in M NaOH. Mass spectra were recorded on an A.E.I. MS-9 spectrometer. Microanalyses were performed by Dr. Franz Pascher, Bonn, BRD.

*Methyl 4,6-O-benzylidene-3-C-nitromethyl-2-O-p-tolylsulfonyl-α-D-glucopyranoside* (**10**). — A suspension of sodium nitromethanide was prepared by the *slow* addition of 1.16 g (24.2 mmol, 10% excess) of a 50% dispersion of sodium hydride in mineral oil, in small portions, to 25 ml of nitromethane stirred in an ice bath. After stirring for 2 h at 5–10°, the suspension was added dropwise during 30 min to a stirred solution of 9.6 g (22 mmol) of methyl 4,6-*O*-benzylidene-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranosid-3-ulose[11] (**1**) in 30 ml of nitromethane at 0°. The mixture was stirred at ambient temperature for 18 h, glacial acetic acid (2 ml) was then added, and the solvent was removed under reduced pressure. The residue was partitioned between 50 ml of chloroform and 100 ml of water. The dried ($Na_2SO_4$) organic phase was evaporated *in vacuo* to give an oil that crystallized from ethyl acetate–hexane. Two further recrystallizations gave **10** (9.0 g, 82%) as colorless needles that showed one spot on t.l.c. (benzene–methanol, 95:5), and had m.p. 143–144°, $[\alpha]_D^{24}$ +41.6° (*c* 1, chloroform); $\nu_{max}$ 3470 (OH), 1555, and 1380 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): τ 6.00 (s, 1 H, OH) lost on addition of $D_2O$, 5.52 (q, 2 H, $J_{AB}$ 13 Hz, $\Delta\nu_{AB}$ 17.5 Hz, $CH_2NO_2$), 5.08 (d, 1 H, $J_{2,1}$ 4.0 Hz, H-2), 4.95 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1).

*Anal.* Calc. for $C_{22}H_{25}NO_{10}S$: C, 53.33; H, 5.09; N, 2.83. Found: C, 53.41; H, 4.96; N, 2.87.

*Methyl 3-O-acetyl-4,6-O-benzylidene-3-C-nitromethyl-2-O-p-tolylsulfonyl-α-D-glucopyranoside* (**11**). — A solution of 12.4 g (25 mmol) of **10** in 100 ml of acetic anhydride, containing 5.0 g (25 mmol) of *p*-toluenesulfonic acid monohydrate, was stirred at room temperature for 12 h. The mixture was then poured into 500 ml of ice-cold, saturated, aqueous sodium hydrogen carbonate and extracted with chloroform (3 × 100 ml). The extract was washed with saturated, aqueous sodium hydrogen carbonate, and the dried ($Na_2SO_4$) chloroform extract was evaporated to give 11.7 g of a syrup that crystallized from absolute ethanol. Recrystallization from ethanol gave 10.2 g (73%) of colorless crystals that showed one spot on t.l.c. (benzene–acetone,

95:5); m.p. 152–153°; $[\alpha]_D^{24}$ +4° (*c* 1, chloroform); $\nu_{max}$ 1760 (C=O), 1575, 1385 ($NO_2$), and 1230 (C–O) $cm^{-1}$. N.m.r. data (100 MHz, $CDCl_3$): $\tau$ 8.00 (s, 3 H, $CH_3CO$), 5.13 (d, 1 H, $J_{2,1}$ 4.2 Hz, H-2), 4.94 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1), 4.81 (q, 2 H, $J_{AB}$ 13.2 Hz, $\Delta\nu_{AB}$ 29.1 Hz, $CH_2NO_2$).

*Anal.* Calc. for $C_{24}H_{27}NO_{11}S$: C, 53.63; H, 5.06; N, 2.61. Found: C, 53.61; H, 4.92; N, 2.53.

*Methyl 2-benzamido-4,6-O-benzylidene-2-deoxy-3-C-nitromethyl-α-D-allopyranoside* (**4**). — Condensation of sodium nitromethanide (20 mmol) and 7.66 g (20 mmol) of methyl 2-benzamido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose[14] (**2**) in 150 ml of nitromethane, as described for **10**, gave a colorless solid. Recrystallization from ethyl acetate–light petroleum (b.p. 60–80°) gave **4** (6.0 g, 67%) as colorless crystals that showed one spot on t.l.c. (benzene–acetone, 4:1), and had m.p. 209–210°, $[\alpha]_D^{24}$ +40.9° (*c* 1, chloroform); $\nu_{max}$ 3500, 3280 (OH, NH), 1555, and 1383 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 6.03 (s, 1 H, OH) lost on addition of $D_2O$, 5.40 (s, 2 H, $CH_2NO_2$).

*Anal.* Calc. for $C_{22}H_{24}N_2O_8$: C, 59.45; H, 5.44; N, 6.30. Found: C, 59.65; H, 5.42; N, 6.29.

*Methyl 3-O-acetyl-2-benzamido-4,6-O-benzylidene-2-deoxy-3-C-nitromethyl-α-D-allopyranoside* (**5**). — Acetylation of 2.22 g (5 mmol) of **4**, as described for **11**, gave 2.2 g (91%) of a foam that could not be crystallized. The product showed one spot on t.l.c. (benzene–acetone, 4:1); $\nu_{max}$ 3280 (NH), 1745, 1675 (CO), 1570, 1385 ($NO_2$), and 1250 (C–O) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 7.80 (s, 3 H, $CH_3CO$), 5.10 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.85 (q, 2 H, $J_{AB}$ 12.4 Hz, $\Delta\nu_{AB}$ 18.8 Hz, $CH_2NO_2$), 1.74 (d, 1 H, $J_{NH,2}$ 9.8 Hz, NH). Mass spectrum: *m/e* 486 [$M^+$] (Calc. for $C_{24}H_{26}N_2O_9$: 486.16382. Found: 486.16249).

*Benzyl 2-acetamido-4,6-O-benzylidene-2-deoxy-α-D-ribo-hexopyranosid-3-ulose* (**3**). — To a stirred solution of 30 g (75 mmol) of benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[16] in 1 litre of anhydrous methyl sulfoxide at 70° was added 17 g (60 mmol as $P_4O_{10}$) of phosphorus pentaoxide. Stirring was continued at 70° for 6 h and the cooled mixture was then poured into chloroform (2500 ml). The chloroform solution was washed with water (5 × 500 ml), dried ($Na_2SO_4$), and concentrated to ~800 ml. The crystalline precipitate was collected. Further concentration *in vacuo* gave a second crop. Recrystallization of the combined product from tetrahydrofuran–light petroleum (b.p. 60–80°) afforded **3** (21.6 g, 72%) as colorless crystals that showed one spot on t.l.c. (chloroform–*p*-dioxane, 95:5); m.p. 249–250°; $[\alpha]_D^{25}$ +108° (*c* 0.63, pyridine); $\nu_{max}$ 1750 $cm^{-1}$ (C=O). N.m.r. data (60 MHz, $CDCl_3$–methyl sulfoxide-$d_6$): $\tau$ 8.03 (s, 3 H, $CH_3CO$), 5.02 (m, 1 H, H-2), 4.72 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 2.08 (d, 1 H, $J_{NH,2}$ 9.0 Hz, NH).

*Anal.* Calc. for $C_{22}H_{23}NO_6$: C, 66.49; H, 5.83; N, 3.52. Found: C, 66.51; H, 5.90; N, 3.57.

*Benzyl 2-acetamido-4,6-O-benzylidene-2-deoxy-3-C-nitromethyl-α-D-allopyranoside* (**6**). — A suspension (22 mmol) of sodium nitromethanide in 35 ml of nitromethane, prepared as for **10**, was added during 80 min to a solution of 7.94 g

(20 mmol) of **3** in 150 ml of nitromethane stirred in an oil bath at 80°. The mixture was stirred at 80° for 3 h and then at ambient temperature for 12 h, cooled, neutralized by the addition of 3 ml of glacial acetic acid, and poured into 1 litre of ice–water. A crystalline precipitate separated after prolonged stirring. The product was collected on a filter and dissolved in 500 ml of chloroform, and the solution was washed consecutively with saturated, aqueous sodium hydrogen carbonate (20 ml) and water (2 × 20 ml). Evaporation of the dried ($Na_2SO_4$) solution gave an oil that contained some starting material (t.l.c.). Remaining **3** (800 mg) was removed by crystallization from hot tetrahydrofuran. Evaporation of the mother liquor gave a residue that was dissolved in hot ethyl acetate. On cooling, colorless crystals of **6** were deposited. The product was collected on a filter and the mother liquor retained. Recrystallization of **6** from ethyl acetate gave 4.28 g (52%, based on **3** consumed) of colorless crystals that showed one spot on t.l.c. (chloroform–*p*-dioxane, 95:5), and had m.p. 212–213°, $[\alpha]_D^{24}$ +148° (*c* 1, chloroform); $\nu_{max}$ 3450, 3360 (OH, NH), 1560, and 1380 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 6.17 (s, 1 H, OH) lost on addition of $D_2O$, 5.68 (q, 1 H, $J_{2,1}$ 4.6, $J_{2,NH}$ 11.0 Hz, H-2), 5.47 (s, 2 H, $CH_2NO_2$), 5.13 (d, 1 H, $J_{1,2}$ 4.6 Hz, H-1), 3.87 (d, 1 H, $J_{NH,2}$ 11 Hz, NH).

*Anal.* Calc. for $C_{23}H_{26}N_2O_8$: C, 60.26; H, 5.72; N, 6.11. Found: C, 60.63; H, 5.65; N, 6.25.

*Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*C*-nitromethyl-α-*D*-gluco-pyranoside* (**12**). — Evaporation of the mother liquor of **6** gave 2.76 g (33%) of a foam that could not be crystallized, but which showed one spot on t.l.c. (chloroform–*p*-dioxane, 95:5) that was indistinguishable from that of **6**. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 8.37 (s, 1 H, OH) lost on addition of $D_2O$, 5.47 (s, 2 H, $CH_2NO_2$).

*Benzyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-3-*C*-nitromethyl-α-*D*-allopyranoside* (**7**). — Acetylation of 6.9 g (15 mmol) of **6**, as described for **11**, gave 7.3 g (97%) of a foam that showed one spot on t.l.c. (chloroform–*p*-dioxane, 95:5) and that crystallized slowly from diethyl ether; m.p. 148–149°; $\nu_{max}$ 3380 (NH), 1745, 1685 (CO), 1570, 1380 ($NO_2$), and 1245 (C–O) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 8.15 (s, 3 H, $CH_3CO_2$), 8.03 (s, 3 H, $CH_3CON$), 4.92 (q, 2 H, $J_{AB}$ 12 Hz, $\Delta\nu_{AB}$ 18.1 Hz, $CH_2NO_2$).

*Anal.* Calc. for $C_{25}H_{29}N_2O_9$: C, 59.99; H, 5.64; N, 5.60. Found: C. 60.00; H, 5.73; N, 5.63.

*Benzyl 2-acetamido-3-*O*-acetyl-4,6-*O*-benzylidene-2-deoxy-3-*C*-nitromethyl-α-*D*-glucopyranoside* (**13**). — Acetylation of 700 mg (1.5 mmol) of **12**, as for **11**, gave 710 mg (93%) of an uncrystallizable foam that showed one spot on t.l.c. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 8.15 (s, 3 H, $CH_3CO_2$), 8.05 (s, 3 H, $CH_3CON$).

*Methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-nitromethylene-2-*O*-p-tolylsulfonyl-α-*D*-ribo-hexopyranoside* (**16**). — To 50 ml of saturated, methanolic ammonia was added 2.69 g (5 mmol) of **11**, with vigorous stirring, at ambient temperature. Stirring was continued for 4 h, and the solid precipitate collected on a filter. The filtrate was retained. Recrystallization of the product from 2-methoxyethanol gave **16** (1.0 g, 42%) as colorless crystals that showed one spot on t.l.c. (benzene–ethyl acetate, 10:1),

and had m.p. 243–244°, $[\alpha]_D^{25}$ −34.7° (*c* 1, chloroform); $\nu_{max}$ 1600 (C=C), 1540, and 1385 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$–methyl sulfoxide-$d_6$): $\tau$ 5.25 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.95 (q, 1 H, H-2, $J_{2,1}$ 4.0, $J_{2,3'}$ 1.8 Hz), 3.24 (t, 1 H, $J_{3',2} = J_{3',4} = 1.8$ Hz, C=CHNO$_2$).

*Anal.* Calc. for $C_{22}H_{23}NO_9S$: C, 55.34; H, 4.86, N, 2.93. Found: C, 55.30; H, 4.94; N, 2.93.

*Methyl 4,6-O-benzylidene-3-deoxy-3-C-nitromethyl-2-O-p-tolylsulfonyl-α-D-erythro-hex-2-enopyranoside* (**19**). — The filtrate obtained from the reaction mixture of **16** was concentrated *in vacuo*. The residue showed two spots on t.l.c. (benzene–ethyl acetate, 10:1), neither of which corresponded with starting material **11**, or product **16**. Chromatographic separation of the mixture on a column of silica gel (Merck, 70–230 mesh ASTM), with chloroform as eluent, gave two components. Evaporation of the combined fractions containing the faster-moving component gave an oil that crystallized on standing. Recrystallization from ethyl acetate gave **19** (470 mg, 20%) as colorless crystals, m.p. 120–121°, $[\alpha]_D^{24}$ +46.4° (*c* 0.8, chloroform); $\nu_{max}$ 1600 (C=C), 1563, and 1375 ($NO_2$) $cm^{-1}$. N.m.r. data (100 MHz, $CDCl_3$): $\tau$ 6.18 (m, 1 H, $J_{5,4}$ 8.4, $J_{5,6eq}$ 2.4, $J_{5,6ax}$ 4.2 Hz, H-5), 5.69 (q, 1 H, $J_{6eq,6ax}$ 8.2, $J_{6eq,5}$ 2.4 Hz, H-6eq), 5.52 (d, 1 H, $J_{4,5}$ 8.4 Hz, H-4), 4.99 (s, 1 H, H-1), 4.92 (s, 2 H, $CH_2NO_2$).

*Anal.* Calc. for $C_{22}H_{23}NO_9S$: C, 55.34; H, 4.86; N, 2.93. Found: C, 55.41; H, 4.78; N, 2.94.

*Methyl 3-amino-4,6-O-benzylidene-3-deoxy-3-C-nitromethyl-2-O-p-tolylsulfonyl-α-D-glucopyranoside* (**22**). — Evaporation of the fractions containing the slower-moving component from the column-chromatographic purification of **19** gave 240 mg (10%) of a foam that could not be crystallized. The product showed one spot on t.l.c. (benzene–ethyl acetate), and had $[\alpha]_D^{24}$ +55.4° (*c* 1, chloroform); $\nu_{max}$ 3380, 3320 (NH), 1560, and 1380 ($NO_2$) $cm^{-1}$. N.m.r. data (100 MHz, $CDCl_3$): $\tau$ 8.94 (broad s, 2 H, $NH_2$) lost upon addition of $D_2O$, 5.48 (d, 1 H, $J_{2,1}$ 4.0 Hz, H-2), 5.17 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.08 (q, 2 H, $J_{AB}$ 12.4 Hz, $\Delta\nu_{AB}$ 51 Hz, $CH_2NO_2$).

*Anal.* Calc. for $C_{22}H_{26}N_2O_9S$: C, 53.43; H, 5.30; N, 5.66. Found: C, 53.67; H, 5.21; N, 5.35.

*Treatment of* **11** *with potassium* tert-*butoxide*. — To a stirred solution of 300 mg (0.56 mmol) of **11** in 8 ml of anhydrous tetrahydrofuran at 0° was added 74 mg (0.66 mmol) of potassium *tert*-butoxide. Stirring was continued at 4° for 15 h. The mixture was poured into 25 ml of ice–water containing 0.2 ml of acetic acid. The product was extracted with dichloromethane (3 × 5 ml), and the extract was washed with saturated, aqueous sodium hydrogen carbonate (5 ml) and water (5 ml). Evaporation of the dried ($Na_2SO_4$) solvent and crystallization of the residue from methanol gave 104 mg (39%) of colorless crystals. The product was identical with **16**, as obtained in the ammonia reaction above, with respect to mixture m.p. and all the usual physical and chemical properties.

*Treatment of* **16** *with pyridine*. — A solution of 200 mg (0.42 mmol) of **16** in 2 ml of freshly distilled pyridine was boiled under reflux for 2 h, and then poured into 50 ml of ice-cold 10% aqueous sodium chloride. The solid, red precipitate, that

showed one major spot on t.l.c., was collected on a filter, washed with water (30 ml), and chromatographed on a small column of silica gel with chloroform–benzene (96:4). The colorless product obtained was crystallized from ethyl acetate–light petroleum (b.p. 60–80°) to give 120 mg (60%) of colorless crystals that was identical with **19** in all the usual physical and chemical properties.

*Methyl 4,6-O-benzylidene-3-deoxy-3-C-nitromethyl-2-O-p-tolylsulfonyl-α-D-allopyranoside* (**23**). — *Method* A. Solid sodium borohydride (76 mg, 2 mmol) was added to a stirred solution of 477 mg (1 mmol) of **16** in 7 ml of acetonitrile at ambient temperature. Stirring was continued for 15 h, and the mixture was then poured into 50 ml of ice–water. Excess of borohydride was destroyed by addition of 1 ml of acetic acid. The product was extracted with dichloromethane (3 × 10 ml), and the extract was washed with saturated, aqueous sodium hydrogen carbonate (10 ml) and water (10 ml). The dried ($Na_2SO_4$) extract was evaporated to give a crystalline residue. Recrystallization from acetone–methanol gave **23** (441 mg, 92%) as colorless crystals, m.p. 166–167°, $[\alpha]_D^{24}$ +52° (*c* 1, chloroform); $\nu_{max}$ 1565 and 1390 $cm^{-1}$ ($NO_2$). N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 6.55 (m, 1 H, H-3), 5.35 (q, 1 H, $J_{2,1}$ 3.2, $J_{2,3}$ 5.2 Hz, H-2), 5.29 (s, 2 H, $CH_2NO_2$), 5.21 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1).

*Anal.* Calc. for $C_{22}H_{25}NO_9S$: C, 55.11; H, 5.26; N, 2.92. Found: C, 55.38; H, 5.13; N, 2.95.

*Method* B. To a stirred solution of 3.0 g (6.3 mmol) of **11** in 50 ml of acetonitrile was added 426 mg (11.2 mmol) of solid sodium borohydride, in small portions during 30 min, at ambient temperature. Stirring was continued for 3 h, and the mixture was then poured into 500 ml of ice–water. Excess borohydride was destroyed by addition of 5 ml of glacial acetic acid. Work-up as in method *A* gave 2.58 g (96%) of colorless crystals that were identical with **23** obtained by method *A*, with respect to mixture m.p., and all the usual physical and chemical properties.

*Benzyl 2-acetamido-4,6-O-benzylidene-2,3-dideoxy-3-C-nitromethyl-α-D-erythro-hex-2-enopyranoside* (**20**). — To a stirred solution of 730 mg (1.46 mmol) of **7** in 10 ml of tetrahydrofuran at 0° was added 330 mg (2.95 mmol) of solid potassium *tert*-butoxide in small portions during 20 min. Stirring was continued for 15 h at 4° and the mixture was then poured into 100 ml of 2% ice-cold, aqueous acetic acid. The product was extracted with dichloromethane (4 × 10 ml), and the extract was washed with saturated, aqueous sodium hydrogen carbonate (5 ml) and water (5 ml). Evaporation of the dried ($Na_2SO_4$) extract left a solid that was crystallized from a mixture of acetone, methanol, and ethanol (1:10:10). Recrystallization gave **20** (480 mg, 75%) as colorless crystals that showed one spot on t.l.c. (chloroform–*p*-dioxane, 95:5), and had m.p. 218–219°, $[\alpha]_D^{26}$ −34.8° (*c* 1.1, chloroform); $\nu_{max}$ 3290 (NH), 1670 (C=O), 1560, and 1380 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$–methyl sulfoxide-$d_6$): $\tau$ 8.00 (s, 3 H, $CH_3CON$), 4.82 (s, 2 H, $CH_2NO_2$), 4.32 (s, 1 H, H-1), 0.91 (s, 1 H, NHAc).

*Anal.* Calc. for $C_{23}H_{24}N_2O_7$: C, 62.72; H, 5.49; N, 6.36. Found: C, 62.18; H, 5.31; N, 6.19.

*Methyl 4,6-O-benzylidene-2,3-dideoxy-3-C-nitromethyl-α-D-erythro-hex-2-*

*enopyranoside* (**21**). — Treatment of 2.2 g (6 mmol) of **9**[5] with potassium *tert*-butoxide in tetrahydrofuran, as described for **20**, gave a syrup that was chromatographed on a column of silica gel, with chloroform as eluent, to give a solid that crystallized from ethanol. Recrystallization gave **21** (1.38 g, 75%) as colorless needles that were clearly distinguishable from **18** on t.l.c. (benzene–ethyl acetate, 10:1), and had m.p. 128–129°, $[\alpha]_D^{24}$ +63.1° (*c* 1, chloroform); $\nu_{max}$ 1575 and 1375 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 5.03 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.97 (q, 2 H, $J_{AB}$ 14.2 Hz, $\Delta\nu_{AB}$ 28.8 Hz, $CH_2NO_2$), 4.17 (m, 1 H, H-2).

*Anal.* Calc. for $C_{15}H_{17}NO_6$: C, 58.63; H, 5.58; N, 4.56. Found: C, 58.43; H, 5.43; N, 4.55.

*Benzyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-nitromethyl-α-*D*-allopyranoside* (**24**). — Reduction of 700 mg (1.4 mmol) of **7** with sodium borohydride in acetonitrile, as described for **23** (Method *A*), gave a mixture of products that showed two spots on t.l.c., (chloroform–*p*-dioxane, 95:5). Chromatographic separation on silica gel (chloroform) gave the faster-moving component as a foam; yield 270 mg (44%); $[\alpha]_D^{24}$ +49° (*c* 1, chloroform); $\nu_{max}$ 3444 (NH), 1670 (C=O), 1560, and 1386 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 8.13 (s, 3 H, $CH_3CON$), 6.52 (m, 1 H, $J_{3,2}$ 4.5 Hz, H-3), 5.55 (m, 1 H, $J_{2,3}$ 4.5 Hz, H-2), 5.18 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.12 (d, 2 H, $J_{3',3}$ 6.6 Hz, $CH_2NO_2$).

*Anal.* Calc. for $C_{23}H_{26}N_2O_7$: C, 62.43; H, 5.92; N, 6.33. Found: C, 62.90; H, 5.85; N, 5.89.

*Methyl 2-benzamido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-nitromethyl-α-*D*-allopyranoside* (**25**). — Reduction of 360 mg of **5**, as described for **23** (Method *A*), gave 186 mg (51%) of a glass that showed one spot on t.l.c. (benzene–acetone, 4:1), and had $[\alpha]_D^{24}$ +44.4° (*c* 0.5, chloroform); $\nu_{max}$ 3450 (NH), 1670 (C=O), 1560, and 1390 ($NO_2$) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 6.45 (m, 1 H, H-3), 5.12 (d, 2 H, $J_{3',3}$ 5.6 Hz, $CH_2NO_2$).

*Anal.* Calc. for $C_{22}H_{24}N_2O_7$: C, 61.68; H, 5.65; N, 6.54. Found: C, 61.50; H, 5.96; N, 6.06.

*Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-*D*-allopyranoside* (**27**). — To a stirred solution of 397 mg (1 mmol) of **3** in 6 ml of acetonitrile was added 152 mg (4 mmol) of sodium borohydride at ambient temperature. Stirring was continued for 2 h, and the mixture was then poured into 100 ml of ice–water and acidified with 1 ml of acetic acid. The mixture was extracted with dichloromethane (3 × 20 ml), and washed consecutively with 5% aqueous sodium hydrogen carbonate (5 ml) and water (15 ml). Evaporation of the dried ($Na_2SO_4$) extract gave a solid. Recrystallization from absolute ethanol gave 381 mg (95%) of colorless needles that showed one spot on t.l.c. (chloroform–*p*-dioxane, 95:5) and had m.p. 218–219°, $[\alpha]_D^{24}$ +112° (*c* 1, chloroform); $\nu_{max}$ 3510 and 3380 (OH, NH) $cm^{-1}$. N.m.r. data (60 MHz, $CDCl_3$): $\tau$ 8.07 (s, 3 H, $CH_3CO$), 7.17 (d, 1 H, $J_{OH,3}$ 6.8 Hz, OH) lost on addition of $D_2O$, 5.35 (q, 2 H, $J_{AB}$ 12.2 Hz, $\Delta\nu_{AB}$ 18.6 Hz, $OCH_2Ph$), 5.10 (d, 1 H, $J_{1,2}$ 4.2 Hz, H-1).

*Anal.* Calc. for $C_{22}H_{25}NO_6$: C, 66.15; H, 6.31; N, 3.51. Found: C, 66.19; H, 6.19; N, 3.49.

ACKNOWLEDGMENT

The capable technical assistance of Miss Rita Paulini is gratefully acknowledged.

REFERENCES

1 (*a*) G. J. LOURENS, *Tetrahedron Lett.*, (1969) 3733–3736; (*b*) G. J. LOURENS, *Carbohydr. Res.*, 17 (1971) 35–43.
2 (*a*) A. ROSENTHAL AND K. S. ONG, *Tetrahedron Lett.*, (1969) 3981–3983; (*b*) A. ROSENTHAL AND K. S. ONG, *Can. J. Chem.*, 48 (1970) 3034–3038.
3 S. W. GUNNER, R. D. KING, W. G. OVEREND, AND N. R. WILLIAMS, *J. Chem. Soc., C*, (1970) 1954–1961.
4 A. ROSENTHAL, K. S. ONG, AND D. A. BAKER, *Carbohydr. Res.*, 13 (1970) 113–125.
5 A. ROSENTHAL AND G. SCHÖLLNHAMMER, *Can. J. Chem.*, 50 (1972) 1780–1783.
6 J. YOSHIMURA, K. SATO, K. KOBAYASHI, AND C. SHIN, *Bull. Chem. Soc. Jap.*, 46 (1973) 1515–1519.
7 H. P. ALBRECHT AND J. G. MOFFATT, *Tetrahedron Lett.*, (1970) 1063–1066.
8 A. ROSENTHAL, M. SPRINZL, AND D. A. BAKER, *Tetrahedron Lett.*, (1970) 4233–4235.
9 (*a*) H. B. HASS, A. G. SUSIE, AND R. L. HEIDER, *J. Org. Chem.*, 15 (1950) 8–14; (*b*) H. H. BAER, T. NIELSON, AND W. RANK, *Can. J. Chem.*, 45 (1967) 991–996.
10 A. I. MEYERS AND J. C. SIRCAR, *J. Org. Chem.*, 32 (1967) 4134–4136.
11 K. ONODERA, S. HIRANO, AND N. KASHIMURA, *Carbohydr. Res.*, 6 (1968) 276–285.
12 J. J. NIEUWENHUIS AND J. H. JORDAAN, *Carbohydr. Res.*, 51 (1976) 207–213.
13 F. W. LICHTENTHALER, *Fortschr. Chem. Forsch.*, 14 (1970) 556–577.
14 B. R. BAKER AND D. H. BUSS, *J. Org. Chem.*, 30 (1965) 2308–2311.
15 F. W. LICHTENTHALER AND P. EMIG, *Tetrahedron Lett.*, (1967) 577–582.
16 P. H. GROSS AND R. W. JEANLOZ, *J. Org. Chem.*, 32 (1967) 2759–2763.
17 H. C. BROWN, J. H. BREWSTER, AND H. SCHECHTER, *J. Am. Chem. Soc.*, 76 (1954) 467–474.