*Carbohydrate Research*, 89 (1981) 255–269
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

# REACTION OF METHYL 2-DEOXY-3-*O*-SULFONYL-2-*p*-TOLUENESULFONAMIDO-α- AND β-D-GLUCOPYRANOSIDE DERIVATIVES WITH HALIDE IONS*

TOSHIAKI MIYAKE, TSUTOMU TSUCHIYA, YOSHIAKI TAKAHASHI, AND SUMIO UMEZAWA
*Institute of Bio-organic Chemistry, 1614 Ida, Nakahara-ku, Kawasaki-shi 211 (Japan)*
(Received June 12th, 1980; accepted for publication in revised form, August 10th, 1980)

ABSTRACT

Methyl 2-deoxy-3-*O*-sulfonyl-2-*p*-toluenesulfonamido-α-D-glucopyranoside derivatives were treated with halides in *N*,*N*-dimethylformamide. The corresponding 3-halo-α-D-glucopyranosides were formed by a double SN2 process in high yields *via* the 3-halo-α-D-allopyranosides, despite the presence of an axial methoxyl group at C-1. The reactions proceeded more readily than the reaction for methyl 4,6-*O*-cyclohexylidene-2-deoxy-3-*O*-*p*-tolylsulfonyl-2-*p*-toluenesulfonamido-β-D-glucopyranoside. The mechanism for the ready displacement at C-3 in the α-D anomers is discussed. Deoxy compounds were prepared from the corresponding 3-halides by action of tributylstannane, or of sodium in liquid ammonia. Treatment of methyl 4,6-*O*-cyclohexylidene-2-deoxy-3-*O*-*p*-tolylsulfonyl-2-*p*-toluenesulfonamido-α-D-glucopyranoside with nucleophiles other than halide ions gave the corresponding 2,3-epimino derivative.

## INTRODUCTION

A number of natural and semi-synthetic 3′-deoxy derivatives of such aminocyclitol antibiotics as kanamycins have been found active against resistant bacteria[2]. However, chemical deoxygenation at C-3′ *via* SN2 reactions is not readily performed[3], owing to the presence of an axial aglycon at C-1′, which hinders the approach of a nucleophile to C-3′. To overcome this problem, radical-type deoxygenations have recently been developed by several groups[4] and by us[5], the procedures proving effective in some instances. However, in the synthesis of tobramycin, successful SN2 displacement by iodine at C-3 of the 2,6-bis(*N*-ethoxycarbonyl)-3-*O*-*p*-tolylsulfonyl-α-D-glucopyranosyl moiety of a kanamycin derivative was achieved by treatment[6] with 50% sodium iodide in *N*,*N*-dimethylformamide (DMF) (20 h, 100°). Haskell *et al.*[7] also reported success in displacement with benzenethiolate at C-3 of the methyl 2-(*N*-benzyloxycarbonyl)-3-*O*-trifluoromethylsulfonyl-α-D-glycopyranoside of 2-amino-2-deoxy-D-glucose.

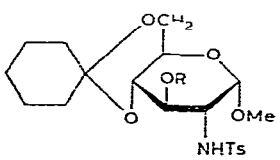
*An outline of this paper was read by T. Tsuchiya at the 5th Anniversary Symposium of the Institute of Bioorganic Chemistry; see ref. 1.

0008-6215/81/0000–0000/S 02.50, 

During studies on chemical transformation of *N*-protected 2-amino-2-deoxy-D-glucopyranosides, we have found that a 3-*O*-sulfonyl-2-*N*-*p*-tolylsulfonyl derivative may be readily converted into the corresponding 3-iodo derivative, a precursor for the 3-deoxy derivative, by sodium iodide. This paper deals with displacement reactions of 3-*O*-sulfonylated derivatives of methyl 2-deoxy-2-*p*-toluenesulfonamido-α- and β-D-glucopyranoside with halide and other ions.

## RESULTS AND DISCUSSION

*Preparation of 2-deoxy-3-O-sulfonyl-2-p-toluenesulfonamido-α- and β-D-glucopyranosides.* — Conventional treatment of methyl 2-deoxy-2-(methoxycarbonyl)-amino-α-D-glucopyranoside[8] with 1,1-dimethoxycyclohexane[9] gave the 4,6-cyclohexylidene acetal (**1**), which was demethoxycarbonylated by alkaline treatment to give the 2-amino analog (**2**). Treatment of **2** with *p*-toluenesulfonyl chloride in aqueous 1,4-dioxane gave methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-*p*-toluenesulfonamido-α-D-glucopyranoside (**3**). The desired 3-*O*-methylsulfonyl, 3-*O*-*p*-tolylsulfonyl, and 3-*O*-benzylsulfonyl derivatives (**4**, **5**, and **6**) were prepared conventionally from **3** by use of the corresponding sulfonyl chlorides. The *N*-methyl-*N*-*p*-tolylsulfonyl derivative (**7**) was prepared by treatment of **5** with diazomethane, and the decyclohexylidenated analog (**8**) was prepared by acid hydrolysis of **5**. Two reference compounds having no *N*-*p*-tolylsulfonyl group, namely, the *N*-methoxycarbonyl-3-*O*-*p*-tolylsulfonyl and *N*-benzyloxycarbonyl-3-*O*-*p*-tolylsulfonyl derivatives (**9** and **11**) were also prepared from **1** (for **9**) and **2** (by way of its *N*-benzyloxycarbonyl derivative **10**).




3 R = H
4 R = Ms
5 R = Ts
6 R = $SO_2CH_2Ph$

Methyl 4,6-*O*-cyclohexylidene-2-deoxy-3-*O*-*p*-tolylsulfonyl-2-*p*-toluene-sulfonamido-β-D-glucopyranoside (**25**) was prepared as follows. 2-Amino-2-deoxy-D-glucose was converted to methyl 2-deoxy-2-*p*-toluenesulfonamido-β-D-glucopyranoside (**23**) *via* the 1-bromide **22**, essentially by the method of Micheel *et al.*[10,11]. Cyclohexylidenation of **23** (to give **24**), followed by 3-*O*-*p*-toluenesulfonylation gave **25**.

*Halide displacement-reactions.* — The reactions of **4**, **5**, and **6** with 50% sodium iodide in *N*,*N*-dimethylformamide (DMF) at 100° were studied initially. The conditions were those used previously for the synthesis[6] of tobramycin. The 3-iodo-α-D-

glucopyranoside derivative (**12**) was produced in high yield (~95%) from **4**, **5**, and **6** by treatment for 3–5 h, the time period being shorter than that (20 h) used in the synthesis of tobramycin. This result shows that 3-iodination readily occurs, despite the presence of an axial 1-methoxyl group. Chlorination of **5** with 3.6% (w/v) lithium chloride in DMF for 2.5 h at 100° also gave the corresponding 3-chloro-α-D-glucopyranoside (**14**) in high yield. However, when the reaction was conducted for 20 min at 120°, two derivatives were produced. The major product was the 3-chloro-α-D-allopyranoside **13**, and the minor one the 3-chloro-α-D-glucopyranoside **14**. The structures of **13** and **14** were proved by their n.m.r. spectra. When the foregoing reaction was prolonged to 1 h, compound **14** was the only product isolated. Similar

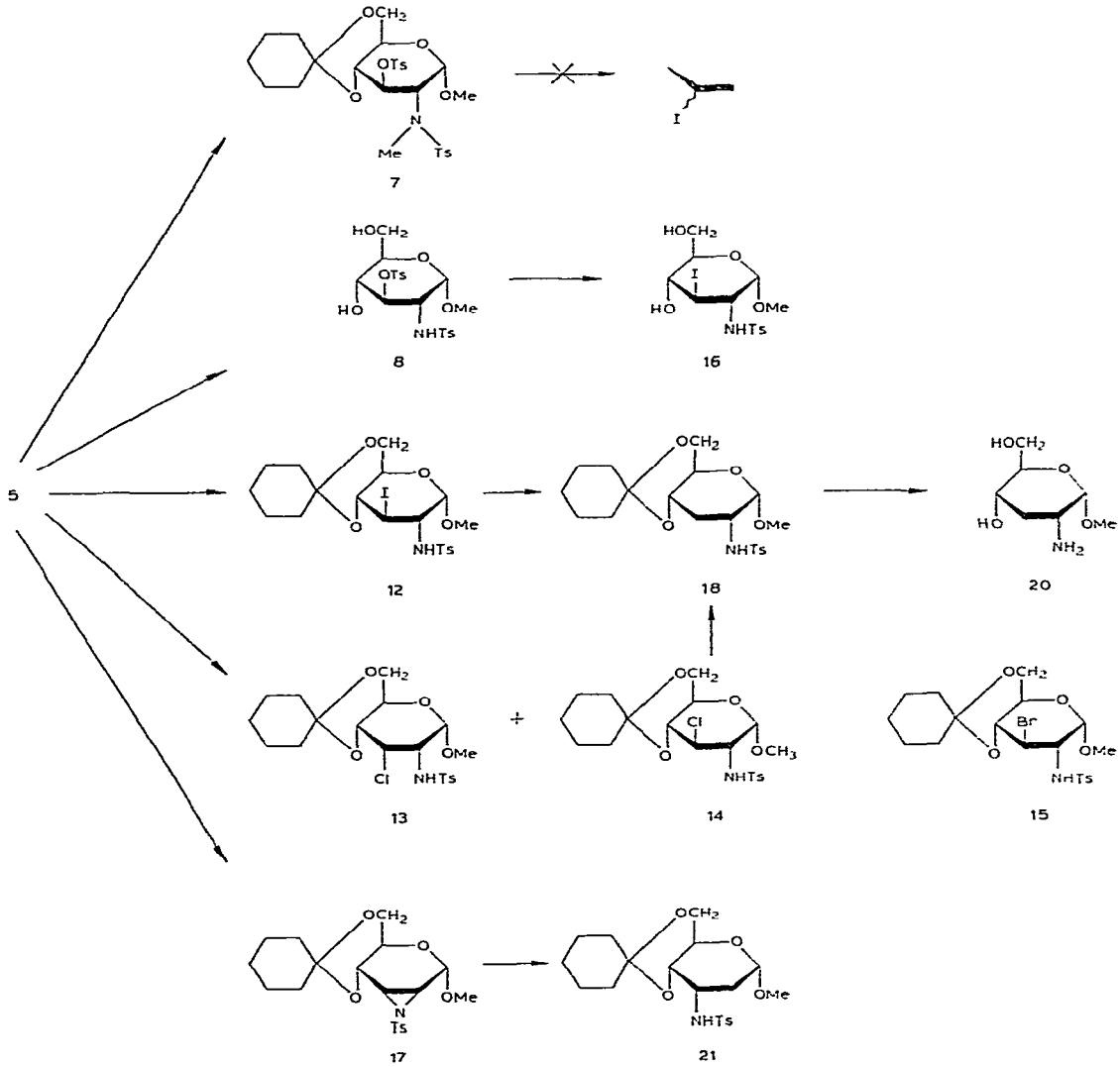


TABLE I

YIELDS OF 3-HALO DERIVATIVES

| *Starting compound* | *Metal halide* | *Temperature (°C)* | *Reaction period (h)* | *Yields (%[a]) of product* | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | **12** | **13** | **14** | **15** | **16** | *Other* |
| **4** | NaI[b] | 100 | 5 | 94 | | | | | |
| **5** | NaI | 100 | 3.5 | 96 | | | | | |
| **6** | NaI | 100 | 5 | 97 | | | | | |
| **8** | NaI | 100 | 40–60 | | | | | 85 | |
| **5** | LiCl[c] | 100 | 2.5 | | | 95 | | | |
| **5** | LiCl | 120 | 20–60 | | 42 | 25 | | | **5**, 15; **13** + **14**, 14 |
| **5** | LiCl | 120 | 1 | | | 98 | | | |
| **5** | LiBr[d] | 120 | 50–60 | | | | 92 | | |

[a]Purified product, except for **16**. [b]~ 35 Mol equiv. for the starting compound; NaI/DMF = 0.5 g/mL; typical procedure shown in the preparation of **12**. [c]Anhydrous LiCl; 10 mol equiv. for starting compound; LiCl/DMF = 0.036 g/mL. [d]Anhydrous LiBr; 10 mol equiv. for starting compound; LiBr/DMF = 0.07 g/mL.

treatment of the isolated **13** also gave **14**. These results (see Table I) appear to show that chlorination occurs first at C-3 by an SN2 process (to give **13**), followed by further chlorination (to give **14**).

To clarify the mechanism of conversion, **13** was heated for 1 h at 120° in DMF without the addition of lithium chloride, whereupon **13** was mostly recovered. This result shows that chloride ion is necessary for conversion of **13** into **14**, and the possibility of epimerization at C-3 appears unlikely. However, epimerization as catalyzed by chloride ion had also to be considered, and hence, compound **13** was treated with lithium bromide. After 0.5 h, the 3-bromo-α-D-glucopyranoside **15** was isolated as the sole product, identical with **15** prepared from **5** with lithium bromide in DMF. After treatment for 3, 5, and 15 h, however, **13** gave a mixture of the 3-bromo- and 3-chloro-α-D-glucopyranosides (**15** and **14**) in the ratios of 1.4:1, 1:1.5, and 1:2, respectively. When **13** was treated similarly with 15% (w/v) lithium iodide in DMF, analogous results were obtained, namely, after reactions for 0.5, 3, 5, and 15 h, **13**, the 3-iodo- (**12**), and 3-chloro-α-D-glucopyranoside (**14**) were obtained in the ratios of 1:2.7:0, 1:4.6:1.5, 1:5:3.5, and 1:4.3:8.6, respectively. The formation of **14** in both reactions may be explained on the basis of the action of chloride ion liberated during the reactions. When sodium bromide or sodium iodide were used instead of lithium salts in the foregoing reaction, **14** was not formed and **15** and **12** were the only products isolated, even after reactions for 5 h. This result may be explained by the removal from the system of the sodium chloride formed, because it is insoluble in DMF. The 3-chloro compound **14** was also partially converted into 3-bromo or 3-iodo derivatives (**15** or **12**) on 10-h treatment with lithium bromide or iodide, respectively. These results (see Table II) suggest that, in the displacement

TABLE II

PRODUCT DISTRIBUTION AT VARIOUS REACTION[a] TIMES

| *Starting compound*[b] | *Metal halide* | *Reaction period (h)* | *Signal strength*[c] *of the* $^1$*H-n.m.r. spectrum of H-1 for:* | | | |
|---|---|---|---|---|---|---|
| | | | **12** | **13** | **14** | **15** |
| **13** | LiCl | 40/60 | | [d] | 1 | |
| | | 1.5 | | | 1 | |
| **13** | LiBr | 0.5 | | | [d] | 1 |
| | | 3 | | | 0.42 | 0.58 |
| | | 5 | | | 0.6 | 0.4 |
| | | 15 | | | 0.67 | 0.33 |
| **13** | NaBr | 1 | | | | 1 |
| | | 5 | | | | 1 |
| **13** | LiI | 0.5 | 0.73 | 0.27 | 0 | |
| | | 3 | 0.65 | 0.14 | 0.21 | |
| | | 5 | 0.53 | 0.1 | 0.37 | |
| | | 15 | 0.31 | 0.07 | 0.62 | |
| **13** | NaI | 5 | 1 | | | |
| | | 20 | 1 | | | |
| **14** | LiBr | 10 | | | 0.67 | 0.33 |
| | LiI | 10 | 0.21 | | 0.79 | |

[a]At 120°. [b]Starting compounds were dissolved in 1.1M metal halide in DMF, respectively (molar ratios of the metal halide/starting compound were always 10). [c]Measured in pyridine-$d_5$ containing a little $D_2O$. [d]Not detectable.

reactions of **13**, no epimerization occurred and, after the first SN2 reaction, repeated double inversions occurred at C-3 to give a mixture of **15** and **14**, or a mixture of **12** and **14**, indicating that compound **14** is thermodynamically more stable than **15** or **12**.

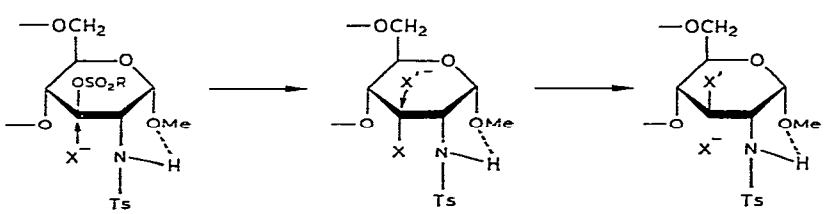
In order to clarify the stereochemical factors influencing the halogen displacement, compounds **7** and **8** were treated with 50% sodium iodide in DMF. From the decyclohexylidenated derivative **8**, the 3-iodo-α-D-glucopyranoside **16** was formed in high yield in a short period (40 min), indicating that removal of the cyclohexylidene group from **5** increased the reactivity at C-3. On the other hand, the *N*-methyl-*N*-*p*-tolylsulfonyl derivative **7** did not respond to the reaction, even after a long time-period (62 h, 100°); the starting material was recovered quantitatively. This result may be explained by either by steric hindrance of displacement at C-3 by the *N*-methyl group, or that the NH hydrogen atom of the sulfonamide group in **5** or the other related compounds is required for SN2 reaction at C-3. In order to clarify this question, the *N*-methyl-*N*-*p*-tolylsulfonyl-β-D-glucopyranoside derivative **27**, prepared from **25** by treatment with diazomethane, was treated similarly. This time a 3-iodo derivative (**28**) was obtained in moderate yield, suggesting that steric hindrance by the *N*-methyl group in the reaction of **7** is unlikely, and the NH hydrogen atom may play an important role in the displacement reaction.

At this stage, we felt further that confirmation of the positive role of the sulfonamide group would be necessary. For this, compounds **9** and **11**, both of which lack the sulfonamide group, were treated with sodium iodide. In both instances, fair amounts of the starting materials were recovered, even after long reaction-periods, with concomitant decomposition. This behavior clearly indicates that the sulfonamide group plays a major role in the displacement reactions.

Subsequently, in order to confirm the importance of the orientation of the anomeric methoxyl group for the halide displacement at C-3, the 3-*O*-*p*-tolylsulfonyl-*N*-*p*-tolylsulfonyl-β-D-glucopyranoside (**25**) was treated with lithium chloride in the manner (1 h, 120°) described for **5**. This time the 3-chloro-β-D-allopyranoside **26** was obtained in moderate yield (71%), without the formation of a 3-chloro-β-D-gluco derivative. This fact shows that, in the β-D anomer, SN2 reaction occurs at C-3, but no double inversion as in **5**. As, in **25**, the anomeric methoxyl group is equatorially disposed and, in general, does not hinder the approach of a nucleophile to C-3, the formation of **26** from **25** is reasonably interpreted.


25 26

One possible mechanism satisfying the results mentioned hitherto is the assumption that hydrogen bonding is present between NH and the alkoxyl oxygen atom at C-1. The slightly negatively charged oxygen atom of the C-1 methoxyl group will be neutralized as depicted in **I**, thus facilitating the approach of the halide ion from below at C-3 to give the 3-halo-α-D-allopyranoside derivative. Ready conversion of the allopyranoside into the 3-halo-α-D-glucopyranoside by attack of another halide ion may also be explained by facile removal of the axial halogen atom of the allopyranoside derivative. As removal of the axial halogen from **II** is not obstructed by the presence of a slightly negatively charged methoxyl group at C-1 (the negative charge is also neutralized in **II**), the formation of **III** will be readily accomplished. In the case of the 3-chloro-β-D-allopyranoside **26**, hydrogen bonding between NH and the methoxyl oxygen atom at C-1 is also possible. However, through hydrogen




I II III

bonding, the *N*-*p*-tolylsulfonyl group is forced to approach close to C-3, thus hindering the approach of a halide ion to C-3 from the upper side, either stereochemically or electronically. Thus, the possible displacement at C-3 is prevented.

*Reactions with other nucleophiles.* — When compound **5** was treated with several other reagents, such as sodium acetate, sodium azide, sodium benzoate, tetrabutylammonium fluoride, and lithium nitrate, the *N*-*p*-tolylsulfonyl-2,3-epimino-α-D-allopyranoside **17** was the principal product in all instances. Compound **17** was also prepared from **5** by treatment with methanolic sodium hydroxide. Ali *et al.*[12] have previously reported the intermediate formation of an *N*-(methylsulfonyl)epimine in the reaction of methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-(methylsulfonyl)-2-methanesulfonamido-α-D-glucopyranoside with sodium azide in DMF. The aforementioned reagents tested seem to act on **5** as bases rather than as nucleophiles. The cause of the remarkable difference in behavior between halide ions ($Cl^-$, $Br^-$, and $I^-$) and the other reagents used is not clear.

Treatment of **17** with lithium aluminum hydride gave the 2-deoxy-3-*p*-toluenesulfonamido derivative **21** as a single product. Direct treatment of **5** with lithium aluminum hydride also gave **21**, possibly via **17**. This result indicates that the direct 3-deoxygenation[13] encountered in the reaction of methyl 4,6-*O*-benzylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside does not occur in this instance.

*Deoxygenations.* — In the final part of this study, preparation of 3-deoxy compounds from the corresponding 3-halo precursors is described. Treatment of the 3-iodo and the 3-chloro derivatives (**12** and **14**) with tributylstannane gave the corresponding 3-deoxy derivative (**18**) in high yields. Desulfonylation of **18** with sodium in liquid ammonia, followed by *N*-methoxycarbonylation with methyl chloroformate, gave methyl 4,6-*O*-cyclohexylidene-2,3-dideoxy-2-methoxycarbonylamino-α-D-*ribo*-hexopyranoside (**19**), identical with the compound prepared by a different route[5c], thus confirming the structure of **19**. The 3-iodo and 3-chloro derivatives (**12** and **14**) were treated with sodium in liquid ammonia, followed by treatment with strong cation-exchange resin, to give methyl 2-amino-2,3-dideoxy-α-D-*ribo*-hexopyranoside (**20**), identical with the compound prepared from **18** by the same treatment. This procedure is, therefore, a convenient route for one-step removal of both halogeno and *p*-tolylsulfonyl groups.

## EXPERIMENTAL

*General.* — Melting points were determined on a Kofler block and are uncorrected. Specific rotations were measured, in a 0.1-dm tube, with a Perkin–Elmer Model 241 polarimeter. $^1$H-N.m.r. spectra were recorded at 90 MHz with a Varian EM-390 spectrometer. Thin-layer chromatography (t.l.c.) was performed on Merck silica gel 60 (pre-coated) with sulfuric acid spray for detection. Silica gel (Wakogel C-200) was used, unless otherwise stated, for separation of the products by column chromatography.

*Methyl 4,6-O-cyclohexylidene-2-deoxy-2-methoxycarbonylamino-α-D-glucopyra-*

*noside* (**1**). — A solution of methyl 2-deoxy-2-methoxycarbonyl amino-α-D-glucopyranoside (2.81 g) in DMF (28 mL) containing *p*-toluenesulfonic acid (420 mg) and 1,1-dimethoxycyclohexane (1.8 mL) was heated for 1.5 h at 50° *in vacuo* (~15 torr) to remove the methanol liberated. Addition of saturated, aqueous sodium hydrogencarbonate (5 mL), followed by evaporation, gave a syrup. A solution of the syrup in chloroform was washed with water, dried (magnesium sulfate), and evaporated. The residue was chromatographed on a short column with 2:1 benzene–ethyl acetate to give a solid; yield 3.59 g (97%), $[\alpha]_D^{25}$ +78° (*c* 1, chloroform); $^1$H-n.m.r. ($CDCl_3$): $\delta$ 3.35 (s, 3 H, $OCH_3$).

*Anal.* Calc. for $C_{15}H_{25}NO_7$: C, 54.37; H, 7.60; N, 4.23. Found: C, 54.48; H, 7.62; N, 4.07.

*Methyl 2-amino-4,6-O-cyclohexylidene-2-deoxy-α-D-glucopyranoside* (**2**). — A mixture of **1** (5.05 g) in 1,4-dioxane (25 mL) and 1.2M aqueous sodium hydroxide (2.5 mL) was stirred for 6 h at 100°. Evaporation gave a residue that was extracted with chloroform. The solution was concentrated to ~20 mL and ether was added to give needles; yield 2.82 g (68%), m.p. 132–134°, $[\alpha]_D^{25}$ +113° (*c* 1, chloroform).

*Anal.* Calc. for $C_{13}H_{23}NO_5$: C, 57.13; H, 8.48; N, 5.13. Found: C, 57.31; H, 8.43; N, 5.15.

*Methyl 4,6-O-cyclohexylidene-2-deoxy-2-*p*-toluenesulfonamido-α-D-glucopyranoside* (**3**). — A solution of **2** (3.00 g) in 50% aqueous 1,4-dioxane (60 mL) containing anhydrous sodium carbonate (1.28 g) and *p*-toluenesulfonyl chloride (2.3 g) was kept for 3.5 h at 5°. Evaporation gave a residue that was extracted with chloroform. The solution was washed with water, dried, and evaporated. The residue was dissolved in 30:1 chloroform–ethanol and passed through a short column of silica gel with the same solvent-system. Fractions containing **3** were evaporated to give an amorphous powder; yield 4.57 g (97%), $[\alpha]_D^{25}$ +51° (*c* 1, chloroform); $^1$H-n.m.r. ($CDCl_3$): $\delta$ 2.45 (s, 3 H, $CH_3$ of Ts), 3.27 (s, 3 H, $OCH_3$), 4.33 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), and 5.25 (d, 1 H, *J* 8.5 Hz, NH; disappeared on deuteration).

*Anal.* Calc. for $C_{20}H_{29}NO_7S$: C, 56.19; H, 6.84; N, 3.28; S, 7.50. Found: C, 56.00; H, 6.74; N, 3.08; S, 7.22.

*Methyl 4,6-O-cyclohexylidene-2-deoxy-3-O-(methylsulfonyl)-2-*p*-toluenesulfonamido-α-D-glucopyranoside* (**4**). — A solution of **3** (49.3 mg) in pyridine (1 mL) containing methanesulfonyl chloride (66.6 mg, 5 mol equiv. for **3**) was kept overnight at 0°. Water (0.05 mL) was added and, after 30 min, the solution was evaporated. A solution of the residue in chloroform was washed (5% potassium hydrogensulfate, 5% sodium hydrogencarbonate, and then water), dried and evaporated. The residue was reprecipitated from chloroform–hexane to give a solid; yield 50.6 mg (87%), $[\alpha]_D^{25}$ +63° (*c* 1, chloroform); $^1$H-n.m.r. ($CDCl_3$): $\delta$ 2.47 (Ts), 3.07 (Ms), 3.37 ($OCH_3$), 4.60 (m, 1 H, H-3), 4.62 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), and 5.52 (d, 1 H, *J* 9.5 Hz, NH).

*Anal.* Calc. for $C_{21}H_{31}NO_9S_2$: C, 49.89; H, 6.18; N, 2.77; S, 12.68. Found: C, 49.79; H, 6.07; N, 2.63; S, 12.75.

*Methyl 4,6-O-cyclohexylidene-2-deoxy-3-O-*p*-tolylsulfonyl-2-*p*-toluenesulfona-*

*mido-α-*D*-glucopyranoside* (**5**). — A solution of **3** (209 mg) and *p*-toluenesulfonyl chloride (470 mg, 5 mol equiv. for **3**) in pyridine (4 mL) was heated for 16 h at 90°. Processing as described for **4** gave a crude product that was chromatographed with 3:1 benzene–ethyl acetate to remove slight impurities and give an amorphous powder; yield 254 mg (86%), $[\alpha]_D^{25}$ +44° (*c* 1, chloroform): $^1$H-n.m.r. ($CDCl_3$): $\delta$ 2.45 (s, 6 H, Ts), 3.32 ($OCH_3$), 4.60 (m, 1 H, H-3), 4.61 (d, 1 H, H-1), and 5.27 (d, 1 H, *J* 9.5 Hz, NH).

*Anal.* Calc. for $C_{27}H_{35}NO_9S_2$: C, 55.75; H, 6.06; N, 2.41; S, 11.02. Found: C, 55.96; H, 5.99; N, 2.17; S, 10.82.

*Methyl 3-*O*-benzylsulfonyl-4,6-*O*-cyclohexylidene-2-deoxy-2-*p*-toluenesulfonamido-α-*D*-glucopyranoside* (**6**). — An ice-cold solution of **3** (47.6 mg) in pyridine (1 mL), containing p-toluenesulfonyl chloride (23.6 mg, 1.1 mol equiv. for **3**) was kept for 50 min at 0°. Processing as described for **4** gave a solid; yield 55.2 mg (85%), $[\alpha]_D^{25}$ +47° (*c* 1, chloroform): $^1$H-n.m.r. ($CDCl_3$): $\delta$ 2.43 (Ts), 3.37 ($OCH_3$), 4.42 (AB q, 2 H, *J* 13.5 Hz, $SO_2CH_2Ph$), 4.65 (d, 1 H, H-1), and 4.7 (broadened q, 1 H, 3-H), 5.22 (d, NH).

*Anal.* Calc. for $C_{27}H_{35}NO_9S_2$: C, 55.75; H, 6.06; N, 2.41; S, 11.02. Found: C, 55.94; H, 6.15; N, 2.26; S, 11.20.

*Methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-*N*-methyl-3-*O*-p-tolylsulfonyl-2-*p*-toluenesulfonamido-α-*D*-glucopyranoside* (**7**). — To a solution of **5** (103 mg) in oxolane (1 mL), diazomethane (~13 mg) in ether (1 mL) was added and the solution was kept overnight at room temperature in the dark (see also the procedure reported by Micheel and Michaelis[11]. In t.l.c. (5:1 benzene–ethyl acetate), the solution showed spots having $R_F$ 0.45 (**5**, minor) and 0.65 (**7**, major). Diazomethane solution (1 mL) was added and the solution was kept for a further 20 h. Evaporation gave a syrup that was chromatographed with 10:1 benzene–ethyl acetate to give a solid; yield 87 mg (83%), $[\alpha]_D^{25}$ +66° (*c* 0.5, chloroform;) $^1$H-n.m.r. ($CDCl_3$): $\delta$ 2.45 (s, 6 H, Ts), 3.00 (s, 3 H, $NCH_3$), 3.30 ($OCH_3$), 4.21 (double d, 1 H, *J* 3.5 and 10.5 Hz, H-2), 4.71 (d, 1 H, *J* 3.5 Hz, H-1), and 5.03 (broadened m, 1 H, H-3); in pyridine-$d_5$: 2.30 and 2.33 (s, 3 H each, Ts) 3.18 ($NCH_3$), 3.27 ($OCH_3$), 4.68 (double d, 1 H, H-2), 4.95 (d, 1 H, H-1), and 5.39 (clear double d, 1 H, *J* 10.5 and 8 (= $J_{3,4}$) Hz, H-3).

*Anal.* Calc. for $C_{28}H_{37}NO_9S_2$: C, 56.45; H, 6.26; N, 2.35; S, 10.76. Found: C, 56.35; H, 6.15; N, 2.25; S, 10.79.

*Methyl 2-deoxy-3-*O*-p-tolylsulfonyl-2-*p*-toluenesulfonamido-α-*D*-glucopyranoside* (**8**). — A solution of **5** (148 mg) in 80% aqueous acetic acid (3 mL) was heated for 2 h at 80°. Evaporation followed by distillation of toluene from the residue gave a solid; yield 128 mg (100%), $[\alpha]_D^{25}$ +46° (*c* 1, chloroform): $^1$H-n.m.r. ($CDCl_3$): $\delta$ 2.43 and 2.48 (s, 3 H each, Ts), 3.27 ($OCH_3$), 3.45 (d, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 10.5 Hz, H-2; peaks clearly appeared in $CDCl_3$–$D_2O$), 4.40 (d, 1 H, H-1), 4.67 (double d, 1 H, *J* 8 (= $J_{3,4}$) and 10.5 Hz, H-3), and 5.08 (d, 1 H, *J* 9.5 Hz, disappeared on deuteration, NH).

*Anal.* Calc. for $C_{21}H_{27}NO_9S_2$: C, 50.29: H, 5.43; N, 2.79; S, 12.78. Found: C, 50.44; H, 5.37; N, 2.59; S, 12.76.

*Methyl 4,6-O-cyclohexylidene-2-deoxy-2-methoxycarbonylamino-3-O-p-tolylsulfonyl-α-D-glucopyranoside* (**9**). — Compound **1** (107 mg) was treated with *p*-toluenesulfonyl chloride (5 mol equiv. for **1**) as described for **5** to give **9** as a solid; yield 143 mg (91%), $[\alpha]_D^{25}$ +42° (*c* 1, chloroform); $^1$H-n.m.r. ($CDCl_3$): δ 2.45 (Ts), 3.42 ($OCH_3$), and 3.70 (s, 3 H, $CO_2CH_3$).

*Anal.* Calc. for $C_{22}H_{31}NO_9S$: C, 54.42; H, 6.44; N, 2.89; S, 6.60. Found: C, 54.33; H, 6.34; N, 2.73; S, 6.25.

*Methyl 2-(benzyloxycarbonyl)amino-4,6-O-cyclohexylidene-2-deoxy-α-D-glucopyranoside* (**10**). — Prepared conventionally from **2** (204 mg), benzyl chloroformate (0.12 mL), and anhydrous sodium carbonate (87 mg) in aqueous methanol (1:1, 4 mL), the yield of **10** was 248 mg (82%); $[\alpha]_D^{25}$ +63° (*c* 1, chloroform).

*Anal.* Calc. for $C_{21}H_{29}NO_7$: C, 61.90; H, 7.17; N, 3.44. Found: C, 62.12; H, 7.22; N, 3.34.

*Methyl 2-(benzyloxycarbonyl)amino-4,6-O-cyclohexylidene-2-deoxy-3-O-p-tolylsulfonyl-α-D-glucopyranoside* (**11**). — Compound **11** had $[\alpha]_D^{25}$ +48° (*c* 0.5, chloroform).

*Anal.* Calc. for $C_{28}H_{35}NO_9S$: C, 59.88: H, 6.28: N, 2.49; S, 5.71. Found: C, 59.71; H, 6.28; N, 2.27: S, 5.93.

*Methyl 4,6-O-cyclohexylidene-2,3-dideoxy-3-iodo-2-p-toluenesulfonamido-α-D-glucopyranoside* (**12**). — A mixture of **5** (199 mg) and sodium iodide (2.0 g) in DMF (4 mL) was heated for 3.5 h at 100°. T.l.c. (5:1 benzene–ethyl acetate) showed a single spot ($R_F$ 0.5) (compare **5**: $R_F$ 0.4). The mixture, which solidified on cooling, was extracted with chloroform and the organic solution was evaporated. A solution of the residue in chloroform was washed with 10% aqueous sodium thiosulfate and water, dried, and evaporated with additions of xylene. The pale-yellow solid was chromatographed with 8:1 benzene–ethyl acetate to give a colorless solid; yield 177 mg (96%), $[\alpha]_D^{25}$ +27° (*c* 1, chloroform); $^1$H-n.m.r. (pyridine-$d_5$ + a little $D_2O$): δ 2.32 (Ts), 3.22 ($OCH_3$), and 4.72 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1).

*Anal.* Calc. for $C_{20}H_{28}INO_6S$: C, 44.70; H, 5.25; N, 2.61. Found: C, 44.82; H, 5.22; N, 2.62.

*Methyl 3-chloro-4,6-O-cyclohexylidene-2,3-dideoxy-2-p-toluenesulfonamido-α-D-allopyranoside* (**13**). — This compound had $[\alpha]_D^{25}$ +73° (*c* 1, chloroform) and gave a positive Beilstein test for halogen; $^1$H-n.m.r. (pyridine-$d_5$ + little $D_2O$): δ 2.28 (Ts), 3.22 ($OCH_3$), 4.71 (narrow m, 1 H, width at half-height 4 Hz, H-3), and 4.93 (s, 1 H, H-1).

*Anal.* Calc. for $C_{20}H_{28}ClNO_6S$: C, 53.87; H, 6.33; N, 3.14. Found: C, 54.14; H, 6.45; N, 3.01.

*Methyl 3-chloro-4,6-O-cyclohexylidene-2,3-dideoxy-2-p-toluenesulfonamido-α-D-glucopyranoside* (**14**). — This compound had $[\alpha]_D^{25}$ +54° (*c* 1, chloroform) and gave a positive Beilstein test; $^1$H-n.m.r. (pyridine-$d_5$ + a little $D_2O$): δ 2.28 (Ts), 3.22 ($OCH_3$), 4.10 (double d, 1 H, $J_{1,2}$ 3.5, $J_{2,3}$ 11 Hz, H-2), 4.33 (incomplete double d,

1 H, $J$ ~8 and ~11 Hz, H-3), and 4.86 (d, 1 H, H-1). Irradiation of H-1 collapsed the H-2 quartet to a doublet.

*Anal.* Calc. for $C_{20}H_{28}ClNO_6S$: C, 53.87; H, 6.33; N, 3.14. Found: C, 53.75; H, 6.19; N, 3.25.

*Methyl 2,3-dideoxy-3-iodo-2-*p*-toluenesulfonamido-α-*D*-glucopyranoside* (**16**). — Needles (recrystallized from acetone–chloroform by addition of ether) were obtained: m.p. 204–205°, $[\alpha]_D^{20}$ +70° (*c* 0.5, methanol): $^1$H-n.m.r. (pyridine-$d_5$): δ 2.27 (Ts), 3.25 ($OCH_3$), 4.58 (t, 1 H, $J$ 11.5 Hz, H-3), and 4.80 (d, 1 H, $J$ 3.5 Hz, H-1).

*Anal.* Calc. for $C_{14}H_{20}INO_6S$: 36.77; H, 4.41; N, 3.06. Found: C, 36.76; N, 4.37; N, 2.90.

*Methyl 3-bromo-4,6-*O*-cyclohexylidene-2,3-dideoxy-2-*p*-toluenesulfonamido-α-*D*-glucopyranoside* (**15**). — This compound had $[\alpha]_D^{25}$ +44° (*c* 1, chloroform); $^1$H-n.m.r. (pyridine-$d_5$ + little $D_2O$): δ 2.31 (s, 3 H, Ts), 3.24 (s, 3 H, $OCH_3$), 4.15 (double d, 1 H, H-2), 4.38 (double d, 1 H, $J_{2,3}$ 11, $J_{3,4}$ 9 Hz, H-3), and 4.82 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1).

*Anal.* Calc. for $C_{20}H_{28}BrNO_6S$: C, 48.98; H, 5.75; N, 2.86. Found: C, 48.66; H, 5.53; N, 2.81.

*Reaction of* **9** *with sodium iodide.* — A mixture of **9** (66 mg) and sodium iodide (650 mg) in DMF (1.3 mL) was heated for 20 h at 100°. T.l.c. with 5:1 benzene–ethyl acetate showed two spots having $R_F$ 0.27 (**9**) and 0.4 (trace, 3-iodo derivative?). On heating for a further 10 h, the spot at $R_F$ 0.4 became stronger, but other minor spots also appeared. The solution was thereafter treated as described for **12** (5:1 benzene–ethyl acetate for chromatography) to give recovered **9** (25 mg, 38%) and the product (15.8 mg) having $R_F$ 0.4.

*Reaction of* **11** *with sodium iodide.* — A mixture of **11** (5.0 mg) and sodium iodide (50 mg) in DMF (0.1 mL) was heated for 44 h at 100°. T.l.c. with 5:1 benzene–ethyl acetate showed several spots at $R_F$ 0.5 (3-iodo derivative?), 0.43 (**11**), 0.32 (trace), and 0.13 (trace). Isolation as described for **12** (without column chromatography) gave a solid product whose $^1$H-n.m.r. spectrum showed it to contain ~50% of **11**, [as judged from the peaks of $OCH_3$ (δ 3.40) and $CH_3$ of tosyl (δ 2.42)].

*Methyl 4,6-*O*-cyclohexylidene-2,3-dideoxy-2,3-epimino-*N*-p-tolylsulfonyl-α-*D*-allopyranoside* (**17**). — A solution of **5** (105 mg) in 0.5M methanolic sodium hydroxide (2 mL) was kept for 3.5 h at 40°. T.l.c. (5:1 benzene–ethyl acetate) showed a single spot ($R_F$ 0.45) for **17** (compare **5**: $R_F$ 0.4). Neutralization with hydrochloric acid followed by evaporation gave a residue that was washed with water. Recrystallization from methanol gave needles; yield 64 mg (86%), m.p. 178–179°, $[\alpha]_D^{25}$ +102° (*c* 1, chloroform): $^1$H-n.m.r. ($CDCl_3$): δ 2.45 (Ts), 3.15 (double d, 1 H, $J_{2,3}$ 7.5, $J_{3,4}$ 2.5 Hz, H-3), 3.42 (OMe), 3.50 (double d, 1 H, $J$ 7.5 and 4.0 Hz, H-2), and 4.92 (d, 1 H, $J$ 4.0 Hz, H-1); in pyridine-$d_5$: δ 2.27 (Ts), 3.33 ($OCH_3$), 3.47 (double d, 1 H, H-3), 3.81 (double d, 1 H, H-2), and 5.11 (d, 1 H, H-1); Irradiation of H-1 collapsed the H-2 quartet to a doublet.

*Anal.* Calc. for $C_{20}H_{27}NO_6S$: C, 58.66; H, 6.65; N, 3.42; S, 7.83. Found: C, 58.83; H, 6.60; N, 3.35; S, 7.62.

*Methyl 4,6-O-cyclohexylidene-2,3-dideoxy-2-*p*-toluenesulfonamido-α-*D*-ribo-hexopyranoside* (**18**). — (*a*) *From* **12**. To a solution of **12** (136 mg) in dry 1,4-dioxane (3 mL), were added tributylstannane (0.4 mL) and α,α′-azobisisobutyronitrile (3 mg), and the solution was heated for 1 h at 80° under nitrogen. T.l.c. (5:1 benzene–ethyl acetate) showed a single spot ($R_F$ 0.48) for **18** (compare **12**: 0.52). Carbon tetrachloride (0.2 mL) was added and the solution was heated for 30 min at 80° to decompose the remaining tributylstannane. Evaporation gave a residue that was chromatographed on a short column with 8:1 benzene–ethyl acetate to give a solid: yield 76 mg (73%), $[\alpha]_D^{25}$ +44° (*c* 0.5, chloroform); $^1$H-n.m.r. ($CDCl_3$): δ 2.47 (Ts), 3.28 ($OCH_3$), 4.27 (d, 1 H, H-1), and 4.98 (d, 1 H, *J* 10 Hz, NH).

*Anal.* Calc. for $C_{20}H_{29}NO_6S$: C, 58.37; H, 7.10; N, 3.40; S, 7.79. Found: C, 58.14; H, 7.01; N, 3.39; S, 7.76.

(*b*) *From* **14**. A solution of **14** (1.21 g) in dry 1,4-dioxane (24 mL) was treated as described for (*a*) except that mixtures of tributylstannane (2.4 mL) and α,α′-azobisisobutyronitrile (10 mg) were added at intervals of 0, 1.5, and 8 h after the reaction had started. The mixture was then treated as described for (*a*) to give **18**: yield 906 mg (81%).

*Methyl 4,6-O-cyclohexylidene-2,3-dideoxy-2-methoxycarbonylamino-α-*D*-ribo-hexopyranoside* (**19**). — Compound **18** (116 mg), dissolved in acetone, was charged onto a column of Sephadex LH-20 (15 mL) that was then developed with acetone. The eluate was evaporated and the residue dried well at room temperature *in vacuo*. This further purification of the analytically pure **18** made the yields of the following radical reaction reproducible. The solid was dissolved in liquid ammonia (~30 mL) at −60° (a Haake constant-temperature circulator KS60W was used), sodium metal (~200 mg) was added with stirring, and the temperature was gradually raised to −50°, and then maintained at this temperature for 1 h. Methanol was added until the blue color disappeared, and the solution was gradually warmed (finally *in vacuo*) to evaporate off the ammonia. An aqueous solution of the residue was charged on a column of Dowex 50W X8 ($NH_4^+$ form, 200–400 mesh, 26 mL) and, after washing the column with water, the product was eluted with M aqueous ammonia. The ninhydrin-positive fractions were evaporated to give a syrup of the desulfonylated product; yield 69 mg (94%). To a solution of the syrup in aqueous 1,4-dioxane (6:5, 2 mL), anhydrous sodium carbonate (28 mg) and methyl chloroformate (26 mg) were added, and the solution was kept overnight at room temperature. Conventional processing gave a solid: yield 75 mg (85%). Recrystallization from hexane gave crystals, m.p. 118–119°. On admixture with an authentic sample prepared by different route, the crystals showed no depression of the m.p. (118–119°).

*Methyl 2-amino-2,3-dideoxy-α-*D*-ribo-hexopyranoside* (**20**). — (*a*) *From* **14**. Compound **14** (204 mg) was pretreated with Sephadex LH-20 (24 mL) as described for **19** and the solid (203 mg) obtained was treated similarly with sodium (~400 mg) in liquid ammonia (~60 mL). An aqueous solution of the residue obtained after evaporation of the ammonia was mixed with Dowex 50W X2 resin ($H^+$) (200–400 mesh, ~20 mL), and the mixture was kept overnight at room temperature,

and then poured onto a column containing the same resin (~6 mL). After washing the column with water, elution with M aqueous ammonia gave a syrup. Column chromatography with CM-Sephadex C-25 ($NH_4^+$ form) with 0→0.1M aqueous ammonia gave **20** as a syrup: yield 71 mg that was made neutral with aqueous hydrochloric acid. The solution was then concentrated. Addition of acetone to the concentrate gave a thick syrup that solidified on treatment with acetone. The solid was dried *in vacuo* at 50° to constant weight: yield 43 mg (74%). $[\alpha]_D^{25}$ +130° (*c* 1, water).

*Anal.* Calc. for $C_7H_{15}NO_4 \cdot HCl$: C, 39.35; H, 7.55; Cl, 16.59; N, 6.56. Found: C, 39.12; H, 7.34; Cl, 16.42; N, 6.32.

(*b*) *From* **18**. Compound **18** (103 mg) was treated as described for (*a*) to give **20** · hydrochloride, 22 mg (73%). $[\alpha]_D^{25}$ +127° (*c* 0.4, water).

Found: C, 39.04; H, 7.33; Cl, 16.40; N, 6.26.

*Methyl 4,6-O-cyclohexylidene-2,3-dideoxy-3-*p*-toluenesulfonamido-α-*D*-ribo-hexopyranoside* (**21**). — (*a*) *From* **5**. To a solution of **5** (50.4 mg) in dry oxolane (1 mL, distilled from lithium aluminum hydride), was added lithium aluminum hydride (~20 mg) and the mixture was heated for 1 h at 60°. Water (1 mL) was added and the mixture was extracted with chloroform. The organic solution was washed with water, dried, and evaporated to a solid: yield 31 mg (86%), $[\alpha]_D^{25}$ +101° (*c* 1, chloroform); $^1$H-n.m.r. ($CDCl_3$): δ 2.43 (s, 3 H, Ts), 3.40 (s, 3 H, $OCH_3$), 4.73 (narrow m, 1 H, H-1), and 5.78 (d, 1 H, NH; disappeared on deuteration).

*Anal.* Calc. for $C_{20}H_{29}NO_6S$: C, 58.37; H, 7.10; N, 3.40; S, 7.79. Found: C, 58.56; H, 7.15; N, 3.28; S, 7.54.

(*b*) *From* **17**. A mixture of **17** (9.9 mg) and lithium aluminum hydride (~5 mg) in oxolane (0.2 mL) was treated as just described to give **21** as a solid: yield 8.6 mg (86%).

*3,4,6-Tri-O-acetyl-2-deoxy-2-*p*-toluenesulfonamido-α-*D*-glucopyranosyl bromide* (**22**). — A mixture of 2-amino-2-deoxy-D-glucose hydrochloride (3.01 g), *p*-toluenesulfonyl chloride (2.98 g), and anhydrous sodium carbonate (1.74 g) in aqueous 1,4-dioxane (1:1, 60 mL) was stirred vigorously for 1 h at room temperature. Evaporation gave a residue that was washed with chloroform. The residue was extracted with acetone, and evaporation of the solution gave a solid (4.16 g, crude 2-deoxy-2-*p*-toluenesulfonamido-D-glucose). A solution of the solid in acetic anhydride (15.3 g) in pyridine (80 mL) was kept for 4 h at room temperature. Addition of water (14 mL) followed by evaporation gave a residue that was dissolved in chloroform. The solution was washed with water, dried, and evaporated as described for **4** to give a solid (1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-*p*-toluenesulfonamido-α-D-glucopyranose); yield 5.72 g; $^1$H-n.m.r. ($CDCl_3$): δ 6.00 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1). An ice-cold solution of the solid (5.72 g) in dichloromethane (85 mL), was saturated with hydrogen bromide and the solution was kept overnight at 0°. The resulting, brown solution was evaporated and the residue dissolved in chloroform. The solution was washed with 5% aqueous sodium hydrogencarbonate and water, dried, and concentrated to ~20 mL. Addition of ether (~20 mL) followed by seeding and refrigeration gave colorless needles; yield 4.94 g (68% based on the starting material),

m.p. 147–148° (melted and decomposed), $[\alpha]_D^{25}$ +129° (*c* 1, chloroform); lit.[10] $[\alpha]_D$ +133.5 ±0.5° (*c* 1, chloroform); $^1$H-m.n.r. ($CDCl_3$): δ 1.73, 2.03, and 2.11 (s, 3 H each, Ac), 2.45 (s, 3 H, Ts), 3.63 (double t, 1 H, *J* 3.5, ~9.5 Hz ×2, H-2), 4.0–4.4 (m, 3 H), 5.0–5.4 (m, 3 H), and 6.33 (d, 1 H, *J* 3.5 Hz).

*Anal.* Calc. for $C_{19}H_{24}BrNO_9S$: C, 43.69; H, 4.63; H, 2.68. Found: C, 43.83; H, 4.66; N, 2.59.

*Methyl 2-deoxy-2-*p*-toluenesulfonamido-β-*D*-glucopyranoside* (**23**). — To a suspension of **22** (4.09 g) in methanol (80 mL), was added pyridine (0.76 mL, ~1.2 mol equiv. for **22**), the mixture was stirred for 20 min at room temperature, and then the clear solution was kept for 17 h at room temperature. Evaporation gave a syrup that was dissolved in chloroform. The solution was washed, dried, and evaporated as described for **4** to give a solid; yield 3.80 g. T.l.c. (2:1 benzene–ethyl acetate) showed a single spot at $R_F$ 0.3 (compare **22**: $R_F$ 0.55). To a solution of the solid in methanol (60 mL), 0.5M methanolic sodium methoxide (3.5 mL) was added and the solution was kept for 2 h at room temperature, made neutral with Dowex 50W X8 ($H^+$ form), the resin filtered off, and the solution evaporated to give a solid; yield 2.61 g (96%), $[\alpha]_D^{25}$ −47° (*c* 1, methanol); lit.[10] −53.5 ±0.5° (*c* 1, methanol); $^1$H-n.m.r. (pyridine-$d_5$): δ 2.23 (Ts), 3.20 ($OCH_3$), and 4.62 (d, 1 H, *J* 7.5 Hz, H-1).

*Anal.* Calc. for $C_{14}H_{21}NO_7S$: C, 48.40; H, 6.09; N, 4.03; S, 9.23. Found: C, 48.21; H, 6.07; N, 3.88; S, 9.02.

*Methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-*p*-toluenesulfonamido-β-*D*-glucopyranoside* (**24**). — Compound **23** (1.14 g) was treated as described for **1** to give a solid; yield 1.31 g (93%), $[\alpha]_D^{25}$ −50° (*c* 1, chloroform).

*Anal.* Calc. for $C_{20}H_{29}NO_7S$: C, 56.19; H, 6.84; N, 3.28; S, 7.50. Found: C, 56.27; H, 6.81; N, 3.17; S, 7.27.

*Methyl 4,6-*O*-cyclohexylidene-2-deoxy-3-*O*-p-tolylsulfonyl-2-*p*-toluenesulfonamido-β-*D*-glucopyranoside* (**25**). — Compound **24** (1.31 g) was treated as described for **5** to give a solid; yield 1.19 g (67%), $[\alpha]_D^{25}$ −33° (*c* 1, chloroform); $^1$H-n.m.r. ($CDCl_3$): δ 2.42 and 2.47 (s, each 3 H, Ts), 2.92 ($OCH_3$), 4.25 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), and 4.82 (t, 1 H, *J* 9.5 Hz, H-3).

*Anal.* Calc. for $C_{27}H_{35}NO_9S_2$: C, 55.75; H, 6.06; N, 2.41; S, 11.02. Found: C, 55.87; H, 6.12; N, 2.22; S, 10.95.

*Methyl 3-chloro-4,6-*O*-cyclohexylidene-2,3-dideoxy-2-*p*-toluenesulfonamido-β-*D*-allopyranoside* (**26**). — A mixture of **25** (153 mg) and anhydrous lithium chloride (116 mg, 10 mol. equiv. for **25**) in DMF (3 mL) was heated for 1 h at 120°. T.l.c. (8:1 benzene–ethyl acetate) showed a major spot at $R_F$ 0.35 (**26**) and trace spots at 0.1 (**25**), 0.15, and 0.3. Isolation as described for **13** (method *a*) 8:1 benzene–ethyl acetate was used for chromatography) gave a solid; yield 87 mg (71%), $[\alpha]_D^{25}$ −58° (*c* 0.5, chloroform); $^1$H-n.m.r. ($CDCl_3$): δ 2.47 (Ts), 3.20 ($OCH_3$), 4.47 (d, 1 H, H-1), 4.55 (narrow m, 1 H, H-3), and 5.42 (d, 1 H, *J* 9 Hz, NH).

*Anal.* Calc. for $C_{20}H_{28}ClNO_6S$: C, 53.87; H, 6.33; N, 3.14. Found: C, 54.17; H, 6.30; N, 3.16.

*Methyl 4,6-*O*-cyclohexylidene-2-deoxy-2-*N*-methyl-3-*O*-p-tolylsulfonyl-2-p-tolu-*

*enesulfonamido-β-*D*-glucopyranoside* (**27**). — Compound **25** (102 mg) was treated with diazomethane (~13 mg) as described for **7** except that, for chromatography, 5:1 benzene–ethyl acetate was used; **27** was obtained as a solid: yield 88 mg (84%). $[\alpha]_D^{25}$ −16° (*c* 1, chloroform): $^1$H-n.m.r. ($CDCl_3$): δ 2.44 (s, 6 H, Ts), 2.87 (s, 3 H, $OCH_3$), 3.10 (s, 3 H, $NCH_3$), 4.38 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), and 4.90 (t, 1 H, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3).

*Anal.* Calc. for $C_{28}H_{37}NO_9S_2$: C, 56.45; H, 6.26; N, 2.35; S, 10.76. Found: C, 56.39; H, 6.22; N, 2.23; S, 10.58.

*Methyl 4,6-*O*-cyclohexylidene-2,3-dideoxy-3-iodo-2-*N*-methyl-2-*p*-toluenesulfonamido-β-*D*-gluco- and/or allopyranoside* (**28**). — A mixture of **27** (30.8 mg) and sodium iodide (300 mg) in DMF (0.6 mL) was heated for 32 h at 100°. T.l.c. (5:1 benzene–ethyl acetate) showed a major spot at $R_F$ 0.48 (**28**) and minor spots at 0.13, 0.24, 0.37 (**27**), 0.59 and 0.63. Isolation as described for **12** gave **28**: yield 11.3 mg (40%) and **27**; yield 4.6 mg (15%). Recrystallization from chloroform–ether gave **28** as needles; $[\alpha]_D^{25}$ −24° (*c* 0.33, chloroform): $^1$H-n.m.r. ($CDCl_3$): δ 2.47 (Ts), 2.83 ($OCH_3$), and 3.32 ($NCH_3$).

*Anal.* Calc. for $C_{21}H_{30}INO_6S$: C, 45.74; H, 5.48; N, 2.54. Found: C, 45.70; H, 5.47; N, 2.39.

## REFERENCES


1 T. Tsuchiya, *Jpn. J. Antibiot.*, 32 (Suppl.) (1979) S129–S135.
2 (*a*) S. Umezawa, *Adv. Carbohydr. Chem. Biochem.*, 30 (1974) 111–182; (*b*) H. Umezawa, *ibid.*, 30 (1974) 183–225.
3 For example, see A. C. Richardson, *Carbohydr. Res.*, 10 (1969) 395–402.
4 (*a*) R. E. Ireland, D. C. Muchmore, and U. Hengartner, *J. Am. Chem. Soc.*, 94 (1972) 5098–5100; (*b*) S. Oida, H. Saeki, Y. Ohashi, and E. Ohki, *Chem. Pharm. Bull.*, 23 (1975) 1547–1551; (*c*) D. H. R. Barton and S. W. McCombie, *J. Chem. Soc., Perkin Trans. 1* (1975) 1574–1585; (*d*) H. Deshayes, J. Pete, C. Portella, and D. Scholler, *J. Chem. Soc., Chem. Commun.*, (1975) 439–440; (*e*) R. H. Bell, D. Horton, D. M. Williams, and E. Winter-Mihaly, *Carbohydr. Res.*, 58 (1977) 109–124; (*f*) D. H. R. Barton and R. Subramanian, *J. Chem. Soc., Perkin Trans. 1* (1977) 1718–1723; (*g*) N. C. Billingham, R. A. Jackson, and F. Malek, *J. Chem. Soc., Chem. Commun.*, (1977) 344–345; (*h*) J. Pete, C. Portella, C. Monneret, J. Florent, and Q. Khuong-Huu, *Synthesis*, (1977) 774–776; (*i*) P. M. Collins and V. R. Z. Munasinghe, *J. Chem. Soc., Chem. Commun.*, (1977) 927–928.
5 (*a*) T. Tsuchiya, I. Watanabe, M. Yoshida, F. Nakamura, T. Usui, M. Kitamura, and S. Umezawa, *Tetrahedron Lett.*, (1978) 3365–3368; (*b*) T. Tsuchiya, F. Nakamina, and S. Umezawa, *Tetrahedron Lett.*, (1979) 2805–2808; (*c*) T. Kishi, T. Tsuchiya, and S. Umezawa, *Bull. Chem. Soc. Jpn.*, 52 (1979) 3015–3018.
6 (*a*) Y. Takagi, T. Miyake, T. Tsuchiya, S. Umezawa, and H. Umezawa, *J. Antibiot.*, 26 (1973) 403–406; (*b*) Y. Takagi, T. Miyake, T. Tsuchiya, S. Umezawa, and H. Umezawa, *Bull. Chem. Soc. Jpn.*, 49 (1976) 3649–3651.
7 T. H. Haskell, P. W. K. Woo, and D. R. Watson, *J. Org. Chem.*, 42 (1977) 1302–1305.
8 D. Ikeda, T. Tsuchiya, and S. Umezawa, *Bull. Chem. Soc. Jpn.*, 44 (1971) 2529–2537.
9 F. H. Bissett, M. E. Evans, and F. W. Parrish, *Carbohydr. Res.*, 5 (1967) 184–193.
10 F. Micheel and H. Wulff, *Chem. Ber.*, 89 (1956) 1521–1530.
11 F. Micheel and E. Michallis, *Chem. Ber.*, 91 (1958) 188–194.
12 Y. Ali, A. C. Richardson, C. F. Gibbs, and L. Hough, *Carbohydr. Res.*, 7 (1968) 255–271.
13 S. Umezawa, T. Tsuchiya, and H. Hineno, *Bull. Chem. Soc. Jpn.*, 43 (1970) 1212–1218.