Neighboring-Group Participation in Carbohydrate Chemistry. II.[1] Neighboring-Group Participation of the *N,N*-Diethylamido Group in a Nucleophilic Displacement of a 5-Tosylate[2]

M. MILJKOVIĆ,* D. MILJKOVIĆ, A. JOKIĆ, V. ANDREJEVIĆ, AND E. A. DAVIDSON

The Department of Biological Chemistry, The Milton S. Hershey Medical Center, Hershey, Pennsylvania 17033

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Tosylation of *N,N*-diethyl-1,2-*O*-isopropylidene-α-D-glucofuranuronamide (**6**) with *p*-toluenesulfonyl chloride in pyridine afforded *N,N*-diethyl-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (**7**), *N,N*-diethyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (**19**), and *N,N*-diethyl-1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (**8**). The ratio of monotosylation to ditosylation was 3:1. The predominant formation of the monotosyl derivatives **7** and **19** was explained by postulating the cyclic ortho ester derivatives **16** and **18** as intermediates. The reaction of **8** and **10** with Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin in refluxing acetic anhydride for 5 days afforded compounds **9** and **11**, respectively. These results clearly demonstrated that the nucleophilic displacement of the 5-*p*-tolylsulfonyl group by acetate in both **8** and **10** proceeded *via* the neighboring-group participation of the *N,N*-diethylamido group. The formation of the positively charged aziridinone intermediate **4** as a transition state was proposed.

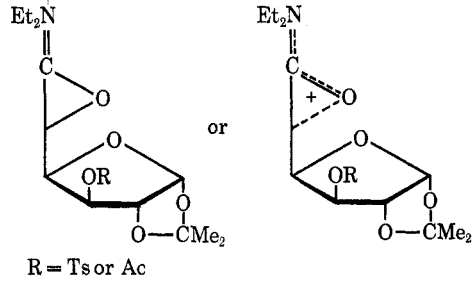
The neighboring-group participation of an acylamido function has been extensively studied,[3,4] and it has been reported that both the carbonyl oxygen and the nitrogen could participate in the reaction.[5] In the former case, a five-membered oxazoline ring (**2**), and, in the latter case, a three-membered aziridine ring (**3**) were formed. The ratio of oxazoline to aziridine formation was *ca.* 1:4,[5] indicating that the nitrogen participation of an acylamido group was considerably favored over that of the carbonyl oxygen. Regardless of which atom of the acylamido group participated, the nucleophilic displacement of an appropriate leaving group (mesylate or tosylate) always proceeded with inversion of configuration at the reacting asymmetric carbon atom. Furthermore, the participation of the acylamido nitrogen always led to the formation of the corresponding epimino sugars, since it was found that the aziridine ring was remarkably resistant toward nucleophilic ring opening. With the exception of azide anion,[6] nucleophiles like H^- and EtO^- had no effect on the aziridine ring in these sugars.[7] We wish to report the nucelophilic displacement of a 5-tosylate with acetate, where, due to the neighboring-group participation of the terminal *N,N*-diethylamido group *via* the aziridinone ionic intermediate **4**,[8] the reaction proceeded with retention of configuration at C-5. This represents, to the best of our knowledge, the first example of neighboring-group participation of an acylamido group where the leaving group (*p*-tolylsulfonyl group) is displaced with an external nucleophile (acetate), with retention of configuration at the involved asymmetric carbon atom (C-5). Direct displacement of the C-5 *p*-tolylsulfonyl group with acetate was not observed.

Results and Discussion

As a model compound for studying the neighboring-group participation of an acylamido group *via* a three-membered aziridinone intermediate, *N,N*-diethyl-1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (**8**) was synthesized.

Treatment of an ethereal solution of 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (**5**), with diethylamine afforded **6**. Tosylation of **6** with *p*-toluenesulfonyl chloride in pyridine gave three products. The ditosyl derivative, which on the basis of mass, nmr, and ir spectra was the expected *N,N*-diethyl-1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (**8**), was obtained in rather low yield (*ca.* 23%). The other two products (*ca.* 73%) were both monotosyl derivatives; thus the overall ratio of monotosylation to ditosylation was *ca.* 3:1.

This result could be possibly explained on the basis of previous findings[9] that the formylation of a hydroxyl group occurs when an alcohol is treated with *p*-toluenesulfonyl chloride in *N,N*-dimethylformamide. Thus, the predominant formation of monotosyl derivatives having a free hydroxyl group either at C-5 (**19**) or C-3 (**7**) could be rationalized assuming that the O-tosylation of the *N,N*-diethylamido group proceeded considerably faster than the tosylation of secondary hydroxyl groups,



R = Ts or Ac

(1) Part I: M. Miljković, A. Jokić, and E. A. Davidson, *Carbohyd. Res.*, **17**, 155 (1971).

(2) This work was supported by a grant (AM12074 from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, U. S. Public Health Service).

(3) L. Goodman, *Advan. Carbohyd. Chem.*, **23**, 127, 143, 151 (1967).

(4) B. Capon, *Quart. Rev. Chem. Soc.*, **18**, 71 (1964).

(5) T. Taguchi and M. Kojima, *J. Amer. Chem. Soc.*, **81**, 4316 (1959).

(6) R. D. Guthrie and D. Murphy, *J. Chem. Soc.*, 5288 (1963).

(7) D. H. Buss, L. Hough, and A. C. Richardson, *ibid.*, 5295 (1963).

(8) It should be noted that the formation of the positively charged aziridinone intermediate **4** is not the only possible explanation for the neighboring-group participation of the diethylamido group in the nucleophilic displacement by acetate in **8**. The neighboring-group participation of an amido group can generally proceed by either O or N attack at the carbon atom bearing a leaving group, and when rings of the same size are formed the O attack is generally favored with un-ionized amide groups, whereas N attack is favored with their conjugate bases.[4] Thus an equally valid explanation for the observed neighboring-group participation of the diethylamido group would involve the formation of the following imino α-lactone intermediate. By analogy with previous findings[4] this intermediate would be favored over **4** since the neighboring-group participation of the diethylamido group must proceed in its un-ionized form. The detailed elucidation of the mechanism of this reaction will be reported elsewhere.

(9) R. A. Edington, *J. Chem. Soc.*, 3499 (1964); J. D. Albright, E. Benz, A. E. Lanziloti, and L. Goldman, *Chem. Commun.*, 413 (1965); H. Schindlbauer, *Monatsh. Chem.*, **100**, 1590 (1969).

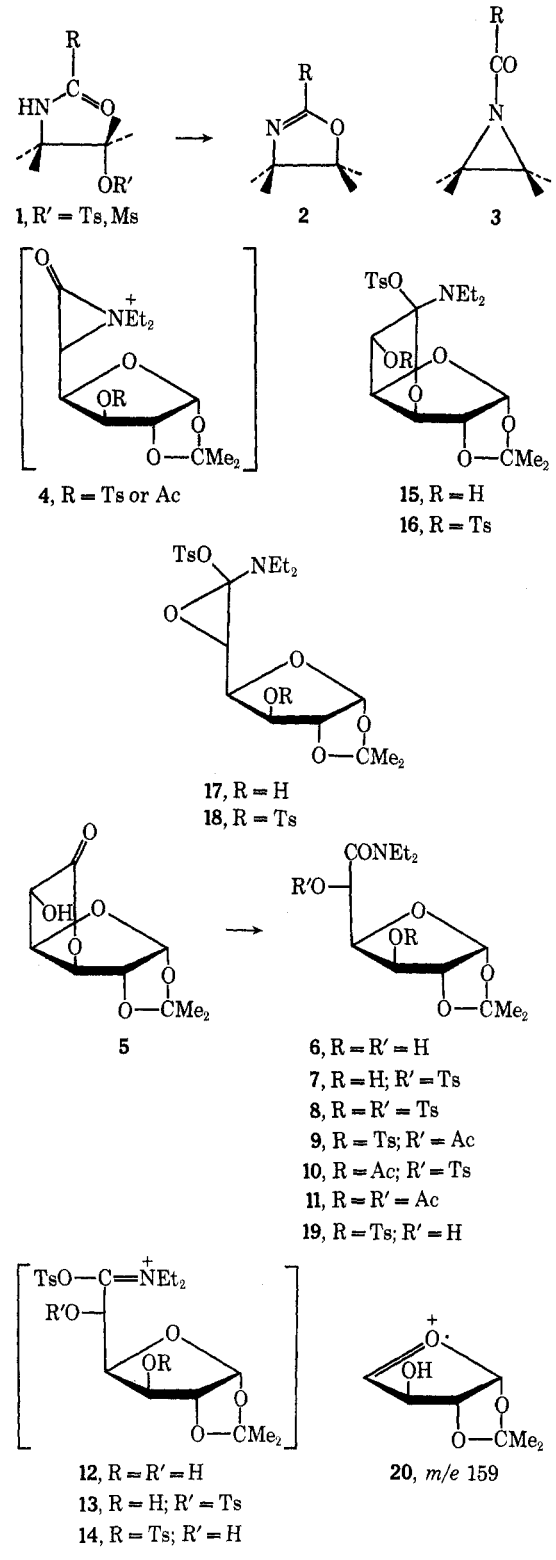
giving as possible intermediates **12**, **13**, and/or **14**. These intermediates could then react intramolecularly with either the C-3 or C-5 hydroxyl group to yield either the five-membered ring (**15** or **16**), or three-membered ring (**17** or **18**) cyclic ortho-ester derivatives; both **15** and **17** can undergo subsequent reaction with *p*-toluenesulfonyl chloride. These cyclic ortho-ester derivatives upon treatment with water would give rise to monotosyl derivatives having free hydroxyl groups either at C-5 (**19**) or C-3 (**7**).

A similar neighboring-group participation by the C-4 hydroxyl group in the benzoylation of D-gluconamide with benzoyl chloride in pyridine was recently reported by Deferrari, *et al.*[10]

The structure of the monotosyl derivatives was deduced from their nmr and mass spectra and subsequently confirmed chemically. In a comparable derivative where the hydroxyl group at C-5 is known to be free (compound **6**), the C-5 proton appears in the nmr spectrum as a doublet at δ 4.66 ($J_{4,5}$ = 9.0 Hz). As expected, acylation (tosylation or acetylation) shifts this resonance signal to lower field (δ 5.32 and 5.44 for **8** and **11**). The major monotosyl product and its acetylated derivative both show resonance signals for the C-5 proton at δ 5.54 and 5.50 ($J_{4,5}$ = 8.8 and $J_{4,5}$ = 9.0 Hz), suggesting that in this derivative the C-5 hydroxyl group is tosylated. This conclusion was supported by examining the mass spectra of this compound and its acetylated derivative, and comparing them with the mass spectra of **6** and its ditosyl derivative **8**. Both the monotosyl derivative and compound **6** showed the *m/e* 159 peak with almost equal intensities (4.0 and 3.5). This fragment is very probably the ionic species **20**, which is known to be present in the mass spectra of glycofuranosyl derivatives[11,12] due to the favored heterolytic scission of the C-4–C-5 bond. The mass spectra of the acetylated monotosyl derivative, as well as those of both compound **11** and the ditosyl derivative **8**, have little or no discernible peaks at *m/e* 159 (0.0, 0.2, and 0.15, respectively). It was therefore concluded that the correct structure for the major monotosyl derivative should be **7** rather than **19**. This conclusion was confirmed chemically by treatment of **10** with Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin in refluxing acetic anhydride to yield **11**.

It is interesting to note that the C-3 proton of **7** appears in the nmr spectrum as a doublet at δ 3.23 ($J_{3,4}$ = 2.4 Hz), whereas the C-3 hydroxyl hydrogen appears as a sharp singlet at δ 7.35. This is rather unexpected, because the C-3 hydrogen of **6** appears in the nmr spectrum at δ 4.41 ($J_{3,4}$ = 2.4 Hz) and the hydroxyl protons in the δ 4.0–5.0 region. The large downfield shift of the C-3 hydroxyl proton could be interpreted in terms of strong hydrogen bonding of the C-3 hydroxyl group with either the nitrogen or the carbonyl oxygen of the diethylamido group. Although the abnormal upfield shift of the C-3 proton of **7**, as compared to that of **6** (δ 4.41, $J_{3,4}$ = 2.4 Hz), is rather puzzling, strong hydrogen bonding between the C-3 hydroxyl and the diethylamido group could result in a striking conformational change, wherein the C-3 hydrogen atom is located above the aromatic ring of the *p*-tolylsulfonyl group. In this case, the strong shielding due to the induced field and proximity of the aromatic ring could result in the observed upfield shift (*ca.* 1.2 ppm) of the C-3 proton.

The structure of the second monotosyl derivative, which was isolated in extremely low yield (*ca.* 2.6%), was deduced from its nmr spectrum and subsequently proved chemically. The fact that the C-5 proton of this monotosyl derivative appears in the nmr spectrum as a doublet at δ 4.36 ($J_{4,5}$ = 9.0 Hz) and the C-3 proton at δ 4.89 (d, $J_{3,4}$ = 2.5 Hz) indicated the C-3 hydroxyl group is tosylated. Furthermore, when the C-5 hy-



(10) J. O. Deferrari, R. M. de Lederkremer, B. Matsuhiro, and M. I. Litter, *Carbohyd. Res.*, **14**, 103 (1970).

(11) K. Biemann, D. C. DeJongh, and H. K. Schnoes, *J. Amer. Chem. Soc.*, **85**, 1763 (1963).

(12) D. C. DeJongh and K. Biemann, *ibid.*, **86**, 67 (1964).

droxyl group is acylated, as is the case for compounds **8** or **11**, the C-5 proton appears in the nmr spectrum at δ 5.32 and 5.44, while the C-5 proton of **6** appears at δ 4.66. Finally, the acetylation of this monotosyl derivative gave a product (**9**) which was identical (ir and nmr spectra) with the product obtained by treating the ditosyl derivative **8** with Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin in refluxing acetic anhydride. Accordingly, the second monotosyl derivative must be *N,N*-diethyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (**19**). It seemed reasonable to assume that there are probably stereochemical reasons for the low yield of this monotosyl derivative **19**.

It is interesting to note that compounds having the C-5 hydroxyl group free are always levorotatory, whereas derivatives with an acylated (acetylated or tosylated) C-5 hydroxyl group are always dextrorotatory.

Refluxing of the ditosyl derivative **8** in acetic anhydride in the presence of Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin gave as a sole product a monoacetyl, monotosyl derivative, which according to its ir and nmr spectrum was different from the acetylated monotosyl derivative **10**, but was identical with the acetylated monotosyl derivative **19**. Reductive desulfonylation of **9** with sodium in naphthalene[13] gave the compound **6**. Therefore, the obtained product had to be 5-*O*-acetyl-*N,N*-diethyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (**9**). Treatment of **10** with Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin in refluxing acetic anhydride afforded the diacetate **11**.

These results clearly show that the nucleophilic displacement of the 5-*p*-tolylsulfonyl group with acetate, in **8** and **10**, proceeds exclusively *via* neighboring-group participation of the *N,N*-diethylamido group through an ionic intermediate such as **4**.[8]

Experimental Section

General.—The silica gel used for all column chromatography was E. Merck (Darmstadt, Germany) silica gel, grain size <0.08 mm. The melting points are uncorrected. Optical rotations were determined with a Cary 60 spectropolarimeter in a 1.0-cm cell. The ir spectra were recorded with a Perkin–Elmer infrared spectrophotometer Model 337, and nmr spectra with a Varian T-60 spectrometer with tetramethylsilane as the internal standard. Chemical shifts (δ) are expressed in parts per million. Mass spectra were recorded on an AEI MS902 mass spectrometer at 70 eV. Samples were introduced *via* the direct insertion probe. The temperature of the ion source is given on each spectrum.

***N,N*-Diethyl-1,2-*O*-isopropylidene-α-D-glucofuranuronamide (6).**—To an ethereal solution (60 ml) of 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (5.0 g, 21 mmol), dry diethylamine (20 ml) was added. The reaction mixture was kept for 65 hr at 0°, after which the solvent and excess diethylamine was removed *in vacuo;* the resulting residue was chromatographed on silica gel (55 g). Elution with 10:1 ethyl acetate–methanol gave 3.7 g of **6** (55%): mp 156–157°; $[\alpha]^{27}D$ −32° (*c* 1, $CHCl_3$); ir ($CHCl_3$) 3580 and 3400 (hydrogen-bonded OH) and 1630 cm^{-1} (amide C=O); nmr ($CDCl_3$ + D_2O) δ 5.96 (d, $J_{1,2}$ = 3.5 Hz, 1, H-1), 4.66 (d, $J_{4,5}$ = 9.0 Hz, 1, H-5), 4.53 (d, $J_{1,2}$ = 3.5 Hz, 1, H-2), 4.41 (d, $J_{3,4}$ = 2.4 Hz, 1, H-3), 4.05 (m, $J_{3,4}$ = 2.4 and $J_{4,5}$ = 9.0 Hz, 1, H-4), 3.9–3.0 (m, 4, methylene H from Et), 1.47 and 1.30 (two s, 6, Me of Ip), 1.18 and 1.16 (two m, 6, Me of Et); mass spectrum (120°) *m/e* (rel intensity) 289 (0.8), 274 (7.5), 271 (3.5), 242 (6), 225 (4), 210 (3), 201 (0.7), 196 (1), 189 (4), 184 (2), 172 (3), 160 (3), 159 (3.5), 143 (3.5), 142 (16), 131 (27), 130 (25), 113 (7), 101 (9), 100 (100), 74 (12), 72 (33), 71 (17).

Anal. Calcd for $C_{13}H_{23}NO_6$: C, 53.97; H, 8.01; N, 4.84. Found: C, 54.17; H, 8.01; N, 4.72.

***N,N*-Diethyl-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (7), *N,N*-Diethyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (19), and *N,N*-Diethyl-1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (8).**—A pyridine solution (40 ml) containing *N,N*-diethyl-1,2-*O*-isopropylidene-α-D-glucofuranuronamide (**6**) (2.00 g, 7 mmol) and *p*-toluenesulfonyl chloride (5.32 g, 27 mmol) was kept for 32 hr at room temperature. The reaction mixture was then cooled to 0° and ethanol was added to destroy the excess of *p*-toluenesulfonyl chloride. The solvent was removed *in vacuo*, and the residue was dissolved in 1:1 ether–ethyl acetate. After removal of insoluble material by filtration, the filtrate was evaporated *in vacuo*, and the residue (oil, 4.80 g) was chromatographed on silica gel (120 g). Elution with 95:5 benzene–2-propanol afforded compound **8** (950 mg, 23%), the monotosyl derivative **19** (82 mg, 2.6%), and compound **7** (2.160 g, 70.5%). Compound **8** was an oil: $[\alpha]^{27}D$ +10° (*c* 1, $CHCl_3$); ir ($CHCl_3$) 1670 (amide C=O), 1610 (aromatic C=C), 1188 and 1176 cm^{-1} (Ts, sym SO_2 stretch); nmr ($CDCl_3$) δ 8.01–7.16 (m, 8, Ts), 5.78 (d, $J_{1,2}$ = 3.8 Hz, 1, H-1), 5.32 (d, $J_{4,5}$ = 8.7 Hz, 1, H-5), 4.96 (d, $J_{3,4}$ = 2.7 Hz, 1, H-3), 4.90 (d, $J_{1,2}$ = 3.8 Hz, 1, H-2), 4.50 (m, $J_{3,4}$ = 2.7 and $J_{4,5}$ = 8.7 Hz, 1, H-4), 3.5–3.0 (m, 4, methylene from Et), 2.80 and 2.60 (two s, 6, Me of Ts), 1.40 and 1.27 (two s, 6, Me of Ip), and 1.13 and 0.90 (two t, 6, Me of Et); mass spectrum (165°) *m/e* (rel intensity) 597 (1.1), 582 (15), 579 (0.01), 538 (0.75), 497 (0.5), 442 (18), 427 (6.5), 426 (28), 425 (16), 396 (15), 384 (15), 368 (9.5), 355 (3), 327 (3.2), 313 (2), 310 (1.5), 297 (0.7), 287 (0.6), 284 (2), 270 (15), 256 (3), 255 (5.5), 254 (40), 253 (9.5), 242 (3.5), 238 (10), 225 (6), 212 (21), 201 (2), 200 (22), 196 (9), 185 (0.8), 173 (15), 159 (0.15), 157 (8.5), 156 (14), 155 (83), 142 (9), 139 (9.5), 130 (14), 129 (10), 113 (7.5), 108 (7.5), 107 (10.5), 101 (34), 100 (100), 92 (35), 91 (90), 78 (50), 77 (8), 72 (83).

Anal. Calcd for $C_{27}H_{35}NO_{10}S_2$: C, 54.25; H, 5.90; N, 2.34; S, 10.07. Found: C, 54.42; H, 5.85; N, 2.17; S, 10.22.

Compound **7** (2.160 g, 70.5%) was crystalline: mp 113–114°; $[\alpha]^{27}D$ +14.0° (*c* 1, $CHCl_3$); ir ($CHCl_3$) 3610 and 3530 (hydrogen bonded OH), 1675 (amide C=O), 1610 (aromatic C=C), 1192 and 1175 cm^{-1} (Ts, sym SO_2 stretch); nmr ($CDCl_3$) δ 7.9–7.2 (m, 4, Ts), 7.35 (s, 1, OH), 5.90 (d, $J_{1,2}$ = 3.6 Hz, 1, H-1), 5.54 (d, $J_{4,5}$ = 8.8 Hz, 1, H-5), 4.55 (d, $J_{1,2}$ = 3.6 Hz, 1, H-2), 4.47 (m, $J_{3,4}$ = 2.4 and $J_{4,5}$ = 8.8 Hz, 1, H-4), 3.6–3.1 (m, 4, methylene from Et), 3.23 (d, $J_{3,4}$ = 2.4 Hz, 1, H-3), 2.45 (s, 3, methyl from Ts), 1.47 and 1.30 (two s, 6, methyl H from Ip), 1.17 and 1.02 (two t, 6, methyl H from Et); mass spectrum (165°) *m/e* (rel intensity) 445 (0.65, 444 (1.8), 443 (3), 430 (1.5), 429 (4.5), 428 (23), 425 (0.15), 386 (0.32), 384 (0.77), 370 (0.55), 368 (1.5), 357 (0.2), 355 (1.1), 343 (0.5), 340 (0.3), 314 (4.5), 297 (0.15), 288 (8.5), 285 (1), 273 (6), 272 (45), 271 (58), 243 (9), 238 (13), 230 (11), 214 (7.7), 210 (8), 196 (5), 185 (2.5), 184 (5), 173 (5.5), 159 (4), 156 (7.3), 155 (42), 144 (23), 143 (25), 142 (57), 139 (4.5), 130 (40), 129 (26), 126 (9), 113 (5.5), 101 (35), 100 (100), 92 (12), 91 (70), 74 (14), 73 (14), 72 (88), 71 (25).

Anal. Calcd for $C_{20}H_{29}NO_8S$: C, 54.16; H, 6.59; N, 3.16; S, 7.23. Found: C, 54.27; H, 6.58; N, 3.04; S, 7.14.

Monotosyl derivative **19** (82 mg, 2.6%) was an oil: $[\alpha]^{27}D$ −33° (*c* 1, $CHCl_3$); ir ($CHCl_3$) 3430 (hydrogen bonded OH), 1645 (amide C=O), 1605 (aromatic C=C), 1190 and 1178 cm^{-1} (sym SO_2 stretch, Ts); nmr ($CDCl_3$) δ 7.9–7.2 (m, 4, Ts), 5.86 (d, $J_{1,2}$ = 3.6 Hz, 1, H-1), 4.89 (d, $J_{3,4}$ = 2.5 Hz, 1, H-3), 4.80 (d, $J_{1,2}$ = 3.6 Hz, 1, H-2), 4.36 (d, $J_{4,5}$ = 9.0 Hz, 1, H-5), 4.00 (m, $J_{3,4}$ = 2.5 and $J_{4,5}$ = 9.0 Hz, 1, H-4), 3.7–2.9 (m, 4, methylene from Et), 2.43 (s, 1, Me from Ts), 1.42 and 1.28 (two s, 6, Me from Ip), 1.12 (m, 6, Me from Et).

5-*O*-Acetyl-*N,N*-diethyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (9).—The ditosyl derivative **8** (500 mg, 0.84 mmol) was dissolved in acetic anhydride (15 ml) and the solution was heated under reflux in the presence of Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin (3.2 g) for 5 days. An additional amount (1.5 g) of Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin was added every 24 hr, bringing the total amount of resin to 9.2 g. The reaction mixture was then cooled to room temperature, the resin was filtered off, and the precipitate was washed with a small amount of chloro-

(13) W. D. Closson, P. Wriede, and S. Bank, *J. Amer. Chem. Soc.*, **88**, 1581 (1966).

form. The filtrate was cooled to 0°, and an excess of methanol was added, after which the solvents were evaporated *in vacuo*. The oily residue was chromatographed on silica gel (12 g). Elution with 2:1 benzene–ether afforded 335 mg (84%) of pure **9**: oil; $[\alpha]^{27}D$ 0° (*c* 1, $CHCl_3$); ir ($CHCl_3$) 1750 (acetate C=O), 1660 (amide C=O), 1600 (aromatic C=C), 1240 (acetate CO), 1191 and 1178 cm^{-1} (sym SO_2 stretch, Ts); nmr ($CDCl_3$) δ 7.9–7.2 (m, 4, Ts), 5.90 (d, $J_{1,2}$ = 3.8 Hz, 1, H-1), 5.23 (d, $J_{4,5}$ = 9.0 Hz, 1, H-5), 5.03 (d, $J_{3,4}$ = 2.6 Hz, 1, H-3), 4.70 (d, $J_{1,2}$ = 3.8 Hz, 1, H-2), 4.60 (m, $J_{3,4}$ = 2.6 and $J_{4,5}$ = 9.0 Hz, 1, H-4), 3.7–3.2 (m, 4, methylene from Et), 2.47 (s, 3, Me from Ts), 1.88 (s, 3, Me from Ac), 1.47 and 1.28 (two s, 6, Me from Ip), 1.21 and 1.10 (two t, *J* = 8.0 and 6.0 Hz, 6, Me from Et).

Anal. Calcd for $C_{22}H_{31}NO_9S$: C, 54.42; H, 6.44; N, 2.89; S, 6.60. Found: C, 54.52; H, 6.35; N, 2.79; S, 6.38.

3-*O*-Acetyl-*N*,*N*-diethyl-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (10).—The monotosyl derivative **7** (1.20 g, 2.7 mmol) was dissolved in acetic anhydride (15 ml), and dry potassium acetate (220 mg) was added. The reaction mixture was kept for 22 hr at room temperature, the potassium acetate was filtered off, and the filtrate was evaporated *in vacuo*. The resulting precipitate was dissolved in ethyl acetate, insoluble material was filtered off, and the filtrate was concentrated *in vacuo*. The crude product (oil, 1.110 g) was chromatographed on silica gel. Elution with 2:1 benzene–acetone afforded a crystalline product (900 mg, 68%), which after recrystallization from ether–hexane gave pure **10** (740 mg, 56%): mp 71–72°; $[\alpha]^{27}D$ +16.0 (*c* 1, $CHCl_3$); ir ($CHCl_3$) 1760 (acetate C=O), 1665 (amide C=O), 1605 (aromatic C=C), 1235 (acetate CO), 1192 and 1180 cm^{-1} (sym SO_2 stretch, Ts); nmr ($CDCl_3$) δ 7.9–7.2 (m, 4, Ts), 5.90 (d, $J_{1,2}$ = 3.6 Hz, 1, H-1), 5.50 (d, $J_{4,5}$ = 9.0 Hz, 1, H-5), 5.36 (d, $J_{3,4}$ = 3.0 Hz, 1, H-3), 4.65 (m, $J_{3,4}$ = 3.0 and $J_{4,5}$ = 9.0 Hz, 1, H-4), 4.53 (d, $J_{1,2}$ = 3.6 Hz, 1, H-2), 3.7–3.0 (m, 4, methylene from Et), 2.42 (s, 3, Me from Ts), 2.15 (s, 3, Me from Ac), 1.47 and 1.27 (two s, 6, Me from Ip), 1.27 and 1.17 (two t, 6, Me from Et); mass spectrum (175°) *m/e* (rel intensity) 485 (0.2), 470 (6.5), 467 (0.025), 428 (0.3), 426 (0.2), 412 (1.1), 396 (1.7), 368 (3.0), 330 (3.5), 315 (3), 314 (21), 313 (8), 298 (0.5), 285 (1.5), 254 (7.5), 238 (4), 201 (1), 196 (4.5), 185 (0.5), 172 (1.5), 159 (0), 155 (20), 143 (5), 142 (4), 130 (8), 113 (2), 101 (15), 100 (100), 91 (27), 72 (33).

Anal. Calcd for $C_{22}H_{31}NO_9S$: C, 54.42; H, 6.44; N, 2.89, S, 6.60. Found: C, 54.45; H, 6.55; N, 2.87; S, 6.80.

3,5-Di-*O*-acetyl-*N*,*N*-diethyl-1,2-*O*-isopropylidene-α-D-glucofuranuronamide (11).—To a pyridine solution (5 ml) containing *N*,*N*-diethyl-1,2-*O*-isopropylidene-α-D-glucofuranuronamide (**6**) (220 mg, 0.76 mmol), acetic anhydride (2 ml) was added and the reaction mixture was kept for 24 hr at room temperature. The pyridine and excess acetic anhydride were removed *in vacuo*, and the residue (300 mg) was chromatographed on silica gel (10 g). Elution with 95:5 benzene–2-propanol afforded pure **11** (238 mg, 83%): mp 84–85°; $[\alpha]^{27}D$ +27.6° (*c* 1, $CHCl_3$); ir ($CHCl_3$) 1755 (acetate C=O), 1660 (amide C=O), 1240 cm^{-1} (acetate C—O); nmr ($CDCl_3$) δ 5.91 (d, $J_{1,2}$ = 3.8 Hz, 1, H-1), 5.44 (d, $J_{4,5}$ = 9.2 Hz, 1, H-5), 5.41 (d, $J_{3,4}$ = 3.2 Hz, 1, H-3), 4.66 (m, $J_{3,4}$ = 3.2 and $J_{4,5}$ = 9.2 Hz, 1, H-4), 4.50 (d, $J_{1,2}$ = 3.8 Hz, 1, H-2), 3.8–3.2 (m, 4, methylene from Et), 2.05 (s, 6, Me from Ac), 1.52 and 1.30 (two s, 6, Me from Ip), 1.28 and 1.17 (two t, 6, Me from Et); mass spectrum (170°) *m/e* (rel intensity) 373 (1), 359 (1.2), 358 (6), 355 (0), 330 (0.4), 328 (0.55), 314 (2.5), 313 (3), 298 (0.4), 285 (1.7), 256 (3.5), 254 (2.5), 238 (2), 226 (1), 210 (2.5), 201 (0.6), 196 (3), 185 (0.5), 173 (1.5), 172 (1), 159 (0.2), 155 (4.5), 143 (2), 142 (3), 130 (2.7), 120 (6), 118 (6.5), 113 (2.5), 101 (6.5), 100 (100), 72 (27).

Anal. Calcd for $C_{17}H_{27}NO_8$: C, 54.68; H, 7.29; N, 3.75. Found: C, 54.69; H, 7.21; N, 3.68.

Reaction of 3-*O*-Acetyl-*N*,*N*-diethyl-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (10) with Dowex 1 (X-10, 200–400 mesh, AcO^-) Ion-Exchange Resin in Refluxing Acetic Anhydride.—A solution of compound **10** (200 mg, 0.41 mmol) in acetic anhydride (10 ml) was refluxed in the presence of Dowex 1 (X-10, 200–400 mesh, AcO^-) ion-exchange resin (1.4 g). An additional amount of resin (1.4 g) was added every 24 hr for a 5-day period. The resin was filtered off, the filtrate was evaporated to dryness, and the residue was chromatographed on silica gel. Elution with 95:5 benzene–2-propanol afforded a pure product (114 mg, 85%) which was identical in every respect with compound **11** (mixture melting point, ir spectra).

Acetylation of *N*,*N*-Diethyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuranuronamide (19).—Compound **19** (48 mg) was dissolved in anhydrous pyridine (1.0 ml), and acetic anhydride was added (1.0 ml). After the reaction mixture was kept at room temperature for 6 hr, the pyridine and acetic anhydride were removed *in vacuo*, and the residue (63 mg) was chromatographed on silica gel. Elution with 95:5 benzene–2-propanol afforded pure **9** (42 mg, 79%).

Reductive Desulfonylation of 9 with Sodium and Naphthalene.—To a solution of naphthalene (774 mg, 6 mmol) in absolute tetrahydrofuran (3 ml), small pieces of sodium (132 mg, 5.7 g-atoms) were added. The solution became deep green in color, and, after all sodium was dissolved, **9** (56 mg) in tetrahydrofuran was added. After 5 min, methanol was added until the green color disappeared and the solution was evaporated *in vacuo*. The residue was dissolved in chloroform; carbon dioxide was bubbled through the solution for 5 min, and the precipitate was removed by filtration. The filtrate was evaporated *in vacuo*, and the residue was chromatographed on silica gel. Elution with 95:5 benzene–2-propanol afforded compound **6** (6 mg, 18%).

Registry No.—**6**, 31120-02-2; **7**, 31143-04-1; **8**, 31081-99-9; **9**, 30694-39-4; **10**, 31129-29-0; **11**, 31129-30-3; **19**, 31129-31-4.

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