amide, 7010-86-8; *N*-methyl-*p*-bromobenzenesulfonamide, 703-12-8; methyl α-bromophenylacetate, 3042-81-7; *N*-methyl-*N*-(α-carbomethoxybenzyl)-*p*-bromobenzenesulfonamide, 52260-15-8; 2-acetamidopropyl acetate, 52260-16-9; *N*-ethyl-*N*-β-hydroxyisopropylamine, 24417-04-7; *p*-toluenesulfonyl chloride, 98-59-9; methyl 2-*p*-toluenesulfonyl-2-phenylacetate, 33829-52-6; *N*-isopropyl-*p*-toluenesulfonamide, 21230-07-9.

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Steric and Electrostatic Interactions in Reactions of Carbohydrates. III.[1] Direct Displacement of the C-2 Sulfonate of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-gluco- and -mannopyranosides[2]

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Heating of an *N,N*-dimethylformamide solution of methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-glucopyranoside (**2**) and methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methysulfonyl-β-D-mannopyranoside (**4**) with potassium benzoate resulted in direct displacement of the C-2 sulfonyloxy group giving the corresponding D-manno- (**14**, 62%) and D-gluco (**13**, 70%) derivatives. Methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (**1**) gave, under the same experimental conditions, only very small amount (~3%) of a product which could be the product of direct displacement (**15**), whereas methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-mannopyranoside (**3**) did not undergo direct displacement at all. The greater reactivity of **4** *vs.* **2** and the unreactivity of **1** and **3** toward the direct nucleophilic displacement was rationalized in terms of torsional strain and electrostatic and steric nonbonding interactions in the corresponding transition states.

In connection with some other work we became interested in direct displacement of the C-2 sulfonyloxy group of pyranosides. Our previous findings that the stereochemical course of the addition of CH_3Li, CH_3MgX, and $NaBH_4$ to the C-2 and C-4 carbonyl carbon atom strongly depended upon the anomeric configuration of the corresponding hexopyranosiduloses[1,3] suggesting that the torsional strain and nonbonding steric and electrostatic interactions in the corresponding transition states are the decisive factors in determining the stereochemical course of these reactions, prompted us to investigate the possible relationship between the anomeric configuration and the reactivity of a C-2 sulfonyloxy group of hexopyranosides toward direct displacement.

Except for displacement of the *p*-tolylsulfonyl group of methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranoside with azide,[4] direct displacement of a C-2 sulfonyloxy group of a furanoside or a pyranoside ring with a charged nucleophile has not been yet reported. The use of an uncharged nucleophile, *e.g.*, hydrazine, did result in displacement of the C-2 sulfonate in both furanoside[5-7] and pyranoside[8] rings. The unreactivity of the C-2 sulfonyloxy group toward displacement with charged nucleophiles was attributed to the electron-withdrawing effect of the anomeric carbon atom and to the unfavorable dipolar interaction in the transition state.[9-13] The greater reactivity of uncharged nucleophiles is displacement of the sulfonyloxy group at the C-2 carbon atom was ascribed to the reversal of polarity of one of the polar bonds in the transition state resulting in a dipolar attractive force.[11] Although some speculations on the reactivity of a C-2 sulfonyloxy group of β-D-glycopyranosides having the C-1 aglycon group equatorially oriented have been entertained,[11] direct displacement of the C-2 sulfonate of a β-D-glycopyranoside was not thus far attempted.

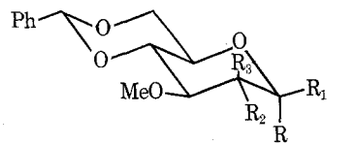
The following substrates were chosen for our study: methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (**1**),[3] methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-glucopyranoside (**2**), methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-mannopyranoside (**3**), and methyl 4,6-*O*-benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-mannopyranoside (**4**).

It is known[14,15] that the reactivity of a sulfonyloxy group directly attached to a six-membered ring (cyclohexane or glycopyranoside) toward direct displacement with a nucleophile will generally depend upon (a) gound-state energy (conformational free-energy) of the substrate and (b) energy of the corresponding transition state.

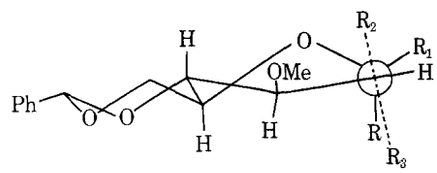
Whereas the ground state energy of α- and β-D-glucopyranosides **1** and **2** and α-D-mannopyranoside **3** should not be significantly different, the conformational free-energy of β-D-mannopyranoside **4**, should be considerably higher due to the unfavorable dipolar interaction between the axially oriented C-2 methylsulfonyloxy group and the C_1–O_1 and the C_1–O_5 dipoles. Consequently, the activation energy for direct displacement of the C-2 sulfonyloxy group of β-D-mannopyranoside **4** should be lower than for displacement of the C-2 sulfonyloxy group of α- and β-D-glucopyranosides **1** and **2**, and α-D-mannopyranoside **3**.

However, as has been already stated, the reactivity of a sulfonyloxy group toward direct displacement does not depend solely upon the ground state energy of a substrate, but also upon the transition state energy level, *i.e.*, torsional strain, nonbonded steric and electrostatic interactions between the approaching nucleophile and/or leaving sulfonate and other substituents of a six-membered pyranoside ring.

Thus, the "axial" attack of a charged nucleophile to the C-2 atom of **1** (α-D-glucopyranoside) resulting in transition



1, R = CH_3O; R_1 = R_3 = H; R_2 = CH_3SO_3
2, R = R_3 = H; R_1 = CH_3O; R_2 = CH_3SO_3
3, R = CH_3O; R_1 = R_2 = H; R_3 = CH_3SO_3
4, R = R_2 = H; R_1 = CH_3O; R_3 = CH_3SO_3
9, R = CH_3O; R_1 = R_3 = H; R_2 = OH
10, R = R_3 = H; R_1 = CH_3O; R_2 = OH
11, R = CH_3O; R_1 = R_2 = H; R_3 = OH
12, R = R_2 = H; R_1 = CH_3O; R_3 = OH
13, R = R_3 = H; R_1 = CH_3O; R_2 = C_6H_5COO
14, R = R_2 = H; R_1 = CH_3O; R_3 = C_6H_5COO
15, R = CH_3O; R_1 = R_2 = H; R_3 = C_6H_5COO
16, R = CH_3O; R_1 = R_3 = H; R_2 = C_6H_5COO



5, R = CH_3O; R_1 = H; R_2 = nucleophile; R_3 = CH_3SO_3
6, R = H; R_1 = CH_3O; R_2 = nucleophile; R_3 = CH_3SO_3
7, R = CH_3O; R_1 = H; R_2 = CH_3SO_3; R_3 = nucleophile
8, R = H; R_1 = CH_3O; R_2 = CH_3SO_3; R_3 = nucleophile

state **5**, will give rise, owing to the flattening of the pyranoside ring, to a strong torsional strain and electrostatic interaction between the leaving C-2 methylsulfonyloxy and the axially oriented C-1 methoxy group. The "axial" attack of a charged nucleophile to the C-2 atom of **2** (β-D-glucopyranoside) resulting in transition state **6**, where the negatively charged nucleophile approaches the C-2 atom from a direction bisecting C_1–O_1 and C_1–O_5 torsional angle, will be subjected to dipolar interactions between the approaching nucleophile and the C_1–O_1 and the C_1–O_5 dipoles. The "equatorial" attack of a charged nucleophile to the C-2 atom of **3** (α-D-mannopyranoside) resulting in transition state **7** will give rise, due to the flattening of the pyranoside ring, to a strong torsional strain and electrostatic interaction between the approaching nucleophile and the axially oriented C-1 methoxy group. Finally, the "equatorial" attack of a charged nucleophile to the C-2 atom of **4** (β-D-mannoyranoside) resulting in transition state **8**, will be free both from torsional strain and dipolar interactions. In addition to the above mentioned interactions, the formation of transition states **5**, **6**, **7** and **8** will also give rise to much weaker nonbonded steric interactions between the approaching nucleophile and the axially oriented hydrogen atoms. Thus, in transition states **5** and **6** there will be in each one 1,3-nonbonded steric interaction between the nucleophile and the C-4 hydrogen atom, whereas in transition states **7** and **8**, there will be in each one 1,4-nonbonded steric interaction between the nucleophile and the C-5 hydrogen atom.

The already mentioned dipolar interactions between the axially oriented C-2 methylsulfonyloxy group and the C_1–O_1 and the C_1–O_5 dipoles in **4** should facilitate the formation of the transition state **8** due to electrostatic and steric relief.

The uncharged nucleophiles (*e.g.*, hydrazine) should be more effective for direct displacement of the C-2 sulfonyloxy group of **2** since there will be no electrostatic repulsion between the approaching neutral nucleophile and the C_1–O_1 and the C_1–O_5 dipoles in transition state **6**. However, there should be little or no difference in reactivity of charged and uncharged nucleophiles in direct displacement of the C-2 sulfonyloxy group of **1**, **3**, and possibly **4**.

Taking into consideration the ground-state energy levels of **1**, **2**, **3** and **4** and the energy levels of SN2 transition states **5**, **6**, **7** and **8**, the following order of reactivity of the C-2 sulfonyloxy group toward direct displacement with a (charged or uncharged) nucleophile could be expected: 3 > 2 ≫ **1** and **4**.

The results of our investigation are reported in this paper.

The C-2 sulfonates **1**–**4** were synthesized by mesylation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-glucopyranoside (**9**),[16] methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside (**10**),[16] methyl4,6-*O*-benzylidene-3-*O*-methyl-α-D-mannopyranoside (**11**), and methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-mannopyranoside (**12**)[1] with methylsulfonyl chloride in pyridine. Methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-mannopyranoside **11** was synthesized by catalytic hydrogenation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-*arabino*-hexopyranosid-2-ulose using platinum on carbon (10%) as the catalyst.

Heating of an *N*,*N*-dimethylformamide solution of **4** with potassium benzoate at reflux for 8 hr resulted in smooth displacement of the C-2 sulfonyloxy group.[17] In addition to small amount of starting material **4** (8%), the only product which could be isolated from the reaction mixture was methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside (**13**, 70%). The structure of **13** was deduced from comparison (mmp, ir and nmr spectra) with an authentic sample, obtained by benzoylation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside (**10**) with benzoyl chloride in pyridine.

Refluxing of an *N*,*N*-dimethylformamide solution of **2** with potassium benzoate resulted also in displacement of the C-2 methylsulfonyloxy group giving, in addition to a small amount of starting material **2** (7%), methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-mannopyranoside (**14**, 62%); however, the reaction was considerably slower (120 hr). The structure of **14** has been proven by comparison with an authentic sample (ir and nmr spectra) obtained by benzoylation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-mannopyranoside (**12**) with benzoyl chloride in pyridine.

Refluxing of an *N*,*N*-dimethylformamide solution of **1** with potassium benzoate for 120 hr afforded, in addition to starting material **1** (77.5%), an extremely small amount of a product (3.5%) which on the basis of comparison with an authentic sample synthesized by benzoylation of **11** with benzoyl chloride in pyridine (ir and nmr spectra) could be methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-α-D-mannopyranoside (**15**).

Refluxing of an *N*,*N*-dimethylformamide solution of **3** with potassium benzoate for 120 hr afforded in addition to small amount of unidentified products the starting material **3** (29%) as the only isolable product. The expected direct displacement product, *i.e.*, methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-α-D-glucopyranoside (**16**), could not be found among the unidentified products.

The above experimental results strongly indicate that the reactivity of the C-2 sulfonyloxy group of a glycopyranosyl-2-sulfonate toward direct displacement depends chiefly upon the anomeric configuration, since the torsional strain and dipolar interactions between an approaching nucleophile or leaving sulfonate and the C-1 alkoxy group in the transition state are the most important factors in these reactions. The belief that the observed "unreactivity" of the C-2 sulfonyloxy group toward direct displacement may be a consequence of the electron-withdrawing effect of the

anomeric carbon atom, a conclusion, which was probably based on unsuccessful attempts to effect the direct displacement of the C-2 sulfonyloxy group of α-anomers of D-glycopyranosides, seems thus to have no justification.

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 267; the nmr spectra were recorded with a Varian T-60 spectrometer using tetramethylsilane as the internal standard. Chemical shifts (δ) are expressed in parts per million.

Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-mannopyranoside (4). To a pyridine solution (10 ml) of **12** (210 mg, 0.71 mmol) methanesulfonyl chloride (0.21 ml, 2.71 mmol) was added and the reaction mixture was kept at room temperature for 45 min. The excess of methanesulfonyl chloride was destroyed by adding methanol, and solvents were evaporated *in vacuo*. The crude reaction product was chromatographed on silica gel. Elution with 95:5 benzene–2-propanol afforded pure crystalline **4** (196 mg, 73%). An analytical sample was obtained by recrystallizing **4** from acetone–isopropyl ether: mp 182–182.5°; $[\alpha]^{27}D$ −79° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 1350 and 1170 cm^{-1} (asymmetric and symmetric SO_2 stretch); nmr ($CDCl_3$) δ 7.6–7.2 (m, 5, phenyl), 5.61 (s, 1, methine H from benzylidene group), 5.16 (br d, $J_{1,2} \leq 1$ and $J_{2,3}$ = 3.0 Hz, 1, H-2), 4.54 (br s, $J_{1,2} \leq 1$ Hz, 1, H-1), 4.5–3.2 (m, 5, H-3, H-4, H-5, H-6, H′-6), 3.57 (s, 6, C-1 and C-3 methoxy groups), 3.15 (s, 3, methyl from C-2 methylsulfonyl group).

Anal. Calcd for $C_{16}H_{22}O_8S$: C, 51.33; H, 5.92; S, 8.57. Found: C, 51.51; H, 6.08; S, 8.67.

Reaction of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-mannopyranoside (4) with Potassium Benzoate in Refluxing *N,N*-Dimethylformamide. An *N,N*-dimethylformamide solution (10 ml) containing **4** (196 mg, 0.52 mmol) and potassium benzoate (225 mg, 1.4 mmol) was heated at reflux for 8 hr. The solvent was then removed *in vacuo* and the residue was chromatographed on silica gel (20 g). Elution with 98:2 benzene–2-propanol gave two fractions. The first fraction (140 mg, 67%) was pure **13**, whereas the second fraction (30 mg) was a mixture of starting material **4**, product **13**, and two unidentified products. After rechromatography of the second fraction on silica gel (5 g) and elution with 98:2 benzene–2-propanol an additional amount (7 mg) of pure **13**, in addition to a small amount (5 mg) of unidentified product and starting material **4** (17 mg; 8%) was isolated. Therefore the total amount of product **13** isolated from the reaction was 147 mg (70%). The compound **13** was identified as methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside by comparison (mixture melting point, ir and nmr spectra) with an authentic sample obtained by benzoylation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside (**10**) with benzoyl chloride in pyridine.

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside (13). To a pyridine solution (5 ml) of **10** (117 mg; 0.39 mmol), benzoyl chloride (0.1 ml, 0.8 mmol) was added and the reaction mixture was kept at room temperature for 18 hr. The residue (282 mg) obtained after removal of pyridine *in vacuo* was chromatographed on silica gel (25 g). Elution with 98:2 benzene-2-propanol gave pure **13** (148 mg; 93%). Analytical sample was obtained by recrystallization from acetone–isopropyl ether: mp 146°; $[\alpha]^{27}D$ −9° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 1723 and 1265 cm^{-1} (C=O and C—O stretch, benzoate); nmr ($CDCl_3$) δ 8.2–7.1 (m, 10, two phenyl groups), 5.56 (s, 1, methine H from benzylidene group), 5.23 (br t, $J_{1,2} \approx J_{2,3}$ = 7.0 Hz, 1, H-2), 4.56 (d, $J_{1,2}$ = 7.0 Hz, 1, H-1), 3.50 and 3.45 (two s, 6, C-1 and C-3 methoxy groups).

Anal. Calcd. for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04. Found: C, 66.11; H, 6.00.

Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-glucopyranoside (2). A pyridine solution (5 ml) containing **10** (100 mg; 0.33 mmol) and methanesulfonyl chloride (0.25 ml, 3.2 mmol) was kept at room temperature for 5 hr. The excess of methanesulfonyl chloride was destroyed by adding methanol (1 ml). Benzene was then added and solvents were removed *in vacuo*. The residue was extracted with 4:1 benzene–ethyl acetate, the extract was evaporated *in vacuo*, and the crude product was chromatographed on silica gel (30 g). Elution with 4:1 benzene–ethyl acetate gave pure **2** (133 mg, 89%) as white crystalline material. Analytical sample was obtained by recrystallization from chloroform–isopropyl ether: mp 126.5° $[\alpha]^{27}D$ −56° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 1370 and 1180 (asymmetric and symmetric SO_2 stretch); nmr ($CDCl_3$) δ 7.5–7.1 (m, 5, phenyl), 5.53 (s, 1, methine H from benzylidene group), 3.60 and 3.53 (two s, 6, C-1 and C-3 methoxy groups), 3.07 (s, 3, methyl from C-2 methylsulfonyl group).

Anal. Calcd for $C_{16}H_{22}O_8S$: C, 51.33; H, 5.92; S, 8.57. Found: C, 51.19; H, 6.01; S, 8.44.

Reaction of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-β-D-glucopyranoside (2) with Potassium Benzoate in Refluxing *N,N*-Dimethylformamide. An *N,N*-dimethylformamide solution (20 ml) containing **2** (164 mg, 0.44 mmol) and potassium benzoate (352 mg, 2.2 mmol) was heated at reflux for 120 hr. The reaction mixture was, after cooling to room temperature, diluted with chloroform and the precipitate was filtered off. The filtrate was evaporated *in vacuo* and the crude product (224 mg) was chromatographed on silica gel (three times). Elution with 99.1 benzene-2-propanol and 9:1 benzene–ethyl acetate afforded, in addition to some starting material **2** (27 mg, 7%), pure **14** (110 mg, 62%) as an amorphous solid. Compound **14** was identified as methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-mannopyranoside by comparison (ir and nmr spectra) with an authentic sample obtained by benzoylation of methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-mannopyranoside (**12**) with benzoyl chloride in pyridine.

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-β-D-mannopyranoside (14). To a pyridine solution (2 ml) of **12** (126 mg, 0.43 mmol) benzoyl chloride (1.0 ml, 8.6 mmol) was added and the reaction mixture was kept at room temperature overnight. Pyridine was then evaporated *in vacuo* and the residue was chromatographed on silica gel (30 g, elution with 98:2 benzene–2-propanol) and Al_2O_3[10 g, activity II; elution with hexane (10 ml), 1:1 hexane–benzene (100 ml), and benzene (100 ml)]. The pure **14** thus isolated (135 mg, 79%) was an amorphous solid: $[\alpha]^{27}D$ −112° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 1715 and 1265 cm^{-1} (C=O and C—O stretch, benzoate); nmr ($CDCl_3$) δ 8.2–7.2 (m, 10, two phenyl groups), 5.83 (q, $J_{1,2}$ = 1.1 and $J_{2,3}$ = 3.2 Hz, 1; H-2), 5.63 (s, 1, methine H from benzylidene group), 4.58 (d, $J_{1,2}$ = 1.1 Hz, 1, H-1), 4.5–3.6 (m, 5, H-3, H-4, H-5, H-6, H′-6), 3.47 and 3.43 (two s, 6, C-1 and C-3 methoxy groups).

Anal. Calcd for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04. Found: C, 66.16; H, 6.05.

Reaction of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-glucopyranoside (1) with Potassium Benzoate in Refluxing *N,N*-Dimethylformamide. An *N,N*-dimethylformamide solution (10 ml) of **1**[3] (132 mg, 0.35 mmol) and potassium benzoate (238 mg, 1.5 mmol) was heated at reflux for 120 hr. After cooling to room temperature, the reaction mixture was diluted with chloroform. The precipitate was filtered off and then dissolved in water. The water solution was extracted with chloroform, the chloroform extract was dried over anhydrous $MgSO_4$ and the chloroform extract, combined with filtrate, was evaporated *in vacuo*. The crude product (192 mg) was chromatographed on silica gel (10 g). Elution with 98:2 benzene–2-propanol afforded two fractions. The first fraction (5 mg, 3.5%) could be the product of direct displacement, *i.e.*, methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-α-D-mannopyranoside (**15**): ir ($CHCl_3$) 1715 and 1265 cm^{-1} (C=O and C—O stretch, benzoate); nmr ($CDCl_3$) δ 8.2–7.2 (m, 10, two phenyl groups), 5.68 (s, 1, methine H from benzylidene group), 5.60 (unresolved m, 1, H-2), 4.85 (d, $J_{1,2}$ = 1.4 Hz, 1, H-1), 3.47 and 3.44 (two s, 6, C-1 and C-3 methoxy groups). The second fraction (102 mg, 77.5%) was, according to ir and nmr spectra, the starting material **1**.

Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-α-D-mannopyranoside (11). An ethyl acetate solution (16 ml) of methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-*arabino*-hexopyranosid-2-ulose (565 mg, 1.92 mmol) was hydrogenated at the atmospheric pressure using 10% Pt on carbon as the catalyst (136 mg). After 2 hr the absorption of hydrogen ceased and the catalyst was then filtered off, washed with several portions of ethylacetate and the filtrate was evaporated *in vacuo*. The residue was chromatographed on silica gel (60 g). Elution with 95:5 benzene–2-propanol gave three fractions. The first fraction (160 mg; 28%) was pure methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-mannopyranoside (**11**) (an amorphous solid), whereas the third fraction (263 mg, 46%) was pure crystalline methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-glucopyranoside (**9**). The second fraction (73 mg), being a mixture of **9** and **11**, was rechromatographed on silica gel (15 g) using 95:5 benzene–2-propanol as eluent, whereby additional amounts of pure **11** (32 mg, 5.6%) and pure **9** (38 mg, 6.7%) were obtained. Thus the total amounts of pure **9** and **11** isolated after catalytic hydrogena-

tion of methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-*arabino*-hexopyranosid-2-ulose were 301 mg (52.9%) of **9** and 192 mg (33.7%) of **11** (the gluco:manno ratio being thus 1.57:1). The analytical sample of **11**, an amorphous solid showed an $[\alpha]^{27}D$ +76° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 3560 (broad peak) and 3470 (shoulder) (OH) nmr ($CDCl_3$) δ 7.6–7.3 (m, 5, phenyl), 5.58 (s, 1, methine H from benzylidene group), 4.77 (d, $J_{1,2}$ = 1.4 Hz, 1, H-1), 4.4–3.6 (m, 6, H-2, H-3, H-4, H-5, H-6 and H′-6), 3.53 and 3.37 (two s, 6, C-1 and C-3 methoxy groups), 2.65 (d, *J* = 1.4 Hz, 1, OH).

Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 61.05; H, 7.00.

Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-mannopyranoside (3). To a pyridine solution of **11** (87 mg; 0.29 mmol) methanesulfonyl chloride (0.100 ml, 0.59 mmol) was added and the reaction mixture was kept at room temperature for 2 hr. The excess of methanesulfonyl chloride was destroyed by methanol and the solvents were evaporated *in vacuo*. The residue was chromatographed on silica gel (20 g). Elution with 97:3 benzene–2-propanol afforded pure crystalline **3** (105 mg, 95%). An analytical sample was obtained by recrystallizing **3** from acetone: mp 185–186°; $[\alpha]^{27}D$ +22° (*c* 0.7, $CHCl_3$); ir ($CHCl_3$) 1363 and 1170 cm^{-1} (asymmetric and symmetric SO_2 stretch); nmr ($CDCl_3$) δ 7.6–7.2 (m, 5 phenyl), 5.62 (s, 1, methine H from benzylidene group), 5.0 (m, 1, H-2), 4.90 (d, $J_{1,2} \leq 1$ Hz, 1, H-1), 4.4–3.8 (m, 5, H-3, H-4, H-5, H-6, and H′-6), 3.56 and 3.40 (two s, 6, C-1 and C-3 methoxy groups), 3.13 (s, 3, methyl from C-2 methylsulfonyl group).

Anal. Calcd for $C_{16}H_{22}O_8S$: C, 51.33; H, 5.92; S, 8.57. Found: C, 51.39; H, 5.90; S, 8.79.

Reaction of Methyl 4,6-*O*-Benzylidene-3-*O*-methyl-2-*O*-methylsulfonyl-α-D-mannopyranoside 3 with Potassium Benzoate in Refluxing *N,N*-Dimethylformamide. An *N,N*-dimethylformamide solution (10 ml) containing **3** (202 mg, 0.54 mmol) and potassium benzoate (202 mg, 1.26 mmol) was heated at reflux for 120 hr. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (30 g). Elution with 2:1 benzene–ethyl acetate afforded four fractions. The third fraction was pure starting material **3** (59 mg, 29%), whereas the other three fractions were unidentified products of decomposition of **3** under the given experimental conditions.

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-methyl-α-D-mannopyranoside (15). To a pyridine solution of **11** (81 mg, 0.27 mmol) benzoyl chloride (0.100 ml, 0.59 mmol) was added and the reaction mixture was kept at room temperature for 2 hr. The pyridine was removed *in vacuo* and the residue was chromatographed on silica gel (20 g). Elution with 98:2 benzene–2-propanol gave slightly impure **15** (111 mg). The rechromatography on slica gel (16 g) and elution with 98:2 benzene–2-propanol afforded pure **15** (110 mg; 100%) as an amorphous solid: $[\alpha]^{27}D$ −48° (*c* 1.0, $CHCl_3$); ir ($CHCl_3$) 1720 and 1265 cm^{-1} (C=O and C—O stretch, benzoate); nmr ($CDCl_3$) δ 8.2–7.2 (m, 10, phenyl), 5.68 (s, 1, methine H from benzylidene group), 5.61 (m, 1, H-2), 4.85 (d, $J_{1,2} \leq 1$ Hz, 1, H-1), 4.5–3.7 (m, 5, H-3, H-4, H-5, H-6, and H′-6), 3.46 and 3.43 (two s, 6, C-1 and C-3 methoxy groups).

Anal. Calcd for $C_{22}H_{24}O_7$: C, 65.99; H, 6.04. Found: C, 66.18; H, 6.20.

Registry No.—**1**, 51016-19-4; **2**, 52260-45-4; **3**, 52260-46-5; **4**, 52260-47-6; **10**, 35775-68-9; **11**, 52260-48-7; **12**, 51364-57-9; **13**, 52260-49-8; **14**, 52260-50-1; **15**, 52260-51-2; methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-*arabino*-hexopyranosid-2-ulose, 29774-59-2.

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Use of Carbon-13 and Proton Magnetic Resonance Studies for the Determination of Glycosylation Site in Nucleosides of Fused Nitrogen Heterocycles

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Several selected fused nitrogen heterocyclic systems, 7-amino-*v*-triazolo[4,5-*d*]pyrimidine (I), pyrazolo[1,5-*a*]pyrimidin-7-one (IV), *s*-triazolo[1,5-*a*]pyrimidin-7-one (VI), and 2-methylthiopyrazolo[1,5-*a*]-*s*-triazin-4-one (IX), and their *N*-ribofuranosides have been studied with respect to the effect of N-ribosylation on the carbon-13 chemical shifts of the neighboring carbons. Large upfield α shifts and small downfield β shifts were observed in the nucleoside when compared to the base anion, thereby providing a convenient general method for the assignment of the glycosylation site in complex fused nitrogen heterocyclic systems.

Recently, several nmr studies in this laboratory have demonstrated the potential use of carbon-13 nuclear magnetic resonance spectroscopy as a general unequivocal method for the assignment of glycosylation site in both five- and six-membered nitrogen heterocycles.[2,3] The assignments were based upon the use of previously reported α- and β-substitution shifts observed in other heterocyclic systems when the neutral species is compared with the anionic form.[4-6] These shift parameters were first described by Pugmire and Grant from studies on the azines and their charged species,[4,5] where nitrogen protonation resulted in an upfield shift for the α carbon and downfield shifts were