Synthetic Nucleosides. LXVII. Studies on the Synthesis of *cis*-2,3-Diamino Sugars. VII. Synthesis and Reactions of Some *N*-*p*-Tolylsulfonyl Derivatives of 2-Amino-2-deoxy-D-altrose, 3-Amino-3-deoxy-D-glucose, and 2,3-Dideoxy-2,3-imino-D-mannose[1a,b]

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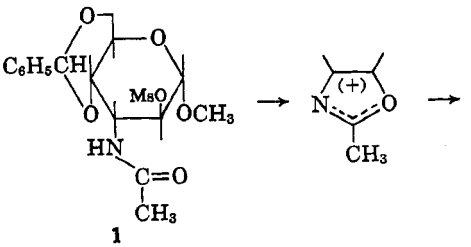
The C-2,C-3-*trans*-diaxial compound, methyl 4,6-*O*-benzylidene-2-deoxy-2-(*p*-tolylsulfonamido)-3-*O*-(*p*-tolylsulfonyl)-α-D-altropyranoside (9) undergoes cyclization to the *N*-tosylaziridine, methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-imino-*N*-(*p*-tolylsulfonyl)-α-D-mannopyranoside (12), in methanolic sodium methoxide with more rapidity than does the C-2,C-3-*trans*-diequatorial compound, methyl 4,6-*O*-benzylidene-3-deoxy-3-(*p*-tolylsulfonamido)-2-*O*-(*p*-tolylsulfonyl)-α-D-glucopyranoside (11). The conformational reasons for this behavior are discussed. The aziridine 12 undergoes *trans*-diaxial ring opening with hydroxide or methoxide ions to give the corresponding 2-amino-2-deoxy-D-altrose derivatives.

The initial studies on the neighboring group displacement of mesylate ester groups by a vicinal-*trans* acetamido function of a carbohydrate molecule (*e.g.*, 1) in weakly basic media resulted in *O*-attack to form an intermediate oxazolinium ion[2a] (eq. 1)[3] which solvolyzed to the *cis*-*N*-acetyl alcohol. Since that time this reaction has been of considerable value[2b] in obtaining



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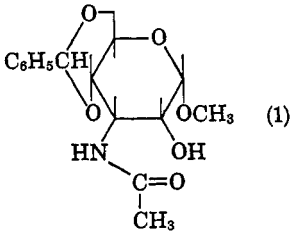
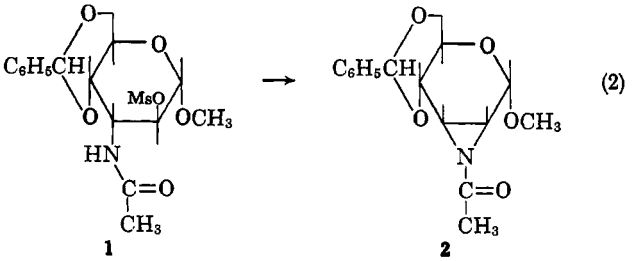


(1)

cis derivatives of carbohydrates. Recent studies, however, have shown that 1, in strongly basic media such as ethereal lithium aluminum hydride or ethanolic sodium ethoxide, undergoes ring closure by *N* attack to furnish the *N*-acetylaziridine (eq. 2).[4]

In recent studies of derivatives of 2- and 3-amino-D-altrose[5–9] which carry trifunctional neighboring groups such as the ureido and thioureido functions vicinal



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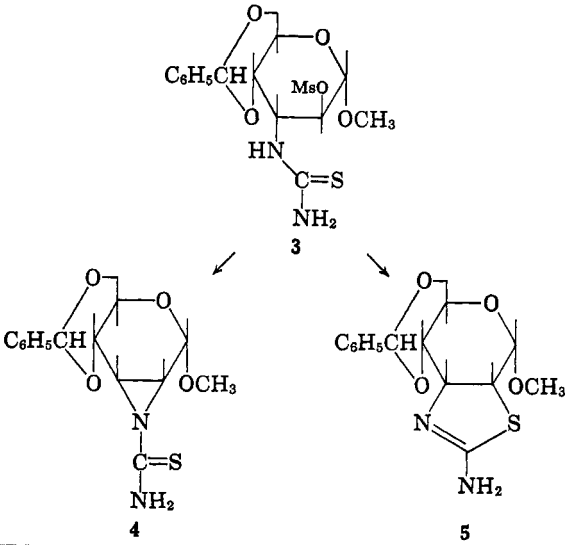
(2)

and *trans* to a suitable leaving group, aziridine derivatives have also been obtained. Thus, treatment of the thioureido compound 3 with methanolic sodium methoxide gave the *N*-thiocarbamoylaziridine 4. Ring closure of 3 in pyridine gave the thiazoline 5. Similar results were obtained for analogous derivatives of 2-amino-D-altrose.[9–11]



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(1) (a) For the previous paper in this series, see B. R. Baker and T. L. Hullar, *J. Org. Chem.*, **30**, 4045 (1965). (b) This work was supported in part by Grant CY-5845 of the National Cancer Institute, U. S. Public Health Service. (c) National Science Foundation Postdoctoral Fellow, 1963–1964.

(2) (a) B. R. Baker and R. E. Schaub, *J. Org. Chem.*, **19**, 646 (1954) *J. Am. Chem. Soc.*, **75**, 3864 (1953); (b) see, for example, the later work of B. R. Baker and co-workers and of R. W. Jeanloz and D. Jeanloz, *J. Org. Chem.*, **26**, 537 (1961).

(3) Abbreviations used: Bz = benzoyl; Ms = mesyl = methanesulfonyl; Ts = tosyl = *p*-tolylsulfonyl.

(4) (a) D. H. Buss, L. Hough, and A. C. Richardson, *J. Chem. Soc.*, 5295 (1963); (b) see also R. D. Guthrie and D. Murphy, *ibid.*, 5288 (1963); (c) R. D. Guthrie, private communication.

(5) B. R. Baker and T. Neilson, *J. Org. Chem.*, **29**, 1047 (1964).

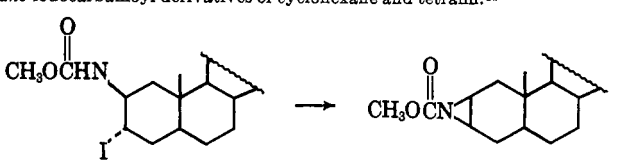
(6) B. R. Baker and T. Neilson, *ibid.*, **29**, 1051 (1964).

(7) B. R. Baker and T. Neilson, *ibid.*, **29**, 1057 (1964).

(8) B. R. Baker and T. Neilson, *ibid.*, **29**, 1063 (1964).

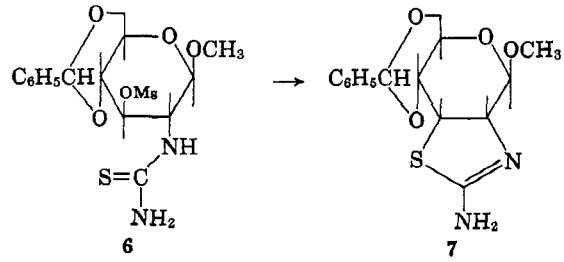
(9) B. R. Baker and T. L. Hullar, *ibid.*, **30**, 4038 (1965).

(10) (a) The formation of an aziridine, when ring closure to a five-membered ring can result, has also been found in a study of derivatives of cholestane. Thus, methyl (3-α-iodo-2-β-cholestane)carbamate, a compound in which the iodo and carbamoyl groups are fixed in a diaxial disposition, undergoes ready reaction in alcoholic potassium hydroxide to give the corresponding aziridine in 96% yield. Similar results were obtained for vicinal, *trans*-iodocarbamoyl derivatives of cyclohexane and tetralin.[11]



(11) A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 3640 (1964).

The thioureido derivatives of 2- and 3-amino-D-glucose (*e.g.*, 6),[12a,6] however, form only thiazolines (*e.g.*, 7) in pyridine or in methanolic sodium methoxide.[12]



6 7

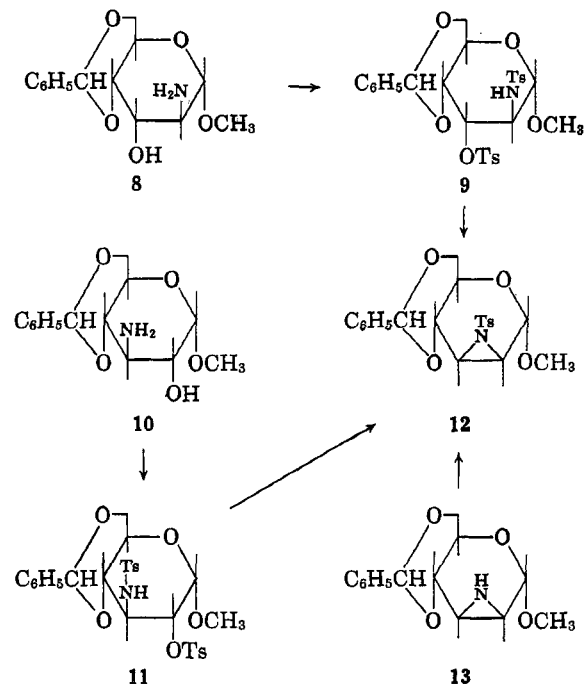
Thus, a trifunctional neighboring group such as the thioureido function exhibits distinct differences in its mode of ring closure depending upon whether it is part of a 2(3)-amino-D-altrose or a 2(3)-amino-D-glucose system. In view of this, it was of interest to study certain D-*altro* and D-*gluco* derivatives containing a neighboring group which can only form azidiridines on ring closure; the *N*-(*p*-tolylsulfonyl) function is such a neighboring group.[13] Consequently a study of the reactivity of selected *N*-tosyl derivatives of 2-amino-D-altrose, 3-amino-D-glucose, and 2,3-imino-D-mannose was undertaken. The results of this study are presented in this paper.

Methyl 4,6-*O*-benzylidene-2-deoxy-2-(*p*-tolylsulfonamido)-3-*O*-(*p*-tolylsulfonyl)-α-D-altropyranoside (**9**) was readily synthesized by reaction of methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (**8**)[9,14] with excess tosyl chloride (Scheme I). In a similar manner, methyl 4,6-*O*-benzylidene-3-deoxy-3-(*p*-tolylsulfonamido)-2-*O*-(*p*-tolylsulfonyl)-α-D-glucopyranoside (**11**) was synthesized from methyl 3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside (**10**).[15]

Ring closure of **9** and **11** both gave the aziridine **12** but at markedly different rates. A solution of **9** in methanolic sodium methoxide at room temperature was rapidly converted to methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-imino-*N*-(*p*-tolylsulfonyl)-α-D-mannopyranoside (**12**). A solution of the gluco derivative **11**, with a similar concentration of sodium methoxide, required heating under reflux for 45 min. to achieve complete conversion to **12**. The structure of **12** was confirmed by the tosylation of methyl 4,6-*O*-benzylidene-2,3-dideoxy-2,3-imino-α-D-mannopyranoside (**13**)[4] to give **12**.

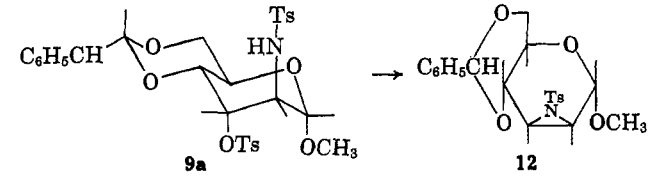
The marked ease of ring closure of the *altro* isomer **9** compared to ring closure of the *gluco* isomer **11** can be explained by stereochemical considerations. The stable conformation of **9** (**9a**) maintains the tosylamide and tosyloxy groups *trans*-diaxial to each other. Thus, the readily formed anion[13c,16] of the amide nitrogen

SCHEME I



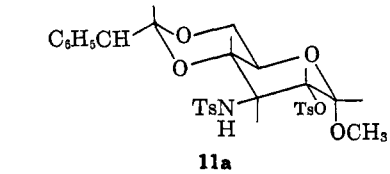
8 9 10 11 12 13

atom is ideally positioned to effect displacement of the tosylate ion. This displacement is undoubtedly accelerated by the release of the strain, caused by the C-1 methoxyl, C-3 tosylate interaction in **9a**, when the tosylate ion is displaced.

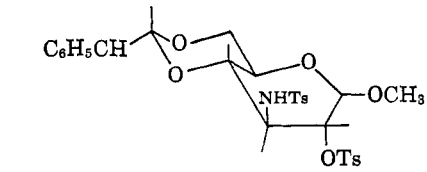


9a 12

The stable conformation of the *gluco* isomer **11** (**11a**) maintains the sulfonamide and sulfonate ester groups in a *trans*-diequatorial disposition. In this conformation the anion of the sulfonamide group cannot approach sufficiently close to C-2 to effect displacement. Consequently **11a** must convert to the chair–boat conformer **11b** in order to achieve the necessary



11a



11b

(12) Recently, methyl 2-benzamido-4,6-*O*-benzylidene-3-*O*-methanesulfonyl-β-D-glucopyranoside, upon treatment with potassium cyanide in *N*,*N*-dimethylformamide, gave the aziridine derivative, methyl 4,6-*O*-benzylidene-*N*-benzoyl-2,3-dideoxy-2,3-imino-β-D-allopyranoside in 17% yield.[12b] (b) W. Meyer zu Reckendorf, *Chem. Ber.*, **97**, 325 (1964).

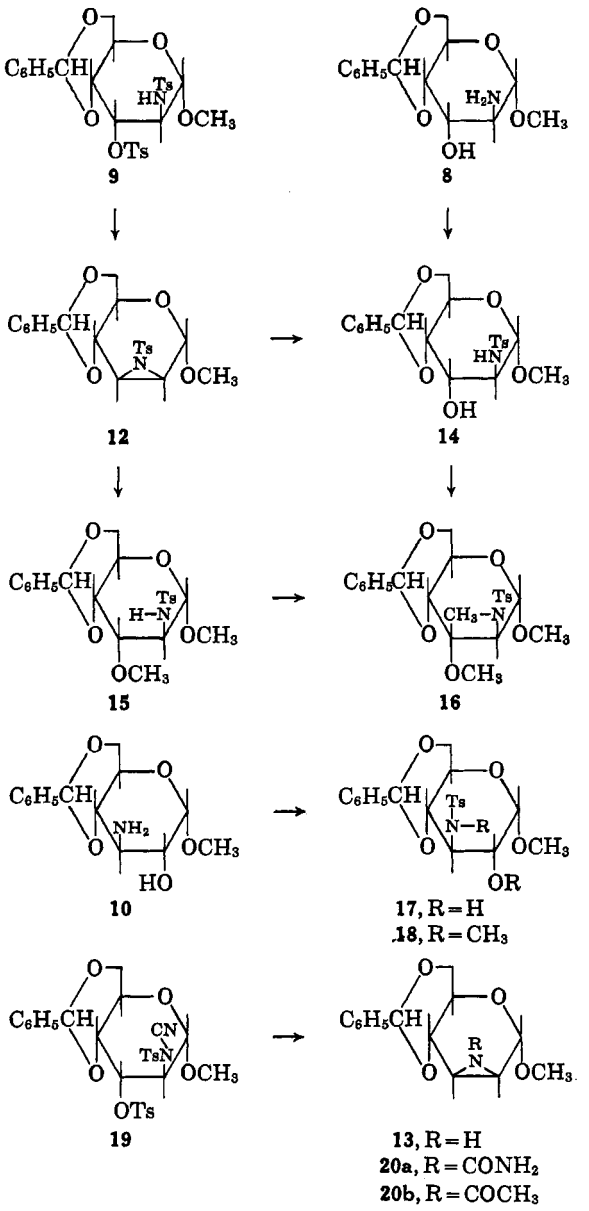
(13) (a) R. Adams, and T. L. Cairns, *J. Am. Chem. Soc.*, **61**, 2464 (1939); (b) M. S. Kharasch and H. M. Priestley, *ibid.*, **61**, 3425 (1939); (c) F. L. Scott and E. Flynn, *Tetrahedron Letters*, 1675 (1964); (d) O. E. Paris and P. E. Fanta, *J. Am. Chem. Soc.*, **74**, 3007 (1952).

(14) G. J. Robertson, W. H. Myers, and W. E. Tetlow, *Nature*, **142**, 1076 (1938); W. H. Myers and G. J. Robertson, *J. Am. Chem. Soc.*, **65**, 8 (1943).

(15) R. D. Guthrie and L. F. Johnson, *J. Chem. Soc.*, 4166 (1961).

(16) (a) T. Taguchi and M. Kojima, *J. Am. Chem. Soc.*, **81**, 4316 (1961). (b) For a brief general discussion of boat forms of cyclohexane and its derivatives, see M. Balasubaramian, *Chem. Rev.*, **62**, 591 (1962). (c) See F. A. Cutler, Jr., L. Mandell, D. Shew, J. F. Fisher, and J. M. Chemerda, *J. Org. Chem.*, **24**, 1621 (1962). See also C. W. Shoppee, *J. Chem. Soc.*, 1032 (1948); V. R. Mattox, R. B. Turner, L. L. Engel, B. F. McKenzie, W. F. McGuckin, and E. C. Kendall, *J. Biol. Chem.*, **164**, 569 (1946), for additional examples of boat forms as intermediates. (d) J. Sicher, M. Tichy, F. Sipos, and M. Pankova, *Proc. Chem. Soc.*, 384 (1960); *Collection Czech. Chem. Commun.*, **26**, 2418 (1961).

SCHEME II



trans-coplanar arrangement of the attacking and departing groups.[16b-d] Formation of conformer **11b** requires bond distortion; **11b** itself suffers from 1,4 interactions ("bowsprit–flagpole" interaction) between the C-2 tosylate and the C-5 hydrogen and 1,2 interactions (eclipsing interaction) between the C-3 tosylamide and the C-4 hydrogen. These factors should render difficult the conversion of **11a** to **11b**. This difficulty in forming **11b** is evident by the slower rate of formation of **12** from **11** compared with formation from **9**.

Since formation of the *N*-tosyl aziridine **12** from **9** is rapid at room temperature, the alkaline stability of **12** was studied by subjecting its precursor, **9**, to alkaline conditions (Scheme II). When **9** was refluxed in 2 *N* sodium hydroxide, methyl 4,6-*O*-benzylidene-2-deoxy-2-(*p*-tolylsulfonamido)-α-D-altropyranoside (**14**) was obtained in 38% yield; authentic **14** was prepared by *N*-tosylation of **8**. Reaction of **9** with sodium methoxide in refluxing methanol for 24 hr. allowed isolation of the *N*-tosylaziridine **12** in 45% yield and of methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-2-(*p*-tolylsulfonamido)-α-D-altropyranoside (**15**) in 30% yield. The structure of **15** was proved in the following manner. Permethylation[17] of **14** and **15** gave the same compound, methyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-methyl-2-methylamino-*N*-(*p*-tolylsulfonyl)-α-D-altropyranoside (**16**), as a glass; the two samples had identical infrared spectra and mobilities on t.l.c. To confirm further this assignment, **10** was *N*-tosylated to give methyl 4,6-*O*-benzylidene-3-deoxy-3-(*p*-tolylsulfonamido)-α-D-glucopyranoside (**17**). Permethylation[17] of **17** gave crystalline methyl 4,6-*O*-benzylidene-3-deoxy-2-*O*-methyl-3-methylamino-*N*-(*p*-tolylsulfonyl)-α-D-glucopyranoside (**18**), clearly isomeric to **16**.

The isolation from these alkaline reactions of only D-altrose derivatives shows that ring opening followed the *trans*-diaxial rule.[18] This result is in accord with the action of ammonia on the corresponding 2,3-anhydro-D-mannoside[2] and with the azide ion on the corresponding 2,3-dideoxy-2,3-imino-D-mannoside.[4c]

It was originally expected that the *N*-tosyl group would labilize the N–C-3 bond sufficiently to allow a facile cleavage of the aziridine ring similar to that enjoyed by a 2,3-epoxide. Thus, treatment of methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside with refluxing methanolic sodium methoxide for 20 hr. is known to give methyl 4,6-*O*-benzylidene-3-*O*-methyl-α-D-altropyranoside in 77% yield.[19] However, the isolation in the present case of **12** in 45% yield after its being refluxed for 24 hr. in methanolic sodium methoxide indicates that this *N*-tosylaziridine is considerably less reactive than the corresponding epoxides. The tosylamido alcohol **14** (derived from **9** through the aziridine **12**) was isolated from boiling aqueous alkali, showing that the *N*-tosylaziridine **12** was labile under these conditions. The aziridine **13** was stable under similar conditions (see below). These facts show that the N-tosyl aziridine ring in **12** is more susceptible to hydrolytic opening than is the nonnitrogen-substituted aziridine ring of **13**.

Alkaline hydrolysis of methyl 4,6-*O*-benzylidene-*N*-cyano-2-deoxy-2-(*p*-tolylsulfonamido)-3-*O*-(*p*-tolylsulfonyl)-α-D-altropyranoside (**19**)[9] gave the aziridine **13** in 57% yield and its *N*-carbamoyl derivative, methyl 4,6-*O*-benzylidene-*N*-carbamoyl-2,3-dideoxy-2,3-imino-α-D-mannopyranoside (**20a**), in 23% yield. As stated above, the alcohol **14** rather than the aziridine **13** is isolated from alkaline treatment of **9**. This result shows that the aziridine ring in **12** does not labilize the *N*-sulfonyl bond sufficiently to permit saponification before ring opening occurs.[20] Consequently, in the alkaline hydrolysis of **19**, detosylation must have occurred *prior to* cyclization to the imine.[21] The isolation of **20a** further substantiates this view.

(17) R. Kuhn, H. Trischmann, and I. Löw, *Angew. Chem.*, **67**, 32 (1955).

(18) (a) A. Furst and P. A. Plattner, Abstracts of Papers, 12th International Congress on Pure and Applied Chemistry, New York, N. Y., 1951, p. 409; (b) E. L. Eliel, "Steric Effects in Organic Chemistry," M. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, pp. 130–134.

(19) G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1193 (1935).

(20) (a) Carboxamides of aziridines are subject to facile alkaline hydrolysis.[4,20b] (b) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, **83**, 4549 (1961); H. C. Brown *ibid.*, **82**, 2016 (1962); H. W. Heine, M. A. Fetter, and E. M. Nicholson, *ibid.*, **81**, 2202 (1959).

(21) The lability to aqueous alkali of an *N*-tosyl group attached to a cyanamide has been noted previously.[22] Consequently the present result is the expected course of reaction. It should be noted, however, that benzylamine in refluxing ethanol did not cleave the sulfonamide bond.[9]

(22) F. Kurzer, *J. Chem. Soc.*, 1034 (1949).

Experimental Section[23]

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-(*p*-tolylsulfonamido)-3-*O*-(*p*-tolylsulfonyl)-α-D-altropyranoside (9).—A solution of **8** (0.282 g., 1 mmole) and tosyl chloride (0.760 g., 4 mmoles) in pyridine (4 ml.) was kept at 50° for 47 hr. protected from moisture, and then poured onto ice (20 g.). The aqueous mixture was extracted with three 20-ml. portions of chloroform, and the combined chloroform extracts were washed with water (two 10-ml. portions), dried, and concentrated to a white solid (0.490 g.). A solution of the solid in chloroform was clarified with decolorizing carbon. Recrystallization from ethyl acetate–petroleum ether at 5° gave **9** (0.425 g., 72%): m.p. 198–199°; λ_{max} 2.96 (NH), 6.22 (C=C), 7.36, 7.50, 8.44, and 8.56 μ (sulfonamide, sulfonate).

Anal. Calcd. for $C_{28}H_{31}NO_9S_2$ (589.7): C, 57.03; H, 5.30; N, 2.38; S, 10.87. Found: C, 57.19; H, 5.44; N, 2.24; S, 10.72.

Methyl 4,6-*O*-Benzylidene-3-deoxy-3-(*p*-tolylsulfonamido)-2-*O*-(*p*-tolylsulfonyl)-α-D-glucopyranoside (11).—To a solution of **10** (0.141 g., 0.5 mmole) in pyridine (4 ml.) at room temperature was added tosyl chloride (0.380 g., 2 mmoles). The yellow solution was kept at 46–48° for 63 hr. protected from moisture, then poured onto crushed ice (20 g.). The aqueous mixture was extracted with three 10-ml. portions of chloroform, and the combined chloroform solutions were washed twice with water (5-ml. portions), dried, and concentrated to a solid (0.303 g., quantitative), m.p. 220–225°. The solid was decolorized in ethanol and then recrystallized twice from chloroform–petroleum ether to give the analytical sample of **11**: m.p. 234–236°; λ_{max} 3.00 (NH), 6.21 (C=C), 7.20, 7.46, 8.42, 8.60 (sulfonamide, sulfonate), 13.35, and 13.96 μ (phenyl).

Anal. Calcd. for $C_{28}H_{31}NO_9S_2$ (589.7): C, 57.03; H, 5.30; N, 2.38; S, 10.87. Found: C, 57.19; H, 5.17; N, 2.58; S, 10.59.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-2,3-imino-*N*-(*p*-tolylsulfonyl)-α-D-mannopyranoside (12). A.—To an ice-cooled solution of **13** (0.094 g., 0.36 mmole) in pyridine (1.0 ml.) containing triethylamine (0.055 ml., 0.39 mmole) was added tosyl chloride (0.136 g., 0.71 mmole). The red solution was kept at 5° for 30 min. and then poured into crushed ice (10 g.). The aqueous solution was extracted with chloroform (three 10-ml. portions), and the combined chloroform solutions were washed with water (two 10-ml. portions), dried, and concentrated to give the analytical sample as a colorless glass (0.130 g., 87%).

Anal. Calcd. for $C_{21}H_{23}NO_6S$ (417.5): C, 60.42; H, 5.55; N, 3.36; S, 7.28. Found: C, 60.60; H, 5.86; N, 3.56; S, S, 7.84.

The analytical sample eventually crystallized when triturated with ethanol to give needles: m.p. 128–129°; λ_{max} 6.24 (C=C), 7.50, 8.60 (sulfonamide), 13.22, 13.56, 14.20, and 14.90 μ (phenyl).

B.—To a suspension of **9** (0.118 g., 0.20 mmole) in methanol (1.2 ml.) at room temperature was added 1 *N* methanolic sodium methoxide (0.8 ml.). A clear solution was immediately obtained. After standing 1 hr. at room temperature, the solution was neutralized by addition of carbon dioxide and diluted with water (5 ml.), and the resulting solution was extracted with chloroform (three 5-ml. portions). The combined chloroform solutions were washed with water (5 ml.), dried, and concentrated to a sirup (0.094 g.). From a solution of the sirup in ethyl acetate–petroleum ether, pure **12** was obtained in two crops (0.065 g., 78%), m.p. 129–131°; the infrared spectrum was identical with that for authentic **12** prepared in part A.

C.—To a suspension of **11** (0.040 g., 0.07 mmole) in methanol (0.3 ml.) was added 1 *N* methanolic sodium methoxide (0.2 ml.). After standing 1.5 hr. at room temperature no dissolution was apparent. Methanol (2 ml.) was added and the mixture was refluxed, the progress of the reaction being followed by subjecting aliquots to t.l.c. After 45 min. of reflux, conversion of **11** to **12** was complete. The solution was processed as in method B to give a sirup (0.022 g., 79%). From a solution of the sirup in ethyl acetate–petroleum ether, **12** crystallized as long needles, m.p. 129–130°; infrared spectrum was identical with that for authentic **12** prepared in **A**.

Methyl 4,6-*O*-Benzylidene-2-deoxy-2-(*p*-tolylsulfonamido)-α-D-altropyranoside (14). A.—To a solution of **8** (0.281 g., 1 mmole) in pyridine (5 ml.) containing triethylamine (0.14 ml., 1 mmole) was added tosyl chloride (0.228 g., 1.2 mmoles). After standing 40 min. at room temperature, the mixture was poured onto crushed ice (10 g.). The aqueous solution was extracted with chloroform (three 10-ml. portions), and the combined chloroform solutions were washed with water (two 10-ml. portions), dried, and concentrated to a yellow solid. The solid was decolorized in ethyl acetate, then recrystallized from ethyl acetate–petroleum ether to give **14** (0.415 g., 93%), m.p. 195–196°. Recrystallization from the same solvents gave the analytical sample: m.p. 198–199°; λ_{max} 2.80 (OH), 3.00 (NH), 7.56, 8.59 (sulfonamide), 13.1, and 14.3 μ (phenyl).

Anal. Calcd. for $C_{21}H_{25}NO_7S$ (435.5): C, 57.92; H, 5.79; N, 3.22; S, 7.36. Found: C, 57.76; H, 5.79; N, 3.19; S, 7.21.

B.—A solution of **9** (0.118 g., 0.2 mmole) in bis(2-methoxyethyl) ether (1.0 ml.) and 2 *N* sodium hydroxide (1.0 ml.) was refluxed for 6 hr. and processed through chloroform as in method A to give a sirup (0.085 g.). From the sirup, crystalline **14** was isolated (0.033 g., 38%), m.p. 190–191°; the infrared absorption was identical with that for authentic **14** prepared in A.

Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*O*-methyl-2-(*p*-tolylsulfonylamido)-α-D-altropyranoside (15).—A solution of **9** (0.170 g., 0.29 mmole) in methanol (3.0 ml.) containing sodium methoxide (1.0 mmole) was refluxed for 24 hr. and then poured into water (10 ml.). The aqueous solution was neutralized and then extracted with chloroform (four 8-ml. portions). The combined chloroform solutions were washed with two 10-ml. portions of water, dried, and concentrated to a glass (0.107 g.). Dissolution of the glass in hot ethanol containing only enough petroleum ether to induce crystallization upon cooling gave **15** (0.039 g., 30%): m.p. 224–226° with softening at 207°; λ_{max} 3.01 (NH), 7.50, 8.56 (sulfonamide), 13.1, 13.3, 14.1, and 14.4 μ (phenyl).

Anal. Calcd. for $C_{22}H_{27}NO_7S$ (449.5): C, 58.78; H, 6.05; N, 3.12; S, 7.13. Found: C, 58.60; H, 6.10; N, 3.09; S, 6.96.

Dilution of the mother liquor with petroleum ether gave crystalline **12** (0.055 g., 45%), m.p. 129–131°, with an infrared absorption spectrum identical with that for authentic **12**.

When a higher temperature was used, a sirup (0.090 g., quantitative) was obtained from which **15**, m.p. 218–221°, was isolated as the sole product.

Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*O*-methyl-2-methylamino-*N*-(*p*-tolylsulfonyl)-α-D-altropyranoside (16). A.—A solution of **14** (0.100 g.) in *N*,*N*-dimethylformamide (2 ml.) and methyl iodide (0.1 ml.) was stirred with silver oxide (0.150 g.) for 30 hr. at room temperature.[17] The mixture was filtered through Celite. The filtrate was diluted with chloroform, washed with 3% potassium cyanide solution (two 10-ml. portions), dried, and concentrated to a clear, colorless sirup (0.125 g.). Precipitation of a sirup from ethyl acetate by addition of petroleum ether gave **16** as an analytically pure sirup (0.095 g.): $[\alpha]^{20}D$ +73.2 ± 1.5° (1.4%); λ_{max} 6.24 (C=C), 7.42, 8.52 (sulfonamide), 12.95, 13.25, and 14.1–14.3 μ (phenyl), no absorption at 3.0 μ (NH).

Anal. Calcd. for $C_{23}H_{29}NO_7S$ (463.6): C, 59.60; H, 6.30; N, 3.02; S, 6.92. Found: C, 59.36; H, 6.36; N, 3.06; S, 6.87.

B.—The product (**15**) (0.020 g.) from the treatment of **9** with sodium methoxide was methylated as in method A to give a sirup (0.020 g.) which gave an infrared spectrum and R_f (0.83) identical with that for **16** prepared above. The optical rotation was $[\alpha]^{20}D$ +70.1 ± 1.1° (1.1%).

The mobility on t.l.c. of authentic **16** from A and **16** from B was identical, R_f 0.82.

Methyl 4,6-*O*-Benzylidene-3-deoxy-3-(*p*-tolylsulfonamido)-α-D-glucopyranoside (17).—To a solution of **10** (0.141 g., 0.5 mmole) in pyridine (5 ml.) containing triethylamine (0.070 ml.,

(23) Melting points were taken with a Fisher-Johns melting block and those below 230° are corrected. Infrared spectra were determined in KBr disks, unless otherwise indicated, with a Perkin-Elmer Model 137B spectrophotometer. Optical rotations were determined in *N*,*N*-dimethylformamide, unless otherwise stated, in a 1-dm. microtube, and concentrations are indicated in grams per 100 ml. as per cent. Petroleum ether used throughout was a fraction of b.p. 30–60°. Thin layer chromatography (t.l.c.) was done with silica gel G using chloroform–acetone (4:1 by volume) as the solvent system; the compounds were detected by exposing the plates to iodine vapor, and the relative proportions of the components were estimated visually. Chloroform extracts were dried over anhydrous magnesium sulfate. All solutions were concentrated by spin evaporation at 60–70° under reduced pressure (aspirator) unless otherwise indicated. Whenever pyridine was employed in a reaction, the residual pyridine in the chloroform extract was always removed by repeated spin evaporation of toluene until the odor of pyridine was absent.

0.5 mmole) was added tosyl chloride (0.114 g., 0.6 mmole). The solution was kept at room temperature for 1.25 hr. and was then poured onto crushed ice (25 g.). The aqueous solution was extracted with chloroform (three 10-ml. portions) and the combined chloroform solutions were washed with water (two 5-ml. portions), dried, and concentrated to afford crude **17** as a yellow crystalline solid (0.190 g., 87%). Decolorization of the solid in ethanol gave a pale yellow solid which was triturated with ethyl acetate to give **17** (0.100 g., 46%), m.p. 270–275°. Recrystallization from chloroform–petroleum ether furnished the analytical sample: m.p. 268–270°; λ_{max} 2.90, 3.06, (OH, NH), 7.50, 8.60 (sulfonamide), 13.35, and 13.90 μ (phenyl).

Anal. Calcd. for $C_{21}H_{25}NO_7S$ (435.5): C, 57.92; H, 5.79; N, 3.22; S, 7.36. Found: C, 58.04; H, 5.74; N, 3.40; S, 7.19.

Methyl 4,6-*O*-Benzylidene-3-deoxy-3-*O*-methyl-3-methylamino-*N*-(*p*-tolylsulfonyl)-α-D-glucopyranoside (18).—A solution of **17** (0.040 g.) in *N,N*-dimethylformamide was methylated as described for **16** to give a sirup (0.040 g.). After decolorization in ethanol, concentration afforded a friable glass (0.036 g., 85%), $[\alpha]^{20}D$ +25.2 ± 1.3° (1.06%). Upon drying *in vacuo* the glass crystallized to give, after trituration with ethyl acetate–petroleum ether, **18** as short needles: m.p. 166–167°; λ_{max} 7.51, 8.61 (sulfonamide), 13.14, 13.90, 14.39, and 14.70 μ (phenyl).

Anal. Calcd. for $C_{23}H_{29}NO_7S$: C, 59.60; H, 6.30; N, 3.02; S, 6.92. Found: C, 59.75; H, 6.50; N, 2.85; S, 6.59.

T.l.c. of **18**, R_f 0.68, and of **16**, R_f 0.82, showed them to be clearly isomeric.

Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-2,3-imino-α-D-mannopyranoside (13).—A suspension of methyl 4,6-*O*-benzylidene-2-cyanamido-2-deoxy-*N*-(*p*-tolylsulfonamido)-3-*O*-(*p*-tolylsulfonyl)-α-D-altropyranoside (19)[9] (1.228 g., 2.0 mmoles) in ethanol (12.5 ml.) and 0.4 *N* aqueous sodium hydroxide (12.5 ml.) was heated on the steam bath for 2.25 hr. The solution then was cooled, neutralized with carbon dioxide, and extracted with chloroform (four 15-ml. portions). The combined chloroform solutions were washed with water (three 10-ml. portions), dried, and concentrated to give a crystalline residue (0.623 g.). Dissolution of the residue in refluxing ethyl acetate (7 ml.) followed by slow cooling to room temperature afforded a crystalline product. The mixture was diluted with petroleum ether (10 ml.) and filtered to give fine needles (0.278 g.), m.p. 139–175°. The needles were chromatographed in two runs on silicic acid (20 g. of 60–200 mesh, 1 × 34 cm. column) using chloroform–acetone (4:1, v./v.), followed by acetone, as the eluents. In order of elution, methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside,[24] m.p. 198–200° (0.082 g.), methyl 4,6-*O*-benzylidene-*N*-carbamoyl-2,3-dideoxy-2,3-imino-α-D-mannopyranoside[9] (**20a**), m.p. 203–205° (0.141 g., 23%), and **13**, m.p. 140–142° (0.045 g., 9%), were thereby isolated as crystalline compounds.

Analysis by t.l.c. of the glass (0.330 g.) obtained from the filtrate from the 0.278 g. showed it to be a mixture of **13** and the 2,3-anhydro-D-allopyranoside in an approximate ratio of 20:1, respectively. Crystallization from ethyl acetate–petroleum ether gave **13** (0.250 g., 48%): m.p. 135–137°; λ_{max} 3.00 (NH), 7.20 (CH, sharp), 12.10 (NH), 13.26, and 14.36 μ (phenyl) (lit.[4] m.p. 145–146°).

Conversion of **13** to its highly crystalline *N*-acetyl derivative **20b** was performed by allowing a solution of **13** (0.050 g., 0.19 mmoles) in pyridine (1 ml.) containing acetic anhydride (0.12 ml. to stand 1 hr. at room temperature. Concentration gave a crystalline residue which was twice recrystallized from ethanol to give pure **20b** (0.043 g., 72%): m.p. 209–211°; λ_{max} 5.89 (amide I), 7.80 (amide III), 13.21, and 14.36 μ (phenyl), no absorption at 3.0 (NH) or at 6.3 μ (amide II) (lit. m.p. 205–206°,[4a] 211–212°[4b]).

Refluxing a solution of **19** (0.400 g.) in aqueous 0.2 *N* sodium hydroxide (20 ml.) for 2 hr. gave a sirupy product containing **13** and unhydrolyzed **19**, the latter presumably because of its insolubility in the medium. Further hydrolysis of this mixture for 2 hr. in a refluxing solution of 0.2 *N* sodium with 50% aqueous ethanol as the solvent gave **13**, m.p. 140–141°, in 73% yield.

(24) This anhydro derivative undoubtedly arises from incomplete ammonolysis during the preparation of **8**.[9]

Synthetic Nucleosides. LXVIII. Studies on the Synthesis of *cis*-2,3-Diamino Sugars. VIII. Derivatives of 2,3-Diamino-2,3-dideoxy-D-ribose and 2,3-Dideoxy-2,3-imino-D-ribose[1a,b]

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The *N*-methanesulfonyl derivative (**3**) of methyl 3-amino-3-deoxy-2,5-di-*O*-methanesulfonyl-β-D-arabinofuranoside (**13b**) undergoes cyclization in aqueous sodium hydroxide or with sodium acetate in hot *N,N*-dimethylformamide to give methyl 2,3-dideoxy-2,3-imino-*N*-methanesulfonyl-5-*O*-methanesulfonyl-β-D-ribofuranoside (**4**). The cyclization of methyl 3-deoxy-2,5-di-*O*-methanesulfonyl-3-(3-phenylureido)-β-D-arabinofuranoside (**15b**) was also investigated.

Neighboring group reactions have been of considerable utility in achieving synthesis of *cis*-substituted sugars.[2] The success of these facile reactions suggested that neighboring groups, suitably substituted with a nitrogen function, would lead to a convenient synthesis of *cis*-2,3-diamino sugars.[3a] Earlier papers[1a,3,4] in this series have described the synthesis and reactions of the nitroguanidino, thioureido, ureido, and guanidino derivatives of 2- and 3-amino-D-altrose and 2- and 3-amino-D-glucose. In these studies the synthesis of several *cis*-2,3-diamino derivatives of D-allose and D-mannose[3c,d,4a] has been achieved.[5] In addition, when the nucleopholic neighboring group was *trans*-diaxial to the adjacent sulfonate ester and contained a hydrogen on the secondary nitrogen atom, aziridines were formed in strongly basic media.[1a,3,4a] As a continuation of these studies it was of interest to examine the cyclization reactions of selected derivatives of methyl 3-amino-3-deoxy-β-D-arabinofuranoside. These studies are described in this paper.

(1) (a) For the previous paper in this series, see B. R. Baker and T. L. Hullar, *J. Org. Chem.*, **30**, 4049 (1965). (b) This research was supported in part by Grant CY-5845, National Cancer Institute, U. S. Public Health Service. (c) National Science Foundation Postdoctoral Fellow, 1963–1964.

(2) (a) B. R. Baker and R. E. Schaub, *J. Org. Chem.*, **19**, 646 (1954), and subsequent papers; (b) R. W. Jeanloz and D. Jeanloz, *ibid.*, **26**, 537 (1961), and previous papers.

(3) (a) B. R. Baker and T. Neilson, *ibid.*, **29**, 1047 (1964); (b) *ibid.*, **29**, 1051 (1964); (c) *ibid.*, **29**, 1057 (1964); (d) *ibid.*, **29**, 1063 (1964).

(4) (a) B. R. Baker and T. L. Hullar, *ibid.*, **30**, 4038 (1965); (b) B. R. Baker and T. L. Hullar, *ibid.*, **30**, 4045 (1965).

(5) Nucleophilic displacement of sulfonate ion by azide ion followed by reduction of the azide has also furnished *cis*-diamino sugars.[6]

(6) (a) R. D. Guthrie and D. Murphy, *J. Chem. Soc.*, 5288 (1963); (b) W. Meyer zu Reckendorf, *Chem. Ber.*, **97**, 1275 (1964).