**Attempted Rearrangement of *p*-Toluidine.**—*p*-Toluidine (0.05 mole) and aluminum chloride (0.11 mole) were complexed, saturated with hydrogen chloride, and maintained at 127–133° for 24 hr. The mixture was poured carefully into an ice slurry of 40 g. of sodium hydroxide in water, and the amine was extracted with ether. Concentration of the ether solution gave a quantitative yield of crude amine which by g.l.c. analysis was at least 99% *p*-toluidine. The column for separation of *m*- and *p*-toluidine was 5% Bentone-34 and 0.5% XF-1150 at 160° and flow rate of 90 cc./min., attenuation 2. Retention time for *p*-toluidine was 279 sec., for *m*-toluidine 378 sec.

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# Synthetic Nucleosides. LXIII.[1,2] Synthesis and Reactions of Some α-Sulfonyloxy Oxo Sugars

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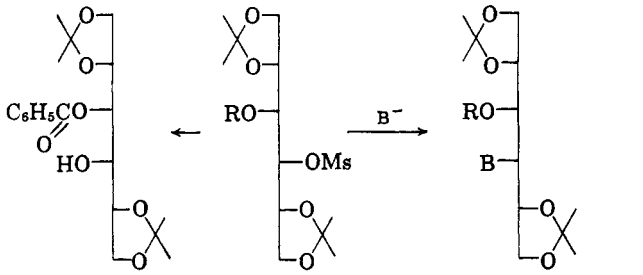
1,2:5,6-Di-O-isopropylidene-3-O-methanesulfonyl-D-mannitol (XVI) was smoothly oxidized to 1,2:5,6-di-O-isopropylidene-4-O-methanesulfonyl-D-*arabino*-3-hexulose (XVIII) in 74% yield by dicyclohexylcarbodiimide and phosphoric acid in dimethyl sulfoxide, the Pfitzner–Moffatt reagent. Similarly, methyl 4,6-O-benzylidene-2-O-(*p*-tolylsulfonyl)-α-D-glucopyranoside (XXVII) was oxidized to methyl 4,6-O-benzylidene-2-O-(*p*-tolylsulfonyl)-α-D-*ribo*-hexopyranosid-3-ulose (XXIX) in 80% yield. Reduction of XXIX by sodium borohydride proceeded by equatorial attack to give methyl 4,6-O-benzylidene-2-O-(*p*-tolylsulfonyl)-α-D-allopyranoside (XXXIIIa) in 92% yield. The sulfonate group of XXXIIIa was removed by O–S cleavage with either sodium methoxide or lithium aluminum hydride to give methyl 4,6-O-benzylidene-α-D-allopyranoside (XXXIV) in 72% yield, thus making this blocked D-allose derivative readily available for other transformations.

Bimolecular displacement reactions with sugar sulfonates are easiest when the sulfonate is on a primary hydroxyl[3,4]; displacement is more difficult at secondary positions on a pyranoside.[5,6] In earlier papers from this laboratory it was shown that open-chain hexitols such as II would undergo displacement if the nucleophile were sufficiently active; for example II could be converted to the azido hexitol (IV) with azide in N,N-dimethylformamide.[7] However, with the weakly nucleophilic fluoride ion, V was not formed, but the product was I formed *via* an ortho ester ion derived from the O-benzoate.[3] When the nonparticipating tetrahydropyranyl blocking group was employed, as in III, displacement of the sulfonate with azide became slower, but an azido derivative (VI) was still obtained[8]; however, displacement of the sulfonate of III with fluoride ion to give VII failed to take place below decomposition conditions.




I II, R = $C_6H_5CO$ IV, B = $N_3$; R = $C_6H_5CO$

V, B = F; R = $C_6H_5CO$

III, R = 

VI, B = $N_3$; R = 

VII, B = F; R = 

If a displacement reaction of a hexitol methanesulfonate by fluoride ion was to be successful, it was clear that a more activated methanesulfonate would be required as a leaving group; such a more active system would be the oxo-α-methanesulfonate XVIII. Sugihara and Yuen[9] have successfully oxidized the monobenzoyl-D-mannitol derivative (X) to the oxo sugar VIII with chromium trioxide in pyridine; that the benzoyloxy group of VIII had not epimerized was clearly demonstrated by their reduction of VIII with lithium aluminum hydride to the mannitol (IX) and altritol (XI) derivatives.

A study of the oxidation of the monomesyl mannitol (XVI)[8] with the chromium trioxide–pyridine reagent under various conditions gave 0–5% yields of a crystalline oxo mesylate which could have structure XVIII or XIX; in contrast, the previously described[9] oxidation of the monobenzoylmannitol X was readily duplicated. Attempts to debenzoylate VIII to the ketol XII with cold methanolic sodium methoxide or ammonia apparently gave an equilibrated mixture of isomers since none of the D-*arabino*-3-hexulose monobenzoate (VIII) could be reisolated after rebenzoylation, nor could a crystalline oxo mesylate (XVIII or

(1) This work was generously supported by Grant CA-05845 from the National Cancer Institute, U. S. Public Health Service. The authors also wish to thank Starks Associates, Inc., and the Cancer Chemotherapy National Service Center, National Cancer Institute, for large-scale preparation of some intermediates mediated by Contract No. SA-43-ph4346.

(2) For the previous paper of this series, see B. R. Baker, R. Harrison, and A. H. Haines, *J. Org. Chem.*, **29**, 1068 (1964).

(3) B. R. Baker and A. H. Haines, *J. Org. Chem.*, **28**, 438 (1963), paper LIV of this series.

(4) R. S. Tipson, *Advan. Carbohydrate Chem.*, **8**, 107 (1953).

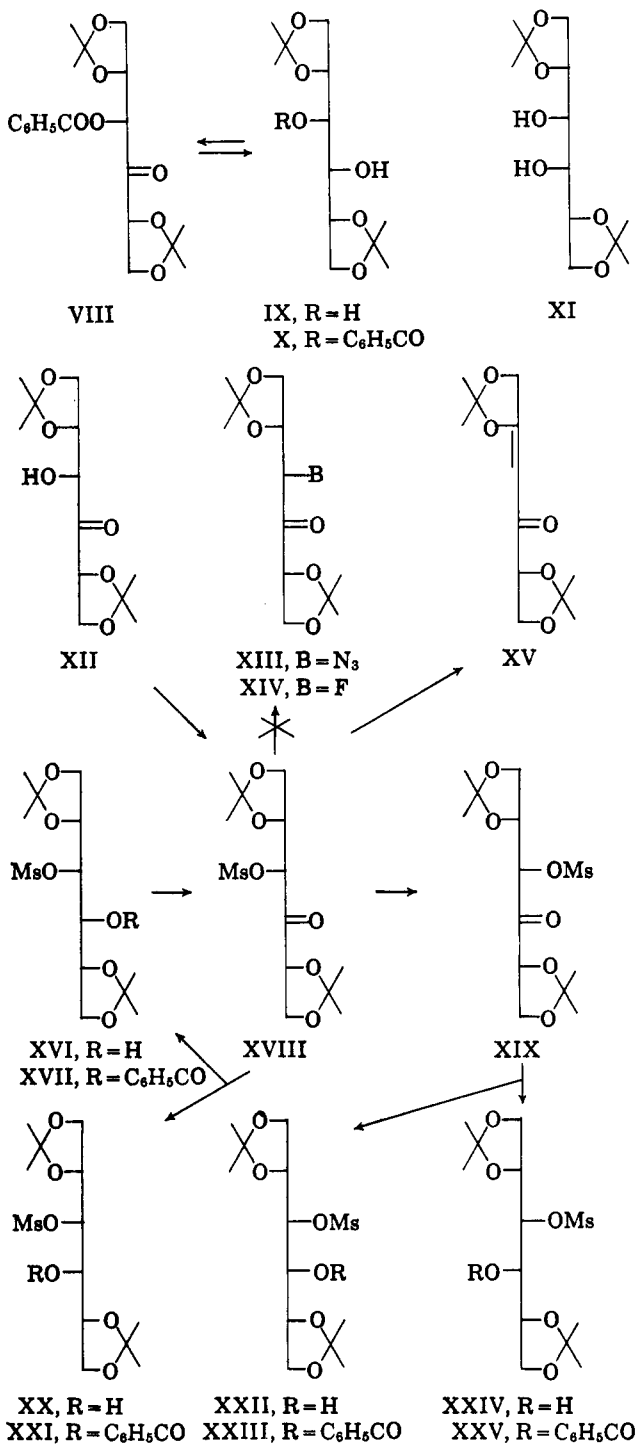
(5) (a) E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **24**, 1618 (1959); (b) E. J. Reist, R. R. Spencer, B. R. Baker, and L. Goodman, *Chem. Ind.* (London), 1794 (1962); (c) E. J. Reist, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 5775 (1958); (d) R. D. Guthrie and D. Murphy, *Chem. Ind.* (London), 1473 (1962); (e) J. Hill, L. Hough, and A. C. Richardson, *Proc. Chem. Soc.*, 346 (1963); (f) W. Meyer zu Reckendorf, *Chem. Ber.*, **97**, 1275 (1964).

(6) C. L. Stevens and co-workers [*J. Am. Chem. Soc.*, **86**, 2937, 2939 (1964)] have used the methods devised in ref. 5a–c for synthesis of sugars and nucleosides related to amicetin.

(7) B. R. Baker and A. H. Haines, *J. Org. Chem.*, **28**, 442 (1963), paper LV.

(8) B. R. Baker and H. S. Sachdev, *ibid.*, **28**, 2132 (1963), paper LVI.

(9) J. M. Sugihara and G. U. Yuen, *J. Am. Chem. Soc.*, **79**, 5780 (1957).




XIX) be isolated by treatment of the debenzoylated products with methanesulfonyl chloride in pyridine.[10]

At this time, Pfitzner and Moffatt[11] reported their new oxidation method for primary or secondary alcohols using dicyclohexylcarbodiimide and anhydrous phosphoric acid in dimethyl sulfoxide; this reagent could apparently oxidize 5′-thymidylic acid to a ketone, although the product was too unstable to isolate.[12]

When the hexitol mesylate XVI was oxidized with the Pfitzner–Moffatt reagent, a 74% yield of crystalline oxo mesylate was obtained, providing the temperature of the reaction was not allowed to rise unduly; this crystalline oxo mesylate could have either structure XVIII or XIX, depending upon whether or not epimerization of the adjacent mesylate had taken place. That this oxo mesylate was different from the oxo mesylate obtained earlier by chromium trioxide–pyridine oxidation was not completely ascertained, although the two samples showed different infrared spectra and both were obtained analytically pure.

That the oxo mesylate obtained by the Pfitzner–Moffatt reagent had structure XVIII and had not inverted to XIX was determined by sodium borohydride reduction, followed by benzoylation of the resultant hydroxyl group; reduction of XVIII would give after benzoylation, XVII and XXI, whereas reduction of XIX would give XXIII and XXV. Thin layer chromatography showed the presence of two products, presumably two isomeric benzoates. These benzoates were separated by chromatography on silica gel with chloroform–acetone (97:3). The faster moving benzoate crystallized and was identical with the previously known isomer of D-*manno* configuration (XVII),[3] thus establishing structure XVIII; the slower moving benzoate, presumably XXI, was an oil that could not be crystallized.

Azide ion was selected for the initial study of the nucleophilic displacement of the sulfonate group of the ketone XVIII since, if the reaction were not successful, it could hardly be expected that the poorly nucleophilic fluoride ion would do better. The reaction of XVIII with sodium azide in N,N-dimethylformamide at room temperature was followed by thin layer chromatography of aliquots removed at appropriate time intervals; after 19 hr., all of the XVIII had reacted. Thin layer chromatography after work-up showed the presence of several products. The crude material no longer contained a sulfonate bond in the infrared near 1180 cm.$^{-1}$ and showed bands due to both azide (2125 cm.$^{-1}$) and carbonyl (1725 cm.$^{-1}$) which might be assigned to the expected azido ketone XIII; the pure azide could not be isolated. A side reaction here could be elimination of the sulfonate group to give the unsaturated hexitol XV which could be expected to be quite unstable to both acid and base since it contains an enol ether group vinylogous to the ketone.

The successful oxidation of the hexitol mesylate (XVI) to the oxo mesylate (XVIII), coupled with the complexity of the displacement reaction to XIII, suggests that some furanose or pyranose ring systems be studied under similar conditions. One of the most readily available compounds for study was methyl 4,6-O-benzylidene-2-O-(*p*-tolylsulfonyl)-α-D-glucopyanoside (XXVII) which can be prepared in excellent yield by selective tosylation of the commercially available XXVI.[13] Oxidation of XXVII with the Pfitzner–Moffatt reagent gave a crystalline oxo sulfonate in 80% yield; although one might anticipate that the oxo sulfonate would have the D-*ribo* configuration (XXIX) which would place the sulfonate in the more stable equatorial conformation, it was necessary to distinguish this compound from the less likely D-*arabino* configuration (XXXI) with an axial sulfonate group. It was

(10) The exploratory experiments described in this paragraph were performed by Dr. H. S. Sachdev and Dr. R. Harrison in this laboratory.

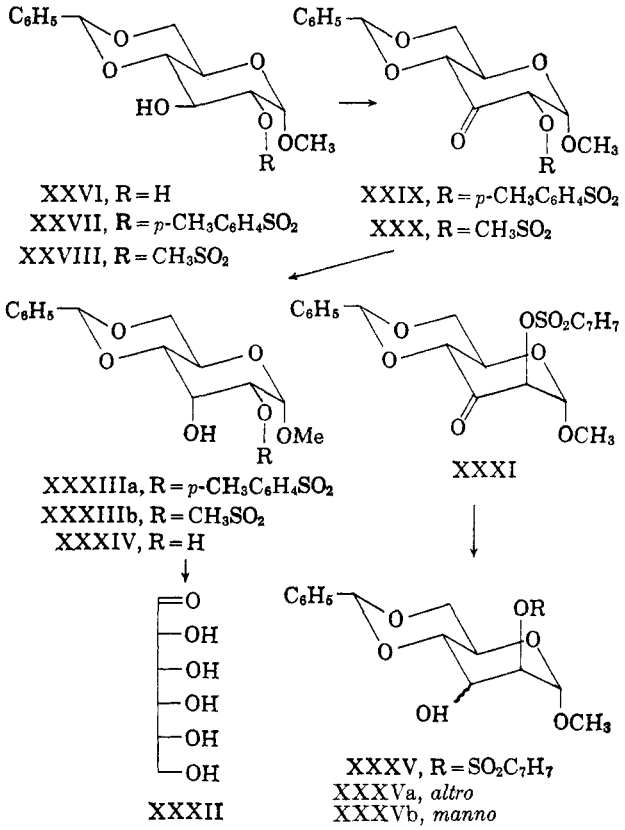
(11) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **85**, 3027 (1963).

(12) A mechanistically similar oxidation method with dimethyl sulfoxide *via* chloroformic esters has been devised by D. H. R. Barton, J. Garner, and R. H. Wightman [*J. Chem. Soc.*, 1855 (1964)] to convert alcohols to ketones.

(13) G. J. Robertson and C. F. Griffith, *ibid.*, 1193 (1935).

also possible, but unlikely, that the C-4 group could epimerize to the axial conformation.

Reduction of the oxo sulfonate with sodium borohydride occurred virtually stereospecifically in 92% yield to a single hydroxy sulfonate which could have any one of four configurations, namely D-*gluco* (XXVII), D-*altro* (XXXVa), D-*manno* (XXXVb), and D-*allo* (XXXIIIa), providing epimerization at C-4 had not occurred. The D-*allo* configuration was considered the most probable since the oxidation product would be expected to have an equatorial sulfonate (XXIX)




and reduction of the oxo group of XXIX was considerably less hindered to equatorial attack by borohydride ion to give an axial hydroxyl (XXXIIIa), than axial attack by borohydride to give an equatorial hydroxyl (XXVII). That the hydroxyl and sulfonate groups were *cis* (either XXXIIIa or XXXVb) was shown by lack of formation of a 2,3-*anhydro* derivative when treated with methanolic sodium methoxide; in fact, this reagent gave O–S cleavage with generation of a crystalline *cis*-glycol.

Since it was remotely possible that epimerization may have occurred at C-4 during oxidation to the ketone XXIX, actually eight different methyl 4,6-O-benzylidine-α-D-hexopyranosides had to be considered before evidence for a *cis*-glycol had been obtained. All but the *allo* (XXXIV) and *talo* isomers are known compounds.[14] Since the glycol isolated had different properties from those reported for five of the six isomers, this narrowed the possibilities down to the *galacto*, *talo*, and *allo* (XXXIV) configurations; the *galacto* was unlikely since its C-3 and C-2 hydroxyls are *trans*. That the *allo* configuration was unequivocally correct was shown by acid hydrolysis of XXXIV to D-allose which was identical with an authentic sample, thus establishing that XXIX had an equatorial sulfonate and that borohydride reduction proceeded by equatorial attack to give an axial hydroxyl in XXXIIIa.[15]

This four-step conversion of methyl 4,6-O-benzylidene-α-D-glucopyranoside (XXVI) to methyl 4,6-O-benzylidene-α-D-allopyranoside (XXXIV) proceeds in good over-all yield and is relatively simple to perform, thus making XXXIIIa and XXXIV available for further transformations on the 2- and 3-hydroxyls of D-allose such as preparation of the mono- and dimethyl ethers at O-2 and O-3; in addition further transformations could be performed at O-4 or O-6 to give derivatives related to mycinose.

Similarly, the 2-O-mesyl derivative (XXVIII) of methyl 4,6-O-benzylidene-α-D-glucopyranoside was converted to methyl 4,6-O-benzylidene-α-D-allopyranoside (XXXIV) *via* the crystalline oxo mesylate (XXX) and XXXIIIb; the over-all yield was somewhat lower than with the 2-O-tosyl blocking group.

Careful time studies were done on attempted displacement of the sulfonate group of the oxo α-sulfonate XXIX with sodium, lithium, or ammonium azide in N,N-dimethylformamide or with sodium azide in dimethyl sulfoxide, methyl ethyl ketone, methanol, or 2-methoxyethanol; disappearance of starting material was followed by thin layer chromatography. When the reactions were essentially complete, a number of products were formed. When the reaction was run in N,N-dimethylformamide, no sulfonate bands were present in the crude product, but the azide band at 2120 cm.$^{-1}$ was strong; a strong, wide band near 1640–1625 cm.$^{-1}$ along with a shift to longer wave length in base in the ultraviolet indicated the possibility of the presence of a chelated 1,3-dicarbonyl system. Apparently, a serious side reaction is again the *trans* elimination of the tosylate with the C-1 proton; since a β-glycoside with a hydrogen *cis* to the tosylate at C-2 would be less likely to undergo elimination, such a system would be worthy of trial in displacement reactions. The pure azide could not be isolated.

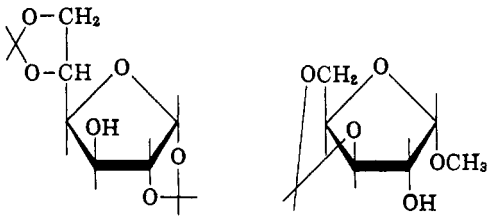
The oxidations of three other sugar derivatives (XXXVI–XXXVIII) by the Pfitzner–Moffatt reagent were investigated; under the standard conditions at room temperature, little oxidation took place as shown by the lack of carbonyl absorption in the infrared in the crude products. It should be noted that, in each case, XXXVI, XXXVII, and XXXVIII have the open hydroxyl group flanked by ether or acetal groups which would decrease the ability of the adjacent C–H bond to break during oxidation and would also hinder the approach of the oxidant. It is also interesting to note that dicyclohexylurea forms rapidly with the Pfitzner–Moffatt reagent; if the reaction is stopped at this early point, then no ketone such as XXIX is obtained, indicating that an intermediate is rapidly formed which

(14) For methyl 4,6-O-benzylidene-α-D-altroside and -D-glucoside, see N. K. Richtmyer and C. S. Hudson, *J. Am. Chem. Soc.*, **63**, 1727 (1941). For the D-idoside and D-galactoside, see E. Sorkin and T. Reichstein, *Helv. Chim. Acta*, **28**, 1 (1945). The D-guloside has been reported by H. G. Fletcher, Jr., H. W. Diehl, and R. K. Ness, *J. Am. Chem. Soc.*, **76**, 3029 (1954), and the D-mannoside by G. J. Robertson, *J. Chem. Soc.*, 330 (1934).

(15) The equatorial attack of a 3-oxo group in pyranosides by borohydride to give an axial hydroxyl group has been previously observed: see ref. 16 and 17.

(16) O. Theander, *Advan. Carbohydrate Chem.*, **17**, 223 (1962).

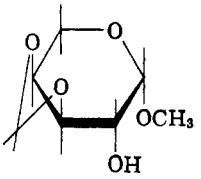
(17) E. E. Grebner, R. Durbin, and D. S. Feingold, *Nature*, **201**, 419 (1964).



XXXVI



XXXVII



XXXVIII

then undergoes a slower oxidation step. In the cases of XXXVI–XXXVIII, dicyclohexylurea forms rapidly, indicating the intermediate has formed, but oxidation of the intermediate by dimethyl sulfoxide does not take place at room temperature.

Of both practical and theoretical interest is that α-sulfonoxy ketones such as XVIII can be prepared by oxidation of a glycol monosulfonate such as XVI in view of the fact that dimethyl sulfoxide can also convert a sulfonate function to a ketone.[18] It is obvious that whatever intermediate is first formed by the Pfitzner–Moffatt reagent, it is more easily oxidized to a ketone than the sulfonate function; any mechanism proposed for oxidation should consider this important factor. Pfitzner and Moffatt[11] have indicated that they are working on the mechanism of this uniquely mild oxidative method and publication of their results is eagerly awaited. It is clear that, even though the Pfitzner–Moffatt reagent has certain limitations, it will take its place among the useful new synthetic methods developed in recent years that are based on dimethyl sulfoxide chemistry. Of course, other oxidizing agents have been used in the carbohydrate area with varying amounts of success, such as chromium trioxide–pyridine,[9,19] chromium trioxide–acetic acid,[20] chromium trioxide–pyridine–acetic acid,[16] chromium trioxide in acetone,[16] ruthenium tetroxide,[21] platinum–oxygen,[22] specific microbiological oxidations,[16,17,23] and mercuric acetate.[24] Each agent may have its own special utility, but the Pfitzner–Moffatt reagent may be one of the most general.

## Experimental[25]

**1,2:5,6-Di-O-isopropylidene-4-O-methanesulfonyl-D-*arabino*-3-hexulose (XVIII).**—To a stirred solution of 1.97 g. (5.78 mmoles) of XVI[8] in 30 ml. of dimethyl sulfoxide was added 4.12 g. (20.0 mmoles) of dicyclohexylcarbodiimide. While the temperature was maintained at 25–30° with cooling, 1.5 ml. (28.6 mmoles) of anhydrous orthophosphoric acid was added dropwise. After being stirred for 18 hr. in a stoppered flask, the mixture was filtered and the dicyclohexylurea was washed with a little dimethyl sulfoxide and acetone. The combined filtrate and washings were diluted with about 150 ml. of chloroform; about 150 ml. of water was then added, and the pH was brought to about 8 with 2.4 *M* aqueous potassium carbonate. The solution was further extracted with four 50-ml. portions of chloroform, and the combined extracts were washed with water until neutral. Spin evaporation of the chloroform *in vacuo* afforded a crystalline residue.[26] Recrystallization from ethanol–petroleum ether gave 1.44 g. (74%) of white crystals, m.p. 99–102°. A second recrystallization gave white crystals: m.p. 100–102°; $[\alpha]^{25}D$ −8.8 ± 2°; $\nu_{max}$ 1735 (C=O), 1365, 1175 (sulfonate), 1070 cm.$^{-1}$ (C–O–C).

*Anal.* Calcd. for $C_{13}H_{22}O_8S$: C, 46.1; H, 6.55; S, 9.48. Found: C, 46.0; H, 6.52; S, 9.37.

Reduction of 68 mg. (0.20 mmole) of XVIII in 10 ml. of methanol with 50 mg. of sodium borohydride for 30 min. at ambient temperature, followed by benzoylation of the resultant mixture of carbinols (XVI and XX) with 0.1 ml. of benzoyl chloride in 5 ml. of pyridine for 14 hr. at room temperature, gave a mixture of XVII and XXI. This mixture was separated by chromatography on Brinkmann silica gel $GF_{254}$ using chloroform–acetone (97:3) as the eluting solvent. Crystallization of the faster moving component from ethanol–water gave white needles of XVII, m.p. 70–74°, that had an infrared spectrum identical with that of XVII[3] and moved identically with XVII on thin layer chromatograms with either chloroform–acetone (24:1) or chloroform–ether (1:1).

**Methyl 4,6-O-Benzylidene-2-O-(*p*-tolylsulfonyl)-α-D-*ribo*-hexopyranosid-3-ulose (XXIX).**—A solution of 4.67 g. (10.7 mmoles) of XXVII[13] in 150 ml. of dimethyl sulfoxide containing 7.74 g. (37.5 mmoles) of dicyclohexylcarbodiimide was treated with 0.29 ml. (5.53 mmoles) of anhydrous orthophosphoric acid as described for the preparation of XVIII. Two recrystallizations[26] from ethanol gave 3.71 g. (80%) of white needles: m.p. 165–167°; $[\alpha]^{25}D$ +44.9 ± 0.9°; $\nu_{max}$ 1765 (C=O), 1600, 1365, 1175 (sulfonate), 1110, 1085, 1060 (C–O–C), 755, 710, 700 cm.$^{-1}$ ($C_6H_5$).

*Anal.* Calcd. for $C_{21}H_{22}O_8S$: C, 58.1; H, 5.10; S, 7.38. Found: C, 57.9; H, 5.07; S, 7.54.

**Methyl 4,6-O-Benzylidene-2-O-methanesulfonyl-α-D-*ribo*-hexopyranosid-3-ulose (XXX).**—Oxidation of 395 mg. (1.10 mmoles) of XXVIII[27] with 0.040 ml. of orthophosphoric acid (0.76 mmole), as described for the preparation of XXIX, gave, after recrystallization[26] from ethanol, 226 mg. (58%) of white plates: m.p. 181–183°; $[\alpha]^{25}D$ +40.1 ± 0.8°; $\nu_{max}$ 1760 (C=O), 1345, 1170 ($SO_2$), 1130, 1115, 1090, 1070 (C–O–C), 763, 702 cm.$^{-1}$ ($C_6H_5$).

*Anal.* Calcd. for $C_{15}H_{18}O_8S$: C, 49.9; H, 5.59; S, 8.90. Found: C, 50.1; H, 5.21; S, 8.91.

**Methyl 4,6-O-Benzylidene-2-O-(*p*-tolylsulfonyl)-α-D-allopyranoside (XXXIIIa).**—To a solution of 668 mg. (1.5V mmoles) of XXIX in 4 ml. of N,N-dimethylformamide was added 100 ml. of methanol; then about 1 g. of sodium borohydride was added in portions. After 30 min. at ambient temperature, the mixture was warmed to the boiling point, then spin evaporated *in vacuo*. The residue was partitioned between chloroform and water. The aqueous layer was thoroughly extracted with chloroform and the combined extracts were washed with water, then spin evaporated *in vacuo*. The product crystallized from absolute ethanol–petroleum ether. Recrystallization from the same solvent pair gave 615 mg. (92%) of white needles: m.p. 166–167°; $[\alpha]^{25}D$ +35.6 ± 0.7°; $\nu_{max}$ 3650, 3500 (OH), 1595,

(18) (a) N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, *J. Am. Chem. Soc.*, **79**, 6562 (1957); (b) N. Kornblum, W. J. Jones, and G. J. Anderson, *ibid.*, **81**, 4113 (1959).

(19) W. G. Overend, *Chem. Ind.* (London), 342 (1963); it is unfortunate that this group has yet to publish any experimental details; we have not been able to duplicate their work.

(20) (a) W. R. Sullivan, *J. Am. Chem. Soc.*, **67**, 837 (1945); (b) D. H. Rammler and C. A. Dekker, *J. Org. Chem.*, **26**, 4615 (1961).

(21) P. J. Beynon, P. M. Collins, and W. G. Overend, *Proc. Chem. Soc.*, 342 (1964).

(22) K. Heyns and H. Paulsen, *Advan. Carbohydrate Chem.*, **17**, 169 (1962).

(23) J. Staněk, M. Černý, J. Kocourek, and J. Pacak, "The Monosaccharides," Academic Press Inc., New York, N. Y., 1963, pp. 496, 632, 723.

(24) R. J. Stoodley, *Can. J. Chem.*, **39**, 2593 (1961).

(25) Melting points were taken in capillary tubes in a Mel-Temp block and those below 230° are corrected. Infrared spectra were determined in Nujol mull with a Perkin-Elmer 137B spectrophotometer. Thin layer chromatograms were run with Brinkmann silica gel G. All optical rotations were determined in N,N-dimethylformamide with a 1-dm. microtube. Petroleum ether used for recrystallization was a fraction boiling at 40–60°.

(26) If the chloroform residue still contained dicyclohexylurea, as shown by urea absorption at 1625, 1575, and 1530, or absorption at 895 cm.$^{-1}$, or t.l.c., the product was dissolved in warm acetone; the solution was filtered to remove the insoluble urea, evaporated *in vacuo*, then recrystallized to purity.

(27) R. W. Jeanloz and D. A. Jeanloz, *J. Am. Chem. Soc.*, **79**, 6257 (1957).

1360, 1172 (sulfonate), 1105 (C–O–C), 760, 720, 700 ($C_6H_5$), no C=O near 1765 cm.$^{-1}$.

*Anal.* Calcd. for $C_{21}H_{24}O_5S$: C, 57.8; H, 5.54; S, 7.34. Found: C, 57.7; H, 5.54; S, 7.30.

Similarly, reduction of 105 mg. (0.29 mmole) of XXX gave, after recrystallization from absolute ethanol–petroleum ether, 97 mg. (92%) of **methyl 4-6-O-benzylidene-2-O-mesyl-α,D-allopyranoside (XXXIIIb)** as white needles: m.p. 143–145°; $[\alpha]^{25}D$ +58.0 ± 1.5°; $\nu_{max}$ 3540 (OH), 1360, 1180 (sulfonate), 1130, 1110 (C–O–C), 755, 700 ($C_6H_5$), no C=O near 1760 cm.$^{-1}$.

*Anal.* Calcd. for $C_{15}H_{20}O_8S$: C, 50.0; H, 5.59; S, 8.90. Found: C, 50.1; H, 5.66; S, 8.77.

**Methyl 4,6-O-Benzylidene-α-D-allopyranoside (XXXIV).** **A.**—A mixture of 200 mg. of lithium aluminum hydride (5.3 mmoles), 427 mg. of XXXIIIa (0.98 mmole), and 30 ml. of dry tetrahydrofuran was refluxed with stirring; after 18 hr. an additional 200 mg. of lithium aluminum hydride was added, and the reaction was refluxed for an additional 25 hr. The excess hydride was decomposed by dropwise addition of ethanol; then water was added until the inorganics formed an insoluble cake. The mixture was filtered and the solids were washed with hot ethanol, then hot acetone. The combined filtrate and washings were spin evaporated *in vacuo*. Crystallization from ethanol–petroleum ether gave 199 mg. (72%) of thick needles, m.p. 174–178°. Recrystallization from the same solvent pair afforded white crystals: m.p. 175–177°; $[\alpha]^{25}D$ +117 ± 2°; $\nu_{max}$ 3500, 3450 (OH), 1120, 1095 (C–O–C), 745, 705 ($C_6H_5$), no sulfonate absorption near 1360 or 1180 cm.$^{-1}$.

*Anal.* Calcd. for $C_{14}H_{18}O_6$: C, 59.7; H, 6.44. Found: C, 59.7; H, 6.60.

Hydrolysis of 137 mg. of XXXIV with hot 1 *N* sulfuric acid gave, after work-up and recrystallization from 1 drop of water by addition of methanol and ethanol, white crystals of D-allose, m.p. 122–126°, that was identical with an authentic sample[28] by mixture melting point and by comparative infrared spectra.

**B.**—A solution of 63 mg. of XXXIIIa and 9.5 mg. of sodium methoxide in 0.75 ml. of methanol was refluxed for 5 hr., then diluted with several volumes of water. Unchanged XXXIII (18 mg., 29%) was removed by filtration. The combined filtrate and washings were extracted with three 10-ml. portions of chloroform. The combined extracts, after being washed with water, were spin evaporated *in vacuo;* yield 23 mg. (80%), m.p. 165–172°. The residue was dissolved in methanol and diluted with water. The trace of unchanged starting material was removed by filtration and the filtrate was evaporated *in vacuo*. Crystallization from absolute ethanol–petroleum ether gave pure XXXIV, m.p. 175–177°, that was identical with preparation A.

Neither methyl 2,3-anhydro-α-D-mannopyranoside nor methyl 2,3-anhydro-α-D-allopyranoside[13] could be detected by thin layer chromatography of the mother liquors. Although this reaction was run only once, it is probable that increasing the reaction time and quantities would give near quantitative yields.

**C.**—Lithium aluminum hydride cleavage of 37 mg. (0.10 mmole) of XXXIIIb, as described in preparation A, gave 16 mg. (55%) of product, m.p. 176–178°, that was identical with preparation A; in this case the oil remaining on spin evaporation was partitioned between water and chloroform prior to crystallization. The water-washed chloroform solution was then spin evaporated *in vacuo*, and the residue was recrystallized.

(28) This sample was kindly provided by Professor I. J. Goldstein of this university who, in turn, had obtained it from Dr. N. K. Richtmyer, National Institutes of Health, Bethesda, Md.

# Synthetic Nucleosides. LXIV.[1,2] Synthesis and Stereospecific Reduction of Some 2(3)-Acylamino-3(2)-oxopyranosides

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Oxidation of methyl 3-benzamido-4,6-O-benzylidene-3-deoxy-α-D-altropyranoside (Ia) and methyl 3-benzamido-4,6-O-benzylidene-3-deoxy-α-D-glucopyranoside (IVa) with phosphoric acid and dicyclohexylcarbodiimide in dimethyl sulfoxide—the Pfitzner–Moffatt reagent—gave the identical ketone, methyl 3-benzamido-4,6-O-benzylidene-3-deoxy-α-D-*arabino*-hexopyranosid-2-ulose (IIa) in 86 and 96% yields, respectively; the axial benzamido group of Ia, after oxidation of the hydroxyl to a ketone, was isomerized to the more stable equatorial configuration of IIa. Much lower yields, but similar results, were obtained with the corresponding 3-acetamido derivatives, Ib and IVb. Reduction of the two ketones with sodium borohydride proceeded virtually stereospecifically by axial attack to regenerate IVa and IVb. Oxidation of methyl 2-benzamido-4,6-O-benzylidene-2-deoxy-α-D-altropyranoside (Va) and methyl 2-benzamido-4,6-O-benzylidene-2-deoxy-α-D-glucopyranoside (XIa) gave the same ketone, methyl 2-benzamido-4,6-O-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose (VIa), in 83 and 95% yields, respectively; the benzamido group adjacent to the ketone again was equatorial, showing an isomerization of the benzamido group during oxidation of Va. Reduction of the ketone VIa with sodium borohydride proceeded virtually stereospecifically by equatorial attack to give methyl 2-benzamido-4,6-O-benzylidene-2-deoxy-α-D-allopyranoside with an axial hydroxyl at C-3. Similar results, but lower yields, were obtained with the corresponding acetamido sugars.

Oxidation of either primary or secondary sugar hydroxyl groups to ketones with phosphoric acid–dicyclohexylcarbodiimide–dimethyl sulfoxide, the Pfitzner–Moffatt reagent,[3] bears promise to take its place among the most useful in the carbohydrate area.[2,3] Its use for oxidizing sugar alcohols bearing an adjacent sulfonyloxy function has been described in the previous paper in this series.[2] In this paper are presented studies on the oxidation of some pyranosidic alcohols bearing an adjacent acylamido group with the Pfitzner–Moffatt reagent and the stereospecific reduction of the resultant ketones by sodium borohydride.

When either methyl 3-benzamido-4,6-O-benzylidene-3-deoxy-α-D-glucopyranoside (IVa)[4,5] or the corresponding altroside (Ia)[5,6] was oxidized with the Pfitzner–Moffatt reagent, the identical ketone was obtained in 96 and 86% yields, respectively; since it was more

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(2) Paper LXIII: B. R. Baker and D. H. Buss, *J. Org. Chem.*, **30**, 2304 (1965).

(3) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **85**, 3027 (1963).

(4) R. D. Guthrie and G. P. B. Mutter, *J. Chem. Soc.*, 1614 (1964).

(5) Methyl 3-amino-4,6-O-benzylidene-3-deoxy-α-D-altropyranoside and methyl 2-amino-4,6-O-benzylidene-2-deoxy-α-D-altropyranoside were prepared by the method of W. H. Myers and G. J. Robertson [*J. Am. Chem. Soc.*, **65**, 8 (1943)]; from the mother liquors of the latter, methyl 3-acetamido- or 3-benzamido-4,6-O-benzylidene-3-deoxy-α-D-glucopyranoside were obtained by selective N acylation.[6]

(6) D. H. Buss, L. Hough, and A. C. Richardson, *J. Chem. Soc.*, 5295 (1963).