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OXIDATION OF CARBOHYDRATES WITH METHYL SULFOXIDE CONTAINING PHOSPHORUS PENTAOXIDE

I. SYNTHESIS OF SOME ALDOSULOSES AND ALDOSIDULOSES*

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ABSTRACT

Methyl sulfoxide containing phosphorus pentaoxide oxidizes secondary alcohol groups of carbohydrates to ketones. Oxidation proceeds most efficiently with *N,N*-dimethylformamide as solvent and with 3–4 molar equivalents of methyl sulfoxide and 1.5–2.0 molar equivalents of phosphorus pentaoxide.

The following carbohydrates were oxidized to afford the corresponding aldosuloses and aldosiduloses in good or moderate yields: methyl 4,6-*O*-benzylidene-2-*O*-(*p*-tolylsulfonyl)-α-D-gluco- and allo-pyranoside (**1** and **18**), methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-gluco- and -allo-pyranoside (**3** and **19**), 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6**), 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylo- and -ribo-furanose (**11** and **13**), 1,2-*O*-isopropylidene-5-*O*-(di-*O*-phenylphosphono)-α-D-xylofuranose (**14**), and 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (**16**).

INTRODUCTION

In recent years, oxidation of "isolated" hydroxyl groups of carbohydrates has been achieved by different methods. The synthetic utility and biological significance of dicarbonyl carbohydrates has prompted a search for more effective and less expensive reagents for oxidation. Many new aldosuloses and aldosiduloses have been synthesized with such oxidants as chromium trioxide, platinum oxide, and ruthenium tetroxide, and have been used successfully in the preparation of amino, branched-chain, and rare sugars[1,2].

Since Kornblum *et al.*[3] reported the oxidation of simple alkyl toluene-*p*-sulfonates and halides with sulfoxides, several systems using sulfoxides, especially methyl sulfoxide, have been developed for oxidation of alcohols[4]. In 1963, an effective oxidation of alcohols to aldehydes and ketones under very mild conditions was described by Pfitzner and Moffatt[5], who used the methyl sulfoxide–*N,N*-dicyclohexylcarbodiimide (DCC) system. This system has proved to be of potential value in the carbohydrate field, as well as with other complex alcohols, such as steroids and alkaloids[6].

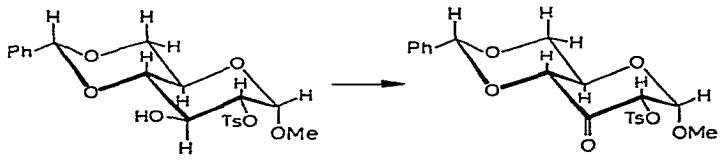
* A preliminary report of this work was given in Ref. 10.

In the course of our study on a polymerization reaction of reducing mono- and di-saccharides[7], we have found that methyl sulfoxide containing phosphorus pentaoxide rapidly oxidises the alcoholic groups of sugars at room temperature to give aldehydes, ketones, or carboxylic acids. The reaction of sulfoxides with phosphorus pentaoxide has been little investigated. Sekera *et al.*[8] used phosphorus pentaoxide in a reaction of sulfonamides with methyl sulfoxide, and Micheel *et al.*[9] suggested that phosphorus pentaoxide in methyl sulfoxide could be a polymerization reagent for reducing sugars, but no comment was made on the oxidation reaction of methyl sulfoxide. At about the time when the preliminary report of our results appeared[10], Albright and Goldman[11] reported that methyl sulfoxide–acid anhydride mixtures were effective for oxidation of alcohols. Since then, several papers have been published[12] on the application of the methyl sulfoxide–acid anhydride system to carbohydrates. In this paper, the synthesis of some aldosuloses and aldosiduloses, using methyl sulfoxide and phosphorus pentaoxide, is described.

RESULTS AND DISCUSSION

The stability of various protective groups and linkages commonly used in carbohydrate chemistry towards the present oxidant was first investigated, because of the previous report[13] that some new reactions of carboxylic acids and other organic compounds proceeded under the reaction conditions used for oxidation. The following, fully substituted carbohydrates were treated with methyl sulfoxide–phosphorus pentaoxide at room temperature: 7-(tetra-*O*-acetyl-β-D-glucopyranosyl)theophylline, 9-(tetra-*O*-acetyl-β-D-glucopyranosyl)-6-benzamidopurine, 2,4:3,5-di-*O*-benzylidene-D-xylose diethyl dithioacetal, phenyl tetra-*O*-acetyl-α-D-glucopyranoside, tri-*O*-acetyl-1,6-anhydro-β-D-glucopyranose, octa-*O*-acetylsucrose, tri-*O*-acetyl-4,6-*O*-benzylidene-D-glucopyranose, 1,2,5-tri-*O*-acetyl-D-glucurono-6,3-lactone, methyl 1,2,3,4-tetra-*O*-acetyl-D-glucuronate, penta-*O*-acetyl-α-D-glucopyranose, tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose, 1,2:3,4-di-*O*-isopropylidene-6-*O*-(*p*-tolylsulfonyl)-α-D-galactopyranose, 5-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone, methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranoside, 1,2,3-tri-*O*-acetyl-4,6-*O*-ethylidene-D-glucopyranose, and methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-dinitrate. The reactions were followed by thin-layer chromatography and by the change of optical rotation. It was found that all of these substances were stable to the oxidation conditions. However, two glycosylamines, *N*-*p*-tolyl-2,3,4-tri-*O*-benzoyl-L-arabinosylamine and *N*-*p*-tolyl-2,3,4,6-tetra-*O*-acetyl-D-glucopyranosylamine, underwent reaction. For example, the reaction mixture containing the latter compound became brown after 15 h at room temperature, and only 10% of the starting material was recovered; no further study of this reaction was made in the present work. From these results, it appears that sulfonyloxy, acetoxy, benzoyloxy, isopropylidene, benzylidene, ethylidene, methoxyl, nitrate, and acetamido groups, and glycosidic bonds involving nucleosidic, phenolic, alkyl, and thioacetal substituents are stable towards the oxidant. Consequently, carbohydrates having these protective groups can be safely employed in the synthesis of dicarbonyl sugars.

The optimal conditions for the oxidation of "isolated" secondary alcoholic groups of carbohydrates were evaluated by using methyl 4,6-*O*-benzylidene-2-*O*-(*p*-tolylsulfonyl)-α-D-glucopyranoside (**1**) as a model compound. Oxidation of this compound was first accomplished by Baker *et al.*[6c] with the methyl sulfoxide–DCC reagent. The oxidation was examined at different temperatures, with different proportions of phosphorus pentaoxide and methyl sulfoxide, and with different solvents and



1 2

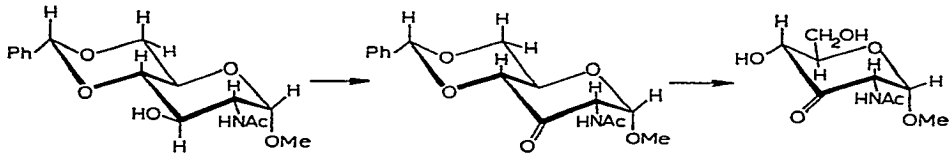
catalysts. The reaction products were easily isolated, and analyzed by n.m.r. spectroscopy and by thin-layer chromatography for the determination of the yield of the keto sugar. It was found that the crude reaction products contained only compounds **1** and **2**; no side reactions were observed. The maximal yield (85–92%) of compound **2** was obtained by treating one mole of reactant **1** with 3–4 moles of methyl sulfoxide and 1–1.5 moles of phosphorus pentaoxide (as P_4O_{10}) in *N*,*N*-dimethylformamide (DMF) for 1.5–2.0 h at 65–70°.

With methyl sulfoxide as solvent, oxidations were best performed at room temperature, since decomposition occurred at higher temperatures, resulting in a decreased yield. The use of too large an excess of phosphorus pentaoxide also decreased the yield of product. A catalytic amount of phosphorus pentaoxide was also ineffective. These results suggest that one mole of phosphorus pentaoxide per mole of alcohol and methyl sulfoxide participate in the oxidation. Other catalysts, such as zinc chloride, aluminium chloride, sulfur trioxide, arsenic oxides (As_2O_3, As_2O_5), antimony oxides (Sb_2O_3, Sb_2O_5), and *p*-toluenesulfonic acid, were all ineffective. Solvents other than methyl sulfoxide and DMF were not effective, and partial replacement of methyl sulfoxide and DMF by benzene or chloroform resulted in a marked decrease in the yield. After the completion of this work, Brimacombe *et al.*[12g] reported that oxidation of compound **1** with methyl sulfoxide–phosphorus pentaoxide gave a 49% yield of compound **2**.

The introduction of a ketonic function into amino sugars is of considerable synthetic utility, since it provides a route to isomeric, branched-chain, and di-amino sugars. Oxidation of compound **3** with methyl sulfoxide–phosphorus pentaoxide in DMF afforded (71% yield) the corresponding ketose (**4**), previously prepared from compound **3** by Baker *et al.*[6c] with the methyl sulfoxide–DCC reagent. Debenzylidenation of compound **4** with 60% acetic acid gave methyl 2-acetamido-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose (**5**).

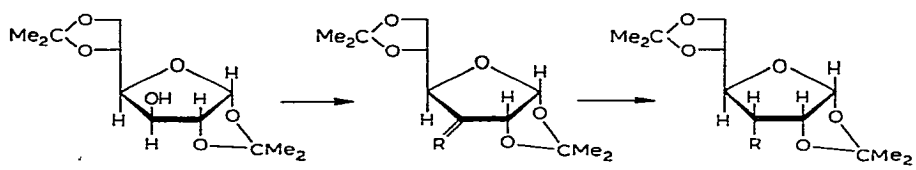
Isopropylidene acetals of carbohydrates have frequently been used in the synthesis of aldofuranosuloses, and typical examples are 1,2:5,6-di-*O*-isopropylidene-α-D-xylofuranose (**6**) and 1,2-*O*-isopropylidene-5-*O*-substituted-α-D-xylofuranose

(**11** and **14**), both of which have a dioxolane ring *cis*-fused to a furanoid ring, and an *exo*-hydroxyl group. The lability of the isopropylidene group towards acid, and the steric hindrance caused by the dioxolane ring have considerable effects on the reactivity of the hydroxyl groups. For example, attempts to oxidize



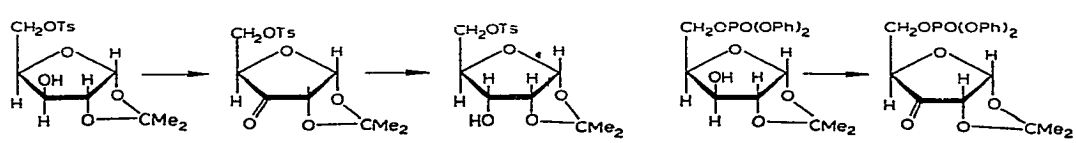
3 **4** **5**

compound **6** with chromium trioxide–pyridine, the Oppenauer reagent, and lead tetraacetate were reported to be ineffective[14]. Since D-*ribo*-hexos-3-ulose derivatives have been found as components of some microbial disaccharides[15], and have much synthetic value[16], the effective oxidation of compounds **6**, **11**, and **14** is of interest.



6 **7** R = O; **8** R = N—OH; **9** R = NH_2; **10** R = NHAc

Oxidation of compound **6** with two molar equivalents of phosphorus pentaoxide in methyl sulfoxide for 1.5–2 h at 60–65° or for 15 h at room temperature afforded 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose (**7**) in 65% yield; the latter oxidation conditions usually gave a better yield. The oxidation in DMF gave a 50–60% yield of product. The ketose, isolated as the hydrate, reacted with hydroxylamine, thiosemicarbazide, or semicarbazide. The *allo*-amine (**9**) was obtained by reduction of the crystalline oxime **8** with lithium aluminium hydride; the *gluco* isomer was not detected on paper chromatograms of the acid hydrolyzate of the crude amine. This result is in accordance with the published behaviour of 1,2-*O*-isopropylidene-α-D-*ribo*- or -*erythro*-aldofuranos-3-ulose on reduction with metal hydrides, which give exclusively, or mainly, α-D-*allo* or *ribo* derivatives[17–19]. Acetylation of the amine **9** gave 3-acetamido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (**10**). The facile oxidation of compound **6** is remarkable, since it is inert to the methyl sulfoxide–DCC reagent[6c], and no other oxidant, except ruthenium tetroxide[2], had been reported to be effective. The C-3 epimer of compound **6**, 1,2:5,6-di-*O*-isopropylidene-α-D-allo-

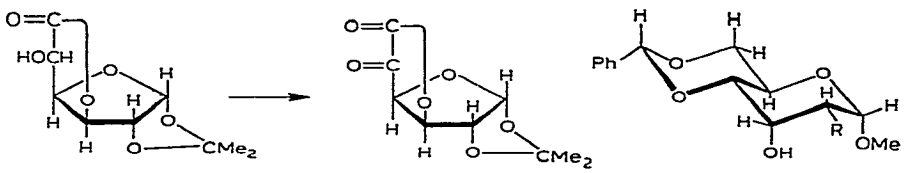


11 **12** **13** **14** **15**

furanose, is easily oxidized[19] catalytically over platinum oxide and with chromium trioxide–pyridine. The oxidation of compound **6** with acetic anhydride and methyl sulfoxide has recently been accomplished by Sowa and Thomas[12a].

Oxidation of 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylofuranose (**11**) and 1,2-*O*-isopropylidene-5-*O*-(di-*O*-phenylphosphono)-α-D-xylofuranose (**14**) was performed in DMF with three molar equivalents of methyl sulfoxide and one molar equivalent of phosphorus pentaoxide for 1–1.5 h at 60–65°. 1,2-*O*-Isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-*erythro*-pentofuranos-3-ulose (**12**) was obtained in 35% yield. Reduction of compound **12** with lithium aluminium hydride gave 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-ribofuranose (**13**). Similarly, 1,2-*O*-isopropylidene-5-*O*-(di-*O*-phenylphosphono)-α-D-*erythro*-pentofuranos-3-ulose (**15**) was obtained from compound **14** in 35% yield, and was characterized as the monohydrate and as the semicarbazone.

Oxidation of 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (**16**) with active manganese dioxide[20] and chromium trioxide[21] has recently been reported. Oxidation of lactone **16** in methyl sulfoxide with phosphorus pentaoxide produced 1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranurono-6,3-lactone-5-ulose (**17**) in 40% yield.



16 17 18, R = OTs
19, R = NHAc

The yield of ketoses in oxidation reactions is usually markedly influenced by the orientation of hydroxyl groups in the pyranoid (axial–equatorial) or fused bicyclic systems (*exo–endo*). As demonstrated above, the methyl sulfoxide–phosphorus pentaoxide reagent oxidizes sterically hindered secondary alcohols. This fact, together with other results[12e,22], may be a reflection of the small influence of steric factors in this oxidation reaction. In the present study, three epimeric pairs of sugar alcohols were treated with methyl sulfoxide–phosphorus pentaoxide. The following compounds, having axial or *endo* secondary hydroxyl groups, were synthesized from the corresponding ketoses: (*a*) methyl 4,6-*O*-benzylidene-2-*O*-(*p*-tolylsulfonyl)-α-D-allopyranoside (**18**), (*b*) methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-allopyranoside (**19**), and (*c*) 1,2-*O*-isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-ribofuranose (**13**). Oxidation of these compounds was performed under conditions similar to those employed for oxidation of the epimeric derivatives. The yield of ketose from compound **18** was 80% (*cf.* 92% for the *gluco* isomer). For compound **19** and its *gluco* isomer, the yields were 58 and 71%, respectively. In the case of compound **13** and its *xylo* isomer, the yields of ketose were 31 and 28%, respectively. These results show that the orientation of hydroxyl groups does not affect the rate of the oxidation by methyl sulfoxide and phosphorus pentaoxide.

EXPERIMENTAL

General. — Melting points were measured on a hot stage. Specific rotations were determined with a Yanagimoto direct-reading polarimeter. Nuclear magnetic resonance (n.m.r.) spectra were recorded at 60 MHz with a Varian A-60 spectrometer, and chemical shifts are expressed on the δ scale in parts per million (p.p.m.) downfield displacement from tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal standard. Infrared (i.r.) spectra were measured on a Shimazu AR-7 spectrometer, using a sodium chloride prism. Paper chromatography was carried out by the descending technique with Toyo Roshi No. 51 filter paper. Thin-layer chromatography (t.l.c.) was performed on Silica Gel G (RSCO).

Methyl sulfoxide was freshly distilled under decreased pressure from Linde Molecular Sieves. Phosphorus pentaoxide (P_4O_{10}) of commercial grade was used for oxidation. Sodium sulfate was used to dry organic solutions.

Fully substituted derivatives of carbohydrates listed in the Discussion were prepared by the literature methods[23,24].

Treatment of fully substituted carbohydrates with methyl sulfoxide–phosphorus pentaoxide. — Each derivative and 1 molar equivalent of phosphorus pentaoxide were dissolved in methyl sulfoxide, and the solution was allowed to stand at room temperature with occasional shaking. The reaction mixtures were examined by t.l.c. (benzene–methanol, 98:2), and for change in optical rotation.

Methyl 4,6-O-benzylidene-2-O-(p-tolylsulfonyl)-α-D-ribo-hexopyranosid-3-ulose (**2**). — A mixture of 7.2 g of methyl 4,6-*O*-benzylidene-2-*O*-(*p*-tolylsulfonyl)-α-D-glucopyranoside[25] [**1**; n.m.r. ($CDCl_3$): δ 4.84 (H-1, $J_{1,2}$ 3.2 Hz), 3.34 (OCH_3)], 5 g of methyl sulfoxide, 8 g of phosphorus pentaoxide, and 200 ml of DMF was heated for 2 h at 65–70° with stirring. The reaction mixture was poured into ice–water, and the solution was kept in a refrigerator overnight. The crystals (6.7 g, 92%) were collected by filtration and washed thoroughly with water. This preparation was found to contain no starting material and no by-products on examination by t.l.c. (benzene–methanol, 98:2) and n.m.r. spectroscopy. Crystallization from ethanol gave white crystals, m.p. 162–164°; $[\alpha]_D^{28}$ +44.6° (*c* 1.0, chloroform) [lit.[6c] m.p. 165–167°, $[\alpha]_D^{25}$ +44.9° (DMF)]; ν_{max}^{Nujol} 1775 cm^{-1} (C=O); n.m.r. ($CDCl_3$): δ 5.26 (H-1, doublet, $J_{1,2}$ 4.1 Hz), 5.12 (H-2, doublet), 3.42 (OCH_3).

For the study of the reaction conditions, 0.3 g of compound **1** was dissolved in 6 ml of solvent. The oxidation was performed on a water bath with occasional shaking, and exclusion of moisture. The reaction mixture was poured into ice–water to effect precipitation. When small proportions of precipitate were obtained, extraction with chloroform was also performed. The white, throughly washed product was subjected to t.l.c. and n.m.r. spectroscopy to determine the yield of the ketose.

A solution of methyl 4,6-*O*-benzylidene-2-*O*-(*p*-tolylsulfonyl)-α-D-allopyranoside[6c] (**18**; 0.3 g), methyl sulfoxide (0.162 g), and phosphorus pentaoxide (0.190 g) in DMF (6 ml) was heated for 2 h at 65–70°. Isolation of compound **2** (80%) was performed as described above.

*Methyl 2-acetamido-4,6-O-benzylidene-2-deoxy-α-*D*-ribo-hexopyranosid-3-ulose* (**4**). — A mixture of 1.8 g of methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside [**3**; n.m.r. (pyridine-d_5): δ 5.26 (H-1, doublet, $J_{1,2}$ 4.0 Hz)], 2 g of phosphorus pentaoxide, and 30 ml of methyl sulfoxide was heated for 15 h at 65–70°. The reaction mixture was diluted with 30 ml of chloroform, and then 30 ml of cold water was added. Upon vigorous shaking, the mixture separated into two phases. The chloroform layer was washed with a small portion of ice–water until neutral, and then dried. Evaporation of the chloroform *in vacuo* at 30–40° afforded 0.8 g (44% yield) of compound **4**. Oxidation with 4 molar equivalents of methyl sulfoxide and 1 molar equivalent of phosphorus pentaoxide in DMF gave a 71% yield of compound **4**. Recrystallization from methanol gave white crystals, m.p. 222°; $[\alpha]_D^{22}$ +128° (*c* 1.0, DMF) [lit.[6c] m.p. 227–228°, $[\alpha]_D^{25}$ +110°]; ν_{max}^{Nujol} 1735 (C=O) cm^{-1}; n.m.r. (pyridine-d_5): δ 4.60 (H-1, doublet, $J_{1,2}$ 4.3 Hz).

A solution of methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-allopyranoside[6c] (**19**; 0.3 g), methyl sulfoxide (0.290 g), and phosphorus pentaoxide (0.27 g) in DMF (6 ml) was heated for 2 h at 65–70°. Isolation of compound **4** (58%) was performed as described above.

*Methyl 2-acetamido-2-deoxy-α-*D*-ribo-hexopyranosid-3-ulose* (**5**). — Debenzylidenation of compound **4** by the method of Jeanloz[26] gave ketone **5** in 80% yield. Recrystallization from methanol afforded white crystals, m.p. 174–176°; $[\alpha]_D^{22}$ +118° (*c* 1.0, water); ν_{max}^{Nujol} 1735 (C=O), 1650, 1555, 955, 850 cm^{-1}; n.m.r. (D_2O): δ 5.20 (H-1, doublet, $J_{1,2}$ 4 Hz), 4.95 (H-2, quartet, $J_{2,4}$ 1.0 Hz), 4.50 (H-4, quartet, $J_{4,5}$ 10.0 Hz).

Anal. Calc. for $C_9H_{15}NO_6$: C, 46.35; H, 6.48; N, 6.01. Found: C, 46.33; H, 6.54; N, 5.99.

*1,2:5,6-Di-O-isopropylidene-α-*D*-ribo-hexofuranos-3-ulose* (**7**). — To a stirred solution of 15 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose [**6**; n.m.r. ($CDCl_3$): δ 5.93 (H-1, doublet, $J_{1,2}$ 3.7 Hz)] in 150 ml of methyl sulfoxide was carefully added 15 g of phosphorus pentaoxide whilst the temperature was maintained at 25–30° with cooling. After being stirred for 20 h at room temperature, the brownish red mixture was diluted with 150 ml of chloroform, and then water (150 ml) was added with cooling. After vigorous shaking, the mixture separated into two phases. The chloroform layer was washed with a small portion of ice–water until neutral, and then dried. Evaporation of the chloroform *in vacuo* at 30–40° afforded a syrup which crystallized upon standing at room temperature. Recrystallization from light petroleum gave white crystals, yield 9.7 g (65%); m.p. 108–112°; $[\alpha]_D^{28}$ +40.0° (*c* 2.0, chloroform). This compound was recrystallized three times from light petroleum to give the monohydrate, m.p. 118–119°, $[\alpha]_D^{28}$ +110° (*c* 1.0, chloroform) {lit.[2] b.p. 97° (0.01 mm), $[\alpha]_D$ +107°; monohydrate[2], m.p. 109–113°, $[\alpha]_D$ +45° in chloroform; monohydrate[19], m.p. 108–110°, $[\alpha]_D^{22}$ +40.2° (*c* 0.5, water)}; n.m.r. ($CDCl_3$): δ 5.87 (H-1, doublet, $J_{1,2}$ 3.8 Hz), 4.28 (H-2, doublet, $J_{2,1}$ 3.8 Hz). A strong ketone absorption was observed at 1770 cm^{-1} in the i.r. spectrum (Nujol) of the syrup that was obtained by heating the monohydrate for 1 h at 100° *in vacuo*.

Compound **7** (3 g) and hydroxylamine hydrochloride (3 g) were dissolved in 20 ml of ethanol and 20 ml of pyridine. The solution was refluxed for 2 h. A syrup obtained on evaporation of solvents was washed with a small portion of cold water, and crystallised from ether to give oxime **8** (2 g). Recrystallization from ether afforded material having m.p. 103–104°; $[\alpha]_D^{28}$ +187° (*c* 1.5, chloroform) {lit.[2] m.p. 103–104°, $[\alpha]_D$ +180°}.

3-Amino-3-deoxy-1,2:5,6-di-O-*isopropylidene*-α-D-*allofuranose*(**9**). — To a stirred solution of compound **8** (250 mg) in 30 ml of anhydrous tetrahydrofuran was added 200 mg of lithium aluminum hydride with cooling. The reaction mixture was refluxed for 3 h with exclusion of moisture. After the addition of 30 ml of ethyl acetate, the mixture was poured into ice–water and extracted with chloroform. The extract was concentrated to give a crystalline residue (120 mg), which was recrystallized from ether to give compound **9**, m.p. 88–90°; $[\alpha]_D^{28}$ +41.3° (*c* 1.2, chloroform) {lit.[27,28] m.p. 88–89°, 92–93°, $[\alpha]_D$ +41.0°, +40.5°}; ν_{max}^{KBr} 1590, 1505, 775, 880, 860, 830 cm^{-1}; n.m.r. ($CDCl_3$): δ 5.77 (H-1, doublet, $J_{1,2}$ 3.5 Hz.), 4.56 (H-2, quartet, $J_{2,3}$ 5.0 Hz), 3.13 (H-3, quartet, $J_{3,4}$ 8.5 Hz), 3.65 (H-4, quartet, $J_{4,5}$ 6.5 Hz), 4.2–3.9 (H-5 protons, multiplet).

Acetylation of amine **9** with acetic anhydride in pyridine gave the *N*-acetyl derivative; m.p. 128–129°; $[\alpha]_D^{28}$ +71.8° (*c* 0.8, chloroform) {lit.[29] m.p. 127–128°, $[\alpha]_D$ +71.3°}; ν_{max}^{KBr} 3320, 1680, 1540, 880, 845, 800 cm^{-1}.

1,2-O-*Isopropylidene-5*-O-(p-*tolylsulfonyl*)-α-D-erythro-*pentofuranos-3-ulose*(**12**). — 1,2-*O*-Isopropylidene-5-*O*-(*p*-tolylsulfonyl)-α-D-xylofuranose [**11**, n.m.r. ($CDCl_3$): δ 5.88 (H-1, doublet, $J_{1,2}$ 4 Hz)] (5 g), phosphorus pentaoxide (8 g), and methyl sulfoxide (0.86 g) were dissolved in DMF (120 ml). The solution was heated for 4 h at 60–65° with stirring, and then extracted with chloroform (50 ml) three times. The extract was washed with cold water, dried, and concentrated *in vacuo*, and the syrupy residue was dissolved in methanol and decolorized with charcoal. After evaporation of the solvent, recrystallization of the residue was effected from methanol–ether–light petroleum to give white needles (1.7 g). Further recrystallization gave the methanolate of the title compound, m.p. 105–106°; $[\alpha]_D^{18}$ +70.5° (*c* 1.0, chloroform); ν_{max}^{Nujol} 3430, 1600, 890, 870, 840 cm^{-1}; n.m.r. ($CDCl_3$): δ 5.87 (H-1, doublet, $J_{1,2}$ 4.0 Hz), 4.37 (H-2, doublet, $J_{2,1}$ 4.0 Hz), 3.27 (OCH_3), 2.45 (C-CH_3, 6 H), 7.81 and 7.35 (aromatic protons, 4 H).

Anal. Calc. for $C_{16}H_{21}O_8S$: C, 51.46; H, 5.76; S, 8.58. Found: C, 51.45; H, 5.93; S, 8.64.

A solution of compound **13** (0.473 g), phosphorus pentaoxide (0.25 g), and methyl sulfoxide (0.25 g) in DMF (8 ml) was heated for 1 h at 65–70°. Isolation of compound **12** (31%) was performed as described above.

1,2-O-*Isopropylidene-5*-O-(p-*tolylsulfonyl*)-α-D-*ribofuranose* (**13**). — Reduction of compound **12** (200 mg) with lithium aluminium hydride for 2 h at 35–40° in tetrahydrofuran gave a white solid (m.p. 99–102°,150 mg). Recrystallization from ether–light petroleum gave compound **13**; m.p. 105–106.5°; $[\alpha]_D^{20}$ +23.6° (*c* 1.4, chloroform); ν_{max}^{Nujol} 3400 (OH), 1590, 890, 870, 850, 815, 810 cm^{-1}; n.m.r. ($CDCl_3$):

δ 5.77 (H-1, doublet, $J_{1,2}$ 4 Hz), 4.6–3.8 (H-2,3,4,5,5', multiplet, 5 H), 2.47 (C-CH_3, 3 H), 1.53, 1.37 (isopropylidene group, 6 H).

Anal. Calc. for $C_{15}H_{20}O_7S$: C, 52.32; H, 5.86; S, 9.32. Found: C, 52.24; H, 6.03; S, 9.11.

1,2-O-Isopropylidene-5-O-(di-O-phenylphosphono)-α-D-erythro-pentofuranos-3-ulose (**15**). — 1,2-*O*-Isopropylidene-5-*O*-(di-*O*-phenylphosphono)-α-D-xylofuranose [**14**; n.m.r. ($CDCl_3$): δ 5.88 (H-1, doublet, $J_{1,2}$ 3.5 Hz)] (1 g) was oxidized with three molar equivalents of methyl sulfoxide and two molar equivalents of phosphorus pentaoxide in 30 ml of DMF for 2 h at 60–65°. Isolation was performed as for compound **12**. The syrup obtained was dissolved in the minimal amount of ethanol, and water was added to produce turbidity. After storage in a refrigerator overnight, white crystals formed, m.p. 65–67°. Recrystallization from water–ethanol gave the title compound (35%), m.p. 75–78°; $[\alpha]_D^{23}$ +44.5° (*c* 1.0, chloroform); ν_{max}^{Nujol} 3350, 1600, 1500, 880, 840 cm^{-1}; n.m.r. ($CDCl_3$): δ 5.77 (H-1, doublet, $J_{1,2}$ 3.5 Hz).

Anal. Calc. for $C_{20}H_{21}O_8P \cdot H_2O$: C, 54.79; H, 5.28. Found: C, 54.31; H, 5.10.

The semicarbazone, prepared by the usual procedure, had m.p. 170–171°; $[\alpha]_D^{20}$ +284° (*c* 1.0, chloroform); ν_{max}^{Nujol} 1780, 1720, 1600, 1500, 890, 880, 840 cm^{-1}.

Anal. Calc. for $C_{21}H_{26}N_3O_8P$: C, 52.61; H, 5.47. Found: C, 52.72; H, 5.60.

1,2-O-Isopropylidene-α-D-xylo-hexofuranurono-6,3-lactone-5-ulose (**17**). — 1,2-*O*-Isopropylidene-α-D-glucofuranurono-6,3-lactone [**16**; n.m.r. ($CDCl_3$): 6.02 (H-1, doublet, $J_{1,2}$ 3.5 Hz)] (10 g) and phosphorus pentaoxide (10 g) were stirred in 115 ml of methyl sulfoxide for 10 min at 35–40° and then for 20 h at 15–20°. The chloroform extract obtained as described for the preparation of compound **7** was concentrated *in vacuo*. Recrystallization of the residue (4.7 g) from hot water gave needles of compound **17**, m.p. 146–148°; $[\alpha]_D^{26}$ +88° (*c* 1.0, methyl sulfoxide) {lit.[20,21] m.p. 146–149°, 145–148°, $[\alpha]_D^{25}$ +76° (water), $[\alpha]_D$ +73° (water)}; ν_{max}^{Nujol} 3350 (OH), 1790 (γ-lactone) cm^{-1}; n.m.r. (pyridine-d_5): δ 6.18 (H-1, doublet, $J_{1,2}$ 3.75 Hz), 5.0 (H-2, doublet, $J_{2,3}$ 0.5 Hz); 5.37 (H-3, $J_{3,4}$ 3.5 Hz), 5.11 (H-4, doublet); (methyl sulfoxide-d_6): δ 5.96 (H-1, doublet, $J_{1,2}$ 3.5 Hz), 4.42 (H-4, doublet), 4.87 (H-3, quartet, $J_{3,4}$ 2.8 Hz), 4.83 (H-2, quartet, $J_{2,3} < 0.1$ Hz), 7.45 and 7.28 (singlets, *gem*-OH).

Compound **17** was treated with cold barium hydroxide solution for 2 h. The solution was poured into a large volume of ethanol to give a white precipitate of the barium salt which was collected by centrifugation and dried: ν_{max}^{Nujol} 1725 (C=O), 1640 cm^{-1} (broad peak, COO^-).

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