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Preliminary communication

Oxidation of glycosides by *Acetobacter suboxydans*: synthesis of methyl α- and β-L-*threo*-pentopyranosid-4-uloses*

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The microbiological oxidation of sugars and their derivatives by the acetic acid bacterium[1] *Acetobacter suboxydans*, has been studied extensively. Alditols and acyclic carbohydrate derivatives are oxidized in accordance with the Bertrand–Hudson rule[2], although there are a few exceptions[3], and cyclitols are oxidized in conformance with rules originally proposed by Magasanik *et al.*[4] and modified by Anderson *et al.*[5]. There have been two reports[6,7] of oxidations of glycosides, but the products were not isolated and characterized. We now report the successful oxidation of methyl α- and β-D-xylopyranosides to give the corresponding glycosid-4-uloses, isolated as their *O*-methyloximes.

TABLE I

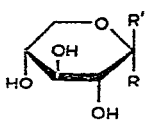
CARBON-13 CHEMICAL SHIFT DATA[a]

Compound	*Carbon atom*						
	1	*2*	*3*	*4*	*5*	C–O*Me*	N–O*Me*
1	104.6	73.1	76.5	69.5	65.6	55.8	–
2	100.1	71.9	73.4	69.9	60.7	54.5	–
3	104.6	75.8[b]	76.7[b]	198.9	66.5	55.0	–
4	102.8	71.4	74.7	205.5	63.7	54.6	–
5	104.4	74.7	70.1	156.2	56.6	55.1	61.4
6	99.7	72.2	69.1	155.1	54.9	55.5	61.4

[a]In p.p.m. downfield from internal tetramethylsilane; spectra were recorded in methyl sulfoxide-d_6.
[b]Assignments for these peak positions may be reversed.

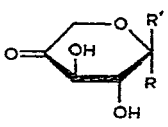
Methyl-β-D-xylopyranoside (1) was treated with a suspension of *A. suboxydans* cells (ATCC 621H, collected from a 2% D-glucitol broth) for 30 days. Paper chromatography revealed the presence of one major and one minor component. A sample of the

*Dedicated to the memory of Professor J.K.N. Jones, F.R.S.



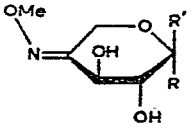
1 R = H
R′ = OMe

2 R = OMe
R′ = H



3 R = H
R′ = OMe

4 R = OMe
R′ = H



5 R = H
R′ = OMe

6 R = OMe
R′ = H

oxidation mixture was reduced with sodium borohydride and the product hydrolyzed with acid, whereupon paper chromatography showed the presence of xylose, arabinose, and a trace of ribose suggesting that oxidation had occurred at both C-3 and C-4. Treatment of the oxidation mixture with methoxylamine hydrochloride[8] afforded one major product. The resultant, crude syrup was extracted with hot dichloromethane to give methyl α-L-*threo*-pentopyranosid-4-ulose (*E*)-*O*-methyloxime (**5**, 28%), m.p. 63–65°. Mild, acid-catalyzed hydrolysis[8] of **5** gave syrupy methyl α-L-*threo*-pentopyranosid-4-ulose (**3**), the major component in the original oxidation mixture. A sample of **3** was reduced with sodium borohydride and the product hydrolyzed with acid, whereupon paper chromatography showed the presence of only xylose and arabinose.

Interestingly, when methyl α-D-xylopyranoside (**2**) was treated with *A. suboxydans* for only 4 days, no starting material could be detected. As in the oxidation of compound **1**, paper chromatography revealed the presence of one major and one minor component; also, paper-chromatographic examination of the product obtained by borohydride reduction of the oxidation mixture and subsequent acid-catalyzed hydrolysis suggested, as before, that oxidation had occurred at C-3 and C-4. Treatment of the mixture with methoxylamine hydrochloride afforded a syrup which, on fractionation on silica gel, gave syrupy methyl β-L-*threo*-pentopyranosid-4-ulose (*E*)-*O*-methyloxime (**6**, 76%). Mild, acid-catalyzed hydrolysis of **6** yielded methyl β-L-*threo*-pentopyranosid-4-ulose (**4**) as a syrup.

The presence of only one geometrical isomer of each oxime (**5** or **6**) was indicated by the ^{1}H and ^{13}C n.m.r. spectra; the latter spectra also permitted assignment of configuration for the oximes. It has been observed[9,10] that, when ^{13}C chemical shifts for ketone derivatives containing C=N bonds are compared with those for the parent carbonyl compounds, the shielding of the *syn*-carbon atom is larger than that of the *anti*-carbon atom. Comparison of the chemical-shift data (see Table I) of compounds **3** and **4** with those of **5** and **6**, respectively, shows that C-5 is shielded by 9.9 and 8.8 p.p.m., whereas C-3 is shielded by only 6.6 and 5.6 p.p.m.; these results suggest that only the *E* isomer of the oxime was formed in each case.

Preliminary experiments on the oxidation of other glycosides have also been completed. Methyl α-D-glucopyranoside is not oxidized at all, and the β-D anomer is only partially oxidized, a result in agreement with that obtained in a previous biochemical study[6].

Other hexopyranosides that have been tested show very limited or no oxidation, whereas all of the pentopyranosides tested showed some oxidation. The results obtained thus far do not permit definition of the stereospecificity of oxidation. However, for the D-xylo-pryanosides at least, it is interesting that the configuration at the anomeric center has a profound effect on the rate of oxidation.

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