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Short Communication

Identification by X-Ray Methods of 6(*R*)-Acetoxy-2(*S*)-methoxy-1(*R*),5(*R*)-3,7,8-trioxabicyclo[3.2.1]octane. A New Compound Isolated after Periodate Oxidation of Methyl α-D-Xylopyranoside in Dimethyl Sulfoxide Followed by Acetylation

Kjell M. Aalmo,[a] Michael G. B. Drew[b] and David G. Nicholson[a]

[a]Department of Chemistry, AVH, University of Trondheim, N-7055 Dragvoll, Norway and [b]Department of Chemistry, The University of Reading, Whiteknights, Reading RG6 2AD, UK

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Yu and Bishop[1] showed that several methyl glycopyranosides are oxidised by periodic acid in dimethyl sulfoxide (DMSO) with the consumption of only one mole of oxidant per mole of glycoside. The product from selective oxidation of methyl β-L-arabinopyranoside between C(3)/C(4) was isolated by them as a crystalline monoacetate in a yield of 37.6%. A double, intramolecular, hemiacetal structure, 7(*S*)-acetoxy-2(*S*)-methoxy-1(*S*),5(*S*)-3,6,8-trioxabicyclo[3.2.1]octane,* was assigned on the basis of its ^{1}H NMR spectrum. A more detailed spectroscopic investigation by Gelas *et al.*[2] confirmed this assignment.

Recently Aalmo[3] has shown by MS and ^{1}H and ^{13}C NMR spectroscopy that oxidation of methyl α-D-xylopyranoside with periodic acid in DMSO is nonselective, giving, after acetylation, two monomeric monoacetylated products in almost a 1:1 ratio. These two compounds could not be separated by thin-layer chromatography, but one of the products was identified as 7(*S*)-acetoxy-2(*S*)-methoxy-1(*S*),5(*S*)-3,6,8-trioxabicyclo[3.2.1]octane, giving an identical ^{1}H NMR spectrum with the oxidation product obtained from methyl β-L-arabinopyranoside by Yu and Bishop.[1] This must be the product obtained after oxidation of the methyl α-D-xylopyranoside between C(3)/C(4) (Fig. 1). The other product is shown by NMR[3] to be a compound produced on oxidation between

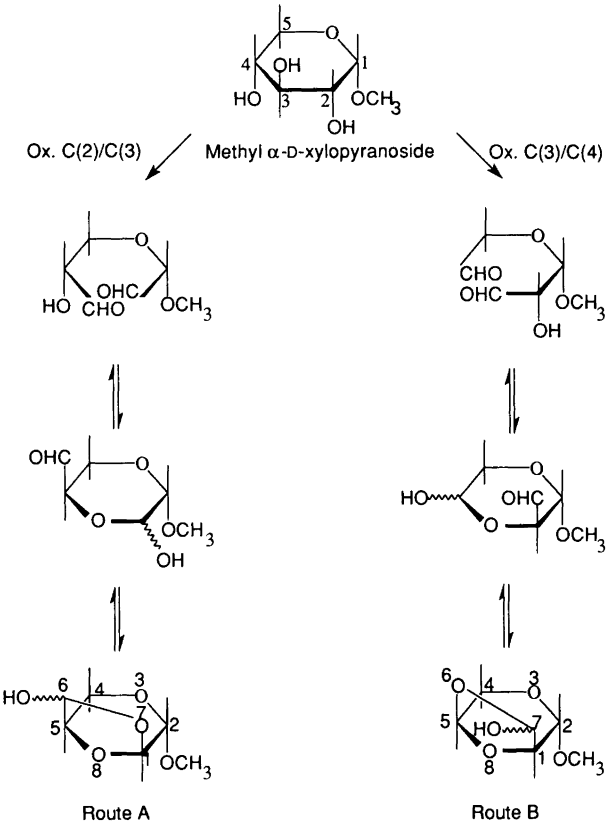

Fig. 1. Possibilities for the formation of a double, intramolecular hemiacetal after oxidation of methyl α-D-xylopyranoside between C(2)/C(3) and C(3)/C(4) by periodic acid in DMSO.

* Yu and Bishop used a different notation; the notation used here is that defined by IUPAC rules (see Ref. 2).

C(2)/C(3) of the methyl α-D-xylopyranoside. A chloroform solution of the two compounds yielded a mixture of crystals and syrup after evaporation of the solvent.

We report here on the identification by X-ray methods of the crystalline compound extracted from this mixture.

Experimental

Preparation. Following the procedure of Yu and Bishop,[1] a sample (6.67 mmol) of methyl α-D-xylopyranoside was oxidised with periodic acid (8.0 mmol) in DMSO (9 mL) for 1.5 h at 5°C, and the products were acetylated and isolated as a yellow syrup. The components of the syrup, which consisted mainly of two acetylated monomers and small amounts of nonacetylated monomers,[3] were separated by preparative TLC, 10 mg of syrup in 0.15 mL chloroform being applied to each plate (20 × 20 cm). The bands were located by dipping reagent[4] on strips (1 cm) cut from each side and the centre of the plate. The silica gel was scraped from the appropriate areas, and extracted with hot ethanol (3 × 15 mL). After filtration and evaporation of the solvent, the main band, which consisted of two monomers in approximately 1:1 ratio as shown by proton and carbon NMR,[3] yielded a syrup. This syrup was dissolved in chloroform and the solution concentrated by slow evaporation to give a mixture of crystals and syrup. Crystals obtained from this mixture were used in this diffraction study.

Crystal data. $C_8O_6H_{12}$, $M = 204$, orthorhombic, $a = 6.135(7)$, $b = 9.476(9)$, $c = 19.193(14)$ Å, $V = 941.4$ Å^3, $Z = 4$, $F(000) = 432$, MoK_α radiation, $\lambda = 0.710\,69$ Å, $\mu = 0.86$ cm^{-1}, $d_c = 1.41$ g cm^{-3}, $d_m = 1.41$ g cm^{-3}. Space group $P2_12_12_1$.

A crystal of approximate size 0.3 × 0.3 × 0.3 mm was set up to rotate about the *a*-axis on a Stoe STADI2 diffractometer and data collected via variable width ω-scan. Background counts were for 20 s and a scan rate of 0.0333° s^{-1} was applied to a width of (1.5 + sin μ/tan θ). Lattice constants were obtained from accurate measurements of axial reflections taken at room temperature. The intensities of 1186 independent reflections were measured out to $2\theta > 50°$ using monochromatised MoK_α radiation. Of these, 689 reflections were classified as observed, i.e. $I_{net} > 2\sigma(I)$, and used in the refinement. Lorentz and polarisation corrections were applied, systematic absences rejected and equivalent reflections merged. (Although the crystal was stable under data collection, the quality of the data was not good enough to yield accurate structural parameters. We therefore examined four other crystals, but to no avail. However, we were able to establish the molecular structure and hence identify the compound.) Scattering factors and dispersion corrections were taken from Ref. 5. The structure was solved by direct methods, and all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were assigned a common isotropic factor and included in calculated positions, and methyl groups were refined as rigid groups. The structure was given a weighting scheme in the form $\omega = 1/[\sigma^2(F) + 0.003F^2]$. The final *R*-value was 0.074 ($R_w = 0.076$).

Table 1. Atomic coordinates (×10^4) with estimated standard deviations in parentheses and equivalent isotropic thermal parameters (in 10^{3}Å^2).

Atom	*x/a*	*y/b*	*z/c*	U_{eq}[a]
O(1)	1575(10)	2052(6)	6969(4)	55(4)
C(2)	3615(18)	2393(10)	7280(5)	61(5)
C(3)	3769(15)	1890(10)	8189(5)	55(5)
O(4)	2048(12)	2485(7)	8643(4)	59(4)
C(5)	1749(17)	3941(10)	8479(6)	63(6)
C(6)	1886(14)	4257(11)	7553(6)	58(4)
C(7)	305(13)	3321(9)	7108(4)	51(5)
O(8)	−108(10)	3967(6)	6322(4)	57(3)
C(9)	−1494(15)	3331(12)	5797(5)	59(5)
O(10)	−2379(13)	2216(9)	5969(5)	77(5)
C(11)	−1678(16)	4144(14)	5037(7)	77(7)
O(12)	3912(10)	3832(7)	7243(4)	60(3)
O(13)	5882(12)	2252(7)	8454(4)	62(4)
C(14)	6448(20)	1603(14)	9205(6)	69(6)

[a] U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Calculations were carried out using the SHELX 76 package[6] and in-house programs on the Amdahl 5870 computer at the University of Reading. In the final cycles of refinement no shift/error ratio was greater than 0.1σ. In the final difference Fourier map the maximum and minimum peaks were 0.53 and −0.46 e Å^{-3}.

The atomic positions are given in Table 1. Additional material, available from the authors, comprises the thermal parameters, structure factors and hydrogen coordinates.

Results and discussion

Figure 1 shows the two different reaction routes, A and B, for the possible formation of a double, intramolecular hemiacetal after oxidation of methyl α-D-xylopyranoside between C(2)/C(3) and C(3)/C(4), respectively. Figure 2 shows the molecular structure of 6(*R*)-acetoxy-2(*S*)-methoxy-1(*R*),5(*R*)-3,7,8-trioxabicyclo[3.2.1]octane, the product from route A with the acetoxy group in an *exo* orientation.

The reaction routes. On oxidation with periodic acid in DMSO, followed by acetylation, methyl α-D-xylopyranoside gave two major, monomeric, monoacetylated products. These products were shown by NMR[3] to be present in solution in an approximately 1:1 ratio, but could not be separated by thin layer chromatography or gas–liquid chromatography. The mass spectrum was in accordance with the formulation of monomeric, mono-*O*-acetylated, methyl acetals.[3]

Concentrating a solution of the products in chloroform gave crystals and a syrup. Five crystals were selected for preliminary X-ray crystallographic examination; the results showed that all five were the same compound (route A; see below and Fig. 1). This was confirmed by

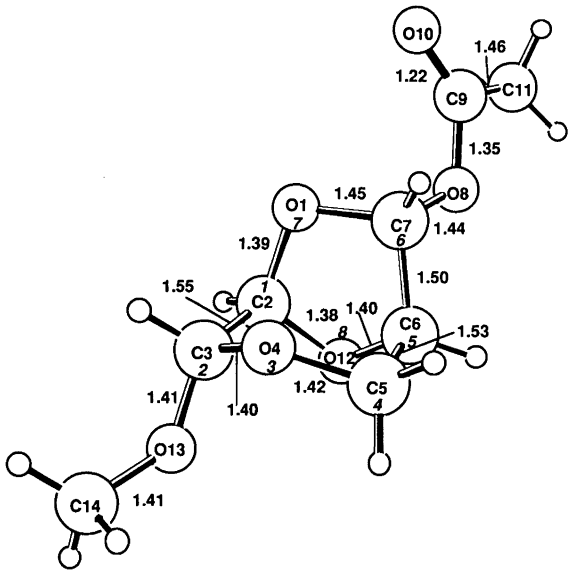

Fig. 2. The molecular structure of 6(*R*)-acetoxy-2(*S*)-methoxy-1(*R*),5(*R*)-3,7,8-trioxabicyclo[3.2.1]octane showing the atom numbering scheme (and also the IUPAC numbering of the rings in italics). The bond lengths (Å) are also included; the e.s.d.s are 0.011 Å.

the fact that the ^{1}H NMR spectrum of the residual syrup exhibited a significant diminution in signal intensities for the product from that route. Moreover, the NMR spectrum of a large crystal from another batch showed it to consist of the route A product. These results show that the present preparation from methyl α-D-xylopyranoside yields the product from route A as a crystalline material, while the product from route B consists of a syrup. We note that Yu and Bishop[1] obtained crystalline material from a procedure that corresponds with route B when using methyl β-L-arabinopyranoside as starting material. The reason for this difference might be due to the selective oxidation of that material, giving mainly one product, or because of the different solvent composition.

The crystal structure shows that the crystalline material consists of the compound 6(*R*)-acetoxy-2(*S*)-methoxy-1(*R*),5(*R*)-3,7,8-trioxabicyclo[3.2.1]octane, obtained from reaction route A, whereas the NMR[3] shows that the syrup is 7(*S*)-acetoxy-2(*S*)-methoxy-1(*S*),5(*S*)-3,6,8-trioxabicyclo[3.2.1]octane (reaction route B). The molecular structure of the former compound is shown in Fig. 2.

The structure of 6(R)*-acetoxy-*2(S)*-methoxy-*1(R),5(R)*-3,7,8-trioxabicyclo[3.2.1]octane.* As expected, the 1,4-dioxane ring takes the lower-energy chair conformation. The five-membered ring fused to the 1,4-dioxane ring adopts the envelope conformation with oxygen O(12) being 0.61 Å out of the plane defined by the four other atoms in that ring.

The 2(*S*)-methoxy substituent takes an orientation in which C(14) is almost antiperiplanar to C(2) [with a dihedral angle of 168° for the fragment C(14)–O(13)–C(3)–C(2) and 72° for the fragment C(14)–O(13)–C(3)–O(4)]. This is the conformation expected for the 2(*S*)-methoxy group from steric considerations of the isolated molecule, since other orientations would give rise to *gauche* butane interactions or 'forbidden' pentane interactions ($g_+ g_-$).

The acetoxy group on C7 adopts the *exo* orientation as expected from steric reasons, thereby giving the 6(*R*) configuration in agreement with earlier findings on similar compounds in solution.[1,7] C(11) takes an antiperiplanar orientation with respect to C(7) [with a dihedral angle of 180° for the fragment C(11)–C(9)–O(8)–C(7) which is consistent with a partial double bond between C(9) and O(8), and which is also reflected by the short bond length of 1.34 Å]. All the other bond lengths are normal.

Thus the crystal structure shows that the molecule in the solid state maintains the same overall conformation to be expected for the free molecule. This means that the molecule is little affected by crystal packing forces.

In conclusion, this study, together with NMR studies,[3] shows that methyl α-D-xylopyranoside is nonselectively oxidised by periodic acid in DMSO, forming, after acetylation, almost a 1:1 ratio of 6(*R*)-acetoxy-2(*S*)-methoxy-1(*R*),5(*R*)-3,7,8-trioxabicyclo[3.2.1]octane and 7(*S*)-acetoxy-2(*S*)-methoxy-1(*S*),5(*S*)-3,6,8-trioxabicyclo-[3.2.1]octane. The product of oxidation between C(2)/C(3) yields 6(*R*)-acetoxy-2(*S*)-methoxy-1(*R*),5(*R*)-3,7,8-trioxabicyclo[3.2.1]octane as a crystalline material, whereas oxidation between C(3)/C(4) leads to 7(*S*)-acetoxy-2(*S*)-methoxy-1(*S*),5(*S*)-3,6,8-trioxabicyclo[3.2.1]-octane as a syrup after evaporation of the chloroform solvent.

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