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Note

Synthesis and configuration of some 2-furylidene acetals of methyl aldohexopyranosides

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The 2-furylidene acetals of, for example, methyl α-D-gluco-[1], β-D-gluco-[2], α-D-galacto-[3], and α-D-manno-pyranoside[1] were prepared almost 50 years ago using 2-furaldehyde, and nitric acid or calcium chloride as the catalyst, at 150–160°/100–200 mmHg in a stream of carbon dioxide. These acetals were obtained in low yield and characterised, but their structures were not determined. We have found[4,5] that the synthesis of cyclic unsaturated acetals of carbohydrates is best effected with an excess of aldehyde, with toluene-*p*-sulphonic acid as catalyst, and with the azeotropic removal of water. This method has also been employed in the synthesis of the 4,6-*O*-(2-furylidene) derivatives (**1**, **4**, and **5**) of methyl α-D-gluco-, β-D-gluco-, and α-D-galacto-pyranoside and the 2,3:4,6-di-*O*-(2-furylidene) derivatives (**8**) of methyl α-D-mannopyranoside. The best results were obtained by using benzene–1,4-dioxane (2:1) or benzene–*N*,*N*-dimethylformamide (1:1) as the reaction medium, and polymerisation of furaldehyde was avoided.

The structures of the furylidene derivatives were elucidated on the basis of ^{1}H-n.m.r. data. In the ^{1}H-n.m.r. spectra of **1**, **4**, and **5**, the protons of the furan ring resonated at δ 7.5 (t, 1 H) and 6.5 (m, 2 H). However, for **8-endo** and **8-exo**, integration of the proton resonances at δ 7.5 and 6.5 gave the ratio 4:2 indicative of diacetals. The chemical shift of the signal for the acetal proton in each of the 4,6-*O*-furylidene derivatives **1**, **4**, and **5** was identical with those of equatorially substituted 2-(2-furyl)-1,3-dioxanes[6]. Thus, in **1**, **4**, **5**, and **8**, the furyl substituent occupies an equatorial position in the 1,3-dioxane ring.

The condensation of methyl α-D-mannopyranoside with 2-furaldehyde gave a crude product mixture having acetal proton signals at δ 5.7, 5.98, and 6.22. Fractionation of the mixture gave the main product in 94% yield with acetal proton signals at δ 5.7 (4,6-acetal) and 6.22 (2,3-acetal) and a small amount of product with signals at δ 5.7 and 5.98. The isomerism of the 2,3-membered acetal relates to the acetal proton being *exo* or *endo* in the *cis*-fused ring system. The *endo* proton (δ 6.22) is readily identifiable since it is deshielded[7]. The preponderance of the *endo*-

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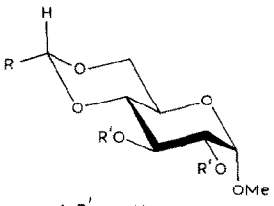
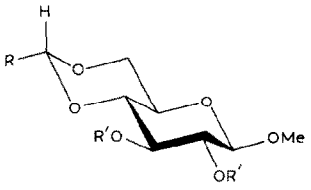
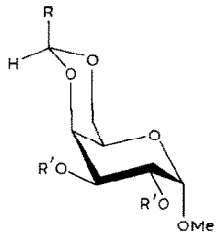


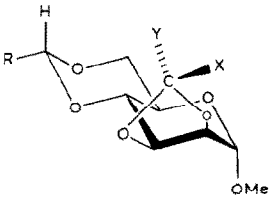
1 R′ = H
2 R′ = Me
3 R′ = Ac



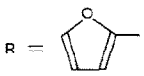
4 R′ = H



5 R′ = H
6 R′ = Me
7 R′ = Ac



8-endo Y = H, X = R
8-exo Y = R, X = H



isomer of methyl 2,3:4,6-di-*O*-(2-furylidene)-α-D-mannopyranoside (**8-endo**) is consistent with our previous observations[5].

O-Furylidene derivatives of methyl aldohexopyranosides are valuable synthetic intermediates in asymmetric synthesis and biologically active polymers[8].

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were measured with a Polamat A Carl Zeiss-Jena polarimeter. I.r. spectra were recorded for KBr discs with a UR-20 spectrophotometer. ^{1}H-N.m.r. spectra were recorded with a Varian HA-100 spectrometer.

2-Furylidene acetals of methyl aldohexopyranosides. — A mixture of methyl aldohexopyranoside (5.0 g), freshly distilled 2-furaldehyde (10–15 mL), benzene (20 mL), and 1,4-dioxane (10 mL) or *N,N*-dimethylformamide (20 mL), containing toluene-*p*-sulphonic acid (0.05 g), was subjected to azeotropic distillation (Dean–Stark apparatus). The mixture was boiled under reflux for 2–8 h, a small amount of pyridine was added, and the solvents were evaporated. The crude product was crystallised from ethanol (**8-endo**), hexane–benzene (5:1, **1** and **4**), or acetone (**5**). A further yield of the product was obtained by concentration of the mother liquor.

Methyl 4,6-*O*-(2-furylidene)-α-D-glucopyranoside (**1**, 95.6%) had m.p. 126–

127°, $[\alpha]_D^{25}$ +125.4° (*c* 1.9, water); lit.[1] m.p. 153–154°, $[\alpha]_D^{25}$ +84.4° (water). ^{1}H-N.m.r. data (Me_2CO-d_6): δ 3.4 (s, 3 H, OMe), 3.5–3.6 (m, 2 H, H-6), 3.6–3.8 (m, 5 H), 4.2 (d, 1 H, $J_{2,3}$ 7.0 Hz, H-2), 4.7 (d, 1 H, H-1), 5.7 (s, 1 H, acetal H), 6.4 (m, 2 H, furan ring), and 7.5 (t, 1 H, furan ring). The 2,3-di-*O*-methyl derivative (**2**) had m.p. 104–105°, $[\alpha]_D^{25}$ +108.6° (*c* 1.3, chloroform); lit.[1] m.p. 119–120°, $[\alpha]_D$ +98.4° (chloroform). The 2,3-diacetate (**3**) had m.p. 124–125°, $[\alpha]_D^{25}$ +89.0° (*c* 1.1, chloroform); lit.[1] m.p. 112–113°.

Methyl 4,6-*O*-(2-furylidene)-β-D-glucopyranoside (**4**, 85.7%) had m.p. 114–115°, $[\alpha]_D^{25}$ −44.8° (*c* 2, pyridine); lit.[2] m.p. 160–162°, $[\alpha]_D^{25}$ −97.2° (pyridine). ^{1}H-N.m.r. data: δ 3.5 (s, 3 H, OMe), 3.2–4.0 (m, 6 H), 4.15 (d, 1 H), 4.3 (s, 1 H), 4.45 (d, 1 H, H-1), 5.68 (s, 1 H, acetal H), 6.45 (m, 2 H, furan ring), and 7.55 (t, 1 H, furan ring).

Methyl 4,6-*O*-(2-furylidene)-α-D-galactopyranoside (**5**, 91.7%) had m.p. 152–153°, $[\alpha]_D^{25}$ +176.5° (*c* 1, water); lit.[3] m.p. 160–161°, $[\alpha]_D^{25}$ +157.6° (water). ^{1}H-N.m.r. data (Me_2SO-d_6): δ 3.35 (s, 3 H, OMe), 3.5–3.8 (m, 4 H), 4.0 (s, 1 H), 4.1–4.2 (m, 1 H), 4.5–4.7 (m, 3 H), 5.62 (s, 1 H, acetal H), 6.5 (m, 2 H, furan ring), and 7.2 (t, 1 H, furan ring). The 2,3-di-*O*-methyl derivative (**6**) had m.p. 136–137°, $[\alpha]_D^{25}$ +125.7° (*c* 1, chloroform); lit.[3] m.p. 138–140°, $[\alpha]_D^{25}$ +127.9° (chloroform). The 2,3-diacetate (**7**) had m.p. 118–120° $[\alpha]_D^{25}$ +206° (*c* 1, chloroform); lit.[3] m.p. 125–126°.

Methyl 2,3(*R*):4,6-di-*O*-(2-furylidene)-α-D-mannopyranoside (**8-endo**, 94%) had m.p. 164–165°, $[\alpha]_D^{25}$ −7.5° (*c* 2, chloroform); lit.[1] m.p. 182–184°, $[\alpha]_D^{25}$ +42.4° (chloroform). ^{1}H-N.m.r. data (Me_2CO-d_6): δ 3.4 (s, 3 H, OMe), 3.6–4.0 (m, 2 H, H-6), 4.1 (d, 1 H), 4.25–4.6 (m, 3 H), 4.95 (s, 1 H, H-1), 5.7 (s, 1 H, dioxane acetal H), 6.2 (s, 1 H, dioxolane acetal H), 6.35–6.55 (m, 4 H, furan ring), and 7.52 (m, 2 H, furan ring). From the mother liquors, methyl 2,3(*S*):4,6-di-*O*-(2-furylidene)-α-D-mannopyranoside (**8-exo**, 2%) crystallised on storage and had m.p. 66–69°, $[\alpha]_D^{25}$ +0.5° (*c* 2, chloroform). ^{1}H-N.m.r. data (Me_2CO-d_6): δ 3.45 (s, 3 H, OMe), 3.1–4.0 (m, 3 H), 4.1–4.6 (m, 3 H), 5.05 (s, 1 H, H-1), 5.7 (s, 1 H, dioxane acetal H), 5.98 (s, 1 H, dioxolane acetal H), 6.35–6.55 (m, 4 H, furan ring), and 7.52 (m, 2 H, furan ring).

Anal. Calc. for $C_{17}H_{18}O_8$: C, 58.28; H, 5.18. Found: C, 58.05; H, 5.11.

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