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Note

N-Acylglycosylamines as intermediates. Synthesis of 2,3,5,6-tetra-*O*-methyl-D-glucofuranose

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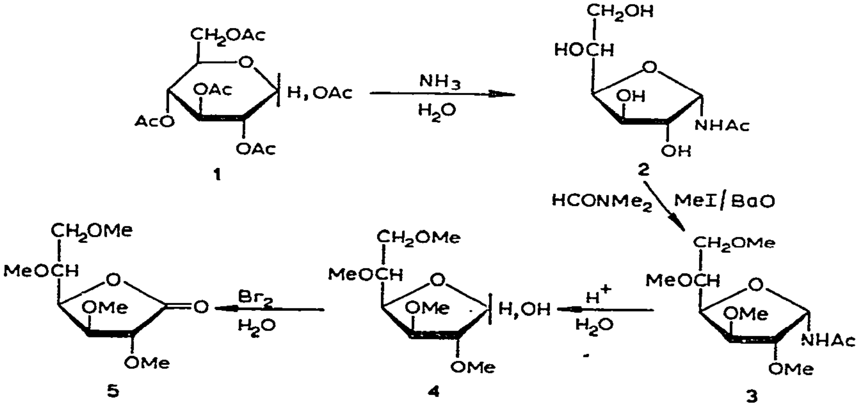
The usual method of synthesis of 2,3,5,6-tetra-*O*-methyl-D-glucofuranose (**4**) is that of methylation[1] of the mixture of methyl D-glucosides obtained[2] by shaking D-glucose with 1% methanolic hydrochloric acid, followed by hydrolysis[1]. The isolation of the mixture of glycosides requires several extractions with ethyl acetate and high-vacuum distillation to eliminate the contaminating free sugar. However, an absolutely pure product is not obtained, as the material still contains some of the pyranose forms[3].

Other ways of synthesis start from partially substituted compounds that have stable furanose structures; these are methylated, and the product hydrolyzed. 1,2-*O*-Isopropylidene-3,5,6-tri-*O*-methyl-α-D-glucofuranose[4], 2,3,6-tri-*O*-methyl-D-glucofuranose[5], penta-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose[6], 5,6-*O*-carbonyl-1,2-*O*-isopropylidene-α-D-glucofuranose[3], and 1,6-anhydro-β-D-glucofuranose[7] have been employed in this way. All of these methods involve several previous stages that make the synthesis of **4** time-consuming.



We used, as the starting material, *N*-acetyl-α-D-glucofuranosylamine (**2**), a compound readily obtained in 53% yield by ammonolysis of penta-*O*-acetyl-β-D-glucopyranose (**1**) with 5% aqueous ammonia. Methylation of **2** was achieved by the method of Kuhn *et al.*[8], with methyl iodide and barium oxide in *N*,*N*-dimethylformamide. Thus was obtained *N*-acetyl-2,3,5,6-tetra-*O*-methyl-α-D-glucofuranosylamine (**3**), which was hydrolyzed under controlled conditions (30 min in 0.5M sulfuric acid) to give compound **4** as a syrup. More-prolonged hydrolysis causes extensive destruction of the product. The formation of **4** was confirmed by its transformation into the corresponding 2,3,5,6-tetra-*O*-methyl-D-glucono-1,4-lactone (**5**).

EXPERIMENTAL

General procedures. — Evaporations were conducted under diminished pressure at 60°. T.l.c. was performed on Silica Gel G (Merck, Germany), with 3% of methanol in benzene as the eluant. The components were detected with 5% sulfuric acid in ethanol and subsequent charring of the plates at 120°. Optical rotations were determined at 25°.

N-*Acetyl-α-D-glucofuranosylamine* (**2**). — Penta-*O*-acetyl-β-D-glucopyranose (20 g) was dissolved in 5% aqueous ammonia and kept for 24 h at room temperature. The solution was evaporated, with intermittent addition of ethanol to eliminate water. The residual syrup was dried in a vacuum desiccator, and dissolved in boiling, absolute ethanol (70 ml); on cooling, compound **2** crystallized (5.9 g, 53% yield), m.p. 196–198°, $[\alpha]_D$ +85.8° (*c* 0.3, water); lit.[9] m.p. 201–202°, $[\alpha]_D$ +86.2°.

N-*Acetyl-2,3,5,6-tetra-*O*-methyl-α-D-glucofuranosylamine* (**3**). — Compound **2** (1 g) was dissolved in *N*,*N*-dimethylformamide (20 ml), and barium oxide (4.2 g) and methyl iodide (7.7 g) were added. The suspension was shaken for 6 h, poured into chloroform (150 ml), and filtered. The filtrate was successively washed with 0.5M sulfuric acid, dilute sodium hydrogen carbonate, and water, dried (anh. sodium sulfate), and evaporated to dryness. The residual syrup was extracted with ethyl ether and the extract was evaporated to a syrup (1.17 g, 93.7%) that was purified by successive dissolutions in water and ethyl ether; $[\alpha]_D$ −15° (*c* 1.0, water).

Anal. Calc. for $C_{13}H_{25}NO_6$: C, 51.98; H, 8.30; N, 5.01. Found: C, 52.12; H, 8.51; N, 4.90.

*2,3,5,6-Tetra-*O*-methyl-D-glucofuranose* (**4**). — Compound **3** (450 mg) was hydrolyzed with 0.5M sulfuric acid for 30 min in a boiling-water bath. The solution was made neutral with barium carbonate, the suspension was filtered, and the filtrate was evaporated to dryness. The residual syrup was purified repeatedly by successive dissolutions in water and ethyl ether. The resulting syrup (370 mg, 96.6%) had $[\alpha]_D$ −7.6° (*c* 2.8, water); lit.[1] $[\alpha]_D$ −7.2° (*c* 2.0, water).

Oxidation of compound **4**. — Compound **4** was oxidized by treatment with bromine water during 18 h. The excess of bromine was removed by aeration, bromide ions with silver carbonate, and silver ions with a sulfonic resin. The solution was evaporated to dryness, the residue was extracted with chloroform, and the extract was evaporated, giving 38 mg of a syrup having $[\alpha]_D$ +32.8° (*c* 0.57, water); lit.[10] $[\alpha]_D$ +32.9° (*c* 0.13, water; 501 h). T.l.c.[11] on deactivated Silica Gel G, with 3:1:1 2-butanone–acetic acid–methanol as the eluant, revealed only one component.

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