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STEREOSELECTIVE SYNTHESIS OF 3-C- AND 5-C-METHYL-α-D-GLUCOFURANOSE DERIVATIVES AND THEIR DIASTEREOMERS

Masuo FUNABASHI*, Haruo SATO, and Juji YOSHIMURA
Laboratory of Chemistry for Natural Products, Faculty of Science,
Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152

The title compounds were stereoselectively prepared from 3-C-methylene-α-D-ribo- and 5-C-methylene-α-D-xylo-hexofuranose derivatives by successive epoxidation and reduction, and from corresponding 3- and 5-uloses by the Grignard reaction, respectively.

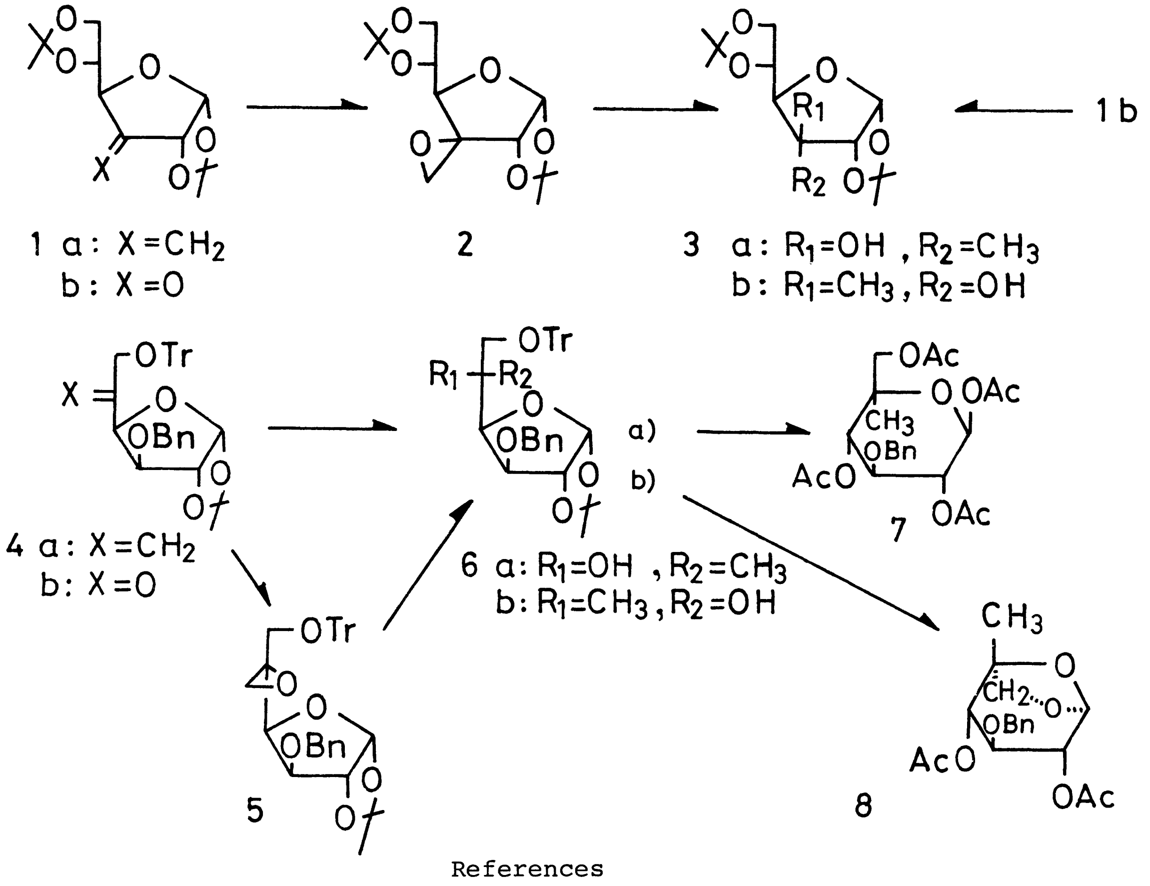
It has generally been known that nucleophilic reaction such as the Grignard and Reformatsky reactions to 1,2;5,6-di-O-isopropylidene-α-D-ribo-hexofuranos-3-ulose takes place from the exo-direction toward the trioxa-bicyclo[3,3,0]octane system to give exclusively the corresponding 3-C-substituted-D-allo derivatives.1) As it seems to be the case applicable to 3-C-methylene derivatives,2) the reversal of the configuration at C-3 by the same principle would be possible to give the diasteromeric 3-C-substituted-D-gluco isomers.

This paper, therefore, deals with a simple stereoselective preparation of the title compounds by applying epoxidation followed by reduction reaction to 3-C- and 5-C-methylene derivatives (1a, 4a) and Grignard reaction to 3- and 5-uloses (1b, 4b).

1,2;5,6-Di-O-isopropylidene-3-C-methyl-α-D-glucofuranose (3a), which is a potentially useful intermediate for a synthesis of some new branched-chain sugars3) such as D-evermicose, D-evalose, L-axenose etc., was, first of all, prepared as follows; 3-C-methylene derivative (1a) obtained from 3-ulose (1b) by a modified procedure using n-BuLi-THF system was converted by oxidation with m-chloroperbenzoic acid in dichloroethane to D-gluco epoxide [2, syrup, $[\alpha]_D$ +55° (c 1.7, methanol); nmr: δ 3.08 (q, epoxymethylene, J_{AB} = 5.0 Hz)] in 85% yield, which was also isolated by the reaction of 1a with diazomethane in a low yield.1b) Reduction of 2 with lithium aluminum hydride in ether gave 3a in 80% yield: mp 66 - 67°C, $[\alpha]_D$ +23° (c 1.0, acetone). 3a is completely different from the D-allo isomer (3b) which is, incidently, prepared from 1a by Grignard reaction: mp 104°C and $[\alpha]_D$ +32° (c 1.0, acetone), [lit.4b) (dithiane method), mp 102 - 103°C, $[\alpha]_D$ +21° (c 1.24, chloroform)]. 3a and 3b can be also differentiated by TLC and GLC.

The same technics were also applied to 3-O-benzyl-1,2-O-isopropylidene-5-C-methylene-6-O-trityl-α-D-xylo-hexofuranose [4a, mp 113 - 114°C, $[\alpha]_D$ -33° (c 1.0, chloroform)] and 3-O-benzyl-1,2-O-isopropylidene-6-O-trityl-α-D-xylo-hexofuranos-5-ulose5) (4b) to prepare the diastereomeric 5-C-methyl-hexofuranoses (6a,b) as analogues of L-noviose3) having 5-C-methyl branch. The reaction of 4b with methylmagnesium iodide in ether gave exclusively 3-O-benzyl-1,2-O-isopropylidene-5-C-methyl-6-O-trityl-α-D-glucofuranose [6a, mp 181 - 182°C, $[\alpha]_D$ -5.7° (c 1.0, chloroform)] in a high yield, and the successive oxidation and reduction of 4a gave the corresponding 5-C-methyl-β-L-idofuranose derivative [6b, syrup, $[\alpha]_D$ -54° (c 1.37, acetone)] as a major product separated from the contaminant 6a by preparative TLC. The ratio was estimated to be 2 : 1 from NMR spectra of the methylene protons at C-6 of the mixture (6).

The configuration at C-5 of both compounds (6a and 6b) was definitely established from the fact that the hydrolysis of 6a and 6b with hot 70% acetic acid and successive acetylation gave 1,2,3,4-tetra-O-acetyl-3-O-benzyl-5-C-methyl-β-D-glucopyranose [7, mp 128 - 129°C, $[\alpha]_D$ -18° (c 1.1, acetone)] and 1,6-anhydro-2,4-di-O-acetyl-3-O-benzyl-5-C-methyl-β-L-idopyranose [8, mp 118 - 119°C, $[\alpha]_D$ +67° (c 1.0, acetone)], respectively in a good yield.



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