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A NEW METHOD FOR THE SYNTHESIS OF 3-DEOXY SUGARS BY GRIGNARD REACTIONS WITH METHYL 5,6-O-CYCLOHEXYLIDENE-3-O-MESYL-α- AND -β-D-ALLOFURANOSIDE[1]

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The 3-deoxy sugars were easily prepared in good yield by the reaction of t-butylmagnesium bromide with the title compounds. The same reaction with 1-O-benzoyl- or -mesyl-cis-cyclododecane-1,2-diol gave cyclododecanone.

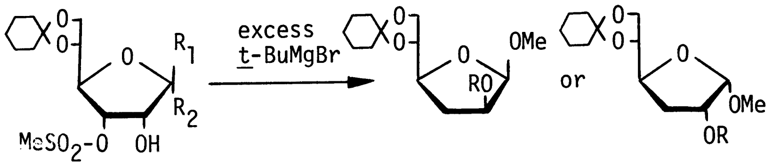
In a recent communication,[2] we reported that the reactions of methyl 5,6-O-cyclohexylidene-3-O-mesyl-β-D-allofuranoside 1a and its α-anomer 1b with an excess of methylmagnesium iodide gave, by one step, branched-chain deoxy sugars, methyl 5,6-O-cyclohexylidene-3-deoxy-2-C-methyl-β-D-arabino- and -α-D-ribo-hexofuranoside, respectively. We have now extended the scope of these reactions to the synthesis of deoxy sugars.

A solid of 1a (2 mmol) was gradually added to a solution of t-butylmagnesium bromide (ca. 24 mmol) in a mixture of ether (20 ml) and benzene (10 ml) at room temperature over a period of 30 min, and the mixture was stirred for another 30 min. The usual workup exclusively afforded methyl 5,6-O-cyclohexylidene-3-deoxy-β-D-arabino-hexofuranoside 2a [syrup, $[\alpha]_D^{25}$ -86.0° (c 1, $CHCl_3$)][3] in 87% yield after column chromatography. Treatment of 2a with benzoyl chloride in pyridine gave a crystalline benzoate 2b [mp 86.0-86.5°, $[\alpha]_D^{25}$ -88.4° (c 1.2, $CHCl_3$)].

In a similar manner, the anomer 1b was reacted with t-butylmagnesium bromide at 60-65° (bath temperature) for 40 min to give methyl 5,6-O-cyclohexylidene-3-deoxy-α-D-ribo-hexofuranoside 3a [syrup, $[\alpha]_D^{25}$ +93.6° (c 1, $CHCl_3$)] in 75% yield. Its benzoate 3b [syrup, $[\alpha]_D^{25}$ +96.0° (c 1, $CHCl_3$)] was obtained by the conventional method.

Both structures of 2a and 3a were determined by means of their elemental analyses, spectroscopic data, and the following chemical conversions. A mixture of 2a (0.4 mmol) and cyclohexanone (0.3 ml) in benzene (1.5 ml) was stirred at room temperature in the presence of a small amount of sulfuric acid for 4 hr. After neutralization with calcium hydroxide, the excess cyclohexanone was reduced with sodium borohydride to give 1,2;5,6-di-O-cyclohexylidene-3-deoxy-β-D-arabino-hexofuranose 4 [syrup, $[\alpha]_D^{24}$ +6.1° (c 1.4, $CHCl_3$)]. Similarly, 3a gave 1,2;5,6-di-O-cyclohexylidene-

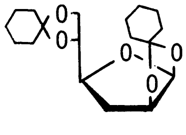
3-deoxy-α-D-ribo-hexofuranose 5 [syrup, $[\alpha]_D^{26}$ +1.4° (c 1.2, $CHCl_3$)]. Although the furanose structures of 4 and 5 were tentatively assigned, the physical data of these compounds were identical with those of the corresponding samples derived from known methyl 4,6-O-benzylidene-3-deoxy-α-D-arabino-[4] and -ribo-hexopyranoside,[5] respectively.



1 2 3

a : R_1=OMe, R_2=H
b : R_1=H, R_2=OMe

a : R=H
b : R=C_6H_5CO-



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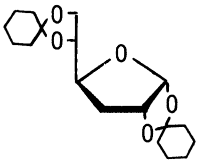

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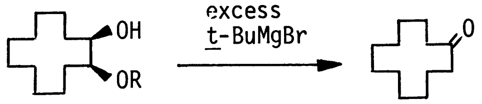

6 7

a : R=$MeSO_2$-
b : R=C_6H_5CO-

The present reactions would involve the formation of 3-deoxy-2-keto sugars via the 1,2-hydride shift[2] from C-2 to C-3, followed by the stereoselective reductions of these ketones with t-butylmagnesium bromide. We have not succeeded in the isolation of the keto-sugars, but 1,2;5,6-di-O-cyclohexylidene-α-D-ribo-hexofuranos-3-ulose[6] was found to be reduced stereoselectively with t-butylmagnesium bromide at room temperature to give 1,2;5,6-di-O-cyclohexylidene-α-D-allofuranose[6] in good yield. When a simple mesylate, 1-O-mesyl-cis-cyclododecane-1,2-diol 6a [mp 97-98°] was treated with a large excess of t-butylmagnesium bromide, cyclododecanone 7 was formed in 82% yield. A similar result could be obtained by the use of 1-O-benzoyl-cis-cyclododecane-1,2-diol 6b [mp 112.5-113.5°] in place of 6a.[7]

REFERENCES AND NOTES

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