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A NOVEL SYNTHESIS OF 2'-DEOXY-α-DISACCHARIDES

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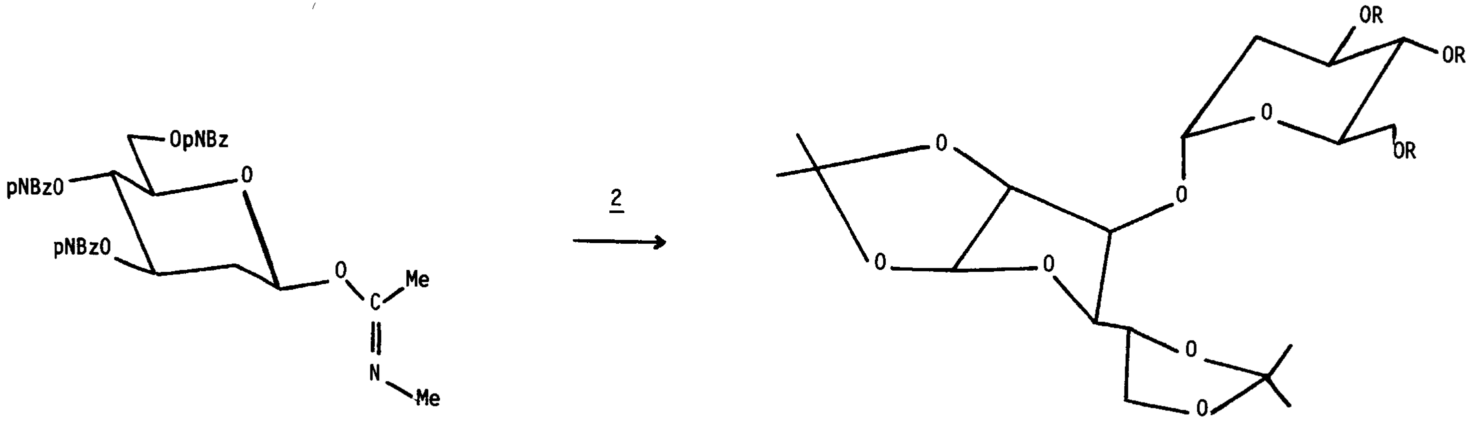
Several 2'-deoxy-α-disaccharides were prepared in excellent yield using the imidate procedure recently introduced in our laboratory for the synthesis of 1,2-cis-disaccharides.

2-Deoxy-α-glycosides are known to be biologically important as structural units in the field of natural products, especially in sugar-containing substances related to the macrolide[1] and anthracycline[2] groups. For this reason, various procedures for synthesis of 2-deoxy-α-glycosides have been investigated[3]. We have recently introduced a new method of selective activation of the anomeric centre of carbohydrates which appears full of promise in the field of glycosidic synthesis[4]. We report in this letter a few examples indicating that the so-called imidate procedure[4] might again be the technique of choice for the synthesis of 2'-deoxy-α-disaccharides.

A benzene solution of 3,4,6-tri-O-p-nitrobenzoyl-2-deoxy-α-D-arabino-hexopyranosyl bromide[5] (1 eq.) was stirred for 12 h at room temperature in the presence of N-methylacetamide (1.5 eq.), silver oxide (3 eq.), diisopropylethylamine (1.1 eq.), and powdered 4 Å molecular sieve to give 1-O-(N-methyl)acetimidyl-3,4,6-tri-O-p-nitrobenzoyl-2-deoxy-β-D-arabino-hexopyranose 1 (57 %) as a syrup which was directly used in glycosidation reactions without further purification[6].

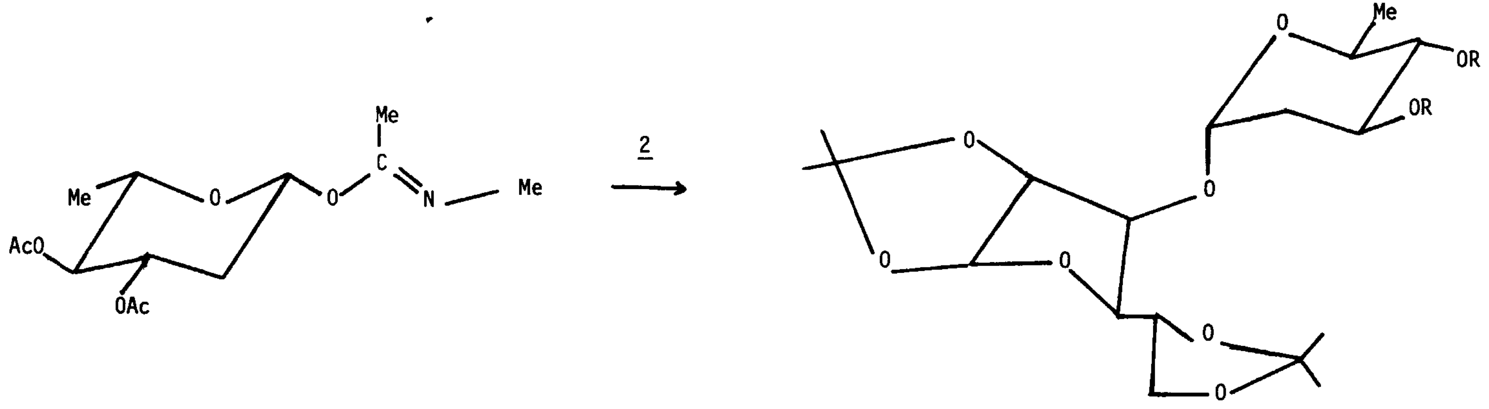
In a typical procedure, a solution of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose 2 (0.25 mmol) in dry benzene (4 ml) was treated at room temperature with the imidate 1 (0.4 mmol) and p-toluenesulfonic acid (0.42 mmol). The solution was stirred for 16 h and neutralized with



1

3 R = pNBz

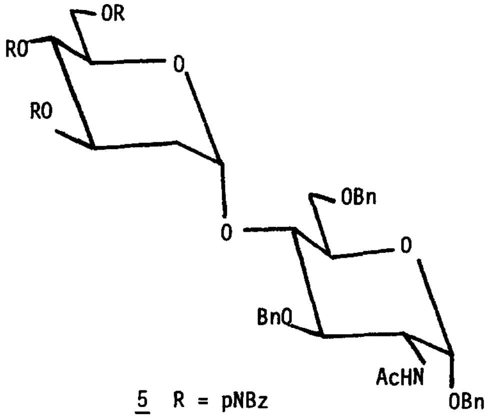
4 R = H



7

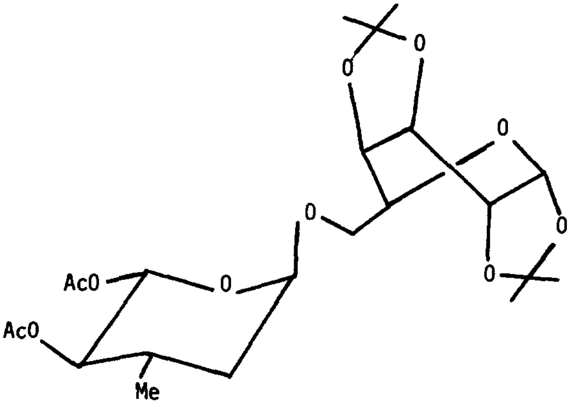
8 R = Ac

9 R = H



5 R = pNBz

6 R = H



10

triethylamine. After workup and purification (silica gel column), disaccharide 3 was isolated as a syrup (88 %), $[\alpha]_D^{20}$ + 9.1° (c 2.4, chloroform). After de-p-nitrobenzoylation (sodium methoxide in methanol), the disaccharide 4 was obtained (94 %), m.p. 99-101° (from ether), $[\alpha]_D^{20}$ + 5.3° (c 1.3, chloroform). Similarly, benzyl 2-acetamido-3,6-di-O-benzyl-2-deoxy-α-D-glucopyranoside[7] was transformed (1h at room temperature) into the disaccharide 5 (82 %), $[\alpha]_D^{20}$+ 76.1° (c 1.7, chloroform). After de-p-nitrobenzoylation, the disaccharide 6 was obtained (94 %), m.p. 152-153° (from acetone), $[\alpha]_D^{20}$ + 105.9° (c 2.7, chloroform). In general, many difficulties have been experienced with the glycosidation of the 4-hydroxyl group of glucopyranoside derivatives and we think that this last example is particularly significant.

In order to extend the procedure to polydeoxy sugars[8], crystalline 3,4-di-O-acetyl-2,6-dideoxy-α-L-arabino-hexopyranosyl bromide[9] was converted into the imidate 7 (79 %), $[\alpha]_D^{20}$ -53° (c 2.4, chloroform). Glycosidation of 2 with the imidate 7 (24 h at room temperature) followed by column chromatography (silica gel) gave the disaccharide derivative 8 (83 %), m.p. 172-173° (from diisopropylether-cyclohexane), $[\alpha]_D^{20}$- 123.1° (c 1.3, chloroform). After deacetylation (methanol-water-trietylamine) the disaccharide 9 was obtained (92 %), $[\alpha]_D^{20}$-89.8° (c 1.4, chloroform). Likewise, the disaccharide derivative 10 was prepared (91 %), $[\alpha]_D^{20}$-103.4° (c 2.4, chloroform) from 1,2:3,4-di-O-isopropylidene-α-D-galactopyranose.

The examples reported herein prove that the imidate procedure has to be considered when dealing with the synthesis of a 2'-deoxy-α-disaccharide and perhaps compares well with alternative methods.

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