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A FACILE SYNTHESIS OF 1,2-O-ISOPROPYLIDENE-ß-L-IDOFURANURONO-6,3-LACTONE[a]

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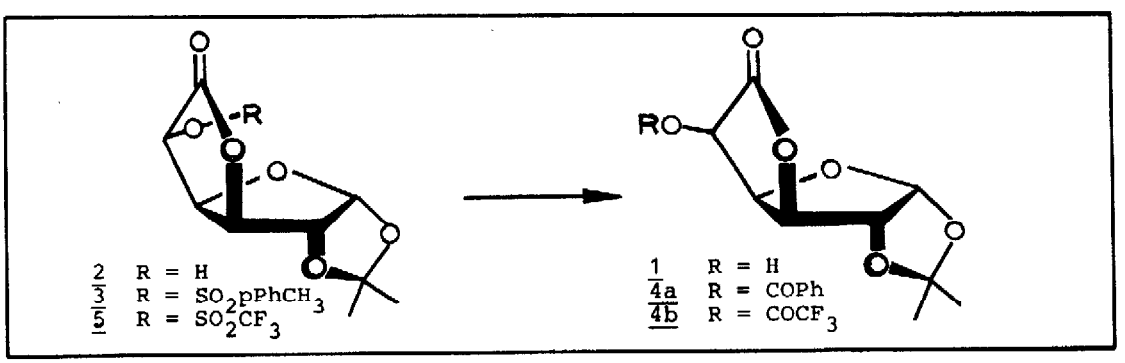
Abstract: A simple, high yield, two step synthesis of 1,2-O-isopropylidene-ß-L-idofuranurono-6,3-lactone is described.

There are several published methods for the synthesis of 1,2-O-isopropylidene-ß-L-idofuranurono-6,3-lactone (1) and derivatives thereof[1-4], either employing 1,2-O-isopropylidene-α-D-glucofuranose[1-3] or 1,2-O-isopropylidene-α-D-glucofuranurono-6,3-lactone (2)[4], both of which are well accessible compounds. All of these approaches are multistep synthesis, involving elaborate procedures and/or separations of diastereomers, resulting in overall yields of 1.7 to 30 %.

Although inversion at C-5 either by nucleophilic displacement of 3 or by direct epimerization of 2 appears to be the method of choice, oxygen nucleophiles in general invariably led to extensive deterioration due to eliminations[4-6].



We want to present a simple, high yield, two step synthesis of 1 starting from 2. The trifluoromethanesulfonyloxy group has been demonstrated to exhibit excellent leaving properties in various carbohydrate transformations[7]. Thus 5-O-trifluoromethanesulfonyl-1,2-O-isopropylidene-α-D-glucofuranurono-6,3-lactone (5), hitherto unknown, when subjected to a variety of oxygen nucleophiles, very smoothly yielded the respective L-ido derivatives practically without by-products contrary to 3. While the removal of acyl groups as in 4a by standard procedures inflicted ring openings as well as eliminations[6], 4b rapidly suffered methanolysis under neutral conditions. The overall yield of 1 thus obtained is 78 %.

In view of this, a variety of substrates with an inherent tendency towards elimination in nucleophilic reactions are presently investigated. This includes epimerizations recently observed with 2 and its derivatives.

In a typical procedure, the 5-O-triflate 5 was prepared by addition of 2 in methylene chloride to trifluoromethanesulfonic acid anhydride dissolved in methylene chloride containing pyridine at -20° and the mixture kept for 30 min. at this temperature. After usual workup[7] the product was used without purification in the next step. It could be obtained in pure form, however, by passing the methylene chloride solution through a short column of celite. The sample showed mp 149 - 150°, $[\alpha]_D^{20}$ 122.2° (c = 0.4, $CHCl_3$). NMR (90 MHz, $CDCl_3$): 1.35, 1.50, 2s, 6H, isoprop.; 4.86, d, 1H, H-2, $J_{1,2}$ = 3.7; 4.93, d, 1H, H-3, $J_{2,3}$ = 0.5; 5.07, dd, 1H, H-4, $J_{3,4}$ = 3.1; 5.42, d, 1H, H-5, $J_{4,5}$ = 4.0; 6.06, d, 1H, H-1.

The 1,2-O-isopropylidene-ß-L-idofuranurono-6,3-lactone (1) was readily obtained by reaction of 5 with sodium trifluoroacetate in DMF at room temperature for 30 min. After removal of solvent a solution of the residue in methanol was passed through a short column of celite, yielding 82 % of 1, mp 132 - 135°, $[\alpha]_D^{20}$ 101° (c = 1.2, acetone), being identical with an authentic sample[4].

5-O-benzoyl-1,2-O-isopropylidene-ß-L-idofuranurono-6-3-lactone (4a) was obtained from 5 with sodium benzoate under conditions described above. Yield 96 %, mp 89-92°, $[\alpha]_D^{20}$ 64.4° (c = 0.4, $CHCl_3$), identical with a sample prepared by benzoylation of 1. NMR (90 MHz, $CDCl_3$): 1.35, 1.39, 2s, 6H, isoprop.; 4.89, d, 1H, H-2, $J_{1,2}$ = 3.7; 4.94, d, 1H, H-3, $J_{2,3}$ = 0.5; 5.15, s, 1H, H-5, $J_{4,5}$ = 0.5; 5.23, d, 1H, H-4, $J_{3,4}$ = 3.4; 6.01, d, 1H, H-1; 7.3 - 8.2, m, 5H, Ph. Attempted debenzoylation of 4a even under very mild conditions invariably resulted in eliminations[6].

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Notes and references:

a. Reactions of D-Glucuronic Acid, part XIV. For part XIII see ref. 4

b. undergraduate fellow

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