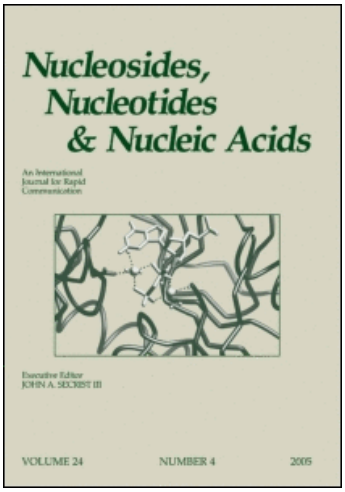

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Glycal Ethers as Starting Materials in C-Nucleoside Synthesis

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GLYCAL ETHERS AS STARTING MATERIALS IN C-NUCLEOSIDE SYNTHESIS

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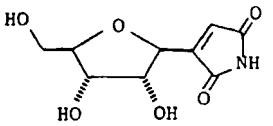
Abstract. When 3,4,6-tri-O-benzyl-D-glucal (3) is treated with thallium (III) nitrate, trihydrate in acetonitrile, 2,5-anhydro-3,4,6-tri-O-benzyl-D-mannose (4), a precursor of the showdomycin analogue (5), is obtained. Ring-contraction of (3) can also be effected by a three-step process [(i) PhSeCl, tetrahydrofuran, (ii) Et_3N, H_2O; (iii) 3-$ClC_6H_4CO_3H$, MeOH]. Other examples of these ring-contraction reactions are described.

Trummlitz and Moffatt have reported[1] a synthesis of the nucleoside antibiotic showdomycin (1), based on 2,5-anhydro-3,4,6-tri-O-benzyl-D-allose (2). Although the latter showdomycin synthesis is elegant, the procedure used[1] for the preparation of (2) was rather lengthy. It occurred to us that it should be possible to prepare analogues of (2), and hence analogues of showdomycin, by the ring-contraction of glycal benzyl ethers.



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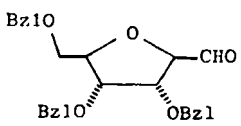

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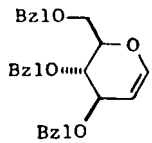

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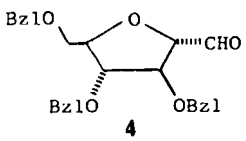

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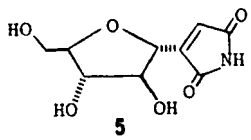

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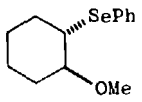
Treatment of 3,4,6-tri-O-benzyl-D-glucal[2] (3) with a stoicheiometric quantity of thallium (III) nitrate, trihydrate[3] (TTN) in acetonitrile solution at room temperature for 1 hr gave[4] what is assumed to be 2,5-anhydro-3,4,6-tri-O-benzyl-D-mannose (4) as the main product. The latter crude aldehyde (4) was converted[4,5] into the showdomycin analogue (5), m.p. 134°C, by the six-step procedure used by Trummlitz and Moffatt[1] to convert (2) into (1). The overall yield of (5) for the seven steps, starting from (3), was ca. 18%.



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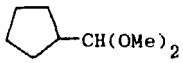

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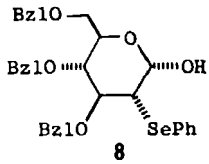

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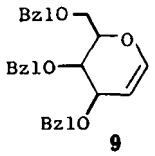
An alternative procedure for ring-contraction was suggested by the recent report[6] that treatment of trans-2-methoxybenzeneselenenocyclohexane (6) with m-choroperbenzoic acid in methanol gave 2-(dimethoxymethyl)tetrahydrofuran (7). When 3,4,6-tri-O-benzyl-D-glucal (3) was allowed to react with a slight excess of benzeneselenenyl chloride in dry tetrahydrofuran at room temperature and the products then treated with triethylamine and water, the benzeneselenenol adduct (8) was obtained[7] and isolated as a crystalline solid, m.p. 98°C, in 67% yield. The configuration at the site of selenenation [i.e. at C(2)], the assignment of which is based on ^{1}H-n.m.r. spectroscopic data, differs from that reported in a related study by Sinaÿ and his coworkers[8]. Treatment of (8) with slightly more than two mol. equiv. of m-chloroperbenzoic acid in methanol at room temperature for 30 min gave the crude aldehyde (4), which was again converted[7] into the α-anomer of ara-showdomycin (5) by Trummlitz and Moffatt's procedure[1]. The overall yield of (5) for the seven steps, starting from (8), was 19.5%.

The reaction between 3,4,6-tri-O-benzyl-D-galactal (9) and TTN proceeded slowly and a complex mixture of products was obtained[7]. However, when (9) was treated first with benzeneselenenyl chloride and then with triethylamine and water, and the resulting benzeneselenenol adduct oxidized with m-chloroperbenzoic acid in methanol, a crude aldehydo-compound with putative structure (10) was obtained[7]. The latter product (10) was readily converted[7] into (11), the α-anomer of lyxo-showdomycin, m.p. 144 - 145°C. The overall yield of (11) was 13% for the nine steps starting from (9). Finally, when 4,6-di-O-benzyl-



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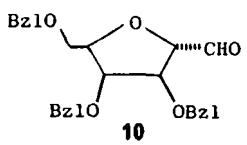

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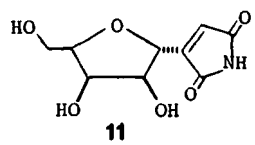

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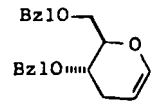

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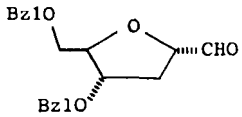

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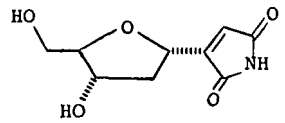

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3-deoxy-D-glucal (12) was treated[4] with TTN in acetonitrile for 30 min at room temperature, the reaction proceeded smoothly and the putative aldehyde (13) was obtained and isolated as its N,N'-diphenylimidazolidine derivative[9], m.p. 47 - 49°C, in 61% yield based on (12). The latter derivative was converted[4] by Trummlitz and Moffatt's procedure[1] into α-2'-deoxyshowdomycin (14), m.p. 112°C. The overall yield of (14) for the nine steps, starting from (12), was ca. 14.5%. The structures of all three showdomycin analogues [(5), (11) and (14)] described above have been confirmed by X-ray crystal structure determinations[4,7].

Acknowledgements

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