A Method for the Preparation of Furanoid Glycals

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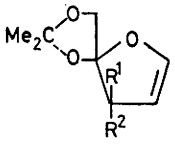
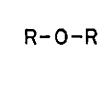
Summary The reduction of furanosyl bromides having base-stable protecting groups with sodium in aprotic solvents gives furanoid glycals.

FISCHER and ZACH's method[1] of preparing pyranoid glycals by zinc-reduction of acetylated pyranosyl halides in acetic acid is not generally useful for the preparation[2] of furanoid

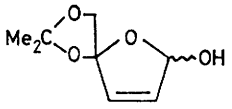
glycals because these unsaturated sugars tend to undergo rapid acid-catalysed allylic rearrangements, unless a poor leaving group is present at C-3.[3] The formation of furanoid glycals by this method,[1,3] as well as by a related method,[2] depends on the generation of an unstable anion at the anomeric position, followed by elimination of a substituent on C-2. We now report that the reduction of suitably protected furanosyl bromides with sodium or potassium in aprotic solvents constitutes an alternative method for the preparation of reactive furanosyl anions. In the examples studied, the initially formed furanosyl anions rearranged rapidly to give 1,4-anhydrohex-1-enitol 3-oxyanions which attacked unchanged furanosyl halide to give 3-*O*-furanosyl furanoid glycals as major products. Also, the reactions of the reducing metal with free furanose present as impurity in the furanosyl bromides gave rise to low yields of 1,1′-disaccharides, apparently through formation of furanosyloxy-anions that attacked starting bromide. During the glycosylation reactions, for which S_N1 character is assumed,[4] the bulky oxyanions attacked from the less hindered sides of the furanosyl bromides.



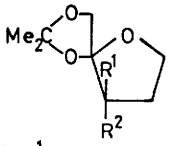
(1); R^1 = 2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranosyloxy, R^2=H
(2); R^1 = OH, R^2=H
(3); R^1 = H, R^2 = 2,3:5,6-Di-*O*-isopropylidene-β-D-allofuranosyloxy



(4); R = 2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranosyl
(5); R = 2,3:5,6-Di-*O*-isopropylidene-β-D-allofuranosyl



(6)



(7), R^1 = 2,3:5,6-Di-*O*-isopropylidene-α-D-mannofuranosyloxy, R^2=H
(8), R^1=H, R^2 = 2,3:5,6-Di-*O*-isopropylidene-β-D-allofuranosyloxy

Thus, 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl bromide[5] reacted smoothly with an excess of sodium in dry tetrahydrofuran (THF) (20 °C, 3 h) to give the furanoid glycal (**1**)† (59% yield) as a distillable oil (180 °C, 0·01 mmHg), $[\alpha]_D$ +13°, *m/e* 413 (M^+ −Me), and a trace of the 1,1′-disaccharide (**4**) (*ca.* 2% yield), m.p. 165 °C, $[\alpha]_D$ +63°, *m/e* 487 (M^+ −Me). Treatment of the mannofuranosyl bromide with sodium sand in toluene (75 °C, 4 h) gave low yields of (**1**) (9%) as well as the 1,4-anhydrohex-1-enitol (**2**) (11%), oil $[\alpha]_D$ −48°, *m/e* 186 (M^+). The glycal (**2**) was unstable and rearranged during chromatography on silica gel to the isomeric compound (**6**), oil, $[\alpha]_D$ −45°, *m/e* 171 (M^+ −Me). No products were obtained when sodium or potassium was replaced in the reaction by magnesium or lithium.

2,3:5,6-Di-*O*-isopropylidene-β-D-allofuranosyl bromide, *m/e* 307 and 309 (M^+ −Me), $J_{1,2}$ 0 Hz, prepared by the method described[5] for the preparation of the analogous mannofuranosyl bromide, behaved similarly on reduction with sodium in THF (20 °C, 3 h) to give the furanoid glycal (**3**) (69% yield), m.p. 108—110 °C, $[\alpha]_D$ +52°, *m/e* 428 (M^+), and the 1,1′-disaccharide (**5**) (*ca.* 2% yield), m.p. 230 °C, $[\alpha]_D$ −60°.

The glycals (**1**) and (**3**) were hydrogenated (Pd–C, EtOAc, 50 lb in^{-2}) to give, respectively, the 1,4-anhydro-2-deoxyhexitols (**7**) (yield 80%), oil, $[\alpha]_D$ +14°, *m/e* 430 (M^+), and (**8**) (yield 75%), m.p. 86 °C, $[\alpha]_D$ −34°, *m/e* 430 (M^+).

The n.m.r. spectra of (**1**), (**3**), (**7**), and (**8**) showed that H-1′ and H-2′ of the furanosyloxy group in each compound were *trans* orientated[6] ($J_{1',2'}$ 0 Hz in all cases).

Compounds (**4**) and (**5**) both displayed the more simple n.m.r. spectra of monosaccharides since the two furanosyl residues in each of the compounds are identical. Again, the $J_{1,2}$ coupling constants (0 Hz) of (**4**) and (**5**) established the *trans* relationship of H-1 and H-2.

The positions of the double bonds in (**1**)—(**3**) and (**6**) were determined by comparison of their n.m.r. chemical shifts and coupling constants with those of known[2,3] furanoid glycals.

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† All new compounds had satisfactory microanalytical and spectral properties. Optical rotations were measured at 20 °C for solutions in chloroform (*c* 1 ± 0·4).

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