A New, Zinc-promoted Synthesis of 1,4-(1,5)-Anhydro-2-deoxy-pent-(hex)-1-enitols (Furanoid and Pyranoid Glycals)

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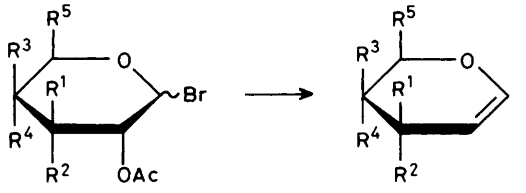
Activated zinc in tetrahydrofuran efficiently converts derivatives of furanosyl and pyranosyl halides into glycals.

Glycals, 1,4-(1,5)-anhydro-2-deoxy-pent-(hex)-1-enitols,[1] are valuable intermediates in carbohydrate and other areas of natural product chemistry.[2]

Inasmuch as the original synthesis of glycals[3] is specifically confined to reactions of 2-*O*-acyl glycopyranosyl halides with zinc in acetic acid, conditions generally incompatible with glycofuranosyl halides,[4] this method only allows pyranoid glycals to be prepared. Since all attempts to change to aprotic solvents, employing Zn, Mg, or Zn/Cu[5] to expand the scope of this glycal synthesis, were also hitherto unsuccessful, more appropriate methods were called for.

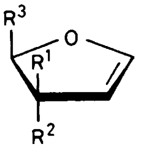
Disregarding special approaches,[6—8] the most useful now at



(1) - (5)

	R¹	R²	R³	R⁴	R⁵
(**1**)	OAc	H	H	OAc	CH$_2$OAc
(**2**)	OAc	H	OAc	H	CH$_2$OAc
(**3**)	OAc	H	H	OAc	H
(**4**)	H	OAc	H	OAc	H
(**5**)	OAc	H	H	X	CH$_2$OAc

X = 2,3,4,6-tetra-*O*-acetyl-β-D-glycopyranosyl



(6), **(7)**

	R¹	R²	R³
(**6**)	OH	H	-CHOCMe$_2$OCH$_2$
(**7**)	H	OH	-CH$_2$OCH$_2$OMe

hand consists in either treatment with sodium iodide of pentofuranosyl bromides, bearing good leaving groups at C-2,[9] or reactions of 2,3-*O*-isopropylidene glycosyl halides with sodium[10] or sodium naphthalenide[5] or, in the latest version, with lithium in ammonia.[11,12] Except for the first of these, none can provide *O*-acylated glycals and invariably either 3-*O*-unprotected[11,12] or 3-*O*-glycosylated products are formed.[10]

An extension of the Fischer–Zach glycal synthesis[3] to aprotic conditions as well as to acetal-protected glycosyl halides has now been accomplished. Thus, when 2,3-*O*-isopropylidene glycofuranosyl halides or per-*O*-acetyl glycopyranosyl halides were subjected to zinc/silver–graphite[13] in tetrahydrofuran, the glycals (**1**)—(**7**) were formed exclusively and in excellent yields (Table 1).† In all

Table 1. Formation of the glycals (**1**)—(**7**).

Product	Temp./°C	Time/min	% Yield	Ref.[a]
(**1**)[b]	−20	10	95.6	15
(**2**)[b]	−20	10	87.3	15
(**3**)[b]	−20 to 25	20	91.9	15
(**4**)[b]	−20 to 25	20	90.1	15
(**5**)[b]	−20 to 25	180	83.1	15
(**6**)[c]	−20 to 30	180	81.0	12
(**7**)[d]	−20 to 30	180	86.4	5

[a] All compounds gave satisfactory microanalytical and spectral data. [b] From the corresponding per-*O*-acetylated glycopyranosyl bromide. [c] From 2,3-*O*-isopropylidene-5-*O*-methoxymethyl-β-D-ribofuranosyl chloride. [d] From 2,3 : 5,6-di-*O*-isopropylidene-β-D-mannofuranosyl chloride.

cases investigated, pyranosyl halides eliminated faster than furanosyl halides.

It is of interest to note that Rieke-zinc,[14] generally considered to be highly reactive, was found to be unsuitable for glycal formation under the conditions given in Table 1.

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† Specifically, to a stirred suspension of zinc/silver–graphite[13] (2.2 mmol) in tetrahydrofuran (THF; 30 ml) the glycosyl halide (2 mmol) THF (5 ml) was added at −20 °C and the temperature slowly increased (*cf.* Table 1). After completion of the reaction and filtration over Florisil, the solution was evaporated and the product purified by chromatography.