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Note

Preparation of acetylated pyranoid glycals from glycosyl halides by chromium(II) complexes under aqueous biphasic conditions

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Abstract

Reactions of chromium(II) aminocarboxylate complexes (ethylenediamine-tetraacetate, nitrilo-triacetate, imino-diacetate) with acetylated glycopyranosyl chlorides or bromides in liquid–liquid or solid–liquid biphasic media (such as water–diethylether, water–ethyl acetate or halosugar–water) give the corresponding glycals in 75–97% yield.

Keywords: Chromium(II) complexes; Biphasic reactions; Glycals

Glycals (1,4- or 1,5-anhydro-2-deoxy-1-enitols) are widely used in carbohydrate and natural product syntheses as starting materials. A recent review[1] covering the synthetic methods for glycals revealed that despite of several existing procedures, further innovations and amendments of known protocols can improve the availability of this important class of compounds.

In this note, we disclose a modification of our recently published method[2] for the preparation of acylated pyranoid glycals from the corresponding glycosyl chlorides or bromides mediated by Cr(II) aminopolycarboxylate complexes in aqueous DMF as the reaction medium. It was demonstrated in our previous study that under the above conditions, competing reactions at the anomeric centre (nucleophilic attack by water or acetate ions to give by-products versus electrontransfer leading to glycals) had comparable rates if less reactive Cr(II)L complexes (L = malonate, glycine, imino-diacetate (IDA)) were used. This resulted in less clean transformations which could be avoided by using complexes of Cr(II) with nitrilo-triacetate (NTA), or ethylenediamine-tetraacetate (EDTA) as ligands.

We reasoned that protection of the glycosyl halides from the non-desirable nucleophilic attack can also be achieved if these sensitive

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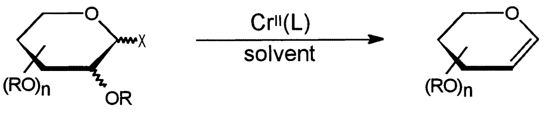
substrates and the reagents are placed into separate phases. Following this hypothesis, the chromium(II) complexes were prepared in water and a solution of a glycosyl halide in either diethyl ether (Table 1, Entries 1–7) or ethyl acetate (Table 1, Entries 8–16) was added and the mixture was vigorously stirred. Yields and purities of the product glycals were comparable with or better than those obtained in the water–DMF homogeneous medium.[2] Under these conditions Cr(II)(IDA) gave results comparable to the ones obtained with the best complexes of NTA and EDTA.

Another version of the biphasic reaction is represented by Entries 19 and 20 in Table 1, where the substrates **1** and **3** remained in the solid phase and the reagent complex was added in pure water. These two-phase reactions also offered an easier work-up procedure as compared to the water–DMF variants for each glycosyl halide.

Although this was not investigated, we speculate that under the biphasic conditions the reaction may take place at the phase boundary. Another possibility is that the acetylated sugar derivatives which are not completely insoluble in water can be present in a limited concentration in the aqueous phase containing the reagent. This latter assumption is supported by the failure of the biphasic transformations of **8** and **9** (Table 1, Entries 17 and 18) which must be much less soluble in water than their acetylated analogues.

Table 1
Preparation of glycals in various biphasic systems



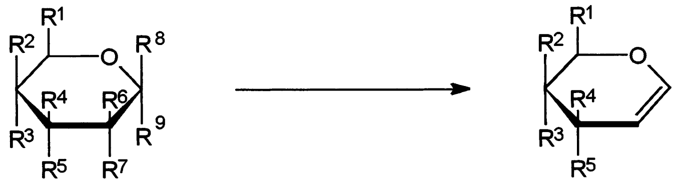
1-9 **10-14**

Entry	Solvent	Starting compound	Ligand (L)	pH	Product	Yield [a,b] (%)
1	water–Et_2O	**1**	IDA	6.2	**10**	84
2	water–Et_2O	**1**	NTA	6.0	**10**	78
3	water–Et_2O	**1**	EDTA	5.0	**10**	80
4	water–Et_2O	**2**	IDA	6.2	**10**	87
5	water–Et_2O	**2**	NTA	6.0	**10**	79
6	water–Et_2O	**2**	EDTA	5.0	**10**	90
7	water–Et_2O	**6**	EDTA	5.0	**13**	85
8	water–EtOAc	**1**	EDTA	5.0	**10**	90
9	water–EtOAc	**2**	IDA	5.8	**10**	76
10	water–EtOAc	**2**	NTA	6.2	**10**	91
11	water–EtOAc	**2**	EDTA	5.0	**10**	91
12	water–EtOAc	**3**	EDTA	5.0	**11**	84
13	water–EtOAc	**4**	EDTA	5.0	**11**	97
14	water–EtOAc	**5**	EDTA	5.0	**12**	44 [c]
15	water–EtOAc	**6**	EDTA	5.0	**13**	75
16	water–EtOAc	**7**	EDTA	5.0	**14**	95
17	water–EtOAc	**8**	EDTA	5.0		no reaction
18	water–EtOAc	**9**	EDTA	5.0		no reaction
19	water	**1**	EDTA	5.0	**10**	80
20	water	**3**	EDTA	5.0	**11**	83

[a] The isolated products had NMR characteristics identical with those of authentic samples **10**, **11**, **13**, **14**[3], **12**.[4]

[b] The purity of the isolated products was higher than 95% based on ^1H NMR spectra of the worked-up reaction mixtures and this means that no resonance other than those of **10**–**14** could be observed in the spectrum.

[c] For the D-xylo configurated compounds, lower yields were obtained also under homogeneous conditions.[2] For this behaviour, the probably higher hydrolytic lability of these compounds may be responsible.



1-9 **10-14**

Compound	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	R^9
1, 10	CH_2OAc	H	OAc	OAc	H	H	OAc	H	Cl
2	CH_2OAc	H	OAc	OAc	H	H	OAc	H	Br
3, 11	CH_2OAc	OAc	H	OAc	H	H	OAc	H	Cl
4	CH_2OAc	OAc	H	OAc	H	H	OAc	H	Br
5, 12	H	H	OAc	OAc	H	H	OAc	H	Cl
6, 13	H	H	OAc	H	OAc	OAc	H	Br	H
7, 14	CH_2OAc	H	*	OAc	H	H	OAc	H	Br
8	CH_2OBz	H	OBz	OBz	H	H	OBz	H	Br
9	CH_2OPiv	H	OPiv	OPiv	H	H	OPiv	H	Br

*2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl.

In conclusion, we have elaborated a simple procedure for the preparation of acetylated pyranoid glycals of high purity in which both glycosyl chlorides and bromides can be applied as starting compounds.

1. Experimental

Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin–Elmer 241 polarimeter at rt. NMR spectra were recorded with a Bruker WP 200 SY spectrometer (^1H, 200 MHz; ^{13}C, 50.3 MHz). TLC was performed on DC-Alurolle, Kieselgel 60 F_{254} (E. Merck), (eluent: 1:1 EtOAc–hexane); the plates were visualised by gentle heating. For column chromatography Kieselgel 60 (E. Merck) was used (eluent: 1:3 EtOAc–hexane). Organic solutions were dried over anhyd $MgSO_4$ and concentrated under diminished pressure at 40–50 °C (water bath).

Aqueous solutions of the Cr(II)L complexes and the glycosyl halides were prepared according to literature protocols described and referenced in detail in our previous paper.[2]

General procedure I for the reaction of acetylated glycosyl halides **1**–**7** *with chromium-(II) complexes in liquid–liquid biphasic medium.*—$Na_2EDTA \cdot H_2O$ (0.893g, 2.4 mmol) was dissolved in water (48.9 cm^3) and KOH (2.42 mol dm^{-3}, 1.1 cm^3, 2.66 mmol) was added. Argon was bubbled into the solution for 15 min. $[Cr(OAc)_2 \cdot H_2O]_2$ (0.750 g, 2.2 mmol Cr(II)) was then added and the colour of the solution turned immediately to sky-blue. A solution of a glycosyl halide (1 mmol) in Et_2O or EtOAc (30 cm^3) was deoxygenated with argon and then added to the complex.

The colour of the aqueous phase turned slowly to blue–violet indicating the formation of Cr(III)EDTA. Intensive stirring was continued for 18 h. The aqueous phase was then saturated with NH_4Cl, then the two phases were separated, and extracted with ether (5×). The ethereal phase was washed with water (3×), dried and the solvent removed under diminished pressure. The residue was of >95% purity as shown by ^1H NMR spectroscopy.

General procedure II for the reaction of acetylated glycosyl chlorides **1** *and* **3** *with* $[Cr(II)(EDTA)]^{2-}$ *complex in solid–liquid biphasic medium.*—Solutions of the complexes were prepared in water (50 cm^3) under argon (General procedure I). A solid glycosyl halide (1 mmol) was added to the solution in one portion. After stirring for 18 h, the work-up was continued as described in General procedure I.

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