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Preparation of Acylated Pyranoid Glycals in Neutral Aqueous Medium by Using Chromium(II) Complexes as Reagents

Gyöngyvér Kovács[a], Krisztina Tóth[a,b], Zoltán Dinya[c], László Somsák*[b1], Károly Micskei*[a2]

[a]*Department of Inorganic and Analytical Chemistry,* [b]*Department of Organic Chemistry,* [c]*Research Group for Antibiotics of the Hungarian Academy of Sciences, Lajos Kossuth University, H-4010 Debrecen 10, HUNGARY*

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Abstract: Reactions of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**3**) with chromium(II)L complexes (L = EDTA, NTA, IDA, GLY, MAL) in neutral (5 < pH < 7) aqueous DMF gave 3,4,6-tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (**13**) in 70-90% yields and >95% purity. Complexes of Cr(II) with L = EDTA, NTA were similarly efficient with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl chloride (**2**) in furnishing glucal **13**, while with L = IDA, GLY, MAL hydrolysis of **2** could not be suppressed. Under the same conditions $[Cr^{II}(EDTA)]^{2-}$ also efficiently gave the corresponding glycals **14-19** from 2,3,4,6-tetra-*O*-benzoyl- (**4**) and 2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranosyl bromide (**5**), per-*O*-acetylated α-D-galactopyranosyl chloride (**6**) and bromide (**7**), α-D-mannopyranosyl chloride (**8**), α-D-xylopyranosyl chloride (**9**), and bromide (**10**), β-D-arabinopyranosyl bromide (**11**), and α-L-rhamnopyranosyl chloride (**12**).

Keywords: carbohydrates; chromium compounds; complexes; glycals

1. Introduction

Glycals (1,4- or 1,5-anhydro-2-deoxy-ald-1-enitols) are among the most versatile chiral building blocks in carbohydrate chemistry and natural product synthesis [1,2]. Although they have been known since the early years of this century [3,4] newer and improved methods for

[1] phone: +36-52-316-666/2453; fax: +36-52-453-836; e-mail: somsak@tigris.klte.hu
[2] phone: +36-52-316-666/2757; fax: +36-52-489-667; e-mail: kmicskei@tigris.klte.hu

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their preparation continuously appear in the literature. This also indicates that no really generalizable procedure could be elaborated for their synthesis.

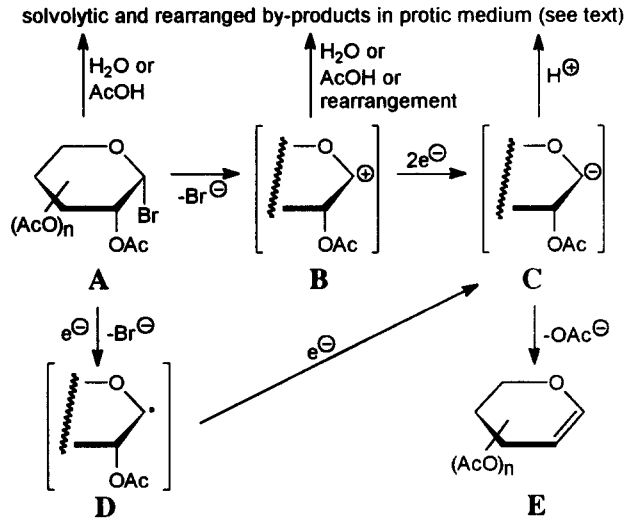
Glycals are most often prepared by the classical Fisher-Zach reductive elimination [3,4] *i.e.* in the reaction of acetobromosugars with (activated) zinc dust in aqueous acetic acid. Since acetobromosugars are prone to solvolytic and other side reactions [5,6] under the aforementioned conditions, and the yield of glycals depends also on the sugar configuration, the general trend to find better procedures for the preparation of glycals has been the use of aprotic conditions and/or other substrates. *Most important are the following methods: a)* Introduction of good leaving groups at C-2 of glycosyl halides [7-9]; *b)* Reactions of variously protected glycosyl halides with reducing agents such as sodium, potassium and sodium-naphtalide [10,11], zinc/silver-graphite [12], potassium-graphite [13], aluminum amalgam [14], samarium(II) iodide [15,16], titanocene dichloride [17,18] in tetrahydrofuran (THF), with lithium in liquid ammonia [19-21], with chromium(II)acetate in *N,N*-dimethylformamide (DMF) in the presence of ethylenediamine (EN) [22], with zinc dust in the presence of a *N*-base in various aprotic solvents [23]; *c)* Sugar derivatives with a C-1–S bond as starting materials: reactions of 1-thioglycosides and glycosyl phenyl sulfones with lithium-naphtalide in THF [24-26]; reactions of 1-thioglycosides with potassium-graphite in THF [27]; reactions of glycosyl phenyl sulfones with samarium(II) iodide in THF with or without hexamethylphosphoric triamide [28,29]; reactions of glycosyl sulfoxides with butyl-lithium in THF [30]; *d)* Electrolysis of acetobromosugars in DMF or acetonitrile [31]; *e)* Radical induced eliminations from 1-thioglycoside-2-xanthates in toluene [25,26], as well as from 2-azido-2-deoxy-selenoglycosides in benzene [32]; *f)* Eliminations from 2-deoxy-pentofuranose derivatives, such as nucleosides [33,34], 1-*O*-mesylates [35], and 1-selenoglycosides [36] as well as from furanose 1,2-diols [37].

Most of the above methods rest on an $E1_{cb}$ elimination of the 2-*O*-substituent from a primarily formed glycosyl anion (**C**→**E**) (see Scheme 1). Detailed mechanistic studies [6] revealed the intermediacy of glycosylium ions **B** yielding **C** by a two-electron reduction in the Fisher-Zach procedure. This can explain the formation of all of the detected solvolytic and rearranged by-products (per-*O*-acetylated sugars, acetylated sugars with a free glycosidic OH, acetylated 1,5-anhydro-alditols, 2-deoxy sugars, and 2,3-unsaturated sugar derivatives) besides the desired glycal. The formation of **B** may most probably be ascribed to the solvent used in the Fischer-Zach conditions. An AcOH–H_2O 1 : 1 mixture due to its protic nature and high polarity (average dielectric constant: $\varepsilon \sim 42$) can ionize and then dissociate [38] the C-Br bond in **A**. This is corroborated by a finding that replacement of water by THF (for an AcOH–THF 1 : 9 mixture: $\varepsilon \sim 7$) largely increases the yield and purity of the glycals [39].

On the other hand, formation of **B** is unfavored in the Zn–*N*-base procedure [23] which can be regarded as an aprotic version of the Fisher-Zach method (dielectric constants of the solvents used are in the range $2 < \varepsilon < 7$, and no ionization can take place). Mechanistic studies [40]

showed that in these reactions **C** is formed via glycosyl radicals **D**. Due to the applied aprotic medium solvolysis of neither **A** nor **C** can occur. Rearrangement of **D** is known to be a slow process [41].

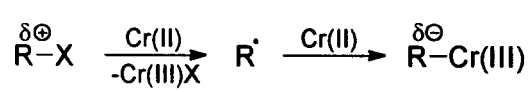
Accordingly, the **A→D→C→E** route produces glycals of very high purity without significant amounts of by-products. Although not investigated in detail, the other aprotic reductive eliminative reactions must also follow the above pathway.



Scheme 1

Recently, carrying out organic reactions in aqueous medium has received particular attention because it offers several advantages: there is no need for anhydrous organic solvents; the burden of solvent disposal on the environment can be moderated; several protection-deprotection steps can be omitted from synthetic sequences; in metal ion assisted reactions separation of the organic product can be simplified; biochemical processes occur in the presence of water [42-46]. Therefore, we envisaged to elaborate a new neutral aqueous synthetic procedure for glycals based on the assumption that the **A→D→C→E** sequence should give glycals of high yield and purity even in a solvolytic milieu if the steps **A→D** and **C→E** are faster than solvolysis.

Chromium(II) compounds are widely used in organic synthesis [47,48] for selective transformations of various functional groups [49,50]. In the present context the most important feature of the chromium(II) ion is its ability to form radicals from alkyl halides [51] which can then give organochromium(III) species [52] of anionic character suitable for further transformations (Scheme 2). Most of this chemistry was performed in a strictly aprotic medium. The use of chromium(II) ion in aqueous medium [53] as well as the application of EN as a complexing ligand to increase the reactivity of Cr(II) was also reported [22,54].



Scheme 2

Based on our experience in the field of complex equilibria of transition metal ions and especially of chromium(II) [55] we have recently published several applications of chromium(II) aminocarboxylate complexes as reagents using the so called "biomimetic setup" for different fields of the synthetic organic chemistry [56-58]. As a part of this program we

describe herein the reactions of Cr(II)L compounds with acylated glycopyranosyl halides in neutral aqueous medium. A preliminary account of this work has been published [59].

2. Results and Discussion

a) Rationale for the use of chromium(II) complexes (Cr(II)L) and their preparation

Reduction of alkyl halides by chromium(II) ion is believed to proceed by an inner sphere electron transfer [60]. The ease of this process depends on the reactivity of the Cr(II) species and is determined by its standard potential (E^0 = −0.41 V for $[Cr(H_2O)_6]^{3+/2+}$). This was clearly demonstrated by the observations that $[Cr^{II}(H_2O)]^{2+}$ can reduce only activated (*eg.* allyl, benzyl, α-carbonyl) halides [53], and addition of EN as a ligand to form $[Cr(EN)_x]^{2+}$ was necessary to successfully reduce primary alkyl halides in aqueous medium [54]. According to the Nernst equation ($E = E^{0'} + RT/F \ln[Cr(III)L]/[Cr(II)L]$) the ligand effect can be described by the formal potential ($E^{0'} = E^0 + RT/F \ln K_{Cr(II)L}/K_{Cr(III)L}$) which is determined by the stability constant of the

1-12 **13-19**

Table 1
Structure of the starting compounds and the products

Starting compound[a]	Configuration	X^1	X^2	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8	Product[b]	Configuration
1	β-D-*gluco*	F	H	CH_2OAc	H	H	OAc	OAc	H	H	OAc	-	-
2	α-D-*gluco*	H	Cl	CH_2OAc	H	H	OAc	OAc	H	H	OAc	13	D-*arabino*
3	α-D-*gluco*	H	Br	CH_2OAc	H	H	OAc	OAc	H	H	OAc	13	D-*arabino*
4	α-D-*gluco*	H	Br	CH_2OBz	H	H	OBz	OBz	H	H	OBz	14	D-*arabino*
5	α-D-*gluco*	H	Br	CH_2OPiv	H	H	OPiv	OPiv	H	H	OPiv	15	D-*arabino*
6	α-D-*galacto*	H	Cl	CH_2OAc	H	OAc	H	OAc	H	H	OAc	16	D-*lyxo*
7	α-D-*galacto*	H	Br	CH_2OAc	H	OAc	H	OAc	H	H	OAc	16	D-*lyxo*
8	α-D-*manno*	H	Cl	CH_2OAc	H	H	OAc	OAc	H	OAc	H	13	D-*arabino*
9	α-D-*xylo*	H	Cl	H	H	H	OAc	OAc	H	H	OAc	17	D-*threo*
10	α-D-*xylo*	H	Br	H	H	H	OAc	OAc	H	H	OAc	17	D-*threo*
11	β-D-*arabino*	Br	H	H	H	H	OAc	H	OAc	OAc	H	18	D-*erythro*
12	α-L-*rhamno*[c]	Cl	H	H	CH_3	OAc	H	H	OAc	H	OAc	19	[d]

[a]Per-*O*-acyl-aldopyranosyl halide; [b]Per-*O*-acyl-1,5-anhydro-2-deoxy-ald-1-enitol; [c]6-deoxy-L-*manno*; [d]6-deoxy-L-*arabino*.

complexes (K). The protonation of the ligand (HL) also affects the system equilibria at the pH applied. Therefore, the use of different ligands (EDTA, NTA, IDA, GLY, MAL; for structures see Table 5) can result in complexes of different formal potential, (*eg.* $E^{0'} \sim -1.3$ V for $[Cr(EDTA)(H_2O)]^{-/2-}$, see more data for different Cr(III)L/Cr(II)L aminocarboxylate complexes in [61]) and, hence, different reactivity. This, on the other hand, means that a possibility for fine tuning the reactivity of the Cr(II) ion arises. Besides this the above ligands, which are solids and available as standard analytical reagents of high purity, can be handled much more easily than EN. Another advantage is that the pH for solutions of complexes with these ligands is in the range 5-7 which is essentially neutral and thus hydrolysis of sensitive substrates (*eg.* glycosyl halides) can be avoided.

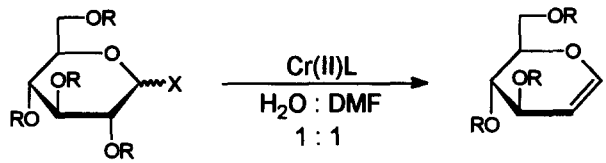
To have reagents with different reactivity the following Cr(II) complexes were prepared on the basis of our earlier solution equilibrium studies [55] from chromium(II)acetate in neutral ($5 < pH < 7$) aqueous medium: $[Cr^{II}(EDTA)]^{2-}$, $[Cr^{II}(NTA)]^{-}$, $[Cr^{II}(IDA)]$, $[Cr^{II}(GLY)]^{+}$, and $[Cr^{II}(MAL)]$. In the reaction mixture monocomplexes were present in exceeding concentration. For preparation of the reactive complexes solution equilibrium calculations [62] using the known formation constants gave the sample compositions at the desired pH (see Experimental).

b) Reactions of acylated glycopyranosyl halides with chromium(II) complexes in aqueous DMF

Preparative studies: The structures for the investigated glycopyranosyl halides (**1-12**) and the obtained pyranoid glycals (**13-19**) are listed in Table 1.

First, per-*O*-acylated D-glucopyranosyl halides (**1-5**) were subjected to the reaction with the prepared monocomplexes of Cr(II) in a 1 : 1 mixture of water and DMF to ensure complete dissolution of the sugar derivatives (Table 2). In this mixture [63] the stability constants of the complexes are practically the same as in pure water [55]. Compounds **1-5** are α-halogeno-ethers which, to the best of our knowledge, have not yet been investigated as substrates of Cr(II) ion mediated reactions in aqueous medium. Halides **2** and **3** failed to react with the least reactive $[Cr^{II}(H_2O)]^{2+}$ (Table 2, Entries 2 and 8), while with chromium(II) complex reagents gave tri-*O*-acetyl-D-glucal (**13**). The reactions of **2** with the less reactive complexes $[Cr^{II}(MAL)]$, $[Cr^{II}(GLY)]^{+}$, and $[Cr^{II}(IDA)]$ produced **13** in lower yield and purity (Table 2, Entries 3-5) indicating that the formation of **13** could not completely override the possible hydrolytic and other side reactions in the reaction mixture. The runs with the more reactive $[Cr^{II}(NTA)]^{-}$ and $[Cr^{II}(EDTA)]^{2-}$ gave **13** as a practically pure crude-product (Table 2, Entries 6, 7) as did the reactions of bromide **3** with each Cr(II) complex (Entries 9-13). No transformation could be observed and the starting material was recovered in the reaction of fluoride **1** with the most reactive $[Cr^{II}(EDTA)]^{2-}$ (Table 2, Entry 1). These observations show that the reactivity range covered by the applied complexes meets the requirements of glucosyl bromide **3**. For chloride **2**

the rate of the first electron transfer is fast enough only with the most reactive complexes. Although glycosyl chlorides are more stable towards nucleophilic attack than the corresponding bromides their lower reactivity towards the Cr(II) complexes allows the hydrolysis to compete with the reduction. Fluoride **1** lies out of the reactivity range provided by the applied ligands.



1-5 **13-15**

Table 2
Reactions of acylated D-glucopyranosyl halides (1-5) with chromium(II) complexes in aqueous DMF

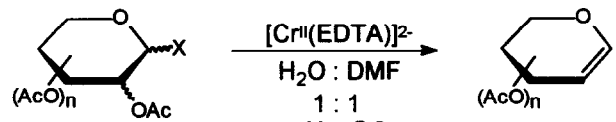
Entry	Starting compound	X	R	Ligand (L)	pH	Product	Isolated yield[a] (%)	Purity[b] (%)
1	1	βF	Ac	EDTA	5.0	-	no reaction[c]	-
2	2	αCl	Ac	H_2O	5.0	-	no reaction[d]	-
3	2	αCl	Ac	MAL	5.7	13	77[g]	~90[f]
4	2	αCl	Ac	GLY	6.6	13	77[g]	~90[f]
5	2	αCl	Ac	IDA	5.9	13	58[g]	~90[f]
6	2	αCl	Ac	NTA	6.0	13	73	>95
7	2	αCl	Ac	EDTA	5.0	13	79	>95
8	3	αBr	Ac	H_2O	5.0	-	no reaction[e]	-
9	3	αBr	Ac	MAL	5.7	13	89	>95
10	3	αBr	Ac	GLY	6.6	13	89	>95
11	3	αBr	Ac	IDA	5.9	13	77	>95
12	3	αBr	Ac	NTA	6.0	13	71	>95
13	3	αBr	Ac	EDTA	5.0	13	87	>95
14	4	αBr	Bz	EDTA	5.0	14	88	>95
15	5	αBr	Piv	EDTA	5.0	15	90	>95

[a]The isolated products had NMR characteristics identical with those of authentic samples **13** [23], **14** [64];
[b]Based on ^{1}H-NMR spectra of the worked-up reaction mixtures. A purity >95% means that no resonances other than those of **13-15** could be observed in the spectrum; [c]Recovery of **1**: 84%; [d]Recovery of **2**: 91%; [e]Recovery of **3**: 81%; [f]2,3,4,6-tetra-*O*-acetyl-D-glucopyranose was the main by-product as judged by the ^{1}H-NMR spectrum of the worked-up reaction mixture; [g]Calculated as if it were pure **13**.

The $[Cr^{II}(EDTA)]^{2-}$ complex was also used for the transformation of the benzoylated **4** and pivaloylated **5** bromides to the corresponding glucals **13** and **14**, respectively (Table 2, Entries 14,15). These reactions show that the type of acyl protecting group does not influence the efficiency of the reaction.

Reactions of the $[Cr^{II}(EDTA)]^{2-}$ complex with glycosyl halides **6-12** are summarized in Table 3. These also produced the expected glycals **13, 16-19** in high yields and purity. The only exception was the reaction of D-xylosyl chloride **9** which gave a more complicated product mixture. Column chromatographic separation yielded D-xylal **17** as the overwhelming major

product as well as 1,2,3,4-tetra-*O*-acetyl-β-D-xylopyranose (**20**) and 2,3,4-tri-*O*-acetyl-1,5-anhydro-D-xylitol (**21**) as minor products (Scheme 3). Compound **20** could form in a nucleophilic substitution by acetate ion from **9** while **21** can be the result of protonation of the probable D-xylopyranosyl chromium(III) intermediate [59].



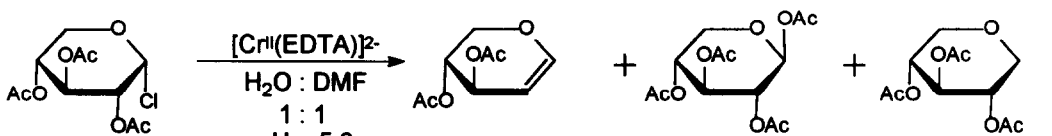
6-12 **13, 16-19**

Table 3
Preparation of per-*O*-acetylated glycals from acetylated glycopyranosyl halides with the $[Cr^{II}(EDTA)]^{2-}$ reagent in aqueous DMF

Entry	Starting compound	Configuration	X	Product	Isolated yield[a] (%)	Purity[b] (%)
1	**6**	D-*galacto*	αCl	**16**	91	>95
2	**7**	D-*galacto*	αBr	**16**	71	>95
3	**8**	D-*manno*	αCl	**13**	80	>95
4	**9**	D-*xylo*	αCl	**17**	72	see text
5	**10**	D-*xylo*	αBr	**17**	66	95
6	**11**	D-*arabino*	βBr	**18**	90	>95
7	**12**	L-*rhamno*	αCl	**19**	61	95

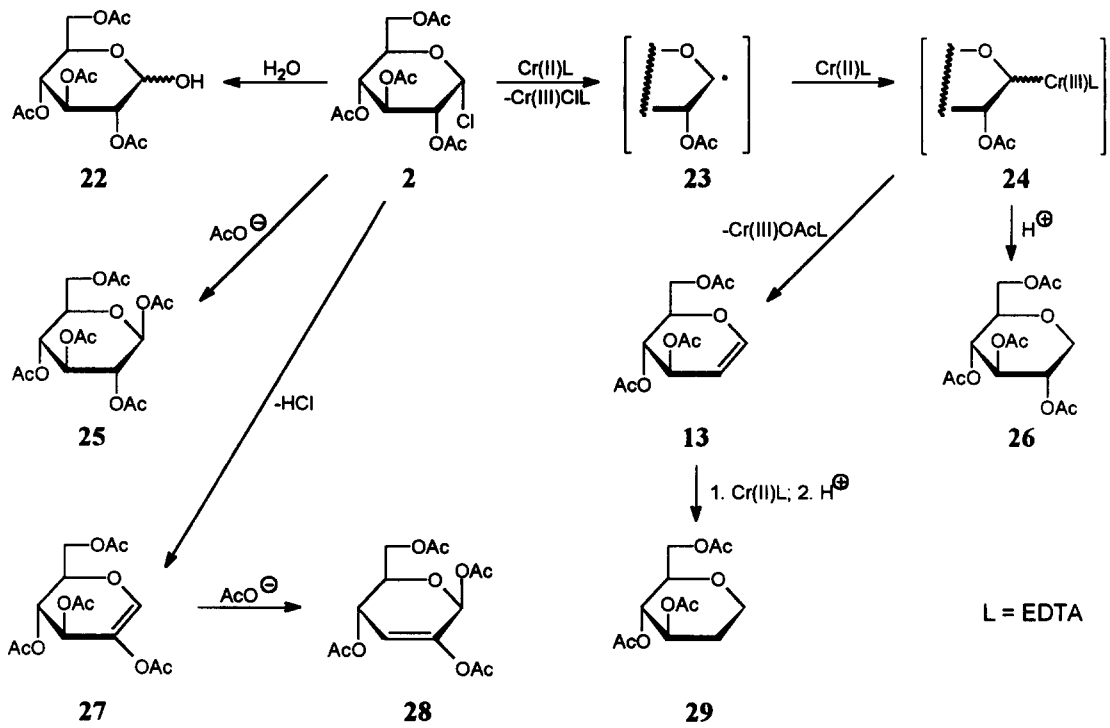
[a]The isolated products had NMR characteristics identical with those of authentic samples **13**, **16**, **18** [23], **17** [65]; **19** [66]; [b]Based on ^{1}H-NMR spectra of the worked-up reaction mixtures. A purity >95% means that no resonances other than those of **13**, **16-19** could be observed in the spectrum.

These findings prove that $[Cr^{II}(EDTA)]^{2-}$ is a useful reagent for the preparation of acylated pyranoid glycals from glycosyl chlorides and bromides in aqueous medium regardless of sugar configuration and protecting groups. The use of this complex can be advantageous for the practicing synthetic chemist because its preparation is the simplest: one merely has to mix stoichiometric amounts of Cr(II) and EDTA and adjust carefully the pH of the solution to 5 (see details in the Experimental section).



9 **17** (72 %) **20** (4 %) **21** (2 %)

Scheme 3



Scheme 4

Mechanistic considerations: In order to obtain a deeper insight into the by-products not seen in the ^{1}H-NMR spectra of the crude-mixtures a GC-MS investigation of the product mixture of the reaction of **2** with $[Cr^{II}(EDTA)]^{2-}$ was carried out. The compounds identified in the reaction mixture as well as their probable way of formation are outlined in Scheme 4. As is evident from the preparative results the main pathway is the formation of **13** *via* glucosyl radical **23** and glucosyl-chromium(III)EDTA intermediate **24**. Radicals **23** could be trapped [67] by electron deficient olefins (*eg.* methyl acrylate or acrylonitrile) to give the corresponding α-*C*-glycosides [68]. Intermediate **24** can also be protonated to give a minor by-product 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-glucitol (**26**). The parallel formation of both **13** and **26** is an unambiguous proof for the intermediacy of **24** whose existence was also shown by UV-Vis spectroscopy [59]. Other minor by-products are formed by attacks of nucleophiles on chloride **2**. Thus, in a reaction with water **2** gives 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (**22**). Attack of acetate ion on **2** can result in a substitution giving per-*O*-acetyl-β-D-glucopyranose (**25**) as well as an elimination furnishing 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (2-hydroxy-D-glucal-peracetate) (**27**). Reaction of **27** with acetate nucleophiles yields **28** in a Ferrier rearrangement [69]. Formation of **29** can be rationalized by the known reduction of the double bond by Cr(II) species [70]. These results show that, in accordance with our original assumption, the high yielding formation of

glycals from glycosyl halides can be realized even in a highly polar aqueous medium ($\varepsilon \sim 58$ for a H_2O–DMF 1 : 1 mixture).

3. Conclusion

The reactions of per-*O*-acylated glycosyl chlorides and bromides with Cr(II) aminocarboxylate complexes, especially with $[Cr^{II}(EDTA)]^{2-}$, are suitable for the high yielding preparation of the corresponding glycals in neutral aqueous medium, practically regardless of sugar configuration and protecting groups.

4. Experimental

Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were determined with a Perkin-Elmer 241 polarimeter at room temperature. 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} (Merck), (eluent: ethyl acetate–hexanes 1 : 1); the plates were visualized by gentle heating. For column chromatography Kieselgel 60 (Merck) was used (eluent: ethyl acetate–hexanes 1 : 3). Organic solutions were dried over anhydrous $MgSO_4$ and concentrated in vacuum at 40-50 °C (water bath).

$CrCl_3 \cdot 6H_2O$ and the applied ligands of analytical grade (Table 5) were purchased from Aldrich. Preparation and reactions of Cr(II) complexes were carried out by using standard Schlenk methodology. The acylated glycosyl halides were prepared by adaptation of known general methods: 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl fluoride (**1**) [71], per-*O*-acetyl-α-D(L)-glycopyranosyl chlorides **2**, **6**, **8**, **9**, **12** [72], per-*O*-acetyl-α(β)-D-glycopyranosyl bromides **3**, **7**, **10**, **11** [65,73,74], 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (**4**) [75], 2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranosyl bromide (**5**) [76].

The components of the crude-mixture from the reaction of **2** with $[Cr^{II}(EDTA)]^{2-}$ were separated and identified by using a VG-7035 GC-MS instrument coupled to a VG-11-250J data system (VG Analytical Ltd., Manchester, England). Full scan data were acquired in positive electron impact ionization mode [EI(+)] over a mass range 30-700 amu using an exponential scan cyclic time of 1 s/decade. The accelerating voltage was maintained at 4 kV, the electron energy at 70 eV and the electron emission current at 200 μA. The total ion chromatograms (TIC) and the mass spectra were recorded at an ion-source temperature of 200 °C. The GC separations were conducted using a DB-5MS fused silica capillary column [(J&W, Folsom, USA) 30 m in length, 0.32 mm in diameter, film thickness 3.0 μm] with a He carrier gas flow rate of 2 cm^3/min. The GC running conditions were as follows: injection 250 °C, splitless for 0.5 min; GC oven temperature program: initial temperature of 120 °C (held for 2 min), 6 °C/min ramp to 280 °C (held for 20 min); direct transfer line temperature of 280 °C.

Preparation of $[Cr(OAc)_2 \cdot H_2O]_2$ by modification of a literature protocol [77]: To a mixture of granulated Zn (45 g, 0.69 mol) and $CrCl_3 \cdot 6H_2O$ (75 g, 0.28 mol) distilled water (90 cm^3) was added under argon. After dissolution of $CrCl_3 \cdot 6H_2O$ the mixture was cooled with an ice bath and excess cc. HCl (105 cm^3) was added to it in one portion. The color of the mixture slowly changed to blue from green as the reaction went on. Cooling was used only in the first part of the reaction. After ~2 h the color of the mixture was sky-blue indicating that the reaction had finished. This solution was then transferred *via* cannula with the help of a small overpressure into a solution of sodium acetate (127 g, 1.55 mol in 300 cm^3 water) which was heated to 50 °C. A red precipitate formed immediately. The warm mixture was pressed through a filter with the help of overpressure. The precipitate was washed with cold deoxygenated distilled water (3×), cold absolute ethanol (3×) and cold diethyl-ether (3×), and dried in an argon gas flow at 40-45 °C, (yield: 45 g, 85 %).

General procedure I for the preparation of chromium(II) complexes. A ligand (see quantities in Table 5, Entries 1-5) was dissolved in a mixture of water (40 cm^3) and DMF (35 cm^3). The calculated amount of a KOH solution was added to the mixture adjusting the pH to the required value which was checked by pH-potentiometry. For the preparation of Cr(II)L complexes solution equilibrium calculations [62] using the known formation constants [55] gave the sample compositions at the desired pH. In this way the protonation of OAc^- was also considered. The magnetically stirred solution was deoxygenated by bubbling with argon for 15 minutes. $[Cr(OAc)_2 \cdot H_2O]_2$ (0.750 g, 2.2 mmol Cr(II)) was added in one portion under argon and the slow change of the color of the solution indicated the formation of the reactive complex $[Cr^{II}(L)(H_2O)_x]^{n+}$. At the applied pH and Cr(II)/L ratio the appropriate monocomplexes form in high concentration.

Table 5
Preparation of the reactive Cr(II)L complexes

Entry	Ligand (L)	Structure of the ligand	Reactive Complex	$lgK_{Cr(II)L}$[a]	Quantity of ligand (g; mmol)	Added KOH solution[b] (cm^3; mmol)	pH	Color
1	EDTA	ethylenediaminetetra-acetic acid[c]	$[Cr^{II}(EDTA)]^{2-}$	12.70	0.893; 2.4	1.1; 2.66	5.0	sky-blue
2	NTA	nitrilotriacetic acid	$[Cr^{II}(NTA)]^-$	6.52	0.459; 2.4	2.8; 6.77	6.7	grey-black
3	IDA	iminodiacetic acid	$[Cr^{II}(IDA)]$	5.01	0.319; 2.4	1.7; 4.11	6.8	sky-blue
4	GLY	glycine	$[Cr^{II}(GLY)]^+$	4.21	0.721; 9.6	0.8; 1.94	6.9	blue
5	MAL	malonic acid	$[Cr^{II}(MAL)]$	3.57	0.250; 2.4	1.9; 4.60	6.2	blue

[a]Taken from [55]; [b]c_{KOH} = 2.42 mol dm^{-3}; [c]$Na_2H_2EDTA \cdot 2H_2O$ form.

General procedure II for the reactions of acetylated glycosyl halides 1-3, 6-12 with chromium(II) complexes in homogenous medium: A glycosyl halide (1 mmol) was dissolved in DMF (5 cm^3) and the solution was deoxygenated with argon. This was added to a solution of the complex prepared as described in General procedure I. The color of the mixture began to turn to different shades of blue-violet characteristic for the forming Cr(III)L complexes. The reaction vessel was then stoppered under a slight overpressure of argon and the stirring was continued for 18 h. Then the mixture was saturated with NH_4Cl and extracted with ether (5×). The salting-out has proven extraordinarily important with the acetylated compounds: without it the yields were 15-20 % lower. The ethereal phase was washed with water (3×), dried and the solvent removed under diminished pressure. The obtained material was investigated by ^{1}H-NMR spectroscopy. If the sample was of 95 % or higher purity the yield of the product was calculated on the basis of the amount isolated by the above procedure (Tables 2 and 3). Further purification was effected by column chromatography.

1,5-Anhydro-3,4,6-tri-*O*-benzoyl-2-deoxy-D-*arabino*-hex-1-enitol (14): The complex $[Cr^{II}(EDTA)]^{2-}$ was prepared from $Na_2EDTA \cdot 2H_2O$ (1.30 g, 3.48 mmol), KOH (2.42 mol dm^3, 1.6 cm^3, 3.87 mmol) and $[Cr(OAc)_2 \cdot H_2O]_2$ (0.57 g, 3.03 mmol Cr(II)) in a mixture of H_2O (26 cm^3) and DMF (45 cm^3) (pH = 5.1). Bromide **4** (0.50 g 0.76 mmol) was dissolved in DMF (9 cm^3), the solution was deoxygenated with argon, and added to the complex. Stirring was continued for 2 d. Work-up was effected according to General procedure II.

1,5-Anhydro-2-deoxy-3,4,6-tri-*O*-pivaloyl-D-*arabino*-hex-1-enitol (15): The complex $[Cr^{II}(EDTA)]^{2-}$ was prepared from $Na_2EDTA \cdot 2H_2O$ (1.30 g, 3.48 mmol), KOH (2.42 mol dm^3, 1.6 cm^3, 3.87 mmol) and $[Cr(OAc)_2 \cdot H_2O]_2$ (0.57 g, 3.03 mmol Cr(II)) in a mixture of H_2O (15 cm^3) and DMF (55 cm^3) (pH = 5.1). Bromide **5** (0.60 g 1.03 mmol) was dissolved in DMF (10 cm^3), the solution was deoxygenated with argon, and added to the complex. Stirring was continued for 1 d. Work-up was effected according to General procedure II. An analytical sample was obtained by column chromatography. Colorless prisms: mp 100-103 °C; $[\alpha]_D$ = –31 (c = 1.01, $CHCl_3$); ^{1}H-NMR: δ ($CDCl_3$) 6.45 (d, 1H, $J_{1,2}$ = 6.2 Hz), 5.32 (dd, 1H, $J_{3,4}$ = 5.8 Hz, H-3), 5.27 (dd, 1H, $J_{4,5}$ = 6.6 Hz, H-4), 4.82 (dd, 1H, $J_{2,3}$ = 2.3 Hz, H-2), 4.35-4.05 (m, 3H, H-5, 6, 6'), 1.23, 1.19, 1.18 (3s, 27H, 9 × CH_3); ^{13}C-NMR: δ ($CDCl_3$) 177.81, 177.49, 176.27 (C=O), 145.34 (C-1), 98.79 (C-2), 73.87, 67.25, 66.38 (C-3,4,5), 61.04 (C-6), 38.56, 38.44 (($CH_3)_3C$), 26.81, 26.75 (CH_3). Anal.: Calcd. for $C_{21}H_{34}O_7$ (398.50): C, 63.30; H, 8.60; Found: C, 63.68; H, 8.39.

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