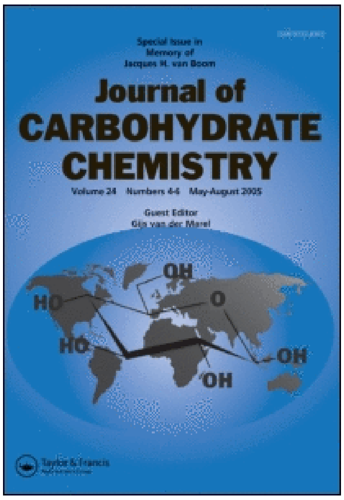


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

The Alkylation and Acylation of Glycals via an Initializing Electrochemical Step

Susanne Fischer[a]; Carl Heinz Hamann[a]
[a] Fachbereich Chemie Carl-von-Ossietzky-Universität, Oldenburg/Oldb., Germany

To cite this Article Fischer, Susanne and Hamann, Carl Heinz(1995) 'The Alkylation and Acylation of Glycals via an Initializing Electrochemical Step', Journal of Carbohydrate Chemistry, 14: 3, 327 — 339

To link to this Article: DOI: 10.1080/07328309508002075

URL: http://dx.doi.org/10.1080/07328309508002075

J. CARBOHYDRATE CHEMISTRY, 14(3), 327-339 (1995)

THE ALKYLATION AND ACYLATION OF GLYCALS VIA AN INITIALIZING ELECTROCHEMICAL STEP

Susanne Fischer and Carl Heinz Hamann*

Fachbereich Chemie
Carl-von-Ossietzky-Universität
Postfach 2503, 26111 Oldenburg / Oldb., Germany

Received April 21, 1994 - Final Form January 3, 1995

ABSTRACT

The method of electrochemically induced formation of ether and ester derivatives of saturated mono- and disaccharides was applied to 1,2-unsaturated monosaccharides (D-glycals). The influence of the supporting electrolyte on the product distribution was investigated by variation of the cation. To provide data for comparison, alkylation was also carried out chemically in the presence of different bases, e.g. LiH and NaH.

INTRODUCTION

The electroreductive conversion of carbohydrates generates anions that react readily with alkylating and acylating reagents to give ether and ester derivatives according to the following scheme.[1]

$$\mathrm{ROH} + e^- \rightarrow \mathrm{ROH}^{\cdot -}$$

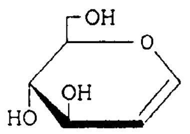
$$\mathrm{ROH}^{\cdot -} \rightarrow \mathrm{RO}^- + \underset{\displaystyle 1/2\mathrm{H}_2}{\overset{}{\mathrm{H}\cdot\!\downarrow}}$$

$$\mathrm{RO}^- + \mathrm{EX} \rightarrow \mathrm{ROE} + \mathrm{X}^-$$

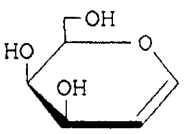
This reaction scheme is valid in aprotic media using electrolyte systems of sufficient electrochemical stability (for instance DMF/LiBr). An electrode material of high electrocatalytic activity (for instance platinized platinum) is essential. The electrode with a working potential of -2.0 V Ag/Ag$^+$ thus replaces common bases (like NaOH, LiH, NaOR etc.) and organometallic compounds used in chemical alkylation or esterification. The anions produced in this electrochemical step are then captured by usual electrophiles such as methyl iodide, benzyl bromide etc. Due to their lack of electrochemical stability at the working potential,[2] these had to be added after electrolysis (ex situ).

The above method of electrochemically initiated introduction of protecting groups was recently applied to several non-reducing saturated mono- and disaccharides.[1,3-5] The substitution patterns observed were chiefly governed by the same parameters as in chemically induced reactions, i.e. acidity and spacial orientation of different hydroxyl groups, and reactivities and steric requirements of the electrophiles. On the other hand electrochemical parameters, such as reduction potential, electrode material or solvent play only a secondary role. In some special cases where the sugar molecule contains a center of high electronic density known to have a repulsive effect towards the negatively charged electrode surface (e.g. benzyl β-lactoside and benzyl 4′,6′-*O*-benzylidene β-lactoside) a marked preference for substitution at the positions farthest from this center of repulsion was noted.

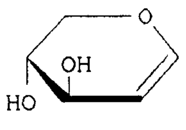
We now report an application of this method for alkylation (benzylation, methylation, tritylation) and acylation of the D-glycals, namely D-glucal (**1**), D-galactal (**2**), D-xylal (**3**), D-arabinal (**4**), 6-*O*-benzyl-D-glucal (**5**) und 6-*O*-benzyl-D-galactal (**6**), using platinum electrodes in the electrolyte systems DMF/LiBr and DMF/NaBr.



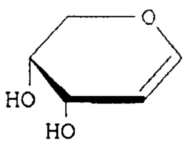
D-Glucal (1)



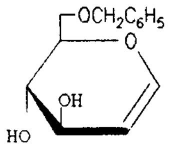
D-Galactal (2)



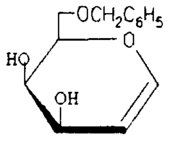
D-Xylal (3)



D-Arabinal (4)



6-*O* -Benzyl-D-glucal (5)



6-*O* -Benzyl-D-galactal (6)

In addition, chemical control experiments were carried out using LiH and NaH to produce the anions of the carbohydrates mentioned above. Trapping occurred after a time equaling the duration of electrolysis. The electrophiles were added in an excess of 10% based on the substrate. Electrochemical and chemical pathways are thus directly comparable. Before carrying out electrolysis, the carbohydrates **1-6** were characterized in view of their electrochemical behaviour by cyclic voltammograms.

RESULTS AND DISCUSSION

The electrochemical behaviour of **1-6** at platinum in LiBr/DMF is in agreement with the current-potential dependencies of saturated mono- and disaccharides.[1] All cyclic voltammograms exhibit a broad cathodic current peak in the potential region of -2.0 to -2.2 V Ag/Ag^+ with corresponding current densities of -1.0 to -2.5 mA/cm^2.

For the substrates **3-6** the current densities clearly increase in the presence of NaBr to -3.0 to -6.0 mA/cm^2. In the case of **1** and **2** in DMF/NaBr no current peaks occurred. Instead, waves with a half-wave potential of -2.2 V **1** and -2.1 V **2**, respectively, were observed. A limiting current of -18.0 **1** or -9.0 mA/cm^2 **2** was recorded at -2.6 V or -2.5 V. On the basis of these results an electrolysis potential of -2.2 V Ag/Ag^+ was chosen.

Regarding the number of electrons transferred in the electrochemical step we used the model compound anthracene, the corresponding cation radical and dication of which are relatively stable.[6] To evaluate the dependency of the peak current densities on the concentration of the used carbohydrates, cyclic voltammetric experiments were carried out in the electrolyte system DMF/$LiClO_4$.

The obtained data allow no conclusion as to the number of transferred electrons. It turned out that the peak current density is not a linear function of concentration.[7] From that it is clear that the electrochemical step is neither diffusion nor passage controlled. It is obvious that the criterion for the determination of the number of transferred electrons by Nicholson and Shain [8] is not applicable.

Tables 1 and **2** illustrate the substitution pattern as well as current [9] and product yields [10] of the obtained ether and ester derivatives of D-glycals in dependence of the conducting agent / base and electrophile.

As can be plainly seen from the tables, the reactivity of the carbohydrate and the electrophile strongly influence the substitution pattern. An important role must also be assigned to the cation which is present during the reaction, whereas the reaction path is of minor significance.

Table 1. Electrochemical results: substitution pattern [%] and current yields [%] of the electrochemically initiated alkylation and acylation of the D-glycals **1-6**.

D-Glycal	Conducting Agent	Electrophile	Product Distribution at C-positions								Current Yields
			3	4	6	3,4	3,6	4,6	3,4,6		
1	LiBr	BnBr	27	47		15	6	5			38
	NaBr		25	23			9	21	22		64
	LiBr	MeI	66	34							25
	NaBr		46.5	19	9		9.5	5.5	10.5		62
	LiBr	TrCl			80					20[a]	65
	NaBr				100						80
	LiBr	Ac_2O					48	36	16		41
	NaBr				8		61	25	6		75
	LiBr	AcCl			70				5		40
	NaBr				78				22		70
2	LiBr	BnBr	13	64	3	6	5	7	1		66
	NaBr		7	9	33	2	6	21	22		90
	LiBr	MeI	26	46		13		12	3		82
	NaBr		12	15	35	4	4	10	20		84
	LiBr	TrCl			89					11[b]	81
	NaBr				100						81
	LiBr	Ac_2O	8	39	8	8	28	7	7		70
	NaBr		5	19	53	3	13	5	2		85
	LiBr	AcCl			25	42			33		70
	NaBr				53		22		25		85
3	LiBr	BnBr	20	75		5					30
	NaBr		20	75		5					55
	LiBr	MeI	50	50							30
	NaBr		45	30		20					60
4	LiBr	BnBr	25	35		35					50
	NaBr		30	30		40					78
	LiBr	MeI	40	50		10					55
	NaBr		50	30		20					60
5	LiBr	BnBr					20	66	14		26
	NaBr						39	46	15		46
6	LiBr	BnBr					17	70	13		54
	NaBr						38	49	13		70

a. Inseparable mixture of several unidentified products.

b. 2-Chloro-2-deoxy-6-*O*-trityl-3,4-di-*O*-acetyl-D-galactose: At present time, no sufficiently proven explanation for the formation of this compound has been found.

Table 2. Chemical results: substitution pattern [%] and product yields [%] of the chemically initiated alkylation of the D-glycals **1-6**.

D-Gly-cal	**Base**	**Electro-phile**	**Product Distribution at C-positions**							**Product Yields**
			3	**4**	**6**	**3,4**	**3,6**	**4,6**	**3,4,6**	
1	LiH	BnBr	28	56	12	6	2	1	1	57
	NaH		17	25	18	5	16	16	3	60
	LiH	MeI	25	45	11		4	5	10	55
	NaH		35	30	25		2	2	12	55
	LiH	TrCl			100					70
	NaH				100					70
2	LiH	BnBr	20	44	20	3	5	5	3	55
	NaH		17	24	14	6	9	10	20	55
	LiH	MeI	15	30	25	5	10	8	7	60
	NaH		15	26	23	9	11	7	10	60
	LiH	TrCl			100					70
	NaH				100					70
3	LiH	BnBr	30	60		10				55
	NaH		30	60		10				55
	LiH	MeI	25	40		35				55
	NaH		13	16		45				55
4	LiH	BnBr	20	40		40				60
	NaH		15	30		45				57
	LiH	MeI	22	38		40				54
	NaH		37	25		37				54
5	LiH	BnBr					50	23	27	50
	NaH						45	30	25	50
6	LiH	BnBr					24	50	26	55
	NaH						35	37	28	60

Reactivity and Steric Properties of the D-Glycal and Electrophile

The reactivity of D-glycals with regard to the substitution of hydroxyl groups will essentially be determined by their nucleophilicity and accessibility. The order of reactivity is: primary > allylic ≥ secondary.[11] Benzylation and methylation of **1** and **2** is selective for 4-OH with lithium ions, e.g. 3- vs. 4-OH = 27:47 or 26:46, and depends on the electrochemical or chemical generation of the anion, compare Table 1 and Table 2. An exception is the electrochemical methylation of **1**, where a clear preference for substitution at OH-3 is observed.

Whilst not consistent with the order of reactivity just mentioned, these results do agree with those obtained by chemically induced benzylation of **1**.[11] We suggest the following explanation. Due to inter- and intramolecular proton migration, the sugar anions generated in the initial step undergo rearrangements that lead to the establishment of an equilibrium distribution. Parameters that direct the adjustment of this equilibrium are the acidity of different OH groups and the possible formation of hydrogen bonds. According to Guthrie et al.,[11] the produced alcoholate species exhibit greater thermodynamic stability when the anionic group is located at C-4. Based on this assumption, substitution will occur mainly at this position, as is corroborated by our results. However, this is only valid if the electrophiles are sterically undemanding.

In the case of the electrochemically initiated benzylation of **5** and **6** as well as in the chemically induced reaction of **6**, the 4,6-di-*O*-substituted products were isolated as the major products (up to 70%, Table 1). From this we conclude that the benzyl group in 6-position does not exert any further steric effect. As another example for the dominance of the thermodynamic stability factors, the benzylation of **3** must be mentioned. Independent of the reaction path and of the cation, the substitution pattern shows a preference for reaction of the hydroxyl group at C-4.

If sterically shielded electrophiles are used, e.g. trityl chloride, the reaction occurs completely under steric control. In case of tritylation of **1** and **2**, only the hydroxyl group at C-6, which is the most accessible one, was transformed into an ether derivative (Table 1, Table 2).

The acylation of **1** and **2** carried out only under electrochemically initiated conditions revealed no regioselectivity caused by the different reactivities of the acylating reagents. In both cases the primary OH-group was preferentially substituted. This lead to the formation of the corresponding mono-, di- and trisubstituted derivatives, whereas the best selectivity – the amount of the 6-*O*-acylester was up to 78% – was achieved by the acylation of **2** using acetyl chloride as the trapping agent. The high degree of 6-substitution is caused by the tendency of ester derivatives to undergo migration of the acyl groups to more accessible positions. Normally, under those conditions, acetates take part in allylic rearrangements to give 2,3-unsaturated derivatives, but none were detected here.

Conducting Agent / Base Cations and Their Interactions with Other Components of the System

The substitution patterns of the alkylations of **1** and **2** indicate an outstanding influence of the cation. A selective reaction as well as preferred substitution at the 4-position was observed in the presence of lithium ions independent of the initializing step. By comparison, the reaction in the presence of sodium ions was generally less selective. The share of 6-*O*-substituted products increased and in the case of methylation and benzylation of **2** the 6-*O*-alkyl ethers were isolated as the main products. However, with the substrates **3-6** the cation did not show significant influence on the substitution pattern.

An influence of the cation can only be explained by the assumption of interactions between it and the newly generated sugar anions, i.e. by the formation of complexes. A requirement of this is first of all the dissociation of the salts. Solvents having a dielectric constant > 30 are able to dissociate salts. According to Prue and other authors [12-14] LiBr as well as NaBr are dissociated in DMF ($\varepsilon = 37$). Due to its nucleophilic character, DMF solvates cations (by electron-donor-acceptor-interaction) rather better than anions, that can only be solvated unspecifically by dispersion forces. (DMF possesses no H-atoms acidic enough for solvation via hydrogen bonding). In consequence the sugar anions achieve high reactivity (naked anions), i.e. a nucleophilic property. According to the HSAB-concept by Pearson,[16] alkali cations are very hard acids and alcoholate ions very hard bases, which will combine eagerly. The formation of a complex is probable. Subsequently the probability distribution of the anionic charge is also influenced by the formation constants of the sugar anions-/alkali cations-complexes. It will move to those positions with the largest complex formation constants. Substitution patterns could therefore become dependent on the alkali cation. This kind of dependence is only observed in reactions of the substrates **1** and **2**. A marked preference for substitution of the terminal hydroxyl group at C-6 in the presence of sodium ions points to an outstanding stability of the $C(6)O^-Na^+$-complex. The formation of that complex must also be the reason for the remarkable current densities attainable with **1** and **2** in DMF/NaBr. In this way the stabilisation of the primarily formed radical anion to an anion is supported, the desorption from the electrode is facilitated.[17]

Reaction Path

Like the disaccharides mentioned in the introduction, the substrates **1-6** contain π-systems capable of interaction with the electrode. An influence of these π-bonds on the adsorption process has been proved.[18,19] Adsorption (and consequently electron transfer) of the H-atoms of the hydroxyl groups farthest from such centers of repulsion is probable. A comparison of the Tables 1 and 2 show differences in the individual patterns, and in some cases these differences are quite remarkable, but the general pattern is maintained. For the investigated 1,2-unsaturated monosaccharides electrochemical and chemical methods follow the same influences (i.e. reactivity, steric requirement, influence of the cation). Adsorption, on the other hand, does not play any detectable role.

EXPERIMENTAL

General Procedure. The electrochemical experiments were carried out in three-compartment cells with working volumes of 10 mL (cyclic voltammograms) and 40 mL

Table 3. NMR data of the alkyl/acyl derivatives of **1** in $CDCl_3$: chemical shifts δ [ppm]; coupling constants J [Hz]

Compound	H-1		H-2		H-3		H-4	H-5	H-6	H-6′	Substituent			
	($J_{1.2}$)	($J_{1.3}$)	($J_{2.3}$)	($J_{2.4}$	($J_{3.4}$)	($J_{3.5}$)	($J_{4.5}$)	($J_{5.6}$)	($J_{5.6'}$)	($J_{6.6'}$)	Bn	Me	Ac	Ph
4,6-Di-*O*-acetyl-3-*O*-benzyl-**1**	6.45dd (6.3)	(1.1)	4.90ddd (2.6)		4.00ddd (5.4)		5.25t	4.20-4.30m (6.5)	4.20-4.30m	4.20-4.30m (11.8)	4.55-4.70d		2.03s	7.20-7.40m
3,6-Di-*O*-acetyl-4-*O*-benzyl-**1**	6.45dd (6.3)	(1.2)	4.90dd (2.6)	(0.8)	5.40ddd (5.9)	(0.5)	3.60ddd	4.20-4.45m	4.20-4.45m	4.20-4.45m	4.55-4.70d		2.03s	7.20-7.40m
6-*O*-Acetyl-3,4-di-*O*-benzyl-**1**	6.45dd (6.1)	(1.1)	4.90ddd (3.0)	(1.3)	4.25ddd (6.0)		3.80ddd (2.9)	4.10ddd (5.0)	4.30-4.40ddd (7.8)	4.30-4.40ddd (12.6)	4.55-4.90d		2.03s	7.20-7.40m
4-*O*-Acetyl-3,6-di-*O*-benzyl-**1**	6.45dd (6.1)	(1.2)	4.90ddd (3.8)	(0.8)	3.90m (6.9)		5.30t (3.0)	4.30m (4.6)	3.60-3.80ddd (6.7)	3.60-3.80ddd (12.3)	4.50-4.65d		2.03s	7.20-7.40m
3-*O*-Acetyl-4,6-di-*O*-benzyl-**1**	6.40dd (6.0)	(1.3)	4.80dd (2.9)	(1.2)	5.40ddd (6.3)		3.95dd (3.2)	4.20m (4.7)	3.80ddd (6.3)	3.80ddd (10.7)	4.50-4.60d		2.03s	7.20-7.40m
3,4,6-Tri-*O*-benzyl-**1**	6.40dd (6.1)	(1.2)	4.85m (3.5)		4.05ddd (6.2)		3.75-3.90m (3.2)	4.20m (4.6)	3.75-3.9m (6.2)	3.75-3.90m (12.2)	4.50-4.60d			7.20-7.40m
3-*O*-Methyl-**1**	6.30dd (6.4)	(2.0)	4.70dd (2.7)		3.65-3.75m		4.22d (7.2)	3.87m (4.8)	3.65-3.75m (3.2)	3.65-3.75m (16.0)		3.50s		
4-*O*-Methyl-**1**	6.38dd (6.2)	(1.3)	4.80dd (3.1)		4.25m (6.4)		3.42dd (8.0)	3.97m (6.1)	3.80-3.95m (2.8)	3.80-3.95m (12.8)		3.55s		
6-*O*-Methyl-**1**	6.38dd (6.4)	(1.3)	4.75dd (3.3)		4.25ddd (7.0)		3.85dd (7.5)	3.95ddd (6.5)	3.35-3.40ddd (2.8)	3.35-3.40ddd (12.8)		3.50s		
3,6-Di-*O*-methyl-**1**	6.35d (6.3)	(1.3)	4.80ddd (2.8)		3.65ddd		3.90dd (7.5)	3.95m (6.5)	3.35-3.40ddd (2.8)	3.35-3.40ddd (12.5)		3.50s		
4,6-Di-*O*-methyl-**1**	6.30d (6.3)	(1.3)	4.80dd (3.0)		4.25ddd (6.7)		3.45dd (7.5)	3.90ddd (5.0)	3.35-3.40ddd (3.2)	3.35-3.40ddd (15.8)		3.50s		
3,4,6-Tri-*O*-methyl-**1**	6.35d (6.3)	(1.3)	4.85 (2.5)		3.40-3.65m		3.40-3.65m (7.4)	3.90ddd (5.7)	3.75-3.90m (3.0)	3.40-3.65m (16.0)		3.50s		
3,4-di-*O*-Acetyl-6-*O*-trityl-**1**	6.30dd (6.2)	(1.0)	4.70dd (3.1)		3.65-3.75m (2.0)	(1.2)	4.22d (3.6)	3.87m (3.6)	3.65-3.75m (8.0)	3.65-3.75m (12.0)			2.03s	7.20-7.40m
4-*O*-Acetyl-**1**	6.43dd (5.9)	(1.5)	4.71dd (2.6)		4.12dd (7.4)		5.30m (6.3)	3.70-4.0m (3.3)	3.70-4.00m (7.4)	3.70-4.00m (12.9)			2.03s	
6-*O*-Acetyl-**1**	6.32dd (6.4)	(1.3)	4.74dd (1.9)		4.27m (7.0)		3.60dd (10.2)	3.95ddd (2.5)	4.12dd (3.8)	4.42ddd (12.1)			2.03s	
3,6-Di-*O*-acetyl-**1**	6.43dd (5.9)	(1.5)	4.74dd (2.6)		5.30ddd (7.0)		3.70d (9.6)	4.00ddd (2.6)	4.40-4.50ddd (7.0)	4.40-4.50ddd (14.7)			2.03s	
4,6-Di-*O*-acetyl-**1**	6.37dd (6.2)	(1.8)	4.84dd (3.0)		4.27d (6.2)		4.95dd (8.4)	4.11ddd (3.1)	4.20dd (5.7)	4.37dd (14.5)			2.03s	
3,4,6-Tri-*O*-acetyl-**1**	6.45dd (6.4)	(1.3)	4.81dd (3.2)	(0.5)	5.35ddd (6.40)	(0.7)	4.40d (6.8)	4.30m (2.4)	4.15ddd (6.4)	4.40ddd (14.5)			2.03s	

Table 4. NMR data of the alkyl/acyl derivatives of **2** in $CDCl_3$: chemical shifts δ [ppm]; coupling constants *J* [Hz]

Compound	H-1 ($J_{1,2}$)	($J_{1,3}$)	H-2 ($J_{2,3}$)	($J_{2,4}$)	H-3 ($J_{3,4}$)	($J_{3,5}$)	H-4 ($J_{4,5}$)	H-5 ($J_{5,6}$)	H-6 ($J_{5,6'}$)	H-6′ ($J_{6,6'}$)	Substituent			
											Bn	Me	Ac	Ph
4,6-Di-*O*-acetyl-3-*O*-benzyl-**2**	6.40dd (6.4)	(1.8)	4.80ddd (3.9)	(0.4)	4.20m		5.50d (4.0)	4.20m	4.20m	4.20m	4.55-4.70d		2.03s	7.20-7.40m
3,6-Di-*O*-acetyl-4-*O*-benzyl-**2**	6.40d (6.1)	(0.6)	4.85dd (4.3)		5.50m (8.1)		4.00dd (4.0)	4.20-4.50m (3.3)	4.20-4.50m (8.0)	4.20-4.50m (11.2)	4.55-4.70m		2.03s	7.20-7.40m
3.4-Di-*O*-acetyl-6-*O*-benzyl-**2**	6.45dd (6.3)	(1.8)	4.65dd (4.0)	(2.0)	5.55m (4.6)	(1.0)	5.45ddd (3.0)	4.30dd (5.9)	3.50-3.70ddd (6.8)	3.50-3.70ddd (10.0)	4.45-4.60d		2.03s	7.20-7.40m
6-*O*-Acetyl-3,4-di-*O*-benzyl-**2**	6.35d (6.3)		4.99ddd (3.3)	(0.8)	4.10m (7.2)		3.90dd (3.5)	4.25-4.50m (4.3)	4.25-4.50m (8.5)	4.25-4.50m (12.0)	4.60-4.85m		2.03s	7.20-7.40m
4-*O*-Acetyl-3,6-di-*O*-benzyl-**2**	6.40dd (6.3)	(3.0)	4.75m (3.9)	(1.9)	4.25m (7.4)	(1.5)	5.50ddd (4.4)	4.30m (6.1)	3.50-3.70ddd (6.3)	3.50-3.70ddd (10.4)	4.50-4.70d		2.03s	7.20-7.40m
3-*O*-Acetyl-4,6-di-*O*-benzyl-**2**	6.35dd (6.2)	(1.4)	4.75m (2.9)	(0.5)	5.50m (7.0)	(1.4)	4.05ddd (3.3)	4.30m (4.8)	3.65-3.80ddd (7.4)	3.65-3.80ddd 10.0)	4.45-4.60d		2.03s	7.20-7.40m
3,4,6-Tri-*O*-benzyl-**2**	6.35dd (6.3)	(1.5)	4.85ddd (2.9)	(1.3)	3.95ddd (3.9)		4.10dd (1.5)	4.20m (5.3)	3.60-3.80ddd (7.0)	3.60-3.80ddd (10.0)	4.40-4.70d			7.20-7.40m
3-*O*-Methyl-**2**	6.43dd (6.4)	(1.4)	4.69ddd (4.0)	(2.0)	3.99dd (6.4)		4.13s	3.92m (6.4)	4.01m (4.8)	3.87m (10.4)		3.44s		
4-*O*-Methyl-**2**	6.35dd (6.4)	(2.0)	4.72ddd (1.8)	(1.8)	4.49m (4.4)		3.65d (3.2)	4.06dd (8.4)	3.75-3.85ddd (4.8)	3.75-3.85ddd (11.8)		3.55s		
6-*O*-Methyl-**2**	6.35dd (6.4)	(1.4)	4.70dd (2.8)		4.35dd (6.2)		4.05d (3.3)	4.20m (6.5)	3.60dd (5.5)	3.60dd (13.5)		3.45s		
3,4-Di-*O*-methyl-**2**	6.35dd (6.4)	(1.3)	4.75dd (3.5)		4.0dd (6.2)		3.65dd (3.4)	4.15m (6.5)	3.95ddd (5.2)	3.85ddd (15.5)		3.50s		
3,6-Di-*O*-methyl-**2**	6.40dd (6.4)	(1.4)	4.75ddd (3.6)		3.95dd (6.5)		4.15m (3.6)	4.14m (6.7)	3.65ddd (5.2)	3.60ddd (14.6)		3.45s		
4,6-Di-*O*-methyl-**2**	6.35dd (6.4)	(1.2)	4.75dddd (3.3)		4.34s (5.3)		3.60m (3.4)	4.14ddd (6.8)	3.60m (5.2)	3.72m (14.6)		3.40s		
3,4,6-Tri-*O*-methyl-**2**	6.35dd (6.4)	(1.4)	4.70ddd (3.5)		3.99dd (6.2)		3.65m (3.6)	4.15ddd (7.0)	3.60m (5.4)	3.60m (15.0)		3.40s		
3,4-Di-*O*-acetyl-6-*O*-trityl-**2**	6.40dd (6.3)	(0.6)	4.90ddd (4.1)	(1.9)	5.60m		5.60m (6.2)	4.20dd (3.3)	3.20-3.40ddd (7.2)	3.20-3.40ddd (16.6)			2.03s	7.20-7.40m
2-Chloro-2-deoxy-3,4-di-*O*-acetyl-6-*O*-trityl-D-galactose	6.31dd (9.7)	(0.8)	5.98dd (3.0)		6.29m (5.7)		5.17dd (2.5)	4.26m (4.1)	3.20ddd (5.9)	3.40ddd (14.9)			1.50-2.10s	7.20-7.40m
3-*O*-Acetyl-**2**	6.51dd (6.3)	(1.8)	4.67ddd (2.2)		5.43m (4.8)		3.90-4.00m (2.2)	4.20d (4.0)	3.90-4.00m (8.8)	3.90-4.00m (12.1)			2.03s	
4-*O*-Acetyl-**2**	6.40dd (6.3)	(1.8)	4.75ddd (2.2)		4.55m (4.8)		5.30ddd (1.5)	4.10dd (5.5)	3.57dd (6.7)	3.77dd (11.8)			2.03s	
6-*O*-Acetyl-**2**	6.37dd (6.3)	(1.5)	4.72m (3.7)	(1.8)	4.34-4.40m (1.5)		3.90dd (3.3)	4.10dd (6.6)	4.34-4.40m (7.4)	4.34-4.40m (11.4)			2.03s	
3,4-Di-*O*-acetyl-**2**	6.49dd (6.3)	(1.8)	4.73ddd (2.7)	(1.7)	5.58ddd (4.6)	(1.2)	5.48ddd (1.7)	4.20dd (5.7)	3.61ddd (6.7)	3.82ddd (12.1)			2.03s	
3,6-Di-*O*-acetyl-**2**	6.43dd (6.3)	(1.8)	4.65ddd (3.8)	(1.7)	5.37m (4.7)		4.30m (1.6)	4.15m (7.7)	4.30m (7.7)	4.15m (12.2)			2.03s	
4,6-Di-*O*-acetyl-**2**	6.40dd (6.2)	(1.6)	4.75m	(2.4)	4.15-4.30m (4.7)		5.48m (1.7)	4.15-4.30m (5.6)	4.15-4.30m (7.4)	4.15-4.30m (12.2)			2.03s	
3,4,6-Tri-*O*-acetyl-**2**	6.40dd (6.3)	(1.8)	4.70ddd (2.5)	(1.7)	5.50m (4.6)	(1.1)	5.35ddd (1.8)	4.10-4.30m (7.1)	4.10-4.30m (5.0)	4.20-4.30m (11.5)			2.00s	

Table 5. NMR data of the alkyl/acyl derivatives of **3** and **4** in $CDCl_3$: chemical shifts δ [ppm]; coupling constants J [Hz]

Compound	**H-1**		**H-2**	**H-3**	**H-4**	**H-5**	**H-5′**	**Substituent**			
	$(J_{1,2})$	$(J_{1,3})$	$(J_{2,3})$	$(J_{3,4})$	$(J_{4,5})$	$(J_{4,5'})$	$(J_{5,5'})$	**Bn**	**Me**	**Ac**	**Ph**
4-*O*-Acetyl-3-*O*-benzyl-**3**	6.60dd (6.3)		4.90m (4.9)	4.70 (2.8)	4.90 (2.0)	4.20dd (3.2)	3.90dd (12.0)	4.55-4.70m		2.03s	7.20-7.40m
3-*O*-Acetyl-4-*O*-benzyl-**3**	6.65dd (6.3)		4.90m (4.9)	4.85m (2.8)	4.72dd (1.9)	3.90dd (3.1)	3.90dd (12.2)	4.55-4.70m		2.03s	7.20-7.40m
3,4-Di-*O*-benzyl-**3**	6.50dd (6.3)		4.90m (4.8)	4.75m	4.75m (2.0)	3.90dd (3.2)	3.90dd (12.0)	4.45-4.60m			7.20-7.40m
4-*O*-Acetyl-3-*O*-methyl-**3**	6.55dd (6.3)		4.90m (4.9)	4.78dd (2.8)	4.89m (2.0)	4.20dd (3.3)	4.00dd (12.0)		3.50s	2.03s	
3-*O*-Acetyl-4-*O*-methyl-**3**	6.53dd (6.3)		4.90m (4.8)	4.85m	4.75dd (1.9)	3.95dd (3.2)	3.85dd (12.0)		3.56s	2.03s	
3,4-Di-*O*-methyl-**3**	6.55dd (6.3)		4.90m (4.8)	4.75m (2.8)	4.82m (2.0)	4.20dd (3.3)	4.00dd (12.0)		3.50s		
4-*O*-Acetyl-3-*O*-benzyl-**4**	6.56dd (6.1)	(1.0)	4.83ddd (4.9)	5.10-5.12m	5.10-5.12m	3.95ddd (3.6)	4.07ddd (10.9)	4.55-4.70d		2.03s	7.20-7.40m
3-*O*-Acetyl-4-*O*-benzyl-**4**	6.55dd (6.0)	(1.0)	4.85ddd (4.8)	5.40ddd (4.1)	4.78m (9.4)	3.95ddd (3.5)	4.05ddd (11.0)	4.55-4.70d		2.03s	7.20-7.40m
3,4-Di-*O*-benzyl-**4**	6.55dd (6.1)		4.82ddd (4.8)	5.15ddd (4.6)	4.75ddd (9.4)	3.95ddd (3.6)	4.0ddd (12.0)	4.45-4.60d			7.20-7.40m
4-*O*-Acetyl-3-*O*-methyl-**4**	6.55dd (6.0)	(1.0)	4.81ddd (4.8)	5.23dd (4.1)	5.10dd (9.5)	3.95ddd (3.6)	4.07ddd (11.0)		3.50s	2.03s	
3-*O*-Acetyl-4-*O*-methyl-**4**	6.62dd (6.0)		4.83ddd (4.7)	5.40ddd (4.1)	4.95dd (9.4)	3.95ddd (3.5)	4.03ddd (10.9)		3.55s	2.03s	
3,4-Di-*O*-methyl-**4**	6.55dd (6.1)		4.82ddd (4.7)	5.27m (4.5)	4.78dd (9.5)	3.95ddd (3.6)	4.10ddd (12.0)		3.50s		

(electrolysis), respectively. The working electrode as well as the counter electrode were bright (cyclic voltammograms, 1 cm^2) or platinized platinum sheets (electrolysis, 6 cm^2). The reference electrode was an Ag/Ag^+-system in acetonitrile.[20] The anolyte and catholyte compartments were separated by a fine-pore glass frit G3. Argon was passed through the magnetically stirred catholyte during electrolysis.

In all experiments (electrochemical, chemical) DMF was used as the solvent. It was dried over CaH_2, distilled under reduced pressure and stored over molecular sieve 4Å. The conducting agents (LiBr, NaBr, (*Fluka*)) were dried in high vacuum at 150 °C. NaH (*Merck*), available as a suspension (80% in paraffin), was liberated from mineral oil by repeated washings with hexane under nitrogen, whereas commercial LiH was used without pretreatment. The carbohydrate derivatives were synthesized as outlined in the literature.[11,21-25]

Substrate concentrations were 0.1 M (cyclic voltammograms, 30 mL) or 0.5 M (electrolysis, 50 mL), whereas the concentrations of the conducting agent were in all cases 0.5 M. Water traces were kept below 250 ppm, as established by Karl-Fischer-titration.[26] The bases were added in a 10% excess based on the amount of car-

Table 6. Physical data: melting points (mp), optical rotation ($[\alpha]^{22}_D$) and elemental analysis data of the reported derivatives of **1**, **2**, **3** and **4** (data only from compounds not mentioned in literature).

Compound	**mp** [°C]	$[\alpha]^{22}_D$	**Elemental analysis**
3,6-Di-*O*-acetyl-4-*O*-benzyl-**1**	57	-2.9 (c 1.2, $CHCl_3$)	
6-*O*-Acetyl-3,4-di-*O*-benzyl-**1**	71	+ 6.5 (c 3.08, $CHCl_3$)	Anal. Calcd for $C_{22}H_{24}O_5$ (368): Found: C 71.58, H 6.50; Calc. C 71.69, H 6.51
3,6-Di-*O*-methyl-**1**			Anal. Calcd for $C_8H_{14}O_4$ (174): Found: C 55.05, H 8.03; Calc. C 55.09, H 8.03
3,4-Di-*O*-acetyl-6-*O*-trityl-**1**			Anal. Calcd for $C_{29}H_{28}O_6$ (472): Found: C 73.68, H 5.90; Calc. C 73.68, H 5.92
4-*O*-Acetyl-**1**			Anal. Calcd for $C_8H_{12}O_5$ (188): Found: C 51.23, H 6.42; Calc. C 51.26, H 6.40
4,6-Di-*O*-acetyl-3-*O*-benzyl-**2**	73	-83 (c 1.3, $CHCl_3$)	Anal. Calcd for $C_{17}H_{20}O_6$ (320): Found: C 63.72, H 6.21; Calc. C 63.70, H 6.24
6-*O*-Acetyl-3,4-di-*O*-benzyl-**2**			Anal. Calcd for $C_{22}H_{24}O_5$ (368): Found: C 71.71, H 6.54; Calc. C 71.69, H 6.51
4-*O*-Methyl-**2**	140		
3,6-Di-*O*-methyl-**2**			Anal. Calcd for $C_8H_{14}O_4$ (174): Found: C 55.02, H 8.00; Calc. C 55.09, H 8.03
3,4,6-Tri-*O*-methyl-**2**		-37 (c 1.0, $CHCl_3$)	Anal. Calcd for $C_9H_{16}O_4$ (188): Found: C 57.35, H 8.45; Calc. C 57.37, H 8.49
3,4-Di-*O*-acetyl-6-*O*-trityl-**2**			Anal. Calcd for $C_{29}H_{28}O_6$ (472): Found: C 73.68, H 5.90; Calc. C 73.68, H 5.92
2-Chloro-2-deoxy-3,4-di-*O*-acetyl-6-*O*-tri-tyl-D-galactose			Anal. Calcd for $C_{31}H_{31}O_8Cl$ (566): Found: C 65.7, H 5.47, Cl 7.05; Calc. C 65.7, H 5.47, Cl 7.23
3-*O*-Acetyl-**2**	110		Anal. Calcd for $C_8H_{12}O_5$ (188): Found: C 51.24, H 6.45; Calc. C 51.26, H 6.40
4-*O*-Acetyl-**2**	90-92		Anal. Calcd for $C_8H_{12}O_5$ (188): Found: C 51.20, H 6.48; Calc. C 51.26, H 6.40
3,4-Di-*O*-acetyl-**2**			Anal. Calcd for $C_{10}H_{14}O_6$ (230): Found: C 52.21, H 6.01; Calc. C 52.17, H 6.08
3,4-Di-*O*-benzyl-**3**			Anal. Calcd for $C_{19}H_{20}O_3$ (296): Found: C 77.5, H 6.81; Calc. C 77.5, H 6.80
3,4-Di-*O*-methyl-**3**		-180 (c 3.0, $CHCl_3$)	Anal. Calcd for $C_7H_{12}O_3$ (144): Found: C 58.3, H 8.32; Calc. C 58.3, H 8.33
4-*O*-Acetyl-3-*O*-benzyl-**4**			Anal. Calcd for $C_{14}H_{16}O_4$ (248): Found: C 68.0, H 6.47; Calc. C 68.0, H 6.47
4-*O*-Acetyl-3-*O*-methyl-**4**			Anal. Calcd for $C_8H_{12}O_4$ (172): Found: C 55.81, H 6.95; Calc. C 55.81, H 6.97
3,4-Di-*O*-methyl-**4**			Anal. Calcd for $C_7H_{12}O_3$ (144): Found: C 55.82, H 6.96; Calc. C 55.81, H 6.97

bohydrate employed. After conversion into anions (pH 8-9, measured with a pH-indicator (*Merck*)) the electrophiles (methyl iodide, benzyl bromide, trityl chloride, acetyl chloride, acetic anhydride) were added in an amount of 1.1 • 10^{-3} mol per 10^{-3} Faraday of transferred charge, or, where chemical methods were employed, in a 10% excess based on the substrate. Stirring of the reaction mixture was continued until the pH value was adjusted to 6-7. Then the solvent was removed under reduced pressure. The crude mixtures of methyl and acetyl derivatives were chromatographed on silica gel KG 60 (*Merck*). Subsequent separation was achieved by HPLC using hexane / ethyl acetate as eluent. In the case of benzyl and trityl ethers the residual syrups were acetylated in pyridine / acetic anhydride. The reaction mixture was poured onto crushed ice, the products were extracted with chloroform, and the extracts washed with water and dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the separation was performed as above.

All experiments were carried out at room temperature, the results are average values (deviation: ± 1%) based on the data derived from at least three individual experiments.

Instrumentation. Electrolyses were performed with a potentiostatic set up (BANK POS 73). HPLC was performed on a Shimadzu LC-4A instrument equipped with analytical (250*4 mm) and preparative (250*16 mm) scale silica gel columns (Polygosil 60-5, Machery-Nagel). NMR spectra were measured on a Bruker AM 300 MHz instrument, using TMS as internal standard. Where necessary, chemical shift assignments were confirmed by spin decoupling. Acetylation of the products makes the substitution pattern evident. The ^{1}H NMR signals of the adjacent ring protons are be shifted to upfield by alkyl protecting groups, whereas acetylation causes a downfield shift. Optical rotations were recorded with a Perkin-Elmer polarimeter MC 241. TLC was performed on aluminium foil precoated with silica gel (Merck 60 F_{254}).

REFERENCES AND NOTES

1. C. H. Hamann, H. Polligkeit and P. Wolf, *DECHEMA Monographien*, **124**, 525 (1991).
2. E. Gileadi, *J. Electroanal. Chem.*, **11**, 137 (1966).
3. C. H. Hamann, S. Fischer, H. Polligkeit and P. Wolf, *DECHEMA Monographien*, **125**, 649 (1992).
4. C. H. Hamann, S. Fischer, H. Polligkeit and P. Wolf, *J. Carbohydr. Chem.*, **12**, 173 (1993).
5. C. H. Hamann, S. Fischer, H. Polligkeit, D. Schleif and P. Wolf, *Zeitschr. Physik. Chem.*, **185**, 69 (1994).

6. O. Hammerich and V. D. Parker, *J. Am. Chem. Soc.*, **96**, 4289 (1974).
7. Z. Gallus, *Fundamentals of Electrochemical Analysis*, J. Wiley, New York, 1976.
8. R. S. Nicholson and I. Shain, *Anal. Chem.*, **36**, 705 (1964).
9. If the reaction is electrochemically initiated, the yield determining partner is the electron being transferred from the electrode to the substrate.
10. The current and product yields were determined by weighing the separated fractions.
11. I. D. Blackburne, A. I. R. Burfitt, P. F. Fredericks and R. D. Guthrie, *Aust. J. Chem.*, **29**, 381 (1976).
12. J. E. Prue and P. J. Sherrington, *Trans. Faraday Soc.*, **57**, 1795 (1961).
13. J. S. Dunnett and R. P. H. Gasser, *Trans. Faraday Soc.*, **61**, 922 (1965).
14. M. D. Archer and R. P. H. Gasser, *Trans. Faraday Soc.*, **62**, 3451 (1966).
15. P. G. Sears, G. R. Lester and L. R. Dawson, *J. Phys. Chem.*, **60**, 1076 (1956).
16. R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.*, **89**, 1827 (1967).
17. R. Holze, F. Köleli and C. H. Hamann, *DECHEMA Monographien*, **117**, 315 (1989).
18. C. H. Hamann and G. Janoske, *Ber. Bunsenges.*, **95**, 1187 (1991).
19. C. H. Hamann and V. Theile, in preparation.
20. R. C. Larson, R. T. Iwamoto and R. N. Adams, *Anal. Chim. Acta*, **25**, 371 (1961).
21. W. Roth and W. Pigman, *Methods Carbohydr. Chem.*, **2**, 405 (1963).
22. M. Sharma and R. K. Brown, *Can. J. Chem.*, **44**, 2834 (1966).
23. B. Iselin and P. Reichstein, *Helv. Chim. Acta*, **27**, 1146 (1944).
24. A. Rosenthal and D. Read, *Methods Carbohydr. Chem.*, **2**, 457 (1963).
25. I. Lundt and C. Pedersen, *Acta Chem. Scand.*, **6**, 25 (1971).
26. E. Scholz, *Karl-Fischer-Titration*, Springer-Verlag, 1984.