REACTIVITY OF HALO SUGARS ON SILVER CATHODES

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Our extensive research on the reductive electrochemistry of glycosyl derivatives has revealed a remarkable electrocatalytic activity of silver cathodes in the reduction of glycosyl halides, which is strictly related to both the electrode active surface and the reaction medium. The peculiarities exhibited by silver cathodes have been extensively characterised (i) by reactivity studies performed on a wide range of halo sugars by cyclic voltammetry and (ii) by preparative electrolyses leading to the formation of simple and mixed glycosyl dimers and, in the presence of suitable acceptors, of glycosides and glycosyl compounds.

Key words: Silver cathode; Halo sugars; Glycosyl dimers; Glycosides; Electrocatalytic activity; Electrosynthesis; Electroreductions; Preparative electrochemistry.

Quite recently, our extensive research work in the field of the reductive electrochemistry of glycosyl derivatives[1–5] has revealed a remarkable electrocatalytic activity of silver cathodes in the reduction of glycosyl halides. Actually silver turned out[5] to be the cathode material on which the above reaction takes place at the lowest cathodic potential, very probably on account of the powerful silver–halide interaction acting as a driving force for leaving group extraction. Moreover, silver turned out to be the best cathode for preparative electrosyntheses of interesting products, several of them being quite unexpected considering usual reaction pathways in organic chemistry, such as glycosyl dimers in high, nearly statistical yields[2–5], and aryl glycosides when performed in the presence of phenols[2,3,5]. These results were interpreted in terms of radical coupling[4,5], the silver cathode providing a sort of “cage effect”.

These interesting features prompted a deeper, extensive investigation of electrocatalytic properties of silver as a function of two modulating factors, notably the electrode active surface and the reaction medium. These studies provide a powerful basis for correlation and rationalisation of previous results concerning glycosyl halide/silver systems. The present work therefore merges our latest studies on electrocatalytic properties of silver with a review/systematisation of the most relevant previous results.

EXPERIMENTAL

Cyclic voltammetry experiments. Voltammetric investigations of a variety of halo sugars were carried out either with an AMEL 466 polarographic analyser, or with a station including an AMEL 553 potentiostat/galvanostat, an AMEL 566 function generator and an AMEL 862a xy recorder, at 200 or 100 mV s^{-1} sweep rate, in HPLC-grade acetonitrile (ACN), with a wide range of supporting electrolytes, and with an aqueous saturated calomel electrode (SCE) as a reference electrode.

Ag working electrodes consisted of differently shaped platinum supports (wires 0.5 mm in diameter and of 2–6 mm length; a disk 0.5 mm in diameter; a hemisphere 0.6 mm in diameter) covered with silver by cathodic deposition against a silver anode from a 10 g dm^{-3} $KAg(CN)_2$ bath, the deposition currents ranging from 0.5 to 5 mA cm^{-2} (the lower value being the standard current density used in the preparation of the silver layer of silver chloride electrodes for thermodynamic experiments[7]). The roughness factor[8] was determined (i) by underpotential deposition[9] of lead in the potential range from –0.600 to –0.750 V *vs* SCE at 5 mV s^{-1} scan rate, with 280 μC cm^{-2} specific charge factor[10], and (ii) by capacitance determination in the potential range from –0.200 to –0.400 V *vs* SCE, with 50 μF cm^{-2} as specific capacitance factor[10].

Preparative electrolysis experiments. Preparative electrolyses were carried out in a two-compartment cell. The cathode consisted of a 1 × 10 × 0.1 cm rectangular Pt plate, electrolytically covered with silver as described above. A silver plate in ACN saturated with tetraethylammonium bromide (TEABr) was used as anode, to provide a harmless counter-reaction (namely, $Ag + Br^- \rightarrow AgBr + e$). An anion-exchange membrane (Sybron® MA3475) or a glass frit were used to separate the cathode and anode compartments. An AMEL 551 potentiostat/galvanostat was used to run electrolyses under both potentiostatic or galvanostatic control.

Commercial acetobromoglucose (Fluka, purum 95%) stabilised by calcium carbonate, was purified by filtration and recrystallisation from diethyl ether.

Direct-phase TLC (hexane/ethyl acetate or propan-2-ol/CH_2Cl_2) were used to monitor the progress of the electrolytic processes. Reaction products were isolated by direct-phase flash chromatography (hexane/ethyl acetate or propan-2-ol/CH_2Cl_2) and identified by means of NMR and MS as described in previous papers[1–5].

RESULTS AND DISCUSSION

Voltammetric Experiments

Effect of Cathode Nature

Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (acetobromoglucose (**1**)) was chosen as a model for testing anomeric glycosyl halide reactivity on a number of metallic cathode materials, including silver, palladium, platinum, mercury and zinc[5]. Silver was found to exhibit the best electrocatalytic activity for acetobromoglucose reduction; acetobromoglucose reduction peak potentials on silver are less negative by 600–700 mV than on mercury, which in turn is much more favourable to acetobromoglucose reduction than a very popular cathode material as glassy carbon[11], having no specific interactions at all with halide ions.

Effect of Ring Configuration

Table I provides a systematised synopsis of the reduction peak potentials on silver and/or mercury for all glycosyl halides hitherto investigated[1–5] (Fig. 1).

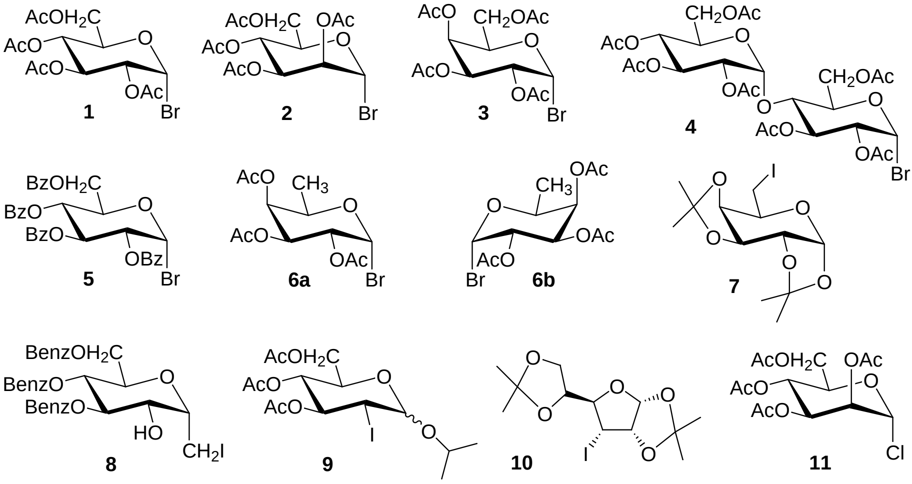


FIG. 1
Structures of compounds characterised by cyclic voltammetry (Table I)

Comparing anomeric bromides it is evident that:

a) their reactivity is influenced by *configuration* of the carbon atom adjacent to the leaving group (mannose, having the large acetate protective group *trans* instead of *cis*, anticipates glucose by 0.3 V on mercury and by 0.1 V on silver). On the contrary, inversion of configuration (galactose) as well as a bulky substituent (maltose) at the C4 carbon are nearly without effect;

b) *enantiomers* have the same reactivity on each cathode material, as expected;

TABLE I
Glycosyl halide reduction peak potentials, (E_p, V *vs* SCE) obtained in 0.1 M acetonitrile/TEAP, at 200 mV s^{-1} scan rate

Bromides	Hg	Ag
Tetra-*O*-acetyl-α-D-glucopyranosyl bromide **1**	–1.90	–1.25 –1.65[a]
Tetra-*O*-acetyl-α-D-mannopyranosyl bromide **2**	–1.60	–1.17 –1.55
Tetra-*O*-acetyl-α-D-galactopyranosyl bromide **3**	–1.90	–1.25
Tetra-*O*-acetyl-α-D-maltopyranosyl bromide **4**	–1.95	–1.35 –1.7[a]
Tetra-*O*-benzoyl-α-D-glucopyranosyl bromide **5**	–1.72 –2.17[b] –2.27[b]	–1.25[a] –1.55 –2.13[b] –2.28[b]
Tri-*O*-acetyl-α-D-fucopyranosyl bromide **6a**	–1.95	–1.20
Tri-*O*-acetyl-α-L-fucopyranosyl bromide **6b**	–1.95	–1.20
Iodides	Hg	Ag
6-Deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose **7**	–1.81	–1.23
(3,4,6-Tri-*O*-benzyl-α-D-glucosyl)iodomethane **8**	–1.435	–1.23
Isopropyl 2-deoxy-2-iodo-3,4,6-tri-*O*-acetyl-D-glucopyranoside **9**	–1.20	–1.05
3-Deoxy-1,2:5,6-di-*O*-isopropylidene-3-iodo-α-D-glucofuranoside **10**	–1.45	–1.23
Chloride	Hg	Ag
Tetra-*O*-acetyl-α-D-mannopyranosyl chloride **11**		–2.65[a]

[a] Shoulder; [b] benzoate peak.

c) benzoate p*rotecting groups*, yet much larger than acetates, improve the glycosyl halide reactivity on mercury probably on account of their greater ability to stabilise the intermediate. Clearly, they are more reactive than acetates, giving reduction peaks of their own, which suggests a possibility of in-site sugar deprotection.

Comparing bromides with other halides, notwithstanding the differences arising from either the sugar configuration or nature of protecting groups (steric hindrance, intermediate stabilisation effects), silver shows a remarkable levelling effect since both glycosyl bromides and iodides (with only one exception) reduce in the same narrow potential range (*ca* from –1.2 to –1.25 V *vs* SCE), while the reactivity sequence I > Br is observed on mercury.

Effect of Active Surface

Figure 2 shows the relationship between the current density for silver deposition and the roughness factor, determined by both underpotential deposition and capacitance for several short-wire electrodes. The results are quite reproducible, though capacity-active surfaces are constantly larger than

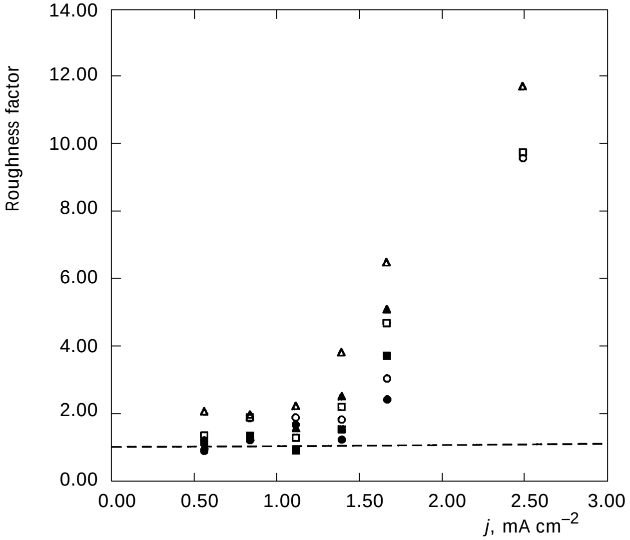


FIG. 2

Roughness factors determined by underpotential deposition (full symbols) and capacity (empty symbols) as a function of the silver deposition current, for short-wire electrodes (geometric surface in cm^2: 0.037 (triangles), 0.094 (squares), 0.110 (circles)) underpotential deposition ones (which is not unexpected, as the two criteria rely on different "probes").

Increasing the silver electrode active surface results in a remarkable positive shift of first-cycle reduction peak potentials, as it is evident from Fig. 3 (nearly +200 mV shift increasing roughness by a factor of ten).

It is remarkable that the first-cycle peak at –1.25 V *vs* SCE was observed to abruptly decrease within a few subsequent cycles, while the signal at –1.75/–1.8 V increased, becoming a well defined peak of height comparable with the initial peak at –1.25 V. Nevertheless, a short anodic pulse or, better, a redox activation cycle including the potential of the reversible couple Ag/AgBr allowed easy restoration of the first-cycle situation. Figure 4 shows a typical pattern obtained with tetraethylammonium perchlorate (TEAP) as supporting electrolyte, a condition implying that the bromide involved in the AgBr reversible wave results from acetobromoglucose reduction. This suggests that some of the reduction products are able to film over the electrode, and that the filmed-over surface loses much of its catalytic activity. Thus the two reduction peaks could be ascribed to "active" and "filmed" silver surface.

Note that the film-over action cannot be ascribed to the bromide ion itself, though evidently remaining on the electrode surface, as working with

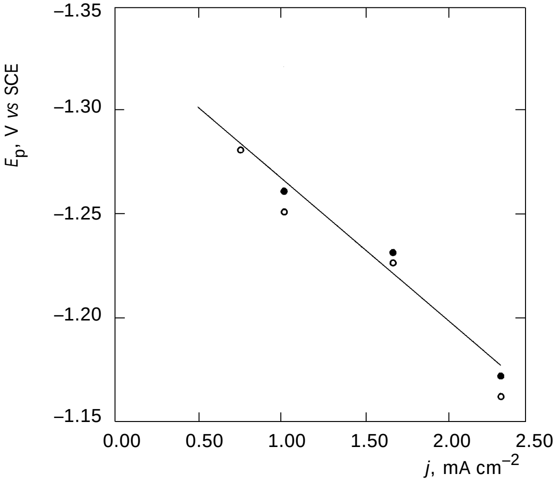


FIG. 3

Acetobromoglucose reduction peak potentials on electrolytically prepared silver cathodes of geometric surface 0.0377 cm^2 (●) and 0.0659 cm^2 (○), as a function of the silver deposition current *j* concentrated bromide supporting electrolytes results in *ca* –200 mV shift only (see below).

Effect of Supporting Electrolyte

The effect of supporting electrolyte has been tested by an extensive scheme of cyclic voltammetry experiments, working with tetramethylammonium perchlorate (TMAP), tetrafluoroborate (TMATFB), chloride (TMACl), and iodide (TMAI); tetraethylammonium perchlorate (TEAP), tetrafluoroborate (TEATFB), bromide (TEABr), and iodide (TEAI); tetrabutylammonium perchlorate (TBAP), tetrafluoroborate (TBATFB), and iodide (TBAI); tetraheptylammonium bromide (THepABr) and iodide (THepAI).

The results are summarised in Table II and visualised in Figs 5a and 5b (where, for comparison, all currents have been normalised at 100 mV s^{-1} on the basis of their dependence on the square root of potential sweep rate).

Peak potentials: Acetobromoglucose reduction potentials are lowest in perchlorate, chloride, and tetrafluoroborate solutions, more negative in bromide solutions, and even more negative in iodide solutions.

Peak currents (see Figs 5a and 5b):

A) Within each anion series, acetobromoglucose reduction currents are regularly modulated by the alkyl chain length of the quaternary ammo-

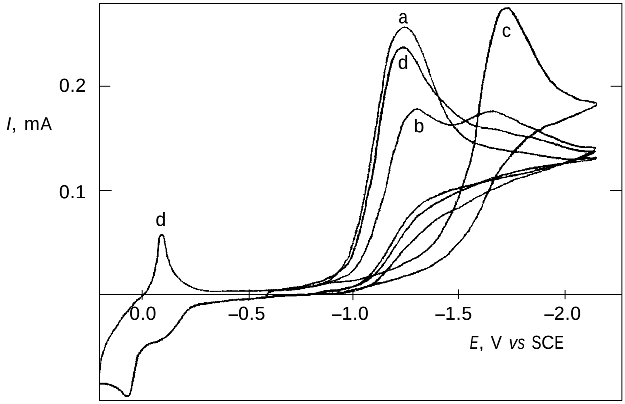


FIG. 4

Typical cyclovoltammetric pattern for 0.003 M acetobromoglucose in acetonitrile with 0.1 M TEAP (or TEATFB) as a supporting electrolyte on a silver-wire cathode (geometric surface 0.16 cm^2, electrodeposition current density 0.5 mA cm^{-2}); a first cycle, b intermediate cycle, c stationary cycle, d after a few reactivation cycles including the Ag/AgBr reversible wave

TABLE II
Cyclic voltammetry (potential range –0.6 to –2.2 V *vs* SCE, scan rate 200 mV s^{-1}) for acetobromoglucose (**1**) reduction on fresh silver-wire electrodes prepared at j = 0.5 mA cm^{-2}

Medium	**1**, mol dm^{-3}	E_{p1}, V vs SCE	I_p, mA 1st cycle	I_p, mA 2nd cycle
		Tetramethylammonium salts		
Acetonitrile/0.1M TMAP	0.003	–1.275	0.112	0.090
	0.006	–1.300	0.246	0.178
	0.009	–1.350	0.328	0.220
	0.012	–1.375	0.400	0.264
	0.015	–1.425	0.496	0.372
+ 0.01 mol dm^{-3} TBATFB	0.015	–1.425	0.404	0.304
+ 0.1 mol dm^{-3} TBATFB	0.015	–1.500	0.364	0.240
Acetonitrile/0.1 M TMATFB	0.003	–1.275	0.226	0.146
	0.006	–1.300	0.382	0.228
	0.009	–1.350	0.532	0.312
	0.015	–1.400	0.84	0.532
+ 0.01 mol dm^{-3} TBATFB	0.015	–1.400	0.812	0.600
+ 0.1 mol dm^{-3} TBATFB	0.015	–1.350	0.748	0.484
Acetonitrile/TMACl sat.[a]	0.01	–1.275	0.078	0.050
	0.02	–1.325	0.134	0.090
	0.03	–1.350	0.190	0.120
Acetonitrile/TMAI sat.[a]	0.01	–1.450	0.096	0.070
	0.02	–1.475	0.178	0.128
	0.03	–1.525	0.256	0.186
		Tetraethylammonium salts		
Acetonitrile/0.1 M TEAP	0.001	–1.200	0.112	0.070
	0.002	–1.225	0.218	0.156
	0.003	–1.225	0.318	0.222
+ 0.1 mol dm^{-3} TEABr	0.003	–1.425	0.312	0.226
+ 0.01 mol dm^{-3} TBAP	0.003	–1.400	0.306	0.236
+ 0.1 mol dm^{-3} TBAP	0.003	–1.400	0.268	0.190
Acetonitrile/0.1 M TEAP[a]	0.001	–1.275	0.086	0.074
	0.002	–1.275	0.174	0.112
Acetonitrile/0.1 M TEATFB[a]	0.001	–1.250	0.106	0.054
	0.002	–1.275	0.190	0.120
	0.003	–1.300	0.216	0.190
Acetonitrile/0.1 M TEABr[a]	0.001	–1.350	0.096	0.062
	0.002	–1.65	0.184	0.116
	0.003	–1.380	0.264	0.164

TABLE II
(*Continued*)

Medium	**1**, mol dm^{-3}	E_{p1}, V vs SCE	I_p, mA 1st cycle	I_p, mA 2nd cycle
Acetonitrile/0.1 M TEAI[a]	0.001	–1.565	0.098	
	0.002	–1.550	0.202	
	0.003	–1.525	0.298	
Tetrabutylammonium salts				
Acetonitrile/0.1 M TBAP	0.001		no peak	
	0.002		no peak	
	0.003		no peak	
	0.004		no peak	
	0.005		no peak	
Acetonitrile/0.1 M TBATFB	0.003	–1.300		
	0.006	–1.350	0.038	0.036
	0.009	–1.400	0.080	0.056
	0.012	–1.450	0.170	0.112
	0.015	–1.450	0.142	0.110
	0.024	–1.450	0.180	0.148
+ 0.1 mol dm^{-3} TEABr	0.024	–1.450	1.360	0.920
Acetonitrile/0.1 M TBAI[a]	0.001	–1.525	0.084	0.062
	0.002	–1.525	0.168	0.130
	0.003	–1.525	0.236	0.172
Tetraheptylammonium salts				
Acetonitrile/0.1 M THepABr	0.003	–1.400	0.288	0.16
	0.006	–1.425	0.444	0.29
	0.009	–1.425	0.712	0.436
	0.015	–1.425	0.96	0.72
Acetonitrile/0.1 M THepAI	0.001	–1.400	0.076	0.046
	0.002	–1.425	0.128	0.76
	0.003	–1.430	0.184	0.112

[a] Scan rate 100 mV/s.

nium ion, with a maximum constantly corresponding to the tetraethylammonium cation. Anyway, the cation modulation is much more evident with anions having little affinity for the silver cathode, such as tetrafluoroborates and perchlorates.

B) In the tetrafluoroborate and perchlorate series, giving the maximum current decrease with increasing length of alkyl chain, the tetrabutylammonium cation is sufficient to nearly (TBATFB) or totally (TBAP) prevent acetobromoglucose reduction, while even longer-chain halide supporting electrolytes result in fairly high currents. Accordingly, it is remarkable that the shielding effect of TBAP or TBATFB can be totally cancelled by addition of 0.1 M halide supporting electrolyte, immediately causing current to jump to high values.

These findings suggest that tetraalkylammonium cations are specifically adsorbed on the silver cathode, thus forming a lipophilic film with the inhibiting effect proportional to its thickness (*i.e.*, to the alkyl chain length); the above film is, however, immediately perturbed by addition of halide ions, which have even stronger specific affinity for silver. In fact, though negatively charged, halide anions are reported to specifically adsorb on silver in aqueous solutions at quite negative potentials (–1.1/–1.2 V *vs* SCE)[12,13]. Now, although no equivalent studies are available for acetonitrile

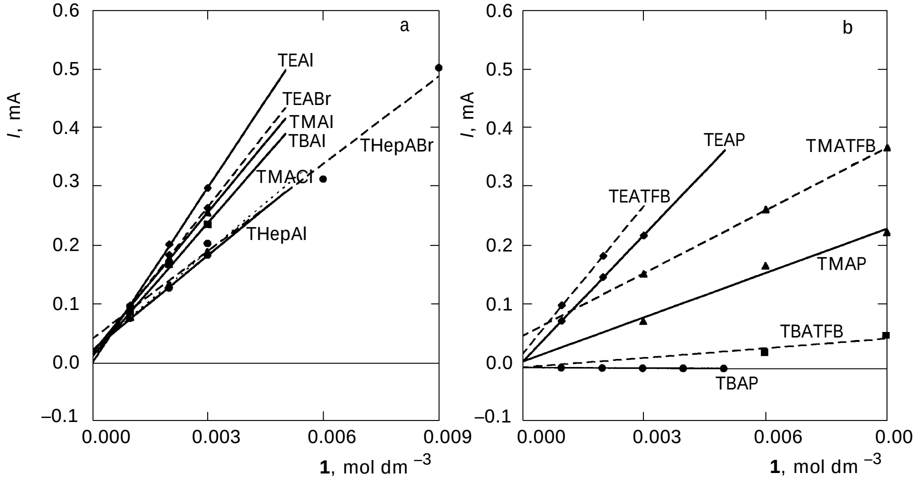


FIG. 5

Supporting electrolyte effect on acetobromoglucose reduction peak currents (normalised to 100 mV s^{-1}) in acetonitrile on silver wire electrodes (surface 0.16 cm^2, electrodeposition current density 0.5 mA cm^{-2}). a Halide supporting electrolytes: iodides (——), bromides (– – –), chloride (·····); b supporting electrolytes: perchlorates (——), tetrafluoborates (– – –)

solvent, it is quite reasonable (and our results may be regarded as a strong, though indirect evidence of this hypothesis) that in this highly polar, aprotic medium, halide ions may adsorb on silver even at more negative potentials, either alone or as an ion pair.

Thus it is reasonable to state that (i) in the case of supporting electrolyte anions having no specific adsorption on silver, such as tetrafluoroborates and perchlorates, the tetraalkylammonium cations are specifically adsorbed on silver so that the inner Helmholtz plane (IHP) is a locus of positive charges; (ii) in the case of supporting electrolytes having strong specific interaction with silver, such as bromide and iodide, the latter are specifically adsorbed on silver either alone or as an ion pair, so that the total charge on the IHP should be negative or, in any case, less positive than under (i). This effect of reversed IHP charge, heavily affecting the activation energy profile at the electrode/solution interface[14] could explain the greater activation energy required by the process in the presence of bromides and iodides.

It is remarkable that the currents obtained with tetraethylammonium salts, being the highest in each anion series, are also showing the lowest dependence on the anion, either specifically interacting with silver or not. Apparently, tetraethylammonium has a very low film-over action so that the active surface is similar to that obtained in the presence of halide ions. Further evidence could be provided by double-layer capacity studies and by SERS or STM (scanning tunneling microscopy)/AFM (atomic force microscopy) experiments.

Preparative Electrolysis Experiments

Cathodic Reduction of Halo Sugars without Acceptors

Acetobromoglucose (**1**) was also chosen as a model substrate for a systematic program of preparative electroreductions on electrodeposited silver cathodes to test the effect of operating conditions on the product distribution. The working conditions chosen are summarised in Table III together with the relevant results which are visualised in the central box of Scheme 1.

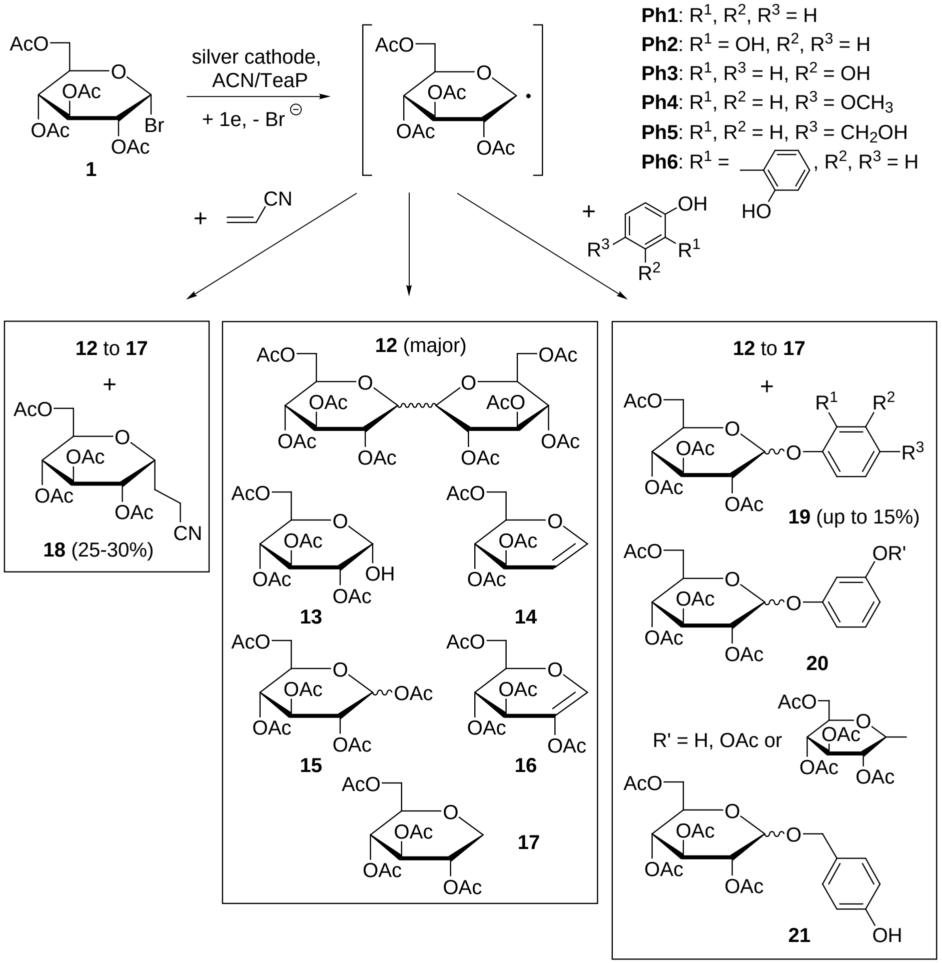
In all cases, except when working with TMAP, the main product is a statistical mixture of three possible C–C glycosyl dimers (α,α-, α,β-, and β,β-), whose formation has been ascribed to a radical intermediate[2–5] and to its peculiarly high local concentration on the silver cathode (a sort of cage effect).

TABLE III
Product distribution (mole %) for the conversion of the same amount of acetobromoglucose (**1**) (6 g, 0.2 M initial concentration) by electroreduction in acetonitrile in divided cell on electrodeposited silver cathode, at constant current (I = 150 mA) after passage of charge Q

Run	Reaction conditions	**12**	**13**	**14**	**15**	**16**	**17**	Byproducts not isolated	Total conversion of **1**
I[a]	Q = 1 600 C, 0.5 M TEAP	55	14	18	9	2	0	0	98
II	Q = 700 C, 0.5 M TEAP	80	11	0	3	0	0	6	67
III	Q = 1 600 C, periodic **1** make up, 0.5 M TEAP, high surface cathode	66	29	0	2.5	2.5	0	0	70
IV	Q = 1 600 C, periodic **1** make up, 0.1 M TEABr	64	11	0	0	0	3	22[b]	65
V	Q = 1 600 C, periodic **1** make up, 0.2 M THepABr	50	48	2	0	0	0	0	61
VI	Q = 1 600 C, periodic **1** make up, 0.2 M TMAP (satureted)	14	15	24	29	8	0	10	59

Blank experiments in the presence of the silver cathode but without passage of charge resulted in very low conversion of 1 (≈2%) maily into tetraacetylglucose. [a] Controlled potential (–1.7 V *vs* SCE maximum). [b] Mixture of 2,3,4,6-Tetra-*O*-acetylglucose and glucose-containing byproduct.

As clearly shown by experiments 1 to 3, to obtain maximum acetobromoglucose conversion into glycosyl dimers (up to 80%), it is necessary to prevent the process from running into diffusion-controlled conditions. In fact, the typical byproducts usually obtained[3,4] when aceto- bromoglucose is totally consumed during the electrolysis (run I), drop almost to nil when electrolysis is either stopped half-way (run II) or acetobromoglucose is periodically added to ensure a constant concentration (run III). Substitution of TEAP with TEABr does not significantly alter the yields of both



SCHEME 1

A survey of acetobromoglucose reactions on silver cathodes dimers and tetraacetylglucose, as the byproducts in run IV, not yet completely elucidated, are very likely glucose-like compounds, probably anomeric C–O–C dimers.

While the dimers *vs* tetraacetylglucose ratio can be improved by controlling the water content and temperature (≈27 °C or lower), the presence, yet to be confirmed, of C–O–C disaccharides could be related to the periodic acetobromoglucose make-up.

The similar product distribution in runs 3 and 4 was not unexpected, since bromide ions are always present in the reaction medium, as they form during the process. The cation effect, as pointed out in the previous section, is more striking. In fact, the longer-chain THepA ion gives almost only dimers and tetraacetylglucose in the 1 : 1 ratio (run V), whereas, remarkably enough, changing TEAP for saturated TMAP (run VI) almost completely inhibit dimerisation, while four monomeric products are obtained in significant yields.

Electrochemical Synthesis of C–C Glycosyl Dimers

The above procedure may be regarded as a powerful way to the synthesis of both homogeneous and crossed C–C glycosyl dimers.

Now, these compounds are looked upon with increasing interest by biochemists as they are structurally very similar to natural C–O–C glycosyl dimers (including fundamental disaccharides such as maltose, lactose, and saccharose) but cannot be metabolised *via* hydrolysis by the same enzymes (in the above case, glucosidase, galactosidase, and invertase, respectively). On the other hand, C–C glycosides are hardly obtainable by non-electrochemical pathways, as already mentioned above.

Thus we have carried out an explorative program of preparative dimerisations[4] including different cases:

1. "Homo" dimerisations in the anomeric position, a case in which three products (α,α-, α,β-, and β,β-) can be expected. After acetobromoglucose, affording high, statistical dimerisation yields (see the previous section), we tested tri-*O*-acetyl-α-D-fucopyranosyl bromide **6a** having a methyl group instead of the CH_2OAc at the C-6 position, obtaining again all of the three possible isomers though in lower yields (total 34%, which, however, could be improved by optimizing the operation conditions).

2. "Homo" dimerisation in non-anomeric, non-prochiral position, in which case only one dimerisation product can be expected. The substrate tested, 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose **7**, gave its dimer as the unique product. This is a remarkable result as the intermediate radical is usually such a good hydrogen abstractor from acetonitrile that in non-electrochemical experiments some coupling of this radical was observed only in the presence of Fe(II); this was interpreted[15] by the hypothesis of the existence of a metal ion/free radical complex of a relatively longer life than a simple alkyl radical.

3. *Cross-dimerisations*: cogeneration by electroreduction on silver of a non-anomeric, non-prochiral radical and a more stable[11] anomeric radical (**7** + **1**; **7** + **6a**). A partial selectivity was observed in both cases. Although six dimers could be expected, products in total yields ≈40–60% almost entirely consisted of the three dimers containing the more reactive radical **7** (ref.[4]).

From these preliminary results, glycosyl halide electroreduction undoubtedly emerges as an extremely competitive methodology for the synthesis of C–C dimers, but the method may turn out to be even much more efficient in terms of both dimerisation yields and selectivity. In fact, all experiments cited above were performed not on electrodeposited silver surfaces (*i.e.*, highly controlled surfaces having high roughness factor) but on silver plates mechanically polished with sandpaper, and, above all, they were carried out only in standard "exhaustive electrolysis" conditions, as in run I, Table III. These conditions proved by no means the most convenient for dimerisation in the recent experiments on model acetobromoglucose. Thus work is in progress to apply the improved methodology to homo- and cross-dimerisations, and to extend it to polysaccharide dimerisation.

Electrochemical Synthesis of Glycosides

Reduction of acetobromoglucose in the presence of acceptors (Scheme 1, left and right boxes) leads to the formation, sometimes stereoselective, of glycosides, a widespread and highly valuable class of natural compounds.

Reduction of acetobromoglucose in the presence of α,β-unsaturated nitriles led to the stereospecific synthesis of 3-glycosylalkanonitriles[1]. In acrylonitrile glucosidation, the yields were 26% on silver and 19% on mercury cathodes.

Reduction of acetobromoglucose in the presence of various phenols[2,3] led to the formation of the corresponding aryl *O*-glucosides in low to moderate yields. In the case of 4-hydroxybenzyl alcohol both the aliphatic and aromatic glucoside were obtained. In the model case of resorcinol, six products were isolated[5], depending on operation conditions, an α- and a β-series, both consisting of monoglucosidated, glucosidated-acetylated, and doubly glucosidated resorcinol.

A remarkable effect of the cathode material[5] on the product distribution was observed. Working under controlled-potential conditions on silver cathode, we obtained selectively α-glucosides and C–C glucosyl dimers as main products (while working under background current conditions we also obtained β-glucosides, which could be explained in terms of a SN2 mechanism started by the phenoxide anion); on palladium cathode, both α- and β-glucosides and again C–C glucosyl dimers as main products; on mercury cathode, α-glucosides in very low yields, and tri-*O*-acetyl-D-glucal as the main product (in agreement with former literature data[16]), whereas the yield of C–C dimers dramatically decreased.

The observation that conditions promoting dimerisations also promote coupling with other acceptors whereas conditions promoting intramolecular reactions constantly give low coupling is consistent with our hypothesis of the "cage effect" provided by an active silver surface. The glycosyl radicals, either true or latent (the bromide acting as a C···Br···Ag link with the silver surface), present in the "cage" in high local concentration, couple with their nearest neighbours, either glycosyl radicals or acceptors. Thus dimerisation and addition are necessarily always in competition, their relative yields depending very likely not only on the acceptor reactivity toward the glycosyl radical, but also on the relevance of its presence inside the "cage". In this context, the present observations about interactions between the silver surface and adsorbed species could be very helpful in designing appropriate reaction conditions to maximise the coupling yields.

The formation of α-glycosides was explained by the Giese–Dupuis hypothesis[17] that the glycosyl intermediate partially maintains sp^3 hybridisation, the α configuration being more stable than the β one due to interaction between the electron in anomeric position and the nonbonding π orbital of the adjacent oxygen atom.

Some exploratory cyclic voltammetry experiments with heterocyclic acceptors such as benzimidazole and purine were also performed in order to test the possibility of C–N glycosidation, with nucleosides as most valuable targets; they gave evidence of specific interaction between the halo sugar, the acceptor and/or the cathode surface.

For preparative purposes, however, the methodology so far used must be radically changed due to a very low solubility of heterocyclic acceptors in acetonitrile and unsuitability of the customary direct-phase separation procedures.

CONCLUSIONS

Silver cathodes, having unique properties, can be regarded as a valuable tool for glycosyl halide reduction. They actually show the best electrocatalytic activity of the tested materials. Their activity can be modulated by an appropriate choice of the operating conditions, in particular the supporting electrolyte. Most important of all, they exhibit a remarkable "cage effect", promoting high local concentrations of glycosyl radicals which can couple or add to other specifically adsorbed species.

Work is in progress to better enlight specific interactions between the selected substrates and the silver surface by means of SERS (surface-enhanced Raman spectroscopy), a powerful technique for silver surface characterisation.

To generalise the peculiar behaviour of organic halides on silver, the extension of the present electrochemical studies to simple alkyl halides is now needed. Actually the reactivity of alkyl halides has been elucidated by very careful and thorough studies[18], yet generally referring to cathodes (platinum, glassy carbon) having little specific interaction with the selected substrates. In this context, testing silver could lead to detection of new and remarkable features.

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REFERENCES

1. Rondinini S., Mussini P. R., Ferzetti V., Monti D.: *Electrochim. Acta* **1991**, *36*, 1095.
2. Benedetto M., Miglierini G., Mussini P. R., Pelizzoni F., Rondinini S., Sello G.: *Carbohydr. Lett.* **1995**, *1*, 321.
3. Rondinini S., Mussini P. R., Sello G., Vismara E.: *J. Electrochem. Soc.* **1998**, *145*, 1108.
4. Guerrini M., Mussini P., Rondinini S., Torri G., Vismara E.: *Chem. Commun.* **1998**, 1575.
5. Rondinini S., Mussini P. R., Cantu G., Sello G.: *Phys. Chem. Chem. Phys.* **1999**, *1*, 2989.
6. Alberti A., Della Bona M. A., Macciantelli D., Pelizzoni F., Sello G., Torri G., Vismara E.: *Tetrahedron* **1996**, *52*, 10241.
7. Ives D. J. G., Janz J. G.: *Reference Electrodes – Theory and Practice*, p. 203. Academic Press, New York 1961.
8. Trasatti S., Petrii O. A.: *Pure Appl. Chem.* **1991**, *63*, 711.
9. Kolb D. M., Przanyski M., Gerischer H.: *J. Electroanal. Chem. Interfacial Electrochem.* **1974**, *54*, 25.
10. a) Vashkyalis A., Demontaite O.: *Elektrokhimiya* **1978**, *14*, 1213; b) Vashkyalis A., Demontaite O.: *Sov. Electrochem.* **1979**, 1950.
11. Comoli M.: *Ph.D. Thesis*. University of Milano, Milano 1998.

12. a) Valette G., Hamelin A., Parsons R.: *Z. Phys. Chem.* **1978**, 113, 71; b) Valette G.: *J. Electroanal. Chem.* **1982**, *132*, 311; c) Valette G.: *J. Electroanal. Chem. Interfacial Electrochem.* **1983**, *146*, 439; d) Valette G., Parsons R.: *J. Electroanal. Chem. Interfacial Electrochem.* **1985**, *191*, 377; e) Valette G., Parsons R.: *J. Electroanal. Chem. Interfacial Electrochem.* **1986**, *204*, 291; f) Bange K., Straehler B., Sass J. K., Parsons R.: *J. Electroanal. Chem. Interfacial Electrochem.* **1987**, *229*, 87.
13. a) Foresti M. L., Innocenti M., Kobayashi H., Pezzatini G., Guidelli R.: *J. Chem. Soc., Faraday Trans.* **1996**, *92*, 3747, and references therein; b) Foresti M. L., Innocenti M., Forni F., Guidelli R.: *Langmuir* **1998**, *14*, 7008, and references therein.
14. a) Conway B. E.: *Theory and Principles of Electrode Processes*, Chaps 4 and 5. Ronald, New York 1965; b) Bianchi G. in: *Elettrochimica* (T. Mussini, Ed.), p. 476. Noguerol, Milano 1963
15. Kochi J., Rust F. F.: *J. Am. Chem. Soc.* **1962**, *83*, 2017.
16. Giese B., Dupuis J.: *Tetrahedron Lett.* **1984**, *25*, 1349.
17. Maran F., Vianello E., Catellani G., D'Angeli F.: *Electrochim. Acta* **1989**, *34*, 587.
18. a) Andrieux C. P., Blocman C., Dumas-Bouchiat J.-M., Savéant J.-M.: *J. Am. Chem. Soc.* **1979**, *101*, 3431; b) Lexa D., Savéant J.-M., Soufflet J. P.: *J. Electroanal. Chem.* **1979**, *100*, 159; c) Andrieux C. P., Merz A., Savéant J.-M., Tomahogh R.: *J. Am. Chem. Soc.* **1984**, *106*, 1957; d) Andrieux C. P., Merz A., Savéant J.-M.: *J. Am. Chem. Soc.* **1985**, *107*, 6097; e) Andrieux C. P., Gallardo I., Savéant J.-M., Su K. B.: *J. Am. Chem. Soc.* **1986**, *108*, 638; f) Andrieux C. P., Savéant J.-M., Su K. B.: *J. Phys. Chem.* **1986**, *90*, 3815; g) Savéant J.-M.: *J. Am. Chem. Soc.* **1987**, *109*, 6788; h) Chami Z., Gareil M., Pinson J., Savéant J.-M., Thiébault A.: *Tetrahedron Lett.* **1988**, *29*, 39; i) Andrieux C. P., Hapiot P., Savéant J.-M.: *J. Phys. Chem.* **1988**, *92*, 5887; j) Lexa D., Savéant J.-M., Su K. B., Wang D. L.: *J. Am. Chem. Soc.* **1988**, *110*, 7617; k) Andrieux C. P., Gallardo I., Savéant J.-M.: *J. Am. Chem. Soc.* **1989**, *111*, 1620; l) Lexa D., Savéant J.-M., Schäfer H., Su K. B., Vering B., Wang D. L.: *J. Am. Chem. Soc.* **1990**, *112*, 6162; m) Chami Z., Gareil M., Pinson J., Savéant J.-M., Thiébault A.: *J. Org Chem.* **1991**, *56*, 586; n) Médebielle M., Pinson J., Savéant J.-M.: *J. Am. Chem. Soc.* **1991**, *113*, 6872; o) Andrieux C. P., Le Gorande A., Savéant J.-M.: *J. Am. Chem. Soc.* **1992**, *114*, 6892; p) Bertran J., Gallardo I., Moreno M., Savéant J.-M.: *J. Am. Chem. Soc.* **1992**, *114*, 9576; q) Savéant J.-M.: *J. Am. Chem. Soc.* **1992**, *114*, 10595; r) Ettayeb R., Savéant J.-M., Thiébault A.: *J. Am. Chem. Soc.* **1992**, *114*, 10990; s) Adcock W., Clark C., Houmam A., Krstic A. R., Pinson J., Savéant J.-M., Taylor D. K., Taylor J. F.: *J. Am. Chem. Soc.* **1994**, *116*, 4653; t) Andrieux C. P., Le Gorande A., Savéant J.-M.: *J. Electroanal. Chem.* **1994**, *377*, 191; u) Andrieux C. P., Batlle A., Espin M., Gallardo I., Jiang Z., Marquet J.: *Tetrahedron* **1994**, *50*, 6913; v) Savéant J.-M.: *Adv. Electron Transfer Chem.* **1994**, *4*, 53; w) Andrieux C. P., Robert M., Savéant J.-M.: *J. Am. Chem. Soc.* **1995**, *394*, 9340; x) Médebielle M., Pinson J., Savéant J.-M.: *Electrochim. Acta* **1997**, *42*, 2049; y) Andrieux C. P., Saveant J.-M., Tardy C.: *J. Am. Chem. Soc.* **1998**, *120*, 4167.