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Carbohydrate Research 338 (2003) 1543–1552
CARBOHYDRATE RESEARCH
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New efficient electrochemical synthesis of 1,5-dithioxylopyranosides in the presence of a sacrificial anode

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Received 14 March 2003; accepted 28 April 2003

Abstract

Electroreduction of the disulfide derivative RSSR (**5**, R = –C_6H_4–CO–C_6H_4–CN) on a mercury pool or a carbon gauze electrode in the presence of 2,3,4-tri-*O*-acetyl-5-thio-D-xylopyranosyl bromide (**1**), using a sacrificial zinc anode gave an α,β anomeric mixture of [4-(4-cyanobenzoylphenyl)] 2,3,4-tri-*O*-acetyl-1,5-dithio-D-xylopyranoside (**6**) in 40–70% yield, according to the experimental conditions used (nature of solvent, electrolyte salt, and temperature). High selectivity favouring the α anomer of **6** is observed starting from the α anomer of **1**. Mechanistic aspects are discussed.

Keywords: Electrosynthesis; Sacrificial anode; Zinc; 5-Thioxylopyranosyl bromide; Dithioxylopyranosides

1. Introduction

In the quest for orally active antithrombotic and antiatherosclerotic agents, a range of synthetic glycopyranosides varying in the nature of the aglycon, configuration, and replacement by sulphur of either the ring-oxygen atom, the oxygen atom linked to the aglycon, or both, has been evaluated in an animal model.[1–3]

Thioglycosides are also key intermediates for oligosaccharide synthesis and they have attracted considerable attention as glycosyl donors.[4] Two synthetic methods are commonly employed,[5] namely the reaction of a peracetylated glycoside with a thiol in the presence of a Lewis acid and the reaction of an acetylated glycosyl halide.[6–8]

However, the development of new and selective methods for thioglycosides synthesis is an area of current interest.

An electrosynthetic approach potentially offers selectivity and mild operating conditions. Moreover, electrochemical methods may involve reaction mechanisms different from conventional chemical processes, leading to compounds with different anomeric configurations.

Only a few electrosyntheses of glycosides have been described; they involve O-glycosylation starting from a thioglycoside,[9–13] glycosyl halide,[14] or glycosyl aryloxides[15] as the glycosyl donor. Recently, an efficient electrochemical N-glycosylation has been reported.[16]

Here, we report an unprecedented electrochemical synthesis of 1,5-dithioxylopyranosides in an undivided cell in the presence of a sacrificial metallic anode. Applications of the technique of electro-organic synthesis started in the early 1980s with the electrocarbonylation of acenathylene.[17] Many papers[18] have demonstrated the successful use of a sacrificial anode in electroreductive organic synthesis performed in a one-compartment cell. One of the most important features of the process is the absence of a membrane because the anodic process does not involve any organic compound. The mechanism of reaction can be schematically given as follows, for a divalent anode-derived ion:

at the anode: $M \rightarrow M^{2+} + 2e^-$

at the cathode: $RX + 2e^- \rightarrow R^- + X^-$

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doi:10.1016/S0008-6215(03)00205-2

in the solution: $R^- + E^+ \rightarrow RE$

overall reaction: $RX + M + E^+ \overset{\text{electricity}}{\rightarrow} RE + MX^+$

(E^+: electrophile present in solution; e.g., carbon dioxide)

This sacrificial metallic anode technique prompted us to the present study of S-glycosylation starting from a 5-thioxylopyranosyl halide, employing the following steps:

i) Preliminary voltammetric investigation of the cathodic reactivity of glycosyl donors and an aglycon, a disulfide derivative, RSSR.
ii) Preparative electrolysis for the synthesis of 1,5-dithioxylopyranosides using various metallic anodes under different experimental conditions (temperature, solvent, electrolyte salt).

2. Results and discussion

2.1. Voltammetric investigation

Fig. 1 shows the cyclic voltammogram of the disulfide RSSR, (**5**, R = –C_6H_4–CO–C_6H_4–CN) in MeCN–0.2 M Bu_4NPF_6 solution on a vitreous carbon electrode. Three reduction peaks were A, B, and C encountered. When the scan was reversed after C, three oxidation peaks C′, B′, and A'_1 were observed. B/B′ and C/C′ present all the characteristics of reversible a system[19] and A'_1 corresponds to the oxidation of the species generated at peak A. On a rotating disk electrode (RDE voltammetry) three corresponding reduction waves are also observed (A: $E_{1/2} = -0.77$ V, B: $E_{1/2} = -1.68$ V and C: $E_{1/2} = -2.18$ V). The intensity height of these three waves are nearly equal (Fig. 2).

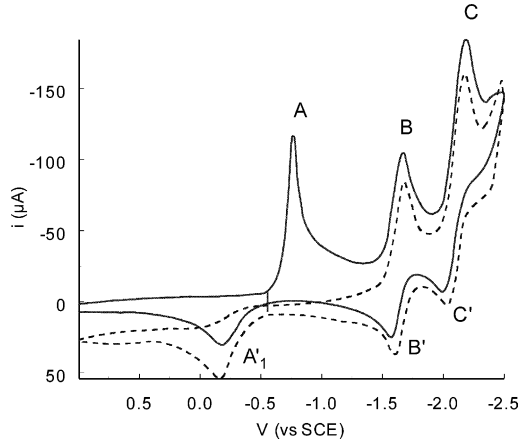


Fig. 1. Cyclic voltammogram of 3.6 mM of RSSR (**5**) at v: 0.1 V s^{-1} in 0.2 M MeCN–Bu_4NPF_6 solution. (a: solid line) **5** alone, starting potential: +1 V; (b: dashed line) after reduction at −1.1 V vs. SCE, starting potential −0.6 V.

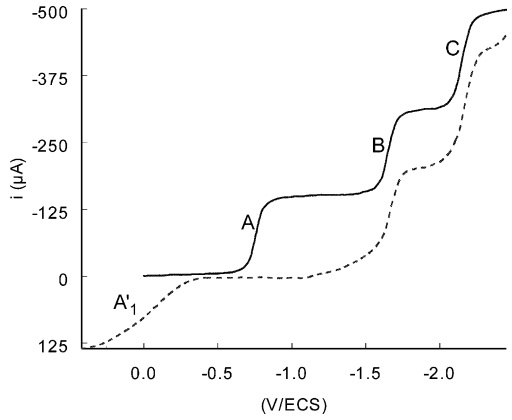


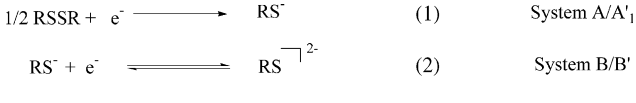
Fig. 2. RDE voltammogram of 3.6 mM of RSSR (**5**) at 0.02 V s^{-1} in 0.2 M MeCN–Bu_4NPF_6 solution. (a: dashed line) **5** alone; (b: solid line) after reduction at −1.1 V vs. SCE. Initial potential: (a) 0; (b) +0.5 V.

We performed the electrolysis of **5** on a mercury pool electrode at a potential of −1.1 V (plateau of wave A). Nearly two mole equivalents of electrons were consumed ($n_{exp} = 2.2$ F) and the solution turned from colorless to red. The cyclic voltammogram of this resulting solution exhibits the system B/B′, C/C′ and the oxidation peak A'_1 (Fig. 1(b)); by RDE voltammetry reduction waves B and C and oxidation wave A'_1 were observed (Fig. 2(b)). These results can be described in terms of Scheme 1.

According to E.C.E. Mechanism (E means electrochemical reaction; C means chemical reaction), the two electroreduction of **5** leads to S–S bond cleavage, and the anion RS^- (**5′**) is obtained.[20] System B/B′ can be probably attributed to reduction of the carbonyl group in RS^- and oxidation of the corresponding radical anion (reaction 2). Peak C corresponds to the one-electron reduction of RS^{2-} giving (formally) a trianion (reaction 3). Anionic species RS^{2-} and RS^{3-} are stable on the cyclic voltammetry time-scale but RS^{2-} decomposes rapidly on the electrolysis time-scale, even at low temperature, yielding a variety of unidentified products.

For comparison with these studies we examined the electrochemical behaviour of diphenyl disulfide (**3**). Similar experimental conditions as just described were followed, and **3** exhibits an irreversible system A/A'_1 in cyclic voltammetry (Fig. 3).

The radical anion formed upon electron transfer to the substrate (reaction 4) cleaves to yield the anion PhS^- and the radical $PhS^\bullet$ (reaction 5). $PhS^\bullet$ is easier to reduce than the starting material, and its reduction is



Scheme 1.

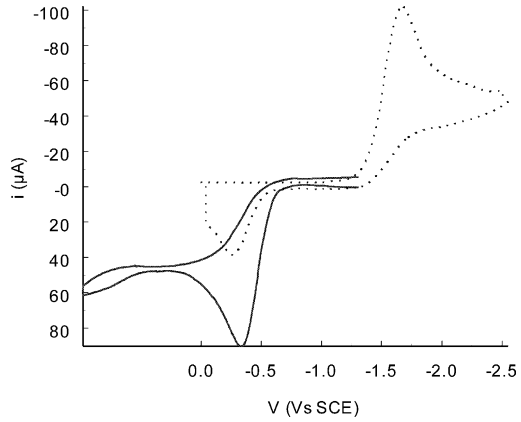
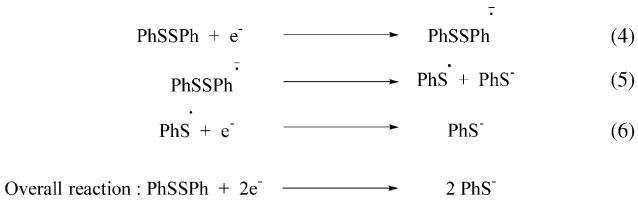


Fig. 3. Cyclic voltammogram of 5.9 mM PhSSPh (**3**), at $v = 0.1\ V\ s^{-1}$ in 0.2 M MeCN–Bu_4NPF_6 solution. (a: solid line) **3** alone, (b: dashed line) after reduction of **3** at −1.6 V. Initial potential: (a) 0; (b) −1.50 V.

described in reaction 6. The overall reduction is thus a two-electron process, which yields to the corresponding phenyl thiolate anion PhS^- (Scheme 2).



Scheme 2.

The oxidation of anion PhS^- induces an irreversible one-electron anodic wave A_1' around −0.3 V giving the $PhS^\bullet$ radical, as described in reaction 7. Further dimerisation yields **3** (reaction 8).

$$PhS^- - 1e^- \rightarrow PhS^- \quad (7)$$

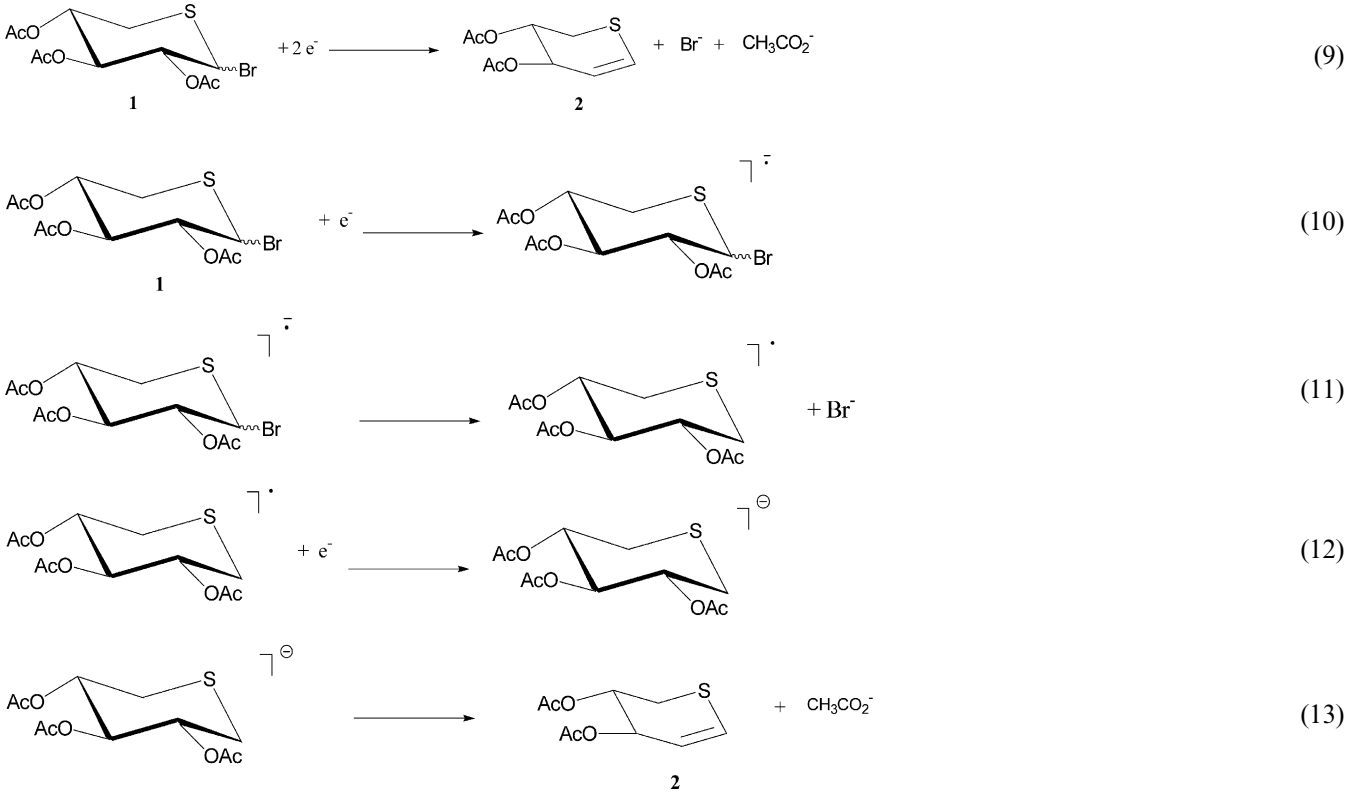
$$PhS^- \rightarrow (1/2)PhSSPh \quad (8)$$

PhS^- can be obtained quantitatively by two-electron reduction of **3** ($n_{exp} = 2.1$ F) on a carbon gauze or mercury pool electrode (see Fig. 3(b)).

The cyclic voltammogram of the acetylated 5-thioxylopyranosyl bromide (**1**) formulated on a vitreous carbon electrode exhibits an irreversible two-electron wave.

The two-electron reduction of **1** on a carbon gauze electrode yields the unsaturated sugar 3,4-di-*O*-acetyl-1,5-anhydro-5-thio-D-*threo*-pent-1-enitol (**2**) (reaction 9)[21] in high yield (see Section 3).

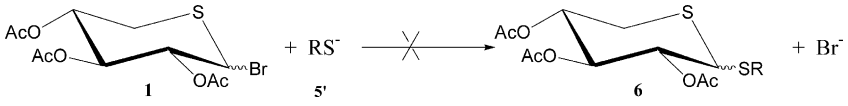
The E.C.E.C. mechanism can reasonably be postulated. Addition of the first electron gives the radical anion (reaction 10), which undergoes fast cleavage of the carbon–bromine bond, leading to the corresponding neutral radical (reaction 11). This radical is easier to reduce than the starting material to give an anion (reaction 12). Finally, the latter unstable anion leads

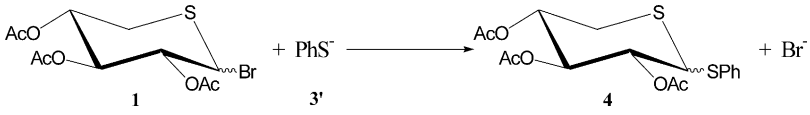


to **2** after β elimination of an acetate group at the C-2 position (reaction 13).

2.2. Reactivity of 1 towards thiolate anions PhS^- (3′) and RS^- (5′) (R = –C_6H_4–CO–C_6H_4–CN)

Fig. 4(a) shows the cyclic voltammogram of PhS^- in MeCN–Bu_4NPF_6 solution; an irreversible peak A_1' is observed. Addition of nearly one molar equivalent of **1** results immediately in complete replacement of peak A_1' by a cathodic irreversible peak D and a new oxidation peak A_2' (Fig. 4(b)). This drastic change induced by **1** addition is due to the formation of the corresponding thioglycoside phenyl 2,3,4-tri-*O*-acetyl-1,5-dithio-D-xylopyranoside (**4**) through reaction 14.





(14)

Peak A_2' corresponds to the oxidation of Br^- (Bu_4NBr in MeCN–Bu_4NPF_6 solution exhibits the same oxidation step A_2') and B to the reduction of **4**.

After appropriate work-up, compound **4** (α and β anomers, ratio = 50/50) was purified chromatographically and identified spectroscopically.

The glycosylation reaction often includes the conception of intimate ion pairs I and II with the definite orientation of counter-ions relative to the central cation, which provides stereospecificity of the nucleophilic anion as shown in Scheme 3.

Stereospecificity of glycosylation can be provided in this mechanism only by the coupling of a nucleophile with ion pairs before further charge separation with the formation of solvent separated ion pairs or a free glycosyl cation III, because the latter are expected to react with the thiolate anion without steric control (case of PhS^-). It becomes clear that the nature of the solvent and counter ion should critically affects the course of the reaction and product composition.

Concerning the thiolate anion **5′**, generated in a divided cell, no reactivity is observed in the presence of **1**. Indeed, by cyclic voltammetry, the oxidation wave A_1' of RS^- is not modified upon addition of one molar equivalent of **1**, even after 2 h of the reaction. This result can explained by the presence of the electron withdrawing carbonyl group of the phenyl derivative and yields **5′**, less nucleophilic than **3′**. This effect can explain the difference of reactivity between **3′** and **5′** towards **1**.

These reasons prompted us to undertake the study of the S-glycosylation reaction from aglycone **5**, using a sacrificial anode in an undivided cell.

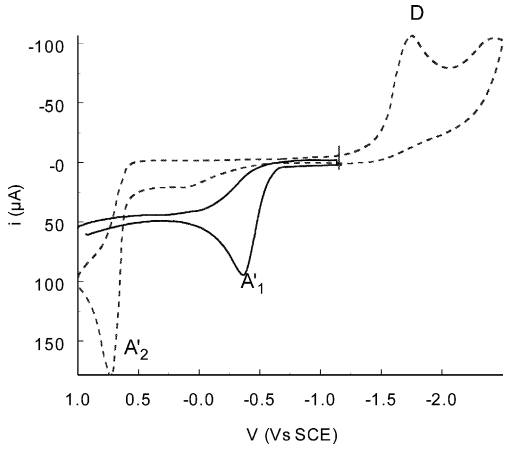
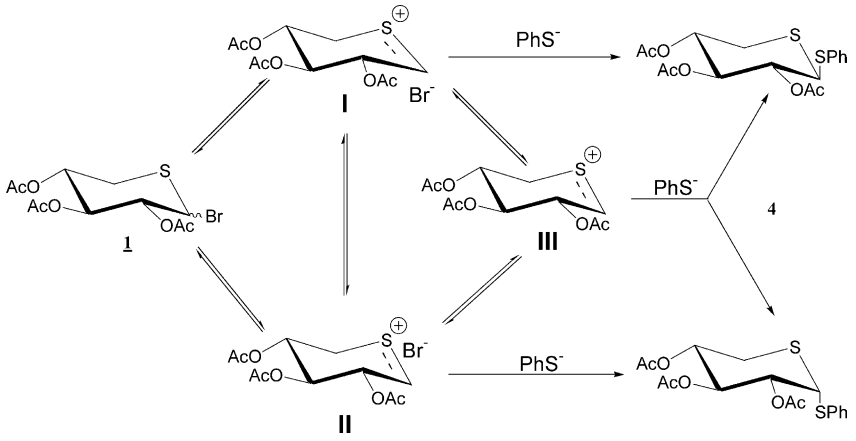


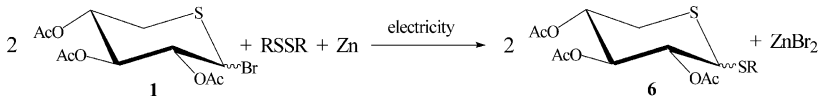
Fig. 4. (a: solid line) Cyclic voltammogram of 11.8 mM PhS^-, at $v = 0.1$ V s^{-1} in MeCN–Bu_4NPF_6 solution; (b: dashed line) after addition of 0.118 mM of **1**. Starting potential: −1.2 V.



Scheme 3.

2.3. Electrosynthesis of 1,5-dithioxylopyranosides in the presence of a sacrificial anode

Electrolysis of the disulfide RSSR (**5**, R = –C_6H_4–CO–C_6H_4–CN) on a mercury pool electrode in the presence of 2,3,4-tri-*O*-acetyl-5-thio-α-D-xylopyranosyl bromide (**1**) using a zinc anode yields, in contrast to the foregoing results, a mixture of the corresponding isomers **6**[1,22–24] (reaction 15).



(15)

We examined the electroreduction of the disulfide RSSR (**5**) in the presence of **1** using a sacrificial anode. All results concerning the 2,3,4-tri-*O*-acetyl-5-thio-α-D-xylopyranosyl bromide (**1**) are listed in Table 1.

Several interesting conclusions may be formulated:

- Only the zinc anode gave compound **6** in appreciable yield. With other metals, such as magnesium, cadmium, aluminium, and tin, no coupling product was obtained (entries 2, 21, 22, 23 and 24). With these anodes, thiolate–metal complexes are not likely to be obtained.
- At the same temperature, no influence of the cathode composition (Hg or C) is observed (entries 2 and 19 at 25 °C, 3 and 20 at 40 °C).
- From THF to MeCN at 40 °C the yield decreases (from 60 to 55%) and the selectivity increases in favour of formation of the anomer α (α/β = 47/53 in THF and 60/40 in MeCN, entries 3 and 15). At room temperature the same observations about the yield can be formulated but the ratios of isomers is not modified (entries 2 and 5). In Me_2SO, 1,4-dioxane, and dichloromethane no reaction occurs (entries 6, 7, and 8). In EtCN, at room temperature, the yield is not modified but the selectivity decreases (entries 2 and 4). In the solvent mixture 1:1 THF–MeCN, the selectivity in favour of isomer α is the highest but the yield decreases drastically (entry 9).
- In MeCN, from −40 to 25 °C, the yield and the α/β ratio increase simultaneously, but at 40 °C the same yield is obtained with an increased α/β ratio (entries 1, 2, and 3).
- In THF, the best yield is obtained at low temperature (63% at 0 °C with an α/β ratio of 67/33, 52% at 25 °C, and 55% and 40 °C). The α/β ratio decreases when the temperature increases (entries 5, 14, and 15).
- In MeCN, at room temperature, several electrolyte salts have been tested. In the presence of a lithium salt ($LiBF_4$ and $LiClO_4$), the yields are lower than those obtained in the presence of the quaternary ammonium salt (entries 2, 11, 12, and 13). In MeCN–$LiBF_4$ solution, a 50/50 α/β ratio is obtained. Using Bu_4NBr as electrolyte salt, the reaction does not occur, probably due to oxidation of bromine ion at the metallic anode.

Under constant current conditions, low increases of the α/β ratio are observed compared to electrolysis performed at constant potential (entries 2 and 17 at room temperature and entries 3 and 18 at 40 °C).

Table 1
Electrolysis of the disulfide RSSR (R = -C_6H_4-CO-C_6H_4-CN) **5** in the presence of **1** (anomer α) using sacrificial anode.

Entry	Solvent/electrolyte salt	E_w [a] or J [b]	T (°C)	RSSR (mol/mol)	Electrode anode/cathode	Yield [c] of **6**	Ratio α/β
1	MeCN–Bu_4NPF_6	−1	−40	1.87	Zn/Hg	40	35/65
2	MeCN–Bu_4NPF_6	−1	25	2.3	Zn/Hg	61	55/45
3	MeCN–Bu_4NPF_6	−1	40	2.2	Zn/Hg	60	60/40
4	EtCN–Bu_4NPF_6	−1	25	2.2	Zn/Hg	60	50/50
5	THF–Bu_4NPF_6	−1.1	25	2.86	Zn/Hg	52	58/32
6	Me_2SO–Bu_4NPF_6	−1.1	25	3	Zn/Hg		
7	1,4-Dioxane–Bu_4NPF_6	−1	25		Zn/Hg		
8	Dichlormethane, CH_2Cl_2–Bu_4NPF_6	−1	25	6	Zn/Hg		
9	THF,MeCN–Bu_4NPF_6	−1.1	25	2.8	Zn/Hg	34	70/30
10	THF, MeCN–$LiBF_4$	−1.1	25	2.2	Zn/Hg	26	67/33
11	THF–Bu_4NBF_4	−1.1	25	2	Zn/Hg	56	68/32
12	MeCN–$LiClO_4$	−1	25	2.1	Zn/Hg	21	65/35
13	MeCN–$LiBF_4$	−1	25	2.5	Zn/Hg	47	50/50
14	THF–Bu_4NPF_6	−1.1	0	2.86	Zn/Hg	63	67/33
15	THF–Bu_4NPF_6	−1.1	40	2.9	Zn/Hg	55	47/53
16	MeCN–Bu_4NBr	−1	25	1.5	Zn/Hg		
17	MeCN–Bu_4NPF_6	0.62	25	2.5 [b]	Zn/Hg		60/40 [d]
18	MeCN–Bu_4NPF_6	0.62	40	2.5 [b]	Zn/Hg		64/36 [d]
19	MeCN–Bu_4NPF_6	−1.2	25	1.99	Zn/C	61	55/45
20	MeCN–Bu_4NPF_6	−1.2	40	2.5	Zn/C		60/40 [d]
21	MeCN–Bu_4NPF_6	−1	25	1.86	Mg/Hg		
22	MeCN–Bu_4NPF_6	−1	25	2.3	Cd/Hg		
23	MeCN–Bu_4NPF_6	−1	25	3	Sn/Hg		
24	MeCN–Bu_4NPF_6	−1	45	2.1	Al/Hg		

[a] Working potential vs. SCE.
[b] Electrolysis performed at constant current J (A m^{-2}).
[c] Determined after chromatography purification.
[d] Determined by NMR spectroscopy without chromatographic purification.

The results from electrolysis of **5** in the presence of **1** (anomer β) using a sacrificial zinc anode are listed in Table 2.

It is noteworthy that in all cases the β anomer is formed preferentially and the α/β ratio depends slightly on experimental conditions (temperature, electrolysis conditions, nature of the cathode and the solvent).

Similar experimental conditions as just described were followed for the reduction of **5** in the presence of 2,3,4-tri-*O*-acetyl-5-thio-D-xylopyranosyl chloride (**7**) comprising an α/β mixture in the ratio of 95/5. The results are indicated in Table 3.

In all cases, the [4-(4′-cyanobenzoylphenyl)] 2,3,4-tri-*O*-acetyl-1,5-dithio-β-xylopyranoside isomer was

Table 2
Electrolysis with 0.1 mol Bu_4NPF_6 of RSSR (**5**, R = –C_6H_4–CO–C_6H_4–CN) in the presence of **1** (β anomer); molar ratio **1/3** = 0.5 using zinc anode

Entry	Solvent	E_w [a] or J [b]	T (°C)	RSSR (mol/mol)	Electrode cathode	Yield [c] of **6**	Ratio α/β
1	CH_3CN	−1 [a]	−40	2.4	Hg	70	10/90
2	CH_3CN	5 [b]	−40	2.3	Hg		10/90 [d]
3	CH_3CN	−1 [a]	25	2.5	Hg		10/90 [d]
4	CH_3CN	4 [b]	25	2.5	Hg		8/92 [d]
5	THF	−0.9 [a]	0	2.1	Hg	68	5/95
6	CH_3CN	−1.3 [a]	25	2.0	C	70	8/92

[a] Working potential vs. SCE.
[b] Current constant J (A m^{-2}).
[c] Determined after chromatography purification.
[d] Determined by NMR spectroscopy without chromatographic purification.

Table 3
Electrolysis with 0.1 mol Bu_4NPF_6 of RSSR (**5**, R = $-C_6H_4-CO-C_6H_4-CN$) in the presence of **7** (95:5 α,β mixture); molar ratio **1**/**5** = 0.5 using zinc anode and mercury pool cathode

Entry	Solvent	E_w [a]	T (°C)	RSSR (mol/mol)	Yield [b] of **6**	Ratio α/β
1	CH_3CN	−1	25	2.4	45	45/55
2	CH_3CN	−1	40	2.3	58	41/59
3 [c]	CH_3CN	−1.1	40	2.5	67	47/53
4	THF	−1.2	0	2.5	41	34/66

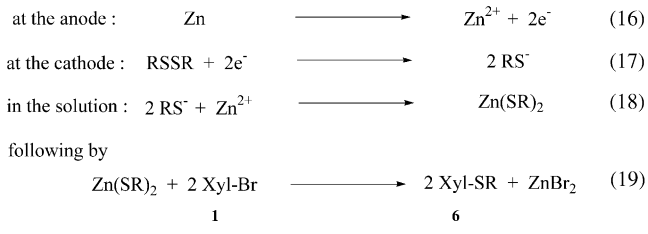
[a] Working potential vs. SCE.
[b] Determined after chromatographic purification.
[c] In the presence of excess of RS^- (3.2 molar equivalents).

formed to a greater extent and the best yield was obtained in MeCN at 40 °C (entries 3). When the yield increases, the α/β ratio also increases, except for entry 3.

2.4. Hypotheses on the glycosylation mechanism in the case of the sacrificial anode

The formation of a thioglycoside by electrochemical synthesis in the presence of a sacrificial zinc anode can be rationalised by Scheme 4.

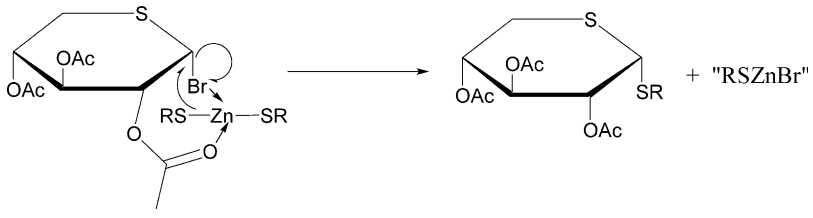
Thiolate anion RS^- (**5′**) generated at the cathode (reaction 17) reacts with the cation Zn^{2+} formed by dissolution of the anode (reaction 16) to give the $Zn(SR)_2$ derivative (reaction 18). The formation of this product is in accordance with the following result. RS^- is electrogenerated by two-electron reduction of RSSR in a divided cell in MeCN–Bu_4NPF_6 solution. This anion is oxidized at the potential of peak A_1' (see Fig. 1). The addition of nearly one mole equivalent (versus RSSR) of the cation Zn^{2+} ($ZnBr_2$ in MeCN) immediately causes the disappearance of the peak A_1'. A similar mechanism has been proposed for the formation of the $Zn(SPh)_2$ complex.[25–27] Then, the cation reacts with **1** to give **6** (reaction 19). Metal–thiolate complexes have attracted interest owing to their biological relevance and the diversity of their structures.[28–30] Recently, the first structural characterisation of a two-coordinate monomeric zinc thiolate $Zn(S\text{-}C_6H_3\text{-}2,6\text{-}SMe)_2$ has been described in which significant deviation from a linear S–Zn–S structure is observed.[31]



Scheme 4.

In thiolate zinc complexes, the divalent zinc ion is very stable and it does not participate in the redox reaction. The d^{10} configuration indicates that zinc complexes are not subject to ligand field stabilisation effects and so coordination number and geometry are only dictated by ligand size and charge. Zinc often shows a strong preference for tetrahedral coordination,[32] which enhances both the Lewis acidity of zinc centre and the nucleophilic properties of the RS groups. In our experimental conditions, the thiolate–zinc complex is probably coordinated with the solvent molecule (MeCN or THF). In 1,4-dioxane, dichoromethane, and dimethyl sulfoxide, formation of thiolate–zinc complex is probably not favored.

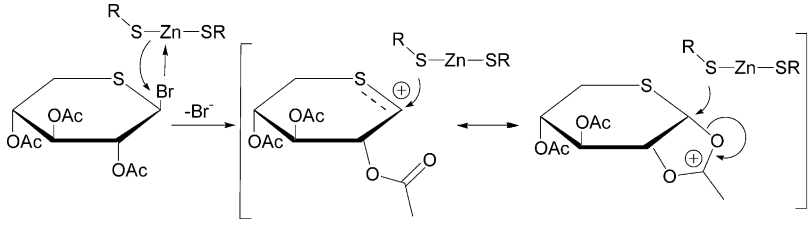
The stereoselectivity observed in the S-glycosylation reaction starting from the 5-thio-α-D-xylopyranosyl bromide [formation of **6** (α anomer) to a greater extent in all cases except entries 1, 4, 15, see Table 1) cannot be explained by the formation of a cation as described in Scheme 3; on the contrary, the formation of a tetracoordinated thiolate–zinc complex as indicated in reaction 20 is more probable. Indeed, an interaction between the metallic atom, the acetyl group, and the bromine atom of the donor may be postulated in the case of the α anomer and this tetra-coordination should increase the nucleophilicity of the RS^- group. Subsequent S_N2-like



(20)

attack of the RS^- group of the thiolate–zinc complex at the anomeric carbon forms the expected glycosidic linkage.

Starting with the 5-thio-β-D-xylopyranosyl bromide, the formation of a tetra-coordination thiolate–zinc complex is not possible and direct activation of the bromide anomeric substituent by the $Zn(SR)_2$ complex occurs. This leads to dissociation with the concomitant formation of an ion-paired, thiocarbenium ion, like I or II (see Scheme 3) with possible participation of the neighbouring acetate group, giving a bridging cation as described in reaction 21. The latter cation, under the influence of the thiolate–zinc complex, yields the β-thioglycoside.



(21)

Donors bearing acyl groups at O-2 ensure β-selectivity in the glycosylation reaction by neighbouring-group participation.[33,34] Recently, density functional methods showed that the precursor cations resulting from neighbouring-group assistance from the 2-acetyl group were found to be the most stable.[35] These authors suggested that side reactions, such as acyl transfer are kinetic products, whereas the desired β-glycoside is the thermodynamic products.

Starting from the acetylated 5-thio-α-D-xylopyranosyl chloride (**7**), formation of the tetra-coordinated thiolate–zinc complex seems to be unfavorable, and so the α anomer of compound **4** is obtained in low yield.

3. Experimental

3.1. Materials and reagents

The disulfide derivative RSSR (**5**, R = $-C_6H_4-CO-C_6H_4-CN$) and 2,3,4-tri-*O*-acetyl-5-thio-D-xylopyranosyl bromide (**1**) were prepared according to literature procedures.[36] Diphenyl disulfide (**3**) and the metallic anode (Goodfellow) were commercial products. THF was distilled under argon from sodium and benzophenone. Acetonitrile (MeCN) was purified by passing the solvent through a column packed with alumina previously dried at 120 °C or was distilled from CaH_2. The supporting electrolytes were 0.2 or 0.1 M (case of a undivided cell using sacrificial metallic anode) Bu_4NPF_6, which was dried and degassed before use.

3.2. Apparatus and general procedures

All experiments were carried out under an Ar atmosphere using standard Schlenck techniques. In voltammetry, the working electrode was a vitreous carbon disc (diameter 1.2 mm) and, for electrolyses a mercury pool or carbon gauze electrode. In all cases, the reference electrode was a saturated calomel electrode (SCE) separated from the solution by a sintered-glass disc. All reagents in solution were added by a syringe previously purged with argon in the cell. The cyclic voltammetry experiments were conducted with a Tacussel PJT 24-1 potentiostat. The electrolyses were carried out with a Amel 552 potentiostat equipped with a Tacussel IG5 integrator.

The ^1H and ^{13}C NMR were performed on a WM 200 or 300 Bruker NMR spectrometer at the CSMUB (Centre de Spectrometrie Moléculaire de l'Université de Bourgogne). The chemical shifts (δ) are given in ppm (downfield from Me_4Si) and the coupling constants (J) in hertz. The multiplicity is as follows: s, singlet; d, doublet; t, triplet. Mass spectra were taken on Kratos Concepts spectrometer. IR measurements were performed on a Nicolet 205 spectrophotometer. Silica gel Merck (280–400 mesh) was used for flash column chromatography and silica gel Merck BOF_{254} for thin-layer chromatography.

The undivided cell was loaded with dry MeCN (20 mL), Bu_4NPF_6 (1.6 g), RSSR and the 5-thioxylopyranosyl halide under N_2. The two electrodes consist of a carbon gauze cathode (or mercury pool) and a zinc ring anode. The electrolysis was performed at a constant potential at the potential of peak A. The reaction was stirred for about 15 h (until the total reaction of **1**). The solution was concentrated and EtOAc added. The supporting electrolyte was precipitated with Et_2O. The mixture was filtered and the organic phase evaporated.

The thioxylopyranoside formed was isolated by chromatography on a silica gel column (9:1 v/v toluene/EtOAc).

3.2.1. [4(4′-Cyanobenzophenone)] 2,3,4-tri-*O*-acetyl-1,5-dithioxylopyranoside (6). The undivided cell was loaded with dry MeCN (20 mL), Bu_4NPF_6 (1.6 g), RSSR (**5**, R = –C_6H_4–CO–C_6H_4–CN) (100 mg, 0.21 mmol), **1** (142 mg, 0.4 mmol) under N_2 to afford a white solid, yield 61%.

The spectroscopic data were consistent with the literature.[37]

3.3. Phenyl 2,3,4-tri-*O*-acetyl-1,5-dithioxylopyranoside (4)

The cell was loaded with dry MeCN (20 mL), Bu_4NPF_6 (1.6 g), PhSSPh (**3**) (251 mg, 1.15 mmol) under N_2. The electrolysis was performed at −1.8 V (versus SCE) corresponding to an initial current of 10 mA. To this solution was added compound **1** (700 mg, 2 mmol). Compound **4** was isolated by chromatography on a silica gel column (9:1 v/v toluene–EtOAc). Evaporation of the solvent yielded **4** as a white solid, yield 30%.

The spectroscopic data were consistent with literature values.[38]

3.3.1. 3,4-Di-*O*-acetyl-1,5-anhydro-5-thio-D-*threo*-pent-1-enitol (2). The divided cell was loaded with dry MeCN (20 mL), Bu_4NPF_6 (1.6 g), and the bromide **1** (500 mg, 1.41 mmol) under N_2. The electrolysis on a mercury pool electrode and carbon as counter electrode was performed at room temperature at a constant potential of −1.9 V (versus SCE). The solution became brown and after having consumed 1.98 F themselves obtained compound **2** (yield: 76%).

The spectroscopic data were consistent with the literature values.[39]

Acknowledgements

One of us (D.B.) gratefully thanks the Conseil Régional de Bourgogne and Laboratoires Fournier 'S.A.' for a three-year grant. This research was supported by The Conseil Régional de Bourgogne and the Laboratoires Fournier (contrat d'Etudes no. 01/5162/54/00023). We are grateful to M.T. Compain for her technical assistance.

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