O-Glycosidation of Telluroglycoside by Electrochemical Oxidation

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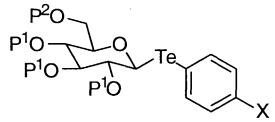
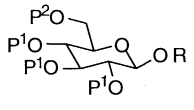
The electrochemical oxidation of telluroglycosides in the presence of primary or secondary alcohols results the *O*-glycosidation with high efficiency. Difference of the oxidation potential is nicely accounted for that of the reactivity of armed- and disarmed-telluroglycosides.

Intensive efforts have been recently directed toward the chemical synthesis of oligosaccharides because of their numerous and diverse biological functions.[1] To this end, a variety of new glycosyl donors have been developed to increase the efficiency of the glycosidation reaction.[2, 3] Among the various glycosyl donors, thio- and selenoglycosides constitute an important class of donors which can be activated under certain conditions.[4] The versatility of these chalcogeno-glycosides prompted us to investigate the glycosidation reaction of telluroglycosides. While the *C*-glycosidation of telluro-glycosides by means of radical reaction has only been reported once in the literature,[5] there has been no report on the *O*-glycosidation, and their potential remains unknown. We found that telluroglycosides **1**, which are readily prepared from sodium aryltelluride and the corresponding bromoglycosides,[6] are easily activated under oxidative conditions and serve as excellent glycosyl donors. Particularly noteworthy is that **1** is activated by electrochemical oxidation[7] which proceeds under neutral conditions and does not use expensive, explosive, or harmful heavy metal chemicals. Thus, the electrolysis of **1** in the presence of suitable glycosyl acceptors affects the first *O*-glycosidation of the telluroglycosides.



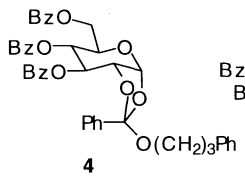
1

a: X = Me, $P^1 = P^2$ = Bz
b: X = H, $P^1 = P^2$ = Bz
c: X = OMe, $P^1 = P^2$ = Bz
d: X = NMe_2, $P^1 = P^2$ = Bz
e: X = Me, $P^1 = P^2$ = Ac
f: X = Me, P^1 = Bn, P^2 = Ac



3

a: $P^1 = P^2$ = Bz, R = $(CH_2)_3Ph$
b: P^1 = Bn, P^2 = Ac, R = $(CH_2)_3Ph$
c: P^1 = Bn, P^2 = Ac, R = C_6H_{11}
d: $P^1 = P^2$ = Ac, R = H
f: P^1 = Bn, P^2 = Ac, R = H



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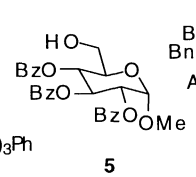

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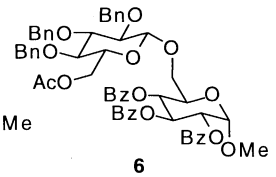

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Electrochemical oxidation was found to be effective for the activation of the telluroglycosides. Thus, the glycosidation of **1a** (Eox = 0.90V *vs.* Ag/AgCl)[8] was carried out using constant potential electrolysis (1.1 V vs. S.C.E.) in the presence of 3-phenyl-1-propanol (**2**, 1.0 equiv) in a 0.1 M $LiClO_4$ solution of MeCN in a divided cell using a carbon fiber anode and a Pt foil cathode. After **1a** disappeared on TLC (3.18 F/mol), the *O*-glycoside **3a** and the orthoester **4** were isolated in 76% and 16% yield, respectively, together with an 85% amount of di-*p*-methylphenyl ditelluride. Structure of **4** was finally confirmed by the ^{13}C NMR, in which the orthoester carbon signal appeared at 121.41 ppm and the three ester carbon signals at 164.74, 165.31 and 166.12 ppm. Careful ^1H NMR and HPLC analyses of the crude mixture revealed the selective formation of the β-anomer (>95% selectivity). The observed β-selectivity as well as the formation of **4** consisted with a neighboring group participation of the 2-acyl protective group. Since **4** was converted to **3a** in 91% yield with high β-selectivity (>95%) by treatment of Me_3SiOTf (1.0 equiv, r.t., 10 min),[9] the overall yield of **3a** from **1a** was 90% (Table 1, entry 1). The stereoselectivity was found to be insensitive to the electrolyte, e.g., Bu_4NClO_4 and Bu_4NBF_4, and the solvent, e.g., EtCN, $EtNO_2$, and CH_2Cl_2. As the reaction proceeded fastest in MeCN, it was used for the following reaction. In all cases, excess electricity (2.5-3.5 F/mol) was required to complete the reaction.

Table 1. Electrochemical glycosidation of telluroglycosides

entry	donor[a]	Eox[b]	acceptor[c]	major product	electrolyte/ solvent[d]	%yield[e]	α:β[f]
1	**1a**	0.90	**2**	**3a**	**A**	76 (90)[g]	5:>95
					B	53 (59)[g]	5:>95
2	**1b**	0.94	**2**	**3a**	**A**	18 (46)[h]	5:>95
					B	50	5:>95
3	**1c**	0.86	**2**	**3a**	**B**	65	5:>95
4	**1d**	0.62	**2**	**3a**	**A**	18 (56)[h]	5:>95
5	**1e**	0.92	**2**	**3d**	**B**	<15	n.d.[i]
6	**1f**	0.82	**2**	**3b**	**B**	70	24:76
7	**1f**		**5**	**6**	**A**	63	29:71
8	**1f**		**7**	**3c**	**A**	68	20:80

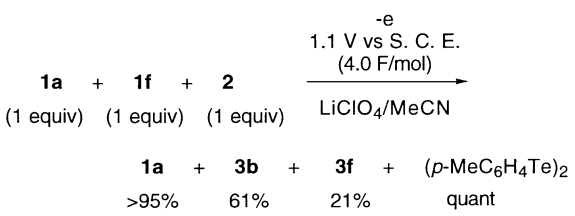
[a]Single β-anomer (>95%) was used, except for **1f** which consisted of a 70:30 mixture of the α and β-anomers. [b]V *vs.* Ag/AgCl. See ref. 8. [c]One equivalent of acceptor was used. [d]**A**: $LiClO_4$/MeCN, **B**: Bu_4NBF_4/MeCN. [e]Isolated yield, except in entry 5 where the yield was determined by ^1H NMR using an internal standard. [f]Determined by ^1H NMR and/or HPLC. [g]Total yield after convertion of **4** to **3a**. [h]Yield based on the reacted telluroglycoside. [i]Not determined.

The efficiency and stereoselectivity of the glycosidation was found to be strongly affected by the para-substituent of the aryltelluro group and the protecting group of the glycosides. The electrolysis of phenyl telluroglycoside **1b** (Eox = 0.94 V *vs.* Ag/AgCl) and *p*-methoxyphenyl telluroglycoside **1c** (Eox = 0.86 V *vs.* Ag/AgCl) afforded **3a** in moderate yield, while that of *p*-dimethylaminophenyl telluroglycoside **1d** (Eox = 0.62 V *vs.* Ag/AgCl) resulted in poor yield (entries 2-4)[10]. Although the electrolysis of acetyl protected telluroglycoside **1e** yielded the 1-hydroxyglycoside **3d** as a major product, that of the benzyl protected telluroglycoside **1f** afforded **3b** in 70% yield as a

24:76 mixture of the α- and β-anomers (entries 5 and 6).

Various glycosyl acceptors, which possessed the sterically demanding hydroxyl group, took part in the glycosidation reaction. It is worth noting that the reaction proceeded efficiently with a stoichiometric amount of glycosyl acceptors (entries 7and 8). Thus, the reaction of **1f** with **5** afforded the corresponding disaccharide **6** in good yield (entry 7). Cyclohexanol (**7**) also participated in the glycosidation reaction to give **3c** (entry 8).

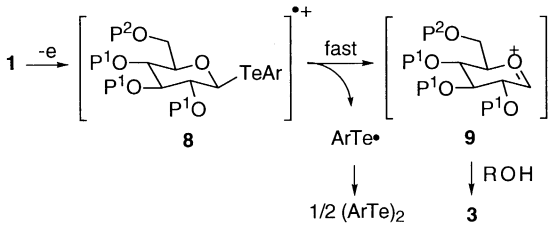
We next examined chemoselective activation of the telluroglycoside based on armed- and disarmed-glycosidation strategy in which C-2 ether protected glycoside reacted faster than C-2 acyl protected glycoside.[11] It is particularly interesting that the 2-benzyl protected glycoside **1f** has lower oxidation potential than that of the 2-benzoyl protected **1a**. Indeed, intermolecular competition of **1a** and **1f** in the presence of one equivalent of **2** at room temperature revealed that all *O*-glycosidation product came from **1f** and that **1a** was recovered quantitatively (Scheme 1).[12] The difference of the oxidation potential of **1f** and **1a** (ΔEox = 0.08 V) corresponds to that of the Gibbs energy of ΔG = 1.84 kcal/mol. This energy difference nicely accounts for the experimental result. While the origin of the energy differences waits further studies, this result would offer the use of oxidation potential for the rational design of the chemoselective glycosidation based on the qualitative analyses of glycoside reactivities.



Scheme 1.

Electrochemical analyses of **1** revealed that the radical cation intermediate had a very short life time. The cyclic voltammetry of **1a** in a 0.1 M $LiClO_4$ solution of MeCN at room temperature showed an irreversible single electron oxidation wave at 0.90 V (*vs.* Ag/AgCl). We could not observe the corresponding reverse reduction wave at a scan speed from 100 mV/sec to 1000 mV/sec, indicating that the lifetime of the radical cation intermediate is very short. Osteryoung square-wave voltammetry[13] at a frequency of 500 Hz also showed an irreversible oxidation wave. These results clearly indicated that the radical cation **8** generated by the single electron oxidation of **1** had a lifetime of less than 2 x 10^{-3} sec, and that **8** spontaneously dissociates to the aryltelluro radical and the oxocarbenium ion **9**. The former dimerizes to a ditelluride and the latter reacts with an alcohol to give **3** (Scheme 2).

In summary, we have demonstrated that easily available telluroglycosides serve as reactive glycosyl donors under neutral conditions. Especially, the mildness of the present reaction



Scheme 2.

conditions would be useful for the selective activation of a telluroglycoside over other chalcogeno-[7b, 7c] and acid labile glycosides. Such chemoselective glycosidations[3] are now under active investigation in this laboratory.

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8 Oxidation potential was measured in 0.1 M MeCN solution of $LiClO_4$ at room temperature using Osteryoung square wave voltammetry, which was recorded on a BAS-100B/W electrochemical analyzer. IR compensation was employed throughout.

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10 Current efficiency of the glycosidation of **1d** was very low, and 68% of **1d** was recovered even after passing 3F/mol electricity.

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12 Partial anomeric epimerization was observed for **1a**. The recovered **1a** consisted of a 20:80 mixture of α- and β-anomers, while the starting material was pure β-anomer.

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