

O-Glycosidation of Telluroglycoside by Electrochemical Oxidation

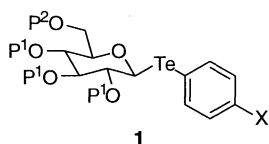
Shigeru Yamago,* Koji Kokubo, and Jun-ichi Yoshida*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering,
Kyoto University, Sakyo-ku, Kyoto 606-01

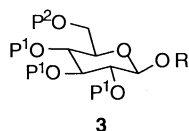
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The electrochemical oxidation of telluroglycosides in the presence of primary or secondary alcohols results the *O*-glycosidation with high efficiency. Difference of the oxidation potential is nicely accounted for that of the reactivity of armed- and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

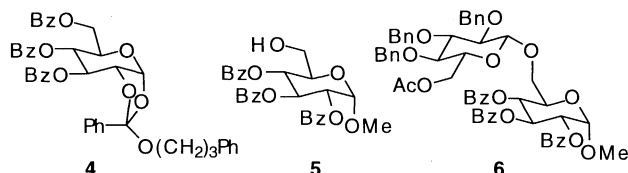
Intensive efforts have been recently directed toward the chemical synthesis of oligosaccharides because of their numerous and diverse biological functions.¹ To this end, a variety of new glycosyl donors have been developed to increase the efficiency of the glycosidation reaction.^{2, 3} Among the various glycosyl donors, thio- and selenoglycosides constitute an important class of donors which can be activated under certain conditions.⁴ The versatility of these chalcogenoglycosides prompted us to investigate the glycosidation reaction of telluroglycosides. While the *C*-glycosidation of telluroglycosides 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 oxidation⁷ 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.



- a:** X = Me, P¹ = P² = Bz
b: X = H, P¹ = P² = Bz
c: X = OMe, P¹ = P² = Bz
d: X = NMe₂, P¹ = P² = Bz
e: X = Me, P¹ = P² = Ac
f: X = Me, P¹ = Bn, P² = Ac



- a:** P¹ = P² = Bz, R = (CH₂)₃Ph
b: P¹ = Bn, P² = Ac, R = (CH₂)₃Ph
c: P¹ = Bn, P² = Ac, R = C₆H₁₁
d: P¹ = P² = Ac, R = H
f: P¹ = Bn, P² = Ac, R = H



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

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

^aSingle β-anomer (>95%) was used, except for **1f** which consisted of a 70:30 mixture of the α and β-anomers. ^bV vs. Ag/AgCl. See ref. 8. ^cOne equivalent of acceptor was used. ^d**A:** LiClO₄/MeCN, **B:** Bu₄NBF₄/MeCN. ^eIsolated yield, except in entry 5 where the yield was determined by ¹H NMR using an internal standard. ^fDetermined by ¹H NMR and/or HPLC. ^gTotal yield after conversion of **4** to **3a**. ^hYield based on the reacted telluroglycoside. ⁱNot determined.

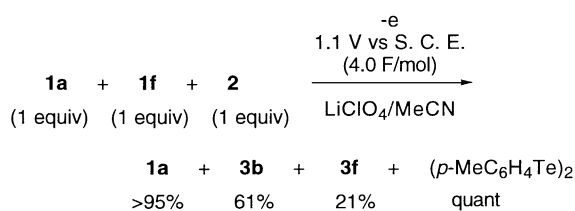
of 3-phenyl-1-propanol (**2**, 1.0 equiv) in a 0.1 M LiClO₄ solution of MeCN in a divided cell using a carbon fiber anode and a Pt foil cathode. After **1a** disappeared on TLC (3.18 F/mol), the *O*-glycoside **3a** and the orthoester **4** were isolated in 76% and 16% yield, respectively, together with an 85% amount of di-*p*-methylphenyl ditelluride. Structure of **4** was finally confirmed by the ¹³C 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 Me₃SiOTf (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., Bu₄NClO₄ and Bu₄NBF₄, and the solvent, e.g., EtCN, EtNO₂, and CH₂Cl₂. 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.

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 7 and 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).

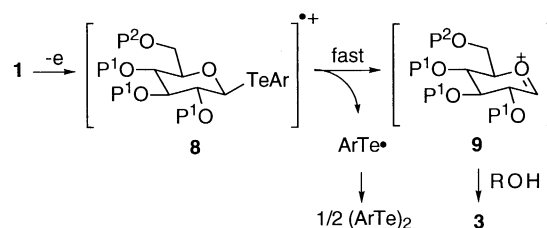
We next examined chemoselective activation of the telluroglycoside based on armed- and disarmed-glycosidation strategy in which C-2 ether protected glycoside reacted faster than C-2 acyl protected glycoside.¹¹ It is particularly interesting that the 2-benzyl protected glycoside **1f** has lower oxidation 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** ($\Delta E_{\text{ox}} = 0.08$ V) corresponds to that of the Gibbs energy of $\Delta G = 1.84$ 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 LiClO₄ 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 voltammetry¹³ 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 2×10^{-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 glycosidations³ are now under active investigation in this laboratory.

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- Oxidation potential was measured in 0.1 M MeCN solution of LiClO₄ 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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- 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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- 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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