（様式２）

学 位 論 文 の 概 要 及 び 要 旨

氏　　名　渋谷章人　印

題　　目　Electrochemical Generation of Glycosyl Dioxalenium Ions and Their Application to the Synthesis of Cyclic β-glucans　（グリコシルジオキサレニウムイオンの電解発生と環状βグルカン合成への応用）

学位論文の概要及び要旨

General Introduction

Electrochemical transformations, powerful tools in organic synthesis, have recently been used for synthesis of natural products. We have been interested in development of the automated electrochemical synthesizer (Figure 1) and demonstrated a method named ‘automated electrochemical assembly’ (AEA), which is based on electrochemical generation of reactive intermediates. In AEA experiments, glycosyl triflate intermediates, generated by electrochemical oxidation, can be accumulated and the subsequent addition of alcohols afford glycosylation products. In principle, reactive intermediates other than glycosyl triflate can be generated and accumulated by this method.

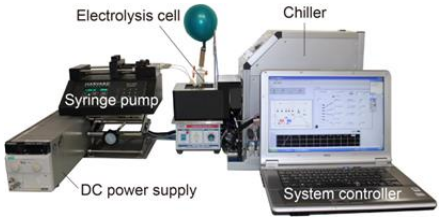


Figure 1.

Cyclic oligosaccharides such as cyclodextrins (CDs) have hydrophilic outer region and hydrophobic inner region. Therefore, they can be used as host molecules that include hydrophobic guest molecules. To date, δ-CD (nonasaccharide) is the largest CD that has been chemically synthesized. Thus, ring sizes and types of glycosidic linkages of synthesized cyclic oligosaccharides are still limited.

We then focused on a natural oligosaccharide shown in Figure 2. This compound is a cyclic dodecasaccharide, isolated from *Bradyrhizobium japonicum* MTCC120, consists of β-(1,3)- and β-(1,6)-glucosidic linkages. Due to its large-sized ring, the compound is expected to be applied to separation of chiral molecules, drug delivery system (DDS) and catalysts. We intended to efficiently synthesize the cyclic β-glucan with the AEA.

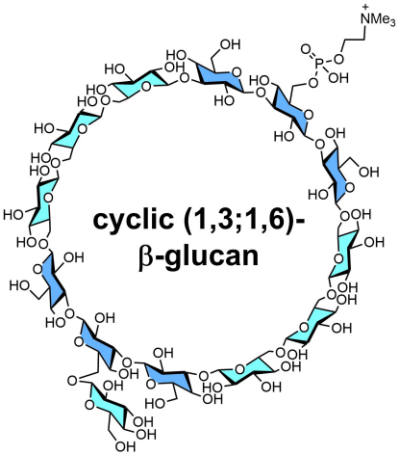


Figure 2.

Chapter 1.

NMR analysis of glycosyl dioxalenium ion intermediates

Stereochemistry is a crucial issue for synthesis of both linear and cyclic oligosaccharides. One of the most reliable methods is using building block equipped with a stereo-controlling group as a protecting group of the hydroxyl group at C-2 position. Activation of the anomeric leaving group affords a glycosyl cation, followed by coordination of the carbonyl oxygen of the acyl group at C-2 position to form a glycosyl dioxalenium ion (Figure 3). Due to steric hindrance of the dioxalenium ion, 1,2-*trans* linkage is selectively formed. Thus, β-glucoside

and α-mannoside can be selectively synthesized by this approach. For efficient synthesis of the above-mentioned cyclic β-(1,3)-β-(1,6)-glucan, it was needed to optimize glycosylation reactions. To begin with, we observed glycosyl dioxalenium ions by VT-NMR measurement (Figure 3). Based on thus-obtained knowledge regarding thermal stability of the dioxalenium ions and influences of protecting groups on them, the reaction conditions were optimized. Under the optimized conditions, β-(1,6)-glucan trisaccharide was successfully synthesized by two cycles of AEA (Table 1).

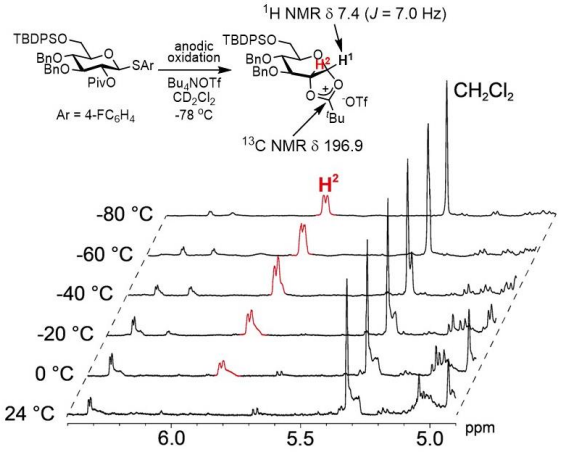
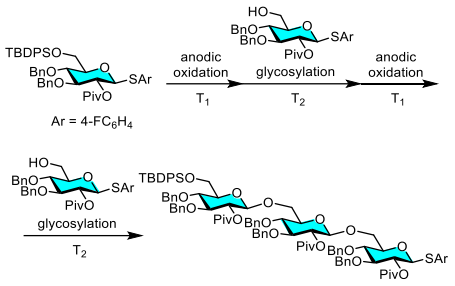


Figure 3

Table 1.



entry	T_1 (°C)	T_2 (°C)	yield	selectivity (α:β)
1	-80	-50	29%	β only
2	-40	-40	46%	β only

Chapter 2

Electrochemical synthesis of cyclic β-(1,3)-β-(1,6)-glucan dodecasaccharides

We set compound **A**, which is a protected analog of the cyclic moiety of the natural product shown in Figure 2, as our target molecule (Figure 4). The compound consists of two types of trisaccharides, which have three β-(1,3)-linkages and three β-(1,6)-linkages, respectively. Therefore, we planned to synthesize the cyclic dodecasaccharide by dimerization and following cyclization of linear hexasaccharide precursors.

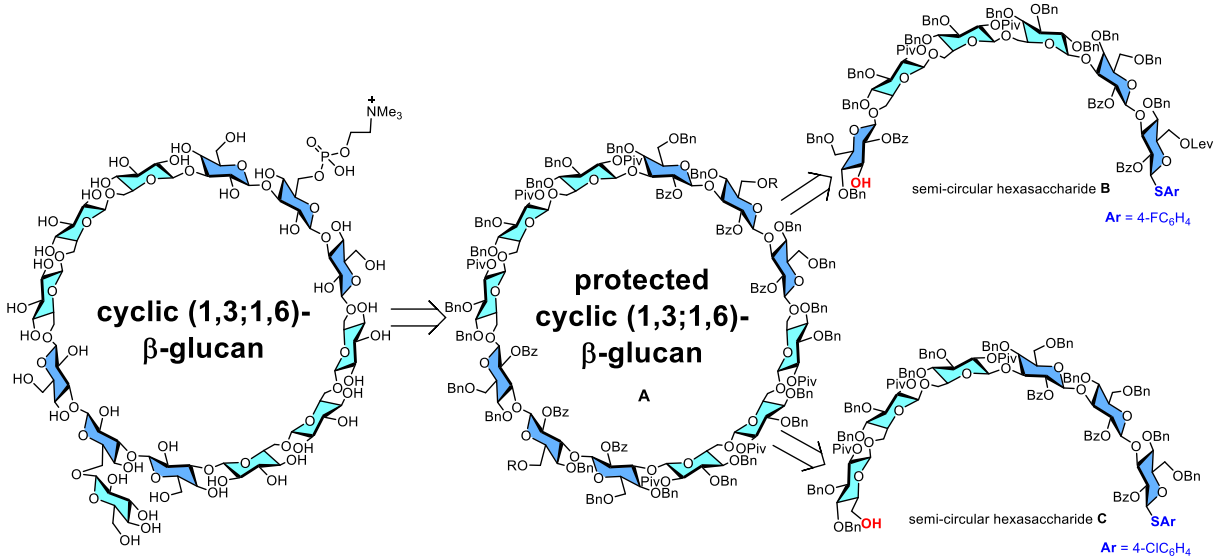


Figure 4.

Optimization of electrolytes of AEA led to efficient formation of not only β-(1,6)-linkages but also β-(1,3)-linkages. Thus, linear hexasaccharide precursor **C** was synthesized by AEA (Figure 5). Under the electrochemical oxidation condition, precursor **C** was dimerized and cyclized to afford cyclic dodecasaccharide **A** in 3% yield (Figure 6). Because the corresponding cyclic hexasaccharide was obtained as the major product,

however, a stepwise process was expected to improve the yield. Glycosylation of hexasaccharide **C** and its protected analog **C'** proceeded in 51% yield and the following TBDPS-deprotection proceeded in 87% yield. Finally, cyclized product **B** was obtained in 23% yield. The total yield in 3 steps was 10%. Although the yield was higher than that of the one-pot process, there is still room for improvement.

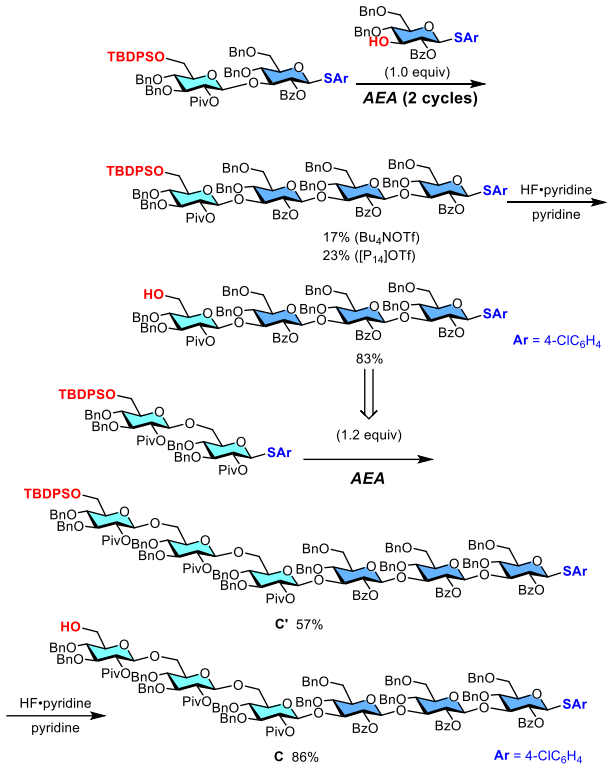


Figure 5.

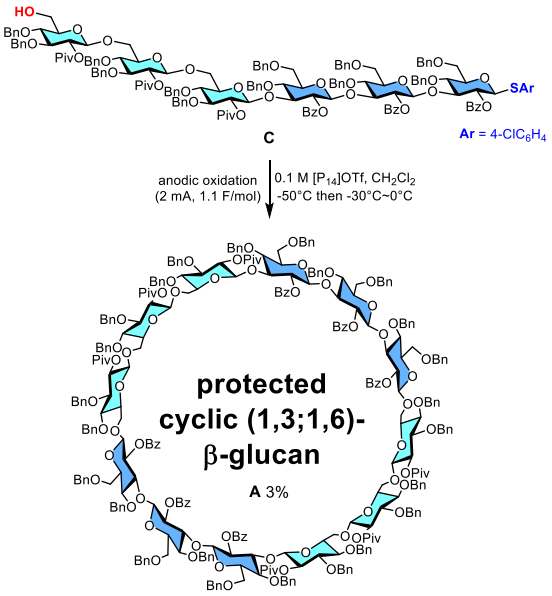


Figure 6.

Chapter 3

Towards rational design of oligosaccharide building blocks of cyclic β-glucans

The linear hexasaccharide which has a β-(1,6)-linkage in the reducing end can be synthesized by AEA one-pot process with two types of monosaccharide and disaccharide building blocks (Figure 7). Contrary to our expectation, under the dimerization-cyclization reaction condition in Figure 6, neither the cyclic dodecasaccharide nor the linear dodecasaccharide was obtained. Therefore, the structures of the reducing ends are supposed to be a key factor for reactivity of the hexasaccharide precursors. As the model oligosaccharides, we currently compare reactivity of the disaccharides in the reducing ends. Based on our knowledge, we consider that reactivity of an oligosaccharide decreases when a hydroxyl group at C-6 position of its reducing end monosaccharide connects to an adjacent monosaccharide.

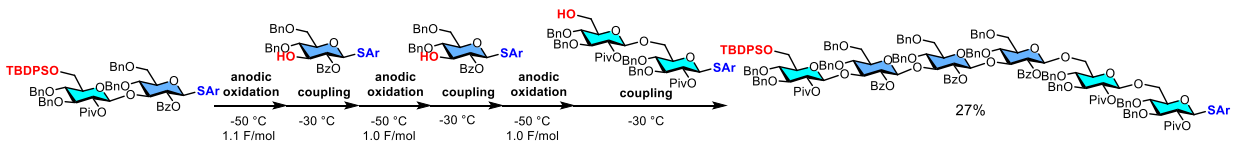


Figure 7.