Halogenated sucrose at the primary position: Comprehensive structure elucidation and reactivity study
(スクロース１級水酸基のハロゲン化：網羅的構造検討と反応性検討)

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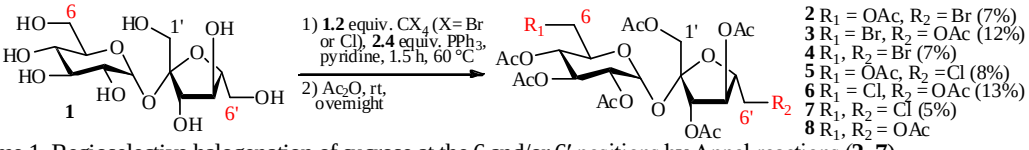
1. Introduction

Regioselective halogenation of sucrose's primary alcohols (at 6-, 6′- or 1′-position) is one of the prior approaches to simplicity synthesis of carbohydrate-based products. Appel reaction—by the used of carbon tetrahalide and triphenylphosphine—is one of the efficient methods to directly convert primary hydroxyl groups to halide. The former subjection of sucrose within limited proportion of Appel reagents gave obscure results between the selectivity of 6- and 6′-alcohols. For decades, halodeoxysucrose derivatives at the primary position have been successfully synthesized. But, the detail reported analyses, especially NMR characterization, have not been completely established. Therefore, the focus of this study is to re-subject sucrose into Appel reaction to archive regioselective halogenations and then fully construct structural elucidation of each compound to indentify sucrose reactivity of this reaction.

2. Methods

Re-subjection of sucrose into Appel reaction was conducted using 1.2 equiv. carbon tetrahalide (bromide or chloride) and 2.4 equiv. triphenylphosphine, which followed by acetylation (Scheme 1). All compounds were assigned by analysis of one- (^{1}H and ^{13}C) and two-dimensional (COSY, HETCOR, HMQC, HMBC, and NOESY) NMR spectroscopy, optical rotation, and mass spectroscopy. Comparison with the literature data for all compounds also described to support the comprehensive structural elucidation.



Scheme 1. Regioselective halogenation of sucrose at the 6 and/or 6′ positions by Appel reactions (**2**–**7**).

3. Results and Discussions

The series of per-*O*-acetylated dihalogenated and monohalogenated at 6- and/or 6′-position (**2**–**7**; Scheme 1) were obtained. The specific splitting pattern in the upfiled region of ^{1}H NMR (Fig. 1), differentiate the substitution site of each compound. The 1′-monohalogenated sucrose was then exclusively synthesized via regioselective chemoenzymatic deacetylation. Thus, allowing the extensive NMR analyses of all monohalogenated sucrose at the primary positions. Further subjection of Appel reaction to 1′-kestose, differs only by the linkage from the second D-fructosyl group to the sucrose, supports the identification of the most hindered and less reactive position through Appel reaction. However, the regioselective Appel reaction of sucrose's primary alcohols followed the halogenation order of 6>6′>>1′.

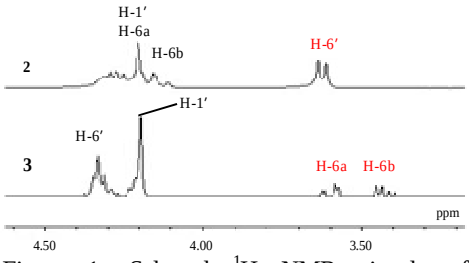


Figure 1. Selected ^{1}H NMR signals of monobrominated sucrose derivatives at 6- and 6′-position (**2** and **3**).

4. Conclusions

Based on comprehensive NMR analyses, previous misinterpreted assignment (*Eur. J. Org. Chem.* **2007**, 3655–3668.) of 6′-bromo-6′-deoxysucrose heptaacetate (**2**) was then revised to 6-bromo-6-deoxysucrose heptaacetate (**3**). The complete structural elucidation of each monohalogenated sucrose at the primary position identified sucrose reactivity by limited proportion of Appel reagents followed the order of 6>6′>>1′.

ref.) Z. P. Tachrim, et al., *ChemistrySelect*, **2016**, *1*, 58–62.