Single-Crystal X-Ray Structural Analysis and Electronic Structures Calculation of Rare Sugar

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Abstract. There are two types of mono-saccharide sugars in nature, which are natural monosaccharide and rare sugar. The sugar that exists in extreme few amount in nature is called as rare sugar e.g. D-psicose and D-allose. The reasons we choose the rare sugar as a research target are because the rare sugar has almost no calories and is very useful for diabetic and dieter patients. Specifically, D-psicose is a no-calorie rare sugar with the sweetness of about 70 % of a sucrose. It has been confirmed that taking the D-psicose with meals suppresses the rise of sugar into the blood. Further, it is very effective in improving and preventing the diabetes. In order to investigate a research on the rare sugars, the first step must be to obtain the correct molecular structure. However, few crystal structures of rare sugars have been reported up to now. Therefore, the purpose of this research is to analyze the single-crystal X-ray structure of unknown rare sugar ‘L-glucose’. In addition, the DV-Xα molecular orbital method is used to compare the differences in a hydrogen bonding between α-D-glucose and α-L-glucose, and to make a novel supramolecular rare sugar.

1. Introduction
The abundance of rare sugars is small and very expensive, so research of rare sugar is difficult. Therefore, much structural analysis of rare sugar and mechanism of synthesis are not yet understood. However, in recent year, researching of Kagawa University has led to the discovery of the isomerization enzyme DTE (D-tagatose -3 epimerase), which isomerizes the natural monosaccharide D-Fructose into the rare sugar D-Psicose, leading to the large-scale synthesis of rare sugars. The discovery of DTE led to the development of a strategic monosaccharide synthesis pathway called ‘Izumoring’ that systematized the relationship between monosaccharides and their molecular structures and enzymes into a ring. In this research, we will focus on research on the 6-membered ring of monosaccharides. There is no difference in chemical formula between rare sugars and natural monosaccharides, both of which are represented by C₆H₁₂O₆ (e.g. D-glucose, L-glucose) and are simply structural isomers. Therefore, the purpose of this study is mainly to analyze the X-ray crystal structure of rare sugar whose crystal structure (absolute coordinates) has not yet been reported. In our laboratory, we succeeded in synthesizing a new rare sugar called supramolecular rare sugar (SRS), which is synthesized from several kinds of rare sugars. However, the mechanism by which different
types of sugar molecules combine has not yet been elucidated. Therefore, it is another purpose to clarify the mechanism of supramolecular rare sugar by using a theoretical calculation method called DV-Xα for calculating and comparing the differences in the hydrogen bonds between α-D-Glucose and α-L-Glucose.

2. Experimental

2.1 Material and methods

The single-crystal X-ray structure analysis can be divided into two stages. The first, X-ray diffraction experiments are performed to collect hkl diffraction data. The second, the obtained data is analyzed to determine the crystal structure. Each process is described below.

In the X-ray diffraction experiment, a single crystal is cut with a design knife to a size suitable for measurement (the dimensions of the sample are 0.2 mm x 0.2 mm x 0.2 mm). Then, the sample was set in the experimental apparatus, and an X-ray diffraction experiment was performed.
Then, when a suitable sample is obtained, it is fixed to the tip of the capillary with an adhesive.

![Image of sample fixed to capillary](image)

**Figure 5.** The sample is fixed.

The sample is placed in a screw bottle to dry and allowed to harden for about a day. Next, an X-ray diffraction experiment is performed. The sample prepared earlier was mounted on a goniometer head of an X-ray diffractometer and centered so that the X-ray radiate the entire crystal. Then, basic information such as the sample name, crystal shape, color, size, and composition formula was input to the data file, and measurement conditions such as voltage, current, and 2θ range to be measured were set, and the measurement program was executed.

![Image of X-ray applied to sample](image)

**Figure 6.** X-Ray is applied to the sample.

### 2.2. Analysis

The reflection data obtained by the X-ray diffraction experiment were subjected to structural analysis using a structural analysis program package “Crystal Structure 3.7” made by Rigaku. The following is a simple flow to the structure determination.

1. **Evaluate** data determines the space group and composition. **Unit Cell Transformation** replace the cell length and cell angle of the a, b, c-axes of the unit cell by the appropriate.
2. **Formula.** If the composition is inappropriate in evaluate data, change the chemical composition.
3. **Space group.** Changes are made when the space group is not appropriate in evaluate data or when unit cell transformation is performed.
4. **Solve.** The peak is obtained using the direct method (We use Sir 2014 for this graduation study).
5. **Default 99** uses the predicted structure to find out the non-hydrogen atom if it does not appear
6. **Least square.** Let you refine the parameters of atoms (coordinates, temperature factors, etc.)
7. **Refinement menu.** This sets the refinement method for all non-hydrogen atoms and the temperature factor of hydrogen. Shelxl 2014 was used in this study.
8. **Fourier.** The hydrogen atom is found by the difference Fourier synthesis.
9. **Least square.** Turn on secondary attenuation effect correction and change weights to sigma for precision. At this time, since maximum shift/error indicates the convergence state of the refinement, when this value becomes 0.01 or less, the structural analysis is finished.
Two types of sugar structures, $\alpha$-D-Glucose and $\alpha$-L-Glucose were used in this calculation. The electronic states are calculated and discussed using structures which have not been reported in the Cambridge Structure Database (CSD). We use DV-X$\alpha$ molecular orbital method to compare the differences in a hydrogen bonding between $\alpha$-D-glucose and $\alpha$-L-glucose, and to make a novel supramolecular rare sugar.

3. Result of this study

![Figure 7. $\alpha$-D-glucose](image1)

![Figure 8. $\alpha$-L-glucose](image2)

|            | $A \cdots H$ | $A \cdots D$ | $A \cdots H$ | $A \cdots D$ | $A \cdots H$ | $A \cdots D$ | $A \cdots H$ | $A \cdots D$ |
|------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| $O_2\cdots H_3A\cdots O_3$ | 1.909 | 0.820 | 2.699 | 161.44 | 0.0391 |
| $O_3\cdots H_6A\cdots O_6$ | 1.811 | 0.888 | 2.699 | 176.72 | 0.0409 |
| $O_5\cdots H_1A\cdots O_1$ | 1.908 | 0.955 | 2.835 | 163.26 | 0.0405 |

Total BOP (Bond Overlap Population) of $\alpha$-D-Glucose was 0.1204 and BOP of $\alpha$-L-Glucose was 0.0941. We can reveal the hydrogen bonding of $\alpha$-D-Glucose in a unit stronger than $\alpha$-L-Glucose. At first glance, the arrangement of hydrogen bonds in the packed molecule is different, but in three-dimensional space, the hydrogen bond pair is the same. Specifically, there are three hydrogen bonds in both, and the positions of hydrogen bonds are the same. (For example, both have $O_2\cdots H_3A\cdots O_3$ hydrogen bonds).
Table 3. Experimental results of α-D-glucose and α-L-glucose.

| Identifier | GLUCSA03 | α-D-Glucose | α-L-Glucose | New data |
|------------|----------|-------------|-------------|----------|
| Former work | Orthorhombic | P2₁2₁2₁ | Orthorhombic | P2₁2₁2₁ |
| This work | Orthorhombic | P2₁2₁2₁ | Orthorhombic | P2₁2₁2₁ |
| Cell Length [Å] | 4.9464(7) | 4.9526(3) | 4.9536(4) | 4.9536(4) |
| | 10.3440(15) | 10.3209(6) | 10.3185(7) | 10.3185(7) |
| | 14.8472(22) | 14.7792(9) | 14.7798(11) | 14.7798(11) |
| Cell Angles[˚] | 90.000 | 90.000 | 90.000 | 90.000 |
| | 90.000 | 90.000 | 90.000 | 90.000 |
| | 90.000 | 90.000 | 90.000 | 90.000 |
| Cell Volume [Å³] | 759.665 | 755.443 | 755.451 | 755.451 |
| Z | 4 | 4 | 4 | 4 |
| R-Factor [%] | 3.7 | 2.85 | 3.33 | 3.33 |

4. Conclusion

In this study, we succeeded in single crystallization and structural analysis of a new monosaccharide of α-L-glucose. As for α-D-glucose, that structure has already been reported, more accurate results have been obtained. In our laboratory, we used the DV-Xα method to calculate hydrogen bonds in both parked selected molecules. As a result, both contain three hydrogen bonds. Although the arrangements of the hydrogen bonds appear to be different at first, the hydrogen bond pairs are actually the same. The Flack parameters for both are very small 2.85 % and 3.33 %, respectively. The R-value is the most important number. The R-value represents the crystal precision at the International Crystallographic Society. The lower the R-value, the higher the precision of the crystal. If the R-value falls below 5 %, the results can be submitted to an international paper. In this study, α-D-Glucose has the lowest R-value of 2.85 %, it the most accurate substance in the world. The R-value of α-L-Glucose is also very small (R-value is 3.33 %), and it is the first substance in the world. The calculated hydrogen bonds in each lattice show that α-D-Glucose has stronger hydrogen bonds than α-L-Glucose. Based on the results, we are thinking of making supramolecular rare sugars by adding a little bit more α-D-Glucose instead of the same amount.

Reference
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