Development of Electronic Lab-book for College Chemistry-Experiment - S_N1 & S_N2 Reactions -

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Abstract: We developed a computer graphics (CG) teaching material (TM) for university students, concerning reactions involving drastic changes in the structure of the reactants in the following chlorination, for example S_N1: formation of *tert*-butyl chloride from *tert*-butanol and S_N2: formation of 1-chlorobutane from 1-butanol. The CG-TM could clearly demonstrate the changes in the structures during the reaction by the ball-and-stick model, in addition to the image of the energy change in terms of the reaction profile. An electronic lab-book for chemical experiments in the students' laboratory at the university was produced, aiming at the integration of observable-level experiments, symbolic chemical equations, and the molecular world. The lab-book displays pictures of apparatus, flow-chart of experimental procedures, and reaction mechanisms with the CG-TM. A preliminary study on the effectiveness of the CG-TM suggested that students were able to obtain images of S_N1 and S_N2 reactions.

1 INTRODUCTION

Based on the understanding of the observed phenomena in chemical reactions (observable or macro level), chemists try to imagine and explain observations in terms of molecules (sub-micro or molecular level). Observation and molecular level models are then represented in terms of a mathematical or chemical equation (representative or symbolic level) (Gilbert, 2009 and Tasker, 2010). Students' difficulties and misconceptions in chemistry often stem from inadequate or inaccurate models at the molecular level (Kleinman, 1987). A molecular structure visualized by computer graphics (CG) allows for a deeper understanding of molecules (Tuvi-Arad, 2006). However, CG teaching material (TM) for objective reactions is not readily available, because creating accurate CG requires molecular structures based on X-ray crystallography experiments or quantum chemistry calculations.

We are attempting to produce a CG-TM based on quantum chemistry calculations, which provides accurate and realizable images of the nature of a reaction (Ikuo, 2006 and 2009). It has been reported that molecular-level animations combined with video clips of macroscopic phenomena enable students to predict the outcome of a chemical reaction better (Velazquez-Marcano, 2004). Many electronic textbooks of chemistry are available, but most of them are very similar to hard copies and very few are related to chemical experiments (Morvant, 2013). Moreover, a combination of the CG movie of a reaction and an experiment is not available. If the CG can be combined with a lab-book of chemical experiments, students can observe the reaction from three levels of thinking: molecular-level CG, which enables students to obtain a realistic image of a symbolic-level chemical equation, and the phenomenon of an actual reaction. Our ultimate goal is to produce an electronic lab-book for chemical experiments, which integrates these three levels of thinking.

Nucleophilic substitution (S_N) reactions, in which a nucleophile displaces another group or atom from a compound, are among the basic reactions in organic chemistry. Therefore, the S_N reaction is often adopted in TM on the university curriculum, including appropriate schemes that aim to show drastic changes in the molecular structure (McMurry, 2001). Teaching materials or schemes that enable students to provide realizable images of the nature of a reaction need to be developed. We have reported that an electronic lab-book with CG-TM is a promising means to provide images of the

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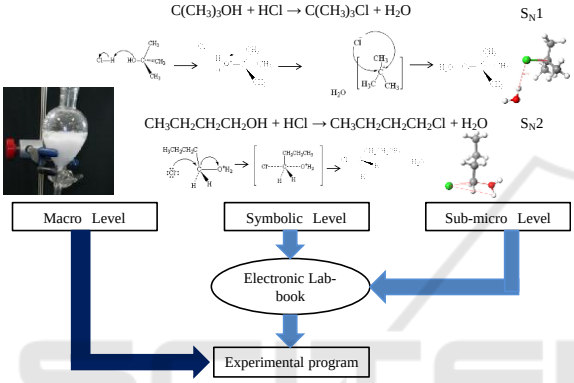
Walden inversion during the S_N2 reaction (Ikuo, 2016).

This paper describes our work on the CG visualization of the chlorination of both *tert*-butanol and 1-butanol as an example of S_N1 and S_N2 reactions, in order to provide realistic images of the mechanisms underlying both types of nucleophilic substitution reactions. The CGs showing the molecular world and experimental procedures for the students' laboratory at the university are combined in the electronic lab-book in order to integrate the observable-level experiment, symbolic-level chemical formula, and the molecular world for the nucleophilic substitution reaction (Scheme 1).

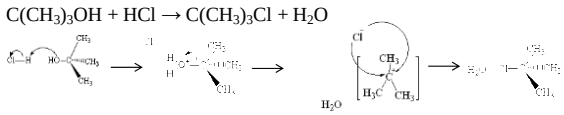


Scheme 1: Development of Electronic Lab-book.

2 METHOD

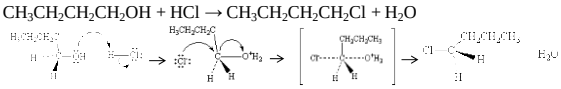
2.1 Development of Experimental Program and Electronic Lab-book

There are two possible mechanisms underlying nucleophilic substitution. In S_N1 reactions (Scheme 2), a carbocation is first formed, which then reacts with the nucleophile. The carbocation is planar, and the anion can attack from either side. Consequently, if the original molecule is optically active, a racemic mixture of products is obtained.



Scheme 2: Mechanism Underlying Chlorination of *tert*-Butanol, S_N1 Reaction.

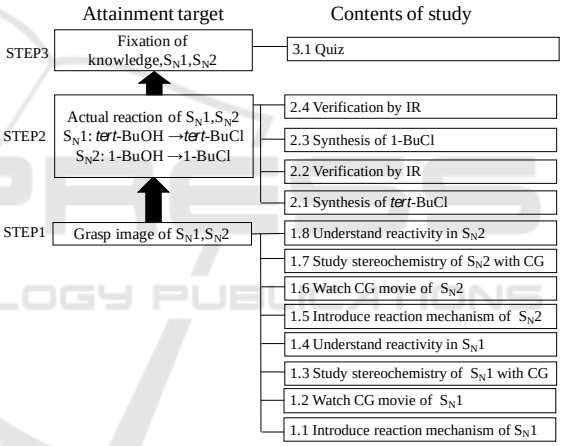
On the other hand, the S_N2 reaction (Scheme 3) is a concerted reaction in which the nucleophile approaches from the left side of the central carbon as the other group leaves to the right.



Scheme 3: Mechanism Underlying Chlorination of 1-Butanol, S_N2 Reaction.

In this case, the configuration of the molecule is inverted. If the original molecule is optically active, the product has the opposite activity, an effect known as the Walden inversion (McMurry, 2001). A schematic representation of the reaction is often used in textbooks, but it is not always easy for the student to obtain the configuration of the molecule or the dynamics of the reaction. The CG-TM may provide such an image.

The attainment targets and contents of an experimental program are shown in Scheme 4.



Scheme 4: Attainment Target and Contents of an Experimental Program.

In STEP1, the S_N1 reaction mechanism is introduced first; then, a learner is expected to grasp a three-dimensional rearrangement image of the reactant molecules during the reaction by watching the CG and CG movie along with the chemical equation and scheme. Subsequently, the stereochemistry is studied using CG. Finally, the reactivity is studied. The S_N2 reaction is studied in a similar manner. This step may take approximately 20 min, which can be assigned as homework.

In STEP2, the actual S_N1 and S_N2 reactions are introduced. Chlorination of both *tert*-butanol for S_N1 and 1-butanol for S_N2 is conducted. The infrared spectral data of the products and reactants are compared. This step may take approximately 2.5 h

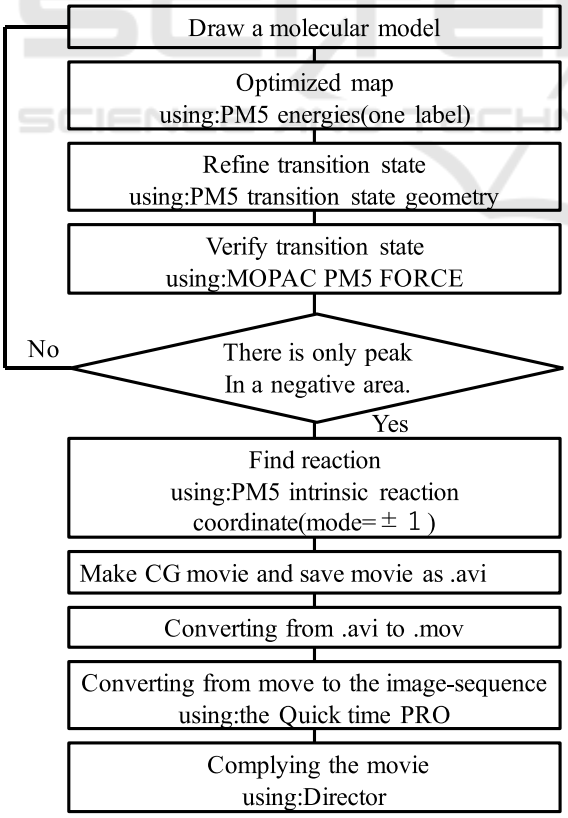
for each reaction.

In STEP3, the learner is expected to integrate his/her knowledge about the S_N1 and S_N2 reactions by participating in a quiz.

2.2 Quantum Chemistry Calculations

The structures of the reactants during the course of the reaction were calculated as follows: the semi-empirical molecular orbital calculation software MOPAC (Stewart, 1989) with PM5 Hamiltonian in the SCIGRESS (ver. 6.01, FUJITSU, Inc.) was used in all the calculations for optimization of the geometry by the Eigenvector following method, for searching the transition state by using the program with saddle point search, and for searching the reaction path from the reactants to the products via the transition state by intrinsic reaction coordinate (IRC) calculation (Fukui, 1970) (Scheme 5).

The structure of the reacting molecules at the transition state was confirmed by a single absorption peak in the imaginary region: -649.8 cm^{-1} (first part of the reaction) and -154.24 cm^{-1} (second part of the reaction) in the chlorination of tert-butanol, S_N1 reaction; and -422.94 cm^{-1} in the chlorination of 1-butanol, S_N2 reaction.



Scheme 5: Procedure for Making CG Movie.

The structures of the initial state, transition state and final state were obtained by the IRC calculation, as shown in Figures 1 and 2. The Gibbs energy changes and interatomic distances obtained by the calculation were in good agreement with the literature values, as seen in Tables 1 and 2.

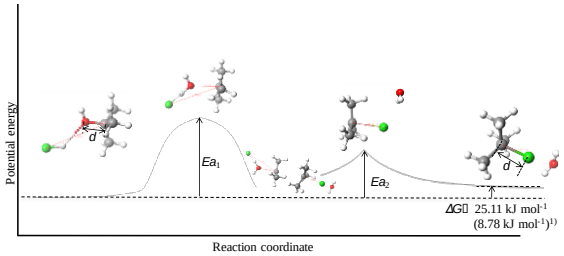


Figure 1: Reaction Path for Chlorination of *tert*-Butanol, S_N1 Reaction. *d*: bond distance; ΔEa: activation energy (Ea_1=266.19 kJ mol^{-1}, Ea_2=60.27 kJ mol^{-1}), ΔG: E_{pro} - E_{rea} 1) Nihonkagakukai (CSJ) Ed., 1984. Kagaku binran kisohen (Handbook of chemistry Basic) 3rd ed., Maruzen, 305.

Table 1: Interatomic Distances of Selected Atoms for Chlorination of *tert*-Butanol, S_N1 Reaction.

Bond	*d* /nm		
	Calculation	Experimental	Subtraction
C−O	0.141	0.143[1)]	0.002
C−Cl	0.184	0.177[1)]	0.007

1) Nihonkagakukai (CSJ) Ed., 1984. Kagaku binran kisohen (Handbook of chemistry Basic) 3rd ed., Maruzen, 717.

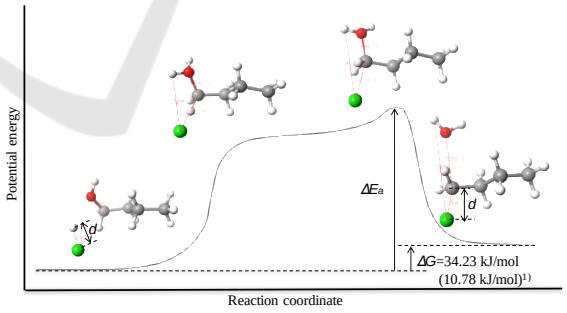


Figure 2: Reaction Path for Chlorination of 1-Butanol, S_N2 Reaction. *d*: bond distance; ΔEa: activation energy (=623.05 kJ mol^{-1}); ΔG: E_{pro} - E_{rea} 1) Nihonkagakukai (CSJ) Ed., 1984. Kagaku binran kisohen (Handbook of chemistry Basic) 3rd ed., Maruzen, 305.

Table 2: Interatomic Distances of Selected Atoms for Chlorination of 1-Butanol, S_N2 Reaction.

Bond	d /nm		
	Calculation	Experimental	Subtraction
H−Cl	0.139	0.143[1)]	0.004
C−Cl	0.180	0.177[1)]	0.003

1) Nihonkagakukai (CSJ) Ed., 1984. Kagaku binran kisohen (Handbook of chemistry Basic) 3rd ed., Maruzen, 717.

Energy changes during the reactions and the structures of the reactants and products were confirmed. Therefore, it was concluded that the reaction path and the molecular geometry obtained by the calculation were appropriate for creating the CG-TM.

2.3 CG-TM and Electronic Lab-book

The AVI file for the reaction path was produced by SCIGRESS such that which changes in the structure of the reacting molecules can be clearly seen and bond formation or bond cleavage is displayed by changes in diameter of the stick in the ball-and-stick model; this diameter is related to the calculated bond order. The AVI file was first converted to a MOV file and then to the image-sequence file by Quick Time PRO (ver. 7.66, Apple, Inc.) (lower part of Scheme 5). The image-sequence file of the ball-and-stick models was combined with the reaction profile (which is the potential energy change during the reaction progress) of the corresponding reaction stage by Director (ver. 12.0, Adobe, Inc.). It was confirmed that the drawn CG of the molecular models of the reactants moved smoothly in the CG movie. The ball, which indicates the progress of the reaction, was arranged on the reaction profile, and simultaneous movements of the ball and the reactants were also confirmed. An electronic textbook was produced with iBooks Author (ver. 2.5, Apple, Inc.) and saved to the tablet (iPad Air 2, Apple, Inc.) by using iTunes (ver. 12.5, Apple, Inc.).

3 RESULTS AND DISCUSSION

3.1 Features of Electronic Lab-book

Teaching materials such as CG or CG movie of the S_N1 and S_N2 reactions were combined with the chemical experiments from students' laboratory for making the electronic lab-book of basic chemistry to provide observations though experiment, molecular-level CG, and symbolic-level chemical equation.

CG-TM such as pop-up CG of the molecule and CG movie of molecular rearrangement in the ball-and-stick model is also inserted (Figure 3). The pop-up CG provides a 3D image of the molecule being described by chemical equations. The CG movie shows the reaction profile, which demonstrates the eaction progress by the ball indicating the potential energy *vs*. reaction coordinate. When student touches the CG-TM in the tablet computer, the image of the structural change during the reaction is displayed. If student touches the material again, the

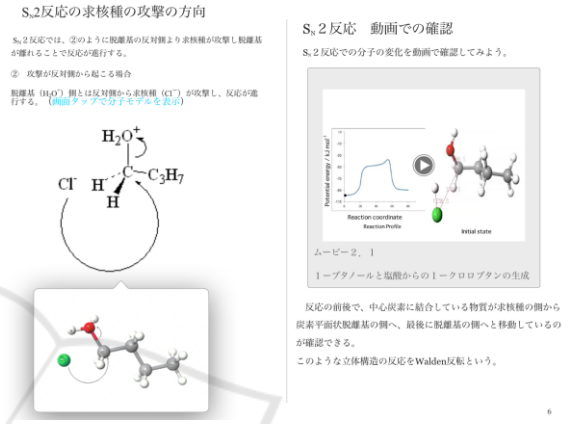


Figure 3: Pop-up CG and CG Movie of S_N2 Reaction in STEP 1.

Quick Time control bar appears and the red ball on the profile can move as per the student's choice. student can manipulate the reaction back and forth until he/she obtains the image of the reaction. A student is expected to obtain a dynamic image of molecular rearrangement.

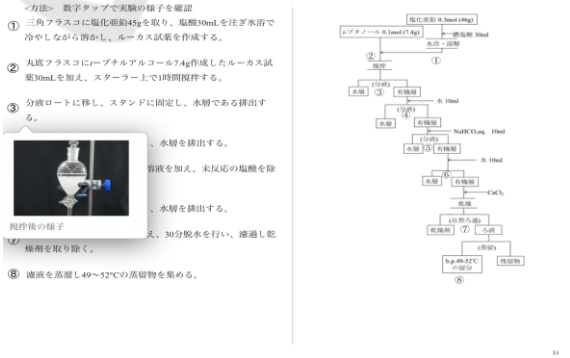


Figure 4: Flow Chart and Pop-up Photo of Apparatus for Experimental Procedure in STEP 2.

A flow chart of the experimental procedure of the (Figure 4) and pop-up photographs of the apparatus were inserted into the electronic textbook for

providing a realistic image of the experimental set up.

In STEP3, the learner is expected to integrate knowledge about S_N1 and S_N2 reactions by participating in a quiz (Figure 5).

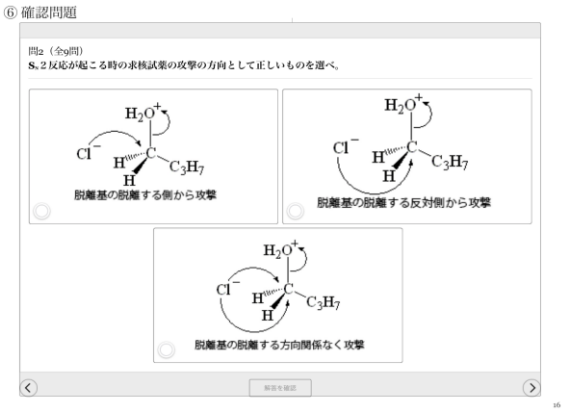


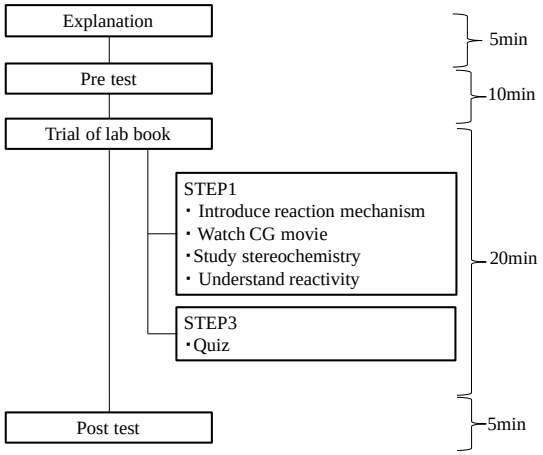
Figure 5: Quiz, Approaching Direction of Nucleophile to Central Carbon for S_N2 Reaction in STEP 3.

3.2 Practicing the Use of the Electronic Lab-book

Four third-year chemistry students of the teachers' training course at Tokyo Gakugei University, who took basic organic chemistry in the first year, were asked to practice STEP1 (grasp the image of S_N1 and S_N2 reactions) and STEP3 (quiz part of the electronic lab-book), as illustrated in Figure 6.

Figure 6: Practice with Electronic Lab-book.

The procedure adopted in the practice session is shown in Scheme 6. First, the usage of the tablet was explained, and then, a pre-test was conducted. After the pre-test, tablets were distributed to each student, and the students were asked to study STEP 1 and try to answer the questions in STEP 3. Finally, a post-test was conducted. Students were confirmed to concentrate on the subject, as they studied STEP 1 in detail and attempted to answer the questions in STEP 3.



Scheme 6: Procedure Adopted for the Lab-book Practice.

The results of the survey are summarized in Table 3. The average number of correct answers was 2.00 out of 6.00 in the pre-test, and it was increased to 5.25 in the post-test. After using the electronic lab-book, students' knowledge in terms of "reactivity," "attacking direction," and "energy change" in the S_N1 and S_N2 reactions was improved. The students added their comments in the free description section of the questionnaire, for example, "After using iPad, image of the reaction became certain" and "the movie helped understanding the reaction mechanism." These comments suggested that the electronic lab-book could provide an image of the S_N1 and S_N2 reactions.

Table 3: Results of Survey.

Question	Contents	Pretest	Posttest
1	Reactivity in SN2	1	3
2	Reactivity in SN1	1	4
3	Attacking direction and product in SN1	1	4
4	Attacking direction and product in SN2	3	3
5	Stereochemistry inSN1 , SN2	2	3
6	Reaction energy in SN1 , SN2	0	4

Although a more detailed study must be carried out on the effectiveness of the electronic lab-book, we can state that the students could obtain an image of the S_N1 and S_N2 reactions.

4 CONCLUSIONS

We developed CG-TM for university students, concerning reactions involving a drastic change in the structures of the reactants in the following chlorination reactions: S_N1, formation of *tert*-butyl chloride from *tert*-butanol; S_N2, formation of 1-chlorobutane from 1-butanol. The CG-TM could clearly demonstrate the changes in the structures during the reaction by the ball-and-stick model, in addition to the image of the energy change by the reaction profile. An electronic lab-book for chemical experiments in the students' laboratory at the university was produced. The lab-book could display pictures of the apparatus, flow chart of the experimental procedure, and reaction mechanism with the CG-TM. A preliminary study on the effectiveness of the CG-TM suggested that students were able to obtain the image of the S_N1 and S_N2 reactions.

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