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Education of Molecular Structures Using Structure-Drawing Software on Personal Computer

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構造式作成ソフトウェアを利用する分子構造の学習

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For the purpose of understanding chemical structures of body constituents, a task work was assigned to the students to draw structural formulae of several organic compounds on personal computer (PC) using structure-drawing software. Concurrently, students' levels of skill in operating software and understanding of structures have been investigated. The students can generally operate the software. However, it was clarified that they had difficulty in fine control to arrange the whole shape of the formula including bond lengths and angles, size of atom label on ring structure, in addition to setting format of the character such as super- and subscripts to indicate charge or number of atoms. In respect of understanding, they had much difficulty in finding the structures asked, and in distinguishing stereoisomers. Two thirds of the errors observed in submitted task papers were concerned with stereochemistry.

Overall, the students felt fun with the structure-drawing software and found it convenient to draw structures, wanted to get skilled, and utilize it for processing papers on laboratory classes. These findings suggest that drawing formulae on PC will be attractive to the students and thus helpful for understanding molecular structures of compounds.

Introduction

Among various clinical examinations, chemical analysis is the one to determine the compounds in blood, urine, and other body fluids. The principles of the assay methods are based on chemical reactivity and physico-chemical property of the compounds, closely related to the molecular structures. Therefore, it is essential to the medical technologist to understand structures of biological organic compounds.

Along with popularization, personal computer (PC) has been also introduced to the field of education (e-learning). Structure-drawing software is designed to draw structural formula

on PC, and the unit of compound can be treated as an object. Probably, this will be the first software for the students from new category. They will take interest in using the software and feel fun to draw structures on PC. Thus it is expected to be a helpful tool in education of chemical structures[1)2)]. The author has been in charge of biochemistry and clinical chemistry classes. In one of them, a drill and task work is given to the students to draw structural formulae of organic compounds on PC using structure-drawing software, for the purpose of understanding structures of body constituents.

So far almost similar errors and unsuitable notations of structural formulae were observed in submitted task papers over the years. Except for misquotation of the compounds, the errors are mostly concerning distinction of isomers, and these will be due to the students' levels of understanding of three-dimensional structures. On the other hand, unsuitable notations are observed in expression of the charge, super- and subscript or insertion of the atom label. These may be caused by inexperience in operation of the software. In this study, we have investigated the students' levels of skill in operating structure-drawing software and understanding of molecular structures, to evaluate education by "drawing" structures.

Apparatus and Methods

Students and Class Subject: The students were 41 freshmen (Class of 2006) of the Department of Medical Technology in College of Medical Sciences, Tohoku University. Those students had finished basic computer literacy class in the college. The laboratory class subject was "Analytical Biochemistry", and one out of the 15 classes was allotted for drill in drawing structures on PC.

Apparatus and Software: The drill class was held in the computer education room furnished with Endeavor AT930C computers (Seiko Epson Corp., Suwa, Japan) operated with "Microsoft Windows XP" (Microsoft Corp., Redmond, WA, USA) on MS-DOS in 2003. For drawing chemical structures, "ISIS/Draw 2.5" (MDL Information Systems, Inc., San Leandro, CA, USA) was employed (Fig. 1). Although we used a Japanese version, manual documents are available only in English. Thus "Quick Start" manual was translated into Japanese and given to the students so that they learnt the operation according to this and by trial and error. We also instructed the students how to download the software from the Web, and many of them carried back the installation program in CD and worked with the software at home. In this case, the models of used PCs are naturally different.

Analyses of students' response and submitted papers: In the task work, the students were assigned to draw 13 structures of 9 compounds including isomers in specified manner. The task paper should be submitted 8 weeks later, and then a questionnaire survey was performed. Concerning the operation of the software, students were requested to classify the difficulty into 4 levels from each of the following technical aspects: 1) drawing chemical bond (line type, length, angle), 2) drawing ring structure, 3) insertion of the atom label, 4) displaying configuration, 5) setting format of the character such as super- and subscript, 6) general operation. In addition, topic with special difficulty they had and general impression of the software was also investigated in free description format. Regarding the task work, the students were requested to describe: 1) how they find the structures required, 2) in which point they felt difficult or got confused, 3) how they solved the problem, 4) general

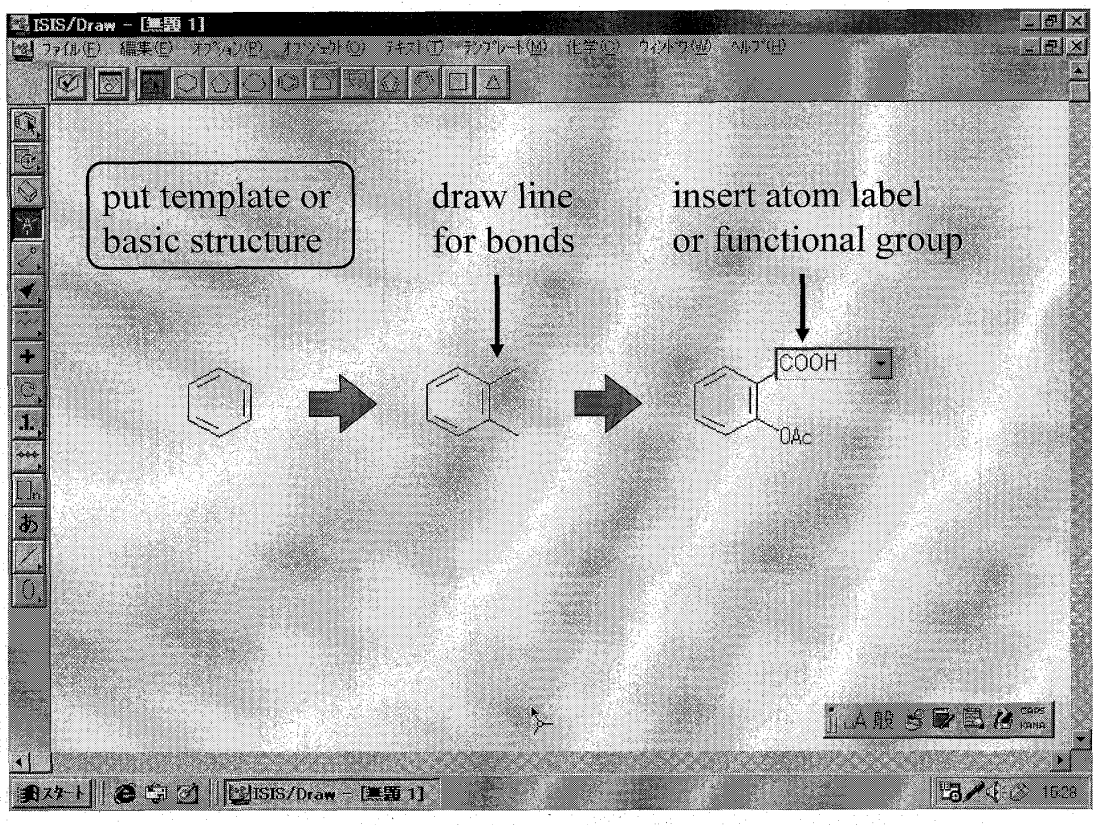

Figure 1. Drawing structural formula using ISIS/Draw. Tool bars specialized for drawing structures are placed on upper and left sides of the window.

impression of the task and drawing structures on PC.

On the other hand, we examined all the structures in submitted papers: correct or incorrect (meet the demands or not), correctness of stereoisomers, format of the characters, valence of the atom, suitability of bond expression. The results were reviewed with those of the questionnaire survey.

Results and Discussion

At first, we directed our attention to students' possession status of PC, levels of their skill in computer literacy, and places they had worked to complete the task. Out of 41 students, 24 (59%) have their own PC and 10 (24%) have sharing PC at home (Fig. 2). Five of seven who do not own PC said that they frequently utilize PC in computer education room at the College, thus only 2 students were rare users. According to the self-evaluation of the skill in literacy, 8 students (20%) replied that they can use PC without inconvenience in normal operation, and all the rest thought themselves as beginners. No one recognized oneself as a power user.

"ISIS/Draw" is a free program for academic and personal use[3], thus we have so far offered the information about the download site. However, students' utilization for processing papers in the laboratory classes was extremely low[4]. Therefore, we actually showed the students for this study, how to download the software, and let them carry back the installation program in CD. As a result, more than half 24 had worked mainly at home,

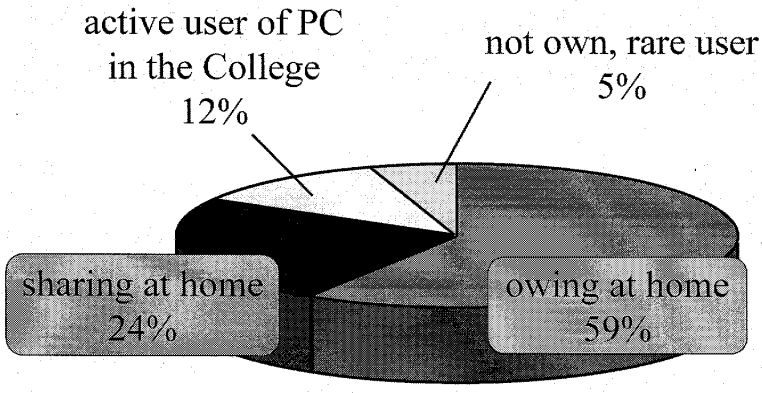

Figure 2. Students' status of possession of PC.

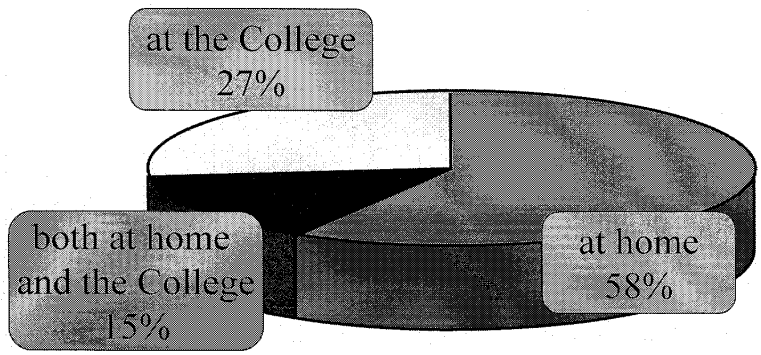

Figure 3. The places students worked to complete the task.

11 at the College, and 6 worked both at home and the College (Fig. 3). We assume that promotion of downloading the software resulted in the increase of students working at home.

In respect to the operation of the software ISIS/Draw, the most students had difficulty in expressing stereostructure and setting of the character format, such as superscript to indicate the electric charge and subscript for the number of atoms. The majority of the students had general impression as difficult (Fig. 4). The concrete difficulties they had in operation are listed in Table 1. Nearly half of the students struggled with the fine control of bond length and direction, balance in whole shape of the molecule, followed by the format of inputting character. These results matched the errors observed in the submitted papers as described below.

As for the difficulty concerning the questions in the task, the topic listed by the most students was about stereostructure of the compounds, followed by finding structures of required compounds and then by meaning of the questions (Table 2). We also asked them how they solved those problems. The most had discussed with classmates, but the effect is doubtful. To the question what they referred to for the structures, an overwhelming majority (38 students) answered that they referred to the books, 90% of which was the textbook used in the class of biochemistry, and the rest 10% for organic chemistry. Furthermore, 35% had additionally used the dictionaries of chemistry, biochemistry or organic compound references together. Fourteen students had searched the

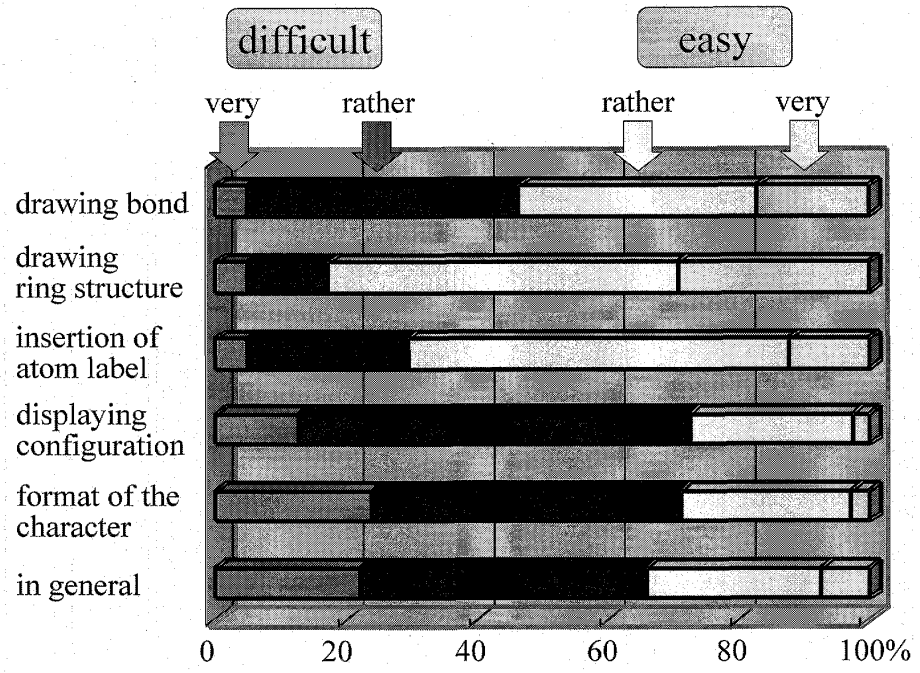

Figure 4. Impression of technical difficulty in operation of the structure-drawing software ISIS/Draw.

Table 1. Difficulties in software operation listed by the students

Rotation and movement of drawn structure or template (4) Direction of the bond line (6) Angle and length of the bond line (5) Connection of the bond lines (2) Margin between the line and characters Proportion of atom label to the line length Arrangement of the whole shape	Fine control to arrange the whole shape of the molecule (20)
Superscripts for charge "+/−" (6) Typing in Greek letter "α, β" (2) Input text was garbled (2) Setting small capital Entering text for the caption PC did not accept insertion of the label	Setting format of the character (13)
Drawing ring structure in good-looking (6) Haworth projection of sugar Configuration of stereoisomers	Notation of ring structure and stereostructure (8)

*Numbers of the similar answers are given in parentheses.

chemical compounds on the Internet, thus we can see the variety in the methods of reference.

Within the 593 structural formulae drawn in the submitted papers, 164 had some errors. The total number of drawn formulae is more than that of correct answers including 13 structures, because the students had drawn unnecessary formulae. The most frequent errors are concerned with stereoisomerisms (Table 3). For example, tartaric acid has two chiral centers in one molecule and appears to have 4 stereoisomers, but actually there are three

Table 2. Difficulties in the working task listed by the students

Problem the students have	Category	How they deal with the problem
Meaning of "(*sn*)" (5) Notation of nucleotide α- and β-side of cholesterol α- and β-anomer Correspondence of the compound between in English and Japanese	Meaning of the question (9)	Ignore the term Asked or discussed with classmates (18) Referred to books, dictionaries, notes on the lectures (34) Searched on the Internet (14) Intuition, Index of the books Refer to molecular models Internet
Hardly find the compound Hardly find the structure of the required compound Time-consuming to find the structure	Finding structures (8)	
Considering stereoisomers (3) Considering the number of isomers (7) Distinction of D-/L-isomers (2) Notation in Reeves projection cis- and trans-form of the ring junction	Stereostructures (14)	

*Numbers of the similar answers are given in parentheses.

Table 3. Errors and unsuitable notation observed in the submitted papers

Stereoisomers	*R*/*S* (D/L-) (mirror image)	Correct	245
		Incorrect	60
		Ignored	25
	Number of the isomers of tartaric acid	Correct	24
		Incorrect	17
		Can not distinguish the identical form	16
	Geometrical isomers	Correct	24
		Incorrect	16
		Ignored	1
Notations	Subscript for suffix	Suitable	5
		Unsuitable	36
		Not in use	30
	Superscript for charge	Suitable	95
		Unsuitable	30
	Small capital for "D-/L-"	Suitable	15
		Unsuitable	158
Incorrect valence			53
Unusual notation of atom and bond			245

isomers because of the symmetry of the molecule (Fig. 5). However, many students could not recognize the fact that (2*S*, 3*R*) and (2*R*, 3*S*) isomers are identical (meso-form).

We assume that the main reason for the errors concerning stereoisomerisms is not the difficulty or inexperience in operating software, but the poor understanding of the structures and sense of spatial recognition. To draw a structure, one should have the concrete image of three-dimensional structure in the mind. The software is just a tool for realizing the image on the display. Therefore, students need practice in recognizing the three-dimensional structures using molecular model or 3D imaging system, and projecting them onto the two-dimensional field. It will be also necessary to cooperate with other classes such as organic chemistry and biochemistry.

Concerning the expression, the observed errors match the result in questionnaire survey that the students felt difficulty in setting character format in operation of the software. Especially, prefixes "D-/L-" to distinguish optical

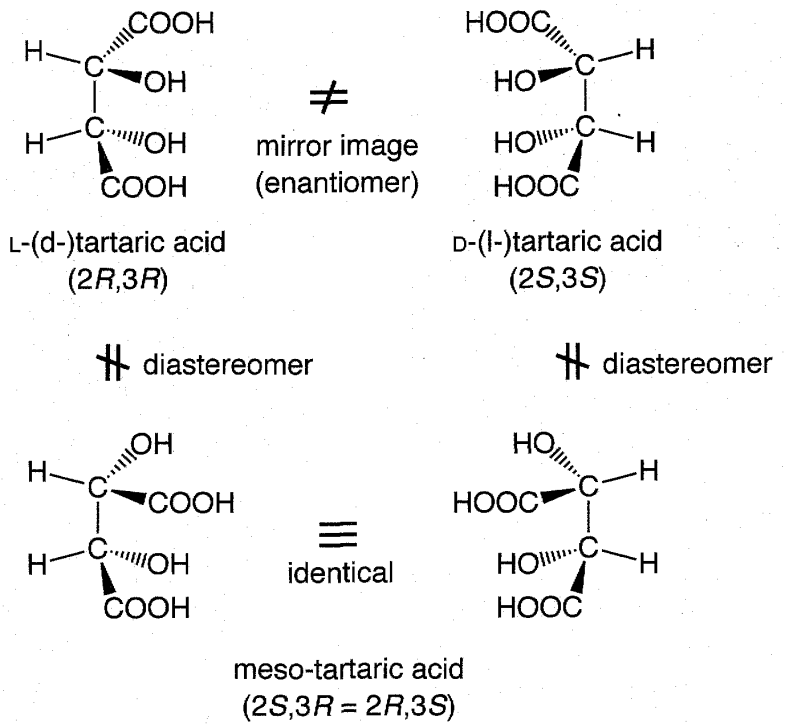

Figure 5. The stereoisomers of tartaric acid.

Table 4. Impression of the software to the students

I worked with fun, pleasant. (20) It is convenient to draw structures. (6) I was deeply impressed by the function of the software. (5)	Five students replied plural answers.
I want to get experienced to utilize in processing papers. (4) I have studied with fun. (3) I will feel familiar with the structure.	
Operation of the software is difficult. (11) I need time to get experienced. (8)	

*Numbers of the similar answers are given in parentheses.

isomers, which should be written in small capital, were not described correctly. However, the primary factor of this case is not the operation skill but that they had forgotten the rule of nomenclature.

Although it is difficult to judge about fine control of whole shape because it includes subjective factors, obvious errors were observed such that the valence is wrong or unusual drawing of atom and bond. We can assume that inexperience of operation is reflected in these errors (Table 3).

As a general impression, two thirds of the students said that the operation of the software is rather difficult. On the other hand, the number of students reached to nearly 90%, who confessed that they found working with the structure-drawing software pleasant and con-

venient (Table 4). We also received positive answers such that "I would like to have a good command of this software", "I would like to utilize even in the future papers", and we infer that they just need time for being experienced with the operation. Furthermore, a student directly answered that this method is useful in understanding structures. It was suggested that "drawing" structural formulae on PC have the possibility to be a helpful tool in education of molecular structures of chemical compounds.

Conclusion

Although the students feel difficult at first and it needs time to get experienced in operation, "drawing" structural formula using software of new category is attractive and pleasant to them. They worked with fun, found convenience, and were prompted to get skilled in operation during the work. The structure-drawing software is expected to be a helpful tool for understanding molecular structures of organic compounds.

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