Discovering Isomerism: A Guided-Inquiry Computational Exercise for Undergraduate Organic Chemistry

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Abstract: This paper provides a guided-inquiry exercise designed to help sophomore level undergraduate students discover isomerism in the organic chemistry curriculum. The activity teaches students to use Gaussian and GaussView software packages to create molecules and setup calculations to explore chemical properties. The students, unknown to them, create cis- and trans- isomers of simple molecules and analyze their potential energies and nuclear repulsion energies. The class uses this information to discover the stability of trans-isomers relative to cis-isomers. This provides students with a clearer understanding of the impact of nuclear repulsions on the final geometry of the molecule. Student assessment of the activity has been highly positive and points to the need for regular integration of such assignments into the Organic Chemistry curriculum.

Introduction

The use of computational programs as instructional tools in all sub-disciplines of Chemistry has become increasingly popular over the past two decades [1–4]. The advent of cheap computational power and ubiquitous access to computational devices has the potential to reshape and enrich traditional teaching and learning methodologies. Recently, there has been a push to integrate more computing into the freshman Chemistry curriculum in the form of specialized courses such as Scientific Computing [5, 6]. These efforts to incorporate computing in chemistry education will particularly impact sophomore and higher-level courses in a few years, and students will appreciate and even anticipate computational approaches in those courses. This requires that instructors have ready access to activities that can be integrated into existing curricula to positively impact student learning.

There are multiple approaches to teaching guided-inquiry and discovery-oriented learning. The POGIL approach has been quite successful and has been adopted by a large community of educators [7–9]. Our approach of guided-inquiry to lead students to discover physical or chemical phenomena has been previously used to create activities for the freshman General Chemistry curriculum [10, 11]. Such efforts have inspired us to now create activities for the Organic Chemistry curriculum. This exercise details the introduction of Gaussian 16 [12] and Gaussview 6 [13] in the first-semester Organic Chemistry curriculum.

There have been numerous endeavours to introduce computational elements in the teaching of organic chemistry. Many of these attempts have focused on simulation and prediction of IR spectra [14, 15], molecular orbital HOMO-LUMO analysis [16], mechanistic pathways [17–20], ring strain [21, 22], and spectral shifts in response to solvent polarity or functional groups [23]. Most of these activities have been designed as laboratory experiments to help students bridge the gap between theory and its application to chemistry. However, there is a dearth of activities that can be used in an interactive teaching scenario where the distinction between lecture and laboratory is blurred and students do not have to differentiate between the two aspects of the discipline.

A strong understanding of molecular geometry and isomers is critical to student success in organic chemistry. Isomerism is typically introduced early in the first semester of the course sequence, with cis/trans isomers serving as the first example of stereoisomers that students encounter. The preference for the trans-isomer is usually explained by a lower potential energy that results from reduced steric strain; however, the concept of nuclear repulsion energy is rarely introduced. Therefore, students are explicitly informed which isomer is more stable, rather than using experimental data to reach this conclusion on their own. As students advance through the course, they must continue to consider molecular geometry and isomer stability when working through reaction mechanisms and predicting products. This critical piece of the curriculum needs to be strengthened for long-term success in the discipline. Our goal in this paper is to present an exercise that can be used in a classroom, laboratory, or integrated classroom-laboratory experience to enable students to discover the energetic differences between cis- and trans- isomers and thus discover the stability rules for this important class of isomers. The exercise is detailed in the Methods section and qualitative student assessment is provided in the Discussion section.

Method

The exercise is designed to accomplish the following learning goals:

- Introduce students to building molecules in a computational interface
- Review hybridization concepts
- Setup and execute calculations using the Gaussian interface
- Compare the results of quantum mechanical calculations for different molecular conformations to arrive at conclusions on stability of structures

The students are provided with a work-sheet that contains detailed instructions to setup and execute the calculations. Working in groups of 2–3, the class completed the exercise in one hour, which is a typical lecture period at many institutions. The exercise can be extended to fit the standard three-hour laboratory period by incorporating the report writing phase of the assignment, or can even be used as a recitation activity.

The activity consists of three parts, increasing in complexity. Students begin by creating methane in the GaussView program and performing a quick optimization of the structure. They measure the bond-lengths and bond-angles and verify that measurements agree with predictions of the sp^3 hybridization model. The next stage invites students to create $H_3C–CH_3$, $H_2C=CH_2$, and HC≡CH molecules, perform a pre-optimization on each molecule, and measure and compare bond length of the central C-C bond in each case. The bond length measurements provide students with a visual reminder of the principles learned in previous courses about the bond length order from single bond to triple bond between carbon atoms. Students also measure the H-C-C bond angles in each molecule, to draw the connection between hybridization and molecular geometry. These two components provide students with a primer on navigating the molecule drawing and editing functionalities of the GaussView interface.

The third part of the activity investigates cis- and trans-isomers. Since this activity precedes any classroom discussion on isomerism, we do not provide names of molecules to the students. Instead, we simply refer to the molecules as Molecule-1, Molecule-2, Molecule-3, and Molecule-4 (Figures 1–4). Students create Molecule-1 to prepare for the first calculation. The structure is subsequently pre-optimized using the "Clean" functionality in GaussView and then students setup a single-point energy calculation at the Hartree Fock level of theory with the 6–31G basis set [24]. The students do not perform a geometry optimization to avoid complicating the experiment. The success of this exercise does not rely on the optimal geometry of the molecules.

Students perform the same steps, pre-optimization and energy calculation, for each of the four molecules in the study. For each molecule, students note the total potential energy and the nuclear repulsion energy. The calculation results are stored in a Google Form that aggregates the data from all participants in the exercise. This provides a pool of data for the class to examine and discuss with the instructor upon completion of the activity.

Results

The results of the calculations described in the previous section are summarized in Table 1.

To facilitate the student data collection process, a Google Form with data validation checks was created. The data validation was enforced with simple rules like checking the input for numerical values, and checking that potential energy values were negative and nuclear repulsion energy values were positive. This data validation was implemented to guard against errors while students were transcribing data to the shared pool.

From the table of values obtained from the students, the differences in potential energy and nuclear repulsion energy between the isomeric forms were calculated. The values entered by the students were converted from Hartrees to kcal/mol prior to performing any calculations, as students are more familiar with the latter unit. The difference in potential energy between the butene isomers is 2.202 kcal/mol, while the nuclear repulsion energy difference is 2058.474 kcal/mol. These two numbers clearly highlight to the student that the cis-form suffers from much stronger nuclear repulsions than the trans-form. Thus, students arrive at the conclusion that the trans-form should be more stable relative to the cis form.

Similarly, the difference in potential energy and nuclear repulsion energy between cis-hexene and trans-hexene (Figures 3–4) are 9.502 kcal/mol and 4045.272 kcal/mol, respectively. The larger magnitude of nuclear repulsion energy for hexene systems helps students to make the connection that nuclear repulsion energy increases as the number of atoms in the system increase.

Discussion

Students were provided with a short survey to assess their response to the activity and to guide future improvements. The survey questions and their results are provided below. Student responses (n = 18) ranged from Strongly Agree (1) to Strongly Disagree (5), with the average values in bold and the standard deviations in parenthesis.

- I enjoyed this activity. **1.67** (0.49)
- I found this activity challenging. **2.56** (0.98)
- I have acquired a better understanding of molecular geometry and its connection with total energy. **1.78** (0.65)
- I have acquired a better understanding of the impact of nuclear repulsion energy on structure. **1.94** (0.56)
- The application of computer interface helped me to understand molecular geometry. **1.72** (0.57)
- This activity stimulated my interest in Organic Chemistry. **2.00** (0.69)
- I would like to perform more activities like this. **1.50** (0.62)

Student feedback was positive overall, with the majority indicating they would like to complete more activities like this. In addition to these survey questions, students provided additional comments that reaffirmed their enjoyment of the activity and their desire to encounter more computational activities in the chemistry curriculum.

Conclusion

We have created a computational activity that can be used to introduce the concept of cis/trans isomerism in molecules. Students learn to create small molecules in the GuassView interface and setup elementary calculations using the powerful Gaussian computational engine. This can serve as a gateway to incorporate additional experiments in the curriculum, leveraging students' familiarity with the computational package. The assessment results clearly highlight student appreciation and readiness to pursue alternate forms of learning that deviate from the standard lecture/ cookbook-laboratory content. This exercise can be easily ported to any other computational chemistry package like GAMESS [25], Q-Chem [26], Psi4 [27], Spartan [28], and others [29]. We have provided the student handout to the exercise in the supporting documents. The student handout can be easily modified to suit the software packages available at the reader's institution. We encourage readers to contact the corresponding author for access to the Google form setup.

Table 1. Calculated energies for cis/trans isomers

Molecule	Potential Energy (kcal/mol)	Nuclear Repulsion Energy (kcal/mol)
cis-2-butene	–97914.280	74579.4749
trans-2-butene	–97916.482	72521.0006
cis-3-hexene	–146873.416	145996.2127
trans-3-hexene	–146882.918	141950.9404

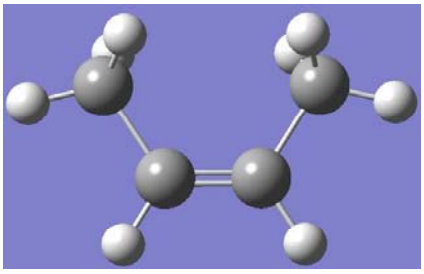

Figure 1. Molecule-1, *cis*-2-butene.

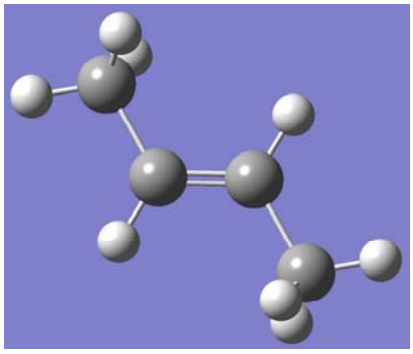

Figure 2. Molecule-2, *trans*-2-butene.

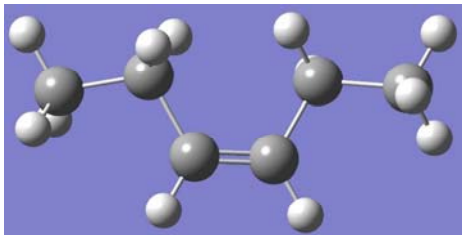

Figure 3. Molecule-3, *cis*-3-hexene.

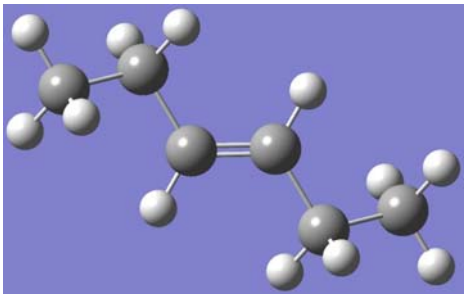

Figure 4. Molecule-4, *trans*-3-hexene.

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Supporting Materials. The activity handout file is available in the supporting material.

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