JOURNAL OF CHEMICAL EDUCATION

pubs.acs.org/jchemeduc

Laboratory Experiment

Integrating iSpartan into a Classic Organic Chemistry Laboratory Experiment

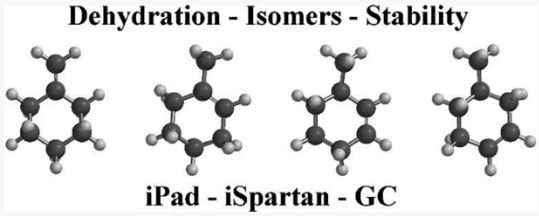
Shanina Sanders Johnson,*[,§] Leyte Winfield,[§] and Shannon H. Sung

Cite This: *J. Chem. Educ.* 2021, 98, 982−985

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: The dehydration of 2- or 4-methylcyclohexanol to obtain isomers of methylcyclohexene is a classic organic chemistry experiment. Students perform a distillation, collecting samples to analyze the progress of the reaction. The reaction produces a major product that can be explained on the basis of the regiochemistry of the π bond formation for the $\alpha-\beta$ elimination process. Minor products can be attributed to the possible rearrangement of the carbocation through a hydride shift. We have added computational analysis to this classic experiment to help students understand alkene stability. The experiment was performed early in the sophomore organic chemistry laboratory, before students were introduced to the mechanistic perspectives that govern the reaction. The iSpartan analysis of the possible methylcyclohexene products combined with gas chromatography data provides students with an inquiry-based laboratory experience. A novice student can analyze the computational information about the products to determine the trend in product stability and determine if a double-bond is formed at an unexpected location in the molecule. The integration of computational tools provides more information to students than performing the experiment in isolation.



KEYWORDS: *Laboratory Instruction, Second-Year Undergraduate, Organic Chemistry, Computer-Based Learning, Inquiry-Based/Discovery Learning, Alkenes, Elimination Reactions*

INTRODUCTION

The American Chemical Society's Guidelines for bachelor's degree programs state that "The ability to compute chemical properties and phenomena complements experimental work by enhancing understanding and providing predictive power."[1] Computational data is commonly incorporated into organic chemistry textbooks to help students understand the relationship between the structure and function of chemical compounds.[2−4] Molecular modeling, in particular, can be a versatile tool that allows students to examine reaction mechanisms and explain experimental results.[5] It is the predictive power of computational data that can aid students' interpretation of experimental data and their ability to rationalize chemical phenomena observed in the laboratory.[3] Examples of the infusion of molecular modeling into organic chemistry laboratory at the introductory and advanced levels have been described for reactions such as the classic Fischer esterification experiment and a contemporary ligand-free Suzuki−Miyaura coupling reaction.[6−10] These efforts emphasize the benefits of combining experimental and computational data and encourage increased exposure to improve students' competencies.

The rise of student-friendly software and less expensive computing resources has made computational chemistry curricula more feasible. Faculty at various institutions, for instance, have implemented the use of iPads in the organic chemistry lecture to minimize the use of paper, support collaborative learning, teach spectroscopy, and aid in the visualization of organic structures.[11−16] Adding to this, applications such as iSpartan contain features that allow users to depict structures in two- and three-dimensional formats that provide visual clarity, demonstrate the spatial connectivity of atoms within the molecule, and allow for the manipulation of a structure. The app also provides access to molecular and atomic properties. The visualizations and energy values afforded through the iSpartan app can help students understand the relationship between the stability of a compound and its energy. Studies show that it is challenging for students to connect ideas from observed chemical reactions to the textbook illustration of reactions.[17] It has also been shown that students may be able to identify products of a reaction correctly, but they do not think about energy and bonding in these transformations.[18] The activity described in this paper provided an opportunity to use iSpartan for this purpose.

Received: September 8, 2020
Revised: December 29, 2020
Published: January 27, 2021

https://dx.doi.org/10.1021/acs.jchemed.0c01134
J. Chem. Educ. 2021, 98, 982−985

Table 1. Possible Products for the Dehydration of 2- and 4-Methylcyclohexanol and Related Energies[a]

Products and Energies for the Dehydration of 2-Methylcyclohexan-1-ol			
	1-Methylcyclohexene	3-Methylcyclohexene	Methylenecyclohexene
Spartan, Gibbs energy of reaction	−3.10	6.69	8.23
iSpartan, heat of formation	−41.4	−33.5	−33.1
iSpartan, steric energy	16.0	27.2	30.9
Products and Energies for the Dehydration of 4-Methylcyclohexan-1-ol			
	1-Methylcyclohexene	3-Methylcyclohexene	4-Methylcyclohexene
Spartan, Gibbs energy of reaction	−3.86	5.93	3.57
iSpartan, heat of formation	−41.4	−33.5	−35.0
iSpartan, steric energy	16.0	27.2	30.0

[a]Energies calculated in Spartan and iSpartan as indicated. The Gibbs energy was calculated at 373.1 K, the minimum temperature utilized by the students for the wet lab portion of the experiment. iSpartan energies are calculated at 298 K. All energies are reported as kJ/mol.

THE ACTIVITY

Five sections of the Organic Chemistry I Laboratory are offered in the fall semester. Each section enrolls a maximum of 16 students. The laboratory courses are taught independently of the lecture course. That is, the delivery of content in the laboratory is not correlated with the lecture course schedule. Over the past decade, the first-semester organic chemistry laboratory at Spelman College has evolved from having a minimal technology presence to using technology as an integral tool for disseminating information, performing assessments, and allowing students to track their progress. For the activity described here, course information was disseminated through the learning management system (LMS). Background information on the laboratory and experimental instructions were provided to students through PowerPoint files accessible through the LMS. Students are required to review the material, along with the information provided in the laboratory manual, before the laboratory period. Prelaboratory quizzes focused on experiment-specific safety and techniques are administered online as well.

The dehydration of alcohols can proceed through a concerted pathway, the E2 mechanism, or through a two-step E1 mechanism involving the ionization of the C−O bond. The latter has the potential to produce a more stable molecule due to the possibility of carbocation rearrangements. For the dehydration of 2-methylcyclohexanol, it has been shown that the presence of minor products increases as the reaction progresses, a phenomenon referred to affectionately as the Evelyn effect.[19] Further kinetic and mechanistic studies have characterized this reaction as *E2-like* with some possible *E1 character*.[20,21] Therefore, the reaction should yield products localized to the α and β carbons defined by the hydroxyl group, *E2-like*. However, minor products appear from carbocation formation and rearrangement, *E1 character*. Although the experiment is straightforward to perform, interpreting the results can be an intricate process.

For this activity, the dehydration of methylcyclohexanols, students were given the experimental procedure but had to determine the outcome of the experiment and explain the product ratio based on computational data. Table 1 shows the energy data for the dehydration of 2-methylcyclohexanol and 4-methylcyclohexanol. The wet lab and computational components were completed by students independently over a period of 2 weeks. Half of the students were assigned the starting molecule 2-methylcyclohexanol, while the other half were assigned 4-methylcyclohexanol as the starting reagent. In week 1, the experiment began with a distillation during which students collect an 8 mL fraction of distillate followed by a 6 mL fraction. The following week, both fractions were analyzed using gas chromatography (GC) to determine the ratio and identity of products formed. Students also utilized iSpartan to draw the two-dimensional structure of each possible product. The structures were transferred to the three-dimensional space in the app where the structures were energy minimized and the steric energies and heat of formations were determined.

Students utilized iSpartan during the laboratory period through a classroom set of iPads (40 total), allowing each student to complete their own calculations. The iSpartan app extracts information from the Spartan Spectra and Properties Database, supplying computational information on more than 5,000 molecules (including chemical properties, NMR and IR spectra data, and orbitals and electrostatic potential maps). Conformational analysis in the iSpartan app utilizes molecular mechanics and provides instantaneous results on the energy minimized conformation of the molecule.[22] The app generates total energies using density functional theory, and for most organic molecules, it also provides an estimated heat of formation using the T1 thermochemistry recipe.[23] On the basis of a combination of quantum chemical models and empirical parameters, the T1 calculation reproduces heats of formation obtained from the G3(MP2) Model using 2−3 orders of magnitude less computation. T1 reproduces experimental heats with an RMS error of ∼8 kJ/mol, the same error as obtained from the G3(MP2) Model.[23] The laboratory activity described here can be adapted for use with WebMO, Mobile Molecular Modeling (-Mo3), or other comparable software. Both WebMO and -Mo3 are available on Android devices, and -Mo3 is free.

To aid the interpretation of the GC results, students were supplied with a reference spectrum. 3- and 4-Methylcyclohexanol are not resolved on the GC being used, and methylenecyclohexane is not formed in any significant quantities.[24] The students used the steric energy generated by iSpartan to describe the relative stabilities of the products present in each fraction. The heat of formation can also be obtained from the app. However, care must be taken to ensure that students understand the limits of this calculation. There is the potential that products are formed by different mechanistic routes, carbocation rearrangements, or isomerization. Therefore, instructor intervention may be needed to ensure that students understand the context and utility of the energy calculation.

https://dx.doi.org/10.1021/acs.jchemed.0c01134
J. Chem. Educ. 2021, 98, 982−985

REFLECTIONS ON STUDENT LEARNING

The Institutional Review Board approved this work at Spelman College. Students provided informed consent before data collection began. To ensure students' anonymity, identifying information was removed from all student work and replaced with participant codes before analysis. Students included here completed the course during the fall semesters in 2013, 2014, 2015, 2016, and 2017. More than 400 students completed the activity, but only 109 lab reports were reviewed to assess the implementation of the activity.

Handwritten student laboratory reports were scanned and analyzed within Atlas.ti, a qualitative data analysis tool that allowed for the coding of student responses. Statements were coded to determine how students explained the relative stability of isomers based on the iSpartan generated energy data, GC results, and the relationship of this information to the product distribution. The portion of a student's discussion that aligned with a given code was highlighted. Once all reports were coded, Atlas.ti tallied the instances of each code across all laboratory reports. Only one instance of a given code was counted per report. A full list of codes used to characterize students' discussion of the results is detailed in the Supporting Information.

A majority of students (85.3%) were able to identify 1-methylcyclohexene as the isomer with the lowest relative energy and noted that this lower relative energy coincided with it being the most stable isomer. Students also recognized that 1-methylcyclohexene was the most abundant product for those using 2-methylcyclohexane. For those using 4-methylcyclohexanol, 1-methylcyclohexene is a minor product. However, explaining this outcome required instructor intervention. Nevertheless, 78.9% of students attempted to address the GC results and their relationship to Zaitsev's rule or product stability, with 55.8% of these doing so successfully. A sample student response from the discussion portion of the lab report as follows:

> *"Because the formation of these two alkenes came from 2-methylcyclohexanol as the starting material, the reaction supports Zaitsev's rule. This reaction also supports the Evelyn effect. 1-Methylcyclohexene had the highest peak on the chromatogram as well as the lowest energy. It is the most stable of the molecules and is produced in the largest yield."*
>
> *"Since 4-methylcyclohexanol was used as the starting material, through reviewing notes on Zaitsev's rule it was concluded that the formation of products follows the rule...the Evelyn effect is not represented in the dehydration of 4-methylcyclohexanol."*

REFLECTIONS ON TEACHING STRATEGIES AND LESSONS LEARNED

The laboratories at Spelman College are undergoing revisions to become more inquiry-based.[25−27] Those efforts have allowed us to revisit the dehydration of methycyclohexanols experiment. The points offered here are a result of these efforts.

1. *Give students an unknown methylcyclohexanol.* Students can make a hypothesis about the major product that will form for the reactions with 2-methylcyclohexanol and 4-methylcyclohexanol. Students can determine their unknown from the GC analysis. This approach can reinforce students' understanding of the E2 mechanics, particularly the location of the elimination and the product outcomes based on Zaitsev's rule.
2. *Give students a known methylcyclohexanol.* Students can make an inference about the identity of their major product and confirm with GC and iSpartan analysis. This option provides less opportunity for the type of critical analysis of the regiochemistry that can occur with option 1 above. However, it does reinforce students' knowledge of Zaitsev's rule and the relationship between steric energy and the compound's stability.
3. *Examine the product ratio analysis.* The outcomes observed by students provide an opportunity to reinforce the competition that occurs between mechanistic pathways. This experiment points toward the competition between the E2 and E1 mechanisms for the reaction involving 4-methylcyclohexanol. Without providing information on the Evelyn effect, ask students to analyze the product ratios from their two fractions, and explain mechanistically any unexpected products.
4. *Have a small group discussion.* Form student groups, either 2 or 4 person groups, pairing students with opposing starting materials. Students can compare outcomes and have an opportunity to challenge misconceptions about the reaction as well as outcomes that result from experimental error. Students could also be asked to consider why the Evelyn effect is relevant for the dehydration involving 4-methylcyclohexanol but not 2-methylcyclohexanol. The group discussion can be summarized as part of their laboratory write-up.

CONCLUSION

iSpartan provides students a user-friendly way to generate energy data that can be used to communicate their rationale of the reaction results. The information also reinforces students' knowledge of the relationship between the energies of a series of molecules and their relative stabilities. It also adds an additional measure of inquiry to the experiment. The teaching strategies and lessons learned provide options for customizing this activity to complement other concepts that could be introduced using this activity.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available at https://pubs.acs.org/doi/10.1021/acs.jchemed.0c01134.

Guidelines for results, discussion, and conclusion (PDF)

AUTHOR INFORMATION

Corresponding Author

Shanina Sanders Johnson − *Department of Chemistry and Biochemistry, Spelman College, Atlanta, Georgia 30314, United States;* orcid.org/0000-0002-7799-9858; Email: ssande15@spelman.edu

Authors

Leyte Winfield − *Department of Chemistry and Biochemistry, Spelman College, Atlanta, Georgia 30314, United States;* orcid.org/0000-0003-3719-5895

Shannon H. Sung − *Institute for Future Intelligence, Natick, Massachusetts 01760, United States;* orcid.org/0000-0001-5704-2920

https://dx.doi.org/10.1021/acs.jchemed.0c01134
J. Chem. Educ. 2021, 98, 982−985

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.jchemed.0c01134

Author Contributions

[§]S.S.J. and L.W. share first authorship for this work.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The work is funded in part by the National Science Foundation Award Numbers 1332575, 1626002, and HRD-1912385. The content is solely the responsibility of the authors and does not necessarily represent the official views of the funding agencies listed.

■ REFERENCES

(1) American Chemical Society Committee on Professional Training. ACS Guidelines for Bachelor's Degree Programs. https://www.acs.org/content/dam/acsorg/about/governance/committees/training/2015-acs-guidelines-for-bachelors-degree-programs.pdf (accessed Jul 25, 2020).

(2) Cheng, G.-J.; Zhang, X.; Chung, L. W.; Xu, L.; Wu, Y.-D. Computational Organic Chemistry: Bridging Theory and Experiment in Establishing the Mechanisms of Chemical Reactions. *J. Am. Chem. Soc.* **2015**, *137* (5), 1706−1725.

(3) Sperger, T.; Sanhueza, I. A.; Schoenebeck, F. Computation and Experiment: A Powerful Combination to Understand and Predict Reactivities. *Acc. Chem. Res.* **2016**, *49* (6), 1311−1319.

(4) Dunlap, N.; Martin, L. J. Discovery-Based Labs for Organic Chemistry: Overview and Effectiveness. *ACS Symp. Ser.* **2012**, *1108*, 1−11.

(5) Baker, J. P. Combining Molecular Modeling with 13C and DEPT NMR Spectroscopy to Examine the Dehydration of 1-Methylcyclohexanol. *In NMR Spectroscopy in the Undergraduate Curriculum: First Year and Organic Chemistry Courses Volume 2*; ACS Symposium Series; American Chemical Society: Washington, DC, 2016; Vol. *1221*, pp 99−106. DOI: 10.1021/bk-2016-1221.ch007.

(6) Csizmar, C. M.; Daniels, J. P.; Davis, L. E.; Hoovis, T. P.; Hammond, K. A.; McDougal, O. M.; Warner, D. L. Modeling S_N2 and E2 Reaction Pathways and Other Computational Exercises in the Undergraduate Organic Chemistry Laboratory. *J. Chem. Educ.* **2013**, *90* (9), 1235−1238.

(7) Hein, S. M.; Kopitzke, R. W.; Nalli, T. W.; Esselman, B. J.; Hill, N. J. Use of ^{1}H, ^{13}C, and ^{19}F-NMR Spectroscopy and Computational Modeling To Explore Chemoselectivity in the Formation of a Grignard Reagent. *J. Chem. Educ.* **2015**, *92* (3), 548−552.

(8) Hii, K. K. M.; Rzepa, H. S.; Smith, E. H. Asymmetric Epoxidation: A Twinned Laboratory and Molecular Modeling Experiment for Upper-Level Organic Chemistry Students. *J. Chem. Educ.* **2015**, *92* (8), 1385−1389.

(9) Schuster, M. L.; Peterson, K. P.; Stoffregen, S. A. Isobutylene Dimerization: A Discovery-Based Exploration of Mechanism and Regioselectivity by NMR Spectroscopy and Molecular Modeling. *J. Chem. Educ.* **2018**, *95* (6), 1040−1044.

(10) Hill, N. J.; Bowman, M. D.; Esselman, B. J.; Byron, S. D.; Kreitinger, J.; Leadbeater, N. E. Ligand-Free Suzuki−Miyaura Coupling Reactions Using an Inexpensive Aqueous Palladium Source: A Synthetic and Computational Exercise for the Undergraduate Organic Chemistry Laboratory. *J. Chem. Educ.* **2014**, *91* (7), 1054−1057.

(11) Amick, A. W.; Cross, N. An Almost Paperless Organic Chemistry Course with the Use of IPads. *J. Chem. Educ.* **2014**, *91* (5), 753−756.

(12) Morsch, L. A.; Lewis, M. Engaging Organic Chemistry Students Using ChemDraw for IPad. *J. Chem. Educ.* **2015**, *92* (8), 1402−1405.

(13) Morsch, L. A. Flipped Teaching in Organic Chemistry Using IPad Devices. In *The Flipped Classroom Volume 1: Background and Challenges*; ACS Symposium Series; American Chemical Society: Washington, DC, 2016; pp 73−92. DOI: 10.1021/bk-2016-1223.ch006.

(14) Balija, A. M.; Morsch, L. A. Inquiry-Based IR-Spectroscopy Activity Using ISpartan or Spartan for Introductory-Organic-Chemistry Students. *J. Chem. Educ.* **2019**, *96* (5), 970−973.

(15) Silverberg, L. J. Use of Doceri Software for IPad in Polycom and Resident Instruction Chemistry Classes. *J. Chem. Educ.* **2013**, *90* (8), 1087−1089.

(16) Winfield, L. L.; McCormack, K.; Shaw, T. Using ISpartan To Support a Student-Centered Activity on Alkane Conformations. *J. Chem. Educ.* **2019**, *96* (1), 89−92.

(17) Kozma, R. The Material Features of Multiple Representations and Their Cognitive and Social Affordances for Science Understanding. *Learn. Instr.* **2003**, *13* (2), 205−226.

(18) Boo, H. K. Students' Understandings of Chemical Bonds and the Energetics of Chemical Reactions. *J. Res. Sci. Teach.* **1998**, *35* (5), 569−581.

(19) Todd, D. The Dehydration of 2-Methylcyclohexanol Revisited: The Evelyn Effect. *J. Chem. Educ.* **1994**, *71* (5), 440.

(20) Cawley, J. J.; Linder, P. E. The Acid Catalyzed Dehydration of an Isomeric 2-Methylcyclohexanol Mixture A Kinetic and Regiochemical Study of the Evelyn Effect. *J. Chem. Educ.* **1997**, *74* (1), 102.

(21) Friesen, J. B.; Schretzman, R. Dehydration of 2-Methyl-1-Cyclohexanol: New Findings from a Popular Undergraduate Laboratory Experiment. *J. Chem. Educ.* **2011**, *88* (8), 1141−1147.

(22) Halgren, T. A. Merck Molecular Force Field. I. Basis, Form, Scope, Parameterization, and Performance of MMFF94. *J. Comput. Chem.* **1996**, *17* (5−6), 490−519.

(23) Ohlinger, W. S.; Klunzinger, P. E.; Deppmeier, B. J.; Hehre, W. J. Efficient Calculation of Heats of Formation. *J. Phys. Chem. A* **2009**, *113* (10), 2165−2175.

(24) Clennan, M. M.; Clennan, E. L. Dehydration of Methylcyclohexanol Isomers in the Undergraduate Organic Laboratory and Product Analysis by Gas Chromatography-Mass Spectroscopy (GC-MS). *J. Chem. Educ.* **2011**, *88* (5), 646−648.

(25) Scott, P.; Pentecost, T. C. From Verification to Guided Inquiry: What Happens When a Chemistry Laboratory Curriculum Changes? *Journal of College Science Teaching* **2013**, 82−88.

(26) Mohrig, J. R.; Hammond, C. N.; Colby, D. A. On the Successful Use of Inquiry-Driven Experiments in the Organic Chemistry Laboratory. *J. Chem. Educ.* **2007**, *84* (6), 992.

(27) Bretz, S. L.; Galloway, K. R.; Orzel, J.; Gross, E. Faculty Goals, Inquiry, and Meaningful Learning in the Undergraduate Chemistry Laboratory. *Technology and Assessment Strategies for Improving Student Learning in Chemistry*; American Chemical Society: Washington, DC, 2016; pp 101−115. DOI: 10.1021/bk-2016-1235.ch006.