

Cis and Trans Isomerization in Cyclic Alkenes: A Topic for Discovery Using the Results of Molecular Modeling

W

Susan E. Barrows and Thomas H. Eberlein*

School of Science, Engineering, and Technology, Penn State Schuylkill, The Capital College, Schuylkill Haven, PA 17972;
*the1@psu.edu

Creative use of commercially available molecular modeling software to illustrate important chemical concepts is growing in popularity. At least 20 articles in this *Journal* alone over the past five years refer to the use of Spartan (1) and similar programs as educational tools. Several representative examples are shown in reference 2. In this article we describe an activity in which students explore the fundamental reasons behind the unusual instability of the trans isomers in medium-sized cycloalkenes by using the results of molecular modeling.

Using molecular modeling to examine cycloalkenes is not unprecedented. Hehre and others have proposed exercises that explore the structures of cycloheptene and cyclooctene (3). The distinctive features of our work lie in the discoveries the students are encouraged to make as they investigate and identify the specific sources of strain in cis versus trans cycloalkenes. In this exercise, discrepant events figure prominently in the learning process (4). Among the surprising findings students will make is the relative ease with which strained double bonds will twist and pyramidalize. We hope this exercise can help to disabuse students of the widespread misperception that alkenes are unyieldingly rigid and planar.

Background for the Exercise

Early in most organic chemistry courses students learn how conformations affect the energy of a molecule (5). For example, in systems that can exhibit free rotation, eclipsed conformers have higher energy than staggered ones. In cyclic molecules, one must consider additional factors that influence the stability of different conformations. These include bond angle strain, unavoidable eclipsing interactions (torsional strain), and several other types of repulsion, such as 1,3-diaxial interactions in substituted cyclohexanes, or transannular interactions in medium-sized rings.

When shifting focus to the structure and reactivity of alkenes, new determinants influencing stability come into play. These are due in part to the relative rigidity of the π system and the reduction in conformational mobility that the π bond introduces. In an effort to summarize the consequences of the geometric constraints enforced by the π bond, many introductory textbooks¹ state or imply a number of generalizations.

π Bond Generalizations

- Alkenes are planar at the double bond.
- Twisting around a C=C double bond breaks the π bond.
- Trans disubstituted alkenes are more stable than their cis counterparts.

Like most generalizations, these “rules” are oversimplifications. The purpose of this molecular modeling exercise is to point out where and why exceptions to the rules occur.

Implementing the Modeling Exercise

Learning Goals

We have several learning goals for students. By completing this exercise, students will:

- Review the factor(s) leading to differences in stability between cis and trans isomers of acyclic alkenes.
- Use the results of molecular modeling studies on cis and trans cycloalkenes (C7–C10) to explore and understand the reasons behind the unusual (relative) instability of the trans isomers in this series. Sources or manifestations of strain in the trans compounds include:
 - twisting about the C=C bond and pyramidalization of the sp^2 carbons, leading to decreased π -bond strength;
 - lengthening of certain C–C bonds; and
 - distortions from ideal C–C–C bond angles.
- Learn that alkene double bonds are not necessarily inflexible and rigidly planar.
- Compare molecular modeling data on heats of hydrogenation of cycloalkenes with corresponding data from the laboratory and note that the close agreement between these data sets lends credence to the notion that molecular modeling data are reliable.

The Exercise

We have found it most effective to implement the modeling exercise as a laboratory activity during the second semester of a one-year sequence in organic chemistry.² In this exercise, students use Spartan to make explicit comparisons

between and among each of the following *cis*–*trans* pairs of cyclic alkenes: cycloheptene, cyclooctene, cyclononene, and cyclodecene (Figure 1). It is important to note that students do not do molecular modeling *per se* to construct the optimized geometries of these molecules. Instead, files containing the pre-optimized geometries are made available to the students.^{3, 4}

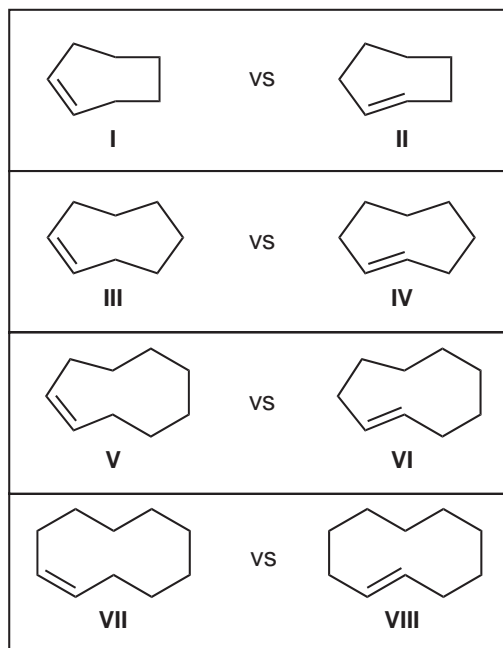


Figure 1. Cycloalkene compounds for which students are to predict the relative stability of each pair of isomers: I and II; III and IV; V and VI; and VII and VIII. Compounds on the left are drawn to show the *cis* isomer and compounds on the right show the *trans* isomer.

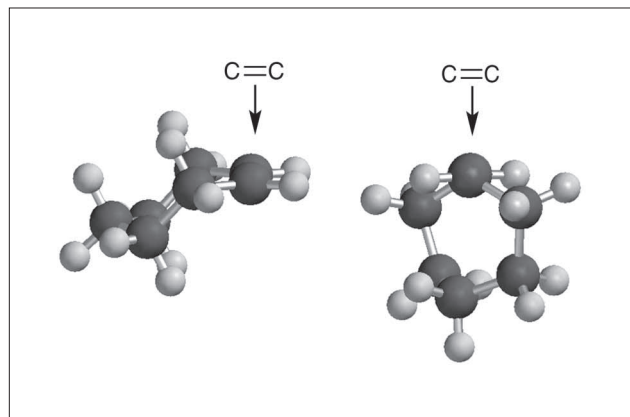


Figure 2. A view down the C=C bond axis of the Spartan models of *cis*- and *trans*-cycloheptene (left and right, respectively). In both models the two carbons are superimposed. Note the angle between the C–H and C–C bonds of the alkene. The decidedly nonplanar nature of the alkene can easily be seen for the *trans* isomer.

The activity is administered in four parts:

1. Students are given a brief review of alkane conformations, cycloalkanes, and the electronic nature of an alkene π bond.
2. Students work in pairs to review the reason why the 2-butene isomers have unequal energies; then they select which member of each pair of cycloalkene isomers pictured in Figure 1 they believe is more stable.
3. Students use Spartan to examine the structures of the cycloalkene isomers to discover the unanticipated fact that, for medium-sized cycloalkenes, *cis* isomers are more stable than *trans*. They use the structural data they gather in this exploration to develop a theoretical basis to justify the results. (For example, the cycloheptenes are depicted in Figure 2; the *trans* isomer clearly shows substantial geometric distortion around the double bond.)
4. Students calculate the actual relative stability of these isomeric pairs based on both laboratory and computed heat of hydrogenation data. The experimental data confirm and support the findings they made in the molecular modeling study. Students also use trends in these data to predict energy differences between isomeric pairs in ring sizes both larger and smaller than those they studied explicitly.

Specific details of the activity, including problems for the students are available in the Supplemental Material.^W Details regarding specific aspects of the implementation are also available in the Supplemental Material in the Instructor Notes.^W

Results

Before examining the Spartan files, our students, by a ratio of greater than 6:1, choose the *trans* isomer in each case to be more stable.⁵ Their reasoning is that *trans* alkenes are always more stable than *cis*, owing to steric repulsion between the alkyl substituents in the *cis* compounds. Upon further investigation of these molecules (provided in a MacSpartan format), however, students observe and report on the following unexpected structural features of the *trans* isomers:

- Bond angles that are nonideal: For example, in the *trans* isomers of cycloheptene and cyclooctene, students find bond angles for tetrahedral carbons that are both appreciably smaller, or appreciably larger, than 112° .⁶
- Bond lengths that are unusual: the longest C–C bond in *cis*-cycloheptene is $1.538 \pm 0.001 \text{ \AA}$, whereas the longest C–C bond in *trans*-cycloheptene is 1.575 \AA .
- Twisting of the double bond and slight pyramidalization of the sp^2 carbons: these effects are especially profound in *trans*-cycloheptene and *trans*-cyclooctene. For beginning students these distortions constitute perhaps the most disconcerting aspect of the unusual molecular geometries of the cycloalkenes.

By the end of the exercise, students understand (and can explain)⁷ how the factors listed above conspire to render the

trans compounds less stable than their cis counterparts in each of the isomeric pairs shown in Figure 1. This surprising result constitutes a “discrepant event” (4), and making the effort to understand it offers students an opportunity to develop a deeper and more sophisticated comprehension of the underlying organic chemistry. By working through this exercise in a guided-inquiry (6, 7) mode, we hope students will revise their mental picture of the supposed conformational immobility of the alkene functional group before it gets too deeply ingrained.

Computational Methods

Geometry optimization calculations and frequency calculations were carried out using MacSpartan Pro (1) and Titan (8). Additional details regarding the choice of computational methods and the sequence of calculations can be found in the Supplemental Material in the Instructor Notes.^W During the exercise, students use SpartanView to manipulate and obtain data from the optimized models. Each student has a personal copy of the SpartanView software, which was included in the textbook (5, McMurry, 5th ed.). Other file formats are available as well (see the Supplemental Materials^W).

Conclusion

As discussed in the introduction, careful examination of the models leads to the discovery of four types of nonideality in the optimized geometry of the trans isomer of cycloheptene, cyclooctene, cyclononene, and (to a lesser extent) cyclodecene that are not found in the cis isomer:

- Twisted π bonds
- Pyramidal sp^2 carbon atoms
- Nonideal sp^3 bond angles
- Unusually long C–C bonds (cycloheptene and cyclooctene only)

Based on deeply-ingrained assumptions as to the structure and rigidity of a π bond, the authors, in preparing this activity for student use, found the distortions that occur at the π bond in the trans cycloalkenes to be the most surprising of the four effects. Perhaps this should not have been a surprise: Mislow (9) concluded that whenever any asymmetry exists in an alkene, some distortion from ideal (planar) geometry must occur. Thus, one of our main goals in presenting this exercise is to help students understand the nature of the geometrically distorted alkene, and to this end we use the cycloalkenes as a case study. For readers wishing additional details, we have submitted two separate manuscripts in which we provide further information regarding specific consequences of geometric distortions in alkenes. One article examines changes in the π system in model studies of *trans*-2-butene with enforced nonideal geometry (10), while the other article provides a more detailed look at the cycloalkenes and related systems (11).

^WSupplemental Material

Supplemental materials include the guided-inquiry Student Exercise. There are also Instructor Notes describing the

implementation of the exercise, details regarding the choice of molecular modeling techniques, and answers for the student exercise. Additional online materials, including files of the optimized geometries of the cycloalkene models, may be found at <http://www.personal.psu.edu/seb16/cycloalkenes> (accessed Jun 2004). Three file formats are provided: *.xyz for use with the Chemscape Chime plug-in; *.pdb for use with Chem 3D; and *.sxf for use with Spartan, SpartanView, or Titan.

Notes

1. We do not wish to imply that no introductory textbooks deal with the issue of trans cycloalkenes. The texts by Hornback and by Brown and Foote (12) both refer to ring strain, cis cycloalkene stability, and the reversal of stability for large cycloalkenes. We are grateful to an anonymous reviewer for calling our attention to these texts. Likewise an exception is found in Carey (5), who suggests a brief molecular modeling exercise involving the cis and trans isomers of cyclooctene. Oddly, however, this exercise prompts students to examine the H–C=C–H dihedral angles—which are barely distorted at all, according to our results—and neglects an examination of the remarkable distortions in the C–C=C–C dihedral angles.

2. Initially we had administered a briefer version of this exercise during the first semester, immediately after the textbook coverage of alkene geometry and electronic properties. Several reviewers pointed out that first-semester students’ understanding of organic chemistry might not be developed to the point where they can fully appreciate the rules, much less the exceptions. We are unaware whether our original practice caused any problems for our students. However, we do concur with the reviewers that is a better strategy to let the rules sink in for a semester (at least), before presenting the exceptions. We now conduct this exercise as a laboratory activity during the second semester. We believe the exercise could also be used effectively as part of an advanced organic laboratory course, although we have not used it for that purpose ourselves.

3. Our students have several opportunities throughout the year to learn how to do molecular modeling on simpler systems that will give reliable results. It is not our intention in this particular exercise to teach molecular modeling. Instead, we wish to use the results of molecular modeling to help students learn an important concept.

4. Finding the lowest energy conformer for each of the rings is not a trivial matter. The minimum energy conformers reported here (and available in the Supplemental Materials^W) are consistent with the experimentally determined structures (13). Attempts to have students perform geometry optimization calculations at the AM1 level led to significant errors, defeating the purpose of the exercise. This problem is described in more detail in the Supplemental Material in the Instructor Notes.^W In this context we note the following caveat from Cramer and coworkers (14), and we heed his advice: “Computational chemistry software has become increasingly affordable and user-friendly, making it simple for beginners to take advantage of sophisticated methods for predicting molecular properties. (Of course, it also makes it simple for beginners to do phenomenally misguided calculations and misinterpret their artifactual results...)”

5. Amusingly, the few students who did indicate they thought the cis cycloalkenes would be more stable than the trans isomers

could not supply a theoretical reason for their belief. Instead, the “explanations” were more along the lines of, “We knew you wouldn’t bother asking this question unless there was something unusual about the cycloalkenes, and so we guessed that the normal stability pattern was reversed.”

6. One should not expect 109.5° C–C–C bond angles for tetrahedral carbon. For example, the central bond angle in propane (112°) is somewhat larger than the tetrahedral angle.

7. Seventeen students participated in this exercise in spring 2003, after which a closed-book quiz was administered. All of the students correctly answered the question “What is the largest ring size for which cis cycloalkenes are more stable than trans?” Most students (percent correct in parentheses) were able to identify the important sources of strain in medium-sized trans cycloalkenes. They cited “bond angle strain” (94%), “twisted π bonds” or “unusually small C–C=C–C dihedral angles” (88%), “unusually long C–C bonds” (59%), “distorted HOMOs” (53%), and “pyramidalized alkene carbons” (41%). Somewhat disconcertingly, several students cited incorrect reasons as well: “steric repulsion” (18%) and “torsional strain” (12%). Perhaps these were leftover misconceptions from before the exercise. Or worse, perhaps these students were just mentioning as many forms of strain as they could remember, without considering whether they pertained to the trans cycloalkenes. See Instructor Notes¹¹ for further details concerning evidence of student learning gains.

Literature Cited

- MacSpartanPro, ver. 5.1, Wavefunction, Inc., 18401 Von Karman, Suite 370, Irvine, CA, 91612.
- Shusterman, G. P.; Shusterman, A. J. *J. Chem. Educ.* **1997**, *74*, 771–776. Poon, T.; Bodolosky, S. A.; Norris, C. M. *J. Chem. Educ.* **1999**, *76*, 983–985. Klassen, J. B.; Graham, K. J.; Muldoon, W. P. *J. Chem. Educ.* **1999**, *76*, 985–986. Cook, A. G.; Kreeger, P. K. *J. Chem. Educ.* **2000**, *77*, 90–92. Hessley, R. K. *J. Chem. Educ.* **2000**, *77*, 202–203. Hessley, R. K. *J. Chem. Educ.* **2001**, *78*, 1183. Lipkowitz, K. B.; Robertson, D. J. *J. Chem. Educ.* **2000**, *77*, 206–209. Graham, K. J.; Skoglund, K.; Schaller, C. P.; Muldoon, W. P.; Klassen, J. B. *J. Chem. Educ.* **2000**, *77*, 396–397. Freeman, F.; Tsegai, Z. M.; Kasner, M. L.; Hehre, W. J. *J. Chem. Educ.* **2000**, *77*, 661–667. Hessley, R. K. *J. Chem. Educ.* **2000**, *77*, 794–797. Hull, L. A. *J. Chem. Educ.* **2001**, *78*, 420–421. Sanger, M. S.; Badger, S. M. *J. Chem. Educ.* **2001**, *78*, 1412–1417. Wladkowski, B. D.; Broadwater, S. J. *J. Chem. Educ.* **2002**, *79*, 230–233. Poon, T.; Mundy, B. P.; Shattuck, T. W. *J. Chem. Educ.* **2002**, *79*, 264–267. Cody, J. A.; Wisner, D. C. *J. Chem. Educ.* **2003**, *80*, 793–795.
- Hehre, W. J.; Shusterman, A. J.; Nelson, J. E. *The Molecular Modeling Workbook for Organic Chemistry*; Wavefunction Inc.: Irvine, CA, 1998; Chapter 7.
- Bodner, G. M. *J. Chem. Educ.* **1986**, *63*, 873–878. Shiland, T. W. *J. Chem. Educ.* **1999**, *76*, 107–112. Herron, J. D.; Nurrenbern, S. C. *J. Chem. Educ.* **1999**, *76*, 1353–1361. Libby, R. D. *J. Chem. Educ.* **1995**, *72*, 626–631. Spencer, J. N. *J. Chem. Educ.* **1999**, *76*, 566–569. Farrell, J. J.; Moog, R. S.; Spencer, J. N. *J. Chem. Educ.* **1999**, *76*, 570–574. DeMeo, S. J. *J. Chem. Educ.* **2002**, *79*, 474–475.
- McMurry, J. *Organic Chemistry*, 5th ed.; Brooks/Cole: Pacific Grove, CA, 2000. Bruice, P. Y. *Organic Chemistry*, 3rd ed.; Prentice Hall: Upper Saddle River, NJ, 2001. Ege, S. *Organic Chemistry*, 3rd ed.; D. C. Heath and Company: Lexington, MA, 1994. Wade, L. G. *Organic Chemistry*, 3rd ed.; Prentice Hall: Upper Saddle River, NJ, 1995. Carey, F. A. *Organic Chemistry*, 5th ed.; McGraw-Hill: New York, 2003.
- Domin, D. *J. Chem. Educ.* **1999**, *76*, 543–547.
- Ditzler, M. A.; Ricci, R. W. *J. Chem. Educ.* **1994**, *71*, 685–688. See also <http://creegan.washcoll.edu/gilabs/> (accessed Jun 2004).
- Titan, ver. 1.0.5, Wavefunction, Inc., 18401 Von Karman, Suite 370, Irvine, CA, 91612 and Schrödinger, Inc., 1500 S.W. First Avenue, Suite 1180, Portland, OR 97201-5815.
- Mislow, K. *Introduction to Stereochemistry*; W. A. Benjamin: New York, 1965; pp 1–15.
- Barrows, S. E.; Eberlein, T. H. *J. Chem. Educ.*, submitted for publication, 2003.
- Barrows, S. E.; Eberlein, T. H. *J. Chem. Educ.*, submitted for publication, 2004.
- Hornback, J. M. *Organic Chemistry*, 1st ed.; Brooks/Cole: Pacific Grove, CA, 1998; p 210. Brown, W. H.; Foote, C. S. *Organic Chemistry*, 3rd ed.; Brooks/Cole: Pacific Grove, CA, 2002; p 167.
- (cis-octene) Mastryukov, V. S.; Chen, K.; Allinger, N. L. *J. Phys. Chem. A* **2001**, *105*, 8562–8566. (trans-octene) Cope, A. C.; Moore, P. T.; Moore, W. R. *J. Am. Chem. Soc.* **1959**, *81*, 3153. Ermer, O.; Mason, S. A. *Acta Cryst.* **1982**, *B38*, 2200–2206. Trættemberg, M. *Acta Chemica Scandinavica* **1975**, *B29*, 29–36. (cis-cyclononene) Pawar, D. M.; Miggins, S. D.; Smith, S. V.; Noe, E. A. *J. Org. Chem.* **1999**, *64*, 2418–2421. (cis-cyclodecene) Pawar, D. M.; Noe, E. A. *J. Am. Chem. Soc.* **1998**, *120*, 5312–5314. (trans-cyclodecene) Pawar, D. M.; Noe, E. A. *J. Am. Chem. Soc.* **1996**, *118*, 12821–12825.
- Cramer, C. J.; Kormos, B. L.; Winget, P.; Audette, V. M.; Beebe, J. M.; Brauer, C. S.; Burdick, W. R.; Cochran, E. W.; Eklov, B. L.; Giese, T. J.; Jun, Y.; Kesavan, L. S. D.; Kinsinger, C. R.; Minyaev, M. E.; Rajamani, R.; Salsbury, J. S.; Stubbs, J. M.; Surek, J. T.; Thompson, J. D.; Voelz, V. A.; Wick, C. D.; Zhang, L. *J. Chem. Educ.* **2001**, *78*, 1202–1205.