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# Computer-Aided Identification of Symmetry Relating Groups of Molecules

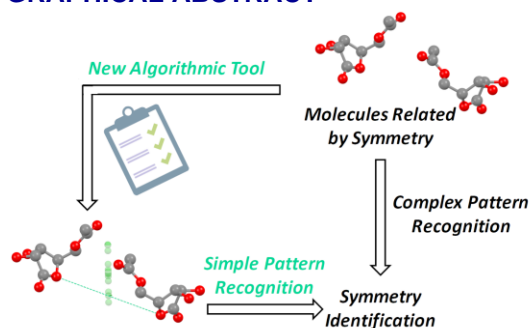
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## ABSTRACT

Molecular symmetry plays an important role in many areas of chemistry, and students are generally taught to identify intramolecular symmetries at the undergraduate level. Intermolecular symmetry, the symmetry among groups of molecules, is of great importance in topics such as X-ray crystallography, but it receives substantially less attention. Even when familiar with such symmetries as translations, screw rotations, and glide reflections, students rarely obtain the same level of proficiency in identifying these symmetries via inspection as they do with the proper and improper rotations involved in point-group symmetry. We describe a tool designed to scaffold the student's ability to mentally manipulate molecules and identify the presence and nature of intermolecular symmetry. The tool consists of an algorithm that the student follows to generate centroids between atoms in putatively symmetry-related molecules. The easily recognized patterns formed by the centroids provide key information about the presence and nature of any intermolecular symmetry relating the molecules. The theoretical basis for the patterns formed by the centroids is provided along with worked examples, an example problem set, and a prescription for generating new exercises.

## GRAPHICAL ABSTRACT



## KEYWORDS

Upper-Division Undergraduate, Graduate Education, Inorganic Chemistry, Computer-Based Learning, Crystallography, Group Theory /Symmetry

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## 25 INTRODUCTION

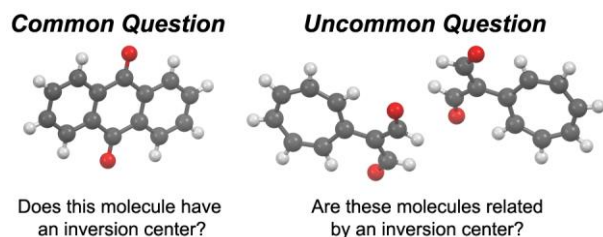
Undergraduate programs in chemistry typically provide students with an introduction to symmetry, including the mathematical formalism of group theory, because of its importance in chemical reactivity and spectroscopy.<sup>1-3</sup> Although surveys of undergraduate chemistry curricula from across the United States have revealed a significant heterogeneity in the manner in which symmetry and group theory are treated,<sup>2-4</sup> they are often considered foundational topics as described in the Inorganic Chemistry Supplement to the Guidelines for Bachelor's Degree Programs prepared by the Committee of Professional Training of the American Chemical Society.<sup>5-6</sup> Students become familiar with the Schönflies notation and the representation of symmetry properties in character tables. They subsequently apply concepts of symmetry and group theory in the contexts of molecular electronic structure (e.g., molecular orbital theory), spectroscopy (e.g., vibrational and electronic), and reactivity (e.g., cyclization reactions).

To fully engage in these chemical applications of symmetry, students are required to gain proficiency in the “mental gymnastics” required to identify the symmetries that map one portion of a molecule onto another.<sup>7-9</sup> Evidence and experience support the hypothesis that this skill is best fostered with active learning exercises using molecular models, computerized modeling software, real-time black/white-board work, and small-group discussion.<sup>10-16</sup> Exercises that employ self-directed, computer-aided study have also provided an important means for students to develop these skills.<sup>17-18</sup>

In the typical curriculum, a heavy, if not exclusive, emphasis is placed on the symmetry of individual molecules, which we will refer to as *intramolecular* symmetry.<sup>3</sup> Far less commonly treated is the concept of *intermolecular* symmetry, the symmetry present within/among a group of molecules. Despite its importance in fields ranging from materials nanoscience to biochemistry,<sup>19</sup> this concept is often only encountered as a special topic in upper-division undergraduate or graduate-level courses. Students commonly encounter particular difficulty with symmetry operations of the second kind (rotoinversions) and symmetries that are a composition of rotation/reflection and translation (screw rotations and glide reflections). A variety of online tools have been developed to help address these and related difficulties.<sup>20-21</sup>

In our experience, we have noticed that although students can gain rapid facility in defining intermolecular symmetries, including screw rotation, glide reflection, rotation, reflection, rotoinversion,

and translation, they do not generally internalize them to the same extent as the intramolecular symmetries encountered in point group determination. For instance, we have observed in a graduate-level X-ray crystallography course that most graduate and senior undergraduate students are comfortable identifying whether a molecule has an inversion center, but many are unable to determine whether a pair of molecules is related by inversion, even when given a computer-manipulatable 3D representation of the molecules (Figure 1). Before continuing, we note that the focus of this paper is not space group assignment but rather the identification of intermolecular symmetry. Even with the use of tangible models,<sup>22</sup> or computerized, manipulatable models,<sup>23</sup> the visual identification of intermolecular symmetry remains a difficult and uncommonly practiced problem.



**Figure 1.** *Left:* A commonly encountered symmetry question. *Right:* An uncommonly encountered symmetry question.

We maintain that it is important for students to viscerally grasp the nature of the symmetries that relate groups of molecules in the same way that they grasp the symmetry within a molecule. At a fundamental level, the spatial reasoning that is exercised when identifying intermolecular symmetry has proved to be an important predictor of success in chemistry more broadly.<sup>10-12</sup> Moreover, active identification of intermolecular symmetry engages the student in cognitive processes that are higher-order than simple memorization of the definitions of these symmetries, which increases the likelihood that this information will be integrated more broadly into their chemistry toolkit.<sup>24</sup> We note that integration of spatial symmetry knowledge into a student's broader chemical skill set can only be successful if their assessments are explicitly linked to clear learning objectives that identify this knowledge integration as an intended outcome of their study.

On the basis of our interactions with both graduate and undergraduate students, we identified two primary difficulties that students encountered when visually identifying intermolecular symmetry: not knowing where to start and not knowing when to stop. Students are often at a loss for where to begin looking for symmetry when presented with an array of molecules instead of a single molecule. The second problem relates to the difficulty in distinguishing between the absence of a symmetry and

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80 an inability to visualize it. For example, a student trying to determine whether or not two molecules are related by a screw rotation may have trouble telling whether the screw rotation is absent or whether they have simply not been able to visualize it yet.

To address these issues, we have developed a tool to aid in identifying intermolecular symmetry. We have thus far restricted ourselves to the screw rotations, rotations, reflections, glide  
85 reflections, rotoinversions, and translations that are consistent with the complete tiling of three-dimensional space. We remind the reader of the nature of the composite symmetry operations: a screw rotation is rotation about an axis followed by translation along that axis; a glide reflection is reflection about a plane followed by translation parallel to that plane; and a rotoinversion is rotation about an axis followed by inversion through a point on that axis. We have elected to use the Hermann-Mauguin  
90 notation as opposed to the Schönflies notation because the latter contains no means of describing symmetries with translational components. In the Hermann-Mauguin notation, the following guidelines apply: a pure rotation is designated as  $M$  and involves rotation of  $360^\circ/M$ ; a screw rotation is designated  $M_n$  and involves rotation of  $360^\circ/M$  followed by translation; a reflection is designated  $m$ , a glide reflection is designated with an italicized letter, the nature of which indicates the direction of  
95 translation, and a rotoinversion is designated as  $\bar{M}$  and involves rotation of  $360^\circ/M$  followed by an inversion.

Our tool consists of an algorithmic, computer-facilitated exercise that the student conducts to scaffold their ability to identify symmetries within a group of molecules. The tool was designed so that the exercise remains a participant-driven, active process as opposed to a passive observation of  
100 animated symmetry operations. So as to not limit the reader to a fixed library of worked examples, we have developed a strategy that allows any group of molecules to be investigated provided that the Cartesian coordinates of the atoms are available. The tool features a well-defined set of algorithmic steps that the student executes, providing them with clear direction on how to start and when to stop searching for a given symmetry. Following the execution of the steps, the student engages in a simple  
105 pattern-recognition exercise that can then be mapped onto the more complex pattern-recognition exercise of *de novo* symmetry identification.

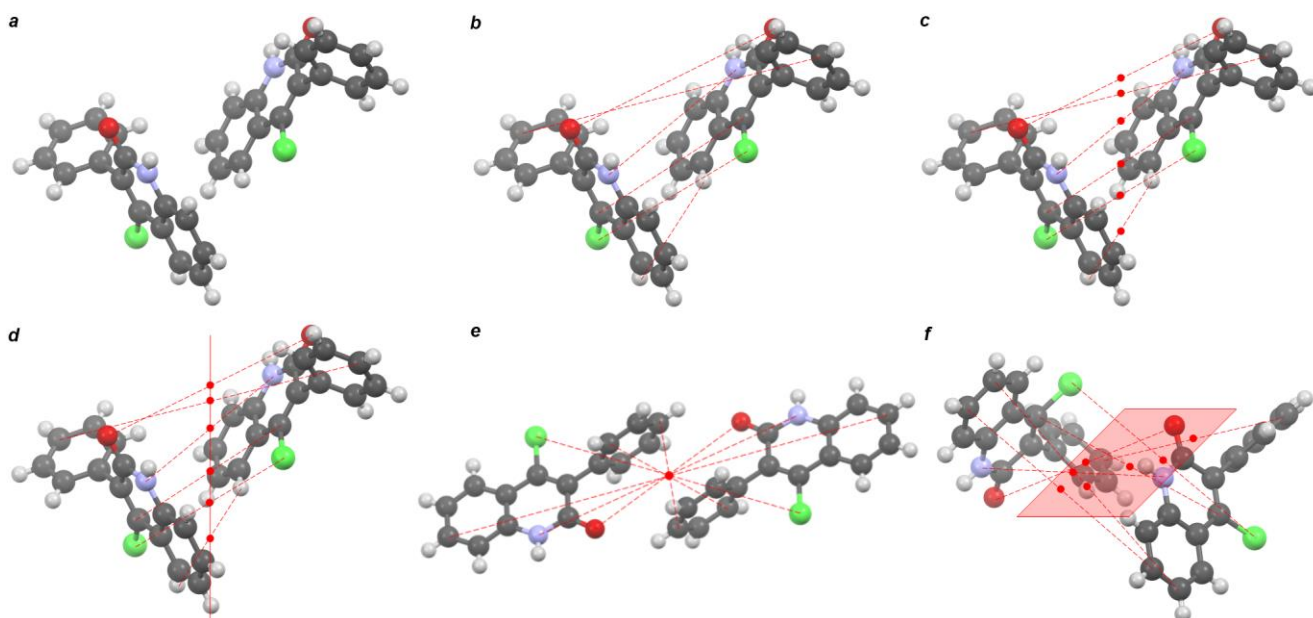
Below we will provide a detailed description of the tool, the theoretical underpinning of the patterns generated when the student conducts the exercise, and a series of worked examples.

Instructions are provided on how to create novel examples. The tool can be used in an upper-division  
110 undergraduate course discussing topics featuring symmetry-related groups of molecules (e.g.,  
supramolecular chemistry, structural biology, inorganic materials, etc.) or graduate-level courses in  
physical inorganic/organic methods, biophysical methods, or X-ray crystallography.

### STRUCTURE OF THE TOOL

The overall structure of the tool comprises the following steps, the first three of which are shown in  
115 cartoon form in Figure 2:

- a) Identify atoms that can be related by symmetry.
- b) Calculate centroids between putatively symmetry-related atoms.
- c) Identify the pattern formed by the centroids and use Table 1 to identify possible symmetries.
- d) Conduct additional tests to determine final symmetry.
- 120 e) Visualize the symmetry that relates the molecules.



**Figure 2.** Schematic depiction of the steps involved in the intermolecular-symmetry-identification tool. a) Two molecules that might be related  
by symmetry. b) Identification of pairs of atoms in the two molecules that could be symmetry related. Pairs of atoms are connected by dashed  
125 red lines. c) Calculation of the midpoints of the lines connecting putatively symmetry-related atoms (centroids between the two atoms).  
Centroids are indicated with red discs. d) Identification of the pattern formed by the centroids. In this case the centroids lie on a line, shown as  
a solid red line connecting the centroids. e) Two molecules in positions different from (a-d). Putatively symmetry-related atoms are connected  
by dashed red lines and centroids are shown as red discs. The centroids all coincide at a single point. f) Two molecules in positions different  
from either (a-d) or (e). Putatively symmetry-related atoms are connected by dashed red lines and centroids are shown as red discs. The  
centroids all lie in a plane which is shown in light red.

130 Some points of clarification or explanation are warranted for each of the points:

- a) It is easiest to begin with atoms that are unique within each molecule. For example, if there is  
only one Br atom in each molecule and the molecules are related by symmetry, then those Br atoms  
must be related by symmetry. If there is a single phenyl ring, then the *ipso*-C atoms in the different

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molecules must be related and likewise for the *para*-C atoms. It may, however, be difficult to  
135 determine which of the *ortho*-C atoms from one molecule may be related to which of the *ortho*-C atoms  
from the other. As described below, when in doubt, the best course of action is to systematically try all  
possible combinations.

b) The centroid  $(\bar{x}, \bar{y}, \bar{z})$  for  $n$  atoms (two or more) can be calculated using equation 1.

$$(\bar{x}, \bar{y}, \bar{z}) = \left( \frac{\sum_{k=1}^n x_k}{n}, \frac{\sum_{k=1}^n y_k}{n}, \frac{\sum_{k=1}^n z_k}{n} \right) \quad (1)$$

140 c) The possible patterns that the centroids can form include point, line, plane, or outline of the  
molecule (molecular graph). The patterns formed by the centroids correspond either to a specific  
symmetry (translation) or to sets of candidate symmetries (rotation/screw rotation, reflection/glide  
reflection, rotoinversions) (Table 1).

d) To distinguish from among the possible candidates, apply the following tests:

- 145 i. Rotation vs screw rotation and reflection vs glide reflection: draw a line connecting the  
putatively symmetry-related atoms. If this line is perpendicular to the line/plane of the  
centroids then the symmetry is a reflection or rotation. If it is non-perpendicular, then  
there is a translational component to the symmetry (screw rotation or glide reflection).
- 150 ii. Rotoinversions:  $\bar{1}$  and  $\bar{4}$  are distinguished by the number of molecules involved (Table  
1).  $\bar{3}$  and  $\bar{6}$  both involve six molecules, but in the latter, three of the six are related to  
the other three by a mirror plane, which can be identified as described above.

As can be appreciated from inspection of Table 1, each symmetry has a unique combination of number  
of molecules involved, pattern of centroids, and angle between the line connecting symmetry-related  
atoms and the centroid pattern.

155 e) It is crucial that, after arriving at the final answer, the student then attempts to visualize how  
this symmetry relates the molecules in question. Recall that the purpose of this tool is to help the  
student ultimately perform the mental gymnastics needed to visualize symmetry relationships between  
the molecules without the use of this tool. To this end, the tool provides them with a clear indication of  
how to start developing this skill and an orthogonal means of actively verifying the presence of a given  
160 symmetry element.

To the best of our knowledge, this methodology has not previously been used to systematically  
identify the presence or nature of intermolecular symmetry, particularly in a pedagogical context. We  
note, however, that Glaser and coworkers have calculated midpoints of pseudosymmetrically related

atoms in krytoracemates<sup>25</sup> to characterize the precision and accuracy of crystallographic

165 pseudosymmetries.<sup>26-27</sup>

**Table 1. Correspondence between Patterns Formed by Centroids, Number of Molecules, and Symmetry Present**

	Symmetry	Number of molecules	Pattern of centroids	Angle between line connecting symmetry-related atoms and centroid pattern
Rotation	2	2	Line	Perpendicular
	3	3	Line	Perpendicular
	4	4	Line	Perpendicular
	6	6	Line	Perpendicular
Screw rotation	2 <sub>1</sub>	2	Line	Non-perpendicular
	3 <sub>1</sub> , 3 <sub>2</sub>	3	Line	Non-perpendicular
	4 <sub>1</sub> , 4 <sub>2</sub> , 4 <sub>3</sub>	4	Line	Non-perpendicular
	6 <sub>1</sub> , 6 <sub>2</sub> , 6 <sub>3</sub> , 6 <sub>4</sub> , 6 <sub>5</sub>	6	Line	Non-perpendicular
Reflection	<i>m</i>	2	Plane	Perpendicular
Glide reflection	<i>a, b, c, d, e, n</i>	2	Plane	Non-perpendicular
Rotoinversion	$\bar{1}$	2	Point	–
	$\bar{3}$	6	Point	–
	$\bar{4}$	4	Point	–
	$\bar{6}$	6	Point	–*
Translation		2	Molecular graph	–

\*Half of the molecules are related to the other half via a mirror plane

## THEORETICAL BASIS

170 The pattern formed by the centroids of symmetry-related atoms can be readily derived by from the mathematical formula describing the symmetry operation. For example, a 2-fold rotation axis along *z* relates an atom at (*x, y, z*) to an atom at (*-x, -y, z*). The centroid between these two would be located at  $(\frac{1}{2}(x-x), \frac{1}{2}(y-y), \frac{1}{2}(z+z)) = (0, 0, z)$ . The final expression reflects the fact that the centroids fall on a line; two coordinates remain constant while one varies. Regardless of the orientation of the screw axis, the result holds that the centroids will form a line. The formulae describing the symmetry operations can be worked out by hand and we leave the explicit calculation of the centroid formulae as an exercise that can be given to students, but the geometric results of these calculations are collected in Table 1.

## PRACTICAL CONSIDERATIONS

180 The tool, as described above, does not require the use of any particular software (or computer software at all, for that matter) but we have found that the freeware program MERCURY, maintained by the Cambridge Crystallographic Data Centre, has several advantages.<sup>28-29</sup> We stress that although the tool described in this article is likely to find use in crystallography courses, it is not specific to X-



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ray crystallography; our suggestion to use crystallographic software stems simply from the advantages of this freeware program. It is free and able to read generic \*.xyz files as well as many other forms of 3D structural information. It possess an intuitive interface, and a detailed user guide is available online.<sup>30</sup> The program interfaces well with the Cambridge Structural Database (CSD)<sup>31-32</sup> and can be used to create a nearly endless supply of exercises in the manner described below, which capitalizes on the power of using databases when teaching chemistry.<sup>33</sup> MERCURY also readily links to the curated CSD Teaching Database.<sup>34-37</sup> The program features facile point-and-click generation of centroids and lines between atoms. Any other program that facilitates these operations would also be serviceable.

## EXAMPLES

In the following examples, the reader is walked through the application of our tool in the identification of a series of representative symmetries. For brevity, the analyses have been restricted to non-H atoms, although they can be readily extended to include H atoms and the same results will be obtained. Although the problems are not related to crystallography *per se*, these examples were created using crystallographically determined coordinates and references are provided for the structure determinations. The examples do not, however, relate any further to the crystal structure; they are simply focused on the identification of a particular intermolecular symmetry element.

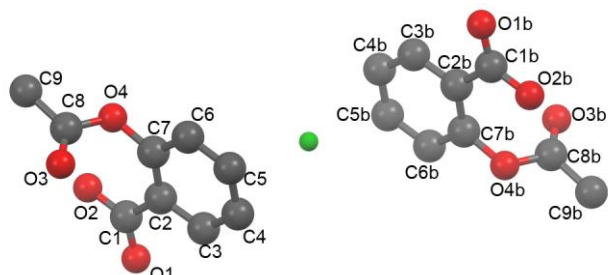
Although a figure is provided for each example below, the reader is strongly encouraged to open the corresponding Supporting Information \*.mrxy file using MERCURY. The structures can then be manipulated to better appreciate the relationships between the molecules, visualize the centroids, and identify centroid patterns, and to more clearly see atom labels.

### Example 1: The inversion center<sup>38</sup>

Consider the two symmetry-related molecules shown in Figure 3. Each molecule has only one benzoic acid functional group, so the hydroxyl O atom of one (O1) must be related to the hydroxyl O atom of the other (O1b); note that the hydrogen atoms are visible in the Supporting Information files. A similar argument holds for the carboxylic acid carbonyl O atoms (O2/O2b) and C atoms (C1/C1b). The atoms of the unique acetyl group are similarly related to each other (O3/O3b, O4/O4b, C8/C8b, and C9/C9b). The arene C atoms are uniquely defined by virtue of their relationship to the substituents. For example, C7 and C7b must be related to each other because they are both attached to the acylated

O atom. Once all centroids are generated, it is apparent that they fall on the same point in space.

Table 1 reveals that if all the centroids fall on a single point and only two molecules are involved, then they are related by  $\bar{1}$  symmetry.



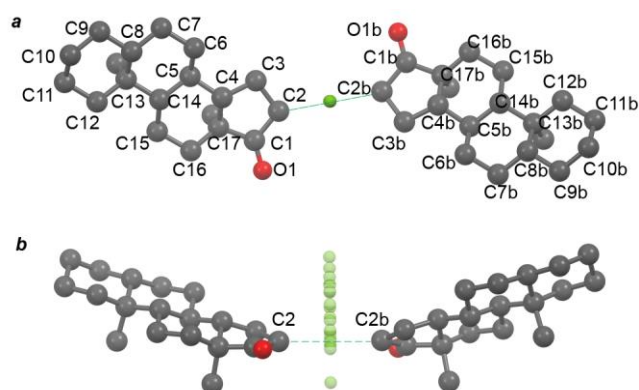
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**Figure 3.** Example 1: molecules related by an inversion center. Color code: red O, gray C, green centroids. All centroids coincide at a single point.

### Example 2: Two-fold rotation<sup>39</sup>

This example may initially seem more intimidating to students who can be overwhelmed by a large number of seemingly similar C atoms from among which they need to identify symmetry-related pairs (Figure 4). Starting from the lone O atom (O1/O1b), however, it is possible to systematically work through the molecule. There is only one C atom in each molecule (C1/C1b) bound to O1/O1b. There is then only one secondary C atom (C2/C2b) bound to C1/C1b. The remaining CH<sub>2</sub> units in these five-membered rings (C3/C3b) must therefore be related. In this way, the series of centroids can be built up by proceeding along the perimeter of the molecule. The centroids form a line indicating that either a screw rotation or a rotation is present. A line connecting C2 and C2b (readily generated using the “measure distance” tool in MERCURY), or any of the other pairs of symmetry-related atoms, intersects the line of centroids at a right angle, indicating that the symmetry is a two-fold rotation without any translational component.

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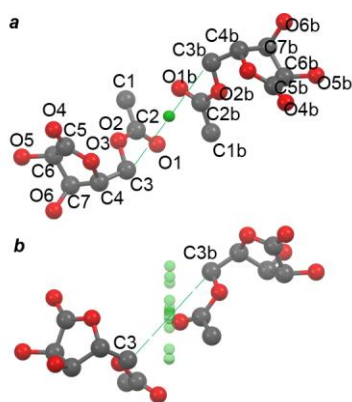


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**Figure 4.** Example 2: molecules related by a two-fold rotation viewed along (a) and perpendicular to (b) the symmetry element. A dashed green line connects C2 and C2b. Color code: red O, gray C, green centroids.

### Example 3: Two-fold screw rotation<sup>40</sup>

In this example (Figure 5), it is again possible to identify unique pairs of putatively symmetry-related atoms. Starting from the terminal methyl, the chain can be followed pairing C1/C1b, C2/C2b, O1/O1b, O2/O2b, and C3/C3b. Within the 5-membered ring, there is then only one C atom attached to the chain (C4/C4b) and one O atom in the ring (O3/O3b). There is then only one carbonyl attached to that oxygen (C5/C5b and O4/O4b). The remainder of the ring can be completed by pairing C6/C6b, C7/C7b, O5/O5b, and O6/O6b. As in the previous exercise, the centroids form a line, but now a line drawn to connect C3 and C3b intersects the line of centroids at an angle other than 90°. The symmetry is therefore a two-fold screw rotation.

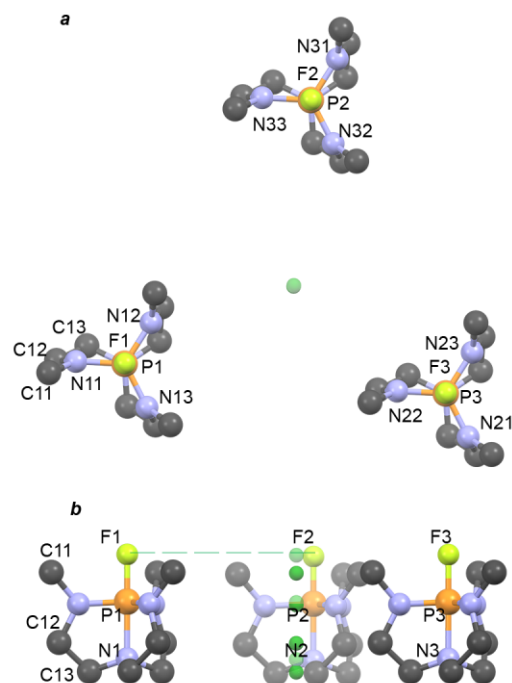


**Figure 5.** Example 3: molecules related by a two-fold screw viewed along (a) and perpendicular to (b) the symmetry element. A dashed green line connects C3 and C3b. Color code: red O, gray C, green centroids.

### Example 4: Higher-multiplicity rotation<sup>41</sup>

In this example (Figure 6), there are three molecules, which suggests that the centroids might form a line for a rotation or screw rotation (Table 1). Recall that the centroids will need to be calculated for triplets of atoms. If symmetry is present, the unique F atoms (F1, F2, F3) must be related, as must the unique P atoms (P1, P2, P3) and transannular N atoms (N1, N2, N3). In this example, however, the symmetry of the molecule raises a question that has not been encountered in previous examples: N11 is related to which equatorial N atoms in the adjacent molecules? Is it related to N22 and N33 or N22 and N31 or N21 and N31? Some students may quickly perceive the three-fold rotational symmetry of this group of molecules and correctly surmise that N11 is related to N21 and N31, but one advantage of our method is that the student is not *required* to have this insight in order to progress. It is possible to methodically work through all possible permutations. If the student believes that N11 is related to

260 N22 and N33, the exercise can be completed and no discernible pattern will be apparent among the centroids. The only permutation that affords one of the geometric elements listed in Table 1 is N11/N21/N31, C11/C21/C31, C12/C22/C32, etc., which gives a line of centroids. A line connecting F1 to F2 is perpendicular to the line of centroids, indicating a pure rotation as opposed to a screw rotation. Note that if none of the permutations had resulted in a meaningful pattern of centroids, then the student would reach the valid conclusion that there is no symmetry relating these molecules (see Example 8).

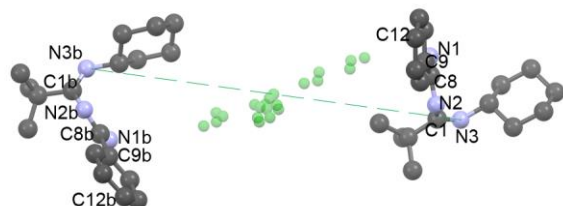


265 **Figure 6.** Example 4: molecules related by a three-fold rotation viewed along (a) and perpendicular to (b) the three-fold axis. A dashed green line connects F1 and F2. Color code: blue N, gray C, orange P, chartreuse F, green centroids.

#### Example 5: Glide reflection<sup>42</sup>

270 Following the strategies outlined above, the centroids can be calculated (Figure 7). A number of unique atom types are present in each molecule and can readily be identified as symmetry-related pairs: the terminal N atoms N1/N1b, the connected C atoms C8/C8b, the *ipso*-C atoms of the phenyl ring C9/C9b, and the *para*-C atoms C12/C12b (Figure 7). The student may initially be confused by which of the *meta*-C atoms are related. In this instance, one set (C10/C10b) is distinguished by the fact that it is syn to the terminal N atom (N1/N1b). It should be borne in mind, however, that the student could also just try both possible combinations: {C10/C10b, C11/C11b, C13/C13b, C14/C14b} or {C10/C14b, C11/C13b, C13/C11b, C14/C10b}. They will find that only the former gives

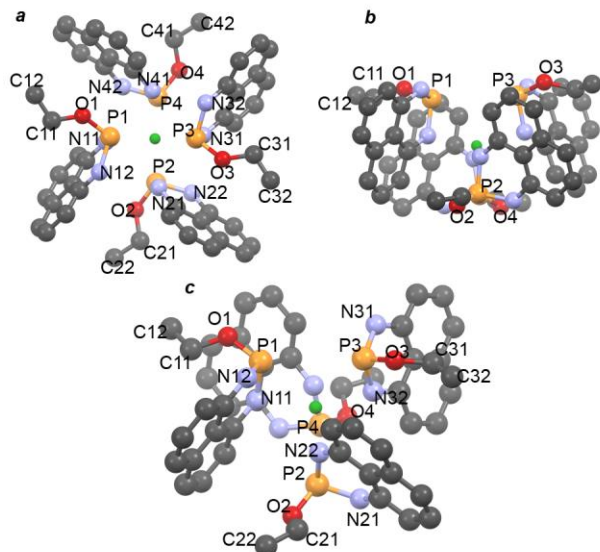
275 a consistent pattern for the centroids. When the exercise is complete, all centroids are seen to fall on a plane. A line drawn between N3 and N3b is not perpendicular to the plane of the centroids and so the symmetry relating the molecules is a glide reflection. Had the line been perpendicular, the molecules would be related by pure reflection.



280 **Figure 7.** Example 5: molecules related by a glide. A dashed green line connects N3 and N3b. Color code: blue N, gray C, green centroids.

#### Example 6: Higher-multiplicity rotoinversion<sup>43</sup>

In this example, the presence of four molecules suggests that either a four-fold rotation, screw rotation, or rotoinversion is operative (Table 1). Centroids are calculated for quartets of atoms. The unique P and O atoms, as well as the C atoms of the ethyl groups, provide a convenient starting point  
285 (Figure 8). Although the centroids for these quartets conspicuously coincide, the pattern formed by the centroids can only definitively be described as a point if *all* centroids overlap. The diammononaphthalene moiety initially looks like it will afford an exercise in exploring the many possible permutations of quartets. Close inspection of the ethyl group reveals, however, that it leans to one side. N11, toward which the ethyl tilts, therefore has to be related to N21, N31, and N41, toward which the ethyl groups  
290 in their respective molecules tilt. In a similar fashion, the entire set of centroids can be calculated. They all coincide at a single point, indicating that the symmetry is  $\bar{4}$ .

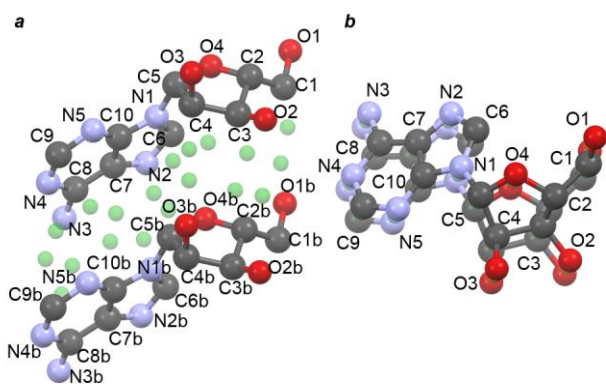


**Figure 8.** Example 6: molecules related by a four-fold rotoinversion viewed along (a), perpendicular to (b), and at a 45° angle to (c) the rotoinversion axis. Color code: blue N, gray C, orange P, red O, green centroids.

295 **Example 7: Translation**<sup>44</sup>

Often forgotten, pure translation is also a symmetry that is encountered in many chemical applications. Translational symmetry is perhaps best visualized by viewing the molecules in question along the translation vector and seeing that they overlap (Figure 9b). Our tool would be deficient, however, if it failed to yield a diagnostic pattern of centroids for this symmetry as well. In this example, all of the atoms in each molecule are chemically distinct, facilitating the identification of symmetry-related pairs. The centroids faithfully reproduce the molecular graph of the molecule, indicating that pure translation is present.

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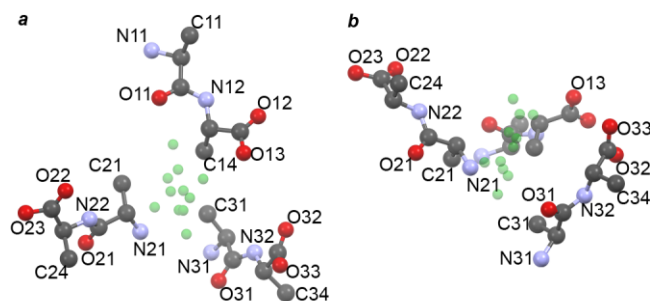
**Figure 9.** Example 7: molecules related by translation viewed perpendicular to (a) and slightly displaced from along (b) the translation vector. Color code: blue N, gray C, red O, green centroids.

305

**Example 8: No symmetry**<sup>45</sup>

It is also possible that molecules might be related by no particularly relevant symmetry. The trivial case arises when the molecules are not structurally identical (e.g., different conformers). Even if the

molecules are identical, however, they might not be related by any of the symmetry operations from  
310 Table 1 (Figure 10). The atoms in each of the cations of this example are chemically unique,  
eliminating any ambiguity as to which atoms would be related across molecules if symmetry were  
present. The centroids calculated between triplets of atoms do not form any discernible pattern.



315 **Figure 10.** Example 8: molecules not related by symmetry viewed along (a) and perpendicular to (b) the normal of the plane that best fits all atoms. Color code: blue N, gray C, red O, green centroids.

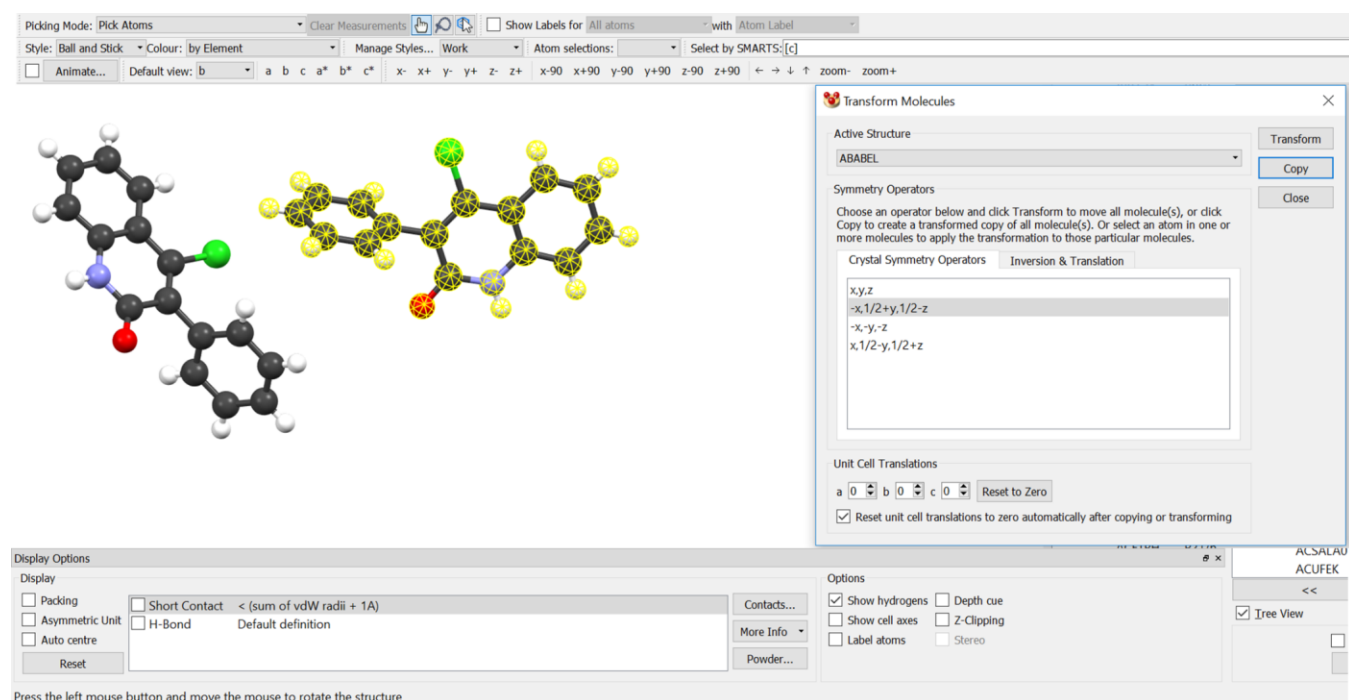
### CREATING NEW EXAMPLES

The \*.xyz files containing the coordinates of the groups of molecules used in these examples are  
supplied as Supporting Information. These files can be used to perform the exercises in MERCURY or  
another molecular visualization program. As Supporting Information, we also provide MERCURY  
320 compressed XML crystal files (\*.mryx) that contain the molecules along with the calculated centroids.  
Note that for the purpose of being able to describe these illustrative examples, the labels given to the  
atoms clearly indicate which are related by symmetry. If the instructor wishes this identification to be  
a part of the exercise, the labels can be changed using the “Edit > Edit Structure > Set atom label” tool  
in MERCURY.

325 The interested instructor is encouraged to use the “Edit > Transform Molecules” function in  
MERCURY to create new examples using crystallographic information files (CIFs) from original  
research, the peer-reviewed literature (CIFs are often provided as free Supporting Information even for  
papers located behind a paywall), or the CSD. To create a new exercise, the CIF is opened with  
MERCURY. By default, the contents of the asymmetric unit are displayed on the screen. For crystal  
330 structures with  $Z = 1$ , a single formula unit will be displayed. The molecule can be highlighted (right-  
click > select molecule), and a symmetry element present within the space group of the crystal can be  
chosen via the “Edit > Transform Molecules” function. Symmetry-related molecules are generated  
using the “Copy” button. The newly created group of molecules can be saved as an \*.xyz file to remove



any information about the space group (Figure 11). Students can then open this \*.xyz file in  
335 MERCURY to conduct the exercise. Again, we stress that the exercises do not explicitly have to pertain  
to crystallography; CIFs are simply a convenient source of groups of symmetry-related molecules. The  
\*.xyz files needed for the exercise can also be created using a molecular builder such as GaussView or  
MOLDEN.



340 **Figure 11.** Screenshot capturing the use of MERCURY to generate symmetry-equivalent molecules when creating new exercises/examples.

### USE IN A COURSE

The most straightforward means by which to use this tool in a pedagogical setting is to have  
students identify the presence of intermolecular symmetry in a set of molecules. The set of molecules  
would be provided in a \*.xyz file prepared as described above. An example of a problem set is provided  
345 as Supporting Information and the authors can be contacted for an answer key. The problem set can  
be given after working through an example with the class or, alternatively, directing them toward this  
paper. As highlighted in the Keywords, this work would be suitable for graduate or upper-division  
undergraduate students. Such problems have been used in the X-ray Crystallography course taken by  
graduate students and upper-division undergraduate students at UC Santa Cruz. Although a full  
350 Chemical Education Research study is outside the scope of the present paper, we note that these



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students have been able to successfully use this tool to identify intermolecular symmetries that they otherwise expressed difficulty in visualizing.

## CONCLUSION

These examples illustrate the application of our tool to help students identify the presence and nature of intermolecular symmetry. They highlight the algorithmic nature of the tool and the determinacy with which it indicates the symmetry that is present. Once the student has determined that a certain symmetry is present, they can then engage in the exercise of visualizing that symmetry. This strategy sidesteps the frustrating situation that can arise when a student is attempting to determine whether a symmetry is present by visualizing it before having practice at this visualization: “Is the symmetry not there, or am I just not seeing it?”

We have found this tool to be useful when training students to visualize intermolecular symmetry, typically in the context of X-ray crystallography. We are currently exploring the applicability of this tool in other contexts and note that we have found it to be useful in finding and describing crystallographic pseudosymmetry.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available on the ACS Publications website at DOI:

10.1021/acs.jchemed.XXXXXXX.

Cartesian coordinates for all examples (XYZ)

MERCURY compressed XML crystal files for all examples (MRYX)

Example problem set and files (DOC and XYZ)

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