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Activity

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Illustrating Catalysis with Interlocking Building Blocks: A BINAP–Ruthenium Complex Catalyzed Asymmetric Hydrogenation

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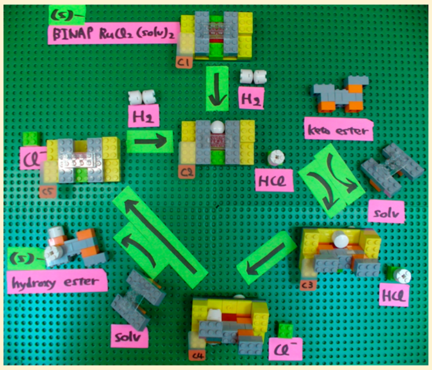
Ⓢ *Supporting Information*

ABSTRACT: A unique method has been developed using an interlocking building-block model equipped with magnets to illustrate the catalytic asymmetric hydrogenation of *β*-keto esters by a BINAP–ruthenium complex to enhance students' understanding of this process. A BINAP–ruthenium block model, mimicking the coordination environment around the metal center in the real complex, can be used to convert the *β*-keto ester model into a *β*-hydroxy ester model. This model was used to provide a greater understanding of the essence of the catalytic reaction and to assist students in their understanding of its mechanism.



KEYWORDS: *High School/Introductory Chemistry, First-Year Undergraduate/General, Inorganic Chemistry, Hands-On Learning/Manipulatives, Catalysis*

Catalytic asymmetric hydrogenation reactions are important processes for the preparation of intermediates of pharmaceuticals, flavors and other fine chemicals.[1,2] The catalytic cycles associated with the hydrogenation reactions, however, are traditionally represented schematically by overcrowded schemes that many students find complicated and difficult to understand. Consequently, many students lose interest in these representations during conventional lectures. Of the many different types of transition metal-catalyzed reactions, the asymmetric hydrogenation of a *β*-keto ester to the corresponding *β*-hydroxy ester by a BINAP–ruthenium [BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] complex[3−5] is educative, because it includes important topics such as the stereoselectivity resulting from the steric hindrance observed between the chiral BINAP moiety and the *β*-keto ester. The proposed mechanism of the reaction together with the two-dimensional illustration of the *β*-keto ester-coordinated BINAP–ruthenium complex are depicted in Figure 1.[3]

The use of interlocking building blocks for chemical modeling is of considerable interest to students of all ages. In most cases, block models have been exploited as tools to illustrate static behaviors, such as molecular, polymer, and crystal structures.[6−8] More recently, however, they have been used to display dynamic behaviors such as chemical reactions and equilibria.[9] The use of block models to illustrate the mechanisms for coordination polymerizations using metallocene catalysts and for olefin metathesis using Grubbs' catalyst was previously reported.[10,11] The block models can illustrate the concepts of the catalytic reactions and help students understand the mechanisms.

Herein, interlocking building blocks are used as a molecular modeling tool to illustrate the catalytic asymmetric hydrogenation reaction of a *β*-keto ester by a BINAP–ruthenium complex. Although the block models do not illustrate the precise molecular structures of the species involved, and cannot take the place of computer visualizations and ball-and-stick systems, they helped high school students and nonchemistry majors to visualize the key concepts of this reaction. In addition, the block model cannot illustrate the process of the electrophilic addition to alkene, which should be covered in a lecture either in parallel or after the activity.

■ PREPARATION

Detailed instructions for constructing the block models used in this study can be found in Videos S1−S5 (Supporting Information). Before conducting the activity, instructors need to construct the block models.

Figure 2 shows block models of the *S* and the *R* isomers of the BINAP–ruthenium complex and corresponding schematic. The block models **M1** and **M2** have been constructed to help students visualize the chirality of the BINAP ligand and the coordination environment around the ruthenium center, respectively. The red, light green, and orange pieces represent the ruthenium, chlorine, and phosphorus atoms, respectively. The yellow pieces have been used to represent the phenyl and naphthyl groups of the BINAP. With regards to **M1**, the BINAP moiety was composed of two main parts [i.e., two $(C_6H_5)_2P(C_{10}H_6)-$] that were connected by rotating blocks.

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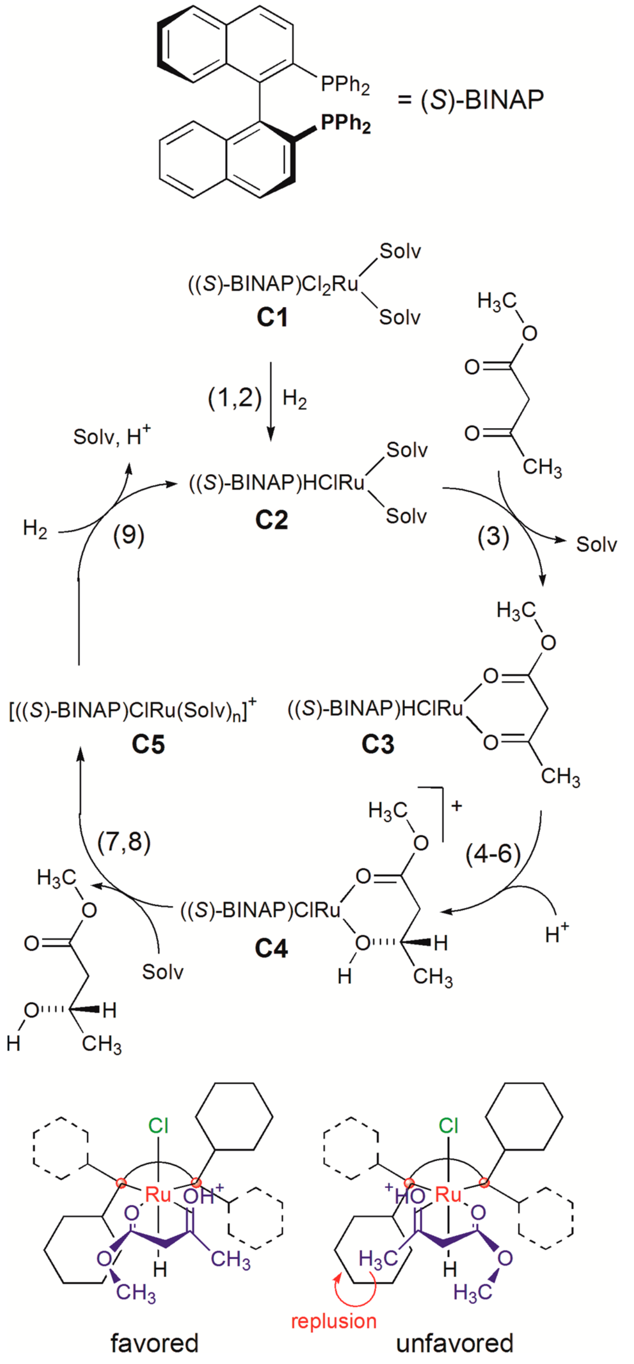

Figure 1. (Top) Asymmetric hydrogenation of β-keto ester to β-hydroxy ester by BINAP−ruthenium catalyst. The labels of compounds and numbers in parentheses correspond to those described in Supporting Information Figures S2 and S3. (Bottom) Coordination geometry of protonated β-keto ester-coordinated (*S*)-BINAP−ruthenium complex. The red circle indicates a phosphorus atom. Naphthalene groups have been omitted for clarity.

The $RuCl_2$ moiety was composed of three 2 × 2 round blocks. As regards **M2**, the red 2 × 2 block was covered with a knobbed, red 2 × 2 plate, to allow for the β-keto ester model to be easily connected and disconnected. The knobbed, yellow 2 × 2 plates being hidden below the light green 2 × 2 blocks similarly allowed for the chlorine block to be easily disconnected.

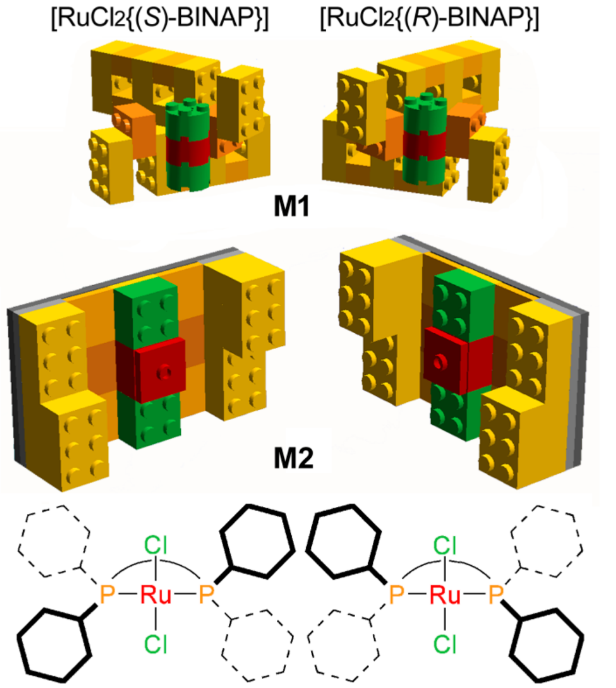

Figure 2. (Top and middle) Assembly of block models of BINAP−ruthenium complex, M1 and M2. M1 highlights the chirality of BINAP ligand, while M2 highlights the coordination geometry around the ruthenium metal. (Bottom) Schematic of coordination geometry of the complex. Naphthalene groups have been omitted for clarity.

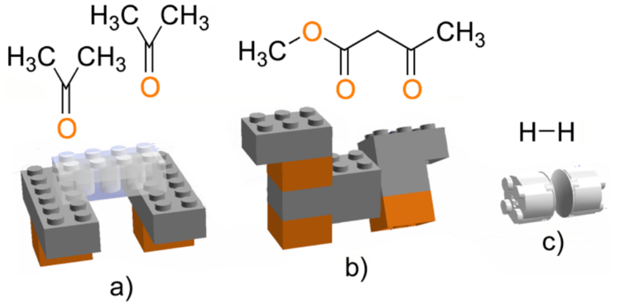

Figure 3. Assembly of block models: (a) coordination solvents 2(acetone), (b) β-keto ester $CH_3OC({=}O)CH_2C({=}O)CH_3$, and (c) hydrogen molecule H_2.

Figure 3a shows a block model of the coordination solvents composed of two acetone molecules. The 2 × 4 transparent block was included as a dummy block to link the two acetone models. Figure 3b shows a block model of a β-keto ester $[CH_3OC({=}O)CH_2C({=}O)CH_3]$, which was composed of two main parts [i.e., $CH_3OC({=}O)CH_2-$ and $-C({=}O)CH_3$] that were connected by rotating blocks. The gray and orange 2 × 2 blocks in the β-keto ester model represent the alkyl backbone and oxygen atoms, respectively. The gray block next to the rotating block was equipped with four magnets to allow for a hydride model to be connected to the gray block. Figure 3c shows a block model of a hydrogen molecule. Each of the hydrogen atoms was equipped with a magnet, so that they could be bound to each other to construct a hydrogen molecule, as well as being bound to the carbon atom of the β-keto ester magnetically.

■ DEMONSTRATION AND DISCUSSION

This activity has been given to science major high school students and nonchemistry major undergraduates. A list of students' comprehension before and after the activity is in the Supporting Information.

Figures S1−S3 and Video S6 (Supporting Information) clearly show how to demonstrate the enantiomer of BINAP with the block models **M1**, and the reaction mechanism of the hydrogenation reaction with the block models **M2**. The total time required for the activity, including explanations of catalyst and chirality, is about 1 h. The chirality and atropisomer of BINAP and chelate coordination can be illustrated by using **M1** models. Students can construct another atropisomer block model by imitating one isomer. The catalytic asymmetric hydrogenation reaction of a β-keto ester by a BINAP−ruthenium complex can be illustrated by using the **M2** model as follows. The reaction of $[\mathrm{RuCl_2\{(\mathit{S})\text{-}BINAP\}(acetone)_2}]$ (**C1**) and H_2 (white/white blocks) generates a BINAP−ruthenium complex $[\mathrm{Ru(H)Cl\{(\mathit{S})\text{-}BINAP\}(acetone)_2}]$ (**C2**) and HCl (white/light green) (Supporting Information Figure S2-(2)). The active catalytic species for the reaction is **C2**, whereas the HCl provides a source of H^+ ions for the protonation of the ketone moiety described below. The β-keto ester then ejects the coordinated solvent molecules from the ruthenium(II) center (red) and coordinates to the metal center through chelation to form a β-keto ester-coordinated complex (**C3**) (Supporting Information Figure S2-(3)). Steric repulsion between the methyl group of the ketone (i.e., gray 2 × 3, and not the methoxy group of the ester) of the β-keto ester and a phenyl group (yellow blocks) of the BINAP forces the $-\mathrm{C(=O)CH_3}$ group to rotate easily in one direction (Supporting Information Figure S2-(4)), which causes the high stereoselectivity of the catalytic reaction (Figure S4, Supporting Information). Following the rotation of the bond, the methyl group of the $-\mathrm{C(=O)CH_3}$ group approaches the H^- ion (white) attached to the metal center, and the oxygen atom (orange) of the group breaks its coordination with the metal center (Supporting Information Figure S2-(4)). The oxygen atom then connects with the H^+ from HCl (Supporting Information Figure S2-(5)), and the carbon atom equipped with magnets is connected with the H^- anion magnetically to form a β-hydroxy ester $[\mathrm{CH_3OC(=O)CH_2C^*H(OH)CH_3}]$ coordinated complex (**C4**) (Supporting Information Figure S2-(7)). The β-hydroxy ester desired product is then ejected by solvent molecules, which coordinate to the metal center (Supporting Information Figure S2-(7, 8)). Finally, the reaction of the complex (**C5**) with a H_2 molecule regenerates the active species **C2** and HCl (white/light green) (Supporting Information Figure S2-(9)). The **C2** active species produces the (*S*)-β-hydroxy ester, whereas the corresponding (*R*) isomer affords the (*R*)-β-hydroxy ester (Figure 4).

In the classroom, the similarities and differences between the block models and actual catalytic system can be emphasized. The steric hindrance observed between the β-keto ester and the BINAP and the hydrogenation process of the block model are similar to those of the authentic catalytic system. Although the catalyst block model has a simple structure mimicking just the coordination environment around the metal center, it can be used effectively to provide a good illustration of the catalytic system. This activity provides a clear illustration of the importance of the coordination environment to the catalytic process involved in asymmetry hydrogenation. With regards to the β-hydroxy ester block model, the angles around the chiral carbon atom were only 90°, which highlights the difference between the block model and the real molecule. Although it can be difficult to represent angles other than 90° using interlocking building block models, this did not limit this activity in any way.

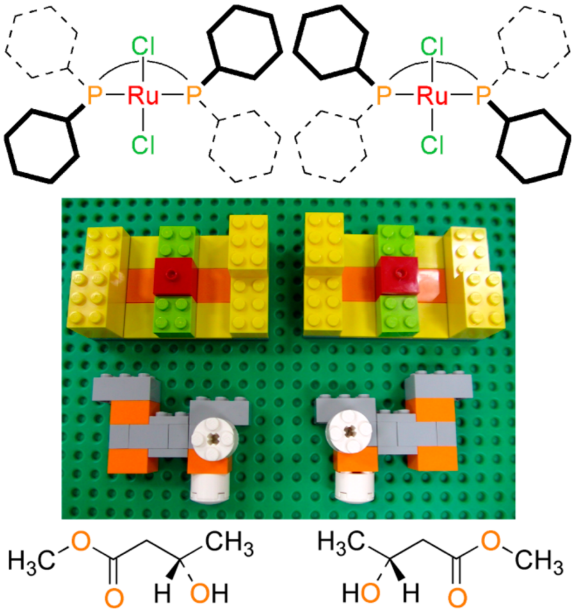

Figure 4. Correlation between the catalyst and β-hydroxy ester models.

This activity is suitable not only for a small class (up to 20 students) but also for science festivals with a small number of participants. Some blocks in this activity may not be readily available. The price of the 2 × 4 transparent clear block in particular is very high. With this in mind, it is recommended to use six 1 × 2 transparent clear blocks instead (Figure S5, Supporting Information).

■ CONCLUSIONS

Developing an effective understanding of catalytic chemical processes can be particularly challenging for students. With the use of block models as teaching aids, a conventional lecture concerning catalytic chemistry can become more straightforward and interesting. This activity provided students with a means to visualize the different steps involved in an asymmetric hydrogenation reaction catalyzed by the BINAP−ruthenium catalyst, which helped them to understand that a small amount of chiral catalyst can generate a large amount of chiral product. Furthermore, the use of this teaching-aid helped students to understand the relationship between the molecular structure of a catalyst and its catalytic properties.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Constructions of block models; video demonstrations of asymmetric hydrogenation reaction by the BINAP−ruthenium catalyst; students' comprehension before and after the activity. This material is available via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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