

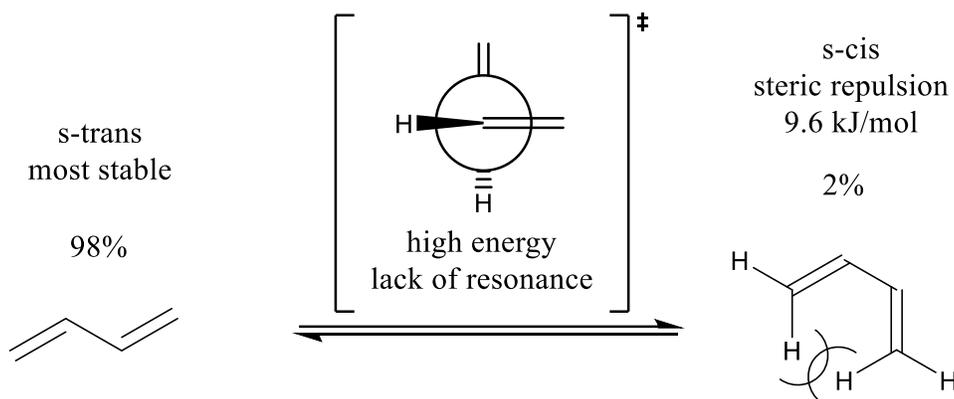
## THE VIRTUAL KINETICS OF A DIELS-ALDER CYCLOADDITION

In this virtual experiment, you will explore the [4+2] cycloaddition of different dienes and dienophiles under various thermal conditions. The kinetics will be measured by the number of virtual minutes passed for the completion of the cycloaddition reaction using the BeyondLabz platform.

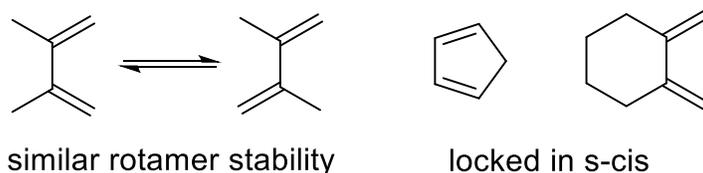
### Introduction

The Diels-Alder reaction, a [4+2] cycloaddition of a conjugated diene and an alkene (the dienophile), provides a powerful synthetic strategy for the synthesis of substituted cyclohexene rings.

The mechanism of the Diels-Alder reaction requires that the diene reacts in the *s-cis* formation. However, 1,3-butadiene favours the more stable *s-trans* rotamer because of the steric hindrance associated with the *s-cis* rotamer. At room temperature, there is enough energy for torsional rotation of 1,3-butadiene about the C<sub>2</sub>-C<sub>3</sub> bond and results in a dynamic equilibrium that largely favours *s-trans* about 98% at room temperature. Other possible rotamers are negligible as they exist as high energy transition states due to broken resonance.

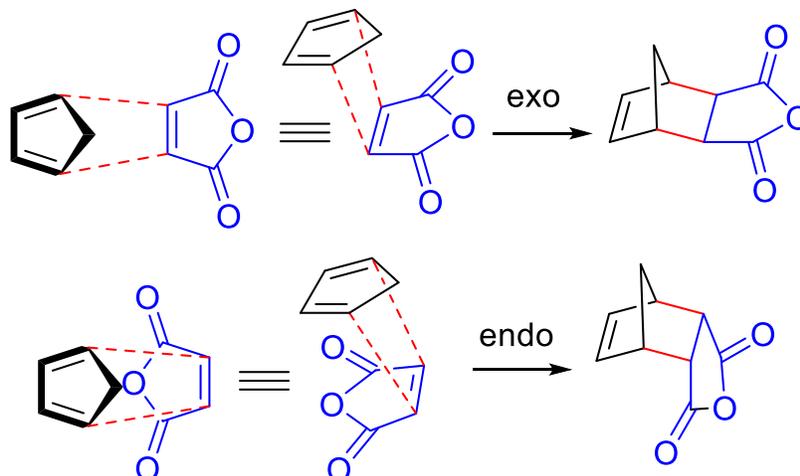


The rate of a Diels-Alder cycloaddition reaction can be increased by favouring the *s-cis* rotamer of a diene or locking the diene as a cyclic diene as shown below. This increases the likelihood of the diene being in the correct rotamer to undergo a Diels-Alder reaction.

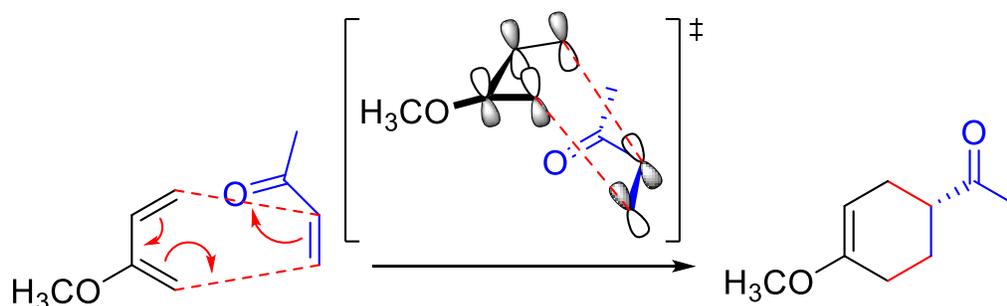


Cyclic dienes react to form bicyclic isomers. For example, the reaction of cyclopentadiene with maleic anhydride can theoretically produce two diastereomers, depending on the direction of the approach of the maleic anhydride relative to the cyclopentadiene in the transition state of the reaction. In practice, the *endo* isomer (product via kinetic control due to favourable  $\pi$  orbital interactions) is favoured under most reaction conditions.





The rate of the reaction can be further enhanced by the presence of electron-donating substituents (such as hydroxy and alkoxy) on the diene, and/or electron-withdrawing groups (such as cyano and acyl) on the dienophile.

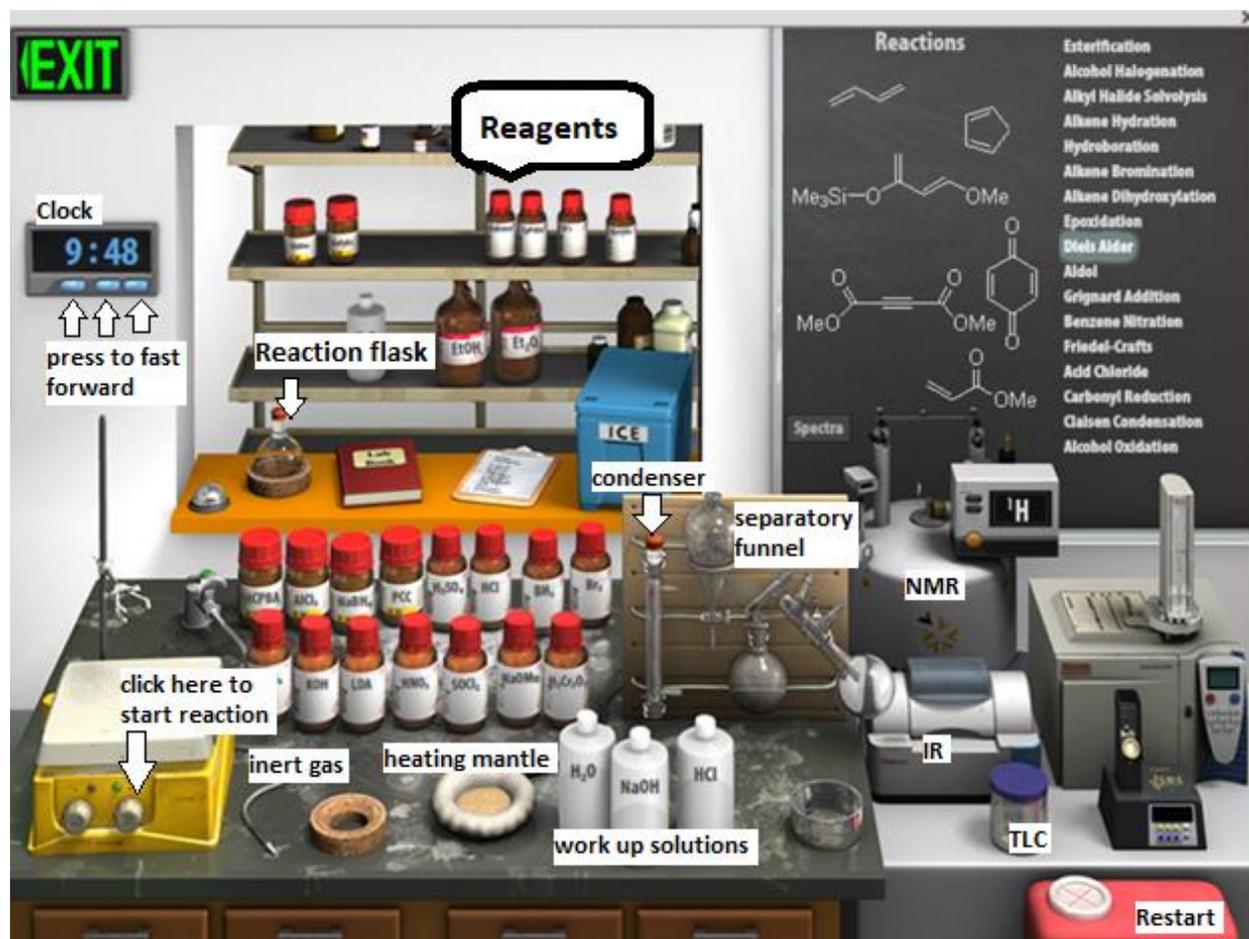


The reaction is often highly regio- and stereo-selective (the concepts of endo and exo carry over to noncyclic compounds as well) depending on the different substituents on the diene and dienophile. The relative polarities of reagents dictate much of the regioselectivity, while the E/Z isomerism of the diene and the presence of  $\pi$ -orbital containing substituents on the dienophile dictate the stereoselectivity on various carbons.

## Procedure

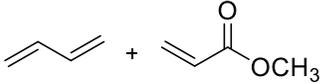
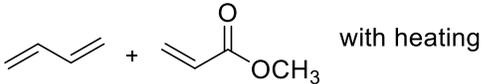
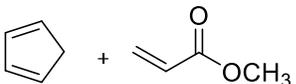
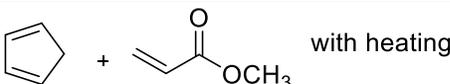
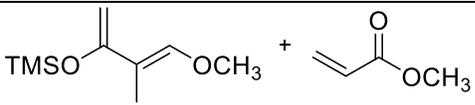
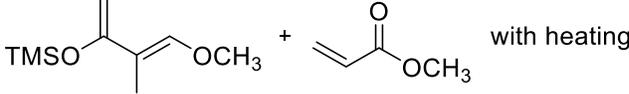
Using the BeyondLabz platform, enter the virtual organic chemistry lab. Click on the Synthesis button on the top left corner and select the Diels Alder reactions on the chalkboard to load the reaction specific reagents onto the stockroom shelves. Click and drag each solvent and reagent to the round bottom flask before moving the flask to the stir plate. Add a water cooled condenser, inert gas line, and heating mantle (if required) before turning the stir plate on and starting the reaction.





You will be comparing the time it takes for the completion of the Diels Alder reaction between various dienes and methyl acrylate at room temperature and with heating. This will be measured by the time it takes for methyl acrylate to disappear from the chalkboard (methyl acrylate cannot be viewed on this particular TLC). You can fast forward in time by clicking on the blue buttons on the clock below the exit sign. Note that you cannot go backwards in time so if you go too far ahead, you must restart the experiment by clicking on the chemical waste bin on the bottom left corner.



Reaction	Start time	Finish time	Rxn minutes
			
			
			
			
			
			

After the reaction has been completed, double click on the separatory funnel and add water to work up the reaction. Drag the organic layer to the cork ring and take  $^1\text{H}$  NMR and IR spectra of the compound by clicking on the NMR or FTIR machine and dragging it to the round bottom flask.

### Discussion

How does heat influence reaction rate? Explain.

Show what happens when the silyl ether is removed upon work-up (5th & 6th reactions).

Attach the  $^1\text{H}$  NMR and IR spectra of the three compounds you virtually synthesized and label all relevant peaks.

### Questions

How would the reaction kinetics change if the reactions were on ice?

Bonus: Given the fact that the Diels-Alder reaction is a reversible reaction, what is one way to limit the reverse reaction? Other than temperature, can you find any other way to speed up the Diels-Alder?

