

14.5: CHARACTERISTICS OF THE DIELS-ALDER REACTION

OBJECTIVES

After completing this section, you should be able to

1. determine whether or not a given compound would behave as a reactive dienophile in a Diels-Alder reaction.
2. predict the stereochemistry of the product obtained from the reaction of a given diene with a given dienophile.
3. recognize that in order to undergo a Diels-Alder reaction, a diene must be able to assume *ans-cis* geometry, and determine whether or not a given diene can assume this geometry.

KEY TERMS

Make certain that you can define, and use in context, the key terms below.

- dienophile
- dimerization

STUDY NOTES

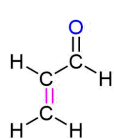
Make sure that you understand that the *s-cis* and *s-trans* forms of a diene such as 1,3-butadiene are conformers, not isomers. Note that some textbooks can confuse the issue further by referring to a compound such as (2*Z*, 4*Z*)-hexadiene as *cis*, *cis*-2,4-hexadiene, and saying that the most stable form of this compound is its *s-trans* conformer!

In fulfilling Objective 2, above, you must recognize that the Diels-Alder reaction is stereospecific.

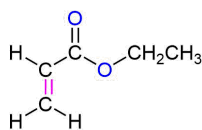
Finally, note reaction **B** in the reading shows 1,3-cyclopentadiene reacting with another molecule of 1,3-cyclopentadiene. When the same compound acts as both diene and dienophile in a Diels-Alder reaction to couple it is a [dimerization](#).

THE DIENOPHILE

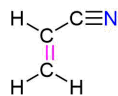
In general, Diels-Alder reactions proceed fastest with electron-withdrawing groups on the dienophile (diene lover). Ethylene reacts slowly while **propenal, ethyl propenoate, and other molecules shown below** are highly reactive in a Diels-Alder reaction.



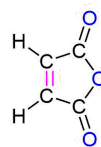
Propenal
(Acrolein)



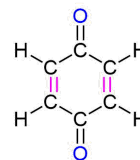
Ethyl propenoate
(Ethyl acrylate)



Propenenitrile
(Acrylonitrile)

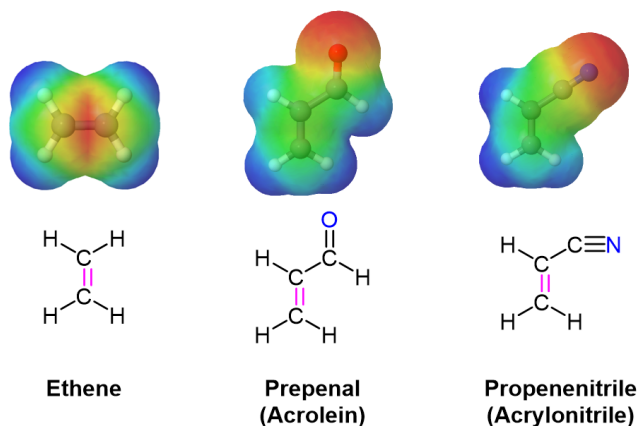


Maleic anhydride



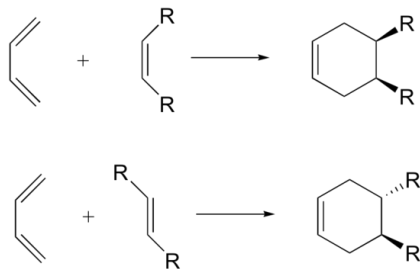
Benzoquinone

In much the same manner as electron-withdrawing substituents on a benzene ring, these are typically a double or triple bond in conjugation with the double bond in the dienophile. A resonance form can be drawn which places a positive charge in the dienophile double bond. This results in the double bond being less electron rich (greater electron density shown in Red/Orange) than ethylene. Electrostatic potential maps show that the electron-withdrawing groups pull electron density away from the double bond.

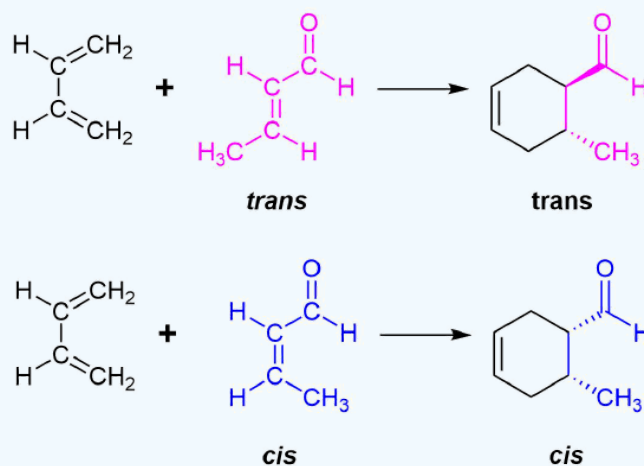


STEREOCHEMISTRY OF DIELS-ALDER (DIENOPHILE)

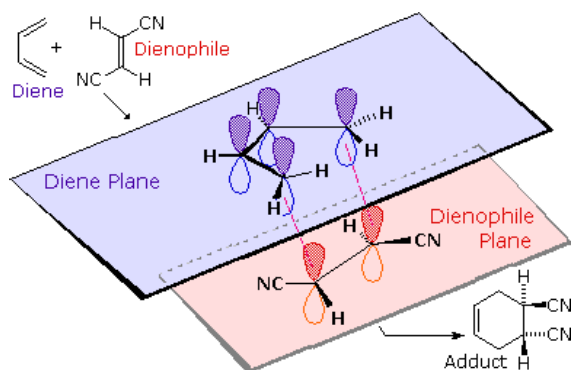
The Diels-Alder reaction is enormously useful for synthetic organic chemists, not only because ring-forming reactions are useful in general but also because in many cases multiple new stereocenters are formed, and the reaction is inherently stereospecific. During a Diels-Alder reaction the stereochemistry of the dienophile is retained in the product. A *cis* dienophile will generate a cyclohexene ring with *cis* (*syn*) substitution on the two carbons from the dienophile. Likewise a *trans* dienophile will generate a cyclohexene ring with *trans* (*anti*) substitution on these two carbon.



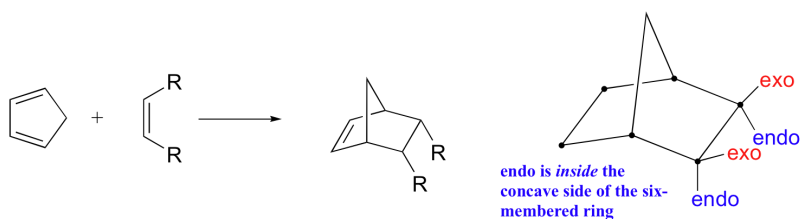
✓ EXAMPLE 14.5.1



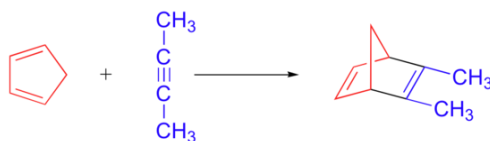
The retention of stereochemistry is due to the planar nature of both reactants and that the forming process is **suprafacial** (i.e. to or from the same face of each plane). This stereospecificity also confirms the concerted nature of the Diels-Alder mechanism. The drawing below illustrates this fact for the reaction of 1,3-butadiene with (E)-dicyanoethene. The *trans* relationship of the cyano groups in the dienophile is preserved in the six-membered ring of the adduct.



Another facet of the stereochemical retention of the dienophile is that only the *endo* product, rather than the alternative *exo* product, is formed. The words *endo* and *exo* are used to indicate relative stereochemistry when referring to bicyclic structures like substituted norbornanes. The *endo* position on a bicyclic structure refers to the position that is *inside* the concave shape of the larger (six-membered) ring. As you might predict, the **exo position** refers to the *outside* position. Diels-Alder reactions with cyclic dienes favor the formation of bicyclic structures in which substituents are in the **endo position**. Preference of the *endo* position is also a facet of the suprafacial nature of the Diels-Alder reaction. The orbital overlap required for the reaction is greater when the dienophile lies directly underneath the diene.

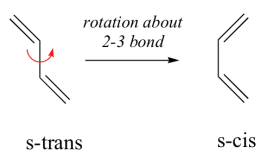


Alkynes can also serve as dienophiles in Diels-Alder reactions:

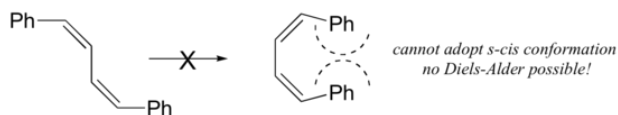


THE DIENE

In general, Diels-Alder reactions proceed fastest with electron-donating groups on the diene (eg. alkyl groups). The Diels-Alder reaction is a single step process, so the diene component must adopt an *s-cis* conformation in order for the end carbon atoms (#1 & #4) to bond simultaneously to the dienophile. For many acyclic dienes the *s-trans* conformer is more stable than the *s-cis* conformer (due to steric crowding of the end groups), but the two are generally in rapid equilibrium, permitting the use of all but the most hindered dienes as reactants in Diels-Alder reactions.



For some dienes, extreme steric hindrance causes the *s-cis* conformation to be highly strained, and for this reason such dienes do not readily undergo Diels-Alder reactions.



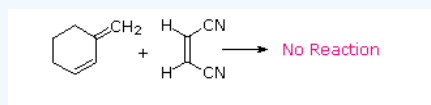
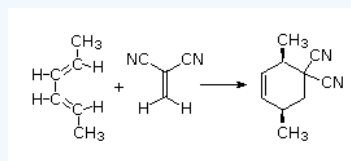
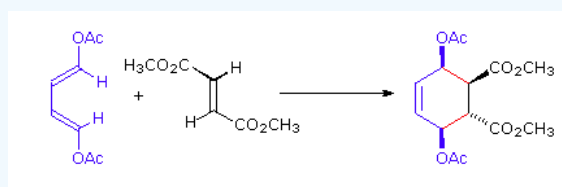
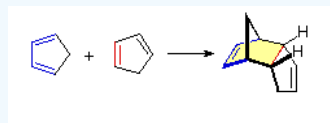
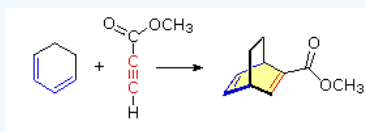
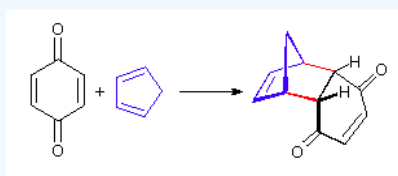
Cyclic dienes, on the other hand, are 'locked' in the *s-cis* conformation, and are especially reactive. The result of a Diels-Alder reaction involving a cyclic diene is a **bicyclic** structure:



STEREOCHEMISTRY OF DIELS-ALDER (DIENE)

The 1 and 4 Carbons in the diene have the possibility of forming two new stereocenters in the cyclohexene product. Similarly to the effects of dienophile stereochemistry, the positioning of substituents on the 1 and 4 carbons in the diene determine the stereochemistry in the product. The diene substituents can be thought of as being either *cis* (both facing in or both facing out) or *trans* and the stereochemistry is retained to form a *cis* or *trans* cyclohexene product.

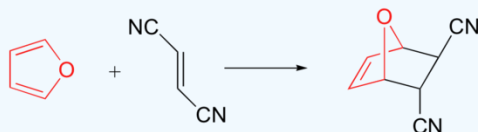
✓ EXAMPLES 14.5.1



THE ESSENTIAL CHARACTERISTICS OF THE DIELS-ALDER CYCLOADDITION REACTION:

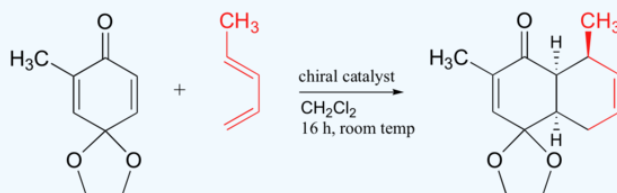
- The reaction always creates a new six-membered ring.
- The diene component must be able to assume an s-cis conformation.
- Electron withdrawing groups on the dienophile facilitate reaction.
- Electron donating groups on the diene facilitate reaction.
- Steric hindrance at the bonding sites may inhibit or prevent reaction.
- The reaction is stereospecific with respect to substituent configuration in both the dienophile and the diene.

✓ EXAMPLES 14.5.2



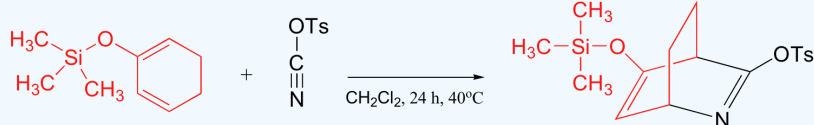
J. Med. Chem. **2008**, 51, 424

link



Org. Lett. **2001**, 3, 1559

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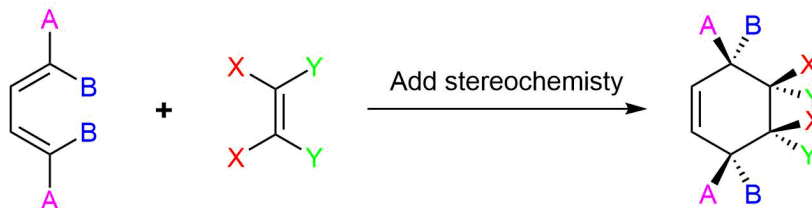
J. Org. Chem. **2003**, 68, 8256

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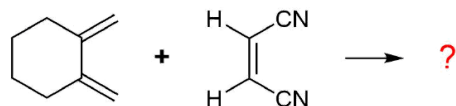
PREDICTING THE PRODUCT OF A DIELS-ALDER REACTION

Start by rotating the diene until it is in the s-cis conformation then point it towards the double bond of the dienophile. Remove the double bonds present in the diene and dienophile. Connect carbons 1 and 4 of the diene to a carbon in the dienophile double bond using a sigma bond to create a six-membered ring. Create a double bond between carbons 2 and 3 of diene.

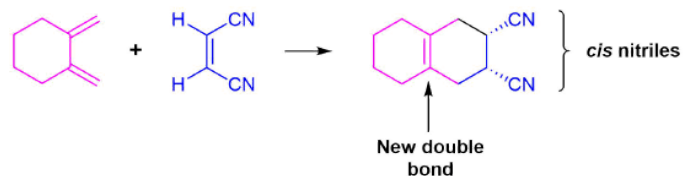
Determine if any substituents attached to either the double bond of the dienophile or carbons 1 and 4 of the diene have a *cis/trans* conformation. If so make sure the substituents have the same configuration in the cycloalkene product.



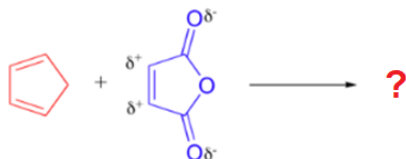
Predict the product of the following reaction:



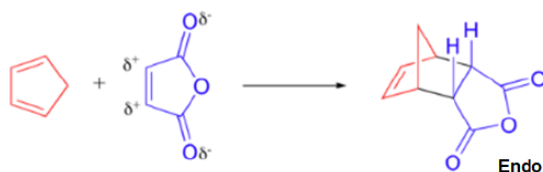
The diene is locked into an s-cis configuration which will promote the reaction. The ring portion of the diene will act as electron donating groups which will also promote the reaction. Because the diene already contained a ring the product will be bicyclic. The dienophile has two nitriles attached to it both of which are electron withdrawing. Since the two nitriles in the dienophile are *cis* to each other the two nitriles will be *cis* to each other in the product.



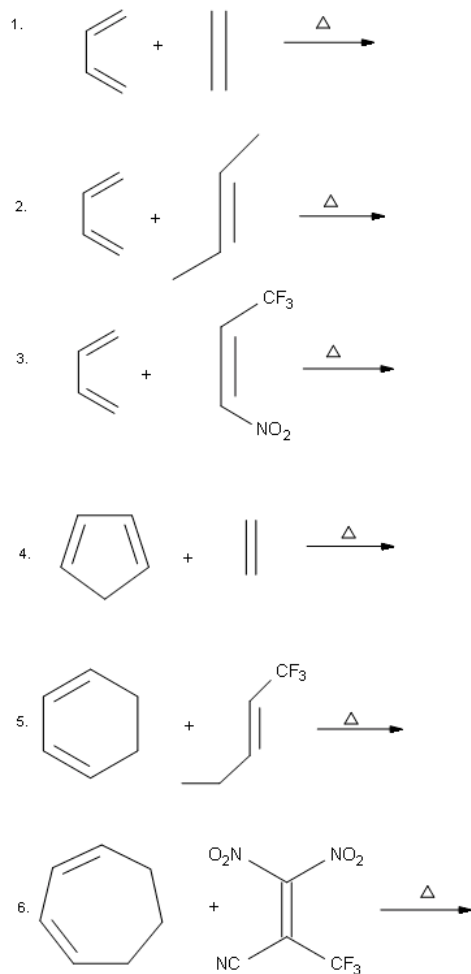
Predict the product of the following reaction:



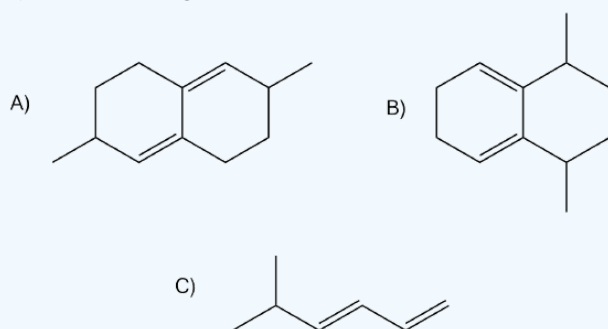
A particularly rapid Diels-Alder reaction takes place between cyclopentadiene and maleic anhydride. Cyclopentadiene is held in the required s-cis configuration so it will make a good diene for a Diels-Alder reaction. Maleic anhydride is also a very good dienophile, because the electron-withdrawing effect of the carbonyl groups causes the two alkene carbons to be electron-poor, and thus a good target for attack by the pi electrons in the diene. Since it is part of a ring, the double bond of maleic anhydride is in a *cis* configuration so the cyclohexene ring will also have a *cis* configuration. Lastly, the product will prefer the *endo* position.



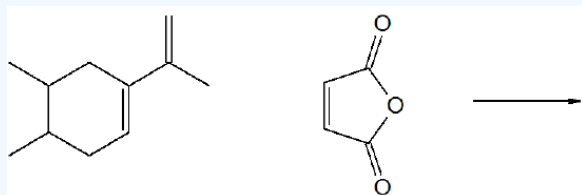
? EXERCISE 14.5.1



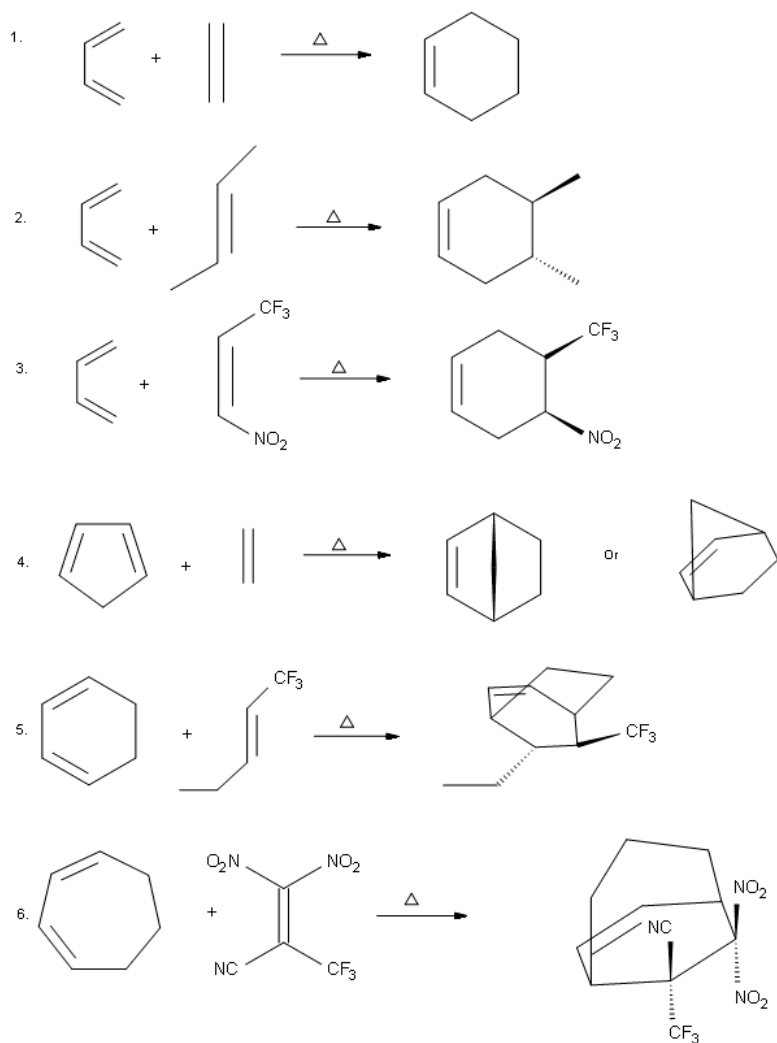
7) Of the following dienes, which are S-trans and which are s-cis? Of those that are s-trans, are they able to rotate to become s-cis?



8) Predict the product of the following reaction.



Answer



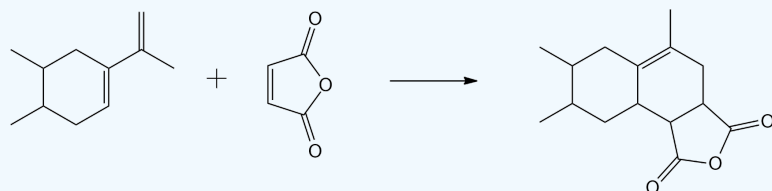
7)

A) s-trans, unable to rotate to become s-cis

B) s-cis

C) s-trans, can rotate to become s-cis.

8)



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