

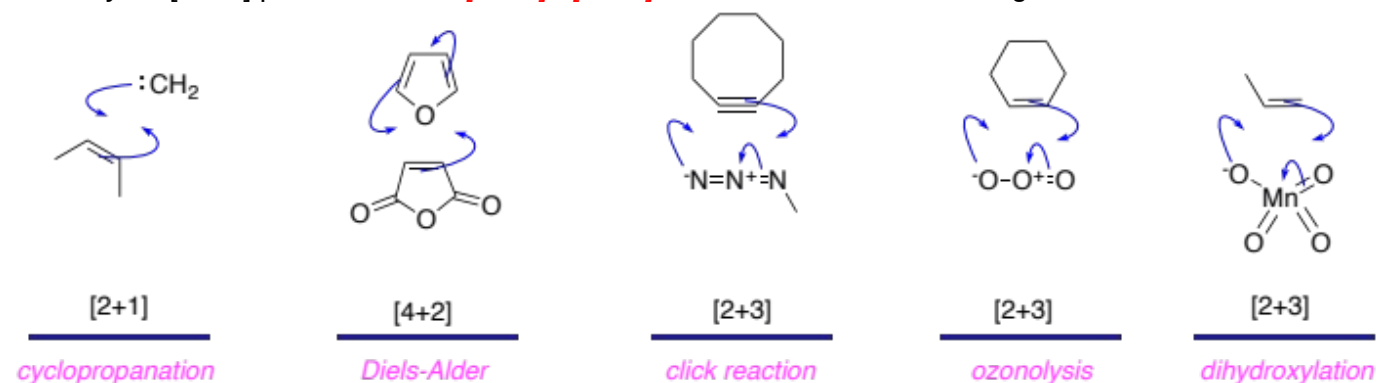
Cycloadditions To Alkenes And Alkynes

from chapter(s) _____ in the recommended text

A. Introduction

B. Nomenclature Of Cycloadditions

can only be [2 + 1] processes, and [3 + 2] / [1 + 4] leads to five-membered rings



C. Carbene Additions [2 + 1] (Cyclopropanations)

Reagents that contribute one atom to a ring in cycloadditions must be able to expand their valency by two: *true*.

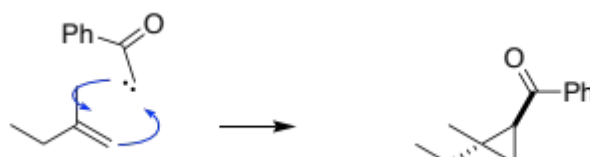
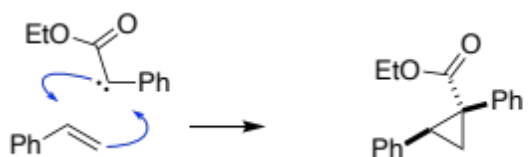
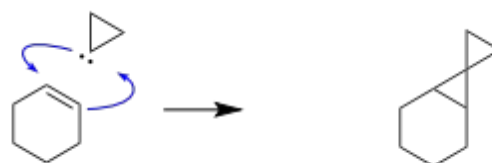
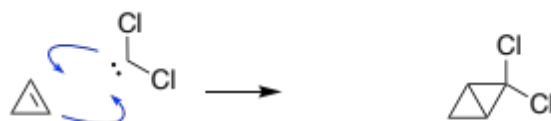
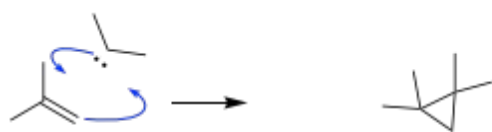
Carbenes have only 6 electrons in the valence shell of carbon.

expanding the valency of the carbon to 4.

A leaving group *is not* required in cyclopropanations featuring carbenes.

Carbenes can be sp^2 hybridized with *an empty p-orbital*, ie *singlet* forms
 sp^3 hybridized with *a diradical structure*, ie *triplet*





show only trans-product

show only trans-product

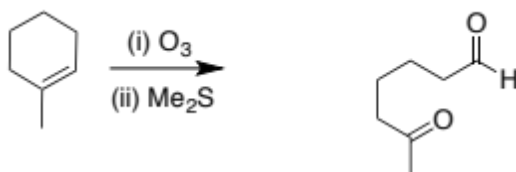
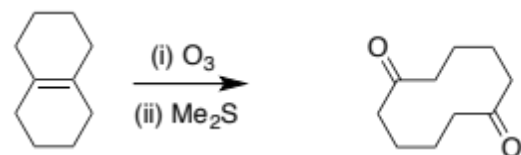
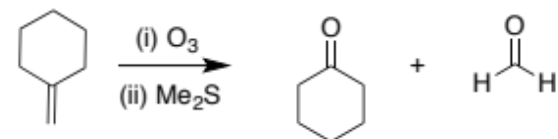
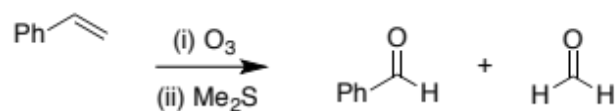
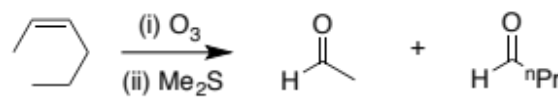
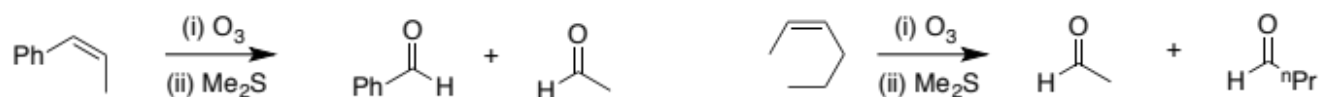
Substances that have two rings sharing a single carbon are called *spiro*.

D. Ozonolysis [2 + 3]

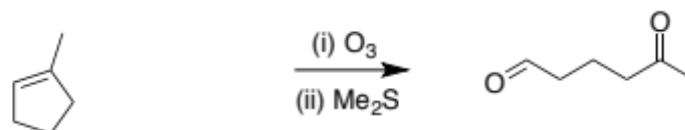
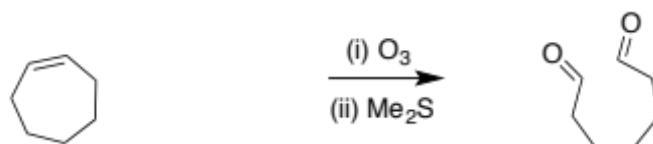
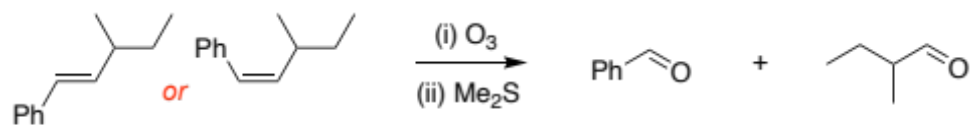
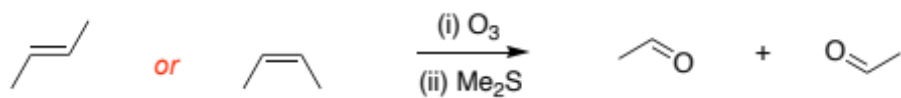
It smells like *a sea breeze / don't smell it, it's highly toxic*

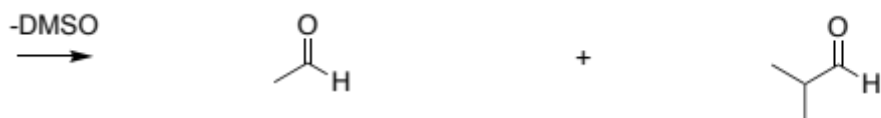
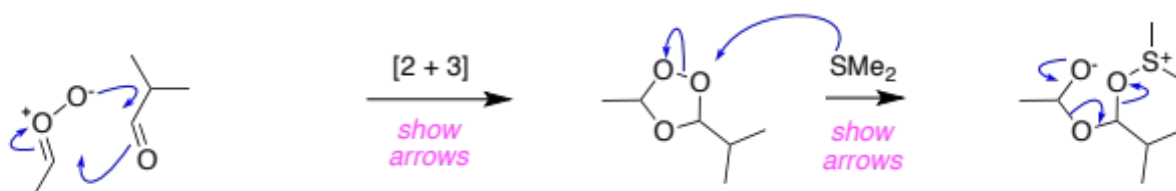
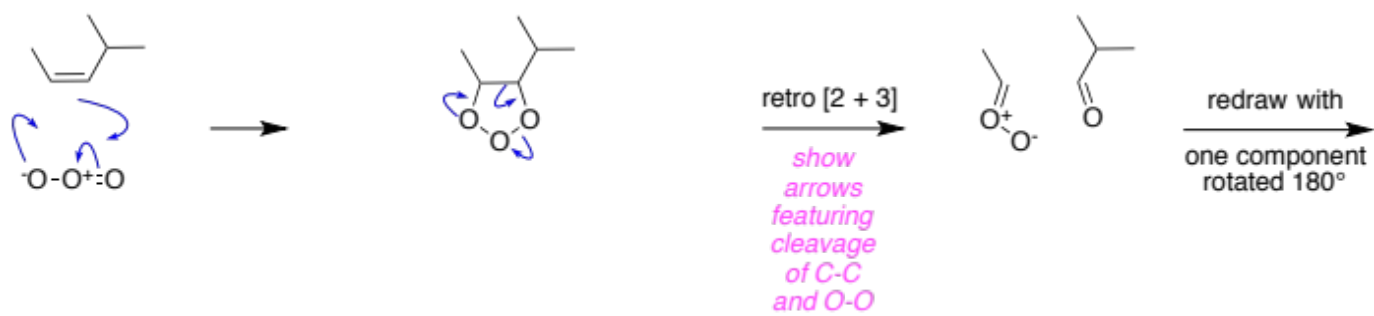
Treatment with ozone, *ie ozonolysis*, then quenching the produce with a mild reducing agent cleaves alkenes to give *aldehydes / ketones* at either terminus

This reducing agent can be *Me₂S / PPh₃ / Zn dust* (dimethyl sulfate cannot be a reducing agent)



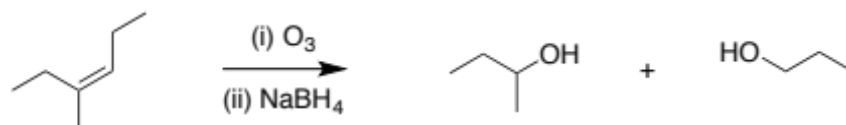
A retro-[2 + 3] is a *ring cleavage to 2 and 3 atoms components*.

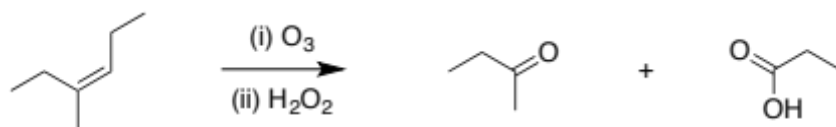




DMSO is Me_2SO

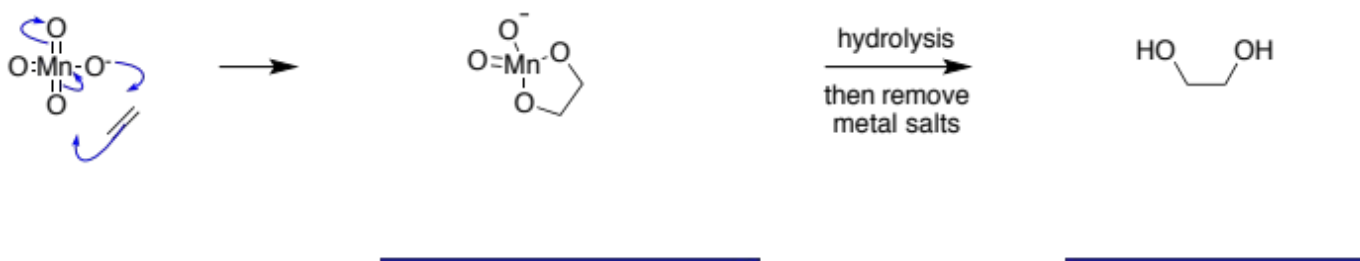
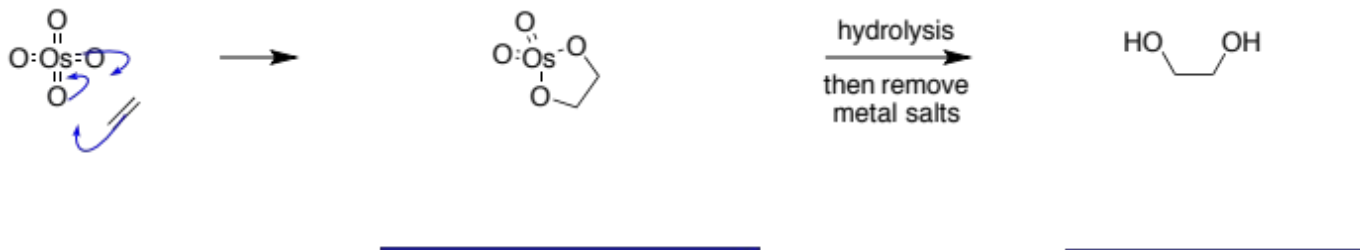
ozonolysis reactions may be *reduced* to alcohols if the mixture is treated with sodium borohydride, or *oxidized* to acids if treated with hydrogen peroxide.



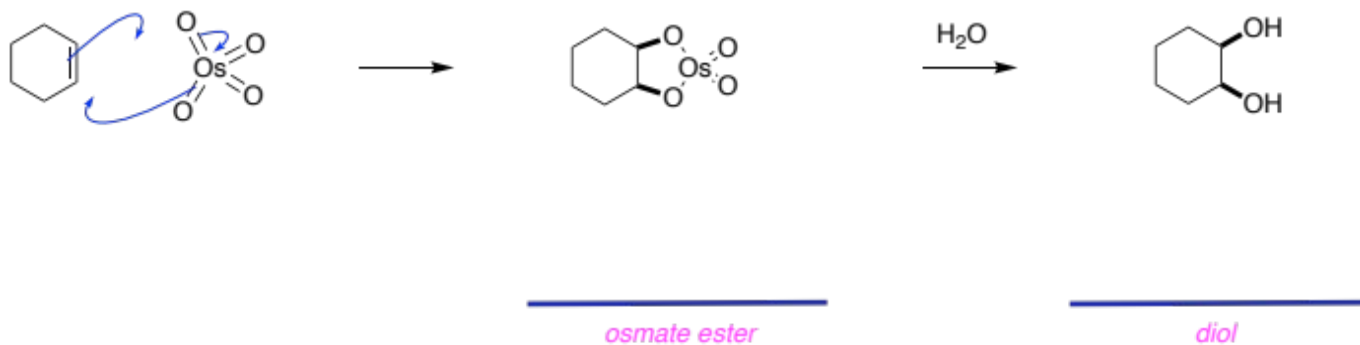


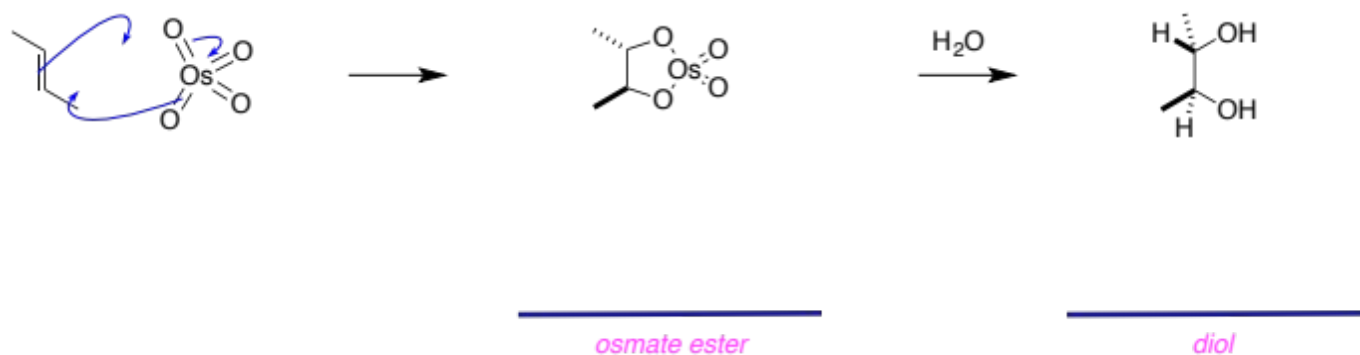
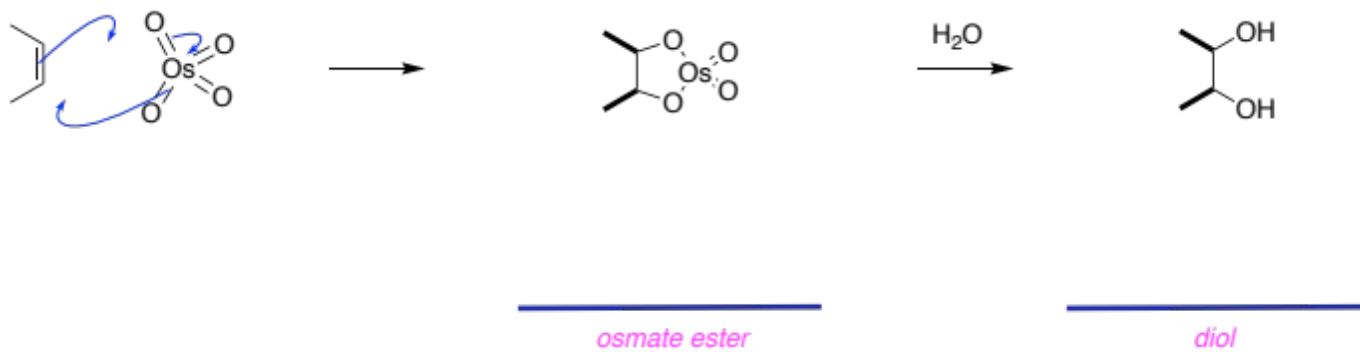
E. *syn*-Dihydroxylation [2 + 3]

A dihydroxylation adds 2 hydroxyl groups to an alkene.



metal oxides to alkenes occur with *syn* face specificity.

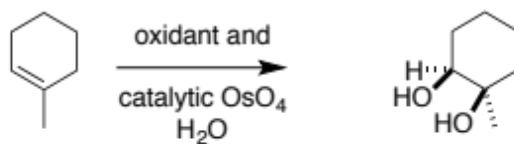
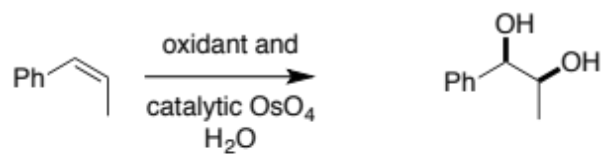




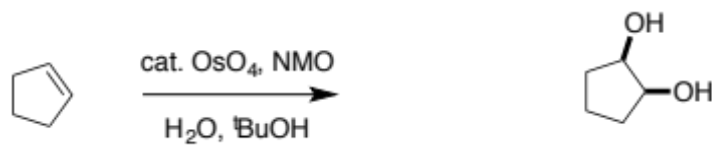
Dihydroxylation with osmium tetroxide is stereospecifically *syn*

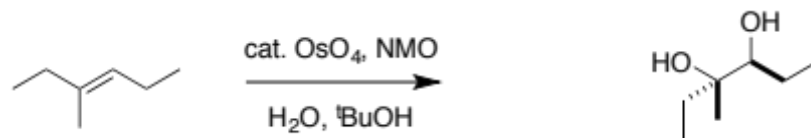
This is *unlike* generation of diols via epoxidations which gives net *anti* addition



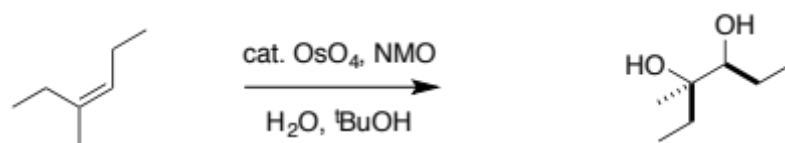


show stereochemistry





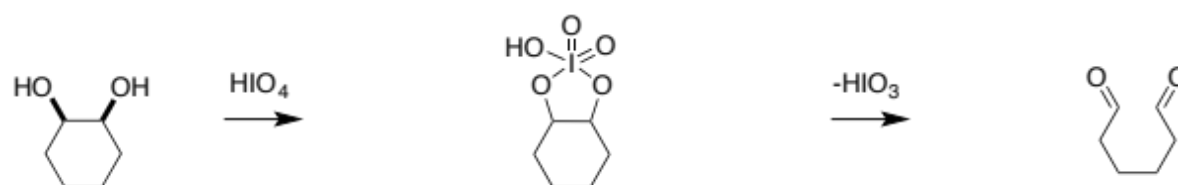
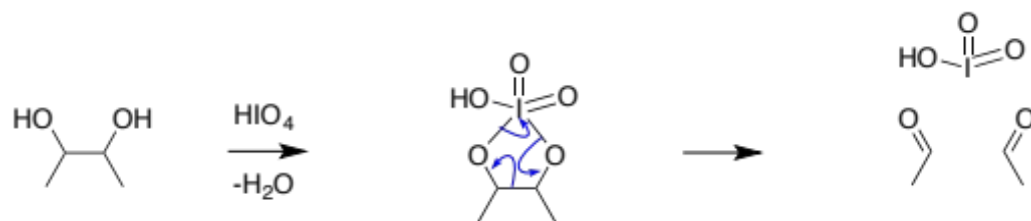
(Of course, both enantiomers form in both the problems shown on this page.)



The products of the two reactions above are *diastereomers*

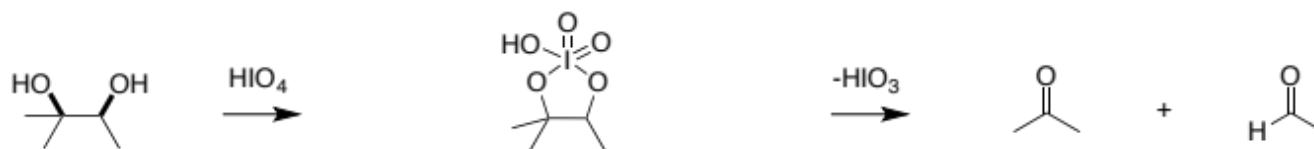
F. Periodate Cleavage

The iodine of periodic acid (HIO_4) is in the **+7** oxidation state; it is **reduced** in this reaction to HIO_3 which is in the **+5** oxidation state.



periodate intermediate

products



periodate intermediate

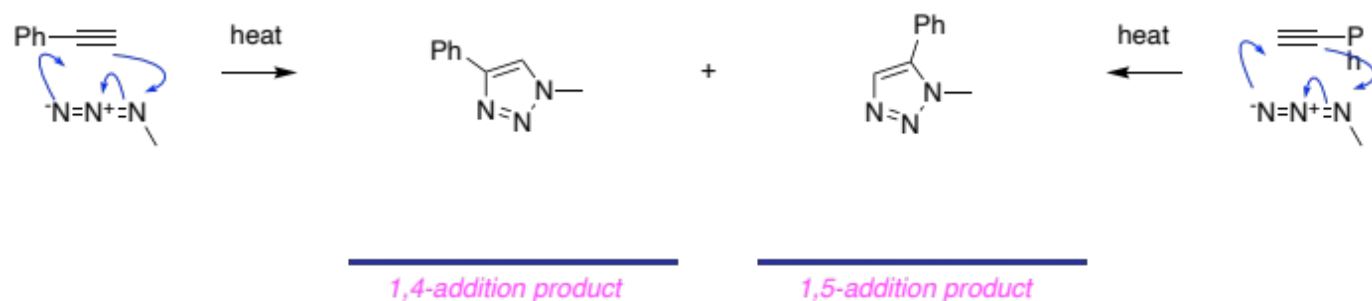
products

G. Azide-Alkyne “Click Reactions” [2 + 3]

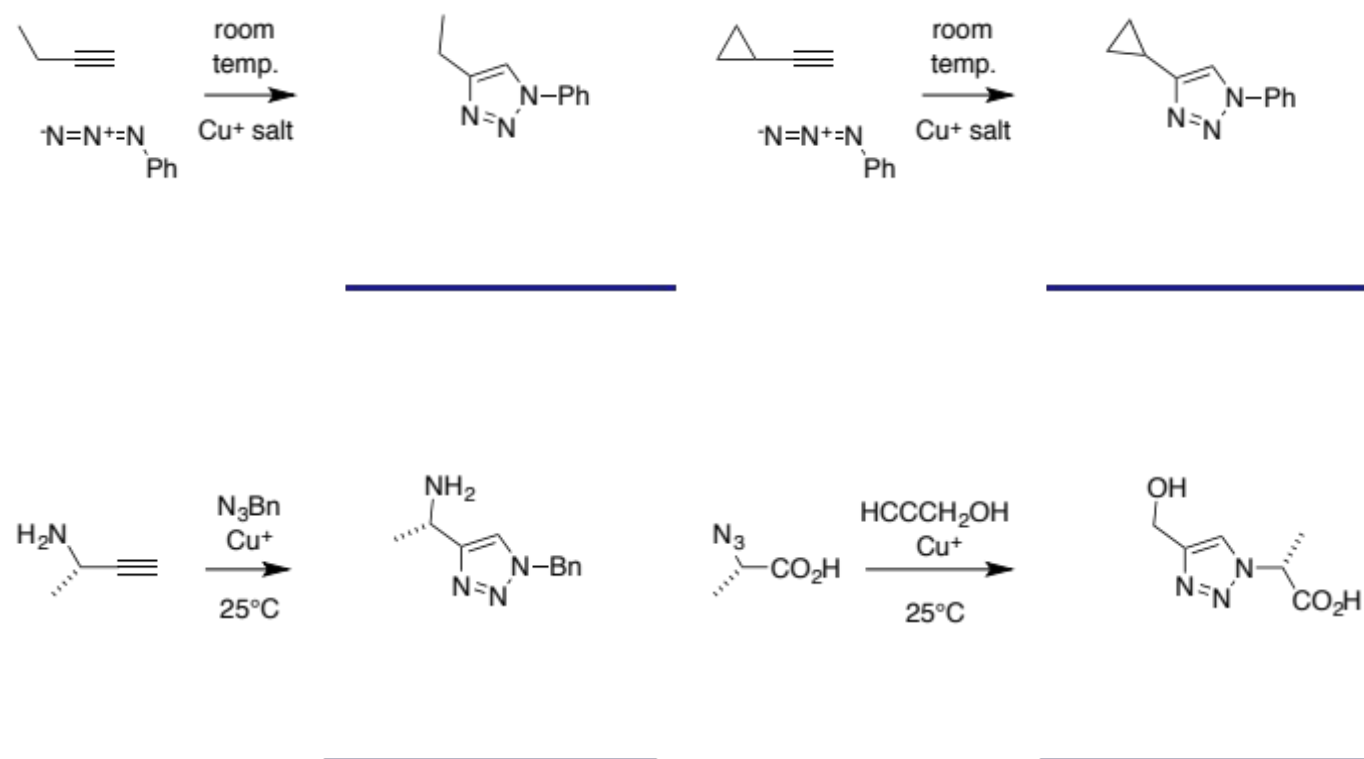
A terminal alkyne is a C – C triple bond *at the end of a chain*.

Heating organic azides and terminal alkynes together causes them to undergo [3 + 2]

Two *regioisomers* are always formed in this reaction, *ie* it is *regioselective*.



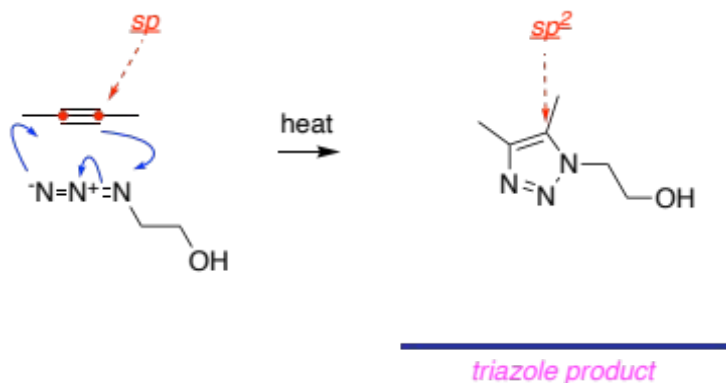
1,4-cycloaddition product, *ie* the reaction becomes 100% *regiospecific*



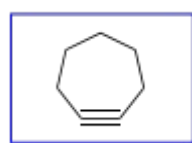
many different organic functionalities, but *none* of them react quickly with azides or with alkynes.

ie this type of click reaction is *chemoselective*.

copper ions are cytotoxic, and cells are *less* stable



the ideal geometry around the "red dot carbons" is 180° , whereas in the triazole product it is 120° .



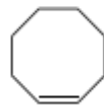
cycloheptyne

3



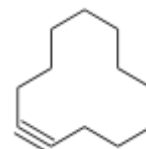
cyclopropyne

4



cyclooctyne

2



cycloundecyne

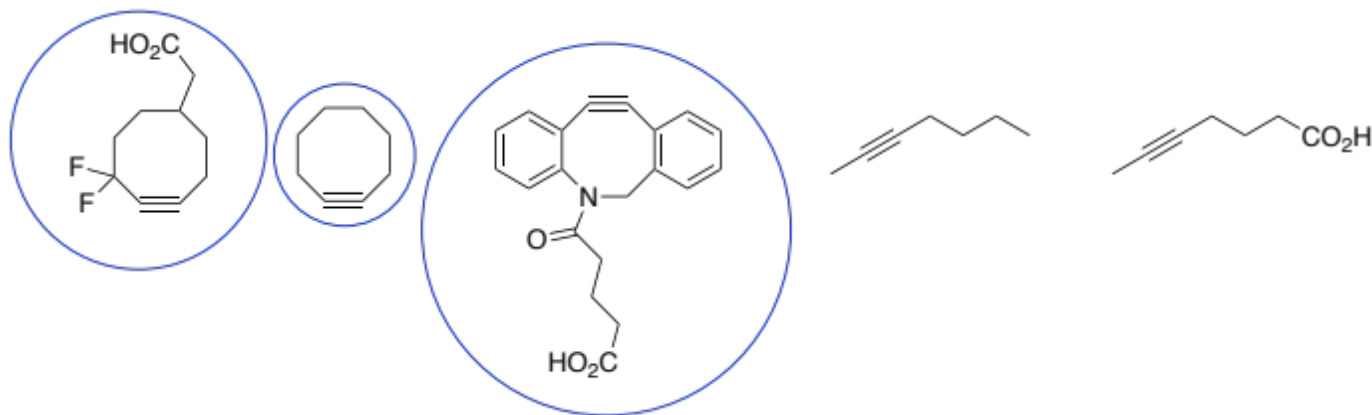
1

and this is called the heat of *hydrogenation* for that substrate.

liberates most heat in this reaction is the *most* strained, ie cyclopropyne.

changes alkyne sp -hybridized carbons to sp^3 , thereby making those carbon atoms *more* able to fit

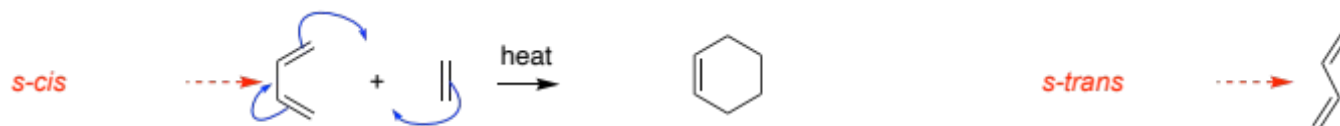
alkyne sp -hybridized carbons to sp^2 , thereby making those carbon atoms *more* able to fit



Reactions like these *do not* need copper salts to proceed at room temperature

on the cell surface, can be observed using *confocal microscopy*.

H. Diels Alder Reactions [4 + 2]

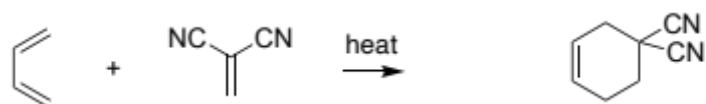


When dienes undergo [4 + 2] cycloadditions, they must be in *s-cis* conformations. conformation about the σ -bond that connects the π -bonds.

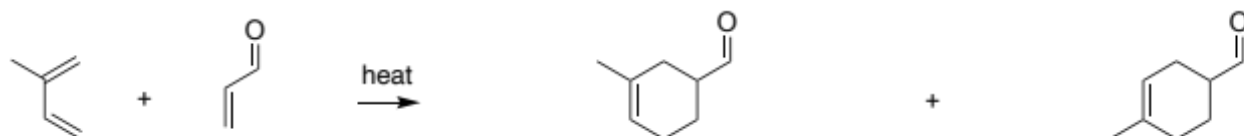
s-cis and *s-trans* conformations *are* in rapid equilibrium at room temperature.

the monoalkene is called the *dienophile* meaning it *loves* dienes.

ie the dienophile adds to *the same* face(s) of the *s-cis* diene conformation. This is called *suprafacial*.

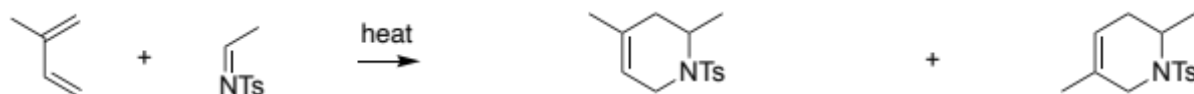


"4,4-dicyanocyclohexene"



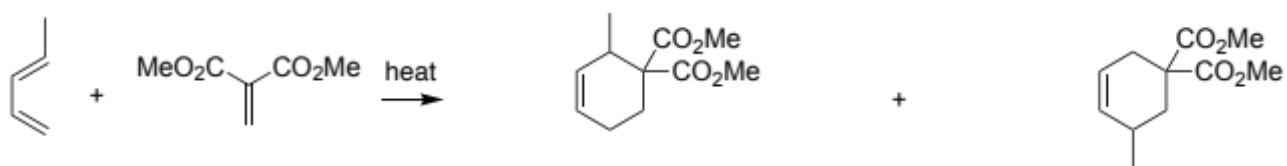
regioisomer 1

regioisomer 2



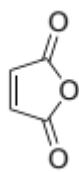
regioisomer 1

regioisomer 2



regioisomer 1

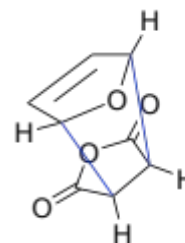
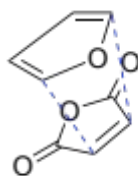
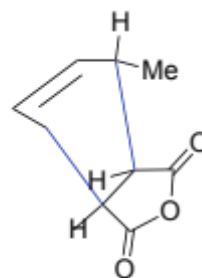
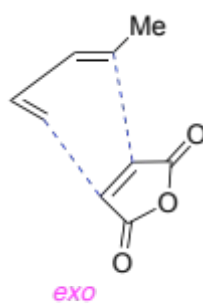
regioisomer 2

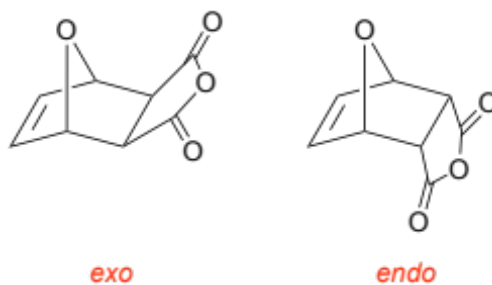


maleic anhydride

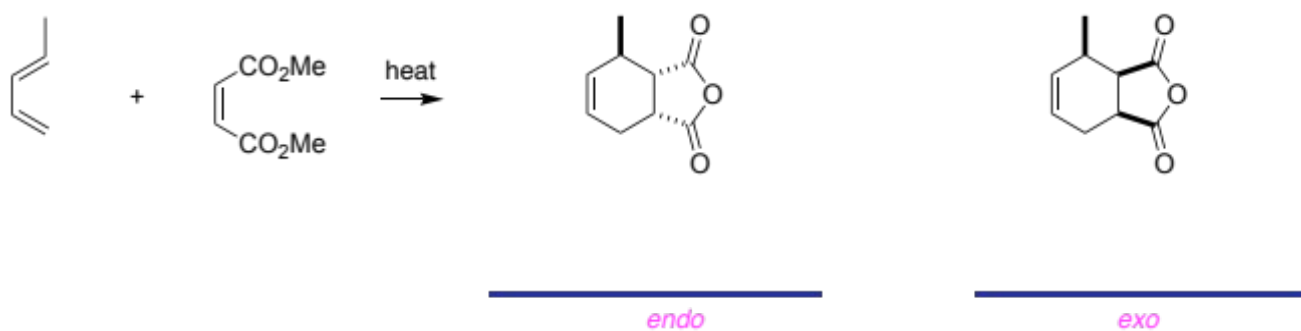
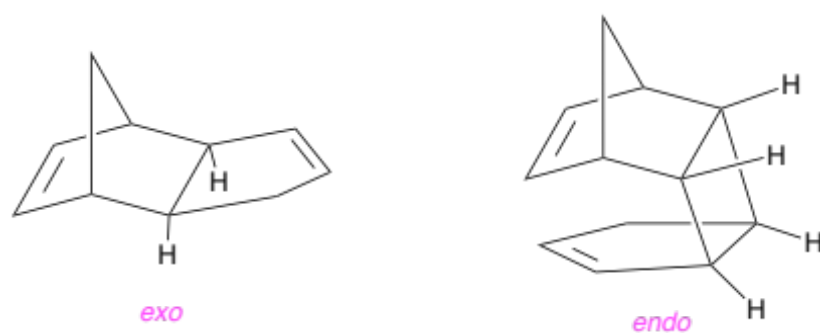


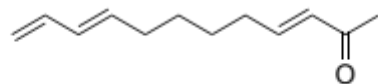
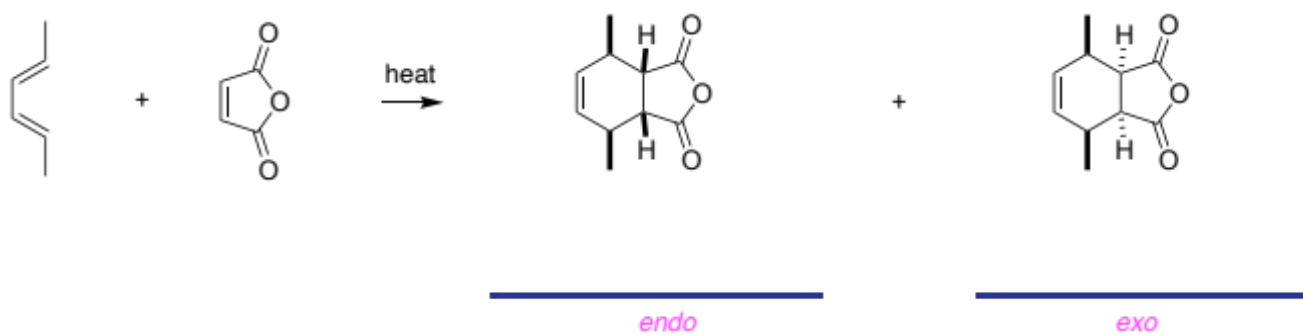
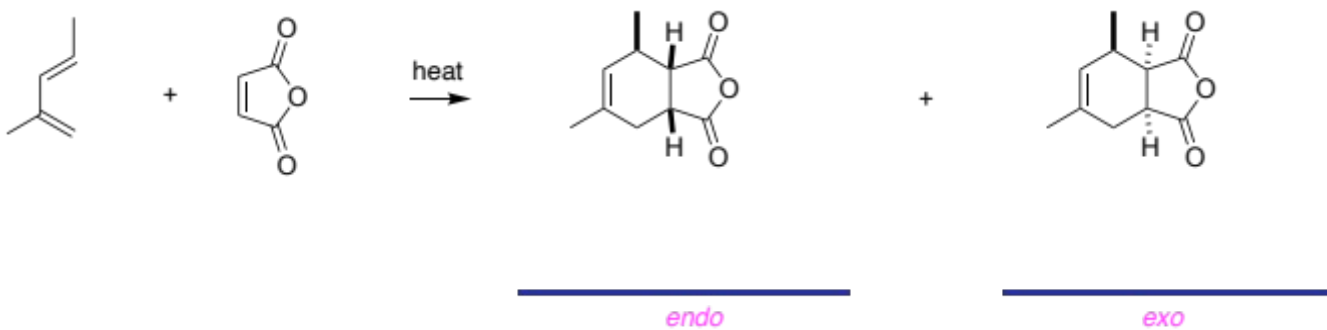
furan



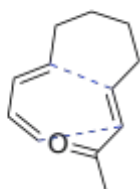


Consequently, the *endo*-isomer is the *kinetic* product, and the *exo*- will predominate at extended reaction time. A pure *exo*-isomer can be isolated in the *late* stages of the reaction and the equilibrium will adjust to *favor*

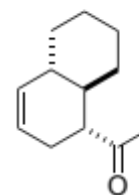




is equivalent to



heat



draw in a suitable conformation

1,3-butadiene gives 4 molecular orbitals of which the lowest energy 2 are filled with two electrons each.



HOMO-LUMO overlap such as that shown above are called *frontierorbital* interactions.

Charge in the *HOMO* redistributed to compensate for the lack of it in the *LUMO* drives these reactions to occur.