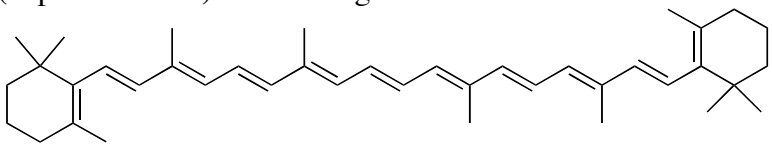
Conjugated Dienes and Colour Continued

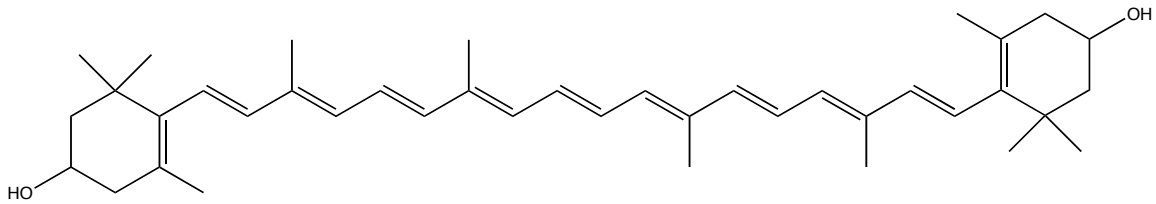
Beta-carotene (depicted below) is the orange-red colour in carrots.



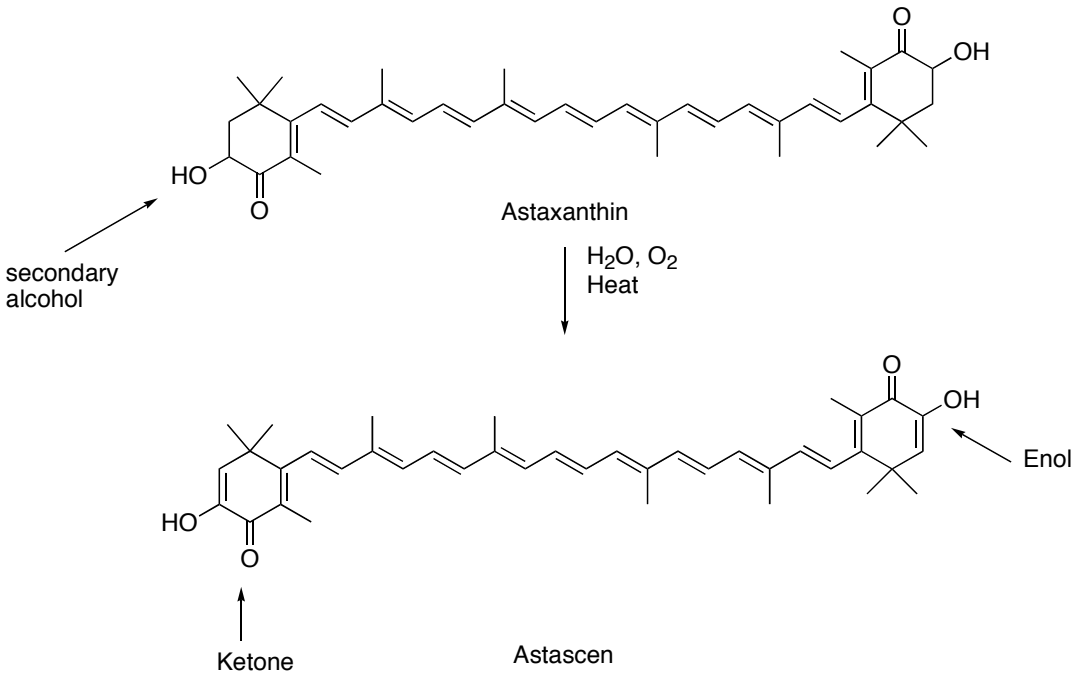
β-carotene

Xanthophylls

Xanthophylls are oxygenated carotene molecules. Zeaxanthin, shown below is purple.



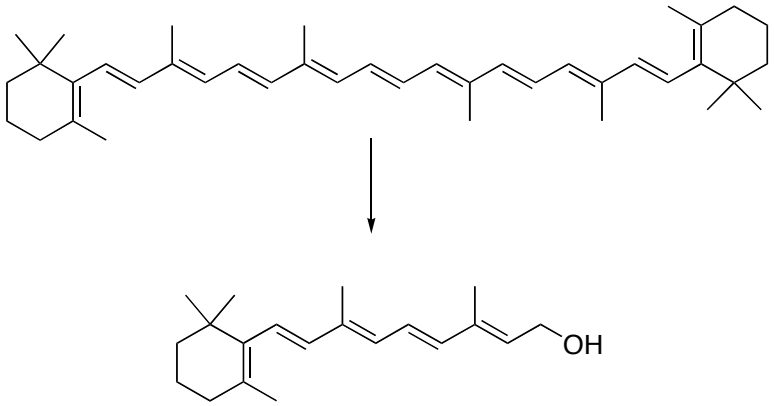
In the below example, astaxanthin, a blue-green pigment in algae, is converted to astascene with the addition of heat, water and oxygen. Astascene is red in colour and contains an enol functional group. Crustaceans (eg. lobsters) eat algae in their natural habitat and therefore ingest astaxanthin. When a lobster is cooked, it turns a bright red colour, which is mainly due to the formation of astascene.



Hemoglobin (red colour in blood) and chlorophyll A (green colour in plants) are two more examples of conjugated molecules that absorb light and serve critical functions.

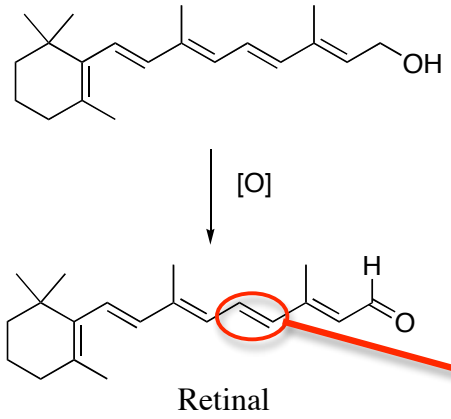
The Chemistry of Vision

Not all conjugated molecules are coloured (need 7 conjugated double bonds). They also make up the light sensitive substances responsible for the visual systems of organisms. A key component of our vision arises from the body's ability to synthesize Vitamin A from beta-carotene (shown below) in which the C_{40} beta-carotene is broken down into the C_{20} vitamin A.



Vitamin A

In the liver, vitamin A is further oxidized to retinal, a process in which the primary alcohol functionality is oxidized to the aldehyde.

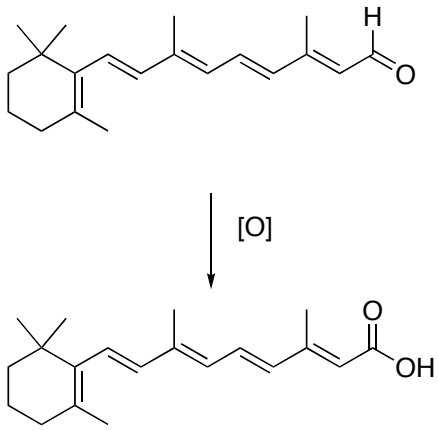


Retinal

This bond changes from trans to cis

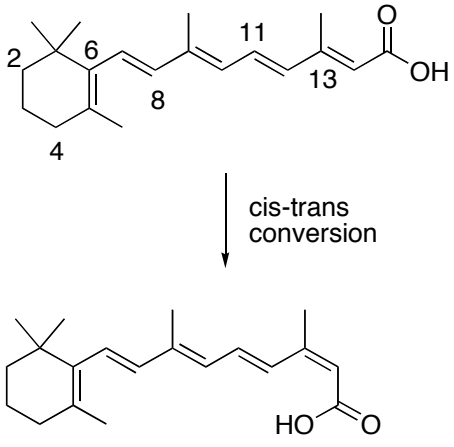
In the eye, retinal reacts with a protein called opsin to give rhodopsin, the visual pigment that is the actual light sensitive substance. Isomerization of the C11-C12 bond from trans to cis causes a conformational change in the 3D structure of the protein that results in nerve impulses being sent to the brain which are perceived as vision.

Further oxidation of the aldehyde to a carboxylic acid in retinal yields retinoic acid, a chemical messenger in the body, which provides signals for fetal development.



Retinoic acid

Conversion of the C13 double bond in retinoic acid to the cis conformation gives the drug Accutane, which is an anti-acne drug. It has teratogenic properties (i.e. can cause malformations and other birth defects)

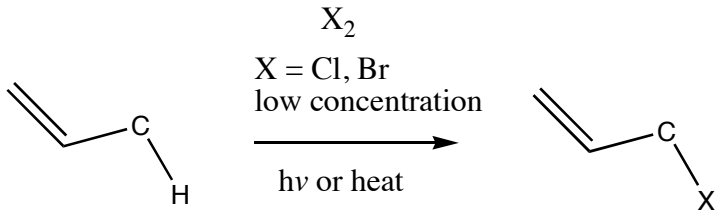


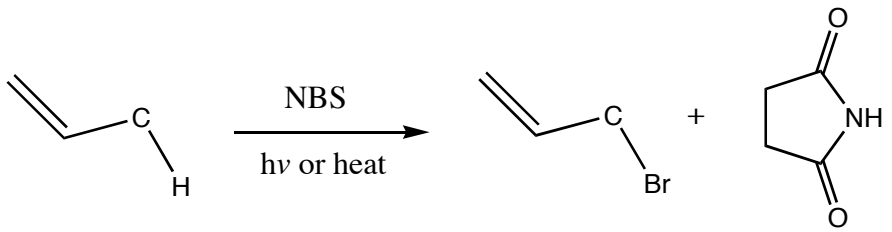
Accutane

Radical Halogenation

Substitution Reaction:

Note that if Hydrogens are not shown, other groups could also be attached for the following 2 examples



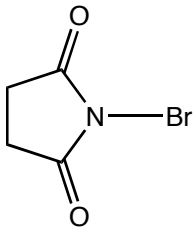


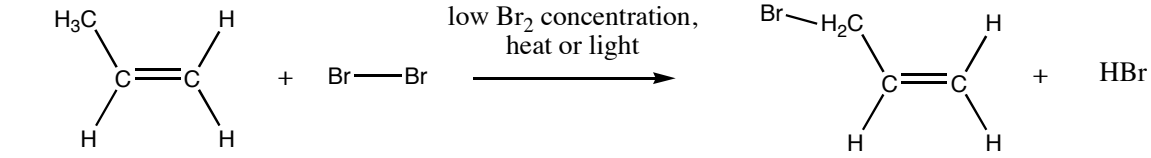
In this case, light is usually used

succinimide

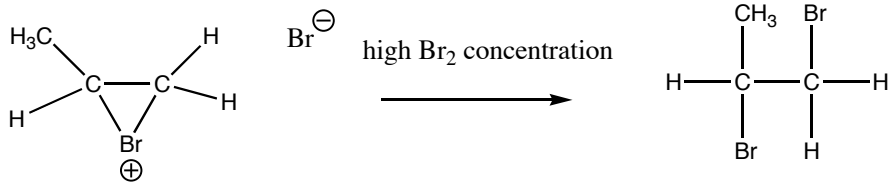
NBS = N-Bromosuccinimide

Know this reagent!



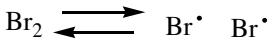


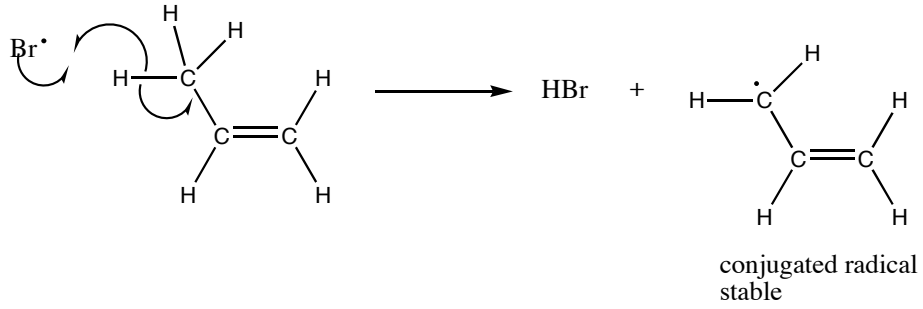
reversible

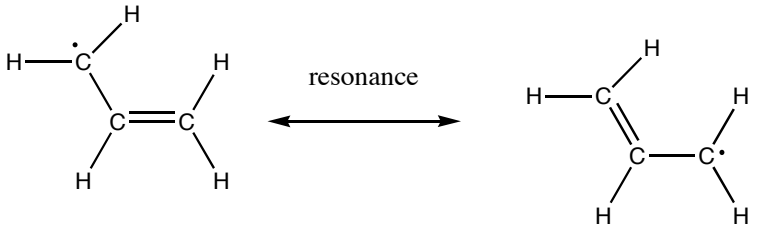


In the above example, the cationic intermediate is formed in both cases. If the bromine concentration is small, it is unlikely that the very small concentration of the Br^- will interact with the cation in order to react, so the cation just reacts back to the initial starting material and the first reaction predominates. If the bromine concentration is high, then it becomes much more likely that the Br^- will react with the cation and the second reaction predominates.

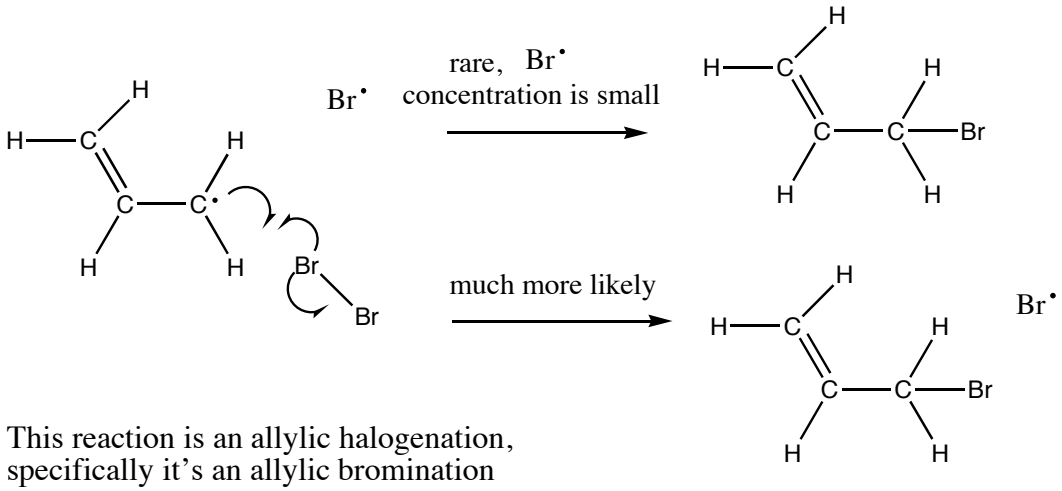
There is another reaction that competes with the first reaction, but it results in the same product:







The C with the radical has sp^2 geometry
The radical lines up with the p orbitals of the π bond

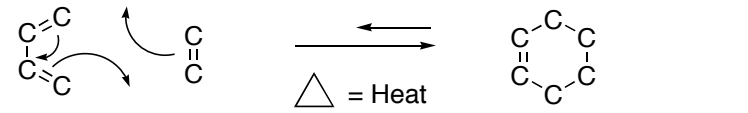


This reaction is an allylic halogenation, specifically it's an allylic bromination

Diels-Alder Reaction

The Diels-Alder reaction was discovered in 1928 by Kurt Alder and Otto Diels. Both later won the Noble Prize in 1950 for their discovery.

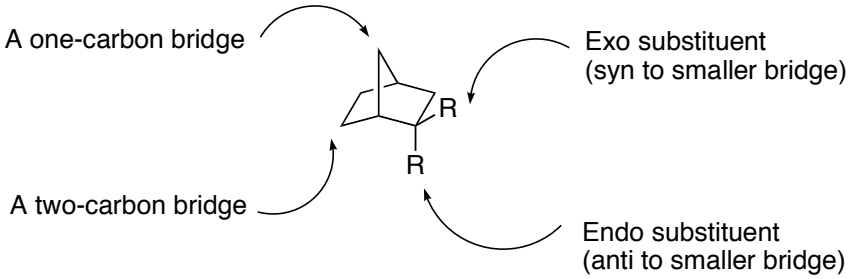
The Diels-Alder reaction consists of a conjugated diene in cisoid form reacting an alkene (also called an olefin, or for these reactions a dienophile because it is 'diene loving'). When heated, it forms two new carbon-carbon bonds in a single step and forms a cyclic molecule (a cyclohexene). The reaction is theoretically reversible but the stability of the product drives the reaction to completion. The Diels-Alder reaction is an example of a [4+2] electrocyclic reaction. The [4+2] refers to the 4 π-electrons from the diene and the 2 π-electrons from the dienophile. The mechanism of the Diels-Alder reaction occurs through a pericyclic process in which the π-electrons move in a cycle or ring.



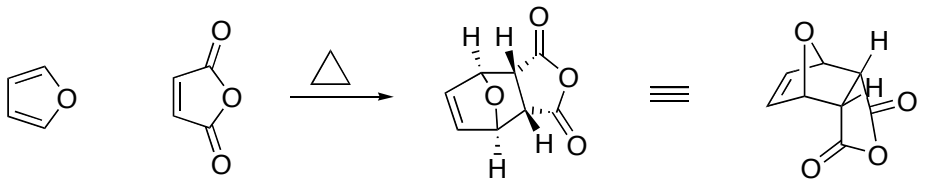
Diene Dienophile Diels-Alder adduct

Although the transoid conformation of dienes is more favoured, the cisoid and transoid conformations are in equilibrium, so as the cisoid reacts with the alkene, more is formed.

The mechanism is **concerted**, which means that all the bonds form and break at the same time (an S_N2 reaction is also concerted). As a result, the reaction is also **stereospecific**, which means that the stereochemistry of the starting materials determines the stereochemistry of the products. Starting from achiral substrates, a racemic mixture of stereoisomers can be formed. The diene and dienophile line up in such a way that the endo product rather than the exo product is formed. Endo and Exo are used to indicate the relative stereochemistry of a bicyclic structure. A substituent on one bridge is said to be endo if it is anti (trans) to the smaller of the two bridges and exo if it is syn (cis).

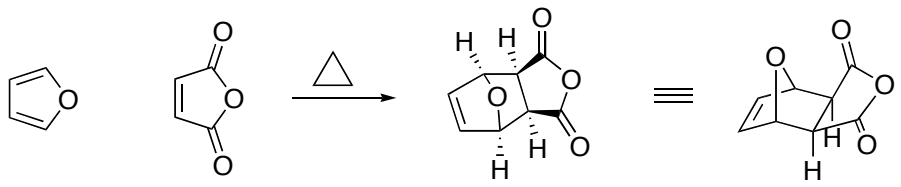


An example to apply to other systems is the Diels-Alder reaction of furan (diene) and maleic anhydride (dienophile). In this reaction, the dienophile approaches the 5-membered ring furan from the bottom side, producing an endo Diels-Alder adduct.



furan maleic anhydride Endo product

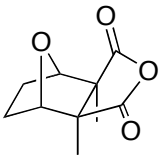
The exo product, which is not favored and not formed, would arise in the following manner.



furan maleic anhydride Exo product

Example of possible Diels-Alder adducts in Nature

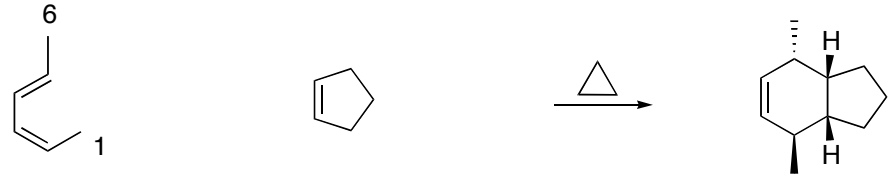
The Spanish fly (*Cantharis vesicatoria*) produces the molecule cantharidin, which contains an exo Diels-Alder product with an anhydride functional group.



Canthardin

Example of Predicting Stereochemistry

The following example uses 2Z, 4E-hexadiene (diene) and cyclopentene (dienophile) to produce an endo product. As shown before with the furan and maleic anhydride reaction, the stereochemistry of the endo product can be predicted. The methyl group at C6 is similar to that of the H in furan and therefore will be pointing down. The position of the C1 methyl group is similar to that of the oxygen in furan and therefore will point up in the endo product (by convention drawn away from (outside of) the cyclohexene ring).

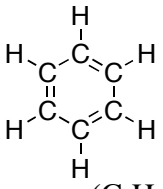


2Z,4E-hexadiene cyclopentene Endo product

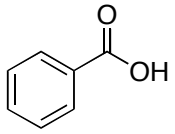
Lecture Outline 2 (Posted on the website)

Aromatic Compounds

Benzene was first isolated in 1825 by Michael Faraday. Its structure was later determined by Joseph Loschmidt and F. August Kekule to contain a cyclic, 6-membered ring containing alternating single and double bonds with 6 π-electrons. The name benzene comes from benzoic acid.

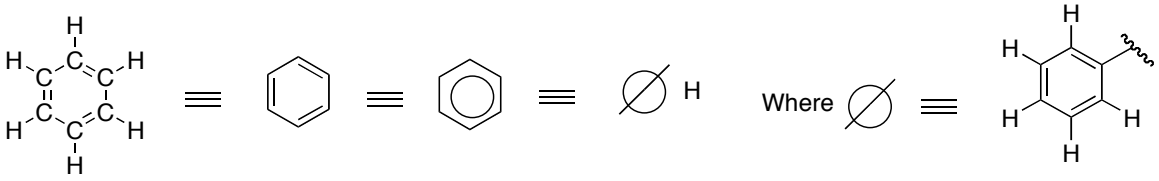


Benzene (C_6H_6)



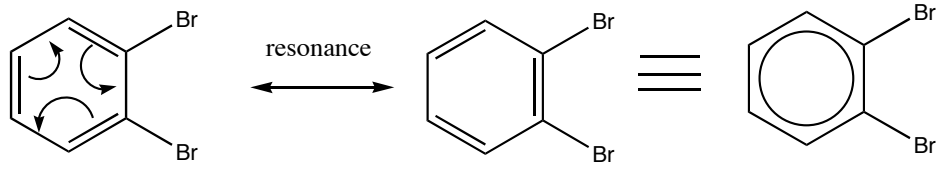
Benzoic acid

There are a few ways of drawing benzene. It is seen as alternating double and single bonds, a central circle or as the Greek symbol ϕ (phi).



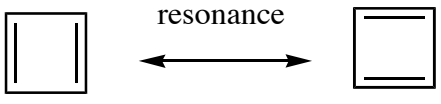
Phenyl group

The central circle is used to represent the resonance within the aromatic ring
Eg.



1,2-dibromobenzene

Benzene's resonance makes it 36 kcal/mol more stable than what is calculated for 'cyclohexatriene'.



cyclobutadiene

Is cyclobutadiene also aromatic?
No! It is actually anti-aromatic (to be described later)
It is extremely unstable

Rules for Aromaticity:

- Cyclic and conjugated about the ring
- Planar
- 4n + 2 π electrons, where n is a positive integer (ie. 1, 2, 3, 4, etc.)

4n+2 rule:

Benzene has 6 π electrons, so for this rule n = 1 (4*1+2 = 6)

Cyclobutadiene has 4 π electrons, which does not allow n to be an integer

4n+2 = 4, n = 0.5 which is not an interger, therefore this cannot be an aromatic molecule