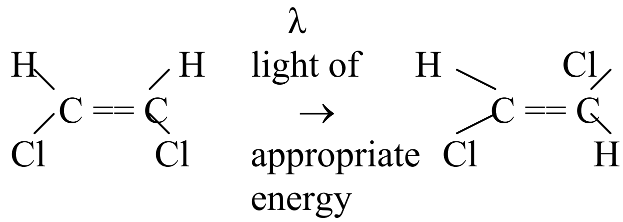
3.4 Photoisomerization reactions

A photoisomerization is the conversion of one isomer into another isomer by light. The examples we will look at involve exclusively the conversion between two geometric isomers.

Example:

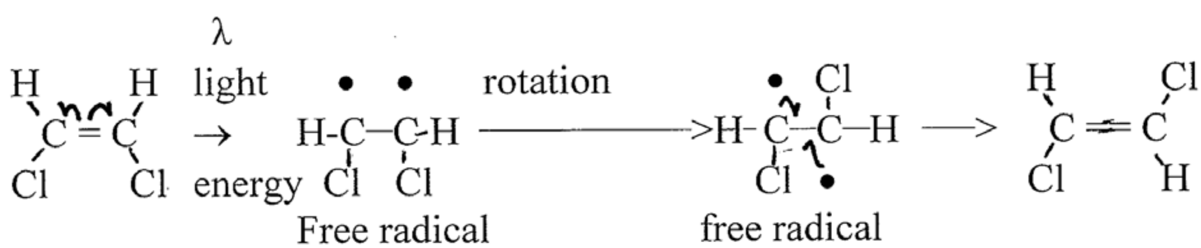


(The Greek letter λ signifies light.)

Reaction Pathway

How does this occur? Light energy (often abbreviated λ) can unpair the electrons in the pi bond so that only a single bond holds the 2 C atoms together. The resultant molecule has two unpaired electrons, and hence is not very stable. We call a molecule with unpaired electrons a **free radical** (no reference to its political status!). Since the free radical molecule has a C-C single bond, free rotation can occur about the C-C bond. After rotation through 180^{o} the unpaired electrons can pair up again and in the process form the other geometric isomer.

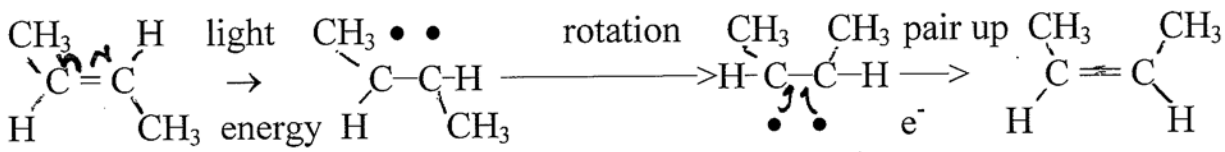
Let's look at a couple of specific examples:



The half arrows signify the movement of one electron from where the arrow starts to where the half arrow is pointing. In the first step of the above example, the two half arrows signify that light energy causes the **unpairing** of the pi electrons in the C=C double bond with one electron going to each of the C atoms. The unpaired electron is signified with a dot. The resulting single bond between the 2 C atoms can undergo free rotation. Eventually the two unpaired electrons can pair up and reform the double bond. This is indicated by the two half arrows that start at the unpaired electron on each separate C atoms and point back into the bond between them. This signifies the reforming of the pi bond.

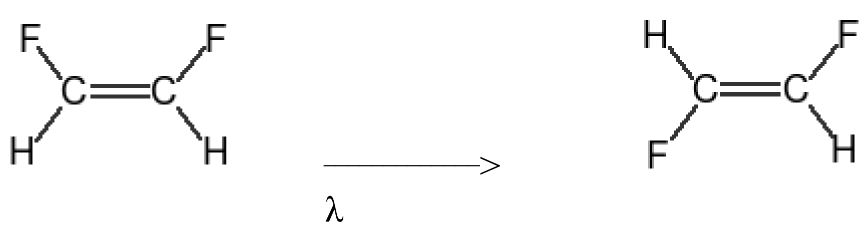
In the above reaction what sort of geometric isomer did we start with? What geometric isomer did we produce as a product?

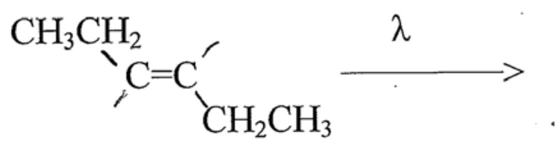
Example 2:



As before, the half arrows signify the movement of **one** electron from where the arrow starts to where the half arrow is pointing. In the first step of the above example, the two half arrows signify the unpairing of the pi electrons in the C=C double bond with one electron going to each of the C atoms. The unpaired electron is signified with a dot. The resulting single bond between the 2 C atoms can undergo free rotation. After a few rotations, the two unpaired electrons can pair up and reform the double bond. This is indicated by the two half arrows that start at the unpaired electron on each separate C atoms and point back into the bond between them. This results in the reformation of the pi bond and the end of free rotation.

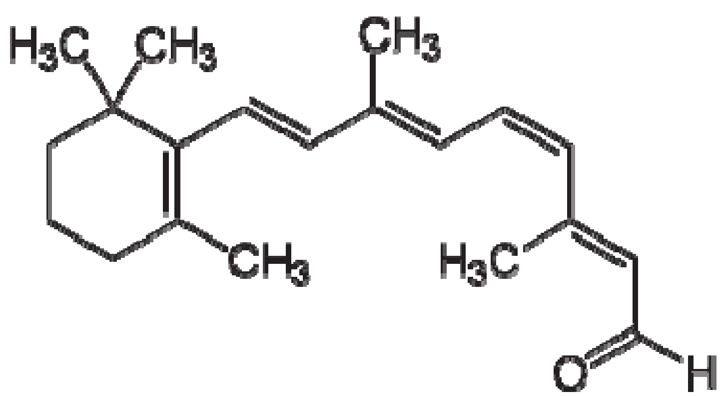
Try writing out the reaction pathway for the following reaction. Identify the beginning and final products as either cis or trans isomers.





Retinal photoisomerization

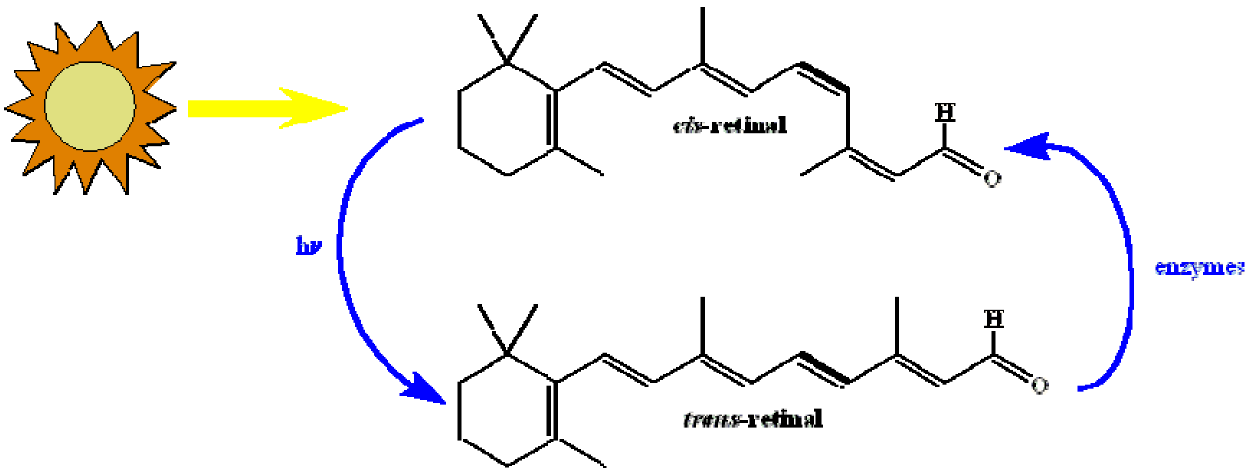
One molecule in which isomerization reactions are particularly important is cis-retinal (a form of vitamin A) shown below:



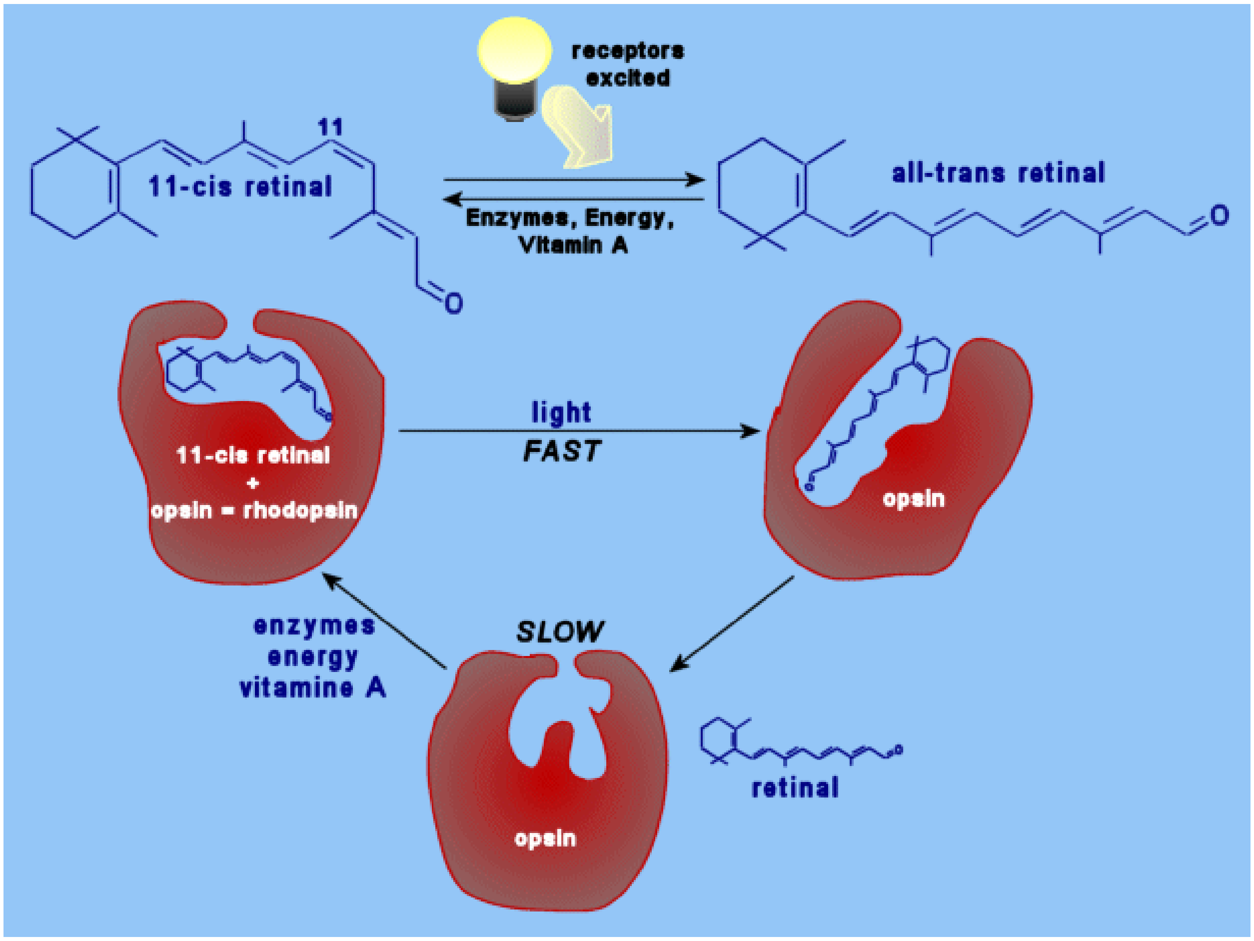
This complex molecule is known as cis-retinal or Vitamin A. Before we look at the isomerization of retinal (vitamin A), let's ask some questions about it.

1. Will it be soluble in water?
2. Label each of the bonds in the chain as cis or trans.

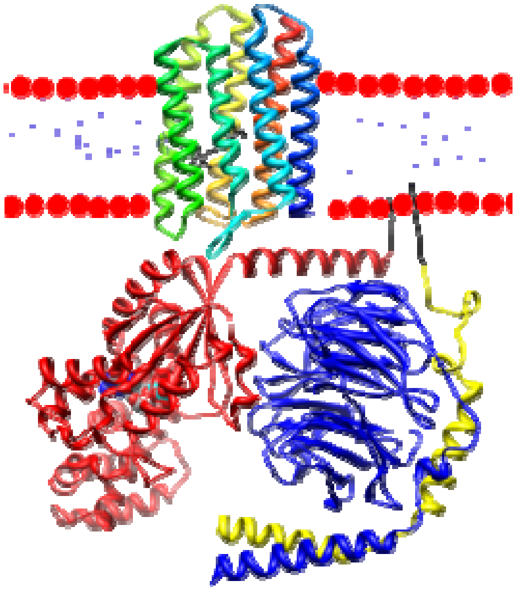
Isomerization of Vitamin A (retinal) in the eye.



In this isomerization, the one cis bond in the polyunsaturated chain is converted into the trans form, which is referred to as trans retinal or all trans-retinal.
Cis retinal is bound to the protein **opsin** imbedded in cell membranes of the retinal cell. The retinal-opsin complex in rod cells is called **rhodopsin.**

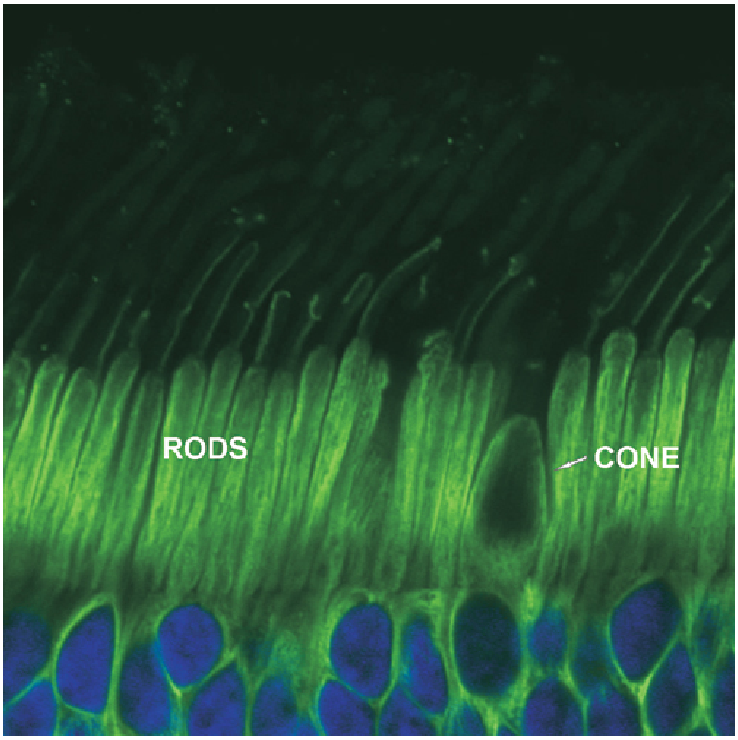


The energy of visible light unpairs the two electrons in the cis pi bond of retinal and when they are unpaired the C-C bond can rotate; when it rotates 180 degrees it converts the cis double bond into the trans geometric isomer. This photoisomerization occurs in about 2 (10^{-13}) seconds. (Now that's what I call fast!!) This chemical reaction causes the trans retinal to drop off of the opsin.



The opsin protein molecule then changes shape and sets off a chain of reaction which results in increased pumping positively charged Na ions across the retinal membrane **out** of the retinal cell, resulting in hyperpolarization. The potential of retinal membranes in the dark is about -30 mV. The pumping of sodium ions out of the retinal cell further polarizes the retinal cell membranes to -35 mV and this causes the retinal neuron to send a message to the brain: "I've just had an isomerization reaction!" Actually it comes across more like a flash of light. The trans form is slowly converted back to the cis form by an enzymatically catalyzed "dark" reaction and Na balance in the retinal neurons is returned. This conversion back to the cis form is much slower than the light induced cis–trans isomerization reaction. If there is a blinding flash of light that converts most of the cis retinal into trans retinal, one will not be able to see again until the trans retinal is converted back to cis and the cis retinal once again binds an opsin molecule. This reaction takes on the order of seconds to minutes rather than the fraction of a picosecond required for the forward photoisomerization reaction. (Although the free radical intermediates usually simply pair up again with each other, they occasionally react with other molecules and damage those molecules. This also reduces the supply of retinal, which must be continuously replaced with new vitamin A from the diet.)

Rhodopsin molecules in the **rod cells** are quite sensitive to light photons, and absorb maximally at 498 nm (green). They provide the black and white night vision in dim light. The **cone cells** are not as sensitive and hence are less useful in dim light, but they have three different forms of opsin protein which bind retinal to form three forms of the protein **photopsin**.



www.brps.org.uk/index.php?pageid=203&tln=aboutrp

The different **photopsin** proteins change the absorption spectrum of the retinal absorption spectrum. Maximally efficient activation of the blue form (short wavelength) of photopsin occurs at **420 nm**; maximally efficient activation of the middle wavelength (yellow) form of photopsin occurs at **534 nm** and long wavelengths (red) form of photopsin occurs at **564 nm;** the brain's sense of color is obtained by a comparison of the intensity of these three forms in a manner which is still not well understood.

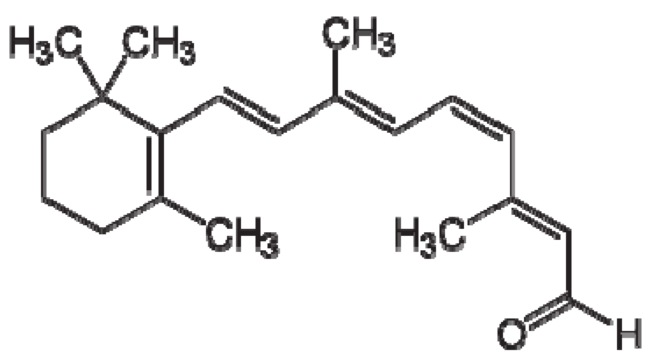
People who lack one of these forms of these cone photopsins will have color blindness with red color blindness being the most common (7% of the male population in the US). Most mammals only have 2 opsin forms in their cone cells, but humans, apes and some monkeys have 3. See "primate color vision" on the internet for more information.

Deficiency of vitamin A results in inability to quickly reform more cis retinal.

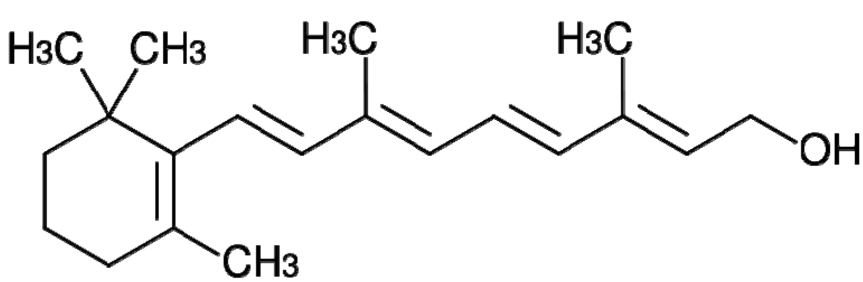
Still another form of retinal-bound opsin called **melanopsin** has been found in specialized cells of the retina where their activation appears to control pupil diameter; melanopsin is also thought to be part of the control of 24 hour circadian rhythms.

The retinal-opsin complex is also found in a salt-loving bacteria, Halobacterium , where it is found in a slightly different form as **bacteriorhodopsin**; these bacteria use bacteriorhodopsin to generate a voltage potential across their membrane. (They then use that voltage potential to make ATP, the energy currency of the cell.)

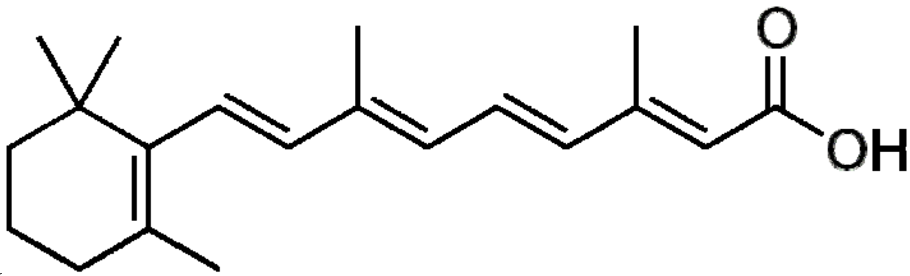
There are 3 chemical forms of vitamin A. They differ only in the functional group at the end of the polyunsaturated C chain. They are:



Retinal



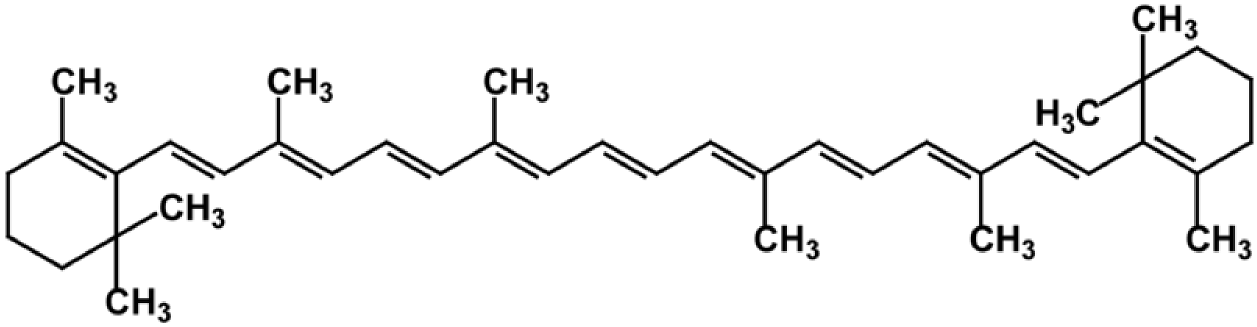
Retinol

retinoic acid 

This last form is of considerable pharmacological interest. It exists in the two forms, **cis retinoic acid** (marketed as **Accutane**) and **trans retinoic acid** (marketed as **Retin-A**).

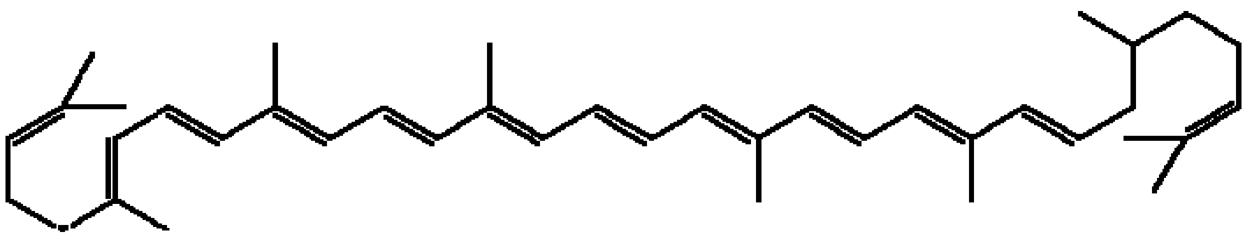
Both of these products are used for the treatment of acne. Retin-A is available as a cream, gel or solution which can be applied to skin for a 6 week course. It frequently causes redness, scaling, and sensitivity to sunlight. In addition to reducing acne, it decrease skin wrinkles slightly. This received publicity in the popular press and resulted in a large number of Retin-A prescriptions for middle aged women who had no problem with acne.

Accutane (cis retinoic acid) is the geometric isomer of Retin-A and is available in pill form. It is normally taken orally (P.O.) twice a day (bid) for a course of 15-20 weeks. Accutane is indicated for severe acne that is unresponsive to other forms of acne treatment. Like Retin-A, it can cause increased photosensitivity. One particular important adverse side effect is that Accutane is **teratogenic** -- it can cause birth defects. As a result, it is extremely important that women taking a course of Accutane should take effective measures to avoid pregnancy. By virtue of the fact that Retin-A is applied topically to the skin, there is much less absorption internally and it can be used during pregnancy.
Your mother may have told you to eat your carrots because they have lots of vitamin A. Carrots don’t contain vitamin A, but they do contain the orange pigment **β carotene**, a precursor of Vitamin A, which can be cleaved in half to produce trans retinal.



Beta carotene

A very similar compound, lycopene, is the primary red pigment found in tomatoes and is claimed to reduce the risk of heart disease and cancer. How is the structure of lycopene different from beta-carotene?



Lycopene