Beta-carotene

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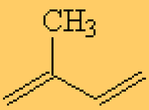
Beta-carotene is the molecule that gives carrots their orange colour. It is part of a family of chemicals called the carotenoids, which are found in many fruit and vegetables, as well as some animal products such as egg yolks. Carotenoids were first isolated in the early 19th century, and have been synthesised for use as food colourings since the 1950s.

Biologically, beta-carotene is most important as the precursor of vitamin A. It also has anti-oxidant properties and may help in preventing cancer and other diseases.

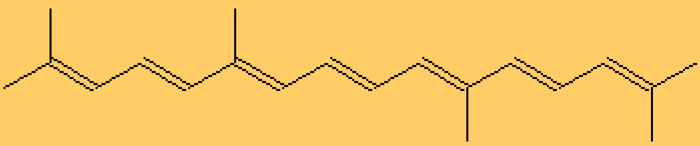
Structure

Beta-carotene is a member of a family of molecules known as the carotenoids. These have a basic structure made up of isoprene units:



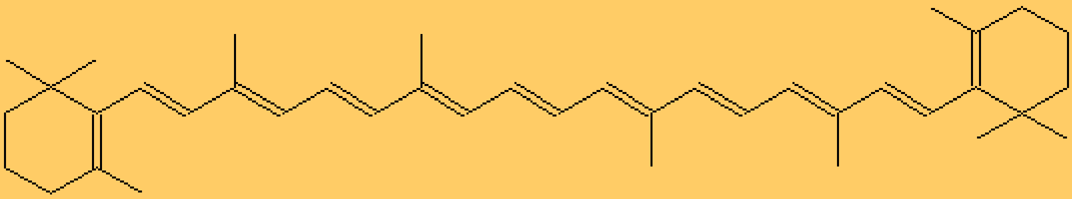
Isoprene

These are joined end-to-end to give a conjugated chain which is common to all carotenoids. Notice that the two centre isoprene units are joined differently to the others ("head-to-head" rather than "head-to-tail") so that the chain has a centre of symmetry.



The central part of a carotenoid

Beta-carotene is made up of eight isoprene units, which are cyclised at each end. It looks like this:



Beta-carotene

The long conjugated chain is responsible for the orange colour of beta-carotene.

History

The bright colours found in nature and the molecules which cause them have always fascinated organic chemists. The earliest studies on carotenoids date back to the beginning of the 19th century. Beta-carotene was first isolated by Wackenroder in 1831, and many other carotenoids were discovered and named during the 1800s, although their structures were still unknown.

Not until 1907 was the empirical formula of beta-carotene, $C_{40}H_{56}$, established by Willstatter and Mieg. The structure was elucidated by Karrer in 1930-31. This was the first time that the structure of any vitamin or provitamin had been established,   and he received a Nobel prize for his work.

Steenbock suggested in 1919 that there could be a relationship between beta-carotene and vitamin A. The concept of provitamins (molecules which are converted into vitamins by the body) was entirely new, and proved to have great significance scientifically and commercially.

The first total syntheses of beta-carotene were achieved in 1950, and Roche started producing it commercially in 1954. Various studies were carried out throughout the 1970s-80s to determine its suitability for use in food, and its activity in the body. In the early '80s it was suggested that beta-carotene might be useful in preventing cancer, and it was found to be an antioxidant. More recently beta-carotene has been claimed to prevent a number of diseases, including cystic fibrosis and arthritis, and there is a flourishing trade in vitamin supplements containing beta-carotene.

Synthesis

The first total syntheses of beta-carotene were reported in 1950 by Karrer and Eugster, Inhoffen *et al* and Milas *et al* . There are now many methods known, and beta-carotene is produced industrially on a large scale.

Beta-carotene contains 40 carbon atoms, *ie* it is a C_{40} carotenoid. There are numerous methods of joining two or three smaller molecules to give the required carbon skeleton. These can be classified as symmetric or unsymmetric. An example of a symmetric synthesis would be

$$C_{16} + C_8 + C_{16} = C_{40}$$

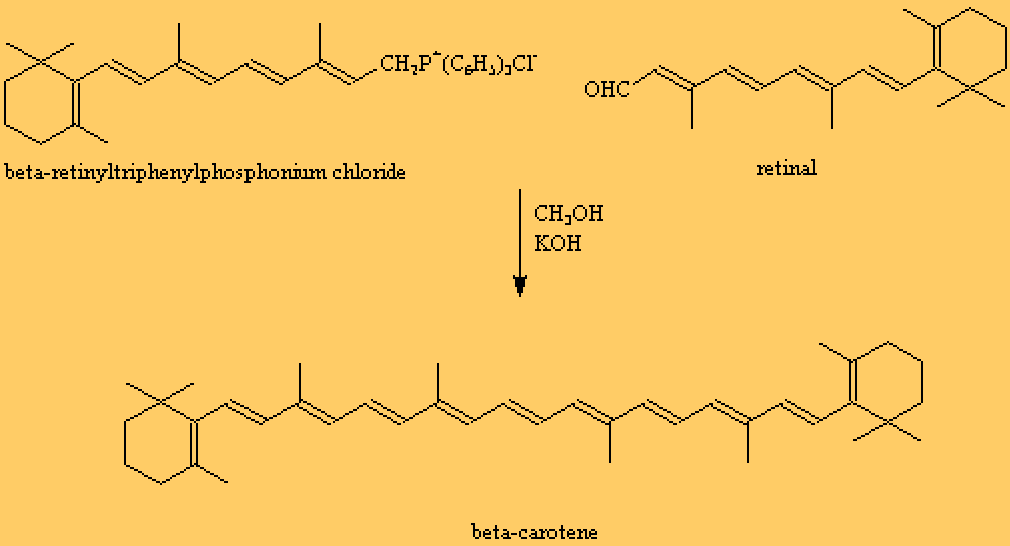
whereas an asymmetric synthesis would be

$$C_{25} + C_{15} = C_{40}$$

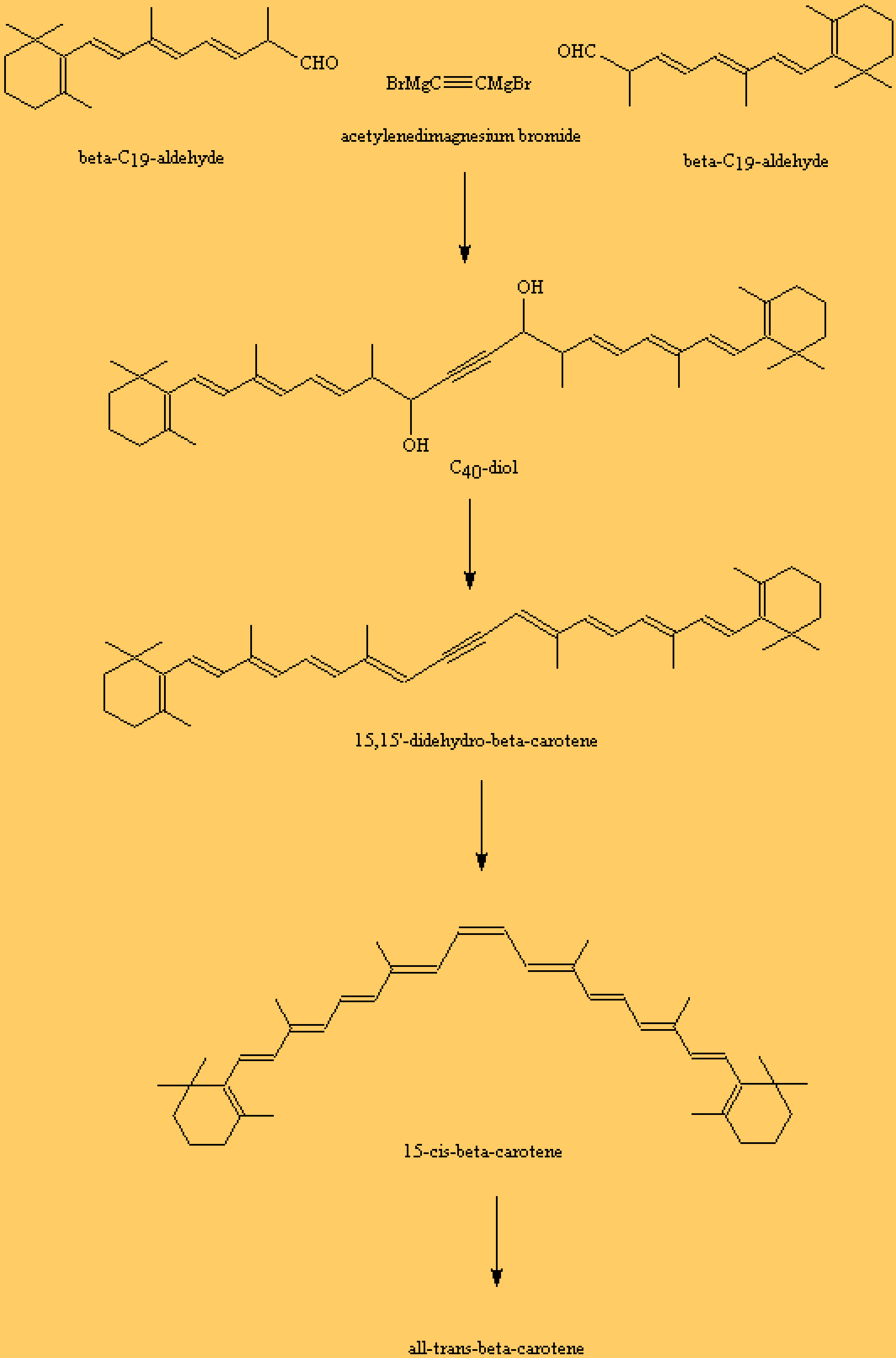
Here are two examples of industrial syntheses. The first was developed by the Badische Anilin- & Soda-Fabrik (BASF) and is based on the Wittig reaction. The second is a Grignard reaction, elaborated by F.

Hoffman-La Roche & Co. Ltd (Roche) from the original synthesis of Inhoffen *et al*. They are both symmetrical; the BASF synthesis is C_{20} + C_{20} , and the Roche synthesis is C_{19} + C_2 + C_{19} .

BASF Synthesis

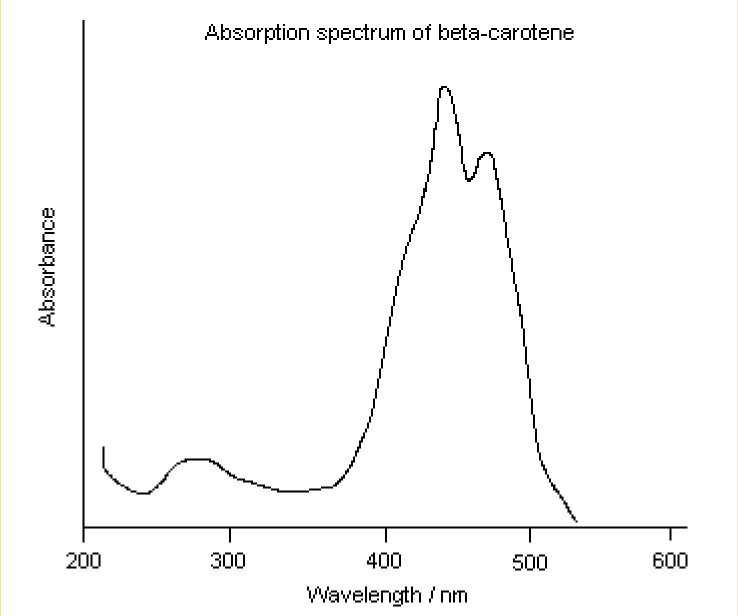


Roche synthesis



Colourings

The conjugated chain in carotenoids means that they absorb in the visible region and hence are coloured. The absorption spectrum below shows that beta-carotene absorbs most strongly between 400-500 nm. This is the green/blue part of the spectrum. So beta-carotene appears orange, because the red/yellow colours are reflected back to us.



After Vetter et al. in Carotenoids (ed. O. Isler), Birkhauser Verlag, 1971 , p194

Natural colours

Carotenoids are one of the most important groups of natural pigments. They are responsible for many of the yellow and orange colours of fruit and vegetables. Beta-carotene is most abundant in carrots, of course, but is also found in pumpkins, apricots and nectarines. Dark green vegetables such as spinach and broccoli are another good source. In these the orange colour is masked by the green colour of chlorophyll. This can be seen in leaves; in autumn, when the leaves die, the chlorophyll breaks down, and the yellow/red colours of the more stable carotenoids can be seen.

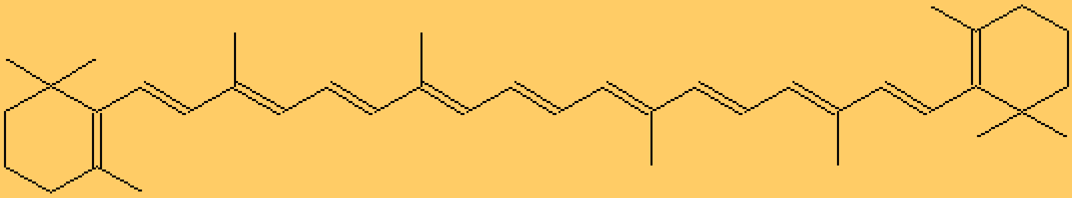
See here for more information on natural sources of beta-carotene.

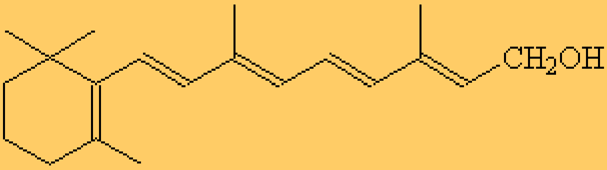
Artificial colours

Natural extracts containing carotenoids, for example carrot extracts and red palm oil, have been used to colour foods for centuries. Synthetic beta-carotene was first marketed as a food colouring by Roche in 1954. It is mainly used for colouring margarine and butter; its vitamin A activity is an added benefit. Other applications include ice-cream, fruit juice and the coatings of tablets. Beta-carotene has an advantage over other artificial colours, for example azo dyes, because it occurs naturally in food and is so known to be safe.

Vitamin A

Beta-carotene is also known as provitamin A, because it is one of the most important precursors of vitamin A in the human diet. If you compare the two molecules, it is clear that vitamin A (retinol) is very closely related to half of the beta-carotene molecule.

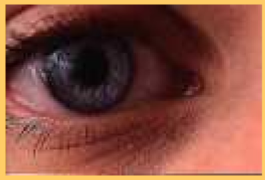




Vitamin A

There are two ways in which beta-carotene can be converted to vitamin A: either by cleavage at the centre or by breaking the molecule down from one end (see here for a diagram illustrating these processes). The second of these is thought to be most important biologically. The breakdown of beta-carotene occurs in the walls of the small intestine (intestinal mucosa) and is catalysed by the enzyme beta-carotene dioxygenase. The retinol formed is stored in the liver as retinyl esters. This is why cod liver oil used to be taken as a vitamin A supplement. It is also why you should never eat polar bear liver if you run out of food in the Arctic; vitamin A is toxic in excess and a modest portion of polar bear liver contains more than two years supply!

Beta-carotene, on the other hand, is a safe source of vitamin A. The efficiency of conversion of beta-carotene to retinol depends on the level in the diet. If you eat more beta-carotene, less is converted, and the rest is stored in fat reserves in the body. So too much beta-carotene can make you turn yellow, but will not kill you with hypervitaminosis.



Vitamin A has several functions in the body. The most well known is its role in vision - hence carrots "make you able to see in the dark". The retinol is oxidised to its aldehyde, retinal, which complexes with a molecule in the eye called opsin. When a photon of light hits the complex, the retinal changes from the 11-cis form to the all-trans form, initiating a chain of events which results in the transmission of an impulse up the optic nerve. A more detailed explanation is given here. Other roles of vitamin A are much less well understood. It is known to be involved in the synthesis of certain glycoproteins, and that deficiency leads to abnormal bone development, disorders of the reproductive system, xerophthalmia (a drying condition of the cornea of the eye) and ultimately death.

References

Links

http://www.roche.com/vitamins/what/general/bc.html
General information about beta-carotene

http://web.indstate.edu/thcme/mwking/vitamins.html#a
More about vitamin A

http://micro.magnet.fsu.edu/vitamins/pages/carotene.html
Picture of beta-carotene under the microscope

http://www.nobel.se/chemistry/laureates/1937/karrer-bio.html
Paul Karrer and his Nobel prize for work in carotenoids

http://webmd.lycos.com/content/dmk/dmk_article_546187
Beta-carotene and arthritis

http://www.tnp.com/article.asp?ID=244
Beta-carotene and cystic fibrosis

http://www.roche.com
F. Hoffman-La Roche & Co. Ltd home page

http://www.basf.com
Badische Anilin- & Soda-Fabrik home page

http://www.arttoday.com
Provided many of the images on these pages

Literature

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Carotenoids (ed. Otto Isler). Birkhauser Verlag, 1971.

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