1. Chemistry, occurrence, functions, uses

2. Biosynthetic principles ("isoprene rule")
Today’s topic on the Arabidopsis node map
Paleogeochemistry of terpenoids

(adapted from Brassel (1994) Isopentenoids and Geochemistry. In: Isopentenoids and Other Natural Products. ACS Symposium Series 562, D. Nes (Ed.), pp. 2-31.)
Terpenoid chemistry – classification (mostly correct)


• **Hemiterpenes** consist of a single isoprene unit. Isoprene itself is considered the only hemiterpene, but oxygen-containing derivatives such as prenol and isovaleric acid are hemiterpenoids.

• **Monoterpenes** consist of two isoprene units and have the molecular formula C\textsubscript{10}H\textsubscript{16}.

• **Sesquiterpenes** consist of three isoprene units and have the molecular formula C\textsubscript{15}H\textsubscript{24}.

• **Diterpenes** are composed for four isoprene units and have the molecular formula C\textsubscript{20}H\textsubscript{32}. They derive from geranylgeranyl pyrophosphate. Diterpenes also form the basis for biologically important compounds such as retinol, retinal, and phytol.

• **Sesterterpenes**, terpenes having 25 carbons and five isoprene units, are rare relative to the other sizes. (The sester-prefix means half to three, i.e. two and a half.)

• **Triterpenes** consist of six isoprene units and have the molecular formula C\textsubscript{30}H\textsubscript{48}.

• **Tetraterpenes** contain eight isoprene units and have the molecular formula C\textsubscript{40}H\textsubscript{64}.

• **Polyterpenes** consist of long chains of many isoprene units. Natural rubber consists of polyisoprene in which the double bonds are cis. Some plants produce a polyisoprene with trans double bonds, known as gutta-percha.
Terpenoid chemistry – classification

Hemiterpenes

Isoprene

Natural Occurrence
Isoprene is produced and emitted by many species of trees into the atmosphere (major producers are oaks, poplars, eucalyptus, and some legumes). The yearly production of isoprene emissions by vegetation is around 600 Tg. This is about equivalent to methane emission into the atmosphere and accounts for ~1/3 of all hydrocarbons released into the atmosphere. After release, isoprene is converted by free radicals (like the hydroxyl (OH) radical) and to a lesser extent by ozone into various species that mix into water droplets and help create aerosols and haze. A second major effect of isoprene on the atmosphere is that in presence of nitric oxides (NOx) it contributes to the formation of tropospheric (lower atmosphere) ozone, which is one of the leading air pollutants in many countries.

Industrial Production
Isoprene is most readily available industrially as a byproduct of the thermal cracking of naphtha or oil, as a side product in the production of ethylene. About 800,000 tonnes are produced annually. About 95% of isoprene production is used to produce cis-1,4-polyisoprene—a synthetic version of natural rubber.

Meroterpenes

trans-Zeatin
(cytokinin hormone)
Terpenoid chemistry – classification

Monoterpenes

Acyclic

Myrcene (hops)

Linalool (lavender)

Monocyclic

(-)-Menthol (mint)

Thymol (thyme)

Carvacrol (oregano)

Bicyclic

(-)-α-Pinene (pine resin)

Eucalyptol (Eucalyptus)
Terpenoid chemistry – classification


Sesquiterpenes

Acyclic

(E,E)-α-Farnesene
(green apple odor)

Monocyclic

α-Humulene
(hops)

Zingiberene
(ginger)

Bicyclic

(-)-β-Caryophyllene
(black pepper)

Tricyclic

(+)-Longifolene
(pine oil)
**Terpenoid chemistry – classification**


**Diterpenoids**

Abietic acid  
(resin acid)

Forskolin  
(activates adenylate cyclase;  
Raises cAMP levels)

Taxol® (paclitaxel)  
(Pacific yew; produced commercially in world’s largest  
cGMP plant cell culture facility)

Stevioside  
(Stevia; ~300-fold sweeter than sucrose)

Salvinorin A  
(Salvia divinorum;  
potent opioid receptor agonist)
Terpenoid chemistry – classification

**Triterpenoids**

β-Sitosterol
(membrane phytosterol)

Brassinolide
(plant hormone; cell elongation)

**Triterpenoid saponins**

Lanatoside
(cardiac glycoside; Digitalis; aglycone: digoxigenin, hapten for immunohistochemistry)

Avenacin A1
(oat)
Terpenoid chemistry – classification

**Tetraterpenoids**

**Hydrocarbons**

Lycopene (pigment of red-colored fruit)

**Alcohols**

Zeaxanthin (xanthophyll)

**Ketones**

Capsorubin (paprika oleoresin)

**Apocarotenoids**

Abscisic acid (plant hormone)

Crocin (saffron)
Polyterpenes

Aircraft tires are made almost exclusively from natural rubber.

Latex from guayule is hypoallergenic.


 cis-Polyisoprene
(Hevea brasiliensis; Latex obtained by tapping trees)
Revisited after 50 Years: The ‘Stereochemical Interpretation of the Biogenetic Isoprene Rule for the Triterpenes’

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In memoriam Leopold Ruzicka and Oskar Jeger

1. Introduction. – In the December issue of Helvetica Chimica Acta, 1955, we published, together with Leopold Ruzicka and Oskar Jeger, a paper entitled ‘Eine stereochemische Interpretation der biogenetischen Isoprenregel bei den Triterpenen’, of which John W. Cornforth in 1961 wrote that it ‘might be termed the apotheosis of the isoprene rule’. In conjunction with a related publication by Stork and Burgstahler, which also appeared in 1955, the paper had a decisive influence on research in the fields of structure determination, biomimetic chemical synthesis, and biosynthesis of polycyclic triterpenoids and steroids in the decades that followed its publication. Today, half a century later, interest in the paper still seems to persist, so that, for example, a young organic chemist, Jeffrey Johnston [6], on his way to write a representative review on biomimetic carbocyclization to terpenes and steroids, recently inquired whether an English translation of the 1955 Helvetica Chimica Acta paper might exist. The answer, quite luckily, happened to be yes, since, about five years ago, Erik Sorensen at Scripps had persuaded Lucy Stark, one of his Ph.D. students, to produce just such a translation of the paper that had been written in an era when major chemistry departments in the US still required their Ph.D students to be capable of reading chemical literature in German. It is this coincidence, besides the fact that, now, after half a century, X-ray analyses of squalene and squalene oxide cyclases have provided experimental evidence for the essential correctness of the paper’s central postulates, that led us, the two surviving authors of the 1955 paper, to consider revisiting it in the light of contemporary knowledge of the chemistry and biochemistry of this family of natural products and ‘celebrating’, so to say, the paper’s hemi-centennial by publishing the English translation in the December issue of the same journal in which the German original had appeared exactly 50 years earlier.
Biosynthetic principles

Formation of isoprenoids by condensation of C5 units

“Head” to “tail”

Monoterpenes (Menthone) | Sesquiterpenes (Cedrol)

“Head” to “head”

Triterpenes (squalene as intermediate) | Tetraterpenes (β-Carotene)

“Head” to “middle”

Monoterpene (Pyrethrin)
Recognizing terpenoid $C_5$ units

Retrobiosynthesis
Recognizing terpenoid C₅ units

Practice examples:
Recognizing terpenoid C₅ units

Practice examples: solutions