Terpenes

MANFRED EGGERSDORFER, BASF Aktiengesellschaft, Ludwigshafen, Germany

1. General

1.1. Definition and Basic Structures

Terpenes are natural products, whose structures are built up from isoprene units. They are classified according to the number of these units:

<table>
<thead>
<tr>
<th>Monoterpenes</th>
<th>C₁₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sesquiterpenes</td>
<td>C₁₅</td>
</tr>
<tr>
<td>Diterpenes</td>
<td>C₂₀</td>
</tr>
<tr>
<td>Sesterpenes</td>
<td>C₂₅</td>
</tr>
<tr>
<td>Triterpenes</td>
<td>C₃₀</td>
</tr>
<tr>
<td>Tetraterpenes</td>
<td>C₄₀</td>
</tr>
</tbody>
</table>

Terpenes can be acyclic, or mono-, bi-, tri-, tetra-, and pentacyclic with 3-membered to 14-membered rings [1–7].

Deviations from the rule occur through rearrangement reactions or degradation of parts of the molecule during biosynthesis. The broader term terpenoids also covers natural degradation products, such as ionones, and natural and synthetic derivatives, e.g., terpene alcohols, aldehydes, ketones, acids, esters, epoxides, and hydrogenation products.

An overview of the most important basic structures demonstrates the structural variety of terpenes [8]. The compounds are normally known by their trivial names, as the systematic nomenclature is frequently less practicable for complicated structures.

© 2012 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

DOI: 10.1002/14356007.a26_205
1.2. Occurrence

Terpenes occur everywhere and in all organisms, in particular in higher plants. Certain components or their combinations are often characteristic of individual types of plant, so terpenes are used for chemotaxonomy [8]. In vegetable raw materials mono- and sesquiterpenes are predominantly found in essential oils [9], [10], sesqui-, di-, and triterpenes in balsams and resins [11], tetraterpenes in pigments (carotenoids) [12], and polyterpenes in latexes [13]. Animal organisms also contain terpenes and terpenoids, which are predominantly incorporated by consumption of plants.

1.3. Biosynthesis

The biosynthesis of terpenes was explained by F. LYNEN. Starting from (3 R)-(-)-mevalonic acid (C_6), isopentenyl diphosphate (IDP) and dimethylallyl diphosphate (DMADP) [8], [14–16] are formed by decarboxylation and isomerization as active C_5 building blocks (Scheme 1). (3 R)-(-)-Mevalonic acid is formed from three C_2 units from acetyl-CoA [8]. Plants synthesize IDP in the chloroplasts, mitochondria, and microsomes; animals synthesize IDP in the liver.

Monoterpenes are formed by stereospecific condensation of IDP with DMADP, whereby a diphosphate anion (PP) is eliminated from DMADP. Geranyl diphosphate is thus formed in a head-to-tail condensation. Neryl diphosphate with the Z-double bond is formed when the S-proton in isopentenyl diphosphate is eliminated stereospecifically. Neryl diphosphate is also formed from geranyl diphosphate by double bond isomerization.

The hydrolysis of geranyl or neryl diphosphate by a prenolpyrophosphatase gives the monoterpane alcohols geraniol and nerol. The acyclic monoterpane hydrocarbons, such as myrcene and ocimene, are formed by dehydration and isomerization of geraniol. The monoterpane aldehydes geranial and neral are formed from geraniol, and the biosynthesis of cyclic monoterpenes involves the loss of diphosphate from neryl diphosphate. The carbonium ion formed is stabilized by ring closure, sometimes after rearrangement, elimination of a proton, or addition of an anion.

The head-to-tail condensation of IDP with geranyl diphosphate gives farnesyl diphosphate, which rearranges further to give geranylgeranyl diphosphate. A large number of sesqui-, di-, and polyterpenes are formed from farnesyl and geranyl diphosphates in the same way as the monoterpenes. Triterpenes (and hence, steroids) are formed by head-to-head condensation of two C_{15} units (farnesyl diphosphate), and tetraterpenes from two molecules of geranylgeranyl diphosphate.

1.4. Biodegradation

Terpenes are degraded by microorganisms, such as Pseudomonas and Aspergillus species [17]. Generally both acyclic and cyclic terpenes are oxidized. Plants are known to be capable of degrading as well as forming terpenes.

In animals acyclic terpenes are degraded by ω-, α- and/or β-oxidation and cyclic terpenes by hydroxylation (elimination as glucuronides).

1.5. Importance and Extraction

Since the study of organic chemistry began, it has been intensively concerned with terpenes. Many
reactions, such as the Wagner–Meerwein rearrangement, theories of conformational analysis, and the Woodward–Hoffmann rules have their basis in terpene chemistry. The postulation of the isoprene rule by O. WALLACH (1887) and its confirmation and extension by L. RUZICKA (1921, 1953) gave this area of chemistry direction and unity.

Monoterpenes and a few sesquiterpenes are important economically as perfumes and fragrances (Perfumes, Flavors and Fragrances). Depending on the properties, terpenes (mostly essential oils) are obtained from the corresponding plants by steam distillation, extraction, or enfleurage. The pure terpenes are mostly isolated from the extracts by fractional distillation.

As readily available, optically active products, some monoterpenes, such as (−)-α-pinene and (−)- and (+)-limonene are used for the synthesis of other optically active products and reagents for cleaving racemates [18].

Various essential oils and the terpenes isolated from them are still used in pharmaceutical preparations, e.g., turpentine, camomile oil, eucalyptus oil, and camphor. The activity of some plants used in medicine and flavoring is due to their terpene content [19]. Terpenes are also used in the production of synthetic resins [20–22], and as solvents or diluting agents for dyes and varnishes [23].

In the following sections only the industrially most important terpenes are dealt with, insofar as they are not part of other articles (Flavors and Fragrances, Turpentines, and Tall Oil). For natural resins, gibberellic acid (Plant Growth Regulators), vitamins A and E (Vitamins, 2. Vitamin A (Retinoids), 3. Vitamins, 4. Vitamin E (Tocopherols, Tocotrienols)).
triterpenes (→ Steroids), tetraterpenes, and the other terpenes the specialist literature must be consulted.

2. Acyclic Monoterpenes

The following acyclic terpenes and terpene derivatives are described elsewhere (→ Flavors and Fragrances):

**Alcohols:** geraniol, nerol, linalool, myrcenol, citronellol, dihydromyrcenol, tetrahydrogeraniol, and tetrahydrolinalool.

**Aldehydes and Acetals:** citral, citral dimethylacetal, citronellal, hydroxydihydrocitronellal, hydroxydihydrocitronellal dimethylacetal, and methoxydihydrocitronellal

**Esters and Nitriles:** geranyl formate, acetate, isobutyrate, isovalerate, phenylacetate, and propionate; neryl acetate; linalyl acetate, butyrate, formate, isobutyrate, and propionate; lavandulyl acetate; and citronellyl acetate, formate, isobutyrate, isovalerate, propionate, and tiglate.

2.2. Myrcene

Myrcene \([123-35-3]\), 2-methyl-6-methylene-2,7-octadiene, \(C_{10}H_{16}\), \(M_r 136.23\), is a colorless liquid with a pleasant odor.

Some physical properties are listed below:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>166 – 168 °C (101.3 kPa)</td>
</tr>
<tr>
<td>(d^{20})</td>
<td>0.7905</td>
</tr>
<tr>
<td>(n^D_{20})</td>
<td>1.4697</td>
</tr>
<tr>
<td>mp</td>
<td>50 °C</td>
</tr>
</tbody>
</table>

Myrcene is very reactive. It polymerizes slowly at room temperature. For this reason it is stored in a cool place from which light and air are excluded. It can be stabilized by the addition of 0.1 % 4-(tert-butyl)catechol.

Although myrcene occurs naturally in many organisms, its extraction is uneconomic; it is produced industrially by pyrolysis of \(\beta\)-pinene [24].

The fragmentation of linalool and linalyl acetate and the catalytic dimerization of isoprene have been described as laboratory methods [25].

Because of its functionality, myrcene is the starting material for a range of industrially important products, e.g., geraniol, nerol, linalool, and isophytol [26]. Addition of hydrogen chloride is industrially important. Depending on reaction conditions, this gives 1-chloro-3,7-dimethyl-2,6-octadiene (geranyl chloride and/or neryl chloride), 3-chloro-3,7-dimethyl-1,6-octadiene (linaloyl chloride), and 7-chloro-7-methyl-3-methylene-1-octene (myrceny1 chloride) [27]. The alcohols are produced from the chlorides by saponification.

The 1,3-diene system of myrcene reacts with a large number of dienophiles. For example, the maleic anhydride adduct is used to characterize and determine the quality of the product [28].

Isophytol is formed by transition-metal-catalyzed addition of malonic ester and subsequent acidification [29].

In the hydrogenation of myrcene 2,6-dimethyl-2,6-octadiene, 2,6-dimethyl-2,7-octadiene, and 2,6-dimethylcyclooctane are formed, depending on the catalyst and the reaction conditions [30:1H 260, 1EIII 1054].
Besides its main use as an intermediate for the production of terpene alcohols, myrcene is used in the production of terpene polymers [20], terpene – phenol resins [21], and terpene – maleate resins [22]. It can also be used as a solvent or diluting agent for dyes and varnishes [23].

2.3. Ocimene

Ocimene [673-84-7], (Z, E)-2,6-dimethyl-2,5,7-octatriene, C₁₀H₁₆, Mᵣ 136.23, is a colorless liquid with a pleasant odor.

The Z/E mixture has the following properties:

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>176 – 178 °C (101.3 kPa)</td>
</tr>
<tr>
<td>d₂⁰</td>
<td>0.800</td>
</tr>
<tr>
<td>nD₂⁰</td>
<td>1.4862</td>
</tr>
<tr>
<td>mp</td>
<td>50 °C</td>
</tr>
</tbody>
</table>

Ocimene is very sensitive to oxidation and therefore can be kept for long periods only with the exclusion of air. At elevated temperatures it rearranges to alloocimene [31].

Ocimene is produced by the flash pyrolysis or photochemical isomerization of α-pinene [32].

Ocimene is mainly used as a perfume component. The derivatives ocimenol (2,6-dimethyl-5,7-octadien-2-ol), produced by acid-catalyzed hydration, and the partially and completely hydrogenated products are also important [33], [34].

2.4. 2,6-Dimethyl-2,4,6-octatriene

2,6-Dimethyl-2,4,6-octatriene exists as two stereoisomers:

(4E, 6Z)-2,6-Dimethyl-2,4,6-octatriene, C₁₀H₁₆, Mᵣ 136.23, is a colorless liquid with an intense odor, and is sensitive to oxidation.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>80 °C (1.9 kPa)</td>
</tr>
<tr>
<td>d₂⁰</td>
<td>0.8161</td>
</tr>
<tr>
<td>nD₂⁰</td>
<td>1.5437</td>
</tr>
</tbody>
</table>

(4E, 6Z)-2,6-Dimethyl-2,4,6-octatriene is produced as a mixture with other products by the thermolysis of α-pinene at 350 °C [35], or by heating Z-ocimene to 190 °C [36]. The products are separated by fractional distillation.

(4E, 6E)-2,6-Dimethyl-2,4,6-octatriene, C₁₀H₁₆, Mᵣ 136.23, has physical properties similar to those of the (4E, 6Z)-isomer.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>79 °C (1.9 kPa)</td>
</tr>
<tr>
<td>d₂⁰</td>
<td>0.8106</td>
</tr>
<tr>
<td>nD₂⁰</td>
<td>1.5438</td>
</tr>
</tbody>
</table>

(4E, 6E)-2,6-Dimethyl-2,4,6-octatriene is formed as a mixture with the (4E, 6Z)-isomer and other products in the thermolysis of pinene at 320 – 330 °C [37], by dehydration of 3,7-dimethyl-3,6-octadien-1-ol [38], and by treating Z-ocimene with base [39].

2,6-Dimethyl-2,4,6-octatriene is used to a small extent in the perfume industry. It is also used as a diluting agent for varnishes and dyes [23], and as a component for terpene polymers [20], [22].

3. Monocyclic Monoterpenes

3.1. p-Menthane

p-Menthane [99-82-1], 1-isopropyl-4-methylcyclohexane, C₁₀H₂₀, Mᵣ 140.25, occurs widely as a cis/trans mixture, e.g., in essential oils in the eucalyptus fruit.
The cis\textit{trans} mixture of \(p\)-menthane is a colorless liquid with a fennel-like odor.

\begin{align*}
\text{cis-1-Isopropyl-4-methylcyclohexane} \\
bp &= 168.8 \, ^\circ\text{C (99.2 kPa)} \\
d_{20}^0 &= 0.8086 \\
n_{20}^D &= 1.4443
\end{align*}

\begin{align*}
\text{trans-1-Isopropyl-4-methylcyclohexane} \\
mp &= -86 \, ^\circ\text{C} \\
bp &= 168.1 \, ^\circ\text{C (99.2 kPa)} \\
d_{20}^0 &= 0.7941 \\
n_{20}^D &= 1.4369
\end{align*}

\(p\)-Menthane is obtained as a \textit{cis/trans} mixture by the catalytic hydrogenation of limonene, terpinols, and \(p\)-cymene [40]. Raney nickel, platinum, or copper and aluminum oxides are used as catalyst [41].

\(p\)-Menthane is predominantly used as a precursor in the production of 1-isopropyl-4-methylcyclohexane hydroperoxide, a catalyst for radical polymerization [42].

### 3.2. \(\alpha\)-Terpinene

\(\alpha\)-Terpinene [99-85-4], 4-isopropyl-1-methyl-1,3-cyclohexadiene, C\(_{10}\)H\(_{16}\), \(M\) 136.23, is the main component of terpinene, the other components being the \(\beta\)- and \(\gamma\)-isomers. It occurs in various essential oils, almost always as a mixture with its isomers.

\(\alpha\)-Terpinene is a colorless liquid with a lemon-like odor. It resinifies on prolonged storage.

\begin{align*}
bp &= 172.5 – 173.5 \, ^\circ\text{C} \\
n_{20}^D &= 1.4780
\end{align*}

\(\alpha\)-Terpinene is obtained by fractional distillation of pine oil [43] and by the thermolysis of \(\alpha\)-pinene in the presence of catalysts, such as manganese oxide [44].

\(\alpha\)-Terpinene is used in essential oils and as an intermediate for perfumes.

### 3.3. Terpinolene

Terpinolene [586-62-9], 4-isopropylidene-1-methyl-1-cyclohexane, C\(_{10}\)H\(_{16}\), \(M\) 136.23, occurs in many essential oils and in sulfate turpentine.

Terpinolene is a colorless liquid with an odor resembling that of turpentine.

\begin{align*}
bp &= 186 \, ^\circ\text{C} \\
d_{20}^0 &= 0.8623 \\
n_{20}^D &= 1.4861
\end{align*}

It forms a hydroperoxide on autoxidation [45], [46].

Terpinolene used to be extracted by fractional distillation of wood turpentine [46]. It is now produced by treating \(\alpha\)-pinene with aqueous H\(_3\)PO\(_4\) at 75 °C [47]. It is preferable to distill terpinolene under vacuum to minimize the formation of polymeric products at elevated temperatures.

Terpinolene is mainly used to improve the odor of industrial and household products [48–50].

### 3.4. \(p\)-Cymene

\(p\)-Cymene [99-87-6], 4-(isopropyl)methylenzene, C\(_{10}\)H\(_{14}\), \(M\) 134.21, is the main component of sulfate turpentine and occurs in many essential oils [51].

\(p\)-Cymene is a colorless liquid with an odor typical of aromatic hydrocarbons.

\begin{align*}
mp &= -67.7 \, ^\circ\text{C} \\
bp &= 177.3 \, ^\circ\text{C} \\
d_{20}^0 &= 0.8573 \\
n_{20}^D &= 1.4906
\end{align*}

The enthalpy of evaporation is 44.670 J/mol.
P-Cymene undergoes catalytic hydrogenation to 1-isopropyl-4-methylcyclohexane [40]. It must be stored in the absence of light and air.

P-Cymene is formed during the sulfite leaching of wood [52]. A range of production processes starting from mono- and bicyclic terpenes have also been described. For example, p-cymene is obtained in good yields from α-pinene in the presence of copper catalysts [53], [54]. In this process a significant proportion of 1-isopropyl-4-methyl-cyclohexane is also formed, which is dehydrogenated in the presence of palladium catalysts at 260 – 280 °C to p-cymene [55]. The Friedel – Crafts alkylation of toluene with propene is used industrially [56]. Products containing more than one isopropyl group are converted into p-cymene with aluminum chloride and hydrochloric acid [57].

P-Cymene is used to improve the odor of soaps and as a masking odor for industrial products. Its use as an intermediate for musk perfumes [58], the oxidation to terephthalic acid, and its addition to antiseptic preparations have also been described [59]. P-Cymene is also used as a solvent for dyes and varnishes.

3.5. 1,8-Cineole

1,8-Cineole [470-82-6], 1,8-epoxy-p-methane, eucalyptol, C_{10}H_{18}O, M_r 154.25, occurs widely in natural essential oils, mainly eucalyptus oil.

\[
\begin{align*}
\text{O} \\
\text{H} \\
\text{H} \\
\text{H} \\
\end{align*}
\]

1,8-Cineole is a colorless liquid. Its odor and taste resemble those of camphor.

\[
\begin{align*}
\text{mp} &\quad 1.55 \degree C \\
bp &\quad 176 – 176.4 \degree C \\
d_{20}^2 &\quad 0.9232 \\
n_{20}^D &\quad 1.4575 \\
[\alpha]_{25}^D &\quad +17.6 \degree (\text{undiluted})
\end{align*}
\]

On warming, particularly in the presence of acids, 1,8-cineole forms other terpenes of the p-methane type. It reacts with a range of substances, forming sparingly soluble products.

1,8-Cineole is extracted exclusively from eucalyptus oils with a high 1,8-cineole content. Various processes are used to separate it from the other terpenes, for example, treatment with H_2SO_4 in the cold [60], distillation in the presence of phenols, such as cresols or resorcinol [61], which form loose addition compounds, or by addition to β-naphthol [62]. 1,8-Cineole can also be enriched by rectification. The yield is increased by gasification in the presence of a chromium – nickel catalyst [63].

1,8-Cineole is used as a perfume and fragrance. In the past it was also used as an expectorant and an antiseptic.

4. Bicyclic Monoterpenes

The industrially most important bicyclic monoterpenes are subdivided into caranes, pinanes, and bicyclo[2.2.1]heptanes, depending on their basic structure.

4.1. 3-Carene

3-Carene [498-15-7], 3,7,7-trimethylbicyclo[4.1.0]hept-3-ene, C_{10}H_{16}, M_r 136.23, occurs in a range of turpentines as the enantiomerically pure compound, but also as the racemate [64], [65].

\[
\begin{align*}
\text{O} \\
\text{H} \\
\text{H} \\
\text{H} \\
\end{align*}
\]

3-Carene is a colorless compound with a sweet, penetrating odor.

\[
\begin{align*}
bp &\quad 176 – 176.4 \degree C \\
d_{20}^2 &\quad 0.9232 \\
n_{20}^D &\quad 1.4575 \\
[\alpha]_{25}^D &\quad +17.6 \degree (\text{undiluted})
\end{align*}
\]

It readily undergoes autoxidation and resini-
Pyrolysis at 300 – 580 °C in the presence of Fe(III) oxide on carriers gives p-cymene as the main product [68].

3-Carene is obtained exclusively by fractional distillation of certain turpentines [69].

3-Carene is predominantly used in the perfume industry for producing essential oils [70]. It is also an intermediate in perfume synthesis and a precursor for insecticides of the pyrethroid type [71], [72].

4.2. Pinane

Pinane [473-55-2], 2,6,6-trimethylnorpinane, 2,6,6-trimethylbicyclo[3.1.1]heptane, C_{10}H_{18}, M, 138.25.

Pinane derivatives occur in wood, the leaves of many plants, algae, and insects. Pinane itself apparently does not occur naturally. However, it is formed on hydrogenation of pinane derivatives [73].

**cis-Pinane (colorless liquid)**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>167.2 – 168 °C</td>
</tr>
<tr>
<td>d_{20}^4</td>
<td>0.8575</td>
</tr>
<tr>
<td>n_{D20}^23</td>
<td>1.4626</td>
</tr>
<tr>
<td>[α]_{D25}^23</td>
<td>-23.6 ° (undiluted)</td>
</tr>
</tbody>
</table>

**trans-Pinane (colorless liquid)**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>164 °C</td>
</tr>
<tr>
<td>d_{20}^4</td>
<td>0.854</td>
</tr>
<tr>
<td>n_{D20}^23</td>
<td>1.4610</td>
</tr>
<tr>
<td>[α]_{D25}^23</td>
<td>+21.4 ° (undiluted)</td>
</tr>
</tbody>
</table>

The oxidation of pinane with air or oxygen gives 2-pinane hydroperoxide or 2-pinanol [74]. In industry, oxidation is carried out in the presence of catalysts [75].

The pyrolysis of (–)-(1S)-cis-pinane at 500 °C gives a mixture of (3R)-3,7-dimethyl-1,6-octadiene and (1R)-isopropyl-2,3-dimethylcyclopentane [76].

cis-Pinane is obtained, together with small quantities of trans-pinane, by the catalytic hydrogenation of α- and β-pinene. If (–)-α- and (–)-β-pinene are hydrogenated, the (–)-enantio-mer is obtained, and from the (+)-pinenes, (+)-cis-pinane. In industry, α-pinene is predominantly used for the hydrogenation. Raney nickel, Pt, or Pd (and their oxides) on carriers are used as catalysts [77], [78]. The hydrogenation with Raney nickel is carried out at 2 – 10 MPa at 150 °C. In the presence of halogen compounds cis-pinane is obtained predominantly [79].

trans-Pinane can be obtained from β-pinene by treatment with sodium borohydride in the presence of boron trifluoride in di(ethylene glycol) and subsequent heating of the reaction mixture in propionic acid [80].

Pinane is used in industry for the production of pinane hydroperoxide [81]. It is also important as an intermediate in the production of 3,7-dimethylocta-1,6-diene, which is used to produce perfumes, such as citronellol, citronellal, and hydroxycitronellal.

4.3. 2-Pinane Hydroperoxide

2-Pinane hydroperoxide [5405-84-5], 2,6,6-trimethylbicyclo[3.1.1]heptane-2-hydroperoxide, C_{10}H_{18}O_{2}, M, 170.25, is a colorless liquid, which is readily flammable and insoluble in water.

The oxidation of pinane with air or oxygen gives 2-pinane hydroperoxide or 2-pinanol [74]. In industry, oxidation is carried out in the presence of catalysts [75].

The pyrolysis of (–)-(1S)-cis-pinane at 500 °C gives a mixture of (3R)-3,7-dimethyl-1,6-octadiene and (1R)-isopropyl-2,3-dimethylcyclopentane [76].

On heating 2-pinane hydroperoxide to > 110 C 1-((1R)-cis-3-ethyl-2,2-dimethylcyclobutyl)ethanone is formed [82]. (1R, 2S)-2-pinanol is
formed in good yields by catalytic hydrogenation.

2-Pinane hydroperoxide is produced by oxidation of pinane with air or oxygen at 95 °C [83–85]. cis-Pinane reacts more rapidly than trans-pinane [86].

2-Pinane hydroperoxide is used as a radical initiator for polymerization reactions [87], e.g., for the polymerization of diolefins and aromatic vinyl compounds, or for hardening unsaturated polyester resins. It is also an intermediate in the production of perfumes, such as pinanol, linalool, nerol, and geraniol [88].

4.4. 2-Pinanol

2-Pinanol [473-54-1], 2,6,6-trimethylbicyclo[3.1.1]heptan-2-ol, C₁₀H₁₈O, Mᵣ 154.25, is obtained as the cis or trans isomer, depending on the production process.

cis-(−)-(1R,2S) trans-(−)-(1R,2R)

cis-2-Pinanol forms colorless crystals with a camphor-like odor.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mp</td>
<td>78 – 79.2 °C</td>
</tr>
<tr>
<td>bp</td>
<td>90 – 91 °C (1.5 kPa)</td>
</tr>
<tr>
<td>[α]D₂⁰</td>
<td></td>
</tr>
<tr>
<td>nD₂⁰</td>
<td></td>
</tr>
<tr>
<td>[α]D₂⁰</td>
<td></td>
</tr>
</tbody>
</table>

trans-2-Pinanol forms colorless needles.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mp</td>
<td>58 – 59 °C</td>
</tr>
<tr>
<td>bp</td>
<td>88 – 89 °C (0.12 kPa)</td>
</tr>
<tr>
<td>[α]D₂⁰</td>
<td></td>
</tr>
</tbody>
</table>

The pyrolysis of 2-pinanol at 500 °C gives linalool. (−)-Linalool is formed from (−)-cis- and (−)-trans-2-pinanol, and (−)-linalool from (−)-cis- and (−)-trans-2-pinanol. The process is used industrially [89], [90].

cis-2-Pinanol is produced industrially by the catalytic hydrogenation of 2-pinane hydroperoxide [91], [92]. Alternatively 2-pinane hydroperoxide can be treated with sodium sulfide in aqueous sodium hydroxide [93] or with sodium methoxide [94]. cis-2-Pinanol can also be obtained directly from pinane by air oxidation in the presence of alkalis, such as sodium hydroxide, at 80 – 100 °C [95].

2-Pinanol is used to produce linalool by pyrolysis [96].

4.5. Camphene

Camphene [5794-03-6], 2,2-dimethyl-3-methylenenorbornane, C₁₀H₁₆, Mᵣ 136.23, occurs in a large number of essential oils in optically active form, both as the R and S enantiomers.

Camphene is a colorless, crumbly crystalline solid with a camphor-like odor. It has a tendency to sublime.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mp</td>
<td>52.5 °C</td>
</tr>
<tr>
<td>bp</td>
<td>157.8 °C (98.8 kPa)</td>
</tr>
<tr>
<td>[α]D₂⁰</td>
<td></td>
</tr>
<tr>
<td>nD₂⁰</td>
<td></td>
</tr>
</tbody>
</table>

Camphene is stable in air and light. At elevated temperatures, in the presence of oxygen, it undergoes autoxidation to camphenilone [97]. Peracids attack the double bond, giving camphene oxide [98]. Catalytic hydrogenation gives the saturated hydrocarbon isocamphane [99].

The extraction of camphene by distillation of turpentine is now hardly used in industry. Instead
Camphene is produced from α-pinene.

\[
\text{HCl} \quad \text{Cl} \quad \rightarrow \quad \text{camphene}
\]

(+)-α-Pinene is converted into (+)-bornyl chloride by the action of dry hydrogen chloride in a Wagner – Meerwein rearrangement. Base-catalyzed dehydrohalogenation of the (+)-bornyl chloride gives racemic camphene [100], [101]. The reaction of α-pinene with borophosphoric acid in the gas phase [102], or on TiO2 catalysts [103] has also been described.

Camphene is used to improve the odor of industrial products. It is an intermediate in the production of camphor, isobornyl esters, and the insecticide Toxaphen.

5. Acyclic Sesquiterpenes

**Farnesene.** α-Farnesene, 2,6,10-trimethyl-2,6,9,11-dodecatetraene, C15H24, Mr 204.36.

α- and β-Farnesenes and their Z- and E-isomers occur in many essential oils, e.g., in apples [104], citrus fruits [105], and hop oil. α-Farnesene is a natural attractant for the larvae of the codlin moth [106]. It is also found in the gland secretions of certain ants [107].

α- and β-Farnesenes are colorless liquids with fruity odors. They are sensitive to autoxidation and can be stored for long periods only with the exclusion of light and air.

Mixtures of α- and β-farnesenes are obtained by heating farnesol with potassium hydrogen sulfate to 160 – 170 °C [108]. Other syntheses of the mixture, involving dehydration of farnesol, nerolidol, and isoprene, have also been described [109], [110].

Farnesene is used in small quantities in the fragrance industry.

6. Monocyclic Sesquiterpenes

6.1. Bisabolene

Bisabolene, C15H24, Mr 204.33, occurs in myrrh oil and limett oil. The isomers α-, β-, and γ-bisabolene are known.

α-Bisabolene, (E, Z)-4-(1,5-dimethyl-1,4-hexadienyl)-1-methyl-1-cyclohexane

bp 95 °C (0.02 kPa)

β-Bisabolene, 1-methyl-4-(5-methyl-1-methylene-4-hexenyl)-1-cyclohexane

bp 148 °C (2.4 kPa)

γ-Bisabolene, (E, Z)-4-(1,5-dimethyl-4-hexenylidene)-1-methyl-1-cyclohexene

bp 132 °C (1.4 – 1.6 kPa)

The individual isomers and their mixtures are colorless liquids with pleasant, balsamic odors.

Isomer mixtures are produced by treating nerolidol and farnesol with acid [111]. Targeted syntheses of α- and β-bisabolene by the Wittig reaction have been described [112–114].

Bisabolene mixtures are used in the perfume and fragrance industries.
6.2. Bisabolol

Bisabolol [515-69-5], C15H26O, Mr 222.37, occurs in various plants.

\[
(+)\alpha\text{-Bisabolol, } (+)-2\text{-methyl-6-(4-methyl-3-cyclohexenyl)-6-hepten-2-ol}
\]

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>120 – 122 °C (0.13 kPa)</td>
</tr>
<tr>
<td>(d^20)</td>
<td>0.9213</td>
</tr>
<tr>
<td>(\delta^20)</td>
<td>1.4919</td>
</tr>
<tr>
<td>([\alpha]_D)</td>
<td>+51.7 ° (undiluted)</td>
</tr>
</tbody>
</table>

\[(-)\alpha\text{-Bisabolol, } (-)-2\text{-methyl-6-(4-methyl-3-cyclohexenyl)-6-hepten-2-ol}\]

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>153 °C (1.59 kPa)</td>
</tr>
<tr>
<td>(d^20)</td>
<td>0.9211</td>
</tr>
<tr>
<td>(\delta^20)</td>
<td>1.4936</td>
</tr>
<tr>
<td>([\alpha]_D)</td>
<td>−55.7 ° (undiluted)</td>
</tr>
</tbody>
</table>

\[rac\text{-Bisabolol, } 2\text{-methyl-6-(4-methyl-3-cyclohexenyl)-6-hepten-2-ol}\]

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>157 °C (1.59 kPa)</td>
</tr>
<tr>
<td>(d^20)</td>
<td>0.9223</td>
</tr>
<tr>
<td>(\delta^20)</td>
<td>1.4917</td>
</tr>
</tbody>
</table>

The bisabolols are colorless liquids with slightly flowery odors.

\[rac\text{-Bisabolol is produced by acid-catalyzed cyclization of farnesol or nerolidol [115]. The individual enantiomers are obtained by extraction from the appropriate plants. Because of their anti-inflammatory and spasmylytic properties [117], both (−)- and rac-bisabolol are predominantly used in the cosmetics industry and to a small extent in the pharmaceutical industry. \]

7. Bicyclic Sesquiterpenes

Caryophyllene. Caryophyllene [87-44-5], 6,10,10-trimethyl-2-methylenebicyclo[7.2.0]-5-undecene, C15H24, Mr 204.36, occurs in many essential oils.

\[Caryophyllene is a colorless, oily liquid with an odor resembling that of cloves.\]

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>254 – 256 °C</td>
</tr>
<tr>
<td>(d^20)</td>
<td>0.9019</td>
</tr>
<tr>
<td>(n^20)</td>
<td>1.4995</td>
</tr>
<tr>
<td>([\alpha]_D)</td>
<td>−9.2 ° (undiluted)</td>
</tr>
</tbody>
</table>

Catalytic hydrogenation on platinum gives tetrahydrocaryophyllene [118], and on palladium a dihydrocaryophyllene [119]. On oxidation with potassium permanganate, a glycol (mp 120 – 120.5 °C) is formed [120], and with perbenzoic acid [121] or peracetic acid, a caryophyllene oxide.

Caryophyllene is best extracted from clove oil. It can also be obtained from other sources, such as certain American pine oil fractions.

Caryophyllene is used as a perfume and fragrance, for example in chewing gum (ca. 200 mg/kg). It is also used as a fixative. It can be used as an intermediate in the synthesis of other perfumes and fragrances [123].

8. Tricyclic Sesquiterpenes

Longifolene. Longifolene [475-20-7], 3,3,7-trimethyl-8-methyleneoctacyclo[5.4.0.9-Z9]undecane, C15H24, Mr 204.36, occurs in the \(d\)- and \(l\)-forms in a range of essential oils. Indian turpentine contains up to 20% longifolene.

\[(+)-(1R,2S,7S,9S)\]

Longifolene is a colorless, oily liquid.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bp</td>
<td>254 – 256 °C (93.9 kPa)</td>
</tr>
<tr>
<td>(d^18)</td>
<td>0.9319</td>
</tr>
<tr>
<td>(n^20)</td>
<td>1.5040</td>
</tr>
<tr>
<td>([\alpha]_D)</td>
<td>+42.73 ° (undiluted)</td>
</tr>
</tbody>
</table>
Longifolene forms crystalline products with hydrogen halides [124]. On treatment with bromine followed by N,N-dimethylaniline, o-bromolongifolene is formed, and with nitrogen oxides o-nitrolongifolene [125].

Longifolene is obtained by distillation, e.g., Indian turpentine. Longifolene is used as a solvent additive. It has been described as a starting material for the production of perfumes, e.g., by oxidation [126], or by treatment with formic acid [127].

9. Acyclic Diterpenes

Phytol. Phytol [150-86-7], (7R, 11R)-3,7,11,15-tetramethyl-trans-2-hexadecen-1-ol, C_{20}H_{40}O, M_r 295.52, is formed by saponification of chlorophyll.

Phytol is a colorless liquid with a slightly flowery odor. The action of acids or heat effects dehydration to phytadiene.

\[
\begin{align*}
\text{Phytol} & \quad \text{Phytadiene} \\
\text{bp} & \quad 136 ^\circ C \ (1.3 \text{kPa)} \\
d_{20}^o & \quad 0.8533 \\
n_25^D & \quad 1.4637
\end{align*}
\]

Phytol can be obtained from natural raw materials by a variety of processes [128]. The industrial synthesis of phytol starts from isophytol. The latter is first treated with formic acid to give phytanyl formate, from which (Z, E)-phytol (isomer ratio 3 : 7) is obtained by saponification or transesterification [129].

Phytol is used in the perfume and cosmetics industries [130]. It can also be used, like isophytol, as the starting material for the synthesis of vitamins E and K_1 [131–133]. The hydrogenation and oxidation products are also known [134].

10. Acyclic Triterpenes

Squalene. Squalene [111-02-4], 2,6,10,15, 19,23-hexamethyl-2,6,10,15,19,23-hexacosa-2,6,10,14,18,22-hexaene, C_{30}H_{50}, M_r 410.73, occurs in liver oils of various species of shark [135], in cod-liver oil [136], in vegetable fats and oils [137], and in human skin fat.

\[
\begin{align*}
\text{Squalene} & \quad \text{a colorless, air-sensitive, almost odorless liquid.} \\
bp & \quad 223 – 226 ^\circ C \ (0.26 \text{kPa)} \\
d_{20}^o & \quad 0.8577 \\
n_25^D & \quad 1.4961
\end{align*}
\]

Squalene is extracted from shark liver [138] or synthesized from hexaphenyl-1,4-butyldilidiphosphonium dibromide and 6,10-dimethyl-5,9-undecadien-2-one (geranylacetone, industrial intermediate in the vitamin E synthesis) [139].

Squalene is hydrogenated on platinum or nickel catalysts to dodecahydro-squalene (perhydrosqualene, squalane, cosbiol) [140], which is widely used in cosmetics [141], [142].

11. Toxicology

There are excellent reviews of the toxicology of terpenes [143]. The known toxicological test results (Table 1) show that most terpenes have low acute oral toxicity and, in spite of occasionally good skin resorption, low dermal toxicity. Some are irritant to the skin of rabbits in concentrated form, but a 4 – 16 % solutions in vaseline, are generally not irritant to humans. Only 3-carene, which occurs in turpentine, has been shown to have a sensitizing potential in humans and animals.

To investigate detoxification in mammals, a metabolism study on rabbits has been carried out. On oral administration several characteristic oxidation reactions have been detected:

1. Stereoselective oxidation: formation of 3-caren-9-ol, 3-caren-9-carboxylic acid, and 3-caren-9,10-dicarboxylic acid from 3-carene
2. Regioselective oxidation: 3,10-myrcenediol, 1,2-myrcenediol, and 2-hydroxymyrcene-1-carboxylic acid from myrcene
3. Allylic oxidation: verbenol and myrtenic acid from \( \alpha \)-pinene, and pinocarveol from \( \beta \)-pinene.


With \( p \)-cymene, three different oxidation products were detected in the first step. The alcohols 2-(4-methylphenyl)-1-propanol and 2-(4-methyl-phenyl)-2-propanol are formed by the \( \omega \)- and (\( \omega \)-1)-oxidation of the isopropyl group.

### Table 1. Toxicity data for terpenes

<table>
<thead>
<tr>
<th>Substance</th>
<th>Acute oral toxicity (rat), LD(_{50}), g/ kg</th>
<th>Acute oral toxicity (rabbit), LD(_{50}), g/ kg</th>
<th>Skin resorption</th>
<th>IRT* (rat)</th>
<th>Skin irritation (R = rabbit; H = human)</th>
<th>Irritation of rabbit eye mucous membrane</th>
<th>Sensitization (H = human; G = guinea pig)</th>
<th>Specific properties/tests</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myrcene</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td>+</td>
<td></td>
<td>R: moderately irritant; H: 4 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[145]</td>
<td></td>
</tr>
<tr>
<td>Ocimene</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td></td>
<td></td>
<td>R: moderately irritant; H: 5 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[145]</td>
<td></td>
</tr>
<tr>
<td>( \alpha )-Terpinene</td>
<td>1.68</td>
<td></td>
<td></td>
<td></td>
<td>H: 5 % not irritant</td>
<td></td>
<td>H: negative damage to liver and blood (forms)</td>
<td>[145]</td>
<td></td>
</tr>
<tr>
<td>( \alpha )-Terpinene</td>
<td>1.68</td>
<td></td>
<td></td>
<td></td>
<td>H: 5 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[145]</td>
<td></td>
</tr>
<tr>
<td>( \alpha )-Terpinene</td>
<td>1.68</td>
<td></td>
<td></td>
<td></td>
<td>H: 5 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[145]</td>
<td></td>
</tr>
<tr>
<td>Terpinolene</td>
<td>4.39</td>
<td>&gt;5</td>
<td></td>
<td></td>
<td>R: not irritant; H: 20 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[145]</td>
<td></td>
</tr>
<tr>
<td>( p )-Cymene</td>
<td>4.74</td>
<td>&gt;5</td>
<td></td>
<td></td>
<td>R: not irritant; H: 4 % not irritant</td>
<td></td>
<td>H: negative affects central nervous system (narcosis)</td>
<td>[145], [146]</td>
<td></td>
</tr>
<tr>
<td>1,8-Cineole</td>
<td>2.48</td>
<td>&gt;5</td>
<td></td>
<td></td>
<td>R: not irritant; H: 16 % not irritant</td>
<td></td>
<td>H: negative cancerization study in progress</td>
<td>[145], [146]</td>
<td></td>
</tr>
<tr>
<td>3-Carene</td>
<td>4.8</td>
<td>&gt;5</td>
<td></td>
<td></td>
<td>R: irritant</td>
<td></td>
<td>H: positive G: positive</td>
<td>[145]</td>
<td></td>
</tr>
<tr>
<td>Camphene</td>
<td>&gt;5</td>
<td>2.5</td>
<td>+</td>
<td></td>
<td>R: slightly irritant; H: 4 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[145], [146]</td>
<td></td>
</tr>
<tr>
<td>Bisabolene</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td>0/12 after 6 h</td>
<td></td>
<td>R: slightly irritant; H: 10 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[145], [146]</td>
<td></td>
</tr>
<tr>
<td>Bisabolol</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td>0/12 after 7 h</td>
<td></td>
<td>R: not irritant; H: 4 % not irritant</td>
<td></td>
<td>H: negative</td>
<td>[146]</td>
<td></td>
</tr>
<tr>
<td>Caryophyllene</td>
<td>&gt;5</td>
<td>&gt;5</td>
<td></td>
<td></td>
<td>R: irritant; H: 4 % not irritant**</td>
<td></td>
<td>H: negative</td>
<td>[146]</td>
<td></td>
</tr>
<tr>
<td>Phytol</td>
<td>&gt;10</td>
<td></td>
<td></td>
<td></td>
<td>R: moderately irritant</td>
<td></td>
<td>H: negative</td>
<td>[145], [146]</td>
<td></td>
</tr>
</tbody>
</table>

*IRT: inhalation risk test (rat, test result dependent on toxicity and volatility; 0/6 after 6 h means that after 6 h exposure in an enriched or saturated atmosphere at room temperature no animals died).

**In light petroleum jelly.

### Table 2. Terpenes licensed as food additives

<table>
<thead>
<tr>
<th>Substance</th>
<th>Licensing authority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myrcene</td>
<td>FDA (GRAS classification), European Council</td>
</tr>
<tr>
<td>Ocimene</td>
<td>FDA, European Council</td>
</tr>
<tr>
<td>( \alpha )-Terpinene</td>
<td>FDA</td>
</tr>
<tr>
<td>Terpinolene</td>
<td>FDA, European Council</td>
</tr>
<tr>
<td>( p )-Cymene</td>
<td>FDA, European Council</td>
</tr>
<tr>
<td>1,8-Cineole</td>
<td>FDA, European Council</td>
</tr>
<tr>
<td>Camphene</td>
<td>FDA, European Council</td>
</tr>
<tr>
<td>Caryophyllene</td>
<td>FDA, European Council</td>
</tr>
</tbody>
</table>

FDA = Food and Drug Administration; GRAS = generally recognized as safe.
References

30. Beilstein, 1 H 260, 1 E III, 1054.
44. BASF, DE 960 988, 1954.

and 4-isopropylbenzyl alcohol by oxidation of the methyl group. The alcohols formed in these different oxidations are either excreted from the organism as their glucuronides or further oxidized [8], [144].

Most of the terpenes described in Table 1 are licensed as food additives by the international bodies responsible (Table 2). This licensing clearly demonstrates the low toxicity of the terpenes concerned.


Zellstofffabrik Waldhof, DE 727 475, 1940.

BASF, DE 961 979, 1953.


S. Arctander: *Perfume and Flavor Chemicals*.


Shell Oil Co., US 2097 744, 1934.


*Beilstein, 27*, 5 E IV, 277.
Further Reading
