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Overview of Flavor and Fragrance Materials

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The nature of this chapter must be that of an overview as the alternative would be a multivolume series! The difficulty is not a shortage of material but rather a surfeit, and a second issue is how to give a rational coverage; should the materials be classified by chemistry, by odor or by application? The approach here is a combination of all three, and is based in part on a précis of The Chemistry and Technology of Flavours and Fragrances [1].

There is, of course, a massive overlap between flavor and fragrance; for example, cis-3-hexenol, discussed below, has a ‘green’, cut-grass odor, and hence contributes freshness to both flavors and fragrances. The division between the two Fs is itself not always a natural one!

1.1 FLAVOR AROMA CHEMICALS

1.1.1 Nature Identical

The vast majority of the aroma chemicals used in flavor are nature identical (NI), that is, they have been identified as occurring in foodstuffs in the
human food chain. This is a key method of identifying the most important components which create a flavor, and until recently, there were also regulatory implications. European Council Directive 88/388/EEC defined these as “flavouring substances identical to natural substances”, with the alternative being “artificial flavouring substances”, with the latter leading to the stigma of “artificial flavors”. The newest regulations, REGULATION (EC) No 1334/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL, no longer differentiates between Nature Identical and artificial, but the concept is still important – as a guide to flavorists, knowing a material is NI is important, and it can be especially so the context of “from the named food” type of flavours. Regulation 1334/2008 now only differentiates between “flavouring substances” and “natural flavouring substances”, which harmonizes to an extent with the USA, where the NI classification has never been used. Even there, though, the NI concept has value, as materials have to be on the FEMA GRAS list, that is they are “Generally Recognized As Safe”, and the vast majority of such substances are found in Nature.

1.1.1.1 Alcohols

It should be noted that ethanol 1 itself is a flavor component of ‘alcoholic drinks’ as anyone tasting alcohol-free drinks will report! In fact it may considered as a solvent (especially in fragrances), as a flavour substance (FEMA 2419) or an additive (E1510)! cis-3-Hexenol 2, mentioned above, is produced in nature as a ‘wound chemical’, that is, when plant tissue is damaged, ingressing oxygen is ‘mopped up’ by reaction with linoleic acid, which generates the unstable cis-3-hexenal, which is enzymatically reduced to the alcohol. Also formed are trans-2-hexenal 3, which has a harsher, more acrid greenness and trans-2-hexenol 4, which is rather sweeter:

![Chemical structures](image)

1-Octen-3-ol, ‘mushroom alcohol’ 5, has the earthy note characteristic of mushrooms. The ‘terpenoid’ alcohols, C10 derivatives, include geraniol 6 and its isomer nerol 7, citronellol 8 and linalool 9 [2]. Cyclic terpenoid alcohols include α-terpineol 10 and menthol 11:
Benzyl alcohol 12 has relatively little odor and is more commonly used as a solvent in flavors; phenethyl alcohol 13 is a component of rose oil and has a pleasant rose-like aroma. Two important phenols are thymol 14 and eugenol 15, which are also major components of thyme and clove oils respectively:

1.1.1.2 Acids

Simple acids contribute sharp notes which often become fruity on dilution. Butyric acid 16 is indisputably ‘baby vomit’ in high concentration; valeric acid 17 is cheesy, whereas 2-methylbutyric acid 18 is fruitier. Longer chain acids such as decanoic 19 are fatty and are important in
dairy flavors. 4-Methyloctanoic acid 20 has the sharp fatty character of roasted lamb:

![Chemical structures](image)

1.1.1.3 Esters

Numerous esters are used in flavors, so it is almost a case of any flavor alcohol combined with any flavor acid! Important simple esters include the fruity ethyl butyrate 21 and 2-methylbutyrate 22; allyl hexanoate 23 has a familiar pineapple aroma and isoamyl acetate 24 is ‘pear drops’. Phenethyl 2-methylbutyrate 25 is ‘rose bud ester’ and the warm sweet aroma of methyl cinnamate 26 makes it valuable in strawberry flavors. Methyl salicylate is the main component of wintergreen oil 27 and methyl N-methylantranilate 28 is found in mandarin, which differentiates this from the other citrus oils:

![Chemical structures](image)
1.1.1.4 Lactones

These cyclic esters are usually found as gamma-lactones (five-membered rings) and delta-lactones (six-membered). Like their acyclic cousins they are used in fruit flavors and also for dairy, especially the delta-lactones such as delta-decalactone 29. Gamma-nonalactone 30, also misleadingly known as Aldehyde C18, has a powerful coconut odor:

\[ \text{29} \]
\[ \text{30} \]

1.1.1.5 Aldehydes

Acetaldehyde 31 is ubiquitous in fruit aromas, though its volatility (b.p. 19 °C) makes it difficult and dangerous to handle as a pure aroma chemical. Unsaturated aldehydes such as the previously mentioned trans-2-hexenal (leaf aldehyde) 3 are very important. trans-2-trans-4-Decadienal 32 is intensely ‘fatty-citrus’; trans-2-cis-6-nonadienal 33 is ‘violet leaf aldehyde’. ‘Citral’, a mixture of the isomers geranial 34 and neral 35, is intensely lemon; it is a key flavor component of lemon and to a lesser extent other citrus oils:

\[ \text{31} \]
\[ \text{3} \]
\[ \text{32} \]
\[ \text{33} \]
\[ \text{34} \]
\[ \text{35} \]

Benzaldehyde 36 is widely used in fruit flavors, especially for cherry, though in fact it is not a key component of cherries. Cinnamaldehyde 37 is found in cassia and cinnamon oils. The most important aromatic
aldehyde, and one of the most significant of all aroma chemicals, is vanillin 38:

\[
\begin{align*}
36 & \quad \text{phenylacetaldehyde} \\
37 & \quad \text{diacetyl (acetacetaldehyde)} \\
38 & \quad \text{vanillin}
\end{align*}
\]

1.1.1.6 Ketones

The C4 ketones diacetyl 39 and acetoin 40 are used in butter-type flavors for margarines and other dairy products and hence are used in very large quantities. The former is very volatile and is believed to have led to respiratory damage amongst people exposed to large quantities of its vapor. The cyclic diketone ‘maple lactone’ 41 occurs as the enolic methylcyclopentenolone (MCP) and has the characteristic sweet, caramel odour of maple syrup. Raspberry ketone 42 is unusual in the bizarre world of flavor and fragrance trade names in that it is actually found in raspberries, tastes of raspberries and is a ketone!

\[
\begin{align*}
39 & \quad \text{diacetyl} \\
40 & \quad \text{acetoin} \\
41 & \quad \text{maple lactone} \\
42 & \quad \text{raspberry ketone}
\end{align*}
\]

1.1.2 Heterocycles [3]

1.1.2.1 Oxygen-containing

The importance of materials containing the five-membered furan ring cannot be overstated [4]. Furfural 43 is formed by the Maillard reaction from pentoses in the cooking process, and 5-methylfurfural 44 from hexoses similarly. The latter has an almond, ‘marzipan’ aroma similar to benzaldehyde but with more naturalistic character. Methyl tetrahydrofuranone, ‘coffee furanone’ 45, is sweet and caramelic, but the most important flavor furan must be 2,5-dimethyl-4-hydroxy-3[2H]-furanone
46, an aroma chemical of many names, including strawberry furanone, and pineapple ketone. This has sweet, fruit and caramel notes, making it of obvious importance in fruit flavors, but it is also important in meat flavors, where it seems to function as a flavor enhancer. Its homologue Soy Furanone 47 is also very sweet, whereas its isomer ‘Sotolone’, or fenugreek lactone 48, has an intense fenugreek tonality, becoming more caramel-like in high dilution. The saturated furan Theaspiran 49 is found in black tea and a number of fruits:

![Chemical structures](image)

The most important pyrans must be Maltol 50 and Coumarin 51. The former is another caramel compound, with the latter having sweet and spicy notes. The saturated furan 1,8-cineole, or eucalyptol 52, is the main component of eucalyptus oil as well as being widespread in other oils such as lavender, distilled lime and rosemary:

![Chemical structures](image)

1.1.2.2 Nitrogen-containing

The pyrrole group is relatively unimportant in flavors, though mention should be made of 2-acetyldihydropyrrole 53, which has the ‘Holy Grail’
aroma of freshly baked bread but is too unstable for commercial use. The most important nitrogenous heterocycles are pyrazines, which are readily formed in the Maillard reaction from amino acids and sugars; simple alkyl pyrazines such as 2,3,5-trimethylpyrazine 54 have roasted, cocoa-like notes making them important for chocolate and roasted notes. Tetrahydroquinoxaline 55 has particularly noticeable roasted notes. 2-Acetylpyrazine 56 has very pervasive roasted, biscuit notes. The alkoxyalkylpyrazines are also found in fresh fruits and vegetables, the intensely odorous 2-methoxy-3-isobutylpyrazine 57 often being known as ‘Bell Pepper Pyrazine’.

### 1.1.2.3 Sulfur-containing

Whilst a few simple thiophenes are used, the most important sulfur heterocycles are thiazoles, especially 2-isopropyl-4-methylthiazole 58 and 2-isobutylthiazole 59, which have peach/tropical and tomato vine character respectively. 4-Methyl-5-thiazoleethanol, Sulfurol 60, is widely used in dairy and savory flavors.

### 1.1.3 Sulfur Compounds [5]

The importance of sulfur compounds reflects their highly odorous character; the most odorous compounds known are sulfur compounds, with odor thresholds down to the $10^{-4}$ parts per billion level. They are the single largest group of ‘High Impact Aroma Chemicals’, materials which provide ‘character impact’ even at very low levels [6].
1.1.3.1 Mercaptans

These are generally the most odorous of the most odorous, as it were, the *capo di capi* of the flavor industry. Methyl mercaptan 61 is widespread in meat aromas, as is 2-methyl-3-furanthiol (MFT) 62; the latter is especially important in beef. Furfuryl mercaptan 63 is a character impact aroma chemical of roasted coffee. The latter two are Maillard reaction products formed from cysteine and pentoses. ‘Fruity’ mercaptans include the blackcurrant/cassis materials 64 and thiomenthone 65, and p-menthene-8-thiol, the Grapefruit Mercaptan 66. The accurately named Cat Ketone, 4-mercapto-4-methyl-2-pentanone 67, is also found in grapefruit and wines.

![Chemical structures of mercaptans](image)

1.1.3.2 Sulfides

The simplest sulfide, dimethyl sulfide (DMS) 68 has a vegetable, sweet-corn odor; sulfides are less odorous than mercaptans, and hence a key aspect of quality is the need to remove all traces of mercaptans; impure DMS is quite repellent. Propyl and allyl sulfides are perhaps the commonest, especially as di- and higher sulfides; allyl disulfide 69 is the major component of garlic oil, with the remainder being mostly higher sulfides. Propyl compounds such as dipropyl trisulfide 70 are found in onion; ethyl compounds are found in Durian fruit, and to human noses other than those raised with the fruit, are at best unpleasant and sewer-like.
Some mercaptans oxidize very easily to form disulfides, such as the formation of bis(2-methyl-3-furyl) disulfide 71 from MFT 62:

There are a number of fruity sulfides, often derived in some way from C6 units with an oxygen atom in the 3-position relative to the sulfur; such a grouping is found in the ‘tropicals’ Tropathiane 72 and 3-methylthiohexanol 73 as well as the potato-like methional 74:

1.2 FLAVOR SYNTHETICS

There are still a number of important flavor materials which have, to date, not been found in nature. They are often used because they have properties which suitable NI materials lack; for example the so-called Ethyl vanillin 75 has a lower odor threshold than vanillin and is more soluble in organic solvents, making it more suitable for use in oil-based flavors, and ‘Ethyl maltol’ 76 is more powerful than maltol. Several glycidate esters are used, such as ethyl 3-methyl-3-phenylglycidate 77, so-called Aldehyde C16, which has a powerful strawberry aroma and is used in flavours as well as fragrances.
Synthetics have proved especially valuable in the area of what might be termed ‘sensates’, the molecules of taste and sensation [7]. For example, the carboxamides 78 and 79 are both cooling agents which are longer-lasting than menthol 81:

\[
\begin{align*}
\text{78} & \quad \text{79}
\end{align*}
\]

Over the years a number of ‘synthetics’ have been found in nature, changing their status, such as the previously mentioned cat ketone and allyl hexanoate, and other materials are surely ‘synthetic’ simply because they are still hiding in foodstuffs! In addition, the “new” European regulations, EC 1334/2008, removes the “artificial” classification, and gives, potentially, a new lease of life to these materials.

### 1.3 NATURAL AROMA CHEMICALS [8]

The seemingly innocent term ‘natural’ is, in fact, a more troublesome one than it seems. In essence ‘natural’ materials are those which are:

(a) obtained by physical means from materials in the human food chain, that is, isolates;

(b) obtained by biological conversions of natural materials, that is, biotechnology; or

(c) obtained by reacting natural materials together in the absence of chemical reagents or catalysts, that is, cooking chemistry or soft chemistry.

These definitions are enshrined in US (CFR 21, 101.22 (a) (3)) and European (REGULATION (EC) No 1334/2008) regulations. As far as aroma chemicals are concerned, “Natural” is a marketing conceit; the marketing departments of flavour and food companies, the supermarkets and other major retailers are unlikely to reverse their policies of promoting their subliminal (and sometimes not so subliminal) formula of Natural = Healthy, especially with the so-called “Clean Label” concept. The importance of the regulations is that they set the criteria which enable a material to be called “Natural”.
1.3.1 Isolates

A number of essential oils consisting of high levels of valuable components, make their direct isolation by physical means commercially viable. Examples include citral 34, 35 from litsea cubeba oil, anethole 80 from star anise oil, methyl N-methyl anthranilate 28 from mandarin petitgrain oil, linalool 9 from ho wood oil, and L-menthol 81 from mint oils. In the latter case, isolation is by cooling the crude mint oil to deposit the familiar large ‘bright crystals’ of commerce:

\[ 
\begin{align*}
34 & \quad 35 \\
80 & \quad 28 \\
9 & \quad 81
\end{align*}
\]

If the value of the end product is sufficiently high and the raw material is cheap enough, then isolation is viable even if the component is at a low level, for example valencene 82 from orange oils and nootkentone 83 from grapefruit oil:

\[ 
\begin{align*}
82 & \quad 83
\end{align*}
\]

1.3.2 Biotechnology

This very modern term actually covers one of our species’ oldest hobbies – brewing! Alcoholic fermentation, as well as forming ethanol,
produces other alcohols such as isobutyl \textsuperscript{84} and isoamyl \textsuperscript{85, 86}. The latter is the main component of fusel oil, the residue after the distillation of liquors such as brandy, which can also be a source of pyrazines such as \textsuperscript{87}.

\[ \text{Acetobacter} \] species, unwanted contaminants in brewing, produce carboxylic acids. Gamma-lactones such as \( \gamma \)-decalactone \textsuperscript{88} can be produced from ricinoleic acid \textsuperscript{89}, a component of castor oil, and vanillin \textsuperscript{38} can be obtained from ferulic acid \textsuperscript{90}, a by-product of cereal production:

\text{1.3.3 'Soft Chemistry'}

This is best illustrated by the formation of esters by heating an alcohol with an acid; if the alcohol has a high boiling point this often takes place rapidly even though no catalyst is permitted. Another important
example is the synthesis of 2,5-dimethyl-4-hydroxy-3[2H]-furanone 46 from the hexose rhamnose 91:

![Chemical structure]

This is the area of greatest contention in the natural aroma chemicals arena. EC 1334/2008 defines the techniques that may be used as “listing of traditional food preparation processes in Annex II, and does not involve, inter alia, the use of singlet oxygen, ozone, inorganic catalysts, metal catalysts, organometallic reagents and/or UV radiation.” but it is often easier to define what cannot be done than what can be: for example, when is a solvent also a reagent? All solvents interact with their solutes – they would not act as solvents otherwise!

1.4 FRAGRANCE AROMA CHEMICALS [9–11]

As noted above, there are many aroma chemicals whose use overlaps both flavor and fragrance; many esters, aldehydes, heterocycles and indeed anything other than the most savory of flavor chemicals, tend to have uses in the fragrance sector. However, the freedom to move away from naturally occurring materials opens up a range of what we might call designer synthetics for the key notes of fragrance.

1.4.1 Musks [12]

The main odiferous component of natural musk is the macrocycle Muscone 92. The scarcity of the natural material and the difficulty of synthesizing large carbocycles has driven chemists to develop synthetics since the late nineteenth century. The first artificial musks were the nitro musks such as Musk Ketone 93, discovered serendipitously during explosives research. Discoloration problems and toxicity issues have restricted the use of the nitromusks and from the 1950s the so-called polycyclic musks were introduced. These have the advantages of stability, especially in household use, as well as ease of synthesis. Galaxolide 94 is the most important of these, with other related materials including Tonalid (Fixolide) 95 and Celestolide 96. The stability and hydrophobicity of
these materials has led to high usage in fabric softeners and detergents as well as fine fragrances.

Advances in synthetic methods have increased the availability of macrocyclic musks. The lactone ring was relatively easy to form, and 15-pentadecanolide 97 has been sold under many names for many years; the corresponding ketone 98 is now available. Modern musk structures such as Nirvanolide 99 combine natural musk character with low odor thresholds:

1.4.2 Amber

‘Amber’ materials are so-called due to their resemblance to *Ambergris*, a material formed in the stomachs of whales, probably as a pathological response to damage by shelly parts of plankton. This was formerly available as a by-product of the ‘whaling industry’, but now is only
found occasionally on beaches (a 15 kg piece was found on a beach in Australia in 2006), making it a rare and expensive material. Ambergris consists mostly of steroidal materials, and this structure forms the basis of classic ambers such as Ambroxan 100 and Amberketal 101. More recently amber molecules lacking this steroidal structure have been produced, such as Karanal 102 and Spirambrene 103:

1.4.3 Florals

Lily of the valley, or ‘muguet’, materials include the aldehydes Lyral 104 and Lilial 105. Methyl dihydrojasmonate 106 is a powerful jasmine molecule, first used in Dior’s famous ‘Eau Sauvage’. For ‘cheap and cheerful’ jasmine-type notes for household fragrances simpler materials such as α-hexylcinnamaldehyde 107 can be used:
The ionones, such as $\alpha$-ionone 108, were amongst the first synthetics to be used in perfumery; these violet-type materials have since been found in nature, for example in raspberry, and are also used in flavors. The damascones, such as $\alpha$-damascone 109, were identified in the oil from rosa damascena; the synthetic analogue Dynascone 110 is used in the popular perfume ‘Cool Water’ by Davidoff:

1.4.4 ‘Woodies’

Materials associated with this note include Iso E Super 111 and Georgywood 112; the macrocyclic ketone Trimofix 113 combines woody and amber notes:

1.4.5 Acetals and Nitriles

Another advantage in the use of synthetics is that stability issues can be addressed; aldehydes are prone to oxidation and Aldol-type condensation reactions, especially under the harsh conditions required for household fragrances. Acetals, such as 2-methylundecanal dimethyl acetal (Aldehyde C12 MNA DMA!) 114 and nitriles such as gerananitrile 115 have similar character to their ‘parent’ aldehydes but are much less prone to these damaging reactions:
1.5 MATERIALS OF NATURAL ORIGIN

1.5.1 Essential Oils

Naturally occurring materials were, of course, the foundation of both the flavor and fragrance industry and organic chemistry. The so-called essential oils are those materials obtained from plant materials by simple physical means, especially cold pressing and steam distillation.

1.5.1.1 Cold-pressing – Citrus Oils

The peels of the citrus family – which includes orange, lemon, lime, bergamot, grapefruit, tangerine, and mandarin – contain glands which release oils when crushed. Cold-pressing the peel gives a mixture of water and oil, which is simply separated. The main component of all these oils is the monoterpenic hydrocarbon limonene 116, typically about 95% in orange and grapefruit, slightly lower in lemon and lime. The character of the oil is determined by ‘trace’ components, which are also considered to be ‘markers’ for the quality of the oil, for example Nootketone 83 in grapefruit (0.1–0.4%), citral 34, 35 in lemon (1–2%), methyl N-methyl anthranilate 28 (0.3–0.6%) in mandarin; it should be emphasized, however, that the quality of the oils is the sum of their parts, not a marker plus carrier!
Citrus essence oils, or phase oils, are by-products of the juice market; concentration of the juice to reduce transport costs leads to oil separating out which can be sold or further processed. Whilst the essence oils are similar in components to their ‘parent’, there are some differences in that the essence oil is nearer to being an extract of the juice. The most important is orange essence oil; this contains more volatiles such as acetaldehyde and ethyl butyrate and a higher level of the sesquiterpene valencene \(^{82}\) than cold-pressed orange oil.

The high levels of hydrocarbons in the citrus oils leads to poor solubility in water, a particular problem for their use in soft drinks. This can be overcome, in part, by folding; the oil is ‘folded’ by distilling off the more volatile monoterpene hydrocarbons, in effect concentrating the more valuable flavor components and removing the most hydrophobic components. The distillates also have value as solvents, diluents and, since the terpenes do carry over some odiferous components, as flavor or fragrance ingredients in their own right; for example in creating a tenfold orange oil, 9 kg of orange terpenes are produced per kg of ‘Orange Oil 10X’.

### 1.5.1.2 Steam-distilled Oils

Most plant materials contain much less volatile oil than the citrus fruits, often less than 1 %, and these are simply steam distilled to obtain the oil; examples include cassia, cinnamon, mint, rose and lavender. This process
can, of course, lead to changes in composition due to thermal decom-
position, oxidation and hydrolysis; by tradition, the best lavender oil is
produced at high altitude, as the lower boiling point of water leads to
less hydrolysis of esters such as linalyl 117 and lavandulyl 118 acetates.

![Chemical structures](image1.png)

Chemical changes can also be beneficial. The most important lime oil
is “Distilled Lime”; this is not redistilled cold-pressed oil but oil which
is steam distilled from the macerated fruit. The high acidity of the juice
leads to hydration of the hydrocarbons, giving high levels of α-terpineol
10 and 1,8-cineole 52. This oil has a fresh, juicy aroma which contrasts
with the waxy, floral odour of the cold-pressed oil.

![Chemical structures](image2.png)

1.5.1.3 A Note on ‘Adulteration’

Historically, especially prior to the routine availability of gas chromato-
graphy, the addition of cheap materials to ‘cut’ or adulterate oils, was
more widespread. It is still a problem; without the use of sophisticated
isotopic analysis, the addition of a quantity of a synthetic material, for
example, cinnamaldehyde to cinnamon oil, is impossible to detect, let
alone prove. Similarly, the addition of a low percentage of terpenes to a
citrus oil which is already over 90 % terpenes, is not going to be detected
easily. Ultimately the answer has to lie in the trust in the supplier, as
applied with a modicum of common sense. Customers are themselves
part of the problem – the desire for lower priced raw materials is itself a driving force in adulteration. Put simply, if you wish to buy an oil at 50% of the market price, then do not be surprised if the product you are buying is only 50% oil!

1.5.2 Absolutes and Other Extracts

This final section in fact covers the oldest approach to flavor and fragrance materials – the extraction of aromatic materials into organic solvents. Extraction of plant material with a nonpolar solvent such as hexane, followed by removal of the solvent, yields a concrete. As the name implies, this is often solid or semisolid due to the presence of plant waxes as well as pigments and nonvolatiles. Extraction into ethanol followed by solvent removal gives an absolute, which is more manageable and the more usual item of commerce. This is a very labour-intensive process and hence absolutes are more expensive than most oils, and are more associated with higher-value materials such as violet flower absolute and orange flower absolute. Oleoresins are more associated with spice oils such as ginger and garlic and are a solution of an absolute-type extract in an essential or solvent such as vegetable oil or propylene glycol.

ACKNOWLEDGMENTS

Many thanks to the contributors to *The Chemistry and Technology of Flavours and Fragrances*, whose work I have cheerfully plundered for this chapter!

REFERENCES


