High Impact Aroma Chemicals Part 2: the Good, the Bad, and the Ugly

by David Rowe, Oxford Chemicals Ltd.

In Part 1, "More Fizz for your Buck", the role of high impact aroma chemicals as character impact materials in foodstuffs was described.[1] In that article, a simple 16-segment flavor wheel was used as the theme to link the materials. Developing this idea further, I have produced a 20-segment wheel, shown in Figure 1.[2]

This expanded wheel enables us to see some broad groupings. The eastern sector is the "sweet" sector (pictured in Figure 2), with "savory" materials in the west (Figure 3); sweet and savory overlap in the southeast.

> "How a more complex flavor uses the synergy between the aromas and the chemicals that create them…"

A second differentiator reflects the origins of the aroma chemicals, and, in turn, their applications. Clockwise from "mushroom" to "vegetable", the materials are formed by biogenesis in plants, and so are of particular interest in creating the flavors of fresh fruits and vegetables (Figure 4). By contrast, most of the others are commonly found as Maillard reaction products (the term "advanced" Maillard products has been used by Shieberle to differentiate them from the first formed Maillard products such as the Strecker aldehydes), and hence are of most interest in flavors for cooked foods (Figure 5). [3]

Whereas the first article emphasized the "separateness" of the flavor types, this article emphasizes how a more complex flavor uses the synergy between the aromas and the chemicals that create them. This can be illustrated by looking at three of the most popular flavors: coffee, roast beef and chocolate.

Coffee

The most obvious aroma associated with coffee (Figure 6) is the "burnt, roasted" note. Furfuryl mercaptan (1) (Figure 7) is the best-known contributor of this note, and in a study on reconstituting the flavor of coffee, it was found to be the single most important aroma chemical. The derivatives of furfuryl mercaptan also have elements of this aroma; the disulfide (2) is rather milder, and the mixed disulfide (3) has sweet, mocha notes. The monosulfide (4) is also mild, and has earthy, mushroom notes, which may contribute to the "earthy" aroma character, one of the four key aroma qualities (earthy, sweet-caramel, sulfury-roasty and smoky) looked at in a reconstitution study.[4] The headspace concentrations of these odorants is lowered by the addition of milk and cream, which may be due to a lipophilic interaction with fats.

Another reconstitution study found that the second most important aroma chemical for coffee was 2-methoxy-4-vinylphenol (5) (Figure 8).[5] This is a familiar material for smoke flavors, and is presumably formed from ferulic acid in the roasting process. Its saturated derivative, 4-ethylguaiacol (6), was also found. Alkylpyrazines, such as 2,3-diethyl-5-methylpyrazine (7), were found to influence the perceived strength of the coffee flavor.

The fourth group of powerful coffee volatiles, prenyl mercaptan (3-methyl-2-butene-1-thiol) (8), 3-mercapto-3-methylbutan-1-ol (9) and its formate (10), can be termed the "prenoids" in that they are in some way related to "prenal", 3-methyl-2-butenal (11) (Figure 9).

These are the more unusual volatiles in coffee. While they contribute less to the flavor than the more familiar materials, the greater volatility of these volatiles — in particular prenyl mercaptan (8) [b.p.130C, c.f. 155C for furfuryl mercaptan (1) and 230C for dithiodimethylenedifuran (2)] — may indicate that they are greater contributors to the "fresh roast" aroma than to the taste.

A second aspect of the prenoids is that several are related to the aroma chemicals found in blackcurrants, cassis and wines, where they contribute the familiar catty note (Figure 10). Indeed, 3-mercapto-3-methylbutan-1-ol (9) is the simplest material having the catty olfactophore (Figure 11).

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Roast Beef

This is both an important flavor in its own right and perhaps also the archetypal "meat" flavor (Figure 12). The single most important group of aroma chemicals in beef is derivatives of 2-methyl-3-furanthiol (MFT) (12) (Figure 13). While MFT is commonly formed in Maillard reactions and present in all meats, it is found at a much higher level in roast beef, up to 28 mg/kg, compared with 9 mg/kg in pork, 11 mg/kg in lamb and only 4.5 mg/kg in boiled chicken.[6] Derivatives are of great importance in roast beef; the disulfide (13) is also very important; it has a strong meaty, roasted odor, and because MFT readily oxidizes to this material, it is characteristic of a more "aged beef" aroma. The odor of (12) and (13) can be described as "beef as it is roasting", whereas (13) resembles a joint of beef when it has been cooked and allowed to stand. 2-Methyltetrahydrofuran-3-thiol (THMFT) (14) is also very powerful, with savory, brothy notes. The sulfide, 2-methyl-3-methylthiofuran (15), is milder with less "beef" character.

A second group of compounds of great importance is furfuryl mercaptan and it's derivatives (Figure 14); essentially the same compounds are found in roast coffee and roast beef. It should also be noted that the levels of furfuryl mercaptan (1) found in meats parallel the pattern seen for MFT; up to 42 µg/kg in roast beef, 10 µg/kg in pork, 14 µg/kg in lamb and 2.4 µg/kg in boiled chicken.[6] 3-Mercapto-2-pentanone (16) is also important, though at up to 73 µg/kg, this was at a lower level than in pork and chicken (117 µg/kg and 100 µg/kg, respectively).

All of these compounds have vicinal oxygen and sulfur, and this may be the "savory olfactophore" (Figures 15 and 16).

Structure-odor relationships have been much less studied in the area of flavors than fragrances, in part because the usage of materials in the former is dominated less by activity and more by the issue of "nature-identical" (and/or natural). There is little value in designing the world's most savory molecule if, in the end, it cannot be used. We might also comment that nature has done rather well in making high impact chemicals herself anyway. The concept can still be useful, however, in the possible identification of aroma chemicals. 4-Methylthiazole-5-ethanol (17) (sulfurol) (Figure 17) is widely used in savory flavors. Most thiazoles have green or fruity odors, and it is also a well known phenomenon that apparently identical batches of sulfurol have different odors, with the desirable "meaty" note not always present. Because sulfurol has a reported odor threshold of over 10,000 ppb, a trace impurity will have a major effect. A strong candidate in the identity of this impurity is the disulfide (13); it has a very similar boiling point to (17) (both ca. 280C), and hence would be carried through the purification by distillation. As a derivative of 2-methylfuranthiol (12), its carbon, oxygen-sulfur framework is actually the same as that in sulfurol; it may be a degradation product or a by-product formed during the synthesis of sulfurol (Figure 18).

Perhaps the major difference between the aroma chemicals for roast beef and for coffee is the presence of fat-derived materials in the former. Fats and their derivatives influence both flavor and "mouth-feel". Aldehydes typically contribute fatty notes, in particular *trans*-2-nonenal (18) and *trans*-2-*trans*-4-decadienal (19) (Figure 19); the latter is reminiscent of chicken fat and has an odor threshold of 0.07 ppb.

Chocolate

To the millions of "chocoholics", this is "nature's perfect food" (Figure 20). A look at the most important aroma chemicals perhaps gives some idea as to why this is. While chocolate is undeniably in the "sweet field", it has both a savory (Figure 21) and sweet (Figure 22) character, the former deriving from Maillard reaction products formed in the roasting of cocoa beans. A study on the key odorants in milk chocolate and cocoa mass was able to identify the origin of most of the top 20 odorants in a milk chocolate (Table 1).[7] As expected, the cocoa mass provided most of the key odorants, especially those with "savory" aspects, such as the pyrazines and the MFT derivative (23) . The sweet lactones probably de-

Figure 1. A Flavor wheel for high impact aroma chemicals

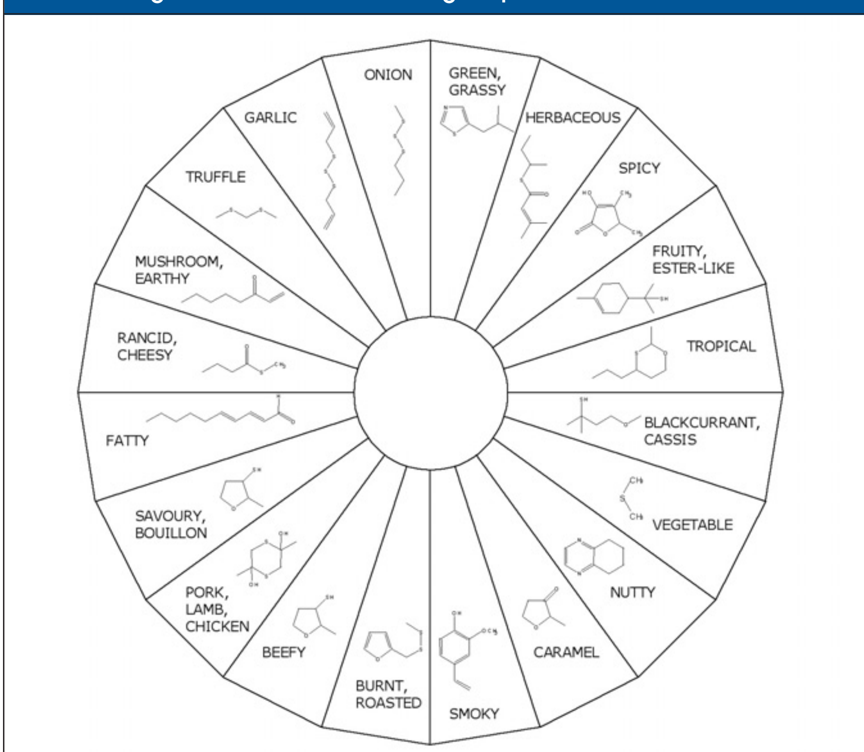


Figure 2. The “sweet” sector

Figure 3. The “savory” sector

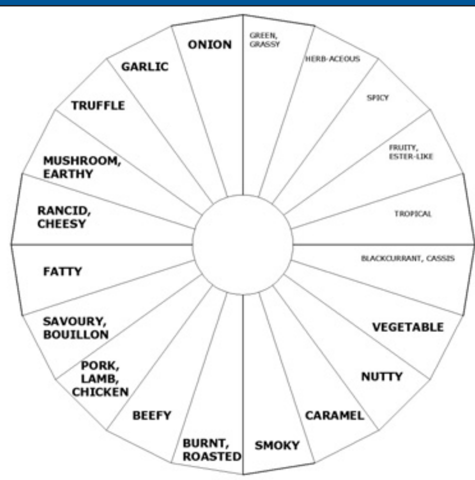


Figure 4. Biogenesis in plants — fresh fruits and vegetables

Figure 5. “Advanced” Maillard products — cooked foods

Figure 6. The coffee wheel

Figure 7. Furfuryl mercaptan derivatives

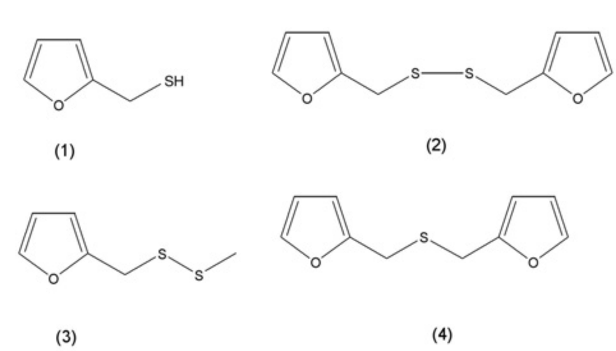
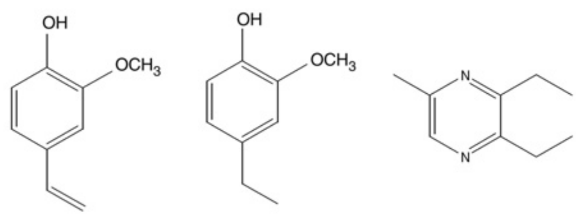


Figure 8. Guaiacols and pyrazines in coffee



(5) (6) (7)

Figure 9. "Prenoid" relationships

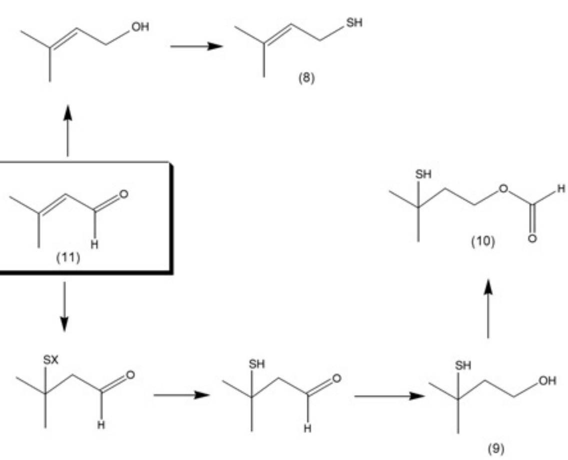
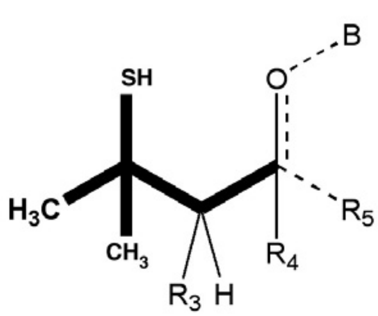


Figure 10. The catty olfactophore



B=H, CH_3, Acyl, absent if carbonyl
R_3 =H, alkyl, ring
R_4=H, CH_3, ring, OR
R_5=H, absent if carbonyl

rived from milk powder, or, in the case of vanillin (24), as essentially an added flavoring. Surprisingly, the "beefy" MFT derivative methyl 2-methyl-3-furyl disulfide (23) has been detected in chocolate and coffee, but not yet in roast beef; a closer look at the latter may well show its presence.

Summary

We can summarize the synergies and correspondences with the diagram presented in Figure 23, in which roast beef, chocolate and coffee are shown with their unique and overlapping characteristics.

Off-Notes

"… I have smelt
Corruption in the dish, incense in the latrine, the sewer in the incense, the smell of sweet soap in
the woodpath…"
— T.S. Eliot, "Murder In The Cathedral" (1934)

Eliot's words, spoken to reflect the tension and mounting horror of the people of Canterbury as the murder of Archbishop Thomas Beckett approaches, convey the powerful sense of "wrongness" that our sense of smell can evoke. Some odors are inherently repulsive, while in other cases a sense of revulsion occurs when incompatible odors are mixed. At Oxford Chemicals, we put together a listing of "off-odors" that we are familiar with in the aroma chemicals business. While we are proud of the quality of our products, we occasionally have problems with off-notes that lead to the material going back for further purification. We take the view that if a supplier claims they never detect any off-notes in their products, this means that the customer is doing their quality control for them From these off-notes we devised the Devil's Flavor Wheel (Figure 24).

There are some terms used that one might not wish to use in polite society, but they are familiar from everyday experience. The wheel is not a random listing of horrors, in that while the off-notes on the eastern side are inherently bad (it is difficult to imagine anyone wanting a sickly, fecal flavor, or a burnt urine fragrance), the western side's odors can be both desirable and repellant. The context is critical; onion and garlic notes are undesirable in a pyrazine, but essential in allyl disulfide. This emphasizes the key notion that off-notes are themselves aroma chemicals, whether present as contaminants or as by-products of synthesis. The amount of contaminating material may be tiny, as many sulfur compounds have odor thresholds below 1 ppb, so a little goes a long way. Sometimes the off-notes are readily identified. For example, "gassy" off-notes may be due to methyl mercaptan, "ammoniacal" due to aliphatic amines or ammonia itself, and "biscuity" due to pyrazines. We have noticed that traces of pyrazines stand out against the fruity notes of esters, and that traces of sulfur compounds give an onion-garlic note that stands out against the earthy-nutty odor of pyrazines. More often, mixtures of trace impurities give the generic type of off-notes such as "dirty", "burnt" and 0"sulfurous". The same principles apply to foodstuffs,

Figure 11. Molecules showing the catty olfactophore

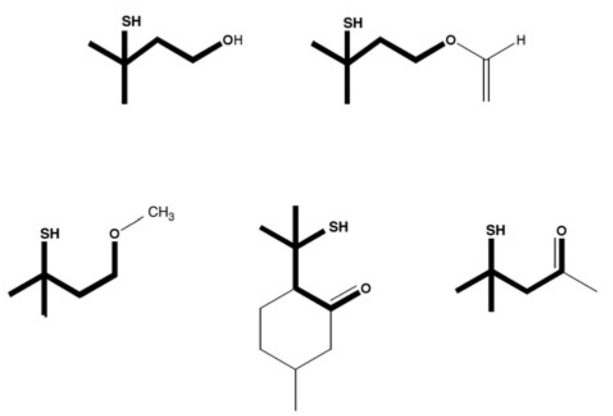
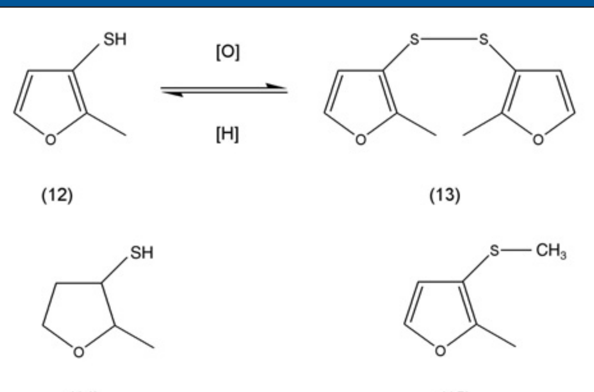


Figure 12. The roast beef wheel

Figure 13. MFT derivatives



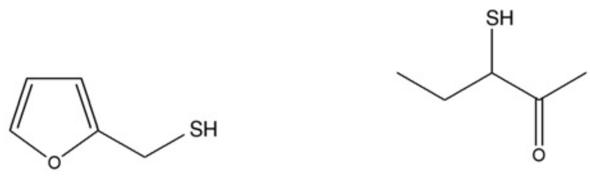
where a number of important aroma chemicals have also been identified as causing off-notes. Again, context is key; perhaps the phrase "one man's meat is another man's poison" is appropriate here. While some off-notes are well known in a number of foods — prenyl mercaptan (8) in "sun-struck" beer, 2-methoxy-4-vinylphenol (5) in orange juice, and lipid breakdown/oxidation products such as decadienal (19) — some are more surprising.[8] Methional (27) and MFT (12) can cause problems in orange juice, sotolon (28) can cause unwanted burnt, spicy notes in citrus soft drinks, and methional (27) is a villain again in causing the "worty" note in alcohol-free beer (Table 2 and Figure 25).[9-11]

The Future(?)

There are three areas where developments are continuing. The first is in synthetic chemistry — materials that are interesting, but too expensive for use at present, may become available at an "accessible" price due to the discovery of a viable synthetic route. The cycle of discovery, synthesis, and manufacture with falling prices has continued since the work on cinnamaldehyde and vanillin in the 19th Century.

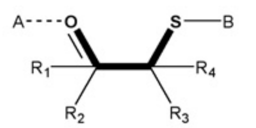
A second area involves further analytical work, which may be in the examination of new "exotic" foodstuffs, or re-evaluation of familiar materials. For example, the cat ke-

Figure 14. More "beefy" mercaptans



(1) (16)

Figure 15. The savory olfactophore



A=ring, absent if carbonyl
B=H, CH_3, Acyl, SR
R_1=ring, absent if carbonyl
R_1, R_2, R_3=ring, H, alkyl

Figure 16. Molecules showing the savory olfactophore

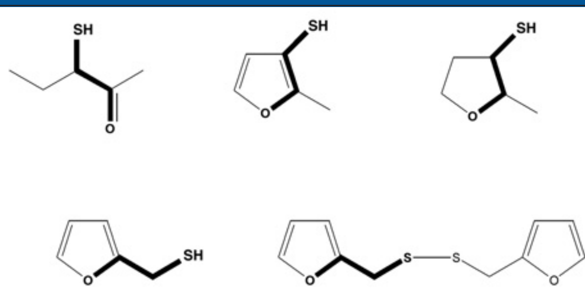


Figure 17. Savory compounds

(17) (13)

Figure 18. Structural relationship between sulfurol and 2-methylfuran-3-thiol derivatives

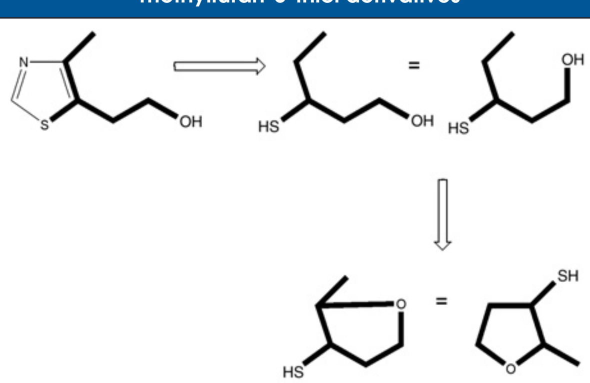
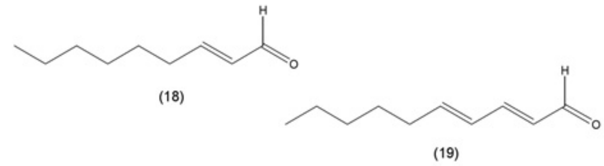


Figure 19. Fatty notes for beef



(18) (19)

Figure 20. The chocolate wheel

tone (29) (Figure 26) was recently found to be an unexpectedly important odorant in grapefruit.[12] We are also now able to go "further down in the noise" on gas chromatography and identify materials at lower levels and even lower odor thresholds; dimethyl selenide (30) has been detected in garlic and garlic breath.[13] Handling and manufacture of such materials may require "glove-box" techniques more familiar from radiation chemistry.

The third area that may have an important effect on the usage of high impact aroma chemicals is work being carried out on delivery systems. A number of very interesting aroma chemicals are also highly reactive and have a short half-life in normal formulations. Systems that can trap and release such materials could enable their use for the first time; examples include the related 2-acetyl-1-pyrroline (31) (basmati rice) and 2-acetyltetrahydropyridine (32) (bread crust).[14]

Why?

A final question that may be asked is, simply: "Why are we so sensitive to these aroma chemicals?"

The functions of our senses of smell and taste are threefold: 1. to find/attract a mate; 2. to find/identify food; and 3. to avoid toxins. It is actually quite difficult to really explain our responses in these simple terms.

1. To find/attract a mate: This is probably the least relevant here. While the extreme sensitivity of insects to sex pheromones is well studied, the fact that these aroma chemicals are found in foodstuffs is something of a compli-

Table 1. Key odorants in chocolate and their probably origins

Odorant	Probable source
vanillin (24)	Vanilla or synthetic
3-methylbutanal	Cocoa mass
2-ethyl-3,5-dimethylpyrazine (20)	Cocoa mass
5-methyl-2-hepten-4-one	Nut paste
2-ethyl-3,6-dimethylpyrazine	Cocoa mass
2,3-diethyl-5-methylpyrazine (21)	Cocoa mass
trans-2-*cis*-6-nonadienal	?
cis-2-nonenal	Cocoa mass
2- and 3-methylbutyric acids	Cocoa mass
methyl 2-methyl-3-furyl disulphide (23)	Cocoa mass
trans-2-*trans*-4-nonadienal	Cocoa mass
trans-2-*trans*-4-decadienal (19)	Cocoa mass?
R-δ-Decalactone (26)	Milk solids
1-octen-3-one	Milk solids or thermolysis?
dimethyl trisulphide (22)	Cocoa mass or thermolysis?
trans-2-nonenal	Cocoa mass
phenylacetaldehyde (25)	Cocoa mass
R-δ-octalactone	Milk solids?
ethyl cinnamate	Cocoa mass
γ-decalactone	Milk solids?

cation; sexual attraction between an animal and its food is unlikely to be a successful evolutionary strategy.

2. *To find/identify food:* At first sight, this is the "obvious" explanation. However, most of the high impact aroma chemicals are formed only when food is cooked; because the cooking of food is of very recent provenance in evolutionary terms, it is unlikely that we have evolved any physical features to respond to this. Some high impact materials are found in fruits, but again, the chemical may only be released when the fruit is actually being eaten; for example allyl disulfide and the other allium sulfides are only released only when the tissues of the garlic clove have been damaged, and a cow certainly doesn't smell of roast beef.

> "Why are we so sensitive to these aroma chemicals?"

3. *To avoid toxins:* There are three main sources of toxins: those present in the environment, those produced as an organism's waste and those produced by the decomposition of food. It is this latter area that gives a clue that this may be the cause of the response to these high impact chemicals; the group of compounds to which we have the greatest sensitivity is mercaptans, and these are produced by the decay of cysteine and methionine in proteins. This

Figure 21. Chocolate's savory side

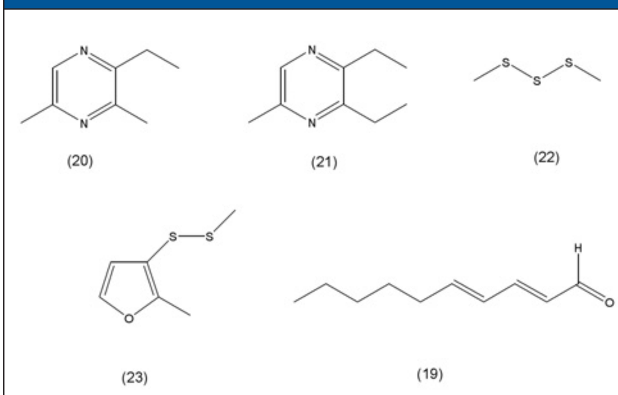


Figure 22. La dolce vita (the seet side of chocolate)

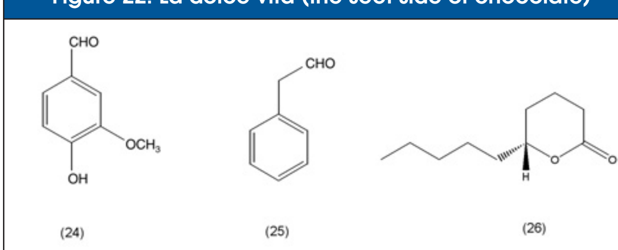


Table 2. Aroma chemicals in the wrong place at the wrong time

AROMA CHEMICAL	AS A DESIRABLE NOTE	AS AN OFF-NOTE
trans-2-*trans*-4-decadienal (19)	chicken meats	cooked potatoes
2-methoxy-4-vinylphenol (5)	coffee	orange juice
methional (27)	fried foods	orange juice
2-methyl-3-furanthiol (12)	beef	orange juice
prenyl mercaptan (8)	coffee	beer
methional (27)	fried foods	alcohol-free beer
sotolone (28)	fenugreek	citrus drinks

Figure 23. The high impact aroma chemicals of roast beef, coffee and chocolate

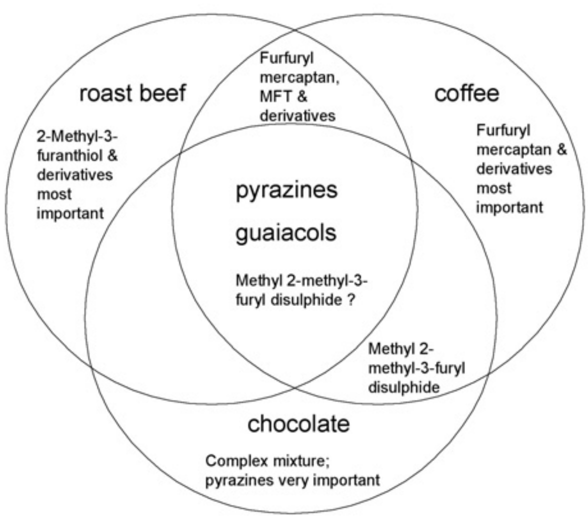


Figure 24. The devil's flavor wheel

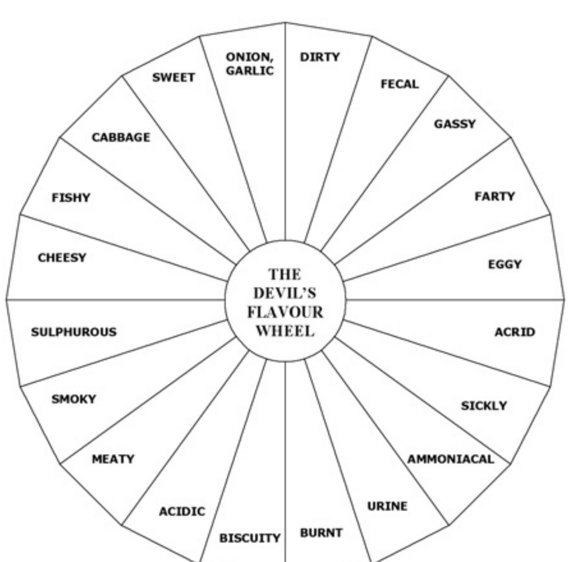


Figure 25. The good, the bad and the ugly

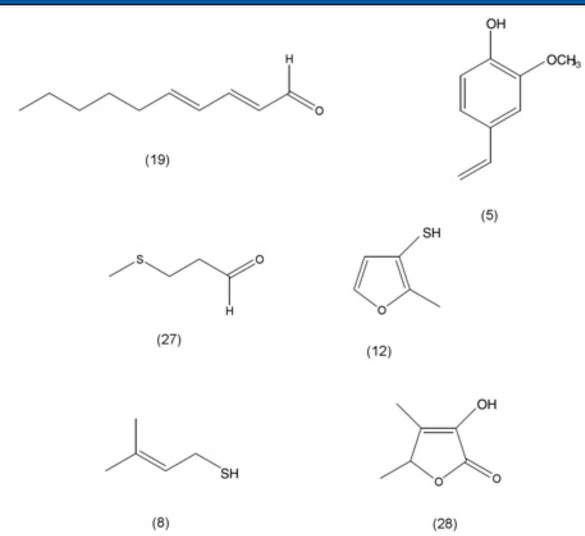
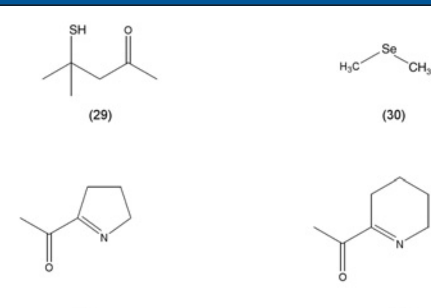


Figure 26. Future high impact aroma chemicals



may be the origin of our response to the simple materials, such as hydrogen sulfide, methyl mercaptan and simple alkyl thiols; the cause of the enhanced response to mercaptans, such as 2-methyl-3-furanthiol and p-menthene-8-thiol, may simply be that these materials happen to trigger the receptors more easily. This is a coincidental response and not a specific "design". To use an analogy from pharmaceutical chemistry, morphine happens to fit our endorphin receptors in the brain with great efficacy, but it is not suggested that we have evolved to develop morphine addiction. Evolution is conservative; a study on mouse olfactory receptor (OR) genes found that while humans have only two-thirds of the OR genes of mice, they occupied a similar receptor space — hence, we retain the ability to recognize a broad range of aroma chemicals.[15] Furthermore, a large number of the OR genes were described as “fish-like”.

These phylogenetic links indicate that our response to these molecules appears to have a very “primitive” origin, and we have yet to meet an individual with specific anosma to these materials. The ability to respond to chemicals in our surroundings is the primary sense. We now differentiate taste and smell, but to the simplest organisms it is as one. Even the simplest and most primitive organisms, the prokaryotic bacteria and archea, have this sense, and this leads us to a fascinating possibility; there is much evidence that life evolved in a sulfur-rich environment, where a sulfur compound would be a nutrient or a toxin, depending on concentration. Does our love for roast beef, coffee and chocolate have its ultimate origins in the days when the only course on the menu was the primordial soup?

Address correspondence to David Rowe, Oxford Chemicals Ltd., North Gare, Seaton Carew, Hartlepool, TS25 2DT, UK.

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