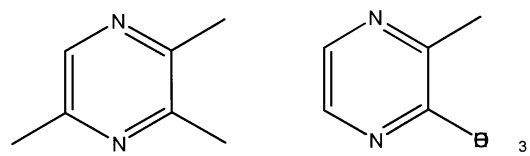
More Fizz for Your Buck: High-impact Aroma Chemicals

By David Rowe, Oxford Chemicals, North Gare, Seaton Carew, Hartlepool, UK

Developments in the flavor and fragrance industry have gone hand-in-hand with advances in the chemical sciences. From the 19th Century, in which saw the identification and synthesis of key materials such as cinnamaldehyde and vanillin, to more recent decades, advances such as 'hyphenated techniques', in particular GC-MS and GC-Olfactometry, have enabled flavor chemists to identify the compounds present in natural materials. Some of these compounds, though present at only trace levels, are key contributors to the odor and flavor of natural materials. This has been augmented recently by the use of solid phase microextraction (SPME) to capture the aroma chemicals at source, such as the IFF's 'Living Flower' and 'Living Flavor' technologies and Givaudan's 'Taste-Trek' studies on aroma chemicals emitted by plants in the rain forest canopy. Many of the materials identified are high-impact aroma chemicals, which will be discussed in this article.

The term 'high-impact aroma chemical' is one that many of us can understand but for which there is no official definition. I will set four key criteria that, for the purpose of discussion, will define these chemicals:

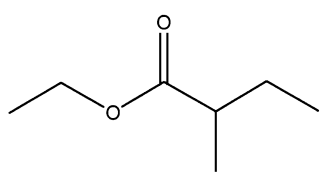
- Low odor threshold. This is an obvious feature, but there is no absolute definition of low to which we can turn. For the purpose here, I have set low odor threshold at less than 10 parts per billion (10 ppb, or 10 in 10^9). Some apparently odorous compounds fall out by this definition. For example, 2,3,5-trimethylpyrazine (1) has an odor threshold[1] of around 1000 ppb and cannot be considered high-impact. However, the 2-alkoxy-3-alkypyrazines, such as 2-methoxy-3-methylpyrazine (2), which has an odor threshold of only five ppb, would constitute a high-impact material by our definition.



(1) (2)

Figure 1. Contrasting pyrazines

- Character impact. The material should have recognizable character, even at the low levels that such a material would be used at. This criterion eliminates many esters, such as ethyl 2-methylbutyrate (3), which has an odor threshold of only 0.1 ppb, but at low levels has only a vague fruitiness, which may be pleasant but not characteristic.



(3)

Figure 2. Esters, odourous but low impact?

- Desirable character impact. Although many chemicals have a powerful odor, this characteristic is not always a desired one. For example, 2,4,6-trichloroanisole (4) is a highly odorous metabolite of a fungus that attacks paper. However, it is highly improbable that this can be considered a high-impact aroma chemical, because it

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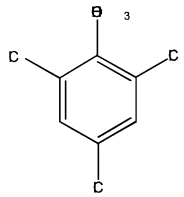
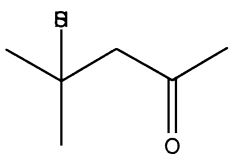
is unlikely that a flavorist or perfumer will have a brief to recreate the aroma or taste of moldy books.



(4)

Figure 3. An unwanted odour

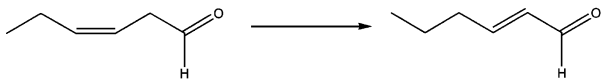
This is of course a matter of context, because many aroma chemicals are repellent when neat or in high concentration. In the correct context, however, they contribute to the desired effect. For example, the nature of 4-mercapto-4-methyl-2-pentanone (5) can be gleaned from its common name of Cat Ketone. However, it is also a key component of sauvignon grape.[2] Depending on the context, it can be used to recreate the bouquet of a fine cabernet sauvignon or the atmosphere of where the local alley cats have marked their territory.



(5)

Figure 4. Cat or vin?

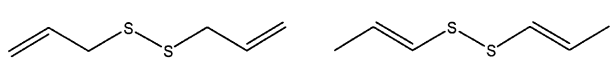
- Availability to the flavorist. There are three aspects here: (i) Regulatory. The material should not be forbidden in the context in which it is to be used. For flavor use, the material should be nature identical, preferably FEMA GRAS. Natural status may be important, especially for the US where the nature identical category is lacking. (ii) Stability. Many materials can be manufactured but have insufficient shelf-life to be useful in a finished flavor. For example, *cis*-3-hexenal (6) is a key aroma chemical emitted by cut grass and other vegetation; it has a low odor threshold (0.25 ppb) and a powerful, desirable green character. Unfortunately, it is chemically reactive, and readily rearranges to the more stable conjugated form, giving the more familiar *trans*-2-hexenal (7). Even the 'half-life' of the isolated material may not be enough to guarantee a useful level of stability. The rearrangement is 'prototropic' and hence catalysed by both acid and base; the rate will be increased by a factor of ten for each pH unit away from its 'optimum' stability point.



(6) (7)

Figure 5. Rearrangement of hexenals

(iii) Economics. Many high-impact chemicals are relatively expensive, which reflects the small market volume and the difficulties associated with manufacturing and handling such materials. However, the material must be commercially available at a price that enables a flavorist or perfumer to add value to their formulation by its use. If the material is captive, the internal costs must not be prohibitive. In short, despite high prices, the high impact of these materials gives 'more fizz for your buck'. An example of this can be seen from garlic chemistry. The major component of garlic oil is allyl disulphide (8) (2-propenyl disulphide). The isomeric 1-propenyl disulphide (9) is also present (*cis*- and *trans*- forms), but whereas the former is readily synthesised, and hence cheap and readily available, no suitable route for large-scale preparation of the latter exists at present. Laboratory syntheses have been reported, but the costs of a material made in such a way means that any advantage in the flavor is outweighed by a vast increase in costs. The added value is therefore insufficient.



(8) (9)

Figure 6. Contrasting garlic disulphides

For the purpose of this discussion, high-impact chemicals are those which fulfil these criteria. Such compounds are powerful materials, highly active at low levels, the Viagra[a] of the flavor and fragrance industry.

Uses

High-impact chemicals have been identified in many foodstuffs and have many applications, to the extent that a simple listing would make dull reading. At first thought it would seem appropriate to use the sixteen key notes of a flavor wheel to illustrate the applications. However, a traditional flavor wheel, as shown below, is not very helpful.

[a]This article is in part based on a presentation given at the ChemSources Association/Society of Flavor Chemists meeting in Cincinnati in April, 2000. At the same meeting, Carl Sheeley (Fontarome, St. Francis, WI) gave a presentation on how aroma chemicals related to the classifications generally used in the chemical industry. Commodity chemicals included solvents, and bulk chemicals, the widely used esters. Flavor and fragrance formulations included specialty chemicals and fine chemicals as active ingredients, whether pharmaceuticals (with Viagra as the example) or high-impact aroma chemicals. The author is very grateful to Carl for this uplifting imagery.

Perfumer & Flavorist **(ISSN 0272-266)** is published bi-monthly by Allured Publishing Corporation, 362 S. Schmale Road, Carol Stream, IL 60188-2787. **Subscriptions:** USA and Canada US$130.00 one year; all other countries US$170.00 one year shipped by air. Periodical postage paid at Carol Stream, Illinois and at additional mailing offices. **Postmaster:** Send address changes to ***Perfumer & Flavorist***, 362 S. Schmale Road, Carol Stream, IL 60188-2787, USA.

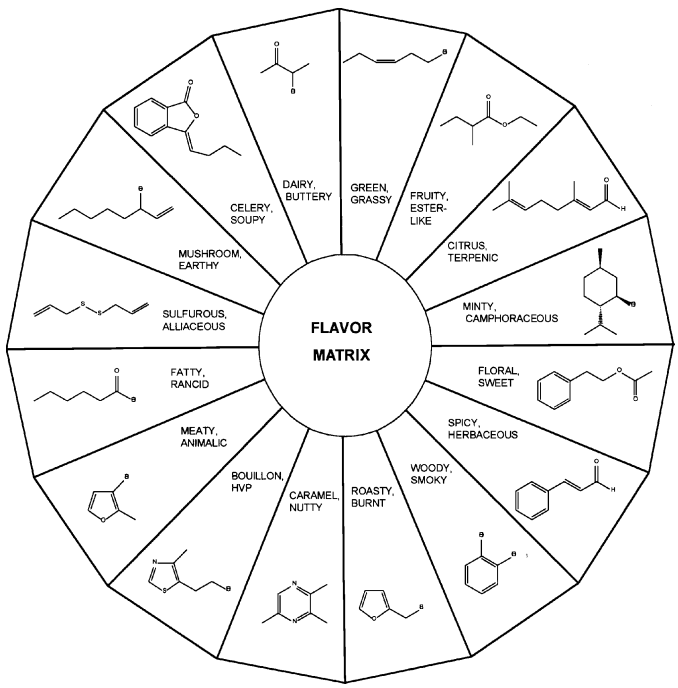


Figure 7. A "Traditional Flavour Wheel"

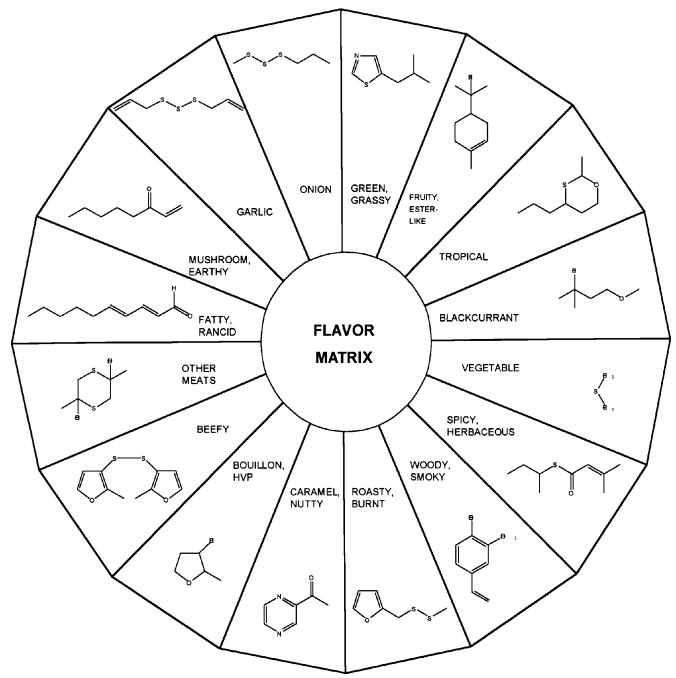


Figure 8. A Flavor Wheel for High Impact Chemicals

There is little to say for mint, camphoraceous that is not known from the menthol/camphor derivatives. There is nothing high-impact for dairy, buttery, and intensely floral, sweet character is best known in the synthetic materials of perfumery. Instead of the traditional wheel, an adapted flavor wheel can be used. The extra areas are extensions of the meaty notes, extensions of the fruity notes into tropical and blackcurrant, and division of the allium into both onion and garlic. Here we can illustrate the uses of high-impact chemicals in these sixteen segments.

Green, Grassy

In this category, the traditional molecules are the hexenyl compounds. As noted above, the true high-impact chemical in this group is the unstable *cis*-3-hexenal (6), the initial cleavage product of linoleic acid. The stable aroma chemicals *trans*-2-hexenal (7) (leaf aldehyde) and *cis*-3-hexenol (10) (leaf alcohol) are widely used. However, with odor thresholds of 17 and 70 ppb, respectively, they are borderline cases as high-impact chemicals. Despite this, their distinctive character is in their favor. A fresh greenness is also associated with the more odorous 2-isobutylthiazole (11) (odor threshold three ppb). This molecule is released by tomato vine and has both tomato and more general green (string bean, geranium leaf) character, especially on dilution.

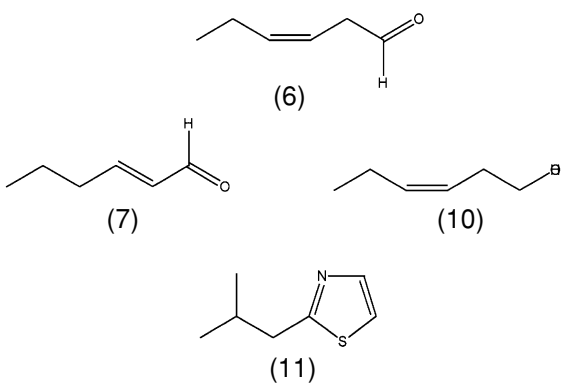


Figure 9. Green, grassy compounds

Fruity, Ester-Like

The esters are obvious candidates here. However, while many have low odor thresholds (ethyl butyrate one ppb, ethyl isobutyrate 0.1 ppb, ethyl 2-methylbutyrate (3) 0.1 ppb, ethyl hexanoate one-two ppb), they lack the character which would make them truly high-impact. Instead, we may illustrate fruity notes with what may be the ultimate high-impact aroma chemical, *p*-1-menthen-8-thiol (12), the grapefruit mercaptan. This has the remarkably low threshold of ~ 10^{-5} ppb, and retains it's character even at

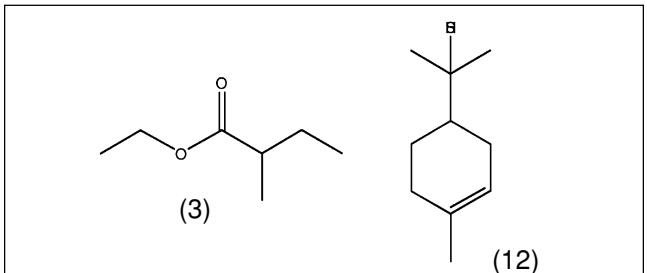


Figure 10. Fruity molecules

low levels. At high concentrations, the molecule simply has a sulphurous, almost rubbery odor common to mercaptans, and requires dilution to at least 0.001% before the fresh grapefruit juice character can be recognized.

Tropical

This is one of the most important areas for high-impact aroma chemicals. Analysis of passionfruit and durian has shown the presence of many powerful sulphur compounds, a large number of which were included in FEMA's GRAS 18 list in 1998. Possibly the best known is tropathiane, 2-methyl-4-propyl-1,3-oxathiane (13),(odor threshold ~3 ppb) ; 3-mercapto-1-hexanol (14) and a number of acylated derivatives were included in FEMA's GRAS 18 list, as were thioesters, including thiohexanoate (15) and thioisovalerate (16).

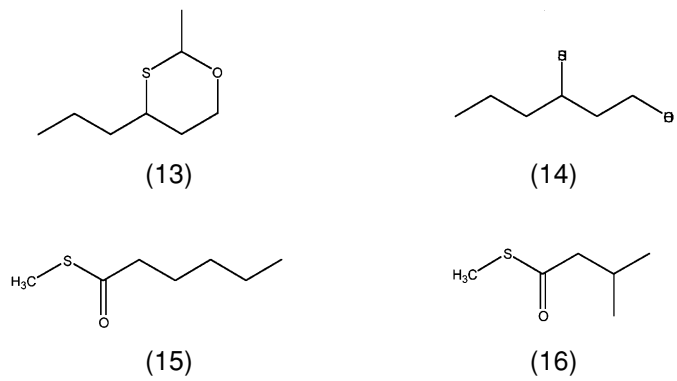


Figure 11. Sulphur compounds for tropical notes

Blackcurrant

This is a very popular flavor in Europe, associated with many health-related products (nutraceuticals or functional foods) and with alcoholic drinks (cassis liqueur, and added as a cordial to some spirits). The key material in blackcurrant is 2-methoxy-4-methyl-4-butanethiol (17); it is also a key component contributing a fruity flavor to olive oil.[3] Two other materials have been used to recreate the rather catty note of blackcurrant; *p*-menthathiolone (18), the main odor-active ingredient of Buchu leaf oil, and 4-mercapto-4-methyl-2-pentanone (5), the cat ketone mentioned earlier.

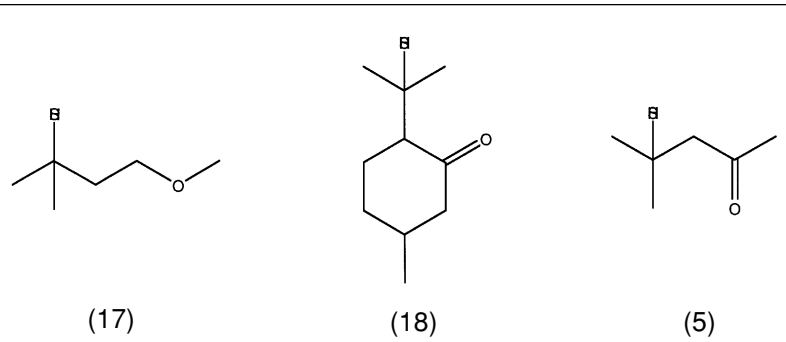
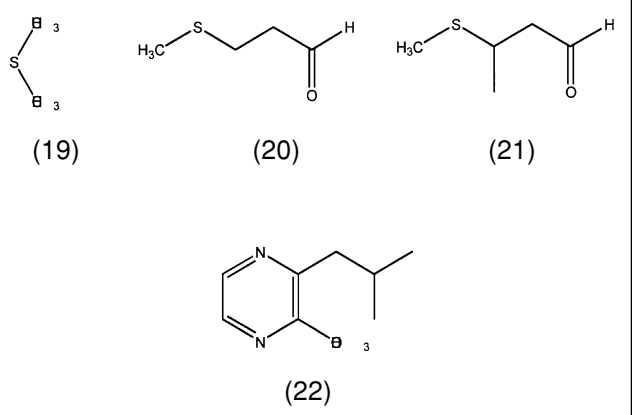


Figure 12. "Catty" mercaptans for blackcurrant

Vegetable

This is obviously rather a large category. A compound of major importance is the ubiquitous dimethyl sulphide (19) (DMS, methyl sulphide, odor threshold ~3 ppb). When pure, this has a clean, crisp, sweet corn odor. Some material on the market

lacks this note and has unpleasant, sulphurous, rotten-cabbage odors. GCMS on such material has shown the presence of dimethyl disulphide and methyl ethyl sulphide. Other powerful compounds for vegetable notes are 3-methylthiopropanal (20) (methional, odor threshold 0.2 ppb) and its homologue, 3-methylthiobutanal (21). On a more specific note, we should mention 2-isobutyl-3-methoxypyrazine (22), the bell pepper pyrazine. It is the main character-impact compound found in green or bell peppers, with a very low odor threshold of 0.002 ppb.

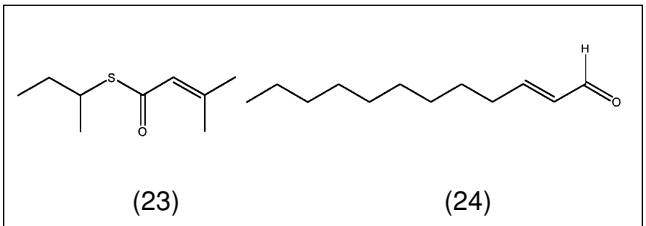


(19) (20) (21) (22)

Figure 13. Molecules for vegetable aromas

Spicy, Herbaceous

This is another very general category. Many essential oils used in flavors and fragrances are derived from herbs and spices, with a vast range of terpenoid components. From the perfumery sector, particular mention may be made of the thioester *sec*-butyl 3-methylbut-2-enthioate (23), a major contributor to the odor of galbanum oil. *Trans*-2-dodecenal (24), possessing a persistent fatty-citrus-herbaceous odor, is a character impact component of coriander.

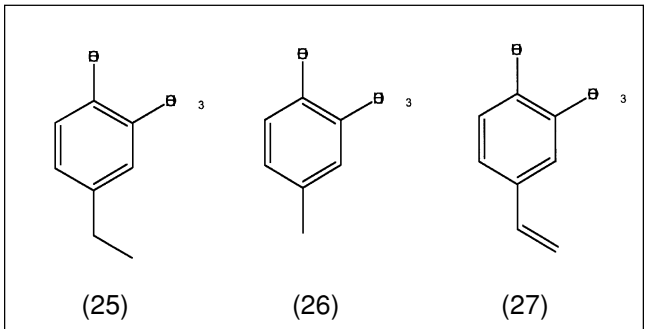


(23) (24)

Figure 14. "Spicy" aroma chemicals

Woody, Smoky

Guaiacols are very important in this area. 4-Ethyl- and 4-methylguaiacols, (25) and (26), have rather phenolic, medicinal odors with thresholds of 90 and 50 ppb, respectively. However, more important is 4-vinylguaiacol (27) (2-methoxy-4-vinylphenol, MVP). This has a spicy, clove-like smokiness particularly associated with smoked ham, and a low odor threshold of only three ppb. It is available in a natural form.

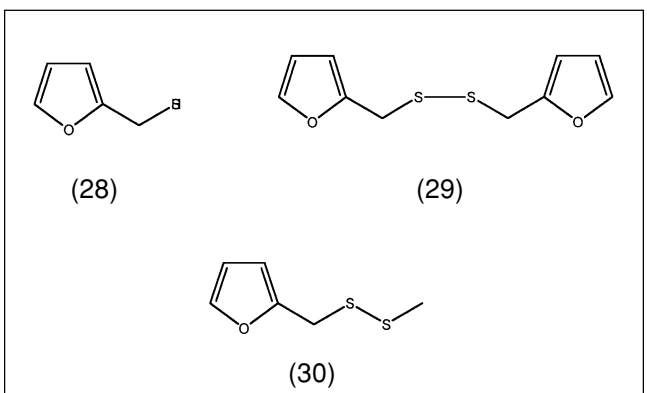


(25) (26) (27)

Figure 15. Guaiacols for smoke flavours

Roasted, Burnt

This sector is the first associated with cooked food; in this and the following sectors the high-impact chemicals are those produced in the Maillard reaction. For roasted and burnt notes, derivatives of furfuryl mercaptan (28) are paramount. The mercaptan itself, with an odor threshold of 0.005ppb, was the first high-impact aroma chemical to be identified. It exhibits one of the classic phenomena associated with high-impact chemicals, the change in the nature of the odor with concentration. At low concentrations (0.01-0.5ppb), the material has a roasted-coffee aroma, becoming burnt and sulphurous in the range 1-10ppb. The neat material has no coffee odor, only an unpleasant oily smell resembling gasoline. Derivatives of furfuryl mercaptan tend to be somewhat less odorous; the disulphide (29) (dithiodimethylenedifuran) is much less obnoxious, and the mixed disulphide furfuryl methyl disulphide (30) has a pleasant sweet coffee (mocha) aroma; the latter has an odor threshold of 0.04ppb.



(28) (29) (30)

Figure 16. Furfuryl mercaptan derivatives for coffee and roasted notes

Caramel, Nutty

These two classifications are at first sight rather disparate, but are again linked by the Maillard reaction. The key materials in this group are pyrazines and furans formed from sugars and amino-acids. The ubiquitous hydroxydimethylfuranone (31) has a sweet, 'cotton-candy' aroma and a low odor threshold of 0.04ppb. 2-Methyltetrahydrofuran-3-one (32) (coffee furanone) is less odorous, but has a very pleasant, sweet-caramel character. Nuttiness is more associated with pyrazines. While it is part of the character of almost all pyrazines, it is particularly associated with the higher pyrazines, such as methyldihydrocyclopentapyrazine (33) (maple lactone pyrazine), and 5,6,7,8-tetrahydroquinoxaline (34) (THQ). 2-Acetylpyrazine (35) is very reminiscent of popcorn; while its odor threshold is rather high at 62ppb, its persistent character earns it membership of the high-impact club.

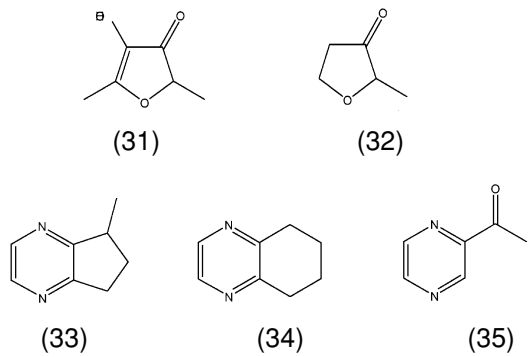


Figure 17. Molecules for "caramel" and "nutty" odours

Bouillon, HVP

The aroma chemical associated with this group is 4-methylthiazole-5-ethanol (36) (sulfurol). However, it has a reported odor threshold of over 10,000 ppb, making this compound scarcely a high-impact chemical. It is also a well-known phenomenon that apparently identical batches of sulfurol have different odors, with the desirable meaty note not always present. A possible identity of this impurity is 2-methyltetrahydrofuran-3-thiol (37). This is an intensely savory molecule, with brothy, casserole, boiled-meat notes and allium overtones. Its carbon, oxygen, sulphur framework is actually the same as that in sulphurol; it may be a degradation product or a by-product formed during the synthesis of sulphurol.

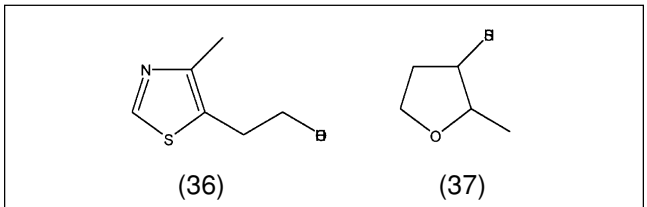


Figure 18. Savoury, bouillon compounds

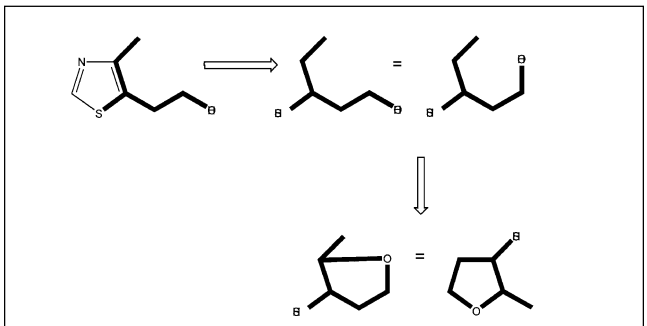


Figure 19. Structural relationship between sulphurol and 2-methyltetrahydrofuran-3-thiol

Meaty, Beefy

This is the province of 2-methylfuran-3-thiol (38) (MFT) and its derivatives. The thiol, it's disulphide (39), mixed disulphide (40) and thioether (41), have all been found in beef. The odor threshold of the disulphide has been reported as being as low as 2×10^{-5} ppb, but our experience of working with these materials indicates that this odor threshold may be due to residual thiol. MFT itself has an initially rather chemical odor, becoming more meaty on dilution. The disulphide has more recognizable character, a rich aged-beef, prime-rib aroma. The GRAS 19 thioether has more roasted character.

Other mercaptans have beef character. 3-Mercapto-2-butanone (42) and 3-mercapto-2-pentanone (43) are commonly found in beef Maillard reactions; the latter has an odor threshold of 0.7ppb.

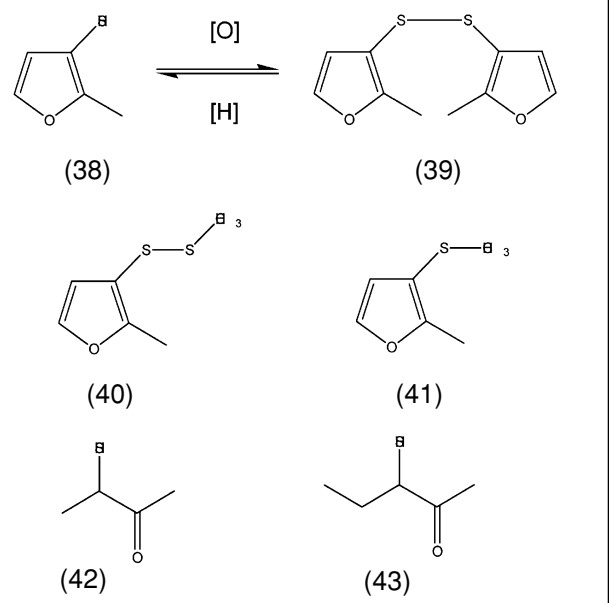


Figure 20. Sulphur compounds for beef

Other Meats

While 2-methyl-3-furanthiol is important in meats other than beef, in particular pork, other high-impact chemicals also occur. Mercaptopropanone dimer (44) has an intense chicken-broth odor, and the unsaturated aldehyde *trans*-2-*trans*-4-decadienal (45) is very reminiscent of chicken fat. The latter has been implicated in the following observation: while 2-methyl-3-furanthiol has been found in chicken, its intensely beefy disulphide is found in lower levels, if at all. It has been proposed that this is due to oxidants being scavenged by unsaturated aldehydes such as (45), and hence not being available for the oxidation of (38) to (39). 2,5-Dimethylfuranthiol (46) has been reported to be present in chicken, but other work has failed to confirm this. The author's experience with this material is that it is more prone to oxidation than 2-methyl-3-furanthiol. This may be preventing its detection; when a sample of neat (46) is left in the laboratory exposed to the air, it rapidly becomes cloudy due to droplets of water formed as the by-product of aerial oxidation. A compound with excellent pork character is pyrazineethanethiol (47). This has not yet been reported in nature, but this again may be an analytical quirk. Because vinylpyrazine (48) has been found in pork (and other meats), and pork is rich in sulphur compounds, including hydrogen sulphide, it is difficult to see how it can't be formed.

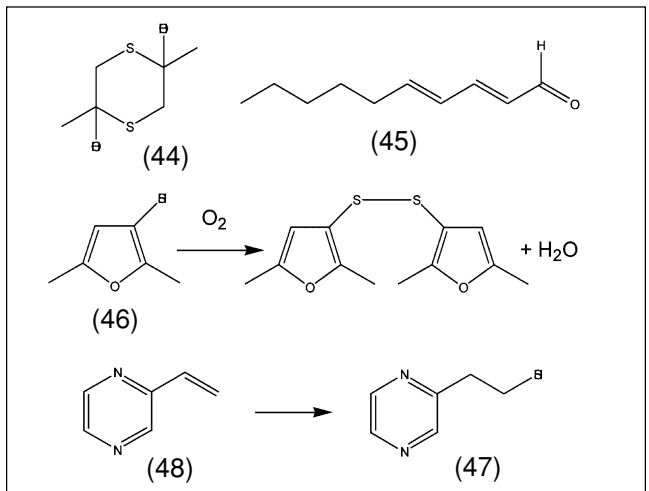


Figure 21. Pork chemistry

Lamb character is associated with two acids, 4-methyloctanoic and 4-methylnonanoic acid. While these have the higher odor thresholds of other carboxylic acids, their sharp-fatty aromas give them at least honorary membership in the high-impact club.

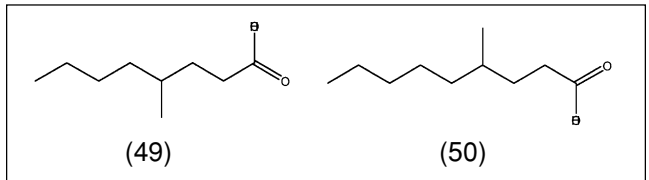


Figure 22. Lamb acids

Fatty, Rancid

This is not at first sight the most desirable of characters, but fattiness is a key character in foodstuffs (as those forced to eat low-fat or reduced-fat foodstuffs know to their cost), and a rancid odor is characteristic of cheese, especially hard and blue cheeses. Aldehydes have very fatty notes, in particular *trans*-2-nonenal (51) and *trans*-2-*trans*-4-decadienal (45). The latter is reminiscent of chicken fat and has an odor threshold of 0.07 ppb. A molecule with great potential in this area is 12-methyltridecanal (52). This tallowy material is found in beef fat and appears to originate from micro-organisms in the rumen of cattle.[4] It is absorbed by the gut as plasmalogens, and released only when the beef is heated over a long period (e.g. stewing). Briefly roasting the meat does not release this chemical. Hence, with the use of this material, we have the potential to create a boiled or stewed beef flavors well-differentiated from roasted or fried beef.

Cheesiness, desirable or otherwise, is often associated with acids, but these have quite high odor thresholds (e.g. valeric acid (53)), which has a nauseating sweaty-cheesiness at high concentration. However, it also has the mercifully high odor threshold of 3000 ppb. Such is the character of these that the impact is greater than the odor threshold might imply. Unsaturated acids such as *trans*-2-hexenoic acid (54) have more powerful, acrid odors. Several *trans*-2-enoic acids (*trans*-2-hept, oct- and non-enoic acid) were included on the GRAS 19 list. Simple thioesters such as methyl thiobutyrate (55) and methyl (2-methyl)thiobutyrate (56) also have an intense cheesy-sweet-fruity odor.

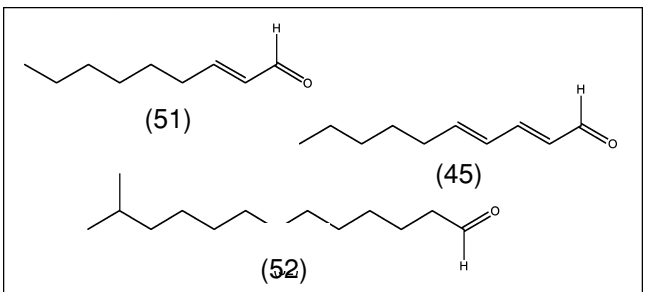


Figure 23. Fatty aldehydes and acids

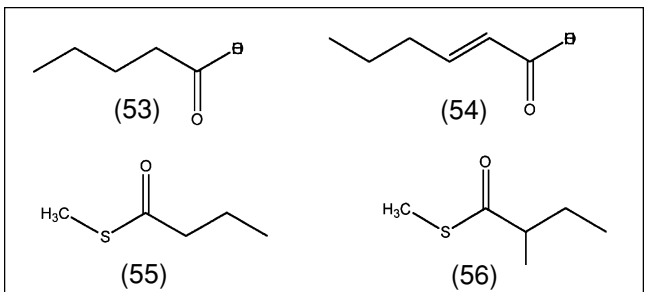
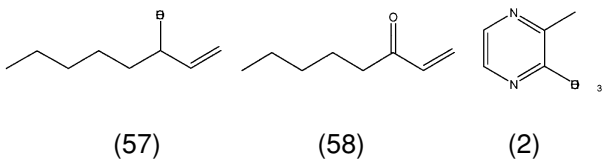


Figure 24. Molecules for cheesy, rancid notes

Mushroom, Earthy

Here we have a classical high-impact aroma chemical, 1-octen-3-ol (57), with an odor threshold of only one ppb, and very characteristic of mushroom. However, this is not the whole story, because the related 1-octen-3-one (58) has a threshold some two-hundred times lower, at only 0.05ppb. This has a very fresh wild-mushroom aroma. It has also been identified as a powerful odorant in materials as diverse as elder flower,[5] raspberry and chocolate. Earthiness is also associated with some pyrazines, especially 2-methyl-3-methoxypyrazine (2).



(57) (58) (2)

Figure 25. Compounds for mushroom and earthy aromas

Garlic

Garlic is rich in sulphur compounds, especially allyl compounds. Indeed, the commonly used term 'allyl' for prop-2-enyl derives from *allium sativum*, or garlic. The major component of garlic oil is allyl disulphide (8), with the mercaptan (59) and higher sulphides, such as the trisulphide (60), and mixed disulphides such as (61). Allyl methyl disulphide is particularly pungent, and has been detected at unexpectedly high concentrations in the breath of garlic eaters.

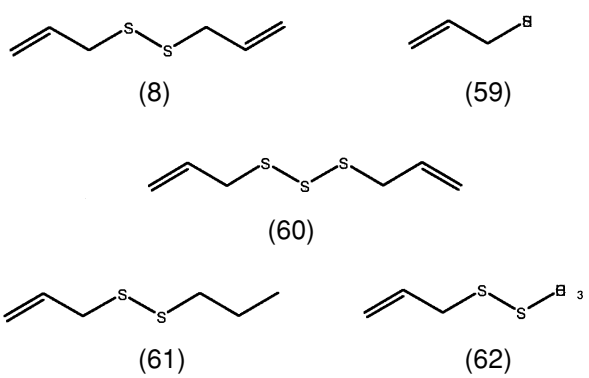


Figure 26. Aroma chemicals for garlic

Onion

As with garlic, onion is high in sulphur compounds, but mostly these are saturated compounds such as the methyl and propyl sulphides (63) – (67). These have less

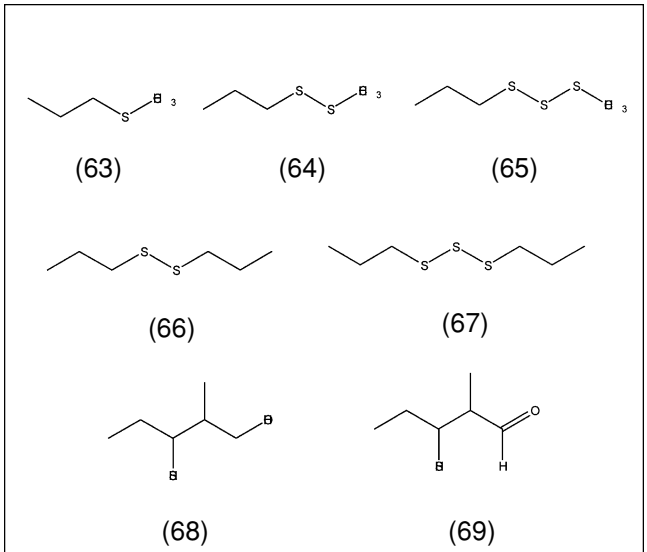


Figure 27. Old and new molecules from onion

harsh, 'sweeter' notes compared to the allyl compounds. Recently, two new highly odorous mercaptans were identified in onion6, 3-mercapto-2-methylpentan-1-ol (68), an onion- and leek-like material with an odor threshold of 0.15 ppb, and 3-mercapto-2-methylpentanal (69), more pungent and meaty, with an odor threshold of 0.95 ppb.

A Note on Associations

While the human nose is an unsophisticated instrument compared with that of some animals, it remains a more powerful organ than we sometimes realize. It appears to have a hotline to the brain; our ability to associate odors with people and with places is well known. The impact of some of the materials discussed above makes them very effective in this. Some of the associations that people have made when exposed to these materials are: greengrocers for 2-isobutylthiazole, presumably due to it's tomato notes; the cinema for 2-acetylpyrazine (via it's popcorn odor.); and fields at 6 am for 1-octen-3-one. Some twenty-five years ago, the commentator had a job starting early in the morning and would go out to pick mushrooms in an adjacent field. Some associations are very personal and depend on very individual circumstances. While most respondents commented on the blackcurrant, fruity aroma of 4-methoxy-2-methyl-2-butanethiol, a colleague with a six month old baby commented that it was reminiscent of wet diapers.

Conclusions

The demand for high-impact chemicals has been driven by the twin engines of increased consumer sophistication in the market for flavors and by improvements in the analytical techniques needed to identify character impact molecules. While much has already been done, the story is still being written with many chapters still to come. As the great 17th Century philosopher Rene Decartes might have said, "odorato ergo sum."

References

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

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