Products of Chemistry

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Chemistry Perfumes Your Daily Life

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One has to rely on chemists to find new aroma chemicals creating new, original notes. In perfumery the future lies primarily in the hands of the chemists.
Ernest Beaux, perfumer who created Chanel Nº 5

Until the middle of the 19th century, perfumes were reserved for the wealthiest strata of society. In contrast, the picture we see today is very different. We have come to accept and expect fragrances to be used not only in haute couture perfumes but in a wide range of consumer products from soaps and detergents to household cleaners, including bleaches. This dramatic change in the use of perfumes has come about with the development of synthetic organic chemistry. Until 100 years ago, perfumes were made of entirely natural materials, whereas the modern perfumery industry makes extensive use of synthetic chemicals: tonnage consumed runs into six figures. Today, it is estimated that out of the 3000 fragrance ingredients available to the perfumers, fewer than 5% come directly from natural sources.

This article gives a brief history of perfumery. The different methods available for extraction of natural perfume ingredients and the development of synthetic materials are introduced. The role of the perfumer in the modern fragrance industry is presented and illustrated by a number of ingredients of the main perfumery odor notes. The perspectives are endless and it all depends upon the chemists to invent molecules never synthesized or smelled before.

The Royal Society of Chemistry has recently published a general overview of the perfumery industry *(1).* General technical and industrial information, along with highlights in fragrance chemistry are summarized in the review.

A Brief History of Perfumery

The use of fragranced materials for all kinds of purposes goes back thousands of years. The word "perfume" comes from the Latin *per fume* "through smoke", reflecting one of the oldest uses of aromatic materials: the burning of incense and herbs as a religious offering *(2).*

The ancient Egyptians were particularly famous for their use of perfumes. They used fragrant materials in many forms: pressed, boiled, dried, powdered, macerated in fat, and even a simple form of distillation. The Crusades made Europeans more aware of perfumery. By the Middle Ages trade in spices from the East was important in Western Europe. The spices were used in perfumes, medicine, and food. During the 17th century, the guild of glove and perfume makers was established in France.

Alchemy gave way to chemistry in the 19th century. In 1882, Paul Parquet created *Fougère Royale* around an accord[1] composed of synthetic coumarin, oakmoss, geranium, and bergamot; with its launch by Houbigant, the new era commenced. In the following years, major achievements in the synthesis of fragrant compounds, as well as the discovery of new odorants, catalyzed the creation of many landmark perfumes. Vanillin, blended resins, animalic notes, and a floral accord with citrusy elements were the basis of *Shalimar,* created by Jacques Guerlain in 1925, and considered the prime example of an oriental fragrance. In 1917 in *Chypre*, François Coty already used the newly available quinolines,[2] especially *iso*-butyl and *iso*-propyl quinoline, though leathery Chypre fragrances like *Bandit* (Piguet, 1944) became fashionable only much later. *Angel* (Thierry Mugler) has been very successful since its 1992 launch. The blue, star-shaped bottle contains a fresh, sparkling oriental fragrance based on a powerful blend of patchouli enveloped by honey, vanilla, and caramel.

Production of Natural Perfume Ingredients

Traditionally, the discovery and development of new synthetic chemicals were based on the analysis of natural sources like plants (such as lavender and jasmine), fruits (for example, lemon and orange) and animals (including musk from the musk deer and ambergris from the sperm whale). The main components contributing to the smell of these natural sources are produced using both old and new methods falling into three basic classes: expression, distillation, and solvent extraction.

Expression is the simplest of the three techniques and is only used for the citrus oils, for example, lemon, orange, and bergamot. When an orange peel is pressed, a fine spray of orange oil is released, which is called an expressed oil.[3]

When steam distillation is used in the manufacture and extraction of essential oils, the plant material (herb, flower, wood, or spice) is placed in a still and steam is forced over the material. The hot steam helps to release the aromatic molecules from the plant material. Usually, the oils co-distil with the steam. They are then separated from the water by means of a Florentine flask, which separates them based on their differing densities (Figure 1).

Perfume materials obtained in this way are referred to as essential oils[4] *(3, 4).* Thus, for example, the oil obtained by steam distillation of lavender is known as the essential oil of lavender or lavender oil. The water that is separated in this process is discarded, in most cases, as it mainly contains waste products. Plant materials such as rose, lavender, or orange are different. The waters, in these cases, contain substantial quantities of odorant ingredients. They are marketed as "floral waters" and are used as perfume and flavor ingredients.

Different processes of extraction can also be used to obtain perfume ingredients: they are summarized in Figure 2. Ethanolic extraction is not used very much for plant materials because of the high proportion of water compared with

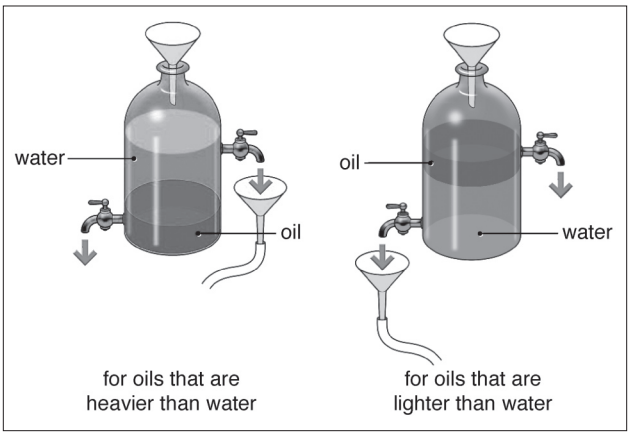

Figure 1. Florentine flasks, used to separate aqueous and oil phases.

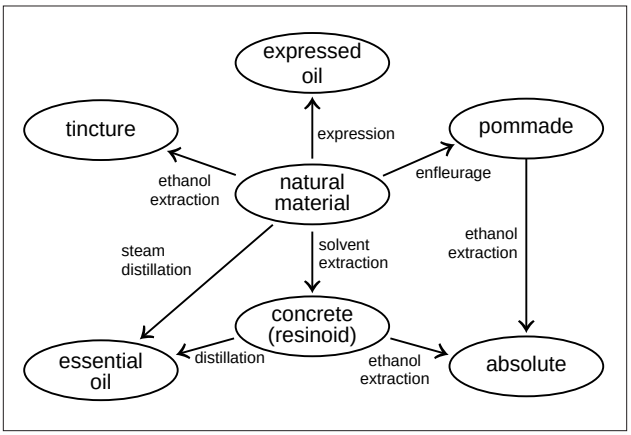

Figure 2. Extraction techniques: processes are written over the arrows and technical names for the products are circled.

oil in the plant (vanilla beans are an important exception). The extraction process is more important with materials such as civet or ambergris, which are secreted by animals. The sperm whale produces a triterpene known as ambreine in its intestinal tract. This compound is excreted into the sea and, on exposure to salt water, air, and sunlight, undergoes a complex series of degradative reactions that produce the material known as ambergris. This extremely valuable and rare waxy substance can be found floating in the sea or washed up on beaches. Extraction of it with ethanol produces the unique tincture of ambergris.

Enfleurage was used by ancient Egyptians to extract perfume ingredients from plant material and exudates. Its use continued up to the 20th century, but it is now of no commercial significance. In enfleurage, the natural material (petals of flowers for example) is laid on purified fat every day for a month. The perfume oils diffuse into the fat over time and then the fat is melted and the whole mixture filtered to remove solid matter. The odorous oils are extracted from the fat with alcohol. Once the ethanol is distilled off, the product is known as an absolute.[5] This technique presents a few disadvantages: the concentration of the odorous oil is low, fat is not the most pleasant material to handle, and it turns rancid after a number of uses.

The most important extraction technique nowadays is simple solvent extraction. Petroleum ether, acetone, hexane, and ethyl acetate, together with various combinations of these, are typical solvents used. Recently, there has been a great deal of interest in the use of carbon dioxide as an extraction solvent. The pressure required to liquefy carbon dioxide at ambient temperature is considerable and thus the necessary equipment is expensive. This is reflected in the cost of the oils produced, but carbon dioxide has the advantage that it is easily removed and produces very high quality oils without any concerns about residual solvent levels. The product of an extraction is called a concrete[6] or resinoid. It can be extracted with ethanol to yield an absolute, or distilled to give an essential oil. The oil can be deterpenated. The use of the word terpene may be misleading to the chemist since, in this instance, it refers specifically to monoterpenoid hydrocarbons. Hence, a terpeneless oil is one from which the hydrocarbons have been removed to leave only the oxygenated species and so increase the strength of its odor.

Essential oils and other extracts vary considerably in price and volume. Lavender, for example, is a relatively inexpensive oil, costing $22–$30 per kg, and 250–300 tons are used annually. Rose and jasmine are more expensive and are used in much smaller quantities. The total annual production of rose oil is 15–20 tons and it costs between $1500 and $4500 per kg, depending on quality. About 12 tons of jasmine extracts are produced annually at prices of up to $3000 per kg. Eucalyptus oil is one of the cheapest oils at $3–$4.5 per kg. The exact balance between volume and price depends on various factors such as ease of cultivation, ease of extraction, and usefulness. For example, eucalyptus trees grow well, the leaves are easy to harvest, trimmed trees grow back vigorously, the oil is easily distilled, and it is useful as a disinfectant as well as a camphoraceous fragrance ingredient. All of these factors combine to make it a high tonnage oil.

As mentioned previously, before the 20th century, perfumes were reserved for the wealthiest people. This is because perfumers relied on natural sources for their ingredients. Most of these ingredients were in limited supply and were expensive to produce. For example, it takes about seven million jasmine flowers to produce only one kg of oil and the flowers have to be picked by hand in the first few hours of the day when their oil content is at its highest. In view of the costs of cultivation and extraction, it is not surprising to find that jasmine oils cost in the region of $3000 per kg.

Some natural oils are much less expensive because of automated farming methods. For example, rows of lavender in a field can be cut almost to ground level and fed directly into a still pot carried on a tractor (Figure 3). The pot is then fitted under a field still and the oil extracted while the harvesting continues. The cost of lavender oil is thus tens, rather than thousands, of dollars per kilogram. Despite this, the modern perfumery industry would not be able to function as it does if it were to rely solely on natural ingredients.

From Natural to Synthetic Perfume Ingredients

The use of synthetic chemicals started to grow in the 19th century with the development of organic chemistry. When in 1921 "Mademoiselle" Chanel decided to launch her own perfume she asked Ernest Beaux to create a new and innovative fragrance for her. The perfumer used for the first

time aliphatic aldehydes to exhale the head notes of a composition rich in jasmine notes. Eighty years later *Chanel N°5* is still among the best selling fragrances. The success inspired other perfumery houses to experiment with synthetic materials and the modern age of perfumery was born.

Synthetic materials are cheaper to produce than natural materials. For example, a very nice Bulgarian rose is one hundred times more expensive to produce from the natural source than it is from synthetic materials. Nowadays, the fragrance represents only 3% of the price of a perfumed product for personal and household care, thus making perfume accessible to all. The organic chemists are now capable of making more robust molecules that will survive acidic, basic, and even oxidizing media. Thus, a wider range of consumer goods products can now be perfumed, where natural oils could not have been used because of degradation of their components, resulting in changes in odor and color. Many of the components of natural oils do not survive in products such as bleaches, laundry powders, and even soaps.

The discovery and application of synthetic fragrance materials towards the end of the 19th century and throughout the 20th century was therefore a momentous event in the history of the industry *(5)*. As techniques for isolation, characterization, and synthesis of organic chemicals improved, the search for new fragrance materials became more structured. In this, the fragrance industry follows the same path as the pharmaceutical industry and relies on the analysis of natural sources like plants, fruits, and animals. The first step is to identify the materials that are available from nature. Particularly in the case of flowers, fragrant volatiles are trapped directly by so-called "headspace" procedures. Using the nondestructive headspace trapping technique and light, portable sampling equipment (Figure 4), the fragrance of any flower, fruit, or other natural source can be collected from the field (or greenhouse) and returned to the laboratory for analysis without disturbing the plant.

Having identified the molecular structure of an odorant, the next task is to prepare an authentic sample. Synthesis serves as the final proof of the correct determination of the structure, but it also makes it possible to produce the material without relying on the natural sources. Synthetic compounds whose structures are the same as those of the natural material are referred as "nature identical". The next step is to prepare a range of analogues that are close in structure but not identical to the natural parent. There are two main reasons for this: firstly, materials that demonstrate improved performance over the natural ones may be discovered; and secondly, information about the structural requirements for the desired odor can often be found. This leads to the development of quantitative structure–activity relationships techniques *(6)*. This sequence can be illustrated by looking in detail at one odor area, for example, that of jasmine. If one looks at a GC trace of jasmine absolute, it is clear that the product is a complex mixture. However, the major components of the mixture (benzyl acetate, benzyl benzoate, phytol, etc.) are not the most important contributors to the characteristic odor of jasmine (Figure 5).

Of the 200 or so materials present in jasmine, the most important for the odor are jasmone and methyl jasmonate. The cis double bond in the side chain introduces extra stages and processing costs in the synthesis and therefore cheaper

Figure 3. Lavender is cultivated in rows in large fields.

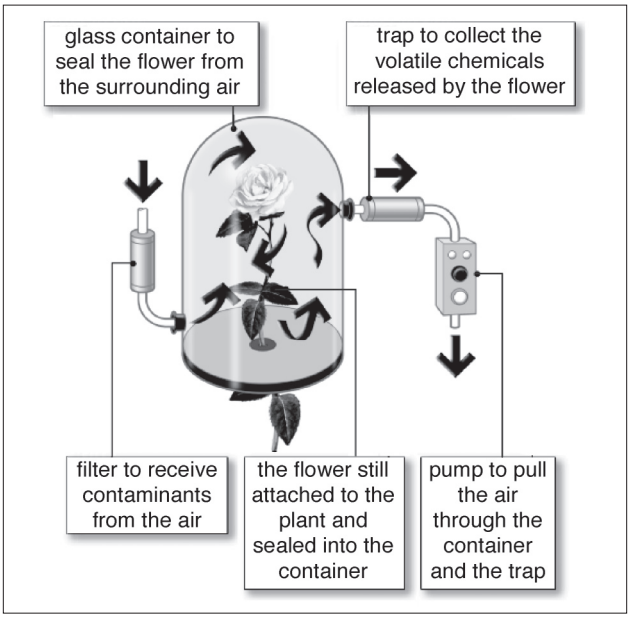

Figure 4. Headspace equipment. The volatile molecules released by the flower are swept into the trap in the stream of air. The air passes through the trap but the volatile molecules are retained. After several hours of sampling the trap is removed and taken back to the lab for analysis.

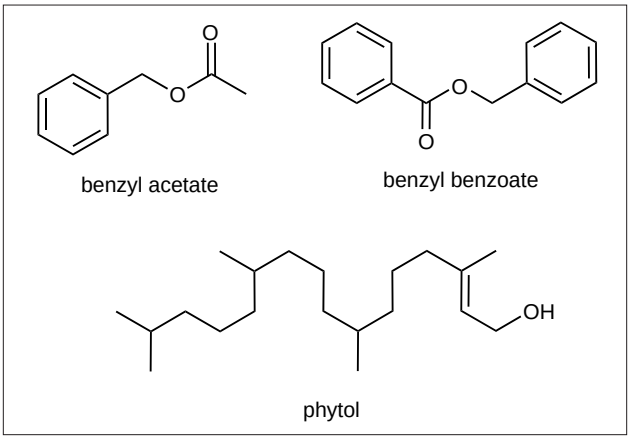

Figure 5. Major components of jasmine.

alternatives to jasmone are dihydrojasmone, jasmatone (Quest) and methyl dihydrojasmonate (Figure 6).

Creating a Perfume, the Prerogative of "Noses"

Perfumers have their own unique way of creating a fragrance. This always involves defining an atmosphere, which will then be translated into feelings either by reference to natural materials or by using synthetic compounds to create a harmonious composition. In all cases, perfumers speak in terms similar to those a composer would use when writing a piece of music. They speak of chords and discords; the shelf of materials they use as ingredients is referred to as an organ (Figure 7) and the individual ingredients are said to contribute notes to the overall composition.

These notes are classified into head notes,[7] heart notes,[8] and base notes.[9] The head notes, often the more volatile materials in the composition, give the initial impact; the heart notes form the bulk of the perfume; and the base notes are the least volatile components, which fix the more volatile elements. When creating a perfume, it is important to get the correct balance of head, heart, and base notes. The components must work together to form a balanced overall composition. The base notes should hold the head notes back so that the volatile elements are not lost immediately, but persist as long as the total perfume lasts. The head notes of natural perfumes are derived from, for example, citrus oils, herbs such as rosemary and lavender, and green notes, which are those associated with crushed foliage. Synthetic materials that can be used to give head notes could be aliphatic aldehydes and monoterpene esters. Aldehydes are very useful head notes materials in fine fragrances, but their use in more functional products is restricted by their instability in the presence of oxidizing agents and at extremes of pH.

The heart notes of perfumes were originally derived from flower oils such as rose, lily, and violet. Today, with all the affordable violet-smelling toilet soaps available, one easily forgets that violet flower oil was the most expensive of all essential oils—at the times when it was still economic to be produced. For the production of one kilogram of this oil 33,000 kg of violet blossoms were needed. It is worth mentioning that violet leaf is still used, but the odor is green, quite unlike the flower character. The ionones were first discovered in 1893 and their violet odor revolutionized perfumery; today almost every perfume includes them, since they blend well with basically all other perfumery materials. The damascones are a group of materials related to the ionones, but in which the enone unit is transposed (Figure 8). They are components of rose oils and have very intense fruity–floral odors. Rose notes are now available through inexpensive synthetics such as geraniol, citronellol, and 2-phenylethanol (Figure 9).

The classical base notes of perfumes fall into the wood, musk, amber, and balsam areas. Woody and amber materials

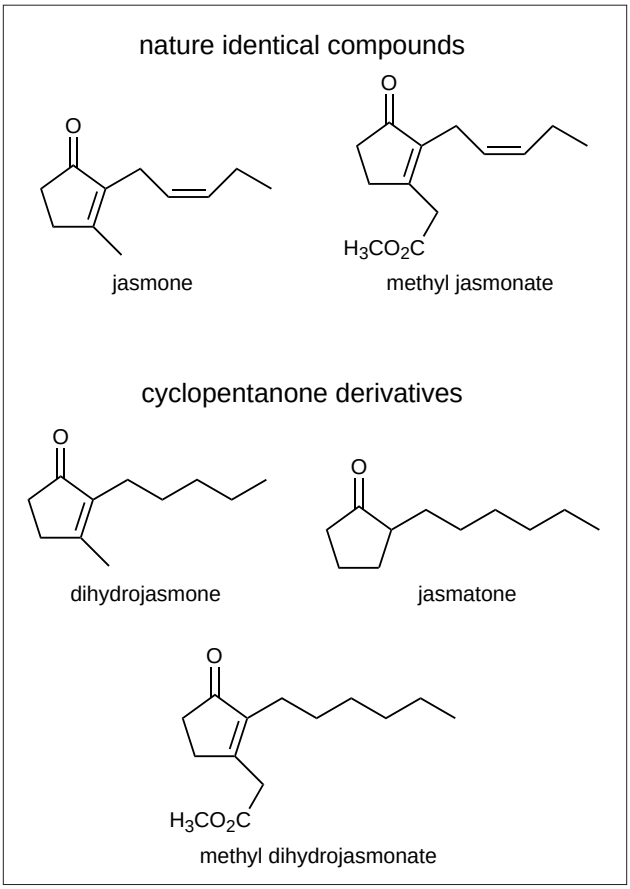

Figure 6. Components with jasmine odor.

Figure 7. Perfumer's organ.

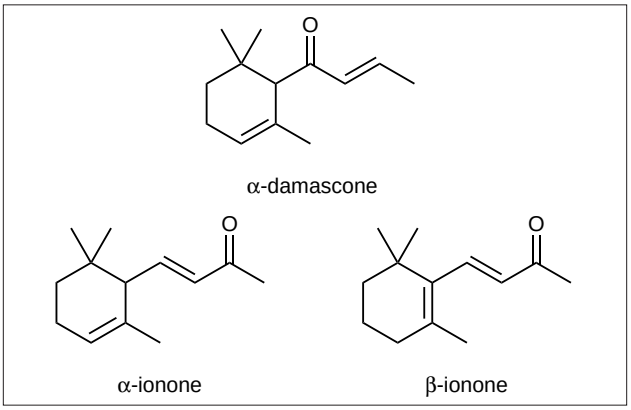

Figure 8. Floral oils components.

generally have complex sesquiterpene-like structures in which precise stereochemistry is frequently important in determining odor type and quality. This segment of the perfumer's organ is thus dominated, at present, by semisynthetic materials obtained by the modification of readily available natural precursors. Some purely synthetic materials are becoming established as woody and amber chemicals and these may supersede the current generation of semisynthetic materials. Musks were originally obtained from various animal (Figure 10) and plant sources such as musk deer (*Moschus moschiferus,* which inhabits the Himalayas from Afghanistan to China), civet cat and ambrette seed oil (distilled from seeds of *Hibiscus abelmoschus*).

Muscone and civetone are the most important odor components of musk and civet respectively (Figure 11). Ambrettolide is a plant product, occurring in the seeds of the ambrette plant, which is cultivated in Madagascar, the Seychelles, Colombia, and Ecuador. In tonnage terms, cyclopentadecanolide is one of the largest of macrocyclic musks.

In 1888, Albert Baur was searching for new types of explosives when he noticed that the product of the Friedel–Crafts reaction of trinitrotoluene (TNT) with *tert*-butyl halides emanated a pleasant musky smell. 2-*tert*-Butyl-4-methyl-1,3,5-trinitrobenzene was an immediate commercial success and became known as "musk Baur". In 1894, Baur discovered and developed musk ketone, which was among the most used perfumery ingredients until the mid-1960s. Phantolide™ (PFW) was first invented in 1951 and introduced to the market a year later, even without knowledge of the correct structure, which was reflected in its name. Phantolide™ (PFW) performs better in detergents and washing powders than musk ketone, so it became the new lead

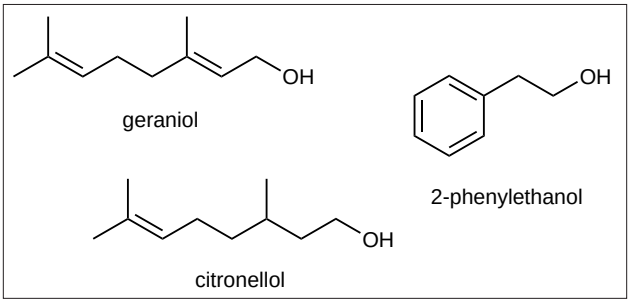

Figure 9. Compounds with rose odor.

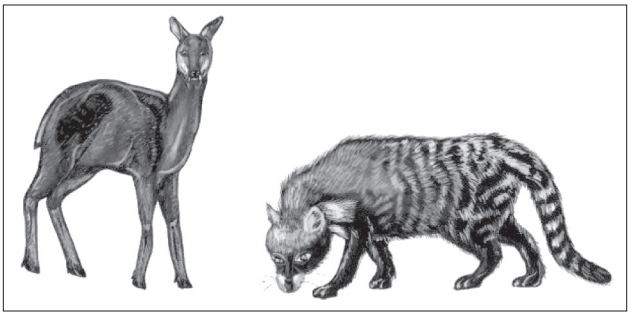

Figure 10. Musk deer and civet cat used to be a source of musks.

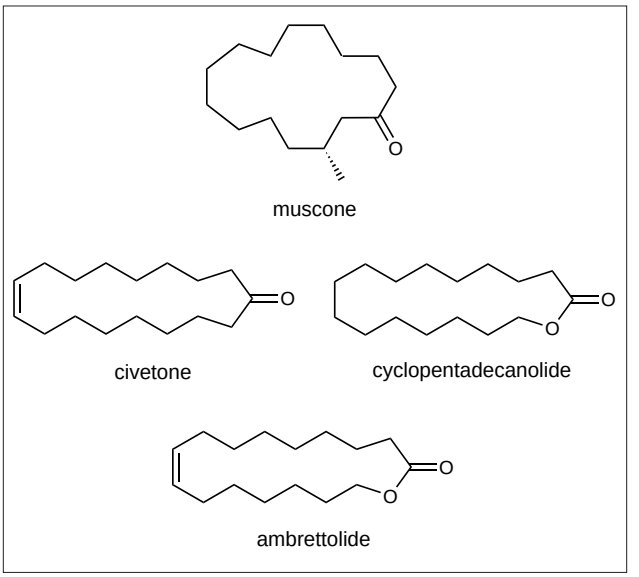

Figure 11. Examples of macrocyclic musks.

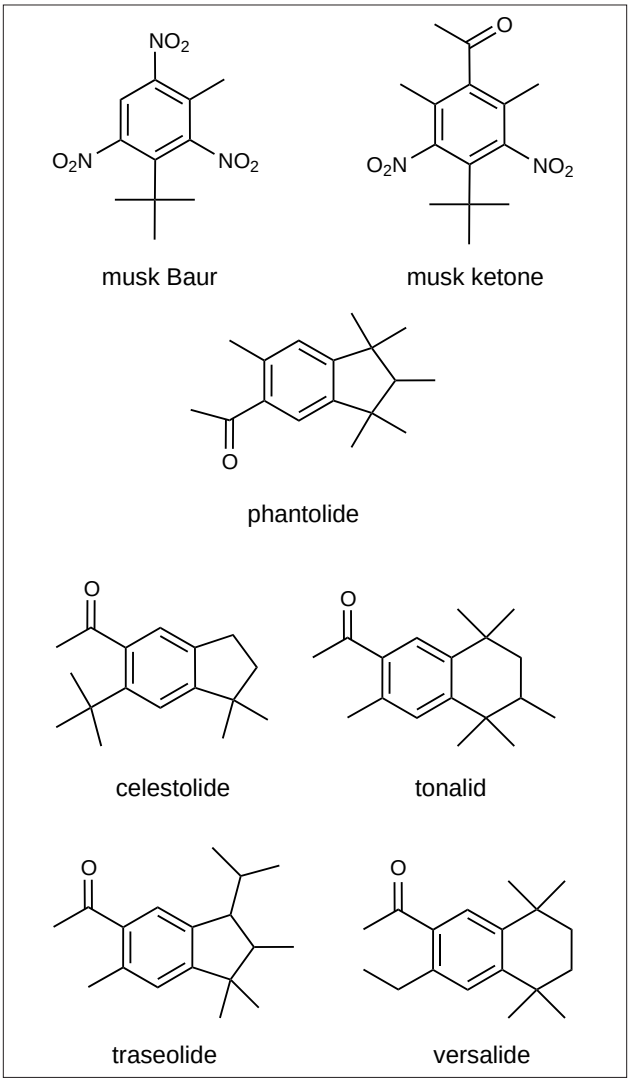

Figure 12. The musk family.

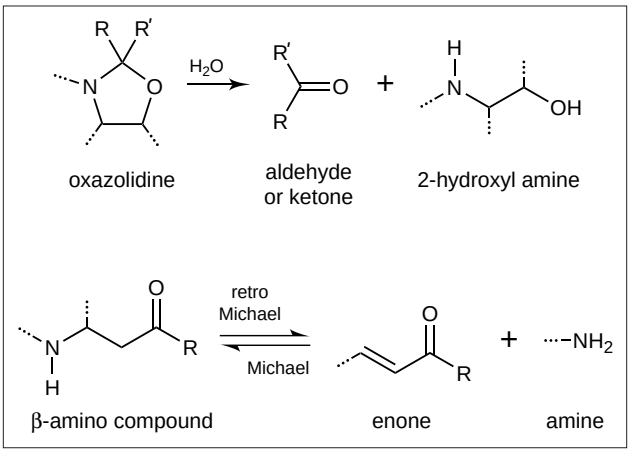

Figure 13. Examples of new fragrance-delivery systems.

structure for musk odorants, and in the following years numerous derivatives were synthesized in the laboratories of the flavor and fragrance industry. Some prominent introductions include Celestolide (IFF), Tonalid (PFW), Traseolide (Quest) and Versalide (Givaudan) (Figure 12).

Future Directions

Many substantive (long-lasting) odorants are known, but a great number of them are too volatile to be perceived more than a few hours after their application. This is the reason why more efficient and effective fragrance-delivery systems, especially for laundry-care products, are intensely sought.

The use of "prodrugs", an inactive drug derivative that is converted in the body into its active form, is a well-established technology to improve the oral bioavailability or the penetration across biological membranes. This concept, widely used by the pharmaceutical industry, was introduced to functional perfumery by Firmenich in the mid-1990s *(7)*. Firmenich and co-workers made use of lipases that are employed in most detergents to degrade fatty stains to hydrolyse esters of fragrant alcohols. This led to the development of a wide range of precursors that are cleaved by hydrolysis during the laundry process to generate in situ fragrance materials, for example, aldehydes and ketones derived from oxazolidines and ionones and damascones from β-amino compounds (Figure 13) have been developed by Procter & Gamble *(8)*. Fragrance chemists are still looking for new systems with improved stability and release properties.

Though fragrances are incorporated into functional products to impart a pleasant odor, some odorants also possess antimicrobial properties or other secondary benefits, for instance, insect repellent activity. Fragrance ingredients such as eugenol, carvacrol, and thymol are known to also have bactericidal activity. However, their use is limited because at a certain concentration their odor becomes unpleasant. In order to overcome this problem, fragrance chemists have been looking for compounds that not only exhibit pleasant odor characteristics, even in higher concentrations, but also possess good antibacterial activity.

The search for molecules with new and innovative odor characteristics is, however, still the main focus of the industry and in almost every odor note there are still plenty of new odorants to be discovered; stronger in odor, more transparent or more easy to overdose, exhibiting better performance in special functional products, or possessing unique combinations of different odor tonalities. There are endless possibilities and variations. Organic chemists will always be needed to create new and ever-improving fragrance ingredients; remember what Ernest Beaux said, "In perfumery the future lies primarily in the hands of the chemists".

Acknowledgments

I would like to thank Charles Sell, Karen Bridge, and Sjack Elings for their helpful comments and critical review.

Notes

1. An accord is a blend of perfume ingredients balanced in odor intensity and having a pleasing effect. It is generally used as a perfume building block.
2. Quinolines are formed by the fusion of a benzene ring with a pyridine ring, with the nitrogen atom next to the benzene ring.
3. An expressed oil is a cold pressed oil in which the oil contained in the outer skin of a citrus fruit is released by rasping or compression of the citrus fruit.
4. Essential oils are steam-distilled oil obtained from plant material.
5. An absolute is the alcoholic extraction of the concrete.
6. The hydrocarbon extraction of the plant material is termed concrete or resinoid.
7. Head notes are the most volatile components of a perfume. They generally last a matter of minutes on the skin and are also referred to as top notes.
8. Heart notes are the heart of a perfume, the main theme. They last for a few hours on the skin and are also referred to as middle notes.
9. Base notes are the substantive part of a perfume comprising the less volatile components of the fragrance composition. They are also referred to as end notes.

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