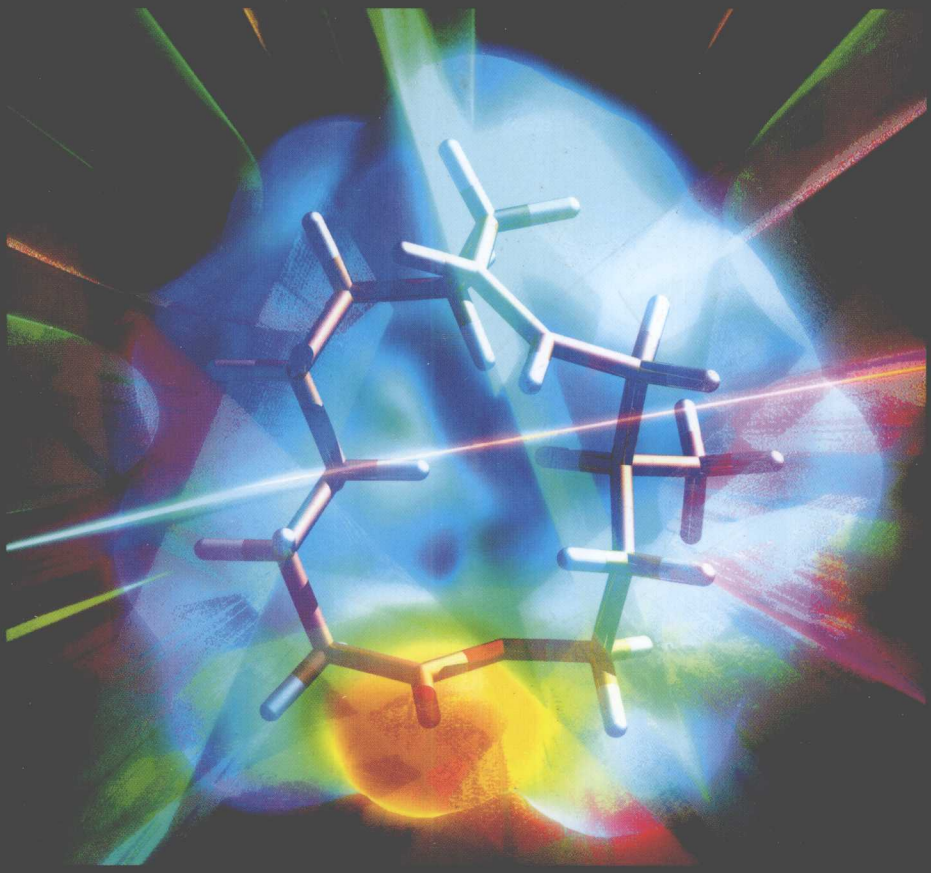
Chemistry and Technology of Flavors and Fragrances



Edited by
David J. Rowe

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Preface

The aim of this book, as I expressed in a letter to the contributors, is to have a work that could be given to a new chemist or technologist joining the industry with the statement 'read this and you'll know what this industry is about'. Several contributors corrected this to '... a little of what this industry is about!' Such comments, and those of the anonymous referees whose remarks were passed on to me, helped to crystallise my thinking on the concepts behind the book. One referee referred to Aroma Chemicals as the core of the book; this is true, and as an organic chemist I make no apologies for this. In this context, the structure could be described as Part I: The origins and identification of the important aroma chemicals of nature, Part II: The chemistry and synthesis of aroma chemicals and Part III: The applications of aroma chemicals. This 'chemical' approach is also aimed at demystifying the industry to a neophyte; whilst no-one would wish to deny the essential creativity of perfumers and flavourists, it is also important to realise that, to quote Steve Herman in his Chapter 'Applications II: Fragrance', '... the fundamental key to dealing with the technical aspects of fragrance is to treat them as mixtures of chemicals'.

The content of the book, in general terms, was my decision, and hence any complaints should be addressed to me rather than, the authors! A book that would please everyone would run into many volumes, and it was necessary to be focused, even at the risk of omitting topics that others might see as crucial. The omission of essential oils was a conscious decision, as these have been extensively covered elsewhere; the exception is as part of the chapter on natural aroma chemicals where these are isolated from essential oils. With this in mind, each author was asked to ensure that the key essentials, as they saw it, were covered. However, I suggested, where appropriate, a section of the chapter could be devoted to an area, that, whilst firmly within the remit of the chapter, was of especial interest to the author; a 'hot topic', if you will. Beyond that, the choice of the material within a chapter was at the discretion of the authors. Ultimately, however, an editor is responsible for his or her book, and hence the sins of omission and commission are mine, and mine alone.

There are those within the industry who treat the two Fs of the Flavour and Fragrance industry as substantially different topics. Obviously there *are* differences; the specific functions of the perfumer and the flavourist are different, and of course, their palettes, as it were, are different. The markets for a musky flavour or a garlic perfume are somewhat limited! However, both areas ultimately have the same aim; to use aroma chemicals, whether as naturally occurring mixtures or as individual compounds, to create an effect

that our chemical senses, taste and smell, find desirable. In this context, the aim of this book is to overcome The Great Divide, or at worst, to ignore it!

Thanks go to the many people with whom I have worked over the past dozen years. Chemistry is a 'social' discipline, and I have learned from many people; I hope that, in a way, this book is giving something back. A particular mention goes to Mark Dewis, Simon Jameson, John Heffernan, Kevin Auty, Peter Setchell, Lee Morgan (the co-designer of 'The devil's flavour wheel'), Gareth Jones, John Johnson, Tracy Brown, Peter Cannon, Rob Gregory, and others who I have now offended by not mentioning, and finally to Duncan Mullis, who first employed me in the Flavour and Fragrance Industry; in a way, Duncan, this book is your fault!

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Chapter 1
Introduction

David J. Rowe

> The earliest recognisable chemists were women, the perfume-makers of Babylon, who used the earliest known stills to produce their wares. The first individual chemist known to history was "Tapputi, the perfume-maker", who was mentioned on a cuneiform tablet from the second millennium BCE in Mesopotamia
>
> Paul Strathern, *Mendeleev's Dream*, Penguin Books, London, UK, 2001

Thus, it is not an exaggeration to say that the roots of modern chemistry lie in the flavour and fragrance industry! As an area of the modern chemical industry, it is low profile compared with the 'big boys' of pharmaceuticals and petrochemicals, the areas that the 'general public' recognise as industrial chemistry. Yet it is a multi-billion dollar, global industry that impacts on everyone's life in the developed world.

1.1 History: in the beginning

In a sense the origins of the industry lie in prehistory. At some point our ancestors found there was pleasure in the aroma of a flower, and that mixing certain herbs with food added relish; when this took place will never be known, but it could be said that at that point we became truly human. Certainly our earliest ancestors had uses for aromatic plants; since burial sites have been well preserved, we know that they used aromatic plants as votive offerings to the gods and the supernatural world. By the time that writing developed in the fertile crescent of the Indus, Nile and Tigris valleys, we have many references to the use of herbs and spices. A crucial point is that the uses of flavourings and fragrances, in whatever form, are a feature of a society where at least one social stratum has the 'disposable income' to obtain them; however important they may be to the quality of life, flavours and perfumes are not (despite the efforts of marketing departments to convince us to the contrary) essential to the continuance of life. Thus throughout history we can see the uses of flavours or fragrances as reflecting either the success of a society, or its decadence, depending on the prejudices of the individual. David Pybus [1] and Paul Jose Teisseire [2] have written excellent and amusing accounts of the development of the uses of fragrance, and the interested reader is directed there for more detailed accounts.

1.2 The classical world

The classical world of ancient Greece and Rome was familiar with many oils, spices and perfumes. Some of the key techniques common to the flavour and fragrance industry and the wider chemical industry had been developed, in particular distillation and the

concept of extraction. The key concept of separation of materials was introduced to the world. Philosophers such as Aristotle were able to introduce some of the ideas which we might recognise today as science. With the rise of the Roman Empire, the resources of the Mediterranean world became available to the privileged few who could live in perfumed luxury surrounded by slaves. Spices from across the empire and beyond were used to flavour food, both for their inherent flavour and to mask the somewhat dubious taste of meat in a pre-refrigeration age. Pliny the Elder wrote a treatise on 'Natural history' which included observations on aromatic plants and their uses. However, throughout this period there was another feature we frequently see in relation to the uses of flavours and fragrance; for some, such as Pliny, they are an 'honest pleasure', whereas for others they represent decadence and vanity. Those in the latter camp were presumably tutting and saying 'told you so' when, as David Pybus [1] puts it, 'Rome succumbed to the barbarian hordes, the lights went out in all the incense burners in Europe, and the rose petals went out with the bathwater'.

1.3 The mediaeval world

The fall of the Roman Empire in the West ushered in the period commonly known as Western Europe's Dark Ages. The 'one world' of the Roman Empire, stretching from Northern England to the Arabian Peninsula, was broken, and instead we had a period of what might be termed 'localisation', in an analogy to today's globalisation. Petty fiefdoms arose in what were earlier merely provinces of the empire. Nowhere is this clearer than in England, where seven kingdoms, the Heptarchy, arose in what was merely part of a single minor province of the Roman Empire. The end result of this was the loss of raw materials and eventually, the knowledge of what to do with them. The foundations of chemistry were lost into the mysticism of alchemy. Some techniques remained in use, especially distillation, but this also became a mystical affair. The classical world used distillation to refine a crude material into a more valuable one, such as an aromatic plant into an essential oil, a basic concept that we are still familiar with today. In the mediaeval mind this became the search for the Philosopher's Stone, to refine base metal into gold or to confer eternal life. Herbs were still used for flavours, but the breakdown of transport meant that these were restricted to what could be grown in local gardens, the 'parsley, sage, rosemary and thyme' of the English folk song. In parallel with this, the powerful mediaeval church frowned on the use of fragrance as earthly vanity. Cleanliness was not next to godliness, rather 'insanitary' was next to 'holy', from the hovels of the early monks to Thomas Beckett's lice-infested hair shirt. Of course, official disapproval has never prevented those with the finances from doing as they will. Spices and oils still made their way into darkened Europe from the Orient and the Arab world. The latter, in particular, kept some of the flame of the classical world burning, which is reflected in the number of words whose origin is Arabic, including alcohol and chemistry itself. The great trading cities of Venice and Genoa controlled much of this trade, with the Silk Road to the East carrying precious spices and oils via Constantinople, the capital of Byzantium, the Eastern Roman Empire. But disapproval there still was; one of the

many things held against England's King John, a man held to be so awful that no other monarch has taken the name in 800 years, was his insufferable vanity – he was said to bathe every month, whether he needed to or not.

1.4 From the Renaissance to the Enlightment

In 1453 Constantinople fell to the Ottoman Turks. The end of the Byzantine Roman Empire, which for a millenium had been the great junction between East and West, had a major impact on trade routes to India and the Orient, the source of the most prized spices. This drove adventurers, especially from the great trading cities of Genoa and Venice, to seek alternative routes to the East. In brief, flavours and fragrances were a major driving force in the European discovery of the Americas (these had been discovered before, of course, by the people who actually lived there, but as they didn't wear trousers, they didn't count). This exposure to new cultures, together with the rediscovery of classical science, often via Arabic texts, led to a new intellectual flowering in Europe. The concepts of science, based on the principles of observation and measurement, were laid down by Galileo. In this context, perhaps the single most important development for the flavour and fragrance industry was the development of the thermometer by Celsius and Fahrenheit. The essentials of modern chemistry were established by the studies of Lavoiser, Davy, Dalton, Priestly, Scheele and others, and the mystical systems the alchemists left behind. It is difficult to overestimate the importance of this change. Though the early chemical laboratory would have looked like an alchemist's workshop with its pots, pans and alembics, chemistry was based on causality; mixing sulfuric acid with sodium chloride always generates hydrogen chloride (or, to use the terminology of the day, mixing oil of vitriol with salt always generates muriatic acid gas) – irrespective of what the operator is wearing, has eaten or has chanted during the process. The difference between alchemy and chemistry is that between astrology and astronomy. Of course, progress is rarely straightforward (witness the number of astrologers in the world); Sir Isaac Newton (1642–1727) believed that his most important work was not on gravity and the calculus but rather his alchemical studies, and in 1794 Antoine Lavoisier found that the Revolution had no need of learned men.

1.5 The industrial age

From the early nineteenth century developments in chemistry, mostly in Great Britain and Germany, began to create the flavour and fragrance industry as we know it. Purification of natural materials, especially essential oils, led to the identification of aroma-active materials such as benzaldehyde, cinnamaldehyde and vanillin. The increased knowledge of organic chemistry, beginning perhaps with the discovery of Wöhler that 'inorganic' and 'organic' materials could be interconverted (i.e. that there was no 'vital force' responsible for creating the complexities of organic materials), meant that these isolated materials could now be synthesised in the laboratory. The great cycle of the chemical industry – identification, laboratory synthesis, large-scale synthesis and commercialisation with falling costs and prices – had now begun. At this time the events and discoveries of importance come so thick and fast that the best way to show them is the timeline (Figure 1.1).

1820 Foundation of Roure by Claude Roure in Grasse under the company name Roure Bertrand
1834 Isolation of cinnamaldehyde
1837 Isolation of benzaldehyde
1852 Cinnamaldehyde synthesised
1852 W.J. Bush established
1858 Microbial resolution of (−)-tartaric acid from a racemic mixture using *Penicillin glaucum*
1859 Synthesis of methyl salicylate
1859 Vanillin purified
1860 Foundation of Fritzsche Brothers
1868 Synthesis of coumarin
1870 Foundation of Haarmann & Reimer
1871 Structure of vanillin determined
1872 Vanillin synthesised
1873 Roure wins its first gold medal at the Vienna International Exposition
1878 Synthesis of cinnamic acid
1879 Saccharin is discovered
1880 Lactic acid, the first known optically active compound to be produced by industrial fermentation
1883 Synthesis of phenylacetaldehdye
1884 Synthesis of cinnamaldehdye
1886 *Bacterium zylinum* identified as cause of vinegar production
1886 Nitromusks discovered
1887 Chirality and taste; enantiomers of asparigine found to have different tastes
1888 First determination of an odour threshold. Ethyl mercaptan by Fischer & Penzoldt
1889 Polak & Schwarz's founded
1889 'Jicky' by Houbigant
1891 Synthesis of the ionones
1892 Allyl disulfide identified in garlic
1894 Fischer's 'Lock & Key' Principle
1896 Foundation of Givaudan by Leon and Xavier Givaudan in Zurich
1898 Foundation of Chuit & Naef by Philippe Chuit & Martin Naef in Geneva
1900 Saccharin first used as a sweetener
1908 MSG identified
1912 Maillard reaction described
1913 Foundation of Fries & Fries in Cincinnati, Ohio by Robert G. Fries and his brother George
1914 Foundation of Polak's Frutal Works (PFW) in the Netherlands by Joseph, Jacob and Henri Polak
1918 A.L. van Ameringen formed
1919 Dragoco founded by Carl-Wilhelm Gerberding
1920 Ruzicka introduces the concept of odourant design
1921 'Chanel No. 5' by Coco Chanel
1922 Takasago founded
1926 Furfuryl mercaptan identified in coffee
1931 Amadori products recognised in the Maillard reaction
1933 Naef, Chuit et Cie. becomes Firmenich & Cie
1937 Non-nutritive sweetener cyclamate discovered
1939 Ruzicka wins Nobel Prize for chemistry
1946 Pauling theorises on the influence on odour of molecular shape and size
1950 Polycyclic musks introduced
1952 GC introduced by James & Martin
1952 Hodge scheme for the Maillard reaction
1954 Roure opens its perfumery school in Grasse
1959 International Flavors & Fragrances formed from van Ameringen-Haebler inc. and Polak & Schwarz NV
1964 GC-Olfactometry introduced
1965 BBA formed from WJ Bush & Co Limited, A. Boake Roberts & Co Limited and Stafford Allen & Sons Limited
1968 Amoore's description of the molecular basis of odour
1969 Cyclamate removed from GRAS list by FDA
1969 Hydroxydimethylfuranone identified in cooked beef
1970 Cyclamate banned in the USA
1970 Damascones identified in rose oil
1972 Sacharin removed from GRAS list by FDA
1981 Aspartame gains FDA approval
1982 Grapefruit mercaptan identified
1989 Solid phase micro-extraction (SPME) introduced
1991 Merger of Givaudan and Roure
1998 Sucralose approved by FDA
2000 Spin off of Givaudan Roure from Roche as Givaudan with a listing on the Swiss Stock Exchange
2001 Bush Boake Allen acquired by IFF

Figure 1.1 Discoveries and foundations from the beginning of the Industrial Age to today.

1.6 The post-war world

Things are different today, I hear every mother say,
Cooking fresh food for her husband's just a drag
So she buys an instant cake and she burns a frozen steak...
The Rolling Stones, *Mother's Little Helper*, 1966

Since the end of Second World War the flavour and fragrance industry has expanded greatly. Several interlocking factors have caused this.

1.6.1 Technical factors

1.6.1.1 Analytical

Development of analytical techniques such as Fourier transform nuclear magnetic resonance spectroscopy (NMR), infra-red spectroscopy and, in particular, gas chromatography (GC) and mass spectrometry (MS) has enabled the key odorants of fragrant flowers and foodstuffs to be identified at ever lower levels; the so-called hyphenated techniques of GC-MS and GC-olfactometry, in conjunction with 'trapping' methods such as GC trapping and solid phase microextraction (SPME), means that we can now identify materials present well below the part per billion level and at quantities down to the picogram level. This means that the trace components, which are often the character impact chemicals of a material, can now be identified. Perhaps someone should calculate how many cows would have to be distilled to prepare sufficient 2-methyl-3-furanthiol, the character impact chemical in roast beef, to be identified by the classical techniques of the nineteenth century.

1.6.1.2 Synthetic

The increase in the 'armoury' of synthetic techniques available to organic chemists has made available to the perfumer or flavourist an enormous number of materials. In particular, it has enabled materials of ever-greater complexity to be available to the applications specialists at a price that, even if the cost per kilo is high, still adds value to the end formulation. The cycle of identifying a potentially valuable material, synthesising it in the laboratory and then developing a commercially viable process (at gradually decreasing cost and sales price) has gone on since the nineteenth century, but the cycle time in today's commercial culture is much lesser.

1.6.2 Social factors

After the end of Second World War, and especially from the 1960s onwards, the developed world, especially North America, western Europe and Japan, has seen a major increase in the standard of living. This has given the 'disposable income' that we have seen is a key factor in the uses of flavours and fragrances. On top of this these regions have seen an unprecedented increase in the social and geographical mobility of their populations.