Tobacco Constituents— Their Importance in Flavor and Fragrance Chemistry

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Tobacco is a common household word throughout all parts of the world. However, very few people are aware of the fact that the word "tobacco" was derived not from English or Latin but from the Spanish word "tubo" for the tube used by American Indians for inhaling the smoke. It was American Indians who first cultivated tobacco, and the substance was introduced into Europe by Christopher Columbus on his return from the New World.

The botanical name for tobacco, "Nicotiana", comes not from the Latin but from the name, Jean Nicot, the 16th century French ambassador to Lisbon, who brought tobacco seeds back to the French Queen, Catherine de Medici. From the French court, tobacco was carried to the farthest reaches of the known world by Portuguese and Spanish sailors.

There is a common saying among people of the developing countries that the first penny earned by a person is spent for bread and butter to satisfy his hunger; the second penny is for soap and detergent to cleanse his body; the third penny, when available, is used to buy tobacco. So it would seem that throughout human civilization tobacco, while not essential to life, is, at the same time, part and parcel of the daily life. However, at least in the civilized world, tobacco is considered neither a foodstuff nor a major fragrance commodity.

But tobacco as a natural product is unique in its own right due to the fact that it contains a great variety of fragrance and flavor molecules: nitrogenous compounds such as pyrazines, pyridines and indole; sulfur compounds such as alkyl sulfides; terpenoids like thymol and geraniol; carotenoid degradation products such as ionones and damascones; labdanoids such as sclariolide, sclareol and Ambrox as well as various aromatic species such as vanillin, benzaldehyde and phenyl ethyl alcohol. To date, no natural product in the flavor and fragrance industry can match tobacco for the number of volatile constituents which have been identified.

It is also said that what is not in tobacco is not in any other natural product. A plethora of publications report in excess of 3000 volatile and nonvolatile components in tobacco products. It is not within the scope of this presentation to review all of these tobacco constituents, but several simple tobacco components which have had a profound influence

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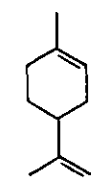
Acidic components of tobacco[13].

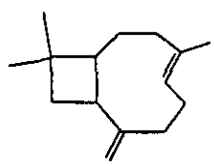
Acid	Virginia %	Burley %	Turkish %
Isovaleric	0.02	nd	nd
n-Valeric	0.01	0.01	0.23
beta Methyl valeric	0.03	trace	18.92
Caproic	0.29	0.03	1.33
Caprylic	0.25	0.28	0.68
Capric	0.08	0.29	0.20

nd = Not Detected

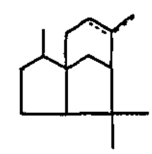
Hydrocarbon constituents of tobacco and other naturals



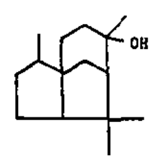
1
Tobacco (trace)[1,2]
Orange, Lemon (95%)[3]



2
Tobacco (dng)[4]
Clove (12%)[5]



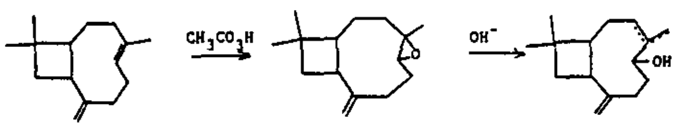
3
Tobacco (dng)[6]
Texas Cedarwood Oil
(22-26%)[7,8]



4
Tobacco (dng)[6]
Texas Cedarwood Oil
(26-32%)[7,8]

dng = Detected but no quantitative data given

Conversion of caryophyllene to useful aroma chemicals



2
Odor: Clove

5
Odor: Rich tobacco

6
Odor: Sweet, woody, peppery[8]

on both flavor and fragrance chemistry will be discussed.

If one considers that the first impression of the aroma of cured tobacco leaf is due to volatile organic molecules, then these compounds can be divided into these general groupings: Hydrocarbons, Acids, Phenols, Nitrogenous Compounds, Sulfurous Compounds, Lactones, Alcohols, Esters, Aldehydes, Ketones, and Ethers.

Hydrocarbons

Even though hydrocarbons probably do not play a critical role in tobacco flavor, some are extremely important for the characteristic flavor and aroma of essential oils. As everyone knows, the simplest alicylic monoterpene, limonene (1)*, is a trace constituent of tobacco[1,2] but it is a major ingredient of many citrus oils, constituting as much as 95% of orange and lemon oils.[3] Limonene (1) is used extensively in fragrance compositions, particularly in soap and detergent products.

At the same time, several other minor sesquiterpene components of tobacco such as beta caryophyllene (2)[4] and cedrene (3)[6] are key constituents in other natural flavor and fragrance materials. Beta caryophyllene (2) represents 12% of clove bud oil,[5] whereas cedrene (3) and cedrol (4) together constitute between 50 and 70% of cedarwood oil.[7,8] Beta caryophyllene (2) is also an important raw material for the production of several fragrance materials such as caryophyllene oxide (5) and hydroxy caryophyllene (6).

Epoxidation of beta caryophyllene (2) gives caryophyllene oxide (5) which has a rich tobacco aroma, and isomerization of this product with aluminum isopropoxide gives a mixture of alcohols (6) with a sweet, woody, peppery odor.[9] Similarly, cedrene (3) and cedrol (4) serve as the starting materials for the production of various important woody fragrance molecules such as cedrene epoxide (7), cedryl methyl ether (8), and the highly reknowned

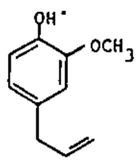
*Numerals in parentheses refer to chemical structures, as numbered in the figures which follow.

Phenolic constituents of tobacco and other naturals

14

Tobacco:
- Virginia (0.17%)[13]
- Burley (0.09%)[13]
- Turkish (0.23%)[13]

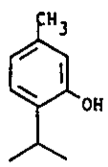
Jasmine absolute (1%)[21,22]
Live jasmine flower (1%)[20]
Live narcissus flower (0.8%)[20]
Ylang oil (dng)[23]
Ambergris tincture (0.1%)[24]
Tonquin musk tincture (0.1%)[25]



15

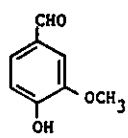
Tobacco:
- Virginia (0.003%)[13]
- Burley (nd)
- Turkish (nd)

Clove bud oil (90%)[27,28]
Carnation oil (30%)[29]
Live carnation flower (80%)[20]
Narcissus oil (dng)[30]



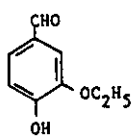
16

Tobacco (dng)[6]
Thyme oil (4%)[31,32]
Live thyme leaf (15%)[33]



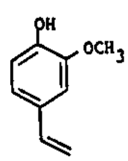
17

Tobacco (trace)[34]
Vanilla (2.5%)[35]
Extract of vanilla (60-80%)[36]
Extract of gum benzoin (8%)[37]



18

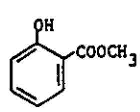
Does not occur in nature.
Odor: intensely sweet, warm and floral



19

Tobacco (trace)[4]
- Virginia (0.08%)[13]
- Burley (0.08%)[13]
- Turkish (0.1%)[13]

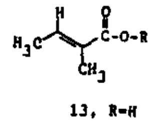
Vanilla extract (dng)[35,36]



20

Tobacco (dng)[26]
Oil of wintergreen (>95%)[41]

Tiglic acid and its esters, content in tobacco and other naturals

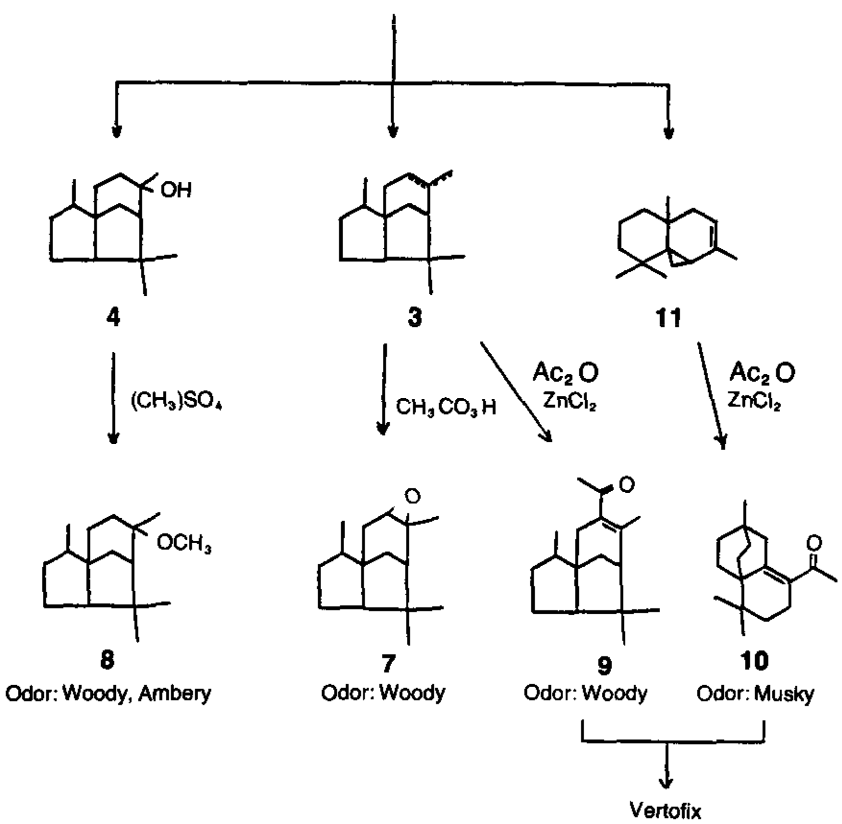


13, R=H

Compound R	Tobacco[4,13] %	Gardenia[16,17] %	Roman Chamomile[18,19] %
CH_3	ang,[4] 0.02[13]	dng	2.7
C_2H_5	nd	1.3	nd
cis-3-Hexenyl	nd	3.0	nd
2-Hexenyl	nd	0.5	nd
Benzyl	nd	1.0	nd
Phenyl ethyl	nd	0.2	nd
Cinnamyl	nd	trace	nd
n-Propyl	nd	nd	0.8
Isobutyl	nd	nd	4.1
sec. Butyl	nd	nd	trace
Methallyl	nd	nd	0.4
n-Butyl	nd	nd	0.14
n-Amyl	nd	nd	0.24

Conversion of Cedarwood Components Into Fragrance Materials

Cedarwood Oil



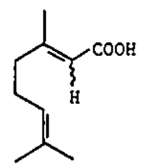
fragrance material, Vertofix (9,10) made by the acetylation of cedrene (3) and thujopsene (11), another component of cedarwood oil.[10,11,12]

Acids

Even though acids have been reported in tobacco as early as 1944, their role in tobacco flavor has not been well documented in the literature before 1982. In that year, Wilson, Mookherjee, and Vinals[13] showed that carboxylic acids served to differentiate, Turkish tobacco from other tobacco types. The common alkanoic acids from C_8 to C_{10} are known for their characteristic cheesy aroma and taste, and, indeed, they are the dominant flavor constituents of various natural cheeses.

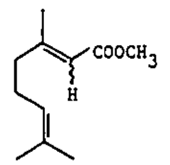
On the other hand, geranic acid (12a), which was first identified in tobacco by Wilson, Mookherjee, and Vinals,[13] and, by itself, probably is not important to tobacco flavor, is, along with its methyl ester (12b), a very important trace constituent of otto of rose[14,15] and gardenia absolute.[16]

Geranic acid and ester content of tobacco and other naturals



12a

Tobacco (0.01%)[13]
Otto of Rose (0.3%)[14,15]
Gardenia (trace)[16]



12b

Tobacco (nd)
Otto of Rose (0.09%)[14,15]

Tiglic acid, trans-2-methyl-2-butenoic acid (13), which was first identified in tobacco by Demole[4] in 1972 and confirmed by Wilson, Mookherjee, and Vinals[13] in 1982, probably plays only a minor role in tobacco flavor. Free tiglic acid (13) also occurs in small amounts in the aroma volatiles of both gardenia absolute[16,17] and Roman chamomile.[18,19]

Even though its importance in these two fragrance oils has not as yet been determined, the esters of tiglic acid are critical for the generation of the true aromas of both gardenia and Roman chamomile. It is interesting to observe that a specific set of esters is critical for the gardenia fragrance,[16,17] while an entirely different set of tiglates is found in the Roman chamomile.[18,19]

With regard to the importance of the tiglates to floral aroma, a very interesting natural phenomenon was discovered by the present authors[20] during the work on living vs dead flower analysis. It was found that, on picking the gardenia blossom, both cis-3-hexenyl tiglate and benzyl tiglate dramatically decreased. This observation strongly suggests that high concentrations of these two esters are important for the more natural aroma of the living flower.

Tiglate content of living vs. picked gardenia flowers

Tiglate	Living gardenia flower (%)[20]	Picked gardenia flower (%)[20]
cis-3-Hexenyl tiglate	7.3	4.4
Benzyl tiglate	1.3	0.7

Phenols

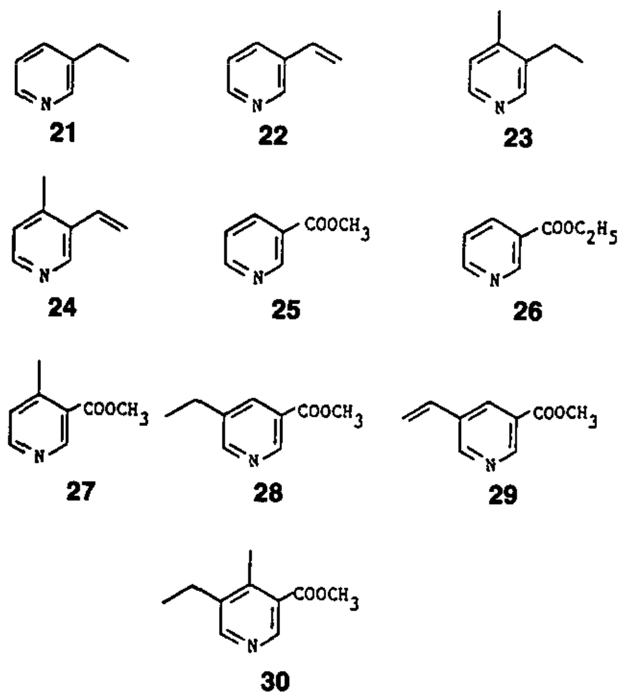
The next class of tobacco compounds which will be discussed is the phenols. Among these, the common compound, para cresol (14), a trace constituent of tobacco,[13] has a tarry, smokey medicinal odor and is animalic in character.

In high concentration, it has a repellant odor, but in extreme dilution it is very floral, and, in fact, it is an important constituent of natural florals such as jasmine,[21,22] ylang,[23] and narcissus[20] as well as highly coveted natural animalic fragrance materials like ambergris[24] and tonquin musk.[25] Similarly, eugenol (15)[13] is a key constituent of clove,[27,28] carnation,[29] and narcissus,[30] and, of course, thymol (16)[6] is the aroma impact component of thyme oil.[31,32,33]

Vanillin (17) is a minor constituent of tobacco,[34] but it is the major flavor impact component of vanilla[35,36] and other naturals like gum benzoin.[37] Not everyone is aware that vanillin was first isolated from vanilla pods as early as 1816. However, the name vanillin was first coined for this compound in 1858 by Gobley[38] who also was the first to assign an empirical formula, albeit an incorrect one. In 1872, Carles[39] assigned the correct formula but did not recognize the aldehydic character of the molecule, and he referred to it as "vanillic acid". The correct structural assignment was finally made by Tiemann and Haarmann[40] in 1874.

Today, thousands of tons of vanillin are produced synthetically each year for use in both flavors and fragrances. The higher homologue, ethyl vanillin (18), although not as yet identified in nature, is also widely employed. It is about 2½ times as strong as vanillin in taste and has the additional advantage, from a fragrance point of view, of possessing a floral aspect to its aroma.

Ethyl vanillin, therefore, finds extensive use in sweet florals such as ylang where it functions both as an aromatic and as a fixative. In this connection, it should be mentioned that para vinyl guaiacol (19), another trace constituent of both tobacco[4,13] and vanilla,[35,36] plays an important role in the flavor industry.



Pyridine and nicotinic constituents of *Jasminium sambac* [42]

Nitrogeneous bases in tobacco[13]

Base	Virginia (%)	Burley (%)	Turkish (%)
PYRIDINES			
2-Methyl pyridine	0.01	0.03	nd
2-Isopropyl pyridine	nd	nd	0.02
3-Isobutyl pyridine	nd	nd	0.17
3-n-Butyl pyridine	0.01	nd	0.04
Nicotine	0.11	3.36	0.01
Methyl nicotinate	nd	dng[6]	nd
PYRAZINES			
Methyl pyrazine	0.01	nd	nd
2,6-Dimethyl pyrazine	0.04	nd	nd
Trimethyl pyrazine	0.03	nd	nd

Methyl salicylate (20), another trace component of tobacco,[26] is the dominant odor and flavor constituent of oil of wintergreen.[41] However, it frequently occurs in trace amounts in many other flavor and fragrance natural products.

It is of interest to note that its parent acid, salicylic acid, occurs naturally in the roots, bark, leaves, blossoms, and fruits of many plants. Its occurrence in sweet birch bark and in the bark of various willows of the genus *Salix*, which probably accounts for its name, was exploited by native Americans for its analgesic properties. This use was passed on to European colonists and served to promote the early isolation and characterization of the acid and the creation of numerous derivatives and analogues such as the modern day Aspirin, acetyl salicylic acid.

Nitrogenous compounds

Among the nitrogenous compounds, pyrazines and pyridines definitely contribute to the aroma and taste of tobacco.[13] It is common knowledge among flavorists that these materials are very important ingredients for the generation of roasted and nutty aromas for cooked meat, especially beef, and for roasted nut products.

However, Mookherjee, Trenkle and Wilson[20] recently found that highly coveted flowers such as jasmine and freesia produce pyrazines as the flowers decay. It is the belief of the present authors that these compounds are artifacts produced by browning reactions.

In 1976, Fujimori, et al[6] reported the occurence in tobacco of methyl nicotinate but did not mention

Pyrazine constituents in head space volatiles of live (on plant) vs picked (after 8 to 12 hours) flowers[20]

Pyrazine	Jasmine Live %	Jasmine Picked %	Freesia Live %	Freesia Picked %	Viburnum Live %
Trimethyl pyrazine	nd	1.94	nd	0.06	nd
2-Ethyl-3,6-dimethyl pyrazine	nd	1.87	nd	0.13	nd
2-Ethyl-3,5-dimethyl pyrazine	nd	3.51	nd	nd	nd
Ethyl trimethyl pyrazine	nd	nd	nd	0.18	nd
2-Isobutyl-3,5-dimethyl pyrazine	nd	0.13	nd	0.21	nd
Ethyl nicotinate	nd	nd	nd	nd	1.0

its odor value. On the other hand, recent work by the present authors[20] on the living flowers of the fragrant viburnum have resulted in the identification of ethyl nicotinate as an aroma impact component.

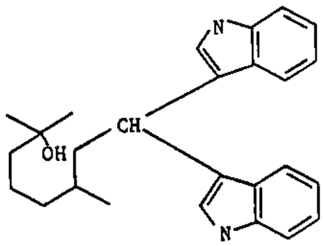
Interestingly, Japanese workers[42] have also identified various pyridines (21-24) and alkyl-substituted nicotinates (25-30) as constituents of oil of *Jasminium sambac,* which is also known as Chinese jasmine. These authors claim that the nicotinates have a "... smokey and somewhat fruity odor, and they seem to harmonize the odors of other ingredients in perfumes."

Probably among all these nitrogenous compounds one which stands out like a star in the history of perfumery is indole (31) which was first reported in tobacco by the present authors.[13] This compound was identified in jasmine by Hess[43] as early as 1899.

Generally, ordinary synthetic indole (31) has a disagreeable fecal odor due to trace impurities like skatole, but highly purified indole at high dilution possesses a very pleasant floral note. In fact, indole (31) plays a very important role in the olfactory effect of many flowers such as jasmine,[20] orange flower,[44] narcissus,[20] lilac,[20] Easter lily,[20] lemon flower,[20] tuberose,[20] and honeysuckle.[20].

Recent work by the present authors[20] on the comparison of living versus picked flowers shows that the indole (31) content is drastically reduced on picking of the blossoms (see table). Therefore, one could easily visualize the importance of indole (31) to modern creative perfumery for the creation of the true-to-nature floral odor.

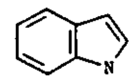
In addition to the importance of free indole (31) in its own right in perfumery, this compound also has a very important function in the creation of a new class of fragrance specialties known as Indolene (32). Indolene (32) is a product made by the reaction of two moles of indole with one mole of various



32

Indolene: a hypothetical structure for the combination of an aldehydic fragrance molecule, e.g. hydroxy citronellal, and indole[45]

Indole Content of Naturals



31

Indole content of living (on plant) and picked (after 8 to 12 hours) flowers[20]

Flower	Live %	Picked %
Jasmine	11.0	2.0
Paperwhite narcissus	4.5	0.3
Purple lilac	2.3	1.5
Easter lily	19.0	2.0
Lemon flower	23.0	13.0
Tuberose	4.4	2.6
Honeysuckle	2.5	nd

Indole content of tobacco and other naturals

Natural	Indole (%)
Tobacco[13]	0.97
Jasmine absolute[22,43]	3.00
Orange flower absolute[44]	0.57

aldehydes such as hydroxycitronellal[45] or phenyl acetaldehyde[45] or any other aldehydic fragrance molecule.

Even though chemists are not certain of the exact chemical structure of these products, this indole Schiff base is extensively used not only in floral formulations like muguet, jasmine, tuberose, hyacinth, narcissus, etc., but also as an enriching floralizer possessing great fixative properties.

Sulfurous compounds

As an additional example of the importance of trace tobacco constituents containing heteroatoms in the flavor and fragrance industry, a very simple two-carbon molecule will be mentioned which, while having a very unaesthetic odor, is, in high dilution, essential for producing the characteristic aroma of several natural flavor and fragrance materials.

This compound is none other than dimethyl sulfide (33) which was identified in tobacco in 1980.[46] It is well known that dimethyl sulfide (33), in high dilution, has the character of several cooked vege-

Dimethyl Sulfide

$$CH_3 - S - CH_3$$

33

tables such as tomato, cabbage, aspargus, broccoli, etc. To produce a cooked tomato flavor, this compound is absolutely essential.

It is very interesting to observe, however, that this cooked vegetable flavor compound plays a dynamic role in one of the most aesthetically pleasing of all fragrance naturals, otto of rose Bulgarian. One cannot make a true rose otto replacement without using a trace of dimethyl sulfide (33).

Lactones

Several neutral odoriferous molecules of tobacco will now be discussed of which lactones will be mentioned first since both flavorists and perfumers are keenly aware of the key roles many of them play in various natural products.

In 1972, Demole and Berthet[4] of Firmenich first reported the presence of butenolide (34) in tobacco, but its importance either to tobacco or to the aroma or flavor of any other natural has not been fully explored. On the other hand, Mookherjee and Shu[47] have shown that not only the tobacco butenolide (34) but also the related butanolides (35-37) are key contributors to the aroma of olibanum or frankincense. Olibanum is not only an incense ingredient but is also used in making all Oriental perfumes.

Interestingly, each of these lactones is characterized by a strong coumarinic odor although structurally they are remarkably different from coumarin (38) itself. Coumarin (38), a tobacco constituent[6] in its own right, is used in the fragrance industry to support herbaceous notes as well as those of lavender and lavandin,[48] rosemary, citrus oils, oakmoss, etc. and as a fixative. Depending on the type of aroma effect desired and the allowable cost, either synethic coumarin or natural material in the form of tonka bean[49] or deertongue[50] can be used.

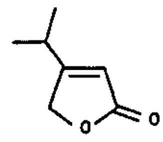
Another series of unsaturated lactones which are found in tobacco[4,51] are bovalide (39) and dihydrobovalide (40) which possess very strong, celery-like notes although they have not, as yet, been identified in celery. Bovalide (39) was first identified in butterfat,[52] but these compounds are usually found at low levels in naturals where their green, celery aroma and flavor can contribute usefully to the characteristic organoleptic effect of the product.

Examples of such naturals are green tea,[54,57] peppermint,[53,58] deertongue,[56] alfafa,[60] patchouli,[63] soy,[55] rice,[59] dried bonito,[61] and endive.[62] To our knowledge, the bovalides have not yet been utilized in the flavor or fragrance industry.

Among all tobacco butanolides, gamma decalactone (41)[64] probably plays the most important role in the flavor and fragrance industry due to the fact that it has a definite coconut, peach, apricot, and heated milk odor and taste, and, indeed, it is a key flavor ingredient of these products.[65-68] Recent work by the present authors[68] has revealed this compound for the first time as a trace constituent of fresh coconut milk. Gamma lactones were, until now, believed not to occur in fresh coconut.[69]

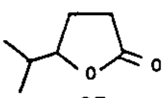
The present authors,[20] moreover, have found that living ripe strawberry fruit contains high levels of gamma decalactone (41) which decrease dramatically after the fruit is picked. Amazingly, just the

Lactones in tobacco and other naturals



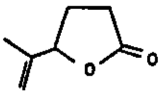
34

Tobacco (dng)[4]
Olibanum (trace)[47]
Odor: strong tonka bean, coumarin note



35

Tobacco (nd)
Olibanum (trace)[47]
Odor: Tonka bean, Coumarin note



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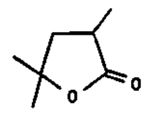
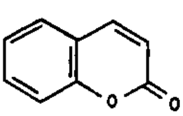
Tobacco (nd)
Olibanum (trace)[47]
Odor: Olibanum with a coumarin note



37

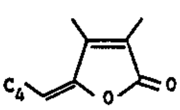
Tobacco (nd)
Olibanum (trace)[47]
Odor: Animalic with a coumarin note



38

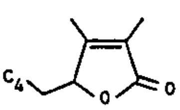
Tobacco (dng)[6]
Lavandin (dng)[48]
Tonka bean (dng)[49]
Deertongue (dng)[50]
Odor: New-mown hay

Lactones in tobacco and other naturals



39

Tobacco (dng)[4]
Butterfat (trace)[52]
Peppermint (0.0001%)[53]
Tea (dng)[54]
Soy (0.05%)[55]
Odor: Strong celery note



40

Tobacco (dng)[51]
Deertongue (dng)[56]
Tea (dng)[57]
Peppermint (dng)[58]
Rice (dng)[59]
Alfalfa (0.2%)[60]
Dried bonito (dng)[61]
Endive (dng)[62]
Patchouli oil (dng)[63]
Odor: Strong celery note

Comparative analysis of gamma decalactone in the head space volatiles of living and picked fruits[20]

Fruit	Living fruit % γ-decalactone	Picked fruit % γ-decalactone
Ripe New Jersey strawberry	9.5	0.3
Ripe New Jersey cling peach	2.5	39.2

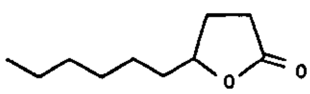
reverse is true in the case of the peach. One can easily visualize why this compound is important to the flavor and fragrance industry.

After the butanolides naturally come the pentanolides. In this class of compounds, the one compound which is not only a tobacco constituent[6] but also an important flavor and fragrance ingredient is delta decalactone (42). As in the case of gamma decalactone (41), delta decalactone (42) is an important flavor constituent of heated milk fat;[70] however, this compound has also recently been found to contribute important notes to many exotic flowers such as gardenia,[71] tuberose,[72] and osmanthus.[73]

Pentenyl pentanolide (43), also known as jasmine lactone, is a key component not only of jasmine absolute,[74] but also of gardenia,[75] osmanthus,[73] and tuberose.[72] This compound is in high commercial demand. It is produced by IFF and is known as Jasmine Lactone BB.

Pentyl pentenolide (44), also called massoia lactone, was first identified in the bark of *Cyptocaria massoia*, hence its name. It has a very heavy, fruity aroma and taste and has been found to be important for osmanthus[73] and tuberose.[72] Pentenyl pentenolide (45), known as tuberolactone, was first identified in tuberose[72] and is also important for osmanthus.[73]

Occurrence of gamma decalactone in tobacco and other naturals



41

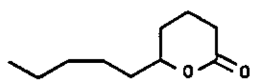
Tobacco (dng)[64]
Butterfat (0.6ppm)[65]
Apricot (dng)[66]
Peach (dng)[67]
Fresh coconut milk (trace)[68]
Odor: Coconut, fruity

Alcohols and esters

Tobacco contains several terpenic and aromatic alcohols and esters which probably play a minimum role in tobacco flavor but which have a profound influence on flavor and fragrance chemistry due to their pronounced floral aroma. Benzyl alcohol (46)[76] is a trace constituent of otto of rose,[77] but it and its acetate (47)[76] are key character-donating components of jasmine absolute.[78] Both, indeed, have a jasmine odor.

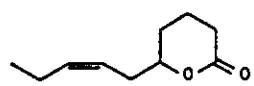
The diterpenic alcohol, phytol (48), and its isomer, isophytol (49), while major constituents of jasmine[80,82] do not possess any odor, but they play an extremely important role due to their fixative properties. Every perfumer knows that, in order to make a good artificial jasmine, one has to use either or both of these two compounds.

Occurrence of delta lactones in tobacco and other naturals



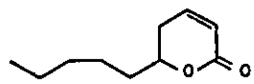
42

Tobacco (dng)[6]
Heated milk fat (dng)[70]
Gardenia (dng)[71]
Tuberose (0.6%)[72]
Osmanthus (0.03%)[73]
Odor: Milky, coconut, fruity



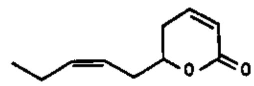
43

Tobacco (nd)
Jasmine absolute (1%)[74]
Gardenia (8%)[75]
Tuberose (1%)[72]
Osmanthus (0.01%)[73]
Odor: Flowery, fruity



44

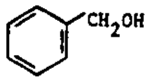
Tobacco (nd)
Tuberose (0.005%)[72]
Osmanthus (0.01%)[73]
Odor: Fruity, flowery



45

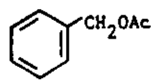
Tobacco (nd)
Tuberose (0.01-0.02%)[72]
Osmanthus (0.02%)[73]

Alcohols and esters of tobacco and other naturals



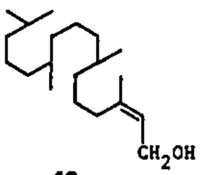
46

Tobacco (dng)[76]
Virginia (2.2%)[13]
Otto of rose (0.01%)[77]
Jasmine absolute (6%)[78]



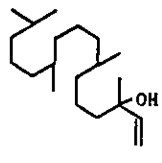
47

Tobacco (dng)[76]
Virginia (0.4%)[13]
Jasmine absolute (33%)[78]



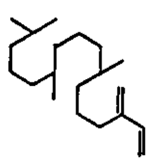
48

Tobacco (dng)[81]
Jasmine absolute (dng)[82]



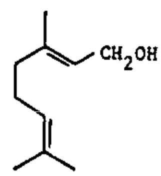
49

Tobacco (dng)[79]
Jasmine absolute (10%)[80]



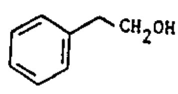
50

Tobacco (dng)[83]
Virginia (2-45%)[13]



51

Tobacco (dng)[4]
Otto of rose (15%)[77]
Jasmine absolute (dng)[84]



52

Tobacco (dng)[76]
Virginia (0.6%)[13]
Otto of rose (1.2%)[77]

It may be of interest to know that, while phytol (48) and isophytol (49) are both present in tobacco,[79,81] neither is a major constituent, whereas neophytodiene (50), which likely arises in tobacco from dehydration of these alcohols,[83] is a major volatile component of tobacco.[13]

One need not stress too much the importance of geraniol (51)[4] and phenyl ethyl alcohol (52)[76] to the flavor and fragrance industry. These two materials are essential to perfumery due to the fact that they possess the rose odor and are the major constituents of Bulgarian otto of rose,[77] a natural which sells for $3000 a pound. It is not out of place to comment that one cannot find a single classical perfume from Joy in 1921 to Giorgio in 1984 which does not contain a drop or two of natural jasmine and rose.

Western people will be interested to know that, while rose is mainly a fragrance material in the West, it is an important flavor commodity in Indian society.

By this time, one can easily realize that trace tobacco constituents are capable of exerting a tremendous influence on the present day perfume and flavor industry.

Carbonyls: ionones

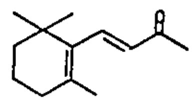
Compounds from the class of carbonyls are not only important to tobacco aroma and taste but have played a great role in modern flavor and fragrance chemistry. Beta ionone (53) was first identified in tobacco by Demole and Berthet[85] in 1971 and alpha ionone (54) by Schumacher and Vestal[86] in 1974.

Interestingly, beta ionone (53) was first synthesized as early as 1893 by Tiemann and Kruger,[87] but it was not identified in nature until 1929 when it was isolated from *Boronia megastigma.*[88] Alpha ionone (54) was not identified in nature until recent times although it also was first made in 1893.[87]

Both of these ionones are essential components of violet flower.[89] Moreover, recently they have also been found to be key ingredients of raspberry[90] and osmanthus.[91]

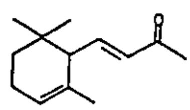
It is interesting to note that dihydro beta ionone, (55), which is also a trace tobacco constituent,[4] constitutes 11% of the volatiles of violet[89] and is also a

Ionones in tobacco and other naturals



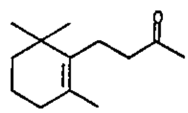
53

Tobacco (dng)[85]
Boronia (dng)[88]
Violet (0.2%)[89]
Raspberry (trace)[90]
Osmanthus (5%)[91]



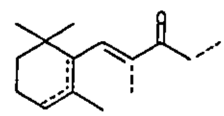
54

Tobacco (dng)[86]
Violet (8.2%)[89]
Raspberry (0.1-1ppm)[90]
Osmanthus (1%)[91]



55

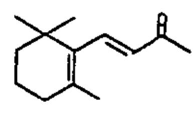
Tobacco (dng)[4]
Violet (11%)[89]
Japanese hybrid tea rose (dng)[92]
Living American tea rose (6.8%)[20]



56

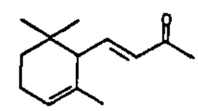
Does not occur in nature

Damascones in tobacco and other naturals



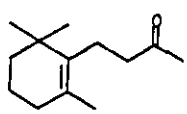
57

Tobacco (trace)[85,94]
Otto of rose (0.05%)[93]
Odor: Tobacco, rose, tea, apple, fruity



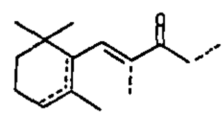
59

Tobacco (trace)[85,93]
Otto of rose (trace)[93]
Odor: Rosey, tobacco, fruity



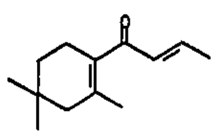
60

Tobacco (nd)
Tea (trace)[97]
Odor: Citrus, tea



61

Not yet detected in nature
Odor: Rosey, fruity



62

Does not occur in nature
Odor: Rose, tobacco, fruity[99]

major component of living American tea rose[20] and Japanese hybrid tea rose.[92] It is described[92] as contributing to the powerful and diffusive rose scent of both violet and hybrid tea rose.

At this point, it will not be out of place to mention a higher homologue in the ionone series called methyl ionone (56) which, while not as yet having been identified in nature, is critical for making modern fancy perfumes due to its characteristic violet odor which is much stronger than that of the ionones.

Carbonyls: damascones

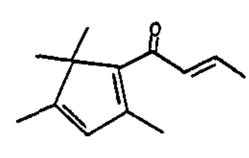
Another class of tobacco carbonyls called isoionones or damascones has truly revolutionized present-day fragrance and flavor chemistry. It is well known that beta damascenone (57) was first isolated in 1930 by Demole and co-workers[93] of Firmenich from *Rosa damascena*. However, the present authors cannot resist commenting at this time on the true story of IFF's first finding of this important molecule in nature; for you see, it happens to occur in tobacco.[85,94]

In 1968, Dr. van Praag,[94] an IFF chemist, isolated a compound from tobacco which he named the "Tobacco 2C Compound". One of the present authors, B. D. Mookherjee[94] deduced the correct structure for beta damascenone (57) on the basis of the IR, NMR and MS spectral data. However, since the UV spectrum of this cross-conjugated molecule does not follow the Woodward UV Rule, IFF hesitated to disclose the structure pending confirmation by synthesis.

In the interim, Firmenich published its identification rationalizing the UV anomaly on the basis of Fermi resonance. Interestingly, in 1985, Kastner[95] of Firmenich disclosed that, on the basis of spectral properties, the structure of beta damascenone (57) was considered as 58. Subsequently, after serious consideration from a biogenetic point of view and through synthesis, the correct structure of beta damascenone (57) was established by the Firmenich chemists.

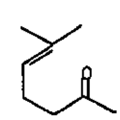
Beta damascone (59) has a more rosey, tobacco, fruity, odor and taste whereas beta damascenone (57) is rose-tea and apple with a pronounced to-

Originally proposed structure for beta damascenone[95]



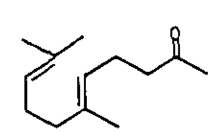
58

Nor-terpenic ketones in tobacco and other naturals



63

Tobacco (1ppm)[100]
Tomato[101]



64

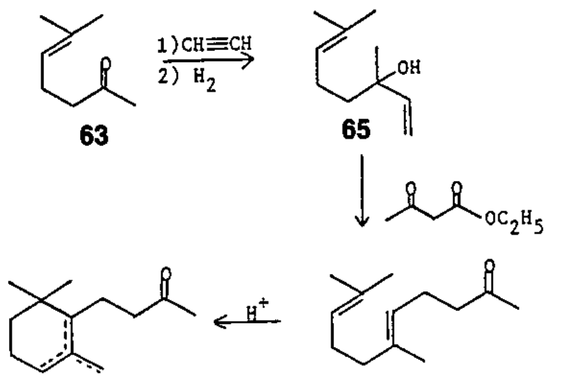
Tobacco (dng)[85]
Tomato (8%)[102]

bacco nuance. Both these materials are extensively used in modern floral perfumes and fruity flavors.

Recently, Ohloff[96] reported that Firmenich is producing approximately 10 metric tons of these rose ketones in the damascone family per year. An isomeric compound, alpha damascone (60), although not as yet identified in rose or tobacco but isolated from tea in 1974,[97] possesses an excellent citrus-tea note and is gaining in popularity for its fine odor and flavor properties.

Due to the unique structure and odor properties of the natural damascones, chemists are constantly constructing new molecules having similar but improved properties. IFF chemists Mookherjee,

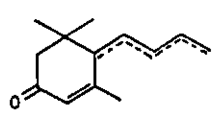
Synthesis of dihydroionones from methyl heptenone



63 65 64

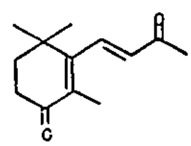
Dihydroionones (alpha, beta, gamma)

Ionone derivatives in tobacco and other naturals



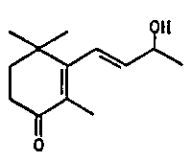
66

Tobacco (dng)[103]
Virginia (5-7%)[13]
Osmanthus absolute (0.05%)[73,104]



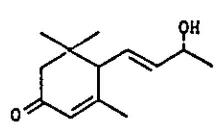
67

Tobacco (dng)[6]
Living freesia flower (5%)[20]
Living osmanthus flower (2%)[20]
Osmanthus absolute (0.1%)[73,104]



68

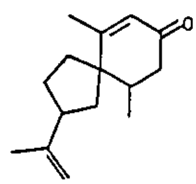
Tobacco (nd)
Living freesia flower (2%)[20]
Living osmanthus flower (0.7%)[20]
Osmanthus absolute 0.3%)[73,104]



69

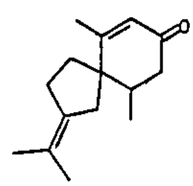
Tobacco (14ppm)[105]

Spiro-ketones in tobacco and other naturals



70

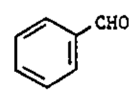
Tobacco (trace)[106]



71

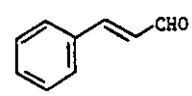
Tobacco (nd)
Vetivert oil (5%)[107]

Aromatic aldehydes in tobacco and other naturals



72

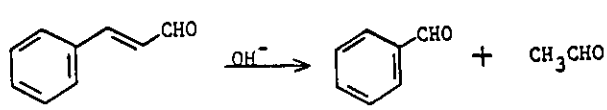
Tobacco (dng)[108]
Bitter almond oil (80-90%)[109]



73

Tobacco (dng)[4]
Cassia oil (80%)[110]

Synthesis of natural benzaldehyde



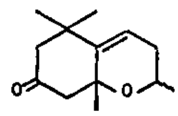
73

Natural cinnamic aldehyde ex cassia oil

72

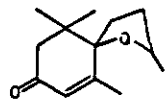
Natural benzaldehyde

Bicyclic ethers in tobacco and other naturals



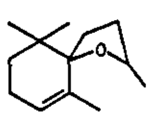
74 (two isomers)

Tobacco (dng)[4]
Purple passionfruit (trace)[111]
Osmanthus (trace)[73]
Odor: Oriental tobacco



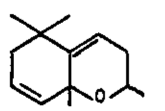
75

Tobacco (dng)[9]
Yellow passionfruit (trace)[113]
Osmanthus (trace)[114]
Tea (trace)[114]
Odor: Tea-like



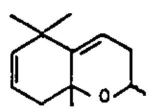
76 (two isomers)

Tobacco (nd)
Yellow passion fruit (0.1-1%)[113]
Osmanthus (0.4%)[73]
Tea (dng)[115]
Raspberry (trace)[116]
Odor: Isomer A: Woody, camphoraceous[117]
Isomer B. Naphthalene-like[117]



77 (two isomers)

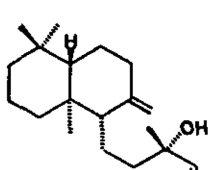
Tobacco (nd)
Purple passionfruit (0.1-1mg/kg)[118]
Cognac (dng)[119]
Odor: Rose-like[112]



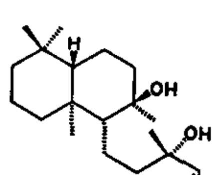
78 (two isomers)

Tobacco (nd)
Purple passionfruit (0.1mg/kg)[118]
Cognac (dng)[119]
Odor: Camphoraceous[118]

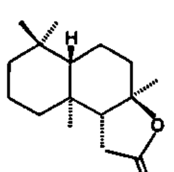
Diterpenic constituents of tobacco



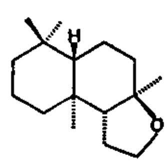
79
(Manool)
Tobacco (dng)[120]



80
(Sclareol)
Tobacco (dng)[120]



81
(Sclareolide)
Tobacco (dng)[121]



82
(Ambrox)
Tobacco (dng)[122]

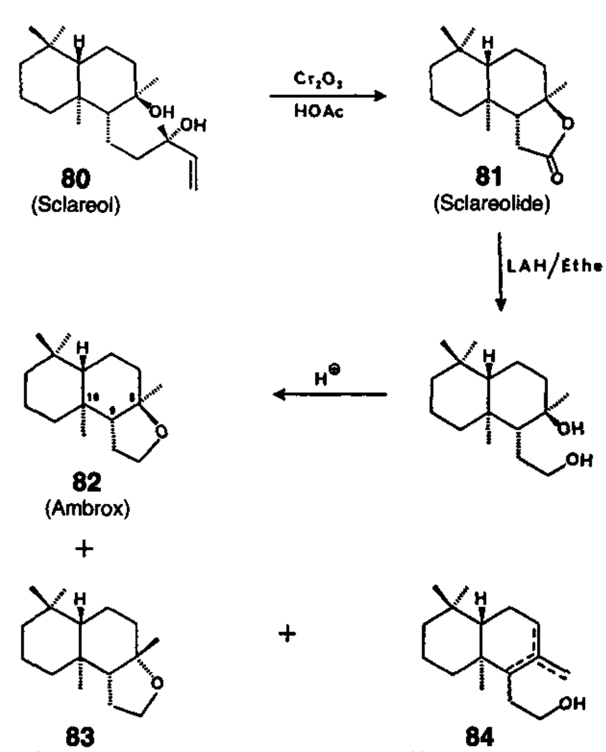
Trenkle, and Wilson,[98] have developed another isomeric compound called trans,trans delta damascone (61) which possesses a more true rose odor without any of the deleterious tobacco notes. At the same time, Dragoco chemists[99] have also introduced a novel compound known as isodamascone (62) which is described as having a rose, tobacco, and fruity aroma.

In the opinion of the present authors, these damascones have brought a new era to the flavor and fragrance industry. One will not find a single new perfume or fruit flavor which does not contain one or more of these compounds.

Two other tobacco ketones, methyl heptenone (63) and geranyl acetone (64), are important to tobacco flavor[85,100] and also play critical roles in the flavor and fragrance industry. Methyl heptenone (63), which has a very green note, is quite important for tomato.[101]

At the same time, it is important starting material for making the most coveted fragrance molecule known, linalool (65), which is, in turn, converted via the Caroll Reaction to geranyl acetone (64). This compound is important not only for general perfumery but also as a raw material for the manufacture of the dihydroionones which were discussed earlier.

Synthesis of Ambrox from sclareol



82 + 83 + 84 = Fixatuer 404
7 : 1 : 3

Other ketones

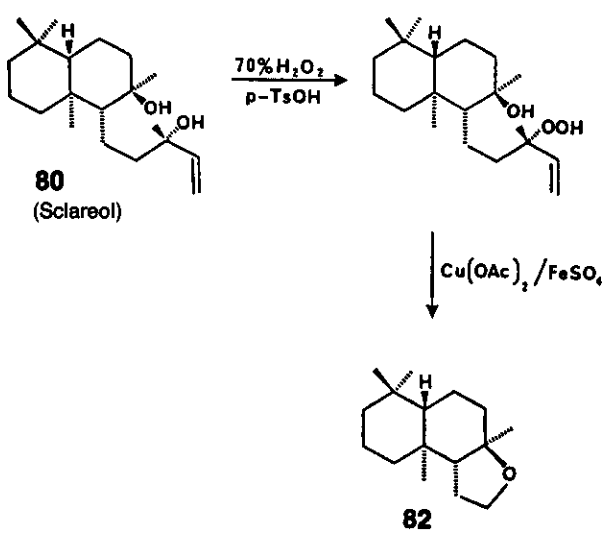
Among the tobacco carbonyls there is one group of isomeric compounds called megastigmatrienones (66)[103] which are closest to being the true-character-impact compounds of tobacco.[13] It is of interest to note that these compounds have recently been found as trace constituents of osmanthus absolute.[73,104]

However, the megastigmatrienones (66) have not as yet found general application in the flavor and fragrance industry. On the other hand, the oxo-ionones (67) and oxo-ionols (68, 69), some of which are important for tobacco flavor,[6,105] have been found, in some cases, to be character impact components in the oil of osmanthus flowers by Mookherjee, Trenkle, and Wilson.[20]

It is interesting to note that these compounds completely disappear from the volatiles of freesia flower on picking and are markedly diminished in the case of osmanthus. It is quite likely that these compounds will play major roles in fragrance chemistry in the near future when they become available.

Another tobacco ketone known as solavetivone (70)[106] should be mentioned not because of its odor properties but because of its structural similarity to a well known sesquiterpenic compound called beta vetivone (71), the key aroma component of vetiver oil.[107] Anyone interested in perfumery knows the true value of vetiver oil and its component, beta vetivone (71).

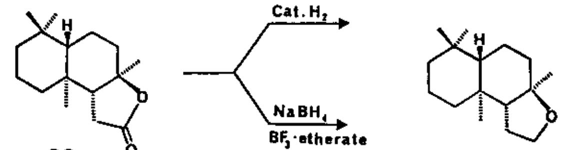
Synthesis of Ambrox from sclareol by H_2O_2 method[124]



80 (Sclareol)

82 (Ambrox)

Synthesis of Ambrox from sclareolide by hydrogenation



80 (Sclareolide)

82 (Ambrox)

Aldehydes

To conclude the discussion of tobacco carbonyls, two minor aldehydes, benzaldehyde (72)[108] and cinnamic aldehyde (73)[4] will be mentioned. Everyone is aware of the importance of benzaldehyde (72) for cherry flavors. It occurs naturally as the glycoside, amygdalin, in bitter almond oil[109] from which it can be obtained and used as a "natural benzaldehyde". Cinnamaldehyde (73) is the dominant flavor constituent of cinnamon spice[110] and is important for general flavor use.

In addition, there is a very important and interesting chemical interrelationship between these two aldehydes. It is well known that, in the present era of the flavor industry, natural flavorants play an increasingly critical role. Natural cinnamic aldehyde (73) is available from cassia oil[110] which comes from China. On treatment with alkali, natural cinnamic aldehyde (73) undergoes a retro aldol reaction to produce natural benzaldehyde (72) which is widely used in the beverage industry.

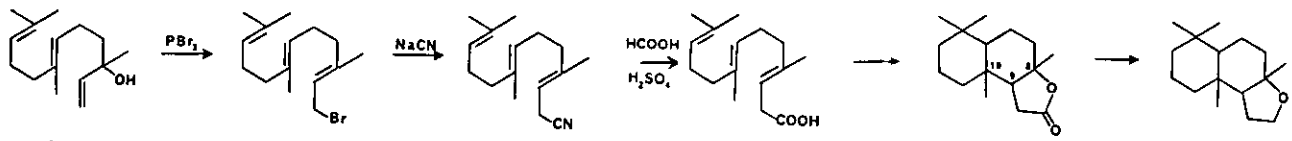
Cyclic ethers

The oxoedulans (74) and theaspirone (75) not only occur in tobacco[4] but also in passionfruit,[111,113] and osmanthus[73] at trace levels. The oxoedulans (74) have been described[112] as possessing an Oriental tobacco aroma whereas the theaspirones (75) are more tealike[114] reflecting the natural product in which they were first identified. These observations have been confirmed by synthesis on the part of the present authors.

At the same time, the corresponding parent compounds, the theaspiranes (76) and the edulans (77, 78), although not as yet identified in tobacco, have been described as possessing odors which are critical to the various naturals in which they have been found. The theaspiranes (76) are reported[117] to be very tealike while the edulans (77) are said[112] to have attractive rose-like aromas.

The present authors have synthesized and carefully purified these compounds and found them to contribute no useful odor properties. In the opinion of the present authors, neither the edulans (77, 78)

Synthesis of DL-ambrox from nerolidol



85 (Nerolidol)	86	87	88	89 (Racemic sclareolide) (three isomers)	90 (Racemic ambrox) (three isomers)

nor the theaspiranes (76) have any flavor or fragrance value.

Diterpenoids

Some diterpenoid compounds of tobacco which are important contributors to tobacco aroma and taste also have a profound influence on the flavor and fragrance industry. These molecules are manool (79),[120] sclareol (80),[120] sclareolide (81),[121] and Ambrox (82)[122] [Ambrox is a registered trade name of Firmenich S.A.].

Of all of these compounds, Ambrox (82) is one of the most coveted chemicals in the flavor and fragrance industry. Manool (79), sclareol (80), and sclareolide (81) possess a faint tobacco-amber odor, whereas Ambrox (82), which was first made by Stoll and Hinder[123] in 1950 as a fragrance chemical, was first reported by Mookherjee and Patel[24] in 1977 to be the key aroma-donating constituent of ambergris, a highly coveted and depleted natural fragrance material.

Ambergris comes from the sperm whale, the killing of which is strictly prohibited under U.S. law. Therefore, one could readily appreciate how critical it is to obtain a synthetic ambergris for the fragrance industry.

Stolland and Hinder[123] of Firmenich performed pioneering work on amber materials, and, indeed, first made Ambrox (82) from sclareol (80) in 1950. This route probably represents the method employed by Firmenich to produce an amber product called Fixateur 404 which sells for $120 a pound. This product contains 90% diluent and the remainder is made up of the active amber ingredients, Ambrox (82), isoambrox (83), and ambra alcohol (84) in the ratio of 7:1:3.

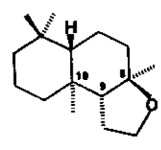
Very recently, in 1987, Decorzant and coworkers[124] of Firmenich published an elegant two-step process for making Ambrox (82) from sclareol (80). Since 70% H_20_2 has been used in this procedure, the practical applicability of this method is in doubt because of the hazards involved in the use of this reagent.

In 1977, when Mookherjee and Patel[24] first reported Ambrox (82) in ambergris, various fragrance companies began to produce pure synthetic Ambrox (82). Subsequently, Henkel introduced pure Ambrox (82) which they called Ambroxan, which is probably made from sclareolide (80) by a known reduction technique.

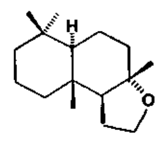
It is interesting to note that Mookerjee and Patel,[24] in connection with their work on ambergris constituents, also proved that sclareolide (81) could be directly converted to pure Ambox (82) by a hydroboration technique; however, the yield is poor. Henkel's Ambroxan is a widely used fragrance material which sells for $550 a pound.

Surprisingly, in 1988, Firmenich introduced a new amber product called DL-Ambrox (90) which sells for $550 a pound. A German company, Wacker, also sells DL-Ambrox (90) which they call "Synambran" for $275 a pound.

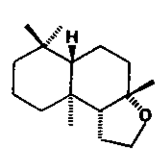
Structure and Odor Threshold of Isomers of Ambrox[127]



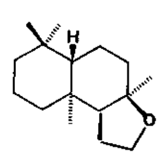
82
(−)-Ambrox
0.3 ppb



ent-82
(+)-Ambrox
2.4 ppb



83
Isoambrox
30 ppb



91
9-Epiambrox
0.15 ppb

It is interesting to note that in 1960 Lucius[125] reported the synthesis of racemic Ambrox (90) starting from nerolidol (85). The present authors believe that both Firmenich and Wacker utilize this or a very similar method to make their DL-Ambrox (90). In the opinion of the present authors, DL-Ambrox (90) does not possess the equivalent odor properties of either Fixatuer 404 or Henkel's Ambroxan.

At this point, it is very appropriate to discuss the odor properties of isomers of Ambrox (82). (−)Ambrox (82), the true constituent of ambergris, possesses a moist, soft, creamy, persistent, warm, animalic, amber odor with a velvety effect.[126] Its odor threshold is about 0.3 ppb.

At the same time, (+)Ambrox (ent 82), not an ambergris constituent, has a higher threshold value, 2.4 ppb, with an accentuated woody note and lacks the strong animalic warmth of its enantiomer, (−)Ambrox (82). It has been called a "poor man's Ambrox" by Firmenich perfumers.

The racemic (±)Ambrox (90) lacks the exotic spicy undertone of (+)Ambrox (ent 82) and its threshold value is 0.5 ppb. Isoambrox (83), which is more thermodynamically stable than Ambrox (82) but is not an ambergris constituent, is generally present in commercially available Ambrox (82) such as Ambroxan and Fixateur 404, and is more than 100 times weaker than (−)Ambrox (82). Surprisingly, (−)−9 epiambrox (91) is the strongest of all with an odor threshold of 0.15 ppb.[127]

Ambrox (82) is such an important commercial fragrance ingredient that its total annual usage exceeds $2 million. Isn't it amazing to see how one chemical can play such an important role in such diverse naturals as tobacco and whale vomit?

In the same way, many additional examples similar to these which have just been described could be cited, but it is felt that it has been amply demonstrated that, whereas tobacco, as such, is not important for the flavor and fragrance industry; indirectly, through its wide variety of trace constituents, it governs modern flavor and fragrance chemistry and its industry.

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