This review deals with the occurrence of pyridine derivatives in food flavors, tobacco, essential oils as well as in model systems. Their formation and olfactory properties are also discussed.

Heterocyclic Compounds in Flavors and Fragrances Part III. Pyridine and Derivatives

By Gaston VERNIN
Laboratorie de Chimie Organique A, Associé au C.N.R.S. (LA N° 126)
Faculté des Sciences et Techniques de St-Jérôme,
Rue H. Poincaré, 13013 Marseille Cédex 04

I—INTRODUCTION

During the last two decades the role of heterocyclic compounds in food flavors has been reviewed by several authors (18, 78, 79, 117-122). While furans (66), pyrroles (68), thiophenes (61), thiazoles (62, 63, 120), oxazoles (65, 57), lactones (64), pyrazines (55, 56) and their reduced systems were periodically treated, surprisingly, pyridines which are among the most widely distributed volatile flavor compounds have not been described in detail (69). Therefore, the purpose of this review is to fill this gap.

II—PYRIDINE COMPOUNDS IN FOOD FLAVORS, TOBACCO, AND ESSENTIAL OILS

1. Occurrences

Since the discovery of the 3-methylpyridine in coffee by RADTKE in 1964 (87), many pyridine derivatives have been found in a great variety of food systems among other heterocyclic compounds. They are present in traces in the following food flavors (see Table 1): fish, meat (beef, chicken, lamb), vegetables (artichoke, dry red beans, leeks, beetroots, asparagus, potatoes, tomatoes), cereals (rice, corn, barley), bread, nut products (almonds, filberts, peanuts, pecan, soya bean), milk and dairy products (cheese), fruits, spices and condiments (pepper, Trassi) nonalcoholic beverages (cocoa, coffee, tea), alcoholic beverages (beer, rum, whiskey), tobacco and essential oils (jasmine).

A detailed list of pyridine compounds iden-

Part I. Heterocyclic Flavoring Compounds in the MAILLARD reaction (in French)

In the first part of this series, heterocyclic compounds occurring in food flavors and model systems were reviewed. The relation between their structure and organoleptic properties were also briefly described. The mechanisms of furans, thiophenes, pyrroles, oxazoles, thiazoles, pyridines, pyrazines and polysulfur-containing rings, formation from food precursors were discussed (60 reférences; Chemical Abstract, *94*, 1550092).

Part II. Heterocyclic Compounds in Food Flavors: Synthesis and Characterization of Flavoring Thiazoles (in French)

The principal synthesis methods for mono-, di-, and trialkylthiazoles, hydroxyalkylthiazoles, alkoxythiazoles and acylthiazoles naturally occurring in food flavors and model systems were reviewed. Physico-chemical data (Kovats indices, ir, uv, ^{1}H- and ^{13}C-nmr, ms) were also reported (102 references; Chemical Abstract, *95*, 132706f).

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tified from the above foods is reported in Table 2.

As it can be seen, the parent compound, its 2-methyl-, 3-methyl-, 2-ethyl-, 2- and 3-acetyl-, 3-carboethoxy-, 2,6-dimethyl-, and 5-ethyl-2-methyl derivatives are the most often encountered.

Gas chromatographic analysis of volatile nitrogen bases of boiled beef shows the presence of pyridine at 0.9 μg/Kg meat (29). α-and β-picolines, 4-ethylpyridine, 2,5- and 2,6-dimethylpyridines were also found to be present in this aroma, in the same way as 2-propylpyridine (56) and 2-amylpyridine (132). Pyridine and 3-methylpyridone were found in cooked meat (96). So far, 16 pyridines from which six 2-alkylpyridines (R = CH_3, C_2H_5, C_3H_7, C_4H_9, C_5H_{11}, C_6H_{13}) were identified in cooked lamb and mutton (7). Some of them were reported in fish (141) and caviar (27).

The parent compound was also isolated from many other food systems including: eggs (49), artichoke (8), asparagus (111), dry red beans (6), beetroots (82), roasted onion (54), baked potatoes (89), potato chips (4), tomatoes (44, 138), popcorn (129), pecan (131), tea (128), beer (32), rum (137), whiskey (75, 133). Its 2-methyl homologue was identified in about the same flavors. 3-Methylpyridine was found to be present in the flavor of beef (29), fish (141), lamb (7), bread (34, 142), rice (139), cheese (71), coffee (126), tea (128), rum (137), whiskey (75, 133) and soyu (77). 3-Butylpyridine was recently reported in an oil of poultry byproduct flavor (30).

2-Acetylpyridine is an important component of potato chips (4), roasted barley (33), roasted filberts (93), roasted peanuts (130), cocoa (140), coffee (126), tea (128) and beer (32). It was recently discovered in the same way as 2-aminopyridine from baked potatoes (9). The 3-acetyl isomer was isolated from white bread (20), roasted filberts (93), coffee (126), beer (32) and tobacco (91). Among 3-substituted pyridines, 3-carbomethoxy-pyridine (or methyl

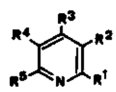
Table 1. Food and Related Systems in which Pyridines have been Identified

Category	Reference(s)
1. Fish, Meat & Poultry Products	
1 Beef (cooked)	29, 52, 56, 132
2 Caviar	27
3a Chicken (heated)	37
3b Eggs	49
4 Fish	141
5 Lamb fat (roasted)	7
6 Meat (cooked)	96
7 Pork	106
8 Poultry byproduct (oil of)	30
2. Vegetables & Allium Species	
9 Artichoke	8
10 Asparagus	111
11 Beans (dry red)	6
12 Beetroots	82
13 Leek	92
14 Onion (roasted)	54
15 Potatoes (baked)	5, 9, 90
16 Potato chips	4
17 Tomatoes	11, 43, 138
3. Cereals & Related Products	
18 Barley (roasted)	33, 100
19 Bread (white)	20, 28, 142
20 Corn (frozen)	3
21 Popcorn	129
22a Rice (cooked)	139
22b Rice bran	115
22c Rice (wild grain)	136
4. Nut Products	
23 Almonds (roasted)	108
24 Filberts (roasted)	93
25 Peanuts (roasted)	130
26 Pecans (roasted)	131
27 Soya bean	1
5. Milk & Dairy Products	
28 Casein	17, 18
29 Cheese	70
30 "Gruyere de Comte" cheese	13, 14
6. Fruits	
31 Artic bramble	45
32 Soursop (Annona muricata)	53
33 Strawberry	86
34 Tamarind	55
7. Spices & Condiments	
35 Pepper (black)	10, 110
36 Trassi (cooked)	102
8. Non-Alcoholic Beverages	
37 Cocoa	
38 Coffee	22-26, 87, 125, 126
39 Tea	128
9. Alcoholic Beverages	
40 Beer	38, 112
41 Rum	137
42 Whiskey	75, 133, 137
10. Tobacco	
43 Burley tobacco	31, 44, 74, 104
11. Essential Oils	
44a Jasmine	109
44b Orange flowers	89
44c Patchouli	34
44d Peppermint oil	107
12. Miscellanous	
45 Phaseolus aureus (roasted)	116
46 Soyu	77

nicotinate) is another important flavoring agent. It was observed in roasted filberts (93), roasted peanuts (130), soursop (57), strawberry (86), coffee (126) and jasmine (109). Its higher homologue was reported in artic bramble (45), beer (112), jasmine (109) and shoyu (77). Another widely distributed compound is 2,6-dimethylpyridine. It was found in beef (29), bread (28, 142), coffee (126), tea (128), whiskey (75), tobacco (91) and shoyu (77).

Among other disubstituted pyridines identified in foodstuffs 2-methyl-5-ethylpyridine was mentioned in lamb (7), dry red beans (6), cheese (36), cocoa (127), tea (128) and whiskey (75).

Table 2. Pyridine Compounds in Food Flavors, Tobacco and Essential Oils



1

Name	Occurrences[a)]	Flavor Description (85, 134, 135)
Pyridine	1, 2, 3b, 4, 5, 6, 9, 10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22a, 22b, 25, 26, 29, 37, 38, 39, 40, 41, 42, 43, 46	-
2-Methylpyridine	1, 2, 3a, 3b, 4, 5, 6, 7, 14, 18, 19, 22a, 25, 29, 37, 38, 39, 40, 41, 42, 43	Popcorn, astringent, hazelnut
2-Ethylpyridine	1, 5, 10, 14, 36, 38, 39, 42, 43, 46	Green
2-Propylpyridine	1, 5, 6	Sweet, green
2-Isopropylpyridine	42	Green, vegetable
2-Butylpyridine	5	-
2-Isobutylpyridine	Not reported	Green pepper
2-Pentylpyridine	1, 5, 24, 25	Fatty, tallowy-like
2-Hexylpyridine	5	-
2-Benzylpyridine	Not reported	Green, astringent
2-Acetonylpyridine	Not reported	-
2-Allylpyridine	Not reported	Green, melon-like
2-Vinylpyridine	43	Green
2-Propen-1-ylpyridine	Not reported	Green, burnt, coffee-like
2-(Hydroxymethyl)pyridine	Not reported	Roasted, moldy
(2-Pyridyl)methanethiol	Not reported	Roasted, pork-like (16), popcorn, nutty, caramel, cereal
2-(2'Pyridyl)ethanethiol	Not reported	Roasted, astringent, earthy
2-(2'Pyridylmethyl)methyl sulfide	Not reported	Bitter, green, earthy
2-(2'Pyridylethyl)ethyl sulfide	Not reported	Astringent, fatty, green
2-Formylpyridine (or pyridine-2-carboxaldehyde)	19	Caramel, fatty
2-Acetylpyridine (or 2-pyridylmethyl ketone)	5, 15, 16, 18, 19, 24, 25, 37, 38, 39, 40, 43	Roasted, coffee-like
2-Propionylpyridine	18	-
(1-Oxoprop-2-enyl)pyridine	18	-
2-Aminopyridine	15	-
2-Phenylpyridine	39, 43	-
3-Methylpyridine (or Beta-picoline)	1, 4, 5, 19, 22a, 22b, 29, 38, 39, 41, 42, 43, 46	Green, earthy, hazelnut
3-Ethylpyridine	5, 38, 39, 43, 44	Buttery, green, caramel
3-Propylpyridine	-	-
3-Butylpyridine	8, 39	-
3-Pentylpyridine	5	-
3-(Hydroxymethyl)pyridine	-	Bitter, green
3-Vinylpyridine	37, 43, 44	-
3-Formylpyridine	43	-
3-Acetylpyridine	19, 24, 38, 40, 43	Burnt, roasted
3-Propionylpyridine	18, 43	-
3-Butyrylpyridine	43	-
3-Carbomethoxypyridine (or methyl nicotinate)	24, 25, 32, 33, 38, 44	-
3-Carboethoxypyridine (or ethyl nicotinate)	31, 40, 44, 46	-

Table 2 Continued

3-Phenylpyridine	37	-
3-Cyanopyridine	43	-
3-Hydroxymethylpyridine		Bitter, green
3-Aminomethylpyridine	43	-
3-Hydroxypyridine	18, 43	-
3-Methoxypyridine	39, 46	-
3-Pyridylpropionate	24, 25	-
4-Methylpyridine	12, 19, 22b, 42, 43	Green
4-Ethylpyridine	1, 19	-
4-Isobutylpyridine	-	Fatty
4-Benzylpyridine	-	Bitter
4-Vinylpyridine	38, 39	-
4-Propen-1-ylpyridine	-	Green, fruity, strawberry-like
4-Formylpyridine	-	Fruity
4-Acetylpyridine	-	Burnt, coffee-like
2,3-Dimethylpyridine	19, 43	Roasted, rubbery
3-Phenylmethylpyridine	37	-
3-Methyl-2-pyridone	1	-
2-Propyl-3-methoxypyridine	30	-
2-Isobutyl-3-methoxypyridine	-	Green pepper
2,4-Dimethylpyridine	19, 22b, 43	Green
4-Phenyl-2-pyridone	34	-
2,5-Dimethylpyridine	1, 5, 42	Roasted, green, earthy
5-Ethyl-2-methylpyridine	5, 11, 30, 37, 39, 42	Fatty, green
2-Ethyl-5-methylpyridine	-	Winey, buttery, caramel, cereal-like
5-Isopropyl-2-methylpyridine	43	-
5-Acetyl-2-methylpyridine	43	-
2-Methyl-5-phenylpyridine	43	-
5-Cyano-2-methylpyridine	43	-
5-Methyl-2-phenylpyridine	5	-
5-Ethyl-2-pentylpyridine	5	-
2,6-Dimethylpyridine	1, 19, 22b, 38, 39, 42, 43, 46	Green
6-Ethyl-2-methylpyridine	39	
2-Acetyl-6-methylpyridine	-	Chocolate-like
2-Acetyl-6-prop-2-ylpyridine	23	-
2,6-Diacetylpyridine	-	Bitter, coffee-like
6-Methylpyridine-2-carboxaldehyde	-	Caramel, fruity
3,4-Dimethylpyridine	22b, 43	Green, almond-like
3-Ethyl-4-methylpyridine	44	Sweet, nutty
Methyl-4-methyl nicotinate	44	-
4-Methyl-3-vinylpyridine	44	-
3-Hydroxy-6-methylpyridine	43	-
3,5-Dimethylpyridine	5, 22b, 43	Green, fatty, roasted
Methyl-5-ethyl nicotinate	44	-
Ethyl-5-ethyl nicotinate	44	-
Methyl-5-vinyl nicotinate	44	-
Ethyl-5-vinyl nicotinate	44	-
2,4,5-Trimethylpyridine	43	-
2-Ethyl-3,5-dimethylpyridine		-
2,4-Dimethyl-5-isopropyl-pyridine	43	-
2,4-Dimethoxy-3-hydroxy-pyridine	23	-
2-Methoxy-3-hydroxy-4-formyl-	23	-
Trimethylpyridine	30	-
2,3,6-Trimethylpyridine	43	-
2,4,6-Trimethylpyridine	43	-
Dimethylcyanopyridine	43	-
Methyl-4-methyl-5-ethyl nicotinate	44	-
Methyl-4-methyl-5-vinyl nicotinate	44	-
Ethyl-4-methyl-5-ethyl nicotinate	44	-

a) For food systems meaning and the corresponding references, see Table I.

Numerous variously substituted pyridines containing alkyl- phenyl-, cyano-, acetyl-, hydroxy- and heteroaryl groups also occur in tobacco (74, 91). Several heteroarylpyridines *2* to *7* patented as tobacco flavoring compounds (40, 41, 42, 72, 140) are listed in Figure 1.

Four alkylated pyridines and ten alkyl substituted nicotinates were found in the basic fraction of the Chinese jasmine (109). Relatively few reduced pyridines occur in processed foods. One of the most important products of this category is 2-acetyl-1,4,5,6-tetrahydropyridine *8* which has a characteristic bread crust aroma (38, 39). *N*-alyl-5,6-dihydro-2-pyridinones *9*, some monoalkylpiperidines *10*, the four dimethylpyridines isomers, 2-piperidinone (*11;* R = H) and its methyl derviative (*11;* R = CH_3) were reported in tobacco (91) (See Figure 2).

N-Nitrosopiperidine found in cured meat is formed during the cooking of meats (15). Hexahydropyridine or piperidine is a component of black pepper (110), fish (141), caviar (27) and soya bean (1) flavors. It is used as flavoring additives in nonalcoholic beverages, meats, soups, and baked goods. Piperine *12* is another important component of black pepper where it accounts for 33 to 35% of the extracts. *N*-Formylpiperidine, dihydropiperidine, isopiperine and piperanine are other components of this spice (10, 109). 1-Ethylpiperidine has been found in a

Figure 1. Heteroarylpyridines found in tobacco (2) or patented as tobacco flavoring compounds (3-7).

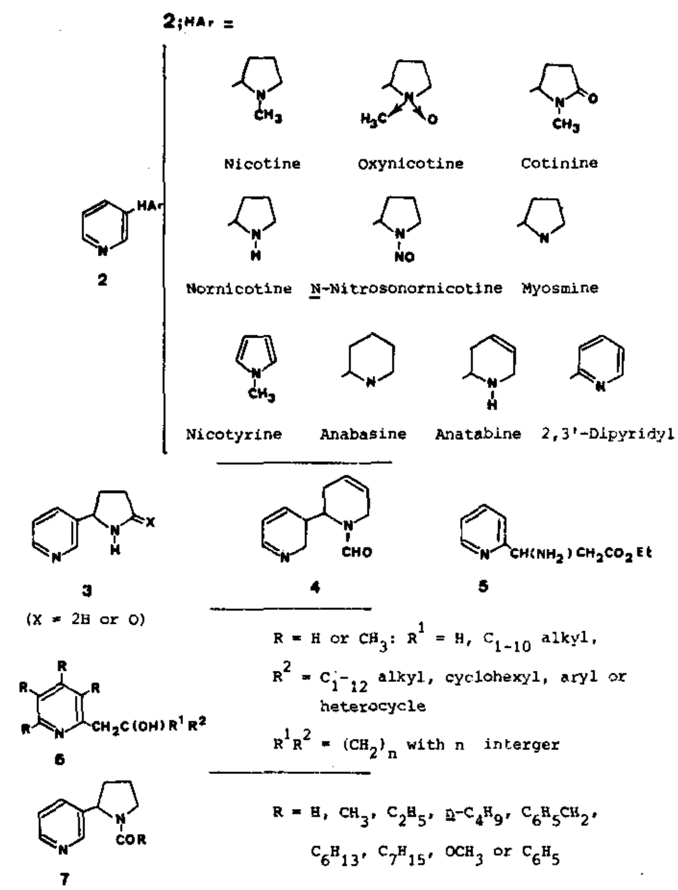
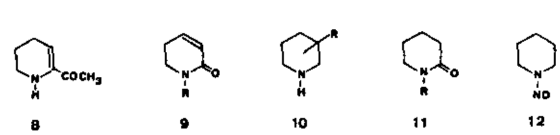


Figure 2



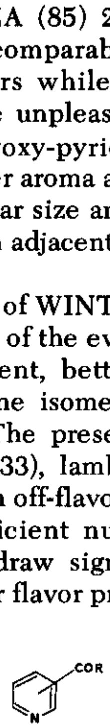
fish flavor (141).

2. Olfactory Properties

Few organoleptic data are available for food-associated pyridines (see Table 2). According to PITTET & HRUZA (85) 2-alkylpyridines as their structurally comparable 2-alkylthiazoles possess green odors while 2-alkoxypyridines were found to have unpleasant phenolic odors. 2-Isobutyl-3-methyoxy-pyridine has a characteristic green pepper aroma as other heterocyclic compounds of similar size and bearing the same functional groups in adjacent position to the ring nitrogen.

From the patents of WINTER *et al.* (134, 135) it appears that most of the evaluated compounds had green, astringent, better earthy or burnt notes. Acetylpyridine isomers had roasted and coffee-like odors. The presence of pyridine in some foods: beer (33), lamb (7) should be responsible for certain off-flavors (12).

However, insufficient number of pyridines were available to draw significant conclusions with regards to their flavor properties.



13

Odor qualities of some alkylpyridyl ketones (*13:* R = CH_3, C_2H_5, n-C_3H_7) were evaluated and structure-activity relations were investigated by SOUTHWICK & SCHIFFMAN (103).

The odor properties did not correlate significantly with the partition coefficients between octanol and water or with a measure of column retention used in high pressure liquid chromatography (HPLC). However, they were correlated with ^{13}C-NMR measurements of the chemical shift of the carbonyl carbon and with mass spectral fragmentation data.

The 2-pyridyl ketones had the greatest odor intensity and appeared to differ qualitatively from their 3- and 4- isomers.

Olfactory detection threshold using pyridine was reported by PERRY et al. (83). The normal range of olfactory thresholds were established for pyridine along with age-related changes in detection. The most diluted solution detected was recorded as minimally perceptible odor (MPO). The mean MPO was $10^{-9.4}$ M which increased with each successively older group (0—15, 16—30, 31—60 and > 60 years old). The ability to detect pyridine with a patient's increasing age suggests MPO should be evaluated on the appropriate age-related curve to determine any abnormal deficiencies.

Owing to their organoleptic properties certain pyridines are used as flavor additives in USA (88) and in the European Community (71) (See Table 3).

III—PYRIDINES IN MODEL SYSTEMS

So far, relatively few pyridines have been found in model systems (see Table 4).

Pyridine and its 2- and 3-methyl derivatives were found by KATO et al. (47) by heating glucose and cysteine at 160°C. Replacing cysteine by cystine, pyridine, 3-methylpyridine and 2-methyl-5-ethylpyridine were observed. The latter compound is also formed when paraldehyde is reacted with ammonia at 200°C (76). TRESSL et al. (113) reacting proline with glucose at 250°C for 2 h. identified a series of 2-substituted pyridines (R = H, CH_3, C_2H_5, CHO) in the same way as 3-methyl- and 2,3-dimethylpyridines. Pyrolysis of a melanoidin resulting from a glucose—ammonia reaction produces pyridine, 2-methylpyridine, 3-hydroxypyridine and 2-methyl-5-hydroxypyridine (114). 2-Hydroxypyridine formation in glucose—hydrogen sulfide—ammonia system was reported by SHIBAMOTO & RUSSELL (94).

A methylpyridine was the only pyridine derivative identified among the thermal degrada-

Table 3. Pyridines Used as Flavorants[a]

	Lists		
Name	FEMA[b]	COE	IOFI[c]
Pyridine	2966	604	2
2-Ethylpyridine	-	+	-
3-Ethylpyridine	3394	-	-
2-Pentylpyridine	3383	-	2
2-Isobutylpyridine	3370	-	2
3-s-Butylpyridine	3371	-	-
2-Acetylpyridine	3251	+	2
2-Pyridinemethanethiol	3232	2279	-
2-Pyridylmercaptan	-	+	-
3-Methylpyridine	-	+	-
2-Ethylpyridine	3394	-	2
3-Isobutylpyridine	3371	-	2
3-Acetylpyridine	3424	-	2
2,6-Dimethylpyridine	3540	-	2
5-Ethyl-2-methylpyridine	3546	-	-
Piperidine	2908	675	2
Piperine	2909	492	2

a) Reference list from Flavor Materials (88);
(-) means a compound which is not listed;
(+) means a listed compound.

b) Average usage ranged from 0.1 to 10 ppm level.

c) International Organization of Flavor Industries list.

Pyridine and Derivatives

Table 4. Pyridines in Model Systems

Compound	Model System(s)
Pyridine	a, b, d, e, p, u, v
2-Methylpyridine	a, c, d, e, m, p, q, u, v
2-Ethylpyridine	d
2-Acetonylpyridine	g
2-Formylpyridine	d, q
2-Acetylpyridine	e, f, r
2-Hydroxypyridine	t
3-Methylpyridine	a, b, d, o, p, q, r, v
3-Vinylpyridine	v
Methyl nicotinate	p
3-Hydroxypyridine	u
4-Methylpyridine	p, v
4-Ethylpyridine	p
2,3-Dimethylpyridine	d
2,5-Dimethylpyridine	k
2-Methyl-5-ethylpyridine	b, c, n
2-Methyl-5-hydroxypyridine	u
2-Ethyl-5-methylpyridine	l, m
2-Amino-5-methylpyridine	g
2,6-Dimethylpyridine	i
3,4-Dimethylpyridine	i, k, p
3-Ethyl-4-methylpyridine	p
Di-(N-methylcarboxamido)-3,4-pyridine	p
3,5-Dimethylpyridine	j, o
2,3,5-Trimethylpyridine	o
2-Ethyl-3,5-dimethylpyridine	j
2-Ethyl-3-hydroxy-6-methylpyridine	h
3,5-Dimethyl-2-ethylpyridine	j

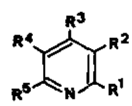
Model Systems:
a = glucose-cysteine (47)
b = glucose-cystine (47)
c = ribose-cysteine/cystine (73)
d = glucose-*L*-proline (36, 113)
e = lactose-casein (17, 18)
f = AMADORI intermediates from glucose-glycine system (80)
g = *L*-rhamnose-ammonia (95)
h = maltol-ammonia (97)
i = furfural-ammonium sulfide (123)
j = glycine-propanal (105)
k = glycine-propanal-crotonal (105)
l = pyrolysis of cysteine (48)
m = hydrolysis of cysteine (48)
n = pyrolysis of alpha-alanine (58)
o = pyrolysis of beta-alanine (58)
p = thermal degradation of trigonelline (124)
q = furfural-hydrogen sulfide-ammonia (2, 84)
r = glucose-alanine (98)
s = paraldehyde-ammonia (76)
t = glucose-hydrogen sulfide-ammonia (94)
u = glucose-ammonia (114)
v = collagen pyrolysis (35)

tion products of 1-deoxy-1-*L*- alanino-*D*-fructose (99).

2-Acetylpyridine formation was observed in the degradation reaction of the rearrangement product (RP) from glucose-glycine system (80). 2-Amino-5-methylpyridine and 2-acetonylpyridine were identified by reacting *L*-rhamnose with ammonia (95). 3,5-Dimethyl-2-ethylpyridine, 3,5-dimethyl-4-ethylpyridine and 3,5-dimethylpyridine were formed by heating the quaternary pyridinium betaines. Pyridinium salts were themselves prepared from the condensation reaction of glycine with propanal (105). Similarly, the thermal decomposition of the condensation products from the glycine-propanal- crotonal system affords 2,5- and 3,5-dimethylpyridine isomers among other unidentified compounds. The lactose-casein browning system investigated by **FERRETTI et al.** (17, 18) also showed the presence of pyridines, namely pyridine and its 2-methyl- and 2-acetyl derivatives.

Recently, SHIBAMOTO et al. (97) observed

Table 5. Pyridines Predicted by the Computer for the Reaction Between Furfural and Ammonia (2,84)



R^1	R^2	R^3	R^4	R^5
OH	OH	H	CH_3	H
OH	CH_3	H	OH	H
CHO	H	H	OH	H
CHO	H	H	H	OH
H	CHO	H	H	OH
H	CHO	H	OH	H
CH_3	H	H	OH	OH
CH_3	OH	H	OH	H
H	OH	OH	CHO	H
CHO	OH	H	OH	H
CHO	H	H	OH	OH
CHO	H	OH	OH	H
CHO	H	OH	H	OH
OH	H	OH	CHO	H
OH	OH	H	CHO	H
CHO	OH	OH	H	H
CH_2OH	OH	OH	OH	H
CH_2OH	H	OH	OH	OH
CH_2OH	OH	H	OH	OH
CH_2OH	OH	OH	H	OH
CH_3	H	H	H	H
H	CH_3	H	H	H
CH_3	H	H	OH	H
H	CH_3	H	OH	H
H	CH_3	OH	H	H
CH_3	H	OH	H	H
CH_3	OH	H	H	H
OH	H	H	CH_3	H
CHO	H	H	H	H
CH_2OH	H	H	H	H

the formation of 2-ethyl-3-hydroxy-6-methylpyridine during the thermal reaction of maltol and ammonia. *N*-Ethyl-3-hydroxy-2-pyridinone and *N*-ethyl-2,6-dioxopiperidine were found by OUWELAND **et al.** (80). during wet and dry degradation of the RP of glucose-theanine system, respectively, 2,6-Dimethyl- and 3,4- (or 3,5)-dimethylpyridines were found by reacting furfural with ammonium sulfide (123).

Pyrolysis of sulfur-containing amino acids alone (48) or in presence of glucose (47) produces certain pyridines. Analogously other amino acids such as α- and β-alanine (58) alone or in presence of glucose (or dicarbonyl compounds) give pyridines. 2-Methylpyridine and 2-methyl-5-ethylpyridine were identified in a pentane-ether extract of the cysteine/cystine-ribose browning system (73).

The thermal degradation of trigonelline is also a source of pyridines, mainly in coffee. Recently, PARIHAR **et al.** (81) reported that model systems containing sesame oil and amino acids formed pyridines and pyrazines during heating. This reaction was catalyzed by Fe and Cu.

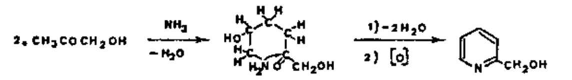
Some pyridine derivatives have been reported among pyrolysis products of collagen (35), chondroitin sulfate (46) and pyridine itself (53). In this latter case, bipyridyl isomers were formed.

Finally, a great number of pyridines, mainly substituted by hydroxyl and formyl groups have been predicted by the computer in the reaction between ammonia and furfural (or its degradation products) (2, 84) (see Table 5).

IV—PYRIDINES FORMATION

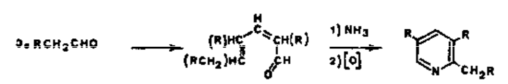
It seems evident from the above results that pyridines are mainly formed in processed foods from carbonyl compounds and ammonia arising from reducing sugars and amino acids. Indeed, their formation from aldehydes, ketones, α,β-unsaturated carbonyl compounds with ammonia (The CHICHIBABINE pyridine condensation) is a well known reaction in organic chemistry (101). All these starting materials were formed during MAILLARD reactions: aldehydes arise from STRECKER degradation of α-amino acids, α-dicarbonyl compounds (glyoxal, pyruvaldehyde, diacetyl . . .) and α-hydroxycarbonyl compounds from retroaldolisation of rearranged AMADORI or HEYNS intermediates, α,β-unsaturated aldehydes from aldol condensation, and ammonia from thermal degradation of amino acids.

Thus 2-hydroxymethylpyridine can be obtained by reacting hydroxyacetone with its enol form, in the presence of ammonia according to the following scheme:



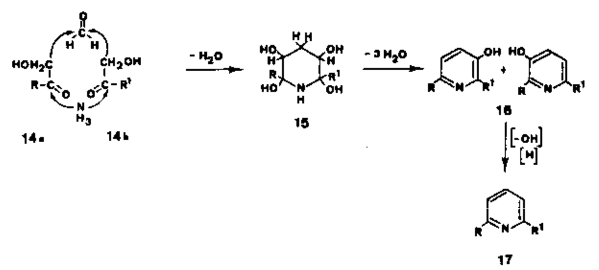
SCHEME 1. Supposed 2-Hydroxymethylpyridine Formation

Trimerisation of aldehydes (R = H or CH_3) produces α,β-unsaturated carbonyl compounds which react with ammonia to give after dehydration and oxidation 2-methylpyridine (R = H) or 3,5-dimethyl- 2-ethylpyridine (R = CH_3) (see Scheme 2).



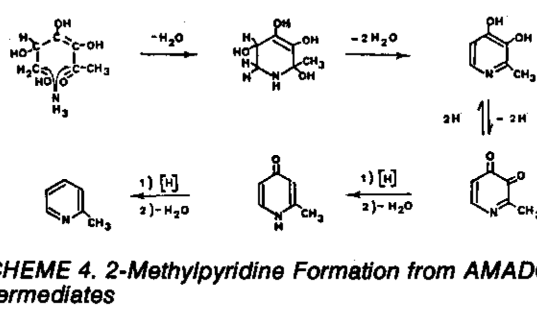
SCHEME 2. Hypothetical 2-Methyl (R = H) and 3,5-Dimethyl-2-Ethylpyridine (R = CH_3) Formation from Aldehydes

By condensing hydroxyketones *14a* and *14b* in the presence of formaldehyde and ammonia, the piperidine derivative *15* was obtained. By dehydration, this latter compound affords the two hydroxypyridine isomers *16* which by dehydroxylation and reduction can lead to 2,6-disubstituted pyridines *17* (see Scheme 3).



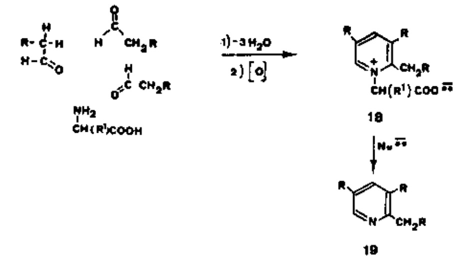
SCHEME 3. Hypothetical 3-Hydroxypyridines Formation

2-Methylpyridine formation from AMADORI Intermediates is shown in Scheme 4.



SCHEME 4. 2-Methylpyridine Formation from AMADORI Intermediates

The formation of variously substituted pyridines from aldehydes and amino acids can be explained by the mechanism shown in Scheme 5 (105).

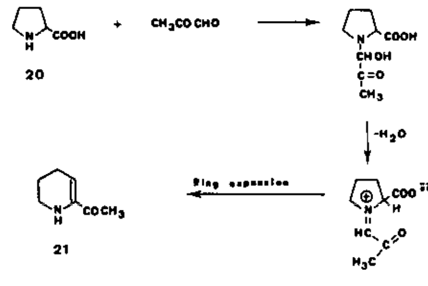


SCHEME 5. Pyridines Formation from Aldehydes and Amino Acids

The last step of the reaction leading to pyridines *19* from betaines *18* is probably a radical nucleophilic displacement ($S_{RN}2$) similar to that reported by KATRITZKY **et al.** (50) for 1-alkyl-2,4,6-triphenylpyridiniums C-alkylate nitroalkane anions. Indeed, pyridiniums are expected to give charge-transfer complexes (CTC) with soft nucleophiles. The electron-transfer processes interconverting pyridiniums and pyridinyls are known to be easy.

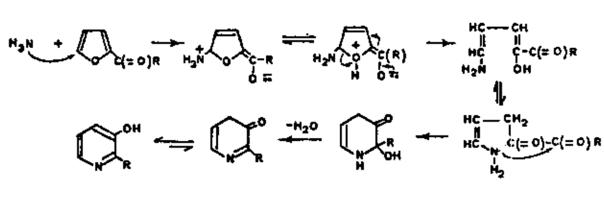
Some pyridines are also formed from cyclized products.

The formation of 2-acetyltetrahydropyridine *21* from proline *20* and pyruvaldehyde has been reported by NURSTEN **et al.** (78) (see Scheme 6).



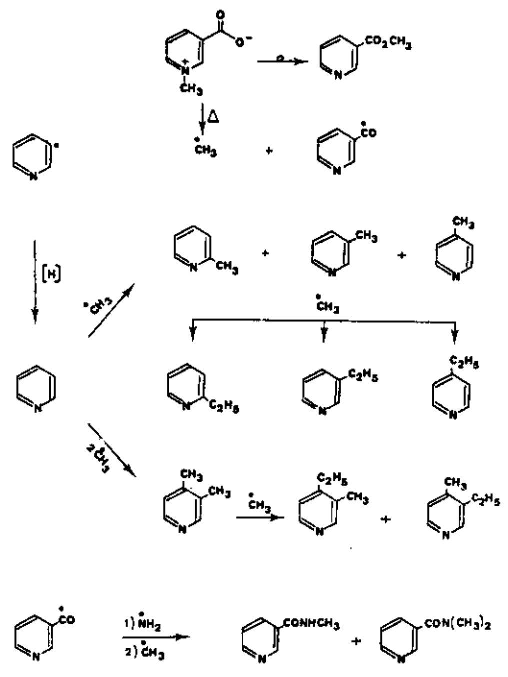
SCHEME 6. 2-Acetyltetrahydropyridine Formation (78)

Furfural or 2-acetylfuran and ammonia can also act as precursors of 3-hydroxypyridines as shown in Scheme 7 (121).



SCHEME 7. 3-Hydroxypyridines Formation from Furfural or 2-Acetylfuran and ammonia (121).

The thermal degradation of trigonelline produces several mono- and dialkylated pyridines. They are probably formed according to a radicalar mechanisms similar to that of the LADENBOURG rearrangement of *N*-alkylpyridinium salts (see Scheme 8)



SCHEME 8. Pyridines Formation from Trigonelline (118)

Pyridines in foods are also formed by many other ways. Heat treatment of certain heterocyclic compounds such as furfurylamine, tetrahydrofurfuryl alcohol, *N*-substituted pyrroles, oxazoles, thiazoles leads to pyridine derivatives (122).

REFERENCES

1. Aria, S., Koyanagi, O. & Fujimaki, M., Agric. Biol. Chem., **31**, 868 (1967).
2. Barone, R., Chanon, M., Vernin, G., Petitjean, M. & Metgzer, J., Parf. Cosm. Arômes, **38**, 71 (1981).
3. Boyko, A. L., Morgan, M. E. & Libbey, L. M., in "Anal. Foods & Beverages" Proc. Symp. 1977 (Publ. 1978), pp. 57-78 (Charalambous, G. Ed.), Academic Press, New York.
4. Buttery, R. G., Seifert, R. M. & Ling, L. C., J. Agric. Food Chem., **18**, 538 (1970); ibid., **19**, 969 (1971).
5. Buttery, R. G., Guadagni, D. G. & Ling, L. C., J. Sci. Food Agric., **24**, 1125 (1973).
6. Buttery, R. G., Seifert, R. M. & Ling, L. C., J. Agric. Food Chem., **23**, 516 (1975).
7. Buttery, R. G., Ling, L. C., Teranishi, R. & Mon, T. R., J. Agric. Food Chem., **25**, 1227 (1977).
8. Buttery, R. G., Guadagni, D. G. & Ling, L. C., J. Agric. Food Chem., **26**, 791 (1978).
9. Coleman, E. C., Chi Tang Ho, & Chang, S. S., J. Agric. Food Chem., **29**, 42 (1981).
10. Debrauwere, J. & Verzele, M., Bull. Soc. Chim. Belges, **84**, 167 (1975).
11. Dirinck, P., Scheyen, L. & Schamp, N., J. Agric. Food Chem., **25**, 759 (1977).
12. Dravnieks, A., McDaniel, H. C. & Powers, J. J., J. Agric. Food Chem., **27**, 336 (1979).

13. Dumont, J. P., Roger, S. & Adda, J., Le Lait, **54**, 31, 386 (1974); ibid., **55**, 479 (1975).
14. Dumont, J. P. & Adda, J., J. Agric. Food Chem., **26**, 364 (1978).
15. Eisenbrand, G., Jankowski, C. & Preussmann, R., "Proc. Intern. Symp. Nitrite Meat Products" (Tinbergen, B., Krol, B. Eds.), 2nd, 1976, 155 (Publ. 1977).
16. Feldman, J. R. & Berg, J. H., U.S. Pat., 3.803.330 (1974).
17. Ferretti, A., Flanagan, V. P. & J. M. Ruth, J. Agric. Food Chem., **70**, 13 (1970).
18. Ferretti, A. & Flanagan, V. P., J. Agric. Food Chem., **19**, 245 (1971).
19. Flament, I., in "Proc. Intern. Symp. Aroma Research", Zeist, Pudoc, Wageningen (1975).
20. Folkes, D. J. & Gramshaw, J. W., J. Food Technol., **12**, 1 (1977).
21. Folkes, D. J. & Gramshaw, J. W., in "Maillard Reactions in Food, Chemical, Physiological and Technological Aspects" (C. Eriksson Ed.), Pergamon Press, Oxford (1982) (in press).
22. Gianturco, M. A., Giammarino, A. S. & Pitcher, R. G., Tetrahedron, **19**, 2051 (1963).
23. Gianturco, M. A., Friedel, P. & Giammarino, A. S., Tetrahedron, **20**, 1763 (1964).
24. Gianturco, M. A., Giammario, A. S., Friedel, P. & Flanagan, V. P., Tetrahedron, **20**, 2951 (1964).
25. Gianturco, M. A., Giammarino, A. S. & Friedel, P., Nature, **210**, 1358 (1966).
26. Goldman, I. M., Seibl, J., Flament, I., Gautschi, F., Winter, M., Willhalm, B. & Stoll, M., Helv. Chim. Acta., **50**, 694 (1967).
27. Golovnya, R. V., Ernaehrungforschung, **15**, 333 (1970); Golovnya, R. V., Mironov, G. A. & Zhuraveleva, I. L., Zh. Anal. Chem., **22**, 612, 956 (1967).
28. Golovnya, R. V., Nahrung, **18**, 143 (1974).
29. Golovnya, R. V., Zhuravleva, I. L. & Kapustin, Yu.P., Chem. Senses Flavour, **4**, 97 (1979).
30. Greenberg, M. J., J. Agric. Food Chem., **29**, 831 (1981).
31. Grob, K. & Vollmin, J. A., J. Chromatog. Sci., **8**, 218 (1978).
32. Harding, R. J., Nursten, H. E. & Wren, J. J., J. Sci. Food Agric., **28**, 225 (1977).
33. Harding, R. J., J. Inst. Brew. (London), **84**, 41 (1978).
34. Heide Ter, R., De Valois, P. J., Visser, J., Jaegers, P. P. & Timmer, R., "Analysis of Foods and Beverages: Headspace Techniques" (Charalambous, G., Ed.), Academic Press, New York, 1978, p. 249.
35. Higman, E. B., Schmeltz, T. & Scholtzhauer, W. S., J. Agric. Food Chem., **18**, 636 (1970).
36. Hodge, J. E., Mills, F. D. & Fisher, B. E., Cereal Science Today, **17**, 34 (1972).
37. Horvat, R. J., J. Agric. Food Chem., **24**, 953 (1976).
38. Hunter, I. R., Walden, M. K., Scherer, J. R. & Lundin, R. E., Cereal. Chem., **46**, 189 (1969).
39. Hunter, I. R. & Walden, M. K., U.S. Pat., 3.425.840 (1969); Idem., 3.620.771 (1971).
40. Japan Tobacco and Salt Public Corp., Japan Kokai Tokkyo Koho, **80**, 136, 278 (1980).
41. Japan Tobacco and Salt Public Corp., Yuki. Gosei Kogyo Co. Ltd., Fuji Flavor Co. Ltd., Japan Tokkyo Koho., 8103, 027 (1981).
42. Japan Tobacco and Salt Public Corp., Japan Kokai Tokkyo Koho, 8145, 143 (1981).
43. Johnson, A. E., Nursten, H. E. & Williams, A. A., Chem. Ind. (London), 1971, 1212.
44. Kabukari, Y., Mikami, Y., Saida, Y., Yoriko, S. & Nakamura, M., J. Agric. Chem. Soc. (Japan), **47**, 799 (1973).
45. Kallio, H., J. Food Sci., **41**, 555 (1976).
46. Kang, J. C., Kornfeld, R. A., Newman, R. H. & Johnson, W. R., J. Agric. Food Chem., **28**, 992 (1980).
47. Kato, S., Kurata, T. & Fujimaki, M., Agr. Biol. Chem., **37**, 539 (1973).
48. Kato, S., Kurata, T. & Fujimaki, M., Agr. Biol. Chem., **37**, 1759 (1973).
49. Kato, Y., Watanabe, K. & Sato, Y., Lebensm.-Wiss. Technol., **11**, 128 (1978).
50. Katritzky, A. R., De Ville, G. Z. & Patel, R. C., Tetrahedron letters, 1980, 1723.
51. Kinlin, T. E., Muralidhara, R., Pittet, A. O., Sanderson, A. & Walradt, J. P., J. Agric. Food Chem., **20**, 1021 (1972).
52. Koelher, P. E., Sason, M. E. & Newell, J. A., J. Agric. Food Chem., **17**, 393 (1969); Idem., J. Food Sci., **36**, 816 (1971).
53. Krumholz, P., Sel. Chim., **8**, 3 (1949).
54. Ledl, F., Z. Lebensm. Unters.-Forsch., **157**, 229 (1975).
55. Lee, P. L., Swords, G. & Hunter, G. L. K., J. Agric. Food. Chem., **23**, 1195 (1975).
56. Leod Mc, G. & Coppock, B. M., J. Agric. Food Chem., **24**, 835 (1976).
57. Leod Mc, A. J. & N. M. Pieris., J. Agric. Food. Chem., **29**, 488 (1981).
58. Lien, Y. C. & Nawar, W. W., J. Food Sci., **39**, 914 (1974).
59. Maga, J. A. & Sizer, C. E., J. Agric. Food Chem., **21**, 22 (1973).
60. Maga, J. A. & Sizer, C. E., in "Fenaroli's Handbook of Flavor Ingredients" (Furia, T. E. & Bellanca, N., Eds.), 2nd Ed. p. 47 (1975).
61. Maga, J. A., CRC Crit. Rev. Food Sci. Nutr., 1975, 241.
62. Maga, J. A., CRC Crit. Rev. Food Sci. Nutri., 1975, 153.
63. Maga, J. A., in "Fenaroli's Handbook of Flavor" (Furia, T. E. & Bellanca, N. Eds.), CRC Press, Cleveland, OH, Vol. **1**, 228 (1975).
64. Maga, J. A., CRC Crit. Rev. Food Sci. Nutr., **8**, 1 (1976).
65. Maga, J. A., J. Agric. Food Chem., **26**, 1049 (1978).
66. Maga, J. A., CRC Crit. Rev. Food Sci. Nutr., **11**, 355 (1979).
67. Maga, J. A., CRC Crit. Rev. Food Sci. Nutr., **14**, 295 (1981).
68. Maga, J. A., J. Agric. Food Chem., **29**, 691 (1981).
69. Maga, J. A., J. Agric. Food Chem., **29**, 895 (1981).
70. Magak' Yan., Prikl. Biokhim. Mikrobiol., **12**, 253 (1976).
71. "Matières Aromatisantes Naturelles, leurs Sources et les Matières Aromatisantes Artificielles Ajoutées," Strasbourg, 1973, Ed. Maisonneuve, 1974.
72. Matsushita, H., Noguchi, M., Kisaki, T., Kata, K., Tsujino, Y. & Saito, A., Japan Kokai Tokkyo Koho, 80,19,076 (1980); Idem., 79,151,980 (1979).
73. Mulders, E. J., Z. Lebensm. Unters.-Forsch., **152**, 193 (1973).
74. Neurath, G. B., Beitr. Tabakforsch., **5**, 515 (1969).
75. Nishimura, K. & Masuda, M., J. Food Sci., **36**, 819 (1971).
76. Noller, C. R., "Chemistry of Organic Compounds", (Saunder, W. B., Ed.), Philadelphia, PA, 1957 p. 627.
77. Nunomura, N., Sasaki, M. & Yokotsuka, T., Agric. Biol. Chem., **42**, 2123 (1978).
78. Nursten, H. E., Food Chemistry, **6**, 263 (1981); Idem., in "Maillard Reactions in Food, Chemical, Physiological and Technological Aspects (C. Eriksson, Ed.), Pergamon Press, Oxford.
79. Ohloff, G. & Flament, I., in "Progress in the Chemistry of Organic Natural Products", Springer-Verlag, Wien, New York, 1980, pp. 231-283.
80. Ouweland Van Den, G. A. M., Peer, H. G. & Tjan, S. B., in "Flavor of Food and Beverages" (Charalambous, G. & Inglett, G. E., Eds.), Academic Press, New York, 1978, pp. 131-144.
81. Parihar, D. B., Vasundhara, T. S. & Vijayayaghavan, P. K., J. Food. Technol., **16**, 313 (1981).
82. Parliment, T. H., Kolor, M. G. & Maing, Y., J. Food Sci., **42**, 1592 (1977).
83. Perry, J. D., Frisch, S., Jafek, B. & Jafek, M., Otolaryngol. Head Neck Surg., **88**, 778 (1980).
84. Petitjean, M., Vernin, G., Metzger, J., Barone, R. & Chanon, M., in "The Quality of Foods and Beverages" (Charalambous, G. & Inglett, G. E., Eds.), Academic Press, New York, Vol **2**, 253-268 (1981).
85. Pittet, A. O. & Hruza, D. E., J. Agric. Food Chem., **22**, 274 (1974).
86. Pyysalo, T. & Honkanen, E., J. Agric. Food Chem., **19**, 27 (1979).

87. Radtke, R., Dissertation, Universität, München (1964).
88. Reference List of Flavoring Substances in Use in the United States, "Flavor Materials—1979" (FEMA Ed.), Allured Publ. Co., Wheaton, IL.
89. Sakurai, K., Toyoda, T., Muraki, S. & Yoshida, T., Agric. Biol. Chem., **43,** 195 (1979).
90. Sapers, G. M., J. Agric. Food Chem., **23,** 1027 (1975).
91. Schmeltz, I. & Hoffmann, D., Chem. Review, **77,** 295 (1977).
92. Schreyen, L., Dirinck, P., Wassenhove, Van, F. & Schamp, N., J. Agric. Food Chem., **24,** 336 (1976).
93. Sheldon, R. M., Lindsay, R. C. & Libbey, L. M., J. Food Sci., **37,** 313 (1972).
94. Shibamoto, T. & Russell, G. F., J. Agric. Food Chem., **25,** 109 (1977).
95. Shibamoto, T. & Bernhard, R. A., J. Agric. Food Chem., **26,** 183 (1978).
96. Shibamoto, T., Kamiya, Y. & Mihara, S., J. Agric. Food Chem., **29,** 57 (1981).
97. Shibamoto, T., Nishimura, O. & Mihara, S., J. Agric. Food Chem., **29,** 643 (1981).
98. Shigematsu, H., Kurata, T., Kato, H. & Fujimaki, M., Agric. Biol. Chem., **36,** 1631 (1972).
99. Shigematsu, H., Shibata, S., Kurata, T., Kato, H. & Fujimaki, M., Agric. Biol. Chem., **41,** 2377 (1977).
100. Shimizu, Y., Matsuto, S., Mizunuma, Y. & Okada, I., Eiyo to Shokuryo, **23,** 276 (1970).
101. Smith, D. M., "Rodd's Chemistry of Carbon Compounds", (Coffey, S. Ed.), Elsevier, Amsterdam, Vol **4,** 27 (1976).
102. Soedarmo Moeljohardjo, Thesis, Wageningen (1972).
103. Southwick, E. & Schiffman, S. S., Chem. Senses., **5,** 343 (1980).
104. Stoffelsma, J., Sipma, G., Kettenes, D. K. & Pypker, J., J. Agric. Food Chem., **16,** 1000 (1968).
105. Suyama, K. & Adachi, S., J. Org. Chem., **44,** 1417 (1979); Idem., J. Agric. Food Chem. **28,** 546 (1980).
106. Swain, Thesis, Missouri (1972).
107. Takahashi, K., Someya, T., Muraki, S., Yoshida, T., Kabuto, C., Ohnuma, T. & Kato, T., Agric. Biol. Chem., **44,** 1535 (1980).
108. Takei, Y. & Yamanishi, T., Agric. Biol. Chem., **38,** 2329 (1974).
109. Toyoda, T., Muraki, S. & Yoshida, T., Agric. Biol. Chem., **42,** 1901 (1978).
110. Traxler, J. T., J. Agric. Food Chem., **19,** 1135 (1971).
111. Tressl Von, R., Bahri, D., Holzner, M. & Kossa, T., J. Agric. Food Chem., **25,** 459 (1977).
112. Tressl Von, R., J. Agric. Food Chem., **26,** 1422 (1978).
113. Tressl Von, R., Grünewald, K. G., Silvar, R. & Bahri, D., in "Progress in Flavour Research" (Land, D. G. & Nursten, H. E., Eds.), Applied Science Publ. Ltd., London, 1978, pp. 193-213.
114. Tsuchida, H., Komoto, M., Kato, H., Kurata, T. & Fujimaki, M., Agric. Biol. Chem., **40,** 2051 (1976).
115. Tsugita, T., Kurata, T. & Fujimaki, M., Agric. Biol. Chem., **42,** 643 (1978).
116. Vasundhara, T. S. & Parihar, D. B., Z. Lebensm.-Unters. Forsch., **172,** 460 (1981).
117. Vernin, G., Parf. Cosm. Arômes, **29,** 77 (1979).
118. Vernin, G., Parf. Cosm. Arômes, **32,** 77 (1980).
119. Vernin, G. Riv. Ital. EPPOS., **53,** 2 (1981).
120. Vernin, G., Riv. Ital. EPPOS., **53,** 190 (1981).
121. Vernin, G. & Metzger, J., Bull. Soc. Chim. Belges, **90,** 553 (1981).
122. Vernin, G., Ed. "Heterocyclic Compounds in Food Flavours" (Ellis Horwood Publ.), Chichester, England, in press (1982).
123. Vernin, G., Unpublished results.
124. Viani, R. & Horman, I., J. Food Sci., **39,** 1216 (1974).
125. Vitzthum, O. G. & Werkhoff, P., Z. Lebensm.-Untersuch., **156,** 300 (1974).
126. Vitzthum, O. G., "Chemie und Bearbeitung des Kaffees", Springer-Verlag, Berlin (1975); Idem., Colloq. Intern. Chim. Cafes (C.R.) 7th 1975, 115.
127. Vitzthum, O. G., Werkhoff, P. & Hubert, P., J. Food Sci., **40,** 911 (1975).
128. Vitzthum, O. G., Werkhoff, P. & Hubert, P., J. Agric. Food Chem., **23,** 999 (1975).
129. Walradt, J. P., Lindsay, R. C. & Libbey, L. M., J. Agric. Food Chem., **18,** 926 (1970).
130. Walradt, J. P., Pittet, A. O., Kinlin, T. E., Muralidhara, R. & Sanderson, A., J. Agric. Food Chem., **19,** 972 (1971).
131. Wang, P. & Odell, G. V., J. Agric. Food Chem., **20,** 207 (1972).
132. Watanabe, K. & Sato, Y., J. Agric. Food Chem., **19,** 1017 (1971).
133. Williams, A. R. & Tucknott, O. G., J. Sci. Food Agric., **23,** 1 (1972).
134. Winter, M., Gautschi, F., Flament, I., Stoll, M. & Goldman, I. M., US. Pat., 3.702.253 (1972); Idem., US. Pat., 3.900.582 (1975).
135. Winter, M., Gautschi, F., Flament, I., & Stoll, M., US. Pat., 3.931.245 (1976); Idem., US. Pat., 3.931.246 (1976).
136. Withycombe, D. A., Lindsay, R. C. & Stuiber, D. A., J. Agric. Food Chem., **26,** 816 (1978).
137. Wobben, H. J., Timmer, R., Heide, R. & De Walms, P. J., J. Food Sci., **36,** 464 (1971).
138. Wobben, H. J., Proc. SOS/73 Intern. Congr. Food. Sci. Technol., 4th, 1974, 22.
139. Yajima, I. Yanai, T., Nakamura, M., Sakakihara, H. & Habu, T., Agric. Biol. Chem., **42,** 1229 (1978).
140. Youram, H. & Sanders, E. B., Eur. Pat. Appl., 15,073 (1980).
141. Zhuravleva, I. L., Prikl. Biokhim. Mikrobiol., **12,** 788 (1976).
142. Zyuz'ko, A. S., Prikl. Biokhim. Mikrobiol., **10,** 443 (1974).