Smoke Composition. An Extensive Investigation of the Water-Soluble Portion of Cigarette Smoke

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Smoke condensate from 70-mm nonfiltered cigarettes smoked under standard conditions was collected in dry ice cooled traps and partitioned between ether and water. The water-soluble portion (~38%) was chromatographed with gradient solvent systems on silicic acid to give nine fractions. Further separation of these fractions by gas chromatography permitted isolation of 479 components. Identifications of most of these components were based on IR, mass, and NMR spectra, GC retention times, and comparison of these data with those of authentic samples. Of the 479 isolates identified, 387 are reported for the first time as tobacco smoke components; these include 19 acids, 61 lactones, 32 esters, 41 amides, 21 imides, 45 aldehydes and ketones, 40 alcohols, 30 pyridine derivatives, 25 imidazoles, 31 lactams, 23 miscellaneous nitrogen heterocyclic compounds, and 14 miscellaneous compounds. These compounds, classified according to functional groups, are listed in Table II.

Considerable effort has been expended for many years to determine the composition of the particulate phase of tobacco smoke. Numerous fractionation schemes have evolved, some of which are summarized by Wynder and Hoffmann (1967). The majority of these involve a partition of the smoke condensate into a water-soluble portion and a nonaqueous soluble portion. The nonaqueous soluble portion, in general, was readily fractionated into its components. However, no work has been published specifically on the water-soluble portion because of the polarity of its components and the difficulties encountered in the separation of highly polar compounds. By employing modern chromatographic techniques, this water-soluble portion of the smoke condensate was studied extensively.

EXPERIMENTAL SECTION

Materials and Equipment. The cigarettes were smoked on a Borgwaldt IIIA smoking machine. The liquid chromatography column adsorbent was Mallinckrodt analytical reagent, silicic acid, 100 mesh. The solvents used were high purity hexane (Exxon), analytical anhydrous ethyl ether and methanol (Mallinckrodt), and acetone (Axton Cross). The acetone was distilled before use, but the other solvents were used as obtained (the purity was checked by concentrating a 500-ml portion to 1 ml and subjecting it to gas chromatography).

The gas chromatography separations were made on Varian 1700 and F&M Model 810 gas chromatographs. IR spectra were run neat between NaCl plates on Perkin-Elmer 21 and 221 infrared spectrophotometers. NMR spectra were run on a Varian A60 spectrometer with deuteriochloroform as the solvent and tetramethylsilane as the internal standard. Mass data were obtained by coupling a Varian 1700 gas chromatograph to a Varian MAT CH-5 mass spectrometer with 70-eV electrons and an ion current of 200 μA.

Production and Partition of Smoke Condensate. Twenty-four thousand nonfiltered (70 mm in length) cigarettes of a cased commercial blend of tobaccos conditioned at 25 °C, 60% relative humidity to 12% moisture content, were smoked to a 23-mm butt. Standard smoking parameters were used: a 35-ml puff of 2-s duration, one puff/min. The condensate was collected in dry ice cooled traps, washed from the traps with acetone, and divided into three portions. Each portion was concentrated on a rota-evaporator under reduced pressure at a temperature less than 40 °C. The dry weights obtained for each portion were: 206.2, 213.7, and 194.1 g; total dry weight recovery: 614 g.

Each of the three portions was partitioned separately between three 1.5-l. portions of ether and one 1.5-l. portion of water and two 750-ml portions of water. The ether layers were combined, as were the water layers, and each in turn was concentrated on a rota-evaporator. The moisture content of each fraction was determined to give on a dry-weight basis 380 g of the ether-layer solubles and 232 g of the water-layer solubles. The ether-layer material was not investigated at this time. The water-layer solubles represented 38% on a dry-weight basis of the original particulate matter collected.

Liquid Chromatography of the Water-Soluble Portion of the Smoke Condensate. The water-soluble portion (232 g) of the smoke condensate was divided into three aliquots. Each aliquot was dissolved in 25 ml of methanol and 100 ml of acetone and the solution mixed with 150 g of silicic acid. The resulting mixture (as a paste) was added to the top of a silicic acid column (42 cm × 8.5 cm). Each of the three columns was simultaneously developed in an "identical" manner with the following sequence of solvents (number of liters in parentheses): 50:50 ether/hexane (3), ether (3), 97.5:2.5 ether/acetone (3), 95:5 ether/acetone (6), 90:10 ether/acetone (3), 80:20 ether/acetone (27), acetone (3), 96:4 acetone/methanol (3), methanol (3), and 90:10 methanol/water (2).

The flow of solvent through the column was facilitated by applying vacuum (188–280 mmHg) via water aspirator. The vacuum line was attached to an adaptor which in turn was connected to the receiver. A second adaptor equipped with a stopcock was placed between the bottom of the column and the vacuum line so that fractions could be taken without interrupting the flow through the column.

Fractions (750 ml) were collected in 1-l. flasks and concentrated on a rota-evaporator. The solvent from the fractions eluted with ether/acetone was recovered from the rota-evaporator and used to make up the ether portion of the next liter of eluent. This was done to conserve solvent and also to provide a gradient elution of the column. The concentrated fractions were combined on the basis of GC data to give the fractions shown in Table I.

The combined weight of the obtained fractions in Table I is 50 g more than was added to the column. This extra weight is due to unremoved solvent as the fractions were not taken to constant weight. This was done to avoid loss of material due to volatility or azeotropic distillation between the solvent and the smoke components. Also, since the fractions were not taken to constant weight the

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Table I. Liquid Chromatography of the Water-Soluble Portion of the Smoke Condensate

Fraction	1	2	3	Wt, g (3 cols combined)
A	1-2	1-2	1-2	1
1	3-10	3-10	3-10	23
2	11-18	11-19	11-19	27
3	19-25	20-25	20-27	45
4	26-30	26-30	28-31	35
5	31-35	31-36	32-37	35
6	36-52	37-50	38-50	40
7	53-65	51-63	51-64	26
8	66-67	64-65	65-66	50
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amount of material remaining on the column could not be determined.

Investigation of Fraction A from Table I. Fraction A in Table I was investigated by GC on a glass column (3 m × 0.63 cm), containing 10% FFAP on Gas-Chrom Q (60–80 mesh). Of the six peaks trapped, four were identified from their IR spectra as benzoic acid, dibutyl phthalate, di-2-ethylhexyl phthalate, and the acetate of a long-chained alcohol. This fraction was also subjected to GC–mass spectroscopy on a 0.25 mm × 30 m FFAP glass capillary column prepared in our laboratory. In addition to the above four compounds, the following were identified: *n*-butyric acid, *n*-valeric acid, 2-methylbutyric acid, isovaleric acid, menthol, phenol, *o*- and *p*-cresol, 2,6-di-*tert*-butyl-4-methylphenol, dimethylphenol, 3-methylthiophene-2-carboxaldehyde, and 5-methylpyrrole-2-carboxylic acid ethyl ester. Isolates from fraction A are listed in Table II.

Investigation of Fractions 1, 2, 3, 5, 6, and 8 from Table I. Fractions 1, 2, 3, 5, 6, and 8 (Table I) were investigated by rechromatography on silicic acid columns. These columns were eluted in a manner similar to the original column except the polarity of the initial solvent was less and the polarity was increased at a much slower rate. In this way, numerous subfractions were obtained (fraction and number of subfractions: 1, 25; 2, 23; 3, 19; 5, 12; 6, 13; 8, 16). Each subfraction was subjected to preparative GC on a glass column (3 m × 0.63 cm o.d.) containing 10% of one of the liquid phases selected from the group FFAP (also 5%), OV-101, PPE-6, Poly-A-103, and Poly-I-110 on Gas-Chrom Q (80–100 mesh). Solid supports Chromosorb W (80–100 mesh) and Gas-Chrom Q (60–80 mesh) were also used, but the Gas-Chrom Q (80–100 mesh) became more or less standard during the latter phases of this work. The gas chromatograms were operated with helium carrier gas, 60 ml/min, and programmed usually from 80 to 275 °C at a rate of 4 °C/min.

The isolates obtained from the preparative GC were rechromatographed on a second column containing a different liquid phase. Peak materials obtained from this chromatography were subjected to IR and mass spectroscopy. When sufficient amounts of material were available, NMR spectra were obtained. Confirmed or tentative identifications were based on comparisons of these spectral data and retention times with corresponding data from known or related compounds reported in the literature and in standard spectra collections ("Documentation of Molecular Spectroscopy", 1966; Pouchet, 1970; Sadtler, 1968). Isolates from these fractions are listed in Table II.

Investigation of Fractions 4 and 7 from Table I. Fractions 4 and 7 (Table I) were subjected directly to preparative GC on the Poly-A-103 column described above; materials were collected from 33 peaks in fraction 4 and 21 peaks in fraction 7. The material in each of these 54 peaks was retrapped on a second column (either on the 10% FFAP or on the 10% Poly-I-110 described above), and IR, mass, and NMR spectra were obtained as described above. Confirmed and proposed identifications were based on GC retention times and spectral data. The isolates from these fractions are also listed in Table II.

Trimethylsilylation of Hydroxy Compounds. Often hydroxylated isolates (alcohols, sugar anhydrides, hydroxy lactones) did not give a parent mass when submitted to mass spectroscopy. After obtaining IR, mass, and NMR spectra, these compounds were trimethylsilylated according to Sweeley et al. (1963) modified as follows. The silylating reagent (100 μl), prepared by mixing 1 ml of anhydrous pyridine, 0.2 ml of hexamethyldisilazane, and 0.1 ml of trimethylchlorosilane, was added to the sample in a 1-ml vial capped with a Teflon-coated rubber seal. The mixture was maintained at room temperature overnight. The trimethylsilyl derivative was isolated from the reaction mixture by GC on the OV-101 column described earlier. IR and mass spectral analyses of the derivatives were used to help determine the parent mass and the number of hydroxyl groups present in each compound.

DISCUSSION

The smoke condensate (614 g) from 24 000 nonfiltered cigarettes was collected in dry ice cooled traps. An ether–water partition of the condensate gave 380 g of ether-soluble material and 232 g of water-soluble material. The ether-soluble material was not studied at this time because the same fraction from similar nonfiltered cigarettes had previously been studied (Newell et al., 1975).

The water-soluble material from the smoke condensate was fractionated by liquid chromatography to give nine fractions. The first of these fractions was studied directly by GC–MS to give 16 compounds. Six of the remaining eight fractions were further fractionated by liquid chromatography. The remaining two fractions plus each of the subfractions from the liquid chromatography columns were preparatively fractionated on appropriate GC columns. The peak materials were collected and rechromatographed on a different GC liquid phase to give individual components. These were identified by IR, mass, and NMR spectra and GC retention times. In most cases, both IR and mass spectra were obtained (only 20 components were identified by MS alone), and when sufficient amounts of material were available, NMR spectra were also obtained. The isolates were identified by comparison of their spectral data with corresponding data of known compounds given in the literature and with those synthesized in these laboratories.

The identification of many compounds containing hydroxyl groups was hindered because of their uncharacteristic mass spectra. In these instances the compounds were trimethylsilylated after obtaining the usual spectral data (IR, mass, and NMR). The silyl derivatives were isolated by GC and their IR and mass spectra obtained. From these spectral data obtained before and after trimethylsilylation, the number of hydroxyl groups and the molecular weight were determined.

The number of compounds recorded in Table II is 478. Table III lists the total number in each structural classification, the number in each structural classification that are new to smoke literature, the number that were identified with compounds synthesized in our laboratory, and the number of compounds with proposed but unconfirmed structures. The proposals for the 150 compounds having unconfirmed structures were based on sound interpretation of their spectral data.

Table II. Isolates from the Water-Soluble Portion of the Smoke Condensate

Compound	Structural status[a]	Fraction found	New to smoke
Acids			
Acetic acid	Lit.	1-6	No[c]
2-hydroxy-, acetate	Lit.	1	Yes
Acrylic acid	Lit.	1	Yes
Benzoic acid	Lit.	A, 1	No[c]
3-hydroxy-	Lit.	1	No[c]
4-hydroxy-	Lit.	1	No[c]
4-hydroxy-3-methoxy-	Lit.	1	No[c]
2-Butenoic acid (crotonic acid)	Lit.	1, 2	No[c]
3-methyl-	Lit.	1	Yes
3-Butenoic	Pro.	1	Yes
3-methyl-	Pro.	1	Yes
Butyric acid	Lit.	A, 1	No[c]
2-hydroxy-	Lit.	3	Yes
2-methyl-	Lit.	A, 1	No[d]
2-Furanacetic acid	Syn.	1	Yes
2-Furoic acid	Lit.	1, 3, 5	No[c]
5-methyl-	Lit.	2, 3	Yes
3-Furoic acid	Lit.	1	Yes
Hexanoic acid, 5-oxo-	Lit.	1	Yes
4-oxo-	Syn.	2	Yes
Isobutyric acid	Lit.	1	No[c]
Isocaproic acid	Lit.	1	No[c]
Isovaleric acid	Lit.	A, 1	No[c]
Lactic acid	Lit.	2, 5, 6	No[c]
Levulinic acid	Lit.	1, 2, 3	No[c]
Methacrylic acid	Lit.	1	Yes
Palmitic acid	Lit.	2	No[c]
Pentanoic acid, 2-methyl-4-oxo-	Syn.	2	Yes
cis-3-Pentenoic acid	Syn.	1	Yes
trans-3-Pentenoic acid	Syn.	1	Yes
Phenylacetic acid	Lit.	1	No[c]
Propionic acid	Lit.	1, 2, 6	No[c]
3-hydroxy-	Lit.	6	Yes
3-hydroxy-, acetate	Syn.	1, 2	Yes
3-phenyl-	Lit.	1	No[d]
Pyrrole-2-carboxylic acid	Syn.	1	Yes
Pyruvic acid	Lit.	2	No[c]
Succinic acid, monomethyl ester	Lit., syn.	1	Yes
Valeric acid	Lit.	A	No[c]
3-methyl-	Lit.	1	No[c]
Lactones			
2-Butenoic acid, 2-acetyl-4-hydroxy-3-methyl-, γ-lactone	Pro.	2	Yes
2,3-dimethyl-4-hydroxy-, γ-lactone	Syn.	1	Yes
4-hydroxy-, γ-lactone	Syn.	1, 2	Yes
4-hydroxy-3-isopropyl-, γ-lactone	Syn.	1	Yes
4-hydroxy-2-methyl-, γ-lactone	Syn.	1	Yes
4-hydroxy-3-methyl-, γ-lactone	Syn.	1, 2	Yes
Butyric acid, 2-acetoxy-3,4-dihydroxy-, γ-lactone	Pro.	2	Yes
4-acetoxy-3,4-dihydroxy-, γ-lactone	Pro.	2, 3	Yes
2-acetoxy-4-hydroxy-, γ-lactone	Syn.	1, 2	Yes
4-acetoxy-4-hydroxy-, γ-lactone	Pro.	1	Yes
2-acetyl-4-hydroxy-, γ-lactone	Lit.	1	Yes
2,4-dihydroxy-, γ-lactone	Syn.	1, 2, 3, 4	Yes
3,4-dihydroxy-, γ-lactone	Syn.	2, 3	Yes
2,4-dihydroxy-3,3-dimethyl-, γ-lactone	Lit.	1	Yes
2,4-dihydroxy-2-hydroxymethyl-, γ-lactone	Pro.	2, 3	Yes
3,4-dihydroxy-2-hydroxymethyl-, γ-lactone	Pro.	3	Yes
3,4-dihydroxy-3-methyl-, γ-lactone	Pro.	2	Yes
4,4-dihydroxy-3-ethynyl-2-methyl-, γ-lactone	Pro.	2	Yes
4,4-dihydroxy-3-methyl-, γ-lactone	Pro.	2	Yes
4-hydroxy-, γ-lactone (butyrolactone)	Lit.	1, 2, 3	No[e]
4-hydroxy-3-hydroxymethyl-, γ-lactone	Syn.	1, 2, 3, 5	Yes
4-hydroxy-2-oxopropyl-, γ-lactone	Syn.	1, 2	Yes
4-hydroxy-2-propionyloxy-, γ-lactone	Syn.	2	Yes
4-hydroxy-4-(3-pyridyl)-, γ-lactone	Syn.	4	Yes
2-methyl-2,3,4-trihydroxy-, γ-lactone (2 isomers)	Syn.	1, 2	Yes
Coumarin, 3,4-dihydro-	Lit.	1	Yes
6-methyl-	Lit.	1	No[f]
7-hydroxy-6-methoxy- (scopoletin)	Lit.	2	No[c]
Cyclohexaneacetic acid, 1,2-dihydroxy-, γ-lactone	Pro.	2	Yes
Cyclohexanecarboxylic acid, 2,3-dihydroxy-3-methyl-, γ-lactone	Lit.	3	Yes
1,3,4,5-tetrahydroxy-, γ-lactone	Lit., syn.	3	No[c]
Cyclohexylideneacetic acid, 2,4-dihydroxy-2,6,6-trimethyl, γ-lactone	Syn.[b]	2	Yes
Glutaric acid, 2-hydroxy-, γ-lactone methyl ester	Syn.	1	Yes

Table II *(Continued)*

Compound	Structural status[a]	Fraction found	New to smoke
Heptanoic acid, 4-hydroxy-5-oxo-, γ-lactone	Pro.	1	Yes
Hexanoic acid, 4,5-dihydroxy-, γ-lactone	Pro.	2	Yes
4-hydroxy-5-oxo-, γ-lactone	Lit.	1, 2, 4	Yes
4-methyl-2,4,6-trihydroxy-, γ-lactone	Pro.	3, 4	Yes
2,4,5-trihydroxy-, γ-lactone (4 isomers)	Pro.	2-5	Yes
2,4,6-trihydroxy-, γ-lactone	Pro.	3, 4	Yes
4,5,6-trihydroxy-, γ-lactone, monoacetate	Pro.	2	Yes
2-Hexenoic acid, 4-hydroxy-2-methyl-, γ-lactone	Lit.	1	No[d]
4-hydroxy-5-oxo-, γ-lactone	Pro.	1	Yes
Bicyclo[3.3.0]octan-2-one, 3,8-dioxa-6-hydroxy-	Pro.	2	Yes
2,4-Pentadienoic acid, 2,3-dimethyl-4-hydroxy-, γ-lactone	Pro.	1	Yes
4-hydroxy-, γ-lactone	Lit.	2, 3	Yes
4-hydroxy-2-methyl-, γ-lactone	Pro.	2	Yes
Pentanoic acid, 2,4-dihydroxy-, γ-lactone (2 isomers)	Syn.	2	Yes
4,5-dihydroxy-, γ-lactone	Pro.	3, 4, 6	Yes
2,5(or 4,5)-dihydroxy-, δ-lactone	Pro.	2-6	Yes
4,5-dihydroxy-2,3-epoxy-, γ-lactone	Pro.	2	Yes
4,5-dihydroxy-3-methyl-, γ-lactone	Pro.	2	Yes
3,5-dihydroxy-, δ-lactone	Pro.	2	Yes
5-hydroxy-3-isopropyl-, δ-lactone	Syn.	2	Yes
5-hydroxy-, δ-lactone	Syn.	2	Yes
3-methyl-2,3,4,5-tetrahydroxy-, γ-lactone	Pro.	3	Yes
2,3,4-trihydroxy-, γ-lactone	Pro.	2	Yes
2-Pentenoic acid, 2,3-dimethyl-4-hydroxy-, γ-lactone	Syn.[b]	1	Yes
4-hydroxy-3-methyl-, γ-lactone	Syn.	1	Yes
5-hydroxy-3-methyl-, δ-lactone	Syn.	1	Yes
4-hydroxy-, γ-lactone	Syn.	1	Yes
3-Pentenoic acid, 4-hydroxy-2-hydroxymethyl-, γ-lactone	Pro.	1, 2	Yes
Esters			
Acetic acid, ethyl ester	Lit.	2	No[c]
5-formyl-2-furfuryl ester	Lit.	2	Yes
2-formyloxy-3-hydroxypropyl ester	Pro.	3	Yes
2-(2-furyl)-2-oxoethyl ester	Syn.	1	Yes
glycolaldehyde ester	Syn.	1	Yes
hydroxybutyl ester	Pro.	1	Yes
2-hydroxyethyl ester	Syn.	1, 2	Yes
hydroxy-, 2-hydroxypropyl ester	Pro.	3	Yes
4-hydroxyphenyl ester	Syn.	1	Yes
2-hydroxypropyl ester	Syn.[b]	1	Yes
1-hydroxy-2-propyl ester	Lit.	1	Yes
3-hydroxypyridyl ester	Syn.	2	Yes
4-methoxybenzyl ester	Lit.	1	Yes
methyl ester	Lit.	1	No[c]
3-oxobutyl ester	Syn.[b]	1	Yes
2-oxopropyl ester	Lit., syn.	1	No[e]
Acetin, diester	Lit.	1	Yes
monoester	Lit.	2, 3, 6	No[c]
1,3-Dioxolan-2-one	Syn.	2	Yes
4-hydroxymethyl-	Lit.	2, 3, 6	Yes
4-methyl-	Lit.	3	Yes
2-Furoic acid, 2-hydroxyethyl ester, acetate	Syn.	6	Yes
Glycerol, monopropionate	Pro.	2	Yes
Glycolic acid, methyl ester	Lit.	4	Yes
Lactic acid, ethyl ester	Lit.	2	Yes
Levoglucosan, monoacetate	Pro.	3, 4	Yes
Malic acid, dimethyl ester	Syn.	1	Yes
Phthalic acid, dibutyl ester	Syn.	A, 1, 3, 6	No[c]
diethyl ester	Syn.	3, 6	No[g]
di-2-ethylhexyl ester	Syn.	A, 1, 3	No[c]
dipropyl ester	Pro.	6	No[c]
Propionic acid, 2,3-epoxy-4-hydroxybutyl ester	Syn.	2	Yes
3-(4-hydroxyphenyl)-, methyl ester	Syn.	1	Yes
1-hydroxy-2-propyl ester	Pro.	2	Yes
Pyrrolecarboxylic acid, 5-methyl-, ethyl ester	Syn.[b]	A, 1	Yes
5-methyl-, methyl ester	Syn.	1	Yes
Sugar anhydride, acetate, mass 186	Pro.	1	Yes
acetate, mass 188	Pro.	2	Yes
acetate, mass 174	Pro.	2	Yes
acetate, mass 188	Pro.	3	Yes
Amides			
Acetamide	Lit.	2-6	No[h]
N-acetonyl-	Syn.	5	Yes
N-allyl-	Syn.	2	Yes
N-butyl-	Syn.	1, 2	Yes
N-methyl-	Lit.	5	Yes
N-propyl-	Lit.	3	Yes

Table II *(Continued)*

Compound	Structural status[a]	Fraction found	New to smoke
Acrylamide	Lit.	3	Yes
N-propionyl-	Pro.	1	Yes
Anatabine, *N*-acetyl-	Syn.	6	Yes
N-formyl-	Syn.[b]	6	Yes
Benzamide	Lit.	2	Yes
2-Butenamide, 2-methyl-	Syn.	2	Yes
cis-2-Butenamide	Pro.	2	Yes
trans-2-Butenamide	Syn.	3	Yes
3-Butenamide	Syn.	3	Yes
3-methyl-	Pro.	2	Yes
Butyramide	Lit.	2, 3	Yes
4-cyano-	Pro.	4	Yes
3-cyano-3-methyl-	Pro.	3	Yes
2-methyl-	Syn.	2	Yes
Formamide	Lit.	5	No[h]
N-methyl-	Lit.	5	Yes
Furamide	Lit.	2	Yes
Hexamide	Lit.	1	Yes
Isobutyramide	Lit., syn.	2, 3	Yes
Isovaleramide	Lit.	1, 2	Yes
Methacrylamide	Lit.	2	Yes
Nicotinamide	Lit.	6	No[c]
N-methyl-	Lit.	6	Yes
Nornicotine, *N*-acetyl-	Syn.	6, 8	No[i]
N-formyl-	Syn.	7	No[i]
2-Pentenamide	Syn.	2	Yes
4-methyl-	Pro.	2	Yes
Phenylacetamide	Lit.	2, 3	Yes
2-Picolinamide	Lit.	2	Yes
Propionamide	Lit.	4, 5	No[h]
3-cyano-	Pro.	4	Yes
N-ethyl-	Syn.	2	Yes
N-methyl-	Syn.	1, 2	Yes
3-phenyl-	Syn.	1, 2	Yes
2-Pyrrolecarboxamide	Syn.	2, 3	Yes
Pyrrolidine, *N*-acetyl-	Syn.	5	Yes
N-formyl-	Syn.	5, 6	Yes
Pyruvamide	Lit.[b]	1	Yes
Valeramide	Lit.	1, 2	Yes
3-methyl-	Lit.	1	Yes
4-methyl-	Lit.	1, 2	Yes
Imides			
Glutarimide	Syn.	2, 3	Yes
3-methoxy-	Pro.	4, 5	Yes
2-methyl-	Syn.	1	Yes
3-methyl-	Lit.	1	Yes
Maleimide, 2,3-dihydroxymethyl-*N*-methyl-	Pro.	4	Yes
2,3-dimethyl-	Syn.	1	Yes
2-ethyl-3-hydroxymethyl-	Pro.	1	Yes
2-ethyl-3-methyl-	Syn.	1, 2	Yes
2-hydroxymethyl-	Pro.	2	Yes
2-methyl-	Syn.	1, 2	Yes
Succinimide	Lit.	1-6	Yes
N,2-dimethyl-	Syn.	1	Yes
2,3-dimethyl-	Syn.	1	Yes
2-ethylidene-	Syn.	1	Yes
2-ethylidene-*N*-methyl-	Syn.	1	Yes
2-ethylidene-3-methyl-	Syn.	1	Yes
2-ethyl-	Syn.	1	Yes
2-ethyl-*N*-methyl-	Syn.	1	Yes
2-ethyl-3-methyl-	Syn.	1	Yes
N-methyl-	Syn.	1, 2	Yes
2-methyl-	Syn.	1	Yes
Lactams			
Cotinine	Lit.	7, 8	No[c]
Dipyrrolo[1,2-*a*;1′,2′-*d*]pyrazine-1,4-dione (pyrocoll)	Lit.	8	No[c]
octahydro-	Syn.	6, 7	Yes
3-Imidazolin-2-one, 5-methyl-	Pro.	2	Yes
Norcotinine	Lit.	8	Yes
Phthalimidine	Syn.	2, 3	Yes
3-methyl-	Pro.	1	Yes
2-Piperidone	Lit.	5, 6	Yes
5-acetyl-5,6-dehydro-	Pro.	2	Yes
3,4-dehydro-	Syn.	5, 6	Yes
4,5-dehydro-	Syn.	5, 6	Yes

Table II *(Continued)*

Compound	Structural status[a]	Fraction found	New to smoke
N-methyl-	Lit.	5	Yes
methyl-	Pro.	1	Yes
Piperazine-2,5-dione, 3-allyl-	Pro.	4	Yes
3-isopropyl-	Pro.	8	Yes
3-methyl-	Syn.	7	Yes
Pyrrolo[1,2-*a*]pyrazine-1,4-dione, hexahydro-	Syn.	7, 8	Yes
hexahydro-3-methyl-	Syn.	7	Yes
hexahydro-3-propyl-	Pro.	4	Yes
1*H*,7*H*-Pyrazolo[1,2-*a*]pyrazole-1,7-dione, 2,3,5,6-tetrahydro-	Pro.	3	Yes
2-Pyridone, *N*-methyl-	Lit.	6	Yes
2-Pyrrolidinone	Lit.	6, 8	Yes
N-methyl-	Lit.	5	Yes
5-methyl-	Lit.	5, 6	Yes
2-Pyrrolin-5-one, 2-(3-pyridyl)-	Pro.	8	Yes
3-Pyrrolin-2-one, *N*-acetyl-3-ethyl-4-methyl-	Syn.	2	Yes
3,4-dimethyl-	Syn.	4-6	Yes
3,5-dimethyl-	Syn.	3	Yes
3,5-dimethyl-4-ethyl-	Pro.	2	Yes
3-ethyl-4-methyl-	Syn.	2, 3	Yes
4-ethyl-3-methyl-	Syn.	3	Yes
3-methyl-	Syn.	4, 5	Yes
3,4,5-trimethyl-	Syn.	2, 3	Yes
Aldehydes and ketones			
Furaldehyde	Lit.[b]	1	No[c]
5-hydroxymethyl-	Lit.	1, 2	No[c]
5-methyl-	Lit.	2, 3	No[c]
2,5-Furandicarboxaldehyde	Syn.	1	Yes
Pyrrole, 2-formyl-	Syn.	1	No[f]
2-formyl-5-methyl-	Syn.	1	Yes
3-formyl-2-methyl-	Pro.	1	Yes
Pyruvaldehyde	Lit.	1	No[j]
Thiophene, 2-formyl-3-methyl-	Lit.[b]	A	Yes
Vanillin	Lit.	1	No[c]
Acetol	Lit.	2	Yes
Acetophenone, 2′,5′-dihydroxy-	Lit.	2	Yes
Benzil	Lit.	7	Yes
1-Butanone, 1-(pyrazinyl)-	Pro.	1	Yes
2-Butanone, 3,4-dihydroxy-	Pro.	3	Yes
2-Butanone, 3,3-dimethyl-4-hydroxy-	Pro.	2, 3	Yes
2-Butanone, 4-hydroxy-	Syn.	2	Yes
1-Buten-3-one, 1-(4-hydroxycyclohexenyl)-	Pro.	1	Yes
Cyclohexane-1,4-dione	Lit.	1, 2	Yes
2-Cyclohexen-1-one	Lit.[b]	1	No[f]
4-(1,3-butadienyl)-3,5,5-trimethyl-	Syn.	1	Yes
4-(2-butenylidene)-3,5,5-trimethyl (4 isomers)	Syn.	1	Yes
4-(3-hydroxy-1-buten-1-yl)-3,5,5-trimethyl-, (4-keto-*a*-ionol)	Syn.	1, 2	Yes
4-(3-hydroxybutyl)-3,5,5-trimethyl-, (4-ketodihydro-*a*-ionol)	Syn.	1	Yes
1,2-Cyclopentanedione, 3,5-dimethyl-	Lit.	1	No[k]
3,4-dimethyl-	Lit.	1	No[k]
3-ethyl-	Lit.	1	No[l]
3-methyl- (cyclotene)	Lit.	1	No[l]
1,3-Cyclopentanedione, 2,4-dimethyl-	Pro.	3	Yes
2-ethyl-	Syn.	3	Yes
2-methyl-	Lit.	5, 6	Yes
2-Cyclopentenone, 2,3-dimethyl-	Lit.	1	No[f]
2,3-dimethyl-4(or 5)-isopropyl-	Pro.	1	Yes
2-methyl-4(or 5)-isopropyl-	Pro.	1	Yes
3-methyl-	Lit.	1	No[f,m]
3-methyl-2-(2-oxopropyl)-	Syn.	2	Yes
2-(2-oxopropyl)-	Pro.	2	Yes
Furan, 2-acetonyl-5-hydroxymethyl-	Pro.	1	Yes
2-acetyl-5-hydroxymethyl-	Syn.	1	Yes
2-acetyl-5-methyl-	Lit.	1	No[e]
2-(1-oxo-2-hydroxyethyl)-	Syn.	1	Yes
2,5-Hexanedione	Lit.	1	Yes
3-hydroxy-	Syn.	2	Yes
3-methyl-	Pro.	1-2	Yes
Imidazole, 2-acetyl-4-methyl-	Syn.	2	Yes
1-Indanone	Lit.	1	No[n]
1,4-Pentanedione, 1-(2-furyl)-	Syn.	1	Yes
2-Propanone, 4-hydroxy-3-methoxyphenyl-	Pro.	1	Yes
4-hydroxyphenyl-	Pro.	1	Yes
4*H*-Pyran-4-one, 5,6-dihydro-3,5-dihydroxy-2-methyl-	Lit.	1	Yes[o]
3,5-dihydroxy-2,6-dimethyl-	Pro.	1	Yes
3,5-dihydroxy-2-methyl-	Lit.	1	Yes

Table II *(Continued)*

Compound	Structural status[a]	Fraction found	New to smoke
2-hydroxy-5-methyl-	Pro.	1	Yes
3-hydroxy-	Lit.	1	Yes
2-hydroxy-3-methyl-	Pro.	1	Yes
3-hydroxy-2-methyl- (maltol)	Lit.	1	No[l]
3-hydroxy-6-methyl- (allomaltol)	Lit.	2	Yes
Pyridine, 3-acetyl-	Lit.	2	Yes
Pyrrole, 2-acetyl-	Syn.	1	No[c]
2-acetyl-5-methyl-	Syn.	1	Yes
2-propionyl-	Syn.	1	Yes
Pyrrolidine, 2-acetonyl-*N*-methyl-4-oxo-	Pro.	3	Yes
2-Pyrrolidinone, *N*-acetonyl-	Syn.	5	Yes
Pyrroline, 2-acetyl-3,4-dimethyl-	Pro.	2	Yes
1-Tetralone	Lit.	3	No[p]
Alcohols			
Allyl alcohol	Lit.[b]	1	No[q]
1,6-Anhydro-β-glucopyranose (levoglucosan)	Lit.	2-6	No[c]
Benzyl alcohol	Lit.	1	No[c]
2,3-Butanediol (*dl* and *meso*)	Lit.	1-5	Yes
1,2,3-Butanetriol	Syn.	5	Yes
3-Butene-1,2-diol	Syn.	2	Yes
Butyl alcohol, 4-(3-methyl-2-pyrazinyl)-	Pro.	5	Yes
4-(4-pyridinyl)-	Pro.	6	Yes
Cyclic diol, mass 128	Pro.	1	Yes
Diethylene glycol	Lit.	5, 6	No[c]
1,3-Dioxalane, 2,2-dimethyl-4-hydroxymethyl-	Lit.	2-6	Yes
Ethyl alcohol, 2-pyrazinyl-	Syn.	5, 6	Yes
2-(3-methyl-2-pyrazinyl)-	Syn.	5	Yes
2-(6-methyl-2-pyrazinyl)-	Syn.	5	Yes
Ethylene glycol	Lit.	2-6	No[c]
3,4-Furandiol, tetrahydro-3-methyl-	Syn.	2	Yes
Furfuryl alcohol	Lit.	1-6	No[c]
Glycerol	Lit.	2-6	No[c]
2,5-Hexanediol	Lit.	2	Yes
Hexanol, methyl-	Pro.[b]	1	Yes
Menthol	Lit.[b]	A	No[c]
Methanol, 5-methyl-2-pyrazinyl-	Syn.	4-6	Yes
2,4-Pentanediol, 2-methyl-	Lit.	1	Yes
2-Phenethyl alcohol	Lit.	1	No[c]
1,2-Propanediol	Lit.	1-6	No[c]
3-chloro-	Lit.	1	Yes
3-*O*-furfuryl-	Syn.	2	Yes
1,3-Propanediol	Lit.	6-8	Yes
1-Propanol, 2,3-oxido- (glycidol)	Lit.[b]	2	Yes
2-Propanol, 1,1-oxydi- [bis(2-hydroxypropyl) ether]	Lit.	2-3	Yes
1-Propanol, 2,2′-oxydi- [bis(1-hydroxy-2-propyl) ether]	Pro.	3	Yes
4*H*-Pyran-5,6-dihydro-5-hydroxy-2-hydroxymethyl-	Pro.	4-5	Yes
isomer of above, mass 130	Pro.	1	Yes
Pyran, 3-hydroxytetrahydro-	Pro.	2	Yes
Pyrrolidine, 2-hydroxymethyl-5-methyl-	Pro.	4	Yes
Sugar dianhydride, mass 144	Pro.	2, 4	Yes
mass 144	Pro.	2-5	Yes
mass 144	Pro.	1-3	Yes
mass 144	Pro.	2-6	Yes
mass 144	Pro.	2-3	Yes
mass 144	Pro.	1	Yes
mass 144	Pro.	1	Yes
mass 144	Pro.	2	Yes
mass 144	Pro.	2	Yes
mass 144	Pro.	2-5	Yes
mass 144	Pro.	2	Yes
Sugar anhydride, mass 162	Pro.	4-5	Yes
mass 146	Pro.	2	Yes
mass 146	Pro.	3-6	Yes
mass 146	Pro.	3	Yes
mass 146	Pro.	3	Yes
mass 146	Pro.	5-6	Yes
mass 146	Pro.	2-3	Yes
mass 146	Pro.	2-4	Yes
mass 146	Pro.	3-4	Yes
Pyridines			
Anabasine, *N*-methyl-	Syn.	8	No[r]
Anatabine, *N*-ethyl-	Syn.	7	Yes
N-methyl-	Syn.	8	Yes
2,3′-Bipyridine	Lit.	3-5	No[c]
5-methyl-	Pro.	2	Yes

Table II *(Continued)*

Compound	Structural status[a]	Fraction found	New to smoke
3,3′-Bipyridine	Lit.	6	Yes
Myosmine	Lit.	6	No[c]
Nicotine	Lit.	6-8	No[c]
5′-hydroxy-	Pro.	8	Yes
3-Picoline	Lit.[b]	2	No[c]
Pyridine, 3-(1-ethyl-2-pyrrolidinyl-) (ethylnornicotine)	Syn.	8	Yes
2-Pyridinol	Lit.	6-7	Yes
3,5-dimethyl-	Syn.	5	Yes
3,6-dimethyl-	Syn.	4-5	Yes
4,6-dimethyl-	Syn.	6-7	Yes
6-ethyl-	Pro.	5	Yes
3-methyl-	Syn.	4-6	Yes
5-methyl-	Syn.	6-7	Yes
6-methyl-	Pro.	6	Yes
3-Pyridinol	Lit.	2-6	No[c]
2,4-dimethyl-	Pro.	5-6	Yes
2,6-dimethyl-	Syn.	6	Yes
4,6-dimethyl-	Pro.	4-6	Yes
5,6-dimethyl-	Pro.	5	Yes
6-ethyl-2-methyl-	Pro.	3	Yes
6-ethyl-4-methyl-	Pro.	3	Yes
2-ethyl-	Syn.	2	Yes
5-ethyl-	Pro.	2	Yes
6-hydroxymethyl-	Pro.	2	Yes
2-methyl-	Syn.	2-5	Yes
4-methyl-	Pro.	2-3	Yes
5-methyl-	Pro.	4	Yes
6-methyl-	Lit.	2-5	No[k]
4- or 5-propyl-	Pro.	6	Yes
C_3-alkyl-	Pro.	6	Yes
C_3-alkyl-	Pro.	6	Yes
C_3-alkyl-	Pro.	6	Yes
Imidazoles			
Benzimidazole, 2-methyl-	Lit.	6	Yes
C_2-alkyl-	Pro.	6	Yes
C_2-alkyl-	Pro.	6	Yes
1*H*-Furo[2,3-*d*]imidazole, 2-methyl-	Pro.	5	Yes
Imidazole	Lit.	8	Yes
2-(2-butyl)-	Syn.	8	Yes
2-(2-butyl)-4-methyl-	Pro.	8	Yes
2,4-dimethyl-	Syn.	8	Yes
4,5-dimethyl-	Syn.	8	Yes
2,5-dimethyl-4-isopropyl-	Pro.	8	Yes
4-ethyl-	Pro.	8	Yes
4-ethyl-2-isopropyl-	Syn.	8	Yes
4-ethyl-2-methyl-	Pro.	8	Yes
4-isobutyl-	Pro.	8	Yes
2-isopropyl-	Syn.	8	Yes
4-isopropyl-	Pro.	8	Yes
2-isopropyl-4-methyl-	Syn.	8	Yes
N-methyl-	Lit.	8	Yes
4-methyl-	Syn.	8	Yes
2,4,5-trimethyl-	Syn.	8	Yes
C_5-alkyl-	Pro.	8	Yes
C_5-alkyl-	Pro.	8	Yes
C_5-alkyl-	Pro.	8	Yes
C_5-alkyl-	Pro.	8	Yes
Imidazo[1,2-*a*]pyridine, 2,3-dimethyl-	Pro.	8	Yes
Miscellaneous nitrogen compounds			
Caffeine	Lit.	4-6	Yes
5*H*-Cyclopentapyrazine, dimethyl-	Pro.	8	Yes
Hydantoin	Lit.	3	Yes
1,5-dimethyl-	Syn.	2	Yes
1-ethyl-	Lit.	2	Yes
5-ethyl-	Syn.	2	Yes
1-isopropyl-	Pro.	1	Yes
5-isopropyl-	Lit.	1, 2	Yes
5-methyl-	Lit.	2, 3	Yes
Oxazolidine-2,4-dione	Syn.	1, 2	Yes
5-methyl-	Syn.	1	Yes
Pyrazine, 2-furyl-5-methyl-	Lit.	5	No[e]
2-hydroxy-3-methyl-	Syn.	5, 6	Yes
2-methyl-5-phenyl-	Pro.	6	Yes
9*H*-Pyrido[3,4-*b*]indole, 1-methyl- (harmane)	Lit.	6	No[c]
9*H*-Pyrido[2,3-*b*]indole, 2-ethyl-	Pro.	6	Yes

Table II *(Continued)*

Compound	Structural status[a]	Fraction found	New to smoke
Pyrimidine, 2,5-dimethyl-6-hydroxy-	Pro.	5, 6	Yes
Pyrrole	Lit.	1	No[c]
methyl-	Pro.[b]	1	Yes
Pyrrolidine, *N*-furfuryl-	Syn.	8	Yes
N-(5-methylfurfuryl)-	Syn.	8	Yes
1*H*-Pyrrolo[1,2-*c*]imidazole-1,3-dione, hexahydro- (proline hydantoin)	Syn.	2	Yes
Pyrrolo[1,2-*a*]pyrazine	Syn.	6	Yes
Theobromine	Lit.	5-7	Yes
Uracil, 3,5-dimethyl-	Syn.	2, 3	Yes
5,6-dihydro-3-ethyl-5-methyl-	Pro.	2	Yes
Miscellaneous			
Acetaldehyde cyanohydrin	Lit.	1	No[s]
Acetone cyanohydrin	Lit.	8	Yes
Tris-2-butoxyethyl phosphate	Lit.	1	Yes
Catechol	Lit.	1	No[c]
o-Cresol	Lit.[b]	A	No[c]
p-Cresol	Lit.[b]	A	No[c]
Ethane, 1,2-dicyano-	Lit.	1	Yes
Hydroquinone	Lit.	3-7	No[c]
methyl-	Lit.	1	No[t]
Maleic anhydride	Lit.	1	Yes
2,3-dimethyl-	Lit.	1, 2	Yes
2-ethyl-3-methyl-	Lit.	1	Yes
2-methyl-3-propyl-	Syn.	1	Yes
Phenol	Lit.	A, 1, 2	No[c]
2,6-di-*tert*-butyl-4-methyl-	Lit.[b]	A	Yes
2,6-dimethoxy-	Lit.	1	No[c]
dimethyl-	Lit.[b]	A	No[c]
2-ethyl-6-methyl-	Lit.	2	Yes
2-methoxy-4-methyl- (4-methylguaiacol)	Lit.	1	Yes
Succinic anhydride	Lit.	6	Yes
2,3-dimethyl-	Lit.	3	Yes
methyl-	Lit.	2	Yes
Thiophene, tetrahydro-1,1-dioxide	Lit.	6	Yes

[a] Lit. = confirmed by literature; syn. = confirmed by syntheses; pro. = proposed structure. [b] Identified by mass spectroscopy only. All others were identified by IR and mass or by IR, mass, and NMR spectroscopy. [c] Stedman, 1968. [d] Kaburaki et al., 1969a,b. [e] Neurath et al., 1971. [f] Shigematsu et al., 1971. [g] Mauldin, 1976. [h] Johnson et al., 1973. [i] Neurath, 1972. [j] Wahl, 1957. [k] Hecht et al., 1974. [l] Elmenhorst, 1971, 1972a,b. [m] Graham, 1970. [n] Testa, 1966. [o] Proposed by Leach and Alford, 1968. [p] Benner et al., 1973. [q] Schuller et al., 1971. [r] Brown and Ahmad, 1972. [s] Nall, 1966. [t] Leach and Alford, 1968.

Table III. Number of Compounds in Each Structural Classification, Number New to Smoke, and Identification Confirmation

Classification	Total	New	Identification[a] L	S	P
Acids	40	19	31	7	2
Lactones	66	61	10	25	31
Esters	40	32	11	17	11
Amides	47	41	21	19	7
Imides	21	21	2	15	4
Lactams	33	31	9	14	10
Aldehydes and ketones	65	47	28	19	18
Alcohols	55	45	18	8	29
Nitrogen heterocyclics					
Pyridines	37	30	8	12	17
Imidazoles	25	25	3	8	14
Miscellaneous	26	23	9	10	7
Miscellaneous	23	14	22	1	
Total	478	389	171	157	150

[a] L = confirmed by comparison of spectral data with those found in the literature. S = confirmed by comparison of spectral data with those of compounds synthesized in our laboratories. P = proposed structure based on the obtained spectral data.

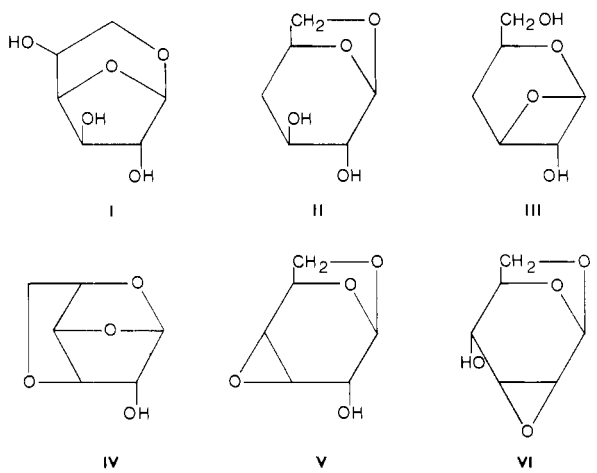
The class of compounds titled nitrogen heterocyclics includes those heterocyclic nitrogen compounds that are not included elsewhere. This group includes 37 pyridines, 25 imidazoles, and 26 miscellaneous compounds. Of the 88 compounds listed in these groups, 50 have confirmed structures based on comparison of their spectral data with those of authentic samples. The assigned structures for most of the 38 remaining compounds in these groups are believed to be sound proposals based on IR, mass, and NMR data, but were not considered as confirmed structures since authentic samples were not available for direct comparison of the corresponding spectral data. Only ten of the compounds in these groups have been previously reported as isolates from tobacco smoke. The list of pyridines includes five alkaloids that are new to tobacco smoke literature. These are ethylnornicotine, *N*-methylanatabine, *N*-ethylanatabine, 3,3′-bipyridine, and 5-methyl-2,3′-bipyridine. A number of these heterocyclic nitrogen compounds have been evaluated as tobacco flavorants and possess good flavor qualities.

Forty-seven amides were obtained in this study. Of these, 31 are primary, 9 are secondary, 6 are tertiary amides, and 1 is an acyclic imide. Very little has been reported on the presence of amides in cigarette smoke. Only six of the amides given in this paper have been previously reported in smoke. In 1956, Buyske et al. reported nicotinamide. More recently, Neurath (1972) reported *N*-acetyl- and *N*-formylnornicotine and Johnson et al. (1973) reported formamide, acetamide, and propionamide. The presence of amides is known to cause problems in some procedures used for the determination of ammonia in smoke (Harrell et al., 1975). This large number of amides present in smoke makes the findings of Harrell et al. even more significant.

Another new class of compounds found in this study is the imides. A total of 21 imides, four glutarimides, six maleimides, and 11 succinimides were found in this study. Three succinimides, the 2-ethylidene, the 2-ethylidene-*N*-methyl, and the 2-ethylidene-3-methyl derivatives, were confirmed as the ethylidene derivatives by synthesis. Also of interest are the three maleimides containing hydroxymethyl groups. These are only proposed structures based on mass and IR spectra and are not conclusive at this time. Studies by Ellsworth (1970) suggest that chlorophyll is a potential source of imides in tobacco and in smoke. The imides that have been evaluated were shown to be good tobacco flavorants.

Of the 33 lactams reported in this work, only cotinine (Quin, 1959) and pyrocoll (Mold et al., 1960) have previously been reported in tobacco smoke. Twenty-three of these newly reported lactams have confirmed structures and the remaining 10 isolates have proposed structures based on IR, mass, and NMR data. Some of these compounds have been evaluated as tobacco flavorants and were found to impart fair to good flavor and aroma during smoking.

Fifty-five alcohols were found in this study, 45 of which are new to smoke literature. These new alcohols include five pyrazinyl alcohols; the structures of four of these have been confirmed, and these four possess good tobacco flavor properties. Also among the new alcohols are 14 cyclic and acyclic diols and triols. These probably arise from humectants which are added to tobacco prior to cigarette fabrication. Another 20 of these new compounds are classified as sugar anhydrides or sugar dianhydrides. One anhydride, mass 162, is suspected to be the furanose derivative (I) of levoglucosan which has been reported as



a pyrolysis product of cellulose (Shafizadeh and Fu, 1973) or it could be either of the 1,6-anhydrogalactoses reported by Leach and Alford (1968). Spectral data were not available for any of these compounds for comparison. Eight other anhydrides, all with mass 146, are believed to have structures of the general types II and III based on IR, mass, and NMR spectra. Also, 11 sugar dianhydrides were isolated in this study. One of these gave the same NMR data as that of 1,4:3,6-dianhydro-D-glucopyranose (IV) (Bedford and Gardiner, 1965). Another dianhydride synthesized in our laboratory with either structure V or VI gave the same spectral data as one of the smoke isolates. Until authentic samples are available, the structures of these anhydrides cannot be confirmed.

Of the 66 lactones reported in this paper, 61 are new to smoke. Over half of these new lactones were hydroxy lactones. Until now the only hydroxy lactones reported in smoke were 1,3,4,5-tetrahydroxycyclohexanecarboxylic acid γ-lactone and 2,3,4,5-tetrahydroxypentanoic acid γ-lactone (Leach and Alford, 1968). Thirty-one of the 61 new lactones have been assigned structures which have not been confirmed. Most of these are hydroxy lactones whose proposed structures were based on IR, mass, and NMR data. Four stereoisomers of 2,4,5-trihydroxyhexanoic acid γ-lactone, two stereoisomers of 2,4-dihydroxypentanoic acid, and two stereoisomers of 2-methyl-2,3,4-trihydroxybutyric acid were isolated in this work. Most lactones when incorporated into tobacco products impart desirable flavor and aroma during smoking.

Compounds listed in Table II also include 65 aldehydes and ketones of which 47 are new, 40 esters of which 32 are new, and 23 miscellaneous compounds of which 14 are new to tobacco smoke literature. Twenty-three of the new ketones and 20 of the new esters contain hydroxyl groups. Most of the compounds in these groups that were tested also impart good flavor and aroma to the tobacco during smoking.

One group of compounds that would be expected to be present in the water layer of smoke but was not found in this work is the amines. The procedure employed in this work involved the use of liquid chromatography on silicic acid columns which undoubtedly irreversibly adsorbed the amines.

Since the compounds isolated during the course of this work are present in tobacco smoke it is obvious that they must play a role in determining the overall flavor of the smoke. It is apparent that many smoke isolates are desirable as flavorants. This is borne out by comparing previous disclosures of tobacco flavoring materials (Leffingwell et al., 1972) with the present list of tobacco smoke isolates. Consequently, many of the new smoke isolates listed in Table II also have the potential of being good tobacco flavorants.

This study was undertaken to determine the composition of the water-soluble portion of the smoke from a typical American-type (blended) cigarette. Casing and flavoring materials are part of this blend and some of the reported compounds, for example, caffeine, arise from the additives. Tobacco leaf constituents are often distilled unchanged into the smoke while other smoke components are formed during the burning of the cigarette. The formation of many of these compounds is a complicated process involving the interaction of tobacco and/or smoke components. Little attempt, therefore, will be made here to speculate on the origin(s) of the reported compounds. Many components found in this study have been shown by GC/MS with glass capillary columns to be present in fresh smoke condensate. This indicates that most of the components are in smoke from the nature of the smoking process and are not due to artifact formation during processing of the smoke condensate.

Finally, some mention should be made about compounds (approximately 25) which were found in fractions of differing polarities. Some of the compounds in this group are the phthalates, acetic, propionic, 2-furoic, and lactic acids, several amides, and some alcohols. No completely acceptable explanation can be given for this. A possibility would be that the compounds were incorrectly identified, but we do not accept this as most of these compounds in question have been previously reported as smoke constituents or were positively identified by synthesis. The phthalic acid esters are known tobacco leaf constituents and have been reported in smoke (Stedman, 1968). On the other hand, it is conceivable since they are plasticizers that they could arise from sources other than tobacco and this might explain their presence in the various fractions.

Other compounds such as furfuryl alcohol and propionic, 2-furoic, and lactic acids, because of their polarity, tend to be slowly eluted during liquid chromatography and consequently are found in many fractions. In a complex and difficult study of this nature involving many fractionation steps and several different investigators these findings are understandable.

ACKNOWLEDGMENT

A tremendous effort was put into this work by people other than the authors. We would like to thank Sterling J. White, Johnny L. Stewart, George W. Young, and Fred A. Thome for spectral services; Joyce H. Dickerson, Fred N. Wendelboe, and Donald L. Roberts for synthetic work; and Anthony L. Angel for technical assistance. We also express our gratitude to Alan Rodgman for his guidance and encouragement during the course of this work and his valuable assistance in the preparation of this manuscript.

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Received for review April 12, 1976. Accepted December 4, 1976. Presented in part at the 29th Tobacco Chemists' Research Conference, College Park, Md., 1975.

Preparation and Herbicidal Activity of the Vinylbenzyl Esters of Various Thio- and Dithiocarbamic Acids

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The vinylbenzyl esters of 14 thio- and dithiocarbamic acids were prepared from vinylbenzyl chloride, carbon oxysulfide, or carbon disulfide, and a secondary amine. These materials were tested for both pre- and postemergent herbicidal activity. The greatest herbicidal activity was manifested with a preemergent application of these chemicals on grassy plants. Compounds with the thiocarbamate moiety (–NCOS–) were found to be more herbicidally active than those containing the dithiocarbamate moiety (–N–CS_2–). An estimation was made of the influence of the vinyl moiety on the herbicidal activity, and it was found to depress this activity when contrasted to the unsubstituted benzyl derivatives.

Certain thio- and dithiocarbamate esters are employed as selective herbicides in various food crops. As a class, they are particularly known for their preemergent herbicidal activity on grassy plants. Benthiocarb (I), EPTC (II), and CDEC (III) are examples of thio- and dithiocarbamate esters which are presently being utilized as selective herbicides. The availability of vinylbenzyl chloride prompted us to prepare some thio- and dithio-

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