Author: Thomas A. Perfetti

Division: Chemical Research

RDM, 1978, No. 34

No. of Pages: 17

Project No: 1250

Smoking Satisfaction
and 'Tar'/Nicotine Control

December 7, 1978

Notebook Pages: 307734-307750;
306301-306306

Dated: December 21, 1977 to
June 15, 1978

Previous Reports: None

INVESTIGATION OF NICOTINE TRANSFER TO MAINSTREAM SMOKE. I. SYNTHESIS OF NICOTINE SALTS

OBJECT:

To synthesize and characterize the properties of nicotine salts of the major acids in tobacco for pyrolysis studies designed to provide information on the mechanism of nicotine transfer to smoke.

SUMMARY:

Thirty nicotine salts including salts of aliphatic monocarboxylic acids, aliphatic dicarboxylic acids, aromatic acids, amino acids and polymeric acids were synthesized for use in studies of the mechanism of nicotine transfer to smoke. The molecular ratio of acid to nicotine in these salts ranged from 1:1 to 3:1.

Infrared spectra and solubility characteristics were obtained for all the salts. Infrared spectra were used to evaluate salt formation and purity. Solubility data are expected to be of use in future work on the nature of the binding of nicotine in tobacco. Infrared spectra of most of the salts prepared have not been reported previously in the literature.

A crystalline 2:1 ratio salt of malic acid and nicotine was obtained. Isolation of this salt has not been reported in the literature.

STATUS:

Synthesis of nicotine salts has been completed. Pyrolysis studies of selected salts of particular interest have also been completed and will be reported separately along with information on the conformation and configuration of these salts.

I. MEMORANDUM:

A great amount of work has been published on the physiochemical properties of nicotine salts. Dezelic and co-workers over a period of 15 years published several articles dealing with the physical properties and syntheses of nicotine salts (3-9,22,23,24). The principle aim in their work was to find new uses of nicotine. At present our aim is to investigate the mechanism of nicotine transfer in the burning cigarette. The initial work centers on the forms of nicotine in tobacco. Since nicotine is a weak base and tobacco contains numerous acids, "bound" or salt forms of nicotine should exist in equilibrium with unionized or "free" nicotine in tobacco. Investigations of the properties of various nicotine salts are being undertaken to provide information on how the form of nicotine in tobacco affects the transfer of nicotine to the mainstream smoke.

The initial studies were divided into three segments.

1. The synthesis of a wide variety of nicotine salts comprising those of the major acids in tobacco plus several other representative acids and a solubility study on these salts.

2. A study of the thermal behavior of these salts to determine temperature profiles for maximum release of nicotine. (Pyrolytic-gas capillary chromatography will be used to obtain qualitative and quantitative information concerning the release of nicotine from these salts), and

3. A study to investigate the transfer of nicotine from tobaccos treated with these salts.

These studies are being conducted in an effort to acquire fundamental knowledge of the mechanism of nicotine transfer. The first segment is the subject of this report.

A. Preparation of Nicotine Salts

Nicotine (Eastman) was purified by treatment with solid sodium hydroxide, filtration and distillation under vacuum. The nicotine obtained was a colorless liquid, b.p., 246-7° C. All acids used in this report were commercially available and were of at least reagent grade quality. Further purification of the acids was not needed. Tables I and II summarize the physical and chemical characteristics of these salts.

1. Low-Molecular Weight Aliphatic Monocarboxylic Acids (3,4,8,22,23)

Nicotine salts of aliphatic monocarboxylic acids have a molecular composition of either 2:1 or 3:1 (acid to base). In the first group are nicotine salts of formic, monochloroacetic and dichloroacetic acids. In the second group are nicotine salts of acetic, propionic, butyric, 2-methylbutyric, 3-methylbutyric and valeric acids.

The general procedure for preparing these salts is straightforward. Each of the salts mentioned above except those of the chlorinated acids was prepared in the following manner: To a 25-ml, round-bottom flask equipped with a magnetic stir bar, was added 0.03 mole of acid (0.02 mole in the case of formic acid). A reflux condenser was mounted onto the flask in the usual manner. While stirring the acid, 0.01 mole of nicotine was added to the flask. Immediately an exothermic reaction took place and reflux began. On cooling a yellow oil was the product in each case. Each oil was viscous and odorless except in the case of nicotine butyrate which had the fragrance of green apples (see Table I).

2. Fatty Acids (14,16)

Nicotine salts of lauric, oleic, linoleic, palmitic and stearic acids have been reported in the literature to be made as colloidal suspensions, dispersions and/or soaps used as insecticides (16). No report of the isolation of these salts was mentioned. Several attempts were made to prepare the nicotine salts of lauric, palmitic and stearic acids. Lauric formed a 3:1 salt with nicotine in the form of a yellow viscous oil in a 50% yield, palmitic acid formed a 3:1 salt in about a 10% yield, but no salt was isolated from stearic acid. The preparation of these salts was similar to that of the monocarboxylic acids. Into a 50-ml round-bottom flask equipped with a magnetic stir bar, 0.03 mole of the acid was added with enough absolute ethanol to dissolve the acid at reflux. To the hot solution 0.01 mole of nicotine was added; an exothermic reaction followed. After cooling, the ethanol was evaporated and a crystalline mass of unreacted acid and salt remained. Ethanol was added again and the acid was removed by filtration. The filtrate contained nicotine and any salt that had been formed. The alcohol filtrate was partitioned with chloroform-water (1:1). The aqueous alcoholic portion contained the excess nicotine. The chloroform portion containing the salt was flash-evaporated and freeze-dried to remove any excess water. The remaining oil was essentially a pure nicotine salt. Molecular ratio was confirmed by ^{13}CMR analysis. Nicotine laurate was formed in a similar fashion in an overall yield of 50% (by ^{13}CMR analysis) while the palmitate had only an approximate 10% overall yield. Nicotine stearate was not obtained under these conditions (see Table I).

3. Aliphatic Dicarboxylic Acids

Nicotine salts of dicarboxylic acids form 2:1 acid:base ratio salts (9). The nicotine salts of tartaric, citric, malic, and oxalic acids were prepared.

a. Nicotine Tartrate (11,19,20)

Into a 50-ml round-bottom flask equipped with a magnetic stir bar 0.02 mole of tartaric acid was added with sufficient cold water to dissolve the acid. Addition of 0.01 mole of nicotine to this solution resulted in an exothermic reaction. The reaction mixture was allowed to cool and

stand for 24 hours. The mixture solidified to a paste of small leaflets. This procedure yielded nicotine bitartrate in a totally pure state without any admixture of the neutral salt (1:1 acid:base ratio salt). The melting point of the 2:1 salt was 88-89° C, yield ~80%.

b. Nicotine Citrate

Into a 50-ml round-bottom flask equipped with a magnetic stir bar was placed 0.02 mole of citric acid dissolved in 4 ml of water. To this solution 0.01 mole of nicotine was added. An exothermic reaction took place. On cooling a yellow oil was formed.

The oil which was soluble in water was placed in a freeze-drier overnight to eliminate water. A thick viscous yellow oil remained which was nicotine citrate (see Table I).

c. Nicotine Malate

Malic acid, 0.02 mole, was dissolved in 5 ml of absolute ethanol in a 25-ml round-bottom flask equipped with a magnetic stirrer. To this solution 0.01 mole of nicotine was added. Immediately an exothermic reaction took place. On cooling for 2 hours in an ice bath crystallization began. After 5 hours the needle-like crystals were filtered and washed with cold ethanol. Nicotine malate was a colorless crystalline solid which melted at 102-103° C. The yield was quantitative.

d. Nicotine Oxalate (17)

Nicotine oxalate was prepared in the same manner as the malate salt. The crystals were small, colorless needles which melted at 110° C. The yield was quantitative.

4. Aromatic Acids

Nicotine salts of aromatic acids have varying acid:base ratios depending on the nature of the acid (3,8).

Nicotine benzoate	1:1
Nicotine phenylacetate	3:1
Nicotine gentisate	1:1
Nicotine gallate	1:1
Nicotine phthalate	1:1
Nicotine salicylate	1:1
Nicotine sulfosalicylate	1:1
Nicotine picrate	2:1

Some nitrated aromatic acids also form 3:1 acid:base ratio salts (3,8).

Nicotine 3,5-dinitrobenzoate ---------- 3:1
Nicotine 4-nitrobenzoate ---------- 3:1
Nicotine 3-nitrobenzoate ---------- 3:1
Nicotine 3-nitrosalicylate ---------- 3:1

a. Nicotine Benzoate (9)

Benzoic acid (0.01 mole) was added to 6 ml of chloroform in a 25-ml round-bottom flask equipped with a magnetic stir bar. To this solution 0.01 mole of nicotine was added. An exothermic reaction took place and the reaction mixture was heated to reflux for 15 minutes. After standing and cooling the chloroform was removed by flash-evaporation. An orange oil remained which changed to a brown oil over a period of several days. The brown oil contained 90-95% nicotine benzoate. No new bands were found in the IR of the brown oil when compared to the IR of the yellow oil. This phenomenon was similar to the discoloration of nicotine when exposed to air for extended periods of time. The IR analysis for nicotine remained essentially the same though visual decomposition had occurred.

b. Nicotine Phenylacetate (6,9)

Into a 25-ml round-bottom flask was added 0.03 mole of phenylacetic acid. To this 0.01 mole of nicotine was added. The solution was allowed to stand for 6 hours. An orange oil was formed which changed to a brown oil containing 90-95% nicotine phenylacetate as determined by IR. The brown oil developed the characteristic odor of phenylacetic acid. No new bands were found in the IR of the brown oil when compared to the IR of the orange oil.

c. Nicotine Gentisate (5,9)

Gentisic acid (0.01 mole) was dissolved in 5 ml of absolute ethanol and to the solution 0.01 mole of nicotine was added. A short time after the addition of nicotine an intense exothermic reaction occurred. After cooling, the newly formed compound crystallized as colorless flakes. The crystals were filtered, washed with cold ethanol, and dried. After recrystallization from absolute ethanol the crystals had a melting point of 147° C. The yield was 88%.

d. Nicotine Gallate (5,9)

Gallic acid (0.01 mole) was dissolved in 5 ml of absolute ethanol and to the solution was added 0.01 mole of nicotine, at which time there was a spontaneous generation of heat. After briefly cooling, a thick crystalline mass was removed and filtered with suction. The crystalline mass was recrystallized from hot water. Well developed tetrahedra formed which had a melting point of 162-163° C. Yield was 92%.

This salt was very hygroscopic and difficult to work with. The salt oxidized in air to tan oil. The tan oil could be crystallized from boiling ethyl acetate to give a dark red-brown solid which was discarded and a tan powder having an IR identical with the original white crystalline salt. The tan powder was stable and melted at 112-114° C. This compound is suspected to be the totally hydrated salt of nicotine gallate.

e. Nicotine Phthalate (9)

To 1.03 g of o-phthalic acid dissolved in boiling ethanol, 1 g of nicotine was added, and the solution was boiled for several minutes on a water bath. After cooling, absolute diethyl ether was added to the reaction mixture which effected precipitation of crystals. The crystals were filtered, dried, and then dissolved in absolute ethanol. The solution was decolorized with carbon and filtered. Crystals were precipitated by the addition of absolute ether. The crystals were filtered, dried, and recrystallized from absolute ethanol. The yield of the reaction was 95% based on the amount of nicotine. Melting point was 126-127° C.

f. Nicotine Salicylate (9)

Nicotine salicylate was purchased from Pfaltz and Bauer and recrystallized twice from ethyl acetate. The procedure for the preparation of this salt from acetylsalicylic acid and nicotine can be found in the literature (3).

g. Nicotine Sulfosalicylate (9)

Sulfosalicylic acid (1.34 g) was dissolved in absolute ethanol, 1 g of nicotine was added to the solution, and the mixture was boiled for several minutes on a water bath. After cooling, absolute diethyl ether was added to precipitate the product which was filtered and dried. The crystals were dissolved in boiling methanol and the solution was decolorized with carbon and filtered. Absolute diethyl ether was added to precipitate the product which was filtered and dried. For IR analysis the compound was recrystallized from 1:1 mixture of ethanol and methanol and dried in a vacuum at 60° C. Melting point was 212-213° C with fuming. Yield of the reaction product was about 88% based on nicotine.

h. Nicotine Picrate (6)

Picric acid (0.01 mole) was added to 100 ml of boiling water in a 500-ml round-bottom flask equipped with a stirring bar. To this boiling solution 0.05 mole of nicotine was added. Immediately, a violent exothermic reaction took place and precipitation of the salt began. The mixture was heated at reflux for an additional 15 minutes. After cooling the yellow crystalline mass was filtered and washed twice with cold 10-ml portions of a 1:5000 picric acid-water mixture and then cold water until the filtrate was colorless. The yellow crystals were allowed to dry overnight. Melting point was 228-229° C. Yield was quantitative (see Table I).

5. Keto- and Amino-Acids (5,27)

a. Nicotine Pyruvate (5)

Pyruvic acid forms a 2:1 acid-base ratio salt with nicotine. Into a 25-ml round-bottom flask equipped with a magnetic stir bar was added 0.02 mole of pyruvic acid. To this 0.01 mole of nicotine was added and an exothermic reaction took place. After cooling a thick viscous yellow oil remained. IR confirmed salt formation had occurred (see Table I).

b. Nicotine Glutamate (27)

Glutamic acid (0.02 mole) was dissolved in 25 ml of boiling water. To this solution nicotine (0.02 mole) was added. Immediately a violent exothermic reaction ensued. After cooling the oily solution was flash-evaporated and a thick oil remained. Absolute ethanol (100 ml) was added to the oil and precipitation began. The precipitate was filtered and washed with ethanol (5 ml) twice and diethyl ether (10 ml) and allowed to dry overnight. The salt was obtained in approximately 90% yield and melted at 199-200° C.

c. Nicotine Aspartate (27)

The same procedure was used as in the case of the glutamic acid salt. The yield was greater than 90%. A melting point of the salt was attempted but there was no decomposition up to 300° C, the upper limit of the Fisher-John melting point apparatus.

6. Polymeric and Macromolecular Salts of Nicotine

a. Nicotine Tannate (2,13)

A solution was prepared containing (0.025 mole) of nicotine in 100 ml of ice water. To the rapidly stirred, cold aqueous solution of nicotine was added rapidly, a solution of 0.0055 mole (0.005 mole plus 10% excess because of usual water content of tannic acid) of tannic acid in 100 ml of ice water. The precipitate was filtered and washed with large quantities of ice water. The product was placed in a vacuum oven at room temperature and then evacuated. After 3 hours at room temperature the oven was heated to 80° C for 15 minutes to complete the vacuum drying. A cream-colored powder was obtained (see Table I).

b. Nicotine Pectate (1,18,25)

A slurry of 3.2 g pectic acid in 54 ml of water was prepared. To this slurry 1.65 g of nicotine was added. The mixture was allowed to stand 24 hours and then the water was flash-evaporated. The syrupy mass that remained was freeze-dried to evaporate the remaining water. An off-white powder remained. Yield was quantitative based on the assumption that pectic acid is essentially all galacturonic acid. The salt began to decompose (b.d.) at 200° C and charred at 240° C.

c. Nicotine Alginate (15,18)

A slurry containing 3.8 g of alginic acid and 25 ml of water was prepared. Nicotine (1.6 g) was then added to the slurry, and an exothermic reaction took place as the nicotine alginate went into solution. The reaction mixture was left standing 24 hours, after which time the water was removed by flash-evaporation under vacuum. A thick oil remained. To this oil 100 ml of absolute ethanol was added and precipitation of the nicotine alginate took place. The alginate was an amorphous beige powder (see Table I).

7. Inorganic Salts of Nicotine (21)

a. Nicotine Dihydrochloride (26)

Nicotine dihydrochloride is commercially available from Pfaltz and Bauer as a tan, deliquescent solid having properties listed in Table I.

b. Nicotine Silicotungstate (14) and Nicotine Chloroplatinate (10,14,21)

Nicotine silicotungstate (14) and nicotine chloroplatinate (10,21) were obtained from Dr. William Squires. They had been formed from the corresponding acid or metal complex, respectively.

B. Spectral Identification of Nicotine Salts (6,7,10,12,24,26)

The infrared spectra of the aforementioned salts and their corresponding acids were prepared by Mr. Sterling White. Dr. Patrick Cooper assisted in the interpretation of the spectra of the salts. All spectra have been filed by the author for future reference.

Many of the nicotine salts prepared exchanged nicotine for potassium in the preparation of samples with KBr. The resulting spectrum of potassium bitartrate was observed, for example, when KBr plates were heated to obtain a melt-IR of nicotine tartrate. Subsequently, AgCl plates were used as the medium for infrared analyses.

Table II shows major IR frequencies observed for salts mentioned in Table I. The infrared spectra of the fatty acid salts had several bands which interfered with those characteristic bands associated with salt formation. Therefore, infrared spectroscopy was not the method of choice for analysis, although infrared spectra of nicotine laurate and palmitate have been recorded. ^{13}CMR spectroscopy was the preferred method for analyses of these crude salts for determination of the acid: base ratios and percent yields. ^{13}CMR was used only on the fatty acid salts prepared.

II. DISCUSSION:

Nicotine as a ditertiary base can form salts or addition molecular compounds of various compositions. In these compounds one molecule of nicotine combines with one, two or three molecules of acids. Several trends exist which can enable one to make a first approximation as to the composition of the salt one is dealing with from its physiochemical data.

1. Acids of the aliphatic homologue series normally form 3:1 (acid-base ratio) salts. The exceptions are halogenated acids of this series and formic acid which form 2:1 salts. Salts of this series are normally yellow oils in the pure state (3,4,8, 22,23).

2. Salts of the aliphatic-dibasic acid series have 2:1 acid-base ratios. Salts of this class of compounds form crystalline solids or oils depending on the structure of the acid. Malonic, succinic, malic and fumaric do not form crystalline compounds with nicotine (9). It appears that the salts become ordered when two carboxyl groups are found adjacent to each other as in oxalic or if hydroxyl groups are found on the carbons between the carboxyl groups as in tartaric acid. If one or more methylene groups are found between the carboxyl groups as in malonic or succinic acid, their nicotine salts will not crystallize. Crystallization is also impared by the double bond in malonic and fumaric acids (9).

   There appears to be at least one marginal case, though for crystallization to occur. Malic acid will form a crystalline solid with nicotine. There are no reports in the literature of a 2:1 acid-base ratio salt of nicotine malate.

3. Nicotine salts of aromatic acids form acid-base ratios of 1:1, 2:1, and 3:1. The structure of the acid and the position and type of functional group attached to the acid dictate whether the salt will be a solid. Benzoic acid, isomeric aminobenzoic acids, phenylacetic acid, mandelic and cinnamic acids do not form crystalline compounds. If there is a hydroxyl group or carboxyl group in the ortho position with respect to the carboxyl group, the compound will crystallize, e.g., the nicotine compounds with salicylic and o-phthalic acids form crystalline solids. But if the hydroxyl group is on the same C atom as the carboxyl group, the compound will not crystallize, e.g., with mandelic acid. Nitro and sulfo groups favorably influence crystallization as shown by the well-crystallized nitrobenzoates and dinitrobenzoates, sulfosalicylates, and the compounds of nicotine with monosulfonic and polysulfonic acids (3,8). In addition, nitro aromatics form well-crystallized nicotine salts such as picric acid, styphnic acid and picrolonic acid (3,8).

4. Most salts of nicotine are colored, amorphous solids (21).

Solubilities of nicotine salts vary considerably as seen in Table I. The nicotine salts of aliphatic monocarboxylic acids, dicarboxylic acids, amino acids and benzoic-type acid salts are soluble in water and alcohol. The nicotine salts of fatty acids, nitro-aromatic acids and polymeric acids are slightly soluble to insoluble in ether and chloroform. The wide range of solubilities is of importance in the extraction of "free" nicotine and "bound" nicotine from tobacco. The implication that the "bound" forms or salt forms of nicotine are simple composites of a single acid and nicotine is unrealistic but fundamental information on these types of salts will add to our understanding of how nicotine transfers to smoke.

The molecular composition of these salts is intriguing, especially since salts exist with molecular compositions in 1:1, 2:1 and 3:1 acid-base ratios. Infrared spectra (Table II) were helpful in determining the conformation of these salts as well as their purity. Infrared data as well as NMR ^{13}CMR, and UV data were used to determine the conformation and configuration of these salts. This part of the study will be reported separately.

Continued work in the area of nicotine and its salts will give a better understanding of its release and the mechanism of transfer to smoke.

Thomas A. Perfetti 1-18-79

Thomas A. Perfetti — Date

Distribution:

Dr. A. H. Laurene, Dr. M. Senkus (file)
Dr. A. Rodgman, Dr. H. J. Bluhm, Library (file)
Mr. J. D. Barnhill
Dr. D. H. Piehl, Dr. M. E. Stowe (file)
Mr. J. A. Giles, Mr. J. P. Clingman, Dr. C. T. Mansfield, Dr. W. L. Clapp, Dr. J. T. Dobbins, Dr. W. M. Henley, Dr. J. N. Schumacher, Library (file)
Dr. T. A. Perfetti

Photo for: Dr. J. A. Difford 1/3/79
Photo for J. A. Sensabaugh, Jr.
Cdh Photo for: Mike Borgerding 9-18-85
Photo: Sam Simmons 11-7-85
Photo: Jerry Lawson 2-4-86
Copy for: J.D. Fredrickson 1-26-87
: Leroy Mack 3-25-87
Copy for: Jerry Lamm copy2 11-17 87

Submitted: August 4, 1978

Completed: February 2, 1979
From manuscript mm

Approved: Mary F. Stowe

Accepted: D H Piehl

Photo for: Sam Simmons 11/7/85

51490 1230

TABLE I

NICOTINE SALTS

Acid	Appearance and Stability	Odor	Molar Ratio[a] of Acid:Nic	M.P. or B.D.	Solubility[b] H_2O	Solubility[b] Alc	Solubility[b] Others
Formic	Yellow oil, Dec. on std.	V.Sl. Acid odor	2:1	--	Sol.	Sol.	--
Acetic	Yellow oil, Dec. on std., to brown oil	V.Sl. Acid odor	3:1	--	Sol.	Sol.	--
Propionic	Yellow oil, Dec. on std., to brown oil	V.Sl. Acid odor	3:1	--	Sol.	Sol.	--
Butyric	Yellow oil, Dec. on std., to brown oil	Green Apples	3:1	--	Sol.	Sol.	--
2-Methylbutyric	Yellow oil, Dec. on std., to brown oil	None	3:1	--	Sol.	Sol.	--
3-Methylbutyric	Yellow oil, Dec. on std., to brown oil	None	3:1	--	Sol.	Sol.	--
Valeric	Yellow oil, Dec. on std., to brown oil	None	3:1	--	Sol.	Sol.	--
Lauric	Yellow oil	Soapy	3:1[c]	--	Insol.	Sol.	--
Palmitic	Yellow oil		3:1[c]	--	Insol.	Sol.	--
Tartaric	Colorless crystals	None	2:1	88-9°	V. Sol.	Sol.	Ether
Citric	Yellow oil viscous;Stable		2:1	--	Sol.	Sol.	--
Malic	Colorless crystals; Stable	None	2:1	102-03°	Sol.	Sol.	--
Oxalic	Colorless crystals; Stable	None	2:1	110°	Sol.	Sol.	--
Benzoic	Orange oil; Stable	None	1:1	--	Sol.	Sol.	--
Gentisic	Colorless crystals; Stable	None	1:1	147°	Sol.	Sol.	Insol. $CHCl_3$ Eth. Acet.
Gallic	Colorless crystals V. Hygroscopic, Dec.	None	1:1	162-3° 113-14°	Sol.	Sol.	Insol. $CHCl_3$
Phenylacetic	Orange oil, Dec. on std.	None	3:1	--	Sol.	Sol.	--
Salicylic	Colorless crystals; Solid	None	1:1	116-17°	Sol.	Sol.	Sol. Ether

TAP 12-19-78

TABLE I (cont'd.)

Acid	Appearance and Stability	Odor	Molar Ratio[a] of Acid:Nic	M.P. or B.D.	Solubility[b] H_2O	Alc	Other
Phthalic	Colorless crystals; Solid	None	1:1	126-27°	Sol.	Sol.	Insol. Ether
Picric	Yellow crystals; Solid; Stable	None	2:1	228-9°	Insol.	Insol.	Insol. Ether
Sulfosalicylic	Light tan; Solid	None	1:1	212°	Sol.	Sol.	Insol. Ether
Tannic	Tan Amorphous; Solid	None	1:5	B.D.> 190° w Evol. of gas	Insol.	Insol.	Insol. Ether
Pectic	Solid Amorphous; Powder; Golden	None	1:3	B.D.> 200° Char 240°	Sol.	Insol.	Insol. Ether
Alginic	Solid Amorphous; Stable	None	1:2[e]	B.D.> 160° Char 200°	V. Sol.	Insol.	Insol.
Hydrochloride	Tan solid; Deliquescent		2:1	154-5°	Sol.	Sol.	--
Chloroplatinate $[C_{10}H_{14}N_2 \cdot PtCl \cdot 2HCl]$	Orange solid	None	1:1	B.D.> 250°	Insol.	Insol.	Insol. Ether
Silicotungstate	Colorless crystals; Solid	None	1:1	Stable > 300°	Insol.	Insol.	Insol. Ether
Pyruvic	Yellow oil; Stable	None	2:1	--	Sol.	Sol.	--
Glutamic	White Amorphous; Solid	None	1:1	199-200°	V. Sol.	Sol.	Insol. $CHCl_3$ Ether
Aspartic	White Amorphous	None	1:1	M.P. >300° No Dec.	V. Sol.	Insol.	Insol. Ether

[a] Molar ratio used in reaction

[b] Observed solubilities in approximately 200 mg/ml of solvent

[c] Analyzed by ^{13}CMR

[d] Hydrated nicotine gallate - tan powder, M.P.-113-114° C

[e] w/w

THP 12-19-78

TABLE II

INFRARED ABSORPTION BANDS (cm^{-1}) OF NICOTINE SALTS

Acid	H-Bonding	-COOH	$-COO^{\ominus}$	$-COO^{\ominus}$	Dimerization, OH-Bonding, and/or C-O Stretching		Others		Spectrum Number[a]
Formic	37-2300	1715	1590 B		1200 B				6778
Acetic	32-2200	1725 1715 B	1570 B	1430- 1360 B	1265 B		1050 1009		53078
Propionic	35-2300	1725	1595 1578	1462 1425	1380 B	1275 1212	1071		52678
Butyric	32-2400	1727 D[b] 1717 D	1582	1460 1442	1400	1270 1200	1092 1041		53078
2-Methylbutyric	32-2400	1722	1598 D 1569 D	1460 1429	1382	1261 1203	1152		53078
3-Methylbutyric	32-2400	1725 D 1717 D	1565 B	1468 1431	1370 1385	1292 1200	1120 1098		53078
Valeric	32-2300	1721	1570	1449 1430-1380 B		1260 1190	1101 1090		52678
Lauric	32-2200	1717	1575	1457	1403	1260-1180	1110		53078
Palmitic	---	Investigated by ^{13}CMR[c]		--	--	--	--		C-666[c]
Tartaric	37-2300	1730	1652 B	1565	1265 1211	1130 1108	1075 1060	872	5478
Citric	37-2200	1728	1585	1400	1215		810		51678
Malic	3400 B 31-2200	1702	1605 1578 B	1450 B	1300	1233 1170	1098		52478
Oxalic	37-2200 3350	1715	1604		1200				5578
Benzoic	2960 B 2780 B	1710 B	1600 1582	1449	1380	1272	1119 1171	1070 1021	5378
Gentisic	32-2400		1575	1482 1430	1340	1275 1235	1192 1121	1022 1011	52278

TMP 12-19-78

TABLE II (cont'd.)

Acid	H-Bonding	-COOH	$-COO^{\theta}$	$-COO^{\theta}$	Dimerization, OH-Bonding, and/or C-O Stretching		Others		Spectrum Number[a]
Gallic	34-2200	1693	1540 B	1350 B	1195 B		1035		5578
Phenylacetic	31-2200	1720	1580	1495 1455					71278
Salicylic		1628	1590		1430	1290	1135		5978
Phthalic	2600- 1900 B	1692	1550	1450 B	1360	1200 B	1120/ 1105/ 1095	1020 1010	5378
Picric[d]			1630 1610	1550 1529	1340 1310	1270 1178	1152 1088		5478
Sulfosalicylic	31-2500	1695	1612 1590		1290 1260	1162 1120	1071 1021		5978
Tannic	37-2200	1712	1601	1595		1325 B	1200 B	1090 1030	5578
Pectic	37-2200 3370	1730	1601		1140	1090			52278
Alginic	37-2300	1740	1609 B	1409		1080 1031	1015		6278
Hydrochloric[d]	34-2200	2050 B 2000	1640 1617	1560 B	1470	1335	1265 1210	1000 1015	5478
Chloroplatinate[d]	3540	3200/ 3160	2720 B	1600	1310	1210	1023	790	5578
	3480	3110/ 3080		1630	1255	1185	1003	668	
Silicotungstate[d]	3530 3370	3070	2720 B	1620 B 1567	1270 1200	1190 1010	912 870	780 675	5578

TAP 12-19-78

TABLE II (cont'd.)

Acid	H-Bonding	-COOH	$-COO^{\ominus}$	$-COO^{\ominus}$	Dimerization, OH-Bonding, and/or C-O Stretching			Others	Spectrum Number[a]
Pyruvic	37-2300 T[b]	1715 B	1622 B		1430 1350	1160 B			51878
Glutamic	32-2200	1670	1642	1610 B[e]	1452	1315	1258 1235	1128	6578
Aspartic	3140 32-2200 B	1690	1620	1560 B[e]	1500	1350 1310	1213 1140	1119 1072	6298

a
The spectrum number represents the data of the spectra run for that compound, for example, nicotine acetate was examined on May 30, 1978 - spectrum number is 53078

b
D = Doublet, B = Broad, T = Triplet

c
Nicotine palmitate was investigated by ^{13}CMR. Its spectrum number represents the 666th carbon spectrum run in 1978.

d
Frequencies do not conform to headings.

e
Indicative of zwitter ion formation.

TAP 12-19-78

III. BIBLIOGRAPHY:

1. Bauer, W. E., Insecticidal Materials of Alkaloid Pectates. U. S. Patent 2,207,694 (July 9, 1940).

2. Balchelder, C. H., Insecticide. U. S. Patent 2,152,236 (March 28, 1938).

3. Dezelic, M., Compounds of Nicotine with Formic, Acetic and Propionic Acids. RAZREDA MAT.-PRIRODSLOV. 263, 157-68 (1939).

4. Dezelic, M., Grujic-Vasic, J. and Ramic, S., Composition of Nicotine with Aliphatic Acids Determined by Stalagmometric Method. BULL. SOC. CHEM. and TECHNOLOG. SARAJEVO(FUGOSLAVIA) 12, 53-53 (1963).

5. Dezelic, M. and Nikolin, B., Salts of Nicotine with Aromatic Acids. GLASNIK DRUSTVA HEM. TEHNOL. NR BOSNE HERCEGOVINE 10, 55-62 (1961).

6. Dezelic, M. and Nikolin, B., Determination of Structure of Some Salts of Nicotine, Pyridine and N-Methylpyrrolidine on the Basis of Their Spectra. SPECTROCHIM. ACTA, Part A, 23, 1149-53 (1967).

7. Dezelic, M., Nikolin, B. and Popvis, R., Determination of the Composition and the Molecular Weight of Some Heterocyclic Bases by UV Spectra. GLASNIK HEMICARA TECHNOL. BOSNE HERCEGOVINE 13/14, 27-36 (1965).

8. Dezelic, M. and Stancic, B., Compounds of Nicotine with Organic Acids. BULL. SOC. CHEM. REPUB. POP. BOSNIE ET HERZEGOVINE 1, 7-19 (1952).

9. Dezelic, M. and Tomic, D., Compounds of Nicotine with Aromatic Acids. KEM. VJESTNIK 17, 39-57 (1943).

10. Diffee, J. T. and Sheppard, M. E., The Preparation and Properties of Salts and Coordination Compounds Containing Nicotine: A Review. RDM, 1972, No. 42 (August 25).

11. Dreser, H., Acid Nicotine Tartrate. ARCH. PHARM. 27, 266-70 (1839).

12. Eddy, R. and Eisner, A., Infrared Spectra of Nicotine and Some of Its Derivatives. J. ANAL. CHEM. 26, 1428-31 (1954).

13. Ginsburg, J. M. and Mann, R. F., Studies with Hydrated Ferric Oxide as Corrective and Sticker for Lead Arsenate and Nicotine Tannate. J. ECON. ENTOMOL. 24, 695-701 (1931).

14. Hansberry, R. and Norton, L. B., Toxicity of Several Nicotine Compounds to Aphis rumicis L.. J. ECON. ENTOMOL. 34, 80-3 (1941).

15. Kercoff, M. (to Laboratoires Feneon), Procede de Preparation d'Alginate Nicotine et Produit Insecticide en Resultant. France 988,608 (August 29, 1951).

16. Moore, W., A Promising New Contact Insecticide. J. ECON. ENTOMOL. 11, 341-2 (1918).

17. Parenty, H. and Grasset, E., Nicotine Oxalate and Other Salts. COMPT. REND. 119, 1273-6 (1894).

18. Perkins, P. R., Nicotine Fortification of Smoking Products Canada 977,233 (November 4, 1975).

19. Pictet, A., Nicotine. BER. 33, 2353 (1900).

20. Pictet, A. and Rotschy, A., Synthesis of Nicotine. BER. 37, 1225-35 (1904).

21. Smith, C. R., Complex Metal-Nicotine Compounds. J. AMER. CHEM. SOC. 75, 2010-2 (1953).

22. Turkovic, I., Compounds of Nicotine with Valeric, Caproic, Enanthic, and Caprylic Acids. KEM. VJESTNIK 15/16, 53-67 (1941-2).

23. Turkovic, I. DOC. PISS. (ZAGREB) (1942).

24. Wada, E., Yamasaki, K., Ihida, M., Sacto, K. and Nakayama, Y., Infrared Absorption Spectra of Tobacco Alkaloids and Some Related Compounds. Scientific Paper of the Central Research Institute, Japan Monopoly Corporation 97, 27-39 (1957).

25. Wilson, C. W., Insecticidal Materials of Alkaloid Pectates. U. S. Patent 2,207,694 (July 9, 1940).

26. Witkap, B., Infrared Diagnosis of the Hydrochlorides of Organic Bases. II. The Structure of Myosmine. J. AM. CHEM. SOC. 76, 5597-99 (1954).

27. Yaichnikov, I. S., Mutual Effect Between Amino Acids and Nicotine. BIOCHEM. Z. 265, 426-8 (1933).