

**THERMAL PATHWAYS FOR THE TRANSFER OF AMINES,
INCLUDING NICOTINE, TO THE GAS PHASE AND AEROSOLS**

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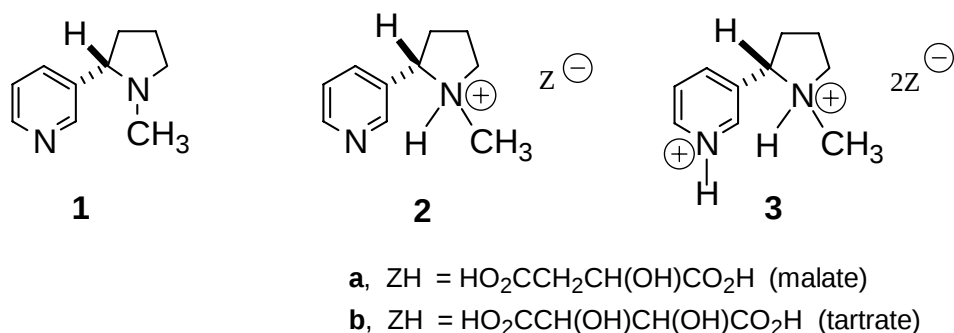
Abstract - Two pathways are proposed to explain the thermal transfer and/or pyrolysis of amines, a major class of plant constituents, to smoke. A crucial distinction is made based on the relative ease of evaporation of the amines compared to the ease of their pyrolytic decomposition. The temperatures required to transfer nicotine to the gas phase from nicotine and nicotine carboxylic acid salts, such as are found in tobacco, are lower than the decomposition temperatures of the nicotine ring system. Thermal gradient studies may better mimic the balance between evaporation and pyrolytic destruction of tobacco volatiles and semi-volatiles during smoking, as such thermolyses are performed by heating the substrate from ambient temperature to a higher temperature under a flow of gas.

INTRODUCTION

Heat-induced generation of gases and aerosols from nonvolatile or semi-volatile substrates is important in many areas of environmental sciences.¹⁻³ Combustion and pyrolysis precursor-product relationships and their attendant mechanisms require the most sophisticated experimentation and careful evaluation because of the physical and chemical instability of both the substrates involved and their products.⁴ Over the past few decades, perhaps the most thorough of studied systems, worthy for numerous reasons, is the formation and characterization of tobacco smoke and an understanding of its properties.^{5, 6}

Because of the acidity of many plant leaf materials, including tobacco, amines such as nicotine that are contained therein are likely to be in their protonated forms.^{5, 7, 8} It is well known, as a fundamental principle of chemistry, that protonated amines (sometimes referred to as “ionized” or “bound amines”) are significantly less volatile than their nonprotonated parents (sometimes referred to as “unprotonated amines” or “free base amines”). It has consequently been postulated that protonated amines will not efficiently transfer their nonprotonated amines to the gas phase upon thermal treatment.⁹⁻¹¹ Indeed, it has recently been claimed that tobacco companies add ammonia to tobacco to convert nicotine acid salts, as are present in tobacco, to nonprotonated or free base nicotine, so that a greater transfer of nicotine to the smoker is achieved.^{1, 3, 9-13} A review has recently been published on this subject.¹⁴

With regard to the burning of plant materials and transfer of amines to the gas phase and to aerosols, two mechanistic schemes are presented below. These two schemes allow the differentiation of protonated and nonprotonated amine behavior with respect to the relative ease of intact amine evaporation, as compared to their relative ease of thermally-induced decomposition. The experiments reported herein demonstrate that (*S*)-(-)-nicotine (**1**) and related nicotine carboxylic acid salts (e.g., **2** and **3**) all transfer nicotine to the



gas phase in high yield with essentially complete retention of configurational purity. The temperatures required to convert this type of nicotine salt to nicotine in the gas phase are lower than the decomposition temperature of the nicotine structure.

EXPERIMENTAL SECTION

Pyrolysis. Samples (10-40 mg) of nicotine and nicotine carboxylic acid salts^{7, 15} were weighed (using a Mettler Toledo Micro Analytical Balance) into a ceramic boat and loaded into the heating zone of the horizontal end of a specially designed quartz pyrolysis tube (7 mm I.D. by 9 mm O.D.) (Figure 1). The “U” section of the pyrolysis tube was placed in a Dewar flask containing liquid nitrogen, and the horizontal end of the tube was secured to a 3/8 inch tee fitted with a thermocouple and gas inlet. A quartz wool plug was placed in the exit end of the pyrolysis tube in order to trap aerosol not condensed in the

cold section of the tube. Voltage was applied to a Nichrome™ wire that was wrapped around the quartz pyrolysis tube. A heating rate of about 400°C/min, from ambient temperature to about 500°C, was obtained. This heating rate was the largest rate obtainable using the described system. Argon or air at a flow rate of about 500 mL/min was passed over the sample. This flow rate corresponded to a flow rate used in kinetic studies on the same compounds published previously.⁷ When the heated zone reached about 500°C, the voltage to the Nichrome™ heater was turned off and the tube was allowed to cool, with the gas flow continuing, for approximately three minutes. The tube was removed from the tee connector and slowly brought to room temperature. The ceramic boat was removed from the pyrolysis tube and the tube rinsed several times with methanol containing an internal standard (isoquinoline). The methanol rinsings were collected in a 25 mL volumetric flask, brought to the 25 mL mark with the same methanol solution, basified with one mL of 20% ammonium hydroxide in methanol, and analyzed by gas chromatography (GC).

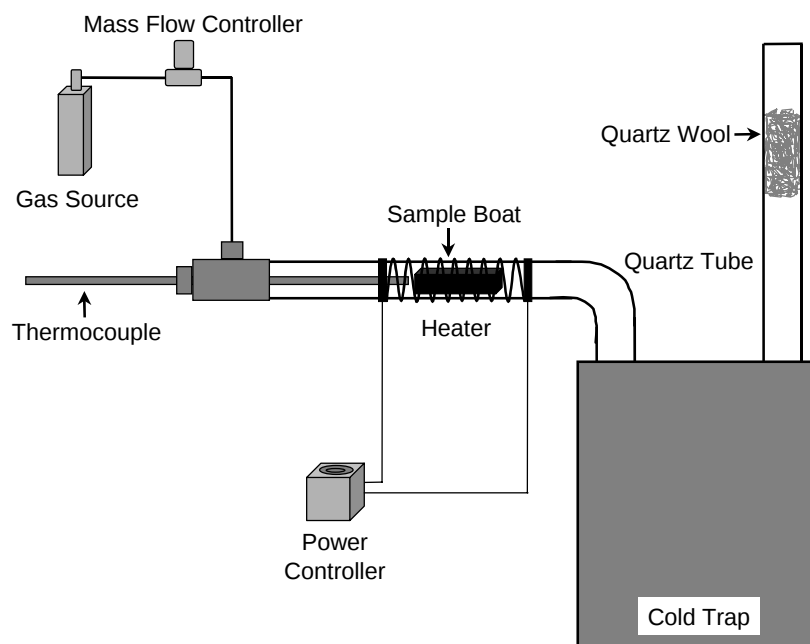


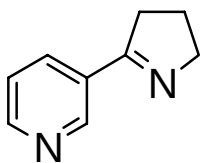
Figure 1. Experimental apparatus used for thermolysis studies.

The percentage of nicotine recovered from each pyrolysis run was determined by taking the average value of three GC injections. All samples were run in triplicate. The reported percent yield of nicotine for each sample in Table I is the average of the three pyrolysis runs. The GC was calibrated with standard solutions containing nicotine and the internal standard isoquinoline. The samples and standards were analyzed using the same packed liner that was prepared and conditioned at the beginning of each analysis.

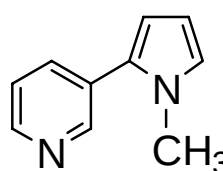
The data were collected using HP Chemstation® software and processed against the standards using the internal standard calculation method.

A Hewlett Packard 5890A GC with a FID detector was used with a Supelco Stabilwax DB™ (15 m x 0.25 mm I.D. x 0.25 µm film thickness) column. The GC conditions were: injector port temperature, 225°C; detector temperature, 250°C; oven temperature program, 150°C to 200°C at 5°C/min, 0 min hold; the carrier gas was He at a flow rate of 30-32 mL/min; the detector makeup was He at 30 mL/min; split flow, 30-35 mL/min; split liner, an inverted cup design, packed with 1 cm Carbowax®/KOH and glass wool at top and bottom. The flow rates for air and hydrogen were 350-400 mL/min and 30 mL/min, respectively. Under these conditions, the observed retention times were 3.1 minutes for nicotine and 4.1 minutes for isoquinoline.

To account for any trapping inefficiency, the percent recovery of nicotine pyrolyzed in argon was normalized to 100% for each of the triplicate pyrolysis runs. This multiplier (the inverse of the average transfer efficiencies of the three runs) was then used to adjust all other pyrolysis experiments. The absence of any decomposition products (see pyrolysis discussion below) in the nicotine samples heated in an argon atmosphere was verified by separate GC/MS analysis (Hewlett Packard 5890 GC with a DB™ 5ms column and a Hewlett Packard 5971 MS). Small quantities of myosmine (4) as well as nicotyrine (5) were observed, via separate GC/MS analysis, in the nicotine samples pyrolyzed in air.¹⁶



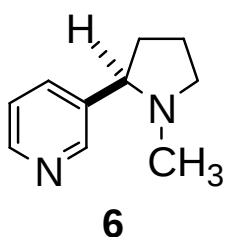
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ANALYTICAL METHODOLOGY

The percentage of R-(+)-nicotine (6) present in the recovered nicotine mixture was determined using an



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HPLC method and analytical equipment previously described.¹⁷ Briefly, 100 µL of a given nicotine sample in methanol (the same samples analyzed by GC as described above) was injected into a 25 x 1 cm I.D. silica HPLC column obtained from Astec (Whippany, NJ). The mobile phase was a mixture of methanol and hexane in the ratio of 80/20 (v/v) and the flow rate was 2 mL/min. The eluent of nicotine, which was

Table I. Summary of experimental results reported herein on the thermolyses of nicotine (**1**), nicotine malates [**2a** and (**2a-3a**)] and nicotine bisbitartrate (**2b-3b**).^a

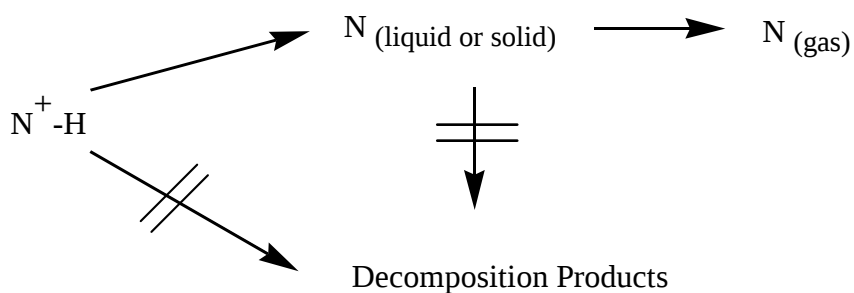
Substrate	Control		Atmosphere					
			Argon			Air		
	R-(+)-nicotine (6) (% of total nicotine)	Enantiomeric Excess	Transfer Yield (%)	R-(+)-nicotine (6) (% of total nicotine)	Enantiomeric Excess	Transfer Yield (%)	R-(+)-nicotine (6) (% of total nicotine)	Enantiomeric Excess
nicotine (1)	n/o ^b	>99.96%	100 ^c	n/o	>99.96%	97.3 (±0.6)	n/o	>99.96%
nicotine malate (2a) (1:0.56 nicotine:malic acid) (pH 5.6)	n/o	>99.96%	95.3 (±0.3)	0.10	99.80%	93.3 (±0.5)	0.16	99.68%
nicotine malate (2a-3a) (1:1 nicotine:malic acid)	n/o	>99.96%	98.4 (±0.6)	0.45	99.10%	94.0 (±1.1)	n/o	>99.96%
nicotine bisbitartrate (2b-3b) (1:2 nicotine:tartaric acid)	0.03	99.94%	95.3 (±0.8)	0.03	99.94%	92.3 (±0.5)	0.04	99.92%

^a Each pyrolysis condition was performed at least three times, and the results reported are the average value. Standard deviations are given in parentheses. ^b “n/o” indicates not observed, that is, no peak was observed at the retention time of R-(+)-nicotine. The error limit (%RSD) for all samples containing $\geq 0.1\%$ R-(+)-nicotine are $\pm 10\%$ ($n = 4$). The error limits for all other samples in the 0.02-0.07% range R-(+)-nicotine are $\pm 30\%$ ($n = 4$). The detection limit was 0.02% R-(+)-nicotine. ^c The average recovery value for six runs was 98.5% (±0.3). GC/MS analysis showed no decomposition products. It is assumed that the efficiency of collection was about 98.5%. A correction factor was thus used in all yield/transfer yield calculations. See the text and the experimental section for details on the correction factors used.

well separated from isoquinoline (used as internal standard for GC analysis) and other impurities, was collected and concentrated by evaporating the solvent with nitrogen gas. The enantiomers of nicotine were then analyzed with a chiral HPLC method. A Chiralcel OJ column, provided by Dr. Ronald Bopp of Chiral Technologies, Inc (Exton, PA), was used as the stationary phase. The mobile phase was hexane/ethanol/trifluoroacetic acid/triethylamine (85/15/0.075/0.0375). The flow rate was 1 mL/min and the UV detection was at 254 nm.

RESULTS AND DISCUSSION

Generalized Thermolysis Pathways for Amines. Schemes I and II present two models for the thermolysis of protonated and nonprotonated amines and the transfer of the amine to the gas phase [$N_{(gas)}$]. Gas phase materials can subsequently condense and form aerosols. In Scheme I, the temperature at which the protonated amine (N^+-H) is converted to the more volatile nonprotonated amine [$N_{(liquid\ or\ solid)}$] is lower than the temperatures required to decompose both N^+-H and $N_{(liquid\ or\ solid)}$. Heating either the protonated amine or the nonprotonated amine leads to the amine in the gas phase.

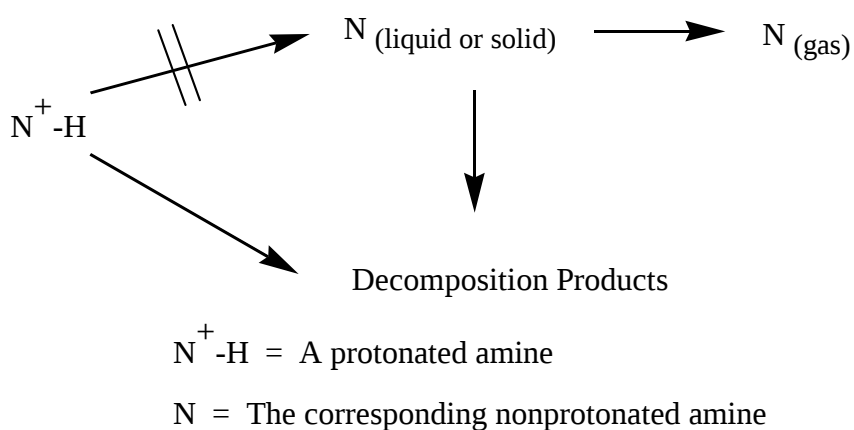


N^+-H = A protonated amine

N = The corresponding nonprotonated amine

Scheme I

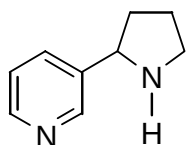
In Scheme II, the temperature at which the protonated amine is transformed to one or more decomposition products is lower than the temperature required to convert it to the more volatile nonprotonated amine [$N_{(liquid\ or\ solid)}$]. Hence, heating N^+-H does not lead to any N in the gas phase. Heating $N_{(liquid\ or\ solid)}$ can lead to both decomposition products and/or $N_{(gas)}$, depending on the relative volatile rates of decomposition and evaporation.



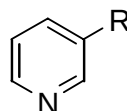
Scheme II

NICOTINE CHEMISTRY

Numerous studies concerning the thermal chemistry of nicotine (**1**) and other tobacco alkaloids have been reported in the literature over the years.^{7, 18-24} All but one⁷ of these studies has been performed by injecting the alkaloid into a preheated oven and trapping and characterizing the evolved reaction products. In general, these studies indicate that nicotine is stable in inert atmospheres up to temperatures in excess of 600°C.^{7, 19, 21, 22, 25} In air, nicotine begins to decompose at ca. 300°C.¹⁸ Some of the pyrolysis and/or oxidation products of nicotine include myosmine (**4**), nicotyrine (**5**), nornicotine (**7**), and a variety of pyrrolidine ring-cleaved compounds, e.g., **8-13**. These pyrolytic conditions are not, however, identical to the conditions experienced by nicotine in a puffing cigarette.^{4, 5, 26-28} A cigarette experiences a wide temperature range of about 30°C to 900°C^{26, 27, 29} and the nicotine experiences notably brief contact times before evaporating and being carried along the cigarette rod into the cooler regions of the cigarette.²⁸



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8, R = H

9, R = CH₃

10, R = CH₃CH₂

11, R = CN

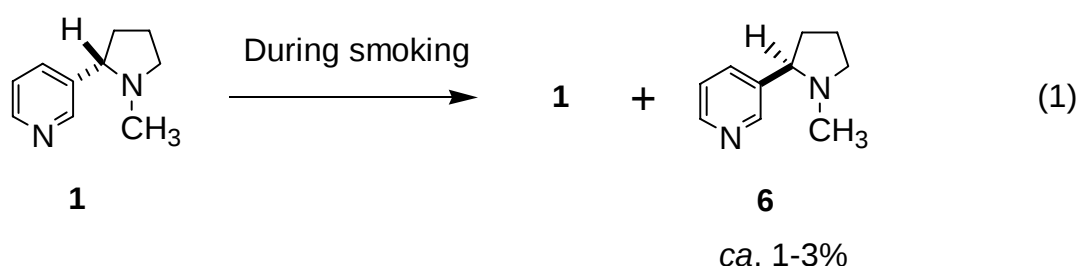
12, R = CH=CH₂

13, R = COCH₃

It is well known that protonated amines are less volatile than their corresponding nonprotonated amines, and this is certainly true in the nicotine series. What is neither unambiguous nor necessarily obvious is

which of the general chemical/physical paths shown in Schemes I and II happens when any particular amines or their protonated forms, such as nicotine and protonated nictines, are heated.

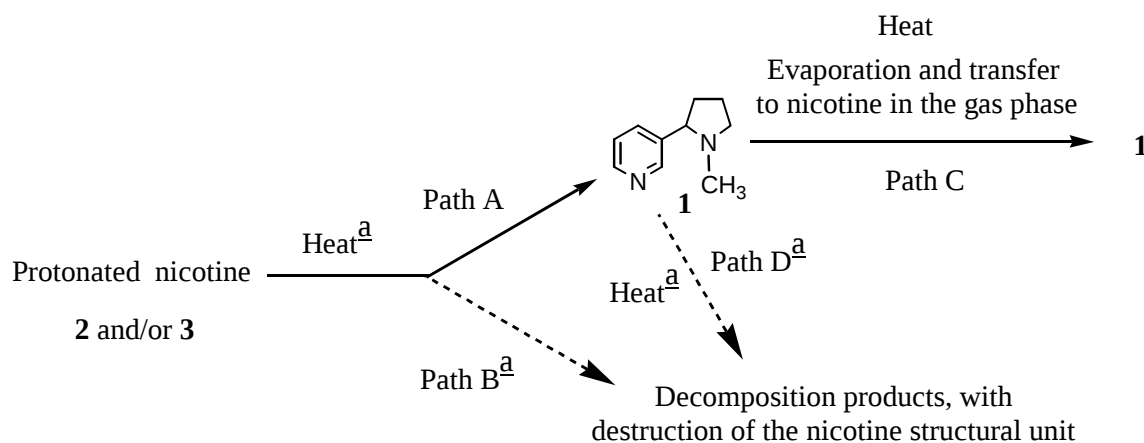
To distinguish between the various paths illustrated in Schemes I and II in the nicotine system, the yields of the thermal transfer from **1** and representative samples of **2** and **3** to nicotine in the gas phase in both air and inert atmospheres were determined. Minor racemization (the most recent and reliable values are *ca.* 1-3%) has been observed in the transfer of nicotine to mainstream cigarette smoke^{23, 30-33} (eq 1). Hence, the enantiomeric yields of nicotine isolated from the thermal treatments were also determined.



Various nicotine-containing substrates, chosen to represent mono- and diprotonated nicotine salts, were heated under either air or argon at a flow rate of *ca.* 500 mL/min and at a heating rate of about 400°C/min. The resultant effluent gases and/or aerosol were trapped, collected, and analyzed by GC using isoquinoline as an internal standard. The enantiomeric excess (purity) of the nicotine precursors and products was determined by HPLC analysis with a chiral stationary phase, using a method which had previous been demonstrated to be highly reproducible and capable of measuring enantiomeric excess (ee) accurately at 99-99.9% levels of purity.¹⁷ The results are reported in Table I and illustrated in Scheme III. Transfer yield, as defined herein, is equivalent to a chemical yield for the reaction described by Path A and/or Path C in Scheme III.

a. Thermal treatment of nonprotonated nicotine (1).

When nicotine was heated from room temperature to 500°C at about 400°C/min under argon at a flow rate of *ca.* 500 mL/min, the trapped material consisted of nicotine in an average yield of *ca.* 98.5% (see Table I). No indication of any degradation products was observed by separate GC/MS analysis. No racemization was observed in either argon or air. On this basis, it is concluded that nicotine transfers essentially quantitatively and with complete chiral retention under these conditions. A correction factor was applied to compensate for the slight percentage (1.5%) of nicotine which was not trapped in the collection device. In an atmosphere of air under the same heating regime, nicotine transfers with a yield of *ca.* 97%. See the experimental section for details.



^a Dashed arrows indicate minor pathways. In the experiments reported herein, heat was applied from ambient temperature to about 500°C under a flow of gas. See the text for details.

Scheme III

b. Thermal treatment of protonated nicotines (2-3).

(*S*)-Malic acid is found in significant concentrations in various tobaccos.³⁴ Two malate salts of nicotine were examined in this work. First, monoprotonated **2a** was prepared by titrating an aqueous nicotine solution with (*S*)-malic acid until a pH of 5.6 was reached (1:0.56 nicotine to malic acid); the oil that resulted following evaporation of the water was used in the pyrolysis. At pH of 5.6 in dilute aqueous solution, nicotine is 99% monoprotonated.^{35, 36} The noncrystalline 1:0.56 nicotine:malic acid salt may well be heterogeneous at room temperature, but because an aqueous solution of this malate has a pH of 5.6, it is referred to as **2a** herein. As shown in Table I, the transfer efficiencies of **2a** to nicotine in an atmosphere of argon and air, are ca. 95% and 93%, respectively. These values are about 4.5% less than the transfer yield from nonprotonated nicotine itself.

Two additional nicotine salts were examined in this work, the crystalline salts of both (*S*)-nicotine (*S*)-malate (**2a-3a**) (1:1) and (*S*)-nicotine bis[(*2R,3R*)-hydrogen tartrate] dihydrate (**2b-3b**) (1:2).¹⁵ The actual structures of these nicotine salts at room temperature are complicated. For example, the crystalline nicotine bisbitartrate contains both monoprotonated (**2b**) and diprotonated (**3b**) nicotine in the crystal unit cell and is thus referred to as **2b-3b** in this report.³⁷ Importantly, the structures of these salts (and the extent of protonation of the nicotine content) will certainly change as they are heated. For example, the crystalline bitartrate **2b-3b** melts in its water of hydration long before thermally induced decomposition occurs; the crystalline substance **2b-3b** is most certainly **3b** in its melt.⁷

These salts (**2a**, **2a-3a**, and **2b-3b**) were independently heated under both an argon and an air atmosphere. The results are summarized in Table I. The first step in each of these thermolyses is melting of the substrate, leading to rapid acid-base equilibration. Additional heating leads to dissociation and/or decomposition of the organic acid anion, followed by evaporation of the resultant nonprotonated nicotine. In argon, the thermal transfer efficiencies to nicotine in the gas phase are in the 95-98% range from the three substrates, and in air the efficiencies are in the 92-94% range. For each substrate, the transfer yield is *ca.* 2-4% higher in an atmosphere of argon than in air. This is consistent with thermal transfer from nonprotonated nicotine itself, which showed *ca.* 3% higher transfer in an argon atmosphere compared with that in air.

Under the conditions of their thermal experiments, very slight contents (ranging from not detected to 0.45%) of the *R*-enantiomer (**6**) of the starting, natural (*S*)-(-)-nicotine (**1**), was observed in the nicotine transferred. See Table I. All but one of the values of the percent **6** present are between “not detected” and 0.1%, that being the thermal treatment of **2a-3a** in argon (0.45%). The same compound, heated in air, resulted in no detectable **6**. In total, these results indicate that very little, if any, racemization occurs for these protonated nicotine salts under either an air or argon atmosphere.

In tobacco, nicotine is protonated by thermally labile carboxylic acids, the decomposition temperatures of which, when in association with nicotine, dictate the upper range of temperatures of nicotine release.⁷ Stronger mineral acids such as HCl are neutralized by mineral bases (e.g., Ca, K, and Mg cations) present in tobacco.³⁴ Hence, salts such as nicotine hydrochloride were not examined in this work.

APPLICATION OF NICOTINE THERMOLYSIS RESULTS TO AN UNDERSTANDING OF NICOTINE CHEMISTRY IN THE SMOKING PROCESS.

The results described above show that examples of **2** and **3** thermally transfer in high yield (92-98%) and with near complete configurational integrity to (*S*)-(-)-nicotine in the gas phase when the sample is heated from ambient temperature at about 400°C/min. In fact, previous studies using thermogravimetric analysis (TGA) demonstrated^{7, 38} that most of the nicotine is evaporated prior to the temperature reaching 250°C. Peak transfer temperatures are: nicotine and nicotine acetate, both *ca.* 110-125°C; nicotine malates, *ca.* 160-210°C; (*S*)-nicotine bis[(2*R*,3*R*)-hydrogen tartrate] dihydrate, *ca.* 195-210°C.

That the transfer yields are high but not quantitative is similar to that found in smoking studies.^{20, 39-42} For example, Houseman added nicotine-2'-¹⁴C-di(*p*-toluoyltartrate) to cigarette tobacco, isolated the various smoke fractions. He found that 15.4% of the original overall ¹⁴C-activity was in the mainstream *particulate phase* and that greater than 95% of this activity was nicotine. Approximately 4% of the

original ^{14}C -activity was in the mainstream *gas phase*, all being nicotine decomposition products.³⁹ Schmeltz, *et al.* observed that when nicotine was passed through an oven preheated to temperatures of 600°C, 750°C or 900°C, it underwent extensive degradation. In contrast, they found that in a burning cigarette, “a substantial portion of nicotine remained intact,” recognizing that the smoking process led to substantial distillation of nicotine.²⁰

In a thermolysis experiment of volatile or semi-volatile substrates, two distinct pathways are possible: volatilization of the intact substrate, or pyrolysis, see Schemes I and II. In experiments using a thermolysis tube, if the heating zone is initially at a temperature below the decomposition temperature of the substrate, the primary volatilization of the substrate may occur prior to substantial substrate decomposition. This is what is observed in the thermolyses of **1-3** described in the results reported herein. Alternatively, if the thermolysis tube is preheated to a temperature already above the decomposition temperature of the substrate and residence times in the heated chamber are sufficiently long, then destruction of the substrate will be observed in preference to distillation of the intact material. In the Schmeltz, *et al.* studies,²⁰ nicotine faced temperatures of 600°C and above, above its thermal stability range and also well above temperatures at which nicotine evaporates.

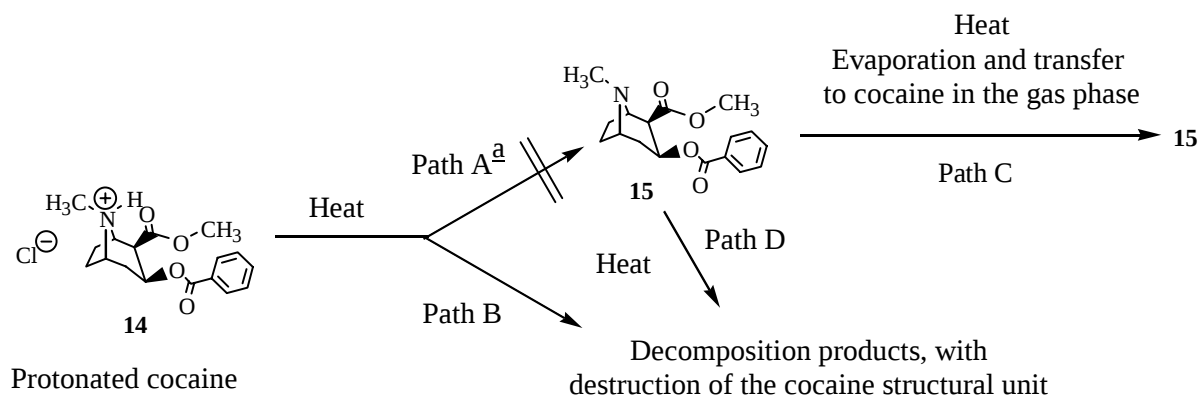
An analogous example is the pyrolysis and smoke chemistry of the volatile substance menthol. Schmeltz and Schlotzhauer⁴³ found significant pyrolysis of menthol at 600°C, but Jenkins, *et al.* observed that 98.9% of the ^{14}C -activity in the mainstream smoke of a cigarette to which ^{14}C -menthol had been added was contained in unchanged menthol.⁴⁴ Clearly, for volatile and semivolatile organic molecules possessing some degree of thermal stability, thermolyses performed from ambient temperature to higher temperatures are likely to better mimic the distillation conditions in a burning cigarette. Dotriacontane⁴⁵ and octatriacontane⁴⁶ also will transfer to mainstream smoke in high yield, although when injected into a preheated tube at high temperatures, both decompose rather than distill unchanged. This is because these molecules, which largely distill under smoking conditions, have at most very brief exposure times to extreme temperatures. Such molecules, however, suffer extensive degradation when experiencing temperatures significantly above those at which they will evaporate. Similar conclusions were recently reached in the evaluation of simple monocyclic aromatic additives to tobacco, such as vanillin, *p*-anisaldehyde, and methyl *trans*-cinnamate.⁴

Schmeltz, *et al.* suggested that nicotine pyrolysis may also be dependent on the form of the nicotine, i.e., nonprotonated or protonated.²⁰ In contrast, the results reported herein found only slight differences (see Table I) based on the form of nicotine pyrolyzed. This is because high yield transfers were observed for all substrates examined at relatively low temperatures.

In total, these experimental results strongly support the validation of Path A and/or Path C with lesser contributions from Path B and Path D (Scheme III) for nicotine and protonated nictines during temperature-ramped thermolysis and also during puffing in the smoking process.

SUBSTANCES WHICH THERMALLY DECOMPOSE BEFORE THEY EVAPORATE

Some protonated amines are much less thermally stable than nicotine and when exposed to heat decompose prior to their evaporation and transfer to the gas phase. Scheme II generalizes this behavior. A specific example of Scheme II chemistry is found in the 8-azabicyclo[3.2.1]octane ring system (e.g., cocaine hydrochloride (**14**), as shown in Scheme IV), in which the strained ring system and thermally labile substituents lead to ring cleavage and elimination reactions.

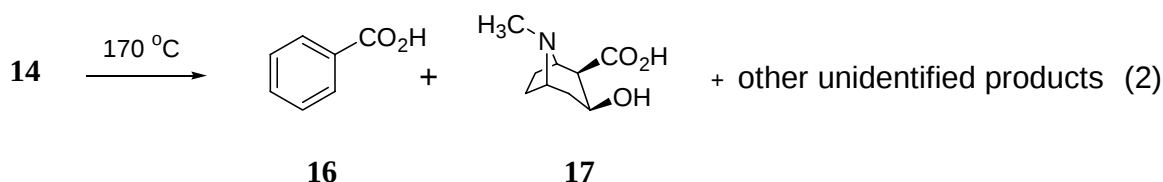


^a Minor pathway, if observed at all.

Scheme IV

No experimental work on any cocaine-containing compounds was performed in our research. However, sufficient literature data on the thermal and smoking properties of **14** and **15** is available to understand their thermal chemistry. Even though the literature thermolysis studies were performed under different conditions in different laboratories, the results are clearly uniform: cocaine (**15**) is not particularly thermally stable⁴⁷⁻⁴⁹ and cocaine hydrochloride (**14**) is thermally very unstable.^{50, 51} Cocaine hydrochloride begins to decompose at about 120°C and one study indicates complete decomposition of **14** at *ca.* 170°C to form benzoic acid (**16**), the hydroxycarboxylic acid (**17**), and a number of other unidentified products (eq 2).⁵¹ For **14**, only Path B transformations are observed, not Path A (Scheme IV). The scientific literature indicates that the temperatures required to convert cocaine hydrochloride

(14) to cocaine (15) in the gas phase are higher than the decomposition temperature of the cocaine ring system. Heating 15 leads to both distillation (Path C) and considerable decomposition (Path D).^{48, 52}



According to the scientific literature, when nonprotonated cocaine (15) is added to tobacco, under smoking conditions, apparently only inefficient transfer of cocaine to the gas phase is observed.⁵⁰ As tobacco is acidic,^{8, 34, 53-55} it is likely that when 15 is added to tobacco, it is converted to protonated cocaine salts and thus decomposes when heated.⁵¹

IMPLICATIONS OF THIS WORK

- During thermal and combustion processes of plant materials, a number of distinct chemical processes control the extent of transfer of intact amines into smoke vs. decomposition. These are the relative thermal stability and ease of evaporation of the nonprotonated and protonated amines, including natural product alkaloids; and the relative stability or volatility of any associated counterions (such as anions of polycarboxylic acids).
- Pathways described by Schemes I and II are helpful to understand and analyze the transfer of amines to the gas phase during the combustion/pyrolysis of plant materials.
- The nicotine ring system is thermally quite stable (decomposes >600°C in inert atmosphere; >300°C in air).
- Nonprotonated nicotine and nicotine carboxylic acid salts thermally transfer nicotine to the gas phase with comparable yield, with near complete configurational integrity (Schemes I and III).
- An example of a protonated amine which does not effectively thermally transfer the intact amine to the gas phase (Scheme II and IV) is cocaine hydrochloride. Decomposition of the molecular structure in Scheme II-type of substrates occurs either exclusively or predominantly.
- Thermal studies may better mimic the balance between evaporation and pyrolytic destruction of volatiles and semi-volatiles during combustion, including cigarette smoking, if the thermolysis is performed by heating the substrate from ambient temperature to a higher temperature under a flow of gas. Injecting the substrate directly into a preheated tube at high temperatures may fail to reveal evaporative processes that happen at lower temperatures.

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