Gas/Particle Partitioning of Two Acid−Base Active Compounds in Mainstream Tobacco Smoke: Nicotine and Ammonia

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Gas/particle (G/P) partitioning constant (K_p) values are reported for nicotine and ammonia for mainstream tobacco smoke (MTS) for a selection of cigarettes, "little cigars", and biddies. As K_p^{nic} decreases as a result of the increasing basicity in the MTS, there is an increase in volatility of nicotine from the smoke particulate matter. The "little cigars" and biddies exhibited generally lower K_p^{nic} values and higher unbound ammonia levels than most of the cigarettes, suggesting a correlation between the two parameters. However, within just the cigarettes, there was little correlation. The water content of MTS particulate matter was found to affect both K_p^{nic} and K_p^{amm}. Unbound ammonia is actual NH_3/NH_4^+; bound ammonia is comprised of compounds such as amides of ammonia; total ammonia is unbound + bound. Most historical studies of ammonia in MTS have not accurately measured either unbound or total ammonia: the acidic solutions historically employed to determine ammonia in MTS will release ammonia from bound forms by hydrolysis, and the release in those studies may not have been complete. This study concludes that a thorough examination of unbound and bound ammonia in MTS will be required before the role of ammonia in affecting volatility of nicotine in MTS can be understood.

INTRODUCTION

Despite well-known concerns about the health effects of long-term tobacco use, worldwide, the production of tobacco has more than doubled since the 1960s, with the total production equaling about 7 million metric tons in 2000 (*1*). Much of this increase has occurred in developing countries, wherein completely unsustainable agricultural practices involving profitable tobacco industries have led to massive deforestation (*2*). It is thus more important than ever before in history that a comprehensive and accurate understanding of the chemistry of tobacco and tobacco smoke be attained.

Mainstream tobacco smoke (MTS) is the aerosol that is drawn directly from a cigarette or other tobacco product by a smoker for inhalation into the lungs or by a machine-smoking device simulating that process. The particle concentration in fresh MTS is enormous, and the current view is that, for most cigarettes, the majority of the nicotine is in the droplets comprising the particulate matter (PM_{MTS}). As an alkaloid, nicotine can exist in a free-base form (**Figure 1**) and in two protonated forms. The diprotonated form is negligible, except under extremely acidic conditions. In a sample of PM_{MTS}, the fraction of the nicotine that is in the free-base form at a given time is denoted α_{fb}^{nic}, with $0 < \alpha_{fb}^{nic} < 1$ (*3*). Henningfield et al. (*4*) discuss connections among (1) the acid/base chemistry of nicotine in

tobacco smoke, (2) nicotine delivery rate and addiction potential, and (3) tobacco industry use of additives.

Only the free-base form of nicotine is directly volatile from PM_{MTS}. Consequently, the overall rate and locational nature of the deposition of smoke nicotine in the respiratory tract (RT) will be
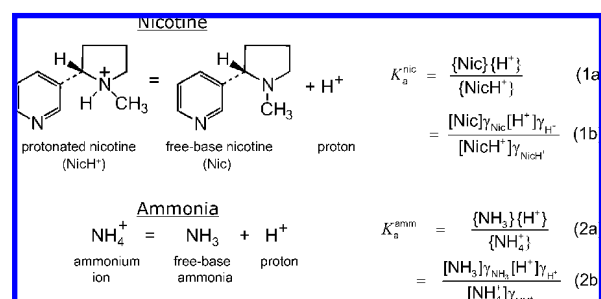

Figure 1. Analogous acid/base reactions for nicotine and ammonia, where K_a^{nic} and K_a^{amm} are the equilibrium acid dissociation constants for protonated nicotine and protonated ammonia, respectively. Both equilibrium constants involve the chemical activities of the involved species, denoted with braces: $\{H^+\}$ is the chemical activity of the proton. Interactions in a solution can make a chemical act differently than what would be expected on the basis of the concentration alone. For species i, the chemical activity $\{i\}$ = $[i]\gamma_i$, where $[i]$ = molal concentration of i and γ_i = molal activity coefficient of i. The value of γ_i is determined by how each unit of i "feels" relative to when i is present in very dilute water: if the same, then γ_i = 1; if more comfortable, then $\gamma_i < 1$; if less comfortable, then $\gamma_i > 1$.
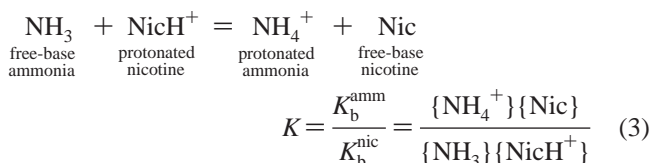
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controlled by α_{fb}^{nic} (*3*). α_{fb}^{nic} may vary as a given cigarette is smoked (*5*) and as the smoke ages locationally within the RT.

The acid/base and solution chemistries of tobacco smoke control the value of α_{fb}^{nic} (*3, 5*): α_{fb}^{nic} increases as the pH of a sample of PM_{MTS} increases, and Pankow et al. (*6*) confirmed that α_{fb}^{nic} in PM_{MTS} increases with increasing levels of the base ammonia. For fresh PM_{MTS} from several commercial brands of cigarettes at 20 °C, Pankow et al. (*5*) reported α_{fb}^{nic} values for initial puffs to be in the range of 0.010 (GPC) up to 0.38 (American Spirit "red"). By a related method, Watson et al. (*7*) reported brand-dependent α_{fb}^{nic} values consistent with those of Pankow et al. (*5*). Besides being important in tobacco smoke, the pH effects of ammonia affect secondary organic aerosol formation in the atmosphere (*8*).
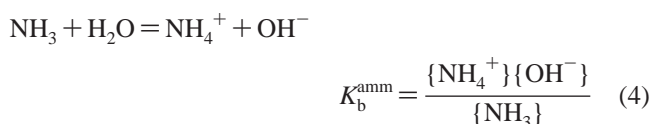
Internal tobacco industry documents obtained during litigation against the industry in the 1990s have provided much information regarding interests and historical practices of companies such as Philip Morris (PhM), RJ Reynolds (RJR), Brown and Williamson (B&W), British American Tobacco (BAT), and Lorillard (LOR). These documents indicate that a variety of nitrogen-containing compounds [ammonia, urea, diammonium phosphate (DAP), protein, etc.] have been added to tobacco materials used in cigarettes. Using the subscript "doc" to denote an internal document, examples are $B\&W_{doc}$ (*9−11*), RJR_{doc} (*12*), and LOR_{doc} (*13*). NaOH and Na_2CO_3 have also been used [RJR_{doc} (*14*) and $PRIG_{doc}$ (*15*), where PRIG = intercompany "Product Regulatory Issues Group"]. Two primary reasons are discussed in the documents for using ammonia-related additives: (1) improving the physical strength of "reconstituted tobacco sheet" (RTS) [PhM_{doc} (*16*), PhM_{doc} (*17*), and RJR_{doc} (*18*)], which is a type of paper produced in the industry to (a) make use of tobacco "fines" and leaf stems [PhM_{doc} (*19*)] and (b) serve as a vehicle for additives [PhM_{doc} (*20*)] and (2) adjusting the sensory potency of cigarette smoke. Various terms have been used regarding sensory potency, including "strength" [BAT_{doc} (*21*), LOR_{doc} (*22, 23*)], "harshness" [RJR_{doc} (*24−26*)], "impact" [BAT_{doc} (*27*), $B\&W_{doc}$ (*28−31*), LOR_{doc} (*32*), RJR_{doc} (*33*)], and "kick" [RJR_{doc} (*34−37*)]. Because increasing smoke potency has been associated with increasing levels of free-base nicotine, many industry documents discuss the view that ammonia-related additives increase smoke potency by increasing the "smoke pH" [e.g., $B\&W_{doc}$, (*9, 38*), LOR_{doc} (*39*), and PhM_{doc} (*40*)].

As a base, ammonia can remove the proton on $NicH^+$ to form Nic (free-base nicotine) according to

$$\underset{\substack{\text{free-base}\\\text{ammonia}}}{NH_3} + \underset{\substack{\text{protonated}\\\text{nicotine}}}{NicH^+} = \underset{\substack{\text{protonated}\\\text{ammonia}}}{NH_4^+} + \underset{\substack{\text{free-base}\\\text{nicotine}}}{Nic}$$

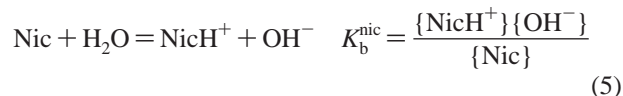$$K = \frac{K_b^{amm}}{K_b^{nic}} = \frac{\{NH_4^+\}\{Nic\}}{\{NH_3\}\{NicH^+\}} \quad (3)$$

The driving force for this reaction is related to the relative strengths of ammonia and nicotine as bases, which are quantified by the temperature-dependent basicity constants K_b^{amm} and K_b^{nic}. In water at 20 °C, ammonia is about 20× stronger as a base than nicotine. At 37 °C, ammonia is ∼13× stronger.

K_b^{amm} relates to the ability of ammonia to remove H^+ from water (including within PM_{MTS}) according to

$$NH_3 + H_2O = NH_4^+ + OH^-$$

$$K_b^{amm} = \frac{\{NH_4^+\}\{OH^-\}}{\{NH_3\}} \quad (4)$$

For nicotine

$$Nic + H_2O = NicH^+ + OH^- \quad K_b^{nic} = \frac{\{NicH^+\}\{OH^-\}}{\{Nic\}} \quad (5)$$

Equations 1a, 2a, 4, and 5 give

$$\frac{K_b^{amm}}{K_b^{nic}} = \frac{K_a^{nic}}{K_a^{amm}} \quad (6)$$

In water at 20 °C, $K_a^{nic} \approx 10^{-8.06}$ (*41*) and $K_a^{amm} \approx 10^{-9.40}$ (*42*), so that $K_b^{amm}/K_b^{nic} \approx 20$ [At 37 °C, $K_a^{nic} \approx 10^{-7.76}$ (*41*) and $K_a^{amm} \approx 10^{-8.89}$ (*42*), so that $K_b^{amm}/K_b^{nic} \approx 13$].

In this work, for commercial cigarettes and other related products, we describe measurements of (1) ammonia and nicotine in PM_{MTS}, (2) ammonia and nicotine in the gas phase of MTS, and (3) water in PM_{MTS}. The measurements are used to obtain an improved understanding of the coupled acid/base-dependent volatility of nicotine and ammonia from PM_{MTS}.

HISTORICAL DETERMINATIONS OF AMMONIA IN TOBACCO SMOKE

Methods used to determine ammonia levels in tobacco smoke have employed a variety of techniques in the final determination step. Using company abbreviations to denote industry affiliations when applicable, ammonia determinations in tobacco smoke have proceeded using colorimetric methods [Harrell et al., RJR (*43*), Labstat (*44*), and PhM_{doc} (*45*)], ion-specific electrode [Sloan and Morie (*46*)], laser spectroscopy [PhM_{doc} (*47*)], gas chromatography (GC) [Ayers, BAT (*48*) and Brunnemann and Hoffmann (*49*)], and ion chromatography (IC) [Huang et al., PhM (*50*), Labstat (*51, 52*), Nanni et al., RJR (*53*) and PhM_{doc} (*54*)]. For the initial sampling step, Ayers, BAT (*48*) and Brunnemann and Hoffmann (*49*) passed MTS through a "bubbler" containing 0.1 N H_2SO_4 to trap smoke ammonia; Brunnemann and Hoffmann (*49*) followed the bubbler with a small "impinger" that also contained 0.1 N H_2SO_4. The H_2SO_4 solutions were then concentrated by evaporation. Sloan and Morie (*46*) collected smoke in 0.1 N HCl, added NaOH to each sample, and then concentrated the ammonia by steam distillation.

Harrell et al., RJR (*43*) suggested that the processing approaches used by Ayers, BAT (*48*), Sloan and Morie (*46*), and Brunnemann and Hoffmann (*49*) carry the potential to release ammonia in tobacco smoke samples by "degradation of amides, nitriles, and other nitrogen compounds". Brunnemann and Hoffmann (*49*) discussed that steam distillation (used to isolate ammonia from smoke extracts) could lead to hydrolysis of amides and the concomitant release of ammonia.

The 1R4F Kentucky reference cigarette has been manufactured by the University of Kentucky in an effort to provide a consistent test cigarette (*55*). It is possible to compare smoke ammonia levels for the 1R4F when smoked by the Federal Trade Commission protocol [IARC (*56*)] but with the smoke analyzed by different methods (it should nevertheless always be remembered that batch−batch and pack−pack variations can never be completely eliminated). Huang et al., PhM (*50*) used a "Cambridge" glass fiber filter to collect PM_{MTS} from the 1R4F and bubbled the smoke gas through an impinger containing 50 mL of "acidic solution". After sampling, the filter was extracted using the solution in the impinger, resulting in reported ammonia levels of 15−20 μg/cigarette. Using a similar approach with 20 mL of 0.1 N H_2SO_4, Labstat (*52*) reported an average ammonia level of 14.5 μg/cigarette. Nanni et al., RJR (*53*) used an electrostatic precipitator capable of "quantitatively trapping" PM_{MTS}. However, rather than using an acidic solution to extract the PM_{MTS}, they employed methanol as a gentler

extraction solvent and reported ammonia levels of ~5 μg/cigarette. These results along with other considerations cited above (e.g., that measured ammonia levels may increase under acidic analysis conditions) are consistent with the view that the correct measurement of unbound ammonia (i.e., $NH_3 + NH_4^+$) levels in MTS may require gentle extraction conditions so that NH_3 is not released from ammonia-containing compounds during analysis.

For the smoke ammonia measurements carried out here, deionized water and 2-propanol were the extraction solvents. The maximum volume for the smoking apparatus was ~1100 mL. For the machine smoking protocol used, all actual cigarettes examined produced <1100 mL of smoke and the mass deliveries M (μg) correspond to consumption of the entire cigarette according to the smoking protocol used. For all of the other products, $\leq$60% of the rod was consumed by the time the sampled smoke volume reached ~900 mL (see below) and the mass deliveries M (μg) correspond to that volume.

For unbound (u) and bound (b) ammonia, for all products

$$M_g^{amm,u} (\mu g) = NH_3 \text{ in the gas phase} \quad (7)$$

$$M_p^{amm,u} (\mu g) = NH_3 + NH_4^+ \text{ in the particle phase} \quad (8)$$

$$M_{g+p}^{amm,u} (\mu g) = M_g^{amm,u} + M_p^{amm,u} \quad (9)$$

$$M_{g+p}^{amm,b} (\mu g) = \begin{array}{l} \text{ammonia that can be released from ammonia-} \\ \text{containing compounds (g + p) in the smoke} \end{array} \quad (10)$$

$$M_{tot}^{amm} (\mu g) = M_{g+p}^{amm,u} + M_{g+p}^{amm,b} \quad (11)$$

When the values obtained by Nanni et al., RJR (*53*) are compared to the other ammonia MTS values cited above, they may suggest that, for the typical commercial cigarette, $M_{g+p}^{amm,u} \approx {}^1\!/_3 M_{tot}^{amm}$.

THEORY

pH$_{eff}$ and α_{fb} for Nicotine and Ammonia. For a solution

$$pH \equiv -\log\{H^+\} = -\log(\gamma_{H+}[H^+]) = -\log \gamma_{H+} - \log[H^+] \quad (12)$$

where $\{H^+\}$ is the chemical activity of H^+, $[H^+]$ is the concentration of H^+, and γ_{H+} is the activity coefficient for H^+, i.e., the correction factor between $\{H^+\}$ and $[H^+]$ (see also **Figure 1**). Interpreting the results of this study requires predictions of how γ values change with varying solution composition. For K_a values for dilute water, all γ_i values are defined relative to how i feels in dilute water: if the same, $\gamma_i = 1$; if more comfortable, $\gamma_i < 1$; if less comfortable, $\gamma_i > 1$. An anthropomorphic analogy that illustrates how different solution environments can affect γ_i values is provided in the Supporting Information.

For the PM portion of the nicotine [Pankow (*3*)]

$$\alpha_{fb}^{nic} = \frac{[Nic]}{[Nic] + [NicH^+]} \quad (13)$$

Molal concentration units [mol/(kg of PM_{MTS})] can be used for [Nic] and [NicH$^+$] in eq 13. Nanograms/(μg of PM_{MTS}) could also be used, but then both [Nic] and [NicH$^+$] are understood to be represented in terms of ng as Nic/(μg of PM_{MTS}). By analogy with nicotine, for unbound ammonia in PM_{MTS}, the fraction that is in the free-base form is defined

$$\alpha_{fb}^{amm} = \frac{[NH_3]}{[NH_3] + [NH_4^+]} \quad (14)$$

If the concentration units used are ng/μg, then both [NH$_3$] and [NH$_4^+$] are understood to be represented in terms of ng as NH$_3$/(μg of PM_{MTS}).

Various methods have been used with the intention of determining "smoke pH" values to elucidate α_{fb}^{nic} values in tobacco PM_{MTS} by eq 1b, with the assumption (incorrect) that activity corrections therein may be neglected. An example is the method of Sensabaugh and Cundiff (*57*), in which PM_{MTS} is allowed to accumulate on a pH electrode previously calibrated with aqueous buffer solutions. However, the existence of severe calibration problems with this and other "smoke pH" methods means that no accurate pH measurement has ever been made for PM_{MTS}: all reported "smoke pH" values are, at best, only roughly correlatable with the true underlying pH values of the corresponding PM_{MTS} samples (*3*). Fortunately, α_{fb}^{nic} in a PM_{MTS} sample can now be measured directly by the method of Pankow et al. (*5*). While values of α_{fb}^{nic} do not allow for direct calculation of values of pH in PM_{MTS} as defined by eq 12, they do allow for calculations of pH_{eff}^{nic} as defined below by eq 18.

Because $[H^+]$, γ_{H+}, and γ_{NicH+} in PM_{MTS} are difficult to measure and because they all appear together in eq 1b with γ_{Nic}, Pankow (*3*) proposed collecting the four parameters in the group $[H^+]\gamma_{H+}(\gamma_{Nic}/\gamma_{NicH+})$ and defining for the effective pH of PM_{MTS} for nicotine that

$$pH_{eff}^{nic} \equiv -\log[[H^+]\gamma_{H+}(\gamma_{Nic}/\gamma_{NicH+})] \quad (15)$$

$$pH_{eff}^{nic} = -\log([H^+]\gamma_{H+}) + \log[(\gamma_{NicH+}/\gamma_{Nic})] \quad (16)$$

$$pH_{eff}^{nic} = pH + \log[(\gamma_{NicH+}/\gamma_{Nic})] \quad (17)$$

$$10^{-pH_{eff}^{nic}} \equiv [H^+]\gamma_{H+}(\gamma_{Nic}/\gamma_{NicH+}) \quad (18)$$

Combining eq 18 with eqs 1b and 13 gives (*3*)

$$\alpha_{fb}^{nic} = \frac{10^{-pK_a^{nic}}}{10^{-pK_a^{nic}} + 10^{-pH_{eff}^{nic}}} \quad (19)$$

and (*3*)

$$pH_{eff}^{nic} = pK_a^{nic} + \log \frac{\alpha_{fb}^{nic}}{1 - \alpha_{fb}^{nic}} \quad (20)$$

As noted above, at 20 °C in water, $pK_a^{nic} = 8.06$ (*41*).

In dilute water, all $\gamma = 1$, so that, by eq 17, $pH_{eff}^{nic} = pH$ and thus an observed α_{fb}^{nic} value can be discussed in terms of the actual pH in the solution. In PM_{MTS}, although all $\gamma \neq 1$, eq 20 allows one to discuss an observed α_{fb}^{nic} in terms of the equivalent pH that would be required, in dilute water, to yield that value; e.g., when $\alpha_{fb}^{nic} = 0.50$ in PM_{MTS} at 20 °C, then $pH_{eff}^{nic} = 8.06$.

For ammonia, by analogy with eqs 15−20

$$pH_{eff}^{amm} = -\log[[H^+]\gamma_{H+}(\gamma_{NH_3}/\gamma_{NH_4+})] \quad (21)$$

$$pH_{eff}^{amm} = -\log([H^+]\gamma_{H+}) + \log[(\gamma_{NH_4+}/\gamma_{NH_3})] \quad (22)$$

$$pH_{eff}^{amm} = pH + \log[(\gamma_{NH_4+}/\gamma_{NH_3})] \quad (23)$$

or equivalently

$$10^{-pH_{eff}^{amm}} \equiv [H^+]\gamma_{H+}(\gamma_{NH_3}/\gamma_{NH_4+}) \quad (24)$$

Combining eq 24 with eqs 2b and 14 yields

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$$\alpha_{fb}^{amm} = \frac{10^{-pK_a^{amm}}}{10^{-pK_a^{amm}} + 10^{-pH_{eff}^{amm}}} \qquad (25)$$

$$pH_{eff}^{amm} = pK_a^{amm} + \log \frac{\alpha_{fb}^{amm}}{1 - \alpha_{fb}^{amm}} \qquad (26)$$

pK_a^{amm} has been measured to be 9.40 at 20 °C in water (*42*). By analogy with pH_{eff}^{nic}, we can use pK_a^{amm} to discuss the extent of protonation of ammonia in PM_{MTS} in terms that relate an observed α_{fb}^{amm} value to the equivalent pH conditions that would be required, in dilute water, to yield that value; e.g., when $\alpha_{fb}^{amm} = 0.50$ in PM_{MTS}, at 20 °C, then $pH_{eff}^{amm} = 9.40$.

Subtracting eq 17 from eq 23 yields

$$pH_{eff}^{amm} = pH_{eff}^{nic} + \log[(\gamma_{NH_4^+}/\gamma_{NH_3})] - \log[(\gamma_{NicH^+}/\gamma_{Nic})] \qquad (27)$$

In dilute water, $pH_{eff}^{amm} = pH_{eff}^{nic} = pH$ because $(\gamma_{NH_4^+}/\gamma_{NH_3}) = 1$ and $(\gamma_{NicH^+}/\gamma_{Nic}) = 1$. In PM_{MTS}, because in general $(\gamma_{NH_4^+}/\gamma_{NH_3}) \neq (\gamma_{NicH^+}/\gamma_{Nic})$, $pH_{eff}^{amm} \neq pH_{eff}^{nic} \neq pH$ and there is an *offset* between pH_{eff}^{amm} and pH_{eff}^{nic}.

The NH_3 molecule is quite polar and hydrophilic. PM_{MTS} is less polar than water, and thus, NH_3 will be less comfortable in PM_{MTS} than in dilute water; perhaps $\gamma_{NH_3} \approx 5$. Because NH_4^+ is ionic, the relative discomfort for NH_4^+ will be greater than for NH_3; perhaps $\gamma_{NH_4^+} \approx 20$. For $NicH^+$, because it is a relatively small organic ion, the comfort level will be lower in PM_{MTS} than in dilute water. However, the effect on $NicH^+$ will likely not be as great as on NH_4^+: the organic portion of $NicH^+$ will be relatively well accommodated in typical PM_{MTS}, so that

perhaps $\gamma_{NicH^+} \approx 10$. For Nic, as a neutral organic molecule, the comfort level will be higher in typical PM_{MTS} than in dilute water, so that perhaps $\gamma_{Nic} \approx 0.25$. These estimates for typical PM_{MTS} (see summary in **Table 1**) give $(\gamma_{NH_4^+}/\gamma_{NH_3}) \approx 0.1 (\gamma_{NicH^+}/\gamma_{Nic})$, so that for the offset we have

$$pH_{eff}^{amm} \approx pH_{eff}^{nic} - 1.0 \quad \text{(estimate at 20 °C)} \qquad (28)$$

which would indicate that, in general, PM_{MTS} solutions feel more acidic to ammonia than to nicotine. As an example, consider a solution in which $pH_{eff}^{nic} \approx 8.0$. If there was no offset, then $pH_{eff}^{amm} \approx 8.0$ and $\alpha_{fb}^{amm} \approx 0.04$. However, because of the offset, $pH_{eff}^{amm} \approx 7.0$ and $\alpha_{fb}^{amm} \approx 0.004$.

K_p and $K_{p,fb}$ Values for Nicotine and Ammonia. Only the free-base form of nicotine is volatile and in direct chemical exchange with the gas phase. The gas/particle (G/P) partitioning equilibrium constant (m³/μg) of free-base nicotine is [Pankow et al. (*3, 5, 6*)]

$$K_{p,fb}^{nic} = \frac{c_{p,fb}^{nic}}{c_g^{nic}} \qquad (29)$$

where c_g^{nic} (ng/m³) is the concentration of nicotine in the gas phase (wherein all of the nicotine is in the free-base form), and $c_{p,fb}^{nic}$ (ng/μg) is the concentration of free-base nicotine in the PM. If the total PM concentration of nicotine (c_p^{nic}, ng/μg Nic) is used instead of $c_{p,fb}^{nic}$, an overall equilibrium constant is obtained

$$K_p^{nic} = \frac{c_p^{nic}}{c_g^{nic}} \qquad (30)$$

Because $c_{p,fb}^{nic} = \alpha_{fb}^{nic} c_p^{nic}$ [Pankow et al. (*3, 6*)]

Table 1. Estimated Effects on γ Activity Coefficient Values for NH_4^+, NH_3, $NicH^+$, and Nic When Going from Dilute Water to PM_{MTS} and Corresponding Estimates for the Offset between pH_{eff}^{amm} and pH_{eff}^{nic}

	in very dilute water			in typical PM_{MTS}			
species	γ	γ ratio	pH_{eff}^{amm} in relation to pH_{eff}^{nic} by eq 26	less or more comfortable compared to being in dilute water?	γ estimate	γ ratio estimate	pH_{eff}^{amm} in relation to pH_{eff}^{nic} by eq 26
NH_4^+	$\gamma = 1$	$\gamma_{NH_4^+}/\gamma_{NH_3} = 1$		NH_4^+ much less	$\gamma \approx 20$	$\gamma_{NH_4^+}/\gamma_{NH_3} \approx 4$	
NH_3	$\gamma = 1$		$pH_{eff}^{amm} = pH_{eff}^{nic} + 0 \; (=pH)$	NH_3 less	$\gamma \approx 5$		$pH_{eff}^{amm} \approx pH_{eff}^{nic} - 1$
$NicH^+$	$\gamma = 1$	$\gamma_{NicH^+}/\gamma_{Nic} = 1$		$NicH^+$ less	$\gamma \approx 10$	$\gamma_{NicH^+}/\gamma_{Nic} \approx 40$	
Nic	$\gamma = 1$			Nic more	$\gamma \approx 0.25$		

Table 2. $K_{H,fb}^{amm}$ and Computed Values of $K_{p,fb}^{amm}$ and ζ_{NH_3} for Ammonia Dissolved in Solvents with Varying Dielectric Constant ε (Dimensionless)

solvent	dielectric constant[a] ε	MW (g/mol)	log $K_{H,fb}^{amm}$ (molal/atm, 20 °C)	log $K_{p,fb}^{amm}$ (m³/μg, 20 °C)	ζ_{NH_3} (20 °C)
water	80.1	18.0	1.89[b]	−8.73	0.088
methanol	33.0	32.0	0.89[c]	−9.73	0.55
ethanol	25.3	46.1	0.75[d]	−9.87	0.56
1-propanol	20.8	60.1	0.72[d]	−9.90	0.48
1,2-dichloroethane	10.4	99.0	−0.06[d]	−10.68	1.54
1,2,3-propanetriol triacetate	7.1	218.2	0.00[e]	−10.62	0.67
chloromethylbenzene	6.9	126.6	−0.34[d]	−10.95	2.21
chlorobenzene	5.7	112.6	−0.41[d]	−11.03	2.91
bromobenzene	5.5	157.0	−0.65[d]	−11.27	3.62
chloroform	4.8	119.4	0.29[d]	−10.33	0.64
1-methylnaphthalene	2.9	142.2	−0.53[f]	−11.15	3.06
toluene	2.4	92.1	−0.46[d]	−11.08	3.93
benzene	2.3	78.1	−0.30[d]	−10.92	3.26
carbon tetrachloride	2.2	154.4	−0.73[d]	−11.35	4.38
cyclohexane	2.0	84.2	−0.88[g]	−11.50	11.18
n-hexane	1.9	86.2	−0.54[f]	−11.16	5.03
1,1′-bicyclohexyl	N/A	166.3	−1.10[f]	−11.72	9.49

[a] *CRC Handbook of Chemistry and Physics* (*60*). [b] Clegg and Brimblecombe (*58*) [c] On the basis of the data in Young and Fogg (*61*) on $NH_{3\,(g)}$ solubility in the range of 273.2−301.6 K. [d] On the basis of the data in Young and Fogg (*61*) on $NH_{3\,(g)}$ solubility at 293.2 K. [e] On the basis of the equation given in Young and Fogg (*61*) on $NH_{3\,(g)}$ solubility as f(*T*). [f] On the basis of the extrapolation of the data in Young and Fogg (*61*) on $NH_{3\,(g)}$ solubility in the range of 300−475 K. [g] Based on data in Young and Fogg (*61*) on $NH_{3\,(g)}$ solubility at 292.5 K.

$$K_p^{nic} = \frac{K_{p,fb}^{nic}}{\alpha_{fb}^{nic}} \quad (K_p^{nic} > K_{p,fb}^{nic}) \tag{31}$$

By analogy with nicotine, only the free-base form of ammonia is volatile and

$$K_{p,fb}^{amm} = \frac{c_{p,fb}^{amm}}{c_g^{amm}} \quad \text{analogue of eq 29} \tag{32}$$

$$K_p^{amm} = \frac{c_p^{amm}}{c_g^{amm}} \quad \text{analogue of eq 30} \tag{33}$$

Note that all c^{amm} values used herein refer to unbound ammonia. For c_p^{amm} (ng/μg), which is the sum of $NH_3 + NH_4^+$ for the PM_{MTS}, the concentration pertains to ng as NH_3 per μg of PM_{MTS}. By analogy with nicotine, $c_{p,fb}^{amm} = \alpha_{fb}^{amm} c_p^{amm}$, so that

$$K_p^{amm} = \frac{K_{p,fb}^{amm}}{\alpha_{fb}^{amm}} \quad \text{analogue of eq 31} \tag{34}$$

$K_{p,fb}^{nic}$ values for fresh PM_{MTS} from 11 brands of commercial cigarettes were measured by Pankow et al. (*5*) to be in the range of $10^{-5.18}-10^{-4.83}$ m^3/μg at 20 °C. These results agree with the range of $10^{-5.24}-10^{-4.91}$ m^3/μg predicted by Pankow (*3*) using eq 38 below and reasonable assumptions concerning the molecular properties of typical PM_{MTS}.

Although we are unaware of any determinations of $K_{p,fb}^{amm}$ values for PM_{MTS} samples, Henry's gas law constant $K_{H,fb}^{amm}$ (molal/atm) for partitioning of free-base ammonia between air and dilute water is well-known. Over the temperature range $T = 273-313$ K, Clegg and Brimblecombe (*58*) give

$$\ln K_{H,fb}^{amm} \text{ (molal/atm)} = -8.09694 + 3917.507/T - 0.00314T \tag{35}$$

At $T = 293.15$ K (20 °C), eq 35 gives $K_{H,fb}^{amm} = 10^{1.89}$ (molal/atm). Unit conversions between $K_{p,fb}^{amm}$ and $K_{H,fb}^{amm}$ yield

$$K_{p,fb}^{amm} \text{ (m}^3/\mu\text{g)} = K_{H,fb}^{amm} RT \times 10^{-9} \tag{36}$$

where R is the ideal gas constant (8.2 $\times$ 10^{-5} m^3 atm mol^{-1} K^{-1}). For 20 °C, eqs 35 and 36 give

$$K_{p,fb}^{amm} = 10^{-8.73} \text{ m}^3/\mu\text{g} \tag{37}$$

The equation governing the G/P partitioning of a neutral compound i (e.g., free-base nicotine and free-base ammonia) to liquid droplets is (*59*)

$$K_{p,i} = \frac{RT}{10^6 \overline{MW} \zeta_i p_{L,i}^o} \tag{38}$$

where $\overline{MW}$ is the number-average molecular weight of the solution phase into which the partitioning is occurring and $p_{L,i}^o$ is the T-dependent liquid vapor pressure (atm) of i. Similar to γ_i, the parameter ζ_i is an activity coefficient "comfort factor" for dissolved i. The comfort factors γ_i and ζ_i are measured relative to different baselines ("reference states"). By way of analogy, if γ_i relates to the comfort of a person of type i measured relative to being completely surrounded by average-person (solvent) clones, then ζ_i relates to the comfort of i measured relative to being completely surrounded by other i. Very dilute water is the solvent reference state for all γ_i values as they are used in K_a values; as noted above, in very dilute water, all $\gamma_i = 1$ and the concentration scale used is molality. For each chemical i, pure liquid i is the reference state for ζ_i
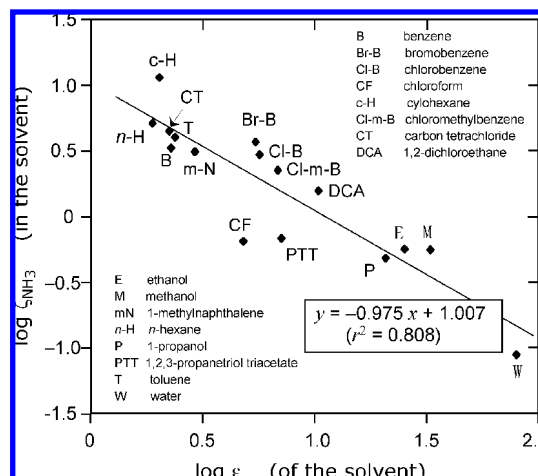

Figure 2. Activity coefficient of ammonia (ζ_{NH_3}) versus the dielectric constant (ε) of the solvent. The ζ_{NH_3} values were calculated herein; the ε values were obtained from Clegg and Brimblecombe (*58*).

Table 3. Estimated Bounds for PM_{MTS} for ζ_{NH_3}, $\overline{MW}$, the Product $\zeta_{NH_3}\overline{MW}$, and log $K_{p,fb}^{amm}$ at 20 °C[a]

ζ_{NH_3} (20 °C)	$\overline{MW}$	$\zeta_{NH_3}\overline{MW}$	log $K_{p,fb}^{amm}$ (20 °C)
estimated lower bounds			corresponding upper bound
0.2	60	12	−9.6
estimated upper bounds			corresponding lower bound
2	129	258	−10.9

[a] Values of log $K_{p,fb}^{amm}$ (20 °C) calculated by eq 38 assuming for ammonia that $p_L^o = 10^{0.91}$ atm at 20 °C.

and the concentration scale used is mole fraction (x). In pure liquid ammonia, $x_{NH_3} = 1$, and thus, $\zeta_{NH_3} = 1$; however, for other chemicals, $\zeta \neq 1$ and $\gamma_{NH_3} \neq 1$. In dilute water, $\zeta_{NH_3} \neq 1$.

For dilute water solutions, $\overline{MW} = 18.0$ g/mol. At 20 °C for ammonia, $p_L^o = 10^{0.91}$ atm (*42*). For ammonia dissolved in water at 20 °C, combining eq 38 with eq 37 yields $\zeta_{NH_3} = 0.088$, which indicates the high comfort that ammonia has when dissolved in water. $K_{H,fb}^{amm}$ values have been measured for many solvents besides water. **Table 2** provides some of those values, corresponding calculated $K_{p,fb}^{amm}$ and ζ_{NH_3} values, and solvent dielectric constant (ε) values. Each dimensionless ε value provides a measure of solvent polarity. The log ζ_{NH_3} and log ε values are well-correlated (**Figure 2**).

Table 2 provides insight regarding probable values of ζ_{NH_3} when ammonia is dissolved in conventional PM_{MTS}. PM_{MTS} is a mixture of many constituents, including low-polarity compounds (e.g., solanesol) as well as significant amounts of relatively polar compounds, including nicotine, organic acids, and water (*62*). It therefore seems reasonable to expect that the overall polarities of different samples of PM_{MTS} will be *inside* the range bounded by water (very polar) and *n*-hexane (nonpolar). We therefore propose that $0.2 < \zeta_{NH_3} < 2$ is reasonable for PM_{MTS}. This range is consistent with the fact that $\zeta_{Nic} \approx 1$ in PM_{MTS} [Pankow et al. (*5, 6*)]. Assuming, as estimated by Pankow (*3*) that samples of PM_{MTS} from conventional cigarettes are characterized by $60 < \overline{MW} < 129$ g/mol, then we estimate that $12 < \zeta_{NH_3}\overline{MW} < 258$. With $p_L^o = 10^{0.91}$ atm at 20 °C for ammonia (*42*), then by eq 38 this suggests for conventional PM_{MTS} that $10^{-10.9}$ m^3/μg $< K_{p,fb}^{amm} <$ $10^{-9.6}$ m^3/μg (see **Table 3**).

MATERIALS AND METHODS

Brands and Smoking. The cigarettes and other smoking products (**Table 4**) were purchased in the U.S. during February−August 2007. All contained cut/shredded filler material. The "other products" included two brands of

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Table 4. Cigarettes and Other Products Considered with TPM (mg), "Tar" (mg), and Mass Fraction Water in PM (f_w^{PM}) As Measured in This Study

abbreviation	brand	weight (g)[a]	type[b]	manufacturer	N[c]	TPM (mg) mean	TPM (mg) standard deviation	"tar" (mg) mean	"tar" (mg) standard deviation	f_w^{PM} mean	f_w^{PM} standard deviation
				Cigarettes							
A	Craven A	0.98	FF, F, K, HP	Rothmans, Benson and Hedges	1	13.51	NA[d]	9.99	NA	0.143	NA
Ba	Basic	0.90	FF, F, K, HP	Philip Morris (PhM)	4	18.84	±1.33	13.29	±1.02	0.147	±0.035
Bl	Am. Spirit Blue	1.06	FF, F, K, HP	RJ Reynolds (RJR)	4	18.90	±2.42	14.99	±2.03	0.087	±0.012
C	Camel	0.93	FF, F, K, HP	RJ Reynolds (RJR)	3	19.70	±1.30	13.69	±0.80	0.173	±0.020
D	Doral	0.91	FF, F, K, HP	RJ Reynolds (RJR)	3	18.36	±1.81	14.40	±1.47	0.121	±0.005
G	GPC	0.92	FF, F, K, HP	RJ Reynolds (RJR)	3	14.09	±1.07	10.15	±0.94	0.211	±0.018
M	Marlboro	0.87	FF, F, K, HP	Philip Morris (PhM)	3	27.12	±5.43	21.58	±4.11	0.125	±0.012
N	Newport (Menthol)	0.89	FF, F, K, HP	Lorillard (LOR)	3	31.83	±3.04	24.56	±2.28	0.154	±0.008
R	Am. Spirit Red	1.06	FF, F, K, HP	RJ Reynolds (RJR)	3	12.30	±1.99	9.68	±1.87	0.097	±0.032
S	Mild Seven	0.90	Charcoal Filter, K, HP	Japan Tobacco	4	19.70	±2.48	14.50	±1.78	0.171	±0.016
T	True	0.97	Ultra-Lights F, K, SP	Lorillard (LOR)	4	10.69	±2.35	7.30	±1.32	0.225	±0.054
V	Virginia Slims	0.95	FF, F, K, HP	Philip Morris (PhM)	3	24.88	±3.86	19.78	±3.12	0.103	±0.007
W	Winston	0.86	FF, F, K, HP	RJ Reynolds (RJR)	4	19.71	±4.15	16.09	±3.94	0.082	±0.035
				Other Products (% of Rod Consumed)							
cb	Cap'n Black (~60%)	1.15	"Little Cigars"[e], F, 100s, SP	Lane Ltd.	3	20.55	±1.19	16.16	±1.01	0.108	±0.027
na	Miramar Natural (~45%)	0.89	"Fine Cigars"[f], NF	Swisher International	3	32.04	±7.97	24.70	±5.61	0.165	±0.022
ne	Mini Neos (~50%)	1.02	"Fine Cigars"[f], NF	JC Newman	3	28.69	±3.47	21.86	±2.04	0.158	±0.010
sa	AGIO Samatra (~40%)	0.98	"Biddies"[f], NF	AGIO Sigaren-Duizel	3	34.04	±2.18	26.37	±1.29	0.137	±0.007
sw	AGIO Sweet (~45%)	1.00	"Biddies"[f], NF	AGIO Sigaren-Duizel	3	22.78	±4.82	17.48	±3.07	0.176	±0.021
zm	Zino Mini (~30%)	0.93	"Fine Cigars"[f], NF	Davidoff and Cie SA	3	21.71	±7.19	18.55	±3.34	0.170	±0.014

[a] Including filter, if any. [b] FF, full flavor; K, king size; SP, soft pack; HP, hard pack; F, filtered; NF, nonfiltered. [c] N = number of replicates. [d] NA = not available. [e] Cut tobacco wrapped with brown paper. [f] Cut tobacco wrapped with leaf.

biddies, three brands of little "fine cigars", and the Captain Black brand, which is marketed as a "little cigar", although it has a paper wrapping and is constructed like a filtered cigarette. For each replicate test, two units of each brand were placed in a short glass dual cigarette holder connected by a 0.64 cm inner diameter TFE Teflon Swagelok union to a glass/TFE Teflon stopcock. One stopcock arm was connected to an initially empty, preweighed, precleaned FEP Teflon bag inside a 4 L chamber. The two units were lit simultaneously and then smoked by removing chamber air, so that MTS would be drawn into the bag. The "Massachusetts" smoking topography (56) was used: 90 mL (45 mL per unit) puffs of 2 s duration every 30 s. Filter vent holes (if any) were 50% blocked. All cigarettes were smoked to a 23 mm "butt length". As noted above, for each of the other products, the size limit of the bag did not allow the entire rod to be smoked, and smoking was halted after 10 puffs (see **Table 4** for the rod fractions consumed). In all smoking experiments, transfer of the PM$_{MTS}$ to the bag was nearly quantitative, with <3% remaining on the walls of the stopcock as estimated by quantitation of nicotine (as a tracer for PM$_{MTS}$).

Determination of Gaseous Nicotine (c_g^{nic}) and Ammonia (c_g^{amm}). c_g^{nic} was determined as described by Pankow et al. (5). For determination of c_g^{amm}, 240 mL of smoke gas was removed from the bag by drawing at 10 mL/min first through a 7 mm diameter, 0.5 μm pore-size Zefluor PTFE Teflon membrane filter (TMF) (Pall Life Science, Ann Arbor, MI) in a TFE Teflon filter holder and then through a Teflon midget impinger containing 1.5 mL of water. Deionized water (18 MΩ/cm) was from a Milli-Q unit (Millipore, Bedford, MA). Impinger solutions were analyzed immediately for dissolved $NH_3 + NH_4^+$ by ion chromatography (IC) using a 180 μL sample loop, an Alltech (Deerfield, IL) universal cation column, and a conductivity detector. Elution at 1 mL/min occurred using 1.5 mF CH_3SO_3H (Sigma-Aldrich, St. Louis, MO).

Determination of PM$_{MTS}$ Levels of Nicotine (c_p^{nic}), Ammonia (c_p^{amm}), and Water (f_w^{PM}). Once a given Teflon bag had been sampled for both gaseous nicotine and gaseous ammonia, the remaining smoke gas volume was removed and measured (virtually all remaining aerosol PM$_{MTS}$ had by then accumulated on the walls of the bag). The bag was sealed and weighed, and the sampled PM$_{MTS}$ mass was computed by difference. Depending upon that mass, between 10 and 20 mL of water-free 2-propanol was added to the bag as an extraction solvent. As an internal standard, 1.5 mg of nicotine-d_3 (Cambridge Isotope Laboratories, Andover, MA) was added to each 2-propanol extract. Nicotine determination was carried out by gas chromatography/mass spectrometry (GC/MS) as described by Pankow et al. (5). For determination of c_p^{amm}, the 2-propanol extract was analyzed by IC in a manner similar to

that used in measuring c_g^{amm}, except that the ammonia standards were prepared in 2-propanol. The water content of each 2-propanol extract was determined by GC following a procedure of Philip Morris (63), allowing the calculation of f_w^{PM}, the water mass fraction of the PM. Briefly, with the GC injector at 220 °C, 4 μL of the extract was introduced splitless into a 3 m × $^1/_8$ in. column containing 80/100 mesh Porapak QS (Supelco, Bellefonte, PA). A thermal conductivity detector (TCD) at 150 °C was employed. Helium was the carrier gas (30 mL/min) and the TCD reference gas (30 mL/min). The GC temperature program was as follows: hold at 160 °C for 4.25 min, 30 °C/min to 200 °C, and hold at 200 °C for 1.75 min.

RESULTS AND DISCUSSION

General Results. Values for total PM (=TPM), water, and "tar" (=TPM − nicotine − water) are given in **Table 4**. For the cigarettes, the range for TPM is 10.7−31.8 and the range for "tar" is 7.3−24.6 mg. For the other products, *for the rod fractions smoked* (see **Table 4**), the range for TPM is 20.6−34.0 mg and the range for tar is 16.2−26.4 mg.

Unbound Ammonia. $M_{g+p}^{amm,u}$ (μg) values are given in **Table 5**. For the 13 cigarette brands, the range for $M_{g+p}^{amm,u}$ is 0.9−7.2 μg. The lowest values are for the "red" and "blue" versions of the American Spirits "additives-free" brand (0.9 and 1.1 μg, respectively). Overall, in comparison to historically reported MTS ammonia levels for cigarettes, the $M_{g+p}^{amm,u}$ values obtained here are consistent with the estimate discussed above for the typical commercial cigarette that $M_{g+p}^{amm,u} \approx {}^1/_3 M_{tot}^{amm}$. For the "other products", for the rod fractions smoked (see **Table 4**), $M_{g+p}^{amm,u}$ ranged from 7.7 to 313 μg. The high values for the three "fine cigars" (Miramar Natural, Mini Neos, and Zino Mini) are consistent with ammonia data reported by Brunnemann and Hoffmann (49) for cigars and cigar-like products.

K_p^{amm} and K_p^{nic}. MTS values of c_p and c_g for 20 °C for ammonia and nicotine are given in **Tables 5** and **6**. Corresponding average values of log K_p^{nic} and log K_p^{amm} for 20 °C calculated on the basis of eqs 30 and 33, respectively, are also given. Pankow et al. (5) reported K_p^{nic} values at 20 °C for fresh MTS from seven of the same brands of cigarettes studied here.

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Table 5. Unbound Ammonia Data As Measured in This Study

abbreviation	brand	N^a	c_g^{amm} (ng/m³) mean	c_g^{amm} (ng/m³) standard deviation	c_p^{amm} (ng/μg) mean	c_p^{amm} (ng/μg) standard deviation	log K_p^{amm} (m³/μg) mean	log K_p^{amm} (m³/μg) standard deviation	unbound ammonia ($M_{g+p}^{amm,u}$, μg) mean	unbound ammonia ($M_{g+p}^{amm,u}$, μg) standard deviation	% NH₃ in gas phase mean	% NH₃ in gas phase standard deviation
						Cigarettes						
A	Craven A	1	1.52×10^5	NA^b	0.06	NA	−6.43	NA	1.7	NA	8.6	NA
Ba	Basic	4	3.73×10^5	$\pm 1.03 \times 10^5$	0.17	±0.05	−6.35	±0.10	3.6	±1.3	4.0	±1.1
Bl	Am. Spirit Blue	4	5.74×10^5	$\pm 2.17 \times 10^5$	0.04	±0.00	−7.09	±0.23	1.1	±0.2	25.8	±8.9
C	Camel	3	4.74×10^5	$\pm 9.81 \times 10^4$	0.22	±0.23	−6.34	±0.11	4.4	±0.1	4.4	±1.4
D	Doral	3	5.54×10^5	$\pm 7.96 \times 10^4$	0.19	±0.01	−6.45	±0.07	3.7	±0.4	4.4	±1.3
G	GPC	3	1.05×10^5	$\pm 2.96 \times 10^4$	0.13	±0.01	−5.90	±0.10	1.9	±0.1	1.7	±0.6
M	Marlboro	3	5.19×10^5	$\pm 1.35 \times 10^5$	0.25	±0.05	−6.32	±0.18	7.1	±2.6	3.5	±2.0
N	Newport (Menthol)	3	3.93×10^5	$\pm 1.21 \times 10^5$	0.22	±0.01	−6.24	±0.13	7.2	±1.0	2.1	±0.9
R	Am. Spirit Red	3	7.27×10^5	$\pm 7.59 \times 10^4$	0.04	±0.01	−7.23	±0.05	0.9	±0.2	43.3	±3.8
S	Mild Seven	4	1.62×10^5	$\pm 6.09 \times 10^4$	0.12	±0.03	−6.13	±0.21	2.4	±0.7	2.3	±1.4
T	True	4	9.56×10^4	$\pm 1.85 \times 10^4$	0.22	±0.05	−5.65	±0.04	2.4	±1.1	1.7	±0.3
V	Virginia Slims	3	5.50×10^5	$\pm 4.46 \times 10^4$	0.16	±0.01	−6.54	±0.01	4.1	±0.5	5.3	±1.3
W	Winston	4	1.05×10^6	$\pm 2.26 \times 10^5$	0.14	±0.02	−6.88	±0.13	3.2	±0.8	16.3	±6.5
						Other Products (% of Rod Consumed)						
cb	Cap'n Black (60%)	3	3.98×10^5	$\pm 1.59 \times 10^5$	0.36	±0.03	−6.02	±0.21	7.7	±0.7	2.4	±1.0
na	Miramar Natural (45%)	3	2.51×10^7	$\pm 3.63 \times 10^7$	7.46	±5.00	−6.16	±0.49	197.1	±166.7	3.9	±3.9
ne	Mini Neos (50%)	3	8.15×10^7	$\pm 6.48 \times 10^7$	8.19	±1.57	−6.92	±0.24	313.3	±92.3	9.7	±3.6
sa	AGIO Samatra (40%)	3	1.56×10^7	$\pm 8.58 \times 10^6$	6.53	±1.56	−6.34	±0.14	196.7	±68.4	3.1	±1.1
sw	AGIO Sweet (45%)	3	4.24×10^7	$\pm 2.57 \times 10^7$	6.28	±1.22	−6.77	±0.25	217.4	±69.9	7.4	±2.6
zm	Zino Mini (30%)	3	2.09×10^7	$\pm 3.07 \times 10^7$	5.61	±2.09	−6.19	±0.57	153.6	±94.3	4.4	±5.6

^{a} N = number of replicates. ^{b} NA = not available.

Table 6. Nicotine Data As Measured in This Study

abbreviation	brand	N^a	c_g^{nic} (ng/m³) mean	c_g^{nic} (ng/m³) standard deviation	c_p^{nic} (ng/μg) mean	c_p^{nic} (ng/μg) standard deviation	log K_p^{nic} (m³/μg) mean	log K_p^{nic} (m³/μg) standard deviation	total nicotine (mg) mean	total nicotine (mg) standard deviation	% nicotine in gas phase mean	% nicotine in gas phase standard deviation
						Cigarettes						
A	Craven A	1	1.41×10^5	NA^b	117.8	NA	−3.08	NA	3.18	NA	0.0042	NA
Ba	Basic	4	2.85×10^5	$\pm 2.11 \times 10^5$	81.6	±11.4	−3.43	±0.34	1.65	±0.26	0.0063	±0.0044
Bl	Am. Spirit Blue	4	1.26×10^6	$\pm 4.19 \times 10^5$	120.0	±9.5	−4.00	±0.14	2.27	±0.38	0.0280	±0.0084
C	Camel	3	2.69×10^5	$\pm 7.53 \times 10^3$	90.7	±11.2	−3.47	±0.05	1.78	±0.17	0.0062	±0.0009
D	Doral	3	1.76×10^5	$\pm 2.58 \times 10^4$	94.5	±7.0	−3.27	±0.03	1.73	±0.09	0.0030	±0.0009
G	GPC	3	8.69×10^4	$\pm 1.70 \times 10^4$	69.1	±5.0	−3.09	±0.06	0.98	±0.13	0.0037	±0.0004
M	Marlboro	3	1.33×10^5	$\pm 4.44 \times 10^4$	78.7	±1.5	−3.21	±0.15	2.13	±0.38	0.0037	±0.0014
N	Newport (Menthol)	3	1.11×10^5	$\pm 2.27 \times 10^4$	74.5	±3.8	−3.17	±0.09	2.36	±0.11	0.0028	±0.0002
R	Am. Spirit Red	3	2.30×10^6	$\pm 8.16 \times 10^5$	117.6	±4.9	−4.27	±0.16	1.45	±0.25	0.0860	±0.0253
S	Mild Seven	4	2.04×10^5	$\pm 1.55 \times 10^4$	92.9	±5.6	−3.34	±0.02	1.82	±0.19	0.0048	±0.0011
T	True	4	1.22×10^5	$\pm 4.16 \times 10^4$	86.9	±5.2	−3.13	±0.13	0.93	±0.22	0.0054	±0.0025
V	Virginia Slims	3	2.45×10^5	$\pm 1.75 \times 10^4$	101.3	±1.3	−3.38	±0.03	2.52	±0.42	0.0039	±0.0011
W	Winston	4	3.92×10^5	$\pm 2.17 \times 10^5$	105.9	±9.8	−3.50	±0.29	2.06	±0.26	0.010	±0.0061
						Other Products (% of Rod Consumed)						
cb	Cap'n Black (60%)	3	4.85×10^5	$\pm 1.65 \times 10^5$	106.2	±9.7	−3.64	±0.12	2.19	±0.28	0.0099	±0.0019
sa	AGIO Samatra (40%)	3	9.04×10^5	$\pm 8.12 \times 10^5$	52.0	±10.1	−4.11	±0.37	1.21	±0.44	0.0301	±0.0218
sw	AGIO Sweet (45%)	3	2.12×10^6	$\pm 6.67 \times 10^5$	88.0	±7.1	−4.37	±0.15	3.01	±0.43	0.0301	±0.0098
na	Miramar Natural (45%)	3	1.46×10^6	$\pm 1.08 \times 10^6$	78.2	±15.4	−4.19	±0.25	2.28	±0.73	0.0250	±0.0138
ne	Mini Neos (50%)	3	1.14×10^6	$\pm 1.68 \times 10^5$	61.5	±8.4	−4.27	±0.13	1.95	±0.39	0.0247	±0.0040
zm	Zino Mini (30%)	3	1.20×10^6	$\pm 5.58 \times 10^5$	78.4	±3.7	−4.15	±0.23	1.94	±0.37	0.0278	±0.0100

^{a} N = number of replicates. ^{b} NA = not available.

Except for Marlboro (see below), the two sets of log K_p^{nic} values are in good general agreement. Log $K_{p,fb}^{nic}$ and α_{fb}^{nic} values could not be measured here by the method of Pankow et al. (*5*), because doing so would have required the addition of ammonia to the sampled PM$_{MTS}$ and that would have prevented measurement of c_p^{amm} and thus determination of K_p^{amm}. The value of $K_{p,fb}^{nic}$ measured by Pankow et al. (*5*) for a certain brand cannot be used in the exact calculation of α_{fb}^{nic} values based on the K_p^{nic} values reported here because unknown within-brand variations in cigarette blend/composition prevent an exact transference.

Among all of the products examined, the largest average K_p^{nic} measured was $10^{-3.08}$ m³/μg for Craven A, and the smallest average K_p^{nic} measured was $10^{-4.37}$ m³/μg for AGIO Sweet Biddies. Among the cigarette brands, the largest K_p^{nic} was

obtained for Craven A and the smallest K_p^{nic} was $10^{-4.27}$ m³/μg for the American Spirit "red". Excluding the American Spirit "red" and "blue", the cigarettes gave generally higher K_p^{nic} values ($10^{-3.50}$–$10^{-3.08}$ m³/μg) than did the other products ($10^{-4.37}$–$10^{-3.64}$ m³/μg). For Marlboro, the K_p^{nic} reported here for MTS from the entire cigarette with 50% vent blocking ($\sim 10^{-3.21}$ m³/μg) is higher than observed by Pankow et al. (*5*) for the first three puffs with no vent blocking ($\sim 10^{-4.10}$ m³/μg). Possible explanations include a higher water content for MTS collected from a whole cigarette versus from the first three puffs, effects of vent blocking, and/or changes in the blend/additives used for the Marlboro pack examined here versus that considered by Pankow et al. (*5*).
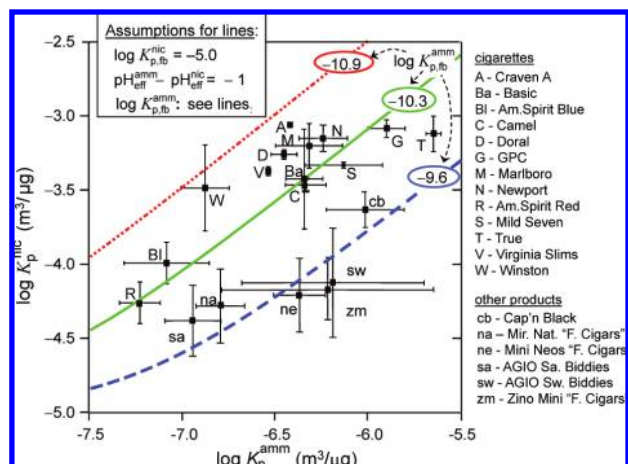
Table 7. Values at 20 °C of α_{fb}^{nic} and Log K_p^{nic} as Functions of pH_{eff}^{nic} Assuming That Log $K_{p,fb}^{nic} = -5.00$[a]

A	B	C	D	E	F
	since $pK_a^{nic} = 8.06$ then:	assuming log $K_{p,fb}^{nic} = -5.00$ then:	assuming $pH_{eff}^{amm} = pH_{eff}^{nic} -1.0$ then:	since $pK_a^{amm} = 9.40$ then:	assuming log $K_{p,fb}^{amm} = -10.30$ then:
pH_{eff}^{nic}	α_{fb}^{nic}	log K_p^{nic}	pH_{eff}^{amm}	α_{fb}^{amm}	log K_p^{amm}
5.0	0.00098	-1.99	4.0	0.0000040	-4.89
5.5	0.0031	-2.49	4.5	0.000013	-5.39
6.0	0.0097	-3.00	5.0	0.000040	-5.89
6.5	0.030	-3.49	5.5	0.00013	-6.39
7.0	0.089	-3.96	6.0	0.00040	-6.89
7.5	0.24	-4.38	6.5	0.0013	-7.39
8.0	0.49	-4.70	7.0	0.0040	-7.89
8.5	0.76	-4.88	7.5	0.012	-8.38
9.0	0.91	-4.96	8.0	0.038	-8.87
9.5	0.97	-4.99	8.5	0.11	-9.34
10.0	0.99	-4.996	9.0	0.28	-9.75
10.5	0.997	-4.999	9.5	0.56	-10.04
11.0	0.999	-4.9996	10.0	0.80	-10.20
11.5	0.9997	-4.9999	10.5	0.93	-10.27
12.0	0.9999	-4.99996	11.0	0.99	-10.29
		⋮			⋮
		$-5.0 = $ log $K_{p,fb}^{nic}$			$-10.3 = $ log $K_{p,fb}^{nic}$

(Column C "exper. data in this range" brace spans rows pH_{eff}^{nic} = 6.0–7.5; Column F "exper. data in this range" brace spans rows pH_{eff}^{amm} = 5.0–7.0.)

[a] Also given are pH_{eff}^{amm}, α_{fb}^{amm}, and log K_p^{amm} as obtained by assuming that $pH_{eff}^{amm} = pH_{eff}^{nic} - 1.0$ and that log $K_{p,fb}^{amm} = -10.30$. Entries in columns A–C are in bold font for the range wherein log K_p^{nic} versus pH_{eff}^{nic} is nearly linear, and entries in columns D–F are in bold font for the range wherein log K_p^{amm} versus pH_{eff}^{amm} is nearly linear.

Among all of the products examined, the largest average K_p^{amm} was $10^{-5.65}$ m^3/μg for the True Ultra Light cigarette and the smallest average K_p^{amm} was $10^{-7.23}$ m^3/μg for the American Spirit "red" cigarette. The cigarette brands gave K_p^{amm} values that are within the range observed for the other products: unlike the K_p^{nic} results, no clear data segregation was observed in the K_p^{amm} values for cigarettes versus the other products.

Log K_p^{nic} versus Log K_p^{amm}. For a given sample of PM$_{MTS}$, log K_p^{nic} and log K_p^{amm} are related: both will increase with increasing true pH, as defined by eq 12. For log K_p^{nic}, the dependence upon pH occurs through pH_{eff}^{nic} because the latter determines α_{fb}^{nic}, which in turn determines K_p^{nic} (see eqs 17, 19, and 31). For K_p^{amm}, the dependence upon pH is through pH_{eff}^{amm}, because the latter determines α_{fb}^{amm}, which in turn determines K_p^{amm} (see eqs 23, 25, and 34). Thus, making specific calculations regarding that relationship for a particular sample of PM$_{MTS}$ (or for a series of PM$_{MTS}$ samples that are generally similar in their main compositional properties) requires information about the value of the $pH_{eff}^{amm} - pH_{eff}^{nic}$ offset for the sample and the values of log $K_{p,fb}^{nic}$ and log $K_{p,fb}^{amm}$.

Table 7 assumes for 20 °C that (1) $pH_{eff}^{amm} - pH_{eff}^{nic} = -1.0$ (see **Table 1**), (2) log $K_{p,fb}^{nic} = -5.0$, which is in the range of values that has been observed for commercial cigarettes [Pankow et al. (5)]; and (3) log $K_{p,fb}^{amm} = -10.3$, the midpoint of the range estimated in **Table 3**. **Figure 3** provides a line for log K_p^{nic} versus log K_p^{amm} based on the calculated values in **Table 7** and lines for two other assumed values of log $K_{p,fb}^{amm}$ (−10.9 and −9.6). Along all three lines, as the solution conditions become more basic, so that nicotine becomes more volatile from the PM$_{MTS}$, log K_p^{nic} decreases essentially linearly with decreasing log K_p^{amm} (slope ≈ +1). Then, as pH_{eff}^{nic} increases above 8.06, that linearity is lost as log K_p^{nic} asymptotically approaches the value of log $K_{p,fb}^{nic}$ that has been assumed (= −5.0). In the nonlinear region, as pH_{eff}^{amm} increases above pK_a^{amm} (=9.40 in water at 20 °C), log K_p^{amm} asymptotically approaches the assumed value of log $K_{p,fb}^{amm}$ (−10.9, −10.3, or −9.6, depending upon the line).

Bold type is used in **Table 7** to mark the extent of the linear range for log K_p^{nic} versus pH_{eff}^{nic} when log $K_{p,fb}^{nic} = -5.0$ and also for

Figure 3. Predicted log K_p^{nic} versus log K_p^{amm} at 20 °C for mainstream tobacco smoke for three values of log $K_{p,fb}^{amm}$ (= −10.9, −10.3, and −9.6) and assuming log $K_{p,fb}^{nic} = -5.0$, $pK_a^{nic} = 8.06$, $pK_a^{amm} = 9.40$, and $pH_{eff}^{amm} - pH_{eff}^{nic} = -1.0$.

log K_p^{amm} versus pH_{eff}^{amm} when log $K_{p,fb}^{amm} = -10.3$. The linear range for log K_p^{nic} is less extensive than the linear range for log K_p^{amm} because nicotine is less basic. The data ranges spanned by the values of log K_p^{nic} and log K_p^{amm} obtained here are marked with braces. Most of the experimental values fall within the respective expected linear ranges. Thus, to the extent that the assumptions underlying the **Table 7** calculations are valid, a plot of log K_p^{nic} versus log K_p^{amm} for the experimentally observed values will be linear with slope ≈ +1. This is examined in **Figure 4**. Most of the points for the cigarettes lie close to or between the lines for log $K_{p,fb}^{amm} = -10.3$ and −10.9. All of the points for the other products lie relatively close to the line for log $K_{p,fb}^{amm} = -9.6$. Overall, the data are consistent with (1) the conclusions reached above regarding likely values of the offset $pH_{eff}^{amm} - pH_{eff}^{nic}$ and log $K_{p,fb}^{amm}$ and (2) the expectation for PM$_{MTS}$ that log K_p^{nic} and log K_p^{amm} values tend to be linearly correlated.

Log K_p^{nic} and Ammonia. The mass delivery of unbound ammonia $M_{g+p}^{amm,u}$ (μg) is defined by eq 9; the mass delivery

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Figure 4. Experimental log K_p^{nic} versus log K_p^{amm} at 20 °C for mainstream tobacco smoke from 13 brands of cigarettes and 6 brands of other products; error bars are ±1 standard deviation (sd). All of the data points for the cigarettes fall within the range of represented by the theoretical lines considered in **Figure 3**, namely, log $K_{p,fb}^{amm}$ = from −10.9 to −9.6 and assuming log $K_{p,fb}^{nic}$ = −5.0, pK_a^{nic} = 8.06, pK_a^{amm} = 9.40, and pH$_{eff}^{amm}$ − pH$_{eff}^{nic}$ = −1.0. Error bars are ±1 standard deviation.
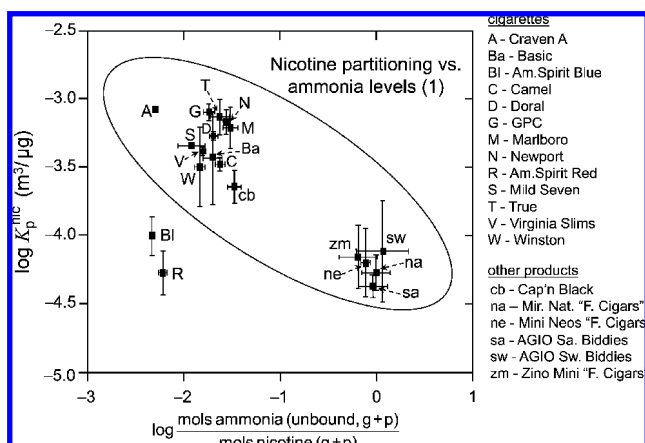
Figure 5. Log K_p^{nic} versus log(mols$_{g+p}^{amm,u}$/mols$_{g+p}^{nic}$). Error bars are ±1 standard deviation.

of total nicotine M_{g+p}^{nic} (μg) is defined analogously (recall that for each of the other products, ≤60% of the rod was smoked). $M_{g+p}^{amm,u}$ and M_{g+p}^{nic} can be converted to mole amounts. **Figure 5** is a plot of log K_p^{nic} versus log(mols$_{g+p}^{amm,u}$/mols$_{g+p}^{nic}$). For the overall data set, excluding the American Spirit "red" and "blue", the results are consistent with log K_p^{nic} for fresh PM$_{MTS}$ tending to decrease with increasing log(mols$_{g+p}^{amm,u}$/mols$_{g+p}^{nic}$) (slope ≈ −0.5). However, within the cigarettes and also within the other products, there is little correlation. The same observations apply to **Figure 6**, which is a plot of log K_p^{nic} versus log($M_{g+p}^{amm,u}$/PM$_{MTS}$).

The relatively low K_p^{nic} values of the two American Spirit cigarette brands at low log(mols$_{g+p}^{amm,u}$/mols$_{g+p}^{nic}$) and log($M_{g+p}^{amm,u}$/PM$_{MTS}$) suggests that relatively large α_{fb}^{nic} values are possible without the presence of significant unbound ammonia. Factors besides unbound ammonia that could increase PM basicity include (1) bound ammonia, because the formation of bound ammonia will involve reactions such as the neutralization of organic acids according to

$$R{-}COOH \ + \ NH_3 \ = \ R{-}CO{-}NH_2 \ + \ H_2O$$

an organic acid   ammonia   a monoamide (as one type of bound ammonia)

$$(39)$$
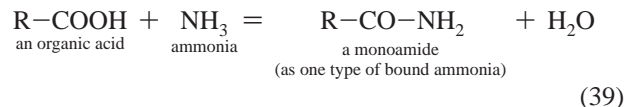
(2) bases other than ammonia and nicotine, (3) low levels of acids relative to bases (including nicotine), and (4) relatively low levels of water in the PM$_{MTS}$. A detailed consideration of the relationship between free-base nicotine in tobacco smoke must therefore examine the role not only of unbound ammonia but also the roles of the above four factors.

Effects of Water in PM$_{MTS}$ on Log K_p^{nic} and Log K_p^{amm}. For cigarettes, the range for the water mass fraction is f_w^{PM} = 0.082−0.225. The range for the other products is similar, f_w^{PM} = 0.108−0.176. Roemer et al. (64) reported f_w^{PM} = 0.13−0.21 for eight commercial and three reference cigarette (the "Massachusetts" machine smoking topography was used).

For two samples of PM$_{MTS}$ that have differing f_w^{PM} values but are otherwise identical, by considering eqs 31 and 34, it can be predicted that both K_p^{nic} and K_p^{amm} will be larger in the sample with the higher f_w^{PM} value. Both nicotine and ammonia will then be less volatile from the sample with the higher f_w^{PM}. First, because water has a rather low molecular weight (18 g/mol), increasing f_w^{PM} will decrease $\overline{MW}$. This will increase $K_{p,fb}^{nic}$ and $K_{p,fb}^{amm}$ (see eq 38). Second, because of the high ε of water (**Table 2**), increasing f_w^{PM} will increase the mean ε of the PM$_{MTS}$, which will tend to decrease both α_{fb}^{nic} and α_{fb}^{amm}: increasing ε favors reactions that lead to the protonation of nicotine and ammonia. These reactions include eqs 4 and 5 as well as

$$R{-}COOH = RCOO^- + H^+ \qquad (40)$$

$$R{-}COOH + Nic = RCOO^- + NicH^+ \qquad (41)$$

$$R{-}COOH + NH_3 = RCOO^- + NH_4^+ \qquad (42)$$
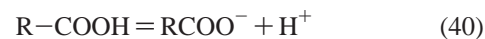
where R−COOH represents a generic organic acid in PM$_{MTS}$. Overall, on the basis of eqs 31 and 34, because increasing f_w^{PM} will cause each $K_{p,fb}$ to increase and each α_{fb} to decrease, both K_p^{nic} and K_p^{amm} will increase with increasing f_w^{PM}.

Figure 7 is a plot of log K_p^{nic} versus f_w^{PM}. Except for the points for the two American Spirit brands and the Captain Black product, the points for the cigarettes and the other products are grouped separately. The degree of scatter for the cigarettes is a consequence of the fact that log K_p^{nic} is significantly affected by numerous variables besides f_w^{PM} (e.g., levels of acids and bases). Nevertheless, the data for the cigarettes (including the American Spirit Red and Blue) are consistent with the expectation that K_p^{nic} values will tend to increase with increasing f_w^{PM}. These considerations are also
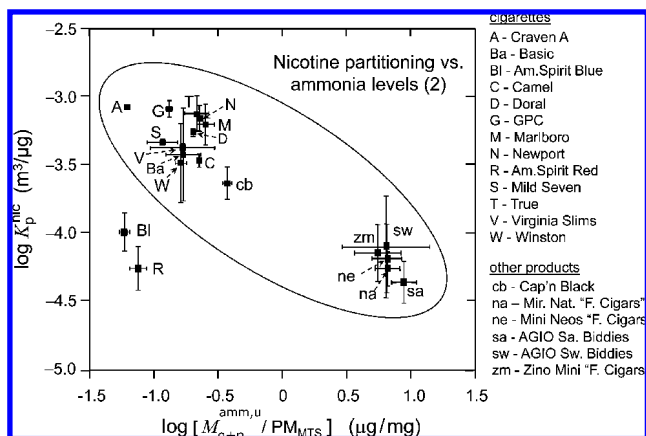

Figure 6. Log K_p^{nic} versus log($M_{g+p}^{amm,u}$/PM$_{MTS}$). Error bars are ±1 standard deviation.

G/P Partitioning of Nicotine and Ammonia in MTS

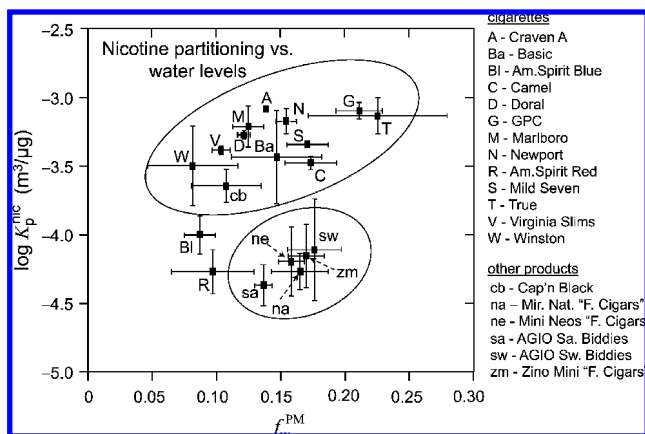*J. Agric. Food Chem.,* Vol. 57, No. 7, 2009 **2687**

Figure 7. Log K_p^{nic} versus f_w^{PM} (fraction of water in the PM). Error bars are ± 1 standard deviation.
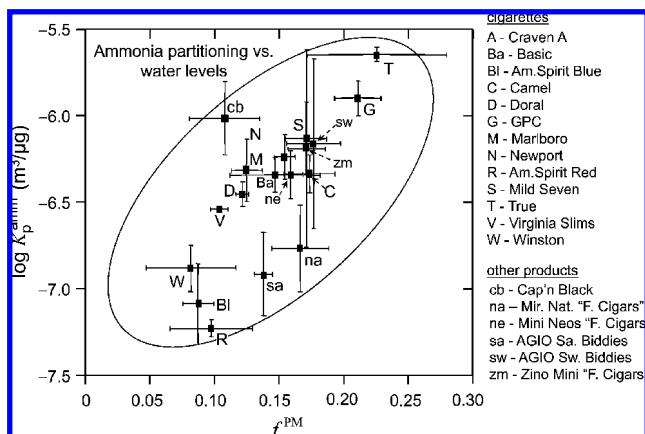

Figure 8. Log K_p^{amm} versus f_w^{PM} (fraction of water in the PM). Error bars are ± 1 standard deviation.

consistent with tobacco industry documents that discuss that (1) reducing free-base nicotine levels in MTS will reduce smoke strength [e.g., BAT_{doc} (21)] and (2) smoke harshness can be reduced by adding moisture and humectants to the tobacco [e.g., BAT_{doc} (65), $B\&W_{doc}$ (66, 67), and RJR_{doc} (68, 69)]. **Figure 8** is the ammonia analogue of **Figure 7**. In this case, the data for the cigarettes and the other products are not grouped separately. The collection of the points provide good evidence that log K_p^{amm} values (and thus also K_p^{nic} values) for smoke from tobacco products are influenced by f_w^{PM} as described above.

Conclusions. The theoretical considerations and experimental data in this study confirm the expected coupled nature of the gas/particle partitioning of nicotine and ammonia in mainstream tobacco smoke (MTS). The predictions made here regarding a correlation of log K_p^{nic} versus log K_p^{amm} values (including the offset between pH_{eff}^{amm} and pH_{eff}^{nic}) are highly consistent with the experimentally observed data: the results indicate that theory and associated assumptions developed here are generally appropriate for MTS. The observed correlation of log K_p^{amm} versus f_w^{PM} suggests that PM water has a stronger effect on gas/particle partitioning for ammonia than for nicotine. A relatively stronger role for water with ammonia than with nicotine may explain a portion of the scatter in **Figure 4**.

Figures 5 and **6** provide evidence that increasing levels of unbound ammonia ($M_{g+p}^{amm,u}$) can lower K_p^{nic} values for MTS. However, within the cigarettes examined here, unbound ammonia alone was not found to be a dominant determinant of K_p^{nic}. Variables in addition to unbound ammonia that will need

to be considered when seeking to explain K_p^{nic} and α_{fb}^{nic} values in MTS include bound ammonia, levels of other bases, levels of acids, and f_w^{PM} (and thus humectants).

Historical measures of ammonia in tobacco smoke did not differentiate between unbound and bound ammonia. Those carried out using acidic solutions to extract ammonia from MTS surely overestimated the true $M_{g+p}^{amm,u}$ values but may also have underestimated M_{tot}^{amm} (unbound + bound ammonia) because of less than quantitative hydrolysis of ammonia-containing amides in the analytical procedures used. Therefore, conclusions such as are discussed by Ingebrethsen (70) regarding how the quantity and/or volatility of ammonia in MTS may affect K_p^{nic} values, α_{fb}^{nic} values, and nicotine deposition in the respiratory tract will need re-examination when the chemistry of bound ammonia becomes better understood in cigarette MTS. In particular, if for a cigarette $M_{g+p}^{amm,u} \approx 1/3 M_{tot}^{amm}$ and if the remaining $2/3$ of the ammonia is essentially nonvolatile from the PM_{MTS} (as higher MW amides), then that significant amount of basicity will tend to be retained in the PM_{MTS} for the entire lifetime of the smoke particles.

ABBREVIATIONS USED

Roman Symbols and Abbreviations

BAT	British American Tobacco Corp.
BAT_{doc}	internal company document pertaining to British American Tobacco Corp.
B&W	Brown and Williamson, Inc.
$B\&W_{doc}$	internal company document pertaining to Brown and Williamson, Inc.
c_g	concentration (ng/m³) in the gas phase
c_g^{amm}	concentration (ng/m³) of ammonia (unbound) in the gas phase (all gaseous unbound ammonia is free-base ammonia, because NH_4^+ is not volatile)
c_g^{nic}	concentration (ng/m³) of nicotine in the gas phase (all gaseous nicotine is free-base nicotine, because $NicH^+$ is not volatile)
c_p	concentration (ng/µg) in the particulate matter (PM)
c_p^{amm}	total concentration (ng/µg) of ammonia in the particulate matter (PM) (unbound; $NH_3 + NH_4^+$ but computed as ng of NH_3/µg of PM)
$c_{p,fb}^{amm}$	concentration (ng/µg) of free-base ammonia (unbound) in the particulate matter (PM)
c_p^{nic}	total concentration (ng/µg) of nicotine in the particulate matter (PM) (Nic + $NicH^+$ but computed as ng of Nic/µg of PM)
$c_{p,fb}^{nic}$	concentration (ng/µg) of free-base nicotine in the particulate matter (PM)
DAP	diammonium phosphate
f_w^{PM}	mass fraction of the particulate matter (PM) that is water
H^+	proton
$[H^+]$	concentration (molal) of the proton
$\{H^+\}$	activity of the proton (on the molal scale)
$[i]$	concentration (molal) of species i
$\{i\}$	activity of species i (on the molal scale); $\{i\} = \gamma_i [i]$
K_a^{amm}	temperature-dependent acidity constant for ammonium ion, i.e., for the reaction $NH_4^+ = NH_3 + H$; at 20 and 37 °C, $K_a^{amm} = 10^{-9.40}$ and $10^{-8.89}$, respectively

K_a^{nic} — temperature-dependent acidity constant for protonated nicotine, i.e., for the reaction $NicH^+ = Nic + H^+$; at 20 and 37 °C, $K_a^{nic} = 10^{-8.06}$ and $10^{-7.76}$, respectively

K_b^{amm} — temperature-dependent basicity constant for ammonia, i.e., for the reaction $NH_3 + H_2O = NH_4^+ + OH^-$

K_b^{nic} — temperature-dependent basicity constant for nicotine, i.e., for the reaction $Nic + H_2O = NicH^+ + OH^-$

$K_{H,fb}^{amm}$ — Henry's gas law constant (molal/atm) for partitioning of free-base ammonia between air and dilute water

K_p — gas/particle equilibrium partitioning constant $(m^3/\mu g)$ for a compound of interest

K_p^{amm} — overall gas/particle equilibrium partitioning constant $(m^3/\mu g)$ for ammonia $(=c_p^{amm}/c_g^{amm} = K_{p,fb}^{amm}/\alpha_{fb}^{amm})$

K_p^{nic} — overall gas/particle equilibrium partitioning constant $(m^3/\mu g)$ for nicotine $(=c_p^{nic}/c_g^{nic} = K_{p,fb}^{nic}/\alpha_{fb}^{nic})$

$K_{p,fb}^{amm}$ — gas/particle equilibrium partitioning constant $(m^3/\mu g)$ for free-base ammonia $(=c_p^{amm}/c_g^{amm})$

$K_{p,fb}^{nic}$ — gas/particle equilibrium partitioning constant $(m^3/\mu g)$ for free-base nicotine $(=c_p^{nic}/c_g^{nic})$

LOR — Lorillard, Inc.

LOR_{doc} — internal company document pertaining to Lorillard, Inc.

M — mass (μg) delivered in mainstream tobacco smoke (MTS) by smoking; for the cigarettes smoked in this work, M pertains to delivery by smoking 100% of the cigarette rod according to the smoking protocol used; for the "other products", less than 100% of the rod was consumed (see **Table 4** for percentages)

$M_g^{amm,u}$ — mass (μg) of gaseous ammonia (unbound, NH_3) delivered in mainstream tobacco smoke (MTS) by smoking (see also the comment on percent of rod consumed found in the definition for the generic M)

$M_{g+p}^{amm,b}$ — mass (μg) of delivered ammonia that is bound in compounds such as amides of ammonia and can be released as molecular ammonia both in the gas and particle phases of mainstream tobacco smoke (MTS) (see also the comment on percent of rod consumed found in the definition for the generic M)

$M_{g+p}^{amm,u}$ — mass (μg) of gas + particle-phase ammonia (unbound, $=M_g^{amm,u} + M_p^{amm,u}$) delivered in mainstream tobacco smoke (MTS) by smoking (see also the comment on percent of rod consumed found in the definition for the generic M)

$M_p^{amm,u}$ — mass (μg) of particle-phase ammonia (unbound, $NH_3 + NH_4^+$) delivered in mainstream tobacco smoke (MTS) by smoking (see also the comment on the percent of rod consumed found in the definition for the generic M)

M_{tot}^{amm} — mass (μg) of total (unbound + bound, $=M_{g+p}^{amm,u} + M_{g+p}^{amm,b}$) ammonia in both the gas and particle phases of mainstream tobacco smoke (MTS) (see also the definition of M for comment on the percent of rod consumed)

$mols_{g+p}^{amm,u}$ — analogue of $M_{g+p}^{amm,u}$ but with units of moles

$mols_{g+p}^{nic}$ — analogue of $mols_{g+p}^{amm,u}$ (moles) but for nicotine

MTS — mainstream tobacco smoke

$\overline{MW}$ — number-average mean molecular weight of a solution phase into which gas/particle partitioning may be occurring

Nic — free-base nicotine

$NicH^+$ — monoprotonated nicotine

$[Nic]$, $[NicH^+]$, $[NH_3]$, $[NH_4^+]$ — concentration (molal) of free-base nicotine, protonated nicotine, ammonia, and ammonium ion, respectively

$\{Nic\}$, $\{NicH^+\}$, $\{NH_3\}$, $\{NH_4^+\}$ — activity of free-base nicotine, protonated nicotine, ammonia, and ammonium ion, respectively (all on the molal scale)

pH — $= -\log\{H^+\}$

pH_{eff}^{nic} — effective pH of the solution relative to the behavior of nicotine in dilute water $(=pK_a^{nic} + \log \alpha_{fb}^{nic}/(1 - \alpha_{fb}^{nic}))$

pH_{eff}^{amm} — effective pH of the solution relative to the behavior of ammonia in dilute water $(=pK_a^{amm} + \log \alpha_{fb}^{amm}/(1 - \alpha_{fb}^{amm}))$

PhM — Philip Morris, Inc.

PhM_{doc} — internal company document pertaining to Philip Morris, Inc.

pK_a^{amm} — $= -\log K_a^{amm}$

pK_a^{nic} — $= -\log K_a^{nic}$

$p_{L,i}^o$ — T-dependent vapor pressure (atm) of i

PM_{MTS} — particulate matter of mainstream tobacco smoke

PM — particulate matter of an aerosol

PRIG — intercompany (tobacco industry) "Product Regulatory Issues Group"

$PRIG_{doc}$ — internal company document pertaining to intercompany (tobacco industry) "Product Regulatory Issues Group"

R — ideal gas constant $(8.2 \times 10^{-5}$ m^3 atm mol^{-1} $K^{-1})$

RJR — RJ Reynolds, Inc.

RJR_{doc} — internal company document pertaining to RJ Reynolds, Inc.

T — temperature (K)

TPM — mass (mg) of total particulate matter in an aerosol (includes water and nicotine in the case of mainstream tobacco smoke)

Greek Symbols

α_{fb}^{nic} — fraction of the total nicotine that is present in the free-base form in the particulate matter (PM)

α_{fb}^{amm} — fraction of the total ammonia that is present in the free-base form in the particulate matter (PM)

γ_i — molal-scale activity coefficient ("comfort factor") of dissolved species i; the species i can be H^+, free-base nicotine (Nic), protonated nicotine $NicH^+$, NH_3, NH_4^+, or any other dissolved species in the solution; γ_i is dimensionless, always >0, and by definition equal to 1.0 in dilute water

ζ_i — mole-fraction-scale activity coefficient ("comfort factor") for dissolved i; the species i could be an chemical that can exist as a pure liquid (e.g., nicotine, ammonia, water, etc.); ζ_i is dimensionless, always >0, and by definition equal to 1.0 in pure liquid i

Supporting Information Available: Analogy for helping to understand the meaning and role of solution-phase molal-scale activity coefficients (γ). This material is available free of charge via the Internet at http://pubs.acs.org.

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