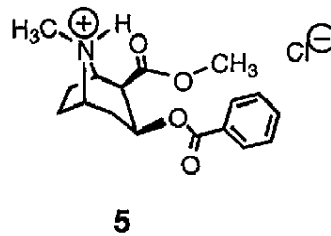
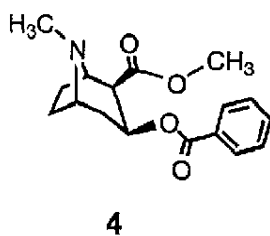


salts (e.g., 2 and 3, such as are found in tobacco), are compared with those of cocaine (4)



and cocaine salts (e.g., cocaine hydrochloride 5, also called "street cocaine",<sup>19</sup> the form in which much of this illegal alkaloid is "marketed," see Figure 1.19-24). The studies reported herein demonstrate that 1 and examples of 2 and 3, when heated, all nearly quantitatively transfer nicotine to the gas phase. The experiments prove that the temperature required to convert this type of nicotine salt, such as is found in tobacco, to nicotine in the gas phase is lower than the decomposition temperature of the nicotine superstructure, i.e., the nicotine ring system.

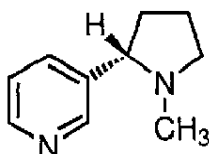
In contrast, a review of the scientific literature summarized herein indicates that the temperatures required to convert cocaine hydrochloride (5) to cocaine (4) in the gas phase is higher than the decomposition temperature of the cocaine superstructure. Heating cocaine hydrochloride typically does not lead to transfer of intact cocaine into the gas phase; instead, destruction of the cocaine ring system as well as loss or modification of its functional group substituents are the significant observed pathways.<sup>20</sup> Both 4 and 5 are thermally very labile.

Thus, the thermal properties of nicotine and of the protonated forms of nicotine, such as occur in tobacco, are quite similar to each other but are considerably different than those of cocaine and protonated cocaine.<sup>25</sup> Any analogies involving the smoke chemistry of these classes of compounds must be carefully examined using experimental data.

## Experimental Section

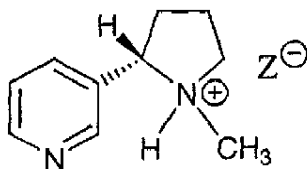
## INTRODUCTION

S-(-)-Nicotine (**1**), hereafter "nicotine", is the principal alkaloid in tobacco. Hypothetically, this well known and extremely well studied substance can exist in one

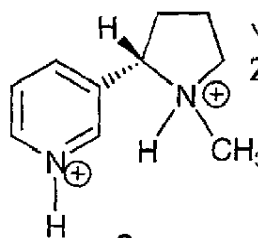


**1**

(or more) of three forms in cigarette blend components: nonprotonated nicotine (**1**), monoprotonated nicotine (**2**) and diprotonated nicotine (**3**).



**2**



**3**

- a,  $Z = \text{CH}_3\text{CO}_2\text{H}$  (as an acetate)  
 b,  $Z = \text{HO}_2\text{CCH}_2\text{CH}(\text{OH})\text{CO}_2\text{H}$  (as a malate)  
 c,  $Z = \text{HO}_2\text{CCH}(\text{OH})\text{CH}(\text{OH})\text{CO}_2\text{H}$  (as a tartrate)
- Handwritten:* HZ

While the efficiency of transfer of nicotine from tobacco to smoke has been the subject of considerable public discussion and attention in the past few years, [Kessler, 1996 #257; Kessler, 1997 #258; Administration, August 28, 1996 #259; Freedman, 1994 #265] hardly any data is available in the peer reviewed scientific literature on these topics. In this paper, we present evidence which indicates; 1) that nicotine is present primarily in one or both protonated forms in tobacco, and 2) that nonprotonated nicotine (**1**) and the nicotine carboxylic acid salts found in tobacco (**2** and **3**) are likely to transfer

*Handwritten:* RGF

2064331062