As a tertiary-tertiary diacid base, nicotine can, on oxidation, give oxides of three types:

\[
\begin{align*}
(I) & \quad \text{Nicotine N-oxide} \\
(II) & \quad \text{Nicotine N'-oxide} \\
(III) & \quad \text{Nicotine N,N'-dioxide}
\end{align*}
\]

Investigation of the oxidation of nicotine began already at the end of last century, but it was concerned almost exclusively with compounds of the first type. In 1891 Pinner and Wolffenstein [1] oxidized nicotine with hydrogen peroxide and isolated a compound C_{10}H_{14}N_{2}O, which was free from carbonyl and alcohol groups and which they called "oxynicotine". In the study of the properties of oxynicotine they obtained two compounds of the same elementary composition, one containing carbonyl and the other noncarbonyl oxygen. The authors proposed the following scheme for their formation:

\[
\begin{align*}
0 \quad \text{(I)} \\
\text{Nicotine} \\
\text{N-oxide}
\end{align*}
\]

\[
\begin{align*}
\text{HCl} & \quad 140^\circ \quad \text{(IV)} \\
\text{Heating} & \quad 200^\circ \quad \text{(V)}
\end{align*}
\]

With regard to oxynicotine (I), Pinner suggested that it was a "polymer" of an aldehyde, because it gave no reactions for the carbonyl group, but was converted into an aldehyde ("pseudooxynicotine" (IV)) when heated with acid. Somewhat later (1901), Auerbach and Wolffenstein [2], on the basis of their work on the oxidation of 1-methylpiperidine with hydrogen peroxide, established the correct structure of oxynicotine and proposed an N-oxide formula with the oxygen attached to the pyrrolidine nitrogen:
The authors showed that the oxygen is readily eliminated by treatment with sulfur dioxide or nitrogen dioxide.

In a study of the action of acetic anhydride on N-oxides of alkaloids, the Polonovskis [3] obtained nor-nicotine (VI) from Pinner’s oxynicotine (I); they considered that the reaction proceeds as follows:

\[
\text{NCH}_3 \xrightarrow{(CH_2CO)_3O} \text{NCH}_3 \quad \text{OCCCH}_3 \quad \text{OOCCH}_3
\]

In 1948 there appeared a short paper by Weil [4] on the photochemical oxidation of nicotine in presence of Methylene blue. The author isolated a viscous yellow oil of elementary composition C19H14N2O2; he suggested that the oxidizing agent acted on the N-CH₃ grouping of the pyrrolidine ring, for 1-methylpyrrolidine is itself readily oxidized under these conditions, whereas various 3-substituted pyridines do not undergo photochemical oxidation. Weil suggested the following scheme of reaction:

1) \( C_{10}H_{14}N_2 + \text{MB} \rightarrow C_{10}H_{13}N_2 + \text{MB}(H_2); \)
2) \( \text{MB}(H_2) + O_2 \rightarrow \text{MB} + H_2O_2; \)
3) \( C_{10}H_{14}N_2 + H_2O_2 \rightarrow C_{10}H_{14}N_2O_2, \)

but gave no proof of the structure of the product, gave no constants for it, and did not characterize it by suitable derivatives. In 1950 Hains and Eisner [5] repeated Pinner’s work and showed that pseudooxynicotine (IV) is not an aldehyde, as Pinner supposed, but 4-methylamino-1-(3-pyridyl)-1-butanone (VII), which was proved by confirmatory synthesis from 1-methyl-3-nicotinoyl-2-pyrrolidone:

\[
\text{Pinner's oxynicotine} \xrightarrow{\text{HCl/160°}} \text{Pinner's pseudooxynicotine}
\]

1-methyl-3-nicotinoyl-2-pyrrolidone

In the same year Reyburg and Harlan [6] determined the true structure of Pinner’s "nicotone" and showed that this compound does not contain a five-membered furan ring (V), but a six-membered oxazine ring (VIII), and they confirmed this by investigation of the ultraviolet absorption spectra.