P5358 CONFORMATIONAL ISOMERS OF NICOTINE, NORNICOTINE AND THEIR HYDRATED CLUSTERS

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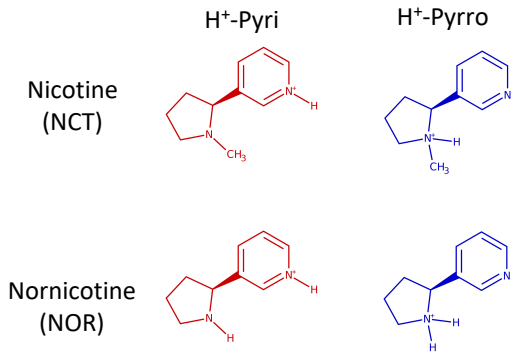
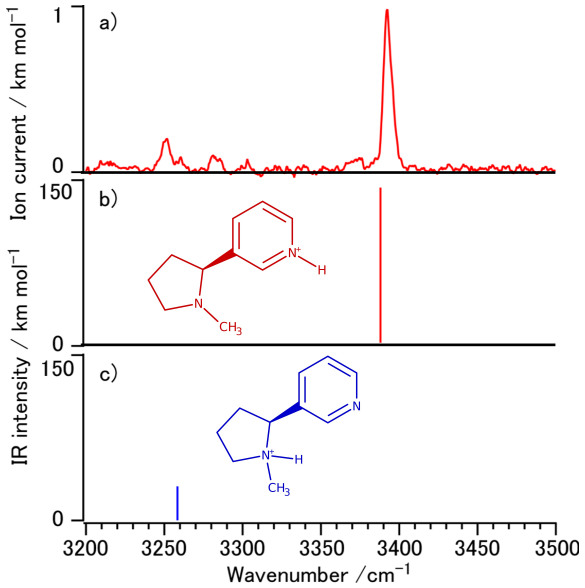
Background

- Nicotine newly classified as a drug.
- Protonation is predicted to have strong effects on binding.
- Protonation sites are not well determined and varies between different environments.
  - Hydrous extracellular matrix.
  - Anhydrous receptor pocket.



How do the the structural differences in alkaloids contribute to differences in binding strength?

Gas phase nicotine is a 2:1 mixture of both pyridine and pyrrolidine protomers



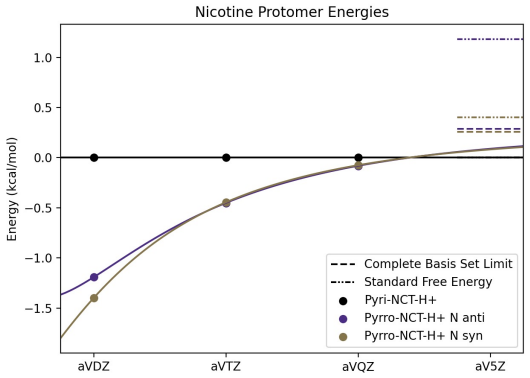


Figure 1. (a) Experimental IRPD spectra of NIC-H⁺ and theoretical IR spectra of (b) Pyri-NCT-H⁺ and (c) Pyrro-NCT-H⁺ in the 3200–3500 cm^{-1} spectral region. Calculations confirm this finding (top).

Gas phase nor nicotine is purely the pyridine protomer

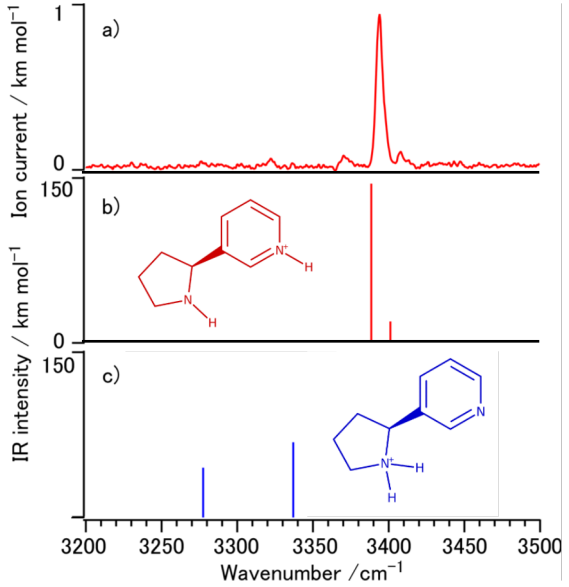


Figure 2. (a) Experimental IRPD spectra of NOR-H⁺ and theoretical IR spectra of (b) Pyri-NOR-H⁺ and (c) Pyrro-NOR-H⁺ in the 3200–3500 cm^{-1} spectral region.

Aqueous nicotine and nornicotine is purely the pyrrolidine protomer

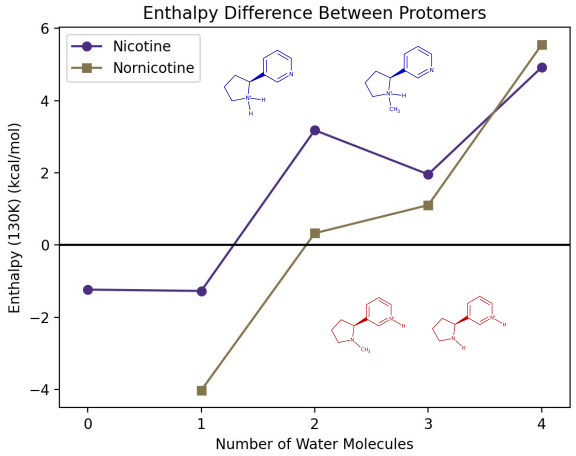


Figure 3. Calculated Enthalpies show a similar transition with hydration number.

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