THE FORMAMIDE$_2$-H$_2$O COMPLEX: STRUCTURE AND HYDROGEN BOND COOPERATIVE EFFECTS

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Peptide groups in biomolecules may adopt \textit{cis} or \textit{trans} configurations. These present a variety of hydrogen bond interactions sites:

- proton acceptor (\textbf{A})
- proton donor (\textbf{D})
- weak hydrogen bonds (\textbf{WD}) (if including the C$_\alpha$-H groups)

**trans-peptide**

\(~99\%\)

**cis-peptide**

\(~1\%\)
They made possible the interaction between peptide groups: The C=O···H-N bond dominate in the hydrophobic core of proteins.
These sites define a variety of possible interactions of peptide group with water: C=O···HOH: ~44 %
In proteins water may mediate in C=O···H-N to nucleate protein folding or in the protein surface where they are exposed to hydrophilic interactions.
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Polarization enhanced HB:
- Shortens the HB lengths
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Resonance enhanced HB:
- Inductive polarization effects
- Shortens the N-C bond lengths
- Enlarges the C=O bond lengths
Previous studies

The interactions with water have been modelled from the study of gas phase microsolvated clusters of simple molecules having the peptide group:

Some examples from MW spectroscopy


2-azetidinone-(H₂O)ₙ, n=1,2: J. C. López et al., PCCP, 2015, 17, 2054.

The observed 1:1 clusters of **formamide** with **water** cover all possible hydrogen bond situations:

**trans-peptide**

14% in globular proteins

**fw-1:1c**

**cis-peptide**

42% in globular proteins

Formamide-water complexes

The signatures of polarization enhanced HB have been observed when the structures of sequential 1:1 and 1:2 cycles:

FW-1:1a

FW-1:2a

Shortening of HB lengths
Stabilization energy

S. Blanco et al., JACS, J. Am. Chem. Soc. 2006, 128, 12111
However no experimental evidence of changes in the $r(C-N)$ or $r(C=O)$ bond lengths.

Ab initio values

$r_{C-N} = 1.361 \text{ Å}$
$r_{C=O} = 1.219 \text{ Å}$

$r(C-N)$ decrease

$r(C=O)$ increase

S. Blanco et al., JACS, J. Am. Chem. Soc. 2006, 128, 12111
We have extended the study of formamide water clusters to new species: (formamide)$_2$-H$_2$O$^1$ and formamide-(H$_2$O)$_3$
To characterize their structure and dynamics
To find the signatures of cooperative effects.
Experiment

Spectrum

**FTMW** spectrometer

**MB-FTMW (4-16 GHz)**

Summary

- Formamide₂-water (f₂w) can be taken as a microsolvated water cluster being formamide the solvent and as a model for water mediated amide interactions and self-association.

- Unambiguous structure characterization based on the observation of isotopologues and hyperfine structure analysis.

- The structure of f₂w show for the first time in gas phase the effect of resonance enhanced cooperative hydrogen bonding of an amide.

- Quadrupole coupling constants are a precious tool to detect the existence on inductive effects due to cooperativity polarization.
Acknowledgement

- Thank you for your attention!