Water's Role in Reshaping a Macrocycle's Binding Pocket: Conformation-Specific Infrared and Ultraviolet Spectroscopy of Benzo-15-crown-5-$(H_2O)_n$ and 4'-aminobenzo-15-crown-5-$(H_2O)_n$ clusters $(n = 1, 2)$

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Crown Ethers' Numerous Facets

Crown Ethers in Host-Guest Chemistry

- Due to the flexibility of the crown cycle they are characterized by their ability to selectively bind substrates, especially cations.
- Since their discovery* more than 40 years ago they served:

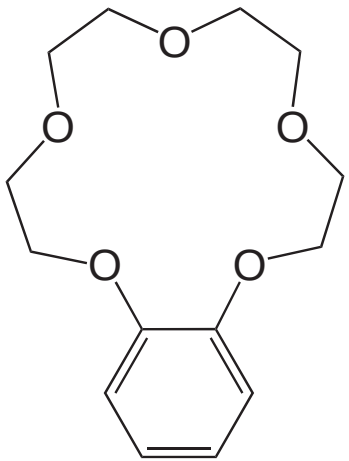
  i) as model compounds for enzyme-substrate interactions,**

  ii) as an aid for ion transport through membranes,†

  iii) as potential scavengers for the combined extraction of cesium and strontium from caustic wastes,‡

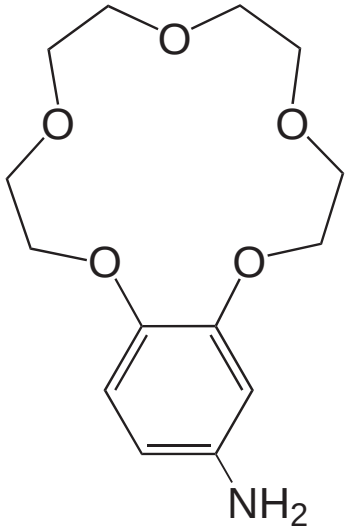
  iv) as a component for a molecular three-input AND logic gate.§

* C. J. Pedersen, *J. Am. Chem. Soc.*, 1967, *89*, 7017.
** J.-M. Lehn, *Pure & Appl. Chem.*, 1979, *51*, 979.
† R. F. Khairutdinov, J. K. Hurst, *Langmuir*, 2004, *20*, 1781.
‡ L. H. Delmau *et al.*, *Solvent Extr. Ion Exch.*, 2006, *24*, 197.
§ D. C. Magri *et al.*, *J. Am. Chem. Soc.*, 2006, *128*, 4950.



Benzo-15-crown-5

B15C



4'-aminobenzo-15-crown-5

ABC

Our Interest

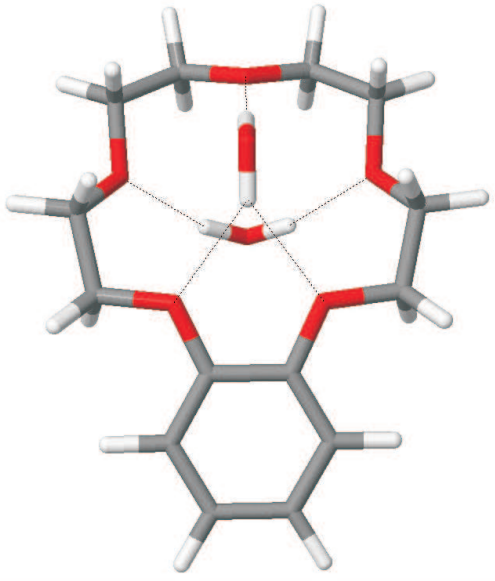
From a microscopic point of view. . .

- We are interested in the intrinsic molecular nature of the multidentate complexation.
- The complexation of water molecules is particularly interesting since the crown ether macrocycle provides many hydrogen bond donor and acceptor sites.
- Applying conformation-specific UV and IR spectroscopy, we would like to extract structural information:

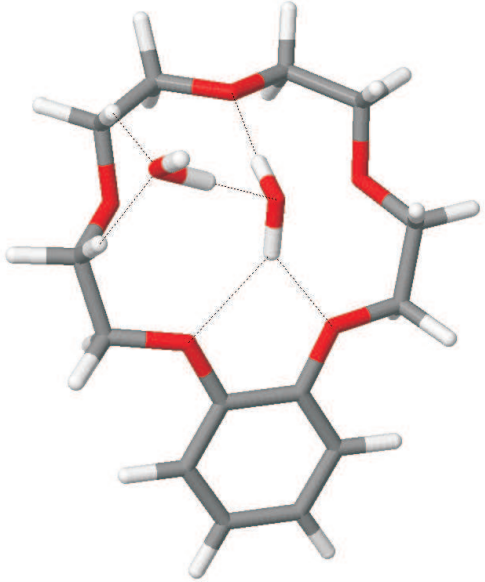
  (1) How flexible is the macrocycle? How variable is the crown ether conformation upon successive complexation?

  (2) Does successive complexation lead to additive or non-additive conformational behavior?

  (3) What determines the relative stability among different water clusters?



B3LYP/6-31+G(d)



Benzo-18-crown-6-ether and Dibenzo-18-crown-6-ether:

R. Kusaka, Y. Inokuchi, T. Ebata, *Phys. Chem. Chem. Phys.*, **2007**, *9*, 4452.

Conformation-Specific Spectroscopy

Methodology

(1) Mass-selective UV spectrum via R2PI

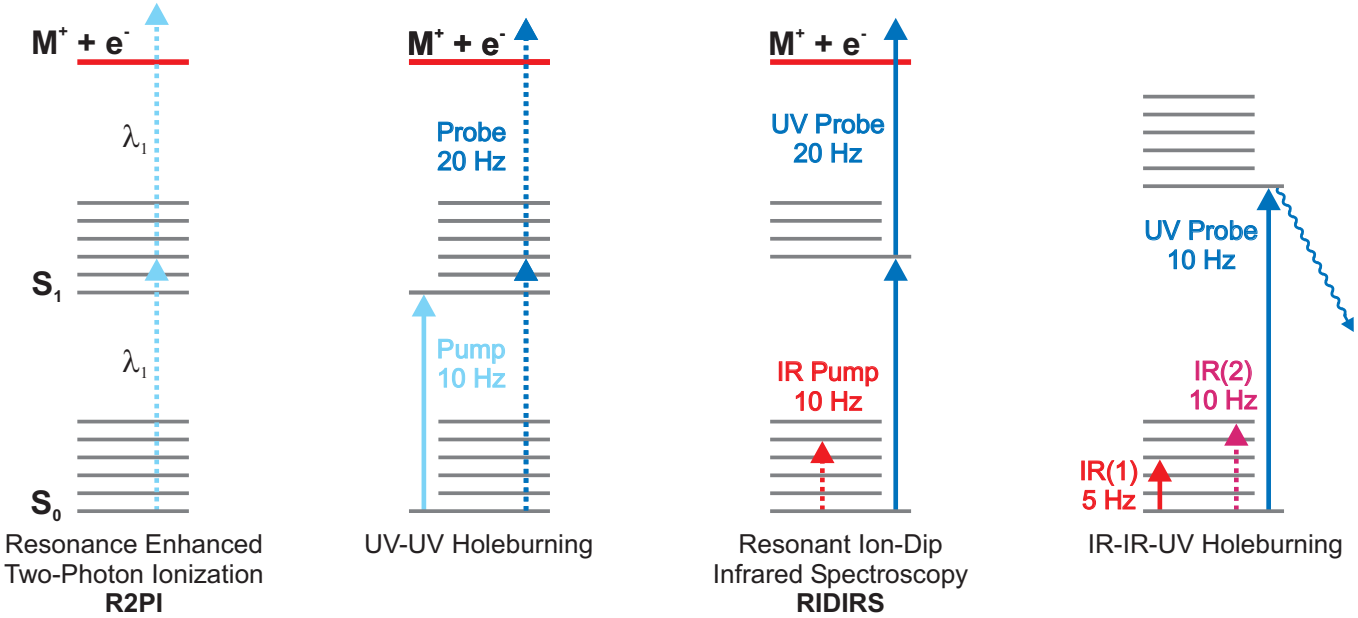
(2) Replacement of ion detection (R2PI) with fluorescence detection (LIF)

(3) Conformation-specific UV spectra via UV-UV/IR-UV holeburning

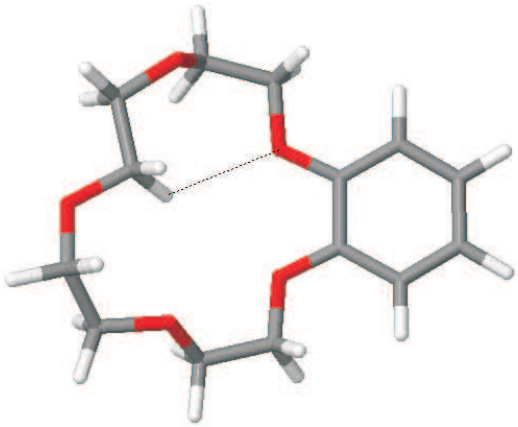
(4) Conformation-specific IR spectra via RIDIR/FDIR spectroscopy

(5) For overlapped electronic spectra:
Conformation-specific IR spectra via IR-IR-UV holeburning

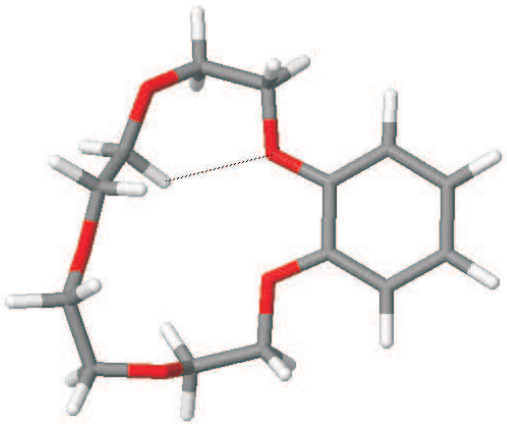
V. A. Shubert, T. S. Zwier, *J. Phys. Chem. A*, 2007, *111*, 13283.



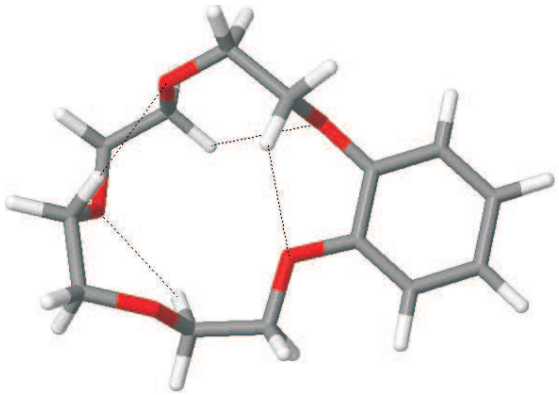
B15C Bare Molecule Conformers



B15C(A)



B15C(B)



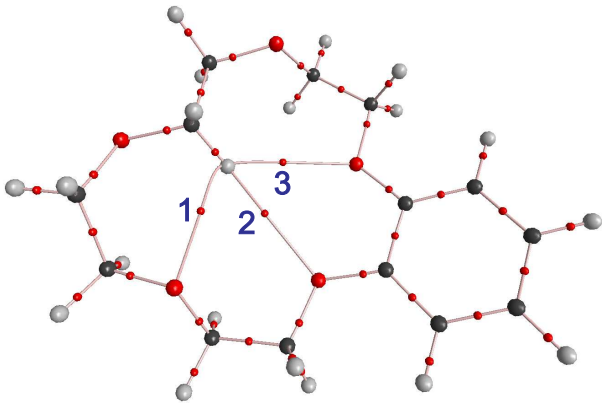
B15C(C)

B3LYP/6-31+G(d)

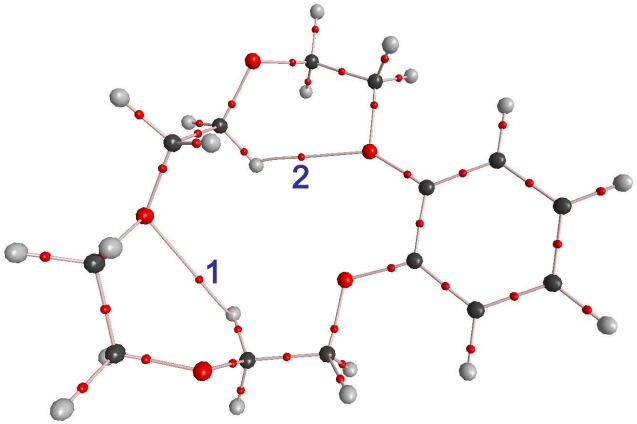
Characteristic Feature

- Blue-shifted alkyl CH stretch bands in the conformation-specific IR spectra.
- Indicative of substantial buckling of the crown structure in order to maximize the number and strength of stabilizing $\mathrm{C-H\cdots O}$ hydrogen bonds.

B15C Bare Molecule Conformers



B15C(A)



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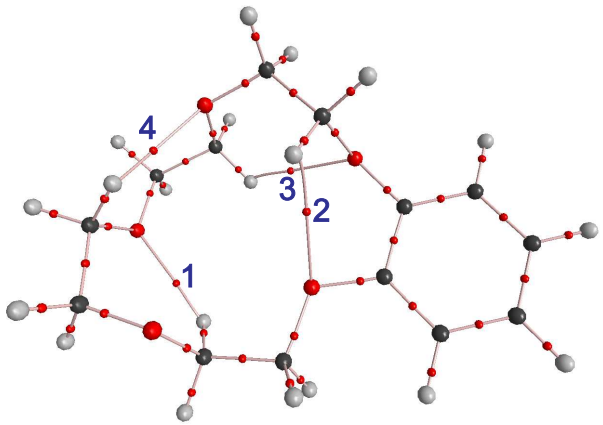

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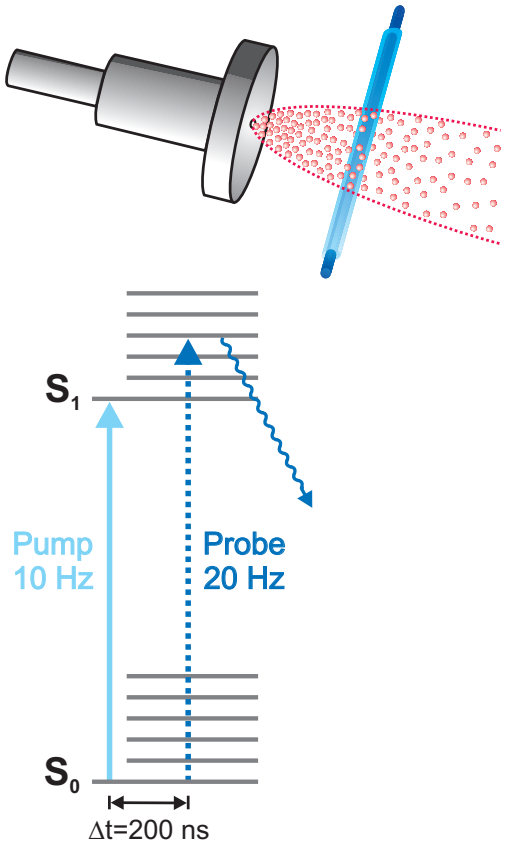
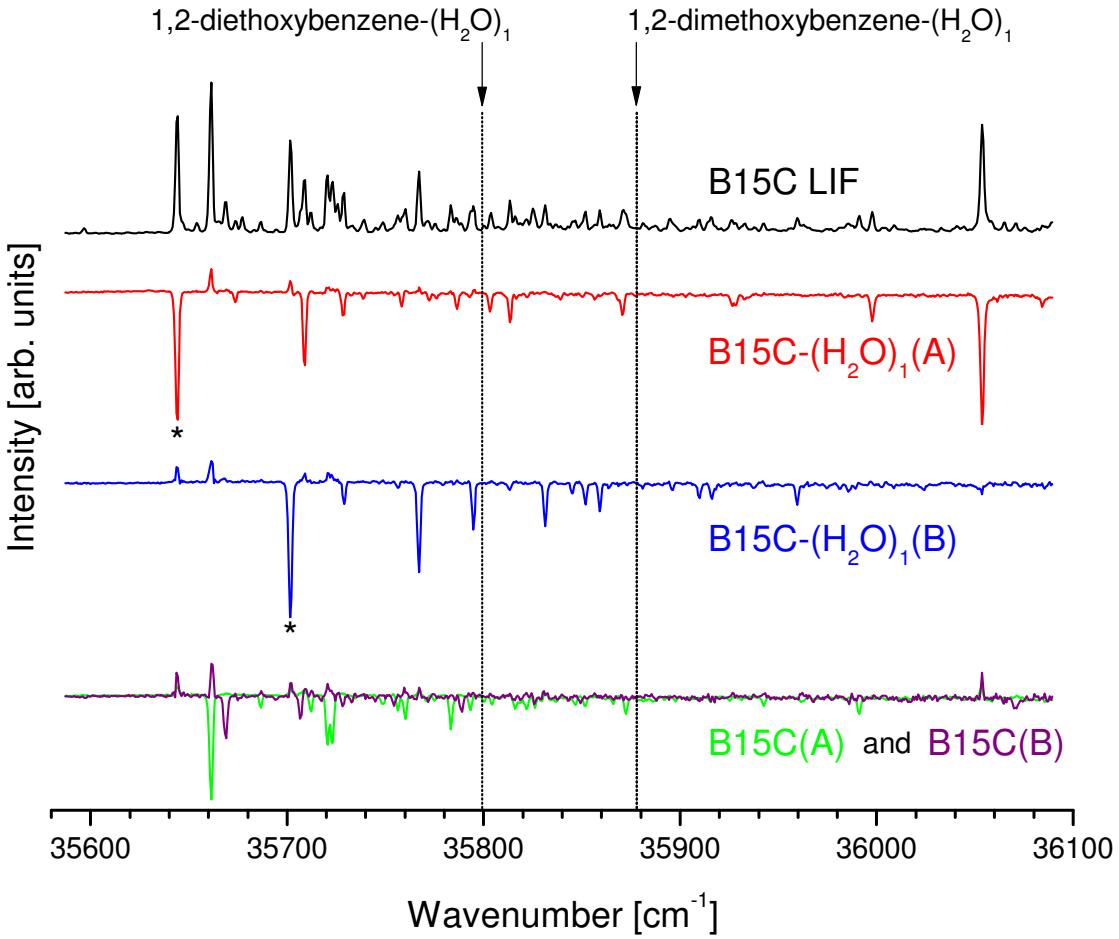
R. F. W. Bader, *Atoms in Molecules. A Quantum Theory*, Clarendon Press, Oxford, 1990.

UV-UV Holeburning Spectroscopy

Conformation-specific UV Spectra — $B15C\text{-}(H_2O)_1$



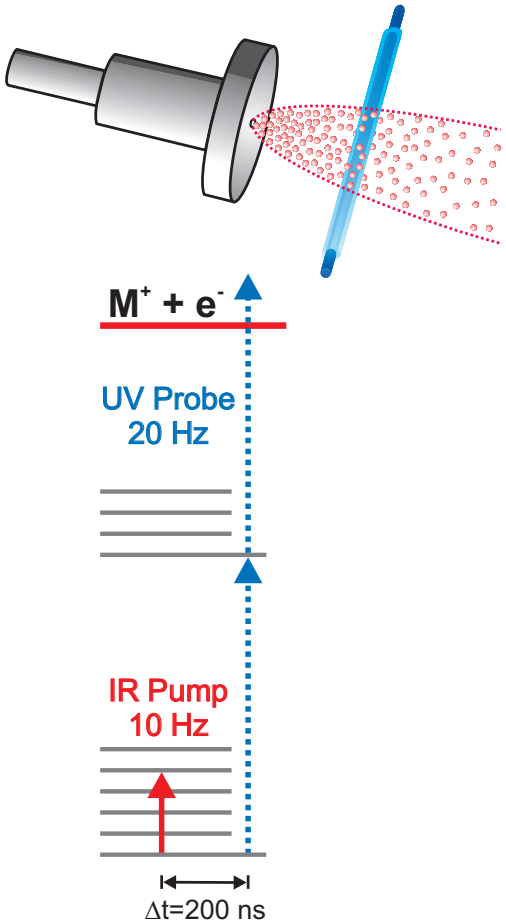


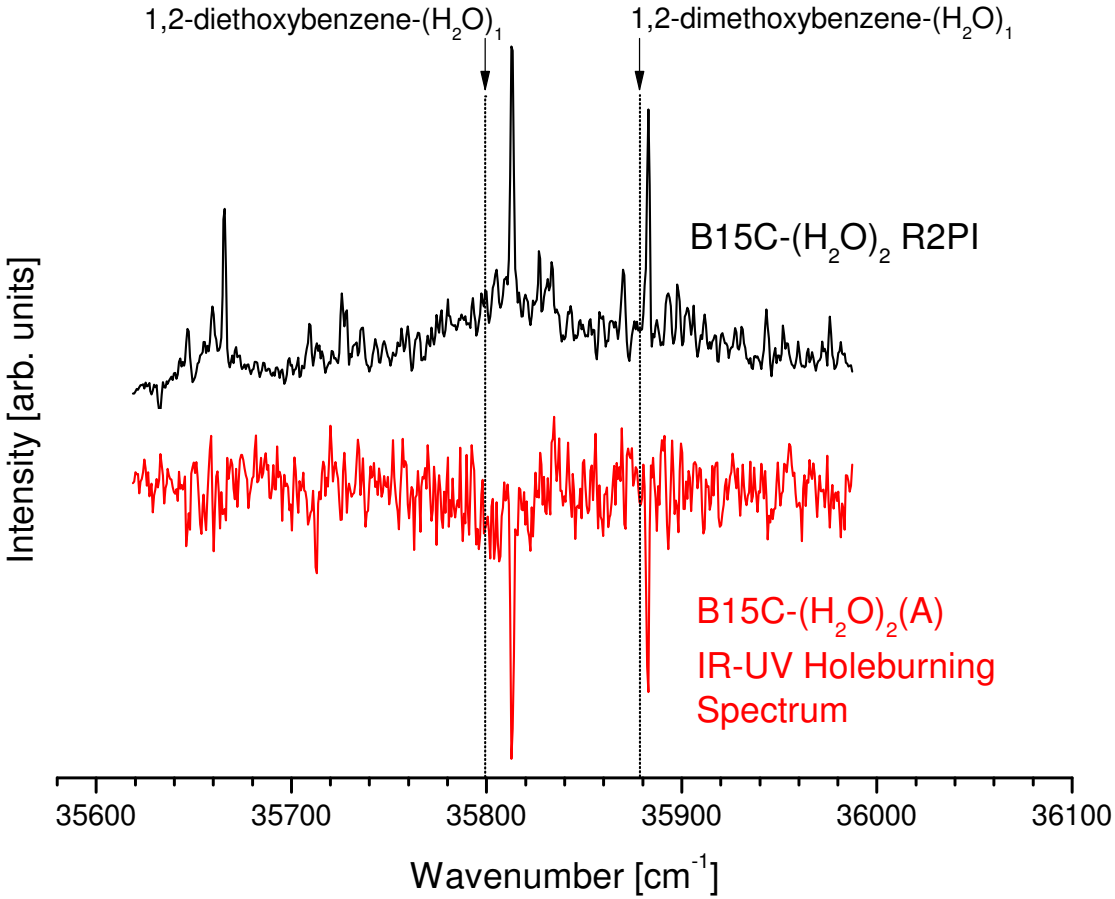
- Two $B15C\text{-}(H_2O)_1$ conformers present in the jet expansion.
- Origin energies are indicative of an all planar arrangement of the atoms near the benzene ring*.

* J. T. Yi, *et al.*, *J. Phys. Chem. A*, **2005**, *109*, 9456.

IR-UV Holeburning Spectroscopy

Conformation-specific UV Spectra — $B15C\text{-}(H_2O)_2$





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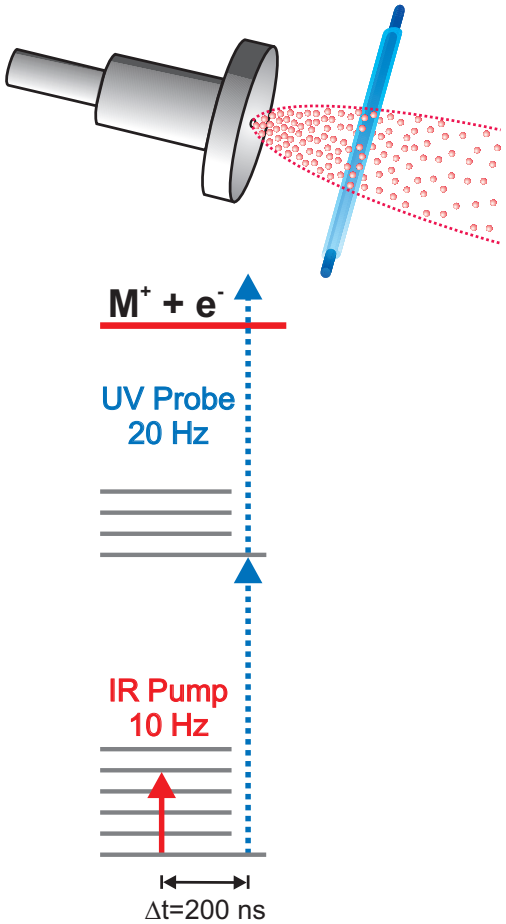
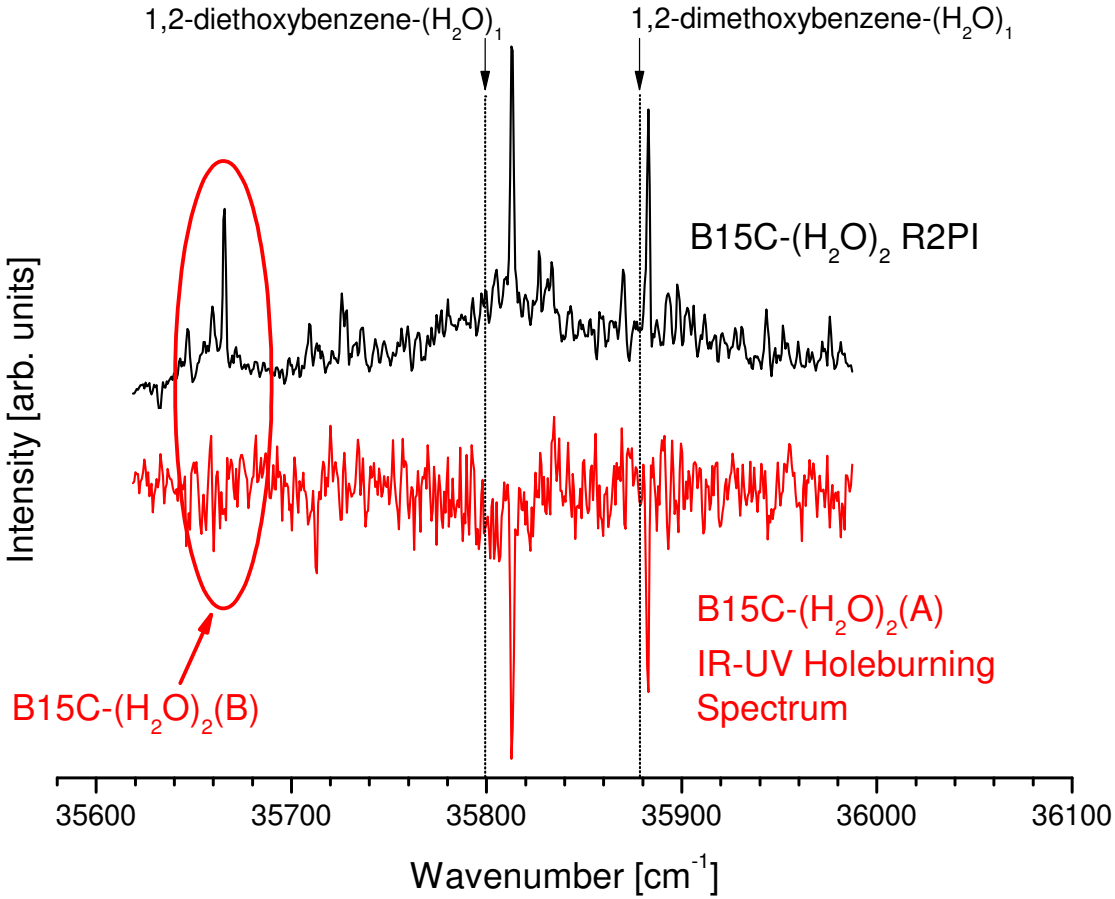
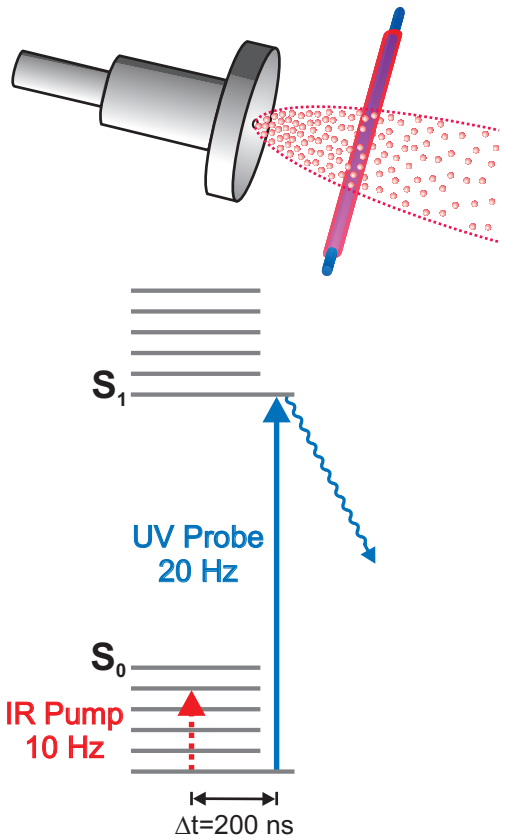


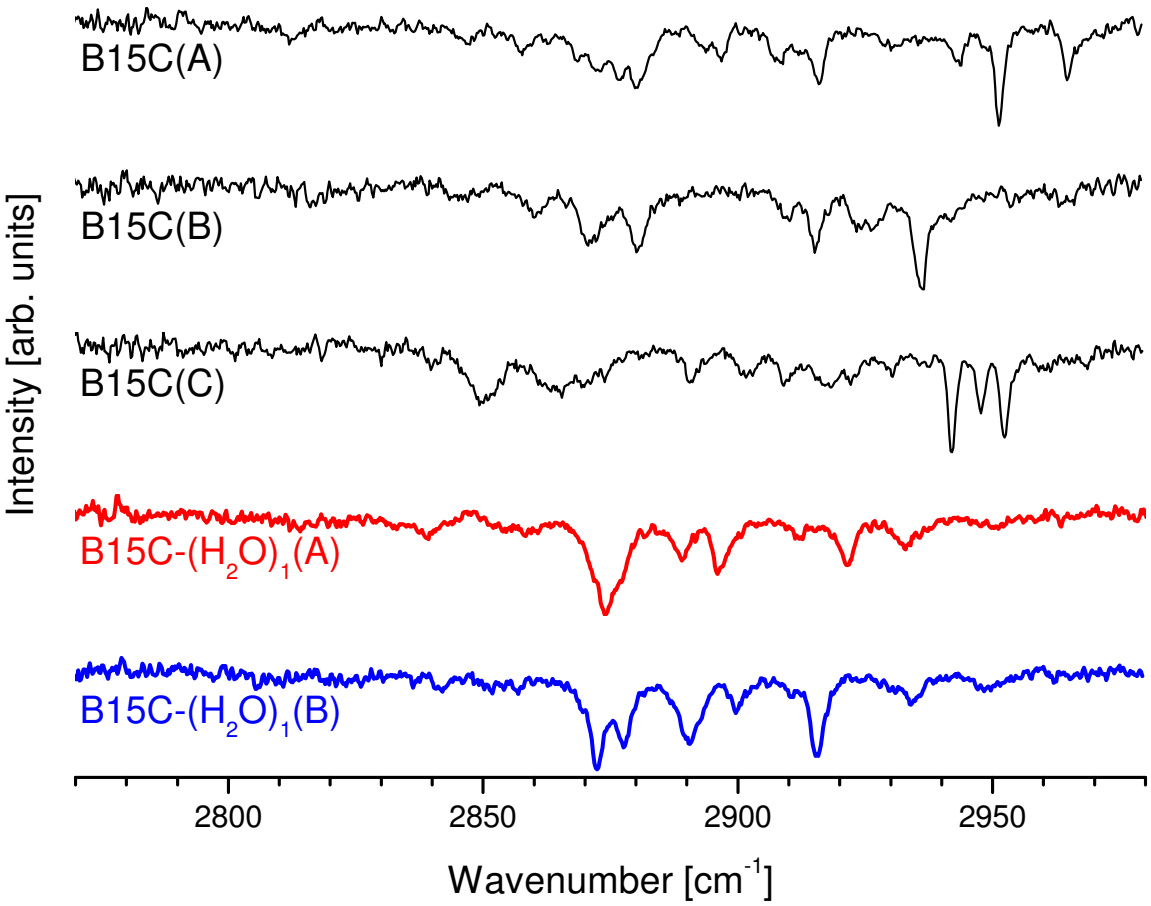


- Two $B15C\text{-}(H_2O)_2$ conformers present in the jet expansion.
- Origin energies are indicative of an all planar arrangement of the atoms near the benzene ring.

Fluorescence-Dip Infrared Spectroscopy

Conformation-specific IR Spectra in the CH Stretch Region — $B15C\text{-}(H_2O)_1$

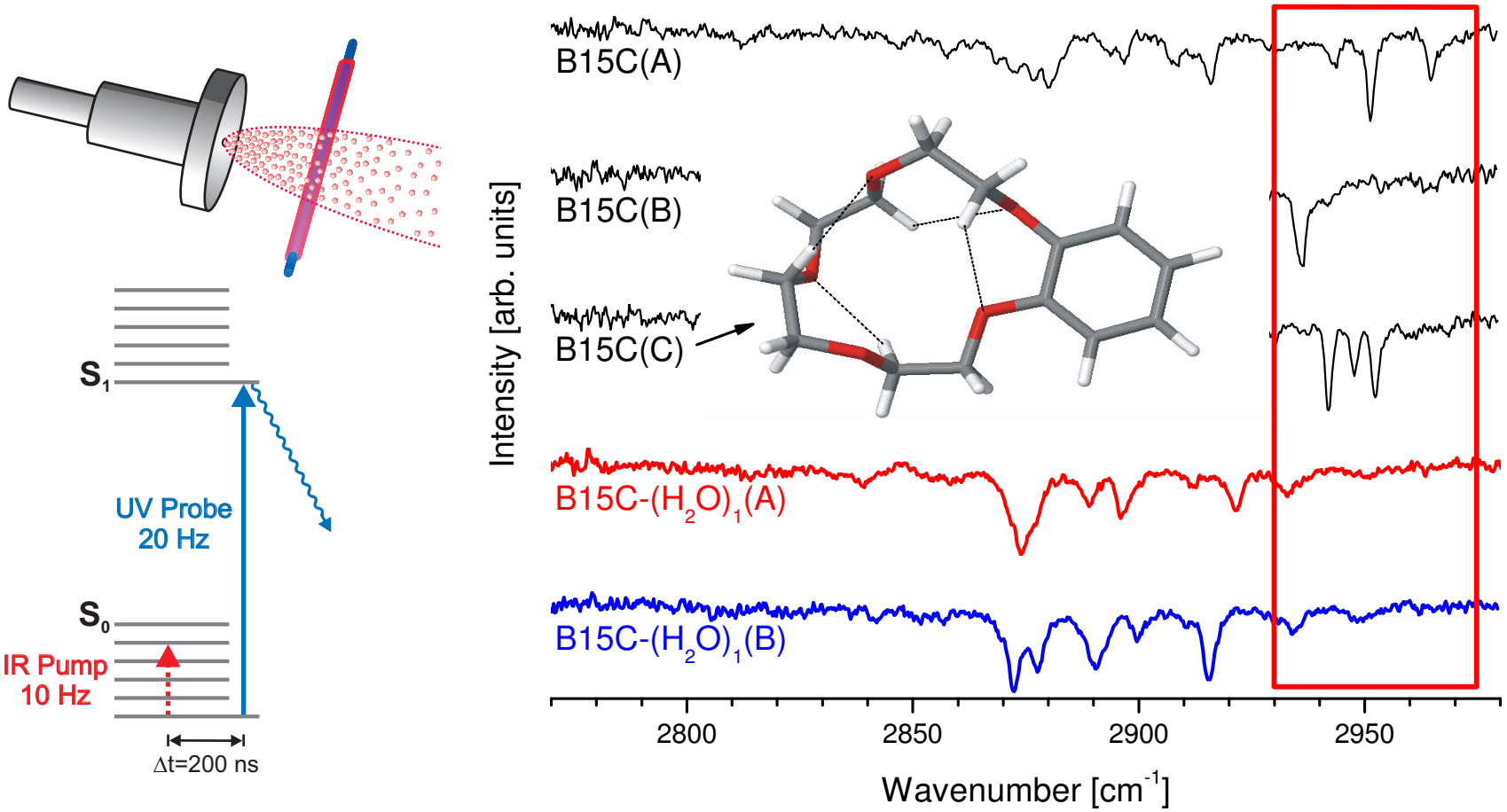




- Similarity of the CH stretch spectra of $B15C\text{-}(H_2O)_1(A)$ and $B15C\text{-}(H_2O)_1(B)$ indicative of similar crown cycle conformations.

Fluorescence-Dip Infrared Spectroscopy

Lack of Blue-shifted $C-H\cdots O$ Hydrogen Bonds — $B15C\text{-}(H_2O)_1$

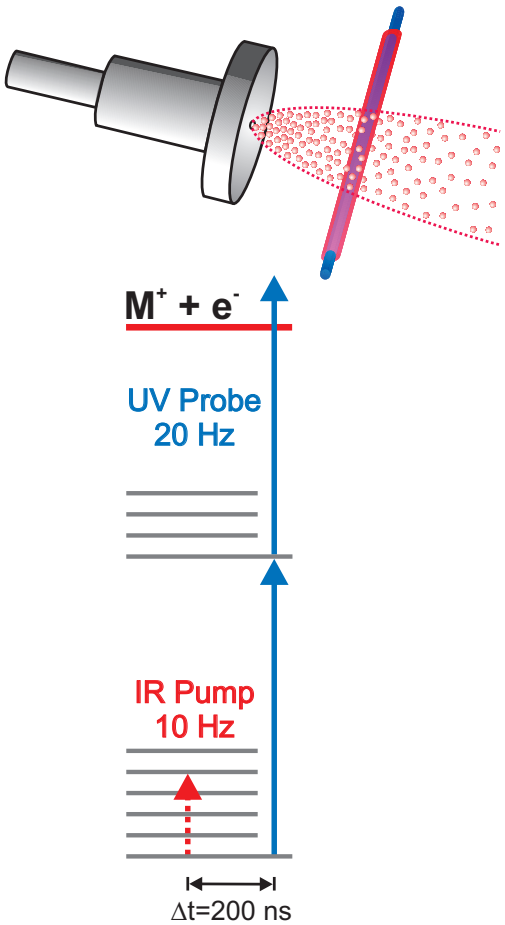


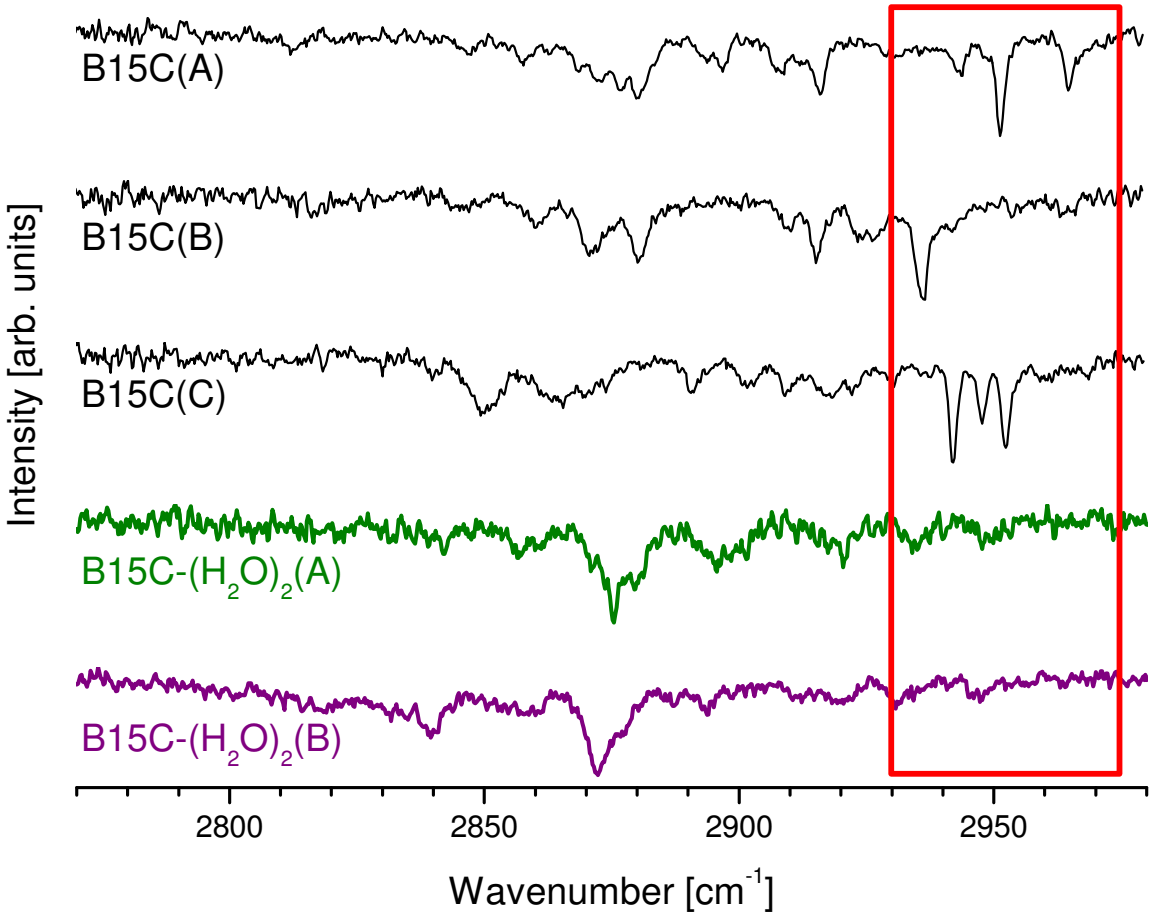
- Lack of spectral features $> 2930\,\mathrm{cm}^{-1}$ indicative of absence of intramolecular $C-H\cdots O$ hydrogen bonds.

$\Rightarrow$ Upon complexation with a single H_2O molecule the crown cycle opens up!

Resonant Ion-Dip Infrared Spectroscopy

Lack of Blue-shifted $C-H\cdots O$ Hydrogen Bonds — $B15C\text{-}(H_2O)_2$



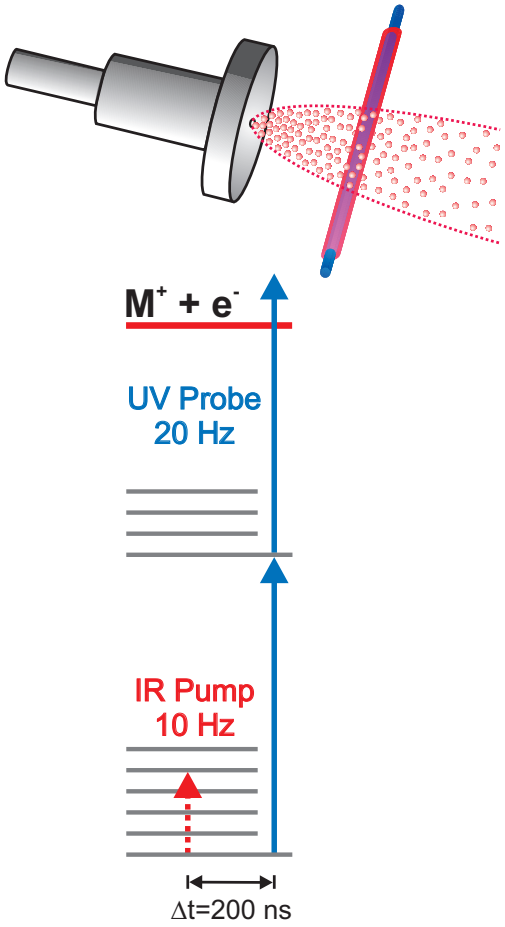


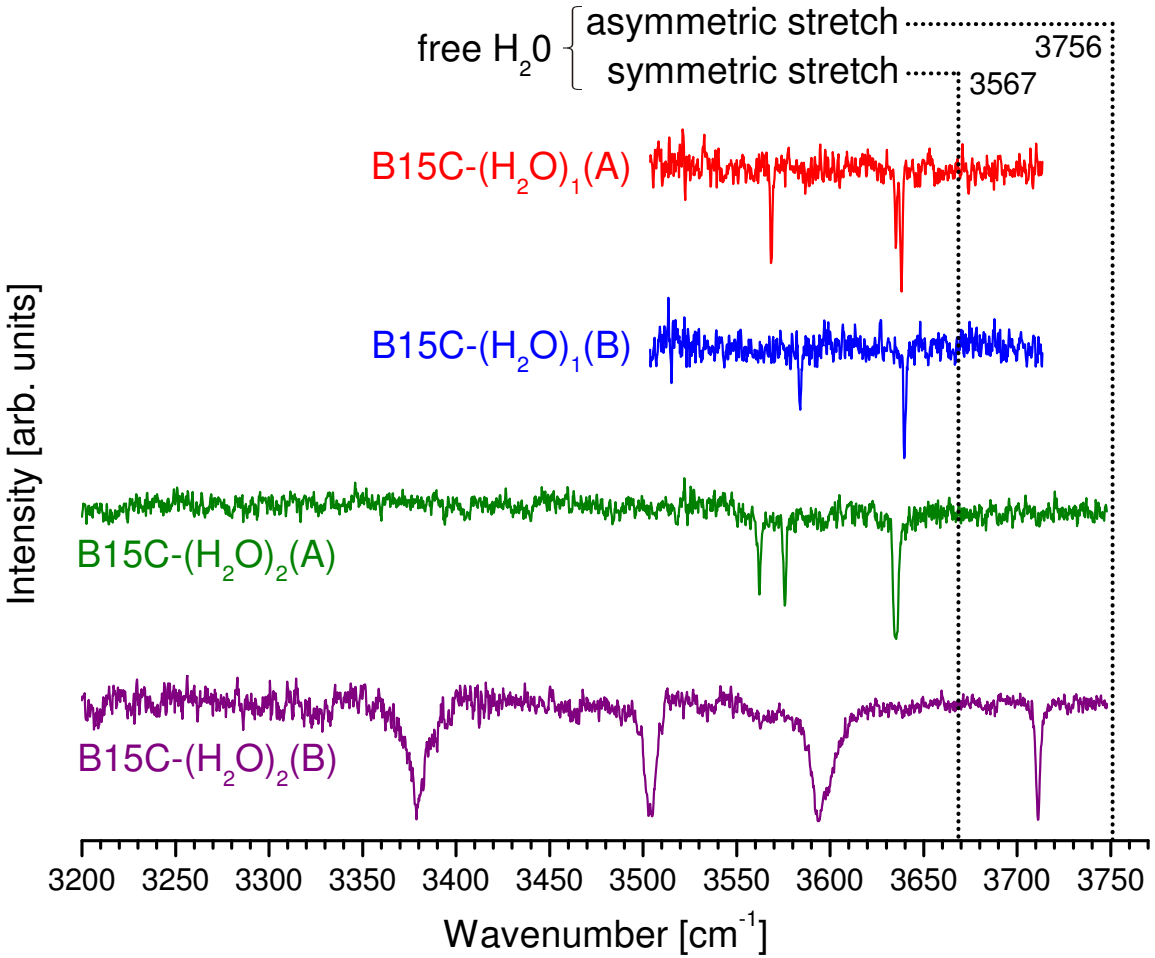
- Lack of spectral features $> 2930\,\mathrm{cm}^{-1}$ indicative of absence of intramolecular $C-H\cdots O$ hydrogen bonds.

$\Rightarrow$ Complexation with the second H_2O molecule leaves the crown cycle open!

Resonant Ion-Dip Infrared Spectroscopy

Conformation-specific IR Spectra in the OH Stretch Region — $B15C\text{-}(H_2O)_1$

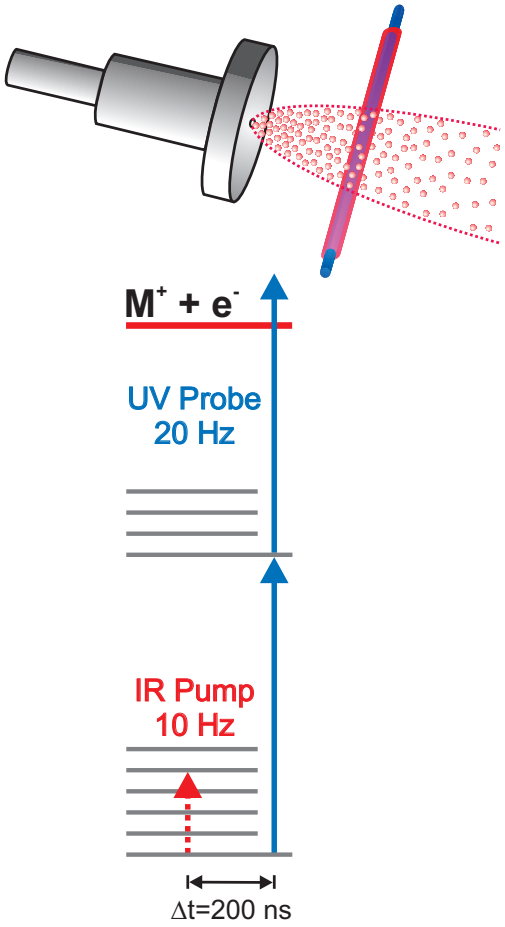


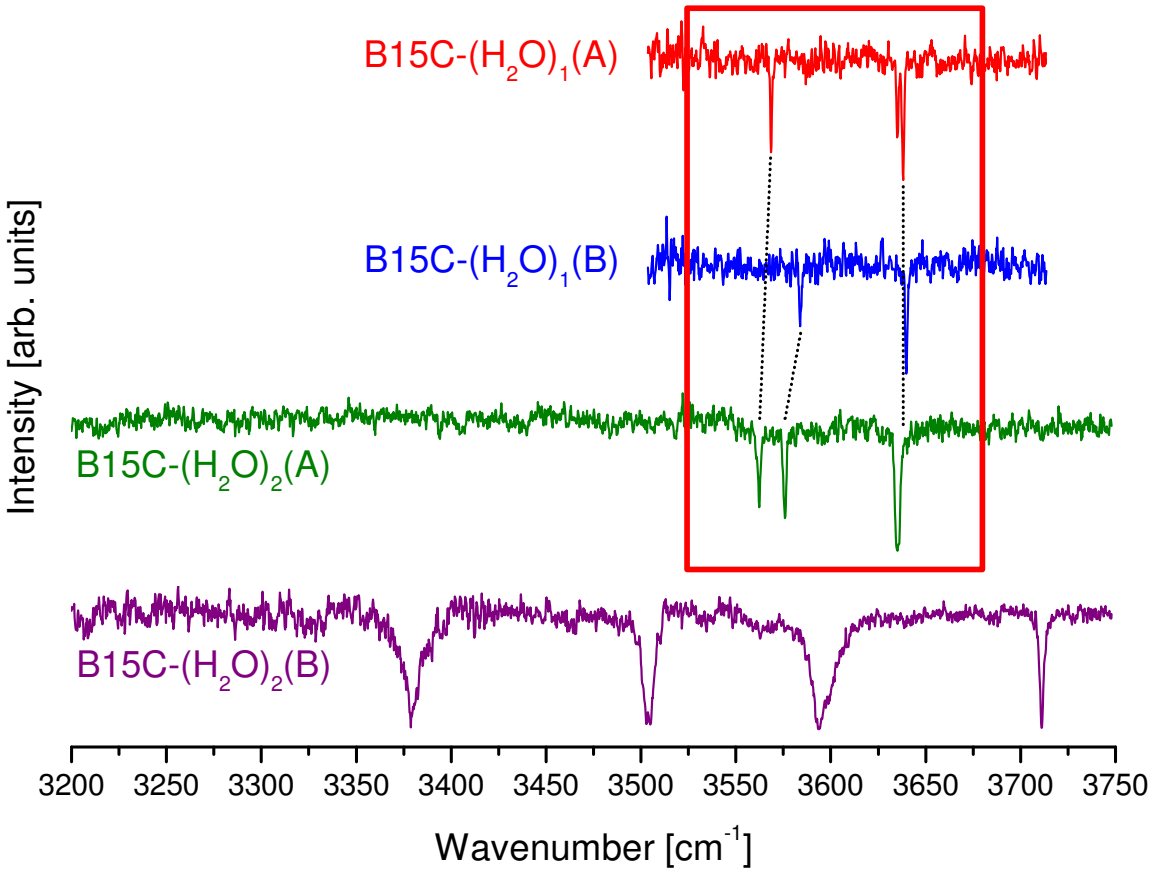


- Monohydrated conformers with very similar crown cycles, only differing in the position of the H_2O molecule.
- Both H_2O hydrogen atoms are involved in hydrogen bonds.

Resonant Ion-Dip Infrared Spectroscopy

Conformation-specific IR Spectra in the OH Stretch Region — B15C-$(H_2O)_2$

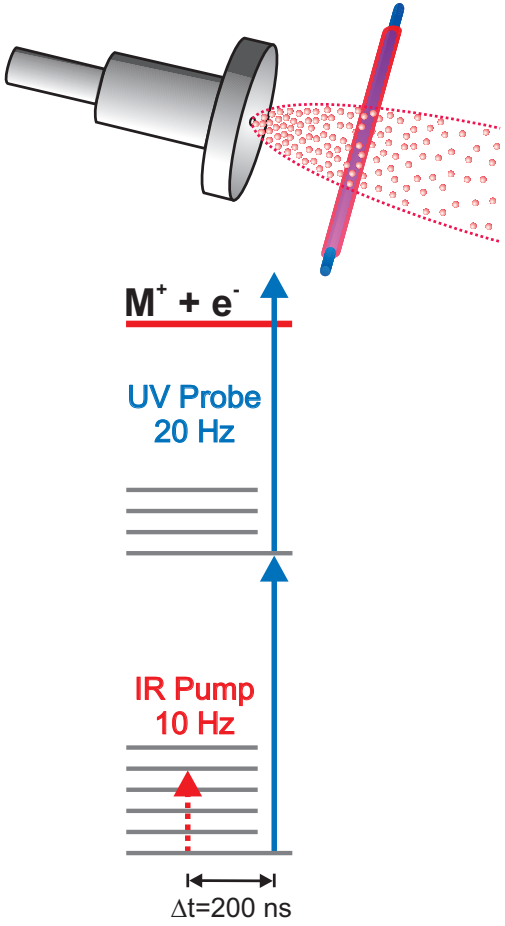


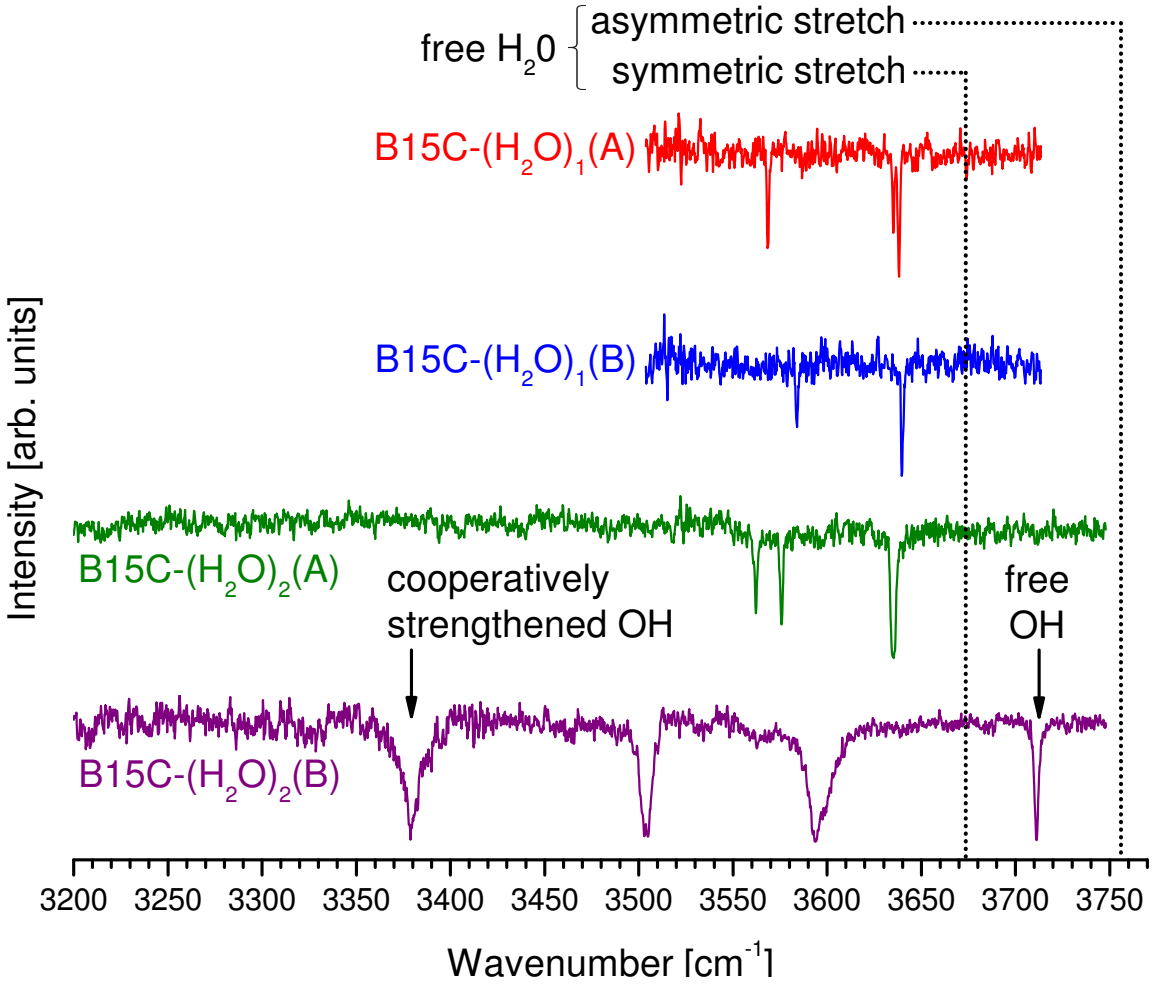


- B15C-$(H_2O)_2$(A) spectroscopically and topologically the sum of B15C-$(H_2O)_1$(A) and B15C-$(H_2O)_1$(B).

Resonant Ion-Dip Infrared Spectroscopy

Conformation-specific IR Spectra in the OH Stretch Region — $B15C\text{-}(H_2O)_2$





- $B15C\text{-}(H_2O)_2(B)$ contains a free OH group and a cooperatively strengthened hydrogen bond.

A Short Checklist

LIF and UV-UV Holeburning Spectra

- Two $\mathrm{B15C\text{-}(H_2O)_1}$ and two $\mathrm{B15C\text{-}(H_2O)_2}$ conformations present in the supersonic jet.
- Origin energies indicative of a planar conformation of the crown cycle near the benzene ring.

RIDIR Spectra in the Alkyl CH Stretch Region

- Similarity of all four crown cycle conformations.
- Lack of blue-shifted intramolecular $\mathrm{C-H\cdots O}$ hydrogen bonds
- The crown cycle opens up upon complexation.

RIDIR Spectra in the OH Stretch Region

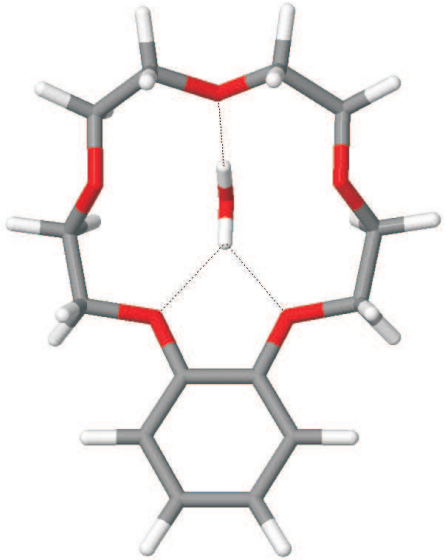
- Both $\mathrm{H_2O}$ hydrogen atoms of the monohydrated complexes are involved in hydrogen bonds.
- One dihydrated complex is the sum of the two monohydrated complexes.
- The second dihydrated complex contains a free OH group and a cooperatively strengthened hydrogen bond.

Ab initio and DFT Calculations

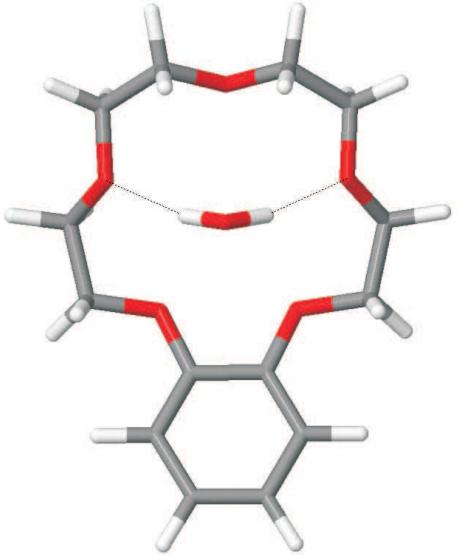
Computational Strategy

- Molecular mechanics force field (MMFs) implemented in Macromodel: 4100 minima below 50 $\frac{\mathrm{kJ}}{\mathrm{mol}}$
- Screening for those conformations in which both H_2O hydrogen atoms are involved in hydrogen bonds: 1524 minima below 50 $\frac{\mathrm{kJ}}{\mathrm{mol}}$
- Submitted to B3LYP/6-31+G(d) geometry optimizations with default grid and loose optimization criteria: 98 minima below 20 $\frac{\mathrm{kJ}}{\mathrm{mol}}$
- Re-optimization with ultrafine grid and tight convergence criteria.
- Harmonic frequencies at B3LYP/6-31+G(d) and single-point energies at MP2/aug-cc-pVDZ level of theory: 6 minima below 20 $\frac{\mathrm{kJ}}{\mathrm{mol}}$
- Screening for those conformations which meet the similarity of the crown cycle and the all-planar condition: 2 minima

B15C-$(H_2O)_1$(A)



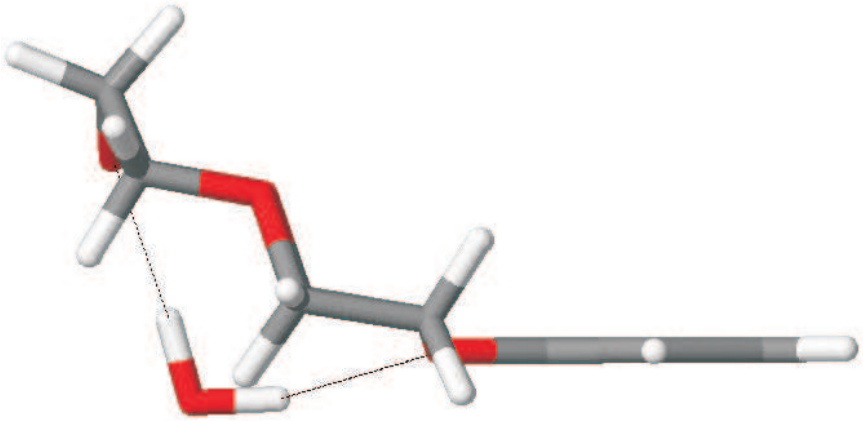
B3LYP/6-31+G(d)



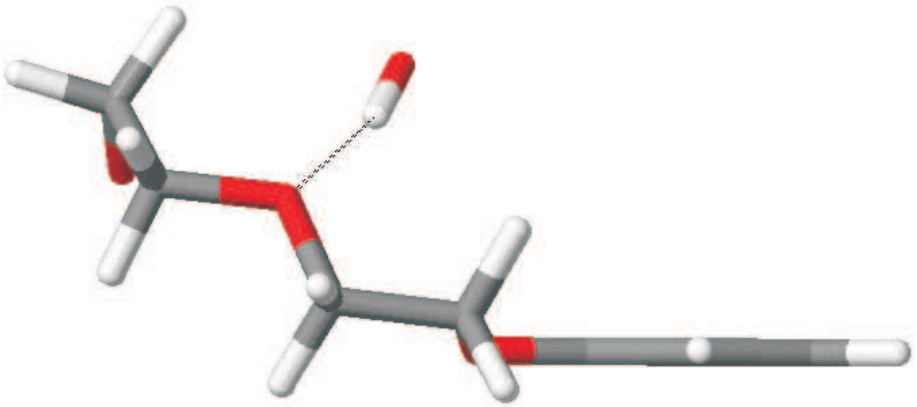
B15C-$(H_2O)_1$(B)

B15C-$(H_2O)_1$ Conformers

B15C-$(H_2O)_1$(A)



B15C-$(H_2O)_1$(B)

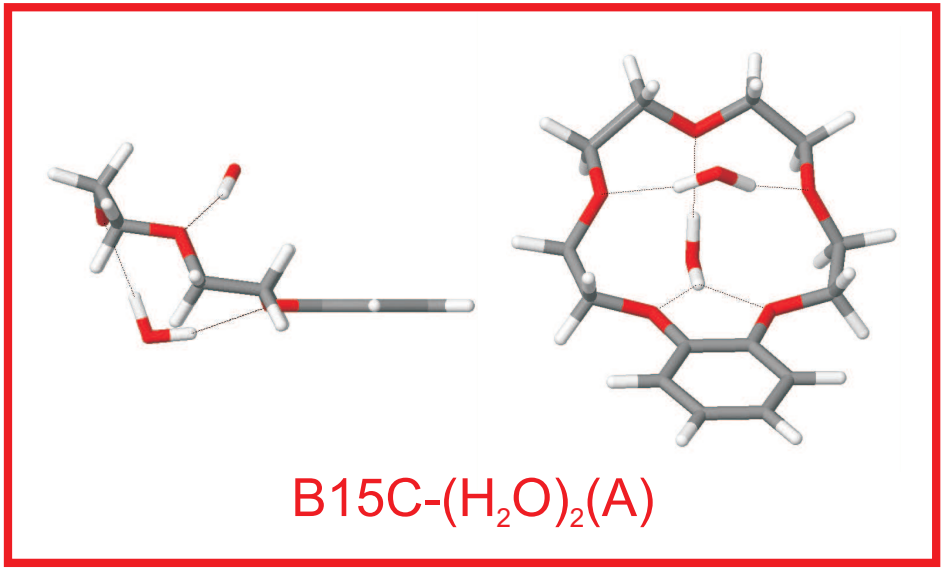


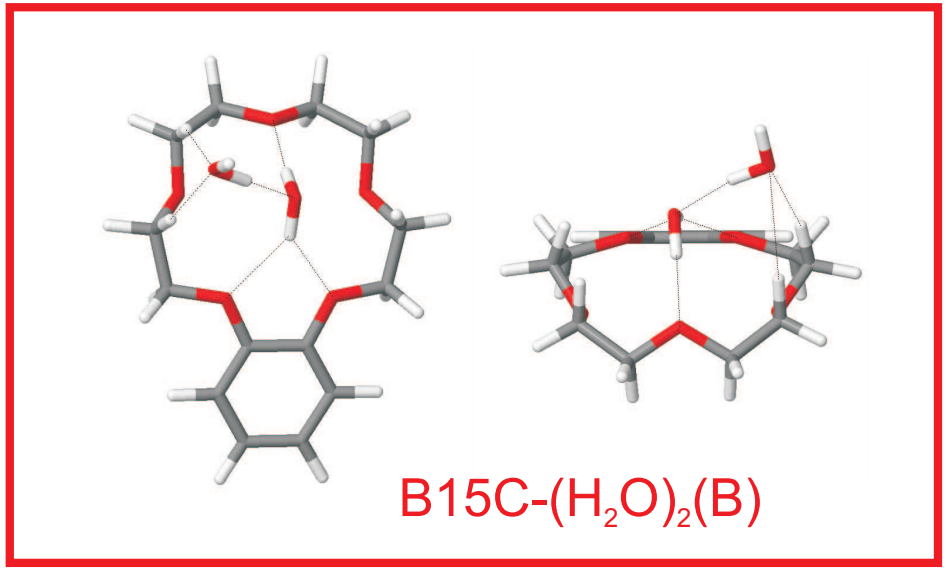
B3LYP/6-31+G(d)

Checklist

- Similarity of the crown cycle conformations.
- Planar conformation of the crown cycle near the benzene ring.
- Lack of blue-shifted intramolecular $C-H\cdots O$ hydrogen bonds
- The crown cycle opens up upon complexation.
- Both H_2O hydrogen atoms are involved in hydrogen bonds.

B15C-$(H_2O)_2$ Conformers





B3LYP/6-31+G(d)

Checklist

- B15C-$(H_2O)_2$(A) is the sum of the two monohydrated complexes.
- B15C-$(H_2O)_2$(B) contains a free OH group and a cooperatively strengthened hydrogen bond.

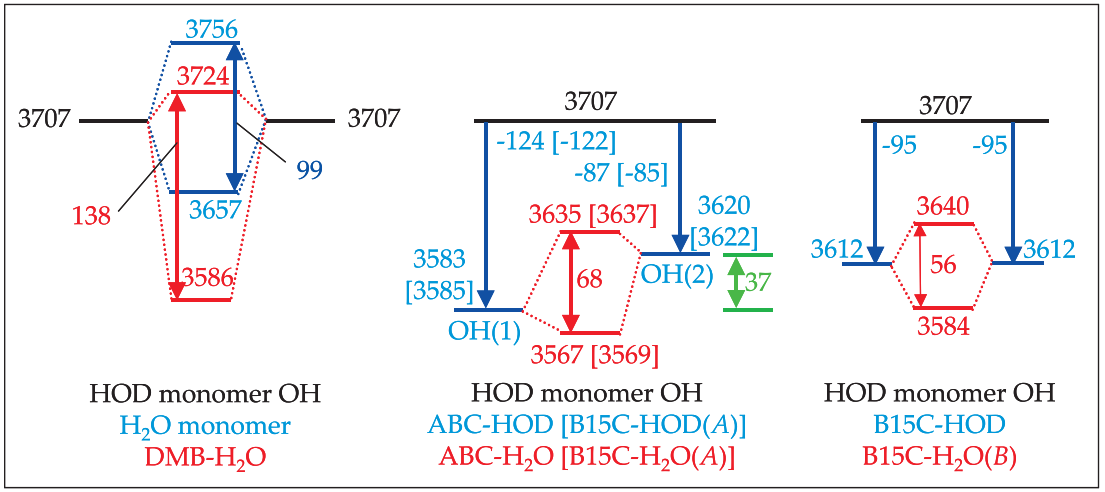
Finally. . .

Summary

- Power & beauty of conformation-specific spectroscopy in elucidating the conformations of flexible molecules and clusters.
- Remarkable flexibility of the crown cycle in binding substrates, drastically altering its conformational preferences from those observed in the uncomplexed monomers.

Present & Future Work

- Investigating the relation between frequency shifts upon complexation and topological properties of the electron density according to Bader's Quantum Theory of Atoms in Molecules (QTAIM).



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LEOPOLDINA

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Computational Chemistry Grid