

## Environmental effects on the nature of hydrogen bonding detected by synchrotron FTIR microspectroscopy

A hydrogen bond forms between a covalently bonded hydrogen atom and an atom with a high electronegativity. The range of the bonding force is wide, from the weakest van der Waals limit to the strongest covalent bond limit, centered on the well-known hydrogen bond between water molecules. Of the three forces that form hydrogen bonds (electrostatic, induction, and dispersion), it is known that the contribution of dispersive interactions such as van der Waals forces is the largest in the weak hydrogen bonds. Van der Waals forces that are easily disturbed by thermal energy around room temperature are sensitive to environmental factors such as temperature and pressure, leading to the attractive and fuzzy properties inherent in biological systems. Assessment of the van der Waals interaction is fundamental to the central quest of understanding the structure that regulates the biological function. The van der Waals interaction, named after Johannes Diderik van der Waals, who first introduced attractive interactions between neutral molecules in his equation of state, is a dispersion interaction of pure quantum physical origin and is due to quantum fluctuation. Very recently, the theoretical treatment of the van der Waals interaction has become possible.

In this research [1], we revealed the environmental effects on the nature of hydrogen bonding in a fully amorphous biocompatible zwitterionic sulfobetaine monomer, DMAPS (Fig. 1), by measurement using terahertz waves and high-intensity synchrotron radiation at SPing-8 BL43IR and analysis with highly accurate first-principles calculations. Biocompatible materials are in high demand for application to drug delivery and/or the coating of artificial organs to avoid the rejection of living organisms. Biocompatible zwitterionic molecules are sensitive to environmental factors such as temperature and pressure, and van der Waals forces govern the stimulus-sensitive properties. Betaine (a specific type of neutral zwitterion) contains a pair of cationic and anionic functional groups at nonadjacent positions in the molecule. A powerful means of detecting the weak interactions is vibrational absorption spectroscopy, which is applicable for many materials including biological substances.

High-intensity synchrotron radiation is useful for small amounts of samples and THz waves are useful for detecting weak hydrogen bonds. THz spectroscopic research has progressed rapidly in recent years, and signal detection and peak assignment on the basis of theoretical calculations have been established for

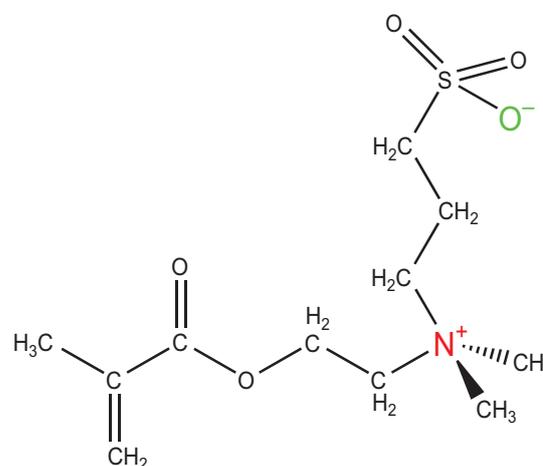


Fig. 1. DMAPS (3-[dimethyl-(2-methacryloyloxyethyl) ammonium] propane sulfonate).

crystalline samples [2-4]. Noncrystalline amorphous samples are more informative from the biological point of view. However, the study of amorphous samples is lagging behind because of the weak signal and the difference from the gas phase and/or the crystal. To overcome the low intensity of THz absorption, we measured the sample without using a filling material such as polyethylene to dilute the sample. Furthermore, typical filling materials such as KBr in far-infrared spectroscopy are not suitable for zwitterionic molecules because of interactions between the filling materials and zwitterionic samples. It is a notable point in the present synchrotron FTIR microspectroscopy measurement that no filling material is required. Theoretically, the effect of surrounding molecules that cause the difference from the gas phase and the difficulty of the nonperiodic amorphous system is incorporated in the dielectric constants.

The complicated far-infrared spectrum of the present amorphous system was found to be well reproduced by incorporating the effect of the surrounding molecules in the dielectric constants. In this frequency region, the overall spectral profile hardly changes with temperature, except for peak sharpening and a slight peak shift to a higher frequency (Fig. 2). A strong temperature dependence was observed, however, as a peak splitting at around  $300\text{ cm}^{-1}$ . The temperature-dependent spectral change around  $300\text{ cm}^{-1}$  is well reproduced by changing the dielectric constant (insert of Fig. 2). A difference in the dielectric

constant negligibly affects the spectral profile in the whole range except for the region around  $300\text{ cm}^{-1}$ . It is possible that the dielectric constant changes with temperature owing to the change in molecular mobility.

The spectral change depending on temperature is caused by the change in the nature of hydrogen bonding depending on the dielectric constant. The nature of three  $\text{CH}\cdots\text{O}$  bonds markedly changes depending on the dielectric constant, from the typical  $\text{CH}\cdots\text{O}$  between the CH donor and the  $>\text{S}=\text{O}$  acceptor to  $\text{CH}\cdots\text{O}$  at the van der Waals contact to no hydrogen bonding.

In summary, the environmental effect on weak intermolecular and intramolecular interactions was revealed by synchrotron FTIR microspectroscopy combined with highly accurate first-principles calculations. High-intensity synchrotron radiation makes it possible to measure small amounts of samples and is suitable for stimulus-sensitive biocompatible materials and amorphous biomolecules. The present results provide a new dimension for designing biocompatible materials with sensitivity to environmental factors such as temperature and pressure.

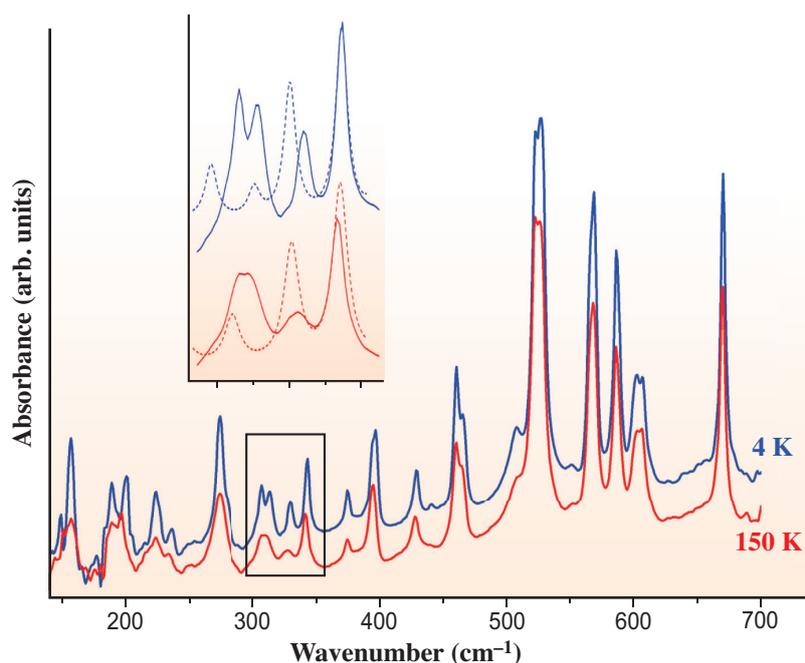


Fig. 2. Far-infrared spectra of DMAPS at 4 K (blue) and 150 K (red). The insert also shows, for comparison, calculated spectra (dashed lines) in the range indicated by the square box. Dielectric constants are 15.20 for the red dashed line and 8.33 for the blue dashed line.

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