

β -Isocyanoalanine as an IR probe: comparison of vibrational dynamics between isonitrile and nitrile-derivatized IR probes



Michał Maj,^{1, 2} Dorota Kossowska,^{1, 2} Kyungwon Kwak,³ Hogyu Han^{2*} and Minhaeng Cho^{1, 2*}

¹Center for Molecular Spectroscopy and Dynamics, Institute for Basic Science (IBS), Korea University, Seoul 136-701, Republic of Korea ²Department of Chemistry, Korea University, Seoul 136-713, Korea ³Department of Chemistry, Chung-Ang University, Seoul 156-756, Korea
*hogyuhan@korea.ac.kr and mcho@korea.ac.kr



Abstract

A vibrational probe based on isonitrile (NC)-derivatized alanine **1** (Ac-Ala(NC)-NHMe) was synthesized and its structure and vibrational dynamics of its NC stretch mode were examined utilizing FTIR and femtosecond IR pump-probe spectroscopy. It has been found that the probe is characterized by very high sensitivity to the hydrogen bonding environment and in comparison to nitrile (CN) the NC stretch mode possesses larger dipole strength when attached to the aliphatic group. Its vibrational lifetime is several times longer than that of azido (N_3) stretch mode in azido-derivatized IR probes and it was determined to be 5.52 ps and 5.53 ps in D_2O and DMF, respectively. Furthermore, to understand the phenomenon of the vibrational solvatochromism of the new IR probe quantum chemistry calculations of methyl isocyanide in water clusters were carried out and the distributed site model for vibrational solvatochromism was applied.

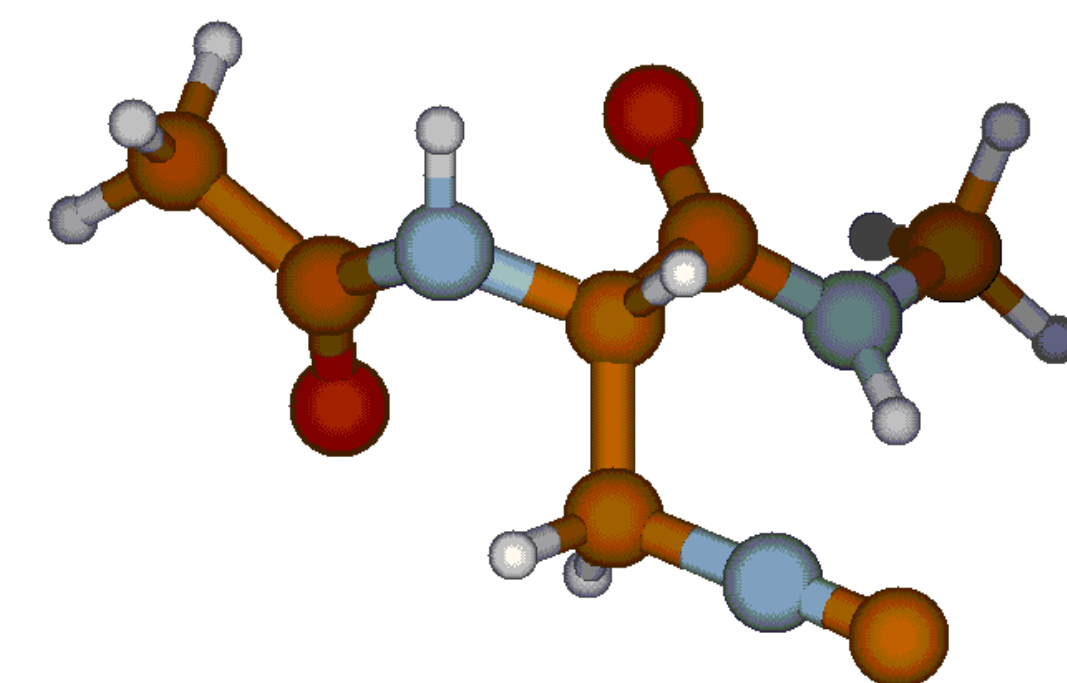


Figure 1. Structure of Ac-Ala(NC)-NHMe.

Results – experimental data

FTIR

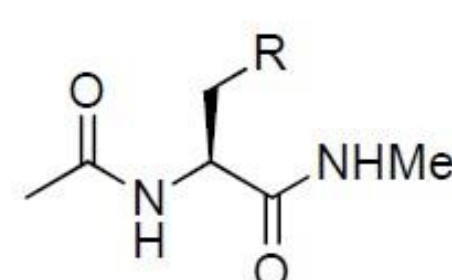


Figure 2. Structures of compounds 0–3 used for IR study.

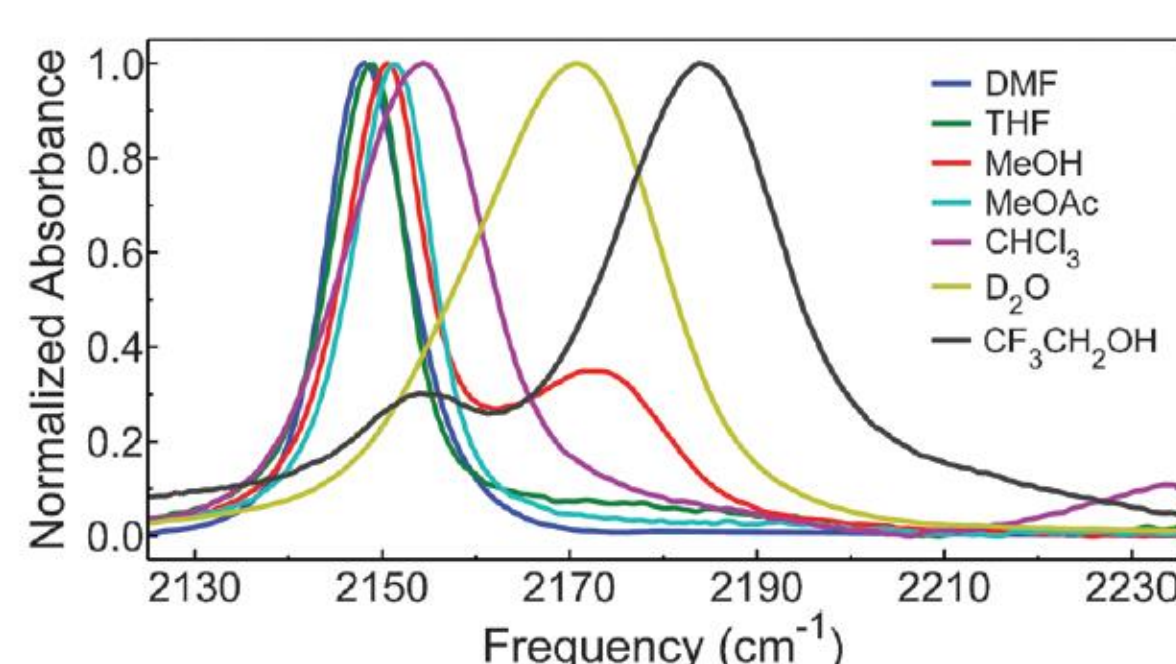


Figure 3. Isonitrile (NC) stretch FTIR spectra of **1** in various solvents.

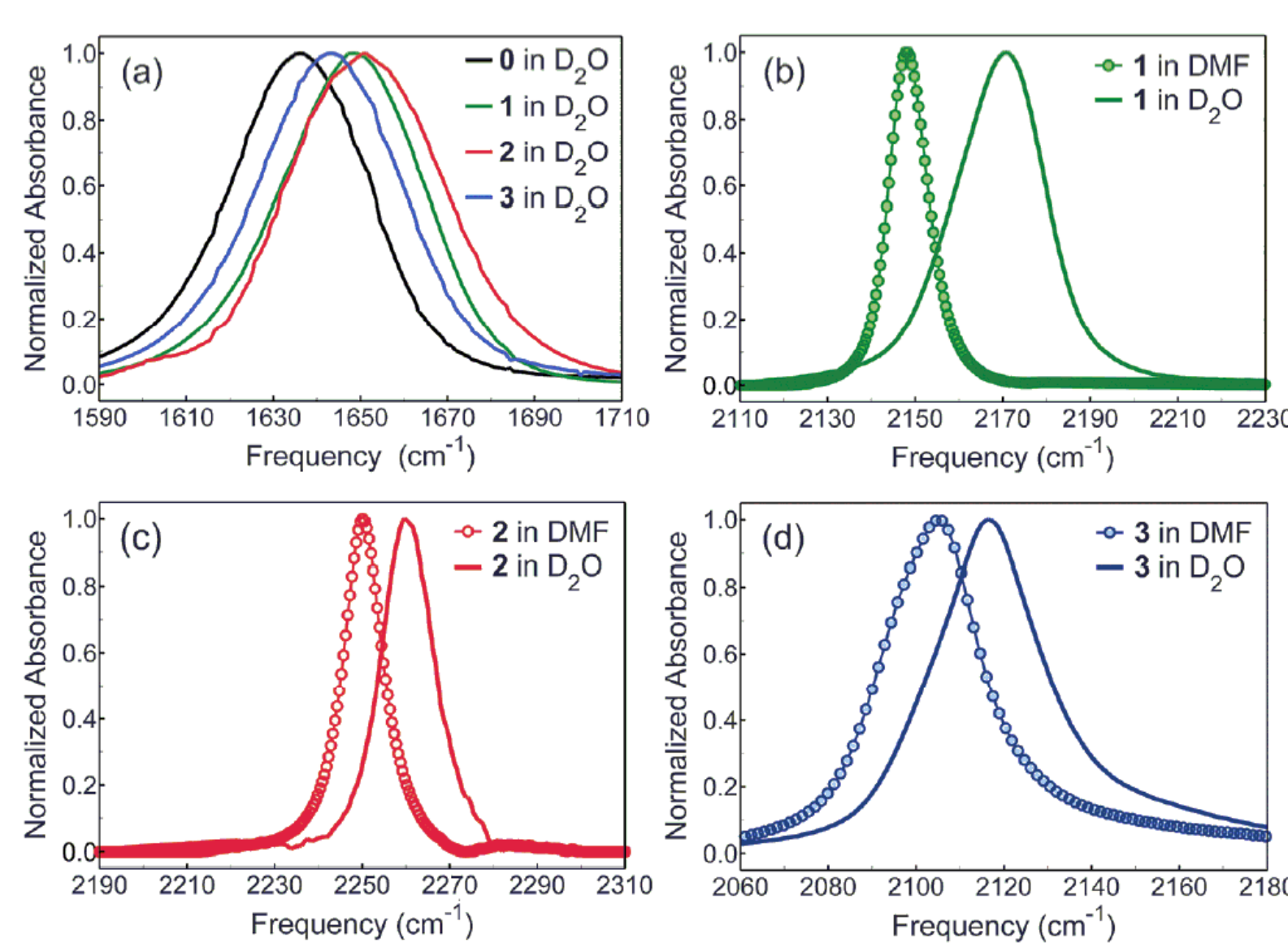


Figure 4. (a) Amide I' FTIR spectra of 0–3 in D_2O . (b–d) Isonitrile (NC), nitrile (CN), and azido (N_3) stretching FTIR spectra of 1–3 in DMF and D_2O .

Polarization controlled IR pump-probe spectroscopy

Figure 5. Contour plots of isotropic PP signals of **1**, before and after applying corrections for heat contribution.

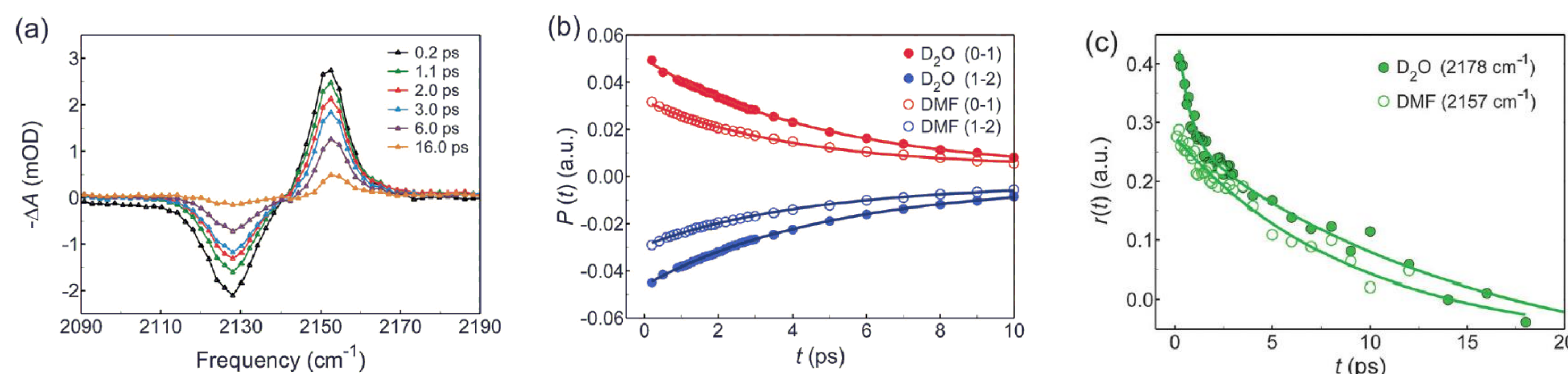
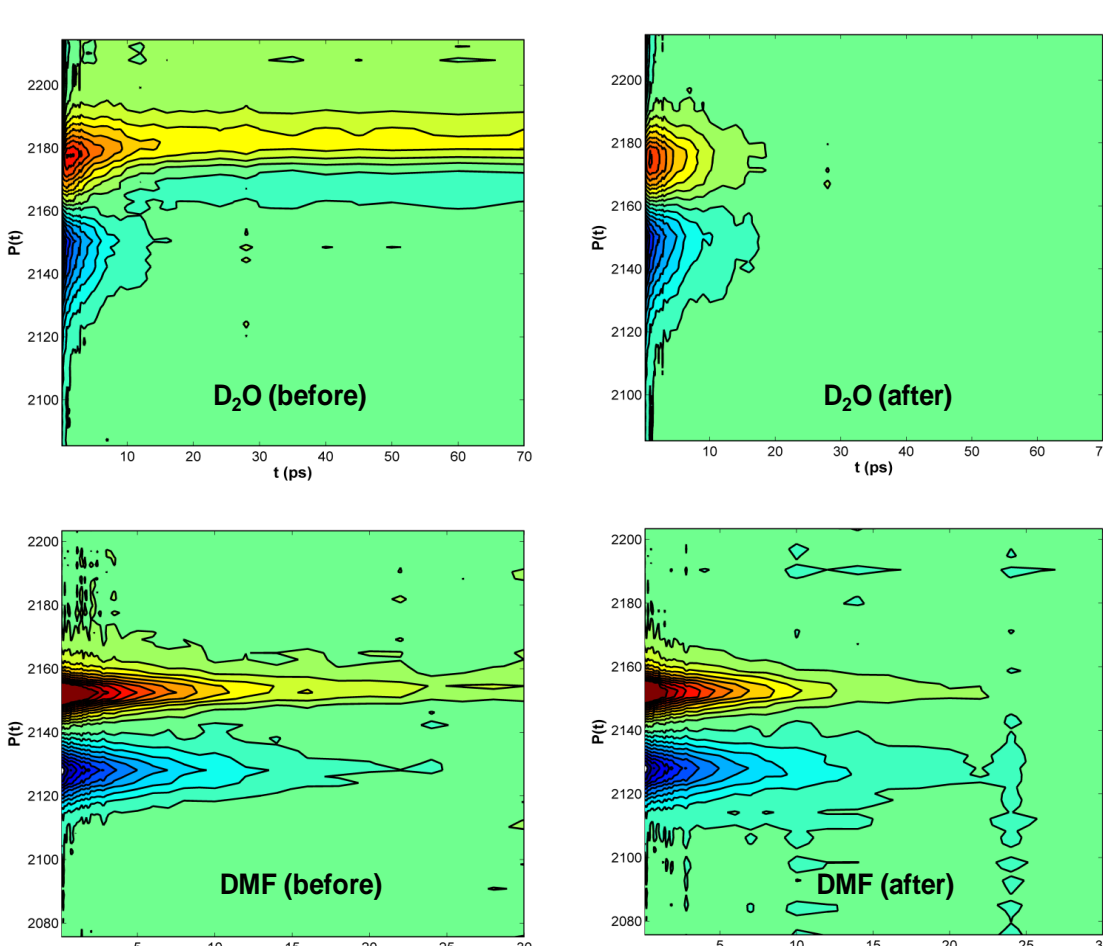


Figure 6. Polarization-controlled IR pump-probe data of **1**. (a) Isotropic IR pump-probe spectra of **1** in DMF at the delay time t . (b) Vibrational population decays of **1** in D_2O and DMF. (c) Anisotropy decays of **1** in D_2O and DMF.

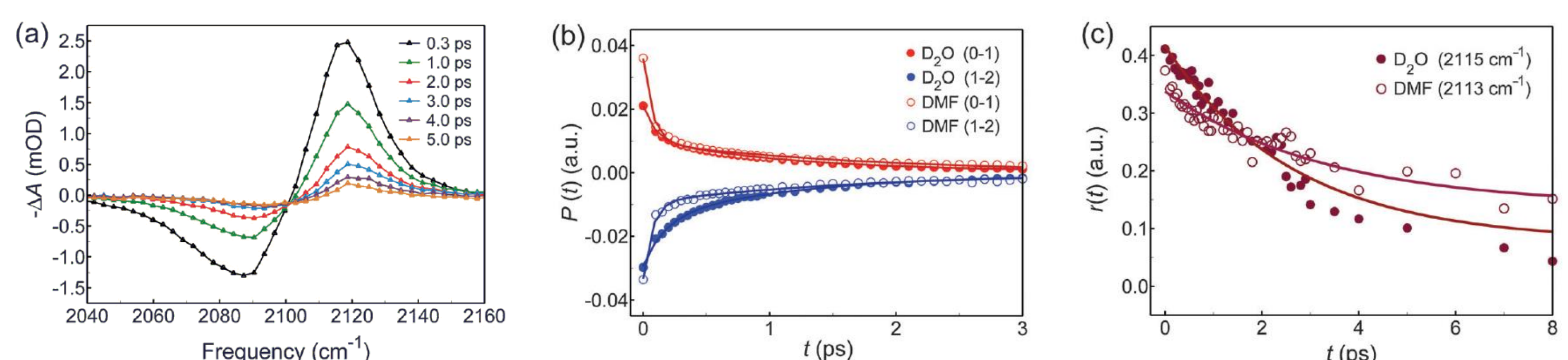


Figure 7. Polarization-controlled IR pump-probe data of **3**. (a) Isotropic IR pump-probe spectra of **3** in D_2O at the delay time t . (b) Vibrational population decays of **3** in D_2O and DMF. (c) Anisotropy decays of **3** in D_2O and DMF.

Table 1. Spectral properties of 1–3.

	1		2		3	
	D_2O	DMF	D_2O	DMF	D_2O	DMF
ω_{center} (cm^{-1})	2169.53	2151.63	2260.37	2250.21	2116.05	2103.59
FWHM (cm^{-1})	24.14	10.58	14.33	10.98	28.95	26.36
ϵ ($cm^{-1}M^{-1}$)	142	390	14	27	349	333
D^* (Debye ²)	1.82	2.21	0.06	0.15	5.49	4.80
T_1 (ps)	5.52 ± 0.18	5.53 ± 0.17	–	–	1.14 ± 0.04 (0.10)**	1.34 ± 0.08 (0.10)**
τ_{or} (ps)	$10.33 \pm 2.24^*$ 0.52 ± 0.20	7.28 ± 0.94	–	–	0.13 ± 0.01 (0.24)**	0.065 ± 0.004 (0.15)**

*From ref. 4. **Amplitudes. ***Major component

Results – computational data

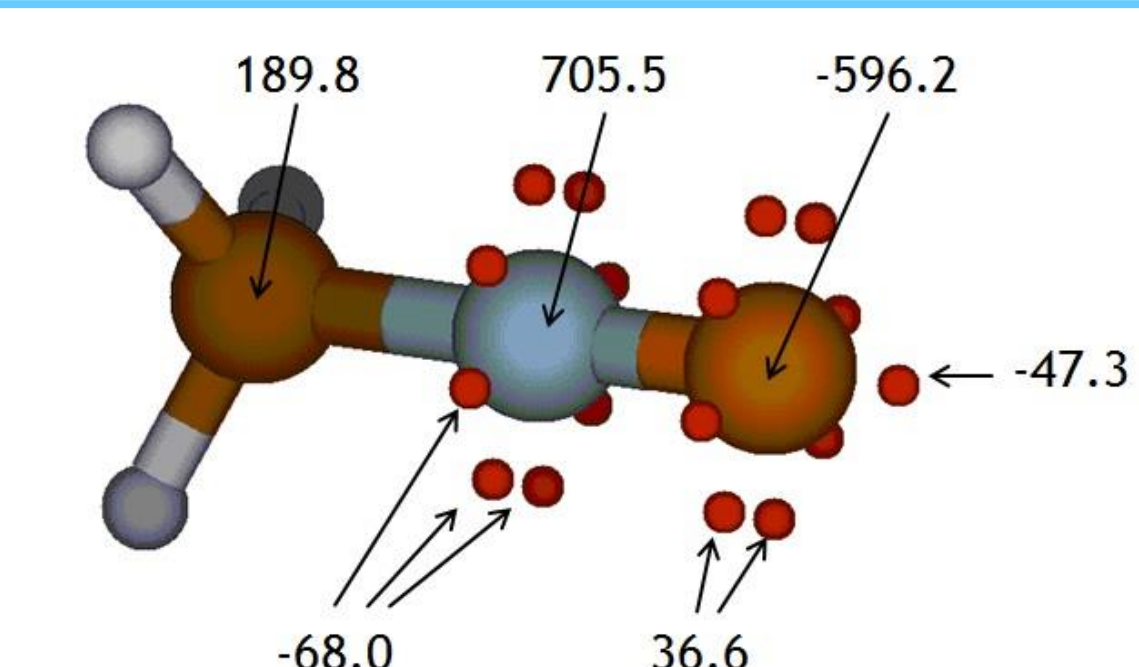


Figure 8. Positions of the distributed interaction sites for MeNC. The unit of solvatochromic coefficients shown is [cm^{-1}/V].

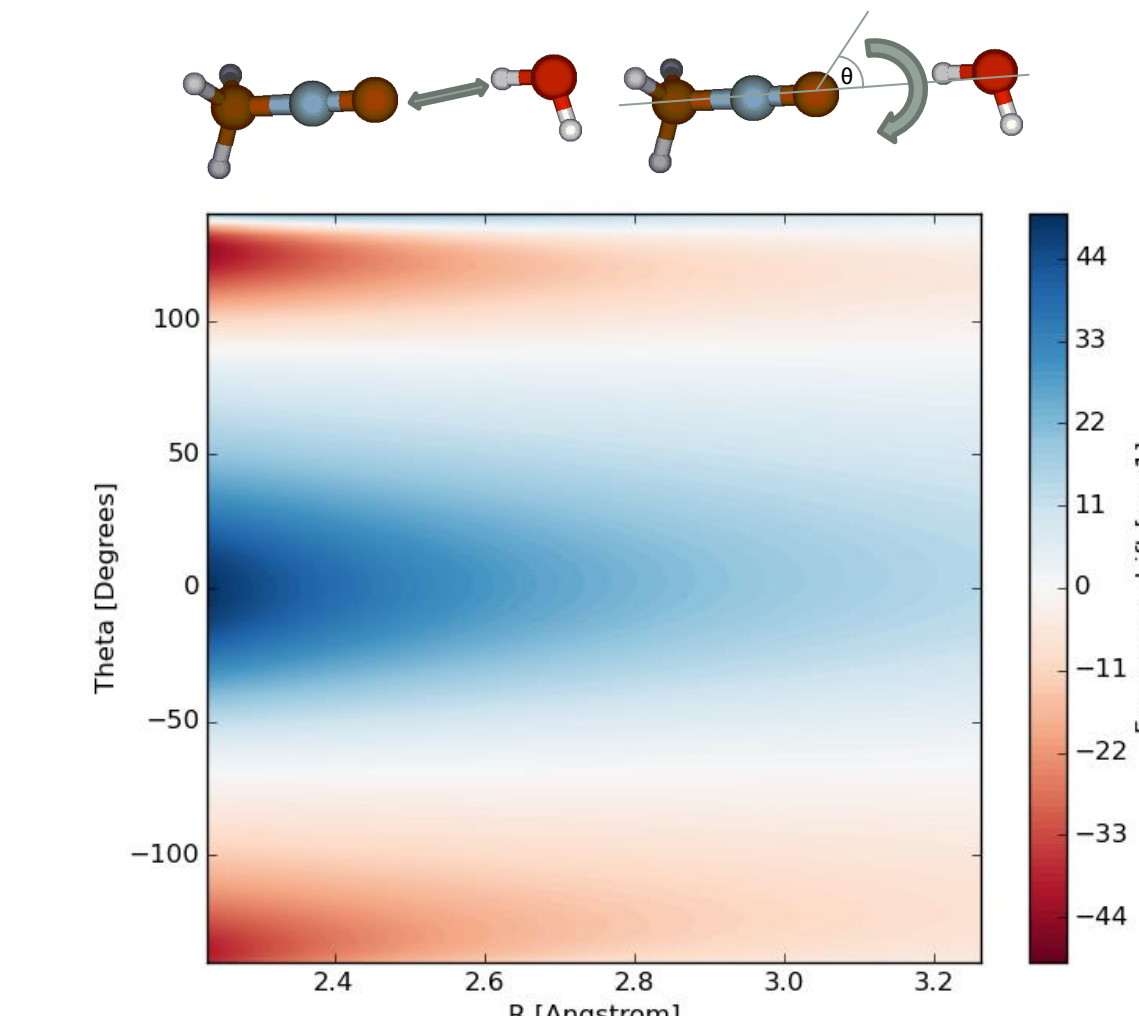


Figure 10. Scan of the frequency shift depending on the MeNC – water hydrogen bond length and the angle θ .

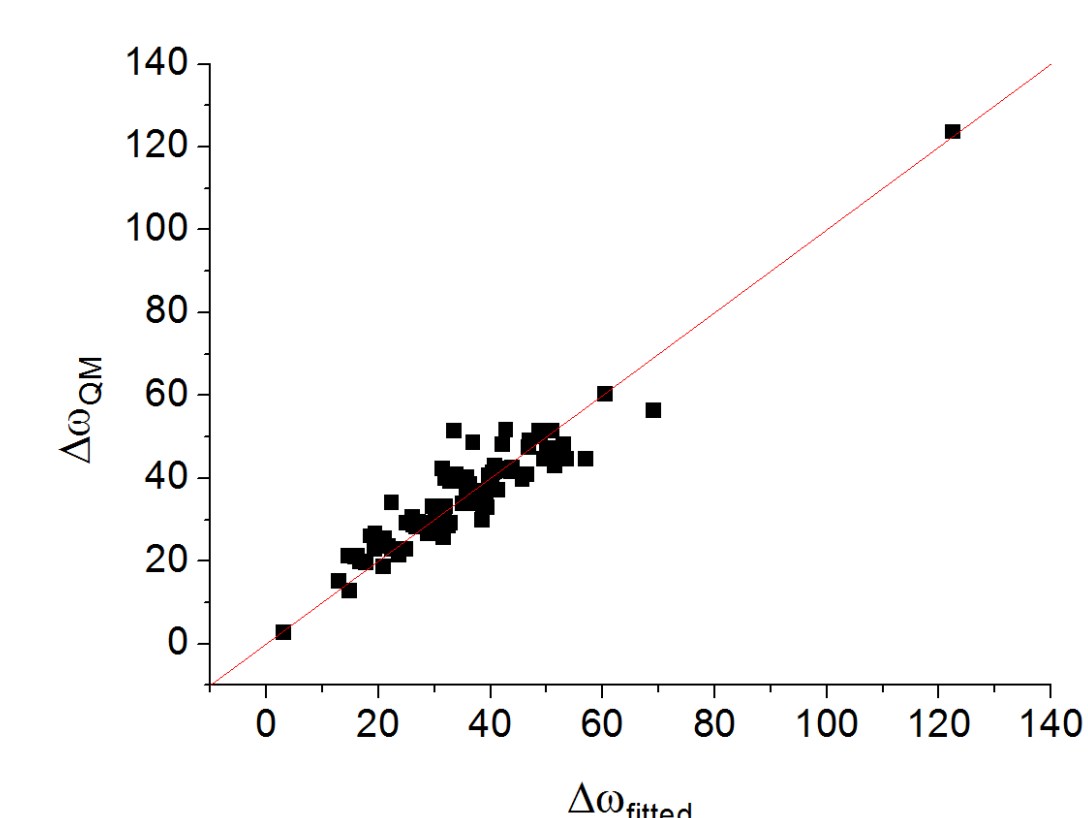


Figure 9. QM calculated vibrational frequency shift $\Delta\omega_{QM}$ versus theoretically calculated $\Delta\omega_{fitted}$ using appropriate equation ($R^2=0.9827$).

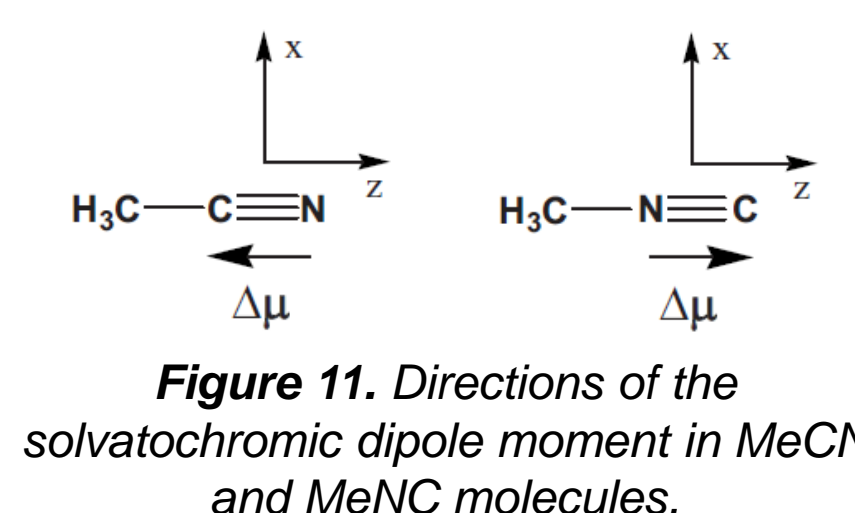


Figure 11. Directions of the solvatochromic dipole moment in MeCN and MeNC molecules.

Interpretation and conclusions:

- Isonitrile group - **highly sensitive reporter of H-bonding** (Fig. 4):
 - Increase of H-bonding strength – **blueshift** of the NC frequency.
 - In hydrogen-bonding solvents – peak **broadening** ($CHCl_3$, D_2O) or **splitting** ($MeOH$, CF_3CH_2OH).
- The frequency shift of amide I' band – **possible perturbation** the backbone conformation of alanine after introduction of isonitrile or nitrile group (Fig. 4a and Table 1). A single symmetric peak – the backbone conformation or solvation has **no notable heterogeneity**.
- A **large dipole strength** ($1.82\text{--}2.21 \times 10^{-2} D^2$) of new probe **1** – 5–40 times larger than CN stretching modes and about 2–3 times smaller than N_3 stretching mode.
- PP spectra – **heating effect** observed and eliminated (Fig. 5).
- Vibrational lifetimes** of the NC stretching mode – 5.5 ± 0.2 ps in both D_2O and DMF (several times longer than N_3 mode) – relaxation processes mainly determined by intramolecular vibrational relaxation (Fig. 6b, Fig. 7b and Table 1).
- The **orientational relaxation time constants** of the NC stretching mode – 0.52 ± 0.20 ps and 10.33 ± 2.24 ps in D_2O (biexponential decay analysed using the wobbling-in-a-cone model) and 7.28 ± 0.94 ps in DMF (Fig. 6c and Table 1)
- From **solvatochromic model** (Fig. 8):
 - For MeNC-water clusters **mainly blueshift** of the NC stretching band.
 - For non-linear H-bonding geometries ($\theta > \sim 70^\circ$) – **redshift** (Fig. 10).
 - Direction of $\Delta\mu$ opposite for MeCN and MeNC.
- Isonitrile stretch mode – potentially an **excellent IR probe** for studying the structure and dynamics of proteins and to probe the local electrostatic potential.

- [1]. M. Maj et al, *Phys. Chem. Chem. Phys.*, 2015, **17**, 11770–11778.
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 [3]. H. Kim and M. Cho, *Chem. Rev.*, 2013, **113**, 5817–5847.
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