Computational Modeling of the Nitrile Stretching Vibration of 5-Cyanoindole in Water

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Table S1. Charges derived from a CHelpG analysis of the electron charge density (Old MM) and those obtained from fitting of the QM interaction potentials (New MM). Atom names are defined in Figure 1.

Atom name	New MM	Old MM
CH2	-0.1839	-0.142679
CZ2	-0.2755	-0.212108
CE2	0.1938	0.207008
CZ3	0.0216	-0.007346
CE3	-0.2753	-0.286345
NE1	-0.4721	-0.470295
CD1	0.0533	0.028534
CG	-0.3405	-0.364845
CD2	0.2657	0.252653
HG	0.1980	0.163512
HD1	0.1685	0.128804
HE1	0.3661	0.375028
HE3	0.1202	0.166148
CN1	0.4616	0.406976
NN1	-0.4772	-0.511574
HH2	0.1535	0.129601
HZ2	0.0222	0.136927

Table S2. Various possible empirical relationships, $\omega_{emp} = \sum_{a,i} c_i^a E_i^a + \omega_{gas}$, and the corresponding correlation coefficients R^2 and root mean square deviations (rmds) from the *ab initio* frequencies. For the *x*-components, the magnitude of the field was used due to the plane of symmetry in the indole ring plane. Entries $E_z^{CN1-NN1}$ and $E_z^{CZ3-CN1}$ refer to the *z*-components of the fields at the center of the respective bonds.

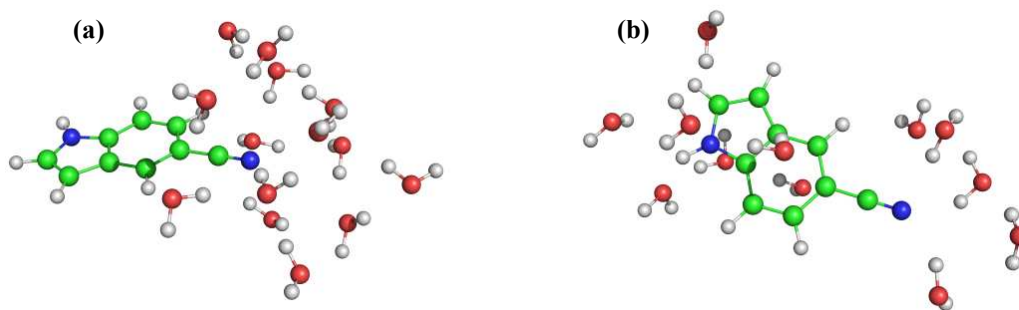| Model	Electric Field Components Used	R^2	rmsd (cm^{-1})
1	$E_z^{CN1}, E_z^{NN1}, E_z^{6m}$	0.81	5.8
2	E_z^{CN1}, E_z^{NN1}	0.64	7.6
3	$E_z^{CN1}, E_z^{NN1}, E_y^{CN1}, E_y^{NN1}$	0.71	6.9
4	$E_z^{CN1}, E_z^{NN1}, E_y^{CN1}, E_y^{NN1}, \left|E_x^{CN1}\right|, \left|E_x^{NN1}\right|$	0.81	5.7
5	$E_z^{CN1}, E_z^{NN1}, E_z^{CN1-NN1}$	0.63	7.6
6	$E_z^{CN1}, E_z^{NN1}, E_z^{CZ3-CN1}$	0.67	7.5
7	$E_z^{CN1}, E_z^{NN1}, E_z^{CZ3}$	0.74	6.9

Figure S1. Representative snapshots of clusters in Set-A (a) and Set-B (b), respectively.
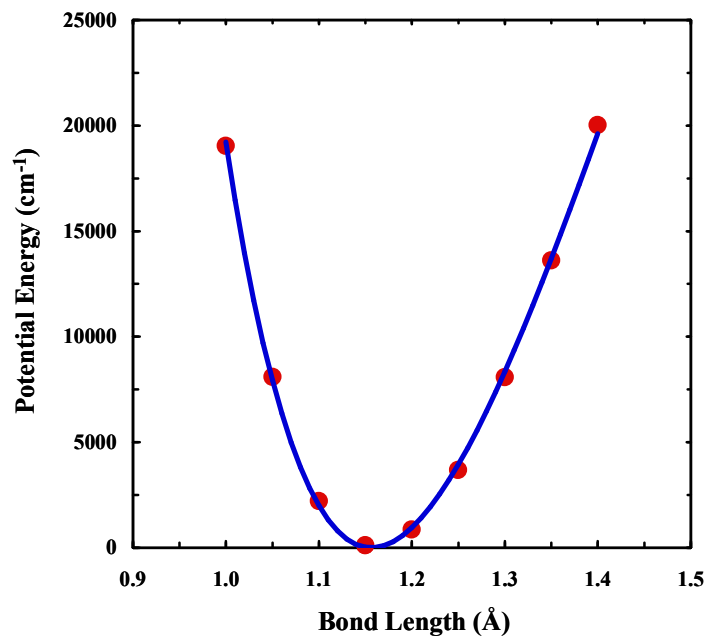
Figure S2. A representative potential energy of 5-cyanoindole as a function of the C≡N bond length. The dots correspond to the *ab initio* single point energies, while the line is the best fit of these data to eq. S-1 using $D = 326$ kcal/mol.
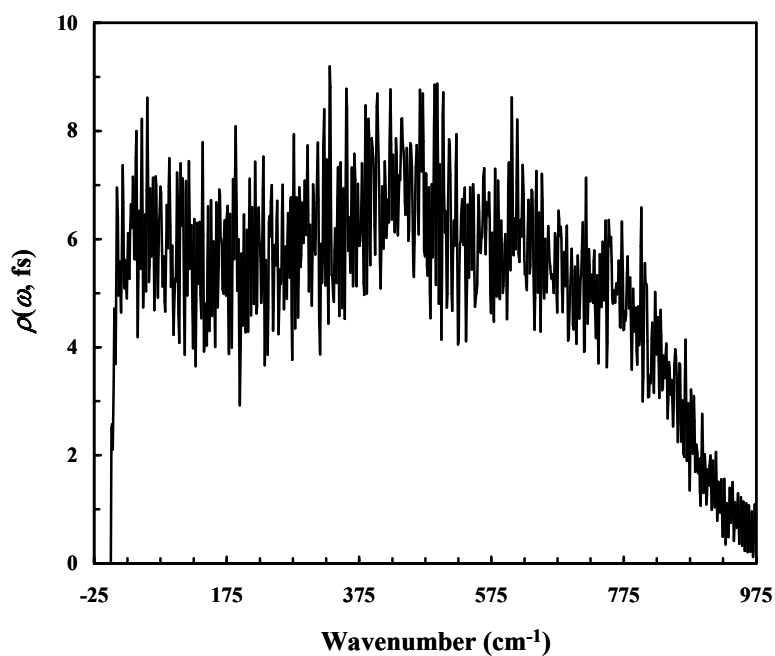

Figure S3. Spectral distribution, $\rho(\omega)$, of 5-cyanoindole in water.

Molecular dynamics simulation

After immersion of 5-cyanoindole in a box of 727 TIP3P waters (1), the energy of the system was first minimized for 2000 steps and then the system was allowed to equilibrate for 1 ns at 300 K and 1 atm. After equilibration, a 1 ns production run was carried out in the NPT ensemble under identical conditions. While the Berendsen barostat was used to relax the system towards equilibrium, the pressure in the production run was maintained at 1 atm using the Nosé-Hoover Langevin piston method. Temperature was controlled by Langevin dynamics; and periodic boundary conditions were used to reduce edge effects. The SHAKE algorithm was employed to constrain all bonds involving the hydrogen atom. A cut-off of 12 Å was used for nonbonded interactions, which were switched to zero between 10 and 12 Å. Full electrostatics were calculated every second step using the particle-mesh Ewald (PME) method. A 2 fs time step was used to integrate the equations of motion and coordinates were saved every 4 fs for analysis.

Electronic structure calculation

Since 5-cyanoindole was not treated as a rigid body in the MD simulation, it undergoes structural fluctuations due to the finite temperature of the system. Such thermally induced fluctuations could modulate the frequency of the nitrile stretching vibration and also lead to uncertainties in the definition of the molecular coordinate system. Thus, in order to eliminate this thermal noise, the structurally distorted molecules in the 5-cyanoindole-water clusters from MD simulation were replaced by the optimized structure of 5-cyanoindole. The C≡N bond of the geometrically optimized molecule was then stretched in a step-wise manner (from 1.0 to 1.4 Å in 0.05 Å steps) by moving both the nitrile carbon and nitrogen, while keeping the center of mass of the nitrile group fixed, allowing determination of the potential energy of the 5-cyanoindole-water clusters as a function of the nitrile bond length (e.g., the one in Figure S2). For all electronic structure calculations, an ultrafine numerical integration grid having 99 radial shells and 590 angular points per shell was used. Tight SCF convergence criteria as defined in the Gaussian 03 software were used for all single point energy calculations.

To determine the anharmonic frequency of the C≡N stretching vibration, those point energies obtained above were then fit to a Morse oscillator function:

$$V(r) = D\left(1 - \exp\left[-\alpha(r - r_0)\right]\right) + V_0 \qquad \text{(S-1)}$$

where D is the bond dissociation energy, α is a constant that determines the width of the potential well, r_0 is the equilibrium bond length, and V_0 is the equilibrium potential energy of the system. By stretching the C≡N bond of the isolated 5-cyanoindole molecule from 1.0 to 12.5 Å and fitting the points to the above equation, the bond dissociation energy D was estimated to be 326 kcal/mol. The ground and first excited vibrational state energies were then calculated according to:

$$E_n = DB\left(n + \frac{1}{2}\right)\left[2 - B\left(n + \frac{1}{2}\right)\right] \qquad \text{(S-2)}$$

where $n = 0$ or 1 for the ground and first excited state, respectively. B is given by

$$B = \frac{\alpha\hbar}{\sqrt{2\mu D}} \qquad \text{(S-3)}$$

where μ is the reduced mass of the nitrile group, i.e. $(12 \times 14)/(12 + 14)$ amu.

Band shape calculation

The electric field on site i of 5-cyanoindole arising from n water molecules was calculated according to:

$$\mathbf{E}_i = \sum_{j=1}^{3n} \frac{q_j}{r_{ij}^2} \hat{\mathbf{r}}_{ij} \tag{S-4}$$

Index j runs over the three atomic sites of the TIP3P water molecule, r_{ij} corresponds to the distance between the ith site on 5-cyanoindole and the jth site on TIP3P water. $\hat{\mathbf{r}}_{ij}$ is the unit vector pointing from atomic site j to site i. The frequency trajectory was obtained by including all water molecules in the box that were within 12 Å of any atom of the 5-cyanoindole molecule, which was placed in the center of the box. Within the framework of a semiclassical picture, the band shape of the C≡N stretching vibration was then calculated using the following equation:

$$I(\omega) \sim \int_{-\infty}^{\infty} dt\, e^{i\omega t} \exp\left[-g(t) - |t|/2T_1\right] \tag{S-5}$$

where T_1 is the vibrational lifetime and $g(t)$ is the line shape broadening function given by

$$g(t) = \frac{1}{\pi} \int_0^{\infty} d\omega \coth(\hbar\omega/2k_B T)\tilde{\xi}_I(\omega)\frac{1-\cos(\omega t)}{\omega^2} + \frac{i}{\pi} \int_0^{\infty} d\omega \tilde{\xi}_I(\omega)\frac{\sin(\omega t) - \omega t}{\omega^2} \tag{S-6}$$

Within a semiclassical picture, $\tilde{\xi}_I(\omega)$ may be approximated by

$$\tilde{\xi}_I(\omega) = M(0)\rho(\omega) \tag{S-7}$$

where $\rho(\omega) \equiv \tanh(\hbar\omega/2k_B T)\widetilde{M}_R(\omega)$ is the spectral distribution function, which is shown in Figure S3. $\widetilde{M}_R(\omega)$ is the real part of the Fourier transform of the normalized frequency autocorrelation function $M(t)$:

$$\widetilde{M}_R(\omega) \equiv 2\int_0^{\infty} dt \cos(\omega t)\left[M(t)/M(0)\right] \tag{S-8}$$

For the numerical evaluation of eq. S-6, spline interpolation on the first 2000 points (8 ps) of the frequency-frequency correlation function obtained from the MD trajectory was performed to generate 800,000 data points. Eq. S-6 was integrated with a step size 1 cm^{-1}. The upper integration limit was 1042.4 cm^{-1}.

References

(1) Jorgensen, W.L.; Chandrasekhar, J.; Madura, J.D.; Impey, R.W.; Klein, M.L. Comparison of Simple Potential Functions For Simulating Liquid Water. *J. Chem. Phys.* **1983**, 79, 926-935.