

A Monte Carlo–quantum mechanical study of the solvatochromism of pyrimidine in water and in carbon tetrachloride

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A sequential combination of Monte Carlo simulation and quantum mechanics calculation is used to study the solvatochromic shift of the $n \rightarrow \pi^*$ absorption transition of pyrimidine in water and in carbon tetrachloride. Super-molecular configurations are generated from NVT Monte Carlo simulations and are used for subsequent extensive quantum mechanical calculations. The auto-correlation function of the energy is used to analyze the statistical correlation between the configurations used in the quantum mechanical calculations. The total number of molecules used in the super-molecules is obtained after analysis of the radial distribution function that defines the solvation shells. For the case of pyrimidine in water, full quantum mechanical INDO/CIS calculations are performed in the super-molecular clusters corresponding to the first, second and third solvation shells, extending up to nearly 11.5 Å away from the center of mass of pyrimidine. For the largest calculation, made for the third solvation shell, it includes 1 pyrimidine and 213 water molecules, with a total of 1734 valence electrons explicitly included. Using the results obtained for the different solvation shells the solvatochromic shift is extrapolated to the bulk limit. This gives our best result of $2223 \pm 60 \text{ cm}^{-1}$, in good agreement with the experimental value of $2700 \pm 300 \text{ cm}^{-1}$ and explicitly confirming that the polarization effects of pyrimidine in protic solvents extend to a very long distance from the solute. For pyrimidine in carbon tetrachloride, a non-polar and aprotic solvent, the use of only the first solvation shell gives a stable result of $\sim 100 \text{ cm}^{-1}$ for the $n \rightarrow \pi^*$ blue shift.

1 Introduction

The influence of solvent effects in molecular properties and spectroscopy has been the subject of considerable attention in recent years.¹ This is of great importance because most laboratory experiments as well as bio-processes occur in solution.² UV–VIS absorption spectroscopy shows a clear dependence on solvents and this can be used to understand solute–solvent intermolecular interactions. Theoretical methods for the study of solvation effects can be classified basically into two distinct categories: Continuum solvent models^{3–13} where the solvent is considered from its macroscopic properties such as refractive index and relative permittivity; and an approach that is gaining wide acceptance, the use of a discrete solvent with a combined quantum mechanics/molecular mechanics (QM/MM) approach.^{14–24} The first method has the advantage of conceptual and computational simplicity and perhaps for this reason has been widely used. Present continuum models include sophisticated procedures such as coupled-cluster models that include high level electron correlation effects in the solute.¹² In that way, the correlation effects on the solute provide accurate reaction fields.¹ The discrete super-molecular QM/MM model, on the other hand, may explicitly include the statistical nature of the liquid and solvent polarization effects. The statistical procedure includes temperature effects. Thus the combined use of quantum

mechanics and Monte Carlo, or molecular dynamics, computer simulation is a very appealing theoretical model. A clear disadvantage is that to include temperature effects ensemble averages have to be considered, thus demanding a very large number of similar calculations. Both models have been used for the study of solvatochromic shifts of organic molecules with relative success. The drawback of having to perform a large number of quantum mechanical calculations to get the average solvatochromic shift may be alleviated by consideration of the auto-correlation function of the energy.²² As Monte Carlo is a Markovian process, the auto-correlation function of the energy gives information on the relative statistical importance of the successive structures generated by the simulation. Of course, highly correlated structures will give very little new statistical information.

In this paper we consider the solvatochromic shifts of the first absorption transition of pyrimidine in water and in carbon tetrachloride. This problem has attracted some attention,^{10,21,23} in particular because of the influence of hydrogen bonds between the hydrogen atom of water and the two nitrogen atoms of pyrimidine. There are some interesting and complementary theoretical results for the known blue shift of pyrimidine in water. Karelson and Zerner,¹⁰ employing INDO/CIS calculations, showed that the $n \rightarrow \pi^*$ blue shift of pyrimidine in water, modeled using a continuum solvation model, can only be adequately predicted with the inclusion of

two explicit water molecules forming hydrogen bonds to the two nitrogen atoms. Zeng and coworkers²¹ performed a systematic study using six different intermolecular pair potentials to represent the pyrimidine–water interaction and concluded that hydrogen bonding accounts for an important part of the observed blue shift in the absorption spectrum of pyrimidine. They also noted that the hydrogen bond may have long range influences on the solvent shift. Recently Gao and Byun²³ using hybrid QM/MM Monte Carlo simulations reported a value of $2275 \pm 110 \text{ cm}^{-1}$ for the $n \rightarrow \pi^*$ blue shift of pyrimidine in water.

The experimental $n \rightarrow \pi^*$ electronic transition of dilute pyrimidine in water has long been of interest.^{25–27} Baba and coworkers reported an experimental excitation energy of $34\,250 \text{ cm}^{-1}$ for the $n \rightarrow \pi^*$ transition of pyrimidine in iso-octane.^{26,27} Assuming that there are small spectral shifts from the gas phase to iso-octane,²⁸ the experimental value^{26,27} of $36\,900 \text{ cm}^{-1}$ found for the $n \rightarrow \pi^*$ transition in water gives a blue shift of 2650 cm^{-1} . Analysis²¹ of several experimental results gives a blue shift of $2700 \pm 300 \text{ cm}^{-1}$ for the $n \rightarrow \pi^*$ transition of pyrimidine in water compared to the gas phase.

In the present work we address the solvatochromic shifts of pyrimidine in water and in carbon tetrachloride. These represent the case of protic (water) and aprotic (carbon tetrachloride) solvents so that the influence of hydrogen bonds manifested in water and absent in carbon tetrachloride may be obtained. We perform a systematic study of the $n \rightarrow \pi^*$ blue shift of pyrimidine, where the solvent molecules are explicitly included in the quantum mechanical calculations. This includes the electrostatic interaction between the solute and the solvent and the corresponding induced polarizations, both in the solute and in the solvent. We use Monte Carlo simulations to generate structures of the liquid and supermolecular quantum mechanical calculations, with all-valence electrons, to obtain the separate contributions of the different solvation shells to the spectroscopic shift, up to the third solvation shell. The largest calculation, made for the third solvation shell, involves the ensemble average of 60 quantum mechanical results obtained with the pyrimidine solute surrounded by as many as 213 water solvent molecules. This latter starts with a self-consistent-field intermediate neglect of differential overlap (INDO) calculation with a properly antisymmetric wavefunction with a total of 1734 valence electrons. This makes the present study the most extensive explicit quantum mechanical calculation of the solvation shell influence on solvatochromic shifts. The transition energies are obtained next using singly-excited configuration interaction (CIS). The final result is estimated after extrapolation to the bulk limit. Thus we not only investigate how the solvation shells influence the shift but we also extrapolate our results to obtain our best estimate of the solvatochromic shift of the $n \rightarrow \pi^*$ transition of pyrimidine in water, compared to the gas phase. A similar study is made for the aprotic and non-polar carbon tetrachloride as solvent. In contrast to the case of pyrimidine in water we find that in the case of pyrimidine in carbon tetrachloride consideration of only the first solvation shell gives a relatively stable result. This will give a clear picture of the long range effects of the polarization on the solvation shift. The largest calculation for pyrimidine in carbon tetrachloride, made for the second solvation shell, involves 100 quantum mechanical INDO/CIS calculations of pyrimidine surrounded by 61 carbon tetrachloride molecules leading to 1982 valence electrons.

2. Theoretical details

2.1 Monte Carlo simulations

Monte Carlo (MC) simulations were carried out for two systems: pyrimidine in water and pyrimidine in carbon tetra-

chloride. Standard procedures,²⁹ including the Metropolis sampling technique³⁰ and periodic boundary conditions using the image method in a cubic box, were used. The simulations were performed in the canonical (NVT) ensemble. The two systems under investigation consisted of 1 pyrimidine molecule plus 350 molecules of carbon tetrachloride and 1 pyrimidine molecule plus 900 molecules of water. The simulation in water is considerably larger because of our interest in examining the long range effects in protic solvents. The volume of the cubic box was determined by the experimental density³¹ of carbon tetrachloride and water, which at $T = 298.15 \text{ K}$ is 1.5867 and 0.9966 g cm^{-3} , respectively. The intermolecular interactions were described by the Lennard-Jones plus Coulomb potential, shown in eqn. (1), with 3 parameters for each atom i (ϵ_i , σ_i and q_i).

$$U_{\text{int}}(r_{ij}) = 4 \sum_i^{\text{on a}} \sum_j^{\text{on b}} \epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] + \frac{q_i q_j}{r_{ij}} \quad (1)$$

where $\epsilon_{ij} = (\epsilon_i \epsilon_j)^{1/2}$ and $\sigma_{ij} = (\sigma_i \sigma_j)^{1/2}$. The set of intermolecular potential parameters^{32–35} employed in the simulations are shown in Table 1.

The intermolecular interactions were spherically truncated within a center of mass separation smaller than the cutoff radius, r_c , of 19.17 and $15.02 \text{ \AA}$, respectively for, carbon tetrachloride and water. Long range corrections were calculated beyond this cutoff distance.²⁹ The Lennard-Jones potential contribution is estimated assuming a uniform distribution $G(r) \approx 1$ after the cutoff radius and the electrostatic potential contribution is estimated with the reaction field method of the dipolar interaction. In all simulated systems, the molecules were kept with rigid geometries. The carbon tetrachloride molecules were within the T_d structure with $r_{\text{CCl}} = 1.766 \text{ \AA}$ and $\angle \text{ClCCl} = 109.47^\circ$. The water molecules were kept in their C_{2v} structure with $r_{\text{OH}} = 1.000 \text{ \AA}$ and $\angle \text{HOH} = 109.47^\circ$. The pyrimidine was held rigid in its C_{2v} structure, optimized at the MP2/6-31++G(d,p) level of theory, with $r_{\text{CN}} = 1.345 \text{ \AA}$, $r_{\text{CC}} = 1.395 \text{ \AA}$, $r_{\text{CH}} = 1.082 \text{ \AA}$, $\angle \text{NCN} = 127.2^\circ$, $\angle \text{CCC} = 116.9^\circ$ and $\angle \text{NCC} = 122.2^\circ$.

In all cases, the initial configurations were generated randomly, considering the position and orientation of each molecule. A new configuration is generated after N MC steps, *i.e.*, after all N solvent molecules randomly attempt to translate in the Cartesian directions and also attempt to rotate around a randomly chosen axis. The maximum allowed displacement of the molecules is self-adjusted after 50 configurations to give an acceptance ratio of new configurations around 50%. The maximum rotation angle was fixed during the simulation as $\delta\theta = \pm 15^\circ$. The simulations consisted of a thermalization

Table 1 Potential parameters used in the Monte Carlo simulations (q_i in elementary charge unit, ϵ_i in kcal mol^{-1} and σ_i in $\text{\AA}$)

Site	q_i	ϵ_i	σ_i
CCl_4^a			
C	0.248	0.050	3.800
Cl	−0.062	0.266	3.470
H_2O^b			
O	−0.820	0.155	3.165
H	0.410	0.000	0.000
$\text{C}_4\text{N}_2\text{H}_4^c$			
C	0.590	0.110	3.750
N	−0.788	0.170	3.250
H	0.000	0.000	0.000

^a All atoms OPLS parameters.³² ^b SPC potential.³³ ^c OPLS parameters³⁴ with the charges calculated using the CHelpG fitting procedure,³⁵ as implemented in the GAUSSIAN98 program,³⁶ at the MP2/6-31++G(d,p) level of theory.

phase of 2.7×10^6 MC steps, followed by an averaging stage of 17.5×10^6 MC steps for carbon tetrachloride solvent and 27.0×10^6 MC steps for water solvent. This is a long simulation by all present standards. After completing the cycle over N solvent molecules a configuration is separated. Thus, the total number of configurations generated by the MC simulation is 50 000 for pyrimidine in carbon tetrachloride and 30 000 for pyrimidine in water.

Instead of performing a quantum mechanical calculation on every configuration generated by the Monte Carlo simulation, we use the auto-correlation or statistical efficiency, to select the statistically relevant structures. In doing so, the subsequent quantum mechanical calculations are performed only on some uncorrelated structures.^{37–42} As in previous studies^{22,37–41} we fit the auto-correlation function of the energy to an exponentially decaying function and obtain the correlation step τ . For pyrimidine in water we obtain here the value $\tau = 250$. Calculating the averages, we select configurations separated by approximately 2τ , or 500. This ensures that the structures used in the quantum mechanical calculations are statistically uncorrelated.⁴³ As the total number of MC configurations generated in the simulation was 30 000, the averages are then taken over 60 configurations. For the case of pyrimidine in carbon tetrachloride we obtain $\tau = 230$. Thus, using a similar reasoning we selected configurations separated by 500 MC steps, generating 100 statistically uncorrelated configurations, in which the properties were averaged out. All simulations were performed with the DICE⁴⁴ Monte Carlo statistical mechanics program.

2.2 Quantum mechanical calculations

To obtain the solvatochromic shifts, the excitation energies were calculated using the ZINDO program,⁴⁵ within the INDO/CIS approach.⁴⁶ The quantum mechanical calculations were performed for the super-molecular clusters, generated by the MC simulations, composed of one pyrimidine and all solvent molecules within a particular solvation shell. As the appropriate Boltzmann weights are included in the Metropolis Monte Carlo sampling technique, the average value of the solvatochromic shift is given as a simple average over a chain of size L of uncorrelated configurations:

$$\langle \Delta E \rangle = \frac{1}{L} \sum_i^L \Delta E_i \quad (2)$$

where $L = 60$ for pyrimidine in water and $L = 100$ for pyrimidine in carbon tetrachloride. ΔE_i corresponds to the difference between the excitation energy obtained for the pyrimidine in the super-molecular configuration i and the corresponding energy in the gas phase. The statistical error of the

average value, $\langle \Delta E \rangle$, is given by

$$\sigma(\langle \Delta E \rangle) = \sqrt{\frac{\langle \Delta E^2 \rangle - \langle \Delta E \rangle^2}{L - 1}}. \quad (3)$$

3 Results and discussion

3.1 Pyrimidine in water

We defined the solvation shells from the radial distribution function between the pyrimidine center of mass and water center of mass, $G_{\text{CM-CM}}(r)$. The radial distribution function is shown in Fig. 1. Three solvation shells can be easily discerned. The first solvation shell starts in 2.85 Å ending at 5.45 Å. The second ends at 8.05 Å and the third at 11.55 Å. After the spherical integration of the $G_{\text{CM-CM}}(r)$ in the corresponding intervals, we obtain 21, 71 and 213 water molecules in these shells, respectively. Table 2 summarizes the contribution of the different solvation shells to the $n \rightarrow \pi^*$ blue shift in water. For each solvation shell 60 quantum mechanical calculations are performed and the average is given in Table 2. Including only those molecules within the first solvation shell gives a blue shift of 364 cm^{-1} . Including all those molecules up to the second solvation shell gives a considerable increase of the blue shift to 959 cm^{-1} . As can be seen, including all solvent molecules up to the third solvation shell gives a blue shift of 1328 cm^{-1} . This represents an increase of $\sim 400 \text{ cm}^{-1}$ compared to the results up to the second solvation shell. Solvent molecules located far out from the solute pyrimidine molecule can still affect the solvation shift of this absorption transition. It has been noted by Zeng *et al.*²¹ that the hydrogen bonds may considerably extend the solvation effects to the outer solvation shells. We have recently⁴⁰ calculated the dipole moment of the

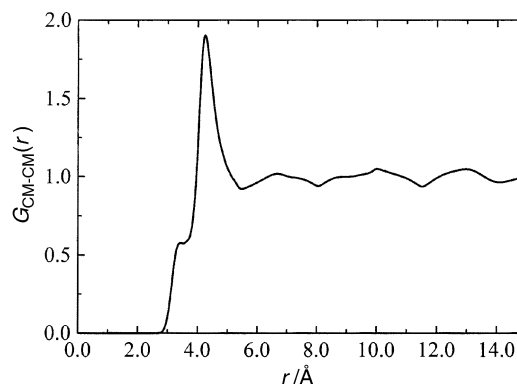


Fig. 1 Computed pair-wise radial distribution function, $G_{\text{CM-CM}}(r)$, between the pyrimidine center of mass and water center of mass.

Table 2 Variation of the calculated (INDO/CIS) blue shift of the $n \rightarrow \pi^*$ transition of pyrimidine in water with the solvation shells. Two results for the blue shift are shown. The left corresponds to the shift of the first $n \rightarrow \pi^*$ transition whereas the rightmost gives an average between the two $n \rightarrow \pi^*$ transitions. N is the number of water molecules included. M is the total number of valence electrons included in the quantum mechanical calculations. L is the number of MC configurations used for ensemble average. R is the distance obtained from the radial distribution function shown in Fig. 1. The statistical error $\sigma(\langle \Delta E \rangle)$ is also shown

Solvation shell	N	M	L	$R/\text{\AA}$	Blue shift/ cm^{-1} $\langle \Delta E \rangle \pm \sigma(\langle \Delta E \rangle)$	
First	21	198	60	5.45	364 ± 70	1570 ± 110
Half-second	59	502	60	7.60	857 ± 75	1831 ± 100
Second	71	598	60	8.05	959 ± 70	1853 ± 100
Half-third	136	1118	60	9.95	1234 ± 80	1948 ± 110
Third	213	1734	60	11.55	1328 ± 75	2000 ± 100
Limit	Bulk				2223 ± 60	2390 ± 100
Gao and Byun ²³					2275 ± 110	
Karelson and Zerner ¹⁰					2600	
Zeng, Hush and Reimers ^{21b}					2450	
Experimental					2700 ± 300	

pyridine-water cluster as obtained from the simulation. Compared to isolated pyridine the dipole moment suffers an increase of $\sim 55\%$. For the case of pyrimidine in water we obtained an increase of $\sim 25\%$. This increased dipole moment due to the hydrogen bonds in protic solvent is one of the possible causes for these long range solvation effects.^{21,40} As noted also by Karelson and Zerner¹⁰ the explicit inclusion of the hydrogen bonded water molecules may be necessary in continuum solvation models to account for the increased dipole moment of the chromophore. Karelson and Zerner¹⁰ and Gao and Byun²³ noted that inclusion of specific hydrogen bonded water causes a near-degeneracy of the two lowest $n \rightarrow \pi^*$ transitions. The symmetry decrease allows the second transition to obtain some intensity leading to absorption broadening. Taking into account the average of the two $n \rightarrow \pi^*$ transitions leads to the results shown in the final column of Table 2. The results of Table 2 cannot be considered converged. This means that it is necessary to go beyond the third solvation shell. The quantum calculations corresponding to the third shell involve as many as 213 water molecules with a total of 1734 valence electrons. It is difficult to supplement further the quantum mechanical calculations. However the monotonic behavior of the solvation shift with the solvation shells suggests that these results may be used to extrapolate the solvation shift up to the bulk limit, as done before.^{39–41} Fig. 2 shows the calculated blue shift of the $n \rightarrow \pi^*$ transition of pyrimidine in water as a function of the inverse size of the solvation shell.^{39–41} Thus our best result for the blue shift of the $n \rightarrow \pi^*$ transition of pyrimidine in water is $2223 \pm 60 \text{ cm}^{-1}$. This is in very good agreement with the estimated experimental^{21,26,27} value of $2700 \pm 300 \text{ cm}^{-1}$ and the theoretical result of Gao and Byun²³ of 2275 cm^{-1} . In the case of the average between the two $n \rightarrow \pi^*$ transitions the solvation shift, in the bulk limit, is obtained as $2390 \pm 100 \text{ cm}^{-1}$. Indeed, as emphasized by Gao and Byun²³ the two procedures gives similar results in the bulk limit. The results presented here give support to Zeng *et al.*²¹ that the effects of hydrogen bonding seem to have long-range consequences for the solvent shift of pyrimidine in water. Similar effects were recently observed for the $n \rightarrow \pi^*$ transition of formaldehyde in water.³⁹

3.2 Pyrimidine in carbon tetrachloride

It is interesting to compare the behaviour of pyrimidine in carbon tetrachloride with pyrimidine in water. Fig. 3 shows the radial distribution function between the pyrimidine center of mass and carbon tetrachloride center of mass, $G_{\text{CM-CM}}(r)$. Three solvation shells are again clearly discernible. The first shell starts at 4.15 Å ending at 7.95 Å, the second ends at 13.25 Å and the third at 18.35 Å. Integration of the $G_{\text{CM-CM}}(r)$

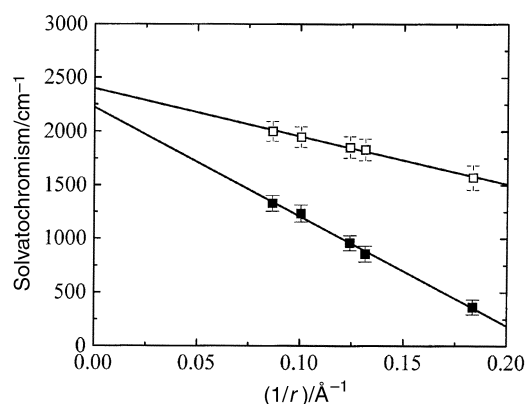


Fig. 2 Calculated blue shift of the $n \rightarrow \pi^*$ transition of pyrimidine in water, as a function of the inverse size of the solvation shell as shown in Table 2.

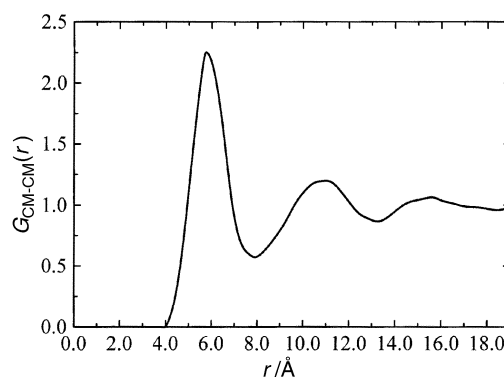


Fig. 3 Computed pair-wise $G_{\text{CM-CM}}(r)$ between the pyridine center of mass and carbon tetrachloride center of mass.

for this system gives a total of 13, 61 and 161 carbon tetrachloride molecules in these shells, respectively. Each carbon tetrachloride molecule has 32 valence electrons and so a calculation with all molecules up to the second solvation shell (61 molecules), involves a large system with 1982 valence electrons. Table 3 summarizes the variation of the calculated solvatochromic shift of the $n \rightarrow \pi^*$ transition of pyrimidine in carbon tetrachloride up to the second solvation shell. In contrast to the case of pyrimidine in water in this case the blue shift is little affected after the first solvation shell. Thus our final result estimates the blue shift of pyrimidine in water as $\sim 100 \text{ cm}^{-1}$. The first shell of solvent molecules is sufficient to model the $n \rightarrow \pi^*$ blue shift in carbon tetrachloride.

4 Summary and conclusions

In this work we applied a sequential Monte Carlo–quantum mechanical treatment to study the solvent effects on the $n \rightarrow \pi^*$ transition of pyrimidine in water and in carbon tetrachloride.

For pyrimidine in water, the solvatochromic blue shift of the $n \rightarrow \pi^*$ transition was analyzed as a function of the solvation shells, starting from the first and extending up to the third solvation shell, with the solute and all solvent molecules treated quantum-mechanically. For the first, second and third solvation shells we found blue shifts of 364 ± 70 , 959 ± 70 and $1328 \pm 80 \text{ cm}^{-1}$, respectively. These results, extrapolated to the bulk limit value of $2223 \pm 60 \text{ cm}^{-1}$, are in good agreement with the experimental value of $2700 \pm 300 \text{ cm}^{-1}$ for the $n \rightarrow \pi^*$ blue shift in water. If an average between the two $n \rightarrow \pi^*$ transitions is considered, the bulk limit value of $2390 \pm 100 \text{ cm}^{-1}$ is obtained. The variation of the blue shift with the solvation shells in water shows that the solvation shifts are affected by long range polarizations extending beyond 11.5 Å.

For pyrimidine in carbon tetrachloride, the calculated $n \rightarrow \pi^*$ blue shift was $101 \pm 11 \text{ cm}^{-1}$. This result was obtained with ensemble averages of 100 quantum mechanical

Table 3 Variation of the calculated (INDO/CIS) solvatochromic shift of the $n \rightarrow \pi^*$ transition of pyrimidine with the number of carbon tetrachloride molecules. N is the number of carbon tetrachloride molecules included. M is the total number of valence electrons included in the quantum mechanical calculations. L is the number of MC nearly uncorrelated configurations used for ensemble average. R is the size of the solvation shell obtained from the minima of the radial distribution function shown in Fig. 3

Solvation shell	N	M	L	$R/\text{Å}$	Blue shift/ cm^{-1}
First	13	446	100	7.95	93 ± 5
Second	61	1982	100	13.25	101 ± 11

calculations of a cluster composed of 61 carbon tetrachloride molecules, a large system with 1982 valence electrons. In contrast to the case of pyrimidine in water the calculated blue shift of pyrimidine in non-polar and aprotic carbon tetrachloride is well obtained considering only the first solvation shell.

The results obtained here give a clear numerical evidence that the solvation shifts of polar molecules in protic solvents leads to long range polarization effects²¹ and these may be rationalized by the increased dipole moment⁴⁰ of the chromophore due to the hydrogen bonds.

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