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Solvent Dependence on Bond Length Alternation and Charge Distribution in Phenol Blue: A Car−Parrinello Molecular Dynamics Investigation

N. Arul Murugan,* Zilvinas Rinkevicius, and Hans Ågren

Department of Theoretical Chemistry, School of Biotechnology, Royal Institute of Technology, SE-10691 Stockholm, Sweden

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Car−Parrinello mixed quantum mechanics/classical mechanics (CP-QM/MM) calculations are performed for phenol blue (PB) in chloroform and water solvents along with Car−Parrinello molecular dynamics (CPMD) calculations on PB in the gas phase. The solvent effect on molecular geometry, particularly of bond length alternation (BLA), has been studied. As reported for similar donor−acceptor polyenic systems, a remarkable solvent effect is seen on the BLA. The calculated BLA parameter suggests that PB is in the neutral form in the gas phase and in chloroform solvent, while in water, it is cyanine-like, which is a mixture of neutral and zwitterionic resonant forms, something that clarifies the controversial reports on the structure of PB in chloroform. We have also verified that the structures obtained from CPMD and CP-QM/MM calculations are correct by calculating absorption spectra for PB in the gas phase and in chloroform solvent and compared with experimental results. To understand the structure for PB in the gas phase and in water solvent, we have carried out Mayer bond order analysis, supporting that the structure of PB in water is cyanine-like. Moreover, PB in water is found to be much more polarized than that in chloroform solvent. Overall, the present work demonstrates that CP-QM/MM calculations can be used to understand the solvent effects on polyenic and merocyanine-like systems, which are usually difficult to model.

1. Introduction

Organic solvatochromic and solvatofluorochromic molecules play an important role as probes to investigate properties of surfaces and the interior regions of dendrimers[1] and proteins[2−5] and also to study the dielectric behavior of supercritical fluids[6] and ionic liquids.[7] An understanding of the chemical and physical properties of surface and interior regions of these biologically important molecules is called for in drug delivery applications and in efficient drug design strategies.[4] The probing nature of these molecules is due to the effect of the polarity of the solvation shell in changing the electron excitation energy of the indicator dye. This change, the so-called solvatochromic shift, reveals the macroscopic nature of the local microenvironment, which is related to several solvent parameters such as dipolarity, polarizability, and hydrogen bond donating and accepting abilities. Among the routinely used solvatochromic dyes, phenol blue (PB) is a molecule with relatively simple structure and that exhibits positive solvatochromic effect,[8,9] something that has motivated the choice of PB as a solvent polarity indicator for many solvents[10,11] and binary solvents.[12] The absorption maximum for PB shifts from 545−552 nm[8,13] in hexane to 654−684 nm[13,14] in water. An interesting structural feature of phenol blue and other solvatochromic dyes is that they can exist in either a neutral form or in a charge-separated zwitterionic form. It is commonly believed that the neutral form is more stable in the gas phase and in less polar solvents, while the population of the zwitterionic form cannot be ignored in polar solvents. Even though there is no controversy on the existence of the neutral form in the gas phase, there are different reports on the nature of the form in solvents.[15−17] The molecular properties such as dipole moment, hyperpolarizability, absorption spectra, and resonance Raman spectra depend on the nature of the form or the percentage population of these two forms (in cases when the molecule is in conformational equilibrium between these two forms), and many of these properties have been reported for PB in different solvents. In particular, the absorption spectra for PB have been reported in polar as well as nonpolar solvents.[10,11,13,14] Furthermore, the solvatochromic shift due to the nature of substituents in the oxygen-containing phenyl group has been investigated,[18] where it has been found that the groups that exhibit inductive or resonance effects which stabilize the charge-separated form result in shifting the absorption maximum toward larger values. Naturally, the charge-separated form has been reported to have a larger dipole moment.[16,17] The hyperpolarizability of PB has been reported in chloroform and other solvents.[19] However, some recent modeling work on the subject[16,17] has been unsuccessful in reproducing the experimental hyperpolarizability and also the solvatochromic shift for PB in chloroform solvent, most likely due to limited theoretical description, that is, the MP2/STO-3G level of theory. The calculations with unconstrained molecular geometry naturally result in a neutral form for PB in chloroform solvent,[16,17] while the calculated solvatochromic shift and hyperpolarizability are closer to the experimental counterparts when the calculations are performed on the PB molecule with the bond lengths constrained to a charge-separated eno form (or zwitter ionic form). On the basis of this circumstance,

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* To whom correspondence should be addressed. Email: murugan@theochem.kth.se.

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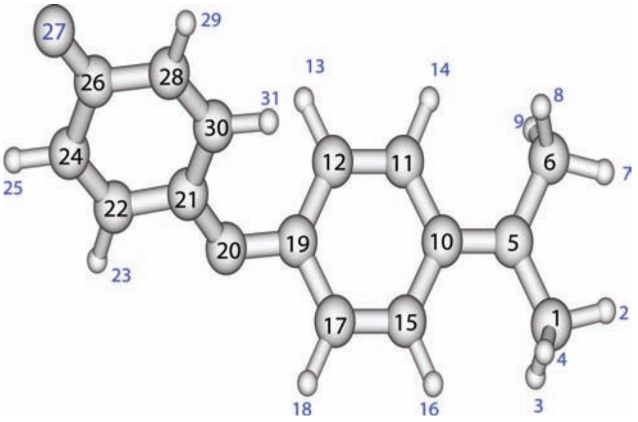

Figure 1. The molecular structure of PB.

Serrano and Canuto[16,17] proposed that in chloroform (and also in other more polar solvents), PB is in a charge-separated form. In contrast, on the basis of the NMR experiments on compounds structurally closer to PB in protic and aprotic solvents and on theoretical calculations at the PM3/COSMO level, Morley and Fitton have reported that PB exists in the neutral quinoneimine form in these solvents.[15] It is important to remember that the NMR experiments are not applied on pure PB but rather on its derivative molecules. The solvent effect on the molecular geometry for PB was investigated by Albert et al. using the INDO-SCRF procedure, which suggests that the molecules remain in a neutral form for the solvents in the dielectric constant range of 2−79 (i.e., from hexane to water).[20] Resonance Raman spectroscopic measurements on PB in different solvents report that the vibrational frequencies of the C═O stretching (appearing around 1640 cm^{-1}) and C═N stretching (appearing at around 1500 cm^{-1}) modes decrease with increasing solvent polarity, which provides a qualitative picture that the electronic structure changes from the neutral to the charge-separated form with increasing solvent polarity.[21,22] It is thus evident that these reports do not clarify the controversy on the molecular structure of PB in chloroform or in other solvents.

The structure of polyenic systems is usually discussed in terms of the bond length alternation (BLA) parameter, which is a measure of the difference between average single and double bond distances in the conjugation pathway[17,23] (see eq 1, which is specific for PB, with atom labeling given in the Figure 1). By convention, this has to be positive for the neutral form, while the opposite is the case for the charge-separated zwitterionic form.[23]

$$\chi = r(\mathrm{N}_{20}-\mathrm{C}_{19}) - r(\mathrm{C}_{21}-\mathrm{N}_{20}) \qquad (1)$$

Unfortunately, there are very few theoretical calculations where the solvent effect on the BLA parameter has been modeled successfully.[23,24] Using hybrid QM/MM calculations with a Monte Carlo based approach for the sampling, the BLA parameter for polyenic systems is shown to be on the order of 0.091 for the gas-phase structure and in chloroform solvent.[24] The BLA parameter has been shown to decrease for the molecular structure in the water solvent. Another successful report was based on the integral equation formalism-polarizable continuum method (IEF-PCM)[23] for the same polyenic system. When going from vacuum to water, the decrease in the BLA has been shown for these polyeninc systems using the IEF-PCM method.[23] The usual theoretical approach to tune the bond length alternation was to apply a static electric field[20,25] or to optimize the structure by placing "sparkles" (negative or positive ions) close to the donor or acceptor groups of these conjugated systems.[26] By applying the electric field in the range of 0−0.2 au, structures with a varying BLA for PB (the range is between −0.04 and 0.072) were obtained. Corresponding properties such as dipole moment, energy gap, polarizability, and hyperpolariability were reported.[20] Unfortunately, when compared to the electric field effect, the solvent effect did not result in any significant change in molecular geometry for PB, as investigated using the INDO-SCRF procedure for different dielectric constants.[20] Using the latter approach (where the positive ion was placed close to the quinone oxygen), the structures with different BLA parameters have been prepared, for which the hyperpolarizabilities were calculated.[17] These calculations report a maximum in hyperpolarizability for a particular value of BLA which corresponds to the charge-separated form. Experimental investigations on the hyperpolarizability for PB in different solvents report a maximum for chloroform solvent.[19] Therefore, Serrano and Canuto suggested that probably PB is in the zwitterionic form in chloroform solvent.[16,17] The way in which the zwitterionic configurations were prepared, the level of theoretical calculations, and the basis set employed in the calculations leave space for reinvestigations of PB in the gas phase and in different solvents.

The solvatochromic molecules undergo large changes in molecular geometry in going from the gas phase to solvents. The change in molecular geometry may be related to either the bond length alternation or to the change in twist angle (as in betaine dyes), which describes the relative orientation of adjacent aromatic rings. In addition to the changes in molecular geometry, there is considerable increase in group charges for the solute molecule going into polar solvents. The force field molecular dynamics technique cannot accurately account for the solvent-induced changes in solute molecular geometry and charge distribution. Therefore, we have used the hybrid Car−Parrinello mixed quantum mechanics/classical mechanics (CP-QM/MM) approach,[27−29] which treats the solute molecule in a more accurate quantum mechanical approach while the solvents are included explicitly and treated using molecular mechanics force fields. Our aim in this work is to investigate the solvent dependence on the BLA parameter and charge distribution for PB in both polar and nonpolar solvents. In order to compare the molecular geometry and charge distribution with the gas phase PB, we have also carried out Car−Parrinello molecular dynamics (CPMD)[30,31] calculations on a single molecule of PB.

2. Computational Details

2.1. Car−Parrinello Molecular Dynamics Calculations. A single PB molecule was optimized at the HF level using the 6-311+G(d,p) basis set using the Gaussian03 software.[32] The optimized structure along with the GAFF[33] force field was used to define the PB for the initial molecular dynamics calculations. Two systems were prepared for PB with chloroform (system I) and water (system II) solvents. In the case of system I, the PB molecule has been solvated with 1385 chloroform molecules in an orthorhombic box with a size of approximately 62.8 × 6.4 × 4.8 Å^3. In the case of system II, the PB molecule has been solvated with 6526 water molecules in an orthorhombic box with a size of approximately 63.4 × 57.0 × 55.2 Å^3. The chloroform and water solvents were described using the GAFF and TIP3P force field,[34] respectively. Systems I and II were allowed to equilibrate under ambient condition using molecular dynamics (MD) calculations in an isothermal−isobaric ensemble for a time scale of 100 ps. The MD calculations were carried out using the SANDER module of the Amber8 software.[35] The final configurations were used as the input configurations for the CP-QM/MM calculations on systems I and II. In our present calculations, we have used the Becke, Lee, Yang, and Parr (BLYP) gradient-corrected functional[36,37] and the Troullier−Martins norm-conserving pseudopotentials.[38] Here, the electronic wave function was expanded in a plane wave basis set. The cutoff used was 80 Ry. We have used 5 au as the time step for the integration of the equation of motion and 800 amu as the fictitious electronic mass. The calculations were carried out in a QM/MM setup,[27−29,39] where the PB molecule is treated at the density functional theory level and the water solvent is treated with a molecular mechanics force field (GAFF in the case of system I and TIP3P in the case of system II). The QM/MM implementation used here includes the coupling between the QM and the instantaneous electrostatic field arising due to the dynamic MM environment. The interaction between the QM and MM systems involves electrostatic, short-range repulsion and long-range dispersion interaction terms (using the empirical van der Waals parameters). The CP-QM/MM calculation starts with a quenching run that relaxes the initial structure within the QM/MM setup. Subsequently, a temperature scaling run was carried out for 0.5 ps to bring the system temperature to 300 K. Finally, the system was connected to the Nose−Hoover thermostat to carry out the Nose run. The lengths of the production runs were approximately 35 and 30 ps, respectively, for systems I and II. For a comparative study of PB in the solution phase with that in the gas phase, we have also carried out CPMD calculations on a single molecule of PB. The molecular geometry of a single molecule of PB was optimized with the CPMD code,[39] and subsequently, the temperature scaling run and Nose production run were performed. The time scale used for the integration of the equation of motion during the scaling and Nose runs was 2 au, and the total time scale for the production run was approximately 5 ps.

2.2. Density Functional Theory Calculations of Mayer Bond Orders and Vibrational Analysis. We have used the Gamess software[40] to calculate the average Mayer bond order for PB in the gas phase and in water solvent. The calculations for the gas phase were carried out for 50 configurations extracted at equal intervals from the CPMD trajectory. Likewise, the calculations for PB in water were carried out for 50 configurations from the CP-QM/MM trajectory. In the case of PB in water, the molecules in the first solvation shell were included explicitly along with the PB molecule. First, the solute all-atoms and solvent center of mass radial distribution function (g_{X-O} rdf) was calculated. For nonglobular molecules like the present one, g_{X-O} rdf has been discussed as an appropriate rdf since it accounts for the solute molecular geometry.[41,42] (see Figure 1s of the Supporting Information for the visualization of PB molecule and the water molecules up to second solvation shell in the g_{X-O} rdf). As we can see from the Figure 2a, the first solvation shell is confined to $r < 3.0$ Å. The number of solvent molecules in the first solvation shell varies between 15 and 25. Figure 2b shows the time evolution of the number of solvent molecules. The average number of solvent molecules in the first solvation shell appears to be around 20. The calculations of the Mayer bond order for PB in the gas phase or in water were carried out using hybrid the Becke3/Lee−Yang−Parr[37,43] (B3LYP) exchange−correlation functional and triple-ζ quality basis set.[44]

In order to understand the solvent effect on C=O stretching and C=N stretching modes of PB, we have also performed the vibrational analysis using Gaussian93 software.[32] The calculations were performed at the density functional level theory using the hybrid B3LYP exchange−correlation functional and the 6-31G(d,p) basis set for all of the atoms. Three different sets of calculations were performed separately for the trajectory corresponding to PB in the gas phase and in chloroform and water solvents. The solvent effect was included using the polarizable continuum model. Since our aim was to access the solvent effect on the C=O and C=N stretching modes qualitatively, we have not included the solvents explicitly. For a quantitative reproduction of the solvent effect on the vibrational frequencies, the explicit inclusion of solvents might be important, particularly in the case of solvents such as water since it forms directional bonds with the solute molecule.

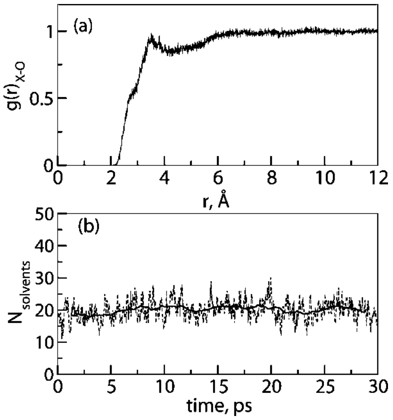

Figure 2. (a) (Solute-all-atoms)−(solvent center of mass) rdf for PB in water. (b) Time evolution of the number of solvent molecules in the first solvation shell for PB in water.

2.3. Density Functional Response Theory Calculations of Absorption Spectra. As discussed in the Introduction, PB has been studied in detail in different solvents, and the properties such as absorption spectra,[10,11,13,14] hyperpolarizability,[19] and resonance Raman spectra[21] have been reported. In order to show that the structure obtained from the CPMD and CP-QM/MM calculations for PB in the gas phase and in solvents are correct, we have aimed to calculate the absorption spectra for PB in the gas phase and in chloroform and to make comparison with the experimentally reported spectra. We have restricted ourselves to chloroform solvent since the main controversy on the structure of PB was related to this solvent. Anyway, it is straightforward to calculate the absorption spectra for any molecule in solvents, except that for some solvents (that lead to directional nonbonded interactions with the solute), it will be necessary to include the solvent molecules (at least up to first solvation shell) explicitly along with the polarizable continuum model.[45−47] The snapshots for PB in the gas phase and in chloroform solvent were extracted from the CPMD and CP-QM/MM trajectory, respectively, as has been discussed in the previous section. The absorption spectra were calculated using time-dependent density functional theory level as implemented in the Dalton 2.0 software[48] in combination with the nonequilibrium PCM solvation model. The calculations were carried out at the B3LYP level with the Ahlrich TVZ basis set augmented with one set of polarization functions.[49] The calculations for PB in chloroform were performed using the polarizable continuum model with the dielectric constant of 4.5 that corresponds to chloroform. The chloroform solvents were not included explicitly in this calculation since, usually, the chloroform molecules are not involved in site-specific interaction with the solute molecule. On the computational side, it is impossible to include the solvent molecules explicitly in this case since there are, on average, 45 chloroform molecules in the first solvation shell. Therefore, the

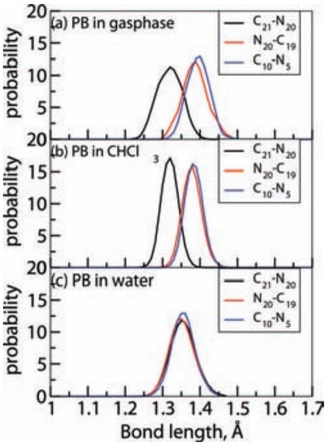

Figure 3. The bond length distribution function for PB in the gas phase and in solvents.

TABLE 1: Average C−N Bond Lengths and Bond Length Alternation Parameter, χ

system	PB in the gas phase	PB in chloroform	PB in water
$C_{21}-N_{20}$	1.319	1.319	1.354
$N_{20}-C_{19}$	1.387	1.379	1.349
$C_{10}-N_5$	1.395	1.383	1.353
χ	0.068	0.060	−0.005

calculations were carried out on the molecular geometries obtained from CPMD and CP-QM/MM runs since this automatically accounts for the temperature and solvent effects on the absorption spectra. The spectra calculations include six lower excitations, which are shown to be sufficient for this type of solvatochromic systems.[16,17,50]

3. Results and Discussions

Molecular properties such as absorption spectra and hyperpolarizabilities have a strong dependence on the magnitude and sign of the BLA parameter. Serrano and Canuto[16] showed that the configurations with positive and negative BLA values exhibited peak positions for the n−π* transition at around 23200 and 17000 cm^{-1}, respectively, while for the π−π* transition, the values were 24900 and 18600 cm^{-1}. The calculated hyperpolarizabilities for these two configurations were, respectively, 24 and 131 × 10^{-30} cm^5 esu^{-1}. Overall, on the basis of the calculated properties, the zwitterionic configuration was proposed as a structure for PB in chloroform, which, however, was objected by the NMR measurements on the molecules structurally similar to PB.[15] To clarify the controversy on the molecular geometry in solvents, we have investigated the molecular geometry of PB in the gas phase and in solvents such as chloroform and water. Figure 3 shows the distribution of bond lengths $C_{21}-N_{20}$, $N_{20}-C_{19}$, and $C_{10}-N_5$ for PB in the gas phase (Figure 3a), in chloroform (Figure 3b), and in water (Figure 3c). The figure clearly shows the remarkable solvent dependence of the bond lengths. The average values for the bond lengths are displayed in Table 1. The bond lengths for the $N_{20}-C_{19}$ and $C_{10}-N_5$ in the gas phase and in chloroform solvent are larger in magnitude when compared to that of the $C_{21}-N_{20}$ bond and are closer to that of a single N−C bond. Instead, the $C_{21}-N_{20}$ has a double bond character which is closer to a C=N bond. On the basis of the magnitude of the bond lengths, we can clearly say that PB is in a neutral form in gas and in chloroform solvents. However, surprisingly, all of these bond lengths are equal for PB in water since all of the peak positions for the bond length distributions appear around the same r value. The magnitude of the bond lengths corresponds neither to a single bond nor to a double bond. This clearly shows that PB in water solvent has a cyanine-like structure which is a mixture of the zwitterionic and neutral forms.

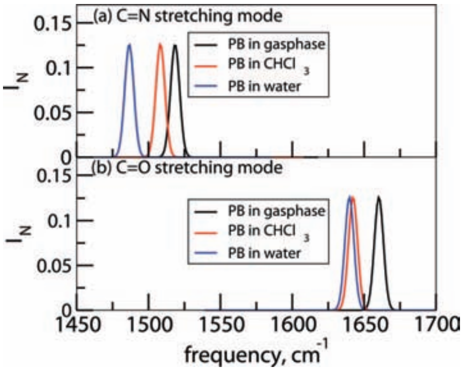

Figure 4. Solvent dependence of peak position for frequencies corresponding to (a) the C=N stretching mode and (b) the C=O stretching mode.

The calculated χ values for PB in the gas phase and in solvents are given in Table 1. The BLA values for PB in the gas phase and in chloroform solvent are, respectively, 0.068 and 0.060. In water solvent, the value is negative and also lower by more than 10 times. This means that the molecular structure in PB adopts a mixed structure of neutral and zwitterionic forms. Therefore, with the increase in dielectric constant, probably the molecule in the neutral form tends to become zwitterionic, in agreement with the observation in similar conjugated polyenic systems[23,24] where the decrease in the BLA parameter has been reported in going from vacuum to water solvent. The resonance Raman studies reported by Yamaguchi et al. indeed support our results.[21] Here, the solvent dependence of the C=N and C=O stretching modes were plotted for various solvents, which shows that the frequencies are decreasing with increasing dielectric constant. This suggests that the C=N and C=O bond lengths are weakened since the frequencies are directly proportional to the square root of the force constant. The C=N bond exists in both neutral and charge-separated forms except that the position of this bond shifts, but this is not the case with the C=O bond. In the neutral form, the CO bond has double bond character and should appear in the range of 1600−1750 cm^{-1}. In contrast, in the zwitterionic form, this has single bond character, which should appear in the frequency range of 1000−1300 cm^{-1}. Therefore, if the PB molecule changes from the neutral form to zwitterionic form due to increasing solvent polarity, this should be clearly seen in the frequency shift of the resonance Raman spectrum. Therefore, the monotonous decrease in the peak position with increasing solvent polarity does support that even in more polar solvent, the PB is not completely zwitterionic. We have also investigated the solvent dependence of the peak position for the frequencies corresponding to C=N and C=O stretching modes, shown in Figure 4a and b, respectively. The peaks were obtained using the following formula

$$I_N = \exp\left(-\frac{(\nu - \langle\nu_i\rangle)^2}{2\sigma_i^2}\right) \qquad (2)$$

where $\langle\nu_i\rangle$ is the average frequency for ith mode, obtained as an average over the Raman spectra calculations for 50 configurations from the CPMD and CP-QM/MM calculations. The frequencies were scaled by a factor of 0.9611, as has been

TABLE 2: Average Bond Orders

bonds	gas phase	PB in water
O_{27}−C_{26}	1.92	1.58
C_{21}−N_{20}	1.65	1.47
N_{20}−C_{19}	1.10	1.21
C_{10}−N_5	1.10	1.20

suggested by Irikura et al.[51] The $2\sigma_i^2$ has been taken to be 10 cm^{-1}. Since our aim was to investigate the solvent dependence of the peak position, we have normalized the intensity to 1. Figure 4a shows the solvent dependence of the peak position corresponding to the C═N stretching mode, while Figure 4b is for the C═O stretching mode. It is clearly seen from Figure 4a and b that both of the peak positions decrease with increasing dielectric constant of the solvent, which is in agreement with resonance Raman studies by Yamaguchi et al., as discussed above.[21]

In order to understand the molecular structure of PB in water when compared to that in the gas phase, we have also calculated the Mayer bond orders (for calculation details, see section 2.2). This analysis was not carried out for the PB in chloroform since, from the bond length distribution, the molecular structure is more or less similar to the gas phase structure. Table. 2 displays the bond orders calculated for a few of the important bonds between the atom pairs, namely, O_{27}−C_{26}, C_{21}−N_{20}, N_{20}−C_{19}, and C_{10}−N_5. The bond orders are shown for PB in the gas phase and in water solvent. The reported bond order values are averages over the calculations carried out for 50 configurations. From the value of the bond orders, we can clearly see that for PB in the gas phase, the bonds O_{27}−C_{26} and C_{21}−N_{20} have double bond character while the N_{20}−C_{19} and C_{10}−N_5 bonds have single bond character, which clearly re-establishes the fact that the molecular structure is in a neutral form in the gas phase. In the case of PB in water, the O_{27}−C_{26}, C_{21}−N_{20}, and N_{20}−C_{19} bonds are associated with bond order values that are between single bond and double bond character. It is also important to note that the bond orders associated with the N_{20}−C_{19} and C_{10}−N_5 bonds increase in water solvent. Overall, this indicates that in water, PB exists in a cyanine-like structure, which is a mixed structure of zwitterionic and neutral conformational states. Therefore, we conclude that in the gas phase and in chloroform, PB exists in a neutral form, while in water solvent, it is in a cyanine-like form. In fact, this is reasonable since chloroform is not a polar solvent like water and the dielectric constant of chloroform is much smaller when compared to that of water. There are many reports on the molecular properties where the effect of chloroform solvent is not very significant. Usually, the molecular dipole moments in chloroform solvent remain close to the gas-phase values.[52,53] For instance, this is the case for the dipole moment of adenosine in chloroform.[54] Overall, our results for PB in chloroform are in disagreement with the reports by Serrano and Canuto[16,17] which suggest a zwitterionic form. There have been no studies on the molecular structure for PB in chloroform or in water, but as we have discussed above, there are reports on other properties of PB in solvents. Therefore, we have calculated the spectra for the PB in the gas phase and in chloroform solvent, as discussed in section 2.1. In the literature, there are detailed reports on the solvent effect on the absorption spectra.[10,11,13,14] The absorption spectra for PB and other solvatochromic molecules are discussed in terms of the lowest two transitions corresponding to π−π* and n−π* excitations. The former one is associated with inter-ring charge transfer, while the latter one corresponds to intraring charge transfer. With PB being a positive solvatochromic dye, the lowest excitation corresponds to the π−π* transition. The absorption maxima for phenol blue have been reported in polar and nonpolar solvents. Probably, the gas-phase values can be compared to hexane and cyclohexane since these two have very low dielectric constants.[55] The reported λ_{max} value in hexane solvent is between 545 and 555 nm, while in cyclohexane solvent, it is about 552 nm. The λ_{max} value for PB in chloroform solvent is 595 nm. Therefore, probably, the solvatochromic shift for PB from hexane to chloroform is approximately 45 nm. We have also calculated the average value corresponding to the π−π* transition, which has been reported to be solvatochromic in the case of PB.[8] Figure 5 shows the distribution of the transition energy corresponding to the π−π* transition for PB in the gas phase and in chloroform; the calculated average values are, respectively, 18059 (or 553.7 nm) and 16955 cm^{-1} (or 590 nm) (see Table 4). The calculated solvatochromic shift for PB from the gas phase to chloroform solvent is 46 nm. Overall, the λ_{max} value calculated for PB in chloroform solvent is in good agreement with the experimental value,[10,11,13,14] which suggests that, indeed, the structure obtained for PB from CP-QM/MM calculations is correct.

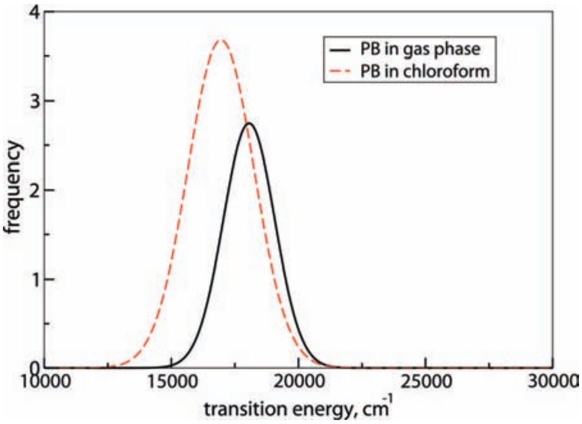

Figure 5. The distribution of transition energies for π−π* for PB in the gas phase and in chloroform.

TABLE 3: Average Group Charges

group charges	PB in the gas phase	PB in chloroform	PB in water
$phenyl_O$	0.1614	−0.0937	−0.3576
$N_{central}$	−0.6056	−0.0837	−0.2354
$phenyl_{NMe_2}$	0.4440	0.1798	0.5942

TABLE 4: Experimental and Calculated Transition Energies for PB in the Gas Phase and in Chloroform

system	PB in the gas phase[a]	PB in chloroform
calculated $E_{\pi-\pi^*}$, nm	554	590
experimental $E_{\pi-\pi^*}$, nm	545−555	595

[a] The experimental transition energy given here is for PB in cyclohexane or hexane.

Finally, we want to compare the values for the atomic charges for PB in chloroform and in water solvents to the gas phase values. It is interesting to see the differences in the charge distribution between PB in the gas phase and in chloroform solvent while the molecular geometry of PB in the gas phase and in chloroform is the same. Table 1s (see the Supporting Information) shows the ESP charges for PB in the gas phase and the D-RESP[28] charges calculated for PB in chloroform and in water. The D-RESP charges are slightly different from the ESP charges since the D-RESP charges account for the instantaneous electric field due to the dynamic solvent environment while the ESP charges account only for the thermal fluctuation in the structure. As we can clearly see from the magnitude of charges for atoms in chloroform and in water, the molecule is more polarized in the latter case. It is striking to note the larger magnitude for many of the atomic charges for PB in the gas phase when compared to those for PB in chloroform solvent. Usually, one can expect a similar dipole moment for the PB in the gas phase and in a nonpolar solvent like chloroform, even though one cannot comment on the charge distribution since different charge distributions can lead to the same dipole moment. Therefore, in order to better understand this, we have calculated the group charges corresponding to the nitrogen atom, the dimethylamino phenyl group (NR_2−Ph), and the phenoxide group (O−Ph group); see Table 3. Interestingly, there is an important feature seen for the molecule in the gas phase when compared to that in solvents. In the gas phase, the negative charge center is located on the nitrogen atom while the positive charges are distributed over the NR_2−Ph and O−Ph groups. It is a bit surprising to note the positive charge on the O−Ph group. In the case of PB in chloroform and in water, the negative charges are located over the N atom and the O−Ph group while the positive charge is located over NR_2−Ph. Even though the magnitude of the group charges for PB in the gas phase are comparable to that for PB in water, the dipole moment is three times lower in the former case due to the opposing directions of individual group dipole contributions, while in the latter case, the reverse is true. It is clearly seen that even though the molecular geometry for PB in the gas phase and in chloroform is similar, there is a remarkable difference in the charge distribution. Still, the calculated dipole moments are of the same order for PB in these two cases. A due comparison with a simple model molecule, 1,2-dichloroethane (DCE), can be useful to understand the nature of the charge distribution. DCE exists in two stable conformational states (namely, gauche and trans forms) in the gas phase and in solvents.[56] The relative population of these two forms is highly solvent-dependent. The trans form appears to be more stable in the gas phase and in nonpolar solvents, while the gauche form appears to be more stable in polar solvents. The trans form is more stable in the gas phase since the like charges on the chlorine atoms are well-separated in this form when compared to those in the gauche form. A similar reasoning can be given for the charge distribution of PB in the gas phase, where the like charges are well-separated. In the case of solvents, the charge centers also interact with the solvent dipoles, and the contribution from the solute−solvent interaction competes with the electrostatic energies of the individual solute molecule.

4. Conclusions

Being a simple organic molecule with a distinct solvatochromic shift, phenol blue has been used as a probe for many decades to explore the dielectric nature of systems as different as biological molecules and ionic liquids. However, despite this fact, a lingering controversy on its molecular structure in polar as well as nonpolar solvents has remained unsolved so far. In an attempt to shed further light on the problem, we have in this work carried out CPMD and CP-QM/MM calculations. Our findings suggest that the molecular structure for PB adopts a neutral form in the gas phase and in chloroform solvent. With sequential CPMD and TDDFT calculations, we were able to obtain the gas-phase absorption spectra. Similarly, with the sequential CP-QM/MM and TDDFT calculations (using the non-equilibrium polarizable continuum model to include the chloroform solvent effect), we were able to reproduce the spectra for PB in chloroform, in good agreement with experimental results.[10,11,13,14] The findings for the molecular structure of PB in chloroform clarify the controversy existing in the literature.[15−17] We suggest a cyanine-like structure for PB in water, something that is supported by Mayer bond order analysis and by resonance Raman spectroscopy measurements.[21] Interestingly, even though the molecular geometries of PB in the gas phase and in chloroform are the same, the charge distribution appears to be different. Also, from the atomic charges calculated for PB in chloroform and in water, we find that PB in water is more polarized than that in chloroform.

Usually, the solvent effect on the polyenic, betainic, and merocyanine systems are difficult to model since, in addition to the changes in the charge distribution, there is a considerable shift in the solute molecular geometry. The present calculations demonstrate that the CP-QM/MM technique can be used successfully to understand the structure of these complex organic solute−solvent systems and, in particular, the solvent-induced changes in the molecular geometry of the solute. We also show that the combined use of the CP-QM/MM technique with the TDDFT approach provides a practical way to understand the solvatochromic behavior of betaine- and merocyanine-like systems.

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Supporting Information Available: Solvation shell structure and average atomic charges. This material is available free of charge via the Internet at http://pubs.acs.org.

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