Ultrafast Proton Transfer Reaction in Phenol–(Ammonia)*n* Clusters: An *Ab-Initio* Molecular Dynamics Investigation.

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ABSTRACT

The ability of phenol to transfer the proton to surrounding ammonia molecules in a phenol-(ammonia)*n* cluster will depend on the relative orientation of the ammonia molecules and a critical field of about 285 MV cm^{-1} is essential along the O–H bond for the transfer process. *Ab-initio* MD simulations reveal that for a spontaneous proton transfer process, the phenol molecule must be embedded in a cluster consisting of at least eight ammonia molecules, even though several local minima with proton transferred can be observed for clusters consisting of 5-7 ammonia molecules. Further, phenol solvated in large clusters of ammonia, the proton transfer is spontaneous with the proton transfer event being instantaneous (about 20-120 fs). These simulations indicate that the rate-determining step for the proton transfer process is the organization of the solvent around the OH group and the proton transfer process in phenol-(ammonia)*n* clusters follows a curvilinear path which includes the O–H bond elongation and out-of-plane movement of the proton and can be referred to as a “Bend-to-Break” process.

INTRODUCTION

The role of the solvent in the proton transfer process is paramount and determines whether or not the proton transfer will occur and the physicochemical properties of the solvent determines the pK_a of the solute and illustrated by the fact pK_a of HCl in water (-7.0) and acetonitrile (10.3) differ by more than 17 units.[1] These differences in the pK_a can be related to the free-energy proton extraction by the solvent and solvation free energy of the proton and the counter anion. One of the interesting aspects of the free-energy proton extraction by the solvent is the role of microscopic solvation of the solute centred around the protic group. More importantly, the general interest is to probe the minimum number of solvent molecules required for acid dissociation and concurrent proton transfer process, to understand the acid dissociation phenomenon at a molecular level.[2-6] In this regard, the role of ammonia as a solvent in the proton transfer process in the phenol-(ammonia)$_n$ clusters have been the subject of intense experimental and theoretical investigations by several research groups over the past three decades to understand the proton transfer reaction in the ground state and hydrogen transfer process in the excited electronic state.[7-16] Additionally, it has been shown that the excited proton transfer reaction of phenol becomes ultrafast at the air-water interface.[17]

The proton transfer reaction in phenol-(ammonia)$_n$ clusters were investigated using the infrared spectroscopic method, which revealed that at least six ammonia molecules are required to observe the features corresponding to the proton transferred form.[14] On the other hand, electronic structure calculations have shown that five ammonia molecules are adequate to extract the proton from phenol, albeit being energetically unfavourable, and the proton transfer process in the phenol-(ammonia)$_n$ clusters becomes increasingly favourable with the increase in the number of ammonia molecules.[16] In a recent work our group, with the aid of electric field calculations along the donor O–H of phenol in the phenol-(ammonia)$_n$ clusters, using at the M06-2X/cc-pVTZ level of theory, has shown that a critical electric field of a critical field of 236 MV cm^{-1} is essential to transfer of a proton from phenol to the surrounding ammonia cluster.[18] Interesting, Additionally, six exceptions to this rule were observed, which indicates that the projection of the solvent electric field over the O–H bond is not an unqualified descriptor of the proton transfer reaction. Based on these observations, it was noted that the critical electric field is a necessary, but not sufficient condition for the proton transfer process. However, the usage of DFT methodologies can lead to artefacts in the proton transfer process, consequently misrepresenting the value of the critical electric field.[19] Furthermore, the unique feature of the proton transfer process in the phenol-(ammonia)$_n$ clusters is the out-of-plane motion of the proton concurrent with the O–H bond elongation leading to a curvilinear path, which has been referred to as a “Bend-to-Break” process.[18] However, the curvilinear path for the proton transfer process was assessed based on the snapshots that were optimized using electronic structure calculations. In this work, the proton transfer process in the phenol-(ammonia)$_n$ clusters is re-evaluated using electric field calculations at the MP2 level theory and Born-Oppenheimer molecular dynamic (BOMD) simulations were carried out to understand the trajectory of the proton motion.

METHODOLOGY

The geometries of 126 PhOH-$(NH_3)_n$ (n=1-10) clusters, calculated using M06-2X/cc-pVTZ method, were reported earlier,[16] and among these 126 structures only 114 structures which show hydrogen bonding between the phenolic OH group to the surrounding ammonia cluster and were considered.[18] These 114 structures were re-optimized using the resolution of identity second-order perturbation theory (RI-MP2) method with cc-pVDZ basis set using ORCA 4.1.2 suite of programs.[20] Following, the electric field along the O–H bond was calculated on the 114 structures using the procedure described elsewhere.[18,21-25] The nomenclature used to label the structures is identical to that reported by Shimizu et al.,[16] wherein each structure is labelled by an alphanumeric. For instance, the label 7A indicates the most stable phenol-(ammonia)$_7$ complex, while the label 5C indicates the third most stable phenol-(ammonia)$_5$ complex. Further, Born-Oppenheimer molecular dynamic (BOMD) simulations were carried out for several phenol-(ammonia)$_n$ clusters were carried out using nineteen (19) selected starting geometries reported earlier,[16] viz. 1A, 2A, 3A, 4A, 4B, 5A, 5C, 6A, 6B, 6E, 7A, 7B, 7C, 8A, 8B, 8C, 9B, 10C, 10E and 10F (see the SI for the coordinates). For the BOMD calculations, the long-range dispersion corrected BLYP-D3 density functional using def2-SVP basis set with a time step of 0.5 fs. All the calculations were carried out using ORCA 4.1.2 suite of programs.[20] The length of the BOMD trajectories was up to 35 ps in some cases to sample the probability of the proton transfer process.

Alternately, initial configurations for BOMD simulations were extracted from the classical MD simulations for PhOH-$(NH_3)_n$ (n=1-8) clusters. For the clusters with $n \geq 3$, the initial configuration for the BOMD simulations consists of phenol moiety in the single donor and double acceptor (DAA) motif. Additionally, MD simulations on a PhOH embedded in ammonia molecules with a 3.4 nm cubic box was carried out and the lowest energy configuration from MD trajectory was taken and truncated the solvation shell after 8 Å from the centre of mass of phenol, yielding a PhOH-$(NH_3)_{63}$ cluster, which was further considered for BOMD simulations. For all these clusters, unrestrained simulation using NVT ensemble were carried out of 30 ps. The temperature was fixed at 150 K using the canonical sampling velocity rescale (CSVR) method with a coupling constant of 1 fs. The BOMD simulations, in this case, were carried out using long-range dispersion corrected BLYP density functional (BLYP-D3) in combination with dzVP basis set. The temperature equilibrated within 1 ps of simulation time and fluctuate around 150 K throughout the trajectories of about 30 ps (Figure S1, see the SI). Thereafter, well-tempered metadynamics simulations were carried out for PhOH-$(NH_3)_n$ clusters consisting of up to seven ammonia molecules by biasing the O–H bond distance with a Gaussian potential of 3 kcal mol^{-1} height and 0.05Å width. Thereafter potentials of mean force along the O–H bond distance were constructed. The BOMD simulations were carried out using CP2K-6.2 package.[26]

RESULTS AND DISCUSSION

(A) Role of electric field

In the case of PhOH-$(NH_3)_9$ clusters two structures within an energy difference of 0.8 kJ mol^{-1} show different behaviour relative to their ability to transfer the proton as can be seen in Figure 1 (these two correspond to structures 9A and 9B in Ref.16). Thus, the ability of the ammonia cluster surrounding the phenol molecule to extract the proton depends on the distribution of the ammonia molecules and not the stabilization energy. Therefore, the proton transfer process from phenol to ammonia is examined in terms of the electric field

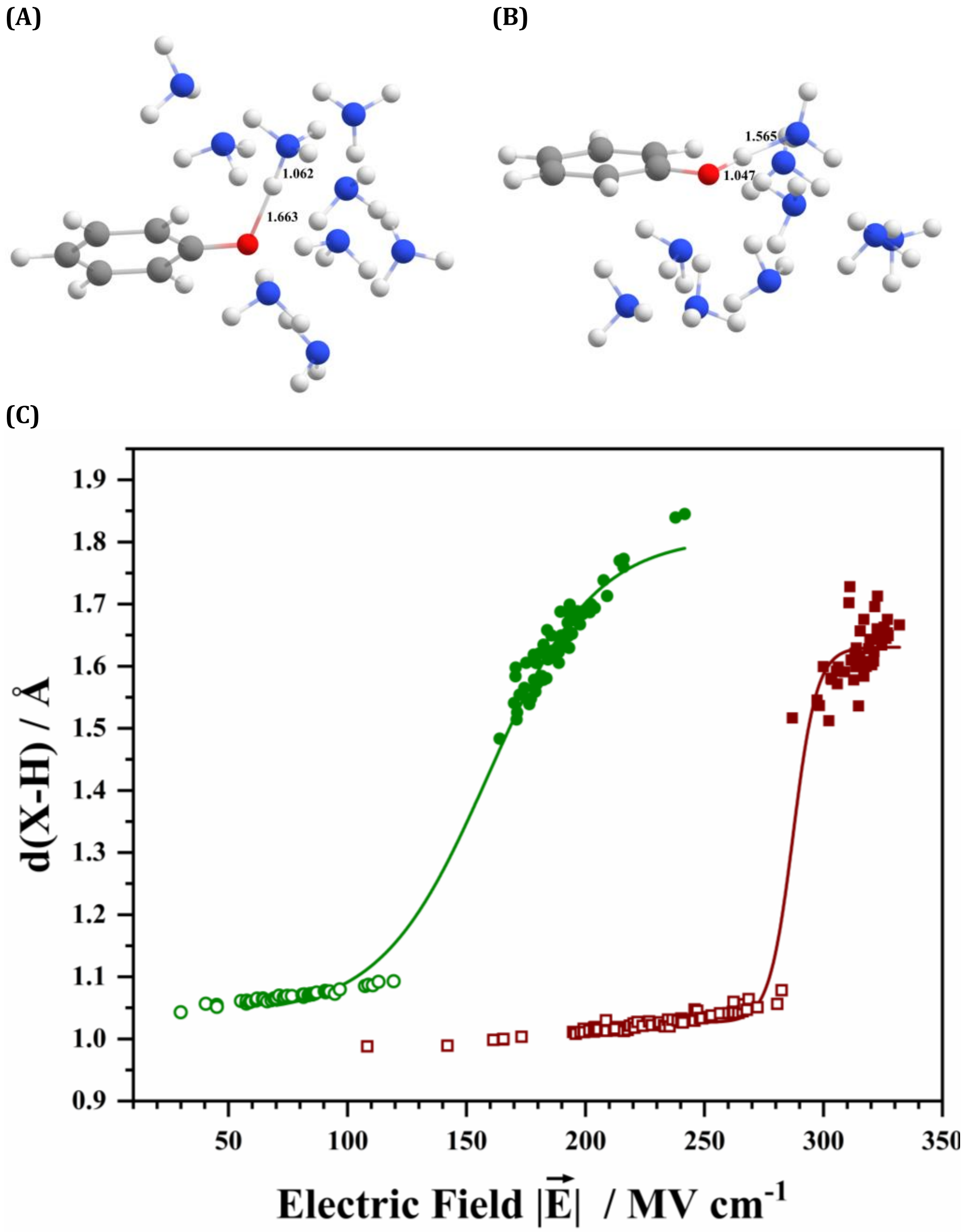

Figure 1. (A, B) Two representative structures of PhOH-(NH_3)$_9$ (9A and 9B) with the stabilization energy difference of 0.8 kJ mol^{-1}, which illustrates the difference in the ability of proton transfer from phenol to ammonia cluster depends on the orientation of the ammonia molecules. Notice the difference in the distribution of the ammonia molecules around phenol in the two structures. (C) The plots of O–H (red squares) and N–H (green circles) distances in Ph-(NH_3)$_n$ clusters against the corresponding electric fields. of the phenol moiety against the calculated electric field along the O–H/N–H bond. The solid lines are the nonlinear Boltzmann sigmoidal fit to the calculated data points around the point of inflection. The points of inflection correspond to electric field values of 285.2 and 159.0 MV cm^{-1} along the O–H and N–H bonds. See the SI for the coordinates of 9A and 9B structures.

along the O–H and N–H bonds of the phenol molecule and ammonium ion, respectively.[18] Figure 1 shows the plot of the O–H/N–H distances against the corresponding electric field and the critical electric fields of 285.2 and 159.0 MV cm^{-1} are required to transfer the phenolic proton to ammonia cluster and transfer of a proton from the ammonium ion to phenolate ions, respectively. In comparison, the M06-2X/cc-pVTZ calculations yield much lower corresponding critical electric field values of 236.2 and 116 MV cm^{-1} (Figure S2, see the SI) .[18] Further, the M06-2X/cc-pVTZ level showed six data points which were exceptions, wherein the proton transfer from phenol to ammonia was not observed even though the electric field along the O–H bond value exceeded the critical electric field value.[18] On the contrary, the present RI-MP2/cc-pVDZ calculations show that for all the structures the proton transfer is observed if the occurs electric field along the O–H bond exceeds the critical electric field, without exceptions. Among the six structures which were exceptions at the M06-2X/cc-pVTZ level, two structures (6E and 6N) did not exhibit proton transfer, while proton transfer was observed in four structures (5K, 8S, 6G, 6L and 8S) at RI-MP2 level of theory. Furthermore, the comparison of the electric field calculated by the M06-2X/cc-pVTZ and RI-MP2/cc-pVDZ indicates that the differences are marginal in the case of hydrogen-bonded structures, whilst the differences are substantial (average difference of about 30.0 MV cm^{-1}) for the proton transferred structures. These results illustrate the limitations of DFT theory to appropriately modelling the proton-transferred structures, which can be attributed to the importance of HF exchange.[19,27]

(B) Proton transfer in BOMD simulations

Several reports in the literature deal with the question of the minimum number of ammonia molecules required in a cluster around phenol for the spontaneous proton transfer, and the consensus is that eight ammonia molecules are required for spontaneous proton transfer from the phenol to ammonia cluster. However, the assessment of the proton transfer process using electric fields indicates that a critical electric solvent electric field along the O–H bond is a necessary requirement for the proton transfer, which depends on the solvent configuration. Electronic structure calculations reveal that some of the PhOH-$(NH_3)_n$ clusters show proton transfer with 5-7 molecules of ammonia, however, these structures are higher

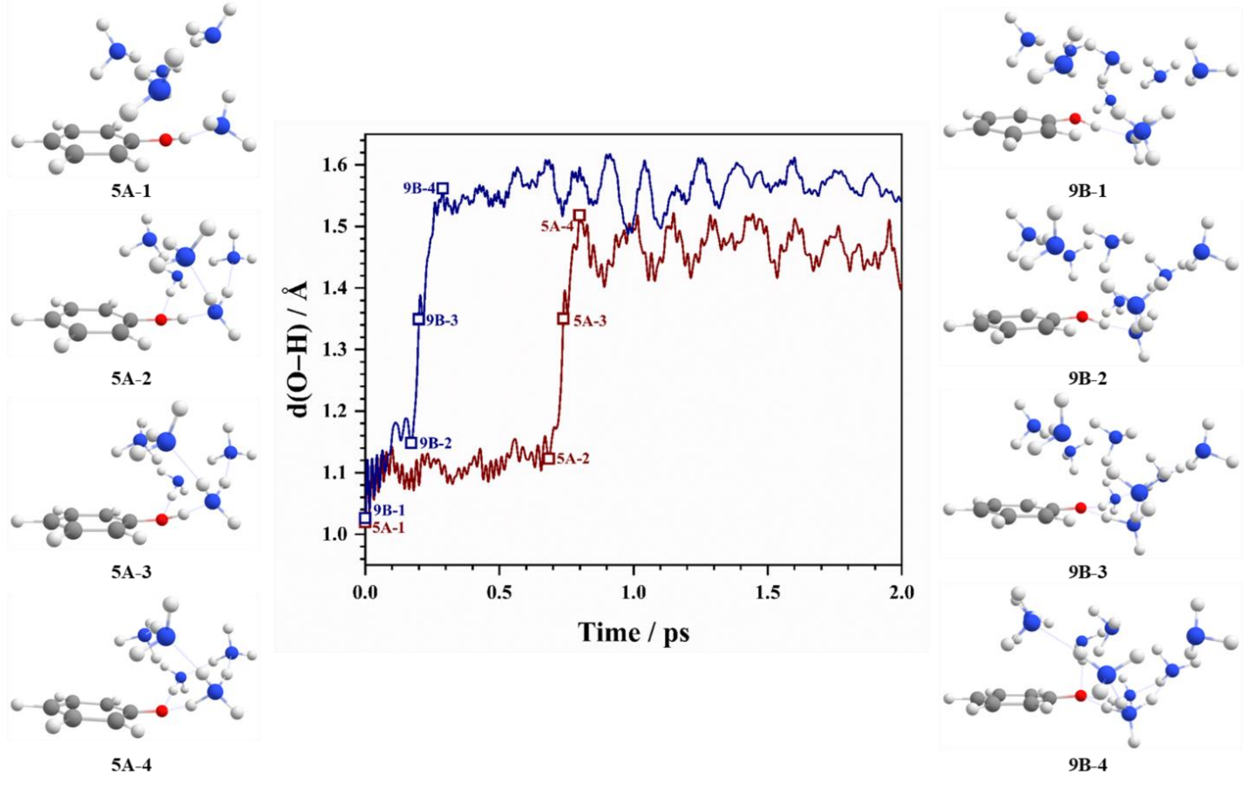

Figure 2. The middle panel shows the plot of O–H distance as a function of simulation time for the two BOMD trajectories starting from the initial structures 5A (red-trace) and 9B (blue trace). In both of the cases, proton transfer from the phenol moiety to the ammonia cluster was observed which is indicated by the lengthening of the OH bond. The left and the right panels show set to structures starting from 5A and 9B as they evolve along the proton transfer trajectory. The time points corresponding to the structures shown are marked on the corresponding trajectories. Notice that the time taken for the proton transfer in the two cases is different and is indicative of the fact that different trajectories sample different parts of the structural landscape. It can also be noticed in both the trajectories, the actual proton transfer process (the sigmoidal part of the cure) occurs almost instantaneously (about 120 fs) from the time-points 5A-2 to 5A-4 and 9B-2 to 9B-4, following solvent reorganization. See the SI for the coordinates of the various snapshots shown in this figure.

in energy relative to the global minimum. In order to access the proton transfer dynamics in PhOH-$(NH_3)_n$ clusters BOMD simulations starting from selected PhOH-$(NH_3)_{1-4}$ clusters (structures 1A, 2A, 3A, 4A, 4B geometries, see the SI for coordinates) were carried out, and the corresponding trajectories reveal that the proton transfer does not occur in the simulation time of 30 ps, even though in this case (for 4B) the O–H bond elongates to 1.10 Å.

On the other hand, in the case of or the $[PhOH-(NH_3)_{2-6}]^+$ cluster cations, proton transfer is spontaneous even in the presence of two ammonia molecules.[28] Further, the BOMD trajectories were also calculated for several $PhOH-(NH_3)_{5-10}$ clusters (starting from 5A, 5C, 6A, 6B, 6E, 7A, 7B, 7C, 8A, 8B, 8C, 9B, 10C, 10E, and 10F geometries, from Ref. 16). Among these, eight trajectories (starting from 5A, 5C, 6E, 7A, 9B, 10C, and 10E) resulted in the proton transfer process, whereas, simulations starting from 6A, 6B, 7A, 7C, 8A, 8B, 8C, and 10F geometries did not yield proton transfer even after 35 ps simulation time. However, the (simulation) time required of the proton transfer varied due to differences in the initial structure and the structural landscape sampled during the simulation. It can be noticed from Figure 2 that the actual proton transfer process occurs almost instantaneously (about 120 fs) from the time-points 5A-2 to 5A-4 and 9B-2 to 9B-4, following solvent reorganization. Table S1 summarizes the proton transfer time and the corresponding C-C-O-H dihedral angle (χ), which captures the out-of-plane movement of the OH proton. For the eight trajectories in which the proton transfer happens the dihedral angle χ varies from 0.6° to 42.0° with an average of 15°, suggesting a curvilinear proton transfer from the phenol to ammonia cluster. These results are in agreement with an earlier work in which it was shown that the proton transfer from the phenol moiety to the surrounding ammonia cluster is accompanied by the out-of-plane motion of the OH proton.[18] It must however be noted that the possibility of proton transfer process along these trajectories will depend on the geometries sampled, therefore do not yield thermodynamic parameters.

(C) Potentials of mean force for the proton transfer reaction

Alternatively, potentials of mean force for the $PhOH-(NH_3)_{1-8}$ clusters were constructed, which are depicted in Figure 3. For $PhOH-(NH_3)_{1-8}$ clusters the free energy for the proton transferred species $[PhO]^- [H(NH_3)_n]^+$ decreases gradually with the increase in the number of ammonia molecules and becomes spontaneous for a cluster consisting of eight ammonia molecules, even though electronic structure calculations suggest that the proton transfer process becomes spontaneous for $n \geq 9$.[14] As shown earlier using BOMD simulations, the proton transfer from the phenol moiety can be observed for clusters consisting of $5 \geq n \geq 7$, however, in these cases the proton transferred structures correspond to local minima on the free energy surface and do not truly represent the spontaneity of the proton transfer process.

Figure 4 shows the change in the phenolic OH distance for the PhOH-$(NH_3)_8$ and PhOH-$(NH_3)_{63}$ clusters along the BOMD trajectory following temperature equilibration. These trajectories signify that the time for the solvent reorganization around the phenolic OH group is the rate-determining step of the proton transfer process and the proton transfer event is almost instantaneous (about 20 fs). Incidentally, the proton transfer event for the two trajectories shown in Figure 2 is about 120 fs. Therefore, based on the BOMD simulations it can be concluded that the rate-determining step for the proton transfer process is the

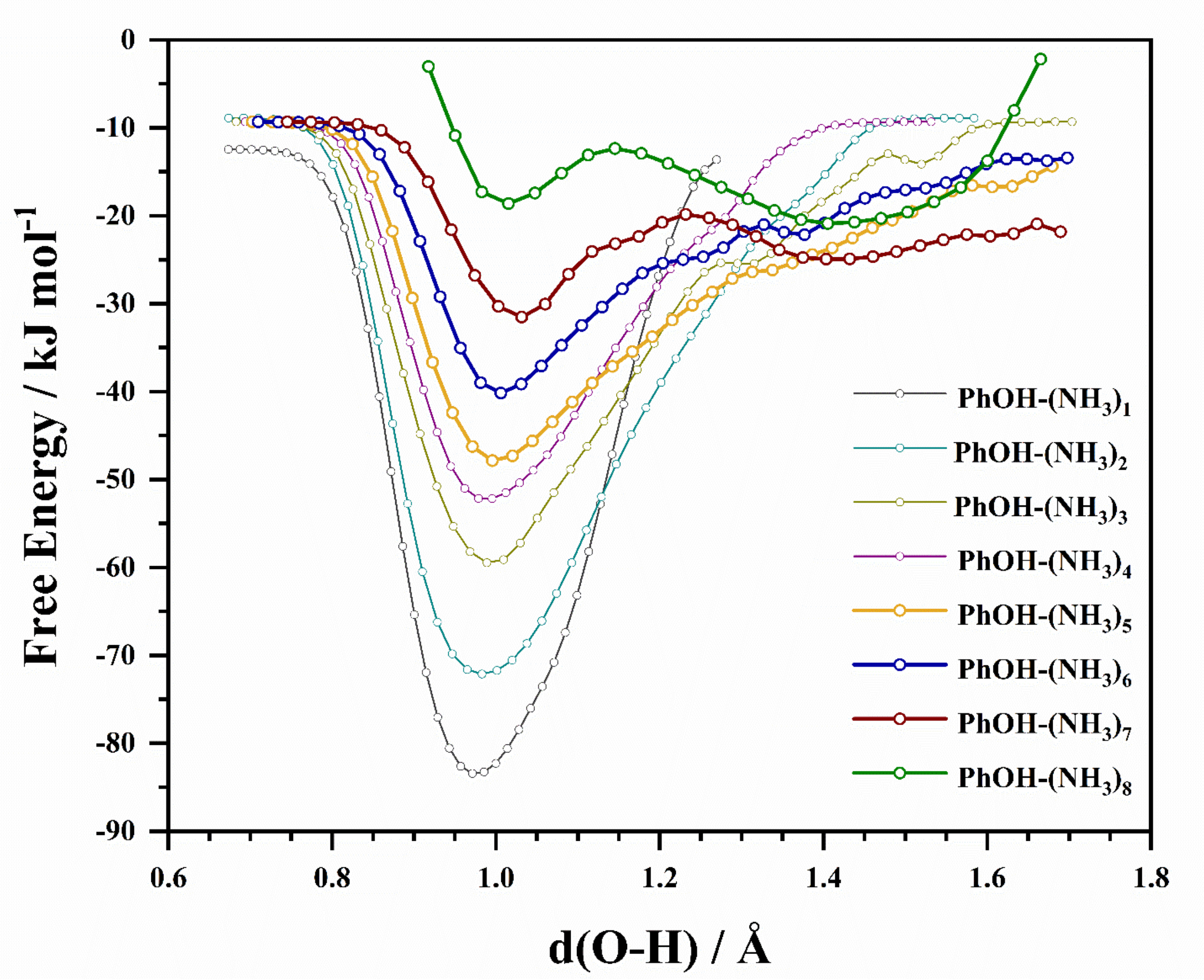

Figure 3. Potential of mean force as a function of phenolic O–H distance obtained from metadynamics simulations by biasing the O–H bond distance with a Gaussian potential of 3 kcal mol^{-1} height and 0.05Å width for PhOH-$(NH_3)_{1-7}$ clusters. In the case of PhOH-$(NH_3)_8$ cluster, the proton transfer was spontaneous, therefore biasing along the O–H bond was not required.

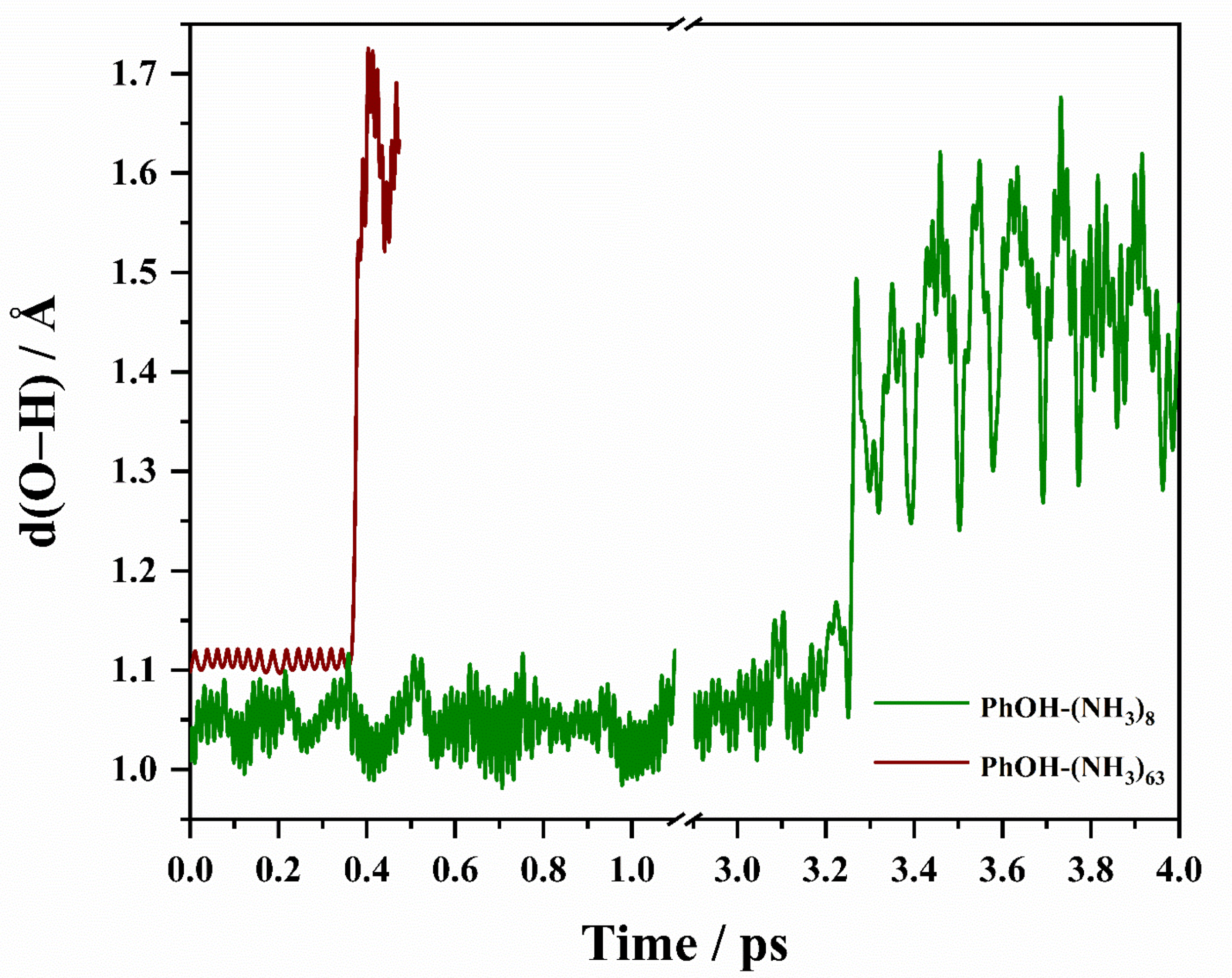

Figure 4. The plot of O–H distance as a function of simulation time for the two BOMD trajectories starting from the PhOH-$(NH_3)_8$ (green curve) and PhOH-$(NH_3)_{63}$ (red curve) clusters, wherein spontaneous proton transfer was observed. The initial part of the trajectory indicates the solvent reorganization followed by instantaneous proton transfer within the time scale of about 20 fs.

organization of the solvent around the OH group. These results suggest that the solvent and the corresponding electric field fluctuations occur until a particular configuration projects the critical field along the O–H bond, resulting in the proton transfer. Additionally, the metadynamics simulations also reveal the out-of-plane motion of the OH proton during the proton transfer process, as indicated by the C-C-O-H dihedral angle (χ), which varies from 46° to 75° (see the SI), once again suggesting a curvilinear proton transfer from the phenol to ammonia cluster. These results are in agreement with an earlier work in which it was shown that the proton transfer from the phenol moiety to the surrounding ammonia cluster is accompanied by the out-of-plane motion of the OH proton, leading to a "Bend-to-Break" process.[18]

CONCLUSIONS

The proton transfer reaction in the phenol-(ammonia)$_n$ clusters was investigated using electronic structure calculations using RI-MP2/cc-pVDZ level of theory in combination with *Ab-Initio* (Born-Oppenheimer) MD simulations. The electric field calculations indicate that a critical electric field of about 285 MV cm^{-1} is required along the O–H bond for the transfer of proton transfer process. Further, the BOMD simulations reveal that the proton transfer does not occur in phenol-(ammonia)$_n$ clusters with $n \leq 4$, while for $n \leq 5$-7, several local minima can be found wherein the proton transfer can occur and finally for clusters with $n \geq 8$ proton transfer is spontaneous. In the case of large clusters and extending the analogy to phenol solvated in ammonia, the proton transfer is instantaneous and spontaneous. The *Ab-Initio* MD simulations suggest that the solvent reorganization around the phenol OH group is the rate-determining step for the proton transfer process. Further, both the electronic structure and BOMD simulations suggest that the proton transfer process in the phenol-(ammonia)$_n$ clusters follows a curvilinear involving the elongation of the O–H bond and the out-of-plane motion of the OH proton.

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Supporting Information

The Supporting Information is available.

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