Proton Exchanges between Phenols and Ammonia or Amines: A Computational Study

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Density functional theory calculations at the B3LYP/6-31+G(d,p) level of theory have been performed to explore proton exchanges between phenols and ammonia or amines, which can be used to account for previous NMR experiments. For the parent phenol−NH_3 system, a transition state with a symmetric phenolate−NH_4^+-like structure, which lies about 35 kcal mol^{-1} in energy above the hydrogen-bonded complex, has been successfully located. An intrinsic reaction coordinate (IRC) analysis indicates that the proton exchange is a concerted process, which can be roughly divided into four continuous subprocesses. A series of *para*-substituted phenol−NH_3 systems have been considered to investigate the substituent effect. Whereas introduction of an electron-withdrawing group on the phenol appreciably reduces the barrier, an opposite effect is observed for an electron-donating group. Moreover, it has been disclosed that there exists a good linear correlation between the activation barriers and the interaction energies between the phenols and NH_3, indicating the important role of proton transfer (or hydrogen bonding) in determining the proton exchange. Also considered are the proton exchanges between phenol and amines and those for some sterically hindered systems. The results show that the phenol tends to exchange hydrogen with the amines, preferably the secondary amines, and that the steric effect is favorable for the proton exchange, which imply that, as the IRC analysis suggested, besides the proton transfer, the flip of the ammonium-like moiety may play a significant role in the course of proton exchange. For all of these systems, we investigated the solvent effects and found that the barrier heights of proton exchange decrease remarkably as compared to those in a vacuum due to the ion pair feature of the transition state. Finally, we explored the phenol radical cation−NH_3 system; the barrierless proton transfer and remarkably low barrier (5.2 kcal mol^{-1}) of proton exchange provide further evidence for the importance of proton transfer in the proton exchange.

Introduction

Hydrogen bonding involving phenols has been the subject of extensive experimental[1−5] and theoretical[6−12] studies because phenol is the simplest aromatic alcohol and its hydrogen-bonding interactions can be regarded as a prototype for the interaction in biological systems, for example, tyrosine residues in proteins. The phenol−NH_3 complex has also served as a good model for the investigation of proton and electron-transfer processes occurring in living matter.[13−20] In most of these efforts, it was generally assumed that the interaction consists solely of the attraction between the lone pair of the amine nitrogen atom and the phenolic hydroxyl proton (i.e., O−H···N hydrogen bond).

Scott et al.[21,22] conducted a spectroscopic and calorimetric study on some phenol−amine systems and observed abnormal enthalpy changes of *n*-butylamine relative to triethylamine when interacting with cresol. To interpret the experimental results, they suggested that both the proton of the phenolic hydroxyl and that of the primary amine might be involved in hydrogen bonding;[21,22] that is, a bifurcated hydrogen bond as depicted in Scheme 1a was formed. This cyclic pattern was adopted thereafter by Jin (one of the authors) and co-workers when they investigated the structure of a 2:1 complex of *para*-cresol with piperazine in the solid state and in solution.[23] The ^{1}H NMR spectroscopy experiments in $CDCl_3$ solution showed unambiguously that the proton peaks assigned respectively to the phenolic hydroxyl and amine groups in pure *para*-cresol and piperazine were merged into one in the complex. They offered a plausible explanation that a cyclic hydrogen-bonded complex may be involved in a fast proton exchange process (see Scheme 1b). More recently, Figueroa-Villar and co-workers[24] performed a nuclear relaxation and molecular diffusion NMR study on this 2:1 *para*-cresol/piperazine complex. They pointed out that the *para*-cresol should be attached to the piperazine via a single O−H···N type hydrogen bond, and the NMR signal of the amine hydrogen in the spectrum of pure piperazine disappeared in the complex, possibly because they were broadened too much to be detected.[24] Nevertheless, the issue of change of ^{1}H NMR spectra upon the formation of phenol−amine complex still remains unresolved.

In the present work, we performed a density functional study on the hydrogen bonding in the phenol−NH_3 complex and put forward an intracomplex identity proton exchange mechanism as illustrated in Figure 1. The transition state linking the two equivalent singly hydrogen-bonded complexes, which possesses a symmetric structure of phenolate−NH_4^+-like, was successfully located. Indeed, the proton exchange or double proton transfer in hydrogen-bonded dimers is ubiquitous,[25−33] and some systems

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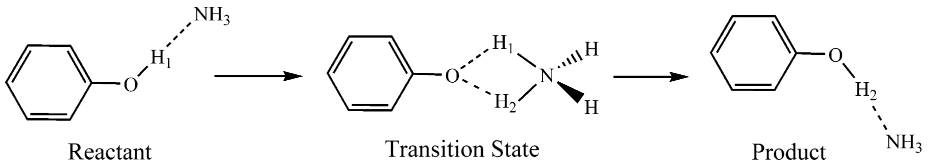
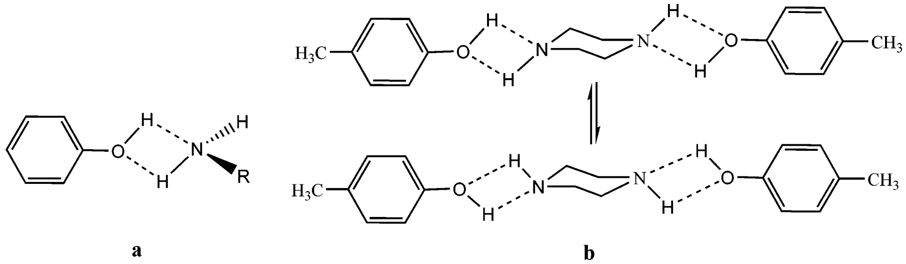


Figure 1. Proposed proton exchange mechanism in the phenol$-$NH$_3$ system.

SCHEME 1



such as CH_3COOH+CH_3OH have been studied theoretically in the context of proton exchange.[27] Particularly, in recent publications[19,20] devoted to investigating the energetics and product branching of the proton-transfer reaction between the phenol radical cation and the deuterated ammonia ($PhOH^{\cdot +}$+ND_3), the H/D exchange via a transition state similar to that of C_{2v} symmetry has been mentioned. This proposed mechanism was then validated by density functional calculations. Substituent effects, the effect of ionization of phenol, and solvent effects upon the proton exchange were also examined. Such a systematical investigation may provide some useful information for our further understanding of the proton transfer, proton exchange, as well as hydrogen bonding in related biological systems.

Computational Details

All of the calculations were carried out with the Gaussian 98 suite of programs.[34] All structures were optimized by density functional theory (DFT) methods, using Becke's three-parameter (B3)[35] exchange functional along with the Lee$-$Yang$-$Parr (LYP) nonlocal correlation functional[36] (B3LYP). The standard split-valence double-ξ basis set with polarization functions on all atoms and diffuse orbitals on heavy atoms, 6-31+G(d,p), was adopted. For the parent phenol$-$NH$_3$ system, ab initio calculations were also performed to validate the rationality of the DFT results at the levels of MP2 (second-order Møller$-$Plesset theory)[37] and CCSD(T) (coupled cluster with single and double excitations of full electrons plus perturbatively included triplet excitations)[38] with the same or larger basis set. No symmetry assumption was made unless otherwise noted. Energy minima and first-order saddle points were determined by analytical computation of vibrational frequencies and by viewing the motion of the imaginary vibrational mode for the transition states. The transition states were further confirmed by the intrinsic reaction coordinate (IRC) procedures. Solvent effects were considered using the polarizable continuum model (PCM).[39] This approach had proven to be able to provide a reasonably good description of the polarization effect of the solvent.[40,41]

The hydrogen-bonding energy (ΔE) was calculated as the difference between the sum of total energies of the two monomers and the total energy of the complex with zero-point energy (ZPE) corrected. The basis set superposition error (BSSE) was taken into account by means of the Boys$-$Bernardi counterpoise method.[42] Bader's atom in molecule (AIM)[43] analyses were carried out using the wave functions generated from the DFT calculations with the help of AIM 2000 software.[44]

Results and Discussion

Hydrogen Bonding and Proton Exchange in the Phenol$-$NH$_3$ System. We first considered the possibility of forming bifurcated hydrogen bonding between phenol and NH$_3$. Such a subject, to the best of our knowledge, has received no attention, albeit the hydrogen bonding and proton transfer in this system have been studied thoroughly.[10,13-15] For this purpose, potential energy surfaces (PESs) associated with the hydrogen bonding for the phenol$-$NH$_3$ dimer have been carefully searched. A geometry optimization starting with the bifurcated hydrogen-bond arrangement always converges to the singly hydrogen-bonded one (reactant or product in Figure 1). Besides, another local minimum where the phenolic OH group acts as a hydrogen-bond acceptor has been located (see Figure 2). This complex also contains a weak C$-$H···N hydrogen bond, which is confirmed by a relatively short interatomic contact (d(H···N) $= 2.63$ Å) and a simple AIM analysis (i.e., there exists a bond critical point (BCP) between the two atoms). Nevertheless, it exhibits significantly higher energy (by about 7 kcal mol^{-1}) as compared to the singly O$-$H···N hydrogen-bonded complex. Bearing these in mind, we can conclude that the proton exchange between phenol and amine through a bifurcated hydrogen bond should be abandoned.

We turn to our proposed intracomplex proton exchange mechanism. The transition state through which the phenol and amine can exchange the hydrogen to form, respectively, the reactant and the product (equivalent hydrogen-bonded complex)

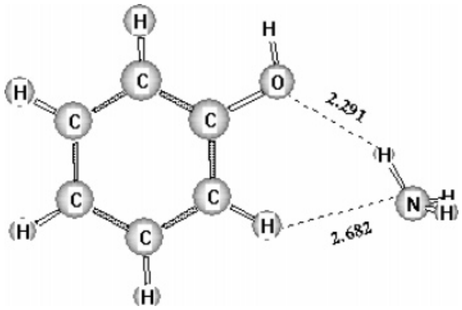


Figure 2. Optimized structure (interatomic distances are in angstroms) for the phenol$-$NH$_3$ complex with the phenolic OH group acting as a hydrogen-bonding acceptor.

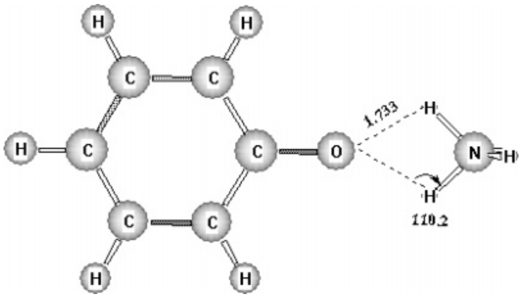


Figure 3. Optimized structure (interatomic distance is in angstroms and bond angle in degree) for the transition state of the phenol−NH_3 system.

TABLE 1: Selected Structural Parameters of the Transition State and Activation Energies for the Parent Phenol−NH_3 System at Various Levels of Theory[a]

methods	d(O···H)	−(O···H−N)	d(N−H)	ΔE_a
B3LYP/6-31+G(d,p)	1.733	110.2	1.060	34.6
	1.733	110.2	1.060	
B3LYP/6-311++G(d,p)	1.738	110.0	1.058	34.2
	1.738	110.0	1.058	
MP2/6-31+G(d,p)	1.756	109.4	1.050	34.9
	1.756	109.4	1.050	
MP2/6-311++G(d,p)	1.744	109.7	1.052	36.4
	1.745	109.6	1.052	
CCSD(T)/6-311++G(d,p)// MP2/6-311++G(d,p)				37.8

[a] Distances are given in angstroms, angles in degrees, and energies in kcal mol^{-1}; CCSD(T) energy is corrected by the zero-point energy calculated at the MP2/6-311++G(d,p) level.

has been successfully located by the B3LYP/6-31+G(d,p) calculations. Normal-mode analysis shows clearly that the transition structure has only one imaginary frequency of 619i cm^{-1}. This symmetrical phenolate−NH_4^+-like structure (Figure 3) exhibits considerably short H···O contacts of 1.733 Å, and its cyclic O···H−NH moiety is almost perfectly coplanar with the aromatic plane, which endows the transition state with some characteristics of the bifurcated hydrogen bond. The existence of the NH···O interactions has been further confirmed in the light of AIM theory. Two BCPs are identified for the two H···O contacts. Besides, a ring critical point (RCP) is also presented. To further validate the transition state, IRC analysis has also been conducted. The result indicates that, along the IRC path, there is (i) proton transfer from phenol to NH_3; (2) flip of the NH_4^+-like moiety to form the transition state; (3) further flip to form the phenolate−NH_4^+-like ion pair complex; and (4) proton transfer from the NH_4^+-like moiety to phenolate, four continuous subprocesses through which the concerted proton exchange is accomplished.

The ZPE-corrected barrier height (ΔE_a) for the proton exchange is predicted to be about 35 kcal mol^{-1} at the B3LYP/6-31+G(d,p) level of theory. To validate the rationality of the DFT result, post Hartree-Fock calculations at the MP2 and CCSD(T) levels of theory with the 6-31+G(d,p) and/or 6-311++G(d,p) basis sets have also been performed. Some selected geometrical parameters of the transition structure and the activation energies (ΔE_a) are summarized in Table 1. It can be seen that the differences of the geometrical parameters and activation energies with different methods are quite limited. In particular, the differences of the N−H bond lengths predicted at various computational levels are never over 0.01 Å. The O···H distances also show small changes when different methods are used, and the variations of the angles −(O···H−N) are within 1°. A comparison of the ΔE_a values calculated at the B3LYP/6-31+G(d,p) level and those with the B3LYP/6-311++G(d,p) and all MP2 methods reveals that the mean deviation is less than 2.3 kcal mol^{-1}. The single-point energy calculated with the CCSD(T) approach amounts to 37.8 kcal mol^{-1}, which does not depart significantly from the B3LYP/6-31+G(d,p) result (34.6 kcal mol^{-1}). These data indicate that the results, with respect to the proton exchange between phenol and NH_3, are insensitive to the methods used. Similarly, it has been demonstrated in a recent work on the hydrogen-bonded phenol−NH_3 system that basis set effects are very small.[7] With these in hand, we expect that the B3LYP/6-31+G(d,p) method should provide a reasonable compromise between the accuracy of calculations and computational costs.

TABLE 2: Calculated Interatomic Distances between the Phenolic Oxygen and the Exchanged Proton, *d*(O···H) (in Å), the Activation Energies of Proton Exchanges, and the BSSE-Corrected Interaction Energies for the *para*-Substituted Phenol−NH_3 Complex[a]

	d(O···H)	ΔE_a	$\Delta E_{a,solv1}$[b]	$\Delta E_{a,solv2}$[b]	ΔE_{HB}
−H	1.733	34.6	27.5	24.9	6.4
$-N(CH_3)_2$	1.715	36.0	29.6	27.1	5.7
$-NH_2$	1.715	35.9	29.7	27.3	6.3
$-OCH_3$	1.721	35.3	28.6	26.1	6.1
−OH	1.724	35.0	28.7	26.2	6.1
$-CH_3$	1.727	35.0	28.3	25.7	6.2
$-SCH_3$	1.750	33.4	25.7	23.0	7.6
−SH	1.752	33.4	25.7	23.1	7.2
−F	1.740	33.9	26.7	24.1	6.9
$-CH{=}CH_2$	1.750	33.6	26.0	23.4	6.6
$-C{\equiv}CH$	1.758	32.9	25.2	22.0	7.1
−Cl	1.749	33.3	25.7	23.1	7.1
$-COCH_3$	1.769	31.7	22.7	19.8	7.4
−COOH	1.775	31.6	23.0	20.0	7.6
−CHO	1.782	31.1	21.9	18.8	8.0
$-CF_3$	1.770	31.7	23.6	20.8	7.8
−CN	1.783	30.8	21.9	19.0	8.2
$-NO_2$	1.801	29.5	19.3	16.0	8.7

[a] All energies are given in kcal mol^{-1}. [b] solv1:chloroform, solv2: acetonitrile.

Considering the fact that the proton exchange is observed experimentally in $CDCl_3$ solution, we also employed PCM calculations to investigate the solvent effect. The results show that the ΔE_a value decreases significantly from 34.6 kcal mol^{-1} in the gas phase to 27.5 kcal mol^{-1} in chloroform solution, and further to 24.9 kcal mol^{-1} in acetonitrile solution; the proton exchange tends to proceed in a more polar medium, which can be ascribed to the ion pair feature in the transition state. Quantitatively, the tendency is easy to understand from the fact that the transition state represents a significantly larger dipole moment than the complex (9.87 vs 4.32 D at the B3LYP/6-31+G(d,p) level).

Proton Exchanges between Substituted Phenols and NH_3. To investigate the substituent effect upon the proton exchange, several *para*-substituted phenol−NH_3 systems were taken into account. Table 2 collects the calculated interatomic distances of the transition structures between the phenolic oxygen and the exchanged proton, *d*(O···H) (all of the values refer to the average of two O···H contacts). Also listed are the activation energies of proton exchanges in the gas phase, in chloroform and acetonitrile solutions, and the BSSE-corrected interaction energies (ΔE_{HB}) of the phenols with NH_3 in the reactants or products.

As can be seen from these data, the ΔE_a values for the substituted phenol−NH_3 systems span over a relatively narrow range, from 29.5 to 36.0 kcal mol^{-1}. The introduction of electron-withdrawing groups at the *para*-position of phenol

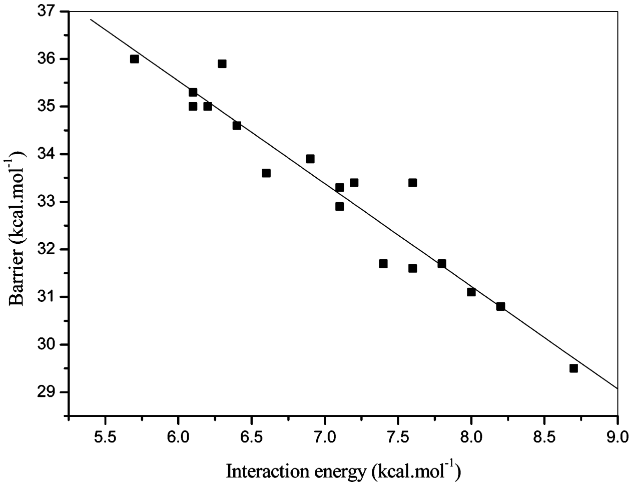


Figure 4. Correlation between the interaction energy of the hydrogen-bonded complex and the barrier of proton exchange.

appreciably reduces the barrier, whereas opposite effects are probed for electron-donating substituents. For example, the CF_3 substituent lowers the barrier height by about 3 kcal mol^{-1} as compared to the parent system; the NO_2 substituent gives rise to an even more pronounced effect, from 34.6 to 29.5 kcal mol^{-1}. This is consistent with the fact that the overall electron-withdrawing ability of the NO_2 group is stronger than that of the CF_3 group. For the most powerful electron-donating group, $N(CH_3)_2$, our calculation predicts an increase of 1.4 kcal mol^{-1} in the barrier height relative to the parent system. Similar effects, although being somewhat small, are also observed for other electron-donating groups (e.g., CH_3, OH). This substituent effect is entirely consistent with that on the hydrogen bonding or proton transfer in the phenol−NH_3 complexes for which the *para*-electron-withdrawing substituents of the phenol lead to increase the hydrogen-bond interaction with NH_3, and therefore favor the proton transfer from phenol to NH_3, whereas the electron-donating substituents impede the occurrence of proton transfer.[7] The consistency indicates that the proton exchange between phenol and NH_3 has close ties with the hydrogen bonding or proton transfer, as disclosed by the IRC analysis for the parent system. Moreover, we found that there exists a good linear correlation between the activation energy of proton exchange and the interaction energy of phenol with NH_3, as depicted graphically in Figure 4. The correlation coefficient is as high as 0.96.

In the above arguments, we have shown that the transition state is also involved in hydrogen bonding-like interactions. According to the calculations, the d(O···H) values in the transition states of substituted phenol−NH_3 systems lie between 1.715 and 1.801 Å (see Table 2), the electron-withdrawing substituents elongate the O···H interatomic distance, and the electron-donating ones cause a shrinkage of this distance. For each system, a BCP between the H and O atoms has been located, and both the electron density at this point and its Laplacian are shown to increase with the electron-donating ability of the *para*-substituted group and to decrease with the presence of electron-withdrawing substituents. These results manifest that the electron-donating substituents enhance the interactions of O···H in the transition states, while the electron-withdrawing substituents yield reverse effect. This is just contrary to the situation of the hydrogen-bonded phenol−NH_3 complexes (reactant or product), because the phenolic OH group is a proton donor in the stable complexes, whereas in the transition states it actually acts as a proton acceptor. Additionally, it is demonstrated from the present results that it is the proton transfer (or phenol−NH_3 hydrogen bonding) but not the phenoate−NH_4^+-like ion pair interaction that plays an important role in the proton exchange, although the latter may provide significant electrostatic stabilization to the transition state.

TABLE 3: Calculated Interatomic Distances (in Å) between the Phenolic Oxygen and the Exchanged Proton, d(N···H), the Activation Energies of Proton Exchanges, and the BSSE-Corrected Interaction Energies for the Phenol−Amine Complex[a]

	d(N···H)	ΔE_{HB}	ΔE_a	$\Delta E_{a,solv1}$[b]	$\Delta E_{a,solv2}$[b]
phenol−NH_3	1.853	6.4	34.6	27.5	24.9
phenol−CH_3NH_2	1.820	7.3	29.6	23.0	20.5
phenol−$(CH_3)_2NH$	1.808	7.3	26.1	20.9	19.2
phenol−piperidine	1.799	7.7	24.7	19.0	16.8
phenol−piperazine	1.803	7.4	24.2	19.0	17.1
2,6-di-mephenol−NH_3	1.918	4.8	33.3	26.7	24.0
phenol−(t-Bu)$_2$NH	1.894	5.1	22.1	17.3	15.7
2,6-di-t-buphenol−NH_3	1.871	3.0	31.5	25.3	22.7
2,6-di-t-buphenol−$NH(CH_3)_2$	1.875	3.4	22.1	17.0	15.0

[a] All energies are given in kcal mol^{-1}. [b] solv1:chloroform, solv2: acetonitrile.

The solvent effects were also examined for all substituted phenol−NH_3 systems. Our calculations using the PCM method show that the ΔE_a values are reduced by 6.1−10.3 kcal mol^{-1} in the chloroform solution, and by 8.5−13.5 kcal mol^{-1} in the acetonitrile, as compared to the corresponding values in a vacuum. As a result, some systems such as 4-nitrophenol−NH_3 represent a considerably low barrier of proton exchange (<20 kcal mol^{-1}) and are likely to be observable in real environment.

Proton Exchange in Phenol−Amine Systems. In Table 3 are listed the interatomic distances of H···N, d(N···H), the interaction energies of the hydrogen-bonded phenol−amine complexes, as well as the corresponding activation energies of proton exchange without and with consideration of the solvent effects. As can be seen, the hydrogen-bonding interactions in all phenol−amine complexes are stronger than that in the parent system, because of larger hydrogen-bond basicity of amine relative to NH_3. The d(N···H) values are shortened by 0.03 Å for phenol−CH_3NH_2, and by ca. 0.05 Å for other complexes; the ΔE_{HB} values with BSSE corrections increase by about 1 kcal mol^{-1}. As one might expect, these systems represent lower activation energies, which range from 24.2 to 29.6 kcal mol^{-1}, lower than that of the parent system by 5−10 kcal mol^{-1}. Especially, the phenol−piperazine system for which fast proton exchange was exactly observed[23] gives a considerably low barrier, 24.2 kcal mol^{-1}. When the polarization effect of the solvent is considered, the ΔE_a value is further reduced to 19.0 kcal mol^{-1} (in chloroform) and 17.1 kcal mol^{-1} (in acetonitrile). Such a low barrier demonstrates the reasonability of the present intracomplex proton exchange mechanism to a great degree. Additionally, it is noteworthy that, for the four phenol−amine systems, there also exists a general trend that the larger is the ΔE_{HB} value of the complex, the lower is the ΔE_a value of the proton exchange. However, these systems do not conform to the correlation (ΔE_a vs ΔE_{HB}) established for the *para*-substituted phenol−NH_3 systems, which will overestimate seriously the proton exchange barriers of them. For instance, the hydrogen-bonded interaction energy for the 4-acetylphenol−NH_3 complex is calculated to be 7.4 kcal mol^{-1}, roughly equal to that for the phenol−piperazine complex; this system, however, gives a significantly higher barrier of proton exchange than the latter. These results mean that the phenols tend to undergo proton exchange with the amines, preferably the secondary amines. On the other hand, it is revealed that, besides

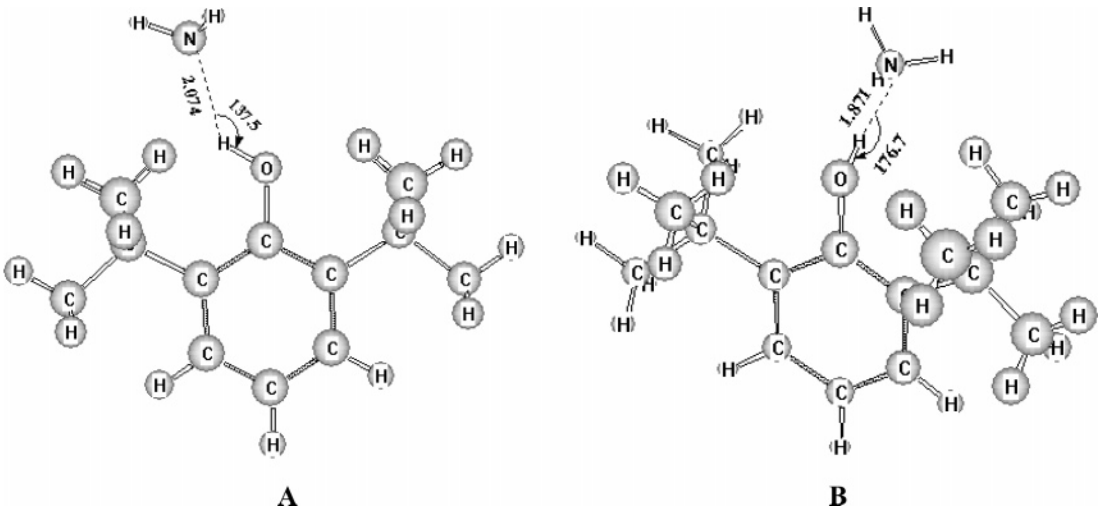


Figure 5. Two different configurations of the complex formed between 2,6-di-*tert*-butylphenol and NH_3.

the hydrogen bonding or proton transfer as mentioned above, the difficulty level of the flip of the ammonium-like moiety (as well as other factors) may affect significantly the proton exchanges between phenols and NH_3 or amines.

Proton Exchange Involving Sterically Hindered Phenols or Amines. The steric effects on hydrogen bonding and proton transfer have recently received considerable attention and been intensively studied.[45−48] In view of the close relationship between the hydrogen bonding or proton transfer and the proton exchange, herein four hindered systems, 2,6-dimethylphenol−NH_3, 2,6-di-*tert*-butylphenol−NH_3, phenol−$NH(^tBu)_2$, and 2,6-di-*tert*-butylphenol−$NH(CH_3)_2$, have been investigated. The hydrogen-bonding interaction energy between 2,6-di-methylphenol and NH_3 is predicted by the B3LYP/6-31+G(d,p) calculation to be 4.8 kcal mol^{-1}, lower than that for the phenol−NH_3 complex by 1.6 kcal mol^{-1}. When the methyl groups proximal to the phenolic hydroxyl are replaced by *tert*-butyl groups, two hydrogen-bonding modes, as shown in Figure 5, have been observed. In complex A (Figure 5), the O−H···N hydrogen bond lies in the plane of the benzene ring but deviates from linearity by about 43° due to the effect of steric hindrance, and the interatomic distance of H···N is 2.074 Å, while in complex B, this hydrogen bond remains essentially linear and lies almost perpendicular to the benzene ring with the H···N distance being remarkably shorter than that in complex A (1.871 Å). A similar perpendicular orientation has also been discerned in a recent study on the hydrogen bond between 2,6-di-*tert*-butyl-4-methylphenol and fatty acid esters.[45] These two complexes are predicted to have comparable stability, with the one with perpendicular configuration being lower in energy than the other by 0.4 kcal mol^{-1}. It suggests in this case that the loss of conjugation between the lone pair of hydroxyl oxygen and the aromatic π electron and the increased hydrogen bonding due to the perpendicular orientation achieve a certain subtle balance. Nevertheless, the hydrogen-bond strength is weaker than the less hindered 2,6-dimethylphenol−NH_3 system ($\Delta E_{HB} \approx 3.0$ kcal mol^{-1} for complex B). As for the complex 2,6-di-*tert*-butylphenol−$NH(CH_3)_2$, only the perpendicular hydrogen-bond mode has been obtained, and the interaction energy between the two partners is 3.4 kcal mol^{-1}, slightly larger than the 2,6-di-*tert*-butylphenol−NH_3 complex because of the stronger hydrogen-bond basicity of $NH(CH_3)_2$. Similarly, a substitution of $NH(^tBu)_2$ for $NH(CH_3)_2$ results in a significant weakening of the hydrogen bonding to the phenol, cf., the ΔE_{HB} values of the two systems phenol−$NH(^tbu)_2$ and phenol−$(CH_3)_2NH$ presented in Table 3.

We investigated the proton exchanges for all of these four hindered systems. The transition state has been located for each system, including the ones having the O−H···N hydrogen bond perpendicular to the benzene ring, which means that the proton exchange can take place in the sterically hindered systems. Additionally, the phenol−$NH(^tBu)_2$ and 2,6-di-*tert*-butylphenol−$NH(CH_3)_2$ complexes, although having a weaker hydrogen bond than the phenol−NH_3 system, represent reasonably low activation energies of proton exchange (ca. 22 kcal mol^{-1}), much lower than that for the parent system. The ΔE_a values of the other two systems, 2,6-dimethylphenol−NH_3 and 2,6-di-*tert*-butylphenol−NH_3, are 33.3 and 31.5 kcal mol^{-1}, respectively. These indicate that the more hindered system gives a lower barrier. Furthermore, according to the PCM calculations, these values of activation energy will be reduced by 4.7−6.6 kcal mol^{-1} in chloroform solution and by 6.4−9.2 kcal mol^{-1} in acetonitrile solution (see Table 3). This steric effect supports further the importance of the flip of ammonium-like moiety in the proton exchange processes, because the more steric hindrance in the hydrogen-bonded complex, the weaker is the interaction between the two moieties after proton transfer, which thus favors the flip of the ammonium-like moiety along the oxygen of the phenoate to accomplish the proton exchange.

Proton Exchange between Phenol Radical Cation and NH_3. Proton transfers of ionized phenol to NH_3 or amines have been investigated extensively as models of some biologically important redox reactions.[7,8,13,49,50] It is well documented that one-electron oxidation of a phenol−amine hydrogen-bonded complex often leads to spontaneous transfer of the phenolic proton to NH_3 or amine.[7,13] Our present calculations show that an optimization starting with PhOH−NH_3 geometry was actually converged to the proton-transferred species, which reproduces prior results of other groups and indicates that the proton transfer from phenol radical cation to NH_3 should be a barrierless process. As for the proton exchange, we have successfully obtained the radical cationic transition state whose structure is quite similar to that for the neutral phenol−NH_3 system, except that the phenoxyl radical and ammonium moieties are more separated (the N···O distances in the neutral and radical cationic transition states are 2.322 and 2.565 Å, respectively). The energetic difference between the transition state and the proton-transferred complex $[PhO{-}NH_4]^{\cdot+}$ is predicted to be only 5.2

kcal mol^{-1}, close to the barrier height (0.23 eV) of proton exchange between PhOH$^{\cdot+}$ and ND$_3$ gained at the MP2/6-31G-(d) level of theory.[19] This result demonstrates that the proton transfer in the phenol−NH$_3$ system, during the course of oxidation, may be concomitant with fast proton exchange. Meanwhile, it provides further evidence for the importance of proton transfer in determining the proton exchange.

Conclusions

In this work, an identity intracomplex proton exchange mechanism has been suggested to account for the experimental observation. Density functional theory calculations were then performed at the B3LYP/6-31+G(d,p) level of theory to validate the proposed mechanism. It has been found that the phenol−NH$_3$ (parent) system possesses a barrier height (34.6 kcal mol^{-1}) of proton exchange. An introduction of electron-withdrawing substituents on the *para*-site of phenol causes the decrease of the barrier height, whereas electron-donating substituents give the opposite effects. Proton exchanges between the phenol and amines have also been examined. It is revealed that the phenol tends to undergo proton exchange with the amines, preferably the secondary amines, and some systems exhibit a reasonably low barrier (ca. 24 kcal mol^{-1} in the gas phase). It has also been demonstrated that proton exchanges in sterically hindered systems are feasible and even more facile. For all of these systems, the proton exchange barriers would be significantly reduced when the solvent effects were considered, which can well be attributed to the ion pair feature of the transition state. From these results, it can be concluded that both the proton transfer (or hydrogen bonding) and the flip of ammonium-like moiety play important roles in the proton exchange as the IRC analysis suggested. Additionally, our calculations show that the phenol radical cation−NH$_3$ system represents a barrierless proton transfer and a quite low barrier (5.2 kcal mol^{-1}) of proton exchange, which supports further the importance of proton transfer in the proton exchange.

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Supporting Information Available: Cartesian coordinates and total energies of all hydrogen-bonded complexes and transition states at the B3LYP/6-31+G(d,p) level of theory. This material is available free of charge via the Internet at http://pubs.acs.org.

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