Theoretical Study of Hydrogen-Bonded Complexes of Chlorophenols with Water or Ammonia: Correlations and Predictions of pK_a Values

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A simple practical method for predicting the acidity constants (as pK_a values) of chlorophenols is proposed based on density functional theory calculations of a series of hydrogen-bonded complexes of phenol and 19 different congeners of chlorophenol, with a single probe molecule, either water or ammonia. Relevant structural parameters and molecular properties of these complexes, primarily involving the acidic hydroxyl group, are examined and plotted against the known pK_a values of 14 chlorophenols and phenol. Strong linear correlations are found for these compounds. Such correlations are used to determine the pK_a values of five chlorophenols whose experimental acidities have large uncertainties. Similar predicted pK_a values are obtained by using different structural parameters and molecular properties for the complexes with either probe molecule. The study may be extended to determine the acidity of other compounds with a single acidic functional group.

1. Introduction

Chlorophenols (CPs) are well-known to be pollutants of environmental waters and soils and are mainly found in effluent discharges from industries, such as those producing paper and pesticides.[1] They are used as general biocides and wood preservatives and may also be introduced into the environment as the products of metabolic degradation of chlorinated pesticides[2,3] and byproducts of chlorine treatment of drinking water.[4] Chlorophenols can represent serious health hazards due to their inherent toxicity and relative persistence in the environment.[5] As a consequence, the US Environmental Protection Agency has listed 2-chlorophenol (2-CP), 2,4-dichlorophenol (2,4-DCP), 2,4,6-trichlorophenol (2,4,6-TCP), and pentachlorophenol (PCP) as priority pollutants, among eleven phenolic compounds.[6]

The chemical behavior and environmental impact of chlorophenols are strongly dependent on the speciation of the molecule in matrices. The ionized form is relatively hydrophilic and more influenced by electrostatic interactions, while the neutral form is more lipophilic and has higher membrane permeability. The ionization of a weakly acidic chlorophenol is described by the acid dissociation constant (or acidity constant, K_a), which is one of the most fundamental properties that affects the fate and transport of chlorophenols in the natural environment. Specifically, the acidity constant of a chlorophenol determines not only its adsorption, mobility, deactivation, and toxicity in biological systems and the environment, but also the efficiency and accuracy of quantitative measurements involving separation and extraction steps.[7,8] Thus, the accurate determination of K_a values (more conveniently expressed as pK_a, the negative logarithm of the acidity constant) of chlorophenols is critical to the understanding of the fate and biological activity of these compounds in the environment.

The acidities (pK_a) of several chlorophenols have been determined by different experimental methods, such as potentiometric titration,[9] spectrophotometry,[10] and chromatography[11−13] in aqueous or aqueous−organic solvent mixtures, and by theoretical methods using free energy calculations.[14−16] Of the 19 possible congeners of chlorophenol (see below), the aqueous pK_a values for five chlorophenols have large uncertainties. The acidity of a compound measures the extent of proton transfer between the molecule and the basic solvent. As a popular theoretical method, the acidity of a compound can be determined by calculating free energies of the compound and the corresponding anion in a continuum medium representing the solvent.[15−17] Alternatively, a large enough set of solvent molecules could be included to explicitly describe acid−solvent structure and interactions.[18,19] However, such a calculation can be complicated and time consuming. As a simple variation of the approach, the acidity of an acid could be predicted from its interaction with a single solvent molecule, as will be explored in this study.

An acid and a base interact strongly at the molecular level, forming a hydrogen-bonded complex. The hydrogen bonding would result in significant changes in the molecular properties at both the acid and the base molecule. Although an actual proton transfer from the acid to the base may not occur without adequate solvation, the covalent bond involving the proton on an acid is considerably weakened under the influence of even a single base molecule. The elongation of the covalent bond and the red shift of the harmonic frequency for the stretch vibration of the bond can be observed when comparing to those of the isolated acid molecule.[20−22] These changes in molecular parameters derived from the hydrogen-bonded complexes may strongly correlate with acidity and indicate the relative strength of that acid.

Hydrogen-bonded complexes involving phenol have been extensively studied by means of both molecular beam spectroscopy experiments[23−27] and theoretical investigations.[27−32] Very few studies have been published for chlorophenol complexes.[28] So far no systematic work has been reported for the complete series of chlorophenol complexes with water or ammonia. Recently, hydrogen-bonded complexes involving phenol and four fluoro- or nitro-phenol derivatives with ammonia have been studied by Abkowicz-Bienko et al. using the density functional method.[32] They found that several molecular

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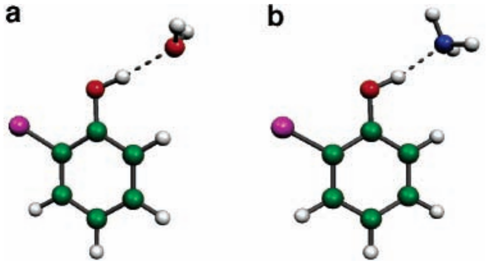

Figure 1. Binding site and configuration (a) for a hydrogen-bonded 2-CP−H_2O complex and (b) 2-CP−NH_3 complex.

parameters resulting from the phenol−ammonia complexes, such as the O−H bond lengths, the O−H stretching frequencies, the hydrogen bond lengths, and the deprotonation energies, correlated reasonably well with the acidity of phenols in the liquid phase. Moreover, the ammine basicity has been found to correlate with the oxidation potentials, product structures, and shapes of potential surfaces in the hydrogen-bonded phenol−ammine complexes.[33]

In the present work, density functional theory (DFT) is used to perform calculations at the B3LYP/611++(d,p) level on the complete series of chlorophenols forming hydrogen-bonded complexes with an ammonia or a water subunit. The DFT/B3LYP method has been shown in the literature to provide reliable structural and vibrational information on the formation of hydrogen-bonded complexes.[27,32] Linear correlations of relevant molecular properties (mainly involving the acidic hydroxyl group of phenols) resulting from the formation of hydrogen-bonded complexes are explored with reliable experimental pK_a values of 14 chlorophenols in the aqueous phase. The pK_a values of the remaining five chlorophenols, whose experimental data are either lacking or of poor quality, are determined by employing the linear correlations. Similar pK_a values can be predicted by using different structural parameters and molecular properties for the complexes with a single probe molecule, either water or ammonia.

2. Method of Calculation

The complete series of chlorophenols are considered to form hydrogen-bonded complexes with ammonia and water. The series includes three monochlorophenols (2-CP, 3-CP, and 4-CP), six dichlorophenols (2,3-DCP, 2,4-DCP, 2,5-DCP, 2,6-DCP, 3,4-DCP, and 3,5-DCP), six trichlorophenols (2,3,4-TCP, 2,3,5-TCP, 2,3,6-TCP, 2,4,5-TCP, 2,4,6-TCP, and 3,4,5-TCP), three tetrachlorophenols (2,3,4,5-TeCP, 2,3,4,6-TeCP, and 2,3,5,6-TeCP), and pentachlorophenol (PCP). The equilibrium geometries and harmonic frequencies of binary complexes of phenol and all 19 chlorophenols with water or ammonia, along with the monomers, have been calculated by using the three-parameter hybrid B3LYP density functional method with the extended basis set 6-311++G(d,p). All calculations are implemented in the Gaussian 98 package.[34]

We focus mainly on the most stable conformation of the molecule-probe complexes, as shown in Figure 1 for 2-CP complexes. For the isolated chlorophenol, the syn conformer is more stable due to intramolecular hydrogen bonding.[35] However, when a probe molecule is introduced, the anti conformer, where the hydroxyl hydrogen is placed away from the closest neighboring chlorine, becomes more stable. This is because a much stronger intermolecular hydrogen bond forms in the anti conformer complex than that in the syn conformer complex. The water or ammonia, as the probe molecule, is positioned at the end of the hydroxyl group of the chlorophenol, and the C_s symmetry is conserved for the hydrogen-bonded system. Specifically, water is positioned toward the hydroxyl hydrogen of the chlorophenol molecule, and the two hydrogens are placed symmetrically above and below the molecular plane of the chlorophenol, as shown in Figure 1a. It should be pointed out that for di-ortho chlorophenols, such a configuration for complexes with water is at the top of the low rotational barrier (ca. 0.3 kcal mol^{-1}) for the water about the hydrogen bond axis. The rotation leads to the water approximately coplanar with the chlorophenol, a minimum energy configuration with C_1 symmetry. To maintain consistency among the various chlorophenols, however, the C_s configuration with the symmetrical arrangement of the water hydrogens, as in the mono-ortho chlorophenols, is considered for all di-ortho chlorophenols. For an ammonia complex, the ammonia is positioned with its lone pair pointing directly toward the hydroxyl hydrogen of the chlorophenol, as shown in Figure 1b.

The acidity of a chlorophenol is a measure of its ability to release a proton from the hydroxyl group to a base such as water or ammonia. In the acid−base complex, the proton of the hydroxyl group is pulled by the lone electron pair of the base in the form of hydrogen bonding. Consequently, the hydroxyl bond length is expected to increase while the hydroxyl bond strength decreases. As a result, several structural or molecular properties of the complex are expected to correlate with the acidity of the chlorophenol. These properties include the O−H bond lengths, r(O−H), the O−H stretching frequencies, ν(O−H), and the C−O bond lengths, r(C−O), which are all related to the hydroxyl group. In addition, the acidity of a chlorophenol should correlate with the strength of hydrogen bonding in the acid−base complex, as represented by the hydrogen bond length, r(OH···O) or r(OH···N), and the binding energy of the complexes, ΔE_{hb}. The binding energy ΔE_{hb}, also recognized as the hydrogen bond energy, is given as the difference between the total electronic energy of the complex and the sum of those of the monomers. The basis set superposition error (BSSE) is not included in the binding energies in this study for two reasons. First, the magnitude of BSSE (ca. 0.2 kcal mol^{-1}) is expected to be small compared to the binding energies (6−11 kcal mol^{-1}). Second, the BSSE is expected to be nearly constant for the same configurations of all complexes considered and will not be reflected in the correlations. It should be noted that other molecular properties, such as the torsional frequency of the hydroxyl group and the C−O stretching frequency, may also relate to the acidity of a chlorophenol. However, these properties are strongly affected by steric effects and coupling with ring vibrations and will not be described in the study. Phenol can be regarded as a parent compound for all chlorophenols, and, as a result, phenol complexes with ammonia and water are included for comparison.

The selected molecular properties of the complexes are plotted against the experimental pK_a values of the chlorophenols in aqueous solution. A least-squares linear regression is then performed on the properties of the complexes of phenol and 14 chlorophenols whose pK_a values are reasonably accurate and cover a wide range (from 4.70 to 9.99). Table 1 summarizes the available experimental pK_a values for phenol and 19 chlorophenols from the literature.[8,36−42] There are large uncertainties in the pK_a values for five of the chlorophenols, 2,3,5-TCP, 2,3,6-TCP, 2,4,5-TCP, 2,4,6-TCP, and 2,3,4,5-TeCP, and the data are not included in the regression fit. The strength of the correlations can be assessed by the correlation coefficient, R^2, and the standard deviation, S.D., from the regression calculations. The linear correlations, once established for phenol

TABLE 1: The pK_a Values for Phenol and Chlorophenols Obtained from Different References in Aqueous Solution at 25 °C

	pK_a lit. data[a]								
compd	A	a	b	c	d	e	f	g	h
phenol	9.92	9.92	9.91	9.99	9.9	9.99	10.00	9.9	
2-CP	8.52	8.52	8.41	8.55	8.3	8.56		8.5	8.56
3-CP	8.79	8.79	8.85	9.10	8.9		9.02		
4-CP	9.37	9.37	9.29	9.43	9.2		9.37	9.4	
2,3-DCP	7.71	7.71	7.66	7.44	7.6				
2,4-DCP	7.90	7.90	7.85	7.85	7.8	7.89	7.85	7.9	7.89
2,5-DCP	7.30		7.30		7.3				
2,6-DCP	6.78	6.78	6.69	6.78	6.6	6.79			
3,4-DCP	8.62	8.62	8.62	8.63				8.6	
3,5-DCP	8.25	8.25	8.25	8.18	8.1				
2,3,4-TCP	6.97	6.97	6.97						
2,3,5-TCP	**6.86**								
2,3,6-TCP	**5.64**	5.80	6.60						
2,4,5-TCP	**7.03**	6.72	6.81	7.37	6.9	7.40			
2,4,6-TCP	**5.61**	5.99	6.00			6.23		7.4	5.99
3,4,5-TCP	7.80			7.84		7.84			
2,3,4,5-TeCP	**6.63**	5.64	5.64			5.14			
2,3,4,6-TeCP	5.22	5.22	5.21		5.2	5.35		5.4	
2,3,5,6-TeCP	5.03	5.03	5.03			5.22			
PCP	4.74	4.74	4.72		4.7	4.70	4.70	4.7	4.70

[a] Column A: pK_a data without boldface used for correlations in this study; compounds with predicted corresponding pK_a values are in boldface. Column a: pK_a from ref 36. Column b: from ref 37 (averaged experimental data). Column c: from ref 38. Column d: from ref 39. Column e: from ref 40. Column f: from ref 41. Column g: from ref 42. Column h: from ref 8.

TABLE 2: Calculated C−O Bond Lengths r(C−O) (Å), O−H Bond Lengths r(O−H) (Å), and OH Stretching Frequencies ν(O−H) (cm^{-1}) for Phenol and Chlorophenol Complexes with Water or Ammonia

	water complex			ammonia complex		
compd	r(C−O)	r(O−H)	ν(O−H)	r(C−O)	r(O−H)	ν(O−H)
phenol	1.362	0.972	3651.0	1.356	0.984	3415.9
2-CP	1.353	0.974	3622.2	1.347	0.987	3356.8
3-CP	1.358	0.973	3633.2	1.352	0.986	3370.8
4-CP	1.360	0.973	3638.9	1.354	0.985	3381.1
2,3-DCP	1.351	0.975	3604.9	1.344	0.988	3325.9
2,4-DCP	1.351	0.975	3609.9	1.345	0.988	3329.7
2,5-DCP	1.349	0.975	3604.7	1.342	0.990	3296.1
2,6-DCP	1.343	0.976	3599.2	1.336	0.992	3265.3
3,4-DCP	1.357	0.974	3623.8	1.351	0.987	3346.7
3,5-DCP	1.354	0.975	3611.7	1.348	0.989	3316.6
2,3,4-TCP	1.350	0.975	3598.7	1.343	0.989	3306.4
2,3,5-TCP	1.347	0.976	3586.8	1.341	0.991	3268.9
2,3,6-TCP	1.341	0.977	3585.4	1.334	0.995	3216.4
2,4,5-TCP	1.348	0.975	3594.6	1.342	0.991	3276.7
2,4,6-TCP	1.342	0.977	3585.5	1.335	0.995	3220.6
3,4,5-TCP	1.354	0.975	3606.5	1.347	0.990	3300.0
2,3,4,5-TeCP	1.347	0.976	3583.5	1.340	0.992	3254.6
2,3,4,6-TeCP	1.340	0.977	3575.4	1.333	0.996	3190.5
2,3,5,6-TeCP	1.339	0.978	3573.5	1.332	0.996	3193.5
PCP	1.339	0.978	3570.2	1.331	0.998	3174.4

and 14 chlorophenols, are used to predict the pK_a values for the five other chlorophenols (with large uncertainties in pK_a).

3. Results and Discussion

3.1. Molecular Properties of Chlorophenols in the Complexes.

Table 2 lists the O−H and C−O bond lengths and O−H harmonic stretching frequencies of the chlorophenol complexes (along with the phenol complexes for comparison) in the conformations shown in Figure 1. The complete geometric and thermodynamic data of the complexes with water or ammonia are available in the Supporting Information, Tables 1 through 4. No experimental data for the chlorophenol complexes are available for comparison. For phenol−water and phenol−ammonia complexes, the calculated OH stretching harmonic frequencies, 3651 and 3415.9 cm^{-1}, are reliable compared with the corresponding experimental anharmonic values of 3524[27] and 3294 cm^{-1}.[43]

As shown in Table 2, the O−H bond length, r(O−H), increases systematically with the number of chlorine substitutions, and is, overall, greater in the complexes with ammonia than that with water. It increases from 0.972 Å to 0.978 Å in the complexes with water and 0.984 Å to 0.998 Å with ammonia. For a given chlorophenol, the O−H bond length with water is about 0.01−0.02 Å shorter than that with ammonia, and the difference increases with the number of substitutions. For a given number of chlorine substitutions, r(O−H) decreases in the order of ortho, meta, and para substituents with respect to the hydroxyl group of chlorophenols. For example, the r(O−H) values for the water complexes with 2,6-DCP, 2,5-DCP, and 3,4-DCP are 0.976, 0.975, and 0.974 Å, respectively. The same trend is also found for the ammonia complexes.

All of the observations for r(O−H) appear to reflect the strength of the hydrogen bond in the complexes. It is known that the hydrogen bond is reflected in the acidity of the hydrogen bond donor (chlorophenol) and the basicity of the hydrogen bond acceptor (water or ammonia). A stronger hydrogen bond to a base results in a larger OH bond length on the phenol and other changes at the acid molecule. Chlorine substitutions enhance the acidity of a chlorophenol as the electronegative chlorine atoms withdraw electron density from the hydroxyl group through the phenol ring. As a result, one would expect a progressive increase in acidity with the number of chlorine substitutions, and for a given number of substitutions, the acidity increases in the order of the para, meta, to ortho position. The strength of hydrogen bonding, as reflected by r(O−H), follows the same trends in acidity. On the other hand, ammonia is a stronger acceptor of hydrogen bonding than water because of the larger proton affinity of ammonia (204 kcal mol^{-1}) versus water (116.5 kcal mol^{-1}).[27] Consequently, the hydrogen bond is stronger for complexes with ammonia than with water, consistent with the increasing r(O−H) of the complexes.

The lengthening of the OH bond in the complexes indicates the weakening of the bond, causing a decrease, or red shift, in the stretching frequency of the bond, ν(O−H). As shown in Table 2, the calculated harmonic frequencies are in the range of 3622.2−3570.2 cm^{-1} for chlorophenol complexes with water and 3356.8−3174.4 cm^{-1} with ammonia. The red shift increases systematically with the number of chlorine substitutions. For example, the red shift is 29 cm^{-1} for 2-CP−water, and is increased to 79 cm^{-1} for PCP−water. Similarly, the red shift is 59 cm^{-1} for the 2-CP−ammonia complex, from the phenol complex, and is increased to 241 cm^{-1} for PCP−ammonia complex. The red shift in ν(O−H) thus correlates with the O−H bond length. Figure 2 (lower panel) shows a strong linear correlation ($R^2 = 0.9927$) between ν(O−H) and r(O−H) for the complexes with ammonia. Similar linear correlations exist for the complexes with water, as shown in Figure 2 (upper panel). It should be noted that hydrogen bonding in the complexes with water is subject to larger steric interference, which will be discussed in a later section, and, as a result, the correlation between ν(O−H) and r(O−H) is divided into two groups, one with di-ortho substitutions and the other with mono-ortho substitutions.

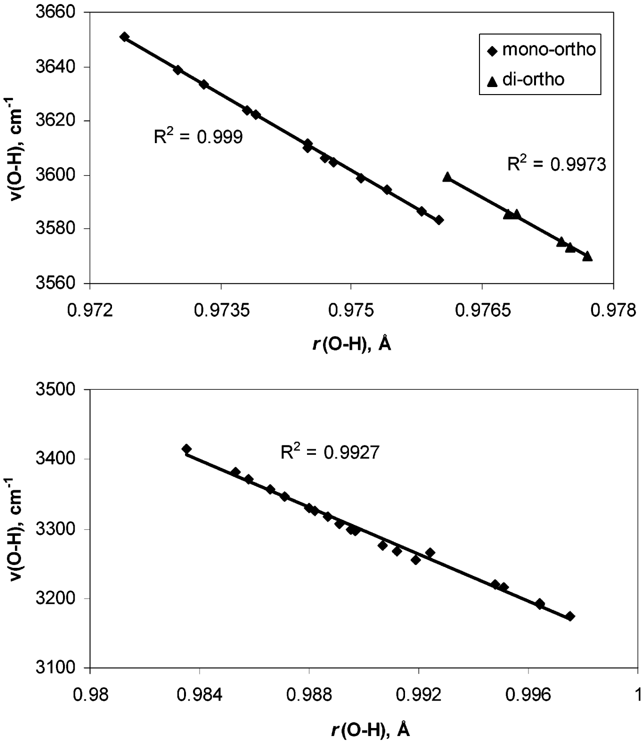

Figure 2. Correlation between the O−H stretching frequency (cm^{-1}) and the O−H bond length (Å) for complexes of phenol and all 19 chlorophenols. The upper panel is for the complexes with water and the lower panel is for the corresponding complexes with ammonia.

In addition to the OH bond length and stretching harmonic frequency, the C−O bond length, r(C−O), of the chlorophenol complexes reflects the strength of hydrogen bonding and, therefore, exhibits systematic correlations with the chlorine substitutions or with the acidity of chlorophenols. The acidity of a chlorophenol increases with the degree of electron withdrawing from the hydroxyl oxygen by the substituted chlorine through the phenol ring. The immediate consequence of such an effect is the reduction in the C−O bond length. As a result, the C−O bond length is expected to decrease with increasing chlorine substitution and, for a given number of substitutions, in the order of the para, meta, and ortho positions. The r(C−O) values in Table 2 confirm such an expectation. For example, the r(C−O) values are 1.358, 1.357, and 1.354 Å for the complexes of 3-CP, 3,4-DCP, and 3,4,5-TCP, respectively, with water, and are 1.352, 1.351, and 1.347 Å with ammonia. For the monochlorophenols, the r(C−O) values are respectively 1.360, 1.358, and 1.353 Å for the complexes of 4-CP, 3-CP, and 2-CP with water, and are 1.354, 1.352, and 1.347 Å with ammonia. It should also be noted that the r(C−O) values for the complexes with ammonia are 0.006−0.008 Å shorter than those for the corresponding complexes with water, consistent with the fact that ammonia is a stronger base than water.

3.2. Intermolecular Properties of the Complexes. Table 3 summarizes the calculated the hydrogen bond binding energies, ΔE_{hb}, hydrogen bond lengths, r(OH···O) or r(OH···N), and the corresponding hydrogen bond angles, ∠OHO or ∠OHN, of the complexes with water or ammonia. It should be noted that the calculated binding energy with ZPE correction for the phenol−water complex, 5.3 kcal mol^{-1}, is in excellent agreement with the experimental value of 5.48 kcal mol^{-1}.[31] No experimental binding energy for the phenol−ammonia complex is available for comparison. The calculated value, 7.2 kcal mol^{-1} with ZPE correction, is consistent with other theoretical values.[29]

TABLE 3: Calculated Binding Energies ΔE_{hb} (kcal mol^{-1}), Hydrogen Bond Lengths r(OH···O) or r(OH···N) (Å), and Hydrogen Bond Angles ∠OHO or ∠OHN (deg) for Phenol and Chlorophenol Complexes with Water or Ammonia

	water complex			ammonia complex		
compd	∠OHO	ΔE_{hb}[a]	r(OH···O)	∠OHO	ΔE_{hb}[a]	r(OH···N)
phenol	174.9	−7.2	1.879	168.2	−9.0	1.885
2-CP	174.6	−8.1	1.852	168.0	−10.1	1.853
3-CP	175.5	−7.9	1.862	168.3	−9.9	1.861
4-CP	176.3	−7.9	1.864	168.8	−9.8	1.866
2,3-DCP	174.9	−8.5	1.838	168.1	−10.6	1.840
2,4-DCP	176.2	−8.6	1.841	168.2	−10.6	1.840
2,5-DCP	177.8	−8.8	1.834	169.6	−11.1	1.827
2,6-DCP	147.4	−5.5	1.934	155.6	−8.2	1.833
3,4-DCP	177.0	−8.4	1.851	168.7	−10.4	1.849
3,5-DCP	178.0	−8.7	1.839	170.0	−10.9	1.838
2,3,4-TCP	176.7	−8.9	1.833	168.3	−11.0	1.832
2,3,5-TCP	177.2	−9.2	1.822	168.9	−11.6	1.816
2,3,6-TCP	148.0	−5.9	1.918	156.0	−8.7	1.810
2,4,5-TCP	178.3	−9.3	1.826	169.1	−11.6	1.818
2,4,6-TCP	148.9	−6.0	1.913	156.3	−8.9	1.812
3,4,5-TCP	179.0	−9.0	1.835	170.1	−11.2	1.830
2,3,4,5-TeCP	178.1	−9.5	1.819	169.0	−11.8	1.810
2,3,4,6-TeCP	149.1	−6.2	1.904	156.1	−9.1	1.801
2,3,5,6-TeCP	147.8	−6.2	1.913	154.7	−9.0	1.806
PCP	148.1	−6.4	1.909	154.7	−9.1	1.800

[a] Binding energy (not corrected for BSSE).

It is apparent from Table 3 that nearly linear hydrogen bonds form in the complexes of chlorophenols having mono-ortho substitutions. The hydrogen bond angles are typically 176° for the complexes with water and 169° for the complexes with ammonia. It is interesting that the hydrogen bonds with ammonia are more bent than those with water and are consistently about 11° from linearity. This is likely due to the repulsion between the hydrogen at the ortho position of the phenol ring and the two hydrogen atoms of ammonia, as shown in Figure 1b. It is a noticeable steric effect for the complexes with ammonia and is nearly absent for the complexes with water, as demonstrated by the two contrasting hydrogen bond angles. For the complexes with di-ortho substitutions, the hydrogen bond angles are dramatically different: 148° for the complexes with water and 155° for the complexes with ammonia. The large deviations from linearity apparently result from the strong repulsion from the ortho chlorine next to the ammonia or water. The bulky chlorine displaces the ammonia or water, causing a severely bent hydrogen bond and other serious steric effects in the hydrogen-bonded system. As a result, molecular properties associated with the complexes of chlorophenols with di-ortho substitutions are intrinsically different from those with mono-ortho substitutions and are expected to follow different patterns. Similar effects were reported for nitro or fluorophenol−ammonia complexes.[21] It is also important to note that the deviations from linearity are considerably larger for the hydrogen bond with water than that with ammonia. This is likely due to the weaker hydrogen bond with water, which is more vulnerable to steric distortion.

As shown in Table 3, the calculated binding energies and hydrogen bond lengths can be discussed separately in two different groups, one for the complexes with mono-ortho substitutions and the other with di-ortho substitutions. The two groups are expected to follow different patterns, as discussed above for the hydrogen bond angles. For the complexes with mono-ortho substitutions, the binding energy, ΔE_{hb}, systematically increases with the number of chlorine substitutions and is considerably larger in the complexes with ammonia than that with water. The ΔE_{hb} values range from -7.2 kcal mol^{-1} to -9.5 kcal mol^{-1} with water and from -9.0 kcal mol^{-1} to -11.8 kcal mol^{-1} for the complexes with ammonia. For a given chlorophenol, the binding energy with ammonia is about 2.0–2.3 kcal mol^{-1} larger than that with water, and the difference increases with the number of substitutions. The ΔE_{hb} values follow almost exactly as expected for the acidity of chlorophenols and the strength of hydrogen bonding in the complexes.

A larger binding energy corresponds to a shorter hydrogen bond length of the complex. Consequently, the hydrogen bond length, r(OH···O) or r(OH···N), is expected to decrease with the number of chlorine substitutions and is slightly shorter in the complexes with ammonia than that with water. The r(OH···O) values range from 1.879 Å to 1.819 Å with water, while the r(OH···N) values range from 1.885 Å to 1.810 Å for the complexes with ammonia.

For the complexes with di-ortho substitutions, both of the binding energies and the hydrogen bond lengths deviate substantially from those with mono-ortho substitutions. The ΔE_{hb} values range from -5.5 to -6.4 kcal mol^{-1} for the complexes with water and from -8.2 to -9.1 kcal mol^{-1} with ammonia. The deviations are larger with water (ca. 3.5 kcal mol^{-1}) than that with ammonia (ca. 2.9 kcal mol^{-1}). The large decreases in ΔE_{hb} for the complexes with di-ortho substitutions directly reflect the steric hindrance for hydrogen bonding in the complexes. Similarly, the hydrogen bond lengths, ranging from 1.934 to 1.904 Å with water and from 1.833 to 1.800 Å with ammonia, consistently follow the trends in the binding energies.

The severely bent hydrogen bonds for the complexes with di-ortho substitutions may also have large consequences for other molecular properties. This is particularly the case with the OH stretching frequencies as noted in the earlier section. Because of the weaker and less effective hydrogen bonding, the red shifts in the OH stretching frequencies are considerably reduced, and are smaller than those typical of the majority of the complexes. As a result, two different sets of linear correlations between ν(O–H) and r(O–H) are used in Figure 2 (upper panel), one with di-ortho substitutions and the other with mono-ortho substitutions.

3.3. Linear Correlations between the Selected Molecular Properties and the Acidity of Chlorophenols. The discussions in the two preceding sections suggest that there exist strong correlations of a number of molecular properties of the complexes with the acidity of the chlorophenols. Figures 3 through Figure 7 are plots of several selected molecular properties, r(O–H), r(C–O), ν(O–H), ΔE_{hb}, and r(OH···O) or r(OH···N), respectively, for the complexes of phenol and 14 chlorophenols against the experimental pK_a values. In each figure, the upper panel is for the complexes with water and lower panel is for those with ammonia. Linear regressions are performed and the results are shown in the plots along with the R^2 values.

It is clear from Figures 3 through 5 that strong linear correlations with the pK_a values of chlorophenols are obtained for the r(O–H), r(C–O), and ν(O–H) of the complexes, as indicated by high R^2 values (ca. 0.96). Specifically, the r(O–H) linearly increases with the acidity or decreases with the pK_a of chlorophenols (Figure 3). Both r(C–O) and ν(O–H) linearly decrease with the acidity or increase with the pK_a (Figures 4 and 5, respectively). These observations indicate that the degree of weakening in the O–H bond from the formation of hydrogen-bonded complexes with ammonia or water increases with the acidity of chlorophenols and is directly proportional to the level of acidity. It should be noted that two separate linear correlations of pK_a vs ν(O–H) exist for the water complexes, one with di-ortho substitutions and the other with mono-ortho substitutions, as shown in Figure 5 (upper panel). A similar pattern has already been found in the correlation of ν(O–H) vs r(O–H). Two sets

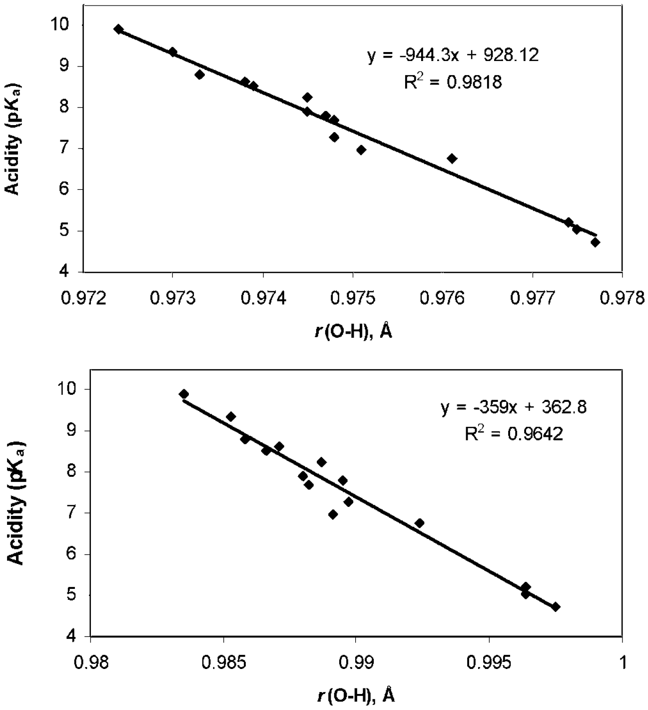

Figure 3. Correlation between the O–H bond length (Å) of complexes of phenol and 14 chlorophenols and the acidity (pK_a) of corresponding phenol compounds in aqueous solution. The upper panel is for the complexes with water and the lower panel is for the corresponding complexes with ammonia.

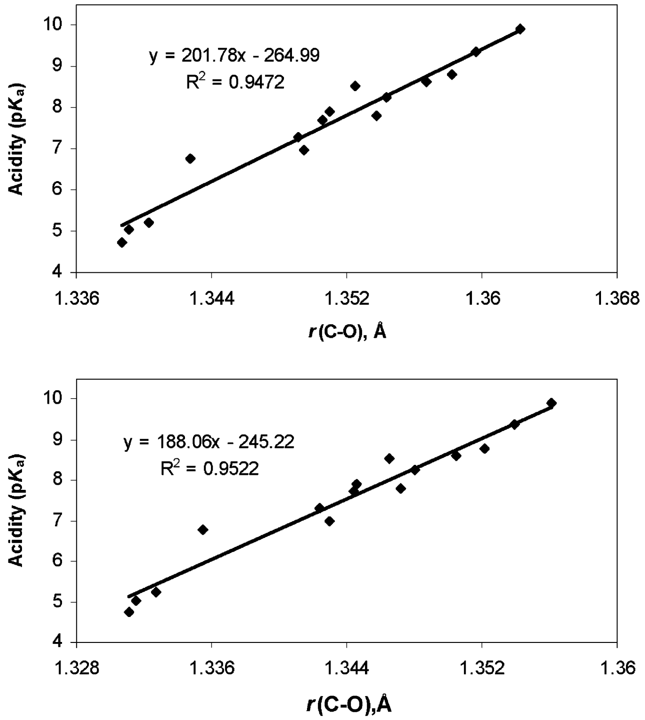

Figure 4. Correlation between the C–O bond length (Å) of complexes of phenol and 14 chlorophenols and the acidity (pK_a) of corresponding phenol compounds in aqueous solution. The upper panel is for the complexes with water and the lower panel is for the corresponding complexes with ammonia.

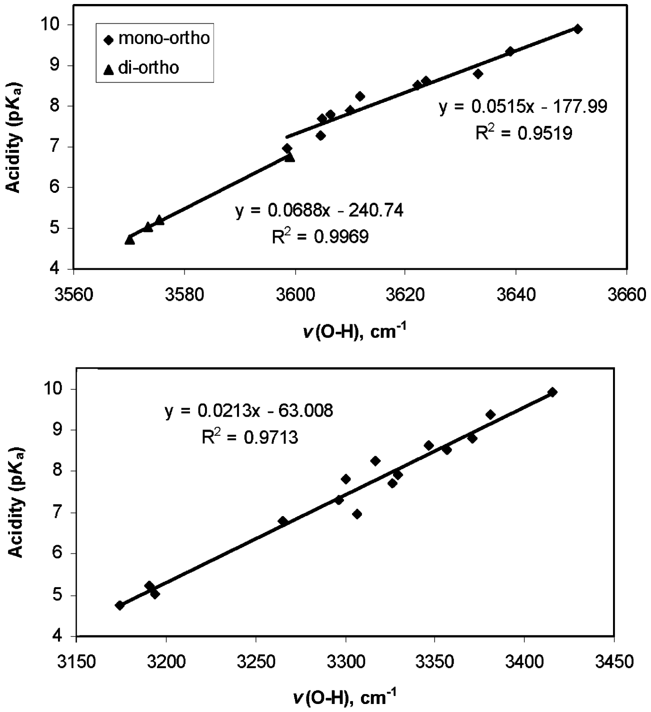

Figure 5. Correlation between the O−H stretching frequency (cm^{-1}) of complexes of phenol and 14 chlorophenols and the acidity (pK_a) of corresponding phenol compounds in aqueous solution. The upper panel is for the complexes with water and the lower panel is for the corresponding complexes with ammonia.

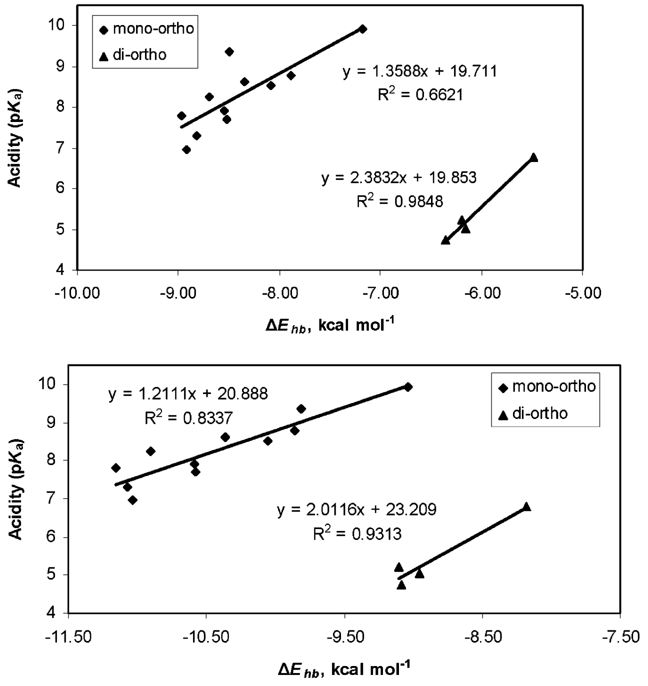

Figure 6. Correlation between the binding energy (kcal mol^{-1}) of complexes of phenol and 14 chlorophenols and the acidity (pK_a) of corresponding phenol compounds in aqueous solution. The upper panel is for the complexes with water and the lower panel is for the corresponding complexes with ammonia.

of correlations are expected due to the severely bent hydrogen bond in the complexes with di-ortho substitutions, as discussed earlier.

Two separate linear correlations with pK_a are also performed for ΔE_{hb} and r(OH···O) or r(OH···N) of all complexes, one with di-ortho substitutions and the other with mono-ortho substitutions, as shown in Figures 6 and 7. Generally, the ΔE_{hb} linearly increases with the acidity of chlorophenols and the r(OH···O) or r(OH···N) linearly decreases with the acidity. Both quantities directly reflect the strength of the intermolecular hydrogen bond, which is enhanced by the acidity. The R^2 values appear overall lower than those for the intramolecular properties associated with the hydroxyl group. Nevertheless, the linear correlations are quite reasonable and are fundamentally compatible with the nature of the properties.

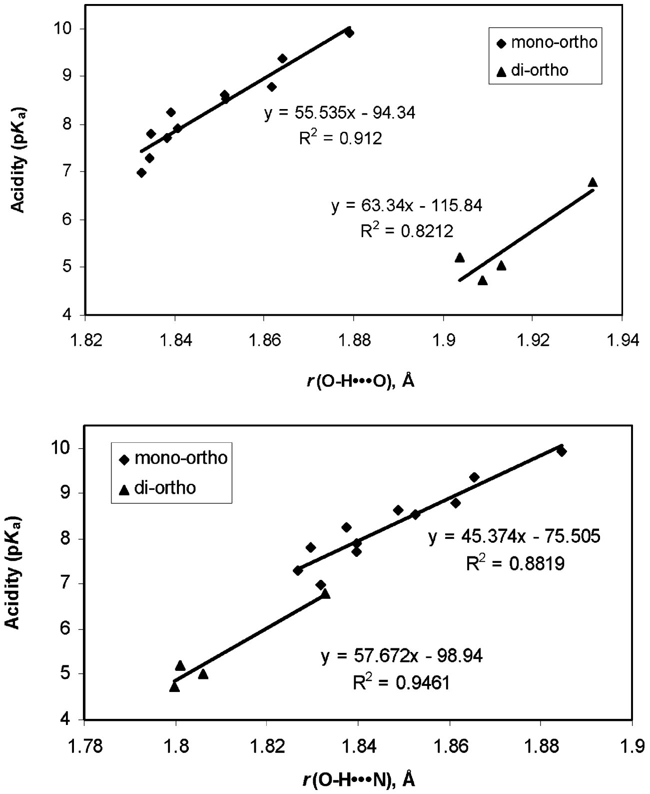

Figure 7. Correlation between the hydrogen bond length (Å) of complexes of phenol and 14 chlorophenols and the acidity (pK_a) of corresponding phenol compounds in aqueous solution. The upper panel is for the complexes with water and the lower panel is for the corresponding complexes with ammonia.

For a given complex, the ΔE_{hb} is determined by the global interaction between the chlorophenol and water (or ammonia). For simplicity, such an interaction may be taken as resulting from electrostatic interactions between the overall dipole of the chlorophenol and that of water (or ammonia). The overall dipole of the chlorophenol is formed mainly from the polarity of the hydroxyl group and that of the substituted chlorine. The leading contribution in ΔE_{hb} comes from the interaction of the hydroxyl group because of its large magnitude and close proximity to the interacting water (or ammonia). Such a contribution is expected to reflect the polarity of the hydroxyl group and thus correlate well with the acidity of the chlorophenol. However, the polarity of substituted chlorine, particularly the orientation of such a dipole component, is strongly dependent upon the relative position. As a result, its contribution in ΔE_{hb} is sensitive to the position of substituted chlorine. The correlation of ΔE_{hb} with the acidity is thus affected by the specific position of substituted chlorine. This may explain the relatively weak correlations of ΔE_{hb} with pK_a. Such interference is expected to be more severe for the complexes with water than with ammonia due to the larger dipole moment of water (1.85 D) compared to ammonia (1.51 D). This is consistent with the corresponding R^2 values, 0.6642 and 0.8308. The hydrogen bond length,

TABLE 4: Predicted pK_a Values for Five Chlorophenols from Linear Correlations[a]

	R^2	S.D.$_{cor}$	2,3,5-TCP	2,3,6-TCP	2,4,5-TCP	2,4,6-TCP	2,3,4,5-TeCP
Water Complex							
r(O−H)	0.9818	0.22	6.67	5.63	7.05	5.73	6.48
r(C−O)	0.9472	0.37	6.89	5.56	7.01	5.72	6.79
ν(O−H)							
mono-ortho	0.9519	0.20	6.73		7.13		6.56
di-ortho	0.9969	0.06		5.94		5.94	
r(OH···O)							
mono-ortho	0.9120	0.27	6.82		7.04		6.67
di-ortho	0.8212	0.47		5.67		5.34	
ΔE_{hb}							
mono-ortho	0.6621	0.54	7.16		7.13		6.79
di-ortho	0.9848	0.14		5.82		5.45	
p$K_{a,\,ave}$			6.85	5.72	7.07	5.64	6.66
Ammonia Complex							
r(O−H)	0.9642	0.31	6.96	5.56	7.14	5.67	6.71
r(C−O)	0.9522	0.35	6.91	5.56	7.06	5.75	6.80
ν(O−H)	0.9713	0.27	6.62	5.50	6.79	5.59	6.31
r(OH···N)							
mono-ortho	0.8819	0.31	6.88		7.00		6.64
di-ortho	0.9461	0.26		5.44		5.54	
ΔE_{hb}							
mono-ortho	0.8337	0.38	6.90		6.90		6.55
di-ortho	0.9313	0.29		5.71		5.37	
p$K_{a,\,ave}$			6.85	5.55	6.98	5.58	6.60
Overall							
p$K_{a,\,ave}$			6.85	5.64	7.03	5.61	6.63
S.D.$_{ave}$			0.16	0.15	0.11	0.19	0.16
p$K_{a,\,exp}$			-	5.80	6.72	5.99	5.64

[a] Experimental values, p$K_{a,\,exp}$, are from ref 36. S.D.$_{cor}$ and S.D.$_{ave}$ are the standard deviations from the linear regressions and from the average pK_a values, respectively.

r(OH···O) or r(OH···N), is largely determined by the intermolecular energy, ΔE_{hb}, and is therefore subject to a similar interference.

Taking into account the expected deviations, all of the properties discussed demonstrate surprisingly consistent linear correlations with the acidity of the chlorophenols. The consistency not only is maintained across the various properties associated with the hydrogen bonding, but it also extends to different probes, from water to ammonia. For a given chlorophenol, the deviations from the linear correlations appear to be consistent from one property to another, from one probe to another. Higher order correlations might be considered as an option, but it is unnecessary from our results as simple linear correlations are adequate in all cases. The physical origin of the linear correlations may be conjectured from the nature of the acidity and correlated properties. The pK_a of an acid directly corresponds to the difference in the free energy between the dissociated and undissociated forms while the latter corresponds to the difference in OH bond strength, which in turn correlates with the OH bond length and stretching frequency in the acid−base hydrogen bond system. Apparent linear correlations have been reported in the literature between bond lengths and other properties, particularly bond dissociation energies.[44,45]

3.4. Predicted pK_a Values for the Five Chlorophenols Based on the Linear Correlations. The established linear correlations for the molecular properties of the complexes with the known pK_a values of the 14 chlorophenols and phenol allow the prediction of pK_a values of similar compounds, particularly the remaining five chlorophenols with uncertain pK_a values. Table 4 summarizes the predicted pK_a values from the different linear correlations for the five chlorophenols, 2,3,5-TCP, 2,3,6-TCP, 2,4,5-TCP, 2,4,6-TCP, and 2,3,4,5-TeCP. The average pK_a values, as recommended by this study, and the corresponding standard deviations are also reported in Table 4, along with the available experimental values.

It is clear that the pK_a values predicted for the five chlorophenols are very consistent with the correlations of different molecular properties and with either probe molecule. This is shown by the small standard deviations, ranging from 0.11 to 0.19, for the average values of pK_a. For example, the pK_a values for 2,3,6-TCP from r(O−H), r(C−O), and ν(OH) are respectively 5.63, 5.56, and 5.94 with water and 5.56, 5.56, and 5.50 with ammonia. Similar pK_a values are predicted from relatively weak correlations for ΔE_{hb} and r(OH···O) or r(OH···N). The average pK_a values for the five chlorophenols, 2,3,5-TCP, 2,3,6-TCP, 2,4,5-TCP, 2,4,6-TCP, and 2,3,4,5-TeCP, are 6.85, 5.64, 7.03, 5.61, and 6.63, respectively. These values should be reliable and are recommended by this study.

Conflicting pK_a values have been reported for the five chlorophenols, some of them with very few experimental sources, as shown in Table 1. The pK_a values for 2,3,6-TCP, 2,4,5-TCP, and 2,4,6-TCP recommended by this study are consistent with the available experimental values of 5.80, 6.72, and 5.99, with the largest difference of 0.38 for 2,4,6-TCP. The pK_a value for 2,4,5-TCP is also in agreement with the reported theoretical value of 6.94 from free energy calculations.[15] On the other hand, the recommended pK_a values for 2,3,5-TCP and 2,3,4,5-TeCP, 6.85 and 6.63, respectively, are considerably different from any of the experimental values, 6.00 or 7.40 for 2,3,5-TCP and 5.14 or 5.64 for 2,3,4,5-TeCP. It should be emphasized that none of these values has reliable experimental sources. The recommended values for the two chlorophenols are consistent with the neighboring pK_a values for their isomers along with the molecular properties while the reported experimental values are inconsistent. For example, based on the molecular properties, the pK_a values are expected to increase in the order of 2,4,5-TCP, 2,3,5-TCP, and 2,4,6-TCP, and the recommended value for 2,3,5-TCP follows the trend. Clearly, the recommended pK_a values are reasonable and may help to resolve the controversies in the experimental values for 2,3,5-TCP and 2,3,4,5-TeCP.

The approach presented in this study is subject to a number of limitations and special considerations. First of all, several variations of such an approach can be taken depending on the availability of the accurate and reliable acidity data. If accurate pK_a values are available for a large number of compounds in the same series, as in the case of the present study, one could generate elaborate correlations of one or several molecular properties with the known pK_a values. Such correlations could then be used for the prediction of pK_a values for other similar compounds. The C−O and O−H bond lengths appear to be the best choices for such correlations, based on this study. In the case of a series lacking a large number of known pK_a values, one could use two or more reliably known values to linearly interpolate or extrapolate to other pK_a values. Second, the hydrogen bonding unit between the acidic group and the probe should remain in the same structure in order to develop the desirable correlation or prediction. Any steric interference to the formation of the hydrogen bond would complicate the correlations, as in the case of the di-ortho chlorophenols. To avoid such a problem, different correlations should be used for complexes with different hydrogen bond structures.

4. Conclusions

Molecular structure and properties for the hydrogen-bonded complexes of phenol and 19 different congeners of chlorophenol with a single probe molecule, either water or ammonia, have been characterized by using density functional theory calculations. Several molecular properties, particularly those associated with the hydrogen bonding of the complexes, have been found to vary systematically with the number and positions of chlorine substitutions, and exhibit strong linear correlations with the known pK_a values for phenol and 14 chlorophenols. Specifically, the pK_a value of a chlorophenol decreases with the increasing of the O−H bond length and the binding energy, and increases with the C−O bond length, the O−H stretching frequency, and the hydrogen bond length. Strong linear correlations have been further used to predict the pK_a values for five of the chlorophenols with controversial values of pK_a in the literature. The predicted pK_a values for these chlorophenols are consistent with all of the molecular properties considered, and should be considered reliable and are valuable for the understanding of the chemical properties and environmental implications of these compounds.

This study has shown systematic linear correlations of molecular properties with the acidity constants of a series of chlorophenols. Such correlations may be employed as a simple and effective approach for studying the acidity of chlorophenols whose acidity is not known or measured. The study can be expanded to include other substituted phenols, carboxylic acids, and other organic acids.

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Supporting Information Available: Figure S1 gives the structure and atom numbering scheme for the chlorophenol complex with water or ammonia; Tables S1 and S2 contain the geometrical parameters of phenol and chlorophenol complexes with water or ammonia from B3YLP/6-311++G(d,p) calculations; Tables S3 and S4 contain the thermodynamic properties of phenol and chlorophenol complexes with water or ammonia. This material is available free of charge via the Internet at http://pubs.acs.org.

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