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Molecular Structures and Properties of the Complete Series of Bromophenols: Density Functional Theory Calculations

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The complete series of 19 bromophenols have been studied by density functional theory (DFT) calculations at the B3LYP/6-311G++(d,p) level. The molecular structures and properties of bromophenols are strongly influenced by intramolecular hydrogen bonding of ortho-bromine, steric and inductive effects of substituted bromine, and other intramolecular electrostatic interactions. Systematic trends in several structural parameters and molecular properties of bromophenols have been found with the increasing number of bromine substitutions, including increase in O−H bond length, decrease in C−O bond length, red shift in O−H stretching frequency, and blue shift in O−H torsional frequency. Correlations among several key molecular parameters as well as those with available aqueous pK_a values are examined. Comparisons with chlorophenols have indicated that the inductive effect of substituted bromine appears larger and bromophenols are slightly stronger acids than chlorophenols.

1. Introduction

Simple bromophenols, including 2-bromophenol (2-BP), 4-bromophenol (4-BP), 2,4-dibromophenol (2,4-DBP), 2,6-dibromophenol (2,6-DBP), and 2,4,6-tribromophenol (2,4,6-TBP), are found in a variety of marine organisms such as marine algae,[1,2] fish,[3] and prawns.[4] These compounds are likely biosynthesized from the organisms' diet[5] and are considered as an important group of key flavor compounds in marine animals at suitable amounts.[6] Moreover, bromophenols are commonly used as brominated flame retardants and are potential to form brominated dioxins and other hazardous combustion byproducts.[7,8] Recently, bromophenols have received increased attention because of their contamination, bioaccumulation, and toxicity in both environmental and biological systems.[8−10] The environmental fate and effects of these substances depend largely on their physical−chemical properties, and therefore, it is important to establish the structure−property relationship for the entire series of bromophenols and understand their chemical and biological activities and environmental impacts.

Only a limited number of studies have been reported on halogenated phenols,[11−17] especially on bromophenols, whereas most studies have focused on the molecular structures and vibrations of phenol and other substituted phenol molecules.[18−29] Among 19 possible bromophenol congeners, only OH stretching frequencies of 2-BP, 2,4-DBP, and 2,6-DBP in liquids have been observed in experiment and the molecular structure and properties of 4-bromophenol in the gas phase have been calculated.[11,13,14] Our previous theoretical study on chlorophenols has revealed systematic trends and correlations in the structure and properties along the complete series of substitutions. In particular, intramolecular hydrogen bonding in *o*-chlorophenols has major consequences on conformational stability and properties as well as on geometry of the remaining molecule.[17]

In the present study, molecular structures and vibrational frequencies of all 19 possible bromophenol congeners are calculated using density functional theory (DFT) at the B3LYP/6-311++G(d,p) level. The stability, conformational variation, and vibrational frequencies of the bromophenols are systematically analyzed and discussed, with a focus on a selected group of data such as O−H bond lengths, C−O bond lengths, O−H stretching, and torsional frequencies. As expected, the molecular structures and properties of bromophenols may be strongly influenced by intramolecular hydrogen bonding of ortho-bromine, steric and inductive effects of substituted bromine, and other intramolecular electrostatic interactions. Correlations among several key molecular parameters as well as those with available aqueous pK_a values are examined. Systematic trends in various molecular parameters and properties are summarized and compared with those of chlorophenols.

2. Computational Methods

Equilibrium geometries of all 19 bromophenols were optimized using density functional three-parameter hybrid model (DFT/B3LYP).[30,31] The 6-311++G(d,p) extended basis set of Pople and co-workers[32,33] for the first-row atoms and hydrogen, expanded by McGratch and Radom to the third-row atoms,[34,35] was employed in all calculations. With the increasing number of bromine substitutions, bromophenols can be grouped into monobromophenols (2-BP, 3-BP, and 4-BP), dibromophenols (2,3-DBP, 2,4- DBP, 2,5- DBP, 2,6- DBP, 3,4- DBP, and 3,5-DBP), tribromophenols (2,3,4-TBP, 2,3,5-TBP, 2,3,6-TBP, 2,4,5-TBP, 2,4,6-TBP, and 3,4,5-TBP), tetrabromophenols (2,3,4,5-TeBP, 2,3,4,6-TeBP, 2,3,5−6-TeBP), and pentabromophenol (PBP). Harmonic vibrational frequencies and corresponding infrared intensities were calculated for the optimized geometries at the same level of theory. Density functional theory has been well tested to give reliable molecular geometries and harmonic frequencies based on comparison with available experimental data.[16,17] All calculations were carried out using the GAUSSIAN 98 computer program package.[36]

A planar geometry is known to be the only stable form of molecular geometry for all halogen-substituted phenols[14−17] and, as a result, the initial geometries of bromophenols considered

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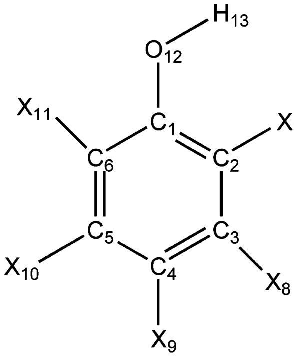
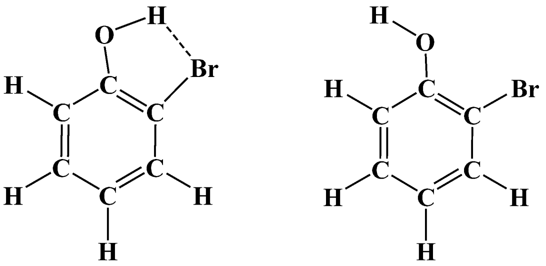


X = H, Br, or both

Figure 1. Structure and atom numbering scheme for the title bromophenol.



2-BP 2-BP (a)

Figure 2. Syn 2-BP and anti 2-BP (a) conformers of 2-bromophenol.

in this study all carry the symmetry of C_s point group. Figure 1 shows the schematic structure of the title molecule and its atomic numbering scheme. For each bromophenol with asymmetric bromine substitution, both syn and anti conformers were examined. In the syn conformer, the hydroxyl group points toward the closest neighboring substituent and it points away in the anti conformer. Figure 2 gives the syn and anti conformers of 2-bromophenol, representing 2-BP and 2-BP(a), respectively.

3. Results and Discussion

3.1. Relative Stability of Bromophenol Isomers. Table 1 summarizes the relative values of various thermodynamic properties (the electronic energy Δ*E*, enthalpy Δ*H*, and free energy Δ*G*), as well as dipole moments for the complete set of bromophenols. The energy values are compared among the isomers of a given number of bromine substitutions, and the most stable isomer is identified as the reference. The relative values for the other isomers are determined relative to that of the most stable isomer. It is clear from Table 1 that the syn conformers of *o*-bromophenols are typically 3.0 kcal mol^{-1} lower in energy and, therefore, more stable than the corresponding anti conformers. On the other hand, the syn and anti conformers of meta- or para-substituted bromophenols are nearly equally stable. The relative stability of monobromophenols decreases in the order of ortho, meta, and para substitution, with relative energies of 0, 1.29, and 1.63 kcal mol^{-1}, respectively. Similarly, 2,5-DBP, 2,4,6-TBP, and 2,3,5,6-TeBP are found to be the most stable isomers for di-, tri-, and tetrabromophenols, respectively, whereas 3,4-DBP, 3,4,5-TBP, and 2,3,4,5-TeBP are the least stable ones. These observations can be explained by effects of intramolecular hydrogen bonding in *o*-bromophenols as well as the inductive (electron-withdrawing) effect and steric repulsion of multiple substitutions, as given below.

TABLE 1: Relative Energies Δ*E* and ΔE_0 (with Zero-Point Energy Correction) (kcal mol^{-1}), Enthalpies Δ*H* (kcal mol^{-1}), Free Energies Δ*G* (kcal mol^{-1}), and Dipole Moments *μ* (Debye) of Bromophenol Conformers at the B3LYP/6-311++G(d,p) Level of Theory[a]

compound	Δ*E*	ΔE_0	Δ*H*	Δ*G*	*μ*
2-BP[b]	0.00	0.00	0.00	0.00	1.11
2-BP(a)	3.22	3.13	3.20	3.05	2.99
3BP	1.29	1.16	1.24	1.04	0.90
3-BP(a)	1.36	1.16	1.25	1.03	3.10
4-BP	1.63	1.43	1.54	1.28	2.31
2,3-DBP	2.77	2.78	2.77	2.90	0.96
2,3-DBP(a)	6.26	6.19	6.23	6.23	3.77
2,4-DBP	0.37	0.41	0.41	0.38	0.87
2,4-DBP(a)	3.52	3.28	3.38	3.16	2.99
2,5-DBP[b]	0.00	0.00	0.00	0.00	1.61
2,5-DBP(a)	3.11	3.08	3.14	2.99	1.32
2,6-DBP	1.85	2.00	1.96	2.06	2.19
3,4-DBP	4.47	4.35	4.43	4.29	2.19
3,4-DBP(a)	4.58	4.38	4.47	4.32	3.41
3,5-DBP	1.44	1.34	1.41	1.21	2.17
2,3,4-TBP	3.91	3.79	3.78	3.97	1.27
2,3,4-TBP(a)	7.48	7.21	7.27	7.31	3.65
2,3,5-TBP	0.49	0.34	0.35	0.42	1.02
2,3,5-TBP(a)	3.86	3.65	3.73	3.64	2.41
2,3,6-TBP	2.11	2.08	2.05	2.21	0.97
2,3,6-TBP(a)	2.41	2.34	2.32	2.46	2.48
2,4,5-TBP	0.90	0.71	0.74	0.74	1.80
2,4,5-TBP(a)	3.88	3.68	3.77	3.63	2.13
2,4,6-TBP[b]	0.00	0.00	0.00	0.00	1.53
3,4,5-TBP	5.55	5.22	5.32	5.24	2.79
2,3,4,5-TeBP	2.33	2.11	2.15	2.14	1.62
2,3,4,5-TeBP(a)	5.78	5.50	5.60	5.45	2.73
2,3,4,6-TeBP	0.67	0.70	0.71	0.69	1.12
2,3,4,6-TeBP(a)	1.11	1.05	1.08	1.02	2.16
2,3,5,6-TeBP[b]	0.00	0.00	0.00	0.00	1.53
PBP					1.73

[a] Relative energies (Δ*E*, ΔE_0, Δ*H*, Δ*G*) are with respect to the most stable isomer with a given number of bromine atoms; absolute values are given in S-Table 1. [b] The most stable isomer with a given number of bromine substitutions

Intramolecular hydrogen bonding may be established due to electrostatic interaction between the ortho-substituted bromine and the hydroxyl group, resulting in a significant stabilization of the syn conformer relative to the corresponding anti conformer. The hydrogen bond energy, determined as an energy difference between the syn and anti conformers, is typically 3.2 kcal mol^{-1} for *o*-bromophenol and increases slightly (ca. 0.3 kcal mol^{-1}) with multiple bromine substitutions. Although hydrogen bonding is absent in *m*- or *p*-bromophenols, the electron-withdrawing bromine might have preferentially stabilized the *m*-bromophenol over the para isomer, as shown by the relative energies. Steric repulsion from multiple bromine substitutions also contributes considerably to the relative stabilities of bromophenols. For example, 3,5-DBP is 1.33 kcal mol^{-1} more stable than 2,3-DBP, despite the intramolecular hydrogen bonding in the latter isomer. Similar results have been found in the series of chlorophenols.[17] Note that the steric effects in bromophenols are more pronounced than those in chlorophenols. For example, the relative energy of 2,3,4,5-tetrachlorophenol is 1.19 kcal mol^{-1} whereas that of 2,3,4,5-TeBP is 2.33 kcal mol^{-1}.

As shown in Table 1, the relative enthalpies Δ*H* and free energies Δ*G* of different isomers follow the same trends as the relative energies Δ*E*, for a given number of bromine substitutions. The molecular dipole moments are typically under 1.6 D for syn conformers and above 2.5 D for anti conformers. The overall dipole of a bromophenol is determined by the contribution from the hydroxyl group and that from the C−Br bonds. In the syn conformers, the two contributions tend to cancel each other out due to the nearly opposite orientations of the O−H

TABLE 2: Ranges of Bond Lengths (Å) and Bond Angles (deg) of Bromophenols Optimized at B3LYP/6-311++G(d,p) Level of Theory

parameters	bromophenol
$r(O_{12}-H_{13})$	0.963−0.970
$r(C_1-O_{12})$	1.346−1.367
r(C−X), X = H	1.080−1.086
r(C−X), X = Br	1.897−1.924
r(C−C)	1.384−1.409
∠CCC	117.1−122.5
$\angle C_1O_{12}H_{13}$	109.1−110.4
$\angle C_2C_1O_{12}$	118.0−123.9
$\angle C_1C_2X_7$, X = H	119.3−120.8
$\angle C_1C_2X_7$, X = Br	116.3−120.1

and C−Br dipoles whereas such a cancellation effect is minimized in the anti conformers.

3.2. Structural Parameters. The overall ranges of optimized geometries of 19 bromophenols using B3LYP/6-311++G(d,p) methods are listed in Table 2. The complete geometrical parameters of 19 bromophenols are summarized in S−Table 2 of the Supporting Information. The bond lengths and bond angles of bromophenols are in relatively narrow ranges typical of the substituted aromatic compounds. Table 3 gives selected bond lengths and bond angles of bromophenols along with those of phenol. Note that the calculated geometrical parameters of phenol are in good agreement with corresponding experimental values.[20] If the environment is the same at both ortho positions, no significant difference results in geometrical parameters between the syn and anti conformers. In other words, significant geometrical variations are expected to occur between the syn and anti conformers only with mono-ortho substitution.

It appears that the O−H bond length, r(O−H), is strongly influenced by the ortho-substituted bromine in the syn conformer. As shown in Table 3, the r(O−H) values in the syn conformers of *o*-bromophenols are typically 0.005 Å longer than that of phenol and those of the anti conformers, increasing slightly with multiple bromine substitutions. For example, the O−H bond lengths of 2-BP, 2,3,4-TBP, and PBP are 0.968, 0.969, and 0.970 Å, respectively. On the other hand, the r(O−H) values in *m*- or *p*-bromophenols are nearly constant and close to that of phenol (0.963 Å). The lengthening of the O−H bond in *o*-bromophenols may be attributed to the interaction between the hydroxyl group and the ortho-bromine, either through intramolecular hydrogen bonding or the larger electron-withdrawing effect of bromine at the ortho position than at the meta or para position. Note that the intramolecular hydrogen bond length decreases with the number of bromine substitutions, as shown in Table 3. The enhancment in the hydrogen bond interaction corresponds to the lengthening of the O−H bond, possibly attributed to the charge transfer from the proton acceptor to the antibonding OH orbital.[37,38] The systematic lengthening of the O−H bond with the number of bromine substitutions may also likely be due to the enhancement in the overall electron-withdrawing character of bromine, which results in the increased acidity of the hydroxyl hydrogen.

Similarly, the C−O bond lengths, r(C−O), are also affected by the number and positions of bromine substitutions. Overall, the r(C−O) values of bromophenols in both conformers are consistently smaller than that of phenol and decrease with the increasing number of bromine substitutions. Specifically, the r(C−O) values of *o*-bromophenols in the syn conformation are systematically smaller (by 0.004−0.006 Å) than those in the anti conformation. It is interesting to note that 2-BP, 2,6-DBP, and 2,4,6-TBP have the shortest C−O bond lengths, 1.357, 1.349, and 1.348 Å, for mono-, di-, and tribromophenols,

TABLE 3: Selected Bond Lengths (Including Intramolecular Hydrogen Bond Lengths) (Å), Bond Angles (deg) of Bromophenols Calculated at the B3LYP/6-311++G(d,p) Level of Theory and Related Experimental pK_a Values in Aqueous Solution

compound	pK_a	r(O−H)	r(C−O)	r_{av}(C−Br)	$\angle C_1C_2X_7$	$\angle C_1O_{12}H_{13}$	$\angle C_2C_1O_{12}$	$r(O_{12}\cdots Br_7)$
phenol	9.99[a]	0.963	1.370		120.1	109.7	122.5	
exp[c]		0.956	1.364			109.0	122.5	
2-BP	8.45[a]	0.968	1.357	1.924	118.5	109.3	123.6	2.494
2-BP(a)		0.963	1.361	1.910	119.7	109.6	118.7	
3-BP	9.03[a]	0.963	1.366	1.919	120.7	110.1	122.2	
3-BP(a)		0.963	1.366	1.918	119.6	109.9	116.8	
4-BP	9.37[a]	0.963	1.367	1.919	120.3	110.0	122.8	
2,3-DBP		0.969	1.354	1.912	117.4	109.4	123.0	2.442
2,3-DBP(a)		0.963	1.360	1.905	118.2	109.6	118.0	
2,4-DBP	7.79[a]	0.968	1.355	1.918	118.6	109.5	123.8	2.504
2,4-DBP(a)		0.963	1.360	1.912	119.8	109.9	118.7	
2,5-DBP		0.968	1.354	1.917	118.7	109.4	123.7	2.501
2,5-DBP(a)		0.963	1.358	1.911	119.9	110.0	118.7	
2,6-DBP	6.67[a]	0.968	1.349	1.916	118.0	109.2	123.5	2.469
3,4-DBP		0.963	1.365	1.909	120.5	110.3	122.5	
3,4-DBP(a)		0.963	1.365	1.909	119.3	110.1	116.9	
3,5-DBP	8.06[a]	0.963	1.363	1.915	120.8	110.3	122.4	
2,3,4-TBP		0.969	1.353	1.908	116.8	109.5	123.4	2.434
2,3,4-TBP(a)		0.963	1.359	1.904	117.5	109.7	118.2	
2,3,5-TBP		0.969	1.352	1.910	117.5	109.5	123.1	2.446
2,3,5-TBP(a)		0.963	1.357	1.906	118.4	110.0	118.0	
2,3,6-TBP		0.969	1.347	1.909	116.9	109.3	122.9	2.420
2,3,6-TBP(a)		0.969	1.348	1.909	117.7	109.1	118.5	
2,4,5-TBP		0.968	1.353	1.910	118.9	109.5	123.9	2.512
2,4,5-TBP(a)		0.963	1.357	1.906	120.1	110.1	118.8	
2,4,6-TBP	6.08[b]	0.968	1.348	1.913	118.1	109.3	123.6	2.476
3,4,5-TBP		0.963	1.363	1.907	120.7	110.4	122.8	
2,3,4,5-TeBP		0.969	1.351	1.906	116.7	109.5	123.6	2.433
2,3,4,5-TeBP(a)		0.964	1.357	1.903	117.5	110.0	118.4	
2,3,4,6-TeBP		0.969	1.346	1.906	116.3	109.4	123.3	2.409
2,3,4,6-TeBP(a)		0.969	1.347	1.906	116.9	109.2	118.8	
2,3,5,6-TeBP		0.970	1.346	1.903	117.3	109.3	122.5	2.413
PBP	4.40[b]	0.970	1.346	1.903	116.4	109.3	122.8	2.394

[a] Reference 39. [b] Reference 7. [c] Reference 20.

TABLE 4: Average Values of C−C Bond Length r_{av} (Å) and Corresponding Standard Deviations, SD, for All Bromophenol Conformers

compound	r_{av}	SD × 10^3	compound	r_{av}	SD × 10^3
2-BP	1.394	4.3	2-CP	1.394	4.2
2-BP(a)	1.393	3.5	2-CP(a)	1.394	3.7
3-BP	1.393	2.5	3-CP	1.393	3.2
3-BP(a)	1.393	3.1	3-CP(a)	1.393	2.7
4-BP	1.394	3.7	4-CP	1.393	2.6
2,3-DBP	1.395	6.2	2,3-DCP	1.395	5.5
2,3-DBP(a)	1.393	4.4	2,3-DCP(a)	1.395	5.5
2,4-DBP	1.393	5.2	2,4-DCP	1.393	4.2
2,4-DBP(a)	1.395	6.4	2,4-DCP(a)	1.393	4.3
2,5-DBP	1.394	3.6	2,5-DCP	1.393	4.8
2,5-DBP(a)	1.393	3.8	2,5-DCP(a)	1.393	4.7
2,6-DBP	1.394	4.8	2,6-DCP	1.394	6.2
3,4-DBP	1.394	3.1	3,4-DCP	1.394	3.6
3,4-DBP(a)	1.394	4.1	3,4-DCP(a)	1.394	3.3
3,5-DBP	1.396	5.7	3,5-DCP	1.392	3.6
2,3,4-TBP	1.397	7.3	2,3,4-TCP	1.396	6.2
2,3,4-TBP(a)	1.395	6.7	2,3,4-TCP(a)	1.396	6.6
2,3,5-TBP	1.396	7.4	2,3,5-TCP	1.394	5.8
2,3,5-TBP(a)	1.394	4.8	2,3,5-TCP(a)	1.395	6.4
2,3,6-TBP	1.394	6.4	2,3,6-TCP	1.395	6.7
2,3,6-TBP(a)	1.396	7.7	2,3,6-TCP(a)	1.395	7.1
2,4,5-TBP	1.395	6.2	2,4,5-TCP	1.394	5.2
2,4,5-TBP(a)	1.395	4.0	2,4,5-TCP(a)	1.394	4.4
2,4,6-TBP	1.395	6.6	2,4,6-TCP	1.394	6.4
3,4,5-TBP	1.397	7.2	3,4,5-TCP	1.395	5.9
2,3,4,5-TeBP	1.398	7.5	2,3,4,5-TeCP	1.397	6.6
2,3,4,5-TeBP(a)	1.397	7.2	2,3,4,5-TeCP(a)	1.398	6.4
2,3,4,6-TeBP	1.398	8.1	2,3,4,6-TeCP	1.396	6.4
2,3,4,6-TeBP(a)	1.397	6.9	2,3,4,6-TeCP(a)	1.397	7.6
2,3,5,6-TeBP	1.399	7.4	2,3,5,6-TeCP	1.396	6.3
PBP	1.402	3.3	PCP	1.400	2.5

respectively, whereas 4-BP, 3,4-DBP, 3,4,5-TBP have the longest C−O bond lengths. The electronegative bromine atom withdraws the electron density from the electron rich hydroxyl oxygen through the phenol ring and, consequently, reduces the electron population in the antibonding orbital of C−O bond. As a result, the C−O bond is strengthened and the C−O bond length is decreased in all bromophenols. In addition, such inductive effects increase with the number of bromine substitutions as well as the proximity of the hydroxyl group from bromine substitution.

The C−Br bond lengths of bromophenols are influenced by the positions and the number of bromine substituents, as shown in Table 3. The average C−Br bond length, r_{av}(C−Br), decreases with the increasing number of bromine substitutions in both conformers. For example, the longest C−Br bond length is 1.924 Å for 2-BP and the shortest is 1.903 Å for PBP. Moreover, r_{av}(C−Br) of *o*-bromophenols is typically 0.012 Å larger in the syn conformer than in the corresponding anti conformer. The elongation of the C−Br bond in the syn conformers of *o*-bromophenols is the consequence of intramolecular hydrogen bonding. The bonding characteristics of a C−Br bond may be enhanced by induction of other substituted bromines, by reducing electron occupation in lone-pair orbitals at Br with antibonding characteristics, leading to a shorter C−Br bond length. This might explain the observed decrease in r_{av}(C−Br) with the increasing number of substitutions.

The C−C bond lengths of the phenol ring are also strongly affected by the number of bromine substitutions. The mono substitution appears to cause a decrease in C−C bond lengths, relative to phenol. As given in Table 4, the average C−C bond lengths, r_{av}(C−C), of monobromophenols are typically 0.001 Å smaller than that of phenol (1.394 Å). The r_{av}(C−C) values are surprisingly increased in higher substitutions, by 0.001 Å for dibromophenols and 0.008 Å for pentabromophenol. This might be again explained by the induction of bromine substitutions. The electron density withdrawn by bromine comes initially from π antibonding orbitals and eventually from π bonding orbitals of the phenol ring. There are noticeable variations in the C−C bond lengths, which also appear to depend on the degree of substitution. Such variations reflect the degree of the ring distortion and are measured by the standard deviation (SD) in C−C bond lengths, as reported in Table 4. It is clear that the ring distortion systematically increases with the number of bromine substitutions, with the only exception of PBP. The restoration of symmetry in PBP with full substitutions at the phenol ring appears to be the reason for the exception.

TABLE 5: Selected Vibrational Frequencies ν (cm^{-1}) and IR Intensities *A* (km mol^{-1}) of Bromophenols and Phenol Calculated with B3LYP/6-311++G(d,p) Level of Theory[a]

	ν(O−H)		τ(O−H)		δ(O−H)		ν(C−O)	
compound	ν	*A*	ν	*A*	ν	*A*	ν	*A*
phenol	3837.3	61.7	311.5	110.8	1191.7	124.5	1274.7	90.7
exp[b]	3656.7	50	309.2	47	1176.5	80	1261.7	62
2-BP	3741.5	98.6	417.5	90.0	1213.3	118.3	1273.1	63.4
exp[c]	3554		404					
2-BP(a)	3834.3	72.9	317.8	96.1	1188.8	80.0	1283.6	20.0
3-BP	3835.3	68.8	316.6	108.9	1193.6	89.4	1269.6	86.9
3-BP(a)	3836.5	75.2	308.1	2.5	1192.3	1123.6	1269.6	26.3
4-BP	3837.9	76.1	311.4	46.0	1186.2	174.5	1279.7	125.7
exp[d]	3607	47.2			1167	33.8	1259	47.3
2,3-DBP	3726.0	98.4	426.3	87.2	1196.3	54.1	1317.9	50.8
2,3-DBP(a)	3833.2	78.7	326.8	85.2	1187.9	24.6	1307.1	109.7
2,4-DBP	3745.4	106.7	405.9	93.2	1208.4	149.7	1269.7	40.1
exp[e]	3528							
2,4-DBP(a)	3836.0	58.0	294.4	74.0	1189.1	72.9	1280.1	4.3
2,5-DBP	3739.0	110.7	416.4	89.8	1209.1	121.8	1269.2	32.9
2,5-DBP(a)	3833.4	77.1	327.4	82.2	1188.3	68.3	1277.1	39.8
2,6-DBP	3732.0	115.0	429.7	82.9	1191.6	45.1	1295.1	17.1
exp[e]	3514							
3,4-DBP	3835.5	77.0	301.2	67.6	1188.5	168.9	1256.9	53.1
3,4-DBP(a)	3836.6	88.9	299.5	97.3	1188.8	165.6	1296.3	96.0
3,5-DBP	3834.5	80.9	314.1	109.3	1186.8	125.1	1273.8	26.6
2,3,4-TBP	3722.5	10.6	430.6	85.0	1220.5	130.1	1309.0	78.8
2,3,4-TBP(a)	3832.2	89.6	329.0	52.0	1207.4	116.9	1305.0	18.0
2,3,5-TBP	3722.9	109.5	430.9	90.1	1187.2	60.6	1293.0	2.5
2,3,5-TBP(a)	3831.1	82.5	331.7	5.2	1235.2	69.4	1288.6	58.6
2,3,6-TBP	3716.0	113.3	438.5	80.6	1169.0	115.1	1235.8	50.3
2,3,6-TBP(a)	3725.1	125.0	432.6	79.4	1245.8	85.3	1288.4	13.7
2,4,5-TBP	3741.0	116.9	408.8	92.0	1208.7	148.7	1322.8	86.1
2,4,5-TBP(a)	3833.2	88.4	312.6	81.1	1177.1	151.6	1277.4	36.0
2,4,6-TBP	3732.9	121.8	424.1	83.8	1260.3	61.2	1288.0	18.9
3,4,5-TBP	3835.4	91.5	313.9	41.8	1190.7	172.6	1260.3	61.2
2,3,4,5-TeBP	3720.2	115.6	431.4	88.9	1219.1	148.7	1423.4	211.2
2,3,4,5-TeBP(a)	3829.1	91.4	312.4	62.1	1192.1	210.7	1369.0	220.4
2,3,4,6-TeBP	3711.9	122.5	437.6	78.8	1208.8	106.1	1450.2	231.3
2,3,4,6-TeBP(a)	3725.2	129.5	424.8	81.5	1220.4	142.6	1450.0	203.4
2,3,5,6-TeBP	3710.4	122.2	445.2	77.5	1244.9	83.8	1412.2	158.3
PBP	3705.7	129.4	444.3	78.2	1291.4	61.5	1407.0	140.6

[a] Abbreviations: ν, stretching vibration; τ, torsional vibration; δ, in-plane bending vibration. [b] Reference 20. [c] Reference 14. [d] Reference 13. [e] Reference 11.

Intramolecular hydrogen bonding between the hydroxyl group and the ortho-bromine results in significant variations in two bond angles directly involved, $\angle C_1O_{12}H_{13}$ and $\angle C_1C_2Br_7$. As shown in Table 4, the bond angle $\angle C_1O_{12}H_{13}$ of *o*-bromophenols is about 0.8° smaller than bromophenols without ortho substitution (about 110.0°). Similarly, the bond angle $\angle C_1C_2Br_7$ of *o*-bromophenols is consistently below 118.0° whereas the angle $\angle C_1C_2H_7$ of bromophenols without ortho substitution is about 120.3°. The $\angle C_1C_2Br_7$ angle of *o*-bromophenols in the syn conformer is usually 0.8° smaller than that in the corresponding anti conformer. Finally, the $\angle C_2C_1O_{12}$ bond angle in the anti conformer is similar to that of phenol (122.5°) and typically 5° larger than that in the syn conformer. The large steric effect resulting from the hydroxyl oxygen and the ortho-bromine might be the major cause of large $\angle C_2C_1O_{12}$ in these syn structures.

3.3. Infrared Vibrational Frequencies. Several important harmonic frequencies and corresponding infrared intensities involving the hydroxyl group are reported in Table 5, along with available experimental data. There are 33 normal vibra-

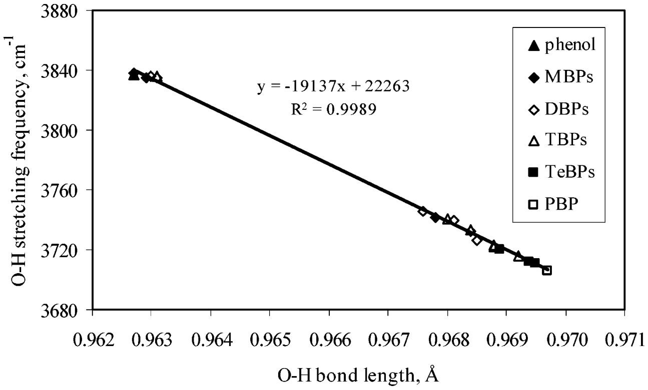


Figure 3. Correlation between the O−H stretching frequency (cm^{-1}) and the O−H bond length (Å) of bromophenols. In the lower-right corner are points for *o*-bromophenols that have relatively longer bond lengths and lower frequencies, whereas points for other bromophenols are located in the upper-left corner. Structural data and frequencies refer to the syn conformers.

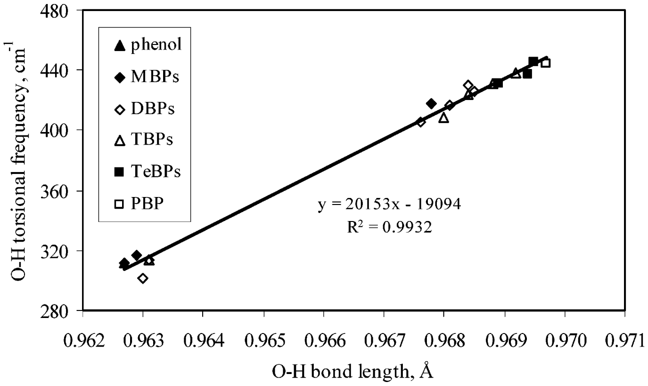


Figure 4. Correlation between the O−H torsional frequency (cm^{-1}) and the O−H bond length (Å) of bromophenols. In the upper-right region are data points for *o*-bromophenols that have relatively higher frequencies and longer bond lengths, whereas points for other bromophenols are located in the lower-left area. Structural data and frequencies refer to the syn conformers.

tional modes for each bromophenol and the complete set of harmonic frequencies and corresponding infrared intensities for all 19 bromophenols are given in S-Table 3 of the Supporting Information. Several important modes are sensitively affected by bromine substitution and the variations in these modes are quantitatively indicative of the effect of bromine substitution. These vibrational modes, including the stretching, torsional, and in-plane bending vibrations of the O−H bond about the C−O axis as well as the stretching vibration of the C−O bond, are analyzed in details as follows.

3.3.1. O−H Stretching Frequencies. Among the 33 normal modes, the O−H stretching vibration is highly localized and only involves the O and H atoms of the hydroxyl group. The calculated harmonic frequencies are known to consistently overestimate the experimental frequencies. Scaled by a factor of 0.963,[14] the calculated O−H stretching frequencies for several bromophenols are in good agreement with the available experimental frequencies.[13,14,20] The O−H stretching frequencies, ν(O−H), of the syn conformers with ortho substitution are considerably lower than those of the anti conformers and decrease progressively with the increase number of bromine substitutions. The red shift in ν(O−H) increases from 96 cm^{-1} for 2-BP to 132 cm^{-1} for PBP relative to phenol. In contrast, the ν(O−H) values for the anti conformers are nearly the same as that of phenol, 3837 cm^{-1}. This can be clearly explained by the effect of intramolecular hydrogen bonding in the syn conformers with ortho substitutions. The intramolecular hydrogen bonding is expected to reduce the force constant of the O−H group, resulting in a decrease or red shift in ν(O−H). Such an effect is intensified with the increasing number of bromine substitutions, and the inductive effects of bromine might be responsible for the shift in frequency.

The red shift of the O−H stretching frequency corresponds to the elongation of the O−H bond length discussed earlier, both reflecting the weakening O−H bond from bromine substitution. As a result, ν(O−H) and r(O−H) should be strongly correlated. Figure 3 shows a plot of the ν(O−H) values verses the r(O−H) values for all syn conformers of bromophenols. It is clear that a strong linear correlation ($R^2 = 0.9989$) exists between ν(O−H) and r(O−H).

3.3.2. O−H Torsional Frequencies. The O−H torsional frequency, τ(O−H), is also highly sensitive to the variations in conformation and bromine substitution. The τ(O−H) values are within the range 417.5−444.3 cm^{-1} for all syn conformers of *o*-bromophenols and are close to the value of phenol (311.5 cm^{-1}) for all anti conformers. The difference can be again attributed to the intramolecular hydrogen bonding present in the syn conformers of *o*-bromophenols, which raise the energy barrier for hydrogen rotation out of molecular plane. Moreover, the τ(O−H) values consistently increase with multiple bromine substitutions, and the blue shift in τ(O−H) relative to phenol increases from 106 cm^{-1} for 2-BP to 133 cm^{-1} for PBP.

Figure 4 shows the strong correlation of the τ(O−H) values with the r(O−H) values, which is consistent with the correlation between ν(O−H) and r(O−H) as they share a common physical origin. An increase in the O−H bond length with multiple bromine substitutions, from 0.968 to 0.970 Å, matches well with increases in both the ν(O−H) red shift and the τ(O−H) blue shift, 36 and 27 cm^{-1}, respectively. Similar correlations (OH bond length versus stretching or torsional frequency) were found for a series of chlorophenols.[17]

3.3.3. O−H In−Plane Bending Frequencies. The O−H in-plane bending strongly couples with other vibrations involving (C−C) stretching and CH bending motions and, as a result, several normal modes exist with different degrees of O−H in-plane bending motions. Table 5 lists the O−H in-plane bending frequency, δ(O−H), corresponding to the highest IR intensity, for each of the 33 bromophenol conformers. With some exceptions, the δ(O−H) values are near 1200 cm^{-1} and increase slightly with the number of bromine substitutions. There is another normal mode around 1350 cm^{-1} with a smaller IR intensity. Note that the δ(O−H) values of meta- or para-substituted bromophenols are lower than those of the ortho isomers and are close to that of phenol (1191.7 cm^{-1}). This may be due to reduced steric interaction from the large bromine atom at the meta or para position relative to the ortho position.

3.3.4. C−O Stretching Frequencies. Similar to the O−H in-plane bending vibration, several vibrational modes contain nuclear motions of the C−O group and the aromatic ring. Table 5 gives the C−O stretching frequency, ν(C−O), with a high intensity for each bromophenol. The values of ν(C−O) for monobromophenols and dibromophenols range from 1273 to 1295 cm^{-1}. With the increasing substitution, ν(C−O) appears to increase systematically, up to near 1450 cm^{-1} for tetrabromophenols and PBP. The increase in ν(C−O) indicates the strengthening of the C−O bond from multiple bromine substitutions, a result consistent with the reduction in the C−O bond.

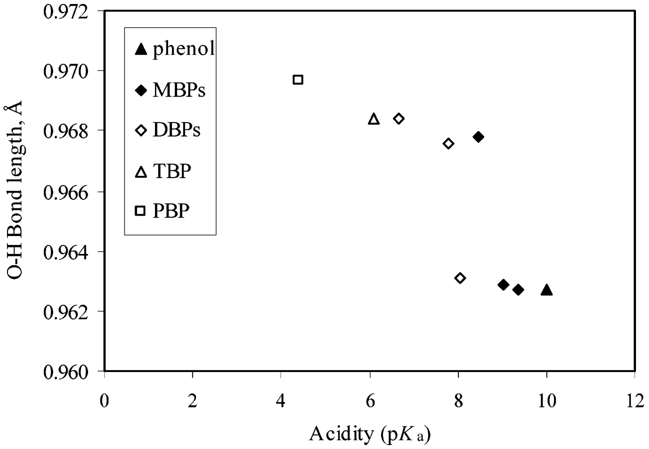


Figure 5. Dependence of the O−H bond lengths (Å) on the known aqueous pK_a values of eight bromophenols. In the upper-left region are data points for *o*-bromophenols that have relatively longer bond lengths and lower pK_a values, whereas data points for other bromophenols are located in the lower-right area. Structural data refer to the syn conformers.

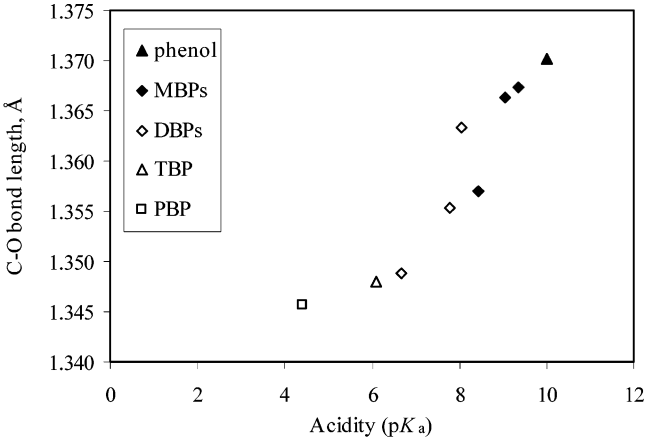


Figure 6. Dependence of the C−O bond lengths (Å) on the known aqueous pK_a of eight bromophenols. With a given number of bromine substitutions, the *o*-bromophenol has a shorter C−O bond length and a lower pK_a value than for the meta or para isomer. Structural data refer to the syn conformers.

3.4. Correlations with Bromophenol Acidity and Comparison with Chlorophenols. The acidity of a bromophenol depends largely on the number and positions of bromine substitution at the phenol ring. It is interesting to note that the O−H bond lengths are correlated with available experimental aqueous pK_a values of eight bromophenols,[7,39] as shown in Figure 5.

o-Bromophenols have relatively longer O−H bond lengths and lower pK_a values, whereas meta and para isomers have shorter O−H bond and higher pK_a values. The weakening of O−H bond enhances the potential for deprotonation of the hydroxyl hydrogen, leading to an increase in the acidity or a low pK_a value. As shown in Figure 6, the C−O bond lengths are also correlated with the available pK_a values. The pK_a values decrease consistently with the C−O bond lengths. The cause of this result might be explained with the electron-withdrawing effect of substituted bromine and the resonance effect of bromine and the aromatic ring. Overall, the acidity of bromophenols increases with the number of substitution. For a given number of substitutions, the acidity increases in the order of para, meta, and ortho positions.

It would be interesting to compare the molecular properties of bromophenols with those of chlorophenols. The two series with meta and para substitutions demonstrate comparable molecular properties, probably due to the lack of intramolecular hydrogen bonding and a diminished induction effect on the hydroxyl group. On the other hand, molecular properties of the two series with ortho substitutions, though following a similar trend, are more sensitive to the number of substitutions in bromophenols than in chlorophenols. For example, an increase of 0.001 Å in the O−H bond length is observed from monochlorophenol to pentachlorophenol, compared to 0.002 Å for bromophenols. Similar differences are observed for the red shifts in the O−H stretching frequency and the blue shifts in the O−H torsional frequencies.

One might be curious about the origin of the differences in various properties between bromophenols and chlorophenols. Chlorine and bromine are two elements in the same main group with a slightly higher electronegativity for chlorine and a larger atomic radius for bromine. Differences in molecular properties involving the two elements have been the topics of intense discussions in the literature.[40] A well-known case is the relative acidity between the two hydrogen halides. On the basis of a conventional argument, HCl would be a stronger acid because of the higher electronegativity of Cl. On the contrary, HBr is a significantly stronger acid. The reason behind this is the larger size of Br that can provide more stability for the resulting bromide ion by diffuseness of charge, another major factor responsible for the acid strength. Electronegativity and diffuseness of charge both contribute to what is called an inductive effect in the halogenated acids. Stronger acidity of HBr than HCl indicates that the second effect prevails in the two hydrogen halides. The similar argument appears to explain the difference in acidity between the two series of halogenated phenols. The overall inductive effect is larger in bromophenols than in the corresponding chlorophenols, as evidenced by the experimental pK_a values as well as the calculated molecular properties discussed in this study.

It should be noted that the inductive effect appears a dominant factor in the acidity of a halogenated phenol although other effects may also have significant contributions. For example, the hydration of an acid and that of the corresponding anion can also play a considerable role. The hydration effect is likely consistent among the halogenated phenol series. The relative acidity of bromophenols verses chlorophenols mirrors that of HBr verses HCl, which implies that inductive effect is dominant.

4. Conclusions

Density functional theory at the B3LYP/6-311++G(d,p) level has been used to study the complete series of 19 bromophenols. The *o*-bromophenol in the syn conformation is found to be the most stable isomer for a given number of bromine substitutions. Intramolecular hydrogen bonding is shown to be responsible for the high stability of the *o*-bromophenol. The steric effect between substituted bromines is another major factor in the relative stabilities of different isomers. Variations in molecular structure and properties along the bromophenol series have been discussed, with a focus on those involved in the hydroxyl group. Systematic trends in several structural parameters and properties have been found from monobromophenols to pentabromophenols, including the increase in the O−H bond length, the decrease in the C−O bond length, the red shift in the O−H stretching frequency, and the blue shift in the O−H torsional frequency. These systematic changes are attributed to the inductive effect of substituted bromine and are correlated to the known acidity values. Comparisons with chlorophenols have been discussed, suggesting that the inductive effect of substituted bromine is larger and bromophenols are slightly stronger acids than chlorophenols.

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Supporting Information Available: S-Table 1 contains various thermodynamic energies of all 19 bromophenols calculated at B3YLP/6-311++G(d,p) level of theory. S-Table 2 contains the optimized geometrical parameters of all 19 bromophenols. S-Table 3 contains the harmonic frequencies and their IR intensities of bromophenols at the same level of theory. This material is available free of charge via the Internet at http://pubs.acs.org.

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