

# How H-Bonding Affects Aromaticity of the Ring in Variously Substituted Phenol Complexes with Bases. 4. Molecular Geometry as a Source of Chemical Information

Tadeusz M. Krygowski,<sup>†</sup> Halina Szatyłowicz,<sup>\*,‡</sup> and Joanna E. Zachara<sup>†</sup>

Department of Chemistry, Warsaw University, Pasteura 1, 02-093 Warsaw, Poland, and  
Department of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00-664 Warsaw, Poland

Received June 3, 2004

Aromaticity of the ring of variously substituted phenols in their H-bonded complexes with various bases was a subject of analysis based on 664 geometries retrieved from CSD and by use of the aromaticity index HOMA. GEO and EN, the components of the HOMA index, describing a decrease of aromaticity due to an increase of bond alternation (GEO term) and bond elongation (EN term), were also studied. There is an approximate monotonic dependence of HOMA and GEO on the H-bond strength estimated by the C–O bond length of the hydroxyl group in phenols.

## INTRODUCTION

Aromaticity is not a clearly defined term,<sup>1–5</sup> but it is one of great use in organic chemistry and related fields.<sup>6,7</sup> Usually it is accepted that cyclic systems with delocalized  $\pi$ -electrons are aromatic if they exhibit the following properties: (i) an increase of stability in comparison with linear unsaturated reference systems [This was originally estimated by resonance energy,<sup>8–10</sup> and now it is usually described by aromatic stabilization energy (ASE).];<sup>3</sup> (ii) a decrease of bond lengths alternation in comparison with linear unsaturated reference systems;<sup>11–14</sup> (iii) a special picture of magnetic properties of the system when exposed to the external magnetic field – specific chemical <sup>1</sup>H NMR shifts and exaltation of the magnetic susceptibility.<sup>15–19</sup> Apart from these features of aromaticity, organic chemists working in synthesis postulate a reactivity criterion stating that (iv) in chemical reactions aromatic systems tend to maintain their  $\pi$ -electron structure. Hence aromatic compounds prefer substitution to addition reaction.<sup>6,7</sup>

A recent definition of aromaticity<sup>20</sup> postulates to name as fully aromatic those systems which follow all four above presented criteria. Even if one of them is not fulfilled, the compound is named as only partially aromatic.

Aromaticity has widely been investigated for individual molecules<sup>3,4</sup> or locally for particular fragments, usually benzene rings in various molecular environments.<sup>21–23</sup> A substantial dependence of the local aromaticity determined for individual rings on their environment was found.<sup>24</sup>

Much less attention has been paid to the intermolecular interactions affecting aromaticity of a given  $\pi$ -electron system. Katritzky<sup>25</sup> has shown that the solvent may affect aromaticity of a given system, and recently it was shown that the H-bonding between the bases in the Crick-Watson pairs causes an increase of aromaticity of  $\pi$ -electron moieties involved in the interactions.<sup>26</sup>

The aim of this paper is to analyze the title question using geometries retrieved from CSD<sup>27</sup> and applying the geometry

based index HOMA<sup>12,14</sup> in its modified version<sup>28</sup> which allows one to show the structural nature of the factors decreasing the aromaticity of the ring.

## METHODOLOGY

Geometries of 664 rings of H-bonded complexes of variously substituted phenol derivatives with various oxygen and nitrogen bases were retrieved from CSD<sup>27</sup> with the following restrictions: (1) the searches were performed for structures containing substituted phenol and a nitrogen or oxygen base having an intermolecular contact between the hydroxyl group of phenol and the nearest O– or N– atom in a base equal to or less than the sum of their van der Waals radii<sup>29</sup> and (2) the searches were restricted to structure measurements with the reported mean estimated standard deviation (esd) of the CC bond  $\leq 0.005$  Å (corresponds to AS flag = 1). The data were retrieved for polysubstituted phenols (by any of the following substituents: halogen, –NO<sub>2</sub>, –NH<sub>2</sub>, –COOH, –CONH<sub>2</sub>, –COCH<sub>3</sub>, –COOCH<sub>3</sub>, –CHO, –OH, –SH, –N=O, –Me, –*i*Pr, –*t*Bu, –Ph, –CPh<sub>3</sub>, –SiMe<sub>3</sub>, –SO<sub>3</sub>H, –H) interacting with N– or O– atom in base. Sometimes the molecules of the solvent were present in the structure lattice.

Principal Component Analysis for collected structural data were done using Vista v.2.1.

Bond lengths of phenol rings were used to estimate the values of aromaticity index HOMA<sup>12,14</sup> in the form with separation of two structural effects decreasing aromaticity: (i) an increase of mean bond length and (ii) an increase of bond length alternation.<sup>28</sup> The definition of this form of HOMA index is as below

$$\text{HOMA} = 1 - \left[ \alpha(R_{\text{opt}} - R_{\text{av}})^2 + \frac{\alpha}{n} \sum_i (R_{\text{av}} - R_i)^2 \right] = 1 - \text{EN} - \text{GEO} \quad (1)$$

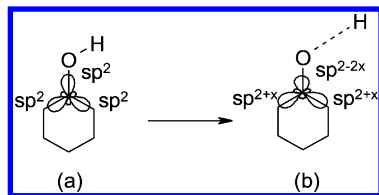
where  $n$  is the number of bonds taken into the summation;  $\alpha$  is a normalization constant (for CC bonds  $\alpha = 257.7$ ) fixed to give HOMA = 0 for a model nonaromatic system and HOMA = 1 for the system with all bonds equal to the

\* Corresponding author phone: +48 22 660 77 55; fax +48 22 628 27 41; e-mail: halina@chemix.ch.pw.edu.pl.

<sup>†</sup> Warsaw University.

<sup>‡</sup> Warsaw University of Technology.

**Scheme 1.** Scheme of the Changes in Hybridization at the Carbon Atom as a Result of an Increase of Negative Charge at the Oxygen Atom



optimal value  $R_{\text{opt}}$  assumed to be realized for full aromatic systems (for CC bonds  $R_{\text{opt}}$  is equal to 1.388 Å);  $R_i$  stands for a running bond length. The EN term describes the decrease of aromaticity due to bond elongation, whereas the GEO term—the decrease due to an increase of bond alternation.  $R_{\text{av}}$  stands for average bond length.

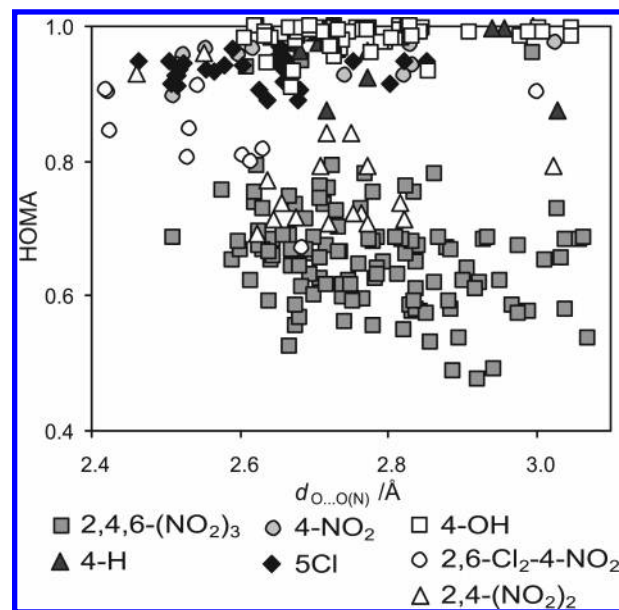
## RESULTS AND DISCUSSION

Recently it has been shown by DFT modeling of the  $\text{ArOH}\cdots\text{F}^-$  system<sup>30</sup> that the C–O bond length is a reliable measure of the intermolecular H-bond strength. The stronger the H-bond is, the shorter the C–O bond length is. On the other hand, it has recently been shown<sup>31</sup> that the changes of geometry parameters near the C–O bond, i.e., both *ipso-ortho* CC bond lengths and the *ipso* bond angle, follow the Bent-Walsh rule<sup>32</sup> and nicely fulfill a linear dependence vs the C–O bond length (with absolute value of the correlation coefficients around 0.95 for the 635 data set). The interpretation was as follows: the increase of the H-bond strength causes the increase of a negative charge at the oxygen atom in the –OH group, and the value of its electronegativity decreases. The changes in the  $\sigma$ -electron structure at the *ipso* carbon atom may be presented as in Scheme 1.

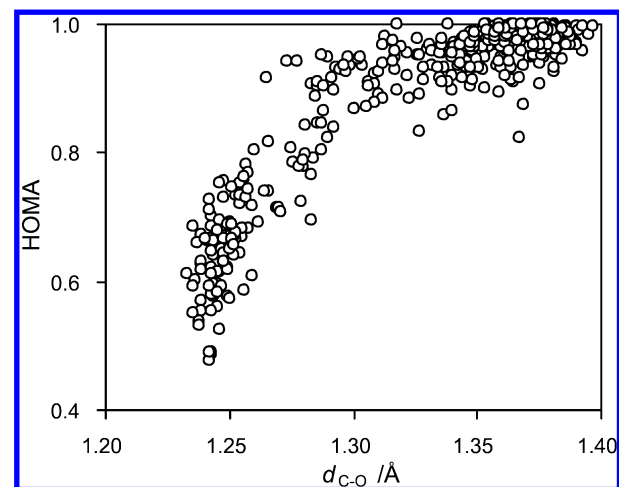
A less electronegative oxygen atom (Scheme 1b) attracts weaker 2p electrons in the  $\text{sp}^2$  hybrid orbital than in the situation presented in Scheme 1a, and this results in a decrease of the p-character in the orbital along the C–O bond. Consequently, two other bond orbitals along *ipso-ortho* bonds contain more 2p character.

One should observe as a structural consequence that *ipso-ortho* bonds become longer and the *ipso* bond angle becomes sharper, as it was observed previously.<sup>31</sup> A question arises whether these local changes are associated with the changes in the aromaticity index HOMA which is based on all CC bond lengths in the ring.

One of the relevant and early applied parameters for the H-bond strength is the O...O (O...N) distance.<sup>33,34</sup> We have used O...O and O...N together at abscissa since the differences in the van der Waals radii of the oxygen and nitrogen atom is almost negligible (1.52 and 1.55 Å, respectively<sup>29</sup>). Figure 1 presents the scatter plot of HOMA values against the O...O(N) distance. Two cluster of data points are observed. These with higher HOMA values ( $>0.8$ ) describe the  $\text{PhOH}\cdots\text{Base}$  interactions, whereas the other, with  $\text{HOMA} < 0.8$ , refer to the  $\text{PhO}^-\cdots\text{HBase}$  interactions. This interpretation is in line with theoretical study based on  $\text{PhOH}\cdots\text{F}^-$  and  $\text{PhO}^-\cdots\text{HF}$  interactions.<sup>35</sup> However, it has been shown that the O...O(N) distance is not too precise a measure of the H-bond strength. It may also be deduced from the Lippincott-Schroeder potential<sup>36</sup> where more components of the potential have to be used to get a reliable estimation of the H-bond energy. To get a deeper interpretation of the



**Figure 1.** Relationship of HOMA on O...O(N) distance,  $d_{\text{O}\cdots\text{O(N)}}$ , for variously substituted phenols.

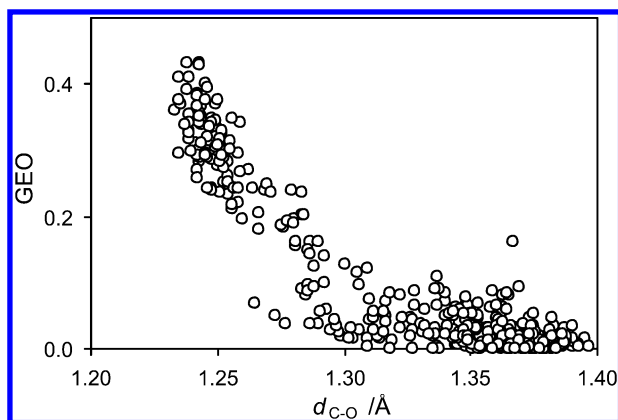


**Figure 2.** Relationship of HOMA on C–O bond length,  $d_{\text{C-O}}$ , for variously substituted phenols.

dependence of aromaticity on the H-bond strength we have used the C–O bond length.<sup>30</sup>

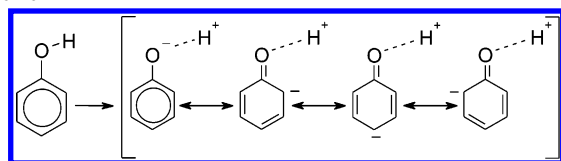
Figures 2–4 show the dependences of HOMA, GEO, and EN indices on the C–O bond length, i.e., the approximate value of the H-bond strength.

The most nicely looking dependences are those for HOMA and GEO vs the C–O bond length—Figures 2 and 3. They both show a regular variation with the increase of the C–O bond length. A change of the H-bond strength causes a substantial decrease of aromaticity. HOMA values fall down from 1.0 to around 0.5, i.e., half of the overall scale of HOMA between the aromatic (1.0) and the nonaromatic (0.0) system. However, the border for the massive population of data points is around 0.55. Alike is the variation of GEO, but in an opposite direction, since in eq 1 GEO is subtracted from 1.0. The descriptor of the bond length alternation (GEO) increases with an increase of the H-bond strength until the  $\text{H}^+$  is transferred on base, and then the interaction changes to  $\text{PhO}^-\cdots\text{HBase}$  and the dependence of HOMA and GEO on  $d_{\text{C-O}}$  is reversed. The changes in GEO are in the range of 0.4, with a massive population along all scatter plots. Note



**Figure 3.** Relationship of GEO term on C–O bond length,  $d_{\text{C-O}}$ , for variously substituted phenols.

**Scheme 2**



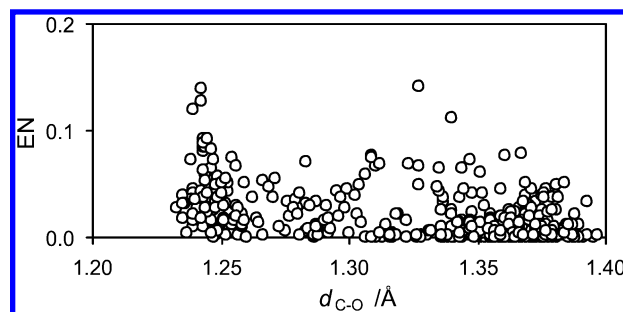
that the dependences in Figures 2 and 3 are not linear, the steeper is the increase of the GEO term and in consequence of eq 1, the smaller is HOMA. This is due to the quadratic form of bond length in the HOMA and GEO terms which are plotted against the linear changes in  $d_{\text{C-O}}$ . From the dependences of  $d_{\text{C-O}}$  on  $\bar{a}$  (the mean value of the *ipso-ortho* and *ipso-ortho'* CC bonds in the ring) result a linear form,<sup>31</sup> thus all other changes in the ring bond length might be assumed as changing in a linear way as well. The worst scatter plot is for the dependence of EN vs C–O bond lengths. However, the range for these data is narrower, with a massive population significantly below the 0.1 HOMA unit. Moreover, there is no clear relationship, rather a random distribution is observed with two clusters: for weak H-bonds (EN  $\sim$ 0.0) and strong H-bonds (EN  $\sim$ 0.05).

It should be pointed out here that among the considered systems there are polysubstituted phenols with five even substituents and their effect on the ring may be strongly steric—leading to substantial elongation of the CC bonds. However, this is not significant as it results from a little variation in EN.

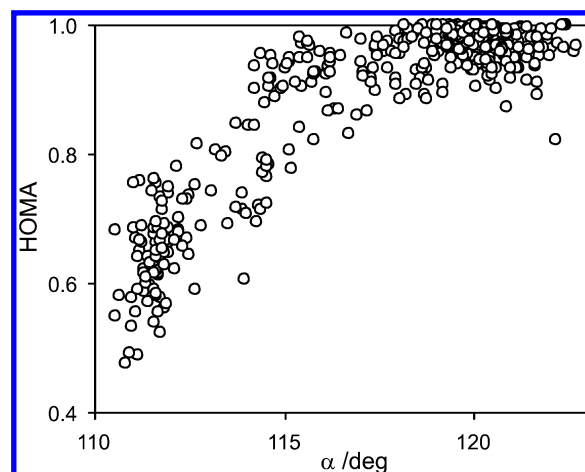
Very important is the dependence of GEO on the C–O bond length (Figure 3). The alternation of bond lengths in the ring behaves regularly with the change of the H-bond strength. Thus one may conclude that an increase of the H-bond strength of phenol derivatives (H-bond donors) leads to a decrease of aromaticity. Moreover, the main structural factor contributing to the decrease of aromaticity of the ring results mostly from bond lengths alternation.

The observation of the decrease of aromaticity of the ring due to the presence of the substituent with an increasing double bond character is in line with the formerly found effect of the decrease of aromaticity of pyrrole rings in porphyrines.<sup>37</sup> A similar observation has been found for pyrazole derivatives.<sup>38</sup> Schematically the H-bond effect on the C–O bond length and then on aromaticity may be shown by Scheme 2.

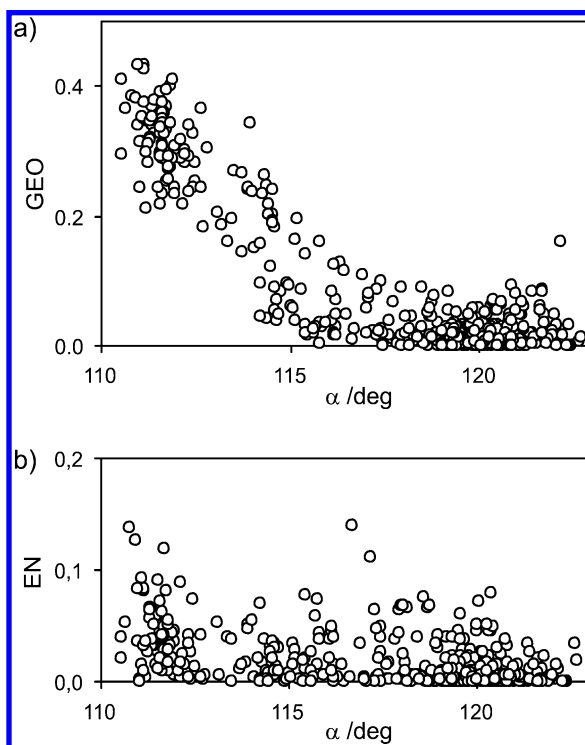
Since the C–O bond length depends linearly on the *ipso* angle<sup>31</sup> ( $\alpha$ ) similar relationships, as in Figures 2–4, are



**Figure 4.** Relationship of EN term on C–O bond length,  $d_{\text{C-O}}$ , for variously substituted phenols.



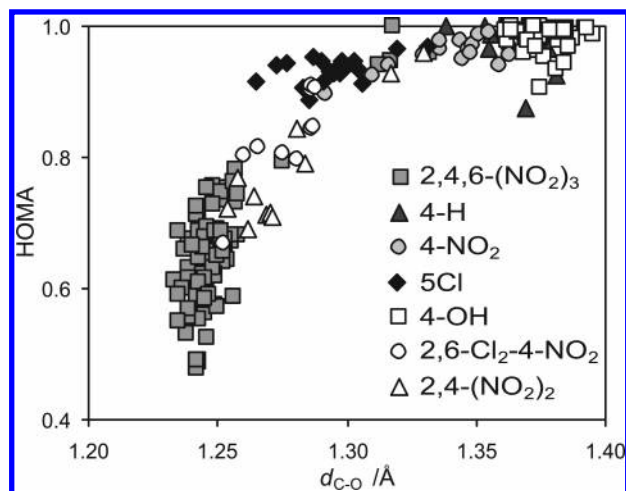
**Figure 5.** Dependence of HOMA on the *ipso* angle,  $\alpha$ , for variously substituted phenols.



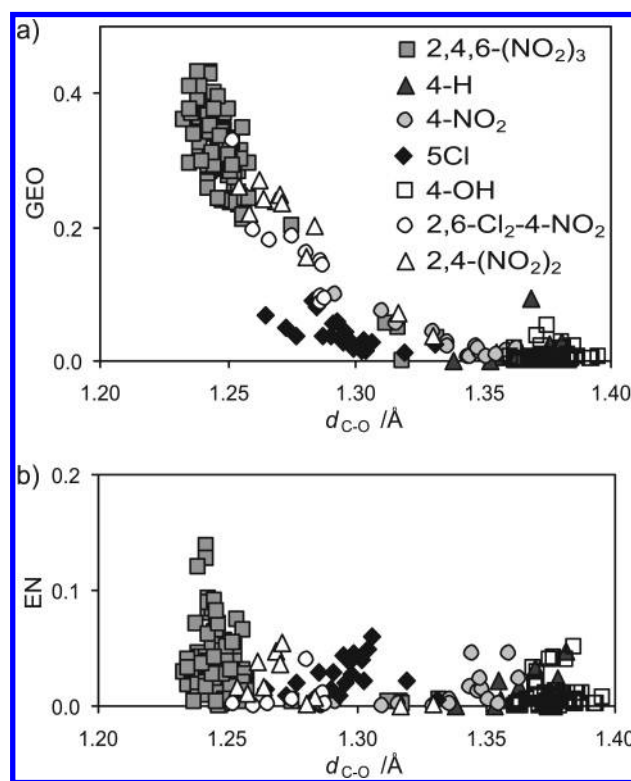
**Figure 6.** Dependence of (a) GEO and (b) EN term on the *ipso* angle,  $\alpha$ , for variously substituted phenols.

observed for the HOMA, GEO, and EN terms plotted against the  $\alpha$  angle as shown in Figures 5 and 6.

When the mean values of HOMA, GEO, and EN are calculated for groups of substituted phenols of a particular kind of substitution (Figures 7 and 8) for which 10 or more



**Figure 7.** Dependence of HOMA on C–O bond length,  $d_{C-O}$ , for 7 types of substituted phenol.

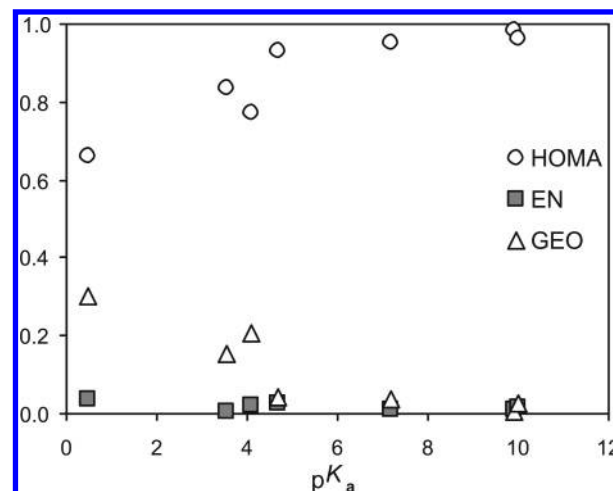


**Figure 8.** Dependence of (a) GEO and (b) EN term on C–O bond length,  $d_{C-O}$ , for 7 types of substituted phenol.

structural data were determined and the  $pK_a$ <sup>39</sup> are known, then the dependence of HOMA and GEO on  $pK_a$  is found, as shown in Figure 9.

The selected data for the groups characterized by  $pK_a$  values exhibit specific features. The data of a given groups range significantly in the C–O bond length and the HOMA and GEO values (Table 1). The mean values of the aromaticity index depend on  $pK_a$  in a logical way (Figure 9).

It is a reasonable dependence, since  $pK_a$  describes the acidity power of phenol, thus the H-bond strength with various bases should depend on this property.<sup>40</sup> In turn, the stronger the H-bonding is, the shorter the C–O (H-bond donor) bond is, and the greater decrease of aromaticity is measured by the mean value of HOMA. Differences in the nature of bases for those complexes contribute to the



**Figure 9.** Dependence of HOMA, GEO, and EN mean values vs  $pK_a$  for 7 types of substituted phenol.

variation of the H-bonding strength. However, taking mean values of the aromaticity descriptors allows one to rationalize this procedure. Figure 9 also shows that an important contribution to the decrease of aromaticity of the ring results from the GEO term, i.e., from the increase of bond alternation. The EN values are almost insignificant.

To study the crystal packing effects on the analyzed data, the full set of compounds presented in scatter plots in Figures 2–6 was a subject of principal component analysis<sup>41</sup> (hereafter abbreviated as PCA) taking into account the following: (a) CC bonds in the ring, (b) ring angles, and (c) ring angles and bonds.

The idea of PCA is based upon the reduction of the data matrix (built up in principle of not orthogonal row- or column-vectors) into the matrix built up of orthogonal vectors. Each obtained vector ('principal components') contributes to the reproduction of the full matrix of variance. The first principal component is in our case representative for geometry changes of the ring and correlates well with the exo-cyclic bond length  $d_{C-O}$ . Other principal components may contain a contribution to changes in the geometry dependent on 'packing forces' and other interactions.

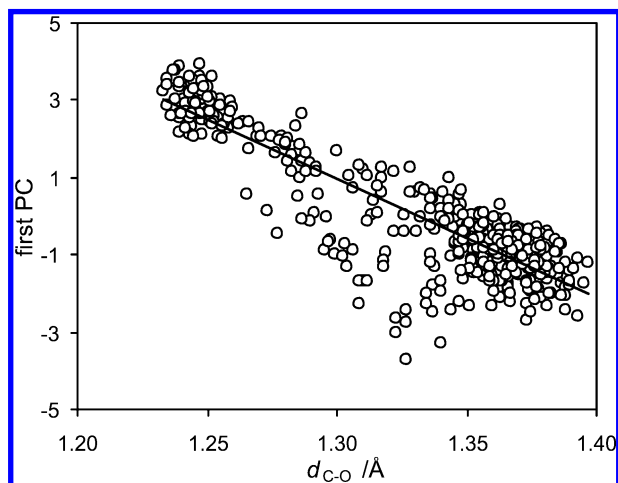
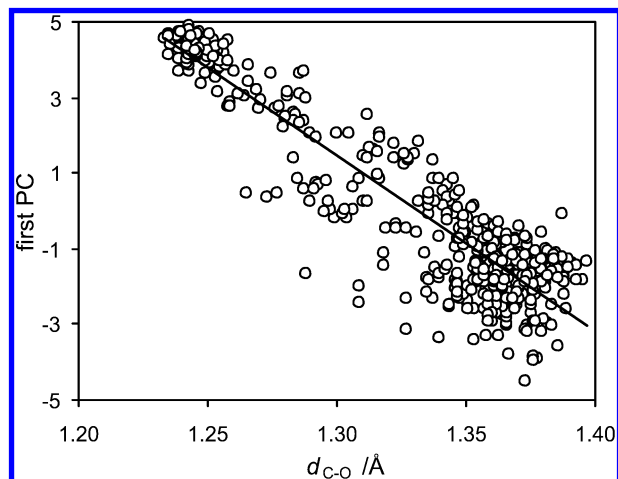
In the first case (a) the first component explains 47.0% of the total variance, and the five principal components are necessary to explain 98.2% of the total variance. In the second case (b) the first component explains 64.1%, and only three components are sufficient to explain 98.1% of the total variance. These results reflect geometrical constraints of the angular deformation in the planar hexagon—the sum of all internal angles is  $720^\circ$ , and, additionally, alpha and beta angles are known to be related by linear regressions.<sup>42</sup> There are no such constraints for bond lengths. When all geometric parameters of the ring are taken into PCA, case (c), then 7 components explain 96.8% of the total variance; however, the main component explains 51.0% of the total variance. It seems that in this case changes in angles and in bond lengths do not necessarily follow the same pattern. It is important to note that in this data set phenol derivatives interact with various bases, they are variously substituted and experience various kinds of crystal packing forces.

Very interestingly, in all cases the main component correlates fairly well with the C–O bond length, as shown in Figure 10, with the correlation coefficient ( $cc$ )  $-0.902$ .



**Table 1.**  $pK_a$ ,<sup>39</sup> Mean Values of Aromaticity Indices, and C–O Bond Length,  $d_{C-O}$ , for All Data Points and for 7 Groups of Substituted Phenol Derivatives Together with Their Estimated Standard Deviation (esd)

phenols	$pK_a$	number of structures	$d_{C-O}/\text{\AA}$		HOMA		GEO		EN	
			mean	esd	mean	esd	mean	esd	mean	esd
all		664	1.332	0.050	0.897	0.133	0.087	0.121	0.016	0.022
2,4,6-(NO <sub>2</sub> ) <sub>3</sub>	0.38	126	1.25	0.016	0.663	0.092	0.302	0.075	0.035	0.028
2,6-Cl <sub>2</sub> -4-NO <sub>2</sub>	3.55	11	1.278	0.013	0.837	0.071	0.156	0.070	0.006	0.012
2,4-(NO <sub>2</sub> ) <sub>2</sub>	4.09	18	1.276	0.020	0.772	0.078	0.207	0.065	0.021	0.020
Cl <sub>5</sub>	4.70	27	1.294	0.013	0.933	0.021	0.043	0.022	0.024	0.014
4-NO <sub>2</sub>	7.16	18	1.334	0.021	0.953	0.025	0.036	0.029	0.011	0.015
4-OH	9.91	70	1.377	0.008	0.984	0.019	0.007	0.010	0.009	0.012
4-H	9.99	13	1.365	0.013	0.962	0.044	0.024	0.032	0.014	0.016

**Figure 10.** Dependence of first principal component of PCA, when bond lengths of the ring were taken into account (case a), on C–O bond length,  $d_{C-O}$ , for variously substituted phenols,  $cc = -0.902$ .**Figure 11.** Dependence of first principal component of PCA, when all geometrical parameters of the ring were taken into account (case c), on C–O bond length,  $d_{C-O}$ , for variously substituted phenols,  $cc = -0.928$ .

Even better correlation (Figure 11) was found for the case (c) with the correlation coefficient  $-0.928$ , whereas for the case (b) the correlation is worse ( $cc = 0.849$ ).

To decide how much the crystal packing forces affect geometrical parameters (bond lengths) determined by X-ray diffraction in a crystalline state, the PCA was applied to a more homogeneous sample, *p*-nitrophenol H-bonded with various bases (18 structures). We have applied here only bond lengths, and the results are very striking. Again, the first component dominates, describing 53.4% of the total variance, and it correlates fairly well with the C–O bond

length. This means that similarly as in the full data set, the main deformation of the ring results from the interaction due to the H-bond. However, all other deformations in the case of the *p*-nitrophenol H-bonded complexes seem to be dependent on the crystal packing forces. Again, to explain the total variance there are five principal components needed, which in this case describes 99.5% of the total variance. Since the isolated *p*-nitrophenol is almost symmetrical (except for the AGIBA effect<sup>43</sup> which is not strong), thus the presence of more than three components evidently indicates the unsymmetrical perturbations of the ring due to potential unsymmetrical intermolecular interactions in the crystal lattice. Application of PCA to the ring geometry parameters (bond lengths) for theoretically modeled systems [*p*-NO<sub>2</sub>-PhO...H...F]<sup>-35</sup> (37 structures) results in one principal component describing 99.6% of the total variance. Thus the deviations in the scatter plots observed in Figures 2–6 may be easily justified by the side effects in the X-ray diffraction data.

## CONCLUSIONS

The investigation demonstrates that intermolecular interactions dramatically affect aromaticity of the ring in H-bonded complexes of variously substituted phenol derivatives with different bases, and the changes depend on the H-bond strength. The variation in the HOMA values range about half of the scale between the aromatic systems (HOMA = 1.0) and the nonaromatic ones (HOMA = 0.0). The best dependences on the H-bond strength were found for the term describing the bond length alternation in the ring (GEO term) and the overall aromaticity index HOMA. The worst, practically without clear feature of any correlation, is the dependence of the term describing the effect of mean bond elongation (EN term) on the C–O bond length. The variation of EN values is three times smaller than those for GEO.

**Supporting Information Available:** Refcodes and appropriate references for 382 hits (664 structures) variously substituted phenol complexes with bases retrieved from CSD. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## REFERENCES AND NOTES

- (1) *Aromaticity, Pseudoaromaticity, Antiaromaticity*; Bergmann, E. D., Pullman, B., Eds.; Proceedings of an International Symposium held in Jerusalem 1970, Israel Academy of Sciences and Humanities, Jerusalem, 1971.
- (2) Agranat, I. In *Aromatic Compounds*; Zollinger, H., Ed.; Butterworth: London, University Park Press: Baltimore, 1973; Vol. 3, Chapter 5, pp 140–171. Agranat, I.; Barak, A. In *Organic Chemistry*; Zollinger, H., Ed.; Butterworth: London – Boston, 1975; Vol. 3, Chapter 1, pp 2–22.

- (3) Minkin, V. I.; Glukhovtsev, M. N.; Simkin, B. Ya. In *Aromaticity and Antiaromaticity, Electronic and Structural Aspects*; Wiley: New York, 1994.
- (4) Topical issue on Aromaticity edited by Schleyer, P. v. R. *Chem. Rev.* **2001**, *101*, 1115–1566.
- (5) Armit, J. W.; Robinson, R. Polynuclear Heterocyclic Aromatic Types. Part II. Some Anhydronium Bases. *J. Chem. Soc.* **1925**, 127, 1604–1618. Balaban, A. T.; Oniciu, D. C.; Katritzky, A. R. Aromaticity as a Cornerstone of Heterocyclic Chemistry. *Chem. Rev.* **2004**, *104*, 2777–2812.
- (6) Smith, B. M.; March, J. In *March's Advanced Organic Chemistry*, 5th ed.; Wiley: New York, 2001.
- (7) Vollhardt, K. P. C.; Schore, N. E. In *Organic Chemistry*, 3th ed.; W. H. Freeman and Company: New York, 1998.
- (8) Pauling, L.; Sherman, J. The Nature of the Chemical Bond. VI. The Calculation from Thermochemical Data of the Energy of Resonance of Molecules Among Several Electronic Structures. *J. Chem. Phys.* **1933**, *1*, 606–617. Pauling, L.; Sherman, J. The Nature of the Chemical Bond. VII. The Calculation of Resonance Energy in Conjugated Systems. *J. Chem. Phys.* **1933**, *1*, 679–686.
- (9) Kistiakovsky, B.; Ruhoff, J. R.; Smith, H. A.; Vaughan, W. E. Heats of Organic Reactions. IV. Hydrogenation of Some Dienes and of Benzene. *J. Am. Chem. Soc.* **1936**, *58*, 146–153.
- (10) Wheland, G. W. In *The Theory of Resonance and its Application to Organic Chemistry*; Wiley: New York, 1947.
- (11) Jug, A.; François, P. Geometry of Nonalternant Hydrocarbons: its Influence on the Transition Energies, a New Definition of Aromaticity. *Theor. Chim. Acta* **1967**, *8*, 249–259.
- (12) Kruszewski, J.; Krygowski, T. M. Definition of Aromaticity Basing on the Harmonic Oscillator Model. *Tetrahedron Lett.* **1972**, 3839–3842.
- (13) Bird, C. W. A New Aromaticity Index and Its Application to Five-Membered Ring Heterocycles. *Tetrahedron* **1985**, *41*, 1409–1414.
- (14) Krygowski, T. M. Crystallographic Studies of Inter- and Intramolecular Interactions Reflected in Aromatic Character of  $\pi$ -Electron Systems. *J. Chem. Inf. Comput. Sci.* **1993**, *33*, 70–78.
- (15) Dauben, H. J.; Wilson, J. D.; Laity, J. L. Diamagnetic Susceptibility Exaltation as a Criterion of Aromaticity. *J. Am. Chem. Soc.* **1968**, *90*, 811–813. Dauben, H. J.; Wilson, J. D.; Laity, J. L. Diamagnetic Susceptibility Exaltation in Hydrocarbons. *J. Am. Chem. Soc.* **1969**, *91*, 1991–1998. Dauben, H. J.; Wilson, J. D.; Laity, J. L. In *Non-Benzoid Aromatics*; Snyder, J. P., Ed.; Academic Press: New York, 1971; Vol. 2.
- (16) Flygare, W. H. Magnetic Interactions in Molecules and an Analysis of Molecular Electronic Charge Distribution from Magnetic Parameters. *Chem. Rev.* **1974**, *74*, 653–687.
- (17) Schleyer, P. v. R.; Maerker, C.; Dransfeld, H.; Jiao, H.; Hommes, N. J. R. v. E. Nucleus-Independent Chemical Shifts: A Simple and Efficient Aromaticity Probe. *J. Am. Chem. Soc.* **1996**, *118*, 6317–6318.
- (18) For recent review see: Lazzeretti, P. Ring Currents. *Prog. Nucl. Magn. Reson. Spectrosc.* **2000**, *36*, 1–88.
- (19) Sadlej-Sosnowska, N. Mutual Relationships between Magnetic Aromaticity Indices of Heterocyclic Compounds. *J. Phys. Org. Chem.* **2004**, *17*, 303–311.
- (20) Krygowski, T. M.; Cyrański, M. K.; Czarnocki, Z.; Häfelfinger, G.; Katritzky, A. R. Aromaticity: a Theoretical Concept of Immense Practical Importance. *Tetrahedron* **2000**, *56*, 1783–1796.
- (21) Krygowski, T. M.; Ciesielski, A.; Bird, C. W.; Kotschy, A. Aromatic Character of the Benzene Ring Present in Various Topological Environments in Benzenoid Hydrocarbons. Nonequivalence of Indices of Aromaticity. *J. Chem. Inf. Comput. Sci.* **1995**, *35*, 203–210.
- (22) Howard, S. T.; Krygowski, T. M. Benzenoid Hydrocarbon Aromaticity in Terms of Charge Density Descriptors. *Can. J. Chem.* **1997**, *75*, 1174–1181.
- (23) Schleyer, P. v. R.; Jiao, H. What is aromaticity? *Pure Appl. Chem.* **1996**, *68*, 209–218.
- (24) Krygowski, T. M.; Cyrański, M.; Ciesielski, A.; Świrski, B.; Leszczyński, P. Separation of the Energetic and Geometric Contributions to Aromaticity. 2. Analysis of the Aromatic Character of Benzene Rings in Their Various Topological Environments in the Benzenoid Hydrocarbons. Crystal and Molecular Structure of Coronene. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 1135–1141. Cyrański, M.; Krygowski, T. M. Separation of the Energetic and Geometric Contributions to Aromaticity. 3. Analysis of the Aromatic Character of Benzene Rings in Their Various Topological and Chemical Environments in the Substituted Benzene Derivatives. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 1142–1145.
- (25) Katritzky, A. R.; Karelson, M.; Wells, A. P. Aromaticity as a Quantitative Concept. 6. Aromaticity Variation with Molecular Environment. *J. Org. Chem.* **1996**, *61*, 1619–1621.
- (26) Cyrański, M. K.; Gilski, M.; Jaskólski, M.; Krygowski, M. K. On the Aromatic Character of the Heterocyclic Bases of DNA and RNA. *J. Org. Chem.* **2003**, *68*, 8607–8613.
- (27) The Cambridge Structure Database, the 5.25 version, November 2003, updated January 2004.
- (28) Krygowski, T. M.; Cyrański, M. K. Separation of the Energetic and Geometric Contributions to the Aromaticity of  $\pi$ -electron Carbocyclics. *Tetrahedron* **1996**, *52*, 1713–1722.
- (29) Bondi, A. van der Waals Volumes and Radii. *J. Phys. Chem.* **1964**, *68*, 441–451.
- (30) Krygowski, T. M.; Zachara, J. E.; Szatyłowicz, H. Molecular Geometry as a Source of Chemical Information. Part 2: An attempt to estimate the H-bond strength – the case of *p*-nitrophenol complexes with bases. *J. Phys. Org. Chem.* **2004**, in press.
- (31) Szatyłowicz, H.; Krygowski, T. M. Molecular Geometry as a Source of Chemical Information. Part I: How H-bonding Modifies Molecular Structure in the Vicinity of Hydrogen Donating Group. The Case of Phenol Derivatives Interacting with Nitrogen and Oxygen Bases. *Pol. J. Chem.* **2004**, *78*, 1719–1731.
- (32) Walsh, A. D. The properties of bonds involving carbon. *Discuss. Faraday Soc.* **1947**, *2*, 18–25. Bent, H. A. An Appraisal of Valence-bond Structures and Hybridization in Compounds of the First-row Elements. *Chem. Rev.* **1961**, *61*, 275–311.
- (33) Pimentel, G. C.; McClellan, A. L. In *The Hydrogen Bond*; W. H. Freeman and Company: San Francisco, 1960.
- (34) Schuster, P.; Zundel, G.; Sandorfy, C. In *The Hydrogen Bond*; North-Holland Publishing Company: Amsterdam, 1976.
- (35) Krygowski, T. M.; Zachara, J. E.; Szatyłowicz, H. Molecular Geometry as a Source of Chemical Information. Part III. How H-bonding Affects Aromaticity of the Ring in the Case of Phenol and Para-Nitrophenol Complexes – a B3LYP/6-311+G\*\* Study. *J. Org. Chem.* **2004**, *69*, 7038–7043.
- (36) Lippincott, E. R.; Schroeder, R. One-Dimensional Model of the Hydrogen Bond. *J. Chem. Phys.* **1955**, *23*, 1099–1106.
- (37) Cyrański, M. K.; Krygowski, T. M.; Wisiorowski, M.; Hommes, N. J. R. v. E.; Schleyer, P. v. R. Global and Local Aromaticity in Porphyrins: An Analysis Based on Molecular Geometries and Nucleus-Independent Chemical Shifts. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 177–180.
- (38) Krygowski, T. M.; Anulewicz, R.; Cyrański, M. K.; Puchała, A.; Raszka, D. Separation of the Energetic and Geometric Contribution to the Aromaticity. Part IX. Aromaticity of Pyrazoles in Dependence on the Kind of Substitution. *Tetrahedron* **1998**, *54*, 12295–12300.
- (39) Kortum, G.; Vogel, W.; Andrusow, A. In *Dissociation Constants of Organic Acids in Aqueous Solution*; Butterworth: London, 1961. Tehan, B. G.; Lloyd, E. J.; Wong, M. G.; Pitt, W. R.; Montana, J. G.; Manallack, D. T.; Gancia, E. Estimation of  $pK_a$  Using Semiempirical Molecular Orbital Methods. Part I: Application to Phenols and Carboxylic acids. *Quant. Struct. – Act. Relat.* **2002**, *21*, 457–472.
- (40) Huyskens, P.; Sobczyk, L.; Majer, I. On a hard/soft bond interaction. *J. Mol. Struct.* **2002**, *615*, 61–72.
- (41) Malinowski, E. R. In *Factor Analysis in Chemistry*; Wiley: New York, 2002. Zalewski, R. I. In *Studies in Organic Chemistry. Similarity Models in Organic Chemistry, Biochemistry and Related Fields*; Zalewski, R. I., Krygowski, T. M., Shorter, J., Ed.; Elsevier Science Publisher: Amsterdam, 1991; Vol. 42, Chapter 9, pp 455–544.
- (42) Domenicano, A.; Vaciago, A. Molecular Geometry of Substituted Benzene Derivatives. I. On the Nature of the Ring Deformations Induced by Substitution. *Acta Crystallogr.* **1975**, *B31*, 221–234. Domenicano, A.; Murray-Rust, P.; Vaciago, A. Molecular Geometry of Substituted Benzene Derivatives. IV. Analysis of Variance in Monosubstituted Benzene Rings. *Acta Crystallogr.* **1983**, *39B*, 457–468.
- (43) Krygowski, T. M.; Cyrański, M. K. Angular Group Induced Bond Alternation (AGIBA). A New Face of Substituent Effect Detected in Molecular Geometry. *Synlett.* **2003**, *7*, 922–936. Correction *Synlett.* **2003**, *10*, 1570–1570.

CI049817S