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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*

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Analysis of geometrical patterns of 635 variously substituted phenols in H–bonding complexes with bases revealed that C_1O, C_1C_2, C_1C_6 bond lengths as well as ipso bond angle change regularly with variation of the acidity (pK_a) of phenols. The Bent-Walsh rule is fulfilled and the approximate linear dependence between the above mentioned geometry parameters works. The perturbation in the OH group, due to H-bonding, is transmitted even on further fragments of the ring. DFT modelling at the B3LYP/6–311+G** level of theory for the simplest cases illustrate nicely the conclusion derived for variously substituted systems.

Key words: hydrogen bond, substituted phenols, Bent-Walsh rule

It is a trivial statement that geometry is a very important characteristic of molecules. According to R. Hoffmann "*There is no more basic enterprise in chemistry than the determination of the geometric structure of a molecule. Such a determination if it is well done, ...provides us with a starting point for understanding of every physical, chemical and biological property of the molecule*" [1]. Obviously, the geometry of any molecule in the condensed phase depends on the interaction with the neighbouring species [2]. Because of the interactions, the isolated molecule geometry may be dramatically changed giving important information due to the deformations observed. The Bürgi & Dunitz principle of the structural correlation [3–6] has given a lot of insight for understanding the initial steps of chemical reaction just from the analysis of the interactions of molecules in a crystalline state [7]. In this way, this nicely illustrated organic addition and elimination reactions, the transformation paths of carbonyl derivatives [8], reaction paths for nucleophilic substitution reactions (S_N2) [9] and the role of hydrogen bonding in molecular assemblies [10]. The structure correlation principle was also very useful in the analysis of ligand – receptor interactions [11]. It was also found that deformations of molecules depend clearly on the distance of neighbouring atoms from other molecules in the crystal lattice [12].

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* Dedicated to Prof. Dr. Z. Galus on the occasion of his 70th birthday.

Another important structural effect on molecular geometry is associated with substituents that due to their inductive and mesomeric interactions with a substituted moiety may cause substantial changes in bond angles and bond lengths. Accumulation of sufficiently precise measurements allowed first studies in this field in the mid-70s and the first systematically studied systems were derivatives of benzene [13]. The variation of the ipso angle in the monosubstituted ring was interpreted in terms of the Walsh-Bent rule [14,15] and VSEPR theory [16]. The linear regression [17] of the ipso angle α *vs*. Huheey group electronegativity [18] χ and inductive substituent constants [19] σ_I was found with correlation coefficient (hereafter abbreviated as *cc*) around 0.9 for 13 and 10 data sets, respectively. Then, following the Bent-Walsh rule it was found that bond lengths, taken as a difference between the *ortho*-*meta* (b) and *ipso*-*ortho* (a) and bonds lengths, $\Delta = (b - a)$, correlate equally well (*cc* = 0.913 for 14 data set) with the ipso angle α for monosubstituted benzene derivatives [20]. In the case of homo-*para*-disubstituted benzene ring derivatives the correlation was even better (*cc* = 0.979, for 10 data points).

The main subject of the paper is related to the H-bonding, the interactions of a great diversification as to the characteristics of energy and geometry [21–23]. Additionally these interactions lead to some kind of a charge separation and in consequence changes in π-electron delocalization [24]. Undoubtedly they refer to one of the most important non-covalent interactions present in chemistry [21]. There are many geometry based analyses dealing with H-bonding itself [25–30], but the aim of this paper is to study how far the molecular geometry undergoes changes in the closest neighborhood of the H-bonding, and to what degree it reflects its strength. In the case of a homogeneous sample a good correlation was found following the Bent-Walsh rule [31]. However, it is not known how the strong variation of substituent(s) attached to the benzene nucleus of variously substituted phenol derivatives affects this regularity. Moreover, various subsituents attached to the ring change the acidity of phenols [32] from $pK_a = 0.71$ for 2,4,6-trinitrophenol up to $pK_a = 10.88$ for 2,4,6-trimethylphenol or even 12.23 for 2,6-di-*t*butyl-4-methyl-phenol. This range of pK_a determines a strong variation in the Broensted acidity which may be related to the strength of the H-bonding formed. This in turn may be additionally affected by different basicities of counter molecules in the H-bonded systems.

RESULTS AND DISCUSSION

The analysis is based on the data for H-bonding complexes of substituted phenols with oxygen and nitrogen bases. All data were retrieved from CSD [33] with the following restrictions: (1) the searches were performed for structures containing substituted phenol and a nitrogen or oxygen base, having an intermolecular distance between oxygen of the hydroxyl group of phenol and the closest O- or N-base equal or less than the sum of their van der Waals radii [34]; (2) the searches were restricted to structure measurements with the reported mean estimated standard deviation (e.s.d.)

of the C–C bond ≤ 0.005 Å (corresponds to AS flag = 1). The data were retrieved for polysubstituted phenols (by any of the substituent such as: halogen, -NO_2, -NH_2, -COOH, -$CONH_2$, -$COCH_3$, -$COOCH_3$, -CHO, -OH, -SH, -N=O, -Me, -*i*Pr, -*t*Bu, -Ph, -CPh_3, -$SiMe_3$, -SO_3H, -H) interacting with N- or O-base and sometimes including molecules of solvent.

Application of the Bent-Walsh rule for interpretation of interrelations between the geometry parameters in phenol moiety in the vicinity of H-bonding. The fixed part of the H-bonding region for polysubstituted phenol derivatives interacting with the bases is the benzene ring and the CO and OH bonds. The latter will not be discussed here, since our study is based on X-ray diffraction measurements which do not provide reliable position of the H-atom. The labeling of geometric parameters is included in Fig. 1.

Table 1 shows pK_a values [32,35,36] and the mean values for geometry parameters for all sets of substituted phenols.

Table 1. Mean values of geometrical parameters and pK_a [32,35,36] for the polysubstituted phenols.

Phenols	pK_a	No. hits	No. obs.	R_{CO}/Å	a/Å	b/Å	c/Å	α/deg	β/deg	γ/deg	δ/deg
2,4,6-$(NO_2)_3$	0.71	69	109	1.248	1.447	1.370	1.380	111.7	124.4	119.1	121.3
2,6-Cl_2-4-NO_2	3.55	8	10	1.277	1.421	1.365	1.383	113.9	123.7	118.7	121.4
2,4-$(NO_2)_2$	4.09	9	17	1.277	1.430	1.371	1.383	114.5	122.8	119.3	121.2
Cl_5	4.70	20	27	1.294	1.414	1.387	1.391	115.3	122.5	120.3	119.0
F_5	5.53	4	5	1.334	1.393	1.376	1.376	115.8	122.3	120.4	118.8
4-NO_2	7.16	13	15	1.337	1.398	1.376	1.384	119.2	120.5	119.2	121.4
2-NO_2	7.23	1	6	1.308	1.413	1.383	1.370	114.3	122.5	121.0	118.7
4-CHO	7.61	1	1	1.357	1.387	1.378	1.391	120.5	119.5	120.9	118.9
4-COMe	8.05	1	2	1.357	1.388	1.379	1.389	119.9	119.7	121.1	118.4
2-$CONH_2$	8.37	1	1	1.354	1.397	1.382	1.380	120.5	118.9	121.0	119.7
3-NO_2	8.38	2	2	1.364	1.382	1.379	1.376	119.9	119.2	122.0	117.6
3,5-$(OH)_2$	8.45	6	22	1.369	1.386	1.386	1.386	121.4	118.6	121.4	118.6
2-Cl	8.48	1	3	1.341	1.404	1.392	1.393	116.6	122.0	120.1	119.2
2-OH	9.12	6	20	1.371	1.387	1.384	1.380	119.8	120.0	120.1	120.1
3-OH	9.15	7	15	1.365	1.387	1.385	1.386	120.6	119.3	121.0	118.8
2-NH_2	9.30	2	2	1.368	1.393	1.389	1.390	119.8	119.9	120.3	119.7
4-Cl	9.42	4	6	1.364	1.380	1.382	1.370	119.6	120.2	119.6	120.9
4-C_6H_5	9.55	2	2	1.374	1.381	1.386	1.394	119.5	120.0	122.0	116.6
4-OH	9.91	37	68	1.377	1.383	1.385	1.383	119.6	120.2	120.2	119.5
Phenol	9.997	9	15	1.368	1.382	1.387	1.376	120.4	119.4	120.3	120.0
3-NH_2	9.99	2	3	1.362	1.402	1.399	1.401	120.3	119.7	120.3	119.8
3-Me	10.08	2	3	1.375	1.378	1.382	1.379	120.9	119.6	119.5	120.9
4-iPr	10.24	3	3	1.378	1.385	1.390	1.391	119.8	119.7	121.5	117.7
4-Me	10.25	3	4	1.375	1.372	1.382	1.372	119.6	119.6	122.0	117.2
2-Me	10.28	1	2	1.373	1.387	1.385	1.380	121.3	118.7	120.7	119.8
2,4,6-Me_3	10.88	1	1	1.386	1.393	1.386	1.387	121.8	117.8	122.5	117.6
4-OH-2,3,5,6-Me_4	11.25	2	2	1.383	1.395	1.403	1.396	122.6	118.7	118.7	122.6
2,6-*t*Bu_2	11.70	1	1	1.392	1.397	1.395	1.373	123.9	116.3	121.6	120.3
2,6-*t*Bu_2-4-Me	12.23	1	1	1.382	1.405	1.395	1.384	123.2	116.3	123.0	118.1

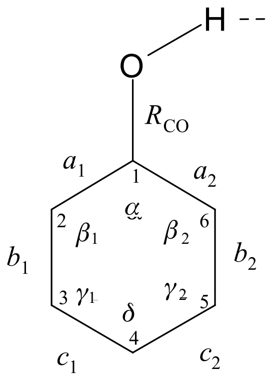

Figure 1. Labeling of geometry parameters. a, b and c in the text are the mean values for these kind of bonds. Alike β and γ.

As we can see, the variations of the mean values cover a very broad range: 0.164 Å for R_{CO}, and 0.067 Å for a bond lengths and 12.2° for the α angle. For individual values, these ranges are even larger. The longest and shortest R_{CO} bonds in the studied H-bonded complexes are 1.397 Å (4-hydroxyphenol) and 1.233 Å (2,4,6-trinitrophenol), respectively. The great variability of R_{CO} and a – bond lengths, and of the α angle may be interpreted in terms of the changes of electronegativity of the oxygen atom. Following Iczkowski and Margrave [37] electronegativity is defined as a derivative of the total energy E, against charge, Q :

$$\chi = -\left(\mathrm{d}E / \mathrm{d}Q\right)$$

thus χ depends on the charge at the oxygen atom. The Mulliken atomic charges at oxygen atom in phenol and phenolate anion computed [38] by use of DFT at the B3LYP/6-311+G** level of theory are –0.274 and –0.533, respectively. Thus, the situation for the studied systems may be illustrated in a simplified way by the canonical structures as shown in Fig. 2.

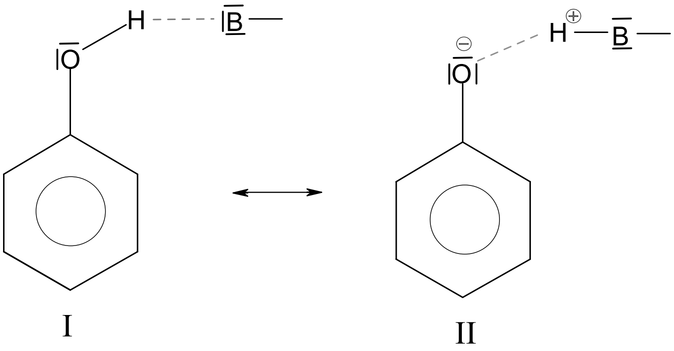

Figure 2. Resonance structures for H-bond interactions between the hydroxyl group of phenol and the basicity centre of the H-bond acceptor B. Influences on the ring geometry are not shown.

As a consequence of the increase of the negative charge at oxygen atom, the value of its electronegativity decreases, and the changes in hybridization, *i.e.* in the sigma electron structure at the ipso carbon atom, may be presented as in the scheme below (Fig. 3):

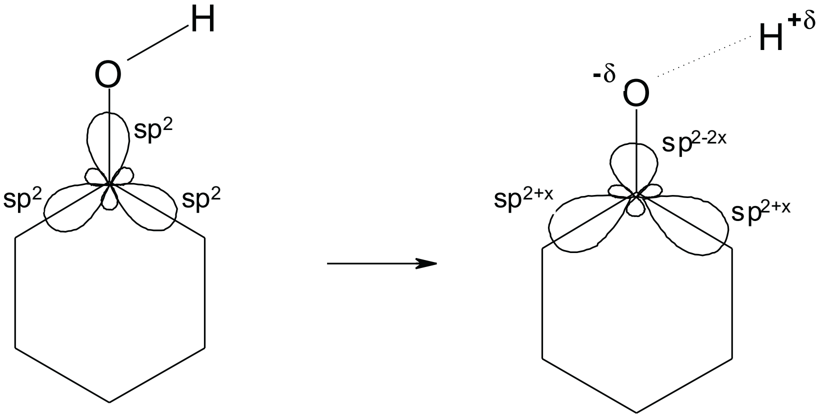

Figure 3. Scheme of the changes in hybridization at the carbon atom as a result of the increase of negative charge at the oxygen atom.

A less electronegative oxygen atom attracts weaker the p electrons in the sp^2 hybrid orbital and this results in a decrease of the p-character in the orbital along the C–O bond; consequently two other bond orbitals along a_1 and a_2 contain more p character.

As the structural consequences of the above described mechanism one should find: a lengthening of the a bonds, a decrease of the α angle and a shortening of the C–O bond lengths. These changes depend on the strength of the H-bonding and should act in a concerted way. In the case of a very limited number of the homogeneous sample [31] (12 pentachlorophenols interacting with different bases) the mutual correlations between R_{CO}, the a – bond lengths and the α angle, were acceptable, with modulo of $cc > 0.93$.

In the simplest case, where are no substituent effects and where do not work any crystal packing forces, we have considered two extreme situations – the phenol molecule and the phenolate anion. The DFT optimization at B3LYP/6–311+G** level of theory [38] gave the result as in Fig. 4. We immediately see a very good agreement with the Bent-Walsh prediction: the α angle decreases by 6.3° and the R_{CO} bond length decreases by 0.101 Å! The changes of a-bond lengths also follow the rule, they are enlarged by 0.051 Å.

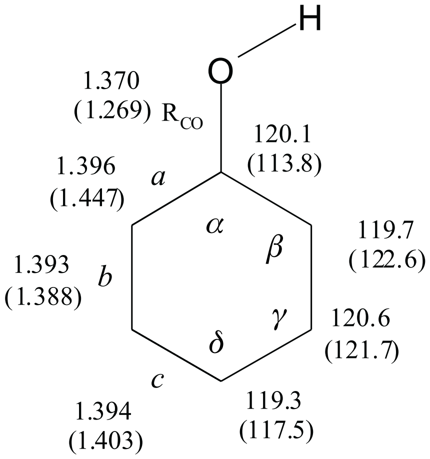

Figure 4. B3LYP/6–311+G** optimized geometry (mean values) of phenol and the phenolate anion (in parentheses).

Three questions arise:

1) Does the variety and complexity of substituents (Table 1) attached to the ring modify this picture?
2) How is the acidity (pK_a values) of phenol derivatives reflected in view of the Bent-Walsh rule applied to the problem of variation in structure, *i.e.* to the interrelation between the geometric parameters in the vicinity of the H-bonding?
3) Are the regularities observed in close vicinity of the H–bonding system encountered at longer distances as well?

To answer the first question, we have made scatter plots for those pairs of structural parameters:

(i) C–O bond length (R_{CO}) *vs.* α;
(ii) C–O bond length (R_{CO}) *vs.* the mean value a of the a_1,a_2 bond lengths; and finally
(iii) α *vs.* the mean value of a.

Figure 5 presents these relationships together with the *cc*-values.

Figure 5 shows the scatter plots for 356 hits, of which 635 data followed the criteria of selection, with correlation coefficients shown in the caption to the figure. It is clear that geometry of the region in the ring (a_1, a_2, R_{CO}–bonds and α angle) close to H-bonding is ruled by the H-bonding itself. The substituent effect works in a negligible way, if it does at all. Comparison of the geometry of 1,3,5-trinitrobenzene and 2,4,6-trinitrophenol shows this clearly, as shown in Fig. 6 – evidently the ipso angle at the OH substituent is dramatically lower than it was in the case of 1,3,5-trinitrobenzene.

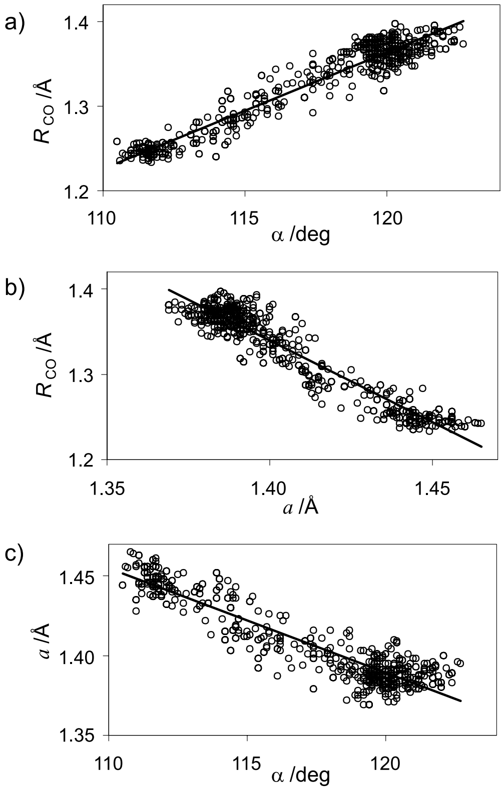

Figure 5. (a) R_{CO} bond lengths *vs.* α angles, $cc = 0.960$. (b) R_{CO} bond lengths *vs.* mean a-bond lengths, $cc = -0.952$. (c) Mean bond lengths a *vs.* α angles, $cc = -0.920$. Number of data $n = 635$.

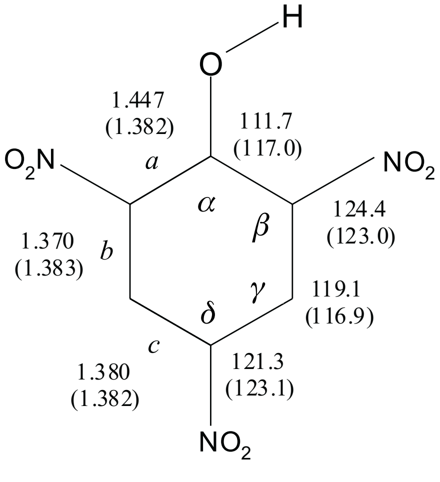

Figure 6. Mean values of the experimental geometrical parameters of the benzene ring for 2,4,6-trinitrophenol and 1,3,5-trinitrobenzene (in parentheses).

The nitro-group is strongly electronegative (Huheey group electronegativity [18] $\chi = 4.33$), and hence, following the Bent-Walsh rule, it will force the α angles (*i.e.* ipso for NO_2 groups) to be larger and in consequence it should even more decrease the ipso angle at OH in 2,4,6-trinitrophenol. As a further consequence, for the H-bonding complexes of 2,4,6-trinitrophenol there should be observed deviations from the main trend of the plot α *vs.* R_{CO} towards smaller values of α. Nothing like this is found, 2,4,6-trinitrophenol complexes do not deviate from the main line of the scatter plots in Fig. 5. Thus it may be concluded that the governing effect on the geometry of the region discussed here results from the H-bonding interaction of OH and the base. Various substituents attached to the ring of polysubstituted phenols do not significantly affect the geometry of the region, otherwise the correlation would be much worse.

Another point of discussion is the dependence of R_{CO} and the a bond lengths and the α angle on the strength of the acidity of polysubstituted phenols, i.e. the pK_a – values. It may be assumed that the magnitude of the Broensted acidity of the proton donating molecule in the H-bonded complex is related to the strength of this bond. For this purpose additional searches were carried out (using the above described criteria) for polysubstituted phenols for which the pK_a values were known (Table 1) which are shown in Fig. 7.

Figure 7 shows the scatter plots presenting the mean values of the geometry parameters for a given kind of substituted phenol plotted against pK_a of this kind of phenol. The high value of *cc* for the R_{CO} bond lengths *vs*. the pK_a (Fig. 7a) results from the fact that the C–O bond is least influenced directly by the substituents in the ring. Slightly worse is the correlation in Fig. 7b presenting the variation of the ipso angle α *vs*. pK_a. In this case substituents attached to the ring may interfere with the direct influence of the H-bonding effect. Almost equally good is the correlation of β *vs*. pK_a, Fig. 9a. This is well known that α and β angles correlate each other [39] due to purely geometrical reasons, as the ring is a planar hexagone. In our case the scatter plot of α *vs*. β has $cc = 0.974$. The worst is the correlation for the mean a bond lengths *vs*. pK_a (Fig. 7c) – in this case the substituents attached to the ring may act most substantially. The points deviating upwards in this scatter plot are mostly those in which the phenol moiety is substituted in position *ortho* – thus the overcrowding effects of bulky substituents from the *ortho* positions acts in the direction of lengthening of *a*-bonds. The deviating points are for: 2,4,6-trinitrophenol, 2,4-dinitrophenol, 2-nitrophenol, and two derivatives with *t*-butyl substituents in both *ortho* positions, thus rather bulky substituents.

These dependences support well a conclusion that the determining property for geometry changes in the ring, at least closer to the OH-region, is the acidity of the OH group deciding about the strength of the H-bond, which obviously depends also on the basicity of the base-molecule, which however does not damage the general picture.

In order to check how the H-bonding affects the more distant geometric parameters of the ring, Fig. 8(a,b,c) present the scatter plots for the dependences of β, γ and δ angles *vs*. pK_a. At least the dependence of β on pK_a is of a similar quality as the one described above in Fig. 7. The dependences of bond lengths b and c *vs*. pK_a are much worse as shown by Fig. 9a,b.

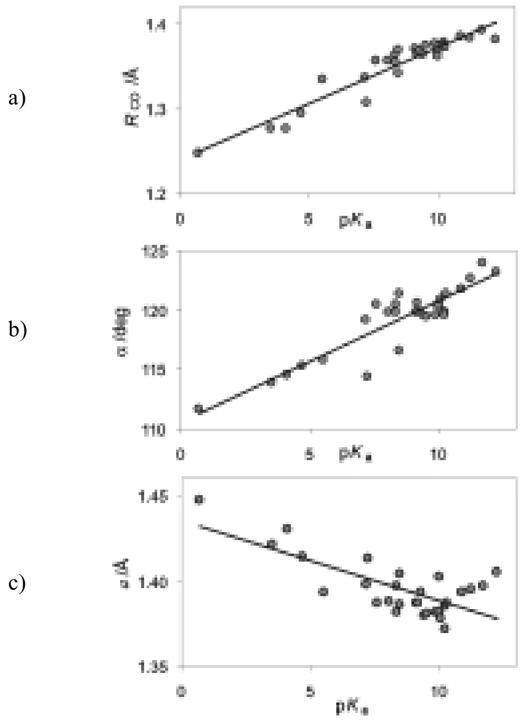

Figure 7. Scatter plots of the mean geometric parameters *vs.* the acidity of phenols. (a) R_{CO} *vs.* pK_a, cc = 0.953; (b) α *vs.* pK_a, cc = 0.905; (c) a *vs.* pK_a, cc = –0.736 for 29 data points (see Table 1).

Another aspect of the relations discussed above is the dispersion of structural parameters, R_{CO}, α and a, which depends in a characteristic way on the pK_a value of a given kind of phenol. The distribution of the R_{CO} length for a sample of complexes of 2,4,6-trinitrophenol (n = 109) is characterized by a cluster, with the variance equal to $0.5 \cdot 10^{-4}$, whereas the data for 4-nitrophenol (n = 15) shows some ten times larger dispersion, with variance value = $4.6 \cdot 10^{-4}$. Again, the data for 4-hydroxyphenol shows a small dispersion, with variance $0.5 \cdot 10^{-4}$.

The interpretation of these findings is as follows. 2,4,6-Trinitrophenol is a strong acid (pK_a = 0.7) which in contact with bases, even very weak ones, leads to an almost complete transfer of the proton to the acceptor. Therefore, we have a very short R_{CO} (mean value 1.248 Å) which may be compared with R_{CO} = 1.210 Å in acetone [40], whereas for CO bond in phenol [41] without any strong intermolecular interactions R_{CO} = 1.362 Å. An opposite situation exists for 4-hydroxy-2,3,5,6-tetramethylphenol for which the pK_a is near 12, thus indicating its very weak acidity. Therefore, only very strong bases can involve the OH group into H-bonding, and even then the interaction is rather weak, hence a small variation in the values of structural parameters. Again a dispersion of data R_{CO} *vs.* α plot is rather small. Figure 10 shows two graphs of variances for R_{CO} bond lengths and α angles taken from the ranges of one unit of pK_a each plotted against the pK_a values.

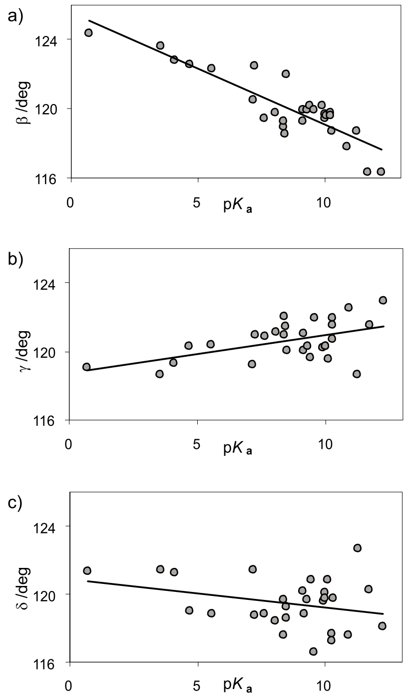

Figure 8. Scatter plots of the mean angles β, γ and δ of the benzene ring *vs.* the acidity of phenols. (a) β *vs.* pK_a, $cc = -0.881$; (b) γ *vs.* pK_a, $cc = 0.518$; (c) δ *vs.* pK_a, $cc = -0.293$. Number of data points $n = 29$.

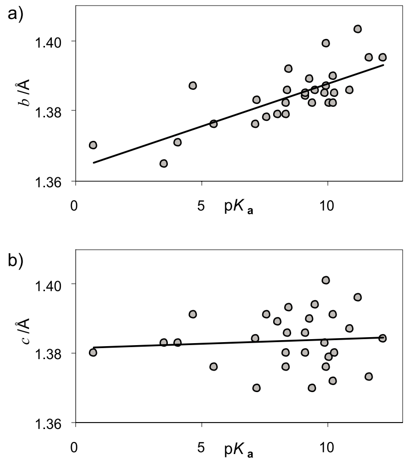

Figure 9. Scatter plots of the mean value of b and c bonds of the benzene rings *vs*. the acidity of phenols. (a) b *vs.* pK_a, $cc = 0.763$; (b) c *vs.* pK_a, $cc = 0.072$. Number of data points $n = 29$.

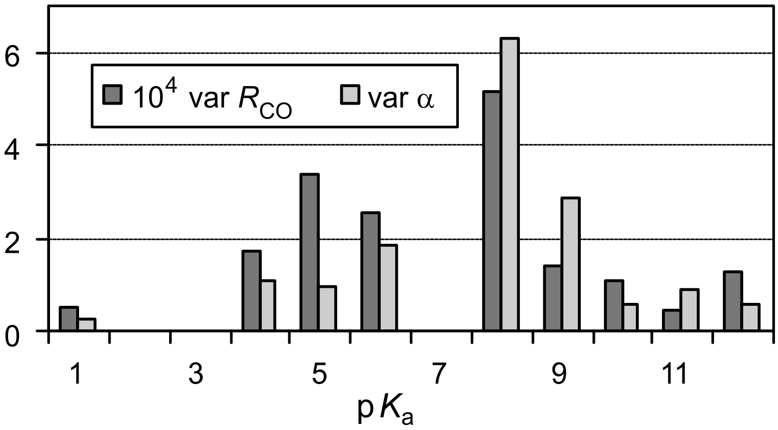

Figure 10. Graph of variances from the R_{CO} bond lengths and α values estimated for the ranges n and n+1 unit of pK_a against pK_a values equal to n+0.5; n runs from 0 to 12.

CONCLUDING REMARKS

The observations presented in this paper have been long time assumed on the basis of resonance theory, applied to the hydroxyl group involved the H-bond but have been never proven on a large and generally defined data set. Hydrogen bonding in the complexes of variously substituted phenol with nitrogen and oxygen bases affects the C–O bond length and geometrical parameters in the closest vicinity in the ring in a regular way – the Bent–Walsh rule is well fulfilled. The more distant parameters follow the above mentioned changes, but in a slightly more dispersed way. The changes in geometry depend linearly on the acidity of the phenol (*i.e.* pK_a values) in the PhOH...B complex. The correlations presented in this paper exist despite of (i) a great diversification in nature and in number of substituent(s) attached to the ring (see Table 1), which definitely affect the ring geometry, (ii) a great diversification of the bases involved in the systems under study, and finally (iii) the source of data is purely experimental – molecular geometry obtained from X-ray diffraction data consists some deformations due to the crystal packing forces [2,12].

Supporting information available. Supplementary references including detail information about phenols considered in this work (REFCODE CSD, chemical name and formula). This material is available *via* e-mail: halina@chemix.ch.pw.edu.pl

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Dedication

This work is dedicated to Professor Zbigniew Galus in recognition of His remarkable contribution in the area of electroanalytical chemistry.

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