

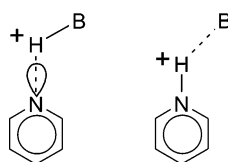
How H-bonding Modifies Molecular Structure and π -Electron Delocalization in the Ring of Pyridine/Pyridinium Derivatives Involved in H-Bond Complexation[†]

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Analysis of the experimental geometry of 397 variously substituted pyridine and pyridinium derivatives has shown very little variation of all bond lengths in the ring and substantial changes in the values of α and β angles, being in line with theoretically modeled data (at the B3LYP/6-311+G** level of theory). No dependence of bond lengths and π -electron delocalization in the ring measured by HOMA index on the changes in bond angle at the N-atom is observed. This is at variance with the patterns observed in substituted phenolate/phenol systems involved in H-bonding. Due to significant differences in magnitude of the *ipso* angle at the nitrogen atom that depend on the location of hydrogen atom in pyridine/pyridinium systems (N, N \cdots H, and N–H), this angle may be used as a valuable indicator of N \cdots H interactions since the X-ray structural analysis does not give a reliable position for the proton.

Introduction

Pyridine is one of the most common heterocyclic components of aromatic compounds—every 4 h, a paper appears with the word “pyridine” included in its title or abstract or as a keyword¹ (see Figure S1, Supporting Information). Pyridine and its derivatives play a very important role in heterocyclic chemistry^{2,3} and are also the subject of numerous studies as far as their aromatic character is concerned.⁴

Pyridine is well-known as a relatively strong basic compound. As a solvent, pyridine is characterized by a

high value of donor number^{5,6} (DN = 33.1) and the Kamlet and Taft hydrogen bond acceptor parameter^{7,8} $\beta = 0.64$ and as a rather weak or moderate Lewis acid quantified by the Reichardt⁹ $-E_T^N$ value 0.302. In both of the above cases the parameters are defined in the range of a 0–1 scale of magnitude. The pK_a value of pyridine¹⁰ is 5.20, and that classifies it as a relatively strong Brønsted base and consequently pyridinium cation (PyH⁺) as a relatively weak acid. Due to its properties as a base, pyridine and its substituted derivatives are often involved in coordination complexes and H-bond interactions.^{11–14} The ionization potential,¹⁵ $I_p = 9.23$ eV, is like that for benzene (9.24 eV) and does not support

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formation of strong EDA complexes.¹⁶ The pyridine complex with I₂ is about 27 kJ weaker than that with benzene.¹⁷

The main subject of this paper is related to the H-bonding and its distant consequences on geometry of the ring. This kind of interaction is much diversified in regard to the energy and geometry characteristics^{11,12,14} and refers to one of the most important interactions (see Figures S1 and S2, Supporting Information) present in chemistry and all fields associated with chemical processes.¹⁴ There are many geometry-based analyses dealing with H-bonding itself,^{18,19} but the aim of this paper is to study how far the molecular geometry undergoes changes in both close and more distant neighborhood of the H-bonding and to what degree this alteration reflects its strength. Following the Hellmann–Feynman theorem,^{20,21} the distribution of electronic density in the molecule determines the forces acting on the nuclei, which in turn define geometry of the molecule in question. A question then arises—how far are these changes reflected in the π -electron delocalization in the ring?

These studies carried out for phenol and phenolate derivatives involved in H-bonded complexes revealed substantial structural consequences,²² also observed as dramatic changes in π -electron delocalization in the ring.^{23–25} In these cases, the oxygen atom in hydroxyl and oxo groups has two 2p-type electrons that may be involved in π -electron delocalization with the π -electron system in the ring. Their mobility depends dramatically on the kind and also the strength of H-bonding.^{24,25} In the case of pyridine and pyridinium moieties involved in H-bonded complexes, the nitrogen atom has only one 2p-type electron able to be delocalized over the ring. This difference in p-electron structure of the nitrogen and oxygen atoms in pyridine/pyridinium and phenol/phenolate couples, respectively, is well reflected in the changes in geometry and π -electron delocalization in aromatic rings in H-bonded complexes and is a main subject of this report.

Methodology

Geometries of 397 H-bonded complexes of variously substituted pyridine and pyridinium cation derivatives with various oxygen and nitrogen acids/bases (see Figure S3, Supporting Information) were retrieved from CSD²⁶ with the following restrictions: (1) the searches were performed for substituted

pyridine (pyridinium cation) interacting with a nitrogen or oxygen acid (base) with an intermolecular contact between the nitrogen of pyridine (pyridinium cation) and the nearest O or N atom in acid (base) equal to or less than the sum of their van der Waals radii;²⁷ (2) the searches were restricted to structure measurements with the reported mean estimated standard deviation (esd) of the CC bond ≤ 0.005 Å (corresponding to AS flag = 1). The data were retrieved for polysubstituted pyridine/pyridinium cation (by any of the following substituents: halogen, –Me, –Et, –CHCH₂, –CN, –COOH, –COOMe, –COOEt, –COOPr, –COMe, –COPh, –CONH₂, –CF₃, –NH₂, –NMe₂, –NO₂, –OH, –OMe, –Ph, –SH, –H) interacting with N or O atom in acid/base partner. Sometimes the molecules of the solvent were present in the crystal lattice.

Becke-style 3-parameter density functional method using the Lee–Yang–Parr correlation functional and 6-311+G** basis set (B3LYP/6-311+G**) were used to optimize the molecules' geometries. All calculations were performed using the Gaussian03 series of programs.²⁸

Results and Discussion

Analyses of Geometry Parameters. Table 1 contains the mean values of geometric parameters for variously substituted rings of pyridine/pyridinium moieties, hereafter abbreviated as Py/PyH⁺, involved in H-bonded complexes. Two possible situations are realized:



The data used for estimation of the mean values for both sets (**1a** and **1b**) are subject to two kinds of interactions affecting independently the geometry patterns: first by various substitution and second by various kinds of H-bonding due to different components of the H-bond interaction (variation in H⁺–B or B in **1a** and **1b**, respectively). For further analysis we have chosen three sets of data for pyridine/pyridinium derivatives: (a) all 397 variously substituted **1a**, **1b**, and its subgroups, (b) 4-substituted **1a**, **1b** (without pyridine/pyridinium cation itself), and (c) unsubstituted **1a**, **1b**. Labeling of structural parameters is given in Chart 1.

Experimental data from CSD may be to some extent biased by imprecision due to the crystal packing forces,²⁴ leading to sometimes unclear conclusions. Hence, some computational support seems to be useful. For this purpose, we applied ab initio modeling to compare the

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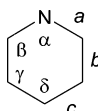
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TABLE 1. Number of Structures, *N*, Mean Bond Lengths and Bond Angles in the Ring of **1a** and **1b** Systems and the Differences in Geometric Parameters between the Values for Pyridine and Pyridinium Derivatives (for Labeling, see Chart 1)

systems	N	<i>a</i> /Å	<i>b</i> /Å	<i>c</i> /Å	α /deg	β /deg	γ /deg	δ /deg
Py ^a	185	1.335	1.381	1.379	117.67	122.99	118.84	118.65
PyH ⁺ ^a	212	1.340	1.372	1.385	122.28	119.77	119.34	119.48
differences		-0.006	0.009	-0.006	-4.61	3.22	-0.50	-0.83
4-X-Py ^b	76	1.335	1.378	1.385	117.52	123.06	119.31	117.72
4-X-PyH ⁺ ^b	47	1.338	1.358	1.406	120.40	121.30	120.07	116.82
differences		-0.003	0.019	-0.021	-2.89	1.76	-0.76	0.89
H-Py ^c	38	1.327	1.375	1.364	117.18	123.22	118.64	119.08
H-PyH ⁺ ^c	40	1.329	1.367	1.372	122.14	119.90	119.13	119.79
differences		-0.002	0.008	-0.008	-4.97	3.32	-0.49	-0.70

^a Various substituted pyridine/pyridinium. ^b 4-Substituted pyridine/pyridinium, without X = H. ^c Unsubstituted pyridine/pyridinium.

CHART 1

geometry patterns of the pyridine/pyridinium pair. Table 2 presents the geometrical parameters. All optimized molecules correspond to minima (no imaginaries frequencies).

A general view of the optimized and experimental geometries is similar: small differences for bond lengths and substantial differences for α and β angles. However, the difference for *a*-bond lengths is clearly greater in the optimized data than in the mean values of the experimentally obtained geometries. For further analysis, at least at this stage, we will discuss mostly the experimental data.

In all cases of pyridine/pyridinium systems (Table 1), the differences in mean *a*-bonds lengths (which are the closest to the “perturbation site”, i.e., the H-bond formation region) are very small, between 0.002 and 0.006 Å (presented as absolute values). Interestingly, the difference for *a*-bond lengths is the smallest for the unsubstituted and the 4-substituted species; for the last one, the differences in length of *b* and *c* bonds are bigger due to the direct substituent effect.

The differences (presented as absolute values) in α bond angles are more substantial and are in the range 2.89–4.97 degrees. The differences for the β angle are also considerable (1.76–3.32 degrees), but these quantities are mutually interrelated due to the geometry constraints of hexagon.²⁹ The differences for the other two bond angles are definitely smaller. In Figure 1a, the geometrical parameters are taken from variously substituted pyridine/pyridinium systems. Thus, in these cases two kinds of variability affect the geometry of the ring: (i) various substituents attached to different sites and (ii) various H-bonding dependent on the nature of the partner of H-bond.

If only unsubstituted pyridine/pyridinium systems are taken into account, then the correlation is even better, as shown in Figure 1b. This is an obvious consequence of a lack of perturbation due to various substituents present in different positions.

The plots of *a*-bond lengths against α angle, shown in Figure 2, do not show any clear trend. The most amazing

one presents the simplest derivative—unsubstituted pyridine/pyridinium systems involved in H-bonding (Figure 2c). The *a*-values are almost in the same range for both the pyridine and pyridinium complexes, whereas the α values differ significantly. In the case of unsubstituted species the difference amounts to 4.97 degrees (Table 1), whereas for 4-substituted and polysubstituted systems the difference is less legible, due to various additional perturbations, but still the mean values represent it nicely, and the difference amounts to 2.89 and 4.61 degrees, respectively. Note that the magnitude of the *ipso* angle, α , at N (formally N···H or NH) may be a useful indicator of proton position. This is particularly important in view of the low precision of H-location by X-ray diffraction studies.³⁰ The above conclusion is well supported by the differences in α -values presented in Tables 1 (experimental data) and 2 (optimized geometry).

All those dependences, *a*-bond lengths on the α angle of the ring in the pyridine/pyridinium systems, are practically independent of the kind of perturbations and differ dramatically from the formally similar situations observed for variously substituted phenol/phenolate systems involved in H-bond formation.²² For 635 variously substituted phenol/phenolate systems the dependence of the *a* bond on the α angle is nearly linear (Figure 3, experimental data) and the correlation coefficient is equal to -0.920. Note that for the pyridine/pyridinium systems the range of *a*-bond lengths (Figure 2) is nearly the same for both forms (**1a**, **1b**). In the case of phenol/phenolate derivatives (Figure 3) they are almost separable along the α -axis.

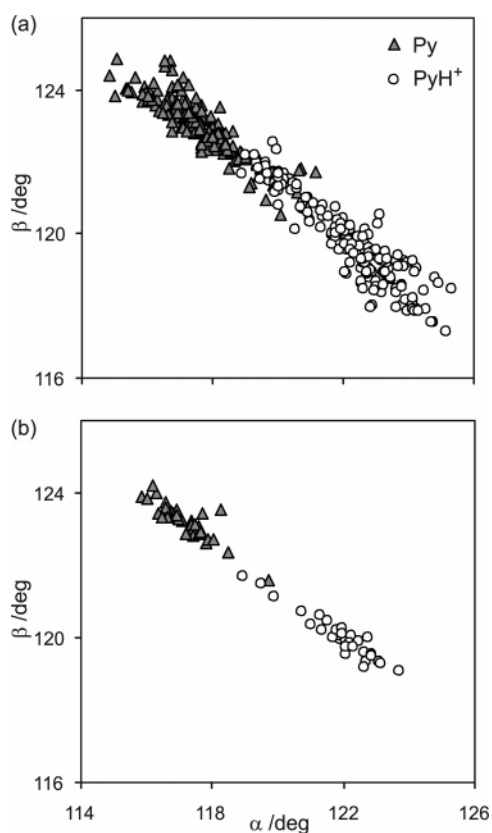
To discuss more deeply the above-presented finding let us look at Chart 2 to compare the differences in the factor perturbing the ring, which is labeled S. In the case of (O···H···base) interactions in phenol/phenolate systems involved in H-bonding (Chart 2b), the center of basicity contains two 2p-type electrons that are able to conjugate with the π -electron system of the ring. In the case of pyridine/pyridinium systems (Chart 2a), there is a substantial difference: the interactions of the lone pair···H⁺···base are associated with the nitrogen atom which contains only one 2p-type electron. Thus, the changes on basicity centers (O in phenol/phenolate and N in pyridine/pyridinium) in the former case may be propagated by two 2p-type electrons able to interact with the ring whereas in the latter case only one 2p-type electron, already part

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TABLE 2. Geometrical Parameters for 4-X-pyridine/Pyridinium Couple Obtained by Optimization at the B3LYP/6-311+G** Level of Theory and the Differences in the Parameters between the Values for Py and PyH⁺

X		a/Å	b/Å	c/Å	α/deg	β/deg	γ/deg	δ/deg
NO ₂	Py	1.336	1.394	1.387	117.85	123.68	116.84	121.12
NO ₂	PyH ⁺	1.350	1.382	1.389	123.55	119.38	117.60	122.50
differences		-0.015	0.012	-0.002	-5.70	4.30	-0.76	-1.38
H	Py	1.337	1.394	1.392	117.32	123.60	118.47	118.54
H	PyH ⁺	1.351	1.381	1.396	123.21	119.28	119.08	120.07
differences		-0.014	0.013	-0.004	-5.90	4.33	-0.61	-1.53
OH	Py	1.337	1.391	1.395	116.58	124.26	118.18	118.56
OH	PyH ⁺	1.355	1.371	1.410	122.14	120.20	119.11	119.24
differences		-0.018	0.021	-0.015	-5.57	4.06	-0.94	-0.68
NH ₂	Py	1.338	1.389	1.403	116.05	124.49	119.01	116.95
NH ₂	PyH ⁺	1.358	1.365	1.422	121.43	120.61	119.92	117.51
differences		-0.020	0.024	-0.019	-5.38	3.88	-0.91	-0.56
O ⁻	Py	1.350	1.382	1.446	114.05	125.72	121.28	111.97
O ⁻	PyH ⁺ ^a	1.373	1.354	1.465	120.55	121.19	121.67	113.74
differences		-0.023	0.028	-0.019	-6.50	4.53	-0.39	-1.77

^a Quinoid form.**FIGURE 1.** Dependence of α vs β for (a) variously substituted pyridine/pyridinium systems involved in H-bonding ($cc = -0.975$) and (b) unsubstituted pyridine/pyridinium systems ($cc = -0.993$). Assignments of Py and PyH⁺ derivatives are the same in both scatter plots.

of the π -electron system of the ring, may be affected by the changes in electronegativity of the basicity center.

Let us consider the problem: what kind of electronic interaction is responsible for the changes in geometry parameters—the a -bond lengths and α angles?

It was shown in a former analysis of pentachlorophenol H-bonded complexes with various bases³¹ that the changes of a -bond lengths are due to mesomeric effects and

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electronegativity, both working in the same direction. However, it was shown that the mesomeric effect predominates.

Following a recent analysis of the substituent effect on geometry of the ring in monosubstituted benzene derivatives, the α angle represents a change in hybridization of the *ipso* atom^{32,33} and, thus, as a consequence, also a change in electronegativity.^{34,35} What is more, the angular deformations in the ring have recently been used for defining a new scale of electronegativity that correlates with most popular scales.³⁶

In summary, the changes of a -bond lengths may be due to a blend of two factors, the changes in electronegativity and in the mesomeric effect, whereas the changes of α are due mostly to the changes in electronegativity.

Approaching the proton to nitrogen atom in pyridine (Chart 2a) increases its electronegativity; hence, the α angle becomes larger. The situation may be compared to that in the case of phenolate anion to which the proton (from the donating molecule) approaches the oxygen atom (Chart 2b). As for as the changes in electronegativity when the oxygen and nitrogen atoms are compared, the situation is roughly similar. However, there is a substantial difference—the nitrogen atom contains one π -electron and is a part of the ring, whereas the oxygen atom contains two pairs of π -electrons and is linked to the ring by one bond. The changes in H-bonding strength cause the changes in electronegativity of the oxygen atom, and these in turn affect the hybridization at C₁ atom of the ring and geometry of the ring. The situation resembles monosubstituted benzene derivatives where substituents of various electronegativity affect the carbon atom and then the geometry and π -electron delocalization in the ring.^{34,35,37}

The changes in a -bonds in phenol/phenolate H-bonded complexes are ruled (mostly) by mesomeric effects,³¹ which act in line with electronegativity effects as inter-

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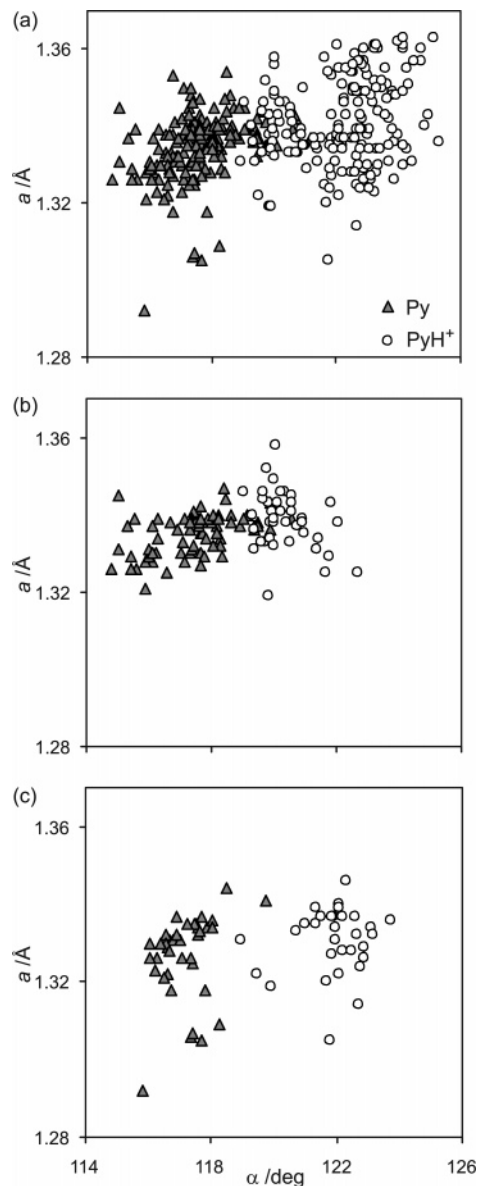


FIGURE 2. Dependence of α -bond lengths on α angle of (a) variously substituted pyridine/pyridinium systems involved in H-bonding, (b) 4-substituted pyridine/pyridinium derivatives without H-bonding, and (c) unsubstituted pyridine/pyridinium systems. Assignments of Py and PyH⁺ derivatives are the same in all scatter plots.

preted by the Bent–Walsh rule.^{32–36} Hence, collinearity of changes in a vs α plots (Figure 3) appears. However, for the pyridine/pyridinium systems with H-bonding of varying strength this is not the case—no linear dependences of a -bond length on α angle are observed as shown in Figure 2. To further consider the problem, an analysis of π -electron delocalization was carried out.

Analysis of π -Electron Delocalization in the Ring.

The retrieved from CSD database geometry of the ring in pyridine/pyridinium moieties involved in H-bonding allows one to apply HOMA,³⁸ the geometry-based index of aromaticity, which may serve as a convenient, reliable,³⁹ and easily accessible quantitative measure of

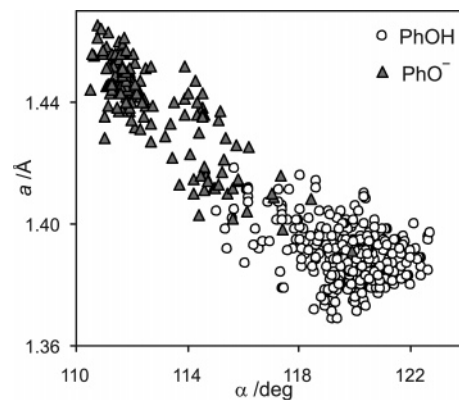
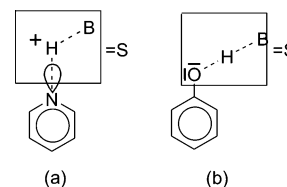


FIGURE 3. Dependence of α -bond lengths on α angle for variously substituted phenol/phenolate systems involved in H-bonding ($cc = -0.920$).

CHART 2



π -electron delocalization⁴⁰ in the ring. The formula for HOMA reads

$$\text{HOMA} = 1 - \frac{1}{n} \sum_{j=1}^n \alpha_i (R_{\text{opt},i} - R_j)^2 \quad (1)$$

where n is the number of bonds taken into the summation; α_i is a normalization constant (for CC and CN bonds $\alpha_{\text{CC}} = 257.7$ and $\alpha_{\text{CN}} = 93.52$) fixed to give HOMA = 0 for a model nonaromatic system and HOMA = 1 for the system with all bonds equal to the optimal value $R_{\text{opt},i}$ assumed to be realized for full aromatic systems (for CC and CN bonds $R_{\text{opt,CC}}$ is equal to 1.388 and $R_{\text{opt,CN}} = 1.334$ Å); and R_j stands for a running bond length. The HOMA index was used successfully for similar studies^{23,24} dealing with the distant consequences of H-bonding on π -electron delocalization in substituted phenols and phenolates.

Figure 4 presents the dependence of HOMA values for pyridine/pyridinium rings on the structural parameter, i.e., the changes in the α angle. Variations in HOMA values are substantial—in the range of 1.0–0.7 units but despite such a wide range of variation of the α angle (from ca. 114 to 125 degrees), the changes in HOMA values are practically independent of α . Note that the variability of HOMA is about two times smaller for pyridine than for pyridinium systems involved in H-bonding, but in both cases the maximal value of aromaticity index is equal to or near 1.0 and the variability of the α angle values is similar.

The difference between the pyridine/pyridinium systems involved in H-bonding and phenol/phenolate ones is significant. In the case of variously substituted phenol/phenolate systems involved in H-bonding the dependence of HOMA on α is typical,^{23,24} as shown in Figure 5. The

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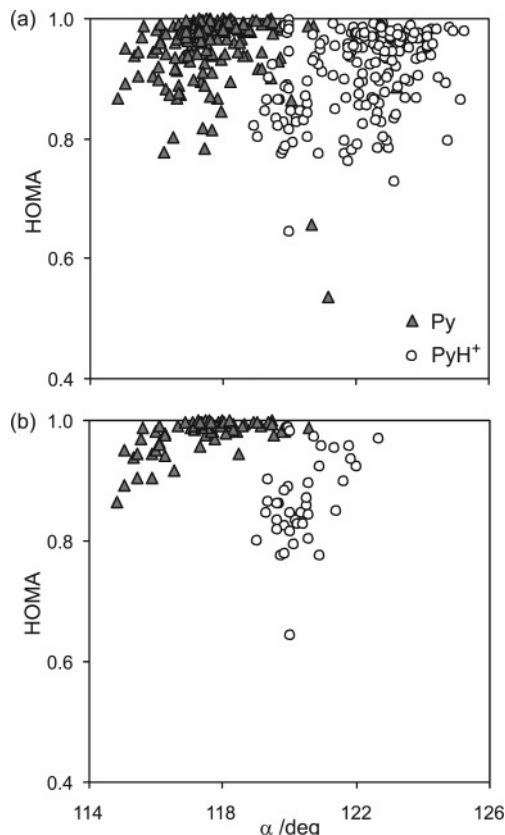


FIGURE 4. HOMA values plotted against the α angle values for (a) variously substituted and (b) 4-substituted pyridine/pyridinium systems, without the unsubstituted one, involved in H-bonding. Assignments of Py and PyH^+ derivatives are the same in both scatter plots.

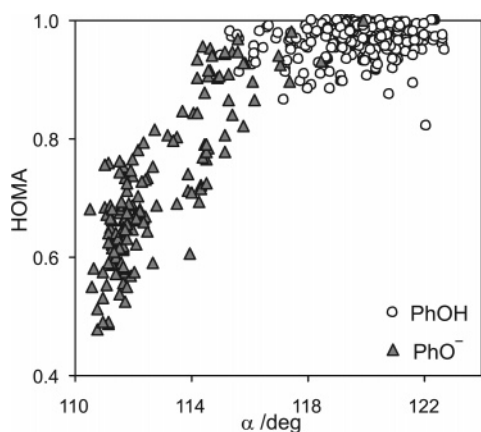


FIGURE 5. HOMA values plotted against the α angle values for variously substituted phenol/phenolate systems involved in H-bonding.

variability of HOMA is about five times smaller for phenol than for phenolate derivatives but the ranges of α angle values are similar in both cases. A decrease of electronegativity of the oxygen atom in hydroxyl group is associated with an increase of the O–H distance due to the strengthening of interactions with base. This in turn enhances the mesomeric effect of the lone pair at the oxygen atom and leads to stronger π -electron localization in the ring observed as a decrease of HOMA values.

The fundamental difference for the above two cases consists of the existence of a clear dependence of HOMA on α for the phenol/phenolate systems and the lack of such a dependence for the pyridine/pyridinium systems. In both cases, the H-bond formation causes a change in hybridization and electronegativity at C_1 (or N) atoms. However, only in the case of phenolate/phenol systems does the mesomeric effect act significantly on α -bond lengths. Thus, the ways in which the perturbing agent (S, Chart 2) affects the ring are dramatically different for the pyridine/pyridinium and phenolate/phenol systems, respectively.

Since in both cases the variation in α is significant, and comparable in magnitude, and moreover this quantity is supposed to depend mostly on the changes of electronegativity of the perturbing agent,^{34–36} S (Chart 2), let us look at the differences in possibilities in which S may interact with the ring.

Consider first the phenol/phenolate systems involved in H-bonding. The H-bond formation in all cases $\text{Ph-OH}\cdots\text{B}$, $\text{Ph-O}\cdots\text{H}^+\cdots\text{B}$, and $\text{Ph-O}^-\cdots\text{H}^+\text{B}$ affects electron charge at the oxygen atom, leading to changes in its electronegativity.⁴¹ As a consequence, the α angles follow these changes. The oxygen atom in both its forms O^- and OH has a 2p-type electron pair that can conjugate with the π -electron system of the ring, and it does it. The strength of this interaction depends on electronegativity of the oxygen atom and in turn on $\text{O}\cdots\text{H}$ interaction in the H-bond. Variation of the strength of H-bonding in phenol/phenolate systems causes the changes in π -electron delocalization monitored by HOMA values plotted against the α angle (Figure 5) and phenyl–oxygen bond length.²⁴

Finally, let us consider the title question, the pyridine/pyridinium systems involved in H-bonding. As shown in Figure 4, a wide range of HOMA values (0.4 units) and of α values (about 10 deg) are comparable with phenol/phenolate systems; however, they are not related to each other at all. The most probable interpretation is that the mesomeric effect of various substituents attached in different positions is independent of their electronegativities. A partly similar situation was observed previously for monosubstituted benzene derivatives with mesomerically active groups.³⁷

Conclusions

The complete lack of difference between ipso-ortho bond lengths in pyridine and pyridinium involved in H-bonding against considerable differences for the phenol/phenolate systems supports the thesis that 2p-type electron in the nitrogen atom is weakly involved in mesomeric and π -electron delocalization due to H-bond formation $\text{N}\cdots\text{HB}$ or $\text{NH}\cdots\text{B}$. The above thesis is also well supported by the lack of systematic variability of HOMA index.

This may refer to a different electron structure in the two systems. In the case of phenol/phenolate systems two p-type electrons may be involved in a mesomeric effect leading to changes in π -electron structure in the ring, i.e., also in geometry. In the case of pyridine/pyridinium

(41) Iczkowski, R. P.; Margrave, J. L. *J. Am. Chem. Soc.* **1961**, *83*, 3547.

systems only one p-type electron may be involved in the mesomeric effect, and hence, the effect on π -electron delocalization in the ring is much smaller.

It results from Tables 1 and 2 that the N \cdots H and N–H interactions are well monitored by the values of α -angle that may be useful indicators for location of proton in H-bonded systems studied by X-ray structural analysis, which, being well-known, does not give a reliable position for the proton.³⁰

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Supporting Information Available: Statistics of papers dealing with pyridine and hydrogen bond published within the past decade.¹ Supplementary references including REFCODE CSD. The Cartesian coordinates of optimized geometry 4-X-pyridines and 4-X-pyridinium cation molecules (where X denotes NO₂, H, OH, NH₂, and O[−]). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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