Review Commentary

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Structural aspects of the intermolecular hydrogen bond strength: H-bonded complexes of aniline, phenol and pyridine derivatives

Halina Szatyłowicz[a*]

This short review is devoted to the description of the effect of the nature and the strength of intermolecular hydrogen bonds on structural properties of H-bonded complexes of aniline, phenol and pyridine derivatives. Several hundreds of such complexes, playing an important role in organic chemistry and biochemistry, have been identified and described in the literature. In the introductory part, the idea of the H-bond is discussed in terms of its historical development, followed by presently accepted classification of H-bonds. Critical review of quantum methods usually used for the calculations of the geometry of H-bonded complexes and the energies of H-bonds is then presented. In the second part, the H-bond-induced geometrical, hybridization and aromaticity index changes are discussed. All correlations based on quantum calculations are compared with those derived from the available crystal structure data. Although the experimental data are more scattered than the calculated ones, their agreement is impressive. This unequivocally shows the power of the calculation methods developed in recent years.

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Keywords: hydrogen bonding; intermolecular H-bond; measures of H-bond strength; *ab initio* calculation; aromaticity; group electronegativity; aniline; phenol; pyridine

INTRODUCTION

'Hydrogen bond' is one of the most important terms used in chemistry,[1–3] biochemistry[4–6] and related fields.[7,8] The effect of H-bond on the reactivity, chemical, physical and structural properties of various types of matter has been increasingly widely studied. In the past 10 years the number of papers devoted to diverse aspects of the H-bond, published yearly, increased two times, reaching 9472 articles in 2007.[9]

The phenomenon of the hydrogen bond formation was mentioned for the first time by Nernst[10] in 1891 as 'dimeric association of molecules with hydroxyl group'. Huggins claimed[11] that he had used the name – hydrogen bridge – for the first time in 1919.[12] He was the author of the first review concerning hydrogen bridges,[13] which ended with the following statement: 'The writer ventures to predict that the most fruitful applications of hydrogen-bridge theory will be to better understanding of the nature and behavior of complicated organic substances such as gels, proteins, starch, cellulose, sugars and other carbohydrates, chlorophyl, hemoglobin and related substances, etc.'

The first monograph on this subject was published by Pimentel and McClellan.[1] According to these authors the H-bond exists when (i) there is evidence of bond formation, and (ii) there is evidence that this bond specially involves a hydrogen atom already bonded to another atom. Lately, Steiner[14] proposed to modify the second point: 'An X-H···A interaction is called a “hydrogen bond”, if 1. it constitutes a local bond, and 2. X-H acts as proton donor to A.' Nowadays the strict definition is still under discussion by a specially established IUPAC task group,[15] which in 2006 decided to propose a short definition and a list of criteria and characteristics for the hydrogen bond. The core, following closely the definition given by Pimentel and McClellan,[1] was given:[16] 'The hydrogen bond is an attractive interaction between a group X-H and an atom or a group of atoms Y, in the same or different molecule(s), when there is evidence of bond formation.' The principal problem is associated with choosing the appropriate evidence of H-bond formation. As the most important, the following criteria have been proposed: (i) the H atom in the X-H group is more electropositive than X and (ii) the physical forces involved in H-bonding should include attractive electrostatic forces, this means that they should not be primarily dispersive ones. The latter suggests a directionality of interactions, which is a very important term in distinguishing between hydrogen bonds and van der Waals forces.[17]

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[*] Correspondence to: H. Szatyłowicz, Faculty of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00-664 Warsaw, Poland
E-mail: halina@ch.pw.edu.pl

[a] H. Szatyłowicz
Faculty of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00-664 Warsaw, Poland

The next problem to be considered is the energy borders setting for strong, moderate, and weak H-bonds. Even the most recent articles[18,19] show different energy values for H-bond energy gradation, especially for the energy of weak H-bonds, which are close to van der Waals interactions. Parthasarathi *et al.*[18] have shown that there is a smooth change in the nature of the interaction from van der Waals to classical H-bonding and, subsequently, to strong H-bonds. Hydrogen bonds in crystals span energies between 0.2 and 40 kcal/mol.[14] In the case of gas phase the upper limit increases (up to about 60 kcal/mol for $[F\cdots H\cdots F]^-$ system[19]). Summarizing, a hydrogen bond, D—H···A, is an interaction where the hydrogen atom is attracted by two atoms, one being a part of D—H bond and another one (A), which is the attractor of proton. This attractive interaction increases with increasing electronegativity of the participants, D and A. From the classical point of view, the H-bonding interactions are mainly electrostatic in nature, but sometimes may be partly covalent. Nowadays, the concept of a hydrogen bond includes also weaker interactions, which in the limiting cases have considerable dispersive-repulsive character, and merge into van der Waals interactions. Desiraju,[20] highlighting some features common to all these bonds, suggested that the term 'hydrogen bridge' is a better descriptor for them: 'Such a descriptor recognizes an interaction without borders and one that admits of much variation in its relative covalent, electrostatic, and van der Waals content.' He proved it by showing the interplay between effects for a number of hydrogen bonds described in the literature; his approach is schematically presented in Fig. 1. The diagram demonstrates H-bond as a borderless interaction: electrostatic with variation toward covalent character (the case of very strong H-bonds) and electrostatic with variation toward van der Waals interaction (the case of weak H-bonds). The central region of the sketch (Fig. 1) corresponds to the classical (conventional) hydrogen bond. A covalent and noncovalent character of the interaction quantify the proton acceptor distance.[21] Moreover, the intermolecular distance, between the proton donor and proton acceptor, and the model of the H-bond (e.g. charge, resonance, polarization-assisted H-bonds, Table 1) are also used to determine nature and strength of the interaction.[22,23]

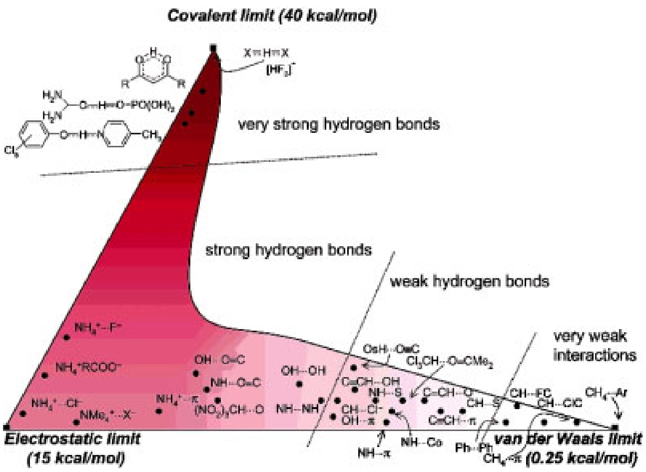


Figure 1. The hydrogen bridge. The composite nature of the interaction is highlighted by the three extreme situation of widely differing energies. The sketch is not strictly quantitative but the coloring attempts to provide a visual scale of energies. The figure serves as a rough guide to the balance of electrostatic, Van der Waals nature, and covalency in any X–H···A interaction. For the weak interaction, the covalent character is very small and may be interpreted as charge transfer. A Van der Waals interaction is considered to have dispersive and repulsive components [Reprinted with permission from Ref. [20]. Copyright (2002) American Chemical Society] [This figure is available in color online at www.interscience.wiley.com/journal/poc.]

In the discussion about the power of a given hydrogen bond, two aspects should be distinguished: (i) effects of hydrogen bonding on physicochemical properties of the interacting

Table 1. Classification of hydrogen bonds (HB) on the basis of their selected features; energy (i.e. dissociation energy) in units taken from original works (1 cal = 4.184 J)

	Very strong	Strong	Moderate	Weak
Energy[a]/kJ/mol		50–100	30–50	
Energy[b]/kcal/mol		15–40	4–15	1–4
$d_{D\cdots A}$ [b]/Å		2.2–2.5	2.5–3.2	>3.2
$d_{H\cdots A}$ [b]/Å		1.2–1.5	1.5–2.2	>2.2
Energy[c]/kcal/mol	30–40	15–30	4–15	0.25–4
Energy[d]/kcal/mol	>10		5–10	<5
Model	Low-barrier HB (LBHB)[e] Single-Well HB (SWHB)[g]	Charge-assisted HB (CAHB)[f] Resonance-assisted HB (RAHB)[f]	Polarization-assisted HB (PAHB)[f]	Isolated HB (IHB)[f]
Bond Critical Point (BCP) criteria[h]	$\nabla^2\rho_{BCP} < 0$ $H_{BCP} < 0$		$\nabla^2\rho_{BCP} > 0$ $H_{BCP} < 0$	$\nabla^2\rho_{BCP} > 0$ $H_{BCP} > 0$
Energy[h]/kcal/mol	>24.0		12.0–24.0	<12.0
Degree of covalence[i]	Covalent $d_{H\cdots A} < 1.2$ Å		Partially covalent $1.2\text{Å} < d_{H\cdots A} < 1.8\text{Å}$	Noncovalent $d_{H\cdots A} > 1.8$ Å
Interaction[j]	Shared–Share (SS)	Covalence degree	Intermediate CS	Closed–Share (CS) Softening degree

[a] Ref. [95]; [b] Ref. [3]; [c] Ref. [18,20]; [d] Ref. [96]; [e] Ref. [23]; [f] Ref. [97, 98]; [g] Ref. [99]; [h] Ref. [100]; [i] Ref. [21]; [j] Ref. [91].

molecules, that is the proton donor and the proton acceptor, and (ii) multiplication factor, that is the number of coexisting H-bonds. The last case could be compared to a typical human-group-like behavior. As separated they may be weak, easy to break, sometimes hard to detect, but acting together they become much stronger and support themselves, that is cooperate. One of the best examples of these effects is the noncovalent synthesis using hydrogen bonding (for review see Prins *et al.*[24]). Cooperativity effect in hydrogen bond interactions was confirmed both in the gas phase ($(H_2CO\cdots(HF)_n$, $n = 1,\ldots,9$, complexes;[25] chain of 4-pyridones;[26] β-sheets of protein[27,28]), in liquid (solutions of H-bonded system of poly(4-vinylpyridine) and acids as proton donor[29]) and in the solid state.[14] H-bonds may not only enhance[7] but also reduce the strength of each other. The latter effect, called 'anticooperativity', has been investigated surprisingly little.[14] From the point of view of medicinal and supramolecular chemistry, the G-quadruplex, schematically presented in Fig. 2, seems to be the most important example of the cooperativity.[30] Guanine[31] (deposited onto an inert substrate) self-assembles into hydrogen-bonded network of quartets (Fig. 2, R=H). The obtained G-quartet structure (observed in a high-resolution variable-temperature STM) is the same as found in quadruplex telomeric DNA (for review see Davis[32]). Furthermore, results of DFT calculations[31] confirm the strong preference of guanine to form quartets (the average energy per hydrogen bond increases from 5.1 kcal/mol in the dimer to 7.1 kcal/mol in the trimer and 9.7 kcal/mol in the quartet). The strengthening of the H-bonds within G-quartet network relative to those in an isolated dimer arises from the cooperative effect.

Recently, it has been found that quadruplexes (four-stranded structures) prevail in the human genome[33] and, moreover, are suspected of regulating telomer replication. Thus, a new rule, rule of 'four', was announced by Armitage.[30]

Intermolecular H-bonds are the main interactions deciding about the molecular architecture and properties of a large variety of materials.[34–38] They occur independently on the state of the matter. Structural rearrangements may take place at different stages of the material formation: during evaporation and condensation[39] and in solutions.[40–43]

The aim of this article is to review effects of the nature and the strength of intermolecular hydrogen bonds on physicochemical and structural properties of H-bonded complexes. Three aspects should be considered: (i) changes in the region of the interaction, that is 'center of the reaction'; (ii) the response of the directly interacting chemical moieties to these changes; (iii) the response of the remaining part of the molecule to the H-bond stimuli. Knowledge concerning short-and long-distance consequences should allow to explain and/or predict properties of more complicated systems.

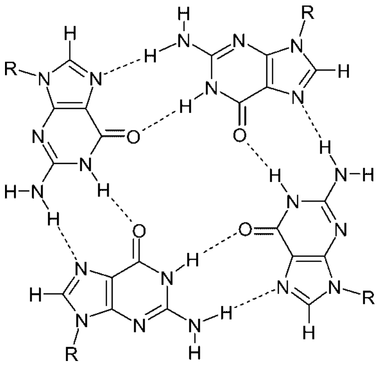


Figure 2. Hydrogen-bond pattern in G-quartet

For this review, benzene derivatives containing H-bond donors and acceptors have been selected. These derivatives not only play an important role in organic chemistry and in biochemistry but also are crucial constituents of more complicated systems such as biologically active molecules (macromolecules), functionalized polymers, supramolecular aggregations and others. In addition, their chemical constitution facilitates direct investigation of the three aspects of the H-bond formation listed above. Finally, H-bonds involving oxygen- or nitrogen-containing groups constitute a large majority of H-bond-type interactions existing in nature. In particular, hydroxybenzene (phenol) derivative,[44–46] aminobenzene (aniline) one[47] and derivatives of pyridine[48] are discussed. In the last case, the nitrogen atom, participating in the formation of the H-bond, is an inherent part of the aromatic ring. For this reason it is possible to follow the transmission of the H-bond-induced effects directly to this chemical moiety.

As it has already been stated (*vide supra*), phenol, aniline, pyridine and their derivatives are involved in the formation of a large variety of H-bonded complexes. Taking into consideration their interactions with oxygen and nitrogen atoms as acceptors or donors, they can act as organic acids or bases. The collected X-ray data (CSD[49]) cover more than 600 structures of H-bonded phenols,[50] 300 of anilines[51] and about 400 of pyridines[52] investigated in the past 30 years. The studied systems interact with a great variety of bases (acids) that differ not only in their basicity (acidity) but also in other properties affecting the H-bond interactions. It is not possible to study experimentally H-bonded complexes with controlled and gradually changing basicity (acidity) of the interacting counterparts. In this case, computational methods exploiting an appropriate model of H-bond interactions, in which interactions are varied in a gradual way, are irreplaceable. Such computational investigations enable the prediction of other properties of given H-bonded complexes, both in close vicinity of the bond formation area as well as at longer distances (short- and long-distance consequences of H-bond formation).

HOW TO MEASURE EFFECTS ORIGINATING FROM THE HYDROGEN BONDING

Generalities

Different experimental techniques are used to study H-bonding,[2] for review see Refs.[53–56] Invaluable sources of data are results of X-ray and neutron diffraction measurements, collected in the Cambridge Structural Database.[49] A great disadvantage of the most popular X-ray diffraction method is that it does not allow for the precise determination of the positions of protons in a given complex,[57] but in some cases this obstacle can be overcome.[58] It is noteworthy to stress that H-bonds interactions (especially weak, noncovalent) have not always been considered in the original papers presenting the X-ray data.[59]

Rich source of information concerning hydrogen bonding are quantum chemical calculations.[7,8] Their results not only allow to find out the geometries of H-bonded complexes, the energy of the interactions and molecular vibrations, but also give supplementary information that can provide insights into the fundamental nature of this phenomenon (covalent, noncovalent, electrostatic). Today, the accuracy of the computational methods can approach that of the experiments.[7] In this respect, appropriate selection of the theoretical level (method and basis set) of the calculations is of crucial importance,[8,56,60,61] particularly in the case of weak interactions.[62,63] The second-order Møller–Plesset perturbation method[64,65] (MP2) and Becke-style 3-parameter density functional method using the Lee–Yang–Parr correlation functional[66–69] (B3LYP) are recommended. The used basis set should include polarization and diffuse functions. It should be stressed that in the case of weak interactions, DFT (Density Functional Theory) procedures may be deficient due to their inability to take into account the dispersion energy.[63,70] In the case of the energetic study of H-bonded complexes, it is necessary to take into consideration the basis set superposition error[7,71,72] (BSSE).

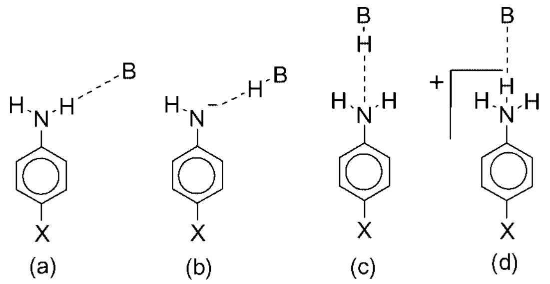
A very useful tool to characterize atomic and molecular interactions is the topological analysis. The Bader's approach,[73] Atom in Molecules theory (AIM), is widely used to study H-bonds. Unquestionable advantage of an analysis of the electron density distribution is the possibility of the comparison of its findings with results of the traditional experiment[74] (accurate X-ray measurements) and vice versa,[75–77] for review see Bertini *et al.*[78] For 83 experimentally studied H-bonds (Y—H···O, Y = C, N, O, X-ray diffraction experiments), Espinosa *et al.*[75] have shown that the length of the H-bond (distance between the proton and its acceptor atom) summarizes essential features of these interactions. The obtained topological properties of the electron density at critical points (CP) of H-bonds (the kinetic and potential energy density) and the strength of the interaction (the dissociation energy of H-bond) depend exponentially on the H···O distance. Similar relations have been found for dihydrogen-bond systems[79] and many other classes of compounds such as Schiff bases and proton sponge complexes, to name a few,[80–83] where interactions are much more diverse than those existing in the systems described by Espinosa.[75]

Alkorta *et al.*[84] demonstrated that logarithmic relationships between the bond length and the electron density at the bond critical point are capable of explaining simultaneously the features of covalent bonds and H-bond. Moreover, the same applies to both the inter- and intramolecular interactions.[82,83]

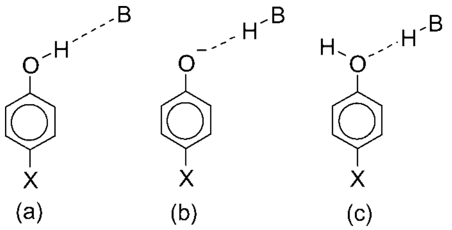
The AIM theory was applied, for the first time, to H-bond complexes by Bader *et al.*[85] Subsequently, an additional set of topological criteria, which a bond must fulfill in order to be considered as H-bond, have been proposed by Popelier and coworker.[86,87] The topological and energetic properties in the H-bond critical point are used as a measure of the H-bonding strength[18,75,79,88–92] and the nature of the interactions.[21,93,94]

Modeling H-bonded systems with gradually varying energy of interactions

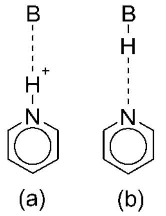
In order to consider structural changes of systems involved in H-bond complexation for simplicity and clarity, it is useful to model the interactions in the way permitting a gradual change in their strength. For this reason, the modeling in accordance with Schemes 1–3 was introduced in a series of papers dealing with various complexes of aniline, phenol and pyridine derivatives.



Scheme 1. H-bonded complexes of aniline derivatives



Scheme 2. H-bonded complexes of phenol derivatives



Scheme 3. H-bonded complexes of pyridine derivatives

In the case of intermolecular hydrogen bond, proton donor and proton acceptor in the H-bonded complex belong to different molecules, either of the same type or different ones. Intermolecular H-bonded complexes of pyridine and *para*-substituted aniline and phenol are presented in Schemes 1–3. Particularly rich in different kinds of interactions is the case of the amino group (Scheme 1). It can be both a proton donor, Scheme 1(a), and a proton acceptor, Scheme 1(c). Their conjugated forms are the anilide anion, Scheme 1(b), and the anilinium cation, Scheme 1(d), respectively. In the case of phenol derivatives (Scheme 2) and pyridine (Scheme 3), two principal processes can be envisioned; these molecules can act as proton donors (phenol or the pyridinium cation) or proton acceptors (phenolate and pyridine), (a) and (b) in Schemes 2 and 3, respectively. The oxygen atom of the hydroxyl group may be a proton acceptor in H-bonded complexes[101] too (Scheme 2c), but it is mainly realized as its second H-bond. All possibilities of the H-bonded complexes formation follow the scheme of interactions between the Broensted acids and bases, but not always with a final proton transfer; thus they cover two generalized (appearance of ionic forms is not shown) reactions:

$$RY - H + B \rightarrow RY - H \cdots B \qquad (1)$$

and

$$RY + HB \rightarrow RY \cdots HB, \qquad (2)$$

where: RY—H means aniline, the anilinium cation, phenol or the pyridinium cation, and RY – the anilide anion, aniline, phenolate or pyridine, respectively. B indicates base (acceptor of proton), and HB its acid form (donor of the proton).

The acidities of RY—H and HB decide which of the H-bonded system, that is RY—H···B or RY···HB, will be formed.[102] Obviously, a stronger acid (RY—H, HB) is a better proton donor, and a stronger base (B, RY) is a better acceptor, but increasing acidity has a limit, since eventually proton transfer occurs,[103,104] so the reactions (1) and (2) could be jointly written as

$$\mathrm{RY} - \mathrm{H} \cdots \mathrm{B} \Leftrightarrow \mathrm{RY} \cdots \mathrm{HB} \tag{3}$$

This reaction may take place when acidities (proton affinity in the gas phase, pK_a in solution) of the participants are comparable, that is their difference is close to zero. The proton transfer reactions are widely studied.[55,103–106] Intermolecular distances in the H-bonded systems formed according to the reaction (3) should be short enough to exhibit low barrier for the proton transfer. Such H-bonds are strong or very strong (Table 1) and are known as low-barrier H-bonds (LBHB) or charge-assisted H-bonds (CAHB). The LBHBs are believed to play an important role in enzymatic reactions,[39,97,107–108] but the opposing views on this idea can also be found in the literature.[109,110]

According to the above-mentioned results,[75] the dissociation energy increases with the shortening of the hydrogen bond. The length of the H-bond may be expressed by the intermolecular distance between heavy atoms, that is proton donor and proton acceptor, $d_{Y\cdots B}$, or by proton–acceptor H-bond distance, $d_{H\cdots B}$. The latter one is mainly used in the discussion of the calculation results and in the case of accurate experimental data, for example in the work of Espinosa *et al.*[75] Nowadays, $d_{H\cdots B}$ as the H-bond length is more frequently used for the comparison of the strength of the interaction (Table 1). It mainly comes from numerous (fruitful) studies of the electron density properties in the critical point of the hydrogen bond.[21,79,84,100,111] Simulation of H-bonded complexes with controlled and gradually changing strength of the interaction can be performed by controllable changing length of the hydrogen bond for all complexes shown in the reactions (1)-(3). The first two, (1) and (2) can be modeled by gradual varying of the length of the H-bond, $d_{H\cdots B}$ or $d_{Y\cdots B}$, with concomitant full optimization of the remaining geometric parameters of the system. A more appropriate method for simulation of proton transfer, Eqn (3), is changing the distance between hydrogen and proton acceptor, $d_{H\cdots B}$, for constant intermolecular distance between heavy atoms, $d_{Y\cdots B}$. Repeating calculations for different separation distances of heavy atoms ($d_{Y\cdots B}$) allows to observe modifications in the energy change profile: the number of minima (one or two potential wells) and their mutual relation (a barrier between them). An elegant illustration of this methodology is the work of Scheiner and Kar,[110] where the idea of LBHBs in enzymatic catalysis was studied.

In all the above-mentioned methods, the change of the H-bond length, resulting in the modification of the strength of the interaction, implies a simultaneous variation in the proton affinity of the interacting counterpart(s). This is the case of proton transfer reaction (3) where shortening (or lengthening) of $d_{H\cdots B}$, for constant $d_{Y\cdots B}$, gives this effect. In the case of the reaction (1), calculations of the complex RY—H···B, for progressively shortened intermolecular distances between the heavy atoms ($d_{Y\cdots B}$), correspond to modeling interaction of RY—H with increasingly stronger base B. Analogous calculations for the RY···HB system, reaction (2) simulate interaction of the proton acceptor RY with stronger acid HB. For both cases the binding energy increases with increasing basicity (acidity) of the interacting counterparts (e.g. relationships found for Ph—NH$_2$···F$^-$, Ph—OH···F$^-$ and Ph—NH$_2$···HF, Ph—O$^-$···HF which are presented in Fig. 3). It is noteworthy to mention again that in the overwhelming majority of cases it is not possible to study experimentally H-bonded complexes with controlled and gradually changing interactions of the H-bonding type.

Modeling of H-bonded complexes with a wide range of strengths of the interaction (from weak to strong HB) has been used mainly to study topological properties of hydrogen bonding. For that purpose, the best objects are small systems, such as hydrogen fluoride[88,91] or water.[112] In the first case the variation of the energy of interaction was simulated by changing the $d_{H\cdots F}$ distance, in the second one – the intermolecular distance between heavy atoms, $d_{O\cdots O}$. The last method was tested for H-bonded systems of *para*-substituted derivatives of phenol,[113] and then successfully applied for pyridine and aniline[51] derivatives. Comparison of the dependence between the total energy of the interaction (binding energy) and the hydrogen bond length, $d_{H\cdots B}$, for experimental data[75] and computational results, both simulated[51,91,113] and optimized,[21,91] is presented in Fig. 3. Binding energy for PhNH$_2$···F$^-$ and H$_2$O···HOH complexes,[112] as a function of the intermolecular distance between heavy atoms is depicted in Figs. 4 and 5, respectively.

First, a great variety of homo- and heteronuclear hydrogen bonds, particularly in the case of fully optimized systems, presented in Fig. 3, should be pointed out. Moreover, the calculations whose results are shown in Figs. 3–5 were performed using different computational methods. CASSCF/6-311++G** was applied by Espinosa *et al.*[91] for simulation of interaction within the HF···HF system and optimization of XH···FY complexes. H-bonded complexes of phenol, aniline and pyridine derivatives with F$^-$ and/or HF (Schemes 1–3) were simulated[113] at B3LYP/

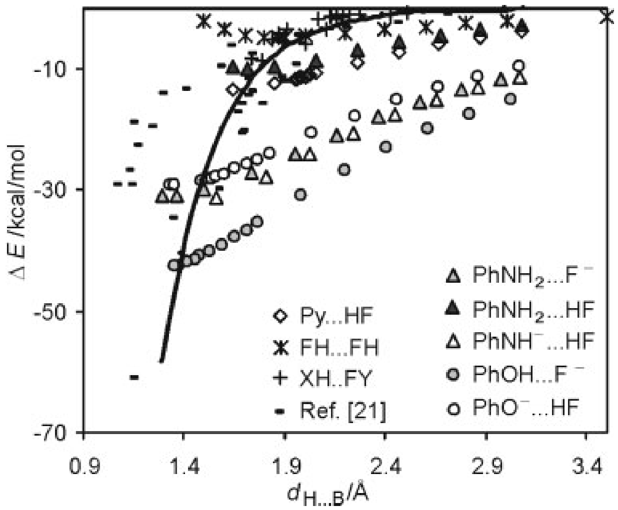


Figure 3. Relationship between the H-bond energy, Δ*E*, and their length, $d_{H\cdots B}$. Curve represents exponential fitting[75] for 83 experimentally observed (Y–H···O, Y = C, N, O) hydrogen bonds. Circles, triangles and diamonds denote simulated H-bonded complexes of phenol,[129] aniline[130] and pyridine, respectively, with B = F$^-$ and HB = HF (Schemes 1–3). Asterisks and pluses mean simulated (HF···HF) and optimal (Y–F···H–X) H-bonded systems.[91] Minuses indicate 34 complexes analyzed by Grabowski *et al.*[21]

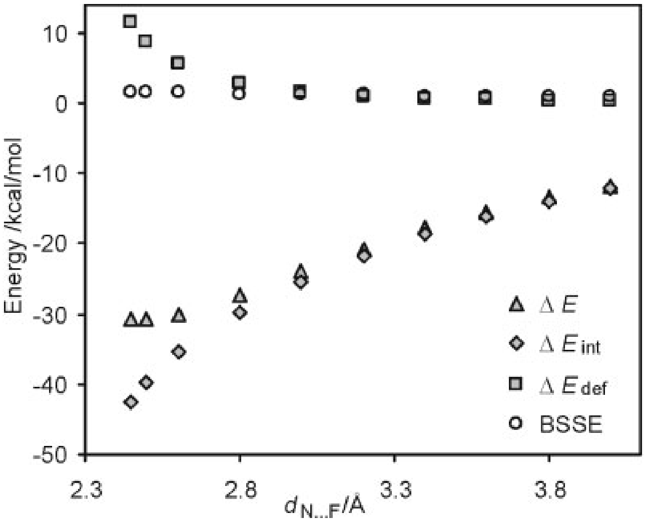


Figure 4. Change in the total energies, ΔE, intermolecular, ΔE_{int}, and deformation, ΔE_{def}, energies, and BSSE for Ph-$NH_2\cdots F^-$ complexes as a function of the N···F separation, $d_{N\cdots F}$[130]

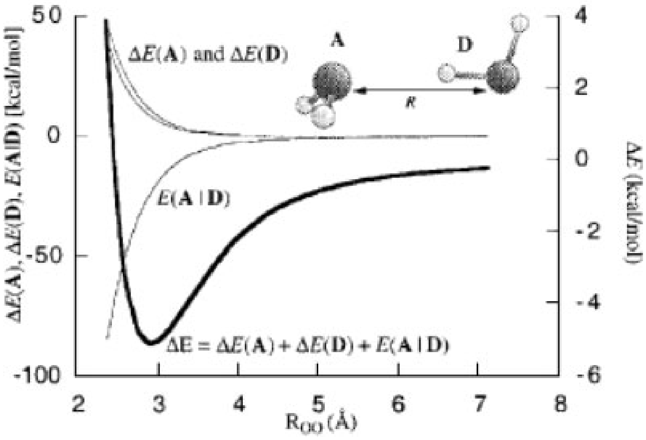


Figure 5. Change in the total (bold), ΔE, internal, ΔE(A) and ΔE(D), and intermolecular, E(A|D), energies of water dimer relative to two free waters and as a function of O···O separation [Reprinted with permission from Ref.[118]. Copyright (2000) John Wiley & Sons, Inc.]

6-311+G** level. For modeling $H_2O\cdots HOH$ and $[HOH\cdots OH]^-$ systems[112] MP2/6-311++G(2d, 2p) scheme was used. Full optimization of 34 complexes (the largest variety of H-bond type, with dihydrogen bond and H···π interaction inclusive) was performed by Grabowski *et al.*[21] using MP2/6-311++G**. Solid curve in Fig. 3 represents exponential fitting[75] for experimentally observed Y—H···O (Y = C, N, O) hydrogen bonds.

In spite of a large variety of interacting molecules and applied methods, the results of the simulation are in line with experimental data. The strength of the intermolecular interaction increases with the shortening of the hydrogen bond. Furthermore, the same rule seems to apply for equilibrium (fully optimized) complexes formed with a large variety of proton donors and acceptors. A systematic study of this phenomenon has not yet been undertaken.

Energy of hydrogen bond

The strength of the intermolecular H-bond is usually calculated as the difference between the energy of the complex and the energies of the isolated monomers, that is as the energy of the reaction:

$$A + B \rightarrow A\cdots B \qquad (4)$$

For energetically stable systems, the estimated energy of the interaction is negative. Positive values (absolute values) are often presented for convenience of the discussion (Fig. 1). They can be considered as corresponding to the process inverse to reaction (4), that is the dissociation of the complex (Table 1). As mentioned above, the energy should be corrected for BSSE.[7,71,72] For even greater accuracy, the energy should be also corrected for the zero-point vibrational energies (ZPE). To compare the computational result with the available experimental data,[51] the thermal energy correction should be included.[114]

The process of H-bond formation may be conceptually divided into two processes: (i) changes in geometry of A and B from the optimized ones to their geometry in the complex (A···B), and (ii) electronic redistribution between the product and the substrates of reaction (4) for all their geometries as in the optimal complex. The first process is called deformation and its energy can be expressed as follows:

$$\begin{aligned}\Delta E_{def} = {} & E_A(\mathrm{basis}_A; \mathrm{opt}_{A\cdots B}) - E_A(\mathrm{basis}_A; \mathrm{opt}_A) \\ & + E_B(\mathrm{basis}_B; \mathrm{opt}_{A\cdots B}) - E_B(\mathrm{basis}_B; \mathrm{opt}_B) \qquad (5)\end{aligned}$$

The second one is 'pure' interaction and is known as the supermolecular approach:

$$\begin{aligned}\Delta E_{int} = {} & E_{A\cdots B}(\mathrm{basis}_{A\cdots B}; \mathrm{opt}_{A\cdots B}) - E_A(\mathrm{basis}_{A\cdots B}; \mathrm{opt}_{A\cdots B}) \\ & - E_B(\mathrm{basis}_{A\cdots B}; \mathrm{opt}_{A\cdots B}) \qquad (6)\end{aligned}$$

where $E_A(\mathrm{basis}_{A\cdots B}; \mathrm{opt}_{A\cdots B})$ means that the energy of molecule A, E_A, is calculated using internal coordinates of the A and B molecules, $\mathrm{basis}_{A\cdots B}$ (i.e., a ghost basis set at the B molecule is included), and for their geometry obtained during optimization of the A···B complex, $\mathrm{opt}_{A\cdots B}$. The other terms in Eqns (5) and (6) should be understood in the same way.

Therefore, the total energy (or binding) of the reaction (4) is the sum:

$$\Delta E = \Delta E_{def} + \Delta E_{int} \qquad (7)$$

The first term, deformation energy, is always positive because it refers to optimal structures of A and B. The second one, intermolecular energy, for interacting counterparts is negative.

Substituting Eqns (5) and (6) to (7) we obtain the well-known expression:

$$\begin{aligned}\Delta E = {} & E_{A\ldots B}(\mathrm{basis}_{A\ldots B}; \mathrm{opt}_{A\ldots B}) - E_A(\mathrm{basis}_A; \mathrm{opt}_A) \\ & - E_B(\mathrm{basis}_B; \mathrm{opt}_{.B}) + \mathrm{BSSE} \qquad (8)\end{aligned}$$

where

$$\begin{aligned}\mathrm{BSSE} = {} & E_A(\mathrm{basis}_A; \mathrm{opt}_{A\ldots B}) - E_A(\mathrm{basis}_{A\ldots B}; \mathrm{opt}_{A\ldots B}) \\ & + E_B(\mathrm{basis}_B; \mathrm{opt}_{A\ldots B}) - E_B(\mathrm{basis}_{A\ldots B}; \mathrm{opt}_{A\ldots B})\end{aligned}$$

This equation is used to calculate the BSSE value by the Gaussian 03 suite of programs.[115]

Individual components of the H-bond energy, Eqn (7), cannot be experimentally measured. However, the described calculation enables to look into H-bond formation, which can be considered as the result of the competition between the deformation and the interaction processes. The results for simulated Ph—$NH_2\cdots F^-$ complexes (Scheme 1a, B = F^-) are shown in Fig. 4. In this system the deformation process takes place only in the aniline molecule. For long hydrogen bonds, the $d_{N\cdots F}$ distance in the range 3 ÷ 4 Å, their strength (binding energy) is almost equal to the intermolecular energy, whose absolute value increases with shortening of the H-bond length. The deformation energy is of the order of BSSE values or lower. In the case of shorter H-bonds ($d_{N\cdots F} < 3$ Å) approaching of the proton acceptor (F^-) results in an increase of both the deformation energy and the absolute value of the intermolecular energy, but the former one increases faster. As a consequence, the sum of the energy parts, Eqn (7), reaches minimum for the fully optimized Ph—$NH_2\cdots F^-$ complex ($\Delta E_{def} = 11.67$ kcal/mol and $\Delta E_{int} = -42.49$ kcal/mol). This large value of the estimated deformation energy can be explained by the delocalization of the lone pair of the nitrogen atom by the C—N bond to phenyl ring (*vide infra*).

In spite of the simplicity of the above presented model, the obtained results are in line with the energy decomposition using localized charge distribution[112,116–118] whose representative example (H-bonding in water) is presented in Fig. 5. The total energy of the interaction arises from two competing contributions: the internal energies of the donor and acceptor molecules [ΔE(D) and ΔE(A)] and their intermolecular energy [E(A|D)]. The latter dominates for large values of the intermolecular distance between the oxygen atoms (R_{OO}), the former is more pronounced for short R_{OO} values. The minimum of the total energy indicates fully optimized water dimer complex.

EFFECT OF H-BONDING ON STRUCTURAL PROPERTIES

Generalities

To quantify the strength of H-bond in terms of structural parameters vicinal to hydrogen bond, the plot of the estimated binding energy, Eqn (7), against C—N(O) bond length and *ipso* angle α, is shown in Fig. 6. Two structural parameters were used for H-bonded complexes of pyridine and phenol and aniline derivatives (the C—Y bond length and the *ipso* angle of the ring, for its definition see Charts 1 and 2) in order to compare the range of their variability induced by the H-bond interactions. Since the C—N bond in pyridine constitutes an inherent part of the aromatic ring, its length is little dependent on the strength of the H-bond (the mean value was used in Fig. 6a). Therefore, the dependence of the α angle, presented in Fig. 6b, seems to be in this case a better measure of the H-bond energy. Obviously, for H-bonded systems of aniline and phenol derivatives, the *ipso* angle is a distant (by one bond) structural parameter.

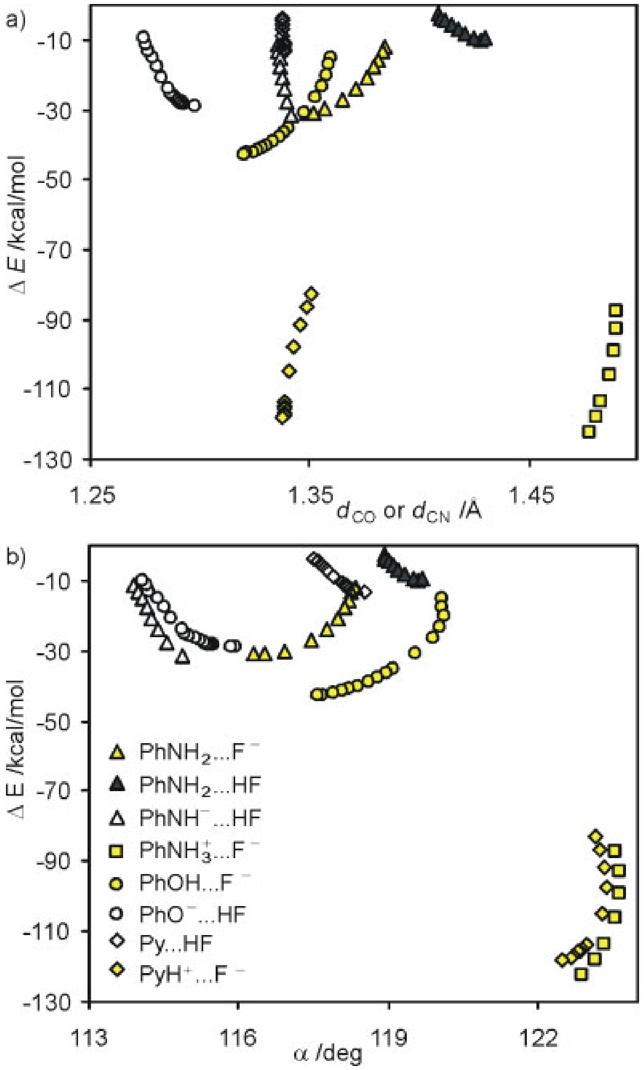


Figure 6. Dependence of the estimated H-bonding energy, Eqn (7), on (a) C–N or C–O bond length, (b) α angle for the B3LYP simulated interaction of aniline (triangles and squares), pyridine (diamonds) and phenol (circles) derivatives with B = F^- or HB = HF, Schemes 1–3. Cases in which N or O constitute a part of proton-donating groups are indicated in yellow. The presented data are a compilation of published[51,129,130] and unpublished results obtained by the author and her coworkers [This figure is available in color online at www.interscience.wiley.com/journal/poc.]

In complexes discussed here, the length of the C—Y (Y = O or N) and the *ipso* angle, α clearly depend on the strength and the nature of the corresponding H-bond. Two cases can be distinguished, in which opposite tendencies can be noticed: (i) when the Y atom is a part of the proton donor group (notation $PhNH_2\cdots F^-$, $PhNH_3^+\cdots F^-$, $PhOH\cdots F^-$, $PyH^+\cdots F^-$, respectively, yellow-filled signs in Fig. 6); (ii) when the Y atom is a proton acceptor ($PhNH_2\cdots HF$, $PhNH^-\cdots HF$, $PhO^-\cdots HF$, $Py\cdots HF$, gray triangles and empty triangles, circles and diamonds, respectively in Fig. 6). In the first case shortening of the C—Y bond gives rise to a strengthening of the corresponding H-bond. The reverse trend is observed in the second case. Lengthening of the C—Y (Y = O, N) bond results in an increase of the strength of the interaction. The direction of the *ipso* angle, α, variability is consistent with the change of the C—Y bond length. Note that for all presented cases of the H-bonded complexes, the relationship between the strength of the H-bond and its length is of the same nature (Figs. 3 and 4) and only the responses of the C—Y bond length and the α angle are different in both discussed cases.

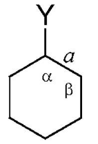


Chart 1.

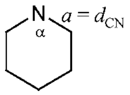


Chart 2.

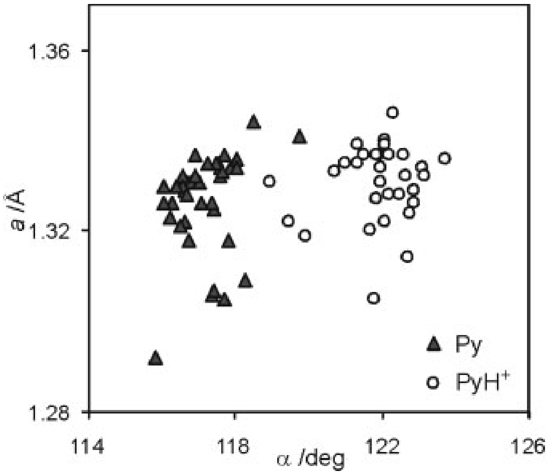


Figure 7. Dependence of *a*-bond, $a = d_{CN}$, on α angle of pyridine/pyridinum systems involved in H-bonding [Reprinted with permission from Ref.[52] Copyright (2005) American Chemical Society]

Properties changes in the region of H-bond interactions

The relationship between the strength of the H-bonding and the C—N bond length (Fig. 6a) for simulated Py···HF and $PyH^+\cdots F^-$ complexes suggests that a change of the bond length as a function of its energy is rather small. In the case of noninteracting pyridine and pyridinium cation,[52] the corresponding bond lengths are equal to 1.337 Å and 1.351 Å, respectively. For the fully optimized system, Py···HF, its length amounts to 1.338 Å. An increase of the binding energy in the $PyH^+\cdots F^-$ system (modeled by approaching fluoride to the nitrogen atom of the pyridinium cation, linearity of the H-bond assumed) results in a shortening of the C—N bond length up to $d_{CN} = 1.338$ Å (for the shortest intermolecular N···F distance of 2.909 Å, before the proton transfers from nitrogen to fluoride). Results of the simulation are in agreement with the X-ray structural data presented in Fig. 7. Analysis of the experimental geometry of H-bonded complexes of variously substituted pyridine and pyridinium derivatives[52] shows a very small variation of all bond lengths in the ring and substantial changes in the values of the α angles. The *a*-bonds lengths (in pyridine and pyridinium $a = d_{CN}$) are almost in the same range for both the pyridine and pyridinium complexes, whereas the α values differ significantly (Fig. 7). Furthermore, for *para-* and poly-substituted systems, the difference of the α angles in pyridine and pyridinum derivatives also exists in spite of various additional perturbations. Summarizing, the magnitude of the *ipso* angle, α, at N may be considered as a useful indicator of the proton position (formally N···H or NH).

An analysis of H-bonded complexes of pentachlorophenol with various bases[119] shows that the changes of the *ortho–ipso* bond lengths are due to the mesomeric effect and the electronegativity, both working in the same direction but the mesomeric effect predominates. Following an analysis of the substituent effect on the ring geometry in mono-substituted benzene derivatives, it can be postulated that a change in the α angle represents a change in the hybridization of the *ipso* atom[120,121] (see below) and, as a consequence, also a change in its electronegativity.[122,123] Moreover, the angular deformations in the ring have recently been used for defining a new scale of electronegativity.[124] Therefore, changes of the *ortho–ipso* bond lengths, *a*, may be due to a blend of two factors: changes in the electronegativity and in the mesomeric effects, whereas changes of the α angle are mostly caused by changes in the electronegativity.

Approaching proton to the nitrogen atom in pyridine (Py···HF, Scheme 3b, HB = HF) increases its electronegativity, hence the α angle becomes larger (Fig. 6b). The lack of a difference between the *ipso–ortho* bond lengths ($d_{CN} = a$) support the hypothesis that the 2p-type electron in the nitrogen atom is weakly involved in mesomeric effect due to the H-bond formation N···HB or NH···B.

A new way of estimating group electronegativity, χ, from angular geometry of the ring in mono-substituted benzene derivatives has been proposed.[124] This method is based on the results of the application of the principal component analysis (PCA).[125,126] It has been found that the main component, describing the observed geometrical changes in the ring,[123] almost solely depends on the changes in the α and β angles (Chart 1) and can be correlated with many scales of electronegativity. In consequence, Domenicano and coworkers[124] introduced the group electronegativity concept (Fig. 8b) in the Pauling electronegativity scale.[127] For geometrical reasons, the changes in α and β angles (Chart 1) mutually depend due to the constraint of the hexagon planarity.[128] Thus, it has been found that it is sufficient to use only α angle to estimate the electronegativity of the group.[129,130] For example, the determined correlation coefficient (*R*) for the linear regression of electronegativity, χ[124],versus *ipso* angle[123],α, relation, was 0.998 for 53 mono-substituted benzene derivatives with 'the first row' substituents (i.e. substituents linked to the benzene ring through an element of the Li—F row of the periodic table).

$$\chi = -41.00(\pm 0.03) + 0.3678(\pm 0.0086)\,\alpha \qquad (9)$$

In parenthesis of the Eqn (9) are given confidence intervals for the significance level of 0.01.

For H-bonded complexes of phenol and aniline derivatives, the variations of the α angle, alike the C—Y (Y = O, N) bond length (Fig. 6), are strongly influenced by the binding energy. Therefore, a significant change of the electronegativity of the substituent, arising from its participating in the H-bond, was found. Influence of H-bonding in phenol/phenolate complexes on the electronegativity of OH/O^- groups[129] is similar to the below presented case of aniline derivatives.[130]

Figure 8a shows the effect of the nature and the strength of the H-bonding in anilide/aniline/anilinium complexes on the electronegativity of $NH^-/NH_2/NH_3^+$ groups.[130] Varying the nature of the H-bonding ($PhNH_2\cdots F^-$, $PhNH_3^+\cdots F^-$, and $PhNH^-\cdots HF$, $PhNH_2\cdots HF$ systems) generates different possibilities of the electron delocalization from the nitrogen atom toward the C—N bond and further to the benzene ring. Nevertheless, the C—N bond lengths and electronegativity of the $NH^-/NH_2/NH_3^+$ groups involved in H-bonding are mutually interrelated. Black squares in Fig. 8a denote noninteracting derivatives: anilide anion ($\chi = 0.89$[130]), aniline and anilinium cation (χ equal to 2.63 and 4.32, respectively[124]). For the $PhNH^-\cdots HF$ complexes, the range of $\chi(NH^-)$ variations extends from 0.90 to 1.26. When the amino group acts as a proton donor in the $PhNH_2\cdots F^-$ complexes, the $\chi(NH_2)$ value ranges from 1.77 to 2.52; however, if it plays the role of a proton acceptor from hydrofluoric acid ($PhNH_2\cdots HF$ complexes), the calculated $\chi(NH_2)$ range is from 2.74 to 2.99. In the case of H-bonded complexes containing the anilinium cation the $\chi(NH_3^+)$ values change from 4.20 up to 4.48. All simulated systems are denoted by crosses in Fig. 8a. Empty squares indicate

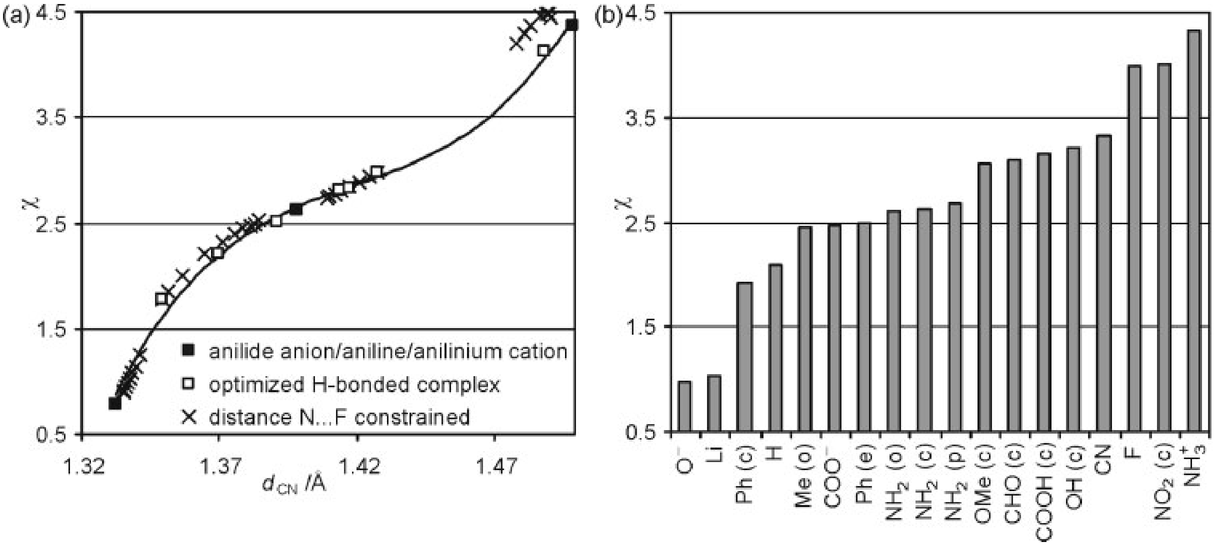


Figure 8. (a) Dependence of the group electronegativity, χ, for various H-bonded complexes of the anilide/aniline/anilinium cation with Broensted bases and acids on the C–N bond length, d_{CN}; black squares mean not interacting derivatives, empty squares denote the optimized H-bonded complexes, crosses designate the H-bonded systems with the constrained N···F distance. The curve (a third degree polynomial) fitted to data for full optimized systems. (b) For comparison a histogram of χ values[124] for various groups known as typical substituents is shown [Reprinted from Ref.[130]. Copyright (2007) with permission from Elsevier]

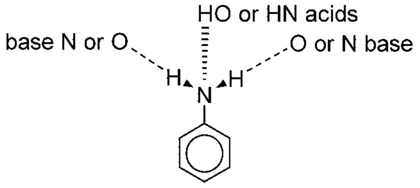
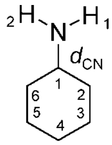


Chart 3.



$\Sigma = H_{(1)}NC_{(1)} + H_{(2)}NC_{(1)} + H_{(1)}NH_{(2)}$

Φ = angle between the planes defined by $H_{(1)}NC_{(1)}$ and $H_{(2)}NC_{(1)}$

Chart 4.

the fully optimized complexes of aniline interacting, via the hydrogen bond, either with a base B (B = F^-, CN^-, OH_2) or with an acid HB (HB = HF, HCN, H_2O), and for the H-bonded complex of the anilinium cation with water. The relationships between electronegativity and the C—N bond length for both types of complexes, that is those with constrained N···F interatomic distance and the fully optimized ones, lead to an equivalent shape of the function presented as a third degree polynomial. Moreover, the range of the χ-values variability for the NH_2 and NH_3^+ groups involved in H-bond complexation, estimated by computational modeling, is in line with that extracted from the X-ray geometry data, as shown in Fig. 9.

Experimental geometries of aniline/anilinium cation in their H-bonded complexes with various oxygen or nitrogen acids and bases were retrieved from CSD.[49] It should be stressed that in a large majority of crystal structures, the amino group forms more than one H-bond. The maximum number is three (Chart 3). In the case of the NH_2 group involved in two H-bonds, they could be of the same type or of different one (i.e. in one of them nitrogen is a proton donor and in the second acts as a proton acceptor). For this reason the number of points in Fig. 9b is larger than in Fig. 9a. Note that H-bond formation in which the NH_2 group is a proton donor induces opposite changes as compared to the case when it is a proton acceptor. Additionally, in the crystal structure, one of these interactions may be superior to the other. Then the appropriate $d_{N\cdots B}$ (B = O or N) distance may be substantially shorter (suggesting a stronger hydrogen bond) and, in consequence, this interaction may determine the electronegativity of the whole group. Let us consider the optimized H-bonded systems of aniline. In general, a modification of the chemical nature of the base (B = F^-, CN^-, OH_2) interacting with aniline results in a more pronounced electronegativity and C—N bond length variations as compared to the case of the interacting acid (HB = HF, HCN, H_2O). In the former, the electronegativity changes by 0.73 and the bond length by 0.04 Å, whereas in the latter by 0.18 and 0.01 Å, respectively. The change of the intermolecular N···B distance is roughly similar for both cases (0.64 Å and 0.55 Å, respectively). The strongest hydrogen bond and the shortest N···B distance are observed for aniline interacting with F^- (as the base) and with HF (as the acid). Their energies are equal to −30.83 and −9.80 kcal/mol, respectively. The former complex is the case of CAHB.[23] If the water molecule, which can be both an acceptor and a donor of proton, interacts with aniline, the estimated H-bonding energy amounts to −3.55 and −4.82 kcal/mol, respectively. Contrary to the case of $PhNH_2\cdots F^-$ and $PhNH_2\cdots HF$, in the complexes of water with aniline ($PhNH_2\cdots OH_2$ and $PhNH_2\cdots HOH$), a shorter intermolecular N···B distance is observed for the complex in which the water molecule acts as a proton donor. This is in agreement with the experimental CSD data, which suggest stronger H-bonding for the $PhNH_2\cdots HO(N)$base interaction (Fig. 9b).[130]

From crystal engineering point of view, the consecutive, interesting and important question is how does the nature and strength of H-bonding affect the shape of the amino group? Its

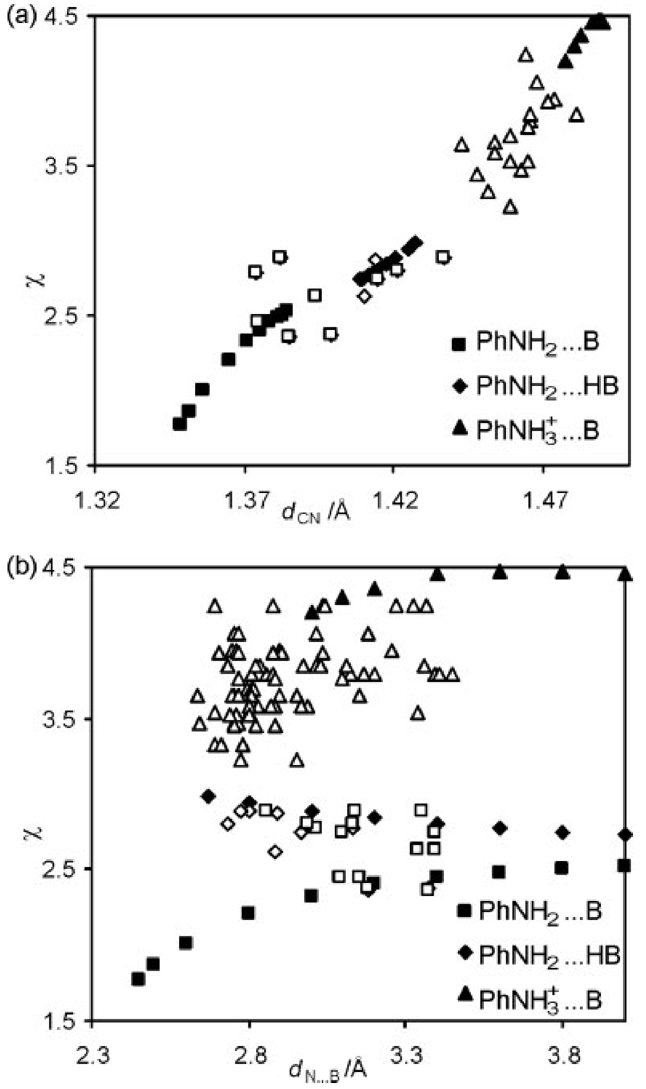


Figure 9. Relationship between the group electronegativity, χ, and (a) the C–N bond length, d_{CN}, (b) the N···B interatomic distance, $d_{N\cdots B}$, for experimental (retrieved from CSD, empty signs) and simulated (black signs, squares denote $PhNH_2\cdots B$, diamonds indicate $PhNH_2\cdots HB$, triangles mean $PhNH_3^+\cdots B$ systems) H-bonded complexes of aniline and the anilinium cation with Broensted bases and acids [Reprinted from Ref.[130]. Copyright (2007) with permission from Elsevier]

shape can be described by the dihedral angle Φ (Chart 4), the sum of the bond angles, Σ, for bonds linking the nitrogen atom to two H atoms and to the carbon atom (Chart 4), or as dihedral angle τ between the plane of the amino group (H—N—H) and the ring plane. For planar NH_2, their values are 180, 360 and 0 deg, respectively. The geometry of the NH_2 group in aniline has been a subject of intensive studies, with a particular interest in its pyramidalization. For aniline, microwave studies[131] lead to $\tau = 37.5 \pm 2$ deg, however a careful reanalysis of the data by Roussy and Nonat[132] gives the value of 42.4 ± 0.3 deg, in agreement with the results of other groups.[133,134] A slightly higher value, 44.30(16) deg, was derived from a semirigid bender analysis[135] of the far-infrared data.[136] Thoroughgoing analysis of gas phase electron diffraction data and *ab initio* molecular orbital calculations at the HF and MP2 levels of theory yielded[137] 44 ± 4, 41.8 and 43.6 deg, respectively. The estimated Σ value varies depending on the calculation method applied: 336.2 deg (estimated on the basis of the data presented by Schultz *et al.*[137]), 339.3 deg,[138] 343.5 and 337.5 deg (calculated using B3LYP/6-311+G** and MP2/aug-cc-pVDZ results,[139] respectively).

It is well known that the substituent influences the properties of aniline via intramolecular interactions. The presence of an electron-attracting group, for example the nitro group,[140] in the *para*-position of the ring results in a substantial intramolecular charge transfer from the amino group through the ring to the nitro group. This transfer leads to changes in the pK_a values of the amino group of substituted anilines, for all geometry parameters applied ($\Sigma = 351.6$ and 342.0 deg for B3LYP/6-311+G** and MP2/aug-cc-pVDZ calculations,[139] respectively) and affects the charge distribution.[141–148] The influence of various substituents on structural parameters and cyclic π-electron delocalization in aromatic systems has recently become subject of increased interest.[149]

H-bonding, as intermolecular interaction, affects the geometry and the electronic structure of the amino group as well. A comparison of both types of the interactions (intra- and inter-ones) is shown in Fig. 10. This figure presents the dependence of

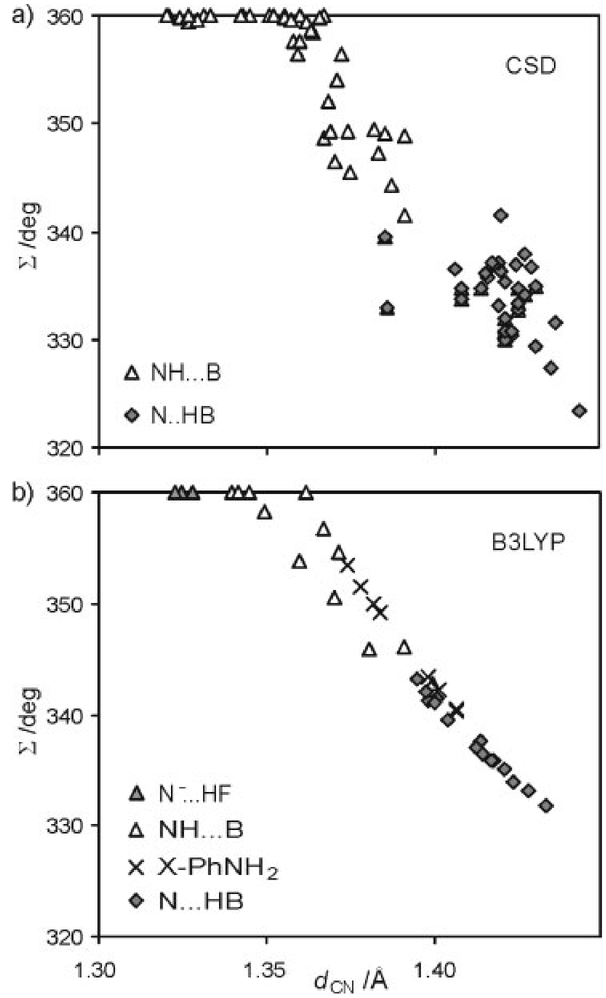


Figure 10. Dependence of Σ on the C–N bond lengths, d_{CN}, for (a) experimental data (CSD) and (b) optimized (B3LYP/6-311+G**) molecules of *para*-X-aniline (X = NO, NO_2, CN, CHO, H, CH_3, OCH_3, OH) and its (X = NO, NO_2, CHO, H, OH) derivatives involved in H-bond complexation [Reprinted (from Supporting Information) with permission from Ref.[138]. Copyright (2007) American Chemical Society]

the pyramidalization of the NH_2 group, expressed by Σ, on the CN bond length, d_{CN}, for experimental data retrieved from CSD[49] and for modeled data computed at B3LYP/6-311+G** level of theory. The experimental data represent H-bonded complexes of different oxygen and nitrogen acids/bases with variously substituted aniline. Optimization was performed for *p*-X aniline (X = NO, NO_2, CN, CHO, H, CH_3, OCH_3, OH) and its (only X = NO, NO_2, CHO, H, OH) H-bonded systems according to the Scheme 1(a-c), B = F^-, CN^-, OH_2; HB = HF, HCN, HOH). Both theoretically and experimentally obtained structural parameters for aniline, its substituted derivatives and H-bonded complexes present a coherent view. Moreover, findings of the B3LYP/6-311+G** and MP2/aug-cc-pVDZ computational methods are also in a good qualitative agreement with each other.[139] A decrease in pyramidalization of the NH_2 group is related to an increase of π-electron accepting power of the *para*-substituent and the H-bonding complexation N—H···B. The reverse trend is observed for N···HB interactions with electron donating substituents. The analysis based on geometrical parameters leads to the same picture as that obtained by Natural Bond Orbital (NBO) studies. The stronger is the through-resonance (intermolecular charge transfer) of the NH_2 group with a counter-substituent, and the more is involved the N—H bond in the interactions with bases, the more planar is the NH_2 group. For CN bond length shorter than 1.35 Å, there appears a high occupancy of the π orbital of this bond.

Pyramidalization of the NH_2 group is related to the C—N bond length (Fig. 10) and associated with a decrease of Σ and Φ values, indicating a change in the hybridization of the nitrogen atom orbitals from sp^2 toward sp^3. The electronegativity, χ, of the amino group also depends on the C—N bond length (Figs. 8a and 9a). To sum up the above discussed findings, χ increases with pyramidalization of the NH_2 group of aniline involved in the H-bond formation.[130]

Another interdependence of the local properties of the H-bond is the correlation between the ^{1}H NMR chemical shift of the proton involved in this interaction and the C—Y (Y = N, O) bond length. Such relation determined for *para*-substituted phenol derivatives complexes with fluoride and hydrofluoric acid[150] is presented in Fig. 11. Two reverse dependences are apparent again (compare Fig. 11 and Fig. 6a). Forming H-bond shifts the proton magnetic resonance toward lower field. If the oxygen atom is a proton donor, *para*-X-PhOH···F^- complexes (Scheme 2a), an increase in the strength of the interaction results in a shortening of the C—O bond length (the positive slope of the linear correlation of $d_{C\text{-}O}$ vs. ^{1}H-NMR chemical shift). The reverse trend (the negative slope), that is an increase of the C—O bond length, is observed for *para*-X-PhO$^-$···HF systems, where oxygen acts as a proton acceptor.

The next dependence, shown in Fig. 12, is predicted by a model based on the relation between bond distances and 'bond orders' (valences), *s*, and an additional bond order conservation rule (for the hydrogen atom involved in H-bond: $s_{Y-H} + s_{H\cdots B} = 1$). Steiner[151] has shown that the valence model of the hydrogen bond correctly works for the geometries of a number of hydrogen bonds (high-precision data retrieved from CSD). The coupling constants have been related to the hydrogen bond geometries and NMR chemical shifts by applying the valence bond order model[152] for both experimental and calculated (DFT method) data. This model was successfully used in the low temperature NMR studies of H-bonded complexes of colloidine with carboxylic acids,[153,154] and small complexes formed between water and pyridine derivatives in solid and liquid phases.[155] For the closed values of bond orders of Y—H and H···B bonds, the proton transfer reaction takes place.[156–158] Lengthening of the covalent bond, Y—H, induces shortening of the hydrogen bond. Results of the simulated H-bonded complexes of aniline, phenol and pyridine derivatives follow the relation predicted by the valence model for hydrogen bond.

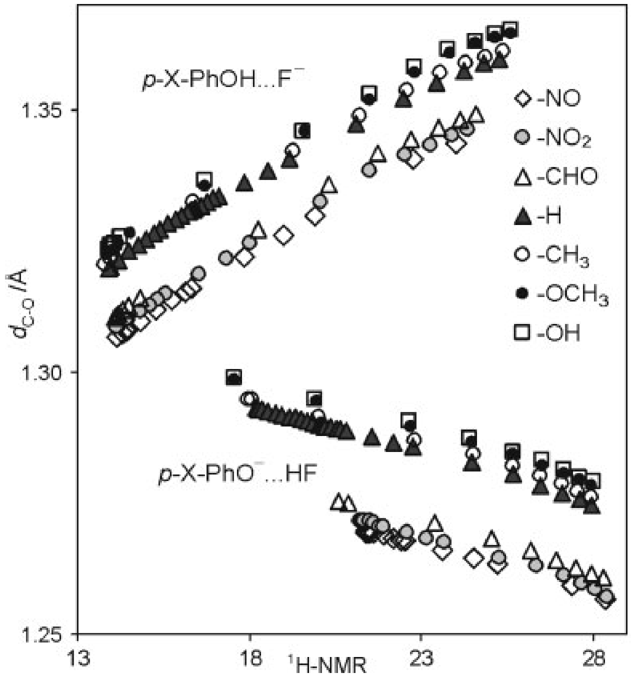


Figure 11. Dependence of two empirical measures of H-bond strengths: the absolute value of chemical shift of the proton involved, ^{1}H-NMR, and C–O bond length, $d_{C\text{-}O}$, for [*p*–X–PhO···H···F]$^-$ complexes [Reprinted with permission from Ref.[150]. Copyright (2005) American Chemical Society]

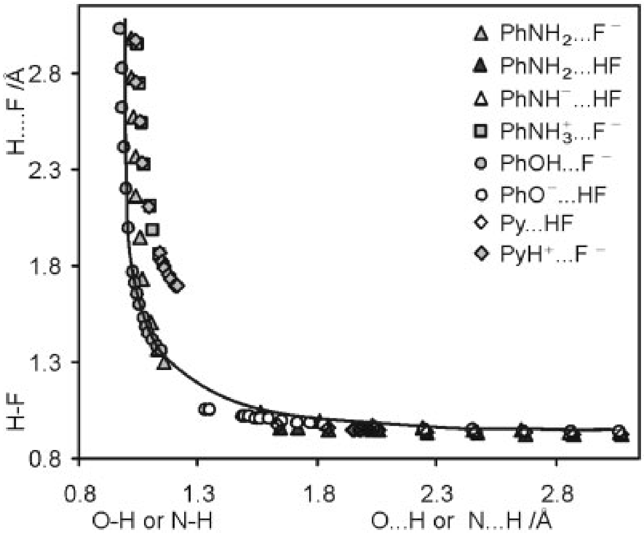


Figure 12. Lengthening of the Y–H (Y = N, O) bond induced by Y–H···F hydrogen bonds and of the F–H bond induced by F–H···Y H-bonds for the B3LYP simulated interaction of aniline (triangles and squares), pyridine (diamonds) and phenol (circles) derivatives with B = F^- or HB = HF, Schemes 1–3, drawn in common diagram. The curve is a fit against the valence model for hydrogen bond (parameters for N–H···O and N···H–O H-bonds were used)[151]

Short-distance consequences of H-bonding

As it has already been stated, the H-bond-induced changes involve lengthening or shortening of the C—Y bond (Y = O, N) and an increase (or a decrease) of the *ipso* bond angle, depending on the role of the substituent in the intermolecular interaction (proton acceptor or proton donor). Simultaneously, an increase in the electron charge (Mulliken charges[159]) at the atom (Y = N, O) participating in H-bonding is observed.[51] H-bond interactions also lead to substantial changes in the hybridization of the Y-atom orbitals. This effect will be discussed in detail. An increase in the negative charge at the Y atom causes changes in the hybridization at the carbon atom following Bent–Walsh rule.[120,121] The rule relates an increase (or a decrease) of electronegativity of the substituent Y (i.e. NH_2 involved in H-bonding, Scheme 4, or OH) with an increase (or a decrease) of the 2p orbital contribution to sp^2- hybridized carbon atom directed to Y and a decrease (or an increase) of this contribution to bond orbitals in two other directions (*ortho–ipso* CC bonds). This, in turn, results in a lengthening (or shortening) of the C—Y bond, shortening (or lengthening) of both *ipso–ortho* CC bonds and an increase (or a decrease) of the *ipso* bond angle. Scheme 4 shows how this rule works in the case of aniline involved in H-bonding. A contribution of mesomeric effect cannot be excluded, but there is no clear relation between C—N bond length and α angle for this kind of interactions.

It was found that Bent–Walsh interrelations appropriately describe both the experimental data and the computational results in H-bonded complexes of aniline[51] and phenol[50,160] derivatives. Structural modifications resulting from the proton transfer in complexes of phenols with pyridines,[161,162] trimethylamine[163] and N-methylmorpholine[164] also follow the Bent–Walsh rule.

Figure 13 shows the relationships between the α angle (Chart 1), the C—N bond length, d_{CN}, and the *ortho–ipso* bond length, *a*, for optimized geometry of 4-substituted aniline, anilide anion and anilinium cation, and their H-bonded complexes. Alike dependences were found for experimental geometries of variously substituted aniline/anilinium cation derivatives in their H-bonded complexes (retrieved from CSD). Obviously, the dispersion of the X-ray data is broader than that of the results obtained for optimized systems.[51] It results from a variety of substituents, their positions and numerous and diversified interactions in the crystal lattice. In spite of this, all interdependences are statistically significant. Computational results show a good qualitative agreement with those based on the X-ray data.

For the H-bonded pyridine and pyridinium complexes, no relation between the C—N bond length and the α angle was found (Fig. 7).[52]

Long-distance consequences of H-bonding

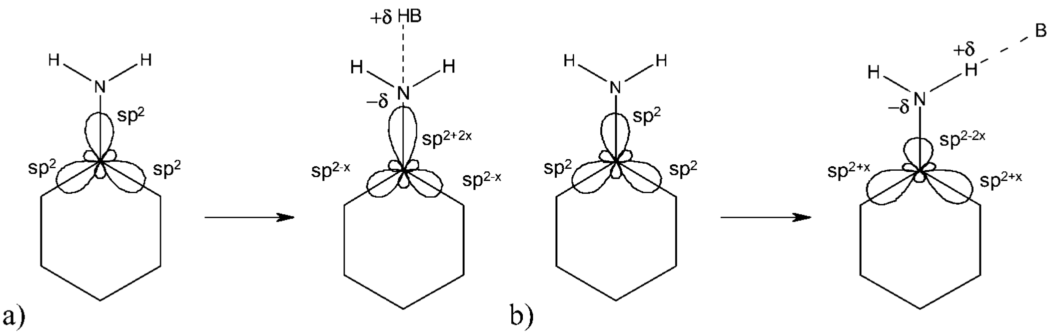
Apart from the above-mentioned consequences of intermolecular H-bond interactions that are rather local, long-distance structural changes can also be observed. A common part of aniline, phenol and pyridine derivatives is the ring, which is characterized by the cyclic π-electron delocalization, that is closely related to aromaticity.[165–168] Another factor that could be associated with π-electron delocalization is the substituent effect.[149] This effect leads to the interaction between the electron-accepting and electron-donating groups, which in turn causes an intramolecular charge transfer, also described as the substituent delocalization effect.[169]

Taking into consideration experimental data (geometry retrieved from CSD), the most appropriate index of aromaticity seems to be the HOMA index[170] (Harmonic Oscillator Model of Aromaticity). This geometry-based index of aromaticity serves as a convenient, reliable[166] and easily accessible (for any type of structural data) quantitative measure of π-electron delocalization[167] in the aromatic ring. The formula for HOMA reads

$$\mathrm{HOMA} = 1 - \frac{1}{n}\sum_{j=1}^{n}\alpha_i\left(R_{opt,i} - R_j\right)^2 \qquad (10)$$

where: *n* is the number of bonds taken into the summation; α_i is a normalization constant (for CC and CN bonds $\alpha_{CC} = 257.7$ and $\alpha_{CN} = 93.52$) fixed to give HOMA = 0 for a model nonaromatic system and HOMA = 1 for the system with all bonds equal to the optimal value $R_{opt,i}$ assumed to be realized for fully aromatic systems (for CC and CN bonds $R_{opt,CC}$ is equal to 1.388 and $R_{opt,CN} = 1.334$ Å); R_j stands for a running bond length.

As previously pointed out, the effect of the strength of H-bonding in complexes of aniline, phenol and pyridine derivatives can also be observed by variability of the C—Y (Y = O or N) bond length or the α angle (Fig. 6). Undoubtedly, trends of the change depend on the nature of the H-bond, that is whether the Y atom is a proton donor or a proton acceptor, but the C—Y bond length can be used as a convenient H-bond strength parameter for aniline and phenol derivative systems. For these complexes, a clear dependence of HOMA index on the C—N and C—O bond lengths is observed. Figure 14 presents results obtained for optimized geometry of *para*-X-substituted aniline, anilide anion and anilinium cation and their H-bonded



Scheme 4. Changes in hybridization at the carbon atom as a result of changes in electronegativity of the nitrogen atom in aniline molecule involved in two kinds of H-bonding.

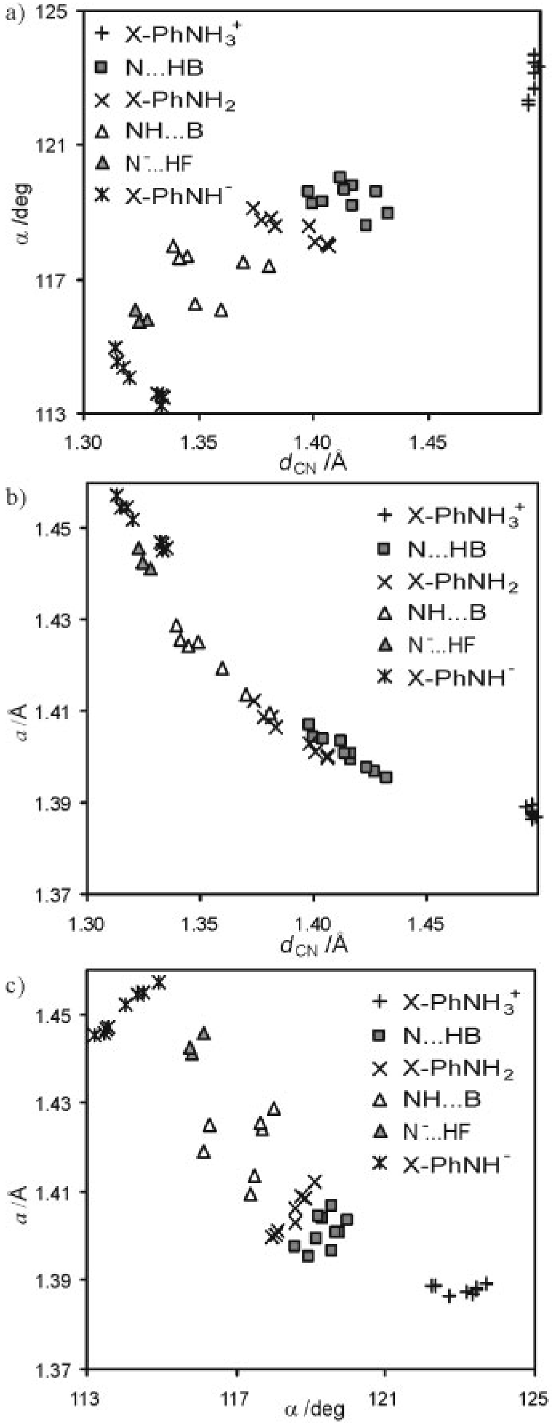


Figure 13. Interrelations between (a) α and C–N bond length, d_{CN}, (b) a and C–N bond length, (c) a bond length and α for optimized geometry of p-X-substituted aniline, anilide anion and anilinium cation (X = NO, NO_2, CN, CHO, H, CH_3, OCH_3, OH), and their H-bonded complexes (only for X = NO, NO_2, CHO, H, OH) [Reprinted with permission from Ref.[51]. Copyright (2007) American Chemical Society]

complexes.[51] The relationship between the C—N bond length and the HOMA index, found for variously substituted aniline and anilinium cation derivatives in their H-bonded complexes (the former retrieved from CSD), is shown in Fig. 15. No crystallographic data for H-bonded anilide anion derivatives are available.

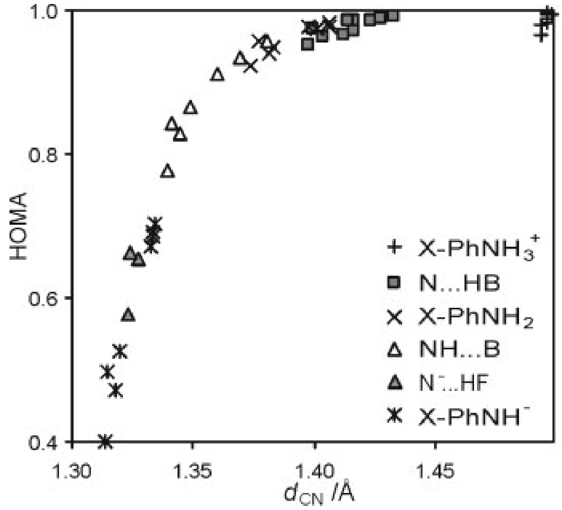


Figure 14. Scatter plot of HOMA versus C–N bond length, d_{CN}, for B3LYP optimized geometry of p-X-substituted aniline, anilide anion and anilinium cation (X = NO, NO_2, CN, CHO, H, CH_3, OCH_3, OH), and their H-bonded complexes (only for X = NO, NO_2, CHO, H, OH) [Reprinted with permission from Ref.[51]. Copyright (2007) American Chemical Society]

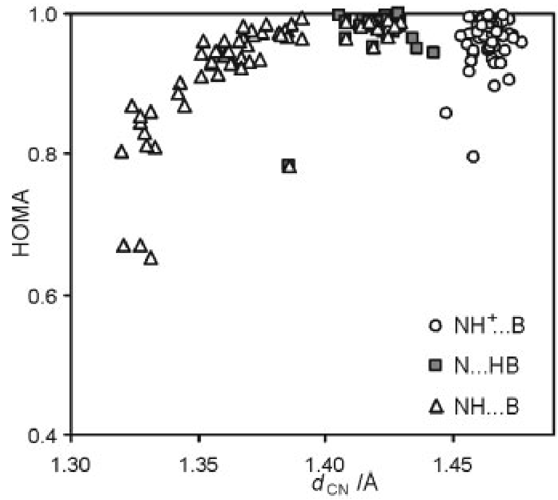


Figure 15. Dependence of HOMA on C–N bond length, d_{CN}, for variously substituted aniline/anilinium cation derivatives in their H-bonded complexes (experimental geometry retrieved from CSD) [Reprinted with permission from Ref.[51]. Copyright (2007) American Chemical Society]

Similar to the case of the relations presented in Fig. 13, the dispersion of the data from the *ab initio* optimization (Fig. 14) is in general smaller than that observed for the experimental scatter plots (Fig. 15). The trends of the dependences of HOMA versus d_{CN}, determined from the calculated optimized data using B3LYP/6-311+G** (Fig. 14) and MP2/aug-cc-pVDZ,[51,160] and those based on the experimental solid state X-ray data (Fig. 15) are very similar. Furthermore, alike relations are observed for H-bonded complexes of phenol derivatives,[50,150,171,172] see Fig. 16. In both cases, namely aniline and phenol H-bonded complexes, shortening of the C—Y (Y = O or N) bond length induces lowering of the HOMA values. Also, magnetism-based index of aromaticity,[173] NICS, used only for optimized and simulated geometries

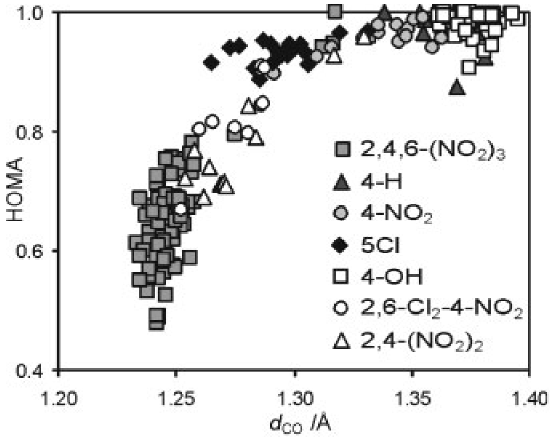


Figure 16. Dependence of HOMA on C–O bond length, d_{CO}, for H-bonded complexes of seven types substituted phenol derivatives[50] [Reprinted with permission from Ref.[150]. Copyright (2005) American Chemical Society]

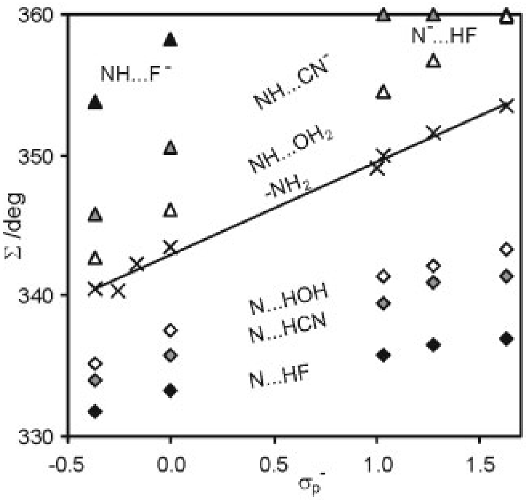


Figure 17. Dependence of Σ for B3LYP/6-311+G** optimized molecules of *para*-X-aniline (crosses) and its derivatives involved in H-bond complexation: N$^-$···HF, N–H···B and N···HB on the substituent constant σ_p^-. Black triangles and diamonds stand for B = F$^-$ and HB = HF, gray ones for B = CN$^-$ and HB = HCN and empty ones for B = HB = OH$_2$ [Reprinted (from Supporting Information) with permission from Ref.[138]. Copyright (2007) American Chemical Society]

of the system, indicates a more limited π-electron delocalization in the ring.[51,171] Furthermore, mutual relation between HOMA and NICSs[174,175] confirms their equivalence.

For the H-bonded pyridine/pyridinium systems, the differences in mean C—N (*a*) bond lengths are very small but a wide range of variability of the α angle is noticed,[52] (Fig. 7). In spite of these strong variations, no dependence between the HOMA index and the changes in the bond angle at the N-atom, α, is observed. This confirms the thesis that 2p-type electron in the nitrogen atom is weakly involved in the mesomeric effect, and hence, its effect on π-electron delocalization in the ring is much smaller. In the cases of aniline and phenol derivatives, two 2p-type electrons may be involved in the mesomeric effect, leading to significant changes in the π-electron structure in the ring.

What about the substituent effect? Let us consider the substituent effect as a long-distance factor. Obviously, substituent influences both the aromaticity of the ring and the strength of H-bonding. As a consequence, it changes the acidity of phenol or aniline derivatives. The analysis of the experimental geometry of H-bonded complexes of substituted phenol derivatives shows a significant dependence of the mean C—O bond length, for a given type of substituted phenol, on its pK_a.[50] The more acidic is the phenol derivative, the shorter is the C—O bond.

Hammett-type approach is a well-known empirical way of estimating the electronic influence of a substituent on the reaction site or another functional group.[176–178] This influence is numerically expressed by substituent constants σ, defined in most cases for disubstituted benzene derivatives.[149,179–181]

Which interactions, intra- (the substituent effect) or intermolecular (hydrogen bond), have 'more power'? Effect of both on the shape of the amino group[139] is shown in Fig. 17. The range of variation Φ (Σ, in parentheses) in aniline H-bonded complexes of NH···B type is *ca* 27 (12) and 49 (20) deg and for N···HB one, ~4 (4) and 4 (5) deg (calculated using B3LYP and MP2, respectively). Obviously, this range is wider if all studied systems are considered: for NH···B *ca* 47 (17) and 53 (23) deg, for N···HB ~12 (11) and 9 (9) deg (calculated using B3LYP and MP2, respectively). This is due to an increase in the donating power of nitrogen if the amino group is involved in the H-bonding. The change in pyramidalization of the amino group, as a result of the substituent effect, is significantly smaller (for Φ it is ~20 and 9 deg, in the case Σ it is ~13 and 8 deg, from B3LYP and MP2 calculations, respectively). The answer to the question is not surprising – 'small' is powerful, particularly when the amino group acts as a proton donor in H-bonded complexes. Similar response suggests changes of the other geometrical parameters for aniline and phenol derivatives and their H-bonded complexes.[51,160] For example, an interesting trend can be observed for relations of the α angle versus the C—N bond length, and *a* versus α (Fig. 13a and c). The substituent effect, for a given kind of systems (labeled inside the figure as triangles, squares, pluses, etc.), has its slope opposite to the general trend (for all data points). Moreover, the variability of the C—N bond length, α angle and the *ortho–ipso* bond length, *a*, due to substituent effects (in subsystems), is dramatically smaller than that for the whole data set. Alike was found for phenol derivatives.[160]

In the case of simulated H-bonded complexes of *para*-substituted phenol derivatives, the substituent similarly effects the relation between the parameters in the center of the reaction,[150] that is the dependence of the C—O bond length on the ^{1}H-NMR chemical shift of the proton involved in the H-bond (Fig. 11). For *para*-X-PhOH···F$^-$ complexes, the slope of the regression line is equal to 0.0038 and 0.0036 for the nitrozo and hydroxyl substituents. In *para*-X-PhO$^-$···HF systems, its value amounts to −0.0018 and −0.0019, respectively. The OH···F$^-$ interactions are twice more sensitive to the substituent effect. Simultaneously, changes of the π-electron delocalization in the ring are observed. The slope of the regression lines of the HOMA values versus ^{1}H-NMR chemical shift is 0.0112 and 0.0039 for —NO and —OH as substituent in *para*-X-PhOH···F$^-$ complexes, whereas −0.0172 and −0.0094 in *para*-X-PhO$^-$···HF systems, respectively. Stronger electron-accepting substituent (—NO) induces a wider variation of the π-electron delocalization. Moreover, the changes of the HOMA index are significantly greater in the case of the O$^-$···HF interactions. In both OH···F$^-$ and O$^-$···HF interactions, stronger electron-withdrawing power of the substituent lowers the HOMA value. Approaching fluoride to the OH group increases the strength of the interaction, which results in a lower value of the H-chemical shift. The more electron donating is the oxygen atom in the system, the greater is the contribution of the quinoid structure which leads to a lowering of the HOMA index. As a consequence, lower aromaticity of the ring is observed. A reverse trend is observed for *para*-X-PhO$^-$···HF systems. In this case approaching HF to the oxygen atom results in an increase of H-bond strength and in a decrease of the ^{1}H-NMR chemical shift. The resulting HOMA value increases. Effects of the substituent in the *para*- position of the ring and the strength of H-bonding are interrelated. Both are connected by the ring, which has the capability of self-adapting via appropriate changes in its π-electron delocalization.

SUMMARY

This brief review devoted to H-bonded complexes of pyridine and derivatives of aniline and phenol – well known components of important supramolecular associations – enables us to draw the following conclusions:

(i) The type of interactions and their strength in H-bonded complexes of the above derivatives depend dramatically on the nature, the number and the position of the substituents attached to the ring.
(ii) Gradual changes of the H-bond strength, simulated by a modification of the intermolecular distance between the heavy atoms of the H-bond, are manifested in various properties of the system. The obtained relationships agree with the results of the fully optimized computational data and, which is even more important, with the crystal structure data retrieved from the Cambridge Structural Database.
(iii) The strength of the H-bonding influences the geometric parameters of the H-bond, the electronegativity of the O$^-$/OH and NH$^-$/NH$_2$/NH$_3^+$ groups, the ^{1}H-NMR chemical shift of the proton involved in the H-bond and the shape of the amino group.
(iv) The trend of the mutual relation depends on the nature of the interaction. When the Y atom (nitrogen and oxygen) acts as a proton donor, an increase in the strength of the interaction induces a shortening of the C—Y bond length. The opposite is observed when the Y atom is a proton acceptor. The above-mentioned local parameters of the H-bond change adequately to the nature of interactions.
(v) In the case of aniline and phenol derivatives, the effect of H-bonding is transferred to the ring following the Bent–Walsh rule. For H-bonded systems of pyridine and pyridinium derivatives, the *ipso* angle, α, at N may be useful indicator of the proton position (formally N···H or NH).
(vi) The H-bonding also influences a variation of properties of groups located outside the region of the interaction, such as the aromatic ring. H-bond-induced changes in its π-electron delocalization are an instructive example of this effect. Mutual interrelations between the H-bond strength, local structural parameters, aromaticity of the ring by means of the HOMA index and by NICS are observed.

LIST OF SYMBOLS AND ABBREVIATIONS USED

AIM	atom in molecules theory
B3LYP	Becke's 3-parameter hybrid functional using the Lee–Yang–Parr correlation functional
BCP	bond critical point
BSSE	basis set superposition error
CAHB	charge-assisted hydrogen bond
CSD	Cambridge Structural Database
DFT	density functional theory
HOMA	harmonic oscillator model of aromaticity
IHB	isolated hydrogen bond
LBHB	low-barrier hydrogen bond
MP2	second-order Møller–Plesset perturbation method
NBO	natural bond orbitals
NICS	nucleus independent chemical shift
PAHB	polarization-assisted hydrogen bond
PCA	principal component analysis
RAHB	resonance-assisted hydrogen bond
SWHB	single-well hydrogen bond

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REFERENCES

[1] G. C. Pimentel, A. L. McClelan, *The Hydrogen Bond*, WH Freeman and Co., San Francisco, **1960**.
[2] P. Schuster, G. Zundel, C. Sandorfy (Eds), *The Hydrogen Bond, Recent Developments in Theory and Experiments*, North-Holland Publishing Company, Amsterdam, **1976**.
[3] G. A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford University Press, Oxford, **1997**.
[4] G. A. Jeffrey, W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer, Berlin, **1991**.
[5] G. R. Desiraju, T. Steiner, *The Weak Hydrogen Bonding in Structural Chemistry and Biology*, Oxford University Press, Oxford, **1999**.
[6] T. W. Martin, Z. S. Derewenda, *Nat. Struct. Biol.* **1999**, *6*, 403–406.
[7] S. Scheiner, *Hydrogen Bonding, A Theoretical Perspective*, Oxford University Press, Oxford, **1997**.
[8] S. J. Grabowski (Ed.), *Hydrogen Bonding – New Insights, Vol. 3, Challenges and Advances in Computational Chemistry and Physics* (Ed.: J. Leszczynski), Springer, The Netherlands, Dordrecht, **2006**.
[9] Institute for Scientific Information, Philadelphia (1996–2008). Retrieved in January **2008**.
[10] W. Nernst, *Z. Phys. Chem.* **1891**, *8*, 110–139.
[11] http://en.wikipedia.org/wiki/Maurice_Loyal_Huggins.
[12] M. L. Huggins, *Undergraduate Thesis, University of California*, **1919**.
[13] W. L. Huggins, *J. Org. Chem.* **1936**, *1*, 407–456. DOI: 10.1021/jo01234a001
[14] T. Steiner, *Angew. Chem. Int. Ed.* **2002**, *41*, 48–76. DOI: 10.102/1521-3773(20020104)41:1<48::AID-ANIE48>3.0.CO;2-U
[15] www.iupac.org/projects/2004/2004-026-2-100.html.
[16] E. Arunan, *Curr. Sci.* **2007**, *92*, 17–18.
[17] J. J. Panek, A. Jezierska, *J. Phys. Chem. A* **2007**, *111*, 650–655. DOI: 10.1021/jp063217+
[18] R. Parthasarathi, V. Subramanian, N. Santhyamurthy, *J. Phys. Chem. A* **2006**, *110*, 3349–3351. DOI: 10.1021/jp060571z
[19] S. J. Grabowski, *Annu. Rep. Chem., Sec. C* **2006**, *102*, 131–165. DOI: 10.1039/b417200k
[20] G. R. Desiraju, *Acc. Chem. Res.* **2002**, *35*, 565–573. DOI: 10.1021/ar010054t
[21] S. J. Grabowski, W. A. Sokalski, E. Dyguda, J. Leszczynski, *J. Phys. Chem. B* **2006**, *110*, 6444–6447. DOI: 10.1021/jp0600817

[22] P. Gilli, V. Bertolasi, V. Ferretti, G. Gilli, *J. Am. Chem. Soc.* **1994**, *116*, 909–915. DOI: 10.1021/ja00082a011

[23] G. Gilli, P. Gilli, *J. Mol. Struct.* **2000**, *552*, 1–15. DOI: 10.1016/S0022-2860(00)454-3

[24] L. J. Prins, D. N. Reinhoudt, P. Timmerman, *Angew. Chem. Int. Ed.* **2001**, *40*, 2382–2426. DOI: 10.1002/1521-3773(20010702)40:13<2382:::AID-ANIE2382>3.0.CO;2-G

[25] M. Ziółkowski, S. J. Grabowski, J. Leszczyński, *J. Phys. Chem. A* **2006**, *110*, 6514–6521. DOI: 10.1021/jp060537k

[26] Y.-F. Chen, J. J. Dannerberg, *J. Am. Chem. Soc.* **2006**, *128*, 8100–8101. DOI: 10.1021/ja0604941

[27] R. Viswanathan, A. Asensio, J. J. Dannenberg, *J. Phys. Chem. A* **2004**, *108*, 9205–9212. DOI: 10.1021/jp047404o

[28] S. Scheiner, *J. Phys. Chem. A* **2006**, *110*, 18670–18679. DOI: 10.1021/jp063225q

[29] J. Kriz, J. Dybal, *J. Phys. Chem. B* **2007**, *111*, 6118–6126. DOI:10.1021/jp070203a

[30] B. A. Armitage, *Nat Chem Biol.* **2007**, *3*, 2003–2004. DOI: 10.1038/nchembio0407-203

[31] R. Otero, M. Schöck, L. M. Molina, I. Lægsgaard, *Angew. Chem. Int. Ed.* **2005**, *44*, 2270–2275. DOI: 10.1002/anie.200461586

[32] J. T. Davis, *Angew. Chem. Int. Ed.* **2004**, *43*, 668–698. DOI: 10.1002/anie.200300589

[33] J. L. Huppert, S. Balasubramanian, *Nucleic Acids Res.* **2005**, *33*, 2908–2916. DOI: 10.1093/nar/gki609

[34] K. Biratha, *Cryst. Eng. Comm.* **2003**, *5*, 374–384. DOI: 10.1039/b309903b

[35] M. Nishio, *Cryst. Eng. Comm.* **2004**, *6*, 130–158. DOI: 10.1039/b313104a

[36] S. Kitagawa, K. Uemura, *Chem. Soc. Rev.* **2005**, *34*, 109–119. DOI: 10.1039/b313997m

[37] J. De Girolamo, P. Reiss, A. Pron, *J. Phys. Chem. C* **2007**, *111*, 14681–14688. DOI: 10.1021/jp0741758

[38] P. Y. W. Dankers, E. W. Meijer, *Bull. Chem. Soc. Jpn.* **2007**, *11*, 2047–2073. DOI: 10.1246/bcsj.80.2047

[39] P. A. Frey, W. W. Cleland, *Bioorg. Chem.* **1998**, *26*, 175–192. DOI: 10.1006/bioo.1998.1097.

[40] R. Custelcean, J. E. Jackson, *Chem. Rev.* **2001**, *101*, 1963–1980. DOI: 10.1021/cr000021b

[41] C. A. Hunter, *Angew. Chem. Int. Ed.* **2004**, *43*, 5310–5324. DOI: 10.1002/anie.200301739

[42] S. H. Bauer, *Struct. Chem.* **2006**, *17*, 595–598. DOI: 10.1007/s11224-006-9098-x

[43] B. N. Solomonov, V. B. Novikov, *J. Phys. Org. Chem.* **2008**, *21*, 2–13. DOI: 10.1002/poc.1281

[44] M. Kartorfy, *The structural chemistry of phenols, in The Chemistry of Phenols* (Ed.: Z. Rappaport), John Wiley & Sons, Ltd., Chichester, **2003**. DOI: 10.1002/0470857277

[45] P. E. Hansen, J. Spanget-Larsen, *NMR and IR spectroscopy of phenols, in The Chemistry of Phenols* (Ed.: Z. Rappaport), John Wiley & Sons, Ltd., Chichester, **2003**. DOI: 10.1002/0470857277

[46] C. Laurence, M. Berthelot, J. Graton, *Hydrogen-bonded complexes of phenols, in The Chemistry of Phenols* (Ed.: Z. Rappaport), John Wiley & Sons, Ltd., Chichester, **2003**. DOI: 10.1002/0470857277

[47] L. Forlani, *Hydrogen bonds of anilines, in The Chemistry of Anilines* (Ed.: Z. Rappaport), John Wiley & Sons, Ltd., Chichester, **2007**. DOI: 10.1002/9780470871737

[48] T. Eicher, S. Hauptmann, A. Speicher, The six-membered heterocycles, in *The Chemistry of Heterocycles*, 2nd Edition, Willey-VCH Verlag, Weincheim, **2004**. DOI: 10.1002/352760183X.ch6b

[49] F. H. Allen, *Acta Crystallogr., Sec. B: Struct. Sci.* **2002**, *58*, 380–388. DOI: 10.1107/S0108768102003890

[50] H. Szatyłowicz, T. M. Krygowski, *Pol. J. Chem.* **2004**, *78*, 1719–1731.

[51] H. Szatyłowicz, T. M. Krygowski, J. E. Zachara-Horeglad, *J. Chem. Inf. Model.* **2007**, *47*, 875–886. DOI: 10.1021/ci600502w

[52] T. M. Krygowski, H. Szatyłowicz, J. E. Zachara, *J. Org. Chem.* **2005**, *70*, 8859–8865. DOI: 10.1021/jo051354h

[53] K. Müller-Dethlefs, P. Hobza, *Chem. Rev.* **2000**, *100*, 143–167. DOI: 10.1021/cr9900331

[54] L. M. Epstein, E. S. Shubina, *Coord. Chem. Rev.* **2002**, *231*, 165–181. DOI: 10.1016/S0010-8545(02)00118-2

[55] L. Sobczyk, S. J. Grabowski, T. M. Krygowski, *Chem. Rev.* **2005**, *105*, 3513–3560. DOI: 10.1021/cr030083c

[56] A. Kovac, Z. Varga, *Coord. Chem. Rev.* **2006**, *250*, 710–727. DOI: 10.1016/j.crr.2005.04.031

[57] F. H. Allen, J. E. Davies, J. J. Galloy, O. Johnson, O. Kennard, C. F. Macrae, E. M. Mitchell, G. F. Mitchell, J. M. Smith, D. G. Watson, *J. Chem. Inf. Comput. Sci.* **1991**, *31*, 187–204. DOI: 10.1021/ci00002a004

[58] S. J. Grabowski, T. M. Krygowski, *Tetrahedron* **1998**, *54*, 5683–5694. DOI: 10.1016/50040-4020(98)00257-9.

[59] J. Lewiński, J. Zachara, I. Justyniak, M. Dranka, *Coord. Chem. Rev.* **2005**, *249*, 1185–1199. DOI: 10.1016/j.ccr2004.11.013.

[60] T. H. Duning,, Jr. *J. Phys. Chem. A* **2000**, *104*, 9062–9080. DOI: 10.1021/jp001507z

[61] I. Rozas, *Phys. Chem. Chem. Phys.* **2007**, *9*, 2782–2790. DOI: 10.1039/b618225a

[62] P. Hobza, Z. Havlas, *Chem. Rev.* **2000**, *100*, 4253–4264. DOI: 10.1021/cr990050q

[63] I. Dąbkowska, P. Jurecka, P. Hobza, *J. Phys. Chem.* **2005**, *122*, 204322 . 204330. DOI: 10.1063/1.1906205

[64] C. Møller, M. S. Plesset, *Phys. Rev.* **1934**, *46*, 618–622.

[65] R. Krishnan, J. A. Pople, *Int. J. Quantum Chem.* **1978**, *14*, 91–100.

[66] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789.

[67] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 1372–1377. DOI: 10.1063/1.464304

[68] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5662. DOI: 10.1063/1.464913

[69] P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623–11627. DOI: 10.1021/j100096a001

[70] J. Ireta, J. Neugebauer, M. Scheffler, *J. Phys. Chem A* **2004**, *108*, 5692–5698. DOI: 10.1021/jp0377073

[71] S. B. Boys, F. Bernardi, *Theor. Chim. Acta* **1970**, *19*, 553–566.

[72] S. Simon, M. Duran, J. J. Dannenberg, *J. Chem. Phys.* **1996**, *105*, 11024–11031. DOI: 10.1073/1.472902

[73] R. F. W. Bader, *Atoms in Molecules: A Quantum Theory*, Oxford University Press, Oxford, **1990**.

[74] E. Espinosa, C. Lecomte, N. E. Ghermani, J. Devemy, M. M. Rohmer, M. Benard, E. Molins, *J. Am. Chem. Soc.* **1996**, *118*, 2501–2502. DOI: 10.1021/ja953193c

[75] E. Espinosa, E. Molins, C. Lecomte, *Chem. Phys. Lett.* **1998**, *285*, 170–173. DOI: 10.1016/S0009-2614(98)00036-0

[76] E. Espinosa, M. Souhassou, H. Lahekar, C. Lecomte, *Acta Crystallogr. B* **1999**, *55*, 563–572. DOI: 10.1107/S0108768199002128

[77] P. Garcia, S. Dahaoui, C. Katan, M. Souhassou, C. Lecomte, *Faraday Discuss.* **2007**, *135*, 217–235. DOI: 10.1039/b606642a

[78] L. Bertini, F. Cargnoni, C. Gatti, *Theor. Chem. Acc.* **2007**, *117*, 847–884. DOI: 10.1007/s00214-006-0208-z

[79] D. Hugas, S. Simon, M. Duran, *J. Phys. Chem. A* **2007**, *111*, 4506–4512. DOI: 10.1021/jp070080u

[80] K. Woźniak, P. R. Mallinson, G. T. Smitch, C. C. Wilson, E. Grech, *J. Phys. Org. Chem.* **2003**, *16*, 764–771. DOI: 10.1002/poc.683

[81] P. M. Dominiak, E. Grech, G. Barr, S. Teat, P. R. Mallinson, K. Woźniak, *Chem. Eur. J.* **2003**, *9*, 963–970. DOI: 10.1002/chem.200390118

[82] P. R. Mallinson, G. T. Smith, C. C. Wilson, E. Grech, K. Woźniak, *J. Am. Chem. Soc.* **2003**, *125*, 4259–4270. DOI: 10.1021/ja029389b

[83] P. M. Dominiak, A. Makal, P. R. Mallinson, K. Trzcinska, J. Eilmes, E. Grech, M. Chruszcz, W. Minor, K. Woźniak, *Chem. Eur. J.* **2006**, *12*, 1941–1949. DOI: 10.1002/chem.200500600

[84] I. Alkorta, J. Rozas, Elguero, *Struct. Chem.* **1998**, *9*, 243–247. DOI: 10.1023/A:1022424228462

[85] R. W. F. Bader, M. T. Carroll, J. R. Cheeseman, C. Chang, *J. Am. Chem. Soc.* **1987**, *109*, 7968–7979. DOI: 10.1021/ja00260a006

[86] U. Koch, P. Popelier, *J. Phys. Chem.* **1995**, *99*, 9747–9754. DOI: 10.1021/j100024a016

[87] P. Popelier, *Atoms in Molecules, An Introduction*, Prentice-Hall, Englewood Cliffs, NY, **2000**.

[88] E. Espinosa, I. Alkorta, I. Mata, E. Molins, *J. Phys. Chem. A* **2005**, *109*, 6532–6539. DOI: 10.1021/jp050776s

[89] S. J. Grabowski, *J. Phys. Chem. A* **2001**, *105*, 10739–10746. DOI: 10.1021/jp011819h

[90] S. J. Grabowski, *J. Mol. Struct. A* **2001**, *562*, 137–143. DOI: 10.1016/S0022-2860(00)00863-2

[91] E. Espinosa, I. Alkorta, J. Elguero, E. Molins, *J. Chem. Phys.* **2002**, *117*, 5529–5542. DOI: 10.1063/1.150113

[92] S. J. Grabowski, *J. Phys. Org. Chem.* **2004**, *17*, 18–31. DOI: 10.1002/poc.685

[93] S. J. Grabowski, W. A. Sokalski, J. Leszczynski, *J. Phys. Chem. A* **2005**, *109*, 4331–4341. DOI: 10.1021/jp0444215

[94] J. Poater, X. Fradera, M. Sola, M. Duran, S. Simon, *Chem. Phys. Lett.* **2002**, *369*, 248–255. DOI: 10.1016/S0009-2614(02)01928-0

[95] J. Emsley, *Chem. Soc. Rev.* **1980**, *9*, 91–124. DOI: 10.1039/CS9800900091

[96] I. Alkorta, I. Rozas, J. Elguero, *Chem. Soc. Rev.* **1998**, *27*(91), 163–170. DOI: 10.1039/a827163z

[97] W. W. Cleland, M. M. Kreevoy, *Science* **1994**, *264*, 1887–1890. DOI: 10.1126/science.8009219

[98] P. A. Frey, S. A. Whitt, J. B. Tobin, *Science* **1994**, *264*, 1927–1930. DOI: 10.1126/science.7661899

[99] P. A. Frey, *Magn. Reson. Chem.* **2001**, *39*, S190–S198. DOI: 10.1002/mrc.953

[100] I. Rozas, I. Alkorta, J. Elguero, *J. Am. Chem. Soc.* **2000**, *122*, 11154–11161. DOI: 10.1021/ja0017864

[101] I. Bandyopadhyay, H. M. Lee, K. S. Kim, *J. Phys. Chem. A* **2005**, *109*, 1720–1728. DOI: 10.1021/jp0449657

[102] P. Gilli, L. Pretto, G. Gilli, *J. Mol. Struct.* **2007**, *844–845*, 328–339. DOI: 10.1016.j.molstruc.2007.05.014

[103] I. Alkorta, I. Rozas, O. Mo, M. Yanez, J. Elguero, *J. Phys. Chem. A* **2001**, *105*, 7481–7485. DOI: 10.1021/jp0116407

[104] E. S. Kryachko, T. Zeegers-Huyskens, *J. Mol. Struct.* **2002**, *615*, 251–256. DOI: 10.1016/S0022-2860(02)00226-0

[105] R. Anulewicz, I. Wawer, T. M. Krygowski, F. Mannle, H.-H. Limbach, *J. Am. Chem. Soc.* **1997**, *119*, 12223–12230. DOI: 10.1021/ja970699h

[106] I. Majerz, Z. Malarski, L. Sobczyk, *Chem. Phys. Lett.* **1997**, *274*, 361–364. DOI: 10.1016/S0009-2614(97)00674-X

[107] C. L. Perrin, J. B. Nielson, *Annu. Rev. Phys. Chem.* **1997**, *48*, 511–544. DOI: 10.1146/annurev.physchem.48.1.511

[108] W. W. Cleland, P. A. Frey, J. A. Gerlt, *J. Biol. Chem.* **1998**, *273*, 25529–25532.

[109] J. P. Guthrie, *Chem. Biol.* **1996**, *3*, 163–170. DOI: 10.1016/S1074-5521(96)90258-6

[110] S. Scheiner, T. Kar, *J. Am. Chem. Soc.* **1995**, *117*, 6970–6975. DOI: 10.1021/ja00131a020

[111] O. Galvez, P. C. Gomez, L. F. Pacios, *J. Chem. Phys.* **2001**, *115*, 11166–11184. DOI: 10.1063/1.1420749

[112] L. C. Remer, J. H. Jensen, *J. Phys. Chem. A* **2000**, *104*, 9266–9275. DOI: 10.1021/jp002726n

[113] T. M. Krygowski, J. E. Zachara, H. Szatyłowicz, *J. Phys. Org. Chem.* **2005**, *18*, 110–114. DOI: 10.1002/poc.875

[114] J. B. Foresman, E. Frisch, *Exploring Chemistry with Electronic Structure Methods*, 2nd Edition, Gaussian Inc., Pittsburgh, **1996**. pp. 165–211.

[115] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, MW Wong, C Gonzalez, JA. Pople, *Gaussian 03, Revision C.02*; Gaussian, Inc.: Wallingford, CT, **2004**.

[116] J. H. Jensen, M. S. Gordon, *J. Phys. Chem.* **1995**, *99*, 8091–8107. DOI: 10.1021/j100020a037

[117] M. S. Gordon, J. H. Jensen, *Acc. Chem. Res.* **1996**, *29*, 536–543. DOI: 10.1021/ar9600594

[118] R. M. Minikis, J. H. Jensen, *Int. J. Quantum Chem.* **2000**, *76*, 341–358. DOI: 10.1002/(SICI)1097-461X.(2000)76:3<341:::AID-QUA4>3.0.CO;2-5

[119] K. Woźniak, T. M. Krygowski, B. Kariuki, W. Jones, *J. Mol. Struct.* **1991**, *248*, 331–343. DOI: 10.1016/0022-2860(91)80040-B

[120] A. D. Walsh, *Discuss. Faraday Soc.* **1947**, *2*, 18–25.

[121] H. A. Bent, *Chem. Rev.* **1961**, *61*, 275–311. DOI: 10.1021/cr60211a004

[122] A. Domenicano, A. Vaciago, C. A. Coulson, *Acta Cryst.* **1975**, *B31*, 1630–1641. DOI: 10.1107/S0567740875005821

[123] R. A. Campanelli, A. Domenicano, F. Ramondo, *J. Phys. Chem. A* **2003**, *107*, 6429–6440. DOI: 10.1021/jp030031r

[124] A. R. Campanelli, A. Domenicano, F. Ramondo, I. Hargittai, *J Phys. Chem. A* **2004**, *108*, 4940–4948. DOI: 10.1021/jp040013p

[125] E. R. Malinowski, *Factor Analysis in Chemistry*, 3rd Edition, Wiley –Interscience, New York, **2002**. pp. 255–294.

[126] R. I. Zalewski, in *Similarity Models in Organic Chemistry, Biochemistry and Related Fields, Studies in Organic Chemistry*, Vol. 42 (Eds.: R. I. Zalewski, T. M. Krygowski, J. Shorter), Elsevier, Amsterdam, **1991**. Chapter 9.

[127] J. Pauling, *The Nature of the Chemical Bond*, Cornell University Press, Ithaca, **1960**. page. 88.

[128] A. Domenicano, P. Murray-Rust, A. Vaciago, *Acta Cryst.* **1983**, *B39*, 457–468. DOI: 10.1107/S0108768183002736

[129] T. M. Krygowski, H. Szatyłowicz, *J Phys. Chem. A* **2004**, *110*, 7232–7236. DOI: 10.1021/jp0605496

[130] H. Szatyłowicz, T. M. Krygowski, *J. Mol. Struct.* **2007**, *844-845*, 200–207. DOI: 10.1016/j.molstruc.2007.04.018

[131] D. G. Lister, J. K. Tyler, J. H. Hog, N. W. Larsen, *J. Mol. Struct.* **1974**, *23*, 253–264. DOI: 10.1016/0022-2860(74)85039-8

[132] G. Roussy, A. Nonat, *J. Mol. Spectrosc.* **1986**, *118*, 180–188. DOI: 10.1016/0022-2852(86)90234-1

[133] M. Quack, M. Stockburger, *J. Mol. Spectrosc.* **1972**, *43*, 87–116. DOI: 10.1016/0022-2852(72)90164-6

[134] N. W. Larsen, E. L. Hansen, F. M. Nicolaisen, *Chem. Phys. Lett.* **1976**, *43*, 584–586. DOI: 10.1016/0009-2614(76)80629-X

[135] B. Kleibomer, D. H. Sutter, *Z. Naturforsch. A: Phys. Sci.* **1988**, *43*, 561–571.

[136] R. A. Kydd, P. J. Krueger, *Chem. Phys. Lett.* **1977**, *49*, 539–543. DOI: 10.1016/0009-2614(77)87033-4

[137] G. Schultz, G. Portalone, F. Ramondo, A. Domenicano, I. Hargittai, *Struct. Chem.* **1996**, *7*, 59–71. DOI: 10.1007/BF02275450

[138] *Molecular Structure by Diffraction Methods* (Vol. 1, 1973; Vol. 2, 1974; Vol. 3, 1975; Vol. 4, 1976; Vol. 5, 1977; Vol. 6, 1978) (Eds: G. A. Sim, L. E. Sutton), The Chemical Society, London.

[139] H. Szatyłowicz, T. M. Krygowski, P. Hobza, *J. Phys. Chem A* **2007**, *111*, 170–175. DOI: 10.1021/jp065336v

[140] O. Exner, T. M. Krygowski, *Chem. Soc. Rev.* **1996**, *25*, 71–75. DOI: 10.1039/CS9962500071

[141] K. C. Gross, P. G. Seybold, *Int. J. Quantum Chem.* **2000**, *80*, 1107–1115.

[142] K. C. Gross, P. G. Seybold, *J. Org. Chem.* **2001**, *66*, 6919–6925.

[143] K. C. Gross, P. G. Seybold, C. M. Hadad, *Int. J. Quantum Chem.* **2002**, *90*, 445–458.

[144] M. E. Vaschetto, B. A. Retamal, A. P. Monkman, *J. Mol. Struct. (Theochem)* **1999**, *468*, 209–221.

[145] P. M. Wojciechowski, W. Zierkiewicz, D. Michalska, P. Hobza, *J. Chem Phys.* **2003**, *118*, 10900–10911.

[146] M. A. Palafox, M. Gill, N. J. Nunez, V. K. Rastogi, L. Mittal, R. Sharma, *Int. J. Quantum Chem.* **2005**, *103*, 394–421.

[147] J. E. Bartmess, J. A. Scott, R. T. McIver, Jr., *J. Am. Chem. Soc.* **1979**, *101*, 6046–6056.

[148] C. Hillebrand, M. Klessinger, M. Eckert-Maksic, Z. B. Maksic, *J. Phys. Chem.* **1996**, *100*, 9698–9702.

[149] T. M. Krygowski, B. T. Stępień, *Chem. Rev.* **2005**, *105*, 3482–3512. DOI: 10.1021/cr030081s

[150] T. M. Krygowski, H. Szatyłowicz, J. E. Zachara, *J. Chem. Inf. Model.* **2005**, *45*, 652–656. DOI: 10.1021/ci049633d

[151] T. Steiner, *J. Phys. Chem. A* **1998**, *102*, 7041–7052. DOI: 10.1021/jp981604g

[152] H. Benedict, I. G. Shenderovich, O. L. Malkina, V. G. Malkin, G. S. Denosiv, N. S. Golubev, H.-H. Limbach, *J. Am. Chem. Soc.* **2000**, *122*, 1979–1988. DOI: 10.1021/ja9907461

[153] P. Lorente, I. G. Shenderovich, N. S. Golubew, G. S. Denisow, G. Buntkowsky, H.-H. Limbach, *Magn. Reson. Chem.* **2001**, *39*, S18–S29. DOI: 10.1002/mrc.946

[154] P. M. Tolstoy, S. N. Smirnov, I. G. Shenderovich, N. S. Golubew, G. S. Denisow, H.-H. Limbach, *J. Mol. Struct.* **2004**, *700*, 19–27. DOI: 10.1016/j.molstruc.2004.02.023

[155] S. Sharif, I. G. Shenderovich, L. Gonzales, G. S. Denosov, D. N. Silverman, H.-H. Limbach, *J. Phys. Chem. A* **2007**, *111*, 6084–6093. DOI: 10.1021/jp071725t

[156] T. Steiner, I. Majerz, C. C. Wilson, *Angew. Chem. Int. Ed.* **2001**, *40*, 2651–2654. DOI: 10.1002/1521-3773(20010716)40:14<2651::AID-ANIE2651>3.0.CO;2-2

[157] I. Majerz, I. Olovsson, *Acta Crytal.* **2007**, *B63*, 650–662. DOI: 10.1107/S0108768107022239

[158] I. Majerz, I. Olovsson, *Acta Crytal.* **2007**, *B63*, 748–752. DOI: 10.1107/S0108768107041225

[159] R. S. Mulliken, *J. Chem. Phys.* **1955**, *23*, 1833–1840. DOI: 10.1063/1.1740588
[160] T. M. Krygowski, H. Szatyłowicz, *Trends Org. Chem.* **2006**, *11*, 37–53.
[161] I. Majerz, A. Koll, *Acta Cryst.* **2004**, *B60*, 406–415. DOI: 10.1107/S0108768104010365
[162] I. Majerz, E. Kwiatkowska, A. Koll, *J. Phys. Org. Chem.* **2005**, *18*, 833–843. DOI: 10.1002/poc.948
[163] E. Kwiatkowska, I. Majerz, A. Koll, *Chem. Phys. Lett.* **2004**, *398*, 130–139. DOI: 10.1016/j.cplett.2004.09.038
[164] I. Majerz, E. Kwiatkowska, A. Koll, *J. Mol. Struc.* **2007**, *831*, 106–113. DOI: 10.1016/j.molstruc.2006.07.029
[165] T. M. Krygowski, M. K. Cyrański, Z. Czarnocki, G. Hafelinger, A. R. Katritzky, *Tetrahedron* **2000**, *56*, 1783–1796. DOI: 10.1016/S0040-4020(99)00979-5
[166] Pv. R. Schleyer, *Chem. Rev.* **2001**, *101*, 1115–1566.
[167] T. M. Krygowski, M. K. Cyrański, *Chem. Rev.* **2001**, *101*, 1385–1420. DOI: 10.1021/cr990326u
[168] M. K. Cyrański, *Chem. Rev.* **2005**, *105*, 3773–3811. DOI: 10.1021/cr0300845
[169] M. Charton, *Progr. Phys. Org. Chem.* **1987**, *16*, 287–315.
[170] T. M. Krygowski, *J. Inf. Comput. Sci.* **1993**, *33*, 70–78. DOI: 10.1021/ci00011a011
[171] T. M. Krygowski, J. E. Zachara, H. Szatyłowicz, *J. Org. Chem.* **2004**, *69*, 7038–7043. DOI: 10.1021/jo049245a
[172] T. M. Krygowski, H. Szatyłowicz, J. E. Zachara, *J. Chem. Inf. Comput. Sci.* **2004**, *69*, 2077–2082. DOI: 10.1021/ci049817s
[173] Pv. R. Schleyer, C. Maerker, H. Dransfeld, H. Jiao, N. J. Rv. E. Hommes, *J. Am. Chem. Soc.* **1996**, *118*, 6317–6318. DOI: 10.1021/ja960582d
[174] Pv. R. Schleyer, M. Manoharan, Z.-X. Wang, B. Kiran, H. Jiao, R. Puchta, N. J. Rv. E. Hommes, *Org. Lett.* **2001**, *3*, 2465–2468. DOI: 10.1021/ol016217v
[175] C. Corminboeuf, T. Heine, G. Seifert, J. Schleyer PvR, Weber, *Phys. Chem. Chem. Phys.* **2004**, *6*, 273–276. DOI: 10.1039/b313383b
[176] L. P. Hammett, *Physical Organic Chemistry*, 1st Edition, 1940 and 2nd Edition, 1970, McGraw-Hill, New York,
[177] H. H. Jaffe, *Chem. Rev.* **1953**, *53*, 191–261. DOI: 10.1021/cr60165a003
[178] C. D. Johnson, *The Hammett Equation*, Cambridge University Press, **1973**.
[179] M. Charton, *Progr. Phys. Org. Chem.* **1981**, *13*, 119–251.
[180] O. Exner, in *Correlation Analysis of Chemical Data* (Eds: N. B. Chapman, J. Shorter), Plenum Press, New York, **1988**. Chapter 10, p. 439.
[181] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165–195. DOI: 10.1021/cr00002a004