NMR Study of Solvation Effect on the Geometry of Proton-Bound Homodimers of Increasing Size

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ABSTRACT: Hydrogen bond geometries in the proton-bound homodimers of quinoline and acridine derivatives in an aprotic polar solution have been experimentally studied using 1H NMR at 120 K. The reported results show that an increase of the dielectric permittivity of the medium results in contraction of the N···N distance. The degree of contraction depends on the homodimer’s size and its substituent-specific solvation features. Neither of these effects can be reproduced using conventional implicit solvent models employed in computational studies. In general, the N···N distance in the homodimers of pyridine, quinoline, and acridine derivatives decreases in the sequence gas phase > solid state > polar solvent.

INTRODUCTION

Hydrogen bonding (H-bonding) is often the main noncovalent interaction in a molecular system under study which defines both its physical properties and its chemical fate. The latter generally involves proton transfer as one of the reaction steps.1 The simplest case is intramolecular proton transfer in small molecules in the solid state.2–5 The presence of competing H-bonds and solvent complicates the analysis.5–8 Sophisticated theoretical tools are required in order to simulate enzymatic reactions and transporters and receptors activity at the atomic level.9–11 At the current stage of knowledge, it is possible to predict the effect of a mutation on the fate of a particular biosystem, to prove this prediction experimentally, and to explain it theoretically.12 However, for many formally simple systems experimental results have not been reproduced in silico at a reasonable approximation; the strength of dispersive interactions in solution,13 spectroscopic signatures of protonated water clusters14,15 and hydrated hydroxyl anion,16 the structure of water-base complexes in aprotic solutions,17 and amorphous solids18–20 are among such problems. In such cases, the measured spectral parameters have to be assigned to a certain geometry or energy using empirical correlations.21–25

In the past, some of us reported on geometry of the proton-bound homodimers of ortho-unsubstituted and ortho-substituted pyridine derivatives in an aprotic polar solution.26 For the ortho-unsubstituted homodimers we observed experimentally a monotonous dependence of the N···N distance on the gas-phase proton affinity (PA) of the involved pyridines. For such homodimers, this dependence can be correlated with a qualitatively similar dependence of the binding energy as established by quantum mechanical calculations of isolated species.27 The effect of the solvent reaction field on the geometries of formally symmetric NHN H-bonds remains a debatable question. Sophisticated calculations predict an increase of the N···N distance in a polar solvent.28,29 The available experimental data contradict this conclusion.30 A discrepancy between experimental and theoretical results was demonstrated recently in an extensive study of bond dissociation equilibria of a variety of proton-bound homodimers.31 In any case, the N···N distance in proton-bound homodimers depends on both the proton-accepting power of the base and the features of solvation. The latter effect should be sensitive to the homodimer’s size.

The objective of the present work is to study experimentally the effect of solvation on the geometry of proton-bound homodimers and its dependence on the size of the complexes. For this purpose, we have measured the 1H NMR chemical shifts of mobile protons in conjugate acids (that are protonated bases in our case) and proton-bound homodimers for two series of quinoline and acridine derivatives in a polar aprotic solvent in the slow intermolecular exchange regime. The values of these chemical shifts have been used to estimate the H-bond geometries of the homodimers. The symmetries of these...
homodimers have been explored by measuring the sign of the primary isotope effects on the NMR chemical shift:

$$\delta(H/D) \equiv \delta(NDN) - \delta(NHN)$$

The species studied are listed in Figure 1.

![Figure 1. Quinoline (a–g) and acridine (h, i) derivatives and anions (j, k) used in this work. 6-chloroquinoline (a), quinoline (b), 3-methylquinoline (c), 7-methylquinoline (d), 4-chloro-2-methylquinoline (e), 2-methylquinoline (f), 2,6-dimethylquinoline (g), 9-chloroacridine (h), acridine (i), tetrakis[bis(3-fluoromethyl)phenyl]borate (Na[BArF]$_4$) (j), and tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ([BArF]$_4$) (k).](image)

### EXPERIMENTAL SECTION

#### Materials. Chemicals were purchased from Sigma-Aldrich and used after additional purification by sublimation or distillation. The deuterated freon gas mixture CDF$_3$/CDFCl$_2$ for the low-temperature NMR experiments, whose composition varied between 1:2 and 1:3, was prepared from chloroform-

Sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (Na[BArF]$_4$) was prepared as described recently. 

**Complexes.** The general procedure of preparing complexes of bases with H[BF$_4$]$^-$ was as follows. Equimolar quantities of the base and of the complex of H[BF$_4$]$^-$ were mixed directly in an anhydrous solvent mixture (e.g., dichloromethane and acetonitrile) and the mixture was then stirred for 3 h at 30 °C. The complexes were then precipitated by the addition of water and dried under vacuum.

**NMR Measurements.** Liquid-state $^1$H and $^2$H NMR spectra were measured on a Bruker AMX 500 spectrometer operated at 11.7 T equipped with a probe-head enabled to perform experiments down to 100 K. The spectra were indirectly referenced to tetramethylsilane (TMS) by setting the central component of the residual CHClF$_2$ triplet of the freon mixture to 7.18 ppm. The standard $^1$H NMR spectra were recorded with recycle times of 3 s.

**XRD Measurements.** X-ray diffraction data for single crystals were collected using a “Bruker APEX-II” CCD diffractometer. The samples were kept at 100 K during data collection. The Olex2 software package was used for the data analysis. The structure was solved with the XS structure solution program using direct methods and refined with the XL refinement package using the least-squares minimization. All non-hydrogen atoms were refined with anisotropic thermal parameters. The disordered solvent molecules of toluene were split into two parts and refined with restraints on bonds, angles (FRAG command) and thermal displacement ellipsoids (SIMU command). The atomic coordinates, the bond lengths, the angles, and the thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC) with reference numbers 1552802 and 1552803.

### COMPUTATIONAL DETAILS

The locations of the binding protons in the crystalline phases were estimated using DFT calculations in the following way. The coordinates of all atoms of the [Acridine-H$_2$]...Acridine$^+$ moiety were taken from the XRD experiment and kept frozen, except the positions of the mobile protons. Their locations were optimized at the B3LYP approximation using the 6-311+G(3df,2p) basis set of the Gaussian 16.A.03 package.

The gas-phase proton affinities (PA) of selected pyridine derivatives and of compounds a–i in the gas phase were calculated as follows:

$$PA = \Delta H_{298}(B) + SRT/2 - \Delta H_{298}(BH^+)$$

Here, $\Delta H_{298}(B)$ and $\Delta H_{298}(BH^+)$ stand for the sums of electronic and thermal enthalpies of a base and its conjugate acid at 298 K. The enthalpies were evaluated at the B3LYP/6-311++G(3df,2p) level. This level provides a reasonable description of the structure and harmonic frequencies of the neutral and charged H-bonded systems in the gas phase. It is also sufficient to obtain correct values of enthalpies. Effective proton affinities (PA') in solutions were calculated at the same level using the polarizable continuum model (PCM) approximation at $\varepsilon = 108.94$ (formamide in the list of Gaussian’s solvents) as follows:

$$PA' = \Delta H_{298}(B) + \Delta H_{298}(BH^+)' - \Delta H_{298}(BH^+)'$$

Here, $\Delta H_{298}(B)$, $\Delta H_{298}(BH^+)'$, and $\Delta H_{298}(BH^+)'$ stand for the sums of electronic and thermal enthalpies of a base, its conjugate acid, and proton at 298 K and the relative permittivity $\varepsilon > 1$.

### RESULTS

In Figure 2 are shown low-temperature NMR spectra of the conjugate acids and the proton-bound homodimers of a–i with [BF$_4$]$^-$ as counteranion and CDF$_3$/CDFCl$_2$ as solvent. Because of salt precipitation at low temperatures, we succeeded to measure spectra using [BArF]$_4^-$ as counteranion only for the homodimers of e and g. In all cases the slow intermolecular
The structural parameters depend on the solvent used for crystallization because the unit cell includes one solvent molecule in addition to the homodimer and the anion. The N···N distances and the angles between the aromatic planes are 2.754 and 2.743 Å, $62^\circ$ and $84^\circ$ in cocrystals with chloroform and toluene, respectively.

X-ray diffraction analysis demonstrates that the structure of the proton-bound homodimer of acridine resembles the one of pyridine.\(^{40}\) In the latter case the N···N distance was shorter (2.655 Å) and the unit cell did not contain the crystallization solvent. The estimated distances in [Acridine···Acridine]\(^{−}\) are N···H = 1.075 and 1.078 Å and H···N = 1.679 and 1.665 Å for the cocrystals with chloroform and toluene, respectively. The H-bonds are linear in both cases. For comparison, in the proton-bound homodimer of pyridine these distances are 1.123 and 1.532 Å, while the NHN angle is $171^\circ$.\(^{40}\)

The sign of the primary isotope effect on the NMR chemical shift is considered to be of diagnostic value for the H-bond symmetry, as has been found in a number of experimental and theoretical studies.\(^{41–46}\) Namely, in most cases, the binding proton is located closer to one side of the H-bond and $\Delta(\text{H/D}) < 0$. There are a few exceptions when the proton is bound equally strong to both partners. In these cases it is located near the center of the H-bond and $\Delta(\text{H/D}) > 0$. However, some of us showed that $\Delta(\text{H/D})$ can be positive for an asymmetric H-bond as well.\(^{47}\) The reason is that the shape of the shielding function of the internal vibrational coordinates can be rather exclusive for each complex. The primary factor that determines the symmetry of the H-bond in a proton-bound homodimer is the electronegativity of the partners.\(^{48,49}\) The bond is expected to be symmetric for fluorine, oxygen, and sp-hybridized nitrogen bases, while asymmetric for sp\(^2\)- and sp\(^3\)-hybridized nitrogen bases.\(^{48}\) The asymmetry can be also induced by steric hindrance. H-bonds in the proton-bound homodimer of pyridine derivatives are asymmetric; the reversible proton transfer between the two pyridines is fast in the millisecond time scale down to 120 K and slower than $10^{11}$ s\(^{−1}\) up to 290 K.\(^{50,52}\) The latter estimate was obtained by means of vibrational spectroscopy. This finding is in agreement with the theoretical estimations of the barrier for the proton transfer of 4 kJ/mol.\(^{51}\)

The rate-limiting step for the proton transfer in this double-well potential is the solvent reorganization.\(^{52–54}\) This effect is important in enzyme catalysis.\(^{55}\) In the proton-bound homodimer of quinoline derivatives b–d, f, and g, $\Delta(\text{H/D})$ is negative as expected.

**DISCUSSION**

**Figure 3.** General view of the proton-bound homodimer of i with [BARF]\(^{−}\) according to X-ray diffraction analysis. The unit cell includes, besides the homodimer and the anion, one molecule of the solvent.

**Figure 2.** Left-hand: the mobile-proton part of the $^1$H NMR spectra of the conjugate acids of a–i. Right-hand: the mobile-proton part of the $^1$H and $^2$H (inserts) NMR spectra of the proton-bound homodimer of a–i. Solvent: CDF\(_3\)/CDCIF\(_2\). Temperature: 120 K. Anion: [BF\(_4\)]\(^{−}\).
estimate the H-bond geometry of the proton-bound homodimers.

For a detailed discussion about geometric and NMR parameter correlations for H-bonds we refer to other publications.37–39 As described in ref 26, the 1H NMR chemical shift of the binding proton correlates with the valence bond orders $p_{fi}^+$ of the N–H and N−⋯H bonds as follows:

$$\delta(1H) = \delta(1H)(p_{fi}^+ + p_{gi}^+) + \Delta_H p_{fi}^+ p_{gi}^+$$

(1)

The parameter $\delta(1H)$ stands for the limiting chemical shift in a fictive free conjugate acid. $\Delta_H$ is an empirical fitting parameter the value of which lies in the range of 10−20 ppm.37,38,40 For the proton-bound homodimer of pyridine it was estimated to be 15.8 ppm;26 this value was used in this work for all species. The parameters $p_{fi}^+$ and $p_{gi}^+$ are dependent and can be expressed as follows:

$$p_{fi}^+ = p - (p(1 - p))^2 (250(p(1 - p))^3 (2p - 1) + 0.85)$$

and

$$p_{gi}^+ = 1 - p - (p(1 - p))^2 (250(p(1 - p))^3 (1 - 2p) + 0.85)$$

where $0 < p < 1$. These parameters were derived numerically for a given $\delta(1H)$ from eq 1. $p_{fi}^+$ and $p_{gi}^+$ define two distances $r_1$ and $r_2$ as follows: $r_1 = -\ln(p_{fi}^+) \times 0.37$ Å + 0.997 Å and $r_2 = -\ln(p_{gi}^+) \times 0.37$ Å + 0.997 Å. Here, we label the shortest one of them as $r_{NH}$ and their sum as $r_{NN}$. We refer to ref 26 for a detailed explanation.

The margin of error for the estimates of $r_{NH}$ and $r_{NN}$ clearly depends on the margin of error for $\delta(1H)$. The latter is 0.01 ppm that provides for the former margin of error a value of 0.0005 Å.26 The systematic error cannot be evaluated at the current stage.

The only complex-specific parameter in our estimations of the N−H and N−N distances is $\delta(1H)$. The best possible estimate of this parameter is the experimental value of $\delta(1H)$ in the conjugate acid of the corresponding base with the noncoordinating anion [BArF]$^-$. Indeed, in the conjugate acids of pyridine derivatives with [BArF]$^-$ the values of $\delta(1H)$ were close to the ones in the conjugate acids of ortho-tert-butylsubstituted pyridines.40,61 [BF4]$^-$ interacts with conjugate acids much stronger than [BArF]$^-$.25 For pyridine derivatives in complexes [pyridine-$H^+][X^-]$, where $X^- = [BF_4]^-$ and [BArF]$^-$, the difference of the 1H NMR chemical shifts was about 3 ppm.40

In contrast, for the proton-bound homodimers of the pyridine derivatives the difference of the 1H NMR chemical shifts in the complexes with [BArF]$^-$ and [BF4]$^-$ was less than 0.1 ppm. Thus, although the interaction of [BF4]$^-$ with the homodimers of ortho-unsubstituted pyridines favored intermolecular exchange down to 120 K,40 this interaction did not affect the geometry of their H-bonds. The proton-bound homodimers of $e$ and $g$ demonstrate that this conclusion is also valid for quinoline derivatives. The value of $\delta(1H)$ in the conjugate acids of $a$–$i$ with [BArF]$^-$ in CDF3/CDClF2 cannot be obtained because of the low solubility. We also could not use another solvent or increase the temperature because $\delta(1H)$ in conjugate acids depends on the solvent polarity. Indeed, for the conjugate acid of pyridine this value is 11.86 ppm15 in CDF3/CDCl3 ($\epsilon \approx 10$)32 and 14.2 ppm35 in CDF3/CDClF2 ($\epsilon \approx 30$).31 In the latter case the temperature dependence of $\delta(1H)$ was specifically noted.26 Thus, $\delta(1H)$ for $a$–$i$ has to be estimated. It is reasonable to assume that for chemically similar compounds this value correlates with their pK, and PA. Strictly speaking, the pK’s of ionizable groups in nonaqueous environment can be estimated theoretically.55 However, such calculations are quite demanding. In contrast, the gas-phase PAs can be easily obtained and do not depend on solvation. The calculated PA’s of selected pyridine derivatives and $a$–$i$ are collected in Tables 2 and 4.

### Table 2. Gas-Phase Proton Affinity (PA) of Some Pyridine Derivatives and 1H NMR Chemical Shifts of the Mobile Protons of Their Conjugate Acids

<table>
<thead>
<tr>
<th>Base</th>
<th>PA, kJ/mol</th>
<th>$\delta(1H)$, ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Py</td>
<td>936</td>
<td>14.2</td>
</tr>
<tr>
<td>4-methylPy</td>
<td>956</td>
<td>13.3</td>
</tr>
<tr>
<td>2,4,6-trimethyl-3-nitroPy</td>
<td>934</td>
<td>13.54</td>
</tr>
<tr>
<td>3-bromo-2,4,6-trimethylPy</td>
<td>968</td>
<td>14.19</td>
</tr>
<tr>
<td>2,6-dimethylPy</td>
<td>972</td>
<td>13.00</td>
</tr>
<tr>
<td>2,4,6-trimethylPy</td>
<td>988</td>
<td>13.01</td>
</tr>
</tbody>
</table>

*The abbreviation Py stands for pyridine.7 Estimated at the B3LYP/6-311++G(3df,2p) level. Reference 26. [BF4]$^-$ and [BArF]$^-$ as anions.

In Figure 4 are plotted the 1H NMR chemical shifts of the conjugate acids of ortho-unsubstituted and o-methyl-substituted

![Figure 4](image_url)

**Figure 4.** 1H NMR chemical shifts ($\delta(1H)$) of the mobile protons of conjugate acids vs the gas-phase proton affinities (PA) of the corresponding bases. Anion [BF4]$^-$: ortho-unsubstituted pyridines (■); o-methyl-substituted pyridines (▲); a−i (▲). Anion [BArF]$^-$: ortho-unsubstituted pyridines (□); o-methyl-substituted pyridines (○). NMR data for the pyridines are taken from ref 26. The dotted line represents the dependence of $\delta(1H)$ on the PA for the conjugate acids of o-methyl-substituted pyridines with [BArF]$^-$.7
dependence of these values. In Table 3 are compared the N···N distances in the proton-bound homodimers of the selected pyridine derivatives that were calculated using (i) the experimental values of \( \delta(1H) \) and (ii) the parameter \( \delta'(1H) \) estimated from PA. The difference between these values represents the margin of error of the further estimations.

Thus, the parameter \( \delta'(1H) \) for the conjugate acids of a–i can be estimated from their PA values using eq 2, Table 4.

| Table 3. Geometry of H-Bonds in the Proton-Bound Homodimers of Some Pyridine Derivatives |
|--------------------------------------|-------|-------|
| base \( ^{a} \)                      | \( r_{NN} \) \( \AA \) | \( r_{NN} \) \( \AA \) |
| Py                                   | 2.618 | 2.618 |
| 4-methylPy                           | 2.624 | 2.632 |
| 2,4,6-trimethyl-3-nitropyridine      | 2.695 | 2.697 |
| 3-bromo-2,4,6-trimethylpyridine      | 2.681 | 2.682 |
| 2,6-dimethylPy                       | 2.670 | 2.664 |
| 2,4,6-trimethylPy                    | 2.665 | 2.668 |

\( ^{a} \) The abbreviation Py stands for pyridine. \( ^{b} \) The N···N distances estimated using the experimental values of \( \delta(1H) \). \( ^{c} \) The same distances estimated using the parameter \( \delta'(1H) \).

**H-bond distances in the proton-bound homodimers of a–i in solution in CDF\(_3\)/CDCIF\(_2\)** are collected in Table 4. In order to simplify the further discussion, we have plotted the estimated N···N distances together with the available N···N distances in the proton-bound homodimers of pyridine derivatives as a function of the PA in Figure 5. The PA values of \( NN,2,6 \)-dimethylpyridine-4-amine and \( NN,2,6 \)-tetramethylpyridine-4-amine are 1013 and 1035 kJ/mol, respectively.

**Solvation Effect on H-Bond Geometries.** Before starting the discussion of Figure 5, we remind the reader of the following points. The binding energies of proton-bound homodimers correlate with the PA in an approximately quadratic manner. 27 We are dealing with structurally similar homodimers for which the binding energy should correlate with the N···N distance. For the species under study, a decrease of the PA of a base causes an increase of the binding energy of its homodimer that should result in contraction of the N···N distance. 26 In aprotic polar solvents, the difference in the PA values is attenuated. 63 The degree of this attenuation should depend on the solvation features. A question arises whether
A decrease of the effective proton affinity in solution as compared to the gas phase is a trivial fact. A critical finding is that the attenuation increases in the sequence pyridine < quinoline < acridine. The effect depends on the size of the species much stronger than on their electronic properties and/or their PA, Table 5. The use of another DFT functional (B97D3) and/or solvation model (SMD) changes the numerical values but not the trend of the attenuation (see the Supporting Information). Thus, if a pyridine derivative Py and an acridine derivative Ac exhibit the same PA in the gas phase, in a polar solvent the effective proton affinity of Ac is smaller than that of Py. As a result, the N···N distance in the proton-bound homodimer of Ac will be shorter compared with that of Py. Figure 5 perfectly demonstrates this effect for pyridines, quinolines, and acridine if to exclude e and h from the examination. Tentatively, the dependence of the solvation effect on the size of solute can be attributed to a local ordering of the solvent molecules. The larger the solute, the more ordering it makes on the solvation shell and thereby increases the local reaction field.

The correlations shown in Figure 5 and their interpretation given above are not well fulfilled by the homodimers of a, h, and e, and somewhat by Coll-2. All these species contain halogens as substituents. The data presented in Table 5 suggest that the solvent polarity does not affect significantly the inductive effect. We can speculate that the presence of halogen substituents affects the local ordering of CDF$_3$ and CDClF$_2$ molecules around the homodimers. This effect can be attributed either to a high localization of the charge at such substituents that competes with the [N···H]$^+$ moiety for the orientation of the solvent molecules, or to a specific solvation of the halogen substituents by chemically similar CDF$_3$ and CDClF$_2$ molecules. Tentatively, we find the latter reason more credible. However, despite recent progress in halogen-bonding we are not aware how strong it can affect the proton-accepting power of heterocycles. Presumably, this effect can be analyzed theoretically.

The data for homodimers of a, h, and e will fit the observed correlation better if their gas-phase PA will be increased by 15 kJ/mol. Thus, the attenuation of the proton affinity for these homodimers is smaller than for similar species. That means the solvation of a, h, and e results in a smaller effective solvent reactive field experiences by their [N···H]$^+$ moieties.

**H-Bond Geometry As a Function of the Dielectric Permittivity.** In Table 6 are collected experimental N···N distances of the proton-bound homodimers of pyridine (Py-1), quinoline (b), and acridine (i) in the CDF$_3$/CDClF$_2$ ($\varepsilon \approx 30$) mixture and in the crystalline state and DFT calculated distances at the gas phase, the PCM ($\varepsilon = 109$), and PCM-SMD ($\varepsilon = 109$) approximations. The calculated N···N distances were dependent on the basis-set used (see the Supporting Information). Thus, the level of our calculations was not sufficient for quantitative conclusions. Here we analyze exclusively the general trend that needs to be studied in detail in the future.

All three homodimers exhibit a contraction of the N···N distances in the sequence gas phase (DFT) > solid state (XRD) > polar solvent (NMR). In contrast, both implicit solvent models predict the opposite behavior for a polar solution that agrees with the results of more sophisticated studies reported in the past. Our results support the conclusion of ref 13 that implicit solvent models employed in computational studies do not reproduce experimental results for proton-bound homodimers. The reason for this result constitutes an open question. Presumably, molecular dynamics simulation with explicit treatment of solvent mixture should be able to reproduce the effect. Here we only mention that the PCM approximation predicts a contraction of the N···N distances compared with the gas phase in complexes of pyridine with phenol and N,N-phenylaniline, as well as in the proton-bound homodimer of azane; in contrast, for the proton-bound complexes of [pyridine−H]$^+$ with N,N-diphenylaniline, the homoconjugated dimers of N,N-dimethylmethanamine and cyano(methyl)cyanamide the behavior is reversed (see the Supporting Information). Thus, both the PCM and PCM-SMD approximations fail to predict the effect of solvation on the geometrical and energetic parameters of bulky charged proton-bound molecular complexes.

**CONCLUSIONS**

In this work, we have experimentally studied the effect of solvation on the geometry of the proton-bound homodimers of pyridines, quinolines, and acridines. The main conclusion of this study is that the N···N distances in these homodimers in solution are shorter than in the gas phase. There are no reasons to doubt that solvation effects reported here can be extended to other H-bonded systems embedded in a polar medium, whether the latter is a solution or an active center of enzyme. The effect of the medium on H-bond geometry cannot be attributed exclusively to the macroscopic dielectric permittivity of the medium. The reactive field also depends on the size of the H-bonded system and the presence in the system of moieties that are subject to specific interactions with solvent.

<table>
<thead>
<tr>
<th>base</th>
<th>$pK_a^{\text{d}}$</th>
<th>PA$^b$</th>
<th>PA$^c$</th>
<th>$\Delta^d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>pyridine</td>
<td>5.2</td>
<td>936</td>
<td>711</td>
<td>225</td>
</tr>
<tr>
<td>4-chloropyridine</td>
<td>3.2</td>
<td>924</td>
<td>701</td>
<td>223</td>
</tr>
<tr>
<td>quinoline</td>
<td>5.0</td>
<td>963</td>
<td>713</td>
<td>250</td>
</tr>
<tr>
<td>4-chloroquinoline</td>
<td>3.6</td>
<td>952</td>
<td>704</td>
<td>248</td>
</tr>
<tr>
<td>5,6,7,8-tetrahydroquinoline</td>
<td>6.3</td>
<td>976</td>
<td>725</td>
<td>251</td>
</tr>
<tr>
<td>acridine</td>
<td>5.6</td>
<td>992</td>
<td>722</td>
<td>270</td>
</tr>
<tr>
<td>9-chloroacridine</td>
<td>4.0</td>
<td>981</td>
<td>712</td>
<td>269</td>
</tr>
<tr>
<td>1,2,3,4,5,6,7,8-octahydroacridine</td>
<td>7.4</td>
<td>1008</td>
<td>739</td>
<td>269</td>
</tr>
</tbody>
</table>

$^a$Reference 64. $^b$Estimated at the B3LYP/6-311+G(3df,2p) level. $^c$Estimated using the polarizable continuum model. $^d$\(\Delta = PA - PA^c\).

**Table 6. N···N Distances (Å) in the Proton-Bound Homodimers of Pyridine, Quinoline, And Acridine**

<table>
<thead>
<tr>
<th>method</th>
<th>Py-1</th>
<th>b</th>
<th>i</th>
</tr>
</thead>
<tbody>
<tr>
<td>NMR in CDF$_3$/CDClF$_2$</td>
<td>2.618$^e$</td>
<td>2.598</td>
<td>2.616</td>
</tr>
<tr>
<td>XRD</td>
<td>2.655$^e$</td>
<td>–</td>
<td>2.743$^e$</td>
</tr>
<tr>
<td>DFT$^{d\text{c}}$</td>
<td>2.687</td>
<td>2.733</td>
<td>2.812</td>
</tr>
<tr>
<td>DFT$^{d\text{f}}$</td>
<td>2.692</td>
<td>2.738</td>
<td>2.820</td>
</tr>
<tr>
<td>DFT PCM, $\varepsilon = 108.94^{a\text{c}}$</td>
<td>2.748</td>
<td>2.793</td>
<td>2.885</td>
</tr>
<tr>
<td>DFT PCM-SMD, $\varepsilon = 108.94^{a\text{c}}$</td>
<td>2.767</td>
<td>2.813</td>
<td>–</td>
</tr>
</tbody>
</table>

$^a$Taken from ref 26. $^b$Cocrystal with toluene. $^c$Cocrystal with chloroform. $^d$Estimated at the B3LYP/6-311++G(d,p) level. $^e$Estimated at the B3LYP/6-311+G(3df,2p) level. $^f$Estimated using the Polarizable Continuum Model at the B3LYP/6-311++G(3df,2p) level and $\varepsilon = 109$. DOI: 10.1021/acs.jpca.7b09285
molecules. In this sense, the solvent is more like a crystal than a gas.
We reach the following specific conclusions from this study.
(i) The geometries of the proton-bound homodimers correlate with the gas-phase proton affinities (PA) of the corresponding bases. In particular, the N–N distance becomes shorter upon a decrease of the PA.
(ii) This correlation remains valid within a series of species of different electronic structure but similar size.
(iii) An increase of the size of the system results in contraction of the N–N distance.
(iv) The correlation can be violated when the system contains substituents that specifically affect solution features in a given solvent. In the case of the CDF$_3$/CDClF$_2$ mixture, such substituents are halogens that causes lengthening of the N–N distance.
(v) Neither the contraction of the N–N distance due to solvation nor the specific effect of substituents can be reproduced using the polarizable continuum model.
(vi) The N–N distance in the homoconjugated dimers of pyridine, quinoline, and acridine derivatives depends on the reaction field of the medium and decreases in the sequence gas phase > solid state > polar solvent.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.jpca.7b09285.

Proton affinities of selected bases at $\varepsilon = 109$ at the 311+ +g(3df,2p) level, the N–N distances in the proton-bound homodimers of pyridine, azane, N,N-dimethylthethamine, and cyano(methyl)cyanamide and the H-bonded complexes of pyridine with phenol, N-phenylaniline, and [N,N-diphenylaniline-H]+ calculated in the gas phase and polar solvents at different approximations, and X-ray crystal data (PDF)

X-ray diffraction structure data for single crystal [Acridine-H÷Acridine][BrF]$_n$ chloroform (CIF)

X-ray diffraction structure for single crystal [Acridine-H÷Acridine][BrF]$_n$ toluene(CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the German-Russian Interdisciplinary Science Center (G-RISC) funded by the German Federal Foreign Office via the German Academic Exchange Service (DAAD) and the Russian Foundation for Basic Research (Project 17-03-00590). We gratefully acknowledge the Gauss Centre for Supercomputing e.V. (www.gauss-centre.eu) for funding this project by providing computing time on the GCS Supercomputer SuperMUC at Leibniz Supercomputing Centre (LRZ, www.lrz.de)

■ REFERENCES


(64) SciFinder. https://scifinder.cas.org/.