

In quest of strong neutral organic bases and superbases—supramolecular systems containing four pyridine subunits

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Abstract—It is shown by a reliable DFT method that supramolecular structures **1** and **2**, constructed using pyridine as an essential building block, act as powerful neutral organic superbases in the gas phase and in acetonitrile due to cationic resonance and hydrogen bonding in the conjugate acids amplified by the NMe₂ groups placed at strategic positions on the molecular backbone.
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Since Alder's seminal work on the first proton sponge, 1,8-bis(dimethylamino)-naphthalene (DMAN),^{1,2} the design and synthesis of neutral organic superbases has received unabated interest. This is not surprising as they have distinct advantages over their inorganic counterparts. They exhibit a high solubility in organic solvents, a low sensitivity to moisture and CO₂ and a very good stability at low temperatures, thus permitting mild reaction conditions.^{3–7} It is also noteworthy that neutral superbases are efficient catalysts, in particular, if immobilized on adequate surfaces they are useful in green chemistry.^{8,9} It has been found that several families of organic compounds provide strong superbases. They encompass acyclic and cyclic guanidines,^{10–13} phosphazenes,^{14–17} guanidinophosphazenes,^{18,19} quinoimines and related systems,²⁰ C₂ diamines²¹ and extended 2,5-dihydropyrrolimines.²² The extensive theoretical and experimental work of the Tartu group should be emphasized.^{18,23–25} Alder's idea of using the intramolecular hydrogen bonding (IMHB) motif in amplifying basicity^{1,2} proved particularly effective when employing multiple hydrogen bonding patterns, thus taking full advantage of the fact that the IMHBs are stronger in protonated species, in addition to formation of a new H-bridge.^{26–28} In the present work, the concept of a single proton embedded in the electrostatic field of four nitrogen lone pairs of the conjugate acid is utilized

(Fig. 1). The gas phase proton affinity and basicity are examined by the DFT B3LYP/6-311+G(2df,p)//B3LYP/6-31G* (thereafter denoted as B3LYP1) method meaning that the molecular structures were optimized at the very economical B3LYP/6-31G* level. On the other hand, the final energy was obtained by carrying out additional single point calculations using the much more flexible 6-311+G(2df,p) basis set. The absolute proton affinities are computed in a standard way as follows:

$$\text{APA}(\mathbf{B}_\alpha) = (\Delta E_{\text{el}})_\alpha + (\Delta E_{\text{vib}})_\alpha + (5/2)RT \quad (1)$$

$$(\Delta E_{\text{el}})_\alpha = E(\mathbf{B}) - E(\mathbf{B}_\alpha\text{H}^+) \quad (2)$$

$$(\Delta E_{\text{vib}})_\alpha = E_{\text{vib}}(\mathbf{B}) - E_{\text{vib}}(\mathbf{B}_\alpha\text{H}^+) \quad (3)$$

The base and its conjugate acid are denoted by **B** and **B_αH⁺**, respectively. The site of proton attack is signified by α . Further, $(\Delta E_{\text{el}})_\alpha$ is the electronic contribution to proton affinity, E_{vib} includes the zero point vibrational energy (ZPVE) and temperature corrections to the 298.2 K enthalpy, while $(5/2)RT$ accounts for the translational energy of the proton as well as for the $\Delta(pV)$ term. The ZPVE values are computed using the B3LYP/6-31G* method without any scaling. The gas phase basicity is defined as the Gibbs free-energy change of the protonation reaction.

The basic structural subunit used here as a fundamental building block is pyridine. It is known that pyridine is a compound of a low basicity. The calculated absolute proton affinity (APA) and basicity [GB] values obtained

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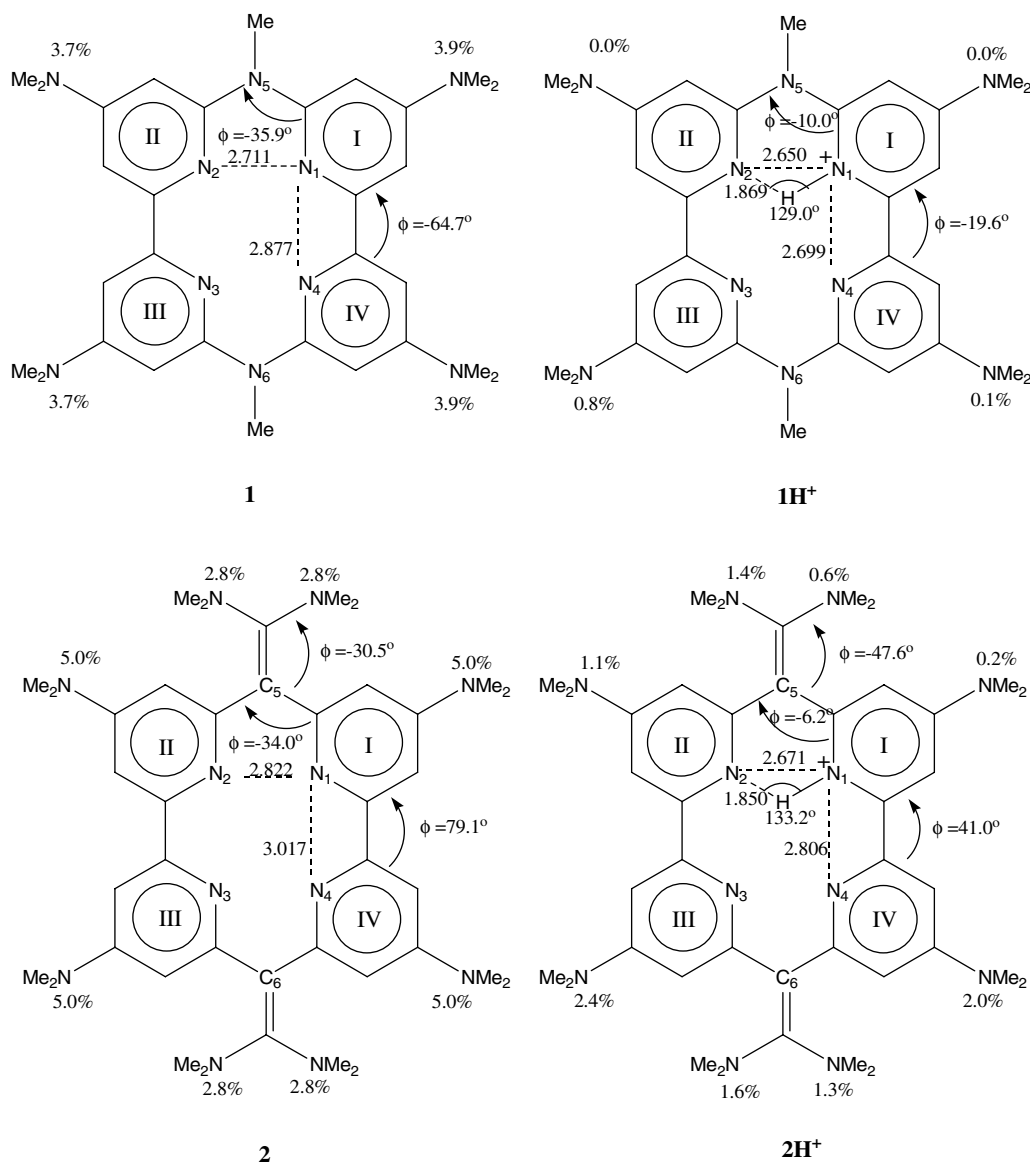


Figure 1.

by the B3LYP1 method are 223.6 [215.9] kcal mol⁻¹, where the basicity is given within square parentheses. They dramatically change in suprastructure **1** involving four pyridine moieties connected by two C(sp²)-C(sp²) bonds of the biphenylene type and two NMe bridges. Each pyridine is substituted by one NMe₂ group at the *para* position, which enables efficient cationic resonance upon protonation. The corresponding APA and GB values are 286.0 [278.4] kcal mol⁻¹. The protonated form **1H⁺** has a strongly asymmetric hydrogen bond (Fig. 1). A full geometric characterization of superbases **1** and **2** and their conjugate acids is outside the scope of the present letter. Therefore, we briefly consider the structural features of the initial base **1** and some characteristic changes caused by protonation in **1H⁺** first. It is useful to use within this context an index, called the degree of pyramidalization (DP%) which is defined as²⁹

$$\text{DP}(\%) = \left[360^\circ - \sum_{i=1}^3 \alpha_i^0 \right] / 0.9^\circ \quad (4)$$

where the summation is extended over three bond angles of the apical atom. It gives quantitative information on the non-planarity of important heteroatoms. A comparison between the DP(%)_N values in the neutral base and conjugate acid sheds some light on the extent of the cationic resonance triggered by protonation. Further, we shall make use of the dimensionless differential bond distance anisotropy $\delta(\text{BDA})$ in the pyridine rings in supermolecules relative to the average distances in free pyridine. This is given by Eq. 5:

$$\begin{aligned} \delta(\text{BDA}) = & (1/2 \text{ \AA}) \sum_{i=1}^2 |d(\text{CN})_i - d(\text{CN})_{\text{av}}| \\ & + (1/4 \text{ \AA}) \sum_{i=1}^4 |d(\text{CC})_i - d(\text{CC})_{\text{av}}| \quad (5) \end{aligned}$$

where the bond distances are in Å. Here, the $d(\text{CN})_{\text{av}}$ and $d(\text{CC})_{\text{av}}$ bond lengths refer to free pyridine.

The critical region in **1** is given by the neighborhood of the N1 atom of the ring I to be attacked by protonation. The first observation made is that the molecule is significantly non-planar. The rings I and II are rotated by a dihedral angle $\phi = -64.7^\circ$. Furthermore, the torsional angle C(II)–N5–C(I)–N1 is -35.9° . Both angles are substantially decreased in absolute values in the protonated species $\mathbf{1H}^+$ assuming values of -19.6° and -10.0° , respectively, which is indicative of a clear tendency toward planarization of the conjugate acid. By the same token, the pyramidalization of the sp^3 nitrogen becomes negligible (Fig. 1), as expected in view of the cationic resonance. The non-bonded contacts in the neutral base **1** are $N1 \cdots N2 = 2.711 \text{ \AA}$ and $N1 \cdots N4 = 2.877 \text{ \AA}$, which in turn are considerably shortened upon the formation of the $N1-H \cdots N2$ bridge to 2.650 \AA and 2.699 \AA , respectively. The H-bridge is highly asymmetric as evidenced by the $d(N1-H)^+$ distance, which is 1.039 \AA , whereas the distance $d(N2 \cdots H)^+$ is as large as 1.869 \AA . Furthermore, it is important to notice that the non-bonded distances between the attached proton and nitrogens N_3 and N_4 are $d(N_3 \cdots H) = 2.819 \text{ \AA}$ and $d(N_4 \cdots H) = 2.311 \text{ \AA}$ implying that the proton is immersed in the Coulomb field of the nitrogen lone pairs. However, one can hardly speak about multicenter hydrogen bonding. Instead, a hydrogen bond with two bridgehead atoms seems to take place here. A favorable Coulomb interaction between the proton and distal nitrogens is difficult to estimate in a quantitative way because the atomic charges in the molecules cannot be determined in an unequivocal manner. The bridge angle $N1-H-N2$ is 129° thus being far from linear. Taking into account structural parameters one is tempted to conclude that the H-bond is of conventional strength. The differential bond anisotropies for two different pyridine rings in **1** are $\delta(\text{BDA})$ (I) = 0.033 and $\delta(\text{BDA})$ (II) = 0.036 , thus being similar. The corresponding magnitudes in the protonated species $\mathbf{1H}^+$ are 0.063 (I), 0.037 (II), 0.034 (III), and 0.040 (IV), where the ring numbering is given within parentheses. The largest increase in the bond localization is found in the directly protonated ring I. This, at first sight surprising finding, is easily understood, if it is taken into account that the cationic resonance stabilization is energetically more advantageous than aromatic stabilization.¹³ As a consequence, pyridine ring I receives a partial quinoid structure due to the double bond character of the linkage between the nitrogen atom of the NMe_2 group and the *para* substituted carbon. This is also evidenced by a decrease in the corresponding bond length, which is 1.387 \AA in **1** and 1.360 \AA in $\mathbf{1H}^+$.

The gas phase proton affinity [basicity] of suprastructure **2** are very high being 291.4 [283.7] kcal mol^{-1} . The structural patterns in **2** and $\mathbf{2H}^+$ are similar to those of **1** and $\mathbf{1H}^+$, respectively. The dihedral angle between the pyridine rings is $\phi = 79.1^\circ$, while the torsion angle $N1-C(I)-C(5)-C(II)$ is -34.0° . They decrease in absolute values to 41.0° and -6.2° , respectively. The degrees of pyramidalization are significantly smaller in $\mathbf{2H}^+$ (Fig. 1). The differential bond distance anisotropy is equal to 0.040 in **2**, while a variation similar to that in $\mathbf{1H}^+$ is found in conjugate acid $\mathbf{2H}^+$, as evidenced by

the $\delta(\text{BDA})$ values of 0.070 , 0.045 , 0.041 , and 0.044 for rings I–IV, respectively. The C–N bond distance of the NMe_2 group *para* substituted to the protonated center N1 is shortened by 0.024 \AA because of the lone pair back donation effect in conjunction with the cationic resonance. There is also evidence of the cationic resonance stabilization within the bis(dimethylamino) substituted double bond containing C5 atom in $\mathbf{2H}^+$. The $d(N1-H^+)$ distance is again 1.039 \AA and the $N1 \cdots N2$ and $N1 \cdots N4$ contacts are significantly shortened upon protonation resulting in the conjugate acid $\mathbf{2H}^+$ (Fig. 1), while the corresponding $d(N_3 \cdots H)$ and $d(N_4 \cdots H)$ distances are 2.946 \AA and 2.483 \AA , respectively. Thus one can safely conclude that the H-bond is bicentric being formed across two bridgehead nitrogen atoms. The $d(N2 \cdots H)^+$ distance is 1.850 \AA thus being smaller than that in $\mathbf{1H}^+$ indicating a somewhat stronger IMHB interaction and stabilization. It is fair to conclude that the global structural features and the qualitative electronic interaction patterns in superbases **1** and **2** as well as in their conjugate acids are similar.

The solvent effect in acetonitrile is estimated by employing the polarized continuum model put forward by Scrocco, Tomasi, and Miertuš.^{30,31} The molecular surface determining a cavity within a solvent is obtained by the isodensity shell of $0.0004e \text{ B}^{-3}$, thus giving rise to the isodensity polarized continuum model (IPCM)³² utilizing $\epsilon = 36.64$ for MeCN. Since the calculation of pKa values require several iterations, a more economical B3LYP/6-311+G**//B3LYP/6-31G* computational procedure is necessary for such large systems. It will be thereafter denoted as B3LYP2. The latter method is used for the calculation of APAs in MeCN, which are subsequently correlated with the experimental pKa values for 10 pyridine compounds.³³ The resulting linear squared fit:

$$\text{p}K_a(\text{MeCN}) = 0.5751 * \text{APA}(\text{MeCN}) - 144.4 \text{ units} \quad (6)$$

is excellent as evidenced by the correlation coefficient $R^2 = 0.993$ and a very low average absolute error of 0.10 . Employing Eq. 5, one can predict the basicity of superbases **1** and **2** in acetonitrile, whose pKa values are 27.2 and 30.0 , respectively.

In conclusion, supramolecular structures **1** and **2**, constructed using pyridine as an essential building block, provide powerful neutral organic superbases in the gas phase and acetonitrile due to cationic resonance and hydrogen bonding in conjugate acids amplified by the NMe_2 groups placed at strategic positions on the molecular backbone. It should be emphasized that cavities in supramolecules **1** and **2** are able to accommodate larger cations, which might lead to interesting host–guest systems. This aspect deserves additional studies.

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