Pyridine and *s*-triazine as building blocks of nonionic organic superbases—a density functional theory B3LYP study†

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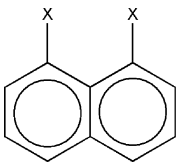
It is shown by reliable DFT B3LYP/6-311+G(2df,p)//B3LYP/6-31G* method that pyridine and *s*-triazine can serve as useful building blocks in tailoring neutral superbases. The former compound is used in constructing the four-fragment macrocycles substituted by a number of NMe_2 substituents placed at strategic positions on the suprastructure's backbone. The calculated proton affinities are within the range of 270–290 kcal mol^{-1}, thus belonging to the upper part of the superbasicity ladder. It is shown that proton affinities of polysubstituted derivatives follow a simple additivity rule, which facilitates prediction and interpretation of the results in multiply substituted systems. The *s*-triazine motif is employed in forming manxane-like systems by using guanidine fragments or 1,1-dimethylaminoethylenes, which exhibit proton affinities spread over the lower part of the superbasicity scale (256–272 kcal mol^{-1}). The amplified basicity in both families of compounds is a consequence of the strong cationic resonance in conjugate acids supported by stabilization provided by intramolecular hydrogen bonds (IMHB). The nature of the IMHBs is examined. It is found that IMHBs in large macrocycles constructed by pyridine moieties is of a bicentric type. They are not cationic resonance supported IMHBs in the first approximation. In contrast, protonation in one of the manxane-like systems yields the IMH bonds that are stabilized by substantial cationic resonance through the hydrogen $H^{\delta+}$ bridge. Consequently, the cationic resonance supported hydrogen bonds (CRSHBs) do exist in some protonated species. The basicity of pyridine macrocycles is examined in acetonitrile. It is found that their pK_a values span a range between 26–30 units meaning that they are also strong superbases in MeCN solutions compared to the threshold given by pK_a(MeCN) of DMAN (18.2 units).

Introduction

Design, preparation and characterization of uncharged organic superbases has been an active research field for several decades.[1] They proved useful as auxiliaries in the chemical syntheses[2,3] exhibiting a number of advantageous properties compared to their ionic inorganic counterparts including better solubility in most organic solvents, insensitivity to moisture and CO_2, stability at low temperatures and pronounced reactivity with the naked anions.[4–6] Last but not least, they are efficient catalysts when immobilized on surfaces[7,8] being recyclable, which is important in the so-called sustainable green chemistry.[9,10] Finally, neutral organic (super)bases are applicable in asymmetric syntheses.[11]

The most important families of strong bases and superbases include cyclic and acyclic guanidines,[12–16] phosphazenes,[17–19] quinonimines and related systems,[20–22] quinolylboranes,[23] extended 2,5-dihydropyrolimines[24] and C_2-diamines.[25] The extensive work of Tartu group[26–29] encompasses preparation, characterization and examination of properties of a large number of organic bases and superbases employing both experimental and theoretical methods. Particular attention has been devoted to the so-called proton sponges—strong bases with a low nucleophilicity starting by Alder's DMAN [1,8-bis(dimethylamino)naphthalene)] **1a**[30] (Scheme 1).

Its basicity is generally accepted as a threshold for superbases with the experimental absolute proton affinity of 245.3 kcal mol^{-1}.[31] Alder's idea was recently generalized by replacing dimethylamino groups by tetramethylguanidino[32,33] and hexamethyltriaminophosphazenyl[34] substituents leading to more powerful superbases TMGN (**1b**) and HMPN (**1c**),



1a X= NMe_2
1b X= $N{=}C(NMe_2)$
1c X= $N{=}P(NMe_2)_3$
1d X= $N{=}P(N{=}C(NMe_2)_3)$

Scheme 1

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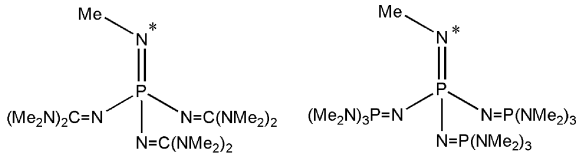
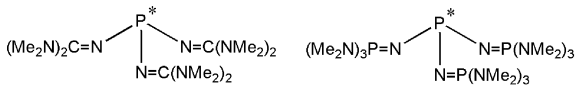
† Electronic supplementary information (ESI) available: DFT B3LYP/6-311+G(2df,p)//B3LYP/6-31G* generated structures of compounds **8a–9g** and their various protonated forms with bond distances (in Å), bond and dihedral angles (in degrees) and pyramidalization of nitrogen atoms (in %) (Fig. S1–15). See DOI: 10.1039/b617914b



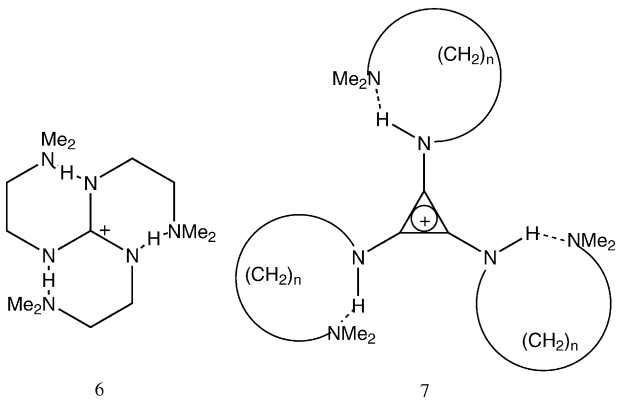
2 **3**



4 **5**

Scheme 2

respectively, which have been successfully synthetized. Theoretical study of a system **1d** (X = N=P(N=C(NMe$_2$)$_2$)$_3$) revealed that it is highly potent superbase exhibiting extremal gas phase PA of 305.4 kcal mol^{-1} and pK_a in acetonitrile of 44.8 units.[35] Very strong superbases[26,36,37] are provided by compounds **2** and **3**, as well as phosphines **4** and **5** depicted in Scheme 2, where the site most susceptible to proton attack is denoted by an asterisk. An important structural motif is given by multiple intramolecular hydrogen bonding (IHB), which leads to high basicity by cooperative IHB effect as in compound **6** and **7**[38,39] (Fig. 1). It should be pointed out that compound **6** was prepared in laboratory recently.[40] The interested reader can find description of the early work on neutral organic superbases in several excellent review articles.[41–49] In designing a large catalogue of noncharged organic superbases we developed a specific strategy,[50] which consists of several steps including: (1) identification of the basic atom usually embedded in a particular functional group, (2) selection of a molecular backbone carrying the functional group, (3) tuning of the basicity by electron releasing substituents placed at the strategic positions and (4) employing some special buttressing effects such as *e.g.* the IMHB concept. In the present work we utilize a somewhat different approach by using pyridine and *s*-triazine fragments instead of some characteristic functional groups. The former is inserted in large supramolecular frameworks thus forming powerful superbases, whereas the latter is substituted by teramethylguanidino groups thus leading to manxane-like compounds, which are very basic too. In both families of molecules a provision of the intramolecular hydrogen bonding is exploited. It will become obvious that the role of substituents is pivotal.



6 7

Fig. 1 Two conjugate acids exhibiting a triple corona effect, *i.e.* three intramolecular hydrogen bond, which in turn close pseudo-rings.

Theoretical framework and computational procedure

The theoretical framework for calculating the absolute proton affinities (APAs) is given by eqn (1)–(4). The APA is defined as a negative value of the enthalpy change for the protonation reaction:

$$B + H^+ \rightarrow B_\alpha H^+ \quad (1)$$

The base and its conjugate acid are denoted by B and $B_\alpha H^+$, respectively, while α denotes the position of proton attack. The absolute proton affinity consists of three terms:

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

$$(\Delta E_{el})_\alpha = E(B) - E(B_\alpha H^+) \quad (3)$$

$$(\Delta E_{vib})_\alpha = E_{vib}(B) - E_{vib}(B_\alpha H^+) \quad (4)$$

Here, $(\Delta E_{el})_\alpha$ is the electronic contribution to proton affinity, E_{vib} includes the zero point vibrational energy (ZPVE) and temperature corrections to the room temperature enthalpy, while $(5/2)RT$ accounts for the translational energy of the proton as well as the $\Delta(pV)$ term. The gas-phase basicity is defined as a Gibbs free energy change of the reaction (1). Our main focus will be the absolute proton affinities, since they provide the main contribution to basicity being more prone to rationalization at the same time.

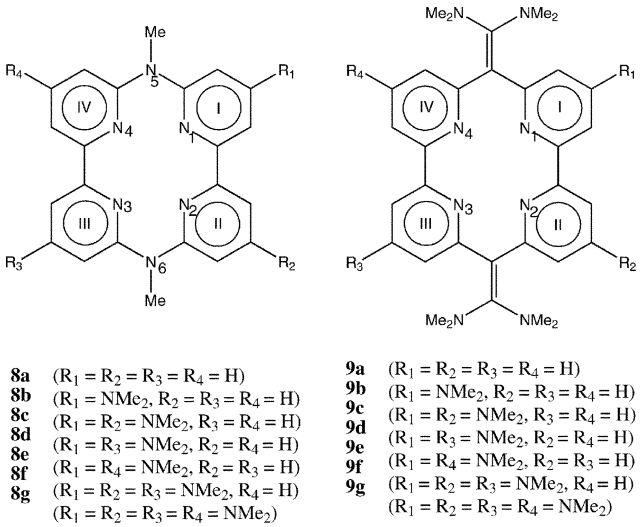
The computational method of choice should be reliable enough and widely applicable in large systems. We have shown that the Hartree–Fock (HF) model is able to reproduce rather closely the MP2 APA values, if properly scaled.[51] More accurate data require explicit account of the correlation energy. A good compromise is achieved by the DFT B3LYP/6-311+G(2df,p)//B3LYP/6-31G(d) approach (thereafter referred to as the DFT(I) method) as amply documented by the earlier work.[35,36,46,47] The true minima on Born–Oppenheimer potential energy surface (BO) are verified by the vibrational frequency analysis at the simple B3LYP/6-31G(d) level. The resulting frequencies are used in calculating the ZPVE contribution and thermal correction without any scaling. All calculations have been carried out by GAUSSIAN 03 program.[52]

Anticipating forthcoming results we can say that both pyridine and *s*-triazine provide useful building blocks in constructing organic superbases, in spite of the fact that they are weak bases themselves. The calculated APAs of pyridine and *s*-triazine are 223.6 and 201.8 kcal mol^{-1}, respectively, whereas larger molecular systems composed of their fragments exhibit APAs between 256 and 290 kcal mol^{-1}.

Results and discussion

Gas phase proton affinities

The results for neutral organic bases **8a–9g**, *s*-triazine and its derivatives **11–15** are given in Table 1. We shall commence discussion with supramolecular systems **8a–9g** containing four pyridine building blocks (Fig. 2). The absolute proton affinities are calculated by using eqn (2). The ZPVE contributions to the APAs retrieved by the B3LYP/6-31G(d) method are practically constant varying between 9.6 and 10.0 kcal mol^{-1}. This is a general feature, which is one of the reasons behind a fairly good performance of the scaled HF method in calculating APAs.[51] It is a consequence of the atomic additivity of the zero point vibrational energy in molecules,[53] which depends only on the number of particular constituent atoms. We note in passing that the second important reason for a reasonable performance of the scaled HF method[51] is approximate additivity of the electron correlation energy too.[54] Since the studied systems are not synthesized as yet, we have to rely on the theoretical proton affinities, which should be fairly reliable according to previous experience. Perusal of the data presented in Table 1 shows that all compounds **8a–9g** are neutral organic superbases. Their APA values range from 265.4 to 291.4 kcal mol^{-1}, thus covering the upper portion of the superbasicity ladder. It should be pointed out that the most basic atom is always $N_{(1)}$. It appears that the supramolecular system **8a** is angularly strained, which also leads to steric crowding. As a consequence the pyridine rings are not equivalent except in couples. It occurs that the rings I and III are equivalent and the same holds for the rings II and IV (Fig. S1 of the ESI†). Therefore, one expects two different pyridine nitrogen sites differing in their basicity. This is indeed the case since APA($N_{(1)}$) and APA($N_{(4)}$) are 265.4 and 264.7 kcal mol^{-1}, respectively. Difference is small, but significant. The reference compound is given by free pyridine, which has relatively low absolute proton affinity (APA) and basicity [GB] of 223.6 [215.6] kcal mol^{-1} as obtained by the DFT(I) method. The parent macrocyclic compound **8a** has APA 265.4 kcal mol^{-1}, corresponding to **8aH**$^{+}_{(N1)}$ conjugate acid, which is 41.8 kcal mol^{-1} higher than the standard. This is a consequence of the combined effects of the cationic resonance spread over the macrocyclic system and the intramolecular H-bond formed in **8aH**$^{+}_{(N1)}$. The latter bridges the $N_{(1)}$ and $N_{(4)}$ atoms and an interesting question arises whether it belongs to a class of the cationic resonance supported hydrogen bonds or not. The cationic resonance supported hydrogen bond (CRSHB) was observed first in the protonated superbase TMGN (**1b**).[33] This finding was corroborated by additional calculations on systems possessing two fragments prone to cationic resonance, placed at appropriate positions on the backbone being bridged by the $H^{\delta+}$-bond upon protonation.[34,35] Here $H^{\delta+}$ denotes proton immersed between two nonbonded nitrogens. The CRSHB should be distinguished from the customary resonance assisted hydrogen bonds (RAHB) within or between neutral molecules, which was intensively discussed over last 15 years.[55–57] Although the RAHB concept is accepted by a number of researchers, it was questioned by Alkorta *et al.*[58,59] recently, on the basis of computed chemical shift of the hydrogen atom on the bridge X–H···Y and the spin–spin coupling constants between the bridgehead atoms X and Y. In spite of this controversy, we found that protonation of 1,8-bis(tetramethylguanidino)-naphthalene **1b** yields a significantly asymmetric intramolecular hydrogen bond (IMHB) N–$H^{\delta+}$···N, where one imine



8a ($R_1 = R_2 = R_3 = R_4 = H$)
8b ($R_1 = NMe_2$, $R_2 = R_3 = R_4 = H$)
8c ($R_1 = R_2 = NMe_2$, $R_3 = R_4 = H$)
8d ($R_1 = R_3 = NMe_2$, $R_2 = R_4 = H$)
8e ($R_1 = R_4 = NMe_2$, $R_2 = R_3 = H$)
8f ($R_1 = R_2 = R_3 = NMe_2$, $R_4 = H$)
8g ($R_1 = R_2 = R_3 = R_4 = NMe_2$)

9a ($R_1 = R_2 = R_3 = R_4 = H$)
9b ($R_1 = NMe_2$, $R_2 = R_3 = R_4 = H$)
9c ($R_1 = R_2 = NMe_2$, $R_3 = R_4 = H$)
9d ($R_1 = R_3 = NMe_2$, $R_2 = R_4 = H$)
9e ($R_1 = R_4 = NMe_2$, $R_2 = R_3 = H$)
9f ($R_1 = R_2 = R_3 = NMe_2$, $R_4 = H$)
9g ($R_1 = R_2 = R_3 = R_4 = NMe_2$)

Fig. 2 Supramolecular systems constructed by four pyridine moieties, which provide four basic site most susceptible to proton attack.

Table 1 Total electronic energies of neutral and protonated (super) bases in au obtained for the supramolecular structures **8** and **9**, *s*-triazine and manxane-like systems **12–15**. The ZPVE contributions to the absolute proton affinities, APAs and GBs are given in kcal mol^{-1}. For the employed theoretical methods see text

Compound	Neutral	Protonated	Δ(ZPVE)	APA	GB
8a$_{(N1)}$	−1178.03428	−1178.47021	9.9	265.4	256.5
8a$_{(N4)}$	−1178.03428	−1178.46925	10.0	264.7	255.9
8b$_{(N1)}$	−1312.04680	−1312.49794	10.0	274.8	266.1
8b$_{(N2)}$	−1312.04680	−1312.48927	9.8	269.5	260.9
8b$_{(N3)}$	−1312.04680	−1312.48501	9.8	266.8	258.4
8b$_{(N4)}$	−1312.04680	−1312.48849	9.8	269.1	260.6
8c$_{(N1)}$	−1446.05928	−1446.51637	9.9	278.4	269.7
8d$_{(N1)}$	−1446.05994	−1446.51637	9.8	278.1	269.6
8e$_{(N1)}$	−1446.05985	−1446.51914	9.9	279.8	271.3
8f$_{(N1)}$	−1580.07275	−1580.53670	9.8	282.8	274.5
8g$_{(N1)}$	−1714.08493	−1714.55377	9.7	286.0	278.4
8g$_{(N4)}$	−1714.08493	−1714.55048	9.7	283.9	276.3
9a	−1679.52930	−1679.98787	9.9	279.3	270.4
9b$_{(N1)}$	−1813.54131	−1814.00914	9.9	285.1	276.4
9b$_{(N2)}$	−1813.54131	−1814.00337	10.1	281.6	272.8
9b$_{(N3)}$	−1813.54131	−1814.00279	10.1	281.2	272.5
9b$_{(N4)}$	−1813.54131	−1814.00526	10.1	282.7	273.9
9c	−1947.55322	−1948.02430	10.0	287.1	278.1
9d	−1947.55302	−1948.02384	10.0	286.9	278.4
9e	−1947.55323	−1948.02583	9.9	288.2	280.0
9f	−2081.56520	−2082.04019	9.9	289.6	281.0
9g	−2215.57737	−2216.05470	9.6	291.4	283.7
10	−280.45531	−280.78766	8.2	201.8	194.9
11	−682.56052	−682.95682	8.8	241.3	233.5
12$_{(N1)}$	−1364.560086	−1365.41754	8.9	256.1	246.6
12$_{(N4)}$	−1364.560086	−1365.42729	9.9	261.3	251.3
13$_{(N1)}$	−1365.01954	−1365.46443	9.3	271.3	264.3
13$_{(N4)}$	−1365.01954	−1365.45505	9.5	265.3	258.0
14	−1316.82497	−1317.27026	9.4	271.5	263.7
15	−1434.78094	−1435.22801	9.6	272.4	264.5

nitrogen is directly protonated, while its imine N atom counterpart is practically semi-protonated.[33] It is important to point out that naphthalene carrier does not transmit the resonance effect from one guanidine fragment to the other. Despite this fact, it turned out that the semi-protonated guanidine group underwent structural changes that indicated roughly 50% of the cationic resonance stabilization induced by the proton forming the $N–H^{\delta+}\cdots N$ bridge.[32,33,35] A similar conclusion holds for protonation of the proton sponge **1c**.[34] These results are not surprising because the cationic resonance is a very strong stabilizing interaction occurring in the conjugate acids particularly in protonated guanidines.[16] Since guanidine moiety is highly susceptible to cationic resonance it is induced to an appreciable extent despite larger $H^{\delta+}\cdots N$ distance. Therefore, it can be safely concluded that the intramolecular CRSHB does take place in some protonated species. Examination of the structural parameters of **8a** and $\mathbf{8aH^+}_{(N1)}$, to be discussed in more detail in a later section, reveals that a large increase in the APA of 41.8 kcal mol^{-1} relative to free pyridine is a consequence of the cationic resonance in $\mathbf{8aH^+}_{(N1)}$ distributed over the right hand side of the system including two apical $N_{(5)}$Me and $N_{(6)}$Me amino groups too (Fig. S2, ESI†). Formation of the $N_1–H^{\delta+}\cdots N_4$ bridge little affects the ring IV, which can be neglected in the first approximation. Obviously, pyridine moiety is less susceptible to cationic resonance than guanidine fragment. Further, distances between $N_{(1)}$ atom and nitrogens $N_{(2)}$ and $N_{(3)}$ are large. Hence, we conclude that the hydrogen bond is essentially bicentric and not of the CRSHB type. However, the Coulomb interactions between proton ($H^{\delta+}$) of the bridge and the lone pairs of distal nitrogens $N_{(2)}$ and $N_{(3)}$ cannot be excluded. Their contribution to the stability of conjugate acid $\mathbf{8aH^+}_{(N1)}$ is difficult to estimate, because the electron density (or the formal atomic charge) residing on particular atoms in molecules is impossible to determine in an unequivocal manner. The single substitution $R_1 = NMe_2$ in **8b** increases APA by additional 9.4 kcal mol^{-1} due to the electron releasing property of the sp^3 nitrogen lone pair of the NMe_2 group and its contribution to the cationic resonance upon protonation. It is interesting to compare it with the increase in APA upon the *para* NMe_2 substitution of a free pyridine.

The corresponding APA [GB] values are 241.7 [233.9] implying that the NMe_2 group enhances proton affinity and basicity of pyridine by 18.1 [18.3] kcal mol^{-1} obviously due to a cationic resonance triggered by protonation and greatly amplified by the *para* positioned NMe_2 group. Therefore, it appears that the corresponding increase in **8b** is by 9.1 kcal mol^{-1} lower, which calls for rationalization. The point is that the *para*-NMe_2 substituted pyridine in **8b** is a part of a complex macrocyclic system (Fig. S4, ESI†). The positive charge in $\mathbf{8bH^+}_{(N1)}$ is predominantly distributed over the right half of the compound and the apical NMe links $C_{(1)}–N_{(5)}$ and $C_{(4)}–N_{(6)}$ as evidenced by the structural data (Fig. S5, ESI†), just like in the case of $\mathbf{8aH^+}_{(N1)}$. Concomitantly, only a portion of the positive charge is available for the cationic resonance with the *para*-substituted NMe_2 group at the ring I. However, taking the system **8b** as a whole, it increases the APA value relative to a free pyridine by 51.2 or 33.1 kcal mol^{-1} higher than the *para*-substituted pyridine by dimethylamino group. The latter value reflects the increase in the cationic resonance relaxation effect of the macrocycle $\mathbf{8bH^+}_{(N1)}$ in addition to the stabilization energy of the IMHB bridge. As to the strength of the IMHB in $\mathbf{8bH^+}_{(N1)}$, it seems that it is practically the same compared to that in $\mathbf{8aH^+}_{(N1)}$ judged by the $N_{(1)}\cdots N_{(4)}$ bridgehead distance, which assumes values of 2.673 and 2.679 Å, in these systems, respectively. In order to get a better insight into the interplay between the IMHB and cationic resonance in protonated macrocyclic system $\mathbf{8bH^+}_{(N1)}$ we examined the conjugate acids obtained by the proton attachment at positions $N_{(2)}$, $N_{(3)}$ and $N_{(4)}$. As a rough measure of the strength of their IMHBs we shall adopt the distance between the bridgehead nitrogen atoms. Protonation at $N_{(2)}$ yields APA($\mathbf{8bH^+}_{(N2)}$) of 269.5 kcal mol^{-1}, thus being lower by 5.3 kcal mol^{-1} than the most basic site $N_{(1)}$. The cationic resonance relaxation effect is obviously less effective than in the APA $\mathbf{8bH^+}_{(N1)}$, since the pyridine ring II is unsubstituted. The IMHB seems to be weaker too, because the length $N_{(2)}\cdots N_{(3)}$ is larger being 2.687 Å. It should be noted in passing that the cationic resonance effect is confined to a large extent to the right half of the $\mathbf{8bH^+}_{(N2)}$ system as expected (Fig. S6, ESI†). The protonation at N_3 atom provides IMHB possessing $N_{(3)}\cdots N_{(2)}$ distance of 2.651 Å, which is lesser than that in the most stable conjugate base. This position is less basic (APA($\mathbf{8bH^+}_{(N3)}$) = 266.8 kcal mol^{-1}) by some 8 kcal mol^{-1} than protonation at $N_{(1)}$ atom. The structural parameters reveal that the cationic resonance is delocalized over the left side of the $\mathbf{8bH^+}_{(N3)}$ system, with a very little influence on the right half of the conjugate acid (Fig. S7, ESI†). This holds also for the case of protonation at $N_{(4)}$ atom (Fig. S8, ESI†). The corresponding APA($\mathbf{8bH^+}_{(N4)}$) = 269.1 kcal mol^{-1} is 5.7 kcal mol^{-1} less basic than the most stable protonated form. The IMHB seems to be the strongest, however, since the $N_{(4)}\cdots N_{(1)}$ distance is the shortest (2.620 Å). This is not surprising since the $N_{(1)}$ atom is the most basic position in the **8b** system, thus being the best IMHB receptor. The overall cationic resonance is on the other hand somewhat less efficient than in the $\mathbf{8bH^+}_{(N1)}$ conjugate acid. It follows that the relative basicities of this polycentric strong base are determined by a subtle interplay between the cationic resonance and the intramolecular hydrogen bonding. Relative contributions of these two stabilizing interactions is very difficult to delineate. The double NMe_2 substitution in **8c–8e** enlarges the APAs by roughly 13.0–14.4 kcal mol^{-1} relative to **8a**. The triple (**8f**) and quadruple (**8g**) substitution amplifies proton affinity by 17.4 and 20.6 kcal mol^{-1}, relative to unsubstituted parent suprasystem **8a**, respectively, thus leading to highly basic compounds as reflected in APA values of 282.8 and 286.0 kcal mol^{-1}. It is of some interest to examine the additivity of the substituent effect in systems **8c–8g**, since it is a common knowledge that the proton affinity of polysubstituted aromatic compounds follows a remarkable additivity rule.[60–62] To put it succinctly, each substituent in the polysubstituted aromatics behaves and affects the proton affinity as if the other were nonexistent. The increment for substitution $R_1 = NMe_2$ is denoted by $I_8(\mathbf{8b}_{(N1)})$ and it is obviously 7.4 kcal mol^{-1}. It is easy to calculate increments describing influence of the NMe_2 groups substituted at the rings II, III and IV, if the proton is attached at the $N_{(1)}$ position. They are 9.4, 2.9, 1.4

and 5.6 kcal mol^{-1}, respectively. The additivity would imply that the proton affinity of the tetrasubstituted compound **8g** is APA(**8g**$_{(N1)}$)^{add} ≅ APA(**8a**$_{(N1)}$) + $\Sigma_{i=1}^{4} I_8$(**8b**$_{(Ni)}$) = 284.7 kcal mol^{-1}. This is comparable with true APA(**8g**) value of 286.0 kcal mol^{-1}. Other additivity values *vs.* true computational results given within parentheses (taken from Table 1) are as follows: APA(**8c**)$_{add}$ = 277.7 (278.4), APA(**8d**)$_{add}$ = 276.2 (278.1), APA(**8e**)$_{add}$ = 280.4 (279.8) and APA(**8f**)$_{add}$ = 281.8 (282.8) in kcal mol^{-1}. Discrepancies between the additive and computational values are rather small thus offering a simple rationalization of the variation in APAs in multiply substituted members of the family **8a–8g**.

The system of compounds formed by the framework **9** provides even stronger superbases (Table 1). It appears that the parent compound **9a** has already a larger APA than its counterpart **8a** by 13.9 kcal mol^{-1}. Tetrasubstituted derivative **9g** is a very powerful superbase as evidenced by APA of 291.4 kcal mol^{-1}. The substituted derivatives **9b–9g** cover a range between 285.1 and 291.4 kcal mol^{-1}, which belongs to the uppermost part of the superbasicity ladder of the neutral organic superbases. The latter is conventionally stretched between DMAN providing a lower limit of 245.3.[63] and the higher limit arbitrarily taken as 300 in kcal mol^{-1}. Perusal of the structural data of conjugate acids **9aH**$^{+}_{(N1)}$ and **9gH**$^{+}_{(N1)}$ (Fig. S13 and S15, ESI†) reveals that the intramolecular hydrogen bonds are not additionally stabilized by the cationic resonance. Instead, protonation of the $N_{(1)}$ atom in **9a** induces the cationic resonance in its half of the molecule including also the C=C(NMe$_2$)$_2$ fragments. In mono and polysubstituted derivatives **9b–9g** one observes again that protonation of particular nitrogen triggers the cationic resonance predominantly over its own half, with small stabilization of all NMe$_2$ groups distributed over the pyridine rings. However, this is a consequence of the direct protonation at particular pyridine N atoms. To put it in another way, it is not caused by additional induction through a particular hydrogen bridge. Estimating increments by analogous way as above, one obtains I_9(**9b**$_{(N1)}$) = 5.8, I_9(**9b**$_{(N2)}$) = 2.3, I_9(**9b**$_{(N3)}$) = 1.9 and I_9(**9b**$_{(N4)}$) = 3.4 (in kcal mol^{-1}). The conjectured additivity value for compound **9g** is APA(**9g**)$_{add}$ ≅ APA(**9a**) + $\sum_{i=1}^{4} I_9$(**9b**$_{(Ni)}$) = 292.7 kcal mol^{-1}, which is quite close to the actual DFT(I) value of 291.4 kcal mol^{-1}. The remaining additivity APAs are the following: APA(**9c**)$_{add}$ = 287.4 (287.1), APA(**9d**)$_{add}$ = 287.0 (286.9), APA(**9e**)$_{add}$ = 288.5 (288.2) and APA(**9f**)$_{add}$ = 289.3 (289.6) kcal mol^{-1}, where the DFT(I) computational results are given within parentheses. The accordance between the additivity values and computational results is highly satisfactory. It means that protonation of complex systems such as **8g** and **9g** can be partitioned in several more or less independent effects, which yield additive contributions to proton affinities.

The energetic data for *s*-triazine and its derivatives **10–15** depicted in Fig. 3 are presented in Table 1. The ZPVE values are again fairly constant being between 9 and 10 kcal mol^{-1}. The parent compound **10** is exception possessing the ZPVE of 8.2 kcal mol^{-1}. It has as low APA as 201.8 kcal mol^{-1} and the corresponding GB value of 194.9 kcal mol^{-1}. Triple NMe$_2$ substitution leading to **11** substantially increases APA to 241.3 kcal mol^{-1} as a consequence of appreciable cationic

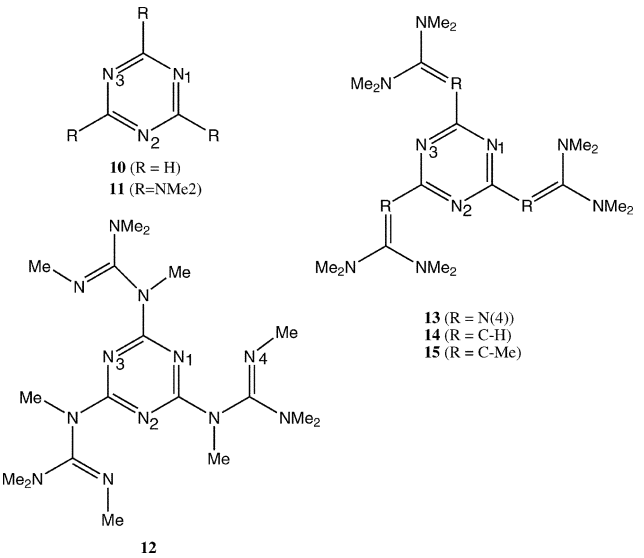


Fig. 3 *s*-Triazine and its derivatives obtained by substituting the ring by three fragments prone to cationic resonance interaction upon protonation.

resonance, which is dramatically increased in the conjugate acid **11H**$^{+}$ by the NMe$_2$ groups. The ambident molecule **12** has two basic sites provided by atoms $N_{(1)}$ and $N_{(4)}$. Their APAs are 256.1 and 261.3 kcal mol^{-1}, respectively, meaning that the imino nitrogen of the guanidine fragment is more basic by some 5 kcal mol^{-1}. It is important to mention that protonation at both sites yields either $N_{(1)}$–$H^{\delta+}\cdots N_{(4)}$ or $N_{(1)}\cdots H^{\delta+}$–$N_{(4)}$ hydrogen bond, which in turn are additionally stabilized by cationic resonance. In other words, if the $N_{(1)}$ is protonated, then the $N_{(4)}$ nitrogen is sort of semi-protonated and *vice versa*. In the system **13** protonation at the ring nitrogen $N_{(1)}$ triggers an efficient cationic resonance spread over the alternating double and single bonds. It encompasses the whole system **13H**$^{+}_{(N1)}$ implying that the IMBH is not supported by the cationic resonance *via* the H-bridge. Proton affinity of a base **13** is 271.3 kcal mol^{-1}, whereas in compounds **14** and **15** it is around 272 kcal mol^{-1}. The electronic pattern in **14H**$^{+}_{(N1)}$ and **15H**$^{+}_{(N1)}$ is similar to that found in **13H**$^{+}_{(N1)}$ meaning that the cationic resonance is triggered by a direct protonation at $N_{(1)}$ position only. Thus, the IMHB bridge does not additionally increase the cationic resonance indicating that CRSHBs are a rather rare phenomenon.

The bottom line is that **11** and manxane-like systems **12–15** are superbases, which in turn cover a lower part of the superbasicity ladder. Another important finding is that **12H**$^{+}$ represents a very interesting charged system where the intramolecular hydrogen bond is supported by cationic resonance by interaction through the H-bridge.

Structural features

Let us first consider in some more detail the structural parameters of the series of compounds **8a–9g** (Fig. S1–S15, ESI†) and their conjugate acids by starting with their building blocks pyridine and its *para*-dimethylamino derivative, with particular emphasis on the cationic resonance and geometry of the

IMHB. It is useful to use for this purpose an index, which is called the degree of pyramidalization (DP %) defined as:[64]

$$\mathrm{DP}(\%) = [360^\circ - \textstyle\sum_{i=1}^{3} \alpha_i]/0.9^\circ \qquad (5)$$

where the summation is extended over three bond angles of the apical atom. It gives quantitative information on the nonplanarity of important heteroatoms. A comparison between the $\mathrm{DP}(\%)_N$ 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 δ(BDA) in the pyridine rings of the supermolecular systems relative to the corresponding distances in free pyridine averaged over the number of bonds. This is given by eqn (6):

$$\delta(\mathrm{BDA}) = (1/2\text{Å})\textstyle\sum_{i=1}^{2} |d(\mathrm{CN})_i - d(\mathrm{CN})_{i(\mathrm{fp})}| + (1/4\text{Å})\sum_{i=1}^{4} |d(\mathrm{CC})_i - d(\mathrm{CC})_{i(\mathrm{fp})}| \qquad (6)$$

where the bond distances are in Å. Here, the $d(\mathrm{CN})_{i(\mathrm{fp})}$ and $d(\mathrm{CC})_{i(\mathrm{fp})}$ bond lengths refer to free pyridine. Hence, the δ(BDA) values provide information about deformation of the rings relative to parent compound.

It is appropriate to begin with the reference structure of pyridine and its protonated form (Fig. 4). The C–N bond distance is shorter than the C–C one, since the bond radius of nitrogen is smaller. The differential bond distance anisotropy δ(BDA) of pyridine is zero by definition. Protonation at nitrogen produces reorganization of the electron density leading to shortening of the vicinal bonds as indicated by the cationic resonance structure. The δ(BDA) value of protonated pyridine is 0.023. Comparison of the *para* (NMe_2) substituted pyridine with the parent molecule is instructive. The N–Me bonds are rotated out of the ring plane by $\pm 7^\circ$ and the nitrogen atom is slightly pyramidal (DP(%) = 1.7%). In spite of this, there is an electron releasing resonance interaction of the NMe_2 nitrogen with the ring, which affects its bond distances. Protonation considerably increases anisotropy of the ring bond distances (δ(BDA) = 0.054) *via* amplified cationic resonance, which significantly shortens the M_2N–C_s distance, where subscript s denotes the substituted carbon of the ring. Moreover, the resonance is spread over the ring from the substitution site in a typical alternating way by stretching and shrinking neighbouring bonds over the π-network (Fig. 4). The heavy atoms are placed in the molecular symmetry plane in order to enhance the cationic resonance effect. Since the NMe_2 nitrogen participates in the resonance interaction by increasing the double bond character of the Me_2N–C_s bond, its π-electron is less available for the hyperconjugate interactions with the Me groups, which in turn takes place in neutral molecule. Consequently, the N–Me bond lengths should be increased, which occurs indeed. This is one of the characteristic features of the cationic resonance triggered by protonation, if the NMe_2 substituents are present. Thus, it could serve as one of its fingerprints.

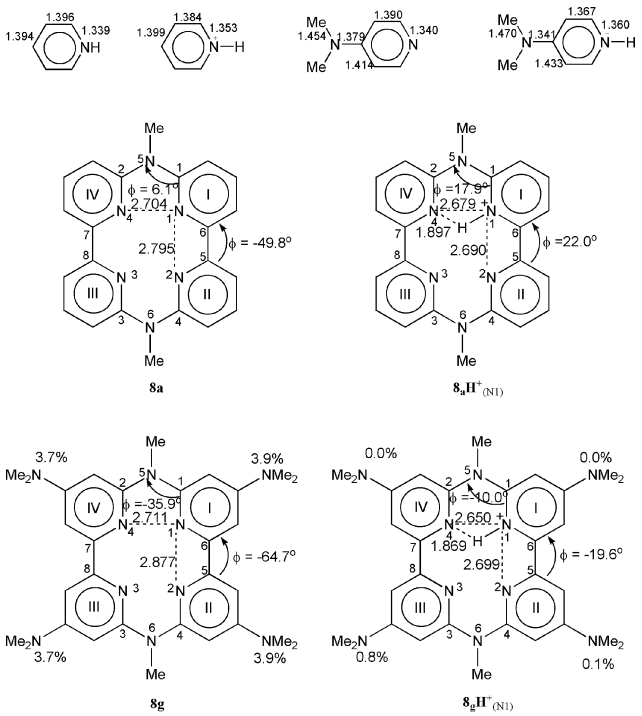


Fig. 4 Some relevant structural parameters of supramolecules **8a**, **8g** and their monoprotonated forms.

Let us continue discussion with the superstructure **8a** (Fig. 4). A striking feature is nonplanarity of this supramolecule as evidenced by a dihedral angle between the directly bonded pyridine moieties *e.g.* I and II of -49.8°. It is worth reiterating that the rings I and III are equivalent and the same holds for II and IV ones. In contrast, the rings *e.g.* I and IV differ and their conjugation interaction with the $N_{(5)}$Me moiety is asymmetric (Fig. S1, ESI†). Obviously, the π-conjugation between $C_{(1)}$ and $N_{(5)}$ atoms is stronger, which is reflected in shorter $d(C_{(1)}$–$N_{(5)})$ distance (1.404 Å) and smaller $N_{(1)}$–$C_{(1)}$–$N_{(5)}$–$C_{(2)}$ dihedral angle of 6.1°. On the other hand, the $C_{(2)}$–$N_{(5)}$ bond distance is longer being 1.420 Å and the dihedral angle $N_{(4)}$–$C_{(2)}$–$N_{(5)}$–$C_{(1)}$ is increased to 38.7°. The $N_{(5)}$ atom is practically planar. The same holds *mutatis mutandis* for the $N_{(6)}$ atom. Protonation at $N_{(1)}$ introduces considerable structural changes (Fig. S2, ESI†). Dihedral angles between I and II pyridines and rings III and IV are diminished in absolute values assuming -23.3 and -27.0°, respectively. The cationic resonance between various moieties is evidenced by decrease in the bond distances $C_{(1)}$–$N_{(5)}$, $C_{(5)}$–$C_{(6)}$ and $C_{(4)}$–$N_{(6)}$. On the other hand, the $C_{(2)}$–$N_{(5)}$ and $C_{(3)}$–$N_{(6)}$ bonds separating left and right parts of the system $\mathbf{8aH}^+_{(N1)}$ are slightly but systematically longer. This means that the cationic resonance is semidelocalized over the right hand side of the conjugate acid $\mathbf{8aH}^+_{(N1)}$. It should be mentioned in this connection that the N_5 and N_6 nitrogens are practically planar in $\mathbf{8aH}^+_{(N1)}$ too. The δ(BDA) values reveal that the ring IV is slightly more deformed than ring I since they are 0.013 and 0.009, respectively. Protonation at $N_{(1)}$ yields the following δ(BDA) values for the rings I–IV: 0.038, 0.009, 0.012 and 0.013, respectively. It follows that deformation of pyridines induced by formation of macrocycle is fairly constant for unprotonated rings being roughly $\delta(\mathrm{BDA})_{av} = 0.012$. If this amount is added to δ(BDA) of protonated pyridine one obtains 0.035, which comes close to the protonated ring in $\mathbf{8aH}^+_{(N1)}$. Formation of the $N_{(1)}$–$H^{\delta+}\cdots N_{(4)}$ bridge diminishes dihedral angle between pyridines III and IV (-27.0°), but examination of the bond

distances reveals that the immersed proton with a charge $H^{\delta+}$ does not induce significant changes in bond distances of the ring IV by through H-bridge direct interaction. It is fair to say that some very small changes are noticeable, but it is safe to conclude that the IMHB in **8aH**$^+_{(N1)}$ is not supported by the cationic resonance at least in the first approximation. It should be noted in passing that the N_5–Me and N_6–Me bonds are lengthened to a small extent upon protonation in **8aH**$^+_{(N1)}$. This means that the some hyperconjugative interaction between methyl groups and the lone pairs of the planar $N_{(5)}$ and $N_{(6)}$ nitrogens in the initial neutral base **8a** is diminished upon protonation, because the corresponding lone pairs participate in the cationic double bond resonance interaction in the $C_{(1)}{=}N_{(5)}{}^{\delta+}$ and $C_{(4)}{=}N_{(6)}{}^{\delta+}$ bonds. This pattern is characteristic for the whole family **8a–8g**. It illustrates the fact that the positive charge in conjugate acids is spread overall the supramolecular systems albeit to different extent in different fragments.

The critical region in the highly superbasic **8g** is given by the neighbourhood of the N_1 atom of the ring I to be attacked by proton. The first observation to be made is that the molecule is significantly nonplanar (Fig. S9, ESI†). The rings I and II are rotated by a dihedral angle $\varphi = -50.2^\circ$ relative to each other. Further, the torsional angle $C_{(2)}$–$N_{(5)}$–$C_{(1)}$–$N_{(1)}$ is 17.4°. Both angles are substantially decreased in absolute values upon protonation at $N_{(1)}$ in **8gH**$^+_{(N1)}$ assuming values of −21.4 and −10.0°, respectively (Fig. S10, ESI†). This is indicative of a clear tendency toward planarization of the conjugate acid, which facilitates the cationic resonance propagated by the mobile π-electrons. By the same token, the pyramidalization of the sp^3 nitrogen atoms becomes negligible (Fig. 4), as expected. The non-bonded contacts in the neutral base **8g** are $N_{(1)}\cdots N_{(4)}$ = 2.711 Å and $N_{(1)}\cdots N_{(2)}$ = 2.806 Å, which in turn are considerably shortened upon formation of the $N_{(1)}$–$H\cdots N_{(4)}$ bridge to 2.650 and 2.699 Å by 0.061 and 0.107 Å, respectively. The H-bridge is highly asymmetric as evidenced by the $d(N_{(1)}$–$H^{\delta+})$ distance, which is 1.039 Å, whereas the distance $d(N_{(4)}\cdots H^{\delta+})$ is as large as 1.869 Å. Further, it is important to notice that the non-bonded distances between the attached proton and nitrogens $N_{(2)}$ and $N_{(3)}$ are $d(N_{(2)}\cdots H^{\delta+})$ = 2.311 Å and $d(N_{(3)}\cdots H^{\delta+})$ = 2.819 Å implying that the proton is immersed in the Coulomb field of the nitrogen lone pairs, but one can hardly speak about the multicenter hydrogen bonding. Instead, a hydrogen bond with two bridgehead $N_{(1)}$ and $N_{(4)}$ atoms takes place here. The bridge angle $N_{(1)}$–$H^{\delta+}$–$N_{(4)}$ is 129° thus being far from linear. Taking into account structural parameters, one is tempted to conclude that the H–bond is of conventional type and medium strength. The differential bond anisotropies for two different pyridine rings in **8g** are δ(BDA)(I) = 0.015 and δ(BDA)(IV) = 0.017, thus being similar. The corresponding magnitudes in the protonated species **8gH**$^+_{(N1)}$ are 0.044 (I), 0.017 (II), 0.010 (III) and 0.019 (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.[16] As a consequence, the 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 1.388 Å in **8g** and 1.360 Å in **8gH**$^+_{(N1)}$, thus indicating a shortening of 0.028 Å. The remaining N–Me bond lengths in the conjugate acid are lengthened by 0.008 Å, which is one of the probes of the cationic resonance as pointed out earlier.

The structural patterns in **9g** (Fig. S14, ESI†) and **9gH**$^+_{(N1)}$ (Fig. S15, ESI†) are similar to those of **8g** and **8gH**$^+$, respectively, but there are some notable differences (Fig. 5). In the first place **9g** is less strained thus allowing for equivalence of the four pyridine fragments (Fig. S12, ESI†). The double bond $C_{(2)}{=}C_{(3)}$ is considerably twisted as evidenced by the dihedral angle $C_{(1)}$–$C_{(9)}{=}$C–N(Me$_2$) of −30.5°. The dihedral angle between the pyridine rings I and II is φ = 79.1°, while the torsion angle $N_{(1)}$–$C_{(1)}$–$C_{(9)}$–$C_{(2)}$ is −34.0°. They decrease in absolute values assuming 41.0 and −6.2° in conjugate acid **9gH**$^+_{(N1)}$, respectively (Fig. S13, ESI†). Degrees of pyramidalization are significantly smaller in **9gH**$^+_{(N1)}$ (Fig. 5). The differential bond distance anisotropy of pyridine fragments is equal to 0.016 in **9g**, while a variation similar to that in **8gH**$^+_{(N1)}$ is found in the conjugate acid **9gH**$^+_{(N1)}$, as evidenced by the δ(BDA) values of 0.048, 0.023, 0.018 and 0.021 for rings I–IV, respectively. The C–N bond distance of the NMe_2 group *para* substituted to the protonated center N_1 is shortened by 0.024 Å 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 involving $C_{(5)}$ atom in **9gH**$^+_{(N1)}$. The $d(N_{(1)}$–$H^+)$ distance is again 1.039 Å and the $N_{(1)}\cdots N_{(2)}$ and $N_{(1)}\cdots N_{(4)}$ contacts are significantly shortened upon protonation in the resulting conjugate acid **9gH**$^+_{(N1)}$ (Fig. 5), while the corresponding $d(N_{(2)}\cdots H)$ and $d(N_{(3)}\cdots H)$ distances are 2.483 and 2.946 Å, respectively. Thus one can safely conclude that the H–bond is bicentric being formed across two bridgehead $N_{(1)}$ and $N_{(4)}$ nitrogen atoms. The $d(N_{(4)}\cdots H)^+$ distance is 1.850 Å thus being smaller than that in **8gH**$^+_{(N1)}$ indicating a somewhat stronger IMHB interaction and larger stabilization. Concomitantly, the bridge angle $N_{(1)}$–$H^+\cdots N_{(4)}$ is somewhat increased by 4° compared to its counterpart in **8gH**$^+_{(N1)}$. Perusal of the bond distances in **9gH**$^+_{(N1)}$ reveals that the cationic resonance is spread over

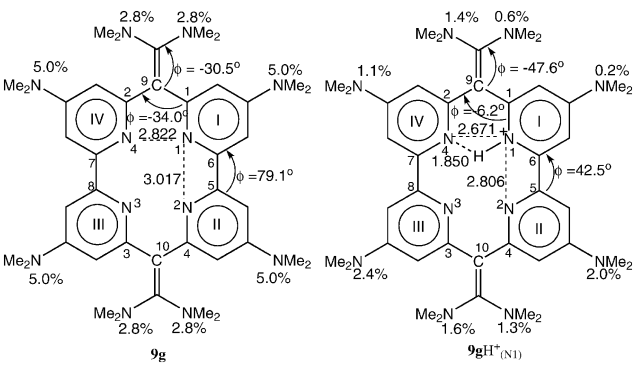


Fig. 5 Structural parameters of superbase **9g** and its conjugate acid **9gH**$^+$.

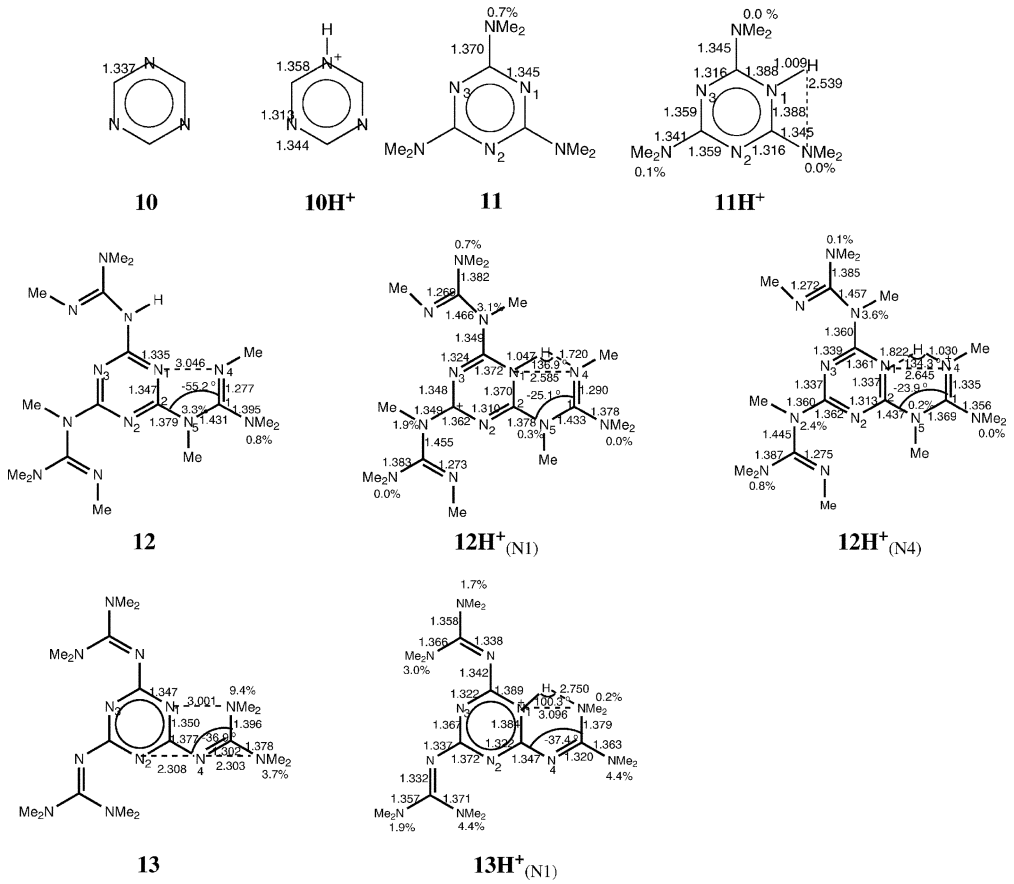


Fig. 6 Important structural parameters of *s*-triazine, its 1,3,5-triamino derivative, manxane-like systems and their protonated forms.

the whole system from the protonated pyridine I to its counterpart ring IV being transmitted through the lower rings II and III *via* the $C_{(10)}$ carbon junction atom. Also, it encompasses the upper $C_{(9)}$═$C(NMe_2)_2$ fragment, but stops at the $C_{(2)}$–$C_{(9)}$ bond, which in turn remains virtually the same (1.486 Å). This is evidenced by contraction of relevant connection bonds $C_{(1)}$–$C_{(9)}$, $C_{(5)}$–$C_{(6)}$, $C_{(4)}$–$C_{(10)}$, $C_{(3)}$–$C_{(10)}$ and $C_{(7)}$–$C_{(8)}$. The changes are sometimes small, but significant enough to detect the π-electron delocalization triggered by protonation. It should be pointed out that the π-AOs are good transmitters of the resonance effect even if they are not parallel, but close considerably large angles between 40–50° instead. The resonance effect over the C–$N(Me_2)_2$ bond occurs at the expense of a decreased hyperconjugation effect between the amino nitrogen and methyl groups. The bond distances between the nitrogen and carbon atoms in the N–Me fragments are invariably increased by small but significant extent. It is important to mention that the IMHB in $\mathbf{9gH^+}_{(N1)}$ is not of the resonance assisted type, since the changes in structure of the ring IV are not induced directly by interaction between the nitrogen N_4 and the proton along the $N_{(4)}\cdots H^{\delta+}$–$N_{(1)}$ bridge, but *via* the through–bonds interaction over the lower rings II and III, as expounded above.

Systems involving *s*-triazine building blocks are particularly interesting, because they exhibit in some specific cases the cationic resonance supported IMHBs. The structures of parent *s*-triazine **10**, its triple NMe_2 derivative **11** and their protonated forms are displayed in Fig. 6. Their geometries speak for themselves providing a compelling evidence that the cationic resonance is strong in $\mathbf{11H^+}_{(N1)}$ being amply enhanced by the NMe_2 groups. The manxane-like compound **12** can be protonated either at $N_{(1)}$ or $N_{(4)}$ atoms. Protonation at $N_{(1)}$ induces lengthening of the $C_{(1)}$═$N_{(4)}$ bond and shortening of the $C_{(1)}$–NMe_2 bond within the guanidine subunit directly through the $N_{(1)}$–$H^{\delta+}\cdots N_{(4)}$ bridge, because the $C_{(1)}$–$N_{(5)}$ and $C_{(2)}$–$N_{(5)}$ are practically unchanged upon protonation. It is safe to conclude that the guanidine moiety is partially protonated too. It should be also noticed that the $N_{(4)}\cdots H^{\delta+}$ distance is rather short (1.720 Å). Hence, it is safe to conclude that CRSHB occurs here. This feature is even more pronounced upon protonation at the $N_{(4)}$ atom in $\mathbf{12H^+}_{(N4)}$. The guanidine fragment undergoes dramatic structural changes triggered by protonation, which in turn are spread over the $C_{(2)}$–$N_{(5)}$ bond. However, considerable changes of the central *s*-triazine ring and distal guanidine moieties exhibit noticeable changes induced through the $N_{(4)}\cdots H^{\delta+}$–$N_{(1)}$ bridge (Fig. 6). It should be mentioned that the nitrogens are planar or very nearly planar in both conjugate acids $\mathbf{12H^+}_{(N1)}$ and $\mathbf{12H^+}_{(N2)}$. In contrast, protonation at N_1 atom in $\mathbf{13H^+}_{(N1)}$ spurs cationic resonance, which is neatly distributed over alternating double and single bonds throughout the system. If there are some changes in the guanidine subunit resulting from a direct interaction through the $N_{(1)}$–H$\cdots$$NMe_2$ group, they are overshadowed by

propagation of the cationic resonance along a network of alternating double and single bonds. Consequently, the CRSHB does not occur in $\mathbf{13H}^{+}_{(N1)}$.

Basicity in acetonitrile

The solvent effect in MeCN is calculated by employing the polarized continuum model put forward by Scrocco, Tomasi and Miertuš. [65,66] The molecular cavity within a solvent is defined by a surface determined by the isodensity shell of 0.0004e bohr^{-3}, thus giving rise to the isodensity polarized continuum model (IPCM).[67] The dielectric constant ε for acetonitrile is 36.64. Since the molecules immersed in a solvent require several iterations in calculating their proton affinities, a somewhat simpler B3LYP method should be applied. We found that the IPCM model coupled with the B3LYP/6-311+G**//B3LYP/6-31G* (thereafter denoted as DFT(II)) method gave an excellent correlation with the experimental pK_a data and calculated APAs of imines in MeCN as evidenced by the regression coefficient $R = 0.997$ and an average absolute error (AAE) of 0.4 units.[68] The explicit correlation reads:

$$\mathrm{p}K_a(\text{theor.})_{\text{guanidine}} = 0.4953\,\mathrm{APA(MeCN)} - 119.7 \text{ units} \quad (7)$$

The problem is, however, that nitrogen atoms in different moieties require different correlation functions, because the aggregation of solvent molecules is different. Hence the pK_a values of pyridine N atoms require a separate scrutiny. For this purpose ten pyridines depicted in Fig. 7 were examined and the relevant energetic data are summarized in Table 2. The resulting linear least squares fit correlation takes a form:

$$\mathrm{p}K_a(\text{theor.})_{\text{pyridine}} = 0.5751\,\mathrm{APA(MeCN)} - 144.4 \text{ units} \quad (8)$$

Both straight lines (7) and (8) are almost parallel. The quality of correlation is very good since R^2 coefficient is very high ($R^2 = 0.993$), whereas the average absolute error is very low ($\Delta_{av} = 0.1$ units). We shall employ eqn (8) in estimating pK_a values of the pyridine N atoms. However, before doing that let us briefly comment on the data presented in Table 2. They reveal a very good accordance with experiment for the APAs in the gas phase obtained by the DFT(II) computational scheme. The average absolute error of 1.8 kcal mol^{-1} is of a systematic type, meaning that taken with opposite sign could be used as an offset value, which in turn would provide an excellent agreement with the measured data. Secondly, proton affinity in acetonitrile is considerably higher compared to the gas phase values due to increased interaction between the conjugate acid and the solvent molecules including stronger intermolecular hydrogen bonds. The difference between APA (solv.) − APA (g) lies in a narrow range between 40.0 (**25**) and 49.3 (**16**) kcal mol^{-1} with an average value of 45.0 kcal mol^{-1}. Substituted pyridines **16–25** exhibit modest basicity both in the gas phase and in MeCN. The largest basicity is found in **25**, undoubtedly because of a strong cationic interaction the six-membered ring and the *para* substituted NMe_2 group. Its pK_a value is 17.7 units.

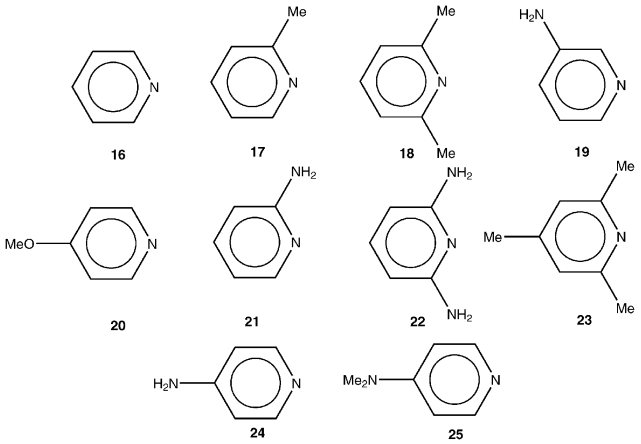


Fig. 7 Pyridine and its derivatives used in deriving semiempirical formula (8) for pK_a.

Employing correlation (8) one arrives at the estimated pK_a values of strong bases and superbases **8a–9g** given in Table 3. They span a range between 22.6 and 30.0 units with systems **9b–9g** possessing pronounced superbasicity in MeCN around 29 and 30 units. It is noteworthy that the increase in APA upon solvation in MeCN relative to the gas phase values lies within the limits of 11.5 and 24.7 kcal mol^{-1} with an average of 16.1 kcal mol^{-1}. This is significantly lower than the corresponding values in substituted free pyridines, which has a simple explanation. The pyridine nitrogen neighbourhood leaves a large free access area for the MeCN molecules, which can easily make aggregates around the protonated N atom. In contrast, proton in the conjugate acids $\mathbf{8aH}^{+}$–$\mathbf{9gH}^{+}$ takes part in the H-bridge, not to mention bulky fragments forming

Table 2 The absolute proton affinities of pyridines (Fig. 6) in the gas phase and MeCN obtained by DFT(II) method. The basicities GB (g) are given for completeness. Theoretical pK_a values are deduced by eqn (8). Comparison with available experimental data reveals a good agreement[a]

Molecule	APA (g)	APA (exptl.)	GB (g)	APA (solv.)	pK_a(calc.)	pK_a(exptl.)
16	223.2 (221.4)	222.0	215.7	272.5	12.2	12.33
17	227.6 (225.8)	226.8	220.1	273.7	12.9	13.11
18	231.5 (229.7)	230.2	224.1	275.2	13.8	13.92
19	230.0 (228.2)	228.1	222.8	275.9	14.2	13.96
20	231.3 (229.5)	229.9	223.7	275.6	14.0	14.04
21	228.2 (226.4)	226.4	220.9	275.8	14.1	14.26
22	230.2 (228.4)	—	224.6	276.7	14.7	14.56
23	235.5 (233.7)	—	227.5	276.8	14.7	14.77
24	236.6 (234.8)	234.2	229.0	281.5	17.4	17.40
25	241.7 (239.9)	238.4	233.9	281.7	17.5	17.74

[a] The APA (g) values within parentheses are obtained by offset value of −1.8 kcal mol^{-1}.

Table 3 The absolute proton affinities of superbases **8a–9g** in MeCN by DFT(II) method and the estimated pK_a values

Molecule	APA (solv.)	APA (solv.) − APA (g)	pK_a
8a	290.1	24.7	22.6
8b	291.8	19.0	23.6
8c	296.5	18.1	26.3
8d	296.3	18.2	26.2
8e	297.5	17.7	26.9
8f	298.3	15.5	27.4
8g	298.7	12.7	27.6
9a	295.6	16.3	25.8
9b	301.0	15.9	28.9
9c	301.5	14.4	29.2
9d	301.5	14.6	29.2
9e	302.2	14.0	29.6
9f	302.6	13.0	29.8
9g	302.9	11.5	30.0

the suprastructures. Hence, the proton is partially solvated within the conjugate (super)acid itself.

It is of some interest to examine a dependence of the pK_a(MeCN) values on the proton affinities APAs (gas). Taking the experimental pK_a(exptl.) data[29] for substituted pyridines **16–25**, one obtains a rather poor correlation pK_a(MeCN) = 0.3016 APA (g) − 55.2 units with R^2 = 0.918 and the average absolute error of 0.5 units. It is fair to say, however, that the qualitative trend of changes is correctly predicted by the gas phase proton affinities. The situation is better in correlating theoretical estimates of pK_a(MeCN) and APA (g) for superbases **8a–9g** as evidenced by a relation pK_a(theor.) = 0.3156 APA (g) − 61.7 units. The correlation parameters are R^2 = 0.976 and AAE = 0.4 units. Obviously, the intrinsic proton affinities strongly affect basicity in acetonitrile too.

Concluding remarks

Although pyridine and *s*-triazine are compounds of low intrinsic basicity in the gas phase and MeCN solvent, they provide very useful building blocks in tailoring suprastructures exhibiting high proton affinities lying in the range of 256.1 and 291.4 kcal mol^{-1} thus covering a large part of the superbasicity scale. The pyridine fragments are used in forming the macrocycles **8a–9g**, which undergo protonation within molecular cavities thus realizing H-bridge essentially between two pyridine nitrogens. This proton ($H^{\delta+}$ atom) is additionally stabilized to some extent by the favourable Coulomb interaction with the N atoms of more remote pyridine fragments. The family of compounds **9a–9g** possess APAs, which belong to the upper part of the superbasicity scale. It is noteworthy that APAs of polysubstituted macrocycles follow additivity rule, which allows for a transparent interpretation of this property along the series **8a–9g**. The corresponding pK_a values are fairly high too reaching a value of 30 units in acetonitrile. On the other hand, *s*-triazine can serve as a central moiety substituted by guanidine or guanidine-like fragments in a way that compounds **12–15** of the manxane shape are formed. They represent a set of superbases whose basicities are placed above the superbasicity threshold of DMAN reaching the middle of the ladder. The most basic site in ambident superbase **12** is imine nitrogen, whereas the ring N atom is more prone to protonation in **13**, **14** and **15**. In all cases the intramolecular H-bonds are formed thus contributing to enhanced basicity. However, the main reason behind superbasic values of proton affinities in compounds **12–15** is the cationic resonance effect in conjugate acids. It is established beyond any doubt that cationic resonance assisted IMHBs occur in conjugate acid systems $\mathbf{12H^+}_{(N1)}$ and $\mathbf{12H^+}_{(N4)}$.

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