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Predicted high proton affinity of poly-2,5-dihydropyrrolimines—the aromatic domino effect†

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ABSTRACT: The basicity of a family of 2,5-dihydropyrrolimines is examined by the Hartree-Fock model. It is found that these systems exhibit high proton affinity, which increases with the number of the five-membered rings present. The origin of the pronounced basicity is identified as the tandem or domino aromatic effect occurring in the conjugate acids. The aromatization is triggered by protonation and spread over whole systems via mobile π-electrons. Proton affinities as high as 300 kcal/mol or more can be achieved in the gas phase, if the aromatization is combined with the favourable substituent effects and with the intramolecular hydrogen bond corona effect. Copyright © 2002 John Wiley & Sons, Ltd.

KEYWORDS: aromaticity; basicity; proton affinity; proton sponges; superbases

INTRODUCTION

The proton affinity (*PA*) and the related basicity are fundamental properties of molecules. They are central to the understanding of proton transfer reactions, which in turn are pivotal in organic chemistry and biochemistry.[1–3] Moreover, the proton is a useful probe of the electronic structure of molecules particularly in studying the electrophilic reactivity of aromatics.[4–7] It is therefore not surprising that much interest and research effort have been devoted to the experimental[6–11] and theoretical[12–17] estimates of *PA*s. Considerable attention has been focused on strong organic bases and the elucidation of their properties, in order to acquire a better understanding of their reactivity.[18–20] The first compound in this category to be prepared was the paradigmatic 1,8-bis(dimethylamino)naphthalene (**DMAN**),[21] which was followed by syntheses of a number of its diamine derivatives. More recently, considerable attention has been shifted to some imines[22] and polyfunctional formamidines,[23] with the intention of extending the existing basicity scale toward superbasic values. Particularly strong organic neutral basis are provided by the Schwesinger proton sponge **SPSG**[24] and **4-phosphazene**[25] (Scheme 1).

The proton affinities of **DMAN, SPSG** and **4-phosphazene** were theoretically estimated to be 245.5, 269.5 and 301.0 kcal mol^{-1}, respectively (1 kcal = 4.184 kJ) (B. Kovačević and Z. B. Maksić, unpublished results). The *t*-Bu group in the last compound was replaced by a CH_3 group in the actual treatment in order to simplify technically highly demanding computations. These strong neutral (super) bases are very important, because unlike anionic bases they require milder reaction conditions while possessing better solubility.[26] Consequently, they have found a wide range of applications in organic syntheses as auxiliary base mediators, often playing a crucial role in such transformations.[27] Having this in mind, we have undertaken comprehensive theoretical investigations, which were able to pinpoint several families of neutral molecules as good candidates for exhibiting high susceptibility towards the proton.[28–31] For this purpose we used a specific strategy, consisting of several steps: (a) identification of an inherently strong basic functional group (imino moiety), (b) judicious selection of appropriate molecular fragments serving as carriers of the functional group of choice (quinonimine, cyclopropenimine), (c) introduction of suitable substituents (NH_2, OCH_3) at the strategic positions,

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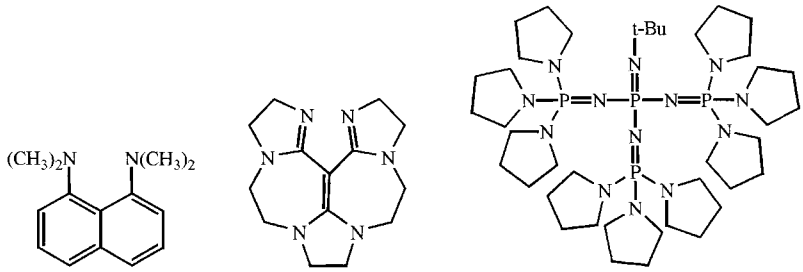


DMAN **SPSG** **4-phosphazene**

Scheme 1

employing the educated guess approach, and finally (d) deliberate exploitation of some special bonding features such as the intramolecular hydrogen bonding corona effect.

The selection of the appropriate molecular skeleton under (b) is of particular importance, since protonation can trigger favorable interactions such as the strong resonance effect as in polyguanides[31] or aromatization of either three- or six-membered olefinic rings such as those in cyclopropenimines and quinonimines,[28–30] respectively. Such effects can dramatically stabilize the conjugate acid, thus contributing to the basicity of the initial neutral base. In this work, we explored molecular systems involving several 2,5-dihydropyrrolimine subunits, which might undergo aromatization in the tandem or domino fashion, triggered by protonation, with the goal of obtaining strong (super)bases exhibiting intrinsic basicities between **DMAN** and **4-phosphazene**. Anticipating forthcoming results, we can say that the aromatic domino effect in five-membered rings is very efficient in propagating the cationic resonance effect along the molecular backbone, induced by proton attack, thus yielding very strong neutral bases. Whereas the latter was the main motivation for the present study, transmission of the information across the system of interlocked rings caused by an event at one end of an extended system (the protonation)—transferred by mobile π-electrons—was an interesting problem *per se*, deserving a closer look.

THEORETICAL

Proton affinities are calculated in the usual way:

$$PA(\mathrm{B}_\alpha) = (\Delta E_{\mathrm{el}})_\alpha - (\Delta ZPVE)_\alpha \qquad (1)$$

where $(\Delta E_{\mathrm{el}})_\alpha = E(\mathrm{B}) - E(\mathrm{B}_\alpha\mathrm{H}^+)$ and $(\Delta ZPVE)_\alpha = ZPVE(\mathrm{B}) - ZPVE(\mathrm{B}_\alpha\mathrm{H}^+)$ are the electronic energies, which include the nuclear repulsion as customary and the zero-point vibrational contributions to the *PA*, respectively. B and $\mathrm{B}_\alpha\mathrm{H}^+$ denote the base in question and its conjugate acid, respectively, and α represents the site of the proton attack. Strictly, the *PA*s are reaction enthalpies. In order to obtain the *PA*s, one should therefore add the thermal adjustment evaluated at 298 K and also corrections due to a loss of three degrees of freedom (of proton) and the presence of the pressure term $p\Delta V$. These corrections are constant and have been implicitly incorporated in ΔE_{el} by a careful choice of the basis set in *ab initio* calculations. The search of the Born–Oppenheimer energy hypersurfaces in our model of choice was performed at the economical Hartree–Fock level, utilizing the 6–31G* basis set. The minima are verified in this approach by vibrational analyses and the corresponding frequencies are subsequently used in deriving the *ZPV* energies.

The final single-point calculations take into account the correlation energy effect at the second order of Møller–Plesset perturbation theory employing the 6–311 + G** basis set. This approach is denoted the MP2/6–311 + G**//HF/6–31G* + ZPVE(HF/6–31G*) model, or more succinctly the MP2 model. Although the MP2 formalism is applicable to relatively large systems, it is not very economical and the larger basis set causes problems in converging the underlying wavefunction. Hence it is gratifying that there is a much simpler and more practical scaled Hartree–Fock ($\mathrm{HF_{sc}}$) model, which exhibits large gains in efficiency and feasibility, with a relatively small sacrifice in accuracy.[32] According to the $\mathrm{HF_{sc}}$ model, the proton affinity is obtained by

$$PA(\mathrm{B})_{\mathrm{N}} = 0.8924\ \Delta E_{\mathrm{el}}(\mathrm{HF/6\text{–}31G^*})_{\mathrm{N}} + 10.4\ (\mathrm{kcal\ mol^{-1}}) \qquad (2)$$

where it is tacitly assumed that the proton is attached to a nitrogen atom. The difference $\Delta\mathrm{E_{el}}(\mathrm{HF/6\text{–}31G^*})_{\mathrm{N}}$ refers to a change in the total molecular energy upon protonation of a nitrogen base under consideration taken with the opposite sign according to the general convention. A fairly constant *ZPVE* contribution to the *PA* is absorbed in the additive constant in Eqn. (2). All calculations were carried out by using the Gaussian 94[33] and GAMESS[34] program packages.

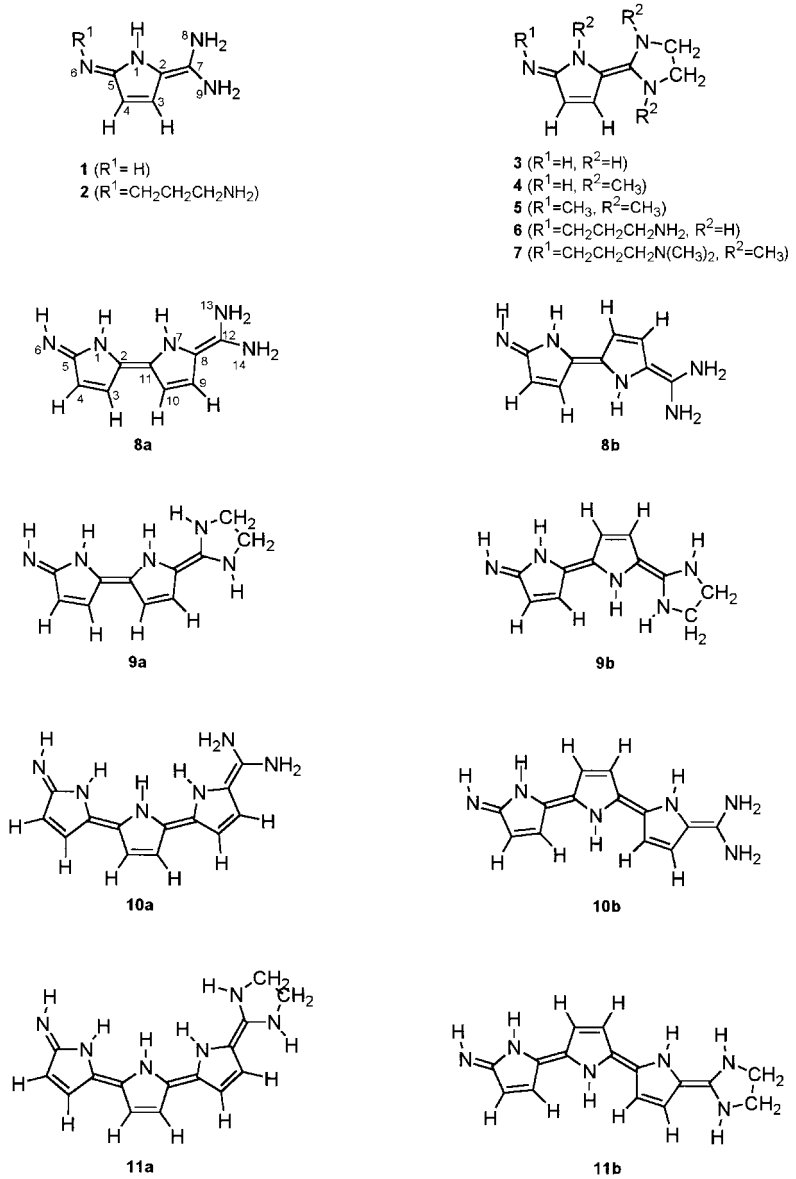


Figure 1. Schematic representation and numbering of atoms of the 2,5-dihydropyrrolimines studied

RESULTS AND DISCUSSION

Energies and proton affinities

We shall first consider the energetic properties of molecules depicted in Fig. 1, focusing on the *PA*. The corresponding data are displayed in Table 1. It should be pointed out that only the protonation at the most basic site (i.e. the imino nitrogen) in these ambident systems is considered, because we are interested solely in the extremal properties. Other protonated positions possess significantly lower *PA*s.

Inspection of the calculated *PA*s shows that all compounds should be more basic in the gas phase than the prototypal **DMAN**. The smallest system **1** already possesses a *PA* as high as 257.0 kcal mol^{-1}. Since compound **1** is small enough for application of the MP2 model to geometry optimization, both MP2 and MP2(fc)/6–311 + G**//MP2(fc)/6–31G* calculations were carried out. The corresponding *PA* values are 258.8 and 258.3 kcal mol^{-1}, respectively. Both values provide good support for the simple HF_{sc} approach, which gave 257.0 kcal mol^{-1}. It is useful to give here a transparent rationalization of its high basicity, since it will allow a better understanding of the forthcoming results. It is now well established that the aromatization of the protonated base amplifies the susceptibility toward the proton attack.[28–30] This is most easily illustrated by Pauling's resonance structures of **1p** (Scheme 2).

The formation of the aromatic sextet within the five-membered ring and accompanying stabilization of the conjugate base are expected, if the resonance effect is

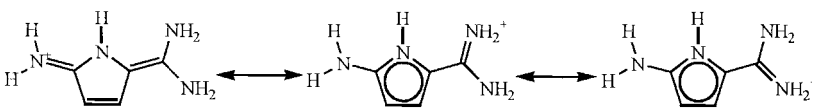
Table 1. Total electronic energies (au) and proton affinities (kcal mol^{-1}) as obtained by the HF/6–31G* and HF_{sc} models, respectively

Molecule	HF/6–31G*	*PA*	Molecule	HF/6–31G*	*PA*
1	−411.74350	—	**2**	−583.86490	—
1p	−412.18388	257.0	**2p**	−584.31853	264.4
3	−488.64497	—	**4**	−605.72002	—
3p	−489.08839	258.7	**4p**	−606.17451	264.9
5	−644.74775	—	**6**	−660.76274	—
5p	−645.20410	266.0	**6p**	−661.22259	267.9
7	−855.88015	—	**8a**	−619.38718	—
7p	−856.35217	274.7	**8ap**	−619.84393	266.2
9a	−696.28400	—	**8b**	−619.38366	—
9ap	−696.74831	270.4	**8bp**	−619.84611	269.4
10a	−827.03332	—	**9b**	−696.27997	—
10ap	−827.50409	274.0	**9bp**	−696.75049	273.9
11a	−903.92739	—	**10b**	−827.02277	—
11ap	−904.40704	279.0	**10bp**	−827.50920	282.8
12	−279.83076	—	**11b**	−903.91938	—
12p	−280.24285	241.2	**11bp**	−904.41360	287.2
13	−487.45590	—	**14**	−695.09874	—
13p	−487.90912	264.2	**14p**	−695.56962	274.1

important. The latter is indeed the case, as evidenced by earlier findings.[31] Note that the delocalization of the peripheral amino nitrogen lone pair electrons is crucial in this respect. It should also be stressed that the resonance in a protonated planar system involves two effects: (a) transfer of the positive charge across the system through the π-electron delocalization and (b) reorganization of the electron density through σ-bonds. The former effect is the well known conjugation, which in turn is much stronger in ionic than in neutral systems. The electron density drift through σ-bonds contributes to a favorable redistribution of atomic charges in order to equalize the electronegativity of atoms within the conjugate acid. The latter is perturbed by the protonation event because the electronegativity of the protonated atom is increased, not to mention the high electronegativity of the proton itself. The latter is reflected in its large total electron density acquired after protonation is completed (0.7 $|e|$). Specifically, alkyl substituents act as pools of the electron density which allow for an effective screening of the positive charge created by the protonation process. Since the σ-channel transfer of the electron density is very important in this respect, we shall classify this mechanism as a relaxation effect. It is noteworthy that the relaxation effect in conjugate acids is similar to that occurring upon inner-shell electron expulsion by x-rays measured by the ESCA technique, which is known to be fairly large.[35] Both mechanisms (a) and (b) lead to appreciable stabilization of the resulting conjugate acids, through reorganization of the electron density distribution. These two effects are intermingled, however, and it is difficult, if not impossible, to delineate them. Consequently, they will be kept together and termed the cationic resonance interaction. However, we shall try to distinguish them in some cases, if one mechanism grossly predominates over the other.

The aromatization of the five-membered rings in conjugate acid **1p** depicted in Scheme 2 will be discussed in some detail in terms of bond distance changes and the accompanying π-bond order variations later on. Here, we shall apply the nucleus independent chemical shift (NICS) approach developed by Schleyer and co-workers,[36,37] which proved useful in considering the aromatic stabilization of annulenes. NICS values are calculated either in the center of a ring or 1 Å above the center corresponding to NICS(0) and NICS(1) indices, respectively. The latter is a somewhat better criterion because NICS measures essentially π-electron delocalization (ring current). Since NICS does not have an absolute meaning, a gauge value is needed, which is provided by that in free benzene. For this purpose we employed the simple and efficient HF/6–31G* model based on gauge invariant (GIAO) atomic orbitals, which for benzene gave the indices NICS(0) = −11.5 and NICS(1) = −12.8.

A brief discussion of the use of the basis sets in the NICS calculations is in place here. Since NICS(1) measures 'the



Scheme 2

Table 2. Schleyer's NICS values for five-membered rings in some selected molecules and their protonated forms[a]

Molecule		NICS(0)	NICS(1)	Molecule		NICS(0)	NICS(1)
1	Ring 1	−3.8	−4.3	**11b**	Ring 1	−4.6	−5.0
1p	Ring 1	−11.6	−10.3		Ring 2	−5.1	−5.4
3	Ring 1	−4.9	−5.4		Ring 3	−4.8	−4.6
3p	Ring 1	−11.8	−10.3	**11bp**	Ring 1	−14.3	−12.4
8a	Ring 1	−4.1	−4.8		Ring 2	−13.3	−11.6
	Ring 2	−4.2	−3.8		Ring 3	−12.0	−11.0
8ap	Ring 1	−12.3	−11.0	**12**	Ring 1	−10.0	−5.0
	Ring 2	−11.3	−9.0	**12p**	Ring 1	−13.0	−8.1
9b	Ring 1	−4.6	−5.3	**13**	Ring 1	−4.8	−5.3
	Ring 2	−4.8	−4.5		Ring 2	−6.4	−3.3
9bp	Ring 1	−13.5	−10.8	**13p**	Ring 1	−12.5	−10.5
	Ring 2	−11.9	−11.1		Ring 2	−13.0	−9.0
10b	Ring 1	−4.9	−4.9	**14**	Ring 1	−4.3	−4.8
	Ring 2	−5.0	−5.2		Ring 2	−4.7	−3.6
	Ring 3	−4.5	−5.1		Ring 3	−6.3	−3.2
10bp	Ring 1	−14.2	−12.7	**14p**	Ring 1	−12.8	−11.9
	Ring 2	−13.2	−11.2		Ring 2	−12.3	−9.4
	Ring 3	−11.7	−11.1		Ring 3	−12.8	−8.9

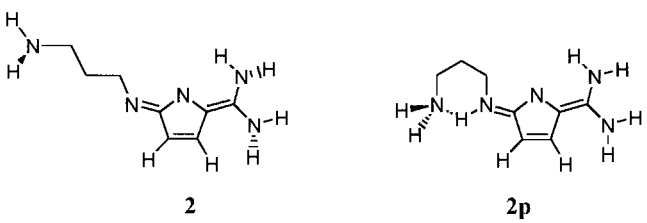
[a] Rings are enumerated starting from the imino nitrogen atom.

magnetic shielding of nothing,' i.e. at a point 1 Å above the plane of a cyclic molecule, which is chosen arbitrarily, it does not have, strictly, a physical meaning as pointed out above. It does have, however, some value as an indicator of the (anti)aromaticity, when this quantity is compared in different rings. In this way we obtain some qualitative information whether the (anti)aromaticity is changed relative to cyclobutadiene and benzene, respectively, and it will be used in this sense here.

Since only relative values have some meaning, we did not compute NICSs employing large basis sets, which are otherwise required for the magnetic properties. It is of interest to compare NICS(1) values of the neutral molecule **1** and its protonated form **1p**. They are −4.3 and −10.3, respectively, which imply relatively low cyclic delocalization in **1**, whereas a considerable aromatic stabilization can be expected in **1p** in view of its NICS(1) value, which is fairly close to that of benzene. It is of interest also to examine NICS values in systems involving two or more sequential rings. They will serve as a guide in establishing the trend of changes in *PA*s. The NICS data given in Table 2 clearly show that the aromatic tandem effect in **8(a,b)p** and **9(a,b)p** and the domino effect in **10ap, 10bp, 11ap** and **11bp** are fairly effective, meaning that the cationic π-electron resonance effect has a long range. It is remarkable that the aromatic spin-off effect is extended over all five-membered olefinic rings. This is the most salient feature of the systems studied, which rationalizes the substantial increase in the *PA* as the number of dihydropyrrolimine rings becomes larger.

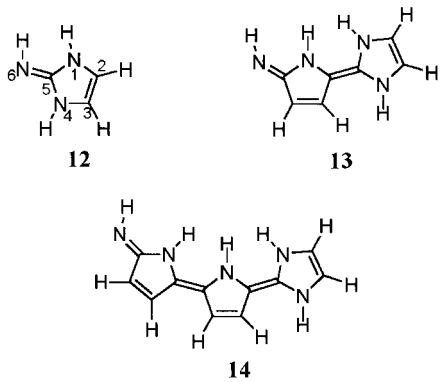
Having identified the basic phenomenon, we shall now focus on some specific characteristics of the systems examined. First we shall examine the corona effect occurring in **2**. Attachment of the side aminopropyl chain at the imino nitrogen leads to a formation of the pseudo-six-membered ring upon the protonation caused by a relatively strong intramolecular hydrogen bond (IMHB). This structural and electronic feature characterizing a very specific IMHB was named the corona or hollow effect,[30] illustrated by Scheme 3.

Comparison of the *PA* values of **1** and **2** shows that the corona effects contributes 7.4 kcal mol^{-1} to the *PA*. Similarly, *PA*(**6**)−*PA*(**3**) and *PA*(**7**)−*PA*(**4**) give increases of 9.2 and 9.8 kcal mol^{-1}, respectively, implying that the intramolecular hydrogen bonding is fairly strong in protonated species. This is not unexpected because (a) the hydrogen atom originating from the incoming proton has the highest positive charge in the conjugate acid and (b) the H-bonding is predominantly Coulombic in nature. Another structural pattern of considerable importance is a distal five-membered ring closure as exemplified by compound **3**. One obtains a small but significant increase in the *PA* by 1.7 kcal mol^{-1}. However, enclosure of distal imino nitrogens into a saturated five-membered ring has important practical consequences, namely, replacement of N—H by N—C bonds precludes the transfer of the proton from amino to imino nitrogen, which could lead to tautomeric forms exhibiting lesser basicity. The remaining hydrogens linked to amino nitrogen atoms can be conveniently substituted by alkyl groups.



2 **2p**

Scheme 3



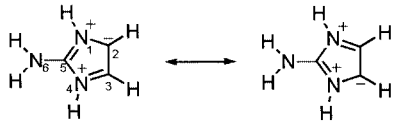
12 **13** **14**

Scheme 4

The next point of interest is the extent of the relaxation effect illustrated here by alkylation of compound **3** yielding derivatives **4** and **5**. It was found by Catalán *et al.*[38] that the permethylation of pyrrazole and imidazole increased their proton affinities by 17 and 14 kcal mol^{-1}, respectively. The corresponding amplification in basicity measured by the proton affinity is given by differences $PA(\mathbf{4})-PA(\mathbf{3})$ and $PA(\mathbf{5})-PA(\mathbf{3})$, which have values of 6.2 and 7.3 kcal mol^{-1}, respectively. Apparently, the alkyl effect considerably increases intrinsic basicity of nitrogen bases. This finding is in accord with our earlier results.[28–31] It is noteworthy that methylation of **6** yielding **7** provides an additional gain in the *PA* of 6.8 kcal mol^{-1}. Hence the resulting proton affinity of **7** is as high as 274.7 kcal mol^{-1}, implying that it is somewhat more basic than Schwesinger proton sponge **2 (SPSG)** in the gas phase.

Inclusion of several five-membered rings leads to substantial amplification of the intrinsic basicity, as indicated by the NICS values. This is evidenced by inspection of the *PA*s along the series **1**, **8b**, **9b**, **10b** and **11b**, i.e. 257.0, 269.4, 273.9, 282.8 and 287.2 kcal mol^{-1}, respectively. It is of interest in this respect to introduce a double bond in the terminal five- membered ring, e.g. in compounds **12–14** (Scheme 4).

The *PA* increases along the family of molecules **12–14** with values of 241.2, 264.2 and 274.1 kcal mol^{-1}, respectively. It is worth mentioning that the MP2(fc)/6–311 + G*//MP2(fc)/6–31G* model yields 240.3 kcal mol^{-1} for the *PA* of **12**. Consequently, it follows that more accurate MP2(fc)/6–31G* geometries have only a marginal influence on the calculated *PA*s in the systems studied. It also appears that inclusion of a terminal double bond increases the *PA*, as evidenced by a comparison of the protonation energies of **13** and **3** and also those of **14** and **9a**. The corresponding values yielding amplification of the *PA* are 5.5 and 3.7 kcal mol^{-1}, respectively. A plausible explanation is provided by the resonance structures depicted in Scheme 5, where the conjugate acid of **12** is considered. These structures, which describe polarization of C—N bonds emanating from the distal C=C double bond, are

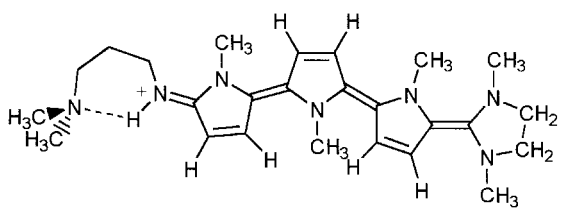


Scheme 5

obviously more important in the protonated form than in the initial base. Note also that an aromatic sextet is formed within the terminal five-membered ring. This conjecture is corroborated by the MO analysis of the π-bond orders (see later).

An additional piece of evidence which supports this interpretation is given by NICS(1) values for the terminal five-membered rings in **12p, 13p** and **14p**, which are −8.1, −9.0 and −8.9, respectively. Other NICS values related to systems **12–14p** presented in Table 2 speak for themselves. Hence, by using the poly-2,5-dihydropyrrolimine framework and employing the hollow and alkyl effects, one can form a ladder of the *PA*s between 241 and 300 kcal mol^{-1}, particularly if judicious selection and positioning of the π-electron donor/acceptor substituents are made. Although most of compounds presented in Fig. 1 are model molecules, a construction of 'true' systems is trivial. For example, let us consider fully methylated compound **11b** supplemented by the dimethylaminopropyl substituent at N-imino position (Scheme 6). The methyl and IMHB corona effect yield $PA(\mathbf{11c}) =$ 302.6 kcal mol^{-1}, as obtained by the HF_{sc} model, thus providing convincing evidence for the claim above.

The substitution of the amino group at the C3 atom in **1** yields $PA(HF_{sc}) = 259.2$ kcal mol^{-1}, thus increasing the *PA* by 2.2 kcal mol^{-1}. Interestingly, if the NH_2 group is attached to the C4 atom in **1**, then the *PA* is reduced by 4.3 kcal mol^{-1}, to 252.7 kcal mol^{-1}. These calculations illustrate well the fact that the right substituent needs to be placed at the proper position in order to ensure a favorable resonance interaction. It is interesting to mention within this context that a double NH_2 substitution at the C3 and C9 carbons in **8a** gives a *PA* value of 271.0 kcal mol^{-1}, implying a substantial increase of 4.8 kcal mol^{-1}. To reiterate, the interplay of aromatization and substituent effects permits the design of a class



11cp

Scheme 6

Table 3. Selected bond distances in some characteristic molecules and their protonated forms, as calculated by the HF/6–31G* model: the corresponding bond indices involve hybrid s-character, Löwdin π-bond orders [π_{bo}(L)], atomic total densities [Q_A(L)] and atomic π-densities [Q_π(L)]

System	Bond	Distance	s-Character	π_{bo}(L)	Atom	Q_A(L)	Q_π(L)	*DP* (%)[a]
1	N1—C2	1.428	32.1–26.0	0.23	N1	−0.36	1.62	22.1
	N1—C5	1.404	33.1–29.2	0.35	C2	0.15	0.81	—
	C2—C3	1.456	33.3–30.9	0.35	C3	−0.20	1.03	—
	C2—C7	1.334	40.5–41.9	0.78	C4	−0.13	0.94	—
	C3—C4	1.330	37.1–36.3	0.87	C5	−0.07	1.15	—
	C4—C5	1.471	30.1–32.9	0.31	N6	−0.48	1.32	0.0
	C5—N6	1.259	37.6–43.0	0.82	C7	0.12	0.92	—
	C7—N8	1.394	28.7–34.5	0.33	N8	−0.55	1.69	28.9
	C7—N9	1.398	29.2–34.3	0.31	N9	−0.54	1.65	27.2
	N6—H	1.005	23.2	—	H(N6)	0.75	—	—
1p	N1—C2	1.408	33.3–26.2	0.30	N1	−0.25	1.57	7.2
	N1—C5	1.344	35.6–28.8	0.49	C2	−0.10	1.23	—
	C2—C3	1.389	37.2–32.6	0.57	C3	−0.07	0.88	—
	C2—C7	1.403	36.6–37.9	0.51	C4	−0.28	1.17	—
	C3—C4	1.382	34.7–33.9	0.65	C5	0.21	0.81	—
	C4—C5	1.398	31.5–38.3	0.55	N6	−0.49	1.75	7.1
	C5—N6	1.344	32.6–37.9	0.45	C7	0.26	0.74	—
	C7—N8	1.334	30.7–38.7	0.45	N8	−0.47	1.64	2.1
	C7—N9	1.329	31.1–39.0	0.47	N9	−0.46	1.64	0.1
	N6—H	0.996	29.1	—	H(N6)	0.68	—	—
12	N1—C2	1.399	34.4–26.2	0.33	N1	−0.31	1.69	0.6
	N1—C5	1.376	34.9–30.6	0.43	N4	−0.29	1.68	0.2
	C2—C3	1.325	38.2–38.1	0.87	N6	−0.58	1.46	—
	C3—N4	1.392	26.5–34.4	0.35	C2	−0.14	1.07	—
	N4—C5	1.370	34.8–28.7	0.43	C3	−0.12	1.05	—
	C5—N6	1.268	40.1–40.1	0.74	C5	0.20	0.81	—
	N6—H	1.002	24.3	—	H(N6)	0.26	—	—
12p	N1—C2	1.400	34.2–25.1	0.36	N1	−0.22	1.59	0.0
	N1—C5	1.326	34.8–32.1	0.56	N4	−0.22	1.59	0.0
	C2—C3	1.326	38.0–38.0	0.86	N6	−0.47	1.75	−0.1
	C3—N4	1.400	25.1–34.2	0.36	C2	−0.09	1.03	—
	N4—C5	1.326	34.8–32.1	0.56	C3	−0.09	1.03	—
	C5—N6	1.327	35.7–38.0	0.50	C5	0.27	0.79	—
	N6—H	0.996	30.9	—	H(N6)	0.34	—	—
8a	N1—C2	1.410	33.2–26.0	0.28	N1	−0.34	1.65	13.3
	N1—C5	1.395	33.7–29.3	0.37	N6	−0.48	1.31	—
	C2—C3	1.458	32.8–30.6	0.34	N7	−0.35	1.57	18.4
	C2—C11	1.333	41.0–40.6	0.78	N13	−0.57	1.72	27.9
	C3—C4	1.330	36.5–36.9	0.87	N14	−0.56	1.22	32.8
	C4—C5	1.474	30.0–32.6	0.30	C2	0.00	1.05	—
	C5—N6	1.259	37.8–42.8	0.81	C3	−0.13	0.95	—
	N7—C8	1.424	32.0–25.7	0.25	C4	−0.19	1.01	—
	N7—C11	1.414	32.2–26.2	0.28	C5	0.15	0.82	—
	C8—C9	1.458	33.2–30.5	0.33	C8	−0.01	1.06	—
	C8—C12	1.328	40.9–41.1	0.81	C9	−0.14	0.95	—
	C9—C10	1.332	36.5–36.8	0.86	C10	−0.19	1.02	—
	C10—C11	1.461	30.4–33.1	0.34	C11	0.04	0.98	—
	C12—N13	1.407	29.4–34.7	0.31	C12	0.07	1.00	—
	C12—N14	1.416	29.4–34.0	0.20	H(N6)	0.29	—	—
	N6—H	1.005	23.3	—	—	—	—	—
8ap	N1—C2	1.397	33.7–26.1	0.33	N1	−0.27	1.54	9.4
	N1—C5	1.360	35.3–27.8	0.43	N6	−0.53	1.72	22.6
	C2—C3	1.364	38.1–33.7	0.65	N7	−0.24	1.54	5.7
	C2—C11	1.431	35.7–36.9	0.39	N13	−0.47	1.63	2.0
	C3—C4	1.413	33.5–32.8	0.53	N14	−0.46	1.66	0.0
	C4—C5	1.369	33.1–40.1	0.64	C2	−0.05	1.14	—
	C5—N6	1.378	31.9–35.4	0.34	C3	−0.12	0.95	—
	N7—C8	1.398	33.2–26.7	0.32	C4	−0.28	1.16	—
	N7—C11	1.351	36.1–26.9	0.48	C5	0.15	0.89	—
	C8—C9	1.389	37.1–32.5	0.56	C8	−0.10	1.21	—
	C8—C12	1.406	36.1–37.9	0.50	C9	−0.10	0.90	—
	C9—C10	1.383	34.9–33.7	0.64	C10	−0.24	1.11	—
	C10—C11	1.397	32.1–36.1	0.56	C11	0.13	0.85	—
	C12—N13	1.333	30.7–38.7	0.46	C12	0.26	0.74	—
	C12—N14	1.328	31.2–39.1	0.47	H(N6)	0.30	—	—
	N6—H	0.999	25.8	—	—	—	—	—

[a] The degree of pyramidalization of nitrogen atoms in degrees is denoted by *DP* (%).

of organic compounds exhibiting closely spaced *PA*s over a wide range of very high values.

Finally, it is noteworthy that isomers **8a**–**11a** are more stable than their counterparts **8b**–**11b** by 2.2, 2.5, 6.6 and 5.0 kcal mol^{-1}, respectively. Consequently, the *PA* of the energetically more favorable isomers is correspondingly lower (Table 1).

Geometries and electron distributions

Selected structural parameters of some characteristic bases and their protonated forms obtained by the HF/6–31G* model are given in Table 3 together with π-bond orders and formal atomic densities as deduced by the Löwdin symmetric orthogonalization procedure.[39] Although the electron density apportioned to atoms has no absolute physical meaning,[40] it is very useful in rationalizing the trend of changes in a family of related molecules caused by protonation. We provide also s-characters of the local hybrid orbitals obtained by the natural bond analysis (NBO)[41] as an index describing the σ part of chemical bonding.

We shall focus first on the changes in bond distances in **1** induced by protonation, because they are paradigmatic for the rest of the systems studied. The data presented in Table 3 show that the alternating double and single bonds in **1p** are considerably lengthened and shortened, respectively, relative to **1** as exemplified by the sequence of bonds N6 = C5—C4 = C3—C2 = C7—N8. This is caused by an obvious tendency of equalization of the π-bond orders. Particularly important is an increase in the π_{bo} index of the N1—C5, C7—N8 and C7—N9 bonds, which are indicative of strong participation of amino lone pairs in the cationic resonance. More specifically, the shortening of the C7—N8 bond in **1p** is as large as 0.086 Å. The lowest π_{bo} (0.30) is found for the N1—C2 bond, since the cationic resonance interaction triggered by protonation at N6 is much better transmitted over alternating double and single bonds than over two consecutive single bonds. In spite of this, the aromatic stabilization of the five-membered ring formally possessing six electrons in **1p** is highly pronounced, as reflected in its NICS(1) value (Table 1). Apparently, even a moderate overlapping along the ring perimeter is sufficient for the aromatic interaction. This is in line with our finding that the non-dynamic correlation of π-electrons in benzene and the artificial localized cyclohexatriene is practically the same.[42] The π-back-bonding of nitrogen lone pairs of the NH_2 groups is followed by their planarization, which is conveniently described by a parameter called degree of pyramidalization [*DP*(%)]:[43]

$$DP(\%) = 360 - \sum_{i=1}^{3} \alpha_i / 0.9 \qquad (3)$$

where α_i represents the three smallest angles merging at the pyramidal apex. The *DP* values of N atoms in **1** (**1p**) for N6, N1, N8 and N9 are 0.0 (7.1), 22.1 (7.2), 28.9 (2.1) and 27.2 (0.1)%, respectively, where values for **1p** are given in parentheses. It is interesting that the largest non-planarity in **1p** is found at the protonated nitrogen, although even in this case it is very small (7.1%). One can say that strong planarization of amino nitrogens is one of the most striking manifestations of protonation

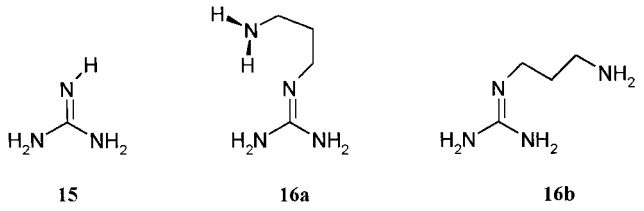
Rehybridization in σ-bond follows changes in π-bond orders. Hence, a decrease in the π-electron density with accompanying bond stretching is connected with an increase in the average p character. The opposite takes place in shortened bonds. It is safe to conclude that the electronic features in the protonated species are governed by the mobile π-electrons.

Examination and comparison of π-bond orders in **12** and **12p** show that they are slightly increased in the latter species along N1—C2 and C3—N4 bonds, whereas the C2—C3 bond exhibits a decrease. Although these changes, induced by protonation, are very small, they are compatible with the resonance picture illustrated by Scheme 4, which provides a rationale for the increased basicity of **12** relative to **1** as discussed earlier.

Changes induced by the protonation of **8a** fit the same pattern (Table 3). The aromatization of the distal five-membered ring is comparable to that in **1p**, as judged by bond distances and the corresponding π-bond orders. The same holds for the resonance of the terminal NH_2 groups, which become almost planar, as found in the archetypal guanidine system.[31,44,45] Therefore, it appears that the resonance effect is very efficiently spread over the whole system. This is also found in extended π-systems **10ap** and **11ap**. It follows as a logical consequence that larger extended systems involving 2,5-dihydropyrrolimine subunits would act as even more powerful bases and that they would perhaps exhibit conductive properties triggered by protonation. Therefore, the preparation of such systems seems to be worthwhile.

CONCLUSION

It has been shown that the poly-2,5-dihydropyrrolimines represent a family of compounds which exhibits high basicities. The origin of their strongly basic behavior is identified as the aromatic stabilization of the first five-membered olefinic ring upon protonation of the imino nitrogen atom. The aromatization within the conjugate acid is then spread over the system of sequential 2,5-dihydropyrrolimine rings in a domino fashion. Moreover, deliberate choice of substituents and their attachment at strategic positions can substantially increase the *PA* of studied compounds, reaching values well above 300 kcal mol^{-1}. A typical example of such structural groupings serving this purpose is given by alkyl groups



15 16a 16b

Scheme 7

such as CH_3, CH_2CH_3 and $C(CH_3)_3$, which would increase the stability of the resulting conjugate acids through the relaxation effect, providing some protection of the double bonds at the same time. Other 'good' substituent groups enhancing the basicity are provided by NH_2 and $N(CH_3)_2$. Formation of the intramolecular hydrogen bond in a corona fashion around the protonation center should also be helpful in this respect. The question of whether the corona effect is effective in solvents is an important one. It should be recalled that neutral organic (super)bases are tailored to be used in organic solvents, which do not form strong intermolecular hydrogen bonds with a solvated base. Consequently, the imino group is not impeded by intermolecular hydrogen bonds with solvent molecules and one can intuitively conclude that the IMHB corona effect should be operative. We shall illustrate this conjecture by calculations of the *PA* values of guanidine (**15**) and its aminopropyl derivative **16a** (Scheme 7) in aprotic solvent such as CH_3CN.

Recently we have shown that the solvent effect of neutral bases in acetonitrile[46] are well described by the iterative (isodensity) Polarized Continuum Model.[47,48] It was found that the *PA* and the accompanying basicity in acetonitrile are determined essentially by an interplay between the intrinsic *PA* in the gas phase and the size of the base in question. The latter factor is easily rationalized by taking into account the fact that the positive charge in the corresponding conjugate base is distributed over all atoms, which is a general characteristic of the relaxation effect in the final state. The more atoms (and the larger molecular surface), the less positive is the charge density on the peripheral atoms (i.e. hydrogens) and concomitantly weaker polarization of the solvent continuum. These features will help in interpreting the *PA*s of **15, 16a** and **16b**. The gas-phase $PA(\mathrm{MP2})_{\mathrm{gph}}$ values for **15** and **16a** are 233.7 and 249.6 kcal mol^{-1}, respectively, where the subscript gph represents gas phase. The aminopropyl amplifies the *PA* by 15.9 kcal mol^{-1}. However, 10.8 kcal mol^{-1} of the latter amount can be ascribed to the IMHB corona effect and the rest (5.1 kcal mol^{-1}) reflects the relaxation effect of the aminopropyl tail as evidenced by the $PA(\mathrm{MP2})_{\mathrm{gph}}$ of the **16b** zig-zag conformation of 238.8 kcal mol^{-1}. The increase in the *PA* in acetonitrile is much smaller, as given by the difference $PA(\mathbf{16a})_{\mathrm{actn}} - PA(\mathbf{15})_{\mathrm{actn}} = 293.7 - 290.4 = 3.3$ kcal mol^{-1}. Nevertheless, this leads to an increase in the pK_a value of 1.6 according to the equation[46]

$$\mathrm{p}K_a = 0.4953\ PA_{\mathrm{actn}} - 119.7 \qquad (4)$$

It is interesting to note in passing the value $PA(\mathbf{16b})_{\mathrm{actn}} = 290.8$ kcal mol^{-1}, implying that the size effect (of the aminopropyl side-chain) almost cancels the increase in the inherent basicity of the aminopropyl derivative of guanidine relative to the parent guanidine in acetonitrile. It is worth of pointing out that the high basicity of the considered poly-2,5-dihydropyrrolimines is rationalized in terms of the aromatic domino effect, which implies a dominant influence of the final state polarization effect.[49] In compounds where the initial state or inductive effects are predominant, there is a good correlation between the ESCA chemical shifts of nitrogen atom to be protonated and the *PA*s.[50] In general, however, the *PA*s are given by an interplay of the initial and final state effects, as we have shown recently.[51]

Finally, it is important to stress that the judicious selection of substituents possessing various electron donor/acceptor properties allows the design of bases exhibiting closely spaced *PA* values, which is a valuable feature for both acid–base chemistry and experimental measurements employing the bracketing technique. It is safe to conclude that the fine tuning enabled by substituents will provide a catalogue of strong neutral organic (super)bases with *PA* values in the range 200–300 kcal mol^{-1}. Finally, the amazing ability and ease with which poly-2,5-dihydropyrrolimines transmit information triggered by protonation along the extended π-system should be strongly pointed out.

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