# Relationships between basicity, structure, chemical shift and the charge distribution in resonance-stabilized iminoamines†

**Siân T. Howard,* James A. Platts and Michael P. Coogan**

*Department of Chemistry, Cardiff University, Cardiff, Wales, UK CF10 3TB.*
*E-mail: howardst@cf.ac.uk*

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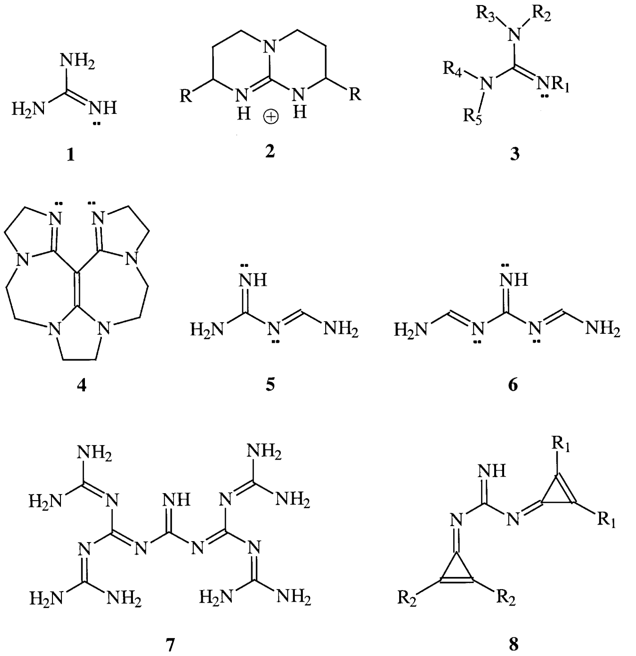
Taking formamidine (gas phase proton affinity ≈950 kJ mol$^{-1}$) and guanidine (gas phase proton affintiy ≈990 kJ mol$^{-1}$) as the prototype iminoamines with resonance-stabilized cations, similar non-cyclic analogs based on a conjugated carbon atom backbone are studied computationally. A simple model of the charge delocalization is developed which predicts theoretical maximum gas-phase proton affinties (PAs) of ≈1114 kJ mol$^{-1}$ (unbranched), 1154 kJ mol$^{-1}$ (singly-branched) and 1209 kJ mol$^{-1}$ (doubly-branched) for such systems. It is also shown that the $^1$H and $^{15}$N chemical shifts of the protons and nitrogens in the imine functions correlate both with basicity and with atoms-in-molecules multipole moments. The properties of these and related compounds are discussed in the context of proton sponges or superbases.

## Introduction

Guanidine **1** (Scheme 1) and its derivatives are important compounds from several different perspectives. It is a substructure in various molecules of biological significance,[1] and the protonated cations form hydrogen-bond mediated structures with *e.g.* phosphate and carboxylate. The guanidine motif is also frequently employed in designing cations such as **2** for anion recognition.[2] Finally, as a highly basic compound it is of interest in the context of proton sponges[3] (organic super-bases) where it can be considered the prototype resonance-stabilized super-basic compound.[4,5] Highly-basic, cyclic amidines and vinamidines such as **3** and **4** have been synthesized which exploit the cation resonance-stabilization mechanism exemplified by guanidine.[6,7] More recently, an extensive synthetic programme has been undertaken by Isobe *et al.* to prepare chiral superbases based on the guanidine motif, with a view to applications in asymmetric synthesis.[8–10] The prototype unbranched amidine formamidine $H_2N–CH=NH$ is known,[11] as are the analogous extended conjugated chain aminines $H_2N–(CH=CH)_n–CH=NH$ $n = 1$ and 3.[11,12] Formamidine is not particularly basic, but it will be shown in this work that extending the conjugated carbon chain backbone has a very marked effect on the gas-phase basicity.



**Scheme 1**

Quantum chemical interest in designing novel superbases based on the guanidine motif was instigated by Gready *et al.*[13,14] They carried out an *ab initio* study (HF/STO-3G and HF/3-21G) for what they termed the 'singly-extended' and 'doubly-extended' guanidine series (see *e.g.* **5**, **6**) predicting significant enhancements of gas-phase proton affinity. Recently, similar ideas were presented at the MP2 level of theory by Maksić and Kovačević,[15] who coined a general term for such compounds as 'polyguanidines'. They demonstrated the saturation of gas-phase PA for linear-chain polyguanidines with increasing chain length, tending towards a limit of ≈1063 kJ mol$^{-1}$. They went on to design exceptionally basic compounds such as a doubly-bifurcated heptaguanidine **7** and also cyclopropenimine-substituted polyguanidines,[16] such as **8**.

The purpose of the present study is to focus on another class of potential iminoamine superbase which exhibits resonance-stabilization of the protonated cation. We shall use the generic term 'iminoamine' because, unlike the compounds proposed by Gready *et al.*, they do not (in general) contain an amidine or guanidine motif, although the simplest unbranched example formamidine $H_2N–CH=NH$ is indeed an amidine, and the simplest singly-branched example is guanidine **1**. The key difference between polyguanidines and the iminoamine compounds studied here (see Scheme 2) is that they are built from a conjugated carbon backbone, with nitrogen-containing groups (one imine and one or more amine) removed to the extremeties of the molecule. Since an unsaturated carbon chain transmits conjugation differently to an alternate =N–C=N–C= structure we might anticipate a different relationship between basicity and chain length(s). Furthermore, such compounds could be expected to exhibit quite different solubility behaviour (*i.e.*

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† Electronic supplementary information (ESI) available: energies and N · · · N distances in geometry-optimised iminoamine bases. See http://www.rsc.org/suppdata/p2/b2/b200899h/

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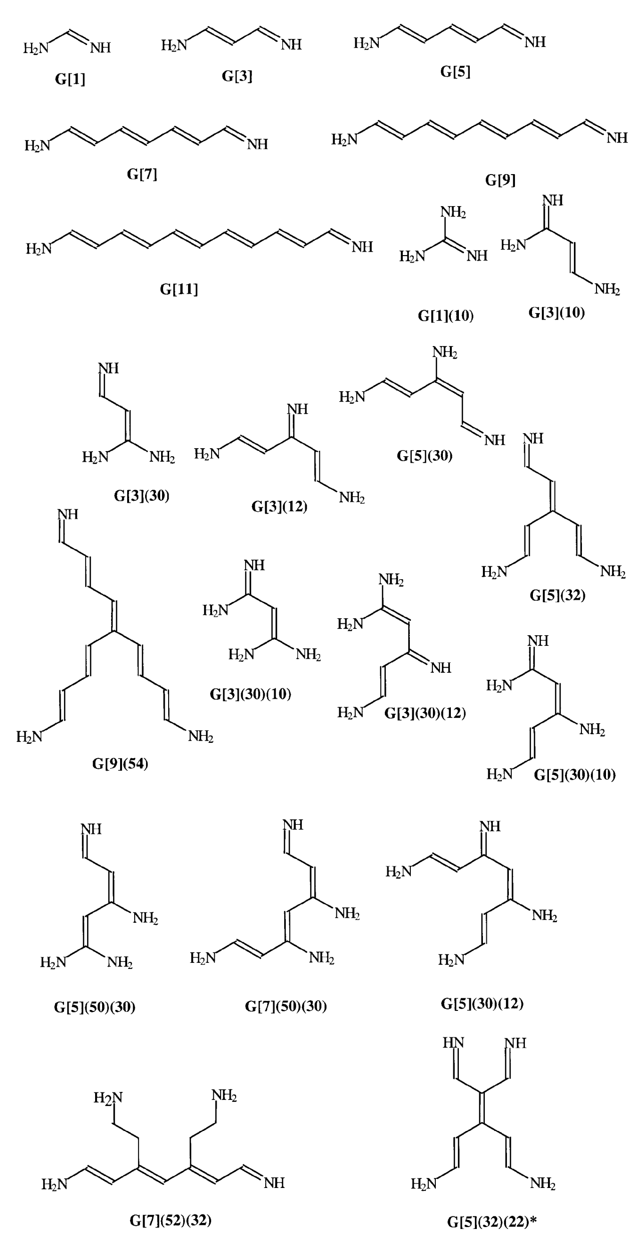


**Scheme 2**

more soluble in apolar solvents) than the polyguanidines proposed in previous studies, thus potentially extending the range of environments in which organic superbases can be employed.

Although all conformers of all compounds have been established as true minimum energy conformations using harmonic frequency calculations, it should be recognized that alternative stable conformers may exist, especially for some of the larger compounds. In particular, we might expect intramolecularly hydrogen-bonded conformers with $[R_1\text{–}NH_2\cdots H_2N\text{–}R_2]^+$ interactions in some of the more extended and flexible species. This latter possibility is discussed later in the paper, with the specific example of a diimine designed to utilize this intramolecular hydrogen bond mechanism to further enhance the basicity. However, the general aim is to establish a basicity–structure design principle for this novel class of compounds, and this does not require finding the lowest energy conformer in every case.

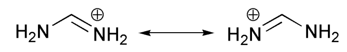
## Computational methods, notation and theory

Hartree–Fock geometry optimizations employed 3-21G[17] and 6-31G** (6d) basis sets[18] in the program GAMESS-UK[19] running on a Silicon Graphics Origin 2000. The molecules were generally optimized without symmetry constraints ($C_1$) at the 3-21G level; in cases where the species is symmetrized during optimization, this higher point group was applied for optimizations with larger basis sets. Harmonic frequency calculations were undertaken for *all* optimized species at the HF/3-21G level, in order to establish that each was at a potential energy minimum, and also to obtain estimates of the vibrational energy at room temperature. Full structural details of all compounds may be obtained from the corresponding author on request.

Scheme 2 shows the unprotonated version of each compound studied, labelled with our own shorthand notation defined as follows. The ‘G’ which begins each label signifies ‘guanidine-type’ since this is the most well-known compound of this category. Then follows in square brackets the number of carbon atoms from the imine function to the end of the longest (primary) chain, G[1] or formamidine being the simplest (unbranched) compound. Singly-branched compounds are then denoted by two numbers in parentheses, which denote the branching point and length (numbers of carbon atoms) of the secondary chain. Thus in this notation guanidine is denoted by G[1](10). Doubly-branched bases naturally require a second pair of numbers in parentheses, giving the same imformation for the tertiary chain. This notation is reasonably compact, and it treats all such iminoamine bases in a common manner, regardless of the number of branches. It should also be apparent from an inspection of Scheme 2 that, for optimal resonance behaviour (in the protonated cation), only odd-numbered branching points should be present.

In order to approximately include the effects of electron correlation in the calculated proton affinities, B3LYP/6-31+G** single point calculations were carried out on all optimized structures of the HF/6-31G** geometries using GAUSSIAN98/DFT[20] running on a 16-processor Compaq Alpha Workstation at the Rutherford-Appleton Laboratories, Chilton. Although the effects of basis set superposition errors on the PA’s have not been included, our previous study[3] of superbases at an identical level of theory (B3LYP/6-31+G**//HF/6-31G**) established that this lowers the PA by 1–3 kJ mol$^{-1}$.

In searching for a simple model to rationalize the data, it was realized that the gas-phase basicity of such iminoamines can be analyzed quite simply, regardless of the ‘dimensionality’ or number of amine branches in a particular compound. Let us assume that the protonated species is stabilized by resonance between two purely ionic wavefunctions (in the classisal valence-bond sense) with negligible contributions from covalent structures, *e.g.* eqn. (1).


(1)

Let us denote the PA of a simple mono-imine such as $H_2C{=}NH_2$, which cannot be stabilized by the same resonance mechanism on protonation, as $PA_1$. As is well known, the effect of resonance in the case of protonated G[1] stabilizes the cation such that its PA will be greater than $PA_1$ by some amount δ. However, the cation is also inevitably *destabilized* by an electrostatic interaction between the two terminal $\text{–}NH_2$ groups, each carrying a localized charge of +0.5 electrons. In the crudest approximation, this repulsive energy might be parametrized (in atomic units) as $-0.5^2/r(N\cdots N)^+$ where $r(N\cdots N)^+$ is the separation in bohrs between the terminal $\text{–}NH_2$ groups in the cation. Whilst this might be a rather poor approximation for G[1], as the chain grows in length we can imagine that this will improve. Thus the PA for the unbranched series, with an asymptotic limit $PA_1 + \delta = a$ as $r(N\cdots N)^+ \longrightarrow \infty$, is given by

$$PA(r(N\cdots N)^+) = a - 1/4r(N\cdots N)^+ \text{ (atomic units)} \quad (2)$$

**Table 1** Gas phase properties[a] of unbranched iminoamines HN=CH(–CH=CH)$_n$–NH$_2$ and additional compounds

|  | δ($^1$H) (imine) (ppm)[b] | δ($^{15}$N) (imine) (ppm)[c] | δ($^{15}$N) (amine) (ppm)[c] | PA/kJ mol$^{-1}$ | $r$(N···N)/Å[d] | $r$(N···N)$^+$/Å[e] | $p$/debye |
|---|---|---|---|---|---|---|---|
| H$_2$C=NH | 11.1 | 329.4 | — | 867.1 | 1.272 | 1.279 | 2.2 |
| G[1] | 6.9 | 195.1 | 59.2 | 950.0 | 2.316 | 2.335 | 3.0 |
| G[3] | 8.8 | 268.1 | 46.5 | 1019.8 | 4.826 | 5.055 | 4.7 |
| G[5] | 9.3 | 284.0 | 45.8 | 1045.9 | 7.311 | 7.924 | 6.1 |
| G[7] | 9.6 | 290.4 | 47.5 | 1062.5 | 9.792 | 9.768 | 7.4 |
| G[9] | 9.7 | 294.1 | 46.0 | 1075.0 | 12.270 | 12.239 | 8.3 |
| G[11] | 9.8 | 295.3 | 47.5 | 1084.1 | 14.746 | 14.708 | 9.3 |
| HN=CH–N=CH–NH$_2$ | 8.7 | 250.4 | 63.1 | 995.6 | 4.680 | 4.585 | 6.0 |

[a] At the B3LYP/6-31+G** level (PA's also include scaled HF/3-21G vibrational energy corrections at 298 K using a factor of 0.893[34]). [b] Relative to the absolute isotropic magnetic shieldings of $^1$H and $^{13}$C in SiMe$_4$ at the same level of theory (B3LYP/6-31+G**), which are 31.5 and 187.5 ppm, respectively. [c] Relative to the absolute isotropic magnetic shielding of $^{15}$N in liquid ammonia at 25 °C of 244.6 ppm.[25] [d] Internuclear distance for the nitrogens of the unprotonated iminoamine. [e] Internuclear distance for the nitrogens of the protonated cation.

**Table 2** Gas phase properties of single-branch iminoamines

|  | δ($^1$H) (imine) (ppm)[b] | δ($^{15}$N) (imine) (ppm)[c] | δ($^{15}$N) (amine) (ppm)[c] | PA/kJ mol$^{-1}$ | $r$(N···N)$^+$/Å[d] | $p$/debye |
|---|---|---|---|---|---|---|
| **7** G[1](10) (Guanidine) | 5.2 | 153.0 | 63.8 | 987.7 | 2.316 | 3.0 |
| **8** G[3](10) | 6.5 | 201.2 | 49.8 | 1042.3 | 3.780 | 3.9 |
| **9** G[3](30) | 8.5 | 256.8 | 41.9 | 1053.3 | 3.780 | 5.2 |
| **10** G[3](12) | 8.6 | 257.7 | 43.8 | 1083.4 | 5.165 | 5.2 |
| **11** G[5](30) | 8.7 | 262.1 | 46.7 | 1080.4 | 5.165 | 6.9 |
| **12** G[5](32) | 9.1 | 277.7 | 46.7 | 1092.5 | 6.452 | 7.1 |
| **13** G[9](54) | 9.2 | 282.4 | 46.4 | 1117.7 | 10.716 | 8.8 |

[a,b,c] See legends of Table 1. [d] The average of the N···N distances in the protonated cation.

**Table 3** Gas phase properties of double-branch iminoamines

|  | δ($^1$H) (imine) (ppm)[b] | δ($^{15}$N) (imine) (ppm)[c] | δ($^{15}$N) (amine) (ppm)[c] | PA/kJ mol$^{-1}$ | $r$(N···N)$^+$/Å[d] | $p$/debye |
|---|---|---|---|---|---|---|
| **14** G[3](30)(10) (cation $C_2$) | 6.8 | 208.4 | 50.4 | 1053.1 | 3.484 | 4.4 |
| **15** G[5](30)(10) | 6.3 | 199.0 | 52.7 | 1088.0 | 4.512 | 5.9 |
| **16** G[5](50)(30) | 8.4 | 255.8 | 49.1 | 1095.5 | 4.512 | 6.4 |
| **17** G[3](30)(12) | 8.1 | 263.4 | 45.2 | 1105.1 | 4.512 | 4.6 |
| **18** G[7](50)(30) (cation $C_2$) | 8.6 | 263.7 | 46.8 | 1106.8 | 5.402 | 4.4 |
| **19** G[5](30)(12) (cation $C_2$) | 8.5 | 261.5 | 45.2 | 1122.7 | 5.402 | 6.0 |
| **20** G[7](52)(32) (cation $C_2$) | 9.0 | 269.9 | 43.4 | 1130.6 | 7.276 | 7.6 |
| **21** (neutral $C_2$) | — | — | — | 1146.5 | 5.516 | 7.3 |

[a,b,c] See legends of Table 1. [d] The average of the N···N distances in the protonated cation.

(note that 1 atomic unit of energy ≈ 2625.5 kJ mol$^{-1}$ and 1 bohr ≈ 0.5292 Å).

This simple analysis isn't limited to the unbranched series: each of the three –NH$_2$ groups of the (protonated) singly-branched iminoamines such as guanidine will carry a charge of approximately +0.33 (for non $C_3$-symmetric examples in fact the charges will differ) and there will be three repulsive interactions between them. However, the asymptotic PA for singly-branched iminoamines should be higher than that of the unbranched case, since more stabilization energy is available corresponding to resonance between three canonical forms as compared with just two. It is therefore a simple step to parametrize the PA for iminoamines bearing $n$ nitrogen atoms:

$$\mathrm{PA}\ (n,r(\mathrm{N}\cdots\mathrm{N})^+) = a(n) - \tfrac{1}{2}n(n-1)q^2/r(\mathrm{N}\cdots\mathrm{N})^+ \quad (3)$$

Here $a(n)$ is the PA of a hypothetical iminoamine with $n$ nitrogens all infinitely separated; $q$ is a *mean* effective charge assigned to the terminal –NH$_2^{\delta+}$ groups in the protonated cation; $r$(N···N)$^+$ is the *mean* N···N distance in the cation; and $n(n - 1)/2$ is the number of repulsive interactions between amine groups in the cation bearing $n$ amino groups. In fact, it is clear from the preceding analysis that we expect $q \approx 1/n$; but by retaining it as a fit parameter, we can test the above hypothesis that the cation positive charge is effectively localized on the terminal –NH$_2$ groups.

Given the dual interest in using NMR as a tool for identifying iminoamine species in solution and the possibility of using chemical shift as a basicity probe, it was decided to study the $^1$H and $^{15}$N chemical shifts of the unprotonated species using the GIAO method.[21] Since such properties are quite sensitive to structure, it was decided to reoptimize all species at the B3LYP/6-31+G** level, and then carry out the chemical shift property calculations at this same level. In this way we are also able to study the influence of the HF approximation on the calculated structures and basicities. Finally, as an additional tool for interpreting the charge distribution in selected compounds we have employed the atoms-in-molecules algorithm as implemented in GAUSSIAN98 to compute atomic multipole moments and Ángyán bond orders.[22,23]

## Results

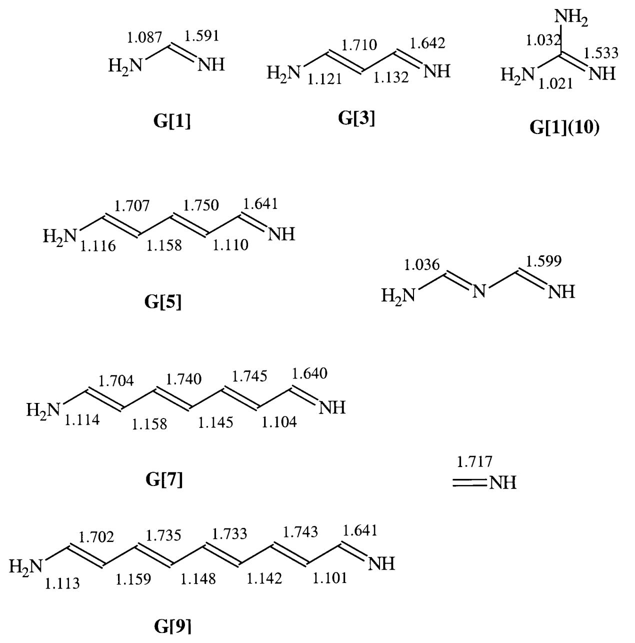
### Structures

Protonation of the imine function to produce –NH$_2^{\delta+}$ naturally results in several of the simplest single-branch and double-branch bases having identical (protonated) structures, and therefore identical values of $r$(N···N)$^+$, as is evident on inspection of Tables 1–3. The N–C bonds in the cations lie between 1.31 Å < $r$(N–C) < 1.35 Å, *i.e.* between typical values for single and double-bonds, as could be expected. Within this range, there is a general trend towards longer N–C bonds for the more extended cations: for example, the (protonated) $C_3$-symmetric series G[1](10), G[5](32) and G[9](54) have N–C bond lengths of 1.337, 1.344 and 1.349 Å respectively.

There is evidence for increased resonance (less localization of electrons in alternant single and double bonds) in the *unprotonated* iminoamine bases, when one looks at the length of the imino function's N=C bond: it has the value of 1.281 Å in G[1]; increases to 1.288 Å in G[3]–G[11] and is still longer in all other species, reaching a maximum value of 1.302 Å in G[5](30)(12). Optimized $H_2C$=NH has a bond length of 1.272 Å at the same level of theory, *i.e.* the most localised double bond. These observations all suggest, in a valence-bond picture, that less-favoured canonical forms with N–C single bonds replacing a purely localized N=C bond are slightly stabilized in the more extended iminoamines, although the effect is small.

## Bond orders

The aforementioned conclusions regarding N–C conjugation are confirmed by the bond orders illustrated in Scheme 3.



Scheme 3

$H_2C$=NH has the highest C–N bond order. The imine and amine C–N bond orders of the unbranched iminoamine series G[1]–G[9] converge to values of 1.113 and 1.641, respectively, with increasing chain length. There are clear patterns of localization–delocalization on comparing the series G[1]–G[9] with guanidine and $H_2N$–C=N–C=NH. Amine bonds adjacent to C=C have lower bond orders than those adjacent to C=N. However, imine bonds adjacent to C=C have higher bond orders than those adjacent to C–N. Thus it could be argued that neither iminoamines nor polyguanidines have the 'upper-hand' in terms of more effective charge delocalization, since one favours delocalization of electrons in the imine bonds, whereas the other favours amine bonds.

## Structure–basicity relationships

The first 6 compounds illustrated in Scheme 2 represent the unbranched ('linear') iminoamine series. The gas-phase PA's reported in Table 1 (and plotted in Fig. 1) show the expected increase with chain length with the 'saturation' effect evident even for just six compounds. A non-linear least-squares fit of the data for unbranched iminoamines in Table 1 using eqn. (3) with $n$ = 2 and $r(\text{N}\cdots\text{N})^+$ equal to the exact N···N separations in the cations finds that the data is well-described by

$$\text{PA} = 0.42447 - 0.35533/r(\text{N}\cdots\text{N})^+ \text{ (atomic units)} \quad (4)$$

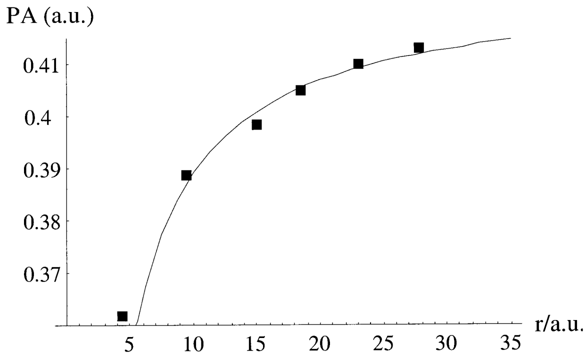


**Fig. 1** Relationship between gas-phase proton affinity and the N···N separation (in the protonated base) for unbranched iminoamine bases. Note that 1 atomic unit of energy = 2625.5 kJ mol$^{-1}$ and 1 atomic unit of distance = 0.5292 Å. Correlation coefficient $R^2$ = 0.978.

The solid line in Fig. 1 represents the fitted curve. The equation above predicts a maximum achievable gas-phase PA for such unbranched iminoamines to be $\approx$1114 kJ mol$^{-1}$. We can also derive an effective charge for the cation terminal –$NH_2$ groups from this fitted equation as $q = \sqrt{(0.35533)}$ which yields +0.60, quite close to the expected value of +0.5 for a unit positive charge shared equally at both ends of the cations.

We turn now to the seven singly-branched ($n$ = 3) compounds G[1](10) through to G[9](54), guanidine being the simplest compound of this type. The two most basic compounds studied are those which, like guanidine, form $C_3$-symmetric cations on protonation: G[5](32) and G[9](54). Since even G[9](54) has a PA lower than the predicted asymptotic PA limit for the unbranced iminoamine series this suggests that, in absolute basicity terms alone, there isn't much to be gained by using singly-branched iminoamines compared to their unbranched counterparts. A least-squares fit of the basicity and mean $r(\text{N}\cdots\text{N})^+$ data in Table 2 (there are now three N···N distances in each cation which are not in general equal) gives the following relationship

$$\text{PA} = 0.43960 - 0.28034/r(\text{N}\cdots\text{N})^+ \text{ (atomic units)} \quad (5)$$

The solid line in Fig. 2 represents the fitted curve. Thus eqn. (4) predicts the maximum achievable gas-phase PA for such a base is around 1154 kJ mol$^{-1}$, with an effective charge

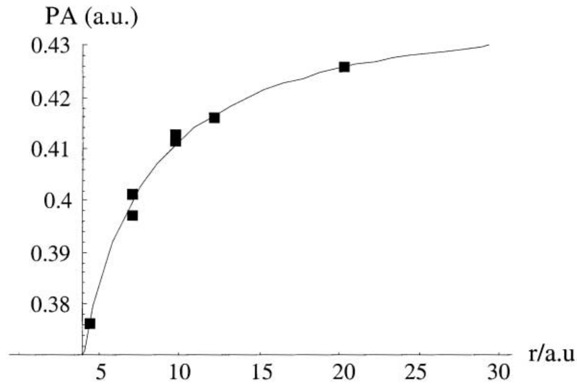


**Fig. 2** Relationship between gas-phase proton affinity and mean N···N separation (in the protonated base) for singly-branched iminoamine bases. Correlation coefficient $R^2$ = 0.990.

**Table 4** Atoms-in-molecules properties of selected compounds

| | Nitrogen of imine function | | | Hydrogen of imine function | | |
|---|---|---|---|---|---|---|
| | $q$/e | $\|p\|$/e bohr | $Q$/e bohr$^{2\,a}$ | $q$/e | $\|p\|$/e bohr | $Q$/e bohr$^{2\,a}$ |
| HN=CH$_2$ | −1.184 | 0.364 | −2.97 | +0.347 | 0.179 | −0.22 |
| G[1] | −1.250 | 0.265 | −4.83 | +0.350 | 0.183 | −0.18 |
| G[3] | −1.204 | 0.288 | −4.08 | +0.334 | 0.188 | −0.21 |
| G[5] | −1.195 | 0.291 | −3.88 | +0.335 | 0.188 | −0.21 |
| G[7] | −1.190 | 0.291 | −3.80 | +0.336 | 0.187 | −0.21 |
| G[9] | −1.188 | 0.291 | −3.75 | +0.338 | 0.187 | −0.20 |
| Guanidine | −1.239 | 0.257 | −5.37 | +0.332 | 0.192 | −0.20 |
| HN=C–N=CH–NH$_2$ | −1.215 | 0.322 | −3.57 | +0.353 | 0.183 | −0.21 |

[a] Traceless tensor definition of atomic quadrupole is used, *i.e.* $Q = 2\langle z^2\rangle - \langle x^2\rangle - \langle y^2\rangle$.

$q \approx +0.31$, quite close to the theoretical value of $\frac{1}{3}$ for the positive charge being localized on and equally shared by the three –$NH_2{}^{\delta+}$ groups.

Finally, Table 3 lists basicities and structural data for seven doubly-branched guanidines, from the simplest G[3](30)(10) to G[7](52)(32). Again, only the two largest compounds studied can compete with the maximum achievable basicity from a very long unbranched iminoamine. However, the maximum achievable basicity for such doubly-branched compounds as predicted by

$$PA = 0.46053 - 0.375781/r(N\cdots N)^+ \text{ (atomic units)} \quad (6)$$

does predict a maximum achievable gas-phase PA of ≈1209 kJ mol$^{-1}$, now considerably in excess of the corresponding value for unbranched compounds. The solid line in Fig. 3 represents the fitted curve. The effective charge $q$ derived from the fit of +0.250 is now identical to the 'ideal' model value of +¼.

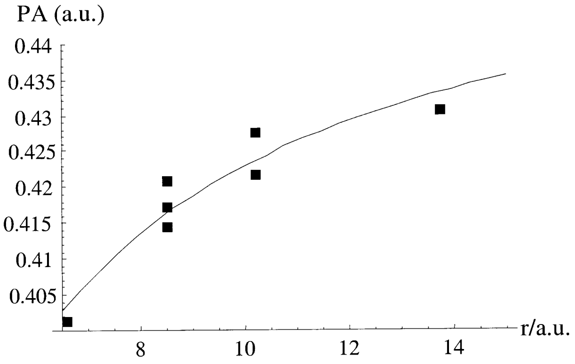


**Fig. 3** Relationship between gas-phase proton affinity and mean N···N separation (in the protonated base) for doubly-branched iminoamine bases. Correlation coefficient $R^2 = 0.899$.

### $^{15}N$ and $^1H$ chemical shifts

Little attention appears to have been paid previously, either experimentally or theoretically, to $^{15}N$ or $^1H$ trends in chemical shifts for (unprotonated) guanidine-type superbases. However, it has been noted that the $^{13}C$ chemical shift of carbon in guanidine[24] can be used to characterize the protonation state; similar observations pertain to the guanidine sub-unit in glycoamidines.[25] Inspection of the data for unbranched iminoamines in Table 1 reveals clear correlations between GIAO-predicted $^1H$ and $^{15}N$ chemical shifts and basicity for the unbranched iminoamine bases, with less-shielded imine nitrogen and hydrogen atoms linked to a higher basicity.

Table 4 reports the atoms-in-molecules multipole moments of the imine function nitrogen and hydrogen atoms for selected molecules calculated at the B3LYP/6-31+G(d,p) level. The values for the unbranched iminoamine series G[1] to G[9] reveal trends which correlate with the $^{15}N$ chemical shift data: specifically, increasing positive charge, increasing dipolar polarization and decreasing quadrupolar polarization correspond to an increasingly less-shielded nitrogen nucleus. In fact, within the unbranched iminoamine series there is an excellent (linear) correlation between imine atomic charge and the chemical shift of the same atom. Such linear or near-linear correlations of atomic partial charge with GIAO-calculated chemical shifts have been noted previously on a number of occasions,[26–31] and have an obvious interpretation. The correlations with higher atoms-in-molecules multipole moments are not quite so simple to interpret, but in the case of the dipole moments at least, we can offer an explanation. Fig. 4 indicates the orientation of the dipole moments of the imine nitrogen atoms in two of the simplest compounds. It can be seen that the positive pole of the dipole, corresponding to enhanced charge density (more shielding), lies approximately in the imine lone pair area. The effect of this dipolar polarization of the charge distrubution is to 'shift' charge from the negative to the positive pole, causing the charge centroid of the atom to no longer be nuclear-centred but shifted somewhat in the direction of the positive pole (evidently the lone pair direction, in this case). Thus the higher the magnitude of the dipole, the further from the nucleus the charge centroid is located, and thus there is less charge density available for shielding at the nuclear position.

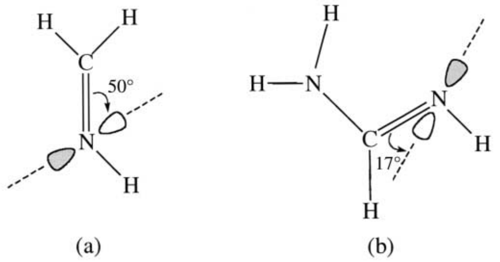


**Fig. 4** Schematic depiction of the atoms-in-molecules imine nitrogen dipole moment orientation in (a) $CH_2$=NH, (b) formamidine.

Like the basicity–structure relationships, the basicity chemical shift data also appear to be asymptotic. After some experimentation we arrived at the following three-parameter asymptotic functional form relating the chemical shift and the PA

$$\delta(PA) = b - c/(PA - d) \quad (7)$$

The fitted functions are shown for the $^1H$ and $^{15}N$ data in Figs. 5a and 5b. The values of the fitted parameters are as follows: $\delta(^1H)$ in ppm, $b$ = 13.6, $c$ = 1155.1 and $d$ = 777.5; and $\delta(^{15}N)$ in ppm, $b$ = 364.7, $c$ = 15231.9, $d$ = 860.2. Although the $^1H$ and $^{15}N$ chemical shifts of the single-branch iminoamines both generally increase with basicity (Table 2), the evidence for the same functional relationship is less clear (see Figs. 6a and 6b): arguably more data points (compounds) are needed to

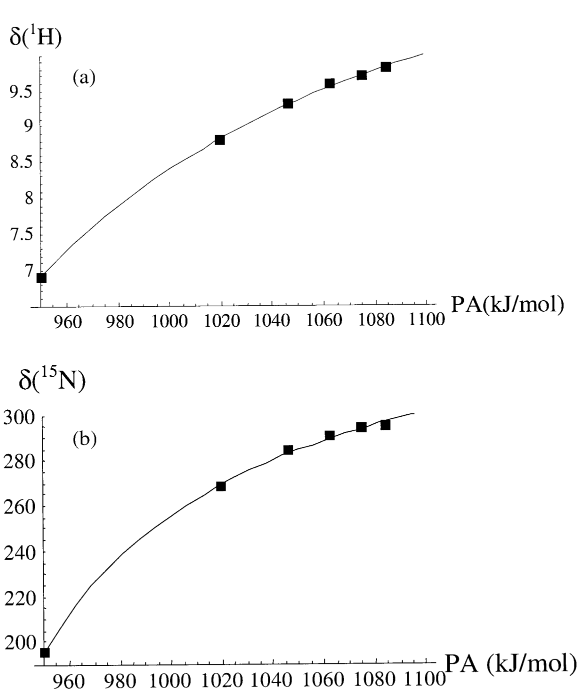


**Fig. 5** (a) Relationship between $^{1}$H NMR of the imine proton and gas-phase proton affinity (in the unprotonated base) for unbranched iminoamine bases, $R^2 = 0.999$. (b) Relationship between $^{15}$N NMR of the imine nitrogen and gas-phase proton affinity (in the unprotonated base) for unbranched iminoamine bases, $R^2 = 0.999$.

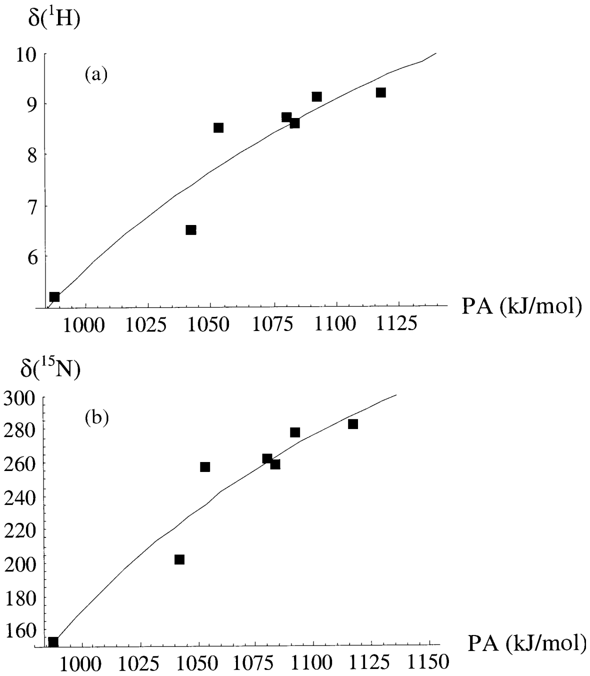


**Fig. 6** (a) Relationship between $^{1}$H NMR of the imine proton and gas-phase proton affinity (in the unprotonated base) for singly-branched iminoamine bases, $R^2 = 0.891$. (b) Relationship between $^{15}$N NMR of the imine nitrogen and gas-phase proton affinity (in the unprotonated base) for singly-branched iminoamine bases, $R^2 = 0.917$.

provide a definitive answer. In any case, fitting eqn. (7) to the data results in the following parameters: $\delta(^{1}\text{H})$ in ppm, $b = 17.9$, $c = 3239.4$, $d = 734.7$; and $\delta(^{15}\text{N})$ in ppm, $b = 534.5$, $c = 89628.3$, $d = 753.8$. These fitted curves are also plotted in Figs. 6a and 6b. Finally with the doubly-branched iminoamine data (Table 3, Figs 7a and 7b), although the general trend of higher basicity with increasing down-field chemical shift remains, the number of data points is insufficient to estimate the functional form of the relationship.

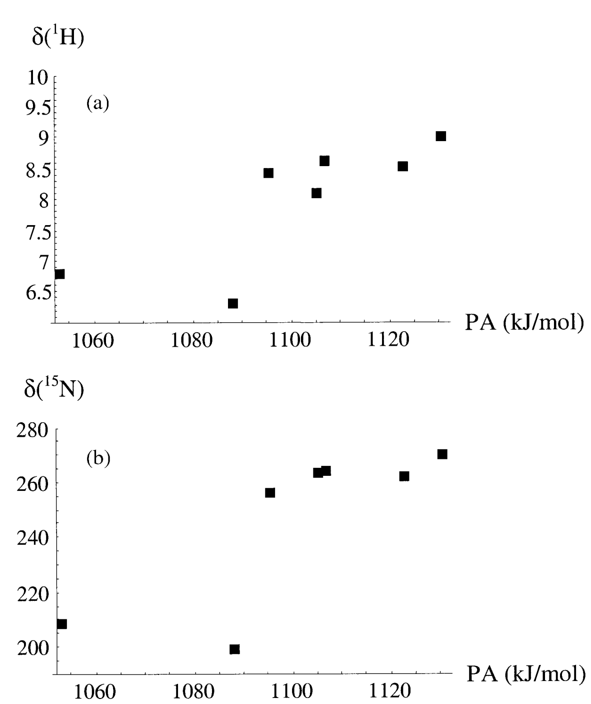


**Fig. 7** (a) Relationship between $^{1}$H NMR of the imine proton and gas-phase proton affinity (in the unprotonated base) for doubly-branched iminoamine bases. (b) Relationship between $^{15}$N NMR of the imine nitrogen and gas-phase proton affinity (in the unprotonated base) for doubly-branched iminoamine bases.

### Diimino bases

Finally we consider how the properties of these compounds can be supplemented to incorporate not only the resonance mechanism of enhanced basicity, but also that of hydrogen bonding as in more conventional proton sponges. The heptaguanidine **7** designed by Maksić and Kovačević[15] provides an example of this: on protonation the –NH$_2$ function which was the imine group before protonation forms two cationic hydrogen bonds to adjacent amine groups. The compound we propose (see Scheme 2) is a simple modification of G[5](32) to incorporate a second imine function, giving an iminoamine with $C_2$ symmetry. In our notation it is G[5](32)(22)*. The asterisk is added here to indicate that it is an atypical compound for optimal resonance stabilization of the cation, since as pointed out earlier this requires only odd-numbered branching points. Despite this, on protonation of an imine function a strong hydrogen bond is formed to the second imine. This results in a PA of 1146 kJ mol$^{-1}$, which is exceptionally basic for such a small organic molecule.

## Conclusions

Like the various acyclic 'polyguanidines' proposed by Gready *et al.* and Maksić *et al.*, the extended iminoamines studied here show enhanced gas-phase basicity compared to guanidine and indeed compared to most known proton sponges. The doubly-branched compound compound G[7](52)(32) has a very similar gas-phase proton affinity to Schwesinger's (polycyclic) proton sponge **4** (around 1143 kJ mol$^{-1}$ according to ref. 3). However, the latter uses both resonance and hydrogen bonding mechanisms of enhanced basicity. We have shown that it is a simple matter to design analogous acyclic iminoamines such as G[5](32)(22)* which additionally employ the H-bonding mechanism of stabilization in the protonated cation (as does Maksić's compound **7**), and in favourable cases the gas-phase PA's are likely to approach and perhaps even exceed 1200 kJ mol$^{-1}$. Calculations of $^{1}$H and $^{15}$N chemical shifts in the imino groups reveal clear correlations of these physical observables with gas-phase basicity, in the sense that less-shielded $^1$H and $^{15}$N are associated with higher basicity. Such relationships may aid both in the identification of the compounds and the estimation of their absolute basicities using measured NMR data. Correlations are also noted between basicity, chemical shifts and charge density parameters derived from an atoms-in-molecules analysis, which points towards useful ways of extracting basicity information from charge distributions obtained experimentally by elastic X-ray scattering.[32]

The iminoamines are distinguished from the polyguanidines by the presence of aliphatic carbon chain linkers, instead of alternate nitrogen heteroatoms. Because the protonated iminoamines only carry *terminal* amine groups the enhanced basicity can be described by a relatively simple model in which the mean charge separation plays a key role. Other differences in physical properties between iminoamines and polyguanidines such as solubility and/or lipophilicity can also be anticipated, which might help to extend the range of applications for superbases in preparative chemistry. Since only a few simple iminoamines have so far been synthesized, it is hoped that this work might provide an impetus for their further study.

All the calculations presented so far refer to the gas phase. Peeters *et al.* have shown how protonation behavior is modified in simple alkyl imines in the presence of at least one solvent water molecule.[33] One important aim therefore is to study how our simple model of acyclic iminoamine basicity is altered by solvent effects, and this work is in progress.

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