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Absolute Proton Affinity of Some Polyguanides

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The problem of the absolute proton affinity (APA) of some polyguanides is addressed by the MP2(fc)/6-311+G**//HF/6-31G* theoretical model. It is shown that the linear chain polyguanides exhibit increased basicity as a function of the number of guanide subunits. However, the saturation effect yields an asymptotic APA value of 254 kcal/mol. Branched polyguanides on the other hand have higher APAs than their linear counterparts. The largest proton affinity is found in a doubly bifurcated heptaguanide, being as high as 285 kcal/mol, thus potentially representing one of the strongest organic bases. Finally, it is found that all polyguanides protonate at imino nitrogen atoms, since they are apparently susceptible the most to the proton attack. The origin of their very high intrinsic basicity is traced down to a dramatic increase in the resonance interaction of the corresponding conjugate bases. For instance, the increase in the resonance energy in the protonated guanidine is estimated to be in a range of 24−27 kcal/mol, which is higher than the aromatic stabilization in benzene. The proton affinity of some polycyclic guanides including Schwesinger proton sponge and porphine is briefly discussed.

1. Introduction

The design of strong organic bases has been a hot topic for some time. Most of the research efforts were concentrated on the absolute proton affinity (APA) of the so-called proton sponges exemplified by 1,8-bis(dimethylamino)naphthalene (DMAN)[1] and its various offsprings.[2−5] However, it was recently realized that the imino group is much more susceptible to the proton attack as illustrated by formamidine, acetamidine, and guanidines.[6−8] We have shown that some quinodiimines[9] and cyclopropeneimines[10] exhibited very high basicity indeed. Our studies underscored the decisive effect of the π-resonance in resulting conjugate acids in determining the high proton affinity of some neutral organic bases. In view of the important role of strong organic bases in acid−base chemistry, we have undertaken the exploration of the proton affinity of some polyguanides, which represented simple extended π-electron systems. These compounds are obtained by replacement of one amino group in guanidine by the $N{=}C(NH_2)_2$ structural fragment. It was of interest to examine the influence of a number of guanidine subunits on the resulting APA. It appears that polyguanides exhibit APAs which are higher by 50 kcal/mol or more than that of the parent guanidine. Consequently, their experimental studies would be highly desirable. These results and their relation to some cyclic polyguanides are discussed in some detail. The examined polyguanide systems considered here are depicted in Figure 1.

2. Methodology

Our approach is well documented elsewhere[9−12] and does not need to be repeated in great detail. Briefly, proton affinities are calculated employing the following formula:

$$\mathrm{APA}(\mathrm{B}_\alpha) = [E(\mathrm{B}) - E(\mathrm{B}_\alpha^+)] + [\mathrm{ZPVE}(\mathrm{B}) - \mathrm{ZPVE}(\mathrm{B}_\alpha^+)] \quad (1)$$

where B and B^+ denote the base and its conjugate acid, respectively, whereas α specifies the site of the proton attack. The theoretical model used is the MP2(fc)/6-311+G**//HF/6-31G* + ZPVE(HF/6-31G*) one and will be abbreviated hereafter as the MP2 model. It involves optimization of the structural parameters and vibrational analyses at the HF/6-31G* level, the latter being utilized in estimating the zero-point vibrational energy (ZPVE) multiplied by a weighting factor of 0.89.[12] The final energies are obtained by the single-point MP2(fc)/6-311+G** calculations. Three features of our model deserve comment: (a) It uses the flexible 6-311+G** basis set in the final calculation to provide a proper description of a rather diffuse character of the nitrogen lone pair. (b) It takes into account the electron correlation effect at the MP2 level. (c) The influence of the ZPVE is explicitly included at the economical HF/6-31G* level. This is important because the resulting conjugate acids have one additional H atom and one

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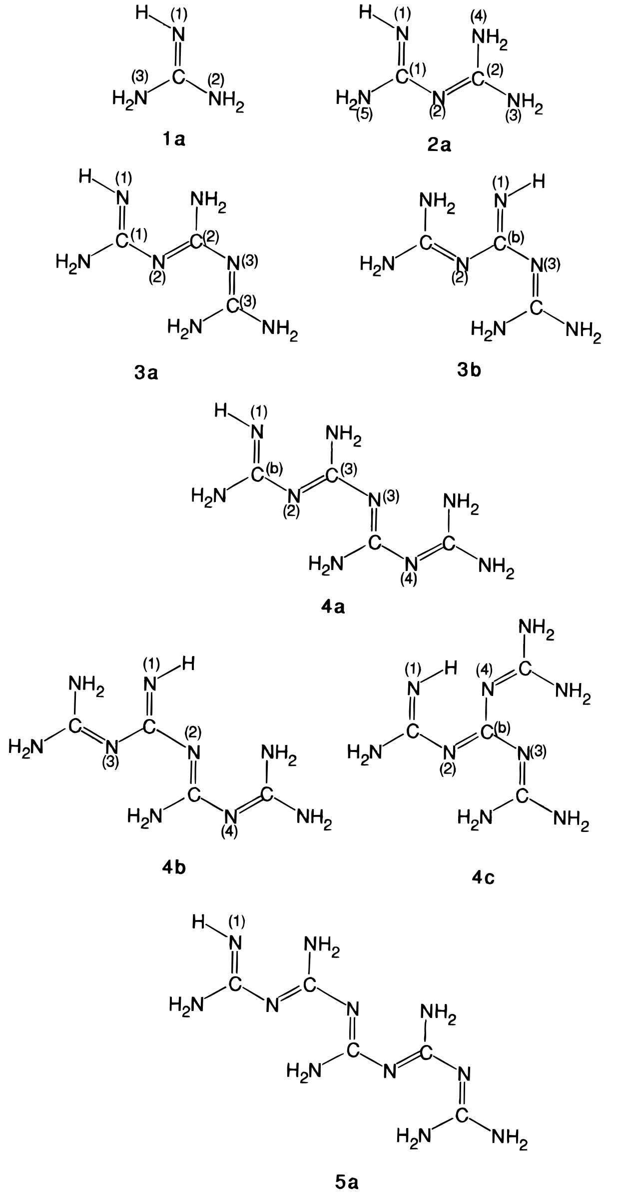
1a
2a
3a
3b
4a
4b
4c
5a

Figure 1. Molecular structures and numbering of atoms in the polyguanides studied in this paper.

Table 1. Total Molecular HF and MP2 Energies E_t (au), Scaled ZPVEs and APAs of Guanidine and Polyguanides As Estimated by the MP2, HFsc, and AM1sc Models (kcal/mol)

compd	E_t(HF)	E_t(MP2)	ZPVE	APA-(MP2)	APA-(HFsc)	APA-(AM1)
1a	−204.119 94	−204.871 36	46.0			
1aH$^+$	−204.521 54	−205.254 50	52.7	233.7	235.3	236.0
2a	−352.065 41	−353.340 27	69.9			
2aH$^+$(N1)	−352.479 62	−353.734 81	77.1	240.4	242.2	247.4
2aH$^+$(N2)	−352.459 63	−353.719 65	77.3	230.6	231.1	227.9
3a	−500.008 41	−501.807 18	93.9			
3aH$^+$(N1)	−500.434 63	−502.211 79	100.8	247.0	249.1	256.8
3aH$^+$(N2)	−500.413 96	−502.197 30	101.5	237.2	237.5	238.7
3aH$^+$(N3)	−500.398 04	−502.185 25	101.0	230.1	228.6	227.0
3b	−499.999 78	−501.801 41	94.1			
3bH$^+$(N1)	−500.434 63	−502.211 80	100.8	250.8	253.9	257.1
3bH$^+$(N2)	−500.412 37	−502.193 82	100.6	241.5	241.4	240.1
4a	−647.951 27	−650.274 17	117.6			
4aH$^+$(N1)	−648.383 02	−650.682 93	124.4	249.7	252.2	262.7
4aH$^+$(N2)	−648.369 60	−650.675 14	125.4	243.8	244.6	247.8
4aH$^+$(N3)	−648.353 18	−650.663 39	125.1	236.7	235.5	236.7
4aH$^+$(N4)	−648.337 01	−650.650 50	124.8	228.9	226.4	224.9
4b	−647.942 91	−650.270 14	117.9			
4bH$^+$(N1)	−648.383 02	−650.682 93	124.4	252.5	256.9	263.8
4bH$^+$(N2)	−648.365 21	−650.671 05	124.9	244.5	246.9	247.9
4bH$^+$(N3)	−648.365 99	−650.670 48	124.7	244.4	247.3	242.1
4bH$^+$(N4)	−648.341 62	−650.653 94	124.8	233.9	233.7	232.1
4c	−647.928 86	−650.258 99	117.5			
4cH$^+$(N1)	−648.386 27	−650.686 38	123.9	261.8	266.5	266.5
5a	−795.894 35	−798.741 68	141.4			
5aH$^+$(N1)	−796.329 78	−799.153 16	148.2	251.4	254.2	265.9

additional N−H bond. Consequently, a change in the ZPVE cannot be neglected.

However, MP2 calculations employing such an involved basis set could be a bottleneck in treating large molecular systems of chemical interest. It is gratifying that the MP2 model can be reduced to Hartree−Fock calculations with only a small sacrifice in accuracy. For that purpose one employs a difference in the Hartree−Fock energies ΔE_{el}(HF/6-31G*) between the base in question and its conjugate acid protonated at the nitrogen atom. The corresponding correlation reads

$$\mathrm{PA}(\mathrm{B_N}) = 0.8924\Delta E_{el}(\mathrm{HF/6\text{-}31G^*})_N + 10.4\ (\mathrm{kcal/mol}) \quad (2)$$

The final results are very close to numbers offered by the MP2 model,[9] being much more economical at the same time. This procedure will be referred to as the scaled Hartree−Fock (HFsc) model. The reason behind a good performance of the HFsc model is the fact that the ZPVE contribution to the proton affinity is fairly constant, being 8.5 ± 0.4 kcal/mol, which is absorbed in the additive constant in eq 2. The other favorable circumstance is that the differences in the electronic energies of bases and conjugate acids at the MP2(fc)/6-311+G**//HF/6-31G* and HF/6-31G* levels are linearly related, i.e., $\Delta E_{el}(\mathrm{MP2(fc)/6\text{-}311{+}G^{**}}) = a\Delta E_{el}(\mathrm{HF/6\text{-}31G^*}) + b$. Hence, it is not surprising that relationship 2 puts HF/6-31G* data in line with the MP2 results. A similar idea can be put forward employing the AM1 semiempirical scheme. For this purpose we made use of ΔH_f(AM1) enthalpies of initial bases and their conjugate acids, which has led to the following formula:

$$\mathrm{PA}(\mathrm{B_N}) = 1.0948\Delta\Delta H_f(\mathrm{AM1})_N + 381.0\ (\mathrm{kcal/mol}) \quad (3)$$

$\Delta\Delta H_f$ refers to differences in the enthalpies of formation, the contribution related to the proton being included in the additive constant.[9] The proton affinities obtained by the AM1 semiempirical method via eq 3 give rise to the scaled AM1sc model, which should roughly approach MP2 results. It should be pointed out that deviations from the ab initio MP2 APA values are larger than in the case of the HFsc model.[9] Consequently, the AM1sc model provides a useful vehicle for pilot calculations in very large systems, if due care is exercised. Finally, all computations were carried out by making use of the GAUSSIAN 94 program.[14]

3. Results and Discussion

3.1. Proton Affinity. 3.1.1. Linear Chain Polyguanides. Total molecular energies, ZPVEs, and the final absolute proton affinities are given in Table 1. It should be pointed out that only the most favorable conformations are discussed here. It appears that the APA value related to the N1 atom in biguanide **2a** is increased by 7 kcal/mol relative to that of the parent guanidine **1a**. It is interesting to emphasize that this fact can be easily rationalized by the increased π-electron

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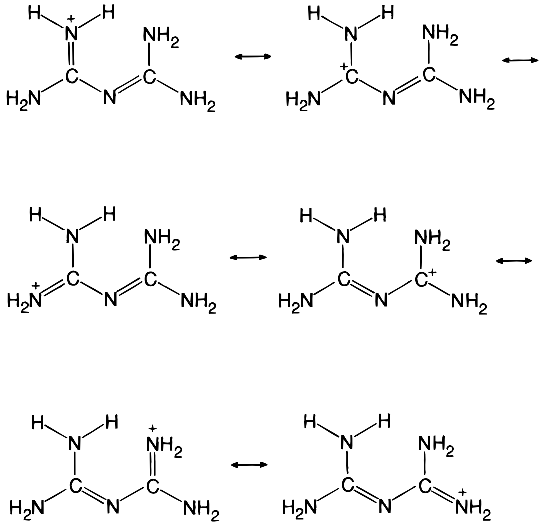
[14] GAUSSIAN 94 (Revision D.1): M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheesman, T. A. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Otiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzales, and J. A. Pople, Gaussian, Inc., Pittsburgh, PA, 1995.

Scheme 1



conjugation induced in the conjugate acid as illustrated in a qualitative manner by the resonance structures presented in Scheme 1. There are two additional resonance structures in **2aH**$^+$(N1) than in the protonated initial system **1aH**$^+$, indicating a larger stability of the protonated species **2aH**$^+$ (N1). This is exactly the reason why the protonation at the N2 nitrogen is less favorable since there are only four resonance structures describing delocalization of the positive charge over the π-system in the protonated form **2aH**$^+$(N2). It should be strongly pointed out in this connection that the resonance effect illustrated by Scheme 1 is broader than sheer π-conjugation. It also involves the relaxation effect due to reorganization of the electron density upon protonation. This type of polarization is similar to the density drift to the positive hole formed by the X-ray ejection of an inner-shell electron as monitored by ESCA spectroscopy.[15] Electronic relaxation upon ionization is appreciable, varying in a large range between 12 and 23 eV depending on the nature of the target atom and the size of the molecular system. A similar effect is expected in protonated bases in view of a broad analogy between the inner-core hole and the protonated atom.[16,17] To put it in another way, the positive charge is easily delocalized over the conjugate acid via the mobile π-electrons through the π-conjugation mechanism. This is energetically profitable because a highly localized positive charge is always disfavored. As a consequence, the electron density of the protonated nitrogen is practically equal to that of the unprotoned one.

There are two different ways to obtain triguanides leading to isomers **3a** and **3b** (Figure 1). In both cases the protonation at the N1 atom is energetically more advantageous. However, we shall first focus attention on the chain polyguanides ***n*a** ($n = 1-5$), where the terminal imino group is always protonated as the most favorable one without exception (Table 1). It appears that the APA steadily increases along the series, but there is an apparent saturation effect (Figure 2). The increments

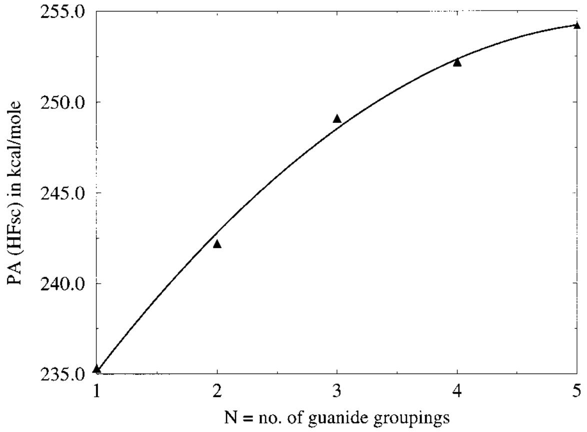


Figure 2. Saturation effect in linear chain polyguanides. The APA values are estimated by the HFsc model. The number of guanine units is denoted by *n*.

$\Delta(n + 1) = \text{APA}((\boldsymbol{n} + \mathbf{1})\mathbf{a}) - \text{APA}(\boldsymbol{n}\mathbf{a})$ for $n = 1-4$ assume values of 6.9, 6.9, 3.1, and 2.0 (kcal/mol), respectively, as estimated by the HFsc model. Attenuation in $\Delta(n + 1)$ is obvious in Figure 2, where the proton affinity asymptotically aproaches a value of 254 kcal/mol, which is practically achieved by pentaguanide **5a** already. It turns out that the guanide fragment, which is distant from the protonated terminal imino group by more than four subunits, does not influence the APA to any significant extent. In contrast, both the nearest-neighbor and the next-nearest-neighbor guanide groups contribute 6.9 kcal/mol each to the proton affinity of the terminal imino nitrogen atom. Although the same magnitude of these two increments is accidental, this finding can be exploited in designing polyguanides possessing high basicity as will be illustrated in the next subsection.

3.1.2. Bifurcated Polyguanides. The simplest branched polyguanide is provided by **3b**, where a chain is forked at the bifurcation carbon atom C(b). The protonation at N1 yields an increase in the APA by 5 kcal/mol relative to that of **3aH**$^+$(N1). Similarly, conjugate acid **4bH**$^+$(N1) is more stable than **4aH**$^+$(N1) by 2.8 kcal/mol. In both cases the reason lies in the greater stability of **3a** and **4a** polyguanides compared to their **3b** and **4b** isomeric counterparts, respectively. It appears, namely, that the protonation of **3a** and **3b** isomers at the N1 atom results in the same conjugate acid. The same holds for isomers **4a** and **4b**. Consequently, the less stable isomer has higher proton affinity. A more profitable gain in the basicity of tetraguanides is obtained, if the bifurcated carbon atom is placed in the guanide fragment next to the protonated one as typified by **4c** and its conjugate acid **4cH**$^+$(N1). This leads to an increase in the APA by 14 kcal/mol relative to that of **4aH**$^+$(N1), providing a high APA value of 266.5 kcal/mol. It should be stressed here that isomers of the protonated polyguanidines, which are related by one or more intramolecular proton shifts, are expected to be in rapid equilibria. The effective proton affinity of such a mixture of isomers is the weighted Boltzmann average of the proton affinities of individual isomers. Since the protonation at the N1 nitrogen atoms is considerably more favorable than the proton attachment at the other basic sites, it is fair to say that PA values of compounds **2a**, **3a**, and **4a** will be very close to values of 240.4, 247.0, and 249.7 kcal/mol, respectively. A simple generalization of the bifurcation principle found

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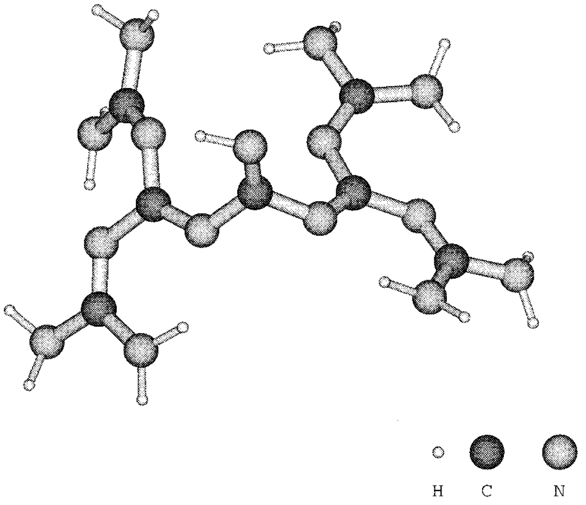
[15] For an extensive review the reader could consult Z. B. Maksić, In *Theoretical Models of Chemical Bonding, Part 3, Molecular Spectroscopy Electronic Structure and Intramolecular Interactions*; Maksić, Z. B., Ed.; Springer-Verlag: Berlin−Heidelberg, 1991; p 289.

[16] Martin, R. L.; Shirley, D. A. *J. Am. Chem. Soc.* **1974**, *96*, 5229.

[17] Smith, S. R.; Thomas, T. D. *J. Am. Chem. Soc.* **1978**, *100*, 5459.



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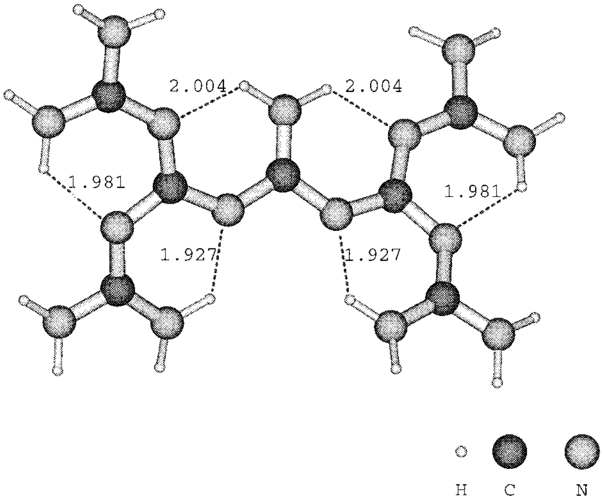
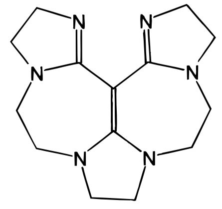


6H$^+$

Figure 3.

in **3b** and **4b** is offered by heptaguanide **6** (Figure 3) possessing two branches each forked in a fairly symmetrical way, thus forming an "octopus-like" distribution of eight NH_2 groups. The resulting APA is 285.3 kcal/mol according to the HFsc model as intuitively expected, implying that **6** should be one of the strongest neutral organic bases as far as the intrinsic (gas-phase) basicity is concerned. Its basicity could be further amplified by additional intramolecular H-bonding corona effect as discussed in the last section (vide infra). It is noteworthy that an apparently strong resonance effect present in **6H$^+$**(N1) is further enhanced by internal hydrogen bonds as schematically depicted in Figure 3. The resonance effect is reflected in a dramatic planarization of the system induced by the protonation. Our computational results obtained so far indicate that the intramolecular hydrogen bonds existing in the initial base are further strenghthened in the conjugate acid. This is in accordance with intuition and a general picture that the positive charge created upon protonation is distributed over the whole protonated species, thus increasing the effective positive charge of all hydrogen atoms and thereby enhancing the Coulomb contribution to the hydrogen bonding. Perusal of the proton affinities calculated by the AM1sc scheme are in good qualitative agreement with MP2 results. On the other hand, quantitative accordance is modest since deviations from the ab initio estimates vary in the range of a couple of kilocalories per mole to 13 kcal/mol found in **4aH$^+$**(N1). Generally, the AM1sc proton affinity is much too high for the most basic site in polyguanides. Concomitantly, the AM1sc procedure can be employed in a search of highly basic compounds, but the final conclusions should be drawn on the more reliable ab initio results. Another point of importance is that correlations of the type given by eq 3 are valid only for compounds belonging to the same family of molecules. If quite different structural and electronic motifs are involved like, e.g., in systems possessing a cyclobutadiene moiety, then separate correlation(s) should be utilized.[9]

Chart 1



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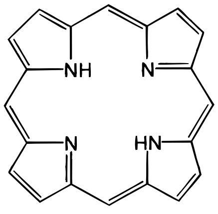

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The proton affinities of linear and bifurcated polyguanides described above favorably compare with the basicity of some polycyclic guanides discussed in the literature. The most basic organic compound prepared so far is given by the Schwesinger proton sponge **7** (Chart 1).[18] Its proton affinity is 269.5 kcal/mol as estimated by our HFsc model,[19] whereas the AM1sc scheme predicts a substantially lower value of 258.7 kcal/mol, presumably because this approximative procedure underestimates the intramolecular H-bonding as observed earlier by Dewar and Dieter.[20] Another supramolecular system, which plays a role of utmost importance in molecular biology, exhibiting appreciable basicity, is porphine **8** (Chart 1). It has a a relatively high proton affinity as evidenced by our HFsc calculations, which yield a PA value of 235.2 kcal/mol.[19] The proton affinity of **8** offered by the AM1sc calculation is 237.8 kcal/mol. It is evident, however, that heptaguanide **6** would supersede the present top position of **7** on the basicity ladder of organic molecules once it was synthesized.

3.2. Resonance Effect. It is useful to have at hand a simple and qualitative interpretation of the variation in the APA of polyguanides. The resonance effect serves the purpose very well because it can rationalize not only the proton affinity in linear chain polyguanides, but also the amplified basicity in branched polyguanides. Similarly the APA values of different nitrogens within the same molecule of these ambident systems are easily understood in a qualitative sense by counting the resonance structures. For instance, the absolute proton affinities APA(N1), APA(N2), and APA(N3) in **3aH$^+$** are 247.0, 237.2, and 230.1 kcal/mol as estimated by the MP2 model, respectively, thus being in harmony with the numbers of resonance structures (8, 6, and 4) occurring in the

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(19) Kovačević, K.; Maksić, Z. B. Manuscript in preparation.

(20) Dewar, M. J. S.; Dieter, K. M. *J. Am. Chem. Soc.* **1986**, *108*, 8075.

respective conjugate acids. The reason behind the decreasing number of resonance structures in this series is that the π-electron conjugation, triggered by the protonation, can be effectively transmitted only across, e.g., the N2═C2 double bond, but not across the N2─C1 single bond in **3a**, if the proton attack takes place at the N2 nitrogen. In other words, the N2─C1 single bond acts as an "insulator" for the resonance effect, whereas the N2═C2 double bond is a "conductor" for the transfer of the protonation effect.

It is not easy to provide quantitative estimates of the resonance effect in higher polyguanides. We shall therefore give an analysis of the resonance contribution to the APA in guanidine, which will serve as a simple and enlightening example. For that purpose, the concept of homodesmic reactions will be followed.[21] The conjugative stabilization of imines (formamidine and guanidine) can be obtained by the following homodesmic reactions:

$$(NH_2)HC{=}NH + H_2C{=}CH_2 \rightarrow (NH_2)HC{=}CH_2 + H_2C{=}NH + \epsilon^1 - E^{(1)}_{\mathrm{conj}} \tag{4}$$

$$(NH_2)_2C{=}NH + H_2C{=}CH_2 \rightarrow (NH_2)_2C{=}CH_2 + H_2C{=}NH + \epsilon^2 - E^{(2)}_{\mathrm{conj}} \tag{5}$$

If the conjugative interaction(s) between the NH_2 group(s) and the C═C double bond ϵ^1 (ϵ^2) are so small that they can be neglected, then a change in energy of reactions 4 and 5 yields to $E^{(1)}_{\mathrm{conj}}$ and $E^{(2)}_{\mathrm{conj}}$, which in turn reflect the conjugation in formamidine and guanidine, respectively, defined as positive entities. However, this is not the case as evidenced by the rotation barrier of aminoethene. If the lone pair of electrons assumes an orientation which prevents π-conjugation, the total electronic energy rises by 5.2 kcal/mol as obtained by the MP2(fc)/6-311+G**//HF/6-31G* model, implying that this value provides a reasonable estimate of π-conjugation stabilization ϵ^1 in aminoethene. The conjugative effect in diaminoethene is deduced by the homodesmic reaction

$$(NH_2)_2C{=}CH_2 + H_2C{=}CH_2 \rightarrow 2[(NH_2)HC{=}CH_2] + 2\epsilon^1 - \epsilon^2 \tag{6}$$

Our adopted MP2 model gives $\epsilon^2 = 13.6$ kcal/mol. Taking ϵ^1 and ϵ^2 into account, one obtains estimates of the π-conjugation in formamidine and guanidine, being $E^{(1)}_{\mathrm{conj}} = 16.1$ and $E^{(2)}_{\mathrm{conj}} = 27.8$ (kcal/mol), respectively, via eqs 4 and 5. It appears that the conjugation effect in initial bases is appreciable due to the strong π-backbonding effect of lone pairs. The resonance effect in the corresponding conjugate acids, however, is even more pronounced. This conjecture follows from the following "gedanken" reactions:

$$(NH_2)HC{=}N^+H_2 + H_2C{=}CH_2 \rightarrow (NH_2)HC{=}CH_2 + H_2C{=}N^+H_2 + \epsilon^1 - E^{+(1)}_{\mathrm{res}} \tag{7}$$

$$(NH_2)_2C{=}N^+H_2 + H_2C{=}CH_2 \rightarrow (NH_2)_2C{=}CH_2 + H_2C{=}N^+H_2 + \epsilon^2 - E^{+(2)}_{\mathrm{res}} \tag{8}$$

In this connection it is useful to keep in mind that eqs 7 and 8 describe the resonance effect, which includes both the π-conjugation and advantageous delocalization of the positive charge, as indicated in the superscript of the resonances energies. The MP2 model yields resonance energies $E^{+(1)}_{\mathrm{res}} = 34.7$ and $E^{+(2)}_{\mathrm{res}} = 51.5$ (kcal/mol), indicating an increase in the stabilization energies spurred by the protonation, which are as large as 18.6 and 24.1 kcal/mol, respectively. It is of interest to test the stabilization energies offered by eqs 5 and 8 in an independent way. Conclusive support is provided by related homodesmic reactions

$$(NH_2)_2C{=}NH + CH_2{=}NH \rightarrow 2[(NH_2)HC{=}NH] + 2E^{(1)}_{\mathrm{conj}} - E^{(2)*}_{\mathrm{conj}} \tag{9}$$

$$(NH_2)_2C{=}N^+H + H_2C{=}N^+H_2 \rightarrow 2[(NH_2)HC{=}N^+H_2] + 2E^{+(1)}_{\mathrm{res}} - E^{+(2)*}_{\mathrm{res}} \tag{10}$$

MP2 calculations show that $E^{(2)*}_{\mathrm{conj}}$ and $E^{+(2)*}_{\mathrm{res}}$ assume values of 27.5 and 54.7 kcal/mol, respectively, which compare well with $E^{(2)}_{\mathrm{conj}} = 27.4$ and $E^{+(2)}_{\mathrm{res}} = 51.5$ (kcal/mol) obtained earlier. It appears that the increase in the resonance effect in the protonated guanidine lies approximately within the range of 24−27 kcal/mol depending on the choice of homodesmic reactions, which should be considered as a fairly good semiquantitative estimate of this intramolecular electronic interaction. It is worth noting that this is higher than the aromatic stabilization in the paradigmatic benzene. The latter is about 20 kcal/mol as estimated independently by the valence bond ab initio calculation[22] and a careful ab initio MO analysis employing homodesmic reactions.[23] One can safely conclude that the resonance effect in conjugate acids plays a decisive role in determining the high proton affinities of polyguanides. It is important to realize that the resonance effect overcomes the hybridization effect of the initial bases in question. It is, namely, well documented by now that basicity is inversely proportional to the s-character of the lone pairs.[24,25] Consequently, if the resonance effect were absent, then the amino nitrogen would be more basic than the imino one. Obviously, the resonance effect prevails, making the imino nitrogen more apt to proton attack. It is important to emphasize that the π-electron conjugation in guanidine, as we put it technically, involves participation of hybridized lone pairs of amino groups, which in turn are significantly pyramidalized. The hybrid AOs of the lone pairs are oriented so that the conjugation is effective as much as possible. It is important to note that the ideal orientation relative to the neighboring π-AO of the C atom is impossible to attain. The situation is drasticaly changed upon protonation, since the NH_2 group becomes planar, thus allowing for the maximal resonance effect. This is described in more detail in the next section.

3.3. Structural Properties. We shall briefly discuss here the shape and size of a couple of polyguanides as

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Table 2. Selected Structural Parameters of Guanidine and Some Simple Polyguanides and Their Protonated Forms As Obtained by the HF/6-31G* Model

molecule	bond distance (Å) or angle (deg)	molecule	bond distance (Å) or angle (deg)
1a	*d*(C=N1) = 1.260 *d*(C−N2) = 1.384 *d*(C−N3) = 1.388 N1−C−N2 = 120.6 N1−C−N3 = 127.3 N2−C−N3 = 112.1	**1aH**$^+$(N1)	d(C−N) = 1.321 N−C−N = 120.0
2a	*d*(C1=N1) = 1.275 *d*(C1−N5) = 1.377 *d*(C1−N2) = 1.378 *d*(N2=C2) = 1.289 *d*(C2−N3) = 1.370 *d*(C2−N4) = 1.345 *d*(H(N4)···N1) = 1.951 N1−C1−N5 = 123.9 N1−C1−N2 = 125.5 N2−C1−N5 = 110.5 C1−N2−C2 = 121.9 N2−C2−N4 = 127.8 N3−C2−N4 = 115.0 N2−C2−N3 = 117.2	**2aH**$^+$(N1)	*d*(C1−N1) = 1.341 *d*(C1−N5) = 1.323 *d*(C1−N2) = 1.318 *d*(N2=C2) = 1.318 *d*(C2−N3) = 1.323 *d*(C2−N4) = 1.341 *d*(H(N4);H(N1)) = 2.395[a] N1−C1−N5 = 118.0 N1−C1−N2 = 125.1 N2−C1−N5 = 116.8 C1−N2−C2 = 126.0 N2−C2−N4 = 125.1 N3−C2−N4 = 118.0 N2−C2−N4 = 116.9
2aH$^+$(N2)	*d*(C1=N1) = 1.251 *d*(C1−N5) = 1.365 *d*(C1−N2) = 1.417 *d*(N2−C2) = 1.348 *d*(C2−N3) = 1.326 *d*(C2−N4) = 1.305 *d*(H(N4)···N1) = 1.937	**2aH**$^+$(N2)	N1−C1−N5 = 129.7 N1−C1−N2 = 119.6 N1−C1−N5 = 110.6 C1−N2−C2 = 127.3 N2−C2−N4 = 121.8 N3−C2−N4 = 120.9 N2−C2−N3 = 117.3

[a] The nonbonded distance between the two closest H atoms.

well as the structural features of their conjugate acids for illustrative purposes. The relevant geometric parameters are given in Table 2. Particular attention should be paid to the degree of pyramidalization of the amino groups and their planarization upon the protonation of the imino nitrogen as a consequence of the resonance effect. For that purpose we shall utilize eq 11, which

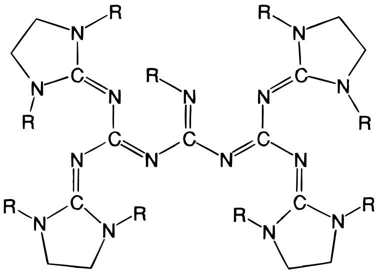
$$\mathrm{DP}\ (\%) = [360 - \sum_{i=1}^{3} \alpha_i]/0.9 \qquad (11)$$

provides the degree of pyramidalization (DP), where the summation is extended over bond angles α_i (deg). It is tacitly assumed that the maximal pyramidalization is achieved if the sum of three angles is equal to 270°, corresponding to three mutually perpendicular 2p AOs. It appears that the NH_2 groups in guanidine **1a** are pyramidalized by 20.8%. In contrast, all three NH_2 groups in the protonated form **1aH**$^+$ become planar, thus enabling optimal π-electron conjugation and the most favorable resonance effect. In biguanide **2a** heavy atoms exhibit a mild nonplanarity. For instance, the dihedral N1−C1−N2−C2 angle is 5.1°. Amino groups involving the N3, N4, and N5 nitrogen atoms are pyramidalized by 17.8%, 8.6%, and 14.8%, respectively. It is conceivable that a decreased pyramidalization of the N4 nitrogen is a consequence of the internal hydrogen bonding with the N1 lone pair electrons. The distribution of σ-bonds around the carbon atoms in **2a** is planar. Nonplanarity in the protonated biguanide **2aH**$^+$(N1) is more pronounced as evidenced by the N1−C1−N2−C2 dihedral angle of 21.5° presumably due to steric congestion and the nonbonded interactions between hydrogens belonging to the $N1H_2$ and $N4H_2$ amino groups. Their arrangement is a compromise between the optimal resonance effect and Coulomb repulsions. Amino structural units $N3H_2$ and $N5H_2$ are planar, possessing a negligible DP value as low as 0.2%. On the contrary, $N1H_2$ and $N4H_2$ amino groups have the same degree of pyramidalization of 5.2%. The distribution of σ-bonds around the carbon atoms remains persistently planar. The protonated form **2aH**$^+$(N2) has some interesting structural features. The central part of the heavy atom skeleton has nonplanarity comparable to that in the parent compound **2a** as reflected by the N1−C1−N2−C2 dihedral angle of 7.5°. Since the resonance effect is operative across the C2=N2 double bond, one expects a considerable planarization of the $N3H_2$ and $N4H_2$ groups. This is indeed the case as evidenced by the corresponding very low DP values of 2.2% and nil, respectively. It is important to realize that the resonance is operative even in not too excessively nonplanar structures. On the other hand, the conjugation is not transmitted over the C1−N2 single bond as expected, resulting in the pyramidalization of the $N5H_2$ amino group with DP = 14.2%, which is close to that (14.8%) found in the parent guanidine **1a**. Similar conclusions can be drawn by analysis of the bond lengths, which reflect the resonance effect rather nicely too. Although the HF distances are not very accurate, their relative changes induced by the protonation are reproduced very well. For example, a uniform CC distance of 1.32 Å in the protonated guanidine **1aH**$^+$ indicates a strong resonance effect. Inspection of the bond distances in **2a** reveals that π-electron conjugation in this compound is more pronounced than in **1a**. Further, protonation at the N1 atom leads to an even stronger π-electron delocalization in **2aH**$^+$(N1), which is spread over the entire system. In contrast, the protonation at the N2 nitrogen atom in **2aH**$^+$(N2) triggers a strong conjugation only in the N2−C2−(N3,N4) fragment of this conjugate acid as surmised earlier. Another interesting detail is given by the N1−C1−N5 part of the system which becomes more isolated and localized as evidenced by an increase in the C1−N2 bond length of 0.039 Å. The finding that there is no spillover of the resonance effect across the C1−N2 single bond upon protonation supports the conjecture reached by examining Pauling's resonance structures, implying that they provide a useful diagnostic tool, if handled with due care.

4. Concluding Remarks

We found that polyguanides possess very high proton affinities. Linear chain poly-guanides exhibit a saturation effect as the number of guanidine units increases, approaching the asymptotic value of 254 kcal/mol. Bifurcation of the polyguanide chain leads to branched (cascade) molecules exhibiting an enhanced basicity. The largest proton affinity is found in a doubly bifurcated heptaguanide, **6**, which assumes a value as high as 285 kcal/mol, thus being a candidate for one of the most potent organic bases. The origin of high PAs is traced down to substantial resonance effect spurred by the protonation. A semiquantitative estimate of the increase in the resonance stabilization in the guanidine upon protonation is calculated to be in the range of 24−27 kcal/mol. This is comparable to the aromatic stabilization in archetypal benzene, which in turn is about 20 kcal/mol.[22,23] Further, it appears that the resonance effect can qualitatively rationalize several general features emerging from the ab initio results. For example, according to the resonance effect, it straightforwardly follows that the terminal imino nitrogen in linear chain polyguanides is the most basic site in these polycentric ambident bases. This is a consequence of the fact that the C═N(p) double bond and C−N(p) single bond behave as a “conductor” and an “insulator” for transmission of the π-resonance interaction, respectively, where N(p) stands for the protonated nitrogen. Finally, attenuation of the resonance effect with the length of the linear chain explains an amplified basicity of branched polyguanides compared to their linear counterparts possessing the same number of guanidine subunits. It should be mentioned that a very high proton affinity of the imino nitrogens in polyguanides could be a drawback, because it might lead to internal transfer of one amino proton of the initial base to the most basic imino position, thus leading to a less basic final isomer. This shortcoming could be circumvented by introducing protecting groups such as, e.g., alkyls. In fact, heptamethylbiguanide has been synthesized already, and it was found that it possessed over 10 times higher catalytic activity due to its high base strength than nucleophilic 1,4-diaza[2.2.2]bicyclooctane in reactions of phenyl isocyanate with 2-ethylhexanol, methanol, and deuterium methoxide.[26] For that purpose we calculated the APA of heptamethylbiguanide and found that it was 258.8 kcal/mol as estimated by the HFsc model. It appears that the APA is increased by 16.6 kcal/mol relative to the proton affinity of the parent biguanide **2a**. This is a nice illustration of the importance of the relaxation effect in the protonated form (supported perhaps by the hyperconjugation), since the π-electron conjugation should be approximately the same as in the parent biguanide **2a**. The present result is in harmony with our earlier findings that alkyl groups have a profound effect on the intrinsic (gas-phase) basicity in a number of strong bases.[9,10,27] There is one additional point, which should be strongly underscored, because it is of importance: our calculations show that a high APA value of isolated heptamethylbiguanide **6** corresponds to increased reactivity and catalytic activity at least in some solvents. It is interesting to mention that the proton affinities of heptamethylbiguanide (258.8 kcal/mol) and pentamethylguanidine (247.8 kcal/mol), as estimated by the HFsc model, are in harmony with the corresponding pK_a = 17.1 and 15.6 values, respectively, measured in benzene.[26] There are also linear correlations between the gas-phase basicity of closely related imines and the pK_a values in some solvents.[28] Hence, it appears that the intrinsic proton affinity is a useful indicator of the basicity in some solutions, if taken with due caution. In this connection it should be kept in mind that polyguanides could be useful only in nonaqueous solutions because the imino group easily hydrolyzes. Further, substitution of NH_2 hydrogens by alkyl groups could be replaced by incorporating amino nitrogens into five-membered rings, which should represent an additional stabilizing factor. For example, instead of heptaguanide **6** one could perhaps try to synthesize compound **9** (Chart 2), which would exhibit a comparable intrinsic basicity. Here R stands for a methyl group. The scaled Hartree−Fock model indicates that the proton affinity of this supramolecular system is 290 kcal/mol. Its basicity can be additionally amplified by substituting a CH_3 group at the most basic imino center by a $CH_2-CH_2-CH_2-NR_2$ group. This would lead to an increased proton affinity due to the internal hydrogen-bonding corona or hollow effect, which contributes about 10 kcal/mol to the resulting APA value.[10] The proton affinity of such a system should reach a very high APA value close to ∼300 kcal/mol. To conclude, we feel confident that branched polyguanides are good candidates for strong organic bases, and consequently their synthesis and characterization are strongly recommended. Another promising pathway in tailoring potent organic superbases is given by a wide family of polycyclic polyguanides, representing extended Schwesinger's proton sponge systems and porphyrins, which might exhibit even more pronounced resonance stabilization in their protonated forms. This work is in progress.

Chart 2



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