Ab Initio Studies of Proton Sponges. 4. Calculating the Strain Energy

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Quantum chemical methods are applied in order to estimate the strain contribution to basicity in diamine proton sponges. Three methods of estimating the strain induced by nitrogen lone pair−lone pair repulsion, are discussed. Strain values in five specific compounds, 1,8-bis(dimethylamino)-naphthalene, 4,5-bis(dimethylamino)phenanthrene, 4,5-bis(dimethylamino)fluorene, 1,8-bis-(dimethylamino)-2,7-dimethoxynaphthalene, and 1,10-bis(dimethylamino)anthracene, are estimated at the HF/6-31G** and BLYP/6-31G** levels of theory. At the Hartree−Fock (HF) level, the values computed for these five compounds vary widely, from 32 to 84 kJ mol^{-1}. The BLYP (electron-correlated) calculations indicate that the HF method overestimates strain values by (on average) around 18 kJ mol^{-1}. None of the three methods discussed here are applicable to every type of proton sponge—certain compounds in which the basic centers are part of heterocyclic systems seem to require some other approach.

Introduction

Diamine proton sponges are compounds with enhanced basicities arising out of the proximity of two basic nitrogen atoms.[1,2] Ab initio calculations have already been applied to predict proton affinities (PAs) of such compounds and to understand the relative magnitudes of the various contributions to basicity and/or pK_a.[3−11] However, while it is relatively straightforward to compute PAs (and with a little more effort, the pK_a in solution[9]), so far little has been achieved in understanding the second part of the problem, i.e., computing the relative magnitudes of different factors to basicity. Calculations at the semiempirical level have proved useful in understanding some basicity trends in proton sponges[12,13] but are not of sufficient accuracy to provide quantitative estimates of these factors. Considering specifically the gas-phase PA (Peräkylä's recent work shows how to use a simple solvation model in order to acount for pK_as[9]), this can be approximated as a sum of four contributions: (i) the proton affinity of a single amine group (assuming asymmetric protonantion of one

Scheme 1
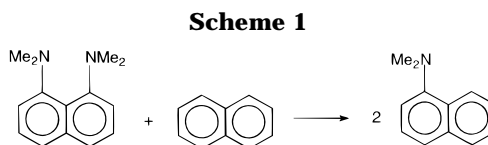
nitrogen, which is usually the case), (ii) the relief of strain (possibly also accompanied by an increase in aromatic stability) and loss of destabilizing lone pair−lone pair repulsion on protonation (Subsequently, the quantity we will refer to as "strain energy" should be understood to include *all* these contributions, if relevant.), (iii) the formation of an intramolecular cationic hydrogen bond [N−H···N]$^+$, which stabilizes the protonated species, and (iv) the change in zero-point or thermal energy on protonation. The various works of Platts, Howard, and Peräkylä make it clear that contribution iv is fairly constant throughout a range of diamine proton sponges, having a value of $\approx$38 ± 7 kJ mol^{-1} at 0 K. This means that the PA of most proton sponges (even large systems) can be estimated with reasonable accuracy at the Har-tree−Fock (HF) level without the need for explicit harmonic frequency calculations which often require huge resources. Although contribution i always dominates the PA, being $\approx$950 kJ mol^{-1} for a group such as R(Me)$_2$N, contribution iii can certainly be 100 kJ mol^{-1} or more according to model gas-phase calculations of the type R$_3$N···H$^+$NR$_3$.[4,8,14] Essentially the only calculations presented so far to estimate the strain contribution are based on isodesmic reactions.[9] Using schemes such as Scheme 1, Peräkylä derived values of 22.8 and 37.2 kJ mol^{-1} for compounds **1a** and **4a**, respectively (see Figure 1). (These values are the enthalpy changes in the above reactions, calculated ab initio.) Here the aim is to point out that there are at least two other methods for obtaining information on these contributions. The first,

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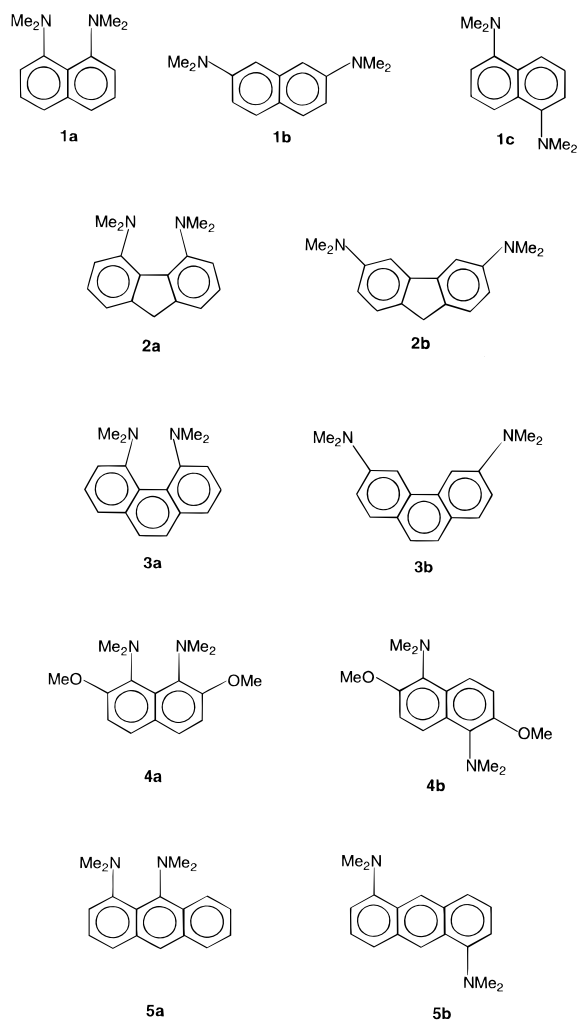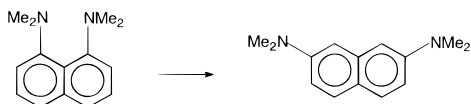(14) Platts, J. A. Ph.D. Thesis, University Of Wales, Cardiff, 1996.

Figure 1. The five proton sponges (and the different isomers) studied in this work.

Scheme 2

and more complete, method is (like Peräkylä's method) specific for a given proton sponge. It associates the strain energy with the enthalpy change of an isomeric shift reaction such as that shown in Scheme 2, the point being that on the right-hand side of the reaction the diamine groups are no longer in proximity, and the structure usually relaxes to a planar form. This method suffers from the potential disadvantage that there are usually several such isomers which could be chosen as the "unstrained" reference compound. There is therefore an electronic (positional) substituent effect, in addition to the loss of strain. However, we note that the isodesmic reaction method is also not free from such effects. The method thus depends on such substituent effects being much smaller in magnitude than the strain energy. For computational expedience, it is natural to choose a reference isomer which has maximal symmetry; e.g., in the case of compound **1a** it could be 2,7-bis(dimethylamino)naphthalene (which may be assumed to be C_{2v}) or 1,5-bis(dimethylamino) naphthalene (C_{2h}). The reference isomer will then have higher symmetry that the corre-

sponding proton sponge (typically of C_2 symmetry), enabling optimization calculations to be carried out more quickly. The effect of choosing different reference isomers is studied here with respect to **1a**, where we have computed the structures and energies of *both* the above-mentioned reference isomers (**1b** and **1c**) and therefore obtained two values for the strain energy. The other alternative method is admittedly crude, both in that it provides a universal curve for *all* diamine proton sponges and that it gives just the lone pair−lone pair repulsion energy. This method associates this repulsive energy in a proton sponge with an internuclear separation, $r(N{\cdots}N)$, as the enthalpy change in the dimer $R_3N{\cdots}NR_3$ when r is increased to ∞. The dimer is arranged in a D_{3h} conformation which mimics the relative geometry of the same groups in a diamine proton sponge. All geometrical parameters may be optimized, except $r(N{\cdots}N)$, which is fixed. The energy so obtained is then subtracted from the energy of two R_3N molecules, to give a value which we shall call $E(LP{\cdots}LP)$, the lone pair−lone pair repulsion energy. Here we will present some sample results for the symmetrical $H_3N{\cdots}NH_3$ dimer.

Computational Details

The HF geometry optimizations employed the 6-31G** (6d) basis set[15] and the July 1995 release of GAMESS,[16] running on DEC Alpha RISC workstations. The "proton sponge" isomers **1a**−**4a** of each compound were optimized within the C_2 point group, and compound **5a** with no symmetry constraints (C_1). C_{2v} symmetry was assumed for the following reference compounds: 2,7-bis(dimethylamino)naphthalene (**1b**), 3,6-bis (dimethylamino)phenanthrene (**2b**), and 3,6-bis(dimethylamino)flourene (**3b**). C_{2h} symmetry was applied in the cases of 1,5-bis(dimethylamino)naphthalene (**1c**), 1,5-bis(dimethylamino)-2,6-dimethoxynaphthalene (**4b**), and 1,6-bis (dimethylamino)anthracene (**5b**). In fact, the unsymmetrical compound **5a** is not a known proton sponge—its inclusion here simply completes the data on possible two and three benzenoid ring based sponges. (In a subsequent paper, we aim to present a comparable study of basicity and strain effects in compounds containing four benzenoid rings[17]). Full structural details of all compounds may be obtained from the authors on request. BLYP/6-31G** (6d) single point calculations were carried out on all optimized structures at the associated HF/6-31G** geometries using GAUSSIAN94[18] running on the EPSRC's Columbus Facility at the Rutherford Appleton Laboratories. These calculations give some idea of the electron correlation contribution to the strain energy. GAUSSIAN94 was also used in the calculation of the HF/6-31G* (6d) potential energy surface (PES) of the D_{3h} species $H_3N{\cdots}NH_3$. The geometrical parameters of the NH_3 monomers were optimized at various fixed values of the intermolecular $N{\cdots}N$ separation and the repulsion energy $E(LP{\cdots}LP)$ taken as $E(H_3N{\cdots}NH_3) - 2E(NH_3)$. Counterpoise or zero-point vibrational energy corrections have not been included. Analysis of the resulting charge distributions employed the AIMPAC program EX-

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Table 1. Total Energies of Optimized Structures (au)

compound/ conformer	HF/6-31G**// HF/6-31G**	BLYP/6-31G**// HF/6-31G**
1a	−649.523 74	−653.496 74
1b	−649.538 34	−653.503 62
1c	−649.536 13	−653.502 72
2a	−764.304 98	−768.975 96
2b	−764.318 81	−768.980 64
3a	−802.164 85	−807.061 53
3b	−802.196 78	−807.084 77
4a	−877.272 31	−882.461 08
4b	−877.294 51	−882.476 51
5a	−802.160 34	−807.057 70
5b	−802.184 08	−807.076 80

Table 2. Derived Strain Energies (kJ mol^{-1}) and Some Structural Features (Å)

compd	HF/6-31G**// HF/6-31G**	BLYP/6-31G**// HF/6-31G**	r(N$\cdots$N)	d^a
1a	38.3, 32.5^b	18.1, 15.7^b	2.791	0.128
2a	36.3	12.3	2.913	0.372
3a	83.8	61.0	2.829	1.135
4a	58.3	40.5	2.760	0.191
5a	62.3	50.1	2.783	0.100, 0.056

^{a}Distance of nitrogen atoms from mean plane. Two values are given for the anthracene proton sponge, since the two nitrogens are symmetry-distinct. ^{b} Two values, calculated as $E(\mathbf{1a}) − E(\mathbf{1b})$ and $E(\mathbf{1a}) − E(\mathbf{1c})$, respectively.

TREME,[19] which evaluated the electron density (ρ) and its Laplacian ($\nabla^2\rho$) at the N$\cdots$N (3,−1) critical point (CP). The CP is defined as the minimum on the line of maximal electron density joining the N nuclei.

Results

The total optimized energies for all compounds are presented in Table 1. The isomers with well-separated diamine groups **1b**−**5b** are more stable than their associated proton sponge counterparts **1a**−**5a** by 0.01−0.03 au (1 au = 2625.5 kJ mol^{-1}). The consequent values of the strain energy are given in Table 2, together with some key structural parameters. At the HF level, values of the strain energy vary over a wide range, from 35 kJ mol^{-1} for **1a**, to 84 kJ mol^{-1} for **3a**. An important point is that the two values of strain energy derived for compound **1a** are very similar, suggesting a mean value of 35.4± 3 kJ mol^{-1}. The "error" induced by positional substituent effects is therefore shown to fulfill the criterion of being much smaller than the strain energy; i.e., 3 kJ mol^{-1} ≪ 35 kJ mol^{-1}. BLYP (electron-correlated) estimates of the strain are also presented in Table 2. These values are consistently lower than their HF counterparts, by 12−23 kJ mol^{-1}, the average "deficit" being 18.8 kJ mol^{-1}. This result should be treated with a little caution, since the structures were not reoptimized at the BLYP level in these calculations (this being computationally prohibitive). However, support for this conclusion may be found in the value for **1a** derived by Peräkylä (also including electron correlation, at the MP2/6-31G* level). Our mean BLYP/6-31G** value of 16.9 ± 1.2 is not far from his value of 22.8 kJ mol^{-1}, and certainly much closer than the HF estimate. Moreover, our BLYP/6-31G** value for **4a** of 40.5 kJ mol^{-1} compares extremely well with Peräkylä's MP2 value of 37.2 kJ mol^{-1}. Table 2 also reports some structural details for

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Table 3. Variation of HF/6-31G* Density Properties and Repulsion Energy in (NH$_3$)$_2$ with Separation

N$\cdots$N distance (Å)	ρ (au)	$\nabla^2\rho$ (au)	repulsive^a energy (kJ mol^{-1})
2.4	0.037	0.167	+124.11
2.6	0.026	0.100	+65.16
2.8	0.018	0.060	+31.61
3.0	0.013	0.037	+13.59

^{a} Relative to two isolated ammonia molecules.

the proton sponge conformer of each compound. There appears to be no correlation between the strain energy and the displacement of the nitrogen atoms from the mean plane. Nor does the N$\cdots$N distance correlate with the strain energy. It was noted that in an earlier paper[7] it was reported that the PA of proton sponges also does not correlate with the N$\cdots$N distance. Table 3 reports the estimates of E(LP$\cdots$LP) obtained via the PES of (NH$_3$)$_2$. A fit to the data of the function E(LP$\cdots$LP) = a/r(N$\cdots$N), which would of course be exact for the repulsive energy of two point charges, gives a reasonable fit (R^2 = 0.984). However, a two-parameter exponential fit of the form E(LP$\cdots$LP) = $ae^{br(N\cdots N)}$ describes the data far better (R^2 = 0.998). The N$\cdots$N separations in the optimized proton sponges **1**−**5** vary from 2.76 to 2.91 Å, which on this basis would suggest E(LP$\cdots$LP) ≈ 20−33 kJ mol^{-1}. In all cases, this is less than the HF-level "strain" estimates presented in Table 2 (in some cases less than half as big). This is to be expected, since the "strain" energy as defined earlier consists of several contributions, not just E(LP$\cdots$LP). Returning to the data in Table 3, the repulsive energy is found to be *linear* with respect to $\nabla^2\rho$ at the N$\cdots$N CP (R^2 = 0.998). It is therefore possible to estimate E(LP$\cdots$LP) in an actual proton sponge either from the distance r(N$\cdots$N) (assuming, for example, that an X-ray or neutron crystal structure is available) or from this electron-density-based parameter (e.g., from an experimental charge density study such as that by Mallinson et al.[20]). Using some previously reported values of $\nabla^2\rho$ at the N$\cdots$N CP calculated ab initio by Platts et al.,[7] E(LP$\cdots$LP) values in compounds **1a**, **2a**, and **3a** are calculated as 26.5, 22.9, and 13.3 kJ mol^{-1}, respectively.

Discussion

In the case of 1,8-bis(dimethylamino)naphthalene, it was demonstrated that the electronic substituent effects induced by changing the diamine group positions are about 10 times smaller than the strain energy. Obviously it would be desirable to make this check in every case, but at the moment this is difficult due to the considerable computing resources required. The size of the strain energies reported here have important consequences for proton sponge design. It may be noted that, according to both the BLYP/6-31G** values and Peräkylä's MP2/6-31G* value, Alder's "prototype" proton sponge 1,8-bis-(dimethylamino)naphthalene has a relatively small (gas phase) strain energy of ≈20 kJ mol^{-1}. So this compound's large basicity is mostly due to the [N−H$\cdots$N]$^+$ hydrogen bond formed on protonation. In fact, the results available so far suggest that the strain energy rarely, if ever, makes a larger contribution to proton sponge basicity than the intramolecular hydrogen bond (often ≈100 kJ mol^{-1} [14]). So it seems that there may be more to be gained by

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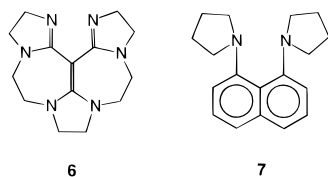
Figure 2. Schwesinger's vinamidine proton sponge (**6**) and 1,8-bis(pyrole)naphthalene (**7**).

designing "flexible" compounds in which the N⋯N distance (after protonation) is as small as possible, rather than an apparently highly strained free base in which the nitrogens are far from the mean plane. Of course, these conclusions remain somewhat tentative at the moment, since they are based on just five examples. When estimates of the strain, basicities, and hydrogen bond energies of many more proton sponges become available, it should clarify this situation. The method for estimating E(LP⋯LP) in actual proton sponges using the (repulsive) $H_3N⋯NH_3$ dimer resulted in values which are consistently much smaller than the HF level isomeric shift estimates contained in Table 2. This suggests that the (mostly electrostatic) lone pair repulsive energy between N atoms typically accounts for no more than half of the overall strain energy. The remainder is presumably made up of bond length and angle strain, with some additional contribution from the disruption of aromaticity due to the distortion of the ring system.

Finally, we should point out the limitations of these techniques for estimating proton sponge strain energies. Compound **6** in Figure 2 is a vinamidine proton sponge first synthesized by Schwesinger and co-workers,[21] which is possibly the most basic organic compound so far known (our own estimates of gas-phase basicity suggest ≈1200 kJ mol⁻¹ for the gas-phase PA[22]). Evidently, it is not possible to write down an isodesmic reaction like that of Peräkylä nor an isomeric shift reaction such as we have used in this work to determine the strain energy. Even the "repulsive dimer" approach for estimating E(LP⋯LP) is also unsatisfactory for such proton sponges in which the basic centers are part of heterocyclic systems. This is because it is difficult to design appropriate model systems/dimer conformations in which the intermolecular repulsive interaction is dominated by just the two basic atoms. Nevertheless, the criterion of applicability is evidently more complex than simply whether the basic centers are part of heterocyclic systems, since the strain energy of, for example, compound **7** (also a known proton sponge, although a very weak one[23]) can be readily determined by either the isodesmic reaction or the isomeric shift methods.

Conclusions

A straightforward method for the estimation of the strain energy in diamine proton sponges has been presented that equates this energy with the enthalpy change of a simple isomeric shift reaction (removing the destablizing N⋯N interaction). Electron correlation is found to play an important role, lowering the strain energy (relative to Hartree−Fock) by 12−23 kJ mol⁻¹. Although it is obviously preferable to include its contribution in any subsequent studies, using an *estimated* HF → BLYP correction of −18± 6 kJ mol⁻¹ would be a reasonable way to proceed for compounds much larger than those studied here, where even BLYP single point calculations may not be computationally feasible. For two of the five compounds, our BLYP/6-31G** strain values may be compared with the MP2/6-31G* values derived in a previous study and computed by a different technique (isodesmic reactions). Encouragingly, the values are very close, which suggests that the strain energies computed may be reasonably independent of the method used. This of course assumes that a method/ basis set is used which is *at least* as good as those just mentioned. The lack of any relationship between strain energy and (i) the displacement of the basic centers from the mean plane or (ii) the N⋯N distance may seem curious at first sight, given that the lone pair−lone pair repulsion energy E(LP⋯LP) is obviously well-correlated with r(N⋯N). However, it should be recalled that we have used an "all-encompassing" definition of strain energy which could be written as:

$$\text{"strain energy"} = E(\text{LP⋯LP}) + E(\text{distortion}) + E(\text{aromatic destabilization})$$

Here E(distortion) is understood to mean the sum of bond stretch, bend, and torsional strain (to use a molecular mechanics notation). Our strain energy as defined above encompasses *all* destabilizing contributions due to the vicinity of the basic centers, and the interplay between these different contributions as a function of molecular geometry is evidently rather subtle. The tentative conclusion (based on just these five compounds) is that proton sponge strain cannot be estimated from structural parameters (i.e., from X-ray or neutron crystallography), ab initio calculations providing the only route to its estimation. On the other hand, E(LP⋯LP) alone can be estimated in a very straightforward way from r(N⋯N) and ancillary ab initio calculations based on repulsive dimer models (although it would be pertinent to carry out more complete and accurate calculations than those presented here).

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