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Theoretical Analysis of Lewis Basicity Based on Local Electron-Donating Ability. Origin of Basic Strength of Cyclic Amines

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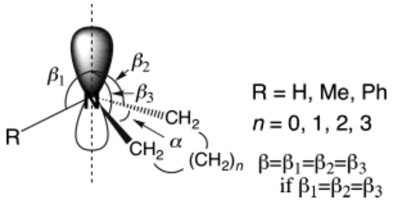
It has been experimentally established that the proton affinities (PA), as well as the solution basicities (pK_{BH^+}), of aziridine derivatives are much smaller than those of the corresponding pyrrolidines and piperidines, though the basic strength of azetidines is close to those of pyrrolidines and piperidines. A simple idea of dependence of the basic strength on bond angles seems to be invalid. Because the basicity of cyclic amines is a fundamental property in organic chemistry, we revisited this topic in order to clarify quantitatively the intrinsic origin of the strength of Lewis basicity of the relevant amines, in particular, based on the local electron-donating ability of the amine nitrogen atoms evaluated in terms of the localized reactive hybrid orbital (RHO) concept. In the cases of representative N-substituents such as hydrogen, methyl, and phenyl groups, the electron-donating energy level of the nitrogen center, obtained by maximizing a kind of superdelocalizability, was shown to be correlated with the magnitudes of experimental and calculated gas-phase proton affinities. The present results strongly support the view that the C−N−C bond angle, i.e., angle strain, in the cyclic amines is not the major source of the difference in strength of basicity of these amines, but rather, the degree of pyramidalization around the nitrogen atom has a significant impact on the electron-donating ability of the nitrogen lone-pair orbital.

Introduction

Bond angle changes about a central atom can greatly alter the electronic properties of a molecule.[1,2] In cyclic amines (1-azacycloalkanes), two bond hybrids which participate in the C−N bonds must increase their p character upon decrease of the C−N−C angle about the amine nitrogen atom. As a consequence, increased s character is seen in the hybrid involved in the N−H bond and the nitrogen lone pair.[3,4] This hybridization effect of the nitrogen atom would lead to a decrease of pyramidalization of the N-substituent and a continuous increase of the basic strength in going from three- to six-membered cyclic amines. This structural relation is known as a type of the Thorpe−Ingold effect,[5] i.e., the smaller the C−N−C angle (α), the larger the pyramidalization angle (*β*) (see Scheme 1).

SCHEME 1



Experimentally, the gas-phase proton affinity (PA) of aziridine **1** (R = H, $n = 0$) is indeed reported to be much weaker than those of pyrrolidine **3** (R = H, $n = 2$) and piperidine **4** (R = H, $n = 3$), while that of azetidine **2** (R = H, $n = 1$) is much closer to those of **3** and **4** (Chart 1, see also Table 1).[6,7] A distinct leveling behavior of **2**−**4** was found in the solution basicity (pK_{BH^+}) (see Table 1) and in the degree of formation of hydrogen bonding of the amine nitrogen with deuterated methanol, which was detected in terms of the shifts in the O−D stretching frequency of deuterated methanol.[6,8] The weak basicity

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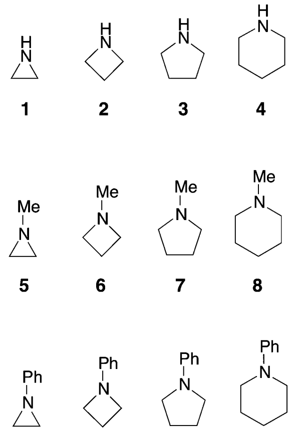
CHART 1



of aziridine **1** has been interpreted in terms of the hybridization effect arising from the small C−N−C angle. On the other hand, the unexpected behavior of azetidine **2** in solution was proposed to be explicable in terms of the intervention of possibly different solvent effects[6,8] and a possible decrease of the ring strain of the azetidine ring upon protonation,[9] leading to enhanced stabilization of the system.

The solution base strength of the *N*-methyl (**5**−**8**) and *N*-phenyl (**9**−**12**) derivatives of the cyclic amines was previously examined (Chart 1)[6,7] and showed a similar trend of ring size effect on the basic strength to that in **1**−**4**. Solution basicity is known to be different from the intrinsic basicity due to complicated solvation effects. On the other hand, the gas-phase proton affinities of the N-unsubstituted cyclic amines (**1**−**4**) and some *N*-methyl derivatives have been studied.[4b] However, the complete data set of the gas-phase PA values of the *N*-methyl (**6**) and *N*-phenyl (**9**−**12**) derivatives is unestablished.[4d]

Furthermore, a recent experimental and theoretical study of the *N*-nitroso derivatives of the relevant cyclic amines (**1**−**4**) (Scheme 1, R = NO) also highlighted the anomalous character of the azetidine derivative despite its small C−N−C angle: *N*-nitrosoazetidine has a bond dissociation energy (BDE) of the N−NO bond as high as those of *N*-nitrosopyrrolidine and *N*-nitrosopiperidine, while the BDE of *N*-nitrosoaziridine was estimated to be much smaller.[10] Angle strain about the C−N−C angle was postulated to weaken the bond strength of the N−NO bond of aliphatic *N*-nitrosoamines, which was consistent with the experimental observations, except for the azetidine derivative.[10]

While the basic strengths of cyclic amines of three to six members have been measured experimentally[6,7,11−14] and theoretically,[14,15] the dependence of the basic strength on bond angles is not clearly understood. Because the basicity of amines is a fundamental property in pure chemistry as well as applied chemistry, such as medicinal chemistry,[16] theoretical prediction and understanding of the basicities of amines and other bases continue to be vital research targets.[17] We decided to revisit this topic in order to define quantitatively the intrinsic origin of the strength of gas-phase Lewis basicity of the cyclic amines, in particular, based on the local electron-donating ability of the amine nitrogen atoms.[18]

Method of Calculations

Full geometry optimization of all the amines, *N*,*N*-dimethylamine and cyclic amines **1**−**12**, and the N-protonated counterparts was carried out at the B3LYP/6-31G* level of theory with a suite of Gaussian 98 programs.[19] The exchange functional in the B3LYP method was the three-parameter hybrid one of Becke,[20] and the correlation functinal was that of Lee, Yang, and Parr.[21] All of the optimized structures were verified to be energy minima or transition structures by vibrational frequency calculations at this level (B3LYP/6-31G*). The final energies were obtained at the B3LYP/6-311+G(3df,2p) level. This basis set was found to be adequate to reproduce the basicity and acidity of molecules containing first-row (third-row) atoms.[22] The energies were corrected with scaled zero-point energy (ZPE) based on B3LYP/6-31G* frequency calculations (scaled by 0.98).[23] To access more accurate proton affinities (PA), the complete basis set method (CBS-Q)[24] and the Gaussian-3 (G3) method[25] were applied. The results of the CBS-Q and G3 calculations available in this work were for the amines except the *N*-phenyl derivatives. Evaluation of the local electron-donating ability of the nitrogen atom of the amines (for **1**−**12**) was carried out by using the MOs obtained

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TABLE 1. Calculated Proton Affinities of Cyclic Amines. Comparison with the Experimental Values[a]

amines	PA(CBS-Q)[b]	PA(G3)[c]	PA(B3LYP)[d]	PA(exp1)[e]	PA(exp2)	pK_{BH+}[i]
1 → **1H**	900.9	903.5	903.7	902.8		8.04
2 → **2H**	935.3	936.3	936.4	932.1	956.8[g]	11.29
3 → **3H**	944.4	946.3	946.2	938.8	956.8[f]	11.27
4 → **4H**	947.8	948.1	949.3	943.4	961.4[f]	11.22
5 → **5H**	926.2	929.0	928.9	927.1		7.86
6 → **6H**	951.1	953.4	951.8			10.40
7 → **7H**	959.4	958.0	955.9	953.5	971.8[f]	10.46
8 → **8H**	963.7	965.2	963.8	957.6	976.1[f]	10.08
9p → **9pH**	890.9	921.8	922.1		926.5[h]	1−2
10p → **10vH**	927.9	931.9	929.2		933.2[h]	3.62
11hc → **11vH**			933.0		941.6[h]	3.57
12tw → **12vH**			958.7		952.9[h]	5.22

[a] Protonation processes of the amines which correspond to calculated proton affinities (PA), given in kJ/mol. [b] Complete basis set (CBS)-Q calculations. At 273.15 K. See ref 23. [c] Gaussian-3 calculation. See ref 24. [d] The values obtained at the B3LYP/6-311+G(3df,2p) level, corrected with scaled zero-point energy based on B3LYP/6-31G* frequency calculations (scaled by 0.980). The structures of the amines were fully optimized at the B3LYP/6-31G* level. [e] Reference 4b. [f] Reference 12. [g] Reference 9. [h] Reference 4d. [i] Reference 7.

at the HF/6-31G* level, applied to the B3LYP/6-31G* optimized structures.[18]

Results and Discussion

Calculated Proton Affinities of Cyclic Amines. Proton affinities (PA) of the cyclic amines, an enthalpy change upon protonation, were evaluated with several levels of calculation, which included single-point calculations at the B3LYP/6-311+G(3df,2p) level (ZPE corrected) on the basis of the B3LYP/6-31G* optimized structures (Table 1). The B3LYP/6-31G*-optimized structures of N-unsubstituted (**1**−**4**) and *N*-methyl cyclic amines (**5**−**8**) together with the corresponding N-protonated ions (**1H**−**8H**) are shown in Figures S1 and S2 (Supporting Information), respectively.

Furthermore, the values of PA were also evaluated with the CBS-Q[24] and G3 methods,[25] and both methods were applied to amines **1**−**10**. The calculated PA values are consistent with the reported experimental values in gas phase (see Table 1).[4b] In the cases of the neutral amines and the corresponding N-protonated ions of the N-phenyl-substituted derivatives, several conformational isomers with respect to rotation of the phenyl group are possible. The relative energies (B3LYP/6-311+G(3df,2p), ZPE corrected) and the optimized structures (B3LYP/6-31G*) of the conformers are shown in Figure 1. The neutral N-phenyl-substituted derivatives aziridine (**9**), azetidine (**10**), and pyrrolidine (**11**) take coplanar structures (**9p**−**11p**) in which the *N*-phenyl group is conjugated with the amine nitrogen lone-pair electrons (Figure 1). In contrast, in the case of piperidine **12**, the conformer with a rotated phenyl group, a twisted phenyl structure (**12tw**), has the minimum energy. Such different conformations of the N-phenyl group of the relevant cyclic amines, depending on the amine ring size, were postulated previously.[7] Upon protonation of the nitrogen atom, the conformers with a vertical (bisected) structure of the phenyl group, perpendicular with respect to the amino ring, are favored in the cases of the azetidine (**10vH**), pyrrolidine (**11vH**), and piperidine (**12vH**), while the coplanar structure is favored in the case of the aziridine (**9pH**). The PA values of the amines obtained by the CBS-Q and G3 methods are comparable to those obtained at the B3LYP/6-311+G(3df,2p)//B3LYP/6-31G* level. Therefore, the proton affinities of amines **1**−**12** calculated at the B3LYP/6-311+G(3df,2p) level are discussed throughout this paper. The calculated PAs correlated well with the experimental ones.

We plotted the calculated proton affinity values of the cyclic amines (Table 1) against the HOMO energies obtained at the HF/6-31G* level (Figure 2). There is no apparent correlation, especially for the *N*-phenyl-substituted derivatives (**9**−**12**). The HOMO is a canonical orbital mainly consisting of the nitrogen nonbonding orbital. Thus, canonical orbitals such as the HOMO of the amines, which are generally delocalized over the whole of the molecule, particularly in the cases of the *N*-phenyl derivatives, seem to be irrelevant to local properties such as the basicity of the nitrogen atom in an amine molecule.[17a,26]

Well-established localized molecular orbital (LMO) methods such as the Rudenberg,[27] Boys,[28] Mezey,[29] and natural localized molecular orbital (NLMO) methods,[30] can create a well-defined nonbonding orbital, localized on the nitrogen atom. The resultant localized orbitals, which represent the nitrogen lone-pair orbitals, have orbital energies much lower than those of the canonical HOMOs (Table 2). These localized orbitals are well localized on the nitrogen atom, but they do not represent the electron-donating reactive orbitals. These conventional LMO methods utilize low-lying s-AOs of the amino nitrogen atom in order to localize the orbitals onto the nitrogen atom. Thus, the energy level of the resulting localized nitrogen lone-pair orbital is lowered.

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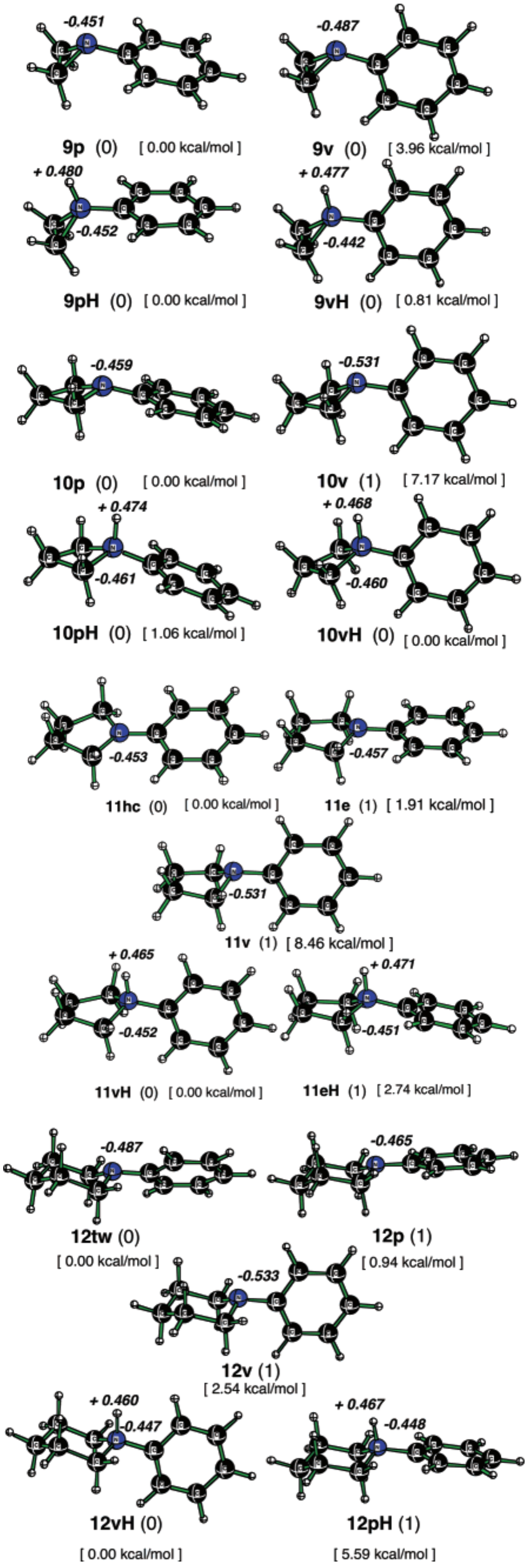

FIGURE 1. B3LYP/6-31G*-optimized structures of *N*-phenyl-substituted cyclic amines and their N-protonated ions. The imaginary frequency number is shown in parentheses, and relative energy is shown in brackets. The natural population analysis charges (B3LYP/6-31G* level) were shown in italic.

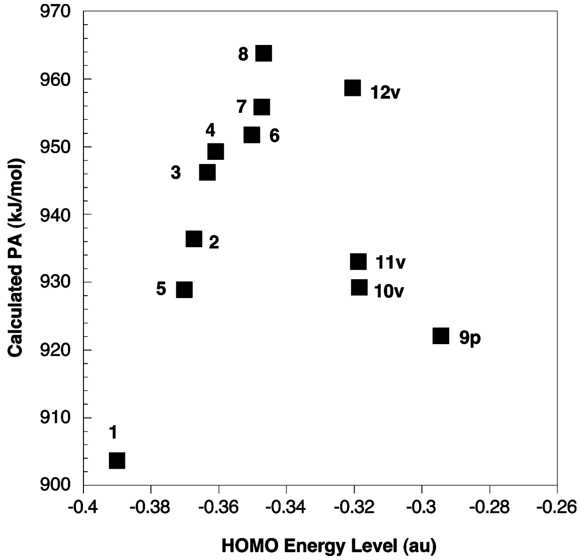

FIGURE 2. Plot of calculated PAs (B3LYP) against HOMO levels obtained at the HF/6-31G* level.

The reactive hybrid orbital (RHO) concept can describe the local electron-donating (-accepting) ability of a reaction center through localization of the reactive orbital as a hybrid of all the occupied (unoccupied) MOs onto the relevant reaction centers.[18] We demonstrate here that the electron-donating ability of the nitrogen atom, evaluated in terms of the RHO concept, is strongly related to the intrinsic strength of basicity of the cyclic amines. We will examine in this paper how the electron-donating ability of the nitrogen atom varies depending on the environment.

Definition of Reactive Hybrid Orbital (RHO) Which Represents Intrinsic Electron-Donating Ability of the Nitrogen Atoms of the Amines. We analyzed the local electron-donating ability of the amines in terms of a reactive hybrid orbital (RHO), which can be generated by a method recently developed by some of the present authors.[18] When an electron-donating orbital ϕ_{oc} is represented by a linear combination of canonical occupied MOs as

$$\phi_{oc} = \left(\sum_i^{oc} d_i \psi_i\right) \Big/ \left(\sum_i^{oc} {d_i}^2\right)^{1/2} \tag{2}$$

the energy level of the orbital can be evaluated as

$$\lambda_{oc} = \left(\sum_i^{oc} {d_i}^2 \epsilon_i\right) \Big/ \left(\sum_i^{oc} {d_i}^2\right) \tag{3}$$

where ϵ_i is the energy level of the canonical MO ψ_i obtained by solving a Hartree–Fock–Roothaan equation. The orbital ϕ_{oc} is then represented by a linear combination of atomic orbitals (LCAO) as

$$\phi_{oc} = \sum_\mu c_\mu \chi_\mu \tag{4}$$

TABLE 2. Local Electron-Donating Abilities of Cyclic Amines, Evaluated by the RHO Method and by Conventional Localized Molecular Orbital (LMO) Methods. Calculated at the RHF/6-31G* Level[a−c]

amines	Rudenberg	Boys	Mezey	NLMO	HOMO	λ_{oc} (f_{oc})	ρ_{oc}	% s[d]
1	−0.541	−0.543	−0.629	-0.575	-0.390	−0.433 (0.920)	2.123	18.89
2	−0.516	−0.510	−0.555	-0.491	-0.367	−0.397 (0.926)	2.333	9.95
3	−0.515	−0.510	−0.545	-0.478	-0.363	−0.393 (0.929)	2.365	9.20
4	−0.513	−0.509	−0.541	-0.473	-0.361	−0.391 (0.927)	2.372	8.71
5	−0.540	−0.540	−0.617	-0.540	-0.370	−0.416 (0.900)	2.162	16.24
6	−0.520	−0.514	−0.553	-0.475	-0.350	−0.385 (0.901)	2.340	8.71
7	−0.519	−0.514	−0.547	-0.467	-0.347	−0.382 (0.903)	2.362	8.25
8	−0.519	−0.514	−0.548	-0.466	-0.347	−0.382 (0.902)	2.364	8.17
9p	−0.554	−0.554	−0.626	-0.530	-0.294	−0.411 (0.870)	2.118	13.94
9v	−0.551	−0.551	−0.634	-0.541	-0.314	-0.427 (0.900)	2.107	15.61
10p	−0.536	−0.529	−0.522	-0.456	-0.275	−0.372 (0.847)	2.277	3.82
10v	−0.528	−0.580	−0.610	-0.470	-0.319	-0.392 (0.908)	2.314	7.50
11e	−0.533	−0.525	−0.505	-0.446	-0.274	−0.367 (0.850)	2.315	2.99
11hc	−0.491	−0.489	−0.444	-0.426	-0.265	−0.356 (0.838)	2.355	0.00
11v	−0.527	−0.521	−0.549	-0.464	-0.319	-0.389 (0.912)	2.343	7.15
12tw	−0.529	−0.522	−0.528	-0.451	-0.285	−0.373 (0.872)	2.338	4.55
12p	−0.532	−0.524	−0.520	-0.450	-0.278	−0.370 (0.854)	2.311	3.72
12v	−0.525	−0.519	−0.550	-0.461	-0.320	−0.388 (0.910)	2.344	6.99

[a] In the RHO method, λ_{oc}, f_{oc} (in parentheses), and ρ_{oc} are the energy level, electron density, and the reactivity index of the amine lone-pair orbital, respectively. [b] The values of λ_{oc}, the orbital energies obtained by the localized molecular orbital methods (Rudenberg, Boys, Mezey, and natural localized molecular orbital (NLMO)) and the HOMO levels are given in au. [c] The structures of the amines are fully optimized at the B3LYP/6-31G* level. [d] Percentage s-character of nitrogen RHO, i.e., the reactive nonbonding orbital of the amine (HF/6-31G*). See also the Supporting Information, Table S32.

Now we extract only the terms containing the AOs on the atom of the reaction center (denoted here by *A*) from eq 4

$$\phi'_{oc} = \sum_{\mu \in A} c_\mu \chi_\mu \tag{5}$$

and then we define functions similar to the frontier density f_{oc} [31] and an index ρ_{oc}, respectively, as

$$f_{oc} = \langle \phi_{oc} | \phi'_{oc} \rangle \tag{6}$$

and

$$\rho_{oc} = -f_{oc}/\lambda_{oc} \tag{7}$$

The value $2f_{oc}$ corresponds to the electrons in ϕ_{oc} belonging to atom *A*, and the formula for ρ_{oc} is similar to that of superdelocalizability based on the Hückel approximation.[32] We obtained a set of d_i values in eq 2, which gives the maximum value of ρ_{oc}, by minimizing $1/\rho_{oc}$ numerically with the Davidon−Fletcher−Powell method.[33] The

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[31] Fukui, K.; Yonezawa, T.; Shingu, H. *J. Chem. Phys.* **1952**, *20*, 722−725.

[32] Fukui, K.; Yonezawa, T.; Nagata, C. *Bull. Chem. Soc. Jpn.* **1954**, *27*, 423−427.

[33] (a) Fletcher, R.; Powell, M. J. D. *Comput. J.* **1963**, *6*, 163−168. (b) Reddy, P. J.; Zimmermann, H. J.; Hussain, A. *J. Comput. Appl. Math.* **1975**, *1*, 255−265.

[34] While the RHO method owes some of its fundamental ideas to the projected reactive orbital (PRO) method,[35b−f] they are essentially different from each other. In the PRO method, a reference function δ_r, which is assumed to represent approximately the interaction with a reagent, is defined prior to calculations. However, determination of the reference function needs a somewhat arbitrary selection of AOs. Furthermore, projection of a reference function represented by a few AOs only on a reaction center results in a low-energy PRO as compared with an interaction frontier orbital.[36] While the set $\{d_i\}$ of eq 2 was determined by projection of a reference function δ_r in the PRO method, we directly optimize $\{d_i\}$ in the RHO method; therefore, an RHO can be calculated without the need of a reference function. By using the present method,[18] a reactive orbital can be uniquely obtained even in complicated cases where a split valence basis set such as 6-31G* or 3-21G* is used. A related method, which determines δ_r that gives the maximum value of λ_{oc}, was proposed by Kurita and Takayama.[37] However, in their method δ_r cannot contain *d*-type AOs in generating a reactive orbital for the formation of new chemical bonds with electrophiles. Also, the localizability of a reactive orbital calculated by their method, particularly for a conjugated or aromatic system, is insufficient. This is because their method focuses on the energy level of a reactive orbital, while paying less attention to the localizability of the orbital. Although their method offers some improvement over the original PRO method in that it provides a procedure for determining a reference function in a unique, analytical manner, the meaning of the reference function became less clear.

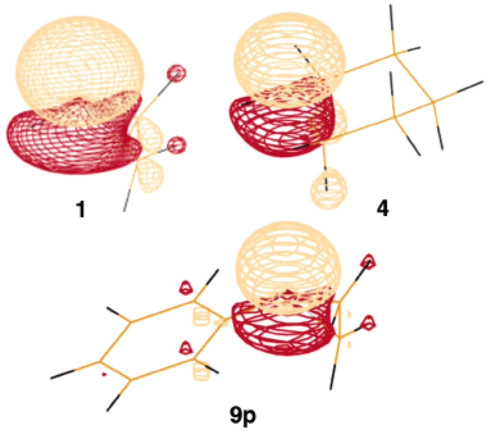

FIGURE 3. Occupied reactive hybrid orbitals of aziridine **1**, piperidine **4**, and *N*-phenylaziridine **9p**.

orbital ϕ_{oc} represented by eq 2 with the optimized d_i values is specifically called the occupied RHO. The occupied RHO is a high-lying orbital (i.e., a small negative λ_{oc} value), but it is localized on the reaction center (i.e., a large f_{oc} value).[34]

The reactive orbitals ϕ_{oc} (occupied RHO) of **1**, **4**, and **9p** are shown in Figure 3. They are well localized on the nitrogen center and look very similar to each other. The results of calculations at the HF/6-31G* level, on the basis of the B3LYP/6-31G* fully optimized structures, are presented in Table 2. The reported analysis based on an interaction frontier orbital obtained for the complex of ammonia (NH_3) and a proton (H^+)[35a] indicated that the lone-pair orbital enhanced the p character in order to create the new N−H bond in ammonium ion (NH_4^+), while the large s component stabilized the molecule in an isolated state (i.e., NH_3). The lone pair orbital obtained in the present RHO method is consistent with that involved in the interaction frontier orbital pair of ammonia and a proton.

One sees that aziridine **1** has a ρ_{oc} value lower than those of **2**, **3**, and **4**, which is consistent with the magnitudes of the experimental and calculated PA values.[4b] The same trend is also observed among *N*-methyl-substituted amines **5**, **6**, **7**, and **8** and among N-phenyl-substituted amines **9**, **10**, **11**, and **12**; aziridines **5** and **9** have low ρ_{oc} values as compared with those of the larger ring-sized amines bearing the same N-substituent. Table 2 indicates clearly that the difference in the ρ_{oc} values between the aziridines and other large ring amines arises mainly from the λ_{oc} term (see eq 7). The orbital energy of the reactive hybrid orbital, λ_{oc} is much closer to that of the HOMO than are those of other LMOs (see Table 2). The extent of localization of the reactive orbital ϕ_{oc} on the nitrogen atom is given by f_{oc} (Table 2). In the cases of the N-unsubstituted and *N*-methylamines, the f_{oc} values are consistent among the amines bearing the same N-substitutent.

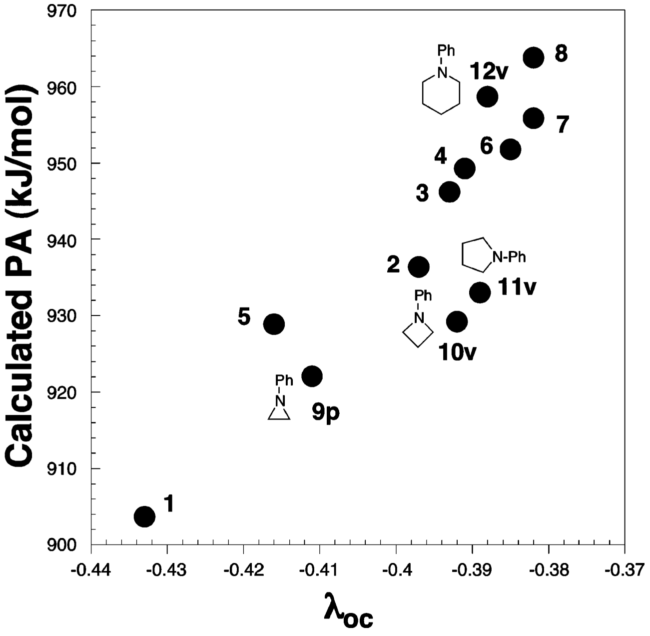

FIGURE 4. Relationship between the orbital energies (λ_{oc}, au, HF/6-31G*) and calculated proton affinities (PAs, kJ/mol, B3LYP/6-311+G(3df,2p)).

In most *N*-phenyl-substituted amines (**10**−**12**), rotation of the phenyl group takes place upon N-protonation, leading to vertical structures of the N-protonated ions (**10vH**, **11vH**, and **12vH**). Therefore, we assumed that the electron-donating abilities of these amines (**10**−**12**) should be evaluated in the vertical structures (**10v**, **11v**, and **12v**). In the case of *N*-phenylaziridine, the coplanar structure (**9p**) was used in the evaluation of the electron-donating ability, because the N-protonated ion keeps a coplanar conformation (**9pH**). In *N*-phenyl-substituted amines (**9p**−**12p**) in a coplanar structure, the f_{oc} values are smaller than those of **1**−**8**. This is because the lone-pair electrons in the coplanar structures **9p**−**12p** are delocalized toward the phenyl ring through conjugation between a lone pair and a phenyl ring, leading to less effective electron donation from nitrogen to a proton. As is apparent in Table 2, the ρ_{oc} values of the *N*-phenyl-substituted amines (except **9**) increased upon rotation from the coplanar structures of the phenyl group (**10p**−**12p**) to the corresponding vertical forms (**10v**−**12v**), probably because the orbital energies (λ_{oc}) were lowered due to the reduction of the out-of-phase interaction of the amine nitrogen lone-pair orbital and the phenyl π orbital.

A plot of the calculated PAs against the λ_{oc} value is shown in Figure 4. The calculated PAs and the λ_{oc} values of all the amines **1**−**12** showed some correlation, though the plots are scattered, especially the values for *N*-phenyl-substituted derivatives. However, the correlation is improved as compared with that found between the calculated PA and the HOMO energy levels (see Figure 2). A similar correlation was also found between the ρ_{oc} values and the calculated PAs. The polarizability effect, i.e., induced dipole stabilization by the *N*-alkyl substituent of the conjugate ion formed on protonation, is known to contribute to the basicities of amines.[11,38] Charge

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[35] (a) Fujimoto, H.; Koga, N.; Hataue, I. *J. Phys. Chem.* **1984**, *88*, 3539−3544. (b) Omoto, K.; Sawada, Y.; Fujimoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 1750−1755. (c) Omoto, K.; Fujimoto, H. *J. Am. Chem. Soc.* **1997**, *119*, 5366−5372. (d) Hirao, H.; Omoto, K.; Fujimoto, H. *J. Phys. Chem. A* **1999**, *103*, 5807−5811. (e) Hirao, H.; Fujimoto, H. *J. Phys. Chem. A* **2000**, *104*, 6649−6655. (f) Ogawa, A.; Fujimoto, H. *Inorg. Chem.* **2002**, *41*, 4888−4894.

[36] Fukui, K.; Koga, N.; Fujimoto, H. *J. Am. Chem. Soc.* **1981**, *103*, 196−197.

redistribution upon N-protonation of the amines was calculated (Supporting Information, Table S29). The natural population analysis charges (B3LYP/6-31G* level) of the N−H atoms of the conjugated ions and the N atom of the neutral amines are compared. The positive charges, which are accumulated within the NH moiety of the ion upon N-protonation, increased as the ring size increased in the cases of the N-substituents such as H and CH_3, while in the case of *N*-phenylamines (here we consider the protonation process shown in Table 1), the change in the charge redistribution upon the increase of the ring size is different from the former N-substituents.[11] In the case of *N*-phenylamines, the smaller positive charge of the NH moiety of the ions indicated a large redistribution effect of the phenyl group. While the polarizability effect depends on the size of the substituent (the larger the size of a substituent, more polariazable),[39] the decrease of the positive charge, accumulated in the NH moiety of the ion upon N-protonation in the cases of N−H and N−CH_3 amines, are contradictory. Furthermore, in the cases of the same ring-size amines, the *N*-methyl substituent leads to the more charge redistribution of the *N*-hydrogen moiety of the ions as compared with the N−H substituent, but not significantly. Thus, the polarizability effect, which indeed contributed to the present protonation process, is unlikely a major origin of the difference of the gas-phase basicities of the present set of the amine bases. Apparently, the relationship shown in Figure 4 is consistent with the idea that the local electron-donating energy level λ_{oc}, and the localizability f_{oc} of the localized reaction orbital, rather than the canonical HOMO and other LMOs, represents the intrinsic strength of basicity; that is, it would be generally anticipated that the stronger the basicity, the negatively smaller the λ_{oc} value (the larger the ρ_{oc} value).

Origin of Structural Effects on the Base Strength. To see the reason the nitrogen centers in the aziridines **1**, **5**, and **9** have weaker basicities relative to the amines having five- and six-membered cyclic structures, and the reason the nitrogen centers in the small cyclic amines, azetidines **2**, **6**, and **10** have basicities close to those of five- and six-membered cyclic amines, we first studied the effect of C−N−C angle. The pyramidalization angle (β_1, β_2, and β_3, see Scheme 1) of inner and outer p-type AO components of the RHO of the amine nitrogen atom (which represents the reactive lone-pair electrons) with respect to the N−C bonds are calculated (see the Supporting Information, Table S30). The average values of three pyramidalization angles both of the inner and outer p-type AO components of the RHOs are almost identical to the values β, which can be obtained under the assumption that the RHO of the amine nitrogen atom extends in the direction which gives the same value (β) for the three pyramidalization angles, β_1, β_2, and β_3 (see Scheme 1). Thus, in the following discussion, the pyramidalization angle β is used. Similar results were obtained when the respective avarage values of β_1, β_2, and β_3 of inner and outer p-type AO components of the RHOs were used. By taking *N*,*N*-dimethylamine (α = 112.8°) as a model, we changed the C−N−C bond angle α (see Scheme 1) to the values obtained by the structural optimization of aziridine (**1**, 60.5°), azetidine (**2**, 90.4°), pyrrolidine (**3**, 104.8°), and piperidine (**4**, 112.1°).[40] Herein, the pyramidalization angles of two C−N bonds and an H−N bond with respect to the lone-pair orbital, defined to be equal (β) in this work, are fixed at 108.6°, which is the optimized pyramidalization angle of *N*,*N*-dimethylamine.[41,42] The localizability f_{oc} of the reaction orbital on the amine nitrogen atom is insensitive to change of the bond angle (α), and all the values are of similar magnitude (Table 3). The λ_{oc} values obtained are −0.416, −0.400, −0.394, −0.393, and −0.394 au, corresponding to values of α of 60.5° (for **1**), 90.4° (for **2**), 104.8° (for **3**), 112.1° (for **4**), and 112.8° (for *N*,*N*-dimethylamine), respectively. The ρ_{oc} values are 2.240, 2.403, 2.467, 2.483, and 2.480, respectively. The electron-donating orbital energy levels λ_{oc} (and electron-donating abilities ρ_{oc}) thus estimated showed linear dependence on the bond angle α, but the slope is small upon change of α (see Figure 5). Therefore, this result indicates that the C−N−C bond angle, i.e., angle strain, is not the major source of the difference in the strength of basicity of these amines.

TABLE 3. Changes in Local Electron-Donating Abilities of *N*,*N*-Dimethylamine upon Changes in the Bond Angle (α) or Pyramidalization Angle (β). Evaluation by the RHO Method. Calculated on the Basis of the RHF/6-31G* MOs[a,b]

angle α (deg)	angle β (deg)	f_{oc}	λ_{oc}	ρ_{oc}
60.5	108.6[c]	0.910	−0.416	2.191
90.4	108.6[c]	0.928	−0.400	2.320
104.8	108.6[c]	0.931	−0.394	2.360
112.1	108.6[c]	0.931	−0.393	2.369
112.8[d]	120.7	0.929	−0.444	2.079
112.8[d]	111.5	0.931	−0.404	2.301
112.8[d]	109.4	0.932	−0.396	2.352
112.8[d]	108.4	0.930	−0.392	2.376
112.8[e]	108.6[e]	0.930	−0.394	2.362

[a] In the RHO method, λ_{oc} (in au), f_{oc} and ρ_{oc} are the energy level, site electron density, and the reactivity index of the amine lone-pair orbital, respectively. [b] Bond angle α and pyramidalization angle β are shown in Scheme 1. See also footnote 42. [c] This β value is the optimized pyramidalization angle of *N*,*N*-dimethylamine. [d] This α value is obtained by structural optimization of *N*,*N*-dimethylamine. [e] The optimized structure of *N*,*N*-dimethylamine was used.

We next examined the effect of the pyramidalization angle β of the reactive orbital (RHO) on the electron-donating ability of the nitrogen center. The calculated pyramidalization angles β of a series of aziridines, **1** (120.7°), **5** (117.1°), and **9** (114.5°) were considerably larger than those of the related pyrrolidine and piperidine

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(37) Kurita, Y.; Takayama, C. *J. Phys. Chem. A* **1997**, *101*, 5593−5595.

(38) Graton, J.; Laurence, C.; Berthelot, M.; Questel, J.-Y. L.; Besseau, F.; Raczynska, E. D. *J. Chem Soc., Perkin Trans. 2* **1999**, 997−1001.

(39) Taft, R. W.; Wolf, J. F.; Beauchamp, J. L.; Scorrano, G.; Arnett, E. M. *J. Am. Chem. Soc.* **1978**, *100*, 1240−1249.

(40) The C−N−C bond angles (α) obtained by the calculation (B3LYP/6-31G* full optimization) were as follows: **1**, 60.5°; **2**, 90.4°; **3**, 104.8°; **4**, 112.1°; **5**, 61.4°; **6**, 90.5°; **7**, 104.8°; **8**, 111.5°; **9p**, 61.8°; **9v**, 60.6°; **10p**, 93.3°; **10v**, 90.6°; **11e**, 109.6°; **11hc**, 112.8°; **11v**, 107.5°; **12tw**, 112.4°; **12p**, 112.1°; **12v**, 114.3°; *N*,*N*-dimethylamine, 112.8°.

(41) The pyramidalization angles (β) obtained by the calculation (B3LYP/6-31G* full optimization) were as follows: **1**, 120.7°; **2**, 111.5°; **3**, 109.4°; **4**, 108.4°; **5**, 117.1°; **6**, 109.3°; **7**, 107.7°; **8**, 107.3°; **9p**, 114.5°; **9v**, 115.9°; **10p**, 102.8°; **10v**, 105.1°; **11e**, 100.1°; **11hc**, 99.4°; **11v**, 99.4°; **12tw**, 105.9°; **12p**, 101.3°; **12v**, 105.5°; *N*,*N*-dimethylamine, 108.6°.

(42) The average values of β_1, β_2, and β_3 of the inner and outer p-type AO components of the RHO of optimized *N*,*N*-dimethylamine are identical to 108.6 (see the Supporting Information, Table S31, and footnote 41).

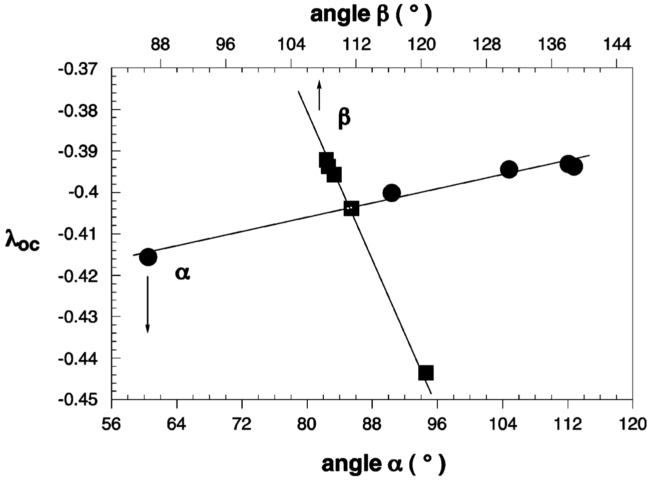

FIGURE 5. Plots of orbital energies (λ_{oc}, au, HF/6-31G*) against bond angle α and pyramidalization angle β. The angle scales have the same interval.

derivatives. Furthermore, the pyramidalization angles β of a series of azetidines, **2** (111.5°), **6** (109.2°), and **10v** (105.1°) were also larger than those of the corresponding pyrrolidine and piperidine derivatives, although the differences were much smaller than those of the corresponding aziridines. When the angle β of *N*,*N*-dimethylamine is hypothetically adjusted to the values of the angles β of the corresponding N-unsubstituted cyclic amines, aziridine (**1**, 120.7°), azetidine (**2**, 111.5°), pyrrolidine (**3**, 109.4°), piperidine (**4**, 108.4°), and *N*,*N*-dimethylamine (108.6°), while keeping the bond angle α constant at the value obtained by structural optimization of *N*,*N*-dimethylamine (112.8°),[41] the λ_{oc} values were calculated to be −0.444, −0.404, −0.396, −0.392, and −0.394 au, respectively (Table 3). The electron-donating orbital energies (λ_{oc}) of the nitrogen center are increased by this structural change, i.e., flattening of the pyramidal nitrogen atoms, and the magnitudes of the resultant λ_{oc} values are consistent with the corresponding values of aziridine (**1**), azetidine (**2**), pyrrolidine (**3**), and piperidine (**4**) (Table 2). The localizability (f_{oc}) was also insensitive to change of the angle β. The ρ_{oc} values were calculated to be 2.162, 2.406, 2.464, 2.491, and 2.480, respectively, upon decrease of the angle β (Table 3). Good linear relationships between the λ_{oc} (Figure 5) or ρ_{oc} and the angle β were obtained, and the slopes were significantly larger than those found for the change of angle α. Therefore, the degree of pyramidalization, which is represented by the angle β appears to have a more significant impact on the electron-donating ability of the amine nitrogen atoms than does the bond angle α. This conclusion can be rationalized in terms of the postulate that the pyramidalization angle (β), rather than the bond angle (α), correlates with the s-character of the nitrogen reactive nonbonding orbital (RHO).[43] This can be recognized in the linear relationship in the plot of the pyramidalization angle (β) against the ratio of the *s*-character of the nitrogen RHO, i.e., the lone pair orbital, calculated at the HF/6-31G* level (Figure 6). Therefore, as the pyramidalization angle (β) increases, the enhanced contribution of the low-lying s-AOs results in reduction of the energy energy levels (λ_{oc}) of the lone-pair orbitals. This can also be seen actually in the smaller λ_{oc} value of the aziridines **1**, **5**, and **9p** as compared with the corresponding pyrrolidines and piperidines (Table 2). The bond angle (α) also modifies the electron-donating orbital energy as shown in Figure 5, though the magnitude is smaller than that induced by change of the pyramidalization angle β. Thus, the amines showed simultaneous changes of the bond angle and pyramidalization angle, depending on the ring size and the N-substituent.

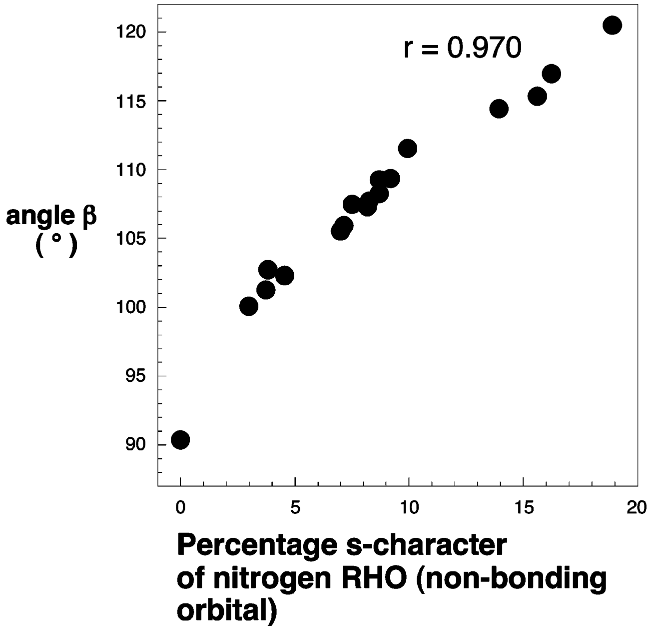

FIGURE 6. Relationship between percentage of s-character of the nitrogen RHO (HF/6-31G*) and pyramidalization angle β.

Conclusion

We calculated the local electron-donating ability (λ_{oc} and ρ_{oc}) of the nitrogen atoms of cyclic amines, based on the reactive hybrid orbital (RHO) theory. The calculated charge redistribution of the NH moiety of the ammonium ion formed upon N-protonation showed reverse polarizability effect, i.e., the positive charge accumulated in the NH moiety of the ion upon N-protonation increased in the cases of N−H and N−CH_3 amines as the ring size increased. We postulated that the local electron-donating ability represents the intrinsic strength of basicity of cyclic amines. We found that the magnitude of the local electron-donating ability is indeed correlated with those of the calculated PAs and the reported experimental PAs. The present results also strongly support the idea that the C−N−C bond angle, i.e., angle strain, in the cyclic amines is not the major source of the difference in strength of basicity of these amines, but rather, the degree of pyramidalization around the nitrogen atom has a significant impact on the local electron-donating ability of the nitrogen atom. That is, as the pyramidalization angle is increased, the local electron-donating ability is reduced. Aziridines have larger pyramidalization angles and, accordingly, show smaller local electron-donating abilities at the nitrogen center as compared with pyrro-

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[43] The s-characters of RHOs of the amines (which represent reactive nonbonding orbital) based on the HF/6-31G* calculations are shown in the Supporting Information, Table S32.

lidines and piperidines, whereas the electron-donating abilities of azetidines are similar in magnitude to those of the related pyrrolidines and piperidines. This accounts well for the PA values of these cyclic amines.

The present work shows that a well-defined local property of the amine nitrogen atoms can aid understanding of the Lewis basicity of the cyclic amines. A similar strategy should be applicable to interpret the data for other nitrogen bases and bases involving other elements and also to predict new molecular systems exhibiting desired levels of basicity.[17]

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Supporting Information Available: Oprimized structures and coordinates of the structures are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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