Hydrogen-bond basicity pK_{HB} scale of aliphatic primary amines

Jérôme Graton,[a] Christian Laurence,*[a] Michel Berthelot,[a] Jean-Yves Le Questel,[a] François Besseau[a] and Ewa D. Raczynska[b]

[a] *Laboratoire de Spectrochimie, Faculté des Sciences et des Techniques, Université de Nantes, BP 92208, F-44322 Nantes Cedex 3, France*
[b] *Institute of General Chemistry, Warsaw Agricultural University, 02528 Warsaw, Poland*

Received (in Cambridge) 26th November 1998, Accepted 17th February 1999

Using 4-fluorophenol as a reference hydrogen-bond donor, equilibrium constants, K_f, for the formation of 1 : 1 hydrogen-bonded complexes have been obtained by FTIR spectrometry for 22 aliphatic primary amines, in C_2Cl_4 at 298 K. The pK_{HB} (log K_f) scale shows that most primary amines are weaker hydrogen-bond bases than many oxygen bases. The pK_{HB} scale of primary amines extends from 2.31 for adamantan-1-amine to 0.67 for $CF_3CH_2NH_2$. The main effects explaining the pK_{HB} variations are (i) field-inductive effects (*e.g.* in $CF_3CH_2NH_2$), (ii) resonance effects (cyclopropylamine), (iii) polarizability effects (alkylamines), and (iv) intramolecular hydrogen bonding (*e.g.* in 2-methoxyethylamine). Except for intramolecularly hydrogen-bonded methoxyamines and diamines, the pK_{HB} and pK_a scales are correlated. The pK_{HB} scale also correlates with the minimum electrostatic potential on the nitrogen lone pair.

The most characteristic property of amines is certainly the ability to behave as bases. In most text books of organic[1] or inorganic chemistry,[2] their base strength is given by the pK_a of their conjugate acid, measured in water, and by the *GB* ($-\Delta G°$ for the protonation reaction) or *PA* ($-\Delta H°$ for the protonation reaction) scales obtained from gas-phase proton transfer measurements. These scales[3] show that amines are generally better proton acceptors, *i.e.* stronger Brønsted bases, than oxygen bases. A simple example comes from the product of the reaction of CF_3SO_3H with 4,4′-bis(dimethylamino)benzophenone: X-rays show that protonation occurs on a nitrogen atom.[4] However the X-ray structure of the hydrogen-bonded complex of the same base with pentafluorophenol establishes that hydrogen bonding occurs to the oxygen atom.[4] In other words, oxygen appears to be a better hydrogen-bond acceptor than nitrogen, a result which cannot be explained by the pK_a scale, but which ought to be from a hydrogen-bond basicity scale.

The first thermodynamic scale of hydrogen-bond (HB) basicity was set up in 1969–1972 by Taft and co-workers[5,6] who defined pK_{HB} as log K_f for the 1 : 1 complexation of bases B with a reference HB donor, 4-fluorophenol, in CCl_4 at 298 K [eqns. (1)–(3)]. Little further work on the pK_{HB} scale was reported

$$B + 4\text{-}FC_6H_4OH \rightleftharpoons 4\text{-}FC_6H_4OH\cdots B \qquad (1)$$

$$K_f/\mathrm{dm^3\,mol^{-1}} = [\text{HB complex}]/[B][4\text{-}FC_6H_4OH] \qquad (2)$$

$$pK_{HB} = \log_{10} K_f \qquad (3)$$

between 1972 and 1988, when we began to extend systematically the pK_{HB} scale to the various families of organic bases, in order that chemists should have at hand a scale comparable to the pK_a scale available for more than 7000 bases.[3] Nitrogen, oxygen, sulfur[7] and π bases[8] have already been studied. In the family of nitrogen bases, we have published the pK_{HB} scale for sp nitrogens (nitriles)[9] and sp^2 nitrogens (amidines[10] and pyridines[11]) but not for sp^3 nitrogens.

We present here the pK_{HB} scale of aliphatic primary amines. The case of anilines, which are not only nitrogen HB bases but also π HB bases, will be studied in a future paper. Previous measurements of equilibrium constants for the hydrogen bonding of phenols to primary amines are scarce. Using dispersive IR spectrometry and phenol, the formation constant of the 1 : 1 HB complex has been obtained[12] for 15 primary amines in CCl_4 at 27 °C, but the sample of amines is little diversified, 14 being alkylamines. Only 4 primary amines have been studied, by F NMR, in the pioneering work on the pK_{HB} scale.[13] At last HB equilibrium constants have been measured, by UV spectrometry, for 5 primary amines against the common HB acceptor 4-nitrophenol in CCl_3CH_3.[14]

We have used FTIR spectrometry in this work and determined the pK_{HB} values of 22 aliphatic primary amines including 7 alkylamines, 3 cycloalkylamines, 4 diamines and 8 amines substituted with various groups (Ph, $H_2C{=}CH$, $HC{\equiv}C$, OMe and CF_3). We have found that the primary amines pK_{HB} scale extends over 1.64 pK units (9.3 kJ mol^{-1}) from adamantan-1-amine (p$K_{HB} = 2.31$) to $CF_3CH_2NH_2$ (p$K_{HB} = 0.67$). The main effects governing these variations are discussed. A correlation is established between pK_{HB} and the minimum electrostatic potential associated with the NH_2 nitrogen lone pair. The comparison with the pK_a scale highlights the importance of building a scale devoted to HB basicity.

Experimental

Materials

All compounds were purchased from Aldrich. Liquids were dried over activated 4 Å molecular sieves and/or chromatographed on basic aluminium oxide (just before use for C_2Cl_4). Allylamine and cyclohexylamine were distilled respectively under high vacuum and at atmospheric pressure. Adamantan-1-amine and 4-fluorophenol were sublimed. Hexadecylamine was fractionally crystallized and dried over P_2O_5. Aminopropionitrile was liberated from its hydrochloride by reaction with excess potassium hydroxide.

Spectra

IR spectra were recorded with a Fourier transform spectrometer, either a Bruker IFS 48 or a Nicolet 510 M, at a resolution of 1 cm^{-1} with 256 scans. An infrasil quartz cell of 1 cm was used. The cell temperature was maintained at 25 ± 0.2 °C.

Equilibrium constants

The equilibrium constant is defined by $K_f = C_c/C_aC_b$ where C_c, C_b and C_a are the equilibrium concentrations of complex, base (amine) and acid (4-fluorophenol). C_a is obtained from the IR absorbance of the free OH band at 3614 cm^{-1}. K_f is calculated as illustrated in Table 1 for the example of propargylamine (prop-2-ynamine), which gives $K_f = 37.2 \pm 1.5$ (95% confidence level). K_f is estimated to be accurate to within 5% and consequently pK_{HB} values are given to within ± 0.02 pK unit. In the case of diamines, we have maintained the amine concentration in fivefold excess, in order to favor the 1 : 1 complex over the 2 : 1 complex. All operations, including the filling of the cell, were conducted in a desiccated glove box.

Calculations

These were performed using the Spartan 4.0 program package[15] running on a Silicon Graphics Indy workstation. Electrostatic potential energy surfaces were calculated from AM1 and PM3 geometry optimised structures (*vide infra*). These surfaces were mapped onto the electron density surfaces (0.001 electron/bohr^3 isosurface) at high resolution.

Table 1 Formation constant of the 4-fluorophenol–propargylamine complex in C_2Cl_4 at 25 °C (4 determinations)[a]

	1	2	3	4
$C_a^0 \times 10^3$[b]	3.7033	3.6731	3.7135	3.7126
$C_b^0 \times 10^2$[c]	0.9927	2.3513	2.9363	5.2487
Absorbance A	0.636	0.470	0.429	0.295
$C_a = (A/\varepsilon l) \times 10^3$[d]	2.7587	2.0382	1.8608	1.2798
$C_c = (C_a^0 - C_a) \times 10^3$	0.9446	1.6349	1.8526	2.4327
$C_b = (C_b^0 - C_c) \times 10^2$	0.8983	2.1878	2.7511	5.0054
K_f[e]	38.12	36.66	36.19	37.98
Complex percentage[f]	26%	45%	50%	66%

[a] All concentrations are in mol dm^{-3}. [b] Initial concentration of 4-fluorophenol. [c] Initial concentration of amine. [d] Beer–Lambert law. $\varepsilon = 230.4$ dm^3 mol^{-1} cm^{-1}. [e] dm^3 mol^{-1}. [f] $100 \times (C_c/C_a^0)$.

Results

Table 2 summarizes the pK_{HB} scale constructed from the hydrogen-bonding formation of 4-FC_6H_4OH with 22 amines in C_2Cl_4 at 25 °C. Also given are the pK_a values in water (generally at 25 °C)[3,16] and the Taft–Topsom substituent constants σ_F and σ_α measuring respectively the field-inductive and the polarizability effects of X substituents in the amines XNH_2. In this work we have preferred C_2Cl_4 to the definition solvent CCl_4 because a few amines precipitate in CCl_4 solutions. Eqn. (4)

$$\mathrm{p}K_{HB}(C_2Cl_4) = 1.005\mathrm{p}K_{HB}(CCl_4) + 0.002 \qquad (4)$$

$$n = 12,\ r\ \text{(correlation coefficient)} = 0.995,$$

$$s\ \text{(standard deviation)} = 0.05,\ F\ \text{(Fisher test)} = 997$$

compares 12 values obtained both in CCl_4 (not given) and C_2Cl_4 and shows that this solvent change does not bring about any variation of pK_{HB}.†

In addition to the $\nu(OH \cdots NH_2)$ band we observe, for $N{\equiv}CCH_2CH_2NH_2$, $MeOCH_2CH_2NH_2$ and $MeOCH_2CH_2CH_2NH_2$, the presence in the IR spectra of a second band attributed to $\nu(OH \cdots N{\equiv}C)$ or $\nu(OH \cdots O)$. This shows that two 1 : 1 HB complexes are formed in solution. In this case the measured formation constant K_f (with amine in excess in order to avoid the formation of 2 : 1 complexes) is a global constant corresponding to the sum of the formation constants of two 1 : 1 complexes: $K_f = K_f(C{\equiv}N) + K_f(NH_2)$ or $K_f = K_f(O) + K_f(NH_2)$. In order to obtain the true amino basicity, $K_f(NH_2)$, we have to subtract $K_f(C{\equiv}N)$, or $K_f(O)$, from K_f. $K_f(C{\equiv}N)$ and $K_f(O)$ have been evaluated by using the relationships between pK_{HB} and $\Delta\nu(OH)$ established in the families of nitriles[9] or ethers.[18] In the same way $K_f = 2K_f(NH_2)$ for diamines, if we assume that the two nitrogens have almost the

---

† Consequently, for the sake of simplicity, we shall retain the same symbol, pK_{HB}, for $\log_{10} K_f$, whether the measurements be made in CCl_4 or C_2Cl_4.

Table 2 pK_{HB} and pK_a scales of primary amines XNH_2. Substituent constants σ_F and σ_α of the X substituent[a]

No	Compound	Formula	pK_{HB}	pK_a[b]	σ_F	σ_α
Alkylamines						
1	Adamantan-1-amine	1-AdamNH_2	2.31	10.58	0	−0.95
2	c-Hexylamine	c-HexNH_2	2.29	10.58	0	−0.76
3	*n*-Octylamine	*n*-OctNH_2	2.27	10.61	0	−0.59
4	*n*-Hexadecylamine	$CH_3(CH_2)_{15}NH_2$	2.26	10.61	0	−0.59
5	*tert*-Butylamine	*t*-BuNH_2	2.26	10.68	0	−0.75
6	Isopropylamine	i-PrNH_2	2.22	10.67	0	−0.62
7	*n*-Butylamine	*n*-BuNH_2	2.21	10.64	0	−0.57
8	*n*-Propylamine	*n*-PrNH_2	2.19	10.57	0	−0.54
9	Ethylamine	EtNH_2	2.17	10.68	0	−0.49
10	c-Propylamine	c-PrNH_2	1.74	9.10	0	−0.62
Diamines						
11	Ethylenediamine	$H_2NCH_2CH_2NH_2$	2.55	9.93 (9.63)[c]	0.04	−0.53
12	1,3-Diaminopropane	$H_2N(CH_2)_3NH_2$	2.62	10.47 (10.17)[c]	0.02	−0.58
13	1,4-Diaminobutane	$H_2N(CH_2)_4NH_2$	2.51 (2.21)[c]	10.65 (10.35)[c]	0.01	−0.60
14	1,6-Diaminohexane	$H_2N(CH_2)_6NH_2$	2.51 (2.21)[c]	10.93 (10.63)[c]	0	−0.62
Substituted amines						
15	2-Methoxyethylamine	$MeOCH_2CH_2NH_2$	2.29 (2.28)[d]	9.44	0.07	−0.52
16	3-Methoxypropylamine	$MeOCH_2CH_2CH_2NH_2$	2.26 (2.25)[d]	9.92	0.03	−0.58
17	Phenethylamine	$PhCH_2CH_2NH_2$	2.16	9.83	0.03	−0.65
18	Allylamine	$H_2C{=}CHCH_2NH_2$	1.94	9.52	0.03	−0.57
19	Benzylamine	$PhCH_2NH_2$	1.88	9.34	0.05	−0.70
20	Propargylamine	$HC{\equiv}CCH_2NH_2$	1.57	8.15	0.12	−0.61
21	Aminopropionitrile	$N{\equiv}CCH_2CH_2NH_2$	1.42 (1.28)[d]	7.80	0.16	−0.59
22	2,2,2-Trifluoroethylamine	$CF_3CH_2NH_2$	0.67	5.61	0.23	−0.46

[a] From ref. 17 and from the estimation rules $\sigma_F(XCH_2) = \sigma_F(X)/1.95$ and $\sigma_\alpha(XCH_2) = \sigma_\alpha(CH_3) + \sigma_\alpha(X)/2.3$. [b] From ref. 3 and 16. [c] Statistically corrected. [d] Value corrected for the presence of a second HB accepting group.

Table 3 Comparison of HB and Brønsted basicities for oxygen and sp^3 nitrogen bases

Base	pK_a	pK_{HB}
DMSO	−1.54[a]	2.53[c]
HMPA	−0.97[a]	3.60[c]
DMA	−0.21[a]	2.44[c]
$EtNH_2$	10.68[b]	2.17[d]
Et_3N	10.72[b]	1.93[c]
Et_2NH	11.02[b]	2.26[d]

[a] A. Bagno and G. Scorrano, *J. Am. Chem. Soc.*, 1988, **110**, 4577. [b] Ref. 3. [c] Ref. 13. [d] This work.

same basicity, and it is easy to refer to the basicity of one nitrogen atom by applying the statistical correction − log 2 to pK_{HB}.

Discussion

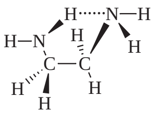
The place of primary amines on the pK_{HB} scale. Comparison of HB and Brønsted basicities

The lead compound of (non gaseous) primary amines, ethylamine, has a pK_{HB} of 2.17, which shows that primary amines are stronger HB bases than pyridines ($pK_{HB} = 1.86$ for pyridine)[11] and nitriles ($pK_{HB} = 0.91$ for acetonitrile).[9] So, like Brønsted basicity, HB basicity increases with the p character of the nitrogen lone pair. However, unlike the Brønsted basicity, primary (also secondary and tertiary) amines are weaker HB bases than many oxygen bases (Table 3).

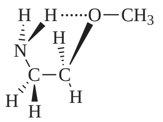
These similarities and dissimilarities between HB and Brønsted basicity scales have already been noticed[5] and explained,[19] phenomenologically, by the existence of family-dependent relationships between scales. For the family of primary amines we indeed find a good correlation [eqn. (5)] between pK_{HB} and pK_a.

$$pK_{HB} = 0.313pK_a - 1.064 \qquad (5)$$
$$n = 18, r = 0.989, s = 0.067, F = 694$$

The methoxyamines **15** and **16** and the two diamines, **11** and **12**, have not been included in this correlation because they deviate from it by more than three times the standard deviation. These four amines appear anomalously stronger HB bases than the alkylamines in spite of the electron withdrawing field effect of the methoxy and amino substituents (*vide infra*). However, as expected from this electronic substituent effect, they are weaker Brønsted bases. Thus it appears that the anomaly belongs to the pK_{HB} values. This deviant behaviour may be explained on the basis of the formation of an intramolecular hydrogen bond NH···N or NH···O, which increases the HB basicity of the HB donor nitrogen.[20] In fact the five-membered ring structures **11** and **15** have been found in the gas phase,[21,22] and six-membered ring structures seem still easier to form in **12** and **16**. These intramolecular hydrogen bonds are expected to occur also in the apolar solvent C_2Cl_4, but not in water[23] because the NH_2 and NH_3^+ groups will interact instead with the more abundant water molecules in a better optimized intermolecular HB geometry.



11



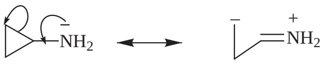
15

Structure–HB basicity relationships

Alkylamines **1**–**9** show an increase of HB basicity both on chain lengthening (in the order $EtNH_2 < n\text{-}PrNH_2 < n\text{-}BuNH_2 < n\text{-}OctNH_2 \sim n\text{-}HexadecNH_2$) and on chain branching (in the order $EtNH_2 < i\text{-}PrNH_2 < t\text{-}BuNH_2$ and cyclohexylamine < adamantan-1-amine). Since alkyl substituents operate in the reverse order of steric hindrance, steric effects must not predominate in the HB basicity of primary amines. In this respect primary amines behave like alcohols[24] and quite differently from ethers.[18] For the gas-phase protonation of alkylamines the increase of basicity on chain lengthening and branching was interpreted[25] as being the result of induced dipole stabilization by the alkyl substituent of the ion formed on protonation (the so-called polarizability effect). The pK_{HB} of alkylamines **1**–**9** appears also to be correlated with the polarizability substituent constant σ_α [eqn. (6)].

$$pK_{HB} = -0.275\sigma_\alpha + 2.063 \qquad (6)$$
$$n = 9, r = 0.836, s = 0.028, F = 16$$

With a pK_{HB} of 1.74 cyclopropylamine does not obey eqn. (6), and appears to be a much weaker base than the related non-cyclic $i\text{-}PrNH_2$ ($pK_{HB} = 2.22$). This low basicity can be interpreted in terms of an electron-withdrawing resonance effect of the cyclopropyl substituent as shown below. The short C–N bond distance (1.429 Å compared to 1.469 Å for $i\text{-}PrNH_2$)[26] indicates an appreciable participation of the resonant form **10b** to the structure of cyclopropylamine.



10a **10b**

Electron-withdrawing field effects also produce a decrease of HB basicity, as exemplified by the very low basicity of $CF_3CH_2NH_2$ ($pK_{HB} = 0.67$) and by the good correlation of pK_{HB} with the field substituent constant σ_F [eqn. (7)] (cyclopropylamine, which needs an additional resonance term, and the amines **11**, **12**, **15** and **16**, which have intramolecular hydrogen bonds, have not been included). The addition of a polarizability term [eqn. (8)] does not significantly improve the correlation, but provides better predictive values for the alkylamines. For gas-phase proton transfer the polarizability term is statistically well-established and chemically well-understood.[27] For a set of 11 substituted primary amines[28] we have established the correlation eqn. (9). The ratios of the sensitivity coefficients to polarizability and field effects are 0.17 for *GB* [eqn. (9)] and 0.05 for pK_{HB} [eqn. (8)]. This reduced importance of polarizability effects on proton sharing in solution compared to proton transfer in the gas phase is expected. However additional work is needed for establishing the existence of polarizability effects on hydrogen-bonding equilibria in solution.

$$pK_{HB} = -6.454\sigma_F + 2.245 \qquad (7)$$
$$n = 17, r = 0.989, s = 0.068, F = 674$$

$$pK_{HB} = -6.256\sigma_F - 0.332\sigma_\alpha + 2.029 \qquad (8)$$
$$n = 17, r = 0.992, s = 0.059, F = 448$$

$$GB/\text{kcal mol}^{-1} = -60.87\sigma_F - 10.30\sigma_\alpha + 208.4 \qquad (9)$$
$$n = 11, r = 0.969, s = 1.75, F = 62$$

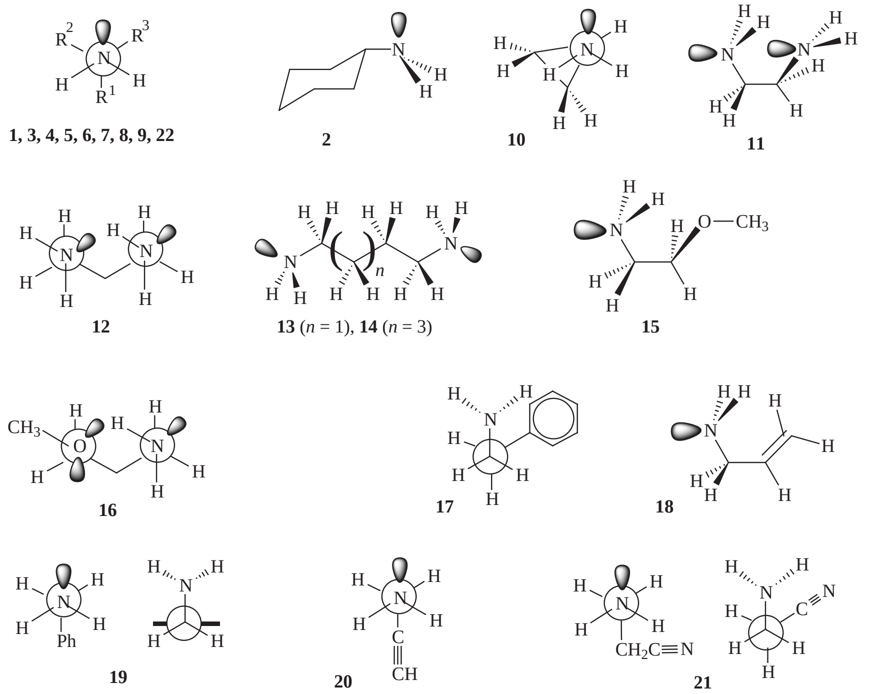
Relationship between pK_{HB} and electrostatic potentials

While the accurate reproduction of the properties of hydrogen-bonded systems needs high-level *ab initio* molecular orbital calculations, a simple analysis based on molecular electrostatic potentials can provide excellent predictions of the HB basicity.[29] Politzer and co-workers proposed to use $V_{s,\min}$, the

Table 4 PM3 calculated electrostatic potential minima, $V_{s,min}(NH_2)$,[a] for amines **1**–**22**, at the geometry shown below

No.	Compound	$-V_{s,min}$	No.	Compound	$-V_{s,min}$	No.	Compound	$-V_{s,min}$
1	1-AdamNH_2	51.87	**9**	EtNH_2	51.04	**17**	$Ph(CH_2)_2NH_2$[b]	51.76
2	c-HexNH_2	51.25	**10**	c-PrNH_2	50.38	**18**	$H_2C{=}CHCH_2NH_2$	48.74
3	*n*-OctNH_2	50.90	**11**	$H_2N(CH_2)_2NH_2$[b]	52.80	**19**	$PhCH_2NH_2$	49.24
4	*n*-HexadecNH_2	50.80	**12**	$H_2N(CH_2)_3NH_2$[b]	55.38	**20**	$HC{\equiv}CCH_2NH_2$	45.71
5	*t*-BuNH_2	51.76	**13**	$H_2N(CH_2)_4NH_2$	49.20	**21**	$N{\equiv}C(CH_2)_2NH_2$	43.13
6	i-PrNH_2	52.08	**14**	$H_2N(CH_2)_6NH_2$	49.86	**22**	$CF_3CH_2NH_2$	35.11
7	*n*-BuNH_2	51.10	**15**	$MeO(CH_2)_2NH_2$[b]	51.73			
8	*n*-PrNH_2	50.87	**16**	$MeO(CH_2)_3NH_2$[b]	54.63			

[a] kcal mol^{-1}. [b] Calculated by constraining the intramolecular HB length to the HF/6-31** calculated distances: $r(H\cdots X)$ = 2.58 (**11**), 2.41 (**12**), 2.56 (**15**), 2.34 (**16**), 2.80 (**17**) Å.



1, 3, 4, 5, 6, 7, 8, 9, 22 **2** **10** **11** **12** **13** (n = 1), **14** (n = 3) **15** **16** **17** **18** **19** **20** **21**

minimum electrostatic potential on the molecular surface defined by the 0.001 electron/bohr^3 contour of the electronic density, to estimate HB basicity.[30] In previous work[31] we predicted the HB basicity of nitriles by means of this quantum mechanical descriptor. We extend today this approach to aliphatic primary amines. Normally, of course, for a simple amine the minimum electrostatic potential corresponds to the nitrogen lone pair. The electrostatic potential at this minimum depends on the electronic structure of the whole molecule. An electron-donating substituent pushes electron density to the amino nitrogen thus increasing the negative value of $V_{s,min}$. Similarly an electron attracting substituent pulls electron density from this nitrogen, and decreases the negative value of $V_{s,min}$.

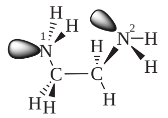
The studied compounds are conformationally challenging because their equilibrium population at 298 K is composed of numerous rotamers. High level *ab initio* methods provide accurate results but are not computationally efficient for the rapid screening of a large number of conformations on many compounds. So we have used the less computationally demanding semi-empirical AM1 and PM3 methods. We have not fully explored the potential energy surface, but have completely optimized the bond lengths and angles of various staggered input structures. The electrostatic potential was then computed for the most stable conformation (generally, *vide infra*), both with the AM1 and PM3 methods. The PM3 results are presented in Table 4. AM1 and PM3 geometries generally agree with each other and with experimental geometries (*e.g.* cyclohexylamine,[32] allylamine,[33] phenethylamine[34] and propargylamine[35]). A discrepancy was found for cyclopropylamine[36] but the $V_{s,min}$ calculated at the experimental and PM3 geometries differ only by 0.4 kcal mol^{-1}. The most serious discrepancies occur for ethylenediamine and 2-methoxyethylamine which exist in a N–C–C–N *gauche* conformation stabilized by intramolecular hydrogen bonds.[21,22] AM1 and PM3 were unable to reproduce these geometries, giving either the *anti* conformation or, in the *gauche* conformation, N···H and O···H distances greater than the sum of van der Waals radii. This is most unfortunate since the electrostatic potentials on amino nitrogen strongly depend on the internal hydrogen bonding (Table 5). In order to remedy the hydrogen bonding deficiencies of AM1 and PM3, we have constrained the H···N and H···O distances to the values given by HF/6-31G** calculations, $d(H\cdots N)$ = 2.58 Å and $d(H\cdots O)$ = 2.56 Å. We have also performed HF/6-31G** geometry optimizations on the diamines **12**–**14** and the methoxyamine **16** in order to study the existence of intramolecular H bonds. We have found that **12** and **16** possess an intramolecular H bond, but not **13** and **14**. Consequently we have also applied the 6-31G** H···N and H···O distances as constraints to the geometry optimization of **12** and **16**. These hydrogen bonding studies also show that the statistical correction log 2 applies only to non-internally hydrogen-bonded diamines **13** and **14** in the correlation of $V_{s,min}$ with pK_{HB} (*vide infra*). In fact ethylenediamine **11** and 1,3-diaminopropane **12** have a much less negative electrostatic potential on the hydrogen-bond acceptor nitrogen than on the hydrogen-bond donor nitrogen (Table 5). This indicates that intermolecular hydrogen bonding occurs mainly on one nitrogen (the latter).

In Fig. 1 we have plotted pK_{HB} *vs.* $V_{s,min}$. We give the equation and statistics of the line in eqns. (10) (PM3) and (11) (AM1).

Table 5 Dependence of amino $V_{s,min}$ on intramolecular hydrogen bonding (PM3 calculations) for ethylenediamine

Conformer	$-V_{s,min}(N^1)$/ kcal mol^{-1}	$-V_{s,min}(N^2)$/ kcal mol^{-1}	$d(N^2 \cdots HN^1)$/ Å
Anti	47.73	47.73	No H bond
Gauche I[a]	53.52[c]	43.12[c]	2.75[e]
	54.81[d]	38.41[d]	2.52[f]
Gauche II[b]	52.11[c]	40.25[c]	2.80[e]
	52.80[d]	38.30[d]	2.58[f]

[a]



[b] Structure **11** of Table 4. [c] Unconstrained PM3 calculation. [d] PM3 result with a constraint on the N^2H distance. [e] PM3 distance. [f] HF/6-31G** distance.

Table 6 Predicted pK_{HB} values from pK_a [eqn. (5)], σ_F [eqn. (7)], $V_{s,min,PM3}$ [eqn. (10)] and $V_{s,min,AM1}$ [eqn. (11)]

Compound	$FCH_2CH_2NH_2$	$F_2CHCH_2NH_2$
pK_a	8.79[a]	7.09[a]
$\sigma_F(X)$	0.12[b]	0.18[b]
$-V_{s,min,PM3}$[c]	47.32	43.91
$-V_{s,min,AM1}$[c]	60.27	56.35
pK_{HB} from eqn. (5)	1.47	1.08
pK_{HB} from eqn. (7)	1.69	1.16
pK_{HB} from eqn. (10)	1.79	1.46
pK_{HB} from eqn. (11)	1.84	1.50

[a] Ref. 23. [b] Ref. 17. [c] kcal mol^{-1}.

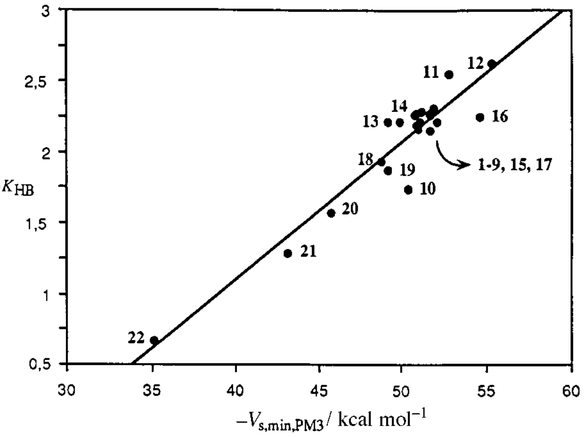


Fig. 1 Correlation of pK_{HB} with PM3 calculated electrostatic potential on the amino nitrogen lone pair. Numbers refer to Table 2.

$$pK_{HB} = 0.097(-V_{s,min}) - 2.797 \qquad (10)$$

$$n = 22, r = 0.946, s = 0.143, F = 171$$

$$pK_{HB} = 0.085(-V_{s,min}) - 3.285 \qquad (11)$$

$$n = 22, r = 0.939, s = 0.152, F = 150$$

Both correlations appear satisfactory considering that $V_{s,min}$ corresponds to one conformation, the lowest-energy one *in vacuo*, whereas pK_{HB} is related to the various conformations existing in a C_2Cl_4 solution. They could usefully predict pK_{HB} for aliphatic primary amines which are not commercially available, not yet synthesized, gaseous, or insufficiently soluble in C_2Cl_4 to be measured. Two examples, 2-fluoroethylamine and 2,2-difluoroethylamine, are given in Table 6. *Ab initio* calculations show the existence of intramolecular hydrogen bonds $NH \cdots F$ in these two compounds, which increase the basicity of the nitrogen lone pair.[20] This effect is taken into account neither by the pK_a values (weak intramolecular HB are broken in water, *vide supra*) nor by σ_F values. Consequently the pK_{HB} values calculated from pK_a or σ_F are too weak and we must prefer pK_{HB} obtained from electrostatic potentials calculated for conformers stabilized by intramolecular hydrogen bonding.

References

1 J. March, *Advanced Organic Chemistry*, Wiley, New York, 1992, ch. 8.
2 J. E. Huheey, E. A. Keiter and R. L. Keiter, *Chimie Inorganique*, De Boeck Université, Paris, 1996, ch. 9.
3 D. D. Perrin, *Dissociation constants of organic bases in aqueous solution*, Butterworths, London, 1965; supplement, 1972.
4 T. Gramstad, S. Husebeye, K. Maartmann-Moe and J. Sæbø, *Acta Chem. Scand.*, Ser B41, 1987, 555.
5 R. W. Taft, D. Gurka, L. Joris, P. von R. Schleyer and J. W. Rakshys, *J. Am. Chem. Soc.*, 1969, **91**, 4801.
6 L. Joris, J. Mitsky and R. W. Taft, *J. Am. Chem. Soc.*, 1972, **94**, 3438.
7 C. Laurence, M. Berthelot, J. Y. Le Questel and M. J. El Ghomari, *J. Chem. Soc., Perkin Trans. 2*, 1995, 2075.
8 F. Besseau, C. Laurence and M. Berthelot, *Bull. Soc. Chim. Fr.*, 1996, **133**, 381.
9 M. Berthelot, M. Helbert, C. Laurence and J. Y. Le Questel, *J. Phys. Org. Chem.*, 1993, **6**, 302.
10 E. D. Raczynska, C. Laurence and M. Berthelot, *Can. J. Chem.*, 1992, **70**, 2203.
11 M. Berthelot, C. Laurence, M. Safar and F. Besseau, *J. Chem. Soc., Perkin Trans. 2*, 1998, 283.
12 D. Clotman and T. Zeegers-Huyskens, *Spectrochim. Acta, Part A*, 1967, **23**, 1627.
13 D. Gurka and R. W. Taft, *J. Am. Chem. Soc.*, 1969, **91**, 4794.
14 M. H. Abraham, P. P. Duce, D. V. Prior, D. G. Barratt, J. J. Morris and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1989, 1355.
15 Wavefunction, Inc., 18401 Von Karman Avenue, Irvine, California 92715, USA.
16 F. M. Jones and E. M. Arnett, *Prog. Phys. Org. Chem.*, 1974, **11**, 263.
17 C. Hansch, A. Leo and R. W. Taft, *Chem. Rev.*, 1991, **91**, 165.
18 M. Berthelot, F. Besseau and C. Laurence, *Eur. J. Org. Chem.*, 1998, 925.
19 M. J. Kamlet, J. F. Gal, P. C. Maria and R. W. Taft, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1583.
20 P. L. Huyskens, *J. Am. Chem. Soc.*, 1977, **99**, 2578.
21 K. M. Marstokk and H. Mllendal, *J. Mol. Struct.*, 1978, **49**, 221.
22 W. Caminati and E. B. Wilson, *J. Mol. Spectrosc.*, 1980, **81**, 356.
23 P. Love, R. B. Cohen and R. W. Taft, *J. Am. Chem. Soc.*, 1968, **90**, 2455.
24 C. Laurence, M. Berthelot, M. Helbert and K. Sraïdi, *J. Phys. Chem.*, 1989, **93**, 3799.
25 D. H. Aue, H. M. Webb and M. T. Bowers, *J. Am. Chem. Soc.*, 1976, **98**, 311.
26 T. Iijima, T. Kondou and T. Takenaka, *J. Mol. Struct.*, 1998, **445**, 23.
27 R. W. Taft and R. D. Topsom, *Prog. Phys. Org. Chem.*, 1987, **16**, 1.
28 T. Silvestro, R. D. Topsom, C. W. Bock and R. W. Taft, *J. Mol. Struct. (THEOCHEM)*, 1989, **184**, 33.
29 P. W. Kenny, *J. Chem. Soc., Perkin Trans. 2*, 1994, 199.
30 H. Hagelin, J. S. Murray, T. Brinck, M. Berthelot and P. Politzer, *Can J. Chem.*, 1995, **73**, 483.
31 J. Y. Le Questel, M. Berthelot and C. Laurence, *J. Chem. Soc., Perkin Trans. 2*, 1997, 2711.
32 E. L. Eliel and S. H. Wilen, *Stereochemistry of organic compounds*, Wiley, New York, 1994.
33 G. Roussy, J. Demaison, I. Botskor and H. D. Rudolph, *J. Mol. Struct.*, 1971, **38**, 535.
34 P. D. Godfrey, L. D. Hatherley and R. D. Brown, *J. Am. Chem. Soc.*, 1995, **117**, 8204.
35 R. Cervelatti, W. Caminati, C. Degli Esposti and A. M. Mirri, *J. Mol. Spectrosc.*, 1977, **66**, 389.
36 D. K. Hendriksen and M. D. Harmony, *J. Chem. Phys.*, 1969, **51**, 700.

Paper 8/09265F