Super-basic Nitriles

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Alkyl substitution on the amino nitrogen, vinylogy (but not benzology), iminology, and alkyl substitution on the functional carbon of the amidine skeleton in cyanamide iminologues increase the hydrogen-bonding basicity of cyanamide and produce, on the pK_{HB} scale, super-basic nitriles more basic than tertiary amines. On the gas-phase basicity scale iminology also increases the basicity of cyanamide, but sp-nitrogen bases remain less basic than sp^2- or sp^3-nitrogen bases.

The most basic nitriles presently known are cyanamides.[1,2] This is generally explained by a 'push–pull' mechanism, schematically described by the resonant structures $R_2N\text{-}C{\equiv}N \longleftrightarrow R_2N^+{=}C{=}N^-$. Interposition of a CH=N imino transmitter group between the 'pushing' NMe_2 and the 'pulling' C≡N groups gives an 'iminologue' of the parent compound $Me_2N\text{-}C{\equiv}N$, in the same way as interposition of a phenylene or of a vinyl group gives, respectively, a cyanamide benzologue or vinylogue. We have recently shown[3] that iminology greatly enhances the hydrogen-bond basicity of cyanamides. We report here other structural effects able to increase strongly the hydrogen-bond basicity of cyanamides and show that these effects are particular to the hydrogen-bond basicity scale.

Results and Discussion

The hydrogen-bond basicity of nitriles is measured by the well-established pK_{HB} scale[4,5] using the logarithm of the formation constant of their complexes with 4-fluorophenol [eqns. (1)–(3) below].

$$R\text{-}C{\equiv}N + p\text{-}FC_6H_4OH \rightleftharpoons p\text{-}FC_6H_4OH\cdots N{\equiv}C\text{-}R \quad (1)$$

$$K_{HB} = [\text{complex}]/[\text{nitrile}][\text{4-fluorophenol}] \quad (2)$$

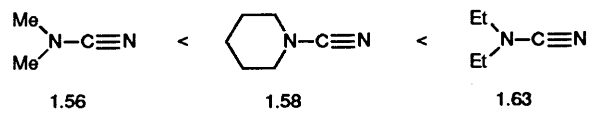
$$pK_{HB} = \log_{10} K_{HB} \quad (3)$$

The formation constant is expressed in $dm^3\ mol^{-1}$ at 298 K in CCl_4. We use very dilute solutions of 4-fluorophenol (*ca.* 0.004 mol dm^{-3}) and of nitriles (0.02–0.1 mol dm^{-3}) to ensure that only complexes of 1 : 1 stoichiometry are formed. In addition to the nitrile nitrogen, the compounds reported in Table 1 have potential amino- and imino-nitrogen sites of fixation for hydrogen bonding. However, in the infrared spectra of the complexes we systematically observed only one symmetrical $\nu(OH\cdots)$ absorption and high frequency shifts of the $\nu(C{\equiv}N)$ band. These observations suggest a unique site of hydrogen bonding on the sp nitrogen of the nitrile group.[1] Actually we do not know examples where hydrogen bonding occurs at the pushing group of 'push–pull' molecules in dilute solutions.[5]

Experimental data are shown in Table 1 together with some pK_{HB} values of various nitrogen bases for comparison.

Comparison of the relative basicities of these nitriles leads to the following trends:

(*i*) Further alkyl substitutions of dimethylcyanamide lead to more basic species.



(*ii*) Benzologues exhibit decreased hydrogen-bonding ability whereas vinylogues and iminologues give more basic compounds.

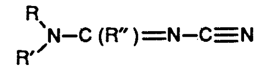
$Me_2N\text{-}C_6H_4\text{-}C{\equiv}N < Me_2N\text{-}C{\equiv}N$
1.23 1.56

$< Me_2N\text{-}CH{=}CH\text{-}C{\equiv}N < Me_2N\text{-}CH{=}N\text{-}C{\equiv}N$
1.70 2.09

(*iii*) Methyl substitution of the imino group gives the most basic nitrile presently known.*

$Me_2N\text{-}CH{=}N\text{-}C{=}N < Me_2N\text{-}C(Me){=}N\text{-}C{\equiv}N$
2.09 2.24

The level of hydrogen-bond basicity attained in the cyanamide iminologues is so high that, on the hydrogen-bond basicity scale, these compounds are actually more basic than many pyridines or tertiary amines (see Table 1). Therefore, it may be predicted that still more basic nitriles could be generated from an appropriate selection of alkyl substituents R, R′ and R″ in the amidine skeleton of cyanoamidines.†



$$\begin{matrix}R\\ \end{matrix}\!\!\!\!\!\begin{matrix}\diagdown\\ \diagup\end{matrix} N\text{—}C(R''){=}N\text{—}C{\equiv}N \quad \begin{matrix}\\ R'\end{matrix}$$

The differences observed[7,8] between hydrogen-bond basicity and Brønsted basicity raise the question of whether these structural features are peculiar to the pK_{HB} scale. We have therefore measured the gas-phase proton-transfer basicity (GB) of a number of nitriles in Table 1. The results are reported in Table 2. For dimethylcyanamide, molecular-orbital calculation by *ab initio* methods with geometry optimization, shows that the proton adds preferentially to the cyano nitrogen.[9] This result is

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* We thank a referee for drawing our attention to *N*′-methyl-N^2-propylcyanoguanidine, another super-basic nitrile. Towards 4-nitrophenol and in 1,1,1-trichloroethane, this compound possesses log K_B 2.90[10] which according to eqn. (11) of that reference should translate to pK_{HB} 2.20.

† From the result obtained for the cyanoguanidine,[10] a referee suggests that NR_2 on the functional carbon might possess an ability similar to that of alkyls for enhancing hydrogen-bond basicity.

Table 1 Hydrogen-bond basicity of cyanamides and related compounds

Compound	pK_{HB}[a]	ΔpK_{HB}[b]	Ref.	Type
4-(Dimethylamino)benzonitrile	1.23	−0.33	4	Cyanamide benzologue
Dimethylcyanamide	1.56	0	*c*	Cyanamide
Piperidine-1-carbonitrile	1.58	+0.02	*c*	Cyanamide
Diethylcyanamide	1.63	+0.07	*c*	Cyanamide
trans-Dimethylaminoacrylonitrile	1.70	+0.14	3	Cyanamide vinylogue
N^2-Cyano-N^1,N^1-dimethylformamidine	2.09	+0.53	3	Cyanamide iminologue
N^2-Cyano-N^1.N^1-dimethylacetamidine	2.24	+0.68	*c*	Cyanamide iminologue
Tri-*n*-butylamine	1.57		4	
Pyridine	1.88		4	
Triethylamine	1.93		4	
4-Picoline	2.03		4	

[a] The precision is estimated to within ±0.03 p*K* units. [b] $\Delta pK_{HB} = pK_{HB}(\text{compound}) - pK_{HB}(Me_2NC{\equiv}N)$. [c] This work.

Table 2 Gas-phase basicity (kcal mol^{-1}) of cyanamides and related compounds

Compound	GB	Ref.
Dimethylcyanamide	197.5	2
Piperidine-1-carbonitrile	201.4	*a*
trans-Dimethylaminocrylonitrile	205.6	*a*
N^2-Cyano-N^1,N^1-dimethylformamidine	204.0	*a*
Pyridine	212.6	*b*
4-Picoline	215.9	*b*
Triethylamine	223.4	*b*
Tri-*n*-butylamine	227.0	*b*

[a] This work. [b] D. H. Aue and M. T. Bowers, in *Gas-phase ion Chemistry*,' Vol. 2, p. 2, ed. M. T. Bowers, Academic Press, New York, 1979.

extended to other 'push–pull' cyanides of Table 2.* For the sake of comparison the GBs of the aforementioned tertiary amines are given in the same table.

Within the nitrile family we observe different sequences in the GB and in the pK_{HB} scales: iminologues are less efficient than vinylogues at increasing the gas-phase basicity. Further similar comparisons involving vinylogues and iminologues of various functional groups are in hand in order to clarify the difference in behaviour between the two transmitting vinyl and imine groups. Moreover, in contrast with the hydrogen-bond basicity, the cyanamide iminologue turns out to be less basic than tertiary amines: even the most basic sp-nitrogen bases do not overcome the basicity of sp^2 or sp^3 nitrogen on the GB scale.

Conclusion

These results emphasize the utility of iminologues and vinylogues for obtaining super-basic nitriles: on the Brønsted gas-phase basicity scale, the vinylogue $Me_2N{-}CH{=}CH{-}C{\equiv}N$ is more basic by 8.1 kcal mol^{-1} than $Me_2NC{\equiv}N$, and on the hydrogen-bonding basicity scale, pK_{HB}, the iminologue $Me_2N{-}C(Me){=}N{-}C{\equiv}N$ is more basic by 0.31 p*K* units than Et_3N. They also illustrate the different responses of the various types of basicity to the interposition of C=C and C=N bonds between the pushing NMe_2 and the pulling C≡N groups of 'push–pull' nitriles.

Experimental

Chemicals.—The cyanamides were purified commercial compounds. The synthesis of $Me_2N{-}CH{=}N{-}C{\equiv}N$ has already been described.[3] $Me_2N{-}C(Me){=}N{-}C{\equiv}N$ is obtained by reaction of dimethylacetamide acetal with cyanamide; m.p. 55–56 °C, δ_H 3.15 and 3.09 (6 H, s), and 2.40 (3 H, s).

IR Measurements.—These were made with a Bruker IFS 45 Fourier-transform spectrometer by selecting 1 cm^{-1} resolution and 256 scans. The method for measuring formation constants of hydrogen-bonded complexes has been previously described.[3]

Gas-phase Basicity Measurements.—The method used to obtain relative GBs by pulsed ICR spectrometry has been described earlier.[2] Piperidine-1-carbonitrile was found to be stronger than Bu^n_2S by 0.5 kcal mol^{-1} and 0.2 kcal mol^{-1} stronger than pyrazine, giving GB = 201.4 ± 0.2 kcal mol^{-1}. *trans*-Dimethylaminoacrylonitrile is equal in basicity to Bu^t_2S and is 0.6 kcal mol^{-1} stronger than isophorone giving GB = 205.6 ± 0.2 kcal mol^{-1}. N^2-cyano-N^1,N^1-dimethylformamidine is weaker than Bu^t_2S by 1.1 kcal mol^{-1}, 0.8 kcal mol^{-1} weaker than isophorone, and 0.5 kcal mol^{-1} weaker than 2-methylbenzotriazole, giving GB = 204 ± 0.5 kcal mol^{-1}.

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* A referee remarked 'the comparison between the solution and gas-phase results of Tables 1 and 2 depends critically on the belief that partial proton transfer as in Table 1 takes place to the same atom as full proton transfer in Table 2. While reasonable in all other cases, this may not be true for the cyanoamidine. The authors of reference 10 give evidence that N^1-methyl-N^2-propylcyanoguanidine, while its hydrogen bond in 1,1,1-trichloroethane is largely or entirely to the nitrile, forms its cation in water by addition of H^+ to the imino-nitrogen, as indeed is probably true for all guanidines[11,12] and is true also for those amidines that have been studied.[13] Of course, that might not be true in the gas phase, but Dr. E. Clayton of ICI pharmaceuticals[14] has found that N^1,N^1,N^2,N^2-tetramethyl-N^3-cyanoguanidine is a stronger proton-transfer base in the gas phase than any other he has ever encountered, which includes aliphatic tertiary amines, a result most reasonably understood if protonation is on imino-nitrogen.'

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Paper 2/06042F
Received 12*th November* 1992
Accepted 14*th January* 1993