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Substituent Constants of the $N{=}CH{-}NMe_2$ Group and their Application to the Prediction of the Basicity of Each Site in Bifunctional Amidines†

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Selected σ-type values of the $N{=}CH{-}NMe_2$ group are estimated and together with literature structure–basicity relationships used to predict the so-called 'microscopic' basicity of each site in bifunctional compounds.

Structure–reactivity relationships have always attracted the attention of chemists. In 1937 Hammett,[1] looking for quantitative models of similarity, proposed eqn. (1), which describes the relationship between the equilibrium or rate constant for substituted (K or k) and unsubstituted (K^0 or k^0) derivatives in a reaction series, the reaction constant (ρ) and the substituent constant (σ).

$$\log K \text{ (or } k) = \log K^0 \text{ (or } k^0) + \rho\sigma \qquad (1)$$

The Hammett equation and its modifications have successfully been applied to different reactions of aromatic and aliphatic systems in solution as well as in the gaseous phase.[2,3] Depending on the reaction series investigated, different types of σ have been proposed,[4,5] *e.g.* σ, σ^0, σ^+ and σ^-, for the description of the total substituent electronic effect, σ^*, σ_I, σ_F for the inductive (field) effect, σ_R, $\sigma_R{}^0$, $\sigma_R{}^+$, $\sigma_R{}^-$ for the resonance (mesomeric) effect and σ_α for the polarizability effect.

In the case of amidines, which are interesting because of their high basicity[6] and biological activity,[7] many structure–basicity relations[6,8–14] have been found but only a few σ-type values for the amidine group have been proposed.[13,15,16] The first estimates of σ_I and $\sigma_R{}^0$ for the $N{=}CH{-}NMe_2$ group (Table 1) were carried out by Shorter[15] on the basis of the ^{13}C chemical shifts obtained for a series of $XC_6H_4N{=}CH{-}NMe_2$ (FDMPs).[17] The proposed σ_I and $\sigma_R{}^0$ values, when compared with the literature data for the NMe_2 group (Table 1), indicate that the $CH{=}N$ group decreases the effects of the NMe_2 group by slightly different factors. For the inductive effect (σ_I) the transmission factor of the $CH{=}N$ group is equal to 0.50 and for the resonance effect ($\sigma_R{}^0$) equal to 0.56.

Taking the values of σ_I (0.03) and $\sigma_R{}^0$ (-0.29), the parameters $\sigma_m{}^0$ and $\sigma_p{}^0$ can be calculated using the equations $\sigma_m{}^0 = \sigma_I + \alpha\sigma_R{}^0$ and $\sigma_p{}^0 = \lambda\sigma_I + \sigma_R{}^0$, which separate the total electronic effect of the substituent into inductive and resonance effects.[4] Values of $\alpha = 0.21$ and $\lambda = 1.16$ for water for FDMPs[18] were used. The $\sigma_m{}^0$ (-0.03) and $\sigma_p{}^0$ (-0.255) values obtained this way are almost the same as those found from the free ν(OH) bond observed for FDMP (X = 4-OH and 3-OH) and phenols:[16] $\sigma_m{}^0 = -0.05 \pm 0.1$ and $\sigma_p{}^0 = -0.25 \pm 0.1$ (Table 1).

Table 1 Comparison of the σ values for amidine and amine groups

Group	σ_I	$-\sigma_R{}^0$	$-\sigma_p{}^0$	$-\sigma_m{}^0$	$-\sigma_p{}^+$	σ_F	$-\sigma_\alpha$
$N{=}CH{-}NMe_2$	0.03[a]	0.29[a]	0.25_5[b] 0.25[d]	0.03[b] 0.05[d]	1.0[b]	0.05[b]	0.40[b]
NMe_2	0.06[e]	0.52[e]	0.32[e]	0.10[e]	1.7[e]	0.10[f]	0.44[f]
$(CH_2)_2N{=}CH{-}NMe_2$						0.01_5[b]	0.52[b]
$(CH_2)_2NMe_2$						0.03[g]	0.57[g]
$(CH_2)_3N{=}CH{-}NMe_2$						0.00_5[b]	0.54[b]
$(CH_2)_3NMe_2$						0.01[g]	0.59[g]

[a]Ref. 15. [b]This work. [c]Ref. 13. [d]Ref. 16. [e]Ref. 4. [f]Ref. 5. [g]Ref. 11.

The σ^0 values for the $N{=}CH{-}NMe_2$ group are smaller than those for the NMe_2 group.[4,5] This means that the $N{=}CH{-}NMe_2$ group is less electron-donating than the NMe_2 group. The same behaviour is found for the $\sigma_p{}^+$ (-1.1) value estimated on the basis of the stretching vibration of the $C{=}O$ group for FDMP (X = 4-COMe) and acetophenones (Table 1).[13] Exceptions are found for the so called 'push–pull' molecules[19,20] in which the amidine group is directly linked with a strong electron-accepting group. IR results obtained for $N{\equiv}C{-}N{=}CH{-}NMe_2$ and $N{\equiv}C{-}N{=}C(N{=}CH{-}NMe_2)_2$ suggest that the $N{=}CH{-}NMe_2$ group is more electron-donating to the resonance effect than the NMe_2 group.

The effective polarizability (α_d) calculated for the $N{=}CH{-}NMe_2$ and NMe_2 groups from the equation proposed by Gasteiger and Hutchings[21] and the literature[5] value for $\sigma_\alpha(NMe_2)$ are used for estimating the $\sigma_\alpha(N{=}CH{-}NMe_2)$. The obtained results ($\alpha_d = 2.89$, $\sigma_\alpha = -0.40$) when compared with those for the NMe_2 group ($\alpha_d = 3.15$, $\sigma_\alpha = -0.44$) show a slightly smaller polarizability of the $N{=}CH{-}NMe_2$ group (Table 1). For the field effect described by σ_F, the transmission factor (0.50) of the $CH{=}N$ group obtained from comparison of $\sigma_I(N{=}CH{-}NMe_2)$ and $\sigma_I(NMe_2)$ is used. Taking the literature[5] value for $\sigma_F(NMe_2)$ we obtained $\sigma_F(N{=}CH{-}NMe_2) = 0.05$ (Table 1). The σ_α and σ_F values for the $(CH_2)_nN{=}CH{-}NMe_2$ group (n = 2 or 3) estimated in the same way as those for the $N{=}CH{-}NMe_2$ group, and the literature[11] values for σ_α and σ_F for the $(CH_2)_nNMe_2$ group are also given in Table 1.

The σ value obtained for the $N{=}CH{-}NMe_2$ group (Table 1) and the literature[4,5] value for σ(X) can be used to predict the so-called 'microscopic' basicities[10] corresponding

Table 2 'Microscopic'[a] and 'macroscopic' (measured) gas phase[b] (GB) and hydrogen bonding[c] ($\log K_{HB}$) basicities for the dibasic compounds: $X{-}N{=}CH{-}NMe_2$

	GB		
X	$N{=}CH{-}NMe_2$	X	Measured
NMe_2	943	901	951
$(CH_2)_2NMe_2$	961	919	982
$(CH_2)_3NMe_2$	966	922	997
OMe	904	750	908
$(CH_2)_2OMe$	952	850	972
$4\text{-}C_6H_4NMe_2$	977	890	975
$4\text{-}C_6H_4OMe$	959	750	961
$4\text{-}C_6H_4CN$	917	830	917.5
	$\log K_{HB}$		
X	$N{=}CH{-}NMe_2$	X	Measured
NMe_2	2.2	<2.0	2.43
$(CH_2)_2OMe$	2.3	1.2	2.75
CN	<0.5	2.1	2.10
$(CH_2)_2CN$	2.0	1.1	2.15
$4\text{-}C_6H_4COMe$	1.5	1.7	1.84
$4\text{-}C_6H_4CN$	1.3	1.2	1.49
$4\text{-}C_6H_4NO_2$	1.2	0.6	1.28

[a]See in text. [b]Refs. 11, 12 and 23. [c]Refs. 13, 14 and 19.

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1997, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

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to the basicity of the individual functional groups in the bifunctional XN=CH—NMe$_2$ with basic sites in the amidine and X groups (Table 2).

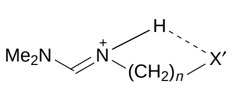
For the gas-phase basicity (GB) prediction of the amidine group in XN=CH—NMe$_2$, linear structure–basicity relationships found previously for the monofunctional RN=CH—NMe$_2$ (FDMs) [eqns. (5) and (8*b*) for alkyl and aryl FDMs from refs. 11 and 12, respectively] and the corresponding σ(X) values are applied. The relationships obtained for the series of RNMe$_2$ [eqn. (8*f*) from ref. 11] and the σ(N=CH—NMe$_2$) values used to estimate the GB(X) in Me$_2$N(CH$_2$)$_n$N=CH—NMe$_2$. For MeO(CH$_2$)$_2$N=CH—NMe$_2$, no equation is used and the estimation of the GB(X) is made on the basic of the literature data for ethers[24] containing a similar number of carbon atoms as the bifunctional amidine. For other derivatives the GB(X) values calculated previously by an AM1 method[12,22] are given in Table 2.

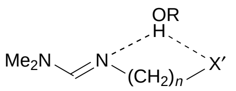
For the estimation of the log K_{HB}(N=CH—NMe$_2$) in XN=CH—NMe$_2$ in CCl$_4$ equations $\log K_{HB} = 2.70 - 4.58\sigma_F$ and $\log K_{HB} = 1.95 - 0.90\sigma^0$ found for the alkyl and aryl FDMs on the basis of literature data,[13,14] together with the σ_F(X) and σ^0(X) values,[4,5] were applied. An exception is N≡C–N=CH—NMe$_2$ for which the log K_{HB} *vs.* $\Delta\nu$(OH) relationship and the value of $\Delta\nu$(OH) for the N=CH—NMe$_2$ group, equal to that for the CN group,[19] are used.

The log K_{HB} *vs.* $\Delta\nu$(OH) relationships obtained for the series of amines, ethers, nitriles and ketones[25,26] and the $\Delta\nu$(OH) values for the NMe$_2$, OMe, CN and COMe groups found for bifunctional amidines[13,14] are used in estimating log K_{HB}(X). For the NO$_2$ group log K_{HB} is estimated according to eqn. (7) from ref. 27. The 'microscopic' and measured basicities are given in Table 2. The results obtained confirm that in the gas phase (as in solution) the amidine group is more basic (by 40–200 kJ mol^{-1}) than the basic group in X (Table 2) and is protonated first. Exceptions may be observed for the so called 'push–pull' molecules.[22].

The hydrogen bond in the non-polar solvent CCl$_4$ is preferentially formed with an electron-accepting group only for so called 'push–pull' molecules (*e.g.* for X = CN).[19,20] When both groups are separated by the phenyl ring their hydrogen bonding basicities are of the same order of magnitude (*e.g.* for X = 4-C$_6$H$_4$COMe and 4-C$_6$H$_4$CN).[13] An exception is the nitro group for which a very weak hydrogen-bond basicity is observed. Separation by the (CH$_2$)$_n$ group eliminates the 'push–pull' effect and a hydrogen bond is preferentially formed with the amidine group [*e.g.* for X = (CH$_2$)$_2$OMe and (CH$_2$)$_2$CN].[14]

Compounds with flexible conformation are interesting cases: X′(CH$_2$)$_n$N=CH—NMe$_2$ containing the OMe or NMe$_2$ group, with $n = 0$, 2 or 3, for which the measured basicities in the gas phase (GB) as well as in non-polar solvents (log K_{HB}) are higher than these predicted for the amidine group (Table 2). In the gas phase this may result from proton 'internal solvation' by two basic groups, the amidine and X′ groups.[23] In a non-polar solvent the formation of a three-centred complex is possible. In such a complex a hydrogen bond may be formed between ROH and two basic sites, the amidine group and the X′ substituent.





Proton chelation by two basic groups increases the gas-phase basicity of bidentate ligands by 8, 22 and 31 kJ mol^{-1} for derivatives with X′ = NMe$_2$ and $n = 0$, 2, 3, and by 4 and 20 kJ mol^{-1} for X′ = OMe and $n = 0$, 2, respectively. The formation of a three-centred complex increases the hydrogen bonding basicity by *ca.* 0.4 log K_{HB} units for derivatives with X = OMe and $n = 2$.

In conclusion the application of σ together with the structure–basicity relationships in the prediction of 'microscopic' basicities for individual sites in bifunctional (or generally polyfunctional) compounds enables the explanation and estimation of additional effects, *e.g.* 'internal' solvation or the formation of a three-centred complex.

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