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Comparison of Thermodynamic Hydrogen Bonding, Brönsted and Gas-phase Basicity with Spectroscopic Hydrogen Bonding Basicity of *N*^{1},*N*^{1}-Dimethylformamidines. Similarities and Differences in Substituent Effects†

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Comparison of the thermodynamic (logK_{HB} with 4-fluorophenol in CCl_4, pK_a in azeotropic ethanol and *GB* in the gas phase) with spectroscopic basicities ($\Delta\nu_{OH}$ of methanol in CCl_4) for *N*^{1},*N*^{1}-dimethylformamidines shows good correlation only between the pK_a and $\Delta\nu_{OH}$ values; no general simple linear model can be applied to the logK_{HB}/$\Delta\nu_{OH}$ and GB/$\Delta\nu_{OH}$ relations.

Basicity of chemical compounds can be measured in different conditions, and thus different basicity parameters are possible.[1] Depending on reagent (acid strength) and solvent (polarity), proton-transfer or hydrogen-bonding reactions may take place. Structural effects observed in these reactions are always complex.[2] They are a mixture of pure structural (internal) and solvation effects (external).[3] Separation of these effects is experimentally impossible. In the gas phase only pure structural effects can be observed.[4] Therefore investigations in the gas phase and in solution, and then comparison of the basicity parameters obtained under different conditions are important. They provide valuable information on structural effects in solution.

For this kind of study a series of *N*^{1},*N*^{1}-dimethylformamidines, $Me_2N{-}CH{=}NR$ (FDM, R = aryl, arylalkyl, alkyl and heteroalkyl) was chosen.[5] FDMs have exceptionally high basicity, which can be measured for a large number of derivatives under different conditions.

In this work the thermodynamic basicity parameters obtained for FDMs in hydrogen-bonding and proton-transfer reactions have been compared with their spectroscopic basicity parameters for the hydrogen-bonding reaction. This comparison supplies valuable information on differences and similarities in the sensitivity of the amidine group to global and partial substituent effects in different reactions.

Basicities for about 50 FDMs were investigated under different conditions (see refs. 16–37, 43 and 44 cited in ref. 5). In each case the imino nitrogen atom was found to be the preferred basic site. The hydrogen bonding basicities in the thermodynamic scale (logK_{HB}) were measured by means of the formation constants of complexes of FDMs with 4-fluorophenol in CCl_4.[6,7] The Brönsted basicities (pK_a) were obtained as the dissociation constants of the cations conjugated with FDMs in azeotropic ethanol.[8,9] The gas-phase basicities (*GB*) were measured as the Gibbs free energies for the deprotonation reaction of the corresponding cations conjugated with FDMs.[10–12] In the spectroscopic scale, the hydrogen bonding basicities ($\Delta\nu_{OH}$) were measured by means of the frequency shift of the stretching frequency of MeOH in CCl_4 [$\Delta\nu_{OH} = \nu_{OH}$(free) − ν_{OH}(hydrogen bonded) in cm^{-1}].[6,7]

In Fig. 1 the logK_{HB}, pK_a and *GB* values obtained for FDMs are plotted against the $\Delta\nu_{OH}$ values. The respective data were taken from refs. 5–12. The comparison shows that only pK_a values correlate well with the $\Delta\nu_{OH}$ values [eqn. (1)]. The good correlation ($r = 0.994$, $s = 0.20$) found for almost all FDMs investigated ($n = 25$) indicates that the interaction of FDMs with methanol in CCl_4 is similar to that with the solvated proton in azeotropic ethanol.

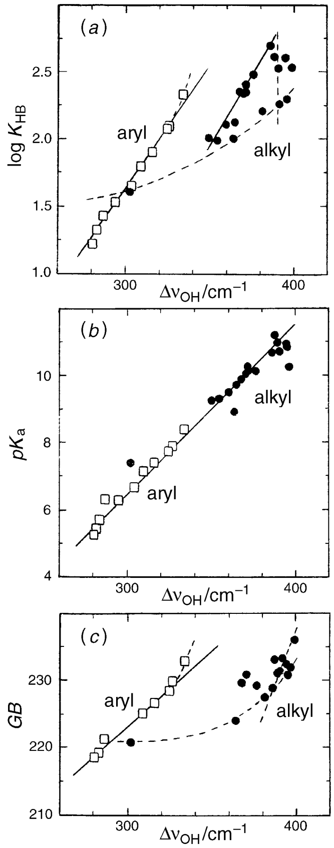

Fig. 1 Plots of the logK_{HB} (*a*), pK_a (*b*) and *GB* (*c*) against $\Delta\nu_{OH}$ for aryl (□) and alkyl (●) derivatives of FDM

$$\mathrm{p}K_a = (0.048 \pm 0.001)\Delta\nu_{OH} - (7.80 \pm 0.38) \qquad (1)$$

Exceptions are found for bifunctional derivatives with heteroalkyl substituents, the $(CH_2)_2OMe$ and $(CH_2)_2CN$ groups, for which the $\Delta\nu_{OH}$ values are higher than expected from relation (1), and additionally for the CH_2CF_3 group which deviates in the opposite direction. Higher $\Delta\nu_{OH}$ for FDM[$(CH_2)_2OMe$] and FDM[$(CH_2)_2CN$] may be explained by a chelation of MeOH by two basic groups, the amidine and OMe or CN groups, respectively.[5] This effect increases the basicity parameter in apolar solvents, just as chelation of the proton by bidentate ligands in the proton-transfer reaction does in the gas phase.[5,11] The deviation of the CH_2CF_3 group may suggest that the $\Delta\nu_{OH}$ value obtained experimentally is too small. This group deviates not only

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Table 1 Correlations between the relative basicities δQ ($\delta\Delta\nu_{OH}$ in cm^{-1} and $-\delta G_{HB}$, $\delta\Delta G_{alc}$, δGB in kcal mol^{-1}) and substituent parameters for aryl and alkyl derivatives of FDMs with use of eqn. (2); see text

No.	δQ	$-\rho_\alpha$	$-\rho_F$	$-\rho_R$	$-c$	r	s	n
FDM(aryl)								
2a	$\delta\Delta\nu_{OH}$	-7.0 ± 8.3	51.8 ± 8.6	49.2 ± 9.1	-1.5	0.969	5.8	10
2b	$-\delta\Delta G_{HB}$	-0.1 ± 0.2	1.4 ± 0.2	1.2 ± 0.2	1.0	0.985	0.1	9
2c	$\delta\Delta G_{alc}$	-0.6 ± 0.7	3.9 ± 0.6	3.2 ± 0.6	4.2	0.979	0.4	9
2d	δGB	-0.4 ± 1.0	12.5 ± 0.9	12.5 ± 1.0	1.7	0.996	0.6	9
FDM (alkyl)								
2e	$\delta\Delta\nu_{OH}$	15.7 ± 7.0	431 ± 67	—	5.0	0.934	3.5	10
2f	$\delta\Delta G_{alc}$	1.2 ± 0.9	17.6 ± 0.9	—	0.6	0.989	0.3	13
2g	δGB	10.8 ± 1.2	41.2 ± 1.2	—	3.9	0.997	0.4	13

from correlation in Fig. 1(*b*), but also from those in Fig. 1(*a*) and 1(*c*).

In the case of the $\log K_{HB}/\Delta\nu_{OH}$ and $GB/\Delta\nu_{OH}$ relationships given in Fig. 1(*a*) and 1(*c*), the linear model: $Q = A\Delta\nu_{OH} + B$ can be applied only locally. Q represents the thermodynamic basicity parameter. For example, the aryl subfamily gives quite good linear relationships: $\log K_{HB}[\text{FDM(aryl)}] = (0.018 \pm 0.001)\Delta\nu_{OH} - (4.0 \pm 0.4)$, $r = 0.989$, $s = 0.48$, $n = 7$, and $GB[\text{FDM(aryl)}] = (0.24 \pm 0.02)\Delta\nu_{OH} + (51 \pm 5)$, $r = 0.987$, $s = 0.91$, $n = 8$. Simple alkyl and heteroalkyl groups strongly deviate from these lines. Their deviations are different and vary from 0 to 1.1 $\log K_{HB}$ units and from 2.3 to 15.6 kcal mol^{-1}, respectively. For arylalkyls together with the Me, cyclopropyl and $CH_2CH{=}CH_2$ groups an additional linear relationship is obtained: $\log K_{HB}[\text{FDM(arylalkyl)}] = (0.021 \pm 0.002)\Delta\nu_{OH} - (5.0 \pm 0.7)$, $r = 0.971$, $s = 0.06$, $n = 10$. In the case of the $GB/\Delta\nu_{OH}$ plots [Fig. 1(*c*] there is only one benzyl group, and thus parameters for a linear model cannot be found for arylalkyls.

Good correlation between the pK_a and $\Delta\nu_{OH}$ values [eqn. (1)] suggests that both parameters are sensitive to the same partial substituent effects. To confirm this suggestion, quantitative analysis of substituent effects based on the Taft and Topsom[13] eqn. (2) has been performed.

$$\delta Q = \rho_\alpha\sigma_\alpha + \rho_F\sigma_F + \rho_R\sigma_R + c \qquad (2)$$

In eqn. (2), δQ is the relative basicity between the substituted [FDM(R)] and methyl derivative [FDM(Me)], and σ_α, σ_F and σ_R correspond to the parameters of the substituent polarizability (P), field/inductive (F) and resonance effects (R).[13,14] The substituent steric effect (S) has not been included in eqn. (2), and thus good analysis cannot be performed for $\log K_{HB}$[FDM(alkyl)], values of which are very sensitive to this effect.[5,7] For alkyl derivatives the $\rho_R\sigma_R$ contribution has been omitted in eqn. (2).[10,11] Derivatives with cyclopropyl and heteroalkyl groups have not been considered. For calculations, the relations $-\Delta G_{HB} = 1.3643\log K_{HB}$ and $\Delta G_{alc} = 1.3643\text{p}K_a$, expressed on the Gibbs free energy scale (in kcal mol^{-1}), as for the *GB*, have been taken.

Correlations for FDM(aryl) show that for each basicity scale the P effect is not an important contribution to δQ (Table 1). This means that the P effect is constant for the aryl groups and does not depend on the substituent on the phenyl ring. It can be neglected when the aryl subfamily is separately considered. Only slight differences in the transmission of the F and R effects are observed. In each basicity scale the ρ_R/ρ_F ratio is close to 1. This explains the good correlations found for the aryl groups in Fig. 1.

Comparison of the ρ_α and ρ_F values obtained for FDM(alkyl) (Table 1) indicates that the contribution of the P effect is very small to the $\delta\Delta\nu_{OH}$ and $\delta\Delta G_{alc}$ and thus it can be neglected. Both the $\delta\Delta\nu_{OH}$ and $\delta\Delta G_{alc}$ depend mainly on the F effect. This explains the good correlation [eqn. (1)] observed in Fig. 1(*b*) The P effect is very important for alkyl derivatives in the gas phase,[10,11] and thus the general $GB/\Delta\nu_{OH}$ relation cannot be expressed by one simple linear model. Two subfamilies can be distinguished in Fig. 1(*c*), one for simple alkyls (for which $\sigma_F = 0$) and the other for alkyls with heteroatom(s) and/or π electrons (for which $\sigma_F \neq 0$) with locally changing A. Similar behaviour is found for the $\log K_{HB}/\Delta\nu_{OH}$ relation because the $\log K_{HB}$ values are sensitive to the P effect.[5] Strong deviations of the *tert*-C_5H_{11} and 1-adamantyl groups from the alkyl subfamily in Fig. 1(*a*) confirm additionally that the $\log K_{HB}$ values are very sensitive to the S effect. This effect decreases the $\log K_{HB}$ of the *tert*-C_5H_{11} and 1-adamantyl groups by *ca.* 0.5 $\log K_{HB}$ units.

All these observations indicate that structure–basicity relationships may be very complicated and simple linear models cannot be generalised for any substituent and any basicity scale. This is in good agreement with the suggestion of Sjöstrom and Wold[15] that linear free energy relationships should be considered as local empirical models of similarity or locally valid linearizations of complicated relationships rather than combinations of 'fundamental' effects.

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