Amine Basicities in Benzene and in Water

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The constants for ion-pair formation with 2,4-dinitrophenol in benzene (K_B), and the pK_a values in water, of thirty-three amines have been measured. According to the class of amine, two different situations can be observed: for primary amines and secondary cyclic amines, the effects of structural variations on basicity are higher in water than in benzene; on the other hand, for tertiary amines these effects are similar in the two solvents. K_B Values of primary amines give a good correlation with σ^*. The Taft and Hancock equation allows a unifying treatment of K_B values of the various classes of amines.

We have recently investigated the mononuclear heterocyclic rearrangements[1] of some arylhydrazones of 3-benzoyl-5-phenyl-1,2,4-oxadiazole into 2-aryl-4-benzoylamino-5-phenyl-1,2,3-triazoles in a number of solvents (dioxane–water,[2] methanol,[3] benzene,[4] dioxane,[3] and acetonitrile[3]) and in the presence of various bases as catalysts.

In our previous study of these rearrangements in benzene[4] we realized that it would have been desirable to have basicity data for a series of amines in this solvent, and in water; literature data in this area are scarce.

Among the various methods designed to measure amine basicities in benzene (ion-pair formation constants,[5] neutralization enthalpy,[6] *etc.*) we concentrated our attention on the determination of ion-pair formation constants between amines and 2,4-dinitrophenol. Indeed, in view of the structure of the transition state proposed for the mechanism of mononuclear heterocyclic rearrangements,[2d,2e,4] ion-pair formation represents a good model for correlation of reactivities in rearrangements with the basicities of the basic catalysts involved.

In order to compare the behaviour of the amines in benzene and in water, we have measured their basicity in water, too. The literature data available are not homogeneous, and there are cases of serious discord between values from different laboratories.

Results and Discussion

The constants for ion-pair formation in benzene (K_B) and the pK_a values in water have been measured essentially by the methods proposed by Pearson and Vogelsong[5a] and by Albert and Serjeant,[7] respectively. The data obtained are collected in Table 1, which also contains some literature data.

Primary Amines.—The four linear aliphatic amines examined (nos. 1—4) show much the same basicity; introduction of a phenyl group causes a reduction in basicity (nos. 5—7) which depends on the distance from the basic centre. Interestingly, the trend of basicities in water (pK_a) parallels that for benzene (log K_B) with a good linear correlation (Figure 1, line a, slope 0.65 ± 0.03, r 0.993, i −4.87 ± 0.36, n 7, confidence level >99.9%) and this indicates that similar steric and electronic factors affect the amine basicity in the two solvents.

Table 1. Constants for ion-pair formation with 2,4-dinitrophenol in benzene (K_B) and pK_a values in water of various amines at 25 °C

No.	Amines	K_B		pK_a[a]	
1	Propylamine	101		10.68	
2	Butylamine	110	(285)[b]	10.75	
3	Pentylamine	136		10.81	
4	Hexylamine	146	(50)[c]	10.85	
5	Benzylamine	17		9.49	
6	2-Phenylethylamine	51		10.08	
7	3-Phenylpropylamine	71		10.37	
8	Pyrrolidine	7 630		11.35	
9	Piperidine	4 490	(2 810)[b]	11.12	
10	Hexamethyleneimine	3 050		10.89	
11	Heptamethyleneimine	2 000		10.78	
12	Piperazine[e]	1 940		10.20	
13	1-Methylpiperazine	660		9.85	
14	Morpholine	70	(250)[b]	8.45	
15	2-Methylpiperidine	2 560		10.93	
16	Diethylamine	1 520	(1 240)[c]	11.02	
17	Dipropylamine	930		11.05	
18	Dibutylamine	880	(950)[c]	11.20	
19	Di-isobutylamine	213		10.59	
20	Benzylmethylamine	153		9.63	
21	Benzylethylamine	90		9.83	
22	*N*,*N*-Dimethylbenzylamine	63		9.03	
23	*N*,*N*-Dimethylethylamine	1 150		10.12	
24	*N*-Methylpiperidine	1 950		10.13	
25	*N*,*N*-Diethylmethylamine	2 290		10.37	
26	Triethylamine	2 700	(2 940)[c]	10.68	
27	Tributylamine	709	(614)[c]	10.89	
28	DABCO[d]	4 950		8.72	
29	1,2-Diaminoethane[e]			10.14	7.49[f]
30	1,3-Diaminopropane[e]			10.70	9.10[f]
31	1,4-Diaminobutane[e]			10.90	9.80[f]
32	1,5-Diaminopentane[e]			11.08	9.99[f]
33	1,6-Diaminohexane[e]			11.19	10.33[f]

[a] Since the corresponding literature pK_a values, where available, are not homogeneous, we do not indicate any alternative pK_a value. [b] Values from T. O. Bamkole, J. Hirst, and I. Onyido, *J. Chem. Soc., Perkin Trans. 2*, 1982, 889. [c] Values from ref. 5*a*. [d] 1,4-Diazabicyclo-[2.2.2]octane. [e] The values for diamines are not corrected for statistical factors. [f] p$K_{a(2)}$ Values.

Secondary Cyclic Amines.—The basicity of the cyclic amines (nos. 8—11) decreases with increasing ring size. The introduction of a second heteroatom [nitrogen (nos. 12 and 13) or oxygen (no. 14)] in the six-membered ring causes a reduction in amine basicity which can be rationalized in terms of field effect or of inductive effect: on the other hand the difference in basicity between the two amines 12 and 14 reflects the higher electron-withdrawing effect of oxygen as compared with nitrogen. An α-methyl group [*cf.* 2-methylpiperidine (no. 15) and piperidine (no. 9)] causes only a small decrease in basicity: here it is probable that there is a balance between the unfavourable effect

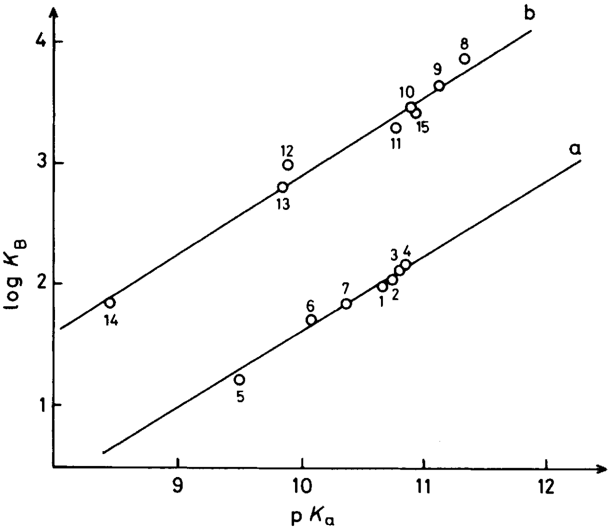

Figure 1. Plot of log K_B *versus* pK_a for primary amines (line a) and for secondary amines (line b) (numbers as in the Table). The values of log K_B and pK_a have been statistically corrected

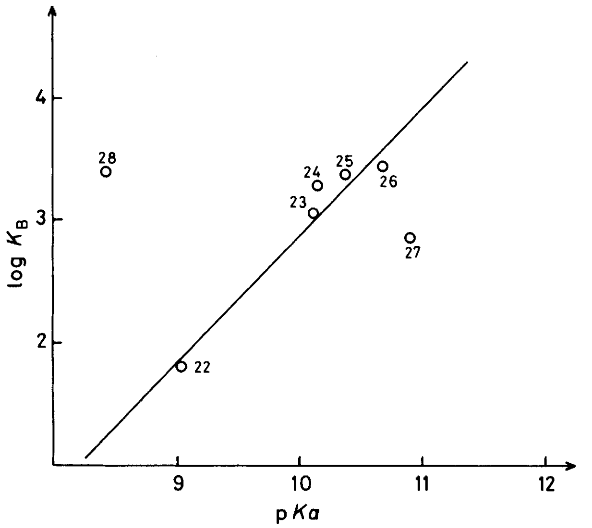

Figure 2. Plot of log K_B *versus* pK_a for tertiary amines (numbers as in the Table). The values of log K_B and pK_a have been statistically corrected

of increasing *B*-strain and the favourable electron-repelling effect of the methyl group. Again in this case there is a good linear correlation between log K_B values and pK_a values (Figure 1, line b, slope 0.65 ± 0.05, *r* 0.990, *i* −3.62 ± 0.48, *n* 8, confidence level >99.9%) as observed for primary amines.

Secondary Amines.—The pattern of basicities in benzene for the six secondary amines examined (nos. 16—21) is different from that in water; thus no correlation is observed between log K_B and pK_a values. However, the relevant plot shows that with some exceptions (*e.g.* see benzylmethylamine and benzylethylamine, or diethylamine and dipropylamine) a trend is observable.

Tertiary Amines.—In spite of their intrinsic heterogeneity five (nos. 22—26) out of the seven tertiary amines studied give a fair linear correlation between log K_B and pK_a (Figure 2, slope 1.06 ± 0.15, *r* 0.970, *i* −7.65 ± 1.55, *n* 5, confidence level >99.0%): the points for tributylamine and DABCO (nos. 27 and 28) fall off the straight line on opposite sides. The steric requirements of these two amines are very different from those of the other tertiary amines and thus their basicity is affected in a different way by the two solvents. In fact, DABCO has a structure such that weak interactions with the poorly solvating solvent (benzene) make interaction with the acid (dinitrophenol) easier: in contrast, the water molecules can build a cage around the DABCO molecules, so lowering its basicity. Opposite effects are observed for tributylamine: in this case the solvation by the water molecules is low, whereas in benzene the three butyl groups surrounding the nitrogen atom prevent it from interacting with the acid partner. The correlation data obtained for the other tertiary amines indicate that amine–solvent interactions are probably small and compensate each other on going from benzene to water: as a consequence, the slope of the relevant correlation is near to unity (Figure 2).

Primary Diamines.—Our attempts at determining the constants for ion-pair formation between some diamines (nos. 29—33) and 2,4-dinitrophenol were unsuccessful. In fact, on mixing the diamine (*e.g.* 1,2-diaminoethane or 1,6-diaminohexane) with 2,4-dinitrophenol, even at very low concentrations (*ca.* 2×10^{-5} M), causes precipitation of the corresponding salt. On the other hand, the expected low K_B values discouraged measurements at low concentrations.

We have measured the basicities of the diamines in water. The pattern of p$K_{a(1)}$ and p$K_{a(2)}$ values is that expected on grounds of p$K_{a(1)}$ and p$K_{a(2)}$ values for dicarboxylic acids. In fact, p$K_{a(1)}$ values vary within a smaller range than p$K_{a(2)}$ values (1 and 3 units, respectively). The difference p$K_{a(1)}$ − p$K_{a(2)}$ is a function of the number of carbon atoms between the two amino groups of each diamine: it amounts to 2.6 units in 1,2-diaminoethane, falls to 1.6 in diaminopropane, and decreases regularly to 0.9 in 1,6-diaminohexane.

Some pK_a values for primary diamines have been measured by Rometsch and his co-workers,[8] and our results essentially duplicate their figures. The previous authors did not collect data for 1,6-diaminohexane: our data fit well their prediction concerning the effect of chain lengthening on pK_a values (for a six-term linear chain p$K_{a(1)}$ − p$K_{a(2)}$ is *ca.* 1.0;[8] the value found is 0.9).

Discussion.—The relative acidities or basicities of two acids or two bases are strongly dependent on the solvent when the species to be compared differ in electron charge (*e.g.* one base is neutral and the other is an anion) or because of specific solvation effects (*e.g.* the two bases show different hydrogen-bonding abilities or have the charge concentrated on different atoms): indeed, solvent changes can also determine a reversal in relative acid or base strengths. Otherwise, the differences are usually small, and linear free energy relationships can be observed between acidities or basicities measured in two different solvents. Accordingly we have obtained some linear correlations between logK_B and pK_a for each homogeneous class of amines (primary amines, secondary cyclic amines, and tertiary amines). The correlation for primary amines shows the same slope as that for secondary amines but a different intercept. This suggests that the entropy variations are constant (*i.e.* zero or proportional to free energy variations) within a class of amines but that they are different for the two classes of amines. Thus, it is possible to correlate logK_B values (*i.e.* free energy variations) with neutralization enthalpies and to obtain three distinct straight lines for the three aforementioned classes of amines. The failure to obtain a unique free energy correlation between logK_B and pK_a for all the amines considered shows that solvation effects are largely dependent on the structure of the amine. The fact induces some other considerations. The most common factors which affect the base strength of amines, together with the electronic effects of the substituents linked to the nitrogen atom, are *B*- and *F*-strain (in some cyclic amines *I*-strain also has to be taken into account): *B*-strain is considered scarcely solvent-dependent.

The substituents linked to the nitrogen atom of the amines studied by us are alkyl groups; thus the relevant electronic and steric effects are measured adequately by σ^* and E_s^c constants, respectively. Accordingly, pK_a values have been correlated using the Taft or the Taft–Hancock equation, for a single class of amines and a range of classes of amines, respectively.

For primary amines there is a good correlation in terms of the Taft equation (1) (*n* 7, *r* 0.975, confidence level >99.9%).

$$\log K_B = -(2.18 \pm 0.21)\sigma^* + 3.93 \pm 0.20 \qquad (1)$$

However, the same treatment cannot be applied to the other classes of amines for the following reasons: (i) in the case of cyclic secondary amines substituent constants are available for only a few of our amines; (ii) in the case of tertiary amines, the substituent constants are available for six amines (nos. 22—27), but the plot of $\log K_B$ *versus* σ^* shows that tributylamine (no. 27) falls off the straight line that can be drawn for the other five amines. On the other hand, this line is not meaningful because it rests on only two points: a cluster of four amines (nos. 23—26) and *N,N*-dimethylbenzylamine. No significant linear correlation can be achieved for open-chain secondary amines.

The data collected allow us to compare the basicities of primary, secondary, and tertiary amines of similar structures. In benzene, triethylamine is a stronger base than diethylamine and presumably stronger than ethylamine also (estimated K_B *ca.* 90—100). The basicity sequences triethylamines > tributylamine and dibutylamine > tributylamine show the influence of steric effects (*F*-strain) superimposed on the electronic ones. Similar conclusions were drawn by Pearson and Vogelsong,[5a] who pointed out that in the series of tertiary, secondary, and primary amines, the basicity order in benzene depends on a combination of electronic and steric effects interacting with each other in different ways.

We attempted to separate polar and steric effects of *N*-substituents of amines $NR^1R^2R^3$ by means of the Taft–Hancock equation (2), where $E_s^c(R^i)$represent the steric effect of a

$$\log K_B = \rho^*\sigma^* + \Sigma_i a_i E_s^c(R^i) + c \qquad (2)$$

component substituent (R^1, R^2, or R^3), and $E_s^c(R^1) \geqslant E_s^c(R^2)$ - $\geqslant E_s^c(R^3)$. The necessary substituent constants were available for all the amines except for DABCO and the three secondary cyclic amines. Following Fujita[9] we assumed that the 'effective' steric effect of the isobutyl group in tertiary amines mimics that of the neopentyl group.

The degrees of independence of the variables are reasonably high, as shown by the partial correlation coefficients (not reported), thus the foregoing procedure is justified. In the statistical analysis, performed in a stepwise manner, the computer program used effects regressions starting with a simple linear regression on the most relevant variable (σ^*) and then bringing in the other variables in the order of decreasing relevance, to some predetermined level of significance. The values of the intercept term, *c*, and of the appropriate regression coefficients, a_1, a_2, *etc.*, and values of statistical quantities, at each stage, are reported in Table 2.

The foregoing analysis indicates that the overall effect of three *N*-substituents can be divided quantitatively into electronic and steric effects according to the equation (3).

$$\log K_B = (-1.474 \pm 0.226)\sigma^* + (1.252 \pm 0.366)E_s^c(R^1) + (1.344 \pm 0.333)E_s^c(R^3) + (3.773 \pm 0.198) \qquad (3)$$

The negative ρ^* value shows that the more the electron-donating ability of the *N*-substituents, the higher the nucleophilicity of the amine. The relative significance of the steric effects of substituents is much more difficult to assess. The foregoing results could mean that in the acid–base association studied the lone-pair electrons of the amine are not strictly oriented in the tetrahedral direction with the substituents but deviate in such a way as to be unaffected by R^2 and to allow the best balance between electron-donating effects and bulkiness of the alkyl substituents.

Experimental

Purification of Compounds.—Benzene,[10] water,[11] 2,4-dinitrophenol,[5a] and amines[4c] were purified according to literature methods. Carlo Erba standard solutions (1N) of hydrochloric acid were used.

Determination of Constants for Ion-pair Formation between Amines and 2,4-Dinitrophenol.—2,4-Dinitrophenol in benzene,

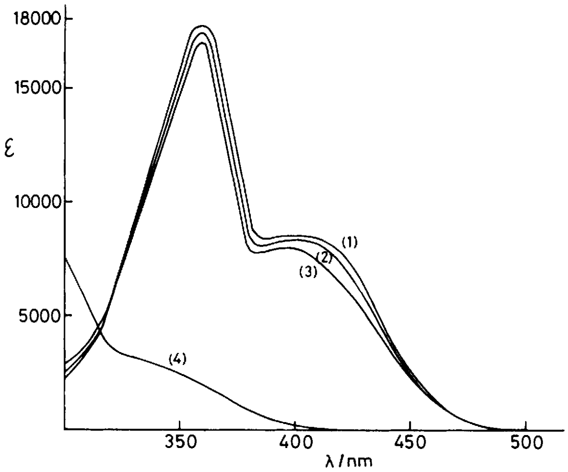

Figure 3. Spectra of 2,4-dinitrophenol at 25 °C: (1) excess of pyrrolidine added; (2) excess of triethylamine added; (3) excess of diethylamine added; (4) no base added

Table 2. Stepwise multiple linear regression analysis of $\log K_B$ in terms of equation (2)

Stage	ρ^*	$a_1 \pm s(a_1)$	$a_2 \pm s(a_2)$	$a_3 \pm s(a_3)$	$c + s(c)$	*R*	*F*
1	-1.197 ± 0.230				3.061 ± 0.142	0.768	27.1
2	-0.916 ± 0.197			1.486 ± 0.417	3.853 ± 0.249	0.871	28.2
3	-1.474 ± 0.226	1.252 ± 0.366		1.344 ± 0.333	3.773 ± 0.198	0.926	33.9
4[a]	-0.804 ± 0.452	0.765 ± 0.452	-0.546 ± 0.324	1.910 ± 0.461	3.839 ± 0.192	0.937[b]	28.9

[a] The regression parameters a_1 and a_2 are statistically significant only at the 0.2 level. [b] The apparent 'improvement' of *R* on increasing the number of variables from 3 to 4 (stage 4) does not have a satisfactory level of significance (see text).

when treated with an excess of various different amines (*e.g.* triethylamine, diethylamine, pyrrolidine, or n-hexylamine), gave similar u.v. and visible spectra with two characteristic maxima at 360 and 400 nm (see Figure 3, ε *ca.* 18 000 and 8 500, respectively). The wavelength used for measurements was 400 nm, at which the starting 2,4-dinitrophenol had a low absorbance (ε 124).

For each determination various solutions containing 2,4-dinitrophenol (*ca.* 1×10^{-4} M) and various concentrations of amine were prepared and thermostatted at 25 °C. Good linear correlations were obtained by plotting reciprocal absorbance *versus* reciprocal amine concentration: from the slopes of these straight lines and by using the ε values of 2,4-dinitrophenoxide anion and of 2,4-dinitrophenol independently determined (see before), on the assumption that ion-pair formation is the only reaction, the equilibrium constants were calculated according to the equation of Pearson and Vogelsong.[5a]

Potentiometric Measurements.—The procedure for the determination of pK_a values described by Albert and Serjeant[7] was used throughout. The values obtained were reproducible to within ±0.01 pK_a units. A Radiometer digital PHM 63 pH meter equipped with a Radiometer GK 2301C combined electrode was used for the determinations.

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