1289. *The Acid–Base Function in Non-aqueous Solution. Part III.*[1] *The Effect of Chain Length and Freedom of Ring Rotation on the Acid–Base Properties of Some Nitrogen Bases in Chlorobenzene*

By John W. Bayles and B. Evans

The nitrogen bases studied are nine *N*-alkyl- and -cycloalkyl-piperidines; five *N*-alkylpyrrolidines; pyrrolidine, piperidine, hexamethyleneimine, and the three cyclohexylamines. The equilibrium in the solvent chlorobenzene was of the form $B + HA \rightleftharpoons B^+HA^-$ where B is the base and in this series HA is 2,4-dinitrophenol. The values of $\Delta G°$, $\Delta H°$, and $\Delta S°$ for this reaction at 25° are measured. There is a correlation between enthalpy and entropy of reaction. The deviations from this are not great and are ascribed to intramolecular sources of entropy change including ring flexion, hydrogen inversion, and ring rotation. It is shown that alkyl chain length has a very small effect on the results. This implies a strict limitation to the kind of effect which may be applied to explain the variation with chain length of the acid–base properties of the alkylamines in water.

In this research we wish to establish the effect of structural factors on the base strength of amines as measured by the energetics of their reaction with 2,4-dinitrophenol in chlorobenzene solution. In Part II [1b] it was demonstrated that chlorobenzene is a solvent which affects minimally the reaction between the butylamines and 2,4-dinitrophenol and we therefore provisionally assume that it will also have a limited solvent effect on the reaction between the amines of this Communication and 2,4-dinitrophenol.

The first series, *N*-n-alkyl-pyrrolidines and -piperidines, were chosen for two reasons. Firstly, the use of tertiary amines eliminates the effects on the reaction of any additional N–H bonds such as are present in primary and secondary amines. This may be a statistical effect (degeneracy of the reaction co-ordinate) which can be allowed for [2] and is therefore not serious, but N–H bonds additional to the one taking part in the reaction would be free to interact with the solvent. For the purpose of this Series we wish to avoid the contributions to ΔG, ΔH, and ΔS which would arise from a change of such interactions in parallel with the reaction with 2,4-dinitrophenol. Secondly, the steric effects expected for tertiary amine reactions should be limited by the structure of the piperidine and pyrrolidine residues, where in effect two of the groups attached to the amine nitrogen are tied together. Thus, any variations in the energetics of their reactions with 2,4-dinitrophenol in chlorobenzene should be related to the variation in length and configuration of the alkyl chain.

The second series, pyrrolidine, piperidine, and hexamethyleneimine, was chosen to obtain a view of the effect of ring size on the behaviour of cyclic amines.

The three cyclohexylamines were measured to obtain a view of the effect of ring rotation on the thermodynamics of proton transfer.

Experimental

Materials.—Chlorobenzene and 2,4-dinitrophenol were purified by the methods described in Part I.[1a] Pyrrolidine (B.D.H.), piperidine (B.D.H.), and hexamethyleneimine (Imperial Chemical Industries Limited) were distilled, dried over sodium wire, and fractionally redistilled. *N*-Methyl- and *N*-ethyl-pipridine were obtained from Messrs. L. Light. The remaining *N*-substituted pyrrolidines and piperidines were prepared from pyrrolidine or piperidine and excess of the alkyl bromide in the presence of sodium carbonate.

These amines were examined by infrared spectrophotometry (Perkin-Elmer Infracord) and where N–H frequencies were found after fractional distillation, the product was treated with toluene-*p*-sulphonyl chloride and the test and treatment were repeated until satisfactory

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[1] (*a*) Part I, J. W. Bayles and A. Chetwyn, *J.*, 1958, 2328; (*b*) Part II, J. W. Bayles and A. F. Taylor, *J.*, 1961, 417.

[2] S. W. Benson, *J. Amer. Chem. Soc.*, 1958, **80**, 5151.

results were obtained. Boiling and melting points agreed with literature values to within the precision of our apparatus (about 0·5°).

RESULTS

Apparatus, Solutions, Units, and Spectra.—Detailed experimental procedures have been described in Part I.[1a] Molal units were used for calculation, but thermodynamic functions are based on mole-fractional units to remove the effect of the molecular weight of the solvent on numerical values. The method of calculation has been described fully in Part II.[1b] Beer's law was found to be satisfied by solutions containing the AHB complex. The absorption of the solvent (chlorobenzene) prevented the spectra from being recorded below 300 mμ. All the AHB spectra show an intense absorption peak ($\varepsilon \simeq 16{,}000$) between 357 and 360 mμ with a shoulder having about two-thirds of this intensity near 410 mμ.

In Table 1, after each amine (B), the first figure is the wavelength (in mμ) of maximum absorption of the AHB complex with 2,4-dinitrophenol (AH), the second is the corresponding molar absorbency, and the third is the molar absorbency at 410 mμ. The latter wavelength was used for determinations of equiibrium position.

TABLE 1

Characteristics of the absorption spectra of 2,4-dinitrophenol in the presence of an excess of various amines

Amine	$\lambda_{\max.}$	$\varepsilon_{\max.}$	ε_{410}	Amine	$\lambda_{\max.}$	$\varepsilon_{\max.}$	ε_{410}
N-Methylpiperidine	357	15,900	9150	*N*-Ethylpyrrolidine	357	16,000	9300
N-Ethylpiperidine	357	16,500	9500	*N*-n-Propylpyrrolidine	358	15,800	9200
N-n-Propylpiperidine	357	15,300	9400	*N*-n-Butylpyrrolidine	358	15,400	9600
N-n-Butylpiperidine	357	17,000	9700	*N*-n-Octylpyrrolidine	357	15,900	9550
N-n-Hexylpiperidine	358	16,300	9400	Pyrrolidine	357	15,900	9700
N-n-Octylpiperidine	357	16,800	9450	Piperidine	360	17,100	10,400
N-n-Hexadecylpiperidine	358	15,800	9750	Hexamethyleneimine	358	16,000	9500
N-Cyclopentylpiperidine	358	16,500	9450	Tricyclohexylamine	360	17,000	11,800*
N-Cyclohexylpiperidine	360	16,400	9750	Cyclohexylamine	360	17,000	11,000
N-Methylpyrrolidine	357	15,900	9300				

* At 400 mμ.

It can be seen that the above AHB spectra are very similar to one another, and this is also borne out by the detailed absorption curves which are so similar that reproduction is unnecessary for the present purpose. These spectra are also the same in general shape as the spectrum of

TABLE 2

Thermodynamic functions for the reaction between some amines and 2,4-dinitrophenol in chlorobenzene

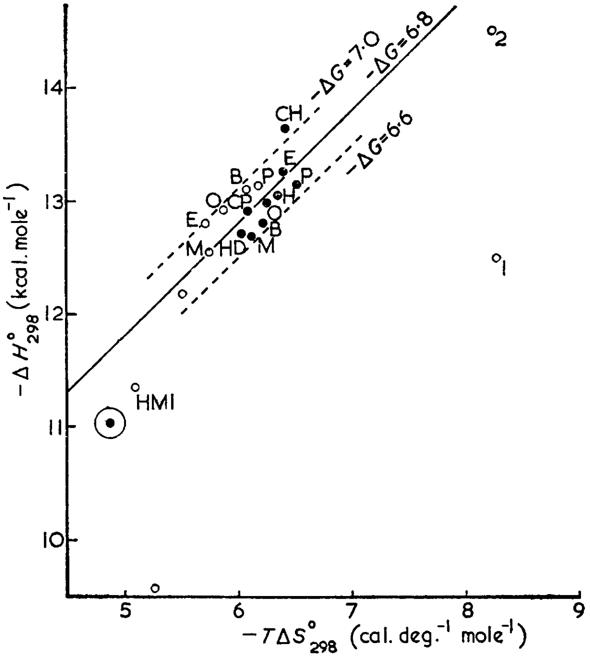
Amine	$-\Delta G^\circ_{298}$ (kcal. mole^{-1})	$-\Delta H^\circ_{298}$ (kcal. mole^{-1})	$-\Delta S^\circ_{298}$ (cal. deg.$^{-1}$ mole^{-1})
Pyrrolidine	6·66 ± 0·01	12·17 ± 0·22	18·47 ± 0·74
Piperidine	6·37 ± 0·01	11·24 ± 0·19	16·33 ± 0·63
Hexamethyleneimine (HMI)	6·25 ± 0·01	11·34 ± 0·08	17·07 ± 0·28
Cyclohexylamine (1)	4·21 ± 0·01	12·49 ± 0·13	27·77 ± 0·44
Tricyclohexylamine (3)	4·34 ± 0·01	9·57 ± 0·15	17·55 ± 0·49
N-*n-Alkylpyrrolidines*			
Methyl	6·80 ± 0·01	12·57 ± 0·13	19·32 ± 0·44
Ethyl	7·09 ± 0·01	12·80 ± 0·09	19·17 ± 0·31
Propyl	6·96 ± 0·01	13·14 ± 0·14	20·75 ± 0·45
Butyl	7·00 ± 0·01	13·07 ± 0·08	20·38 ± 0·28
Octyl	7·04 ± 0·01	12·91 ± 0·18	19·68 ± 0·61
N-*n-Alkylpiperidines*			
Methyl	6·56 ± 0·01	12·67 ± 0·19	20·50 ± 0·63
Ethyl	6·85 ± 0·01	13·25 ± 0·05	21·48 ± 0·18
Propyl	6·62 ± 0·01	13·14 ± 0·12	21·88 ± 0·40
Butyl	6·58 ± 0·01	12·80 ± 0·11	20·84 ± 0·38
Hexyl	6·70 ± 0·01	13·04 ± 0·11	21·29 ± 0·35
Octyl	6·73 ± 0·01	12·98 ± 0·14	20·97 ± 0·46
Hexadecyl (HD)	6·67 ± 0·01	12·70 ± 0·21	20·22 ± 0·69
N-Cyclopentylpiperidine (CP)	6·82 ± 0·01	12·91 ± 0·11	20·45 ± 0·36
N-Cyclohexylpiperidine (CH)	7·22 ± 0·01	13·64 ± 0·10	21·53 ± 0·34

2,4-dinitrophenol in aqueous alkali. Since such a comparison was made in Part I we do not repeat it here. We consider therefore that we are justified in treating the complex as one in which proton tranfer has taken place giving (A^-HB^+).

Equilibrium Constants and Thermodynamic Quantities.—The concentration of AHB at equilibrium was found spectrophotometrically as described in Part II and a check was made that the graphs of m_{AHB} against $m_{AH}\cdot m_B$ were linear. The ranges of molal concentrations of amine and nitrophenol found suitable for measurement in all the systems in this work were $0{\cdot}6 \times 10^{-4}$ to $5{\cdot}0 \times 10^{-4}$ for the piperidines and pyrrolidines and 2×10^{-4} to 12×10^{-4} for cyclohexylamine and tricyclohexylamine. The temperature range was 20° to 60° and five different solution compositions exploiting the above ranges were measured, each at four different temperatures. We checked that these results for each system fitted on a single linear relation between log K and T^{-1}. The results are shown in Table 2.

DISCUSSION

It was pointed out long ago [3] that simple relationships between ΔG° and structure may only be expected at the absolute zero of temperature, and it has also been made clear [4] that the price we must pay for the convenience of room-temperature measurements of equilibrium is to measure variations with temperature. Only so may we disentangle the effects of nuclear perturbations of structure prevalent at room temperature from the electronic effects which usually remain unperturbed from the absolute zero up to temperatures well above the boiling points of most solutions. It is simply a question of which molecular states become statistically accessible between zero and room temperature, and these states make their contributions, usually in a fairly obvious way, to enthalpies, entropies, and the temperature dependence of enthalpy (ΔC_p).



Entropy–enthalpy correlation for the reaction with 2,4-dinitrophenol of some pyrrolidines (open circles), piperidines (full circles), mono-, di-, and tri-cyclohexylamines, and hexamethyleneimine. Point labels indicate the initial letter of the N-substituents or are keyed in Table 2. The large circle (bottom left, piperidine) represents the average probable error

The limited accuracy of photometric measurements and the tendency of polar species such as A^-HB^+ to aggregate at concentrations above 5×10^{-3}M has so far prevented the estimation of ΔC_p values accompanying proton transfer in non-aqueous solvents. We shall see, however, that ΔH and ΔS can show very significant parallel variation which therefore tend not to be reflected in free-energy changes and hence equilibrium constants.

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[3] M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, 1936, **32**, 1333.
[4] D. H. Everett, *Ind. chim. belge*, 1951, **16**, 647—658.

Entropy–Enthalpy Correlation.—The Figure shows that there is a correlation between the enthalpies and entropies of reaction. Such correlation is to be expected if (*a*) the enthalpy of reaction is related to $N^+–O^-$ distance as would be expected from a simple coulombic model, and (*b*) if the loss of entropy brought about by reaction is solely a consequence of the altered force-field in this bond. The formation of this bond causes three translational and three rotational degrees of freedom to be replaced by six internal modes of the complex. One of these is the $N^+–O^-$ stretching mode, and the others are deformations (bending or torsional). They are low-frequency modes and therefore make an important contribution to the entropy of complex formation. The strength of the bond between the two parts of the complex will govern the entropy contributions due to these modes, low enthalpy losses giving rise to a higher entropy in the complex and therefore low entropy losses. If entropy losses are possible by mechanisms not directly related to $N^+–O^-$ distance, then deviations from the enthalpy–entropy relation may be expected. We shall discuss the effect of ring flexions, the presence of the NH inversion mode, and the inhibition of ring rotation in this context.

The correlation for alkyl-pyrrolidines and -piperidines is approximately linear, and there is a strong suggestion that the piperidines and pyrrolidines fall on neighbouring and not coincident lines. The analysis below shows that this is because of the different contributions of ring entropies. These linear enthalpy–entropy correlations are common in physical chemistry, but have not previously been demonstrated for amines because, in the first place, not enough temperature-coefficient work has been done, and in the second, all available results are for aqueous systems where solvation plays a part difficult to assess quantitatively.

The base strengths of amines chosen for this work do not vary over a wide enough range to give a satisfactory picture of enthalpy–entropy correlation in the whole field of proton transfer in non-aqueous solution. Later Parts of this Series have been designed to produce evidence on this point.

Effect of Alkyl-chain Length.—Our aim in making measurements on a series of cyclic bases differing only in the length of alkyl group attached to the nitrogen atom has been to decide whether alkyl-chain length, in the absence of solvation effects, has any effect on the proton affinity of a nitrogen atom. This could operate (*a*) if the alkyl chain were exceptionally long and there were some reason why it should form a coil in the vicinity of the basic nitrogen atom or, (*b*) if on changing from methyl to ethyl or propyl substituents there were an abnormally high occlusion of the reaction field and hence an increased entropy loss for the reaction.

Table 2 reveals that, despite the above possibilities, there is very little variation of ΔS or ΔH with chain length within each series (*N*-substituted pyrrolidines and piperidines) considered separately. Median values, with standard deviations shown in parentheses, are:

	ΔH	ΔS
Pyrrolidines	12·9 (0·2)	19·9 (0·6)
Piperidines	12·9 (0·2)	21·0 (0·7)

This shows clearly that both enthalpies and entropies of reaction are independent of chain length and it excludes both (*a*) and (*b*) above.

It is known that the p*K* values of amines in water vary little with chain length, and this is thought to be because the inductive effect is constant, and, for ordinary alkyl chains, because there is no steric hindrance to the approach of a proton. However, one must await the determination of accurate values of ΔH and ΔS before this interpretation can be confirmed, for, as will be shown in a later Part of this Series (in preparation), constancy in ΔG can be the result of approximately equal variations in ΔH and $T\Delta S$. If there is found to be any chain-length effect in water, it must be ascribed to one of the effects of solvent–solute interaction [5,6] and not, for instance, to the coiling of long chains by inter-segment van der Waals attractions.

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[5] A. G. Evans and S. D. Hamann, *Trans. FaradaySoc.*, 1951, **47**, 34.

[6] D. H. Everett, D. A. Landsman, and B. R. W. Pinsent, *Proc. Roy. Soc.*, 1952, *A*, **215**, 403.

Difference between the Thermodynamics of Quaternisation in Piperidines and Pyrrolidines. Effect of Ring Entropy.—The absence of a chain-length effect on entropy or enthalpy enables us to obtain an averaged value for the difference between the enthalpy and entropy changes accompanying quaternisation in alkylpiperidines compared with those for the corresponding pyrrolidines. One may do this by comparing the average (nearly constant) values of the ΔS°_{298} and ΔH°_{298} for the reactions of the two series and we obtain (in a self-explanatory notation):

$$\Delta(\mathrm{C_5H_{10}NAlk} \longrightarrow \mathrm{C_4H_8NAlk})\ \Delta\,(\equiv\mathrm{N} \longrightarrow \equiv\mathrm{N^+})_{\mathrm{HA}}S^\circ_{298} = 19{\cdot}9 - 21{\cdot}0 = -1{\cdot}_1 \text{ cal. deg.}^{-1} \text{ mole}^{-1}.$$

$$\Delta(\mathrm{C_5H_{10}NAlk} + \mathrm{C_4H_8NAlk})\ \Delta\,(\mathrm{N}\equiv \longrightarrow \equiv\mathrm{N^+})_{\mathrm{HA}}H^\circ_{298} = 12{\cdot}9 - 12{\cdot}9 = 0{\cdot}_0 \text{ cal. mole}^{-1}.$$

(Subscript HA indicates reaction with 2,4-dinitrophenol.)

We suggest that $\Delta\Delta H^\circ$ is near zero because the solvent interactions of the alkylpiperidines and alkylpyrrolidines are very similar, and confined to the region of the nitrogen atom. We suggest that the marginally greater loss of entropy when the alkylpiperidines quaternise is because ring flexion modes occur in six-membered rings and are inhibited by quaternisation.

Effect of Ring Size.—For both $-\Delta H$ and $-\Delta S$ the order is the same, *viz.*, pyrrolidines > hexamethyleneimine > piperidine.

It is interesting that the order of pyrrolidine and piperidine is inverted relative to that of the *N*-alkyl compounds, and this inversion cannot be explained by the probable errors. It seems likely that the presence of a hydrogen atom in place of an alkyl group is responsible for the increase in entropy of pyrrolidine relative to that of piperidine. This may be because the presence of H on N is associated with a lower potential barrier to molecular inversion and consequently the removal of degeneracy from the XNY deformation mode. Of course such a situation would be more important in pyrrolidine and less important in the heavier piperidine. The position of hexamethyleneimine is consistent with its having more entropy to lose on quaternisation than piperidine because it has a larger number of ring flexion modes which will be lost when the nitrogen atom goes from the ternary to the more rigid quaternary orbital structure.

Ring Rotation.—The ring in cyclohexylamine is free to rotate, and a simple statistical mechanical calculation predicts about 7 cal. deg.$^{-1}$ mole^{-1} for its entropy. On quaternisation with 2,4-dinitrophenol the bond angles of the nitrogen become much more resistant to deformation and this, together with the presence of the nitrophenol residue, may lead to loss of entropy of ring rotation. Such an effect will lead to abnormally high entropy losses ($-\Delta S$) for the reaction, and one may expect as much as 7 cal. deg.$^{-1}$ mole^{-1} per ring. However, in tricyclohexylamine, models show that the rings are not able to rotate because of steric hindrance, and we can deduce therefore that the maximum entropy effect to be derived from inhibition of ring rotation in the cyclohexylamines cannot be much greater than 7 cal. deg.$^{-1}$ mole^{-1} and will be the greatest for the reaction of mono- or possibly di-cyclohexylamine. The effect can clearly be seen in the following respective values of $-\Delta S^\circ_{298}$: 27·8 ± 0·4,* 27·5 ± 0·9,† 17·6 ± 0·5 where the very high values for the first two amines are ascribed to this effect.

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* Value obtained in this work agrees with a previously unpublished result of A. Chetwyn.

† Obtained by A. Chetwyn and not previously published. The complete result is: $-\Delta G^\circ_{298} = 6{\cdot}27 \pm 0{\cdot}13$, $-\Delta H^\circ_{298} = 14{\cdot}5 \pm 0{\cdot}2$, $-\Delta S^\circ_{298} = 27{\cdot}5 \pm 0{\cdot}9$.