Aggregation of 4-Substituted Pyridine *N*-Oxide–Trifluoroacetates in Benzene

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The practical molal osmotic coefficients and molal activity coefficients of 4-chloro-, 4-methyl-, 4-phenoxy-, and 4-methoxy-pyridine *N*-oxide complexes with trifluoroacetic acid in benzene solutions over the concentration range 0.03—0.6 mol kg^{-1} were determined by vapour pressure osmometry. The non-ideal behaviour of the investigated systems is interpreted on the basis of two association models and the association constants are derived. The logarithms of these constants are linearly correlated with the square of the dipole moments of free *N*-oxides as expected from theory. For 4-methoxypyridine *N*-oxide trifluoroacetate the value of $\Delta H°$ obtained is −12.4 kJ mol^{-1}. These results are discussed in terms of the structure of aggregates.

THE non-ideal behaviour of complexes of pyridine and quinoline *N*-oxides with carboxylic acids is known.[1-3] Due to the relatively high dipole moments of *N*-oxides [4] and their complexes,[5] and the low permittivity of the solvents, interactions between solute molecules are dominant, while those between solute and solvent molecules are considerably lower. With increasing concentration, the monomeric complexes aggregate to quadrupoles or even to higher oligomers, while at the highest dilution the hydrogen bonds can be broken.[6,7] The extent and degree of association depend on the size and shape of the solute molecules,[7-9] and additionally on the nature of the solvent.[10] In the present paper, the non-ideal behaviour of complexes of four 4-substituted pyridine *N*-oxides with trifluoroacetic acid in benzene solution has been studied by vapour pressure osmometry (v.p.o.) and semi-ideal models applied to discuss the association process. The aim of this work has been to elucidate the effects of ΔpK_a on the association process in an aprotic solvent of low permittivity.

EXPERIMENTAL

Complexes were prepared as previously.[11] Benzene and benzil were purified and dried as in ref. 3. Osmometric concentration were determined with a Knauer vapour pressure osmometer in benzene calibrated with benzil at 27, 35, 40, 45, and 55 °C (for details see ref. 3).

RESULTS AND DISCUSSION

The principles of osmometric measurements of vapour pressure lowering and the practical application of the method have been reported in the literature.[12-18] When a non-volatile solute is dissolved in a solvent, the vapour pressure of the solvent is lowered. The temperature difference is determined by matched thermistors and is measured by the imbalance V in the Wheatstone bridge reading between the solvent on both thermistors and the solvent on one and the solution on the other. It can be shown that the V values depend linearly on the osmotic concentrations ($\phi \cdot m$) of the solute, so that the relation (1) is valid if no dissociation of the solute in the solvent occurs. In equation (1) V is the measured imbalance (μV), k is the calibration constant dependent on temperature, type of solvent, and instrument, ϕ is the practical molal osmotic coefficient, p and p_0 are the partial pressures of the solvent over the solution and the pure solvent, respectively, a_1 is the thermodynamic activity of the solvent, M_1 is the molecular weight of the solvent, and m is the stoicheiometric (analytical) solute concentration (in mol kg^{-1}). The value of k can be obtained by the use of ' standard solutes ' which form ideal binary solutions with the solvent.

$$10^3 V/kM_1 = 10^{-3}\phi \cdot mM_1 = -\ln a_1 = -\ln(p/p_0) \qquad (1)$$

The practical molal osmotic coefficients of the investigated complexes, calculated from equation (1), were fitted into a polynomial of the form (2) where A_i is constant, and q is the degree of the orthogonal polynomial. The constants A_i were obtained by a least-squares method so as to give minimum values of equation (3) where n is the number of experimental points, and W_i is the statistics weight of the ith point. The degree of polynomial ϕ_{calc} which approximates satisfactorily the n experimental points, has been determined from the condition (4).[19]

$$\phi_{\text{calc}} = 1 + \sum_{i=1}^{q} A_i m^i \qquad (2)$$

$$S_q = \sum_{i=1}^{n} W_i(\phi_{\text{exp}} - \phi_{\text{calc}})^2 \qquad (3)$$

$$\frac{S_q}{n-1} < \frac{S_q + 1}{n-q-1} \qquad (4)$$

The polynomial ϕ_{calc} of the lowest degree q which fulfils conditions (4) has been chosen for further analysis. The coefficients A_i and standard error S_q of the estimate are given in Table 1.

The molal activity coefficients of the solute investigated, γ_2, were calculated using Bjerrum's relation (5) in the forms (6) or (6a) which were obtained from

$$\ln\gamma_2 = (\phi - 1) + \int_0^{m'} \frac{\phi - 1}{m}\,dm \qquad (5)$$

$$\ln\gamma_2 = \sum_{i=1}^{q} \frac{i+1}{i} A_i m^i \qquad (6)$$

equation (5) after integration between the limits of $m' = 0$ and m' taking into account equation (2).

$$\log \gamma_2 = 0.43429 \sum_{i=1}^{q} \frac{i+1}{i} A_i m^i \qquad (6a)$$

The values of ϕ and γ_2 obtained (Table 1 and Figure 1) are far below the ideal value of one. This indicates that in benzene solution strong self-association of the complexes takes place. Deviation from ideal solution behaviour increases with increasing ΔpK_a values (Figure 1), but decreases with increasing size of the substituent (*e.g.* PhO) and temperature. The influence of steric effect on aggregation was also noted in case of complexes of triphenylarsine oxide and triphenylphosphine oxide.[7] The above sequence of ' nonideality ' also reflects the probable strength of dipole–dipole association of the complexes.

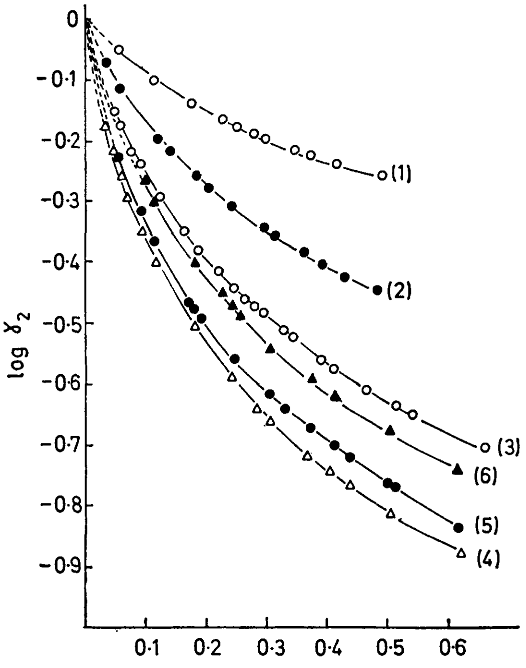

FIGURE 1 Concentration dependence of log γ_2 for the complexes of 4-R-pyridine *N*-oxides with trifluoroacetic acid in benzene: (1) R = Cl (27 °C); (2) R = PhO (27 °C); (3) R = Me (27 °C); (4) R = MeO (27 °C); (5) R = MeO (40 °C); (6) R = MeO (55 °C)

The experimental values of $\phi \cdot m$ and m are the quantities which are utilized to obtain equilibrium constants for aggregations. Assuming that differences between $\phi \cdot m$ and m must be considered to arise solely from molecular aggregation, we consider two models. In model I, the monomer and one other polymeric species of degree of aggregation n are assumed to be in equilibrium in the system [20] $nA_i \xrightleftharpoons{K_n} A_n$. K_n is given by equation (7) where m_1 and m_n are the molal concentrations of monomer and polymer of order n, respectively. The stoicheiometric molal concentration may be written as (8).

$$K_n = m_n/(m_1)^n \qquad (7)$$

$$m = m_1 + n \cdot m_n = m_1 + n \cdot K_n(m_1)^n \qquad (8)$$

The concentration determined experimentally (osmotic concentration) is given by (9). By substituting equation (9) into equation (8) and rearranging, equation (10) is obtained.

$$\phi \cdot m = m_1 + m_n' = m_1 + K_n(m_1)^n \qquad (9)$$

$$K_n = \frac{(m - \phi \cdot m)(n-1)^{n-1}}{(n \cdot \phi \cdot m - m)^n} \qquad (10)$$

Model II assumes that an extended series of multimers are formed (Scheme). It has been assumed in some studies, for the purposes of simplification, that a series of equilibrium constants are equal and not dependent on n [equation (11)].[21,22] By analogy with equations (8)—(10) we may write (12)—(14).

$$K_{12} = K_{23} = \ldots K_{(n-1)n} \equiv K \qquad (11)$$

$$m = m_1 + \sum_{i=2}^{n} i \cdot K^{i-1}(m_1)^i \qquad (12)$$

$$\phi \cdot m = m_1 + \sum_{i=2}^{n} K^{i-1}(m_1)^i \qquad (13)$$

$$K = (m - \phi \cdot m)/(\phi \cdot m)^2 \qquad (14)$$

The values of the equilibrium constants are given in Table 2. A set of internally consistent equilibrium constants is obtained for 4-chloropyridine *N*-oxide complex both with model I ($n = 2$) and II. This suggests that monomer and dimer are the main species which exist in solution. For other complexes, internally consistent equilibrium constants are obtained only with model II. The stepwise association constants increase

TABLE 1

Values of regression coefficients A_i, of equation (2) and standard error of estimate S_q for complexes of 4-R-pyridine *N*-oxides with trifluoroacetic acid in benzene

R	t/°C	A_1	A_2	A_3	A_4	A_5	A_6	A_7	No. of points	10^4S_q
Cl	27	−1.2227	2.9728	−4.0263	2.2711				11	0.19
Me	27	−3.9657	16.9933	−40.6970	47.6864	−21.3162			20	11.73
PhO	27	−2.5107	9.2884	−19.9370	16.7653				15	4.48
MeO	27	−7.0604	61.9644	−364.2505	1 284.1885	−2.596.4477	2 765.7077	−1 199.6709	15	2.13
	35	−6.0452	39.1403	−156.1138	348.5380	−399.7684	183.0601		11	0.85
	40	−5.8116	36.5708	−143.8248	324.4231	−382.6562	181.7581		15	0.63
	45	−4.9310	30.2988	−126.5574	306.4219	−382.6970	189.4572		12	17.06
	55	−4.1441	17.7017	−45.5830	60.9571	−32.2892			11	0.80

with increasing ΔpK_a of the complexes and the dipole moment of the base,[23] and decrease with increasing size of the substituent and with temperature.

Treiner *et al.*[24] have shown that a plot of the logarithms of the dipolar association constants (log K) against the square of dipole moments (μ^2) is linear. Since dipole moments of the investigated complexes are unknown, we have correlated log K with the square of the dipole moments of free N-oxides.* The correlation is approximately linear (Figure 2).

$$2A_1 \xrightleftharpoons{K_{12}} A_2$$
$$3A_1 \xrightleftharpoons{K_{13}} A_3$$
$$A_2 + A_1 \xrightleftharpoons{K_{23}} A_3$$
$$nA_1 \xrightleftharpoons{K_{1n}} A_n$$
$$A_{n-1} + A_1 \xrightleftharpoons{K_{n-1}} A_n$$

SCHEME

All these results taken together demonstrate that the monomeric complexes associate to form aggregates such that the pyridine rings are oriented to maximize the dipole–dipole interactions.

TABLE 2

Values of the association constants for the complexes of 4-R-pyridine N-oxides with trifluoroacetic acid in benzene

R	ΔpK_a [11]	Dipole moment of N-oxides [23] (μ/D)	t/°C	K/ kg mol^{-1}	K_2/ kg mol^{-1}
Cl	0.13	2.82	27	0.99 ± 0.13	1.59 ± 0.08
Me	1.06	4.74	27	4.37 ± 0.44	
PhO	2.44		27	2.36 ± 0.17	
MeO	1.82	5.08	27	7.93 ± 0.28	
			35	7.58 ± 0.16	
			40	6.95 ± 0.27	
			45	5.80 ± 0.14	
			55	5.39 ± 0.13	

The relative abundances of each successive aggregate can be obtained by solving the polynomials (12) and (13) with a finite number for n, neglecting those higher terms which contribute less to the values of m and $\phi \cdot m$ than the accuracy of the osmometric determination. For the investigated systems values of n up to 15 satisfy this requirement.

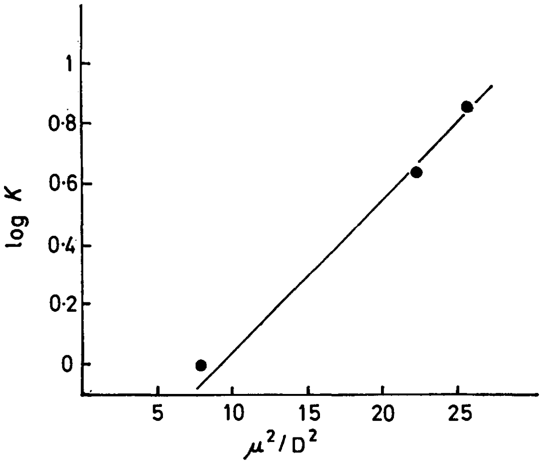

FIGURE 2 Dependence of association constants on dipole moments

Figure 3 presents the distribution of dominant aggregates of 4-methoxypyridine N-oxide–trifluoroacetate in the concentration range studied at 27 °C. The standard enthalpy $\Delta H°$ and entropy $\Delta S°$ for the stepwise aggregation were calculated from relation (15).

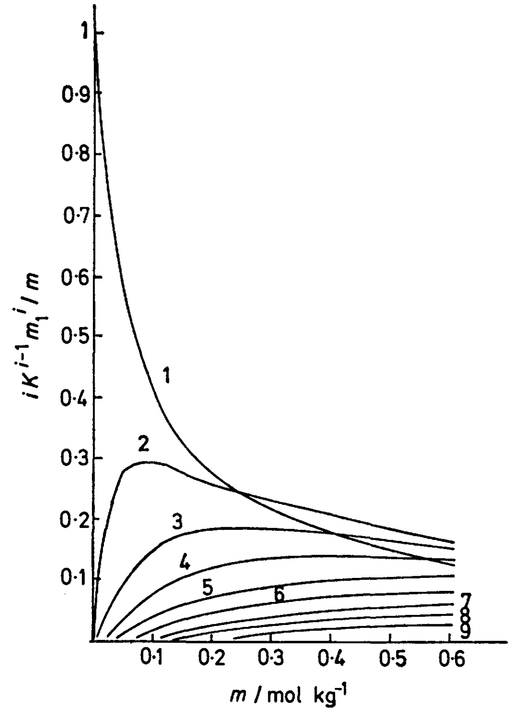

FIGURE 3 The distribution of the major associated species for the 4-methoxypyridine N-oxide–trifluoroacetic acid complex in benzene at 27 °C

$$\ln K = -\Delta H°/RT + \Delta S°/R \qquad (15)$$

For the 4-methoxypyridine N-oxide–trifluoroacetic acid–benzene system $\Delta H°$ is -12.50 ± 0.26 kJ mol^{-1} and $\Delta S°$ -24.16 ± 0.59 J mol^{-1} K^{-1}.

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* The formation of a hydrogen bond produces an excess of dipole moment, $\Delta\mu$, which is directed from B to AH and increases with hydrogen bond strength.[25] We expect that a plot of log K *versus* $(\mu + \Delta\mu)^2$ would be linear with a different slope.

REFERENCES

[1] M. Szafran, E. Grech, and Z. Dega-Szafran, *Bull. Acad. polon. Sci. Sér. Sci. chim.*, 1971, **19**, 643.

[2] Z. Dega-Szafran, E. Grech, and M. Szafran, *J.C.S. Perkin II*, 1972, 1839.

[3] Z. Dega-Szafran, M. Szafran, and J. Rychlewski, *J.C.S. Perkin II*, 1978, 536.

[4] A. R. Katritzky and J. M. Lagowski, 'Chemistry of the Heterocyclic N-Oxides,' Academic Press, London, 1971.

[5] D. Hadži, H. Ratajczak, and L. Sobczyk, *J. Chem. Soc.* (*A*), 1967, 48.

[6] M. Szafran and Z. Dega-Szafran, *Wiad. Chem.*, 1977, **31**, 1.

[7] M. Grundwald, E. Grech, and M. Szafran, *Roczniki Chem.*, 1975, **49**, 133.

[8] M. Grundwald, M. Szafran, and J. Rychlewski, *Pol. J. Chem.*, 1979, **53**, 829.

[9] B. Brycki, Z. Dega-Szafran, and M. Szafran, *Pol. J. Chem.*, 1980, **54**, 221.

[10] Z. Dega-Szafran and M. Szafran, *J. Mol. Structure*, 1978, **45**, 33.

[11] B. Brycki, Z. Dega-Szafran, and M. Szafran, *Adv. Relax. Interact. Processes*, 1979, **15**, 71.

[12] A. P. Brady, H. Huff, and J. W. McBain, *J. Phys. Colloid. Chem.*, 1951, **55**, 304.

[13] R. H. Müller and H. J. Stolten, *Analyt. Chem.*, 1953, **7**, 1103.

[14] W. I. Higuchi, M. A. Schwartz, E. G. Rippie, and T. Higuchi, *J. Phys. Chem.*, 1954, **63**, 996.

[15] N. E. White and M. Kilpatrick, *J. Phys. Chem.*, 1955, **59**, 1044.

[16] L. H. Scroggins and C. L. Ogg, *J. Assoc. Official Analyt. Chem.*, 1968, **51**, 992.

[17] A. S. Kertes and G. Markovits, *J. Phys. Chem.*, 1968, **72**, 4202.

[18] Operating and Service Manual, Model 302 B, Vapour Pressure Osmometer, Hewlett-Packard, 1968.

[19] A. Ralston, 'A First Course in Numerical Analysis,' PWN, Warszawa, 1975, pp. 246—255.

[20] H. Kim, R. C. Deonier, and J. W. Williams, *Chem. Rev.*, 1977, **77**, 659.

[21] J. C. Davis, jun., and K. K. Deb, in 'Advances in Magnetic Resonance,' ed. J. S. Waugh, Academic Press, London, 1970, vol. 4, p. 201.

[22] E. H. Schrier, *J. Chem. Educ.*, 1968, **45**, 176.

[23] A. R. Katritzky, E. W. Randall, and L. L. Sutton, *J. Chem. Soc.*, 1957, 1769.

[24] C. Treiner, J. F. Skinner, and R. M. Fuoss, *J. Phys. Chem.*, 1964, **68**, 3406.

[25] L. Sobczyk, H. Engelhardt, and K. Bunzl, in ' The Hydrogen Bond. Recent Developments in Theory and Experiments,' North-Holland Publishing Co., Amsterdam, vol. III, 1976, p. 937.