

## Kinetics and Mechanisms of Nucleophilic Displacements with Heterocycles as Leaving Groups. Part 20.<sup>1</sup> Aggregation of Some Quaternary Pyridinium Salts in Chlorobenzene

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The practical molal osmotic coefficients ( $\phi$ ) and average aggregation numbers ( $\bar{n}$ ) of five pyridinium salts in chlorobenzene solution over the concentration range  $(0.5\text{--}3.2) \times 10^{-2} \text{ mol kg}^{-1}$  were determined by vapour pressure osmometry. The non-ideal behaviour of the investigated systems is interpreted in terms of the stepwise aggregation model, and the association constants are derived. For the tetrafluoroborates, the association constants increase with the planarity of the cation. For 1-benzyl-2,4,6-triphenylpyridinium and 1-benzyl-2,4-diphenyl-5,6-dihydrobenzo[*h*]quinolinium tetrafluoroborates,  $H^\circ$  values are obtained of  $-7.19$  and  $-9.44 \text{ kcal mol}^{-1}$ , respectively. The structure of the aggregates is discussed. Aggregation is negligible at concentrations  $\leq 2 \times 10^{-3} \text{ M}$ , in the range used for kinetic measurements.

The pyrylium-mediated transformation of amines into other functionality by a two-step process (Scheme) has been developed by one of our groups.<sup>2</sup> The first step of this transformation involves the reaction of the primary amine with a pyrylium salt to give the corresponding pyridinium derivative; the second step is a nucleophilic substitution reaction in which the *N*-substituent is transferred from the pyridine nitrogen atom to the nucleophile. Extensive investigations of the kinetics of such displacements reactions have led to mechanistic conclusions of considerable significance to the theory of nucleophilic displacement at saturated carbon (for a review, see ref. 3). The kinetics of the transfer of pyridinium *N*-substituents to nucleophiles have been measured in nonpolar solvents, e.g. chlorobenzene, at concentrations  $3.2 \times 10^{-5}$ – $1.6 \times 10^{-3} \text{ mol l}^{-1}$ .

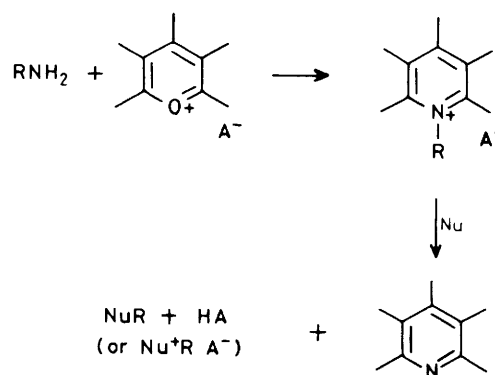
The interpretation of the kinetic data was based on the existence under these conditions of the quaternary pyridinium salts as contact ion pairs. The presence of free ions was excluded by conductivity experiments.<sup>4</sup> As the association of ion pairs ( $A^-B^+$ ) in solvents of low dielectric constant to form higher aggregates [ $(A^-B^+)_n$ ] is well documented,<sup>5,6</sup> we deemed it important to determine the extent of aggregation of some representative quaternary pyridinium salts (1)–(5) by vapour pressure osmometry.

### Experimental

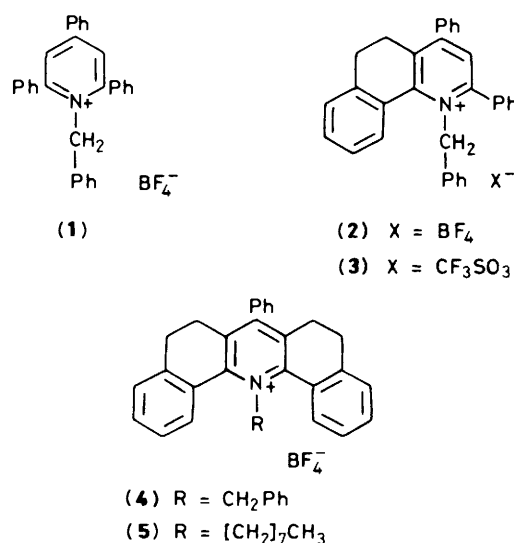
**Preparation of Compounds.**—We previously reported the synthesis and the physical properties of 1-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate (1), m.p. 196–197 °C;<sup>7</sup> 1-benzyl-2,4-diphenyl-5,6-dihydrobenzo[*h*]quinolinium tetrafluoroborate (2), m.p. 193 °C,<sup>8</sup> and trifluoromethanesulphonate (3), m.p. 133 °C,<sup>9</sup> 14-benzyl-5,6,8,9-tetrahydro-7-phenyl-dibenzo[*c,h*]acridinium tetrafluoroborate (4), m.p. 184 °C<sup>10</sup> (ref. 11, m.p. 159–160 °C); and 14-*n*-octyl-5,6,8,9-tetrahydro-7-phenyldibenzo[*c,h*]acridinium tetrafluoroborate (5), m.p. 147 °C.<sup>10</sup>

**Reagents.**—Chlorobenzene (Fluka AG) was distilled from phosphorus pentoxide and stored over molecular sieves (grade 4A). Benzil (Fluka AG) was used as a standard solute in chlorobenzene to obtain the calibration constant.

**Instrument and Measurements.**—A Knauer vapour pressure osmometer was used. The instrumental calibration procedure



Scheme.



and the method of measurement were similar to those described previously.<sup>12,13</sup> Osmotic coefficients ( $\phi$ ) were calculated from equation (1), where  $V$  is the measured imbalance ( $\mu\text{V}$ ),  $K_C$  is the

$$V/K_C = C\phi/M = m\phi \quad (1)$$

**Table 1.** Osmotic coefficients ( $\phi$ ) and equilibrium constants ( $K$ ) for 1-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate (1) and 1-benzyl-2,4-diphenyl-5,6-dihydrobenzo[*h*]quinolinium tetrafluoroborate (2) salts in chlorobenzene

Cmpd.	30 °C			40 °C			50 °C			60 °C		
	$m \times 10^2$ mol kg <sup>-1</sup>	$\phi$	$K$ kg mol <sup>-1</sup>	$m \times 10^2$ mol kg <sup>-1</sup>	$\phi$	$K$ kg mol <sup>-1</sup>	$m \times 10^2$ mol kg <sup>-1</sup>	$\phi$	$K$ kg mol <sup>-1</sup>	$m \times 10^2$ mol kg <sup>-1</sup>	$\phi$	$K$ kg mol <sup>-1</sup>
(1)	0.7426	0.834	32.11	0.4526	0.919	21.15	0.4598	0.948	15.47	0.4584	0.960	9.53
	0.9247	0.794	35.45	0.7319	0.868	23.94	0.7463	0.905	15.54	0.7204	0.913	14.58
	1.4575	0.732	34.36	0.9181	0.846	23.34	0.9284	0.885	15.72	0.9129	0.901	13.34
	1.8454	0.690	35.22	1.3516	0.803	22.61	1.3311	0.847	16.07	1.3769	0.872	12.22
	2.3399	0.671	31.22	1.8162	0.759	23.06	1.8068	0.814	15.52	1.8118	0.860	10.49
	2.7757	0.640	31.67	2.2817	0.737	21.18	2.2797	0.784	15.42	2.3018	0.847	9.23
	3.1355	0.626	30.43	2.7264	0.710	21.04	2.7524	0.760	15.12	2.7918	0.824	9.25
(2)				3.1867	0.677	22.16	3.1939	0.730	15.90	3.2564	0.790	10.32
	0.7386	0.741	63.86	0.4697	0.858	41.30	0.4438	0.921	21.08	0.4842	0.929	17.12
	0.9271	0.704	64.37	0.7182	0.815	38.66	0.7225	0.878	21.86	0.7521	0.900	16.36
	1.3962	0.631	66.55	0.8986	0.777	41.02	0.9351	0.851	21.93	0.9716	0.874	16.88
	1.8191	0.587	65.89	1.3466	0.721	39.95	1.3679	0.802	22.49	1.4286	0.853	14.10
	2.2728	0.556	63.37	1.8668	0.670	39.36	1.8000	0.798	21.79	1.8131	0.814	15.44
	2.7136	0.533	60.70	2.2232	0.640	37.52	2.2496	0.736	21.67	2.2678	0.779	16.08
			2.7346	0.621	35.98	2.8037	0.675	25.36	2.8282	0.752	15.52	

calibration constant, and  $m$  is the stoichiometric solute concentration (mol kg<sup>-1</sup>). The stepwise aggregation constant,  $K$ , was calculated from equation (2); for details see ref. 14.

$$K = [m - m\phi]/(m\phi)^2 \quad (2)$$

Measurements on compounds (1) and (2) were carried out at 30, 40, 50, and 60 °C.

### Results and Discussion

Osmotic coefficients,  $\phi$ , for the five quaternary salts (1)–(5) are given in Tables 1 and 2. As the concentration increases,  $\phi$  decreases rapidly, indicating strong association. As expected at constant concentration  $m$ ,  $\phi$  increases with temperature (Table 1).

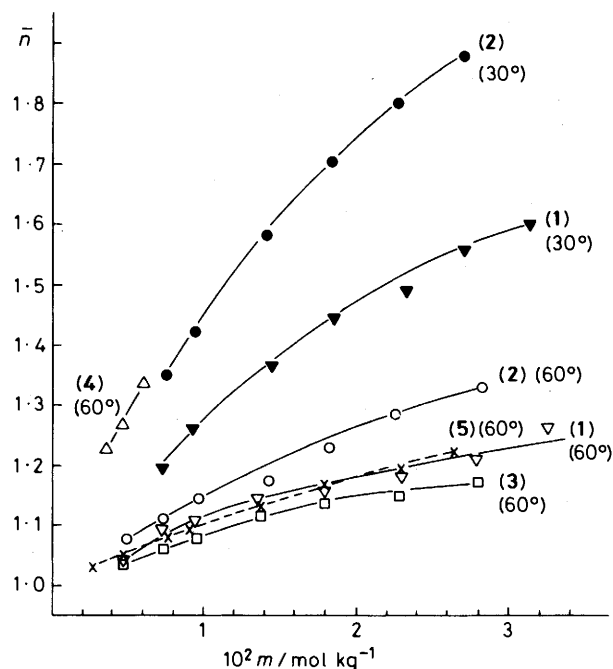
The present data were interpreted neglecting all solute–solvent interactions and assuming that all solute species behave ideally, *i.e.*, with activity coefficients of unity. The non-ideality of the binary system is thus treated in terms of the solute aggregation reactions, *i.e.*, formation of dimers, trimers, *etc.* For such an interpretation, it can be shown that  $\phi$  is directly related to the average aggregation number,  $\bar{n}$ :  $\phi = 1/\bar{n}$ .

As seen from the Figure, at the highest available concentration ( $\bar{n} = 1.88$ ) the association is significantly larger than that required for triple ions (the maximum value of  $\bar{n}$  for triple ions is 1.5), but has not proceeded much beyond the quadrupole state.

Table 3 lists the stepwise aggregation constants calculated from equation (2). The associated species could have been either non-ionic (quadrupoles or higher dipole–dipole aggregates) or ionic (*e.g.*, triple ions).<sup>5,15</sup> However, although all ionic species were neglected, a set of internally consistent equilibrium constants is obtained for all salts. This is not surprising since in chlorobenzene the dissociation constant of quaternary salts into simple ions is of the order of  $10^{-7}$ .<sup>16</sup>

The standard enthalpy  $\Delta H^\circ$  and entropy  $\Delta S^\circ$  for stepwise aggregation were calculated from equation (3). For (1)  $\Delta H^\circ = -7.19 \pm 0.02$  kcal mol<sup>-1</sup> and  $\Delta S^\circ = -16.79 \pm 0.45$  cal mol<sup>-1</sup> K<sup>-1</sup>; for (2)  $\Delta H^\circ = -9.44 \pm 0.50$  kcal mol<sup>-1</sup> and  $\Delta S^\circ = -22.91 \pm 1.59$  cal mol<sup>-1</sup> K<sup>-1</sup>.

$$\ln K = -\Delta H^\circ/RT + \Delta S^\circ/R \quad (3)$$



**Figure.** Variations of aggregation number ( $\bar{n}$ ) with molality at various temperatures

The aggregation numbers found are between 1 and 1.3 in chlorobenzene at 60 °C and are slightly lower than those for quaternary phosphonium salts ( $C_{16}H_{33}P^+Bu_3Cl^-$ ).<sup>17</sup>

Kraus<sup>5</sup> postulates that the extent of association of quaternary ammonium salts in organic solvents of low polarity is determined primarily by the size and structure of the ions and by the dipole moment of the ion pair. Horner and Gerhard<sup>18</sup> have shown that the association of quaternary ammonium salts slightly decreases with increasing bulk of the cation in the order  $Et_4N^+ > Bu_4N^+ > (C_8H_{17})_4N^+$ . The molecular weights of the salts investigated here are practically constant, but the introduction of ethylene bridges between the pyridine and phenyl rings increases rigidity and planarity. The association

**Table 2.** Osmotic coefficients ( $\phi$ ) and equilibrium constants ( $K$ ) for 1-benzyl-2,4-diphenyl-5,6-dihydrobenzo[*h*]quinolinium trifluoromethanesulphonate (3), and 14-benzyl- and 14-n-octyl-5,6,8,9-tetrahydro-7-phenyldibenzo[*c,h*]acridinium tetrafluoroborates (4) and (5)

(3)			(4)			(5)		
$m \times 10^2$ mol kg <sup>-1</sup>	$\phi$	$K$ kg mol <sup>-1</sup>	$m \times 10^2$ mol kg <sup>-1</sup>	$\phi$	$K$ kg mol <sup>-1</sup>	$m \times 10^2$ mol kg <sup>-1</sup>	$\phi$	$K$ kg mol <sup>-1</sup>
0.4549	0.962	8.92	0.3680	0.809	79.66	0.2753	0.972	10.75
0.7385	0.939	9.46	0.4592	0.789	74.06	0.4605	0.951	11.90
0.9307	0.926	9.26	0.5976	0.745	77.07	0.7276	0.927	11.60
1.3917	0.890	9.99				0.9126	0.914	11.32
1.8159	0.876	8.88				1.3606	0.880	11.42
2.2862	0.867	7.71				1.8066	0.857	10.79
2.8001	0.851	7.32				2.3159	0.838	9.97
						2.6598	0.815	10.42

**Table 3.** Values of the association constants and the associated enthalpy and entropy for the pyridinium salts in chlorobenzene

Compd.	Temp. (°C)	$K$ kg mol <sup>-1</sup>	$\Delta H^\circ$ kcal mol <sup>-1</sup>	$\Delta S^\circ$ cal mol <sup>-1</sup> K <sup>-1</sup>
(1)	30	32.92 ± 2.04		
	40	22.31 ± 1.11	-7.19 ± 0.02	-16.79 ± 0.45
	50	15.16 ± 0.28		
	60	11.12 ± 2.03		
(2)	30	64.12 ± 2.07		
	40	39.11 ± 1.90	-9.44 ± 0.50	-22.91 ± 1.59
	50	22.33 ± 1.41		
	60	15.93 ± 1.02		
(3)	60	8.79 ± 0.95		
(4)	60	76.93 ± 2.80		
(5)	60	11.02 ± 0.65		

constants appear to be related to the planarity of cations [(5),(4) > (3),(2) > (1)]. Further the change of *N*-substituent from the relatively rigid benzyl (4) to the more flexible *n*-octyl (5) lowers the association constant.

Whereas small aggregates of quaternary salts are considered to be lamellar micelles with the polar heads together and the hydrophobic groups tail to tail, with organic solvents between them,<sup>19-21</sup> aggregates of planar aromatic quaternary salts should have a different structure.

The most stable structure for an isolated molecule of *N*-methylpyridinium chloride, according to EHT calculations,<sup>22</sup> places the anion on the axis perpendicular to the ring plane. This structure is stabilized mainly by electrostatic attractions; charge transfer is negligible in the ground state. By analogy, and in view of their planarity, the salts now investigated should be associated in stacks, and the stacks should be held together primarily by electrostatic attractions. If the anions are indeed located between the stacks of rings, the effect of anion variation on aggregation could be used to test this structural proposal.

The present work shows clearly that aggregation is negligible in the concentration range (< 2 × 10<sup>-3</sup> M) used for kinetic measurements.

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