

## Salting-in Effects of Alkyl-Substituted Pyridinium Chlorides on Aromatic Compounds

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Solubilities of naphthalene and 1-naphthyl  $\beta$ -D-glucopyranoside in water and cosolute solutions were determined radiochemically and spectrophotometrically. The role of aromatic character of the solute and the cosolutes is discussed in terms of the determined Setschenow constants and the aliphatic-aromatic nature of the cosolutes, substituted pyridinium chlorides. The influence of cosolute on the structure of water is studied through its salting-in effect. The structural effects of non-electrolyte solutes are investigated by comparing the salting-in effects of naphthalene and 1-naphthyl  $\beta$ -D-glucopyranoside.

Cosolute effects, known as salting-in or salting-out phenomena, have received increasing interest recently. The study of the anomalous salting-in properties of quarternary ammonium salts bears a major responsibility for this but, in addition, the thorough and systematic elucidation of the subjects has been laid as a basis for many published papers.<sup>1–4</sup> However, the theories developed in the area do not agree satisfactorily with experiments, which can clearly be seen in a review of Schneider.<sup>5</sup> Especially the lack of a suitable theoretical background for salting-in effects is evident, the main difficulty being the understanding of the effects that large organic ions exert on the structure of the solvent, water.

The role of the solute to be salted in or out is rather ambiguous. The model compounds employed have mostly been inert molecules. Aromatic compounds like benzene and naphthalene have been widely used because of the facility of their solubility determinations. Attention has been paid to the inertness of the solute, while the aromatic character has not been considered to be of equal importance. However, the problem of the behavior of an aromatic

molecule in water is quite an interesting one. Does this molecule possess similar structure-making properties as an aliphatic long chain compound which induces the growth of waterlike structure in its neighbourhood?<sup>6</sup> In other words, is the aromatic molecule sufficiently inert in its water solution? Another question is the role of cosolute in this connection. It would be of interest to know the influence of an aromatic salting solute on the solubility of the substrate. The standard Gibbs energies of transfer of solutes from H<sub>2</sub>O to D<sub>2</sub>O which also reflect structure making and structure breaking properties give somewhat controversial information about the behavior of an aromatic molecule in water.<sup>7</sup>

In the present paper, special attention is paid to aromatic molecules as solutes and cosolutes in water through salting-in and -out phenomena. These effects are studied by measuring the solubility of naphthalene in solutions of substituted pyridinium salts. The predominance of the aromatic character is elucidated by comparing the results with those obtained with a substituted naphthalene, 1-naphthyl  $\beta$ -D-glucopyranoside. Besides the pyridinium cosolutes, KCl and *meso*-inositol were used for reference as they cause a conventional salting-off effect on the solutes.

### EXPERIMENTAL

*Reagents.* Radioactive [1-<sup>14</sup>C]naphthalene was purchased from the Radiochemical Centre and had a specific activity of 7400 MBq/mmol. The naphthalene used in the experiments was prepared by mixing the active naphthalene with an inactive naphthalene (BDH, analytical reagent) and recrystallizing the mixture from absolute ethanol. 1-Naphthyl  $\beta$ -D-glucopyranoside (*purum* quality)

was a product of Fluka AG and was used as received. The cosolutes, substituted pyridinium chlorides, were prepared from the appropriate pyridines and a standard HCl solution diluted from Merck's ampoule. The substituted pyridines were purchased from Koch-Light Laboratories Ltd. and they were distilled prior to use. Special care was taken to prevent the ionization of the pyridinium ions. This was achieved with a small excess of HCl so that the final pH value of each solution was suppressed under 3. Potassium chloride and *meso*-inositol were of reagent grade. The water employed was distilled and degassed water.

**Apparatus and procedure.** The equilibration of the samples was carried out in stoppered Sovirel tubes with a volume of approx. 10 ml. A mass of 0.2 g of [ $^{14}\text{C}$ ]naphthalene and 5 ml of water with appropriate cosolute were added to the tube. With 1-naphthyl  $\beta$ -D-glucopyranoside as substrate an approx. 5 times smaller scale was employed. The tubes were then equilibrated by periodical shaking for a week in a thermostated water bath, the temperature of which was maintained constant (298.2 K) with the aid of a Lauda thermostat. The samples were taken by a Finnpiquette through a glass wool plug. The radiochemical analyses of naphthalene were performed by counting the radioactivity of the weighed samples (0.3–0.5 g) on an LKB-Wallac 81000 liquid scintillation counter. After the quenching correction the solubilities were calculated by comparing the cpm (counts per minute) values for the samples to those obtained for standard solutions of [ $^{14}\text{C}$ ] naphthalene.<sup>7</sup>

The sizes of the samples taken for a spectrophotometrical analysis of 1-naphthyl  $\beta$ -D-glucopyranoside varied between 25–100  $\mu\text{l}$ . A standard curve, absorbance *vs.* concentration, was first constructed. To delete the absorption caused by pyridinium ions a cation exchange chromatographic technique (Dowex 50 W  $\times$  8 20/50 mesh,  $\text{H}^+$ -form) was applied by which a complete elimination of this interfering factor was achieved. The concentration of the eluate of a known volume was then calculated from the absorbance value measured at 285 nm on a Perkin Elmer 46 BCD spectrophotometer.

## RESULTS AND DISCUSSION

The solubility values measured in various cosolute solutions are reported in Table 1. The value for the solubility of naphthalene in water,  $s_0 = (2.54 \pm 0.06) \times 10^{-4} \text{ mol dm}^{-3}$  (mean value from six determinations) agrees excellently with those found in literature, the most recent value being  $(2.48 \pm 0.02) \times 10^{-4} \text{ mol dm}^{-3}$  determined separately by MacKay and Shiu<sup>8</sup> in 1977 and May *et al.*<sup>9</sup> in 1978. The radio-

chemical method of analysis thus seems quite suitable for the purpose in spite of the greater standard error observed. The advantage of the present method is its selectivity. As far as we know, the solubility of 1-naphthyl  $\beta$ -D-glucopyranoside in water has not been measured. The value of  $0.0227 \pm 0.0009 \text{ mol dm}^{-3}$  determined here seems quite reasonable from the point of view that the solubility of naphthalene can be expected to increase with the attachment of a polar, waterlike, substituent.

Salting effect for nonelectrolytes is correlated by eqn. (1) where  $c$  is the concentration of the salt

$$\log(s_0/s) = Kc \quad (1)$$

(cosolute),  $s$  the respective solubility of the nonelectrolyte, and  $K$  the so-called Setschenow constant.<sup>5</sup> The plots of  $\log(s_0/s)$  versus  $c$  are presented in Fig. 1 separately for both nonelectrolyte solutes. Because of nonlinearity of some of the curves in Fig. 1 the constants,  $K$ , are obtained by extrapolation *via* eqn. (2). The constant,  $K$ , expressed by

$$K = \lim_{c \rightarrow 0} \frac{1}{c} \log(s_0/s) \quad (2)$$

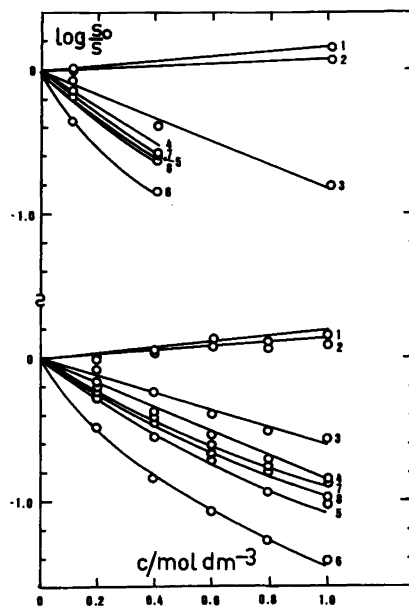


Fig. 1. Plots of  $\log(s/s_0)$  against the concentrations of cosolutes for naphthalene (lower curves) and 1-naphthyl  $\beta$ -D-glucopyranoside (upper curves) at 298.2 K. For the numeration of the cosolutes see Table 1.

Table 1. Solubilities of naphthalene and 1-naphthyl  $\beta$ -D-glucopyranoside in water and various solutions of cosolutes at  $T=298.2$  K.

Cosolute	Cosolute concentration $c/\text{mol dm}^{-3}$	Naphthalene solubility $s/10^{-4} \text{ mol dm}^{-3}$	1-Naphthyl $\beta$ -D-glucopyranoside solubility $s/\text{mol dm}^{-3}$
1. KCl	—	2.54(6) <sup>a</sup>	0.0227(9) <sup>a</sup>
	0.100		0.0222
	0.200	2.64	
	0.400	2.19	
	0.600	1.77	
	0.800	1.92	
2. <i>meso</i> -Inositol	1.00	1.77	0.0151
	0.100		0.0217
	0.200	2.59	
	0.400	2.16	
	0.600	2.06	
	0.800	2.14	
3. Pyridinium chloride	1.00	2.04	0.0183
	0.100		0.0267
	0.200	3.07	
	0.400	4.28	
	0.600	6.11	
	0.800	7.99	
4. 2-Methylpyridinium chloride	1.00	9.15	0.139
	0.100		0.0306
	0.200	3.70	
	0.400	6.01	
	0.600	8.65	
	0.800	12.8	
5. 2,6-Dimethylpyridinium chloride	1.00	17.6	0.0850
	0.100		0.0339
	0.200	4.87	
	0.400	9.08	
	0.600	12.8	
	0.800	22.0	
6. 2,4,6-Tri-methylpyridinium chloride	1.00	28.7	0.0833
	0.100		0.0511
	0.200	7.53	
	0.400	17.2	
	0.600	30.3	
	0.800	47.6	
7. 2-Ethylpyridinium chloride	1.00	68.3	0.197
	0.100		0.0314
	0.200	4.16	
	0.400	6.52	
	0.600	9.99	
	0.800	14.6	
8. 2-Methoxy-pyridinium chloride	1.00	18.2	0.0861
	0.100		0.0306
	0.200	4.41	
	0.400	7.13	
	0.600	11.2	
	0.800	15.4	
	1.00	21.6	0.0933

<sup>a</sup> Mean values from six determinations.

Table 2. Observed Setschenow constants for various cosolutes.

Cosolute	Naphthalene $K/\text{dm}^3 \text{mol}^{-1}$	1-Naphthyl $\beta$ -D- glucopyranoside $K/\text{dm}^3 \text{mol}^{-1}$
1. KCl	0.20(7)	0.17
2. <i>meso</i> -Inositol	0.11(5)	0.10
3. Pyridinium chloride	-0.61(6)	-0.82
4. 2-Methylpyridinium chloride	-0.84(4)	-1.2
5. 2,6-Dimethylpyridinium chloride	-1.52(6) <sup>a</sup>	-1.9 <sup>a</sup>
6. 2,4,6-Trimethylpyridinium chloride	-2.56(5)	-3.4 <sup>a</sup>
7. 2-Ethylpyridinium chloride	-1.13(2) <sup>a</sup>	-1.5 <sup>a</sup>
8. 2-Methoxy-pyridinium chloride	-1.30(9) <sup>a</sup>	-1.8 <sup>a</sup>

<sup>a</sup> Extrapolated to cosolute concentration  $c=0$  owing to the non-linearity of the plots.

eqn. (2) is proportional to the free energy of transfer of the nonelectrolyte from water to a hypothetical ideal cosolute solution of unit concentration. The determined Setschenow constants are presented in Table 2. As expected, the pyridinium salts exhibit negative constants, *i.e.*, exert a salting-in effect on both naphthalene and 1-naphthyl  $\beta$ -D-glucopyranoside. Salting-out is observed both in KCl and *meso*-inositol solutions. The Setschenow constant for KCl–naphthalene system,  $0.20 \pm 0.07 \text{ dm}^3 \text{ mol}^{-1}$ , agrees well with those reported earlier, *viz.*  $0.204^{10}$  and  $0.186^{11}$  although the accuracy of the radiochemical method has its minimum in this case when the solubility of the substrate is decreased.

The salting-out behavior of naphthalene with increasing KCl concentration is expected and has

also been interpreted theoretically.<sup>12</sup> Salting-out by *meso*-inositol is not a surprising phenomenon either. The effect of *meso*-inositol like other polyols on the structure of water is relatively weak. This kind of solute is accommodated without difficulty in the waterlike structure. The resulting effect is therefore small although characteristic for a polar compound.

Pyridinium salts, on the contrary, affect more profoundly the solution structure, as we see from the observed salting-in effects. These effects are even stronger than those of the tetraalkylammonium cosolutes.<sup>1,2</sup> It is known that the aliphatic character plays a central role in the large organic ions causing salting-in of nonelectrolytes.<sup>1</sup> This is because the aliphatic character clearly has a stabilizing effect on the structure of water solutions. It is somewhat surprising that an aromatic ion, like pyridinium ion, seems to have a similar effect. Fig. 2 clearly indicates that the magnitude of salting-in increases with the increasing aliphatic–aromatic ratio of pyridinium cosolutes. The aliphatic–aromatic ratio is here expressed simply in terms of the ratio of the numbers of aliphatic and aromatic hydrogen atoms in the molecules of cosolutes. In this manner, a good linear correlation is obtained, with the exception of 2-methoxy-pyridinium ion. To explain the latter, further investigations with oxygen containing cosolutes would be required. The salting-in effect caused by large organic ions has sometimes been explained by a formation of an addition complex which finally leads to a micelle formation.<sup>1</sup> The solute in question resides inside this micelle. This explanation seems reasonable when the cosolutes with carbon chains long enough are concerned. The pyridinium ions considered in this work

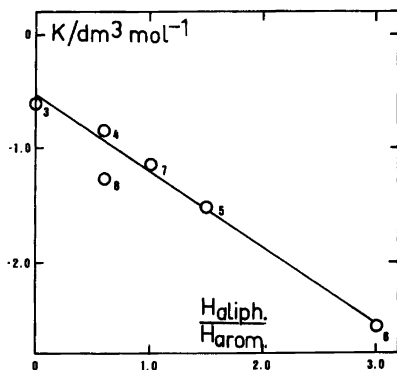


Fig. 2. The Setschenow constants,  $K$ , for naphthalene in various solutions of substituted pyridinium chlorides plotted against the aliphatic–aromatic ratios,  $H_{\text{aliph.}}/H_{\text{arom.}}$ , of the cosolutes. For the numeration of the cosolutes see Table 1.

have no long chained substituents so that the above approach seems improbable. On the other hand, there may be a considerable interaction between the  $\pi$ -electrons of the aromatic ring of the solute and the electron-deficient pyridinium ring. The possible formation of charge transfer complexes cannot be excluded under these circumstances. Some observations can be explained by this phenomenon. For instance, the salting-in effect of tetraalkylammonium ions is greater on naphthalene than on benzene.<sup>1,2</sup> This can be understood on the basis of the larger  $\pi$ -electron system of naphthalene which brings about stronger interactions with cosolutes.

The existence of relationships between the salting-in power of a cosolute and the capacity of the cosolute molecule to accommodate in the structure of water is seen when the Setschenow constants and the standard Gibbs energies of transfer from  $H_2O$  to  $D_2O$  for the respective pyridines are examined. As shown in Fig. 3 two lines can be drawn. One represents the effect of chain lengthening in the position 2 of the pyridinium ion, the other the effect of the number of methyl groups in the pyridinium ion. It seems that the latter property has considerably greater influence on salting-in than has the lengthening of the carbon chain.

To investigate the effect of a polar group attached to naphthalene on the salting-in behavior of the parent compound, corresponding measurements were made with 1-naphthyl  $\beta$ -D-glucopyranoside. It was somewhat surprising that the salting-in

effect occurred in this case even to a greater extent than in naphthalene. Roseman and Jencks have also measured a salting-in effect on uric acid greater than on naphthalene when cosolutes of similar types as in the present work were used.<sup>3</sup> The differences between salting-in behaviors of naphthalene and its derivative are, however, relatively small. The assumption that the aromatic character of the solute-substrate plays a central role in their solutions is perhaps not too tentative. The very recent data of Fromon and Treiner also support this conclusion.<sup>13</sup> In their study the salting-in effect by alkylammonium ions on benzene compared to that on tetrahydrofuran is much stronger (for instance,  $Bu_4NBr$  causes for benzene  $K = -0.60 \text{ dm}^3 \text{ mol}^{-1}$  and for THF  $K = -0.10 \text{ dm}^3 \text{ mol}^{-1}$ ).

The salting-in effects on naphthalene have been observed by Masterton *et al.* with salts containing the *trans*- $[Co(en)_2NCS \text{ Cl}]^+$  cation.<sup>14</sup> Of the theories developed for salting-in and -out effects they demonstrated the approach of McDevit and Long<sup>15</sup> to be too inadequate to explain the results. In this expression the Setschenow constant is proportional to the partial molal volume of the solute and to the amount of electrostriction of the solvent by the salt (cosolute). The temperature and the compressibility of water are also taken into account. The electrostatic approach of Bockris<sup>12</sup> which involves van der Waals forces, thus paying more attention to the instantaneous dipole moments of atoms in the solute molecule, gave a better explanation for the experimental results. Accordingly, the dispersion forces seem to play a considerable role in salting-in by complex ion electrolytes.

It would be interesting to test the existing theoretical approaches also within the context of the present work which has a certain resemblance with that of Masterton *et al.* Difficulties are, however, encountered because no data on pyridinium salts are available for molar volumes in liquid state, polarizabilities *etc.* Therefore, tests for approaches arising from other starting points must be carried out.

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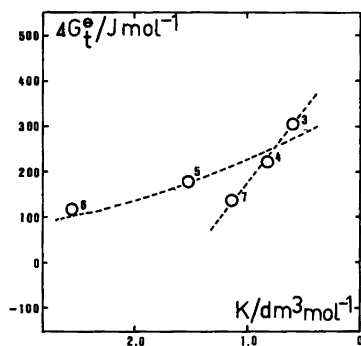


Fig. 3. The standard Gibbs energy of transfer of substituted pyridines from  $H_2O$  to  $D_2O$  plotted against the Setschenow constants obtained for naphthalene in solutions of the respective pyridinium chlorides. For the numeration of the cosolutes see Table 1.

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