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Selective Solubilization of Isomers in Hydrotrope Solutions: *o-/p*-Chlorobenzoic Acids and *o-/p*-Nitroanilines

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Selective Solubilization of Isomers in Hydrotrope Solutions: *o-/p*-Chlorobenzoic Acids and *o-/p*-Nitroanilines

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ABSTRACT

Selective solubilization of *o*-/*p*-chlorobenzoic acids and *o*-/*p*-nitroanilines has been attempted using aqueous solutions of sodium butyl monoglycol sulfate as the hydrotrope. An association model is proposed to fit the solubility data of these isomers and to characterize the hydrotrope–hydrotrope and hydrotrope–solute interactions. The solubility of an *o*-isomer in the aqueous hydrotrope solutions is higher than the solubility of the corresponding *p*-isomer, and thus the *o*-isomer can be selectively solubilized. The solubility of nitroanilines remains unaffected in the presence of the other isomer while chlorobenzoic acids modify the solubility of each other. Thus the separation is affected by the composition of the mixture as well as by the concentration of the hydrotrope. The solubilized material can be recovered by dilution with water.

Key Words. Hydrotropy; Hydrotropes; Sodium butyl monoglycol sulfate; *o*-/*p*-Chlorobenzoic acids; *o*-/*p*-Nitroanilines; Selective solubilization; Association model

INTRODUCTION

"Hydrotropism" is a word coined by Neuberg (1) in 1916 to describe the large increase in the solubility of a variety of sparingly water-soluble organic compounds in the aqueous phase in the presence of certain organic salts.

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These salts, which are themselves highly water-soluble, are termed "hydrotropes" and conventionally include alkali and alkaline earth metal salts of short-chain alkylbenzenesulfonic acids and alkylbenzene carboxylic acids. The phenomenon of hydrotropy is operative in the high concentration range of the hydrotrope, and a minimum hydrotrope concentration (MHC) is usually required to exhibit the increase in solubility (2). The solubility of a solute is usually correlated with the concentration of the hydrotrope using the following equation:

$$\ln(S/S_W) = k_s C_s \quad (1)$$

where S and S_w are solubilities in hydrotrope solution of concentration C_s and in water, respectively; k_s is the salting coefficient, a characteristic of the solute–solvent system.

Hydrotropes have been extensively used in detergent formulations and drug solubilization. The recent interest in hydrotropy has its origin in the development of several new applications of hydrotropes ranging from providing a safe aqueous medium for conducting organic reactions (sometimes with a catalytic effect) to separation of close boiling point isomeric and nonisomeric mixtures using liquid–liquid extraction, extractive distillation, and selective solubilization (3–10).

Understanding hydrotropic mechanisms therefore becomes important since we have found an enhancement of rates of a number of heterogeneous reactions such as alkaline hydrolysis of esters (4, 5), Cannizarro and cross-Cannizarro reactions (11), Hantzsch pyridine synthesis (12), etc. by several times. Hydrotropes are capable of increasing the solubility of sparingly soluble substances by 2 to 3 orders of magnitude and thereby increase the rates of the corresponding reactions. The other remarkable feature of hydrotropic solubilization is the selectivity in solubilization, even for isomers. We have earlier reported various separation techniques using hydrotropes (13). The use of hydrotropes in these applications is particularly attractive because of various factors such as easy recovery of products and high selectivity. As the hydrotropy is operative only at a high concentration of the hydrotrope, simple dilution of the solution precipitates the solute. The hydrotrope solution can then be recycled after any necessary concentration step.

The earlier impression of hydrotropy was of a phenomenon analogous to the salting-in process because of the strong electrolyte nature of the hydrotropes or even as a complex formation between the solubilizate and the hydrotrope (3, 14). However, in recent years we have demonstrated the aggregation behavior of common hydrotropes by several techniques (2). The possibility of a stack-type association of hydrotrope molecules was recognized by Saleh and his coworkers (15, 16), and the presence of an aromatic

ring was considered to be essential for the formation of such stacks. In a previous paper, however, we showed that *a short chain amphiphilic molecule*, such as sodium butyl monoglycol sulfate (Na-BMGS), without an aromatic ring, can also show a remarkable hydrotropic character (2). Most hydrotropes have a distinct amphiphilic structure and do show a mild aggregation behavior by forming aggregates which are reminiscent of surfactant micelles although the cooperativity is far lower than that of surfactants. It also appears that the formation of such aggregates is a prerequisite for the hydrotropic effect. The microenvironmental features of hydrotrope aggregates, such as polarity and microviscosity, are similar to those of micelles (2). However, hydrotropic solubilization differs from micellar solubilization in several aspects. The amount of solubilization is far higher than that for micellar solubilization; not all hydrophobes are dissolved by hydrotropes, thus giving high selectivity; and a very high concentration of hydrotrope, usually in the molar region, is required for solubilization.

In this paper we further explore the aggregation behavior of hydrotrope and the solubilization of industrially important isomeric mixtures of chlorobenzoic acids and nitroanilines. Since aggregation of the hydrotrope is necessary for the solubilization of a solute, an association model is proposed. The model attempts to explain the increase in the solubility of a hydrophobic solute in an aqueous solution of a hydrotrope in terms of the associations between hydrotrope–hydrotrope and hydrotrope–solute molecules.

ASSOCIATION MODEL

The tendency of aggregation of amphiphilic substances is due to short-range hydrophobic and dispersive forces between the hydrophobic parts and is opposed by the long-range electrostatic forces between the charged head groups. Perhaps the small hydrophobic part of the hydrotrope has prompted earlier work to neglect the possibility of aggregation of the hydrotrope (3, 6).

The aggregation of a hydrotrope is also driven by hydrophobic interactions and opposed by the electrostatic repulsion between the charged groups as the hydrotrope, being a strong electrolyte, has been assumed to be fully dissociated in the solution. If the formation of a micelle or an aggregate of a particular aggregation number is favored because of the hydrophobic interaction, then the following equation should represent the aggregation process:

$$nH_1 \leftrightarrow H_n$$

Such an aggregation process would show sudden changes at a critical concentration followed by a linear change in such properties as solubilization capacity with concentration.

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The macroscopic properties of hydrotrope solutions, such as surface tension, conductivity, etc., unlike surfactant solutions, do not show a break but a gradual variation with hydrotrope concentration (2). The sharp break in the case of conventional surfactants is indicative of micellar phase formation with a preference for the formation of an aggregate of a finite and well-defined aggregation number. In the absence of such a break it would be difficult to justify the preferred existence of a particular aggregate in hydrotrope solutions. In the case of hydrotropes, the shorter hydrocarbon chain would warrant stronger repulsion between the charged head groups, which also would make the aggregates somewhat open. Sodium butyl monoglycol sulfate (Na-BMGS), which is used as a hydrotrope in the present study, is a linear molecule and is more likely to form structures similar to spherical micelles than the stacks which have been suggested for aromatic hydrotropes (15). The gradual variation in different properties of hydrotrope solutions with concentration indicates hydrotrope aggregation to be a stepwise process rather than a highly cooperative process like micelle formation. The association constant for the successive addition of a hydrotrope molecule to an aggregate may, however, decrease with the aggregation number, for no aggregates of large aggregation numbers have been observed which otherwise would make hydrotrope solutions exhibit the properties of colloids. The association model can be written using the mass action law:

$$\begin{aligned} H_1 + H_1 &\overset{K_2}{\Leftrightarrow} H_2 \\ H_2 + H_1 &\overset{K_3}{\Leftrightarrow} H_3 \\ H_3 + H_1 &\overset{K_4}{\Leftrightarrow} H_4 \\ H_{n\text{-}1} + H_1 &\overset{K_n}{\Leftrightarrow} H_n \end{aligned} \tag{2}$$

The general case with individual values of K for each of the reactions is much more complex, and it is impossible to evaluate all these constants unless they are related to each other in some way. If K_2 is the dimerization constant, then the successive K's will be less than K_2 because of electrostatic repulsion between the charges on the head groups. If these K's were to be the same in the presence of mild or no electrostatic repulsion, the aggregation process of the hydrotrope would then approach the micelle formation of conventional surfactants. It is assumed that the decrease in K is related to the aggregation number (n) in the aggregate as follows:

$$K_n = K_2/n$$

where K_2 is a constant characterizing hydrotrope–hydrotrope association. Thus, at any concentration there is a polydispersity of the hydrotrope aggregates, with the lower oligomers predominantly present in the solution.

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The total concentration of the hydrotrope (C_s) and the monomer concentration (H_1) can be related by the following equations:

$$C_s = \sum_{n=1} nH_n$$
$$C_s = H_1[2\exp(K_2H_1) - 1] \quad (3)$$

The hydrotrope aggregates are presumably able to dissolve the organic solutes by trapping the solute within the aggregate. The association of the solute can be governed by specific interactions with the hydrotropic assemblies and the geometrical constraints on the final structure of the aggregate because, unlike micelles, there is no fluidlike core for the solubilization of organic solutes in hydrotrope aggregates.

If the solute itself is capable of forming aggregates, then it may take part in the association process of the hydrotrope. However, in the present studies the effect of the presence of the solute on the aggregation constant of the hydrotrope has been assumed to be insignificant.

It has been assumed that the solute associates with an *n*-mer ($n \geqslant 2$) of the hydrotrope in the following manner (Eq. 4). It is expected that the solute becomes distributed among hydrotrope aggregates of different aggregation numbers. It is assumed that hydrotrope aggregates of size H_n will have a population of different solute concentrations which is decided by the following mass action equilibria:

$$H_{n0} + S_1 \overset{K_s}{\Leftrightarrow} H_nS_1$$
$$\underline{H_nS_1} + \underline{S_1} \overset{K_{s2}}{\Leftrightarrow} \underline{H_nS_2} \quad (4)$$
$$H_nS_{(m\text{-}1)} + S_1 \overset{K_{sm}}{\Leftrightarrow} H_nS_m$$

Thus an *n*-mer can have a polydispersity of the dissolved solute at equilibrium. The above equations can be related to the hydrotrope–solute interaction parameter (K_{sm}) as follows:

$$H_nS_m = K_{sm}[H_nS_{m-1}]S_1 \quad (5)$$

If K_{sm} increases with the solute concentration (m) in an *n*-mer, then the solubility can be significant and may lead to a completely homogeneous system. A solute molecule which is likely to reside between the hydrotrope molecules can reduce the electrostatic repulsion between the charged groups of hydrotrope molecules, thus effectively tightening the aggregate structure and providing an additional geometrical constraint to the incorporation of additional solute molecules into the same aggregate. Usually the solubility curve shows a plateau in solubility at the higher extreme of the hydrotrope concentration (2). It is thus assumed that K_{sm} decreases with m in a manner similar to the hydrotrope aggregation, i.e., $K_{sm} = K_s/m$, where K_s is the association con-

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stant for an empty *n*-mer with the first solute molecule. It is also assumed that the solute's preference for a hydrotrope aggregate is not affected by the size of the aggregate. K_s is expected to characterize the hydrotrope–solute interaction.

The amount of solute associated with an *n*-mer, therefore, is

$$\begin{aligned} S_n &= [H_nS_1] + 2[H_nS_2] + 3[H_nS_3] + \cdots \\ S_n &= [H_{n0}]K_s[S_1]\exp(K_s[S_1]) \end{aligned} \tag{6}$$

where S_1 is the concentration of free solute in the aqueous phase and $[H_{n0}]$ is the concentration of *n*-mer without any solute at the equilibrium conditions and subjected to the condition

$$\begin{aligned} H_n &= H_{n0} + \sum_m H_nS_m \\ &= H_{n0}\exp(K_s[S_1]) \end{aligned} \tag{7}$$

Thus the concentration of solute associated with the *n*-mer will be

$$S_n = K_s[S_1][H_n] \tag{8}$$

The total amount of the solute associated with the hydrotrope aggregates will be

$$\begin{aligned} S_T &= \sum_{n=2}^{\infty} S_n \\ &= 2\left(\frac{K_s}{K_2}\right)[S_1][\exp(K_2H_1) - (1 + K_2H_1)] \end{aligned} \tag{9}$$

Equation (9) is somewhat more complex than the usual exponential equation (Eq. 1) used to represent the solubility of a solute in the hydrotrope solution. However, the constants involved do characterize the hydrotrope–hydrotrope and solute–hydrotrope interactions while explicitly accounting for the aggregation behavior of the hydrotrope.

The amount of solute associated with the hydrotrope (Eq. 9) can be related to the total concentration of the hydrotrope (Eq. 3), which is a measurable quantity. These two equations can be used to estimate the values of the interaction parameters K_s and K_2 from the solubility data. They characterize the hydrotrope–hydrotrope and hydrotrope–solute interactions, respectively.

We have selected mixtures of *o*-/*p*-chlorobenzoic acids and *o*-/*p*-nitroanilines for study because of their industrial importance. We reported earlier the solubility of chlorobenzoic acids in aqueous solutions of Na-BMGS where the *o*-chlorobenzoic acid shows a much higher solubility than the *p*-chlorobenzoic acid (17). These acids are synthesized by oxidation of the respective isomers of chlorotoluenes. The separation of chlorotoluenes by distillation is a difficult task owing to their close boiling points. Oxidation of the mixture followed

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by separation of the acids seems to be a better alternative. A mixture of these acids can also be separated by exploiting the differences in their dissociation constants (18).

o-/*p*-Nitroanilines are used primarily in the dye industry and are synthesized by ammonolysis of the corresponding isomers of nitrochlorobenzenes. Nitration of chlorobenzenes using a mixed acid gives a mixture of the *o*-/*p*-/*m*-nitrochlorobenzenes which are separated by fractional crystallization and distillation. Ammonolysis of the *o*-/*p*-nitrochlorobenzenes gives a mixture of the nitroanilines which should be amenable to separation by different techniques, particularly by exploiting the difference in their basic strengths or solubilities in organic solvents. For example, Jagirdar and Sharma (19) separated this mixture using the dissociation extraction process with HCl solution as well as HCl gas where the *p*-isomer reacted preferentially. The use of such reactive techniques for *p*-nitroaniline-rich mixtures results in a considerable loss of *o*-nitroaniline. Also, in a mixture rich in *p*-isomer, the removal of the *o*-isomer impurity is more important (19). As reported earlier, hydrotropes can distinguish between *o*-/*p*-isomers. Also, there is a greater enhancement in the solubility of the *o*-isomer than that of the *p*-isomer in the presence of the hydrotrope. Hence, an attempt was made to separate these isomers by selective solubilization of the *o*-isomer where the loss of *p*-isomer can also be reduced.

MATERIALS AND EXPERIMENTAL METHODS

Sodium butyl monoglycol sulfate (Na-BMGS) (manufactured by Huls, Germany, and marketed as a 50% wt/wt solution) was used as the hydrotrope. The solubilities of *o*- and *p*-nitroanilines were measured at temperatures of 303, 313, and 323 K. For each solubility test about 5 g of the solid was stirred in a fully baffled reactor in the hydrotrope solution of known concentration for 2 hours to ensure equilibrium. The reactor assembly was thermostated with an accuracy of ± 1 K. The solution was filtered and the concentration of the solute in the solutions was obtained spectrophotometrically at their respective λ_{max} (224 nm for *o*-nitroaniline and 227 nm for *p*-nitroaniline). For individual anilines the hydrotrope solution was diluted to a sufficient extent that the absorbance was in the 0.2–0.8 range. The solubility measurements of chlorobenzoic acids were reported earlier by us (17).

From the individual solubility studies it was observed that at any hydrotrope concentration and temperature, the solubility of the *o*-isomer was higher than that of the *p*-isomer. Hence, separation of the isomeric mixtures was conducted by using hydrotrope solutions in a volume just sufficient to dissolve the *o*-isomer with the intention of obtaining pure *p*-isomer in the solid phase. For each separation experiment the mixture of the isomers and the hydrotrope solution was stirred in a fully baffled vessel for 3 hours. After this period the sus-

pension was filtered. The solid residue obtained after filtration was washed with cold water. Because of the very low solubilities of nitroanilines and chlorobenzoic acids in pure water, the loss of any material by solubilization during this washing stage is negligible and thus the washwater was discarded. The residue was analyzed for its composition by high performance liquid chromatography using RP-C_{18} as the stationary phase and MeOH-water as the mobile phase.

RESULTS AND DISCUSSION

The solubilities of *o*-/*p*-nitroanilines (*o*-NA and *p*-NA) in water are 9×10^{-2} and 6×10^{-2} mol/L, respectively, while those of *o*-/*p*-chlorobenzoic acids (*o*-CBA and *p*-CBA) are 1.35×10^{-2} and 0.51×10^{-3} mol/L, respectively. The solubility of both isomer pairs increases with the concentration of the hydrotrope and with temperature. Figures 1 to 3 show the solubility of *o*- and *p*-nitroanilines in Na-BMGS solutions at three different temperatures (303, 313, 323 K). Figures 4 to 6 show the solubility values of *o*- and *p*-

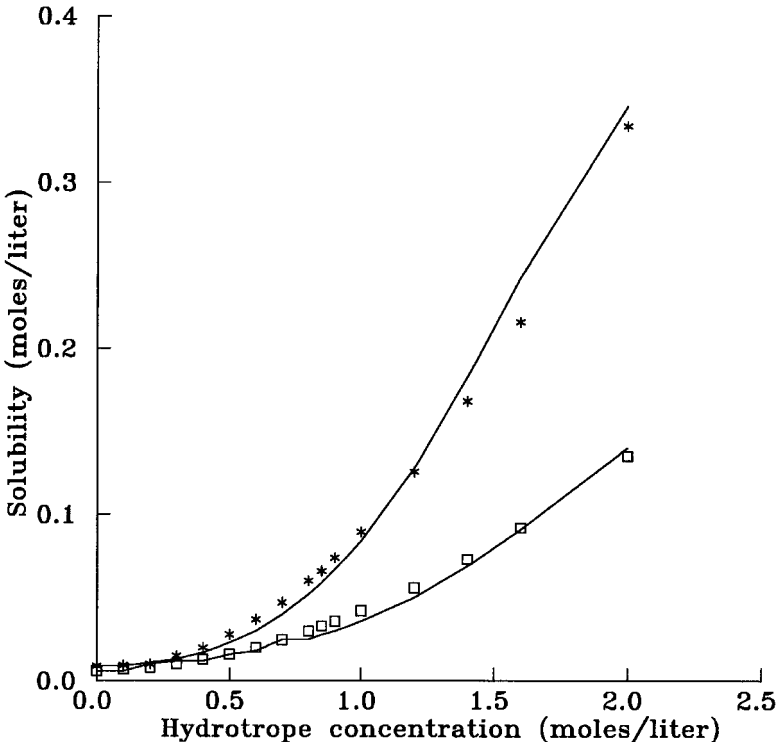

FIG. 1 Solubility of *o*-nitroaniline (∗) and *p*-nitroaniline (□) in aqueous solutions of Na-BMGS at 303 K.

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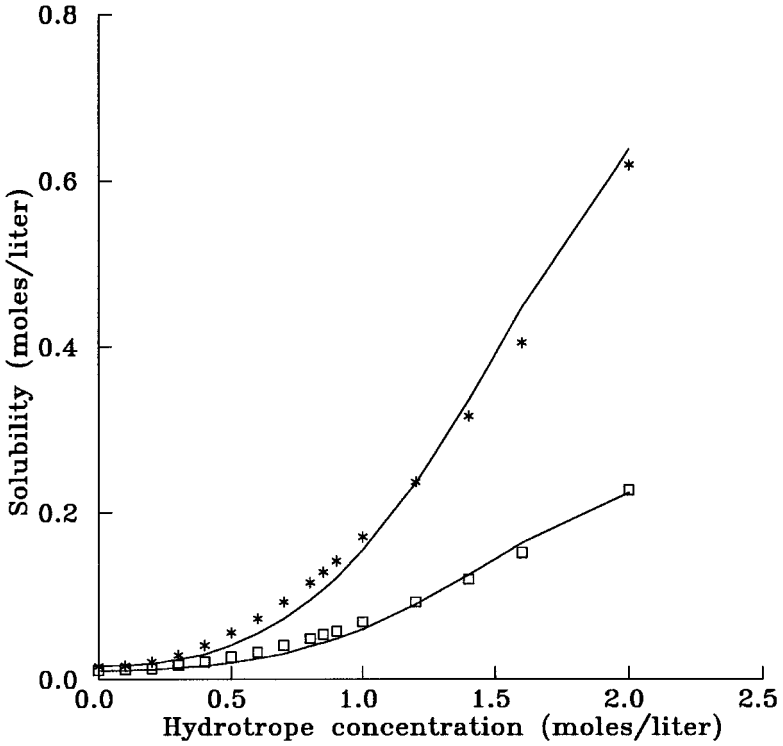

FIG. 2 Solubility of *o*-nitroaniline (∗) and *p*-nitroaniline (□) in aqueous solutions of Na-BMGS at 313 K.

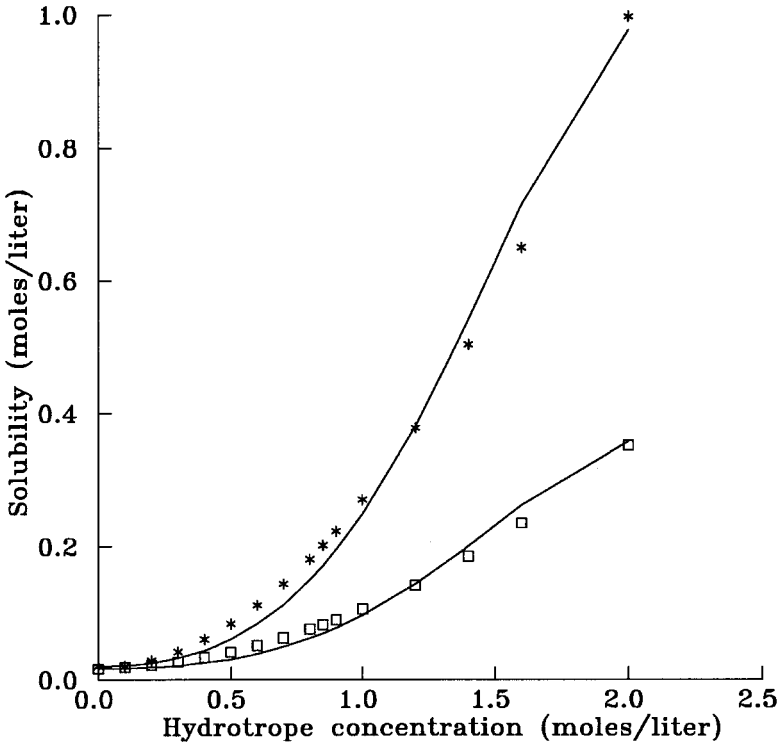

FIG. 3 Solubility of *o*-nitroaniline (∗) and *p*-nitroaniline (□) in aqueous solutions of Na-BMGS at 323 K.

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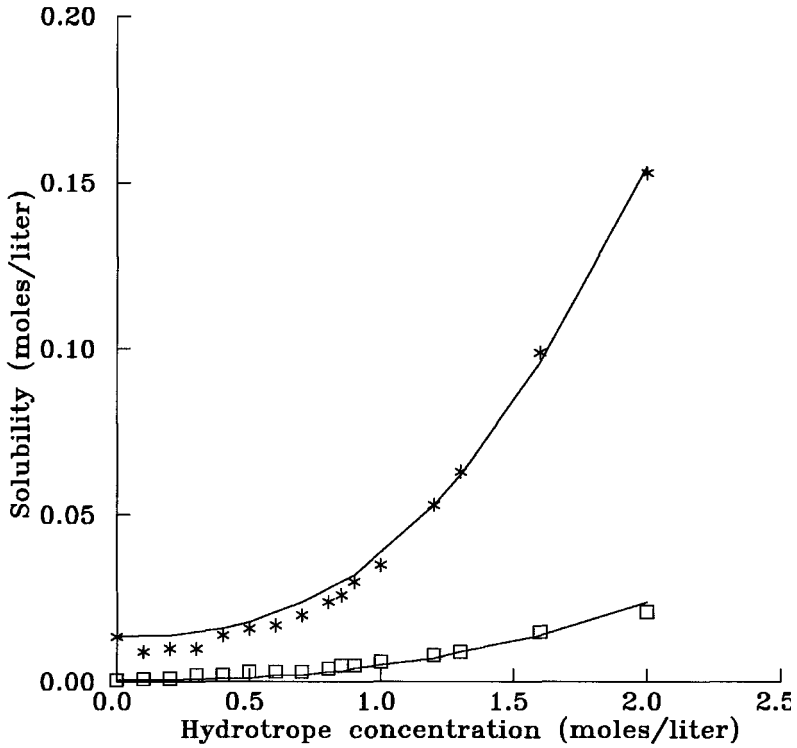

FIG. 4 Solubility of *o*-chlorobenzoic acid (∗) and *p*-chlorobenzoic acid (□) in aqueous solutions of Na-BMGS at 303 K.

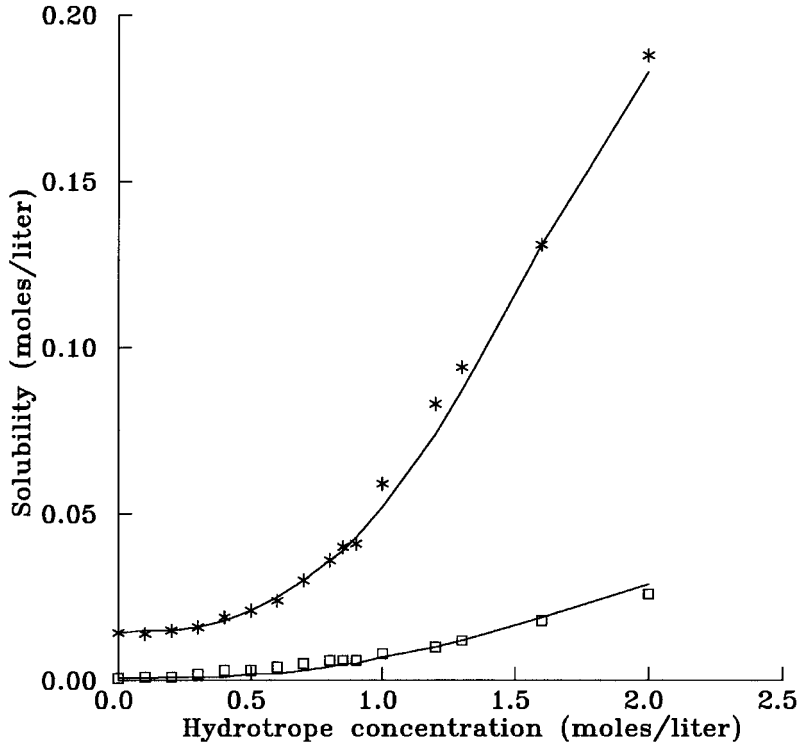

FIG. 5 Solubility of *o*-chlorobenzoic acid (∗) and *p*-chlorobenzoic acid (□) in aqueous solutions of Na-BMGS at 313 K.

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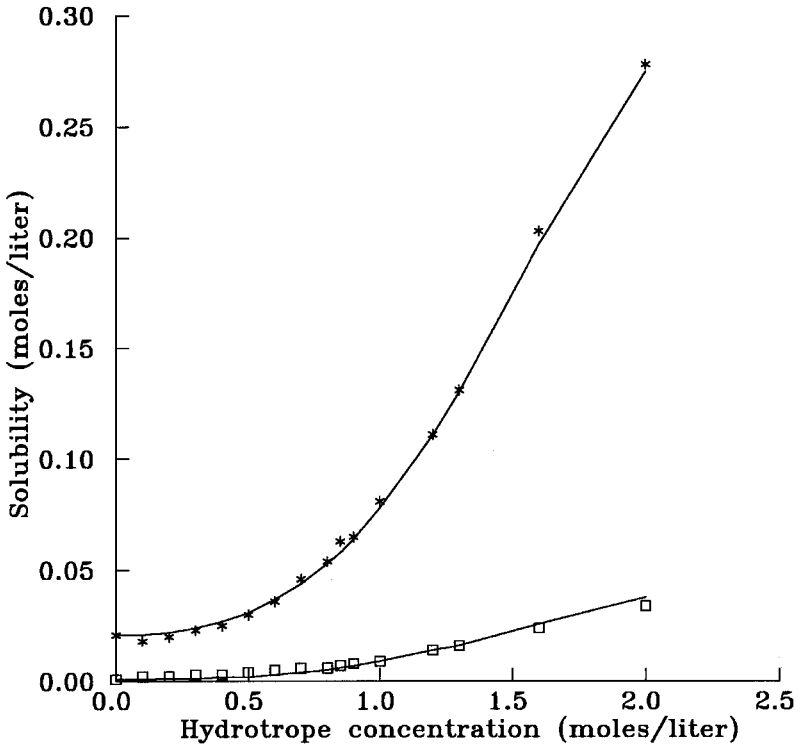

FIG. 6 Solubility of *o*-chlorobenzoic acid (∗) and *p*-chlorobenzoic acid (□) in aqueous solutions of Na-BMGS at 323 K.

chlorobenzoic acids in Na-BMGS solutions at 303, 313, and 323 K, respectively.

o-NA and *p*-NA show a considerable rise in the solubility with hydrotrope concentration. For example, the solubilities of *o*-NA and *p*-NA are 0.334 and 0.135 mol/L in a 2.0 M solution of Na-BMGS at 303 K. The solubility values of *o*-CBA and *p*-CBA are 0.153 and 0.021 mol/L, respectively, in a Na-BMGS solution at the same concentration. The increase in the solubility of each of these isomers in a 2.0 mol/L solution of Na-BMGS with respect to their water solubilities is given in Table 1. This increase is an indication of the selectivity exhibited by hydrotrope solutions toward these solutes. The solubility of *o*-CBA is higher than the solubility of *p*-CBA, but the relative increase ($\Delta S/S_w$) is higher for *p*-CBA than for *o*-CBA in 2.0 M Na-BMGS solutions.

Temperature has a marked effect on the solubility in the presence of the hydrotrope. Temperature may affect the solubility of the solute due to modification of the aggregate structure of the hydrotrope and also by modifying the intermolecular interactions between the hydrotrope and the solute whereby the overall solvent property of the liquid may be significantly altered. The solubility of chlorobenzoic acid and nitroaniline isomers shows a significant rise

TABLE 1
Relative Increase in the Solubility of Isomers[a]

Solute	Temperature (K)	$\Delta S/S_w$
p-Chlorobenzoic acid	303	40.13
	313	35.91
	323	36.88
o-Chlorobenzoic acid	303	10.29
	313	12.11
	323	12.38
o-Nitroaniline	303	36.11
	313	37.69
	323	48.6
p-Nitroaniline	303	21.51
	313	19.64
	323	19.71

[a] ΔS values are in 2.0 M solution of sodium butyl monoglycol sulfate.

with an increase in temperature. The solubilities of these isomers in water are also affected by temperature. However, if we compare the rise in the solubilities of *o*- and *p*-isomers with temperature, it is seen that the difference in their solubilities also increases with temperature. For example, in the case of chlorobenzoic acids the difference in the solubilities of *o*-CBA and *p*-CBA is 3.838×10^{-2} mol/L at 303 K which increases to 24.43×10^{-2} mol/L at 323 K in a 2.0 mol/L Na-BMGS solution. Similarly, in the case of nitroanilines the difference between the solubilities of *o*-NA and *p*-NA increases from 19×10^{-2} mol/L 303 K to 64.47×10^{-2} mol/L at 323 K in 2.0 M Na-BMGS solution.

The solubility data have been fitted using the least-square approach in the proposed aggregation model to estimate the hydrotrope aggregation constant (K_2) and the solute–hydrotrope interaction constant (K_s). The free solute concentration in the solutions is taken to be the solubility of the solute in water. The lines in Figs. 1–6 are the curves predicted from the model using these values of K_s and K_2. The values of K_s and K_2 are reported in Table 2. The relative error in the estimated solubility ranges from 4 to 26%. We expect that these errors are due to the simplifying assumptions made during derivation of the solubilization model. The model inherently predicts an increase in the solubility of the solute. However, some of the solutes do indicate a small salting-out at the lower concentrations of the hydrotrope because of the influence of the highly ionizing head group before hydrotropic solubilization sets in. Thus

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TABLE 2
K_2 and K_s Values from the Solubility Data[a]

	K_2 (L/mol)	K_s (L/mol)	Relative error (%)
o-Nitroaniline:			
303 K	0.145	27	10.3
313 K	0.155	28	13.8
323 K	0.162	34	14.1
p-Nitroaniline:			
303 K	0.12	14	21.3
313 K	0.16	14	11.4
323 K	0.16	14.5	14.2
o-Chlorobenzoic acid:			
303 K	0.115	9.5	16.9
313 K	0.15	8.9	4.0
323 K	0.15	8.8	4.3
p-Chlorobenzoic acid:			
303 K	0.115	44	23.6
313 K	0.15	28	26.7
323 K	0.155	30	23.2

[a] Error = $\frac{1}{N}\sum\frac{\sqrt{(S_e - S_{pr})^2}}{S_e}$ 100, where S_e = experimental value of solubility in hydrotrope solution; S_{pr} = predicted solubility; N = number of experimental points

the free solute concentration of the solute may be different than its water solubility. The second assumption of no effect of the solute on the aggregation number of the hydrotrope assemblies may not be completely valid, particularly for solutes which themselves have a molecular structure conducive to the formation of aggregates of their own or with the hydrotrope. Our independent spectroscopic studies indicate such a co-aggregation behavior of the solute and the hydrotrope (20). Despite these shortcomings the model predicts the trend in solubilization and particularly the selectivity in solubilization as discussed later in this article. Interestingly, the K_2 value at higher temperature also shows an increase where the amount of solute solubilized is higher.

The hydrotrope association constant is much lower than the hydrotrope–solute association constant which indicates that although hydrotrope molecules aggregate in the solution, their aggregation is very weak and the aggregation number may not be high. The hydrotrope used in this study has a hydrophobic group of only four carbon atoms. The repulsive forces between the strongly ionic sulfate groups thus must be much stronger than the short-range forces between these hydrocarbon chains. The higher values of K_s, which differ for different solutes, even among the isomers, however, indicate stronger molecular interactions between hydrotrope assemblies and the solute. Thus the na-

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ture and the concentration of the solute may have an effect on the aggregation of the hydrotrope. In such a case, the hydrotropic solubilization seems to occur because of the co-aggregation of the solute with the hydrotropes. It is thus likely that hydrotrope aggregation would show significant changes with the concentration of the solute. This fact was assumed to be insignificant in the derivation of the model equations in order to simplify the mathematical treatment. At a higher solubility of the solute, the present treatment would not give proper values. Hydrotropic solubilization also seems to be driven by molecular interactions and not by aggregation of the hydrotrope alone.

The K_s values of *o*-nitroaniline at all temperatures are higher than those of *p*-nitroaniline, indicating greater interactions between *o*-NA and the hydrotrope. Thus *o*-NA shows a greater rise ($\Delta S/S_w$) in the solubility with an increase in hydrotrope concentration. Solute–hydrotrope interactions play an important role in solubilization, and these interactions are much stronger for *o*-nitroaniline than for *p*-nitroaniline. However, in the case of chlorobenzoic acids, higher values of K_s were obtained for the *p*-isomer, indicating stronger interactions between *p*-CBA and the hydrotrope compared to *o*-CBA.

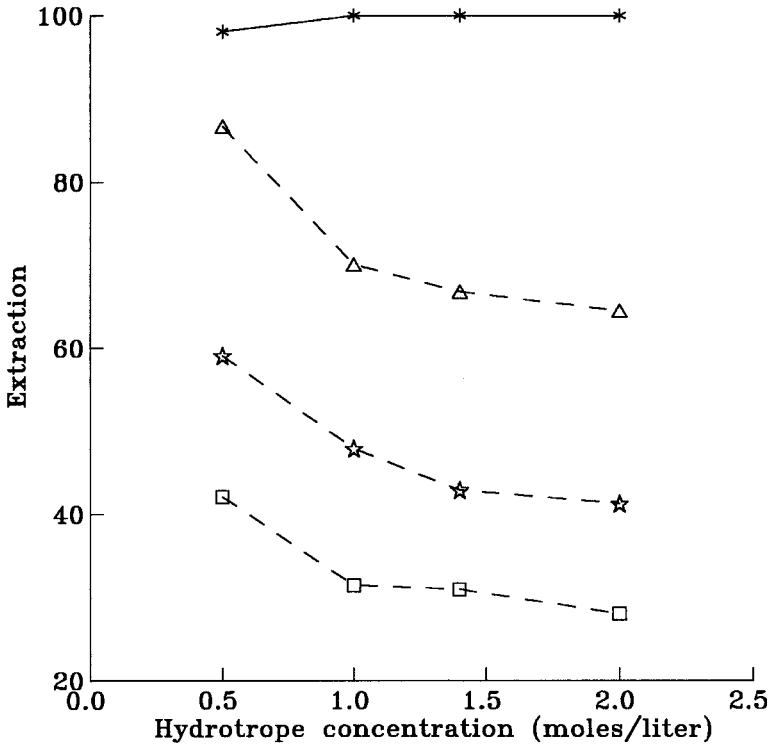

FIG. 7 Extraction of *o*-nitroaniline and *p*-nitroaniline in aqueous solutions of Na-BMGS at 303 K and different compositions of the solid mixture. The lines indicate the expected extraction from the individual solubilities: (——) *o*-nitroaniline, (- - - -) *p*-nitroaniline, (Δ) (*o*/*p* = 60:40), (☆) (*o*/*p* = 50:50), (□) (*o*/*p* = 40:60).

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SEPARATION STUDIES

o-/*p*-Nitroanilines

Individual solubility studies showed the selectivity of hydrotrope solutions toward *o*-nitroaniline. Therefore, the separation of the mixtures of nitroanilines was studied as a function of hydrotrope concentration and temperature. Three different compositions (60:40, 50:50, 40:60%) of nitroanilines were studied. Since the solubility of *o*-nitroaniline is higher than that of *p*-nitroaniline, the amount of hydrotrope solution was chosen to completely solubilize the *o*-isomer with the intention of obtaining pure *p*-isomer. The volume of hydrotrope solution needed can be calculated from the solubility data and by assuming that the presence of the other isomer does not affect the solubility of the *o*-nitroaniline. The effect of the composition of the mixture and the hydrotrope concentration on the extraction into the hydrotrope solutions is shown in Figs. 7–9 at three different temperatures. The solid lines show the expected extraction based on the individual solubilities of the isomers. These figures also show the effect of temperature on separation by solubilization.

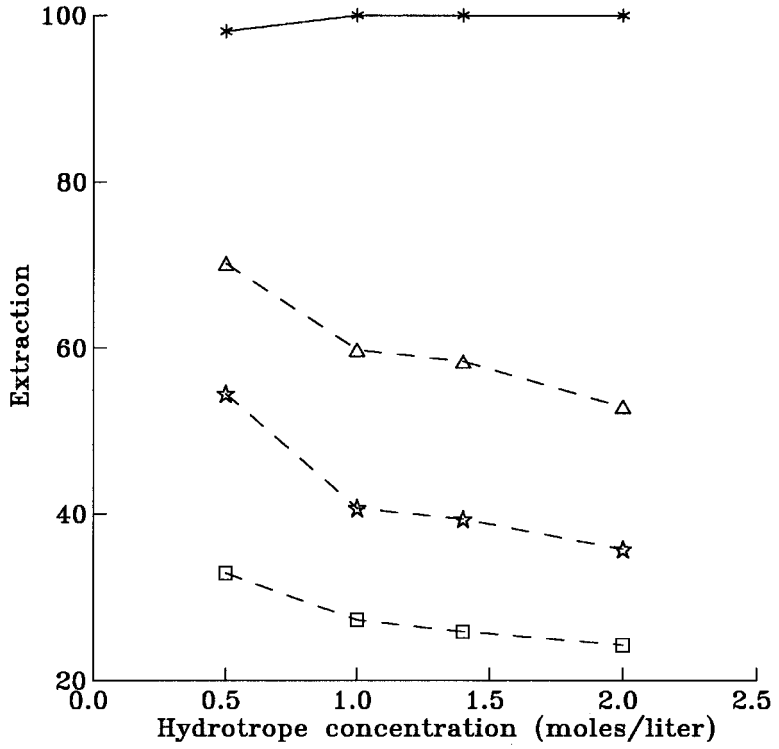

FIG. 8 Extraction of *o*-nitroaniline and *p*-nitroaniline in aqueous solutions of Na-BMGS at 313 K and different compositions of the solid mixture. The lines indicate the expected extraction from the individual solubilities: (——) *o*-nitroaniline, (- - - -) *p*-nitroaniline, (Δ) (*o*/*p* = 60:40), (☆) (*o*/*p* = 50:50), (□) (*o*/*p* = 40:60).

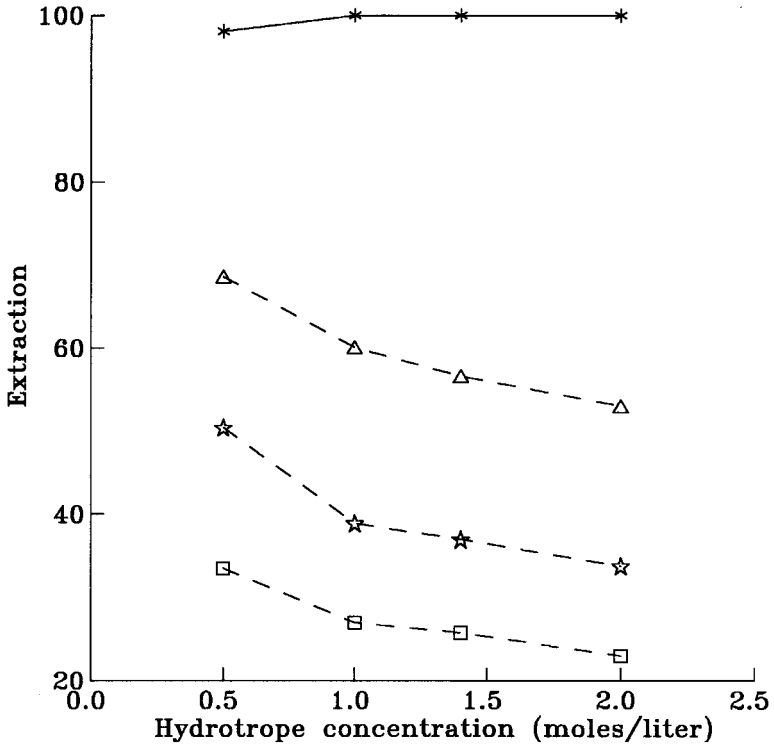

FIG. 9 Extraction of *o*-nitroaniline and *p*-nitroaniline in aqueous solutions of Na-BMGS at 323 K and different compositions of the solid mixture. The lines indicate the expected extraction from the individual solubilities: (——) *o*-nitroaniline, (- - - -) *p*-nitroaniline, (Δ) (*o*/*p* = 60:40), (☆) (*o*/*p* = 50:50), (□) (*o*/*p* = 40:60).

In all cases the remaining solid residue was pure *p*-nitroaniline. However, the loss of *p*-nitroaniline into the hydrotrope solution was higher at lower concentrations of the hydrotrope where a large volume of the solution has to be utilized to dissolve the *o*-isomer fully. At higher concentrations of the hydrotrope, for a given amount of *o*-nitroaniline, the volume of solution is lower, resulting in less loss of *p*-nitroaniline. The same effect has also been observed at higher temperatures. The solubility of both isomers increases with temperature, but the volume effect alone is sufficient to reduce the loss of *p*-nitroaniline. The difference in the individual solubilities of these isomers also increases with temperature at a given concentration of the hydrotrope. At higher temperatures the comparative rise in the solubility of *p*-nitroaniline was less than that of *o*-nitroaniline. Thus, an increase in separation efficiency was expected.

The selective solubilization of *o*-nitroaniline gives pure *p*-isomer, but with an increase in the percentage of *o*-nitroaniline in the mixture, the loss of *p*-nitroaniline also increases. Thus hydrotropic solubilization may not be advantageous for the purification of *o*-nitroaniline but can be used effectively for the

purification of *p*-nitroaniline. There was no effect of one isomer on the solubility of the other isomer.

o-/*p*-Chlorobenzoic Acids

The solubility of *o*-chlorobenzoic acid is more than that of *p*-chlorobenzoic acid in hydrotrope solutions by at least an order of magnitude. However, from the aggregation model and $\Delta S/S_w$ values the *p*-isomer shows a better interaction with the hydrotrope assemblies. This mixture was thus expected to show a behavior different from nitroanilines.

Four different compositions were studied as a function of the hydrotrope concentration at 303 K. Since *o*-chlorobenzoic acid has a higher solubility than *p*-chlorobenzoic acid, the volume of the hydrotrope solutions was adjusted to solubilize *o*-chlorobenzoic acid. With the increase in the *o*-CBA content of the mixture, the solubility of *p*-CBA increased with a corresponding decrease in the solubility of *o*-CBA. The stronger interaction of *p*-chlorobenzoic acid seems to have a competitive edge in replacing a part of *o*-CBA from the hydrotrope solution. Figures 10 and 11 depict the changes in the solubility

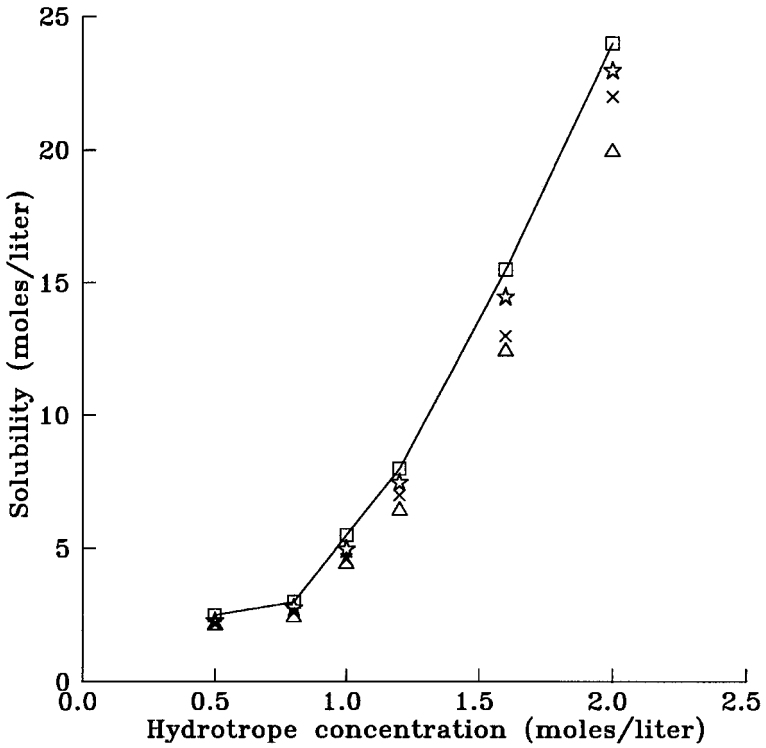

FIG. 10 Solubility of *o*-chlorobenzoic acid in Na-BMGS solutions at 303 K in the presence of *p*-chlorobenzoic acid. The line indicates solubility in the absence of *p*-chlorobenzoic acid. (□) (*o*/*p* = 80:20), (☆) (*o*/*p* = 60:40), (×) (*o*/*p* = 50:50), (Δ) (*o*/*p* = 40:60).

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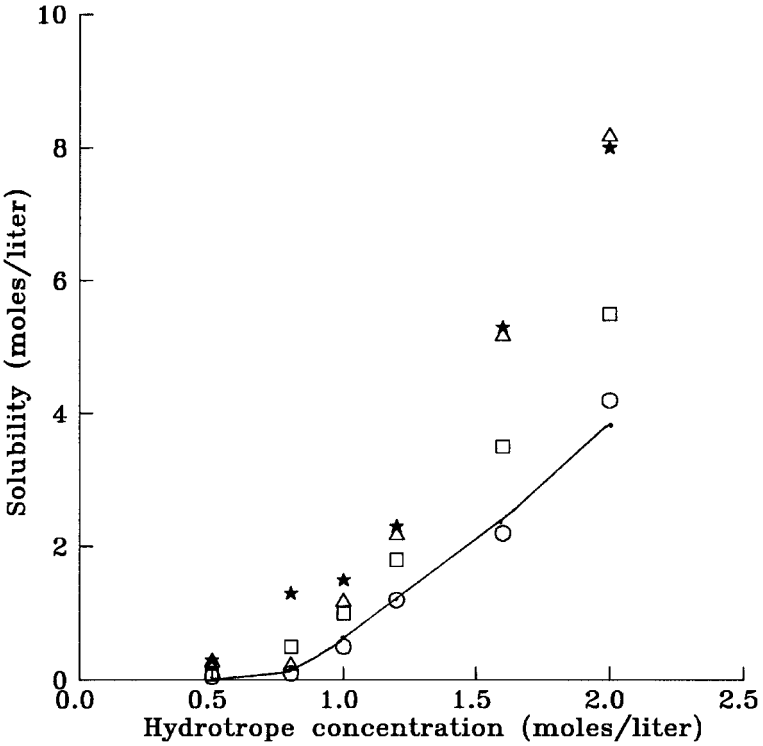

FIG. 11 Solubility of *p*-chlorobenzoic acid in Na-BMGS solutions at 303 K in the presence of *o*-chlorobenzoic acid. The line indicates solubility in the absence of *o*-chlorobenzoic acid. (○) (*o*/*p* = 80:20), (□) (*o*/*p* = 60:40), (★) (*o*/*p* = 50:50), (Δ) (*o*/*p* = 40:60).

of *o*-CBA and *p*-CBA, respectively, as functions of the composition and the concentration of the hydrotrope. The change in solubility was more at higher concentrations of the hydrotrope and also for mixtures rich in *p*-CBA. Although the residue obtained after filtration was relatively pure *p*-isomer, the loss of *p*-CBA into the hydrotrope solution was also significant. The solubilization behavior of chlorobenzoic acids has shown a competitive solubilization indicating the limited capacity of hydrotropic assemblies and also solute–solute interactions in hydrotrope solutions.

If co-aggregation of the solute with the hydrotropic assembly is necessary for hydrotropic solubilization, then a solute having an amphiphilic structure, or at least with distinct hydrophilic and nonpolar groups, should show a large increase in solubility. In the case of nitroanilines, *o*-nitroaniline has an appropriate structure. *p*-Nitroaniline, on the other hand, has polar groups on both ends and thus may not be easily accommodated within the hydrotrope aggregates. *p*-Chlorobenzoic acid, which has a hydrophobic Cl group in the para position, can thus associate with hydrotrope molecules and show a greater change in solubility. The extension of the proposed association model to such

competitive solubilization is difficult. Nevertheless, the model does predict qualitatively the selectivity shown by the hydrotrope aggregates toward a particular isomer from a mixture.

Recovery of Solutes from Hydrotrope Solutions

The hydrotropic phenomenon is a strong function of hydrotrope concentration, and the dissolved solute can be recovered by simple dilution with water. We investigated if further purification is possible during dilution by conducting the dilution in steps. A 50-mL solution of Na-BMGS saturated with *o*-NA and *p*-NA was diluted in steps. Table 3 indicates the concentration of the hydrotrope at each dilution step. The yield was calculated on the basis of the amounts of the individual isomers present in the solution at the beginning. Table 3 also shows the purity of the precipitated solid. In both cases (nitroanilines and chlorobenzoic acids) the initial precipitate was pure *p*-isomer. The percentage of *o*-isomer increased in the latter fractions. However, it was

TABLE 3
Recovery of Solutes from Hydrotrope Solutions by Dilution[a]

Concentration of hydrotrope (mol/L)	% in the solid		% Yield	
	o-	*p*-	*o*-	*p*-
	o-/*p*-*Nitroanilines*			
1.48	—	100	0	22.9
1.24	80.7	19.3	24.4	14.07
1.13	80.5	19.5	12.04	5.92
1.02	75.8	24.2	16.05	10.5
0.84	70.9	29.1	8.1	6.67
	o-/*p*-*Chlorobenzoic Acids*			
1.5	—	100	0	38.1
1.24	80.4	19.6	38.14	16.9
1.13	75.6	24.4	22.8	15.35
1.00	73.9	26.1	15.8	10.07
0.84	75.6	24.4	11.62	6.8

[a] Temperature: 303 K.

	NA	CBA
Initial volume of the hydrotrope solution (2.5 M):	50 cm^3	100 cm^3
Amount of isomers in the initial saturated solution:	*o*- = 2.75 g	2.9 g
	p- = 1.40 g	1.18 g

Yield = (precipitated amount/initial amount) × 100.

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not possible to obtain a pure *o*-isomer by this technique. The concentration of the hydrotrope and the temperature need to be manipulated simultaneously for the further purification of *o*-isomer.

CONCLUSIONS

Selective solubilization of isomeric mixtures of *o*-/*p*-nitroanilines and *o*-/*p*-chlorobenzoic acids has been attempted in aqueous solutions of sodium butyl monoglycol sulfate. Analysis of the solubility data of individual components using a stepwise aggregation model showed a weaker hydrotrope aggregation process but a much stronger hydrotrope–solute association. The association model predicted the trend in the solubility of the isomers, including selectivity in the solubilization of a particular isomer from the mixture. The simplifying assumptions need to be removed to increase the accuracy of the model. However, this may make parameter estimation difficult. In the cases of both nitroanilines and chlorobenzoic acids, pure *p*-isomer was obtained by selective solubilization of the *o*-isomer into the hydrotrope solutions. The concentration of the hydrotrope, the temperature, and the composition of the mixture have a significant effect on separation efficiency.

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