

# Effect of Symmetrical Tetraalkylammonium Salts on Cloud Point of Nonionic Surfactants

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**Abstract** □ The salting in and salting out of the nonionic surfactant octoxynol NF by halides of ammonium and the four lowest symmetrical tetraalkylammonium cations were investigated by measuring their effect on the cloud point at various salt concentrations. The chloride anion tended to salt the surfactant out, lowering its cloud point. The iodide anion tended to salt it in, raising the cloud point, while the bromide ion had no pronounced effect. The ammonium and tetramethylammonium cations tended to lower the cloud point, the latter more extensively than the former. The tetraethylammonium cation had no pronounced effect, while the tetra-*n*-propylammonium and tetra-*n*-butylammonium cations tended to raise the cloud point, the latter more extensively than the former. The salt effect on the cloud point generally increased with increasing salt concentration. Tetramethylammonium chloride was the most efficient salt in lowering the cloud point (by 4° at the 0.10-molal level and by 20° at the 1.00-molal level), while tetrabutylammonium halides were the most efficient salts in raising the cloud point (by 18–19° at the 0.10-molal level for chloride and bromide). Cloud point increases were attributed to the formation of mixed micelles or to hydrotropy. The salting-out efficiency of tetramethylammonium chloride and bromide was ascribed to their ability to increase the structure of water.

**Keyphrases** □ Surfactants, nonionic—octoxynol, effect of tetraalkylammonium salts and ammonium halides on cloud point, various salt concentrations □ Octoxynol—effect of tetraalkylammonium salts and ammonium halides on cloud point, various salt concentrations □ Tetraalkylammonium salts—effect on cloud point of octoxynol, various salt concentrations □ Ammonium halides—effect on cloud point of octoxynol, various salt concentrations □ Cloud point—octoxynol, effect of tetraalkylammonium salts and ammonium halides, various salt concentrations

Two major trends were observed during a systematic investigation of the effect of inorganic cations on the cloud points of polyoxyethylated nonionic surfactants (1, 2). All polyvalent cations plus lithium form complexes with the ether oxygens of simple, model ethers like dioxane as well as with those of the polyoxyethylene moiety of nonionic surfactants. In this complex formation, which competes with the hydration of the cations, the flexible polyoxyethylene chains probably act as polydentate ligands (1, 2). The result is salting in of the surfactants, which manifests itself as an increase in cloud point. The reason that increases in this upper consolute temperature represent salting in is that they correspond to an increase in solubility, namely, an extension of the temperature range in which the nonionic surfactants exist in single-phase, undersaturated solutions (3).

The only inorganic cations incapable of forming complexes with the oxygen of ether groups or of water are sodium, potassium, ammonium, cesium, and, probably, rubidium. Their effect on nonionic surfactants is to lower the cloud points, salting them out (1, 2).

## BACKGROUND

The cations of symmetrical tetraalkylammonium halides are of considerable physicochemical and biological interest. Their effect on the structure of water results in unusual behavior of their aqueous solutions such as peculiar activity and osmotic coefficients (4, 5) and conductance (6), high viscosity with large temperature coefficients (7), and unusual partial molal volumes (8–11).

Examples of tetraalkylammonium derivatives of biological importance are choline, found in lecithins and sphingomyelins; acetylcholine, crucial in the transmission of nerve impulses; and naturally occurring betaines including trimethylglycine. Examples of quaternary ammonium compounds with pharmacological activity include many alkaloidal salts and synthetic neuromuscular blocking drugs. An interesting type of interaction, pertinent to the present research, is supplied by the work of Belleau. The binding of tetraalkylammonium halides to the surfaces of acetylcholinesterase and of muscarinic and nicotinic receptors was shown to involve the structure of water in the vicinity of the receptor sites (12, 13).

The purpose of the present investigation was to examine the effect of tetraalkylammonium halides on the cloud point of a polyoxyethylated nonionic surfactant. It represents a logical sequence in our studies of the effect of the various categories of cations on cloud points and solubility of nonionic surfactants. Ether groups cannot act as ligands for tetraalkylammonium cations as they do for inorganic polyvalent cations. However, ion-dipole attraction (14) and hydrophobic interaction between the alkyl groups of the salts and the ethylene groups of the polyoxyethylene moiety of nonionic surfactants may take place.

Since the properties of symmetrical tetraalkylammonium halides strongly depend on the length of the alkyl groups (4–13), the number of carbon atoms per alkyl group was varied from zero (unsubstituted ammonium) to four.

The anion of the tetraalkylammonium halides was varied for two reasons. First, anions can enhance or reduce the structure of water. Structure-forming anions such as fluoride and chloride lower cloud points, salting the nonionic surfactants out, while structure-breaking anions such as iodide and thiocyanate have the opposite effect (2, 15). Second, large and poorly hydrated anions such as iodide are prone to ion-pairing, either of the usual electrostatic kind or "water structure enforced" (4–6).

Finally, there is the possibility of using the surfactant through its cloud point as a probe to obtain information on the structure and behavior of aqueous solutions of tetraalkylammonium salts.

## EXPERIMENTAL

The nonionic surfactant employed was octoxynol NF<sup>1</sup>, a branched octylphenol with an average of nine to 10 ethylene oxide units. It was selected because it is a monograph in the National Formulary and because it has been employed extensively in cloud point measurements (16), particularly when these were used as a criterion for salting in or out (1, 2). Its properties were given in Ref. 2 under Surfactant I.

The viscous liquid was dried over anhydrous calcium sulfate<sup>2</sup> to constant weight, losing less than 1% of moisture. The tetra-*n*-alkylammonium halides<sup>3</sup> were also dried to constant weight over anhydrous calcium sulfate. Sodium *m*-xylenesulfonate<sup>4</sup> was used as received. All other reagents were ACS reagent grade. Water was double distilled.

The procedures for preparing the ternary electrolyte-surfactant-water mixtures and for measuring cloud points were described previously (1). The surfactant concentration was 1.00% (w/w) based on the amount of water present, except for the hydrotropy experiments described in the Appendix where it was 2.00%. Such relatively small differences in surfactant concentration have no effect on the cloud point (17). Electrolyte concentrations are expressed as molality or as percent (w/w) based on the amount of water present in the mixtures.

## RESULTS

The cloud point of octoxynol as a function of the concentration of the various electrolytes is listed in Table I.

<sup>1</sup> Triton X-100, Rohm & Haas Co.

<sup>2</sup> Drierite, W. A. Hammond Drierite Co., Xenia, Ohio.

<sup>3</sup> Tokyo Kasei Kogyo Co., Tokyo, Japan.

<sup>4</sup> Supplied as 2,4-dimethylbenzenesulfonic acid sodium salt, Eastman Organic Chemicals No. 2131.

**Table I—Cloud Point of Octoxynol as a Function of the Concentration of Added Electrolytes<sup>a</sup>**

Cation	Molality	Cloud Point for Anion			
		Chloride	Bromide	Iodide	Nitrate
Ammonium	0.10	60.8°	63.1°		62.7°
	0.20	60.0°	62.5°		63.2°
	0.50	56.9°	62.1°		63.1°
	1.00	52.3°	61.1°		63.0°
	1.50	48.8°	61.8°		61.5°
	2.00	46.5°	61.7°		59.7°
	3.00	—	—		54.5°
Tetramethylammonium	0.10	60.5°	62.0°	65.3°	
	0.20	59.6°	61.5°	67.0°	
	0.50	53.2°	59.1°	70.4°	
	1.00	45.0°	55.3°	73.4°	
	1.50	37.8°	51.0°	—	
	2.00	31.0°	—	—	
Tetraethylammonium	0.10	61.8°	63.0°	66.5°	
	0.20	61.0°	64.0°	69.1°	
	0.50	60.1°	65.2°	73.0°	
	1.00	57.4°	66.2°	78.5°	
	2.00	47.0°	61.8°	—	
Tetra- <i>n</i> -propylammonium	0.10		67.3°	71.0°	
	0.20		72.8°	78.5°	
	0.50		87.5°	—	
	0.10	73.5°	74.0°		
Tetra- <i>n</i> -butylammonium	0.10	83.0°	84.1°		

<sup>a</sup>Concentration of octoxynol was 1.00% (w/w) based on the weight of water. Its cloud point in the absence of electrolytes was 64.3°.

**Effect of Anion**—The anions are ranked in the following order of decreasing effectiveness for salting out (lowering the cloud point) or increasing effectiveness for salting in (raising the cloud point): chloride > nitrate ≈ bromide > iodide. This order is the same as the Hofmeister or lyotropic series (18), which was also followed by the anions of inorganic salts (1, 2, 15). The large, polarizable iodide ion is particularly effective in breaking the structure of water.

The destructuring of water increases the concentration of nonassociated water molecules. These molecules become available to hydrate the ether groups of the nonionic surfactant, increasing its solubility and raising its cloud point (1, 2). The effect of the anions on the cloud point is minor compared to the large effect of the cations.

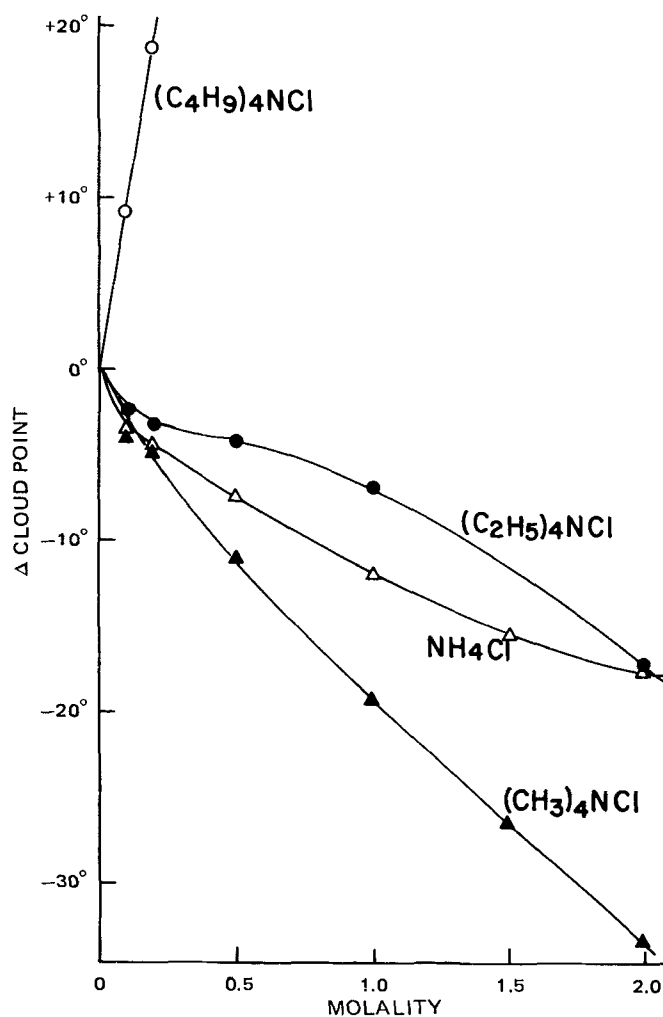
**Effect of Cation Size**—The behavior of the electrolytes underwent profound changes as the number of carbon atoms per alkyl group was increased from zero to four. As is seen from Figs. 1–3, tetramethylammonium salts had the strongest salting-out efficiency. The chloride lowered the cloud point by more than 30° at the 2-molal level. Only the iodide raised the cloud point, because of the strong salting-in tendency of the anion.

The salts of ammonium and tetraethylammonium at low and intermediate concentrations produced moderate decreases or increases in cloud point, depending on the anion. Except for ammonium bromide and tetraethylammonium bromide, the tendency to lower or to raise the cloud point of octoxynol became stronger with an increasing concentration of the electrolyte. As the alkyl groups were increased to *n*-propyl and *n*-butyl, the salting-in effect became very pronounced. The 20° increase in cloud point produced by 0.10 molal tetrabutylammonium chloride and bromide was considerably greater than the increases produced by inorganic salts at comparable concentrations. A 20° increase in the cloud point of octoxynol required over 2 molal sulfuric or hydrochloric acid, over 3 molal cadmium or magnesium nitrate, 4 molal nickel nitrate, and nearly 6 molal calcium nitrate (1).

The salt effect of the tetraalkylammonium halides as a function of the number, *p*, of carbon atoms per alkyl group is illustrated in Fig. 4. The ammonium and tetramethylammonium salts lowered the cloud point, salting the surfactant out. The curves have a minimum for *p* = 1. As *p* increased beyond 2, the cloud point underwent steep increases. The tetrapropyl- and tetrabutylammonium cations were very effective at salting the surfactant in.

## DISCUSSION

The influence of the chain length of the alkyl groups on the nature and magnitude of the salt effect must be attributed to more than one factor, because the effect changes from salting out for *p* = 0 and 1 to salting in



**Figure 1—Change in the cloud point of octoxynol as a function of the molal concentrations of added chlorides.**

for *p* = 3 and 4. Attempts to explain these observations in terms of existing theories of salt effects and water structure are made here.

**Internal Pressure Theory**—Long and McDevit (19) derived the following equation, which explains the effect of electrolytes on the solubility of nonelectrolytes in terms of internal pressure:

$$\ln \frac{S_n^o}{S_n} = \left[ \frac{\bar{V}_n^o (V_e - \bar{V}_e^o)}{\beta RT} \right] C_e \quad (\text{Eq. 1})$$

The subscripts *n* and *e* designate the nonelectrolyte (*i.e.*, the nonionic surfactant) and electrolyte, respectively. The superscript *o* designates the property of the solute in water. Thus, *S<sub>n</sub><sup>o</sup>* and *S<sub>n</sub>* are the molar solubilities of the surfactant in water and in a solution containing *C<sub>e</sub>* moles/liter of electrolyte, respectively;  $\bar{V}_n^o$  represents partial molal volumes at infinite dilution; and *V<sub>e</sub>* is the partial molal volume of the pure "liquid" electrolyte. The difference (*V<sub>e</sub>* -  $\bar{V}_e^o$ ) represents the extent of electrostriction of water by the electrolyte. If *V<sub>e</sub>* >  $\bar{V}_e^o$ , this difference is positive as is the logarithm of the ratio *S<sub>n</sub><sup>o</sup>/S<sub>n</sub>*. Hence, *S<sub>n</sub><sup>o</sup>/S<sub>n</sub>* > 1 and *S<sub>n</sub><sup>o</sup>* > *S<sub>n</sub>*. Physically, a positive (*V<sub>e</sub>* -  $\bar{V}_e^o$ ) means that dissolution of the electrolyte produces a contraction in the volume of water. The solvent medium is compressed by the electrolyte, and the nonelectrolyte is squeezed out of solution or salted out.

The difference (*V<sub>e</sub>* -  $\bar{V}_e^o$ ) was found to be negative for the three tetraalkylammonium bromides tested, namely, -10, -23, and -32 ml/mole for the tetramethyl-, tetraethyl-, and tetrapropylammonium bromides, respectively (20). These three salts loosen the solvent medium and should thereby increase the solubility of the nonelectrolyte, salting it in. This effect was observed with the nonpolar compound benzene (20). However, when the nonelectrolyte was the amphiphilic surfactant octoxynol, of the three salts only tetrapropylammonium bromide raised its cloud point, salting it in as predicted by the theory. Tetramethylammonium bromide salted it out, while tetraethylammonium bromide had no pronounced effect on the cloud point.

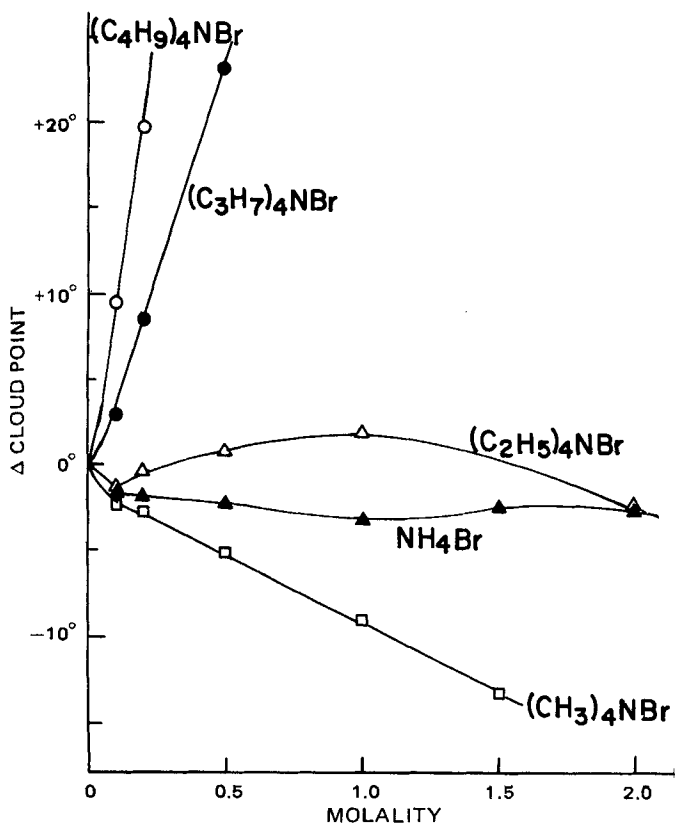


Figure 2—Change in the cloud point of octoxynol as a function of the molal concentrations of added bromides.

Thus, the internal pressure theory does not apply to the present situation, either because the nonelectrolyte is a large molecule or because it is a polar molecule (19). This finding represents a further limitation of the theory. Previously (2), it was found to fail because it did not take into account association between electrolytes and the nonelectrolyte by complex formation.

**Effect of Alteration of Water Structure**—Tetraalkylammonium salts are known to enhance the structure of water; the larger the alkyl groups, the greater is this effect (4). These hydrophobic groups do not attract or orient the water molecules in their immediate vicinity as strongly as does the next shell of water molecules, which surrounds the water molecules nearest to the hydrocarbon groups. Thus, the nearest water molecules are oriented and hydrogen bonded more strongly to the water molecules beyond them than would be the case if there were a strong counterattraction from the side of the hydrocarbon groups. This produces a tightening of the structure of the water surrounding these groups. Such an increase in water structure results in a large decrease in

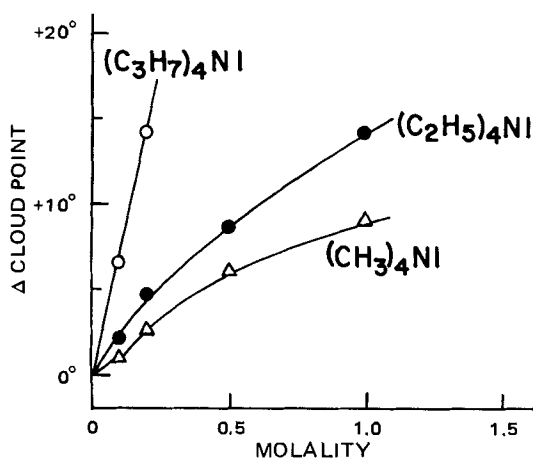


Figure 3—Change in the cloud point of octoxynol as a function of the molal concentrations of added iodides.

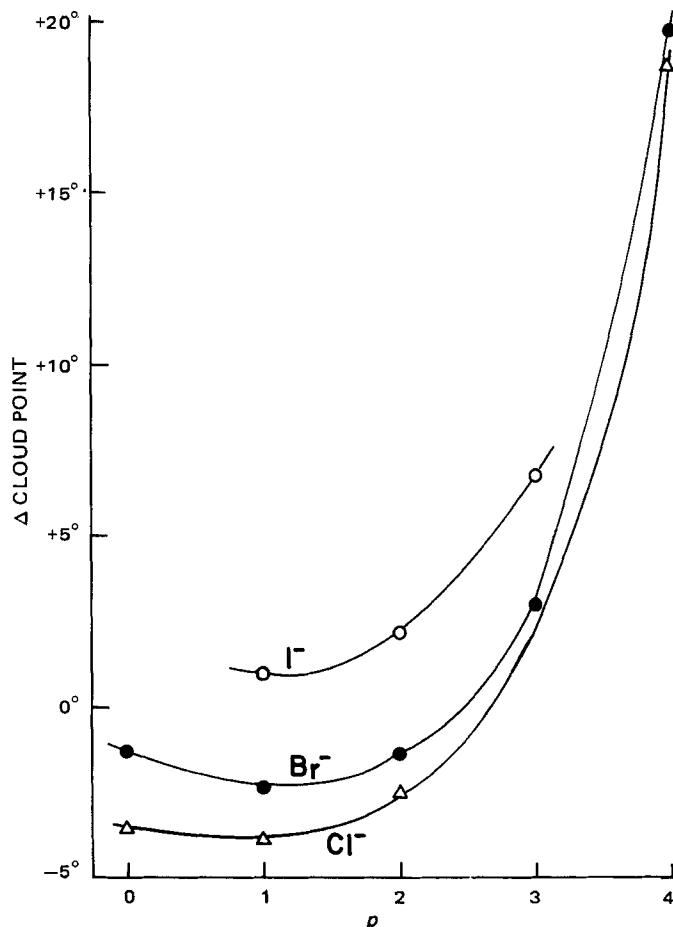


Figure 4—Effect of chain length of the tetraalkylammonium ion on the cloud point of octoxynol at 0.10-molal electrolyte concentration;  $p$  = number of carbon atoms per alkyl group.

entropy on dissolving a tetraalkylammonium salt in water compared with its dissolution in an unstructured organic solvent (4). Evidence of the enhanced water structure is the high viscosity and molal heat capacity of aqueous solutions of tetraalkylammonium halides (7).

As structure makers, tetraalkylammonium halides enhance the association among water molecules to the detriment of the hydration of the surfactant molecules. Thus, these electrolytes should salt the surfactant out. The observed increases in cloud point produced by the tetrapropyl- and tetrabutylammonium salts are in direct opposition to their structure-making activity. This finding indicates that a mechanism other than their effect on water structure is responsible for their salting-in or cloud point-raising ability. The new mechanism must be strong enough to overcome the effect of enhanced water structure formation by the tetrapropyl- and tetrabutylammonium ions, because this effect consists in reducing the solubility of nonelectrolytes or salting out. It is likely that at the cloud point temperature of 64° in the absence of electrolytes, the "icebergs" or "flickering clusters" (21) are largely melted or broken up. The tetrapropyl- and tetrabutylammonium salts boosted the cloud point to even higher temperatures, the latter above 80°, where these water structures cannot persist even in the presence of structure-making salts.

**Electrolyte Association**—Tetraalkylammonium halides reportedly associate in aqueous solution, either by cation-cation pairing (22) or by micelle formation (5, 23–25). The evidence for micellization is not supported by surface tension measurements (26) and could also be construed as indicating hydrotrophy (27). The latter possibility is discussed in the Appendix. However, there is a strong likelihood that octoxynol and the tetraalkylammonium halides form mixed micelles, since the critical micelle concentration (CMC) of octoxynol is far below the 1.00% use level even at room temperature. Nonionic surfactants have a pronounced tendency to form mixed micelles with anionic (28) and cationic (29) surfactants at temperatures above the Krafft point of the ionic surfactants. The cloud points of the nonionic surfactants are considerably raised by comicellization (16, 30).

Of the four cations, ammonium salts do not form micelles. Tetramethylammonium bromide slightly increased the surface tension of water (26) in the manner of inorganic salts and is, therefore, also unlikely to associate into micelles. For the remaining tetraalkylammonium bromides, the decrease in surface tension with increasing salt concentration was steeper the larger their alkyl groups (26). This fact indicates that the tetrabutylammonium salts have the greatest tendency and the tetraethylammonium salts the least tendency toward forming micelles by themselves or mixed micelles with octoxynol. It corroborates the proposed concept of salting in of octoxynol through comicellization.

Ammonium and tetramethylammonium chloride and bromide salt octoxynol out because they are incapable of forming mixed micelles with it. The greater salting-out efficiency of tetramethylammonium salts compared to the corresponding ammonium salts may be due to their greater ability to increase the "ice-like" structure of water and/or to the smaller structure breaking caused by increasing temperatures in their presence. This assumption is corroborated by the observation that, in a group of salts including 15 different cations and eight anions, the tetramethylammonium ion had the largest negative activation energy for viscous flow of all the ions examined. These ions included barium and magnesium, the alkali metal cations and the halide anions, iodate, chlorate, hydroxyl, and sulfate. The ammonium ion had a small negative value. The activation energies of the higher tetraalkylammonium ions were positive and increased in the order tetraethyl-, tetrapropyl-, and tetrabutylammonium (7).

#### APPENDIX: EFFECT OF A HYDROTROPE ON CLOUD POINT

Hydrotropy is an increase in the water solubility of compounds of low intrinsic solubility by the addition of relatively large amounts of a second solute of high solubility. Such hydrotropic solubilizing agents, while amphiphilic in nature, are not surface active. They do not associate into micelles because their hydrophobic moiety is not large enough (27). Typical hydrotropes are alkali salts of benzene-, toluene-, xylene-, or cymenesulfonic acids and of benzoic, salicylic, or phthalic acids (27, 31, 32).

Even though hydrotropes are widely used as solubilizing or salting-in agents, their effect on the cloud point of polyoxyethylated nonionic surfactants has not been investigated. To examine the possibility that the salting-in action of the tetrapropyl- and tetrabutylammonium salts discussed may be one of hydrotropy, it became necessary to measure the effect of a typical hydrotrope on the cloud point of octoxynol to compare its direction and magnitude with those of the higher tetraalkylammonium salts.

The hydrotrope selected was sodium *m*-xylenesulfonate. The cloud points of solutions containing 2.00% (w/w) octoxynol at different hydrotrope concentrations were as follows: 64.7° in the absence of hydrotrope, 82.5° in the presence of 0.061 molal (1.25%) hydrotrope, 92.5° in the presence of 0.123 molal (2.50%) hydrotrope, and above 99° in the presence of 0.253 molal (5.00%) hydrotrope.

Interpolation places the cloud point of octoxynol in 0.10 molal sodium xylenesulfonate at 90°, compared to 83 and 84° in 0.10 molal tetrabutylammonium chloride and bromide, respectively (Table I). Sodium xylenesulfonate is more effective in raising the cloud point of the surfactant than the two tetrabutylammonium salts. If the trend of larger cloud point increases with increasing *p* values (Fig. 4) can be extrapolated, the tetrabutylammonium iodide or the tetrapentylammonium bromide would be more effective in salting the surfactant in than the anionic hydrotrope. The cloud point increases produced by the higher tetraalkylammonium salts and by a typical hydrotrope are thus of the same order of magnitude. Therefore, hydrotropy is another possible mechanism for the salting in of octoxynol by tetraalkylammonium salts instead of the formation of mixed micelles proposed.

The phenomenon of hydrotropy is poorly understood at the molecular

level (27, 33). In our opinion, solutions of hydrotropes at the customary concentrated use levels contain patches that are largely oleophilic because of high local concentrations of aromatic groups. These hydrocarbon patches are not unlike the hydrocarbon cores of micelles but lack the precise boundaries of the latter. The formation of such patches with an increasing hydrotrope concentration is much more gradual than the sudden formation of micelles by surfactants once the CMC is exceeded. Nevertheless, the two phenomena may be so similar that the differences in the salting in of octoxynol by tetrapropyl- and tetrabutylammonium salts *via* mixed micelle formation and *via* hydrotropy are more semantic than based on physical reality. The higher tetraalkylammonium salts resemble some conventional hydrotropes in general composition (33). That the latter are usually anionic whereas the former are cationic is immaterial as far as their interaction with a nonionic surfactant is concerned.

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