

The Effects of Zwitterionic Surfactant Systems upon Aromatic Nucleophilic Substitution

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Reactions of OH^- with 4-chloro-3,5-dinitrobenzoic acid (1) and 2-chloro-3,5-dinitrobenzoic acid (2) have been examined in solutions of *N,N*-dimethyl-*N*-tetradecylglycine (DTG) and *N,N*-dimethyl-*N*-hexadecylglycine (DHG). DTG and DHG inhibit hydroxydehalogenation of (1) and kinetic profiles for this reaction tend towards a plateau which assumes different values depending on the pH; hence the inhibition does not stop the reaction. Reactions of (2) with OH^- in the presence of DTG and DHG exhibit a 'non-effect'. The important factor underlying this difference of behaviour between (1) and (2) in the presence of zwitterionic surfactants is probably the orientation of the substrates within the micro-aggregates.

Recent studies have proved that reaction rates and equilibria in water are markedly affected by a variety of colloidal species.¹ For example, some micelles and oil-in-water microemulsions² are self-assembling, but others, like synthetic vesicles, are metastable and their formation depends on the input of energy by sonication or evaporation.^{1,3,4}

Experimental data about small synthetic vesicles⁵ suggest that the physical-chemical properties of these systems have a great dependence on experimental conditions, particularly on the counter-ions present. It seems that such systems in homogeneous phases have a common behaviour independent of the structural properties of the hydrocarbon chain of the surfactant.

With this in mind, the study of zwitterionic surfactant systems, such as *N,N*-dimethyl-*N*-tetradecylglycine (DTG) and *N,N*-dimethyl-*N*-hexadecylglycine (DHG), is of interest since the presence of both a carboxylate group and an ammonium group in these molecules induces important changes which may affect the catalytic activity of micelles and their use as models in, for example, enzymatic reactions. In fact, in spite of some limitations, the study of the effect of functionalization on micellar properties could provide some insight into the function of biological systems. The class of zwitterionic surfactants with important biological and applied aspects therefore constitutes an intriguing current research area.^{6,7}

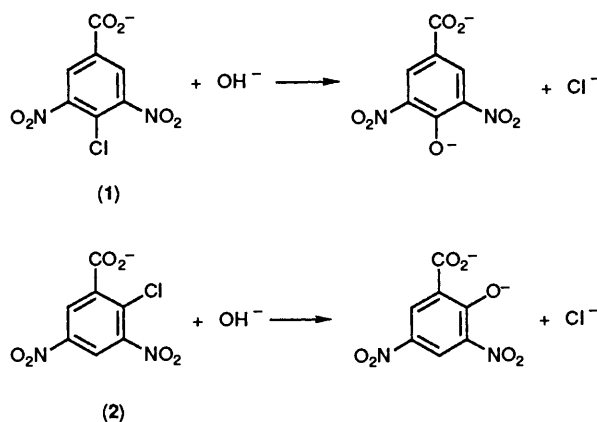
Attention is also drawn to the study of the effects of catalytic activity of zwitterionic surfactant systems in an attempt to rationalize the differing abilities of different surfactants to discriminate between different substrate orientations.^{8,9}

The current paper reports on an examination of the hydroxydehalogenation of two aromatic substrates, 4-chloro-3,5-dinitrobenzoic acid (1) and 2-chloro-3,5-dinitrobenzoic acid (2) (see the Scheme), in the presence of DTG and DHG.

Results and Discussion

Zwitterionic surfactants such as DTG (3) and DHG (4) have both a carboxylate group and an ammonium group in the same molecule. Low critical micelle concentration (CMC) values for these surfactants indicate a certain stabilization of their micellization process. The CMC values at 25 °C for DTG and DHG in the absence and presence of added electrolytes are shown in the Table, where they are compared with those for cetyltrimethylammonium chloride (CTACl).

Substrates (1) and (2) both have two nitro groups *ortho* or *para* to the halogen leaving group, and both contain a



Scheme.

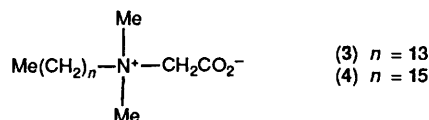


Table. Critical micelle concentration (CMC) values for *N,N*-dimethyl-*N*-tetradecylglycine (DTG), *N,N*-dimethyl-*N*-hexadecylglycine (DHG), and cetyltrimethylammonium chloride (CTACl) in the absence and in the presence of added electrolytes at 25 °C.

Surfactant	Electrolyte	[Electrolyte]/mol dm ⁻³	CMC/mol dm ⁻³
DHG			2.0×10^{-5}
DHG	HCl	1×10^{-2}	2.1×10^{-5}
DHG	NaCl	3×10^{-1}	2.2×10^{-5}
DHG	NaCl	1×10^{-2}	2.2×10^{-5}
DHG	NaOH	1×10^{-3}	2.0×10^{-5}
DHG	NaOH	3×10^{-1}	2.3×10^{-5}
DTG			1.5×10^{-4}
CTACl			1.3×10^{-3}
CTACl	HCl	1×10^{-2}	2.9×10^{-4}
CTACl	NaOH	1×10^{-3}	1.0×10^{-3}
CTACl	NaOH	3×10^{-1}	3.5×10^{-5}

carboxylic group which is ionized in the basic conditions used. It is reasonable to assume that this charged group would be present at the micelle-water interface, allowing better solvation

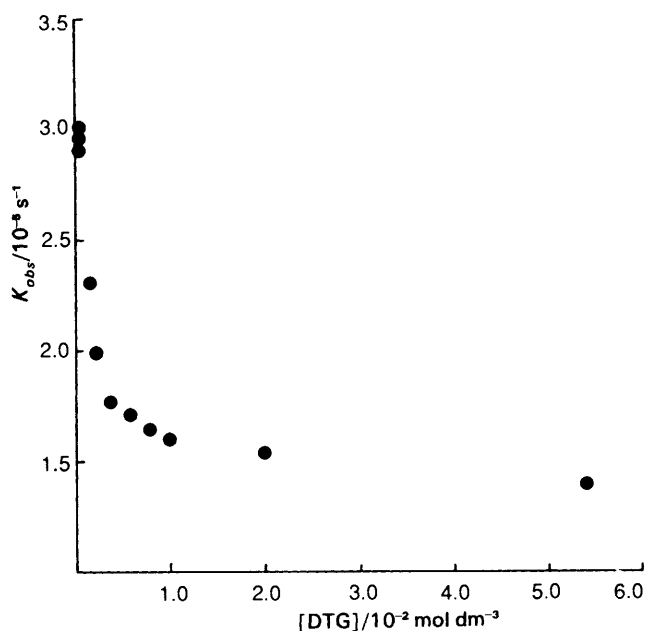


Figure 1. Reaction of (1) with 0.05 mol dm⁻³ NaOH in the presence of DTG.

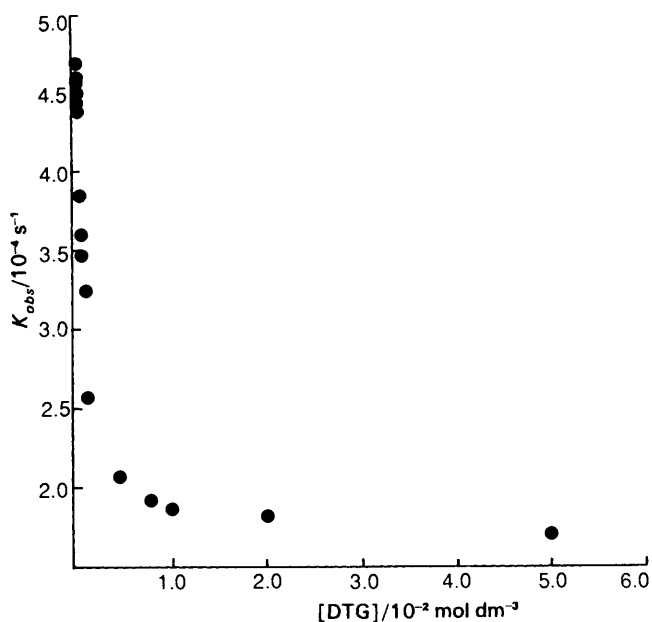


Figure 2. Reaction of (1) with 0.5 mol dm⁻³ NaOH in the presence of DTG.

in the aqueous pseudophase than in the less polar micellar pseudophase. In (2) the halogen leaving group is *ortho* to the carboxylate group and hence should be aligned close to the micelle-water interface, but in (1) the chlorine is *para* to the carboxylate group and hence should be more deeply buried in the micellar pseudophase.

The variation of observed rate with surfactant concentration for the reaction of (1) with NaOH at different concentrations in the presence of DTG and DHG is shown in Figures 1-3.

The presence of both DTG and DHG results in overall inhibition for the reaction of (1) with NaOH. Kinetic profiles for this reaction tend towards a plateau which assumes different values according to the working pH; hence the inhibition does not stop the reaction. Furthermore, the reaction of (1)

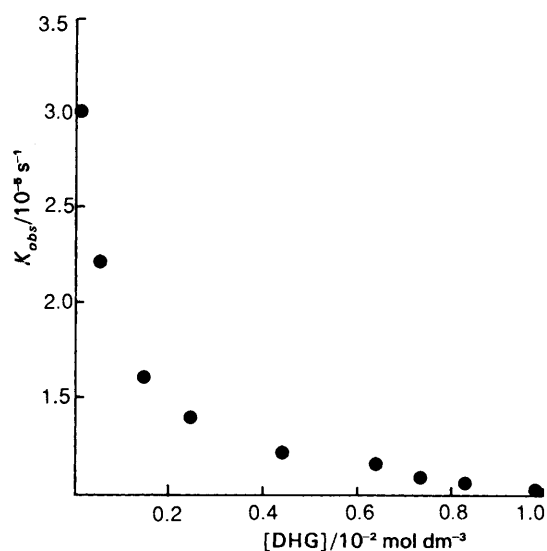


Figure 3. Reaction of (1) with 0.05 mol dm⁻³ NaOH in the presence of DHG.

with 0.05 mol dm⁻³ NaOH in the presence of an anionic surfactant such as sodium lauryl sulphate (NaLS) shows a 'non-effect' as if either OH⁻ ions or the substrate only were in the aqueous pseudophase [$k_{\text{obs}} = (3 \pm 0.05) \times 10^{-5} \text{ s}^{-1}$]. This is compatible with the presence of anionic groups at the micellar surface.

Hence the overall inhibition of the reaction of OH⁻ with (1) in the presence of zwitterionic surfactants may signify that in the presence of zwitterionic micelles either OH⁻ ions or substrate are in the aqueous pseudophase or the micellar pseudophase.

Zwitterionic micelles are formally neutral, but coulombic interactions between micelles and free ions depend, to a high degree, upon the charge density at the micellar surface.^{10,11}

According to Bunton's model,¹² if we consider zwitterionic micelles as smooth spheres with the anionic residues extending from the quaternary ammonium centres, the charge density at the spherical surface through these cationic centres will be greater than that at the spherical surface through the anionic centres, and there will be a net attraction of anions. This 'smooth' micellar model is only an approximation because we do not know the conformation of the zwitterionic head group in the micelle, but it indicates how zwitterionic micelles could bind OH⁻, albeit weakly.

Overall inhibition of the reaction of OH⁻ with micellar bound (1) is not inconsistent with weak binding of OH⁻ by the zwitterionic micelles.

The second-order rate constant for this reaction at the surface of cationic micelles has been calculated¹³ and is lower than that in water by a factor of *ca.* 2-3 for cetyltrimethylammonium chloride, bromide, hydroxide, didodecyldimethylammonium chloride, and ditetradecyldimethylammonium chloride, but because of the increased concentration of OH⁻ there is an overall rate increase. However, the concentration effect in zwitterionic micelles is so small¹² that the overall reaction is inhibited.

These considerations do not explain the fact that the inhibition does not stop the reaction, but (1) is hydrophobic and may bind to monomeric surfactant or small submicellar aggregates.^{14,15} Such small zwitterionic aggregates would be formally neutral and should not attract OH⁻, and the consequent inhibition should decrease as the surfactant concentration increases, micelles form and OH⁻ is attracted to their surfaces.

In the presence of both DTG and DHG there is a 'non-effect' for the reaction of (2) with 0.5 mol dm^{-3} NaOH [DTG: $k_{\text{obs}} = (2.20 \pm 0.05) \times 10^{-5} \text{ s}^{-1}$; DHG: $k_{\text{obs}} = (2.15 \pm 0.05) \times 10^{-5} \text{ s}^{-1}$], but this fact does not signify that either OH^- ions or substrate only are in the aqueous pseudophase.

The important factor underlying this difference of behaviour between (1) and (2) in the presence of zwitterionic surfactants is probably the orientation of the substrates within the micelle. In fact, for (2) the halogen leaving group is *ortho* to the carboxylate group and hence should be aligned close to the micelle-water interface.

Therefore, like the single- and twin-tailed surfactants and hydroxy-functionalized surfactants,^{8,9,13} the zwitterionic surfactants discriminate between different substrate orientations in the micellar pseudophase.

It is also of interest to note the great similarity in the catalytic activity of the two zwitterionic surfactants, DTG and DHG, for the reaction of (1) or (2) with NaOH. It therefore seems that these surfactants exhibit common behaviour independent of the structural features of their hydrocarbon chain, and that the physical-chemical properties of such colloidal systems have a great dependence on their charge distribution and the experimental conditions.

In summary, the presence of both a positive charge and a negative charge in the same molecule plays an important role in the process of aggregation of the single molecules of surfactant and in the association of charged substrates.

Experimental

Materials.—N,N-Dimethyl-N-tetradecylglycine (DTG). A mixture of sodium monochloroacetate (10 g), dimethyl-tetradecylamine (21 g), anhydrous ethanol (100 cm^3), and acetonitrile (100 cm^3) was refluxed for 40 h. The insoluble inorganic salt (sodium chloride) was removed and the filtrate was concentrated and then refluxed with anhydrous diethyl ether. Cooling produced a white solid (DTG), m.p. 158°C . The solid was crystallized from ethyl acetate and acetone and dried over phosphorus pentoxide. The purity of the DTG was tested by means of surface tension measurements: plot of surface tension *vs.* $-\log[\text{surfactant}]$ has no minimum.

N,N-Dimethyl-N-hexadecylglycine (DHG). A mixture of sodium monochloroacetate (15 g), dimethylhexadecylamine (30 g), anhydrous ethanol (150 cm^3), and acetonitrile (150 cm^3) was refluxed for 10 days. The insoluble sodium chloride was removed, the filtrate concentrated and then refluxed with anhydrous diethyl ether. Cooling produced a white solid (DHG), m.p. 205°C (anhydrous diethyl ether-anhydrous ethanol; dried over P_2O_5). The purity of the DHG was tested as for DTG.

4-Chloro-3,5-dinitrobenzoic acid (Aldrich), 2-chloro-3,5-di-

nitrobenzoic acid (Fluka), cetyltrimethylammonium chloride (Kodak), and sodium lauryl sulphate (Fluka) were commercially available.

Surface Tension Measurements.—All measurements were made with a Fisher Surface Tensiometer Model 20 using the ring method. Distilled water was used to prepare the solutions. Techniques were followed to ensure that the ring and glassware used in the measurements and preparation of the solutions were scrupulously clean. Measurements were made at $25 \pm 0.1^\circ\text{C}$ in cells thermostatted by means of a constant temperature bath. The CMC values were determined from the surface tension *vs.* $-\log[\text{surfactant}]$ curves, either in the presence or in the absence of added electrolytes.

Kinetics.—Reactions were followed spectrophotometrically at 25.0°C using a Beckman Model 35 or a Perkin-Elmer 551S spectrophotometer. All solutions of surfactants were made up using CO_2 -free, redistilled water. Substrate solutions were made up using acetonitrile. Substrate concentrations were generally *ca.* $6 \times 10^{-5} \text{ mol dm}^{-3}$ in the cell holder. Reactions of (1) were followed at 438 nm and those of (2) at 367 nm.

References

- 1 J. H. Fendler, 'Membrane Mimetic Chemistry,' Wiley-Interscience, New York, 1982.
- 2 R. A. Mackay, *Adv. Colloid Interface Sci.*, 1981, **15**, 131.
- 3 J. H. Fendler and W. Hinze, *J. Am. Chem. Soc.*, 1981, **103**, 5439.
- 4 I. M. Cuccovia, F. H. Quina, and H. Chaimovich, *Tetrahedron*, 1982, **38**, 917.
- 5 A. Cipiciani, R. Germani, G. Savelli, and C. A. Bunton, *Tetrahedron Lett.*, 1984, 3765.
- 6 J. N. Israelachvili, 'Intermolecular and Surface Forces,' Academic Press, London, 1985.
- 7 P. G. Nilsson, B. Lindman, and R. G. Laughlin, *J. Phys. Chem.*, 1984, **88**, 6357.
- 8 T. J. Broxton, J. R. Christie, and R. P.-T. Chung, *J. Org. Chem.*, 1988, **53**, 3081.
- 9 T. J. Broxton, J. R. Christie, and X. Sango, *J. Org. Chem.*, 1989, **54**, 1919.
- 10 G. Gunnarsson, B. Jonsson, and H. Wennerstrom, *J. Phys. Chem.*, 1980, **84**, 3114.
- 11 C. A. Bunton and J. R. Moffatt, *J. Phys. Chem.*, 1985, **89**, 4166.
- 12 C. A. Bunton, M. M. Mhala, and J. R. Moffatt, *J. Org. Chem.*, 1987, **52**, 3832.
- 13 A. Cipiciani and S. Primieri, unpublished results.
- 14 D. Piskiewicz, *J. Am. Chem. Soc.*, 1977, **99**, 7695.
- 15 C. A. Bunton, Y. S. Hong, L. S. Romsted, and C. Quan, *J. Am. Chem. Soc.*, 1981, **103**, 5788.

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