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Micellar Activation of Nucleophilic Cu^{2+}-complexes of Surfactant Imidazole Ligands by Co-surfactants for the Hydrolysis of *p*-Nitrophenyl Picolinate. Importance of the Charge Site on Surfactant Ligand

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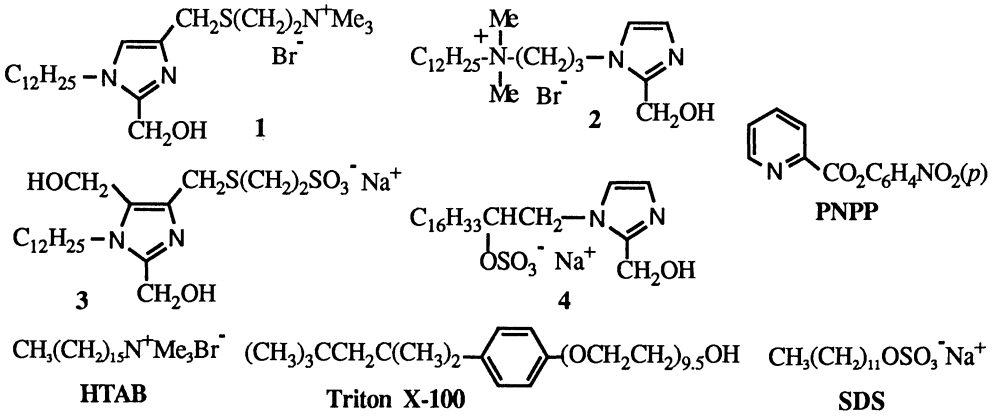
The micellar activation of the nucleophilic Cu^{2+}-complexes of four surfactant imidazole ligands has been examined for the hydrolysis of *p*-nitrophenyl picolinate. A dramatic difference in the effect of co-surfactant was observed between the ligands having a charged group at the polar terminal and those having it at the inner site apart from the imidazole head group.

Surfactant micelles have been the subjects of extensive investigations as models of enzyme proteins or as attractive reaction media.[1-3] A typical surfactant such as hexadecyltrimethylammonium bromide (**HTAB**) or sodium dodecyl sulfate (**SDS**) has a charged group at the chain terminal, and aggregates in aqueous media to form a spherical micelle with the charged groups on the micellar surface. Such a micelle can affect an ionic reaction through micellar effects, but the surfactant monomer itself is normally unreactive. On the other hand, there have been known a number of functional surfactants which directly participate in a reaction as a reagent or a catalyst.[1,3] Structurally, such functional surfactants may be classified into two classes. In the first class, a charged group occupies the terminal of the surfactant chain with a functional group inside. Conversely, in the second class, a functional group occupies the terminal with a charged group inside. In both classes, a spacer unit connects the functional and the charged groups. From a reactivity viewpoint, however, information is very limited which rationalizes such classification. We now report herein an example which shows a remarkable difference in reactivity between these two classes of functional surfactants.

Four surfactant imidazole ligands **1-4** were examined for their nucleophilic reactivities toward *p*-nitrophenyl picolinate (**PNPP**) in the presence of Cu^{2+} and in co-micellar solutions of three surfactants, **HTAB**, **SDS**, and non-ionic **Triton X-100** at pH 7 and 25 °C. A pair of cationic **1** and anionic **3**, and another pair of cationic **2** and anionic **4** are class 1 and class 2 surfactants, respectively.



Ligand **1** has been newly prepared in this study,[4] while the other three ligands were reported previously.[5,6] All the ligands have a 2-hydroxymethyl group which acts as a potent nucleophile when complexed with Cu^{2+}, as established in the previous model studies on hydrolytic metalloenzymes.[5-8] The kinetic measurements were carried out by dissolving **PNPP** in a buffered co-micellar solution of a ligand with a main surfactant. The pseudo-first-order rate constants (k_{obsd}) were then determined as usual by monitoring the release of *p*-nitrophenolate anion at 400 nm by using a stopped-flow spectrophotometer.

Figure 1 shows the observed dependency of k_{obsd} on Cu^{2+} concentration measured in **HTAB** micelles. Here, the **HTAB** monomer concentration was 100 times larger than the ligand concentration. As can be seen from the figure, a remarkable rate increase was observed for all the ligands with increasing Cu^{2+} concentration.[9] Interestingly, however, the curve for the ligand **4** was very different from those for the other ligands. Three saturation curves for the latter seem to be normal and were analyzed based on the rate equations which assume a 2:1 ligand/Cu^{2+} complex as reported previously.[5-8] The former curve seems to be unusual, i.e. a rate maximum was seen at $[Cu^{2+}]=1/2[\mathbf{4}]=0.5\times10^{-4}$ mol dm^{-3}, then the rate dropped sharply when Cu^{2+} became equimolar to the ligand. Similar results, as

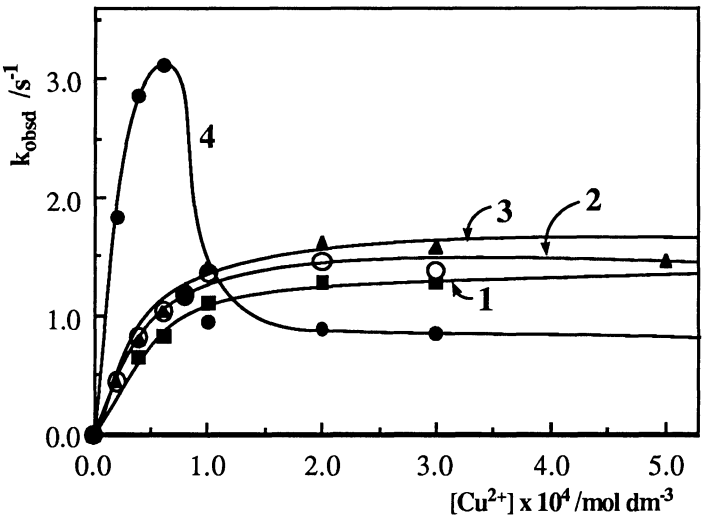


Fig. 1. Plots of pseudo-first-order rate constants *vs.* Cu^{2+} concentration for the hydrolysis of **PNPP** in **HTAB** micelles, [Ligand]=1.0×10^{-4}mol dm^{-3}, [**HTAB**]=1×10^{-2}mol dm^{-3}, [**PNPP**]=2.0×10^{-5}mol dm^{-3}, 25 °C, pH 7.0(2,6-lutidine/HNO_3 buffer 0.1 mol dm^{-3}, μ=0.1 mol dm^{-3}(KNO_3)). The numbers in the figure refer to ligands.

regards both the shapes of saturation curves and the magnitudes of activity, were observed for **Triton X-100** micelles.

Another set of results observed for **SDS** micelles is shown in Fig. 2. For ligands **1** and **3**, both the curve shapes and the net activities were almost the same as those observed for **HTAB** micelles (Fig.1). However, a large rate reduction took place with ligand **2**. In contrast, for ligand **4** the rate reduction after the maximum was much smaller than that in **HTAB** micelles (Fig. 1).

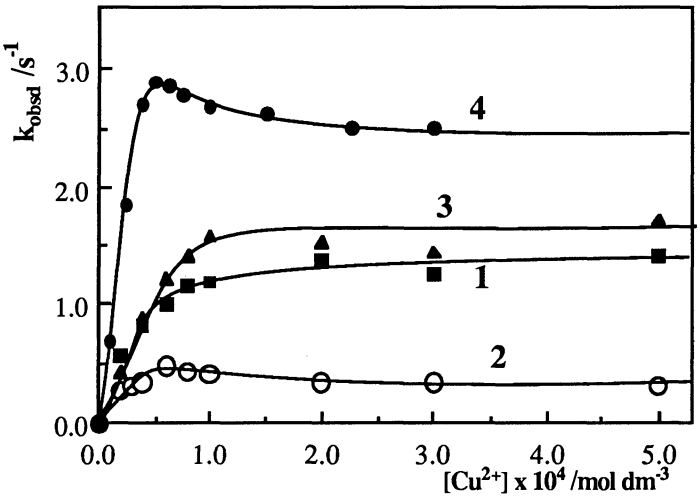


Fig. 2. Plots of pseudo-first-order rate constants *vs.* Cu^{2+} concentration for the hydrolysis of **PNPP** in **SDS** micelles, [ligand]=1x10^{-4}mol dm^{-3}, [**SDS**]=1x10^{-2}mol dm^{-3} and [**PNPP**] =2x10^{-5}mol dm^{-3}. The numbers in the figure refer to ligands. See Fig. 1 for other conditions.

The above mentioned observations clearly indicate that the effect caused by changing a co-surfactant from **HTAB** to **SDS** on the activity (rate) is small for ligands **1** and **3** which are classified as class 1 surfactants, whereas the effect is remarkably large for ligands **2** and **4** which are classified as class 2 surfactants. What is the origin of such a difference? It is a difficult question to answer at the present stage of investigation. Yet the followings are conceivable and worthy of discussions. In the present systems, the active site in each ligand is the moiety of 2-hydroxymethylimidazole complexed with Cu^{2+}, and the charged group may be located in the micellar surface. If such is the case, the active site of each ligand, **1** or **3**, is located beneath the micellar surface, while that of each ligand, **2** or **4**, is located above the micellar surface. Thus, the active sites of the former ligands are relatively inert to the change of microenvironment occurring in the micellar surface. Whereas those of the latter ligands should be relatively sensitive to such change. In the case of **4** in **HTAB** micelles, its unusual saturation curve can be accounted for by postulating a series of events which occur along with the increase of Cu^{2+} concentration as illustrated in Fig. 3. That is, **4** exists as an ion-pair with **HTAB** in the absence of Cu^{2+}, then this ion-pair forms a 2:1 ligand/Cu^{2+} complex, and this complex is further transformed into another complex in which two negative charges of ligands are bound to a second Cu^{2+} in place of two **HTAB** positive ions. Although the reason why the former complex should be more active than the latter is not easy to explain, it is conceivable that the salt bridge by Cu^{2+} in the latter complex deforms its active conformation. Similar transformation in the complex structures can also be considered in **Triton X-100** micelles, although the counter cation (Na^{+}

or K^+) is different. On the other hand, such a bridged complex of **4** in **HTAB** micelles should be less important in **SDS** micelles because of competing salt formation between Cu^{2+} and **SDS**. The rate reduction in the case of **2** in **SDS** micelles may also be ascribed to the ion-pairing between the ligand and the surfactant molecules which results in either the change of microenvironment or the deformation of the active complex conformation.

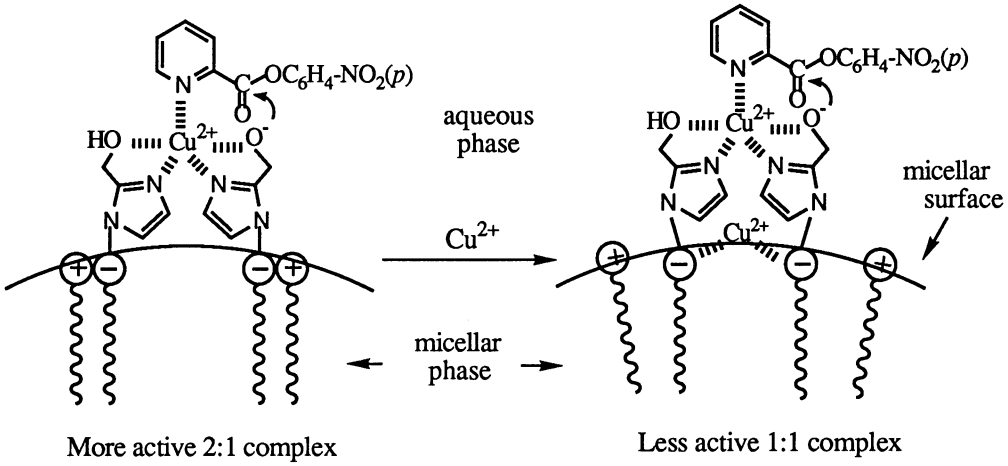


Fig. 3. Oversimplified picture to account for the change of activity of Cu^{2+}/ligand **4** complexes in **HTAB** micelle.

Obviously much are left to be clarified, in particular such information as to support the structures proposed in Fig. 3 is required. Nevertheless, the above mentioned findings and classification appear to present a new insight into the micellar reaction.

References

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9) The rates in the absence of Cu^{2+} and a ligand were 1.9×10^{-5} (**HTAB**), 1.0×10^{-5} (**SDS**), and 1.5×10^{-5} s^{-1} (**Triton X-100**), respectively.

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