Rate-enhancing Multi-site Interaction in the Hydrolysis of a Cationic Ester Catalysed by a Cu^{2+} Complex of an Anionic Surfactant Ligand in Anionic Sodium Dodecyl Sulfate Micelles

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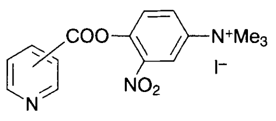
The rate of hydrolysis of 2-nitro-4-trimethylammoniophenyl 2-picolinate is remarkably enhanced when catalysed by a Cu^{2+} complex of surfactant imidazole ligand possessing 2-hydroxymethyl and anionic charged groups in the co-micelles of sodium dodecyl sulfate; the rate enhancement is discussed in terms of multi-site interaction in the formation of a reactive ternary complex.

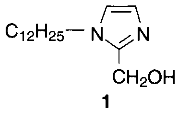
We have been interested in the design of highly active models of hydrolytic metalloenzymes.[1–3] Our previous studies have disclosed that a Zn^{2+} or Cu^{2+} complex of a lipophilic or surfactant imidazole ligand having a metal ion-chelating 2- or 4-hydroxymethyl group becomes a highly active catalyst for the hydrolysis of aryl 2-picolinates when co-micelled with an appropriate non-functional surfactant.[1,2] We now report that a remarkable rate enhancement occurs when the hydrolysis of an ester substrate having a positively charged group is catalysed by a Cu^{2+} complex of a surfactant ligand having a negatively charged group in sodium dodecyl sulfate (SDS) co-micelles. The importance of electrostatic interactions between a substrate and a nucleophile in micellar reactions is already known,[4,5] but information is still very limited, in particular for the micellar models of hydrolytic metalloenzymes.

The ester substrates examined were isomeric 2-nitro-4-trimethylammoniophenyl 2-picolinate (**2-TMP**), 3-picolinate (**3-TMP**) and 4-picolinate (**4-TMP**). The ligands examined were neutral (**1**),[1] cationic (**2**)[2] and anionic (**3** and **4**).[2] The non-functional co-micellar surfactants used were anionic SDS and cationic hexadecyltrimethylammonium bromide (HTAB)

The rates of hydrolysis were determined by the spectrophotometric observation of the release of 2-nitro-4-trimethylammoniophenol. The spontaneous rates at pH 7.05 (25 °C) were quite slow for all esters. The rates of alkaline hydrolysis in the absence of any other catalytic species at pH 10.3 (25 °C) were as follows: **2-TMP**, 0.265; **3-TMP**, 0.0299; **4-TMP**, 0.251 s^{-1}. The kinetics for the catalysed reaction were studied by adding an ester substrate to a mixture of a ligand and Cu^{2+} in the micelles of co-surfactant. The aggregation number of monomers needed to form a SDS or HTAB micelle is known to be less than 100, presumably around 60.[5] Therefore, a micelle contains less than one ligand on average and the microenvironment of the catalyst should be largely governed by the co-micelles.



2-, 3- and 4-TMP



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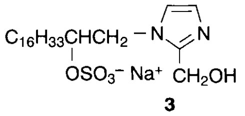

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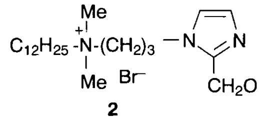

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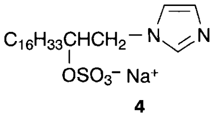

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$Me(CH_2)_{11}OSO_3^- Na^+$
SDS

$Me(CH_2)_{15}N^+Me_3 Br^-$
HTAB

As shown in Fig. 1, the pseudo-first-order rate constants (k_{obs}) obtained by using the co-micellar solutions of anionic ligand **3** and anionic SDS increased with increasing concentration of Cu^{2+} up to a saturation level which was far larger than those of the other systems. The necessity of the 2-hydroxymethyl group for high ligand activity is clearly indicated by the low activity of the **4**·Cu^{2+} complex. As for the substrate, the 2-picolinyl function is essential for high activity as evidenced by the rates of three esters in the presence of Cu^{2+} (1×10^{-4} mol dm^{-3}) and **3** (1×10^{-4} mol dm^{-3}), *i.e.* **2-TMP**, 5.68; **3-TMP**, 3.3×10^{-5} and **4-TMP**, 2.58×10^{-4} s^{-1}.

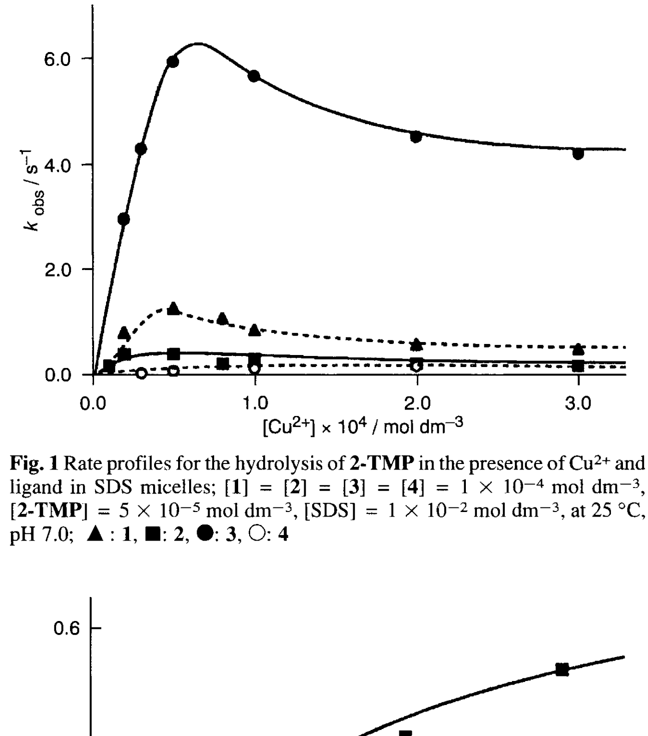

Fig. 1 Rate profiles for the hydrolysis of **2-TMP** in the presence of Cu^{2+} and ligand in SDS micelles; [**1**] = [**2**] = [**3**] = [**4**] = 1×10^{-4} mol dm^{-3}, [**2-TMP**] = 5×10^{-5} mol dm^{-3}, [SDS] = 1×10^{-2} mol dm^{-3}, at 25 °C, pH 7.0; ▲ : **1**, ■: **2**, ●: **3**, ○: **4**

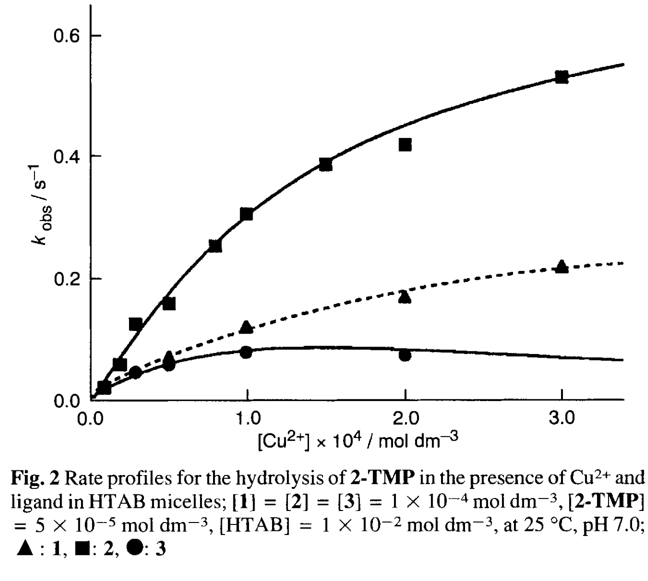

Fig. 2 Rate profiles for the hydrolysis of **2-TMP** in the presence of Cu^{2+} and ligand in HTAB micelles; [**1**] = [**2**] = [**3**] = 1×10^{-4} mol dm^{-3}, [**2-TMP**] = 5×10^{-5} mol dm^{-3}, [HTAB] = 1×10^{-2} mol dm^{-3}, at 25 °C, pH 7.0; ▲ : **1**, ■: **2**, ●: **3**

Similar kinetics to those indicated in Fig. 1 were observed by using HTAB co-micelles. As can be seen in Fig. 2, the activity of **3** in these co-micelles was reduced *ca.* 1/20–1/60 fold compared to that in SDS co-micelles at rate saturation. It can also be seen that the activities of **1** and **2** were essentially the same in the two co-micelles.

It is likely that a surfactant ligand posessing a charged group forms a tight amphiphilic ion pair[6] with a co-micellar surfactant having an opposite charge, as for the pairs **2**·SDS and **3**·HTAB. Such an ion pair may lose flexibility on the surface of the micellar Stern layer in order to adopt a favourable geometry in forming a ternary complex for catalysis with Cu^{2+} and substrate, and this may be why **2** in Fig. 1 and **3** in Fig. 2 show only low activity.

For efficient micellar catalysis to occur, it is necessary to incorporate a substrate onto the micellar surface, which is expected for a cationic substrate such as **2-TMP** in anionic SDS micelles. However, substrate incorporation alone is not sufficient to explain such high activity of **3** in SDS co-micelles, since neutral **1** is less active. Therefore, it seems to be important that the anionic charge of **3** is left free in the SDS micelle because of charge repulsion. It is possible to construct a CPK molecular model for an intermediate ternary complex as illustrated in Fig. 3.

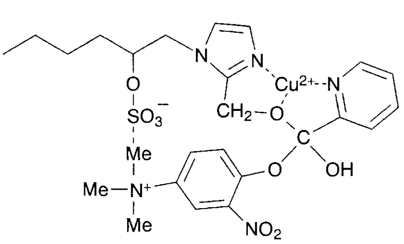

Fig. 3 Proposed structure of the ternary complex of **3**-Cu^{2+}–**2-TMP** in SDS micelles

It is quite reasonable to expect that electrostatic ion pairing between a negatively charged ligand and a positively charged substrate reduces the activation energy to form such a tetrahedral addition intermediate. Thus, the observation of a multi-site interaction in forming a reactive complex for the design of an efficient model of hydrolytic metalloenzymes, is important.

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