CHEMISTRY LETTERS, pp. 2289-2292, 1987.

Acyl Transfer Reaction Catalyzed by Cu^{2+} Ion Complex of a Lipophilic Hydroxyimidazole-ligand in AOT Reverse Micelles. Effects of Change of Core Solvent from Water to DMF

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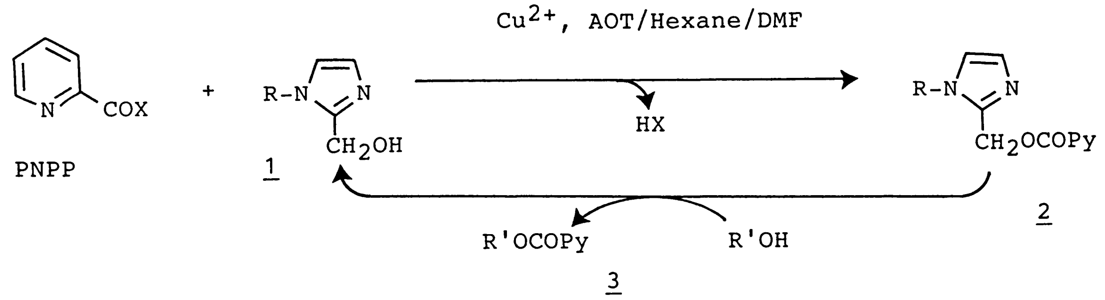
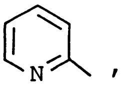
The transfer of acyl group of p-nitrophenyl picolinate to alcohol acceptors has been investigated kinetically in AOT reverse micelles using hexane and DMF as the bulk and the core solvents, respectively. The reaction was found to be remarkably catalyzed by a 1:2 complex of Cu^{2+} ion and N-dodecyl-2-hydroxymethylimidazole ligand involving the acylated ligand as the intermediate. It was also observed that the reaction in the reverse micelles was much faster than that in pure DMF.

Sodium 1,2-bis(2-ethylhexyloxycarbonyl)-1-ethanesulfonate (AOT) is known to solubilize water in hydrocarbon solvents to form reverse micelles, in which water is entrapped in the micellar core as water pool.[1-5] This water pool has attracted much attentions as the model of polar media of enzyme active sites.[1] However, the informations are relatively limited as for the model catalysis of functional groups such as imidazole or hydroxyl groups in such water pools.[1,6] Recently, we reported that the hydrolysis of p-nitrophenyl picolinate (PNPP) is remarkably catalyzed by a Cu^{2+} ion complex of N-dodecyl-2-hydroxymethylimidazole (1) in AOT/hexane/water reverse micelles.[7] By using the same system, we also examined a possibility of acyl group transfer from 1 to certain alcohol acceptors. However, the hydrolysis was the predominant reaction. We now wish to report that the water pools can be replaced by dimethylformamide(DMF) pools, retaining advantageous micellar effects for rate acceleration. Furthermore, as expected, this novel system allows the acyl group transfer to certain alcohol acceptors via the acylation of ligand 1. To the best of our knowledge, there has been no precedent in the literature for use of DMF or related polar solvents as the core solvent in the reactions in AOT reverse micelles.

The outline of the present reaction system is shown in Scheme 1. In the absence of DMF and AOT, the copper salt ($Cu(NO_3)_2$) is practically insoluble and the substrate (PNPP) is also hardly soluble in hexane. The reaction kinetics were carried out by mixing a 15μl of PNPP benzene stock solution with a 3 ml of reverse micellar solution of hexane containing desired concentrations of Cu^{2+} ion and ligand 1. The rates of reaction were measured by monitoring the release of p-nitrophenol spectrophotometrically (310 nm) according to the previous methods.[7,8]



Scheme 1. R=$C_{12}H_{25}$, Py=  , X=$OC_6H_4NO_2$(p) , R'=CH_3 , $HOCH_2CH_2$

As shown in Fig. 1, the pseudo-first-order rate constants (k_{obsd}) increased with increasing AOT concentration to give two curves A and B. The curve A was obtained in the presence of constant concentration of DMF (0.1 mol/dm^3);[9] the rate in the absence of AOT(intercept) increased 3.3 fold at the maximum by adding AOT, then decreased by further AOT addition. This rate maximum suggests the presence of an optimum value in [DMF]/[AOT] ratio (≃2). The curve B shows a saturation of rate increase which was obtained by maintaining the [DMF]/[AOT] ratio (=1) constant. When water is the solvent, it is considered that the size of water pools in the micellar core is determined by [Water]/[AOT] ratio,[1-5] and the micelle concentration is equal to that of AOT divided by the aggregation number. If this holds true also in the present case of DMF, the saturation curve B can be accounted for by assuming the saturation of substrate incorpora-

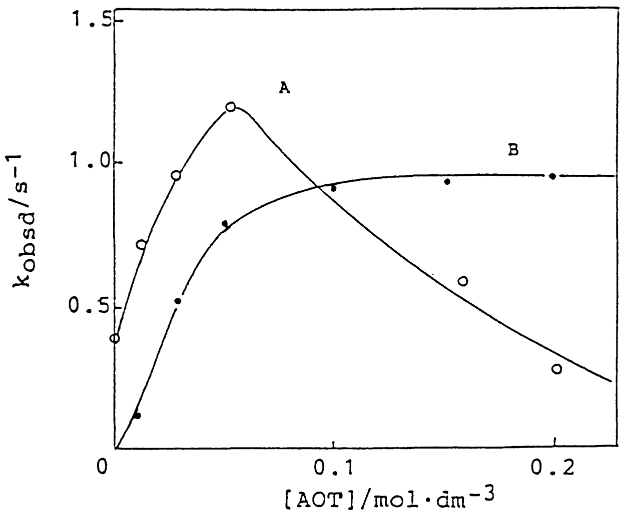


Fig. 1. Dependence of the pseudo-first-order rate constants on AOT concentration at 25 °C. $[Cu^{2+}]=1\times10^{-4}$ mol·dm^{-3}, $[\underline{1}]=2\times10^{-4}$ mol·dm^{-3}, $[PNPP]=5\times10^{-5}$ mol·dm^{-3} : A, [DMF]=0.1 mol·dm^{-3}; B, [DMF]/[AOT]=1.

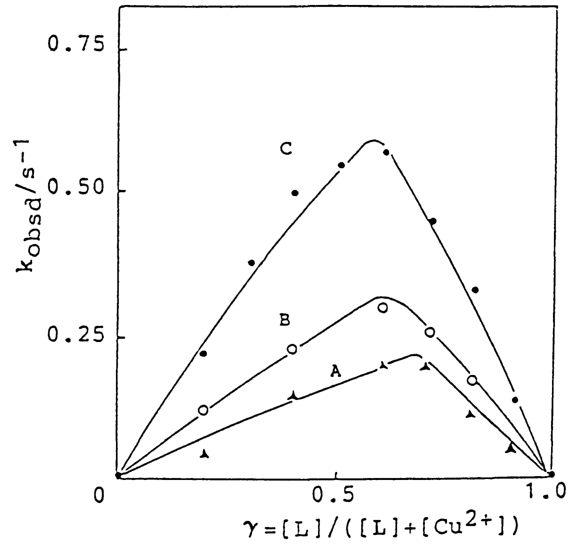


Fig. 2. Job plots for the hydrolysis of PNPP at 25 °C. $([\underline{1}]+[Cu^{2+}])=5\times10^{-4}$ mol·dm^{-3}, $[PNPP]=5\times10^{-5}$ mol·dm^{-3} : A, in DMF; B, [AOT]= 0.05 mol·dm^{-3}, [DMF]=0.05 mol·dm^{-3} in hexane; C, [AOT]=0.05 mol·dm^{-3}, [DMF]=0.227 mol·dm^{-3} in hexane.

tion into micelles, in which the rate is much faster than in the bulk hexane/DMF mixed solvent.

In order to see the composition of the active complex for catalysis, the kinetic version of Job plots were examined as shown in Fig. 2. The figure shows clearly that both ligand and Cu^{2+} ion are necessary for higher rates. The plots for non-micellar reaction (A), obtained in the absence of AOT and in pure DMF, indicate that the maximum rate is attained at $\gamma=0.67$ which implies a 2:1 complex of ligand and Cu^{2+} ion being the active complex for the catalysis. The rate maximum for the other two plots for the micellar reactions (B and C) are found in between $\gamma=0.5$ and 0.67. The former $\gamma=0.5$ corresponds to a 1:1 complex of ligand and Cu^{2+} ion as the active complex. Thus, it is likely that both 1:1 and 2:1 complex are active in the present reaction systems, although the latter is predominating in non-micellar DMF solution. Whatever the details, it is important to notice that a polar reaction such as the present one is faster in hexane containing only 50-227 mmol/dm^3 DMF than in pure DMF. That may be accounted for as a concentration effect. Namely, as implied in Fig. 1B, the substrate (PNPP) and the reagent (ligand 1) are incorporated and concentrated in much smallar volume of reverse micelles than that of bulk hexane, resulting in an enhanced rate of second-order reaction.

The results in Figs. 1 and 2 were obtained by using an excess ligand over the substrate, so that they do not tell anything about the intermediate 2 or about the acyl transfer step (Scheme 1). In Fig. 3 are shown the kinetic results obtained under the conditions of an excess substrate over the ligand. The curve A indicates that in the absence of added alcohol acceptor, the reaction stops after the liberation of one mole of p-nitrophenol corresponding to the amount of ligand, leaving excess substrate unreacted. The acylated product 2 was detected quantitatively by HPLC analysis. On the other hand, the reaction proceeds further in the presence of alcohol acceptors (B,C,E, F). The curves B and C obtained in the presence of methanol are of typical biphasic burst kinetics. Such curves can be accounted for by a rapid acylation of the catalyst hydroxyl group followed by a relatively slow transacylation to the added acceptors (alcohol and water).

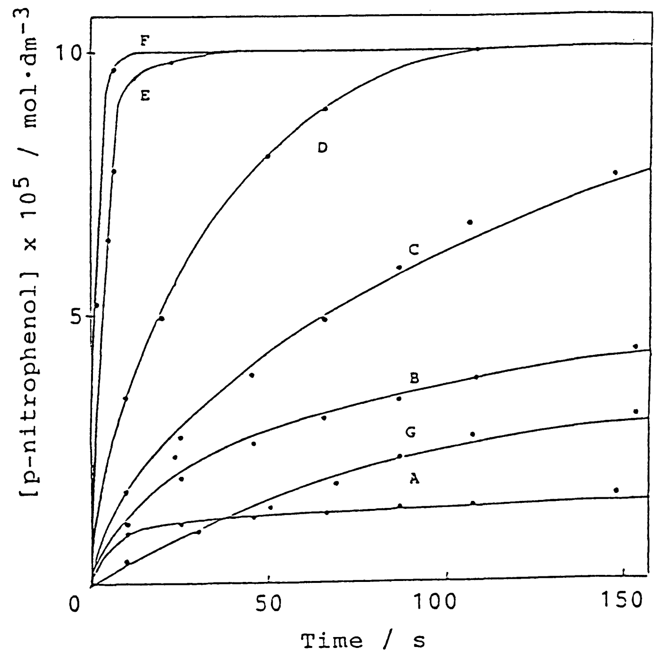


Fig. 3. Burst kinetics for the "alcoholysis" of PNPP in hexane at 25 °C. [AOT]=0.025 mol·dm^{-3}, [DMF]=0.05 mol·dm^{-3}, [Cu^{2+}]=1x10^{-4} mol·dm^{-3}, [1]= 1x10^{-5} mol·dm^{-3}, [PNPP]=1x10^{-4} mol·dm^{-3} : A, no alcohol acceptor; B, [CH_3OH]=2.5x10^{-2} mol·dm^{-3}; C, [CH_3OH]=5.0x10^{-2} mol·dm^{-3}; D, [$(CH_2OH)_2$]=1.3 x10^{-2} mol·dm^{-3}, no ligand; E, [$(CH_2OH)_2$]=1.3x10^{-2} mol·dm^{-3}; F, [$(CH_2OH)_2$]=2.6x10^{-2} mol·dm^{-3}, G, [CH_3OH]=2.5x10^{-2} mol·dm^{-3}, no ligand.

[10,11] The reaction was very rapid in the cases of 1,2-ethanediol (E,F). Even in the absence of ligand, the reaction occurred rapidly (D). However, the comparison of curves D and E indicates that the reaction is much faster in the presence of ligand than in its absence. It is likely that the reactivity of 1,2-ethanediol is enhanced through the chelation with Cu^{2+} ion. In the case of methanol and 1,2-ethanediol, the final acyl transfer products 3 could be isolated quantitatively. In the latter diol, the only product detected was the monoacylated one.

Further works are in progress to examine the possibilities of applying the above system for organic synthesis such as ester exchange reactions.

This work was partly supported by Grant-in Aid from the ministry of education, Science and Culture in Japan.

References

1) J. H. Fendler, "Membrane Mimetic Chemistry," Wiley, New York (1982).
2) A. Kitahara, Adv. Colloid Interface Sci., 12, 109 (1980).
3) M. Zalauf and H. F. Eicke, J. Phys. Chem., 83, 480 (1979).
4) P. L. Luisi and B. Straub, "Reverse Micelles-Technological and Biological Relevance," Plenum, New York (1980).
5) F. M. Menger, J. A. Donohue, and R. F. Williams, J. Am. Chem. Soc., 95, 286 (1973).
6) K. Kon-no and A. Kitahara, J. Colloid Interface Sci., 67, 477 (1978).
7) T. Fujita, O. Tanaka, K. Ogino, and W. Tagaki, 52th National Meeting of The Chemical Society of Japan, Kyoto, April, 1986, Abstr. II, 1172, to be published in a full paper.
8) T. Eiki, M. Mori, S. Kawada, K. Matsushima, and W. Tagaki, Chem. Lett., 1980, 1431.
9) The maximum solubility of DMF in hexane was determined to be 0.59 mol/dm^3 (25 °C) by NMR and UV-turbidity methods.
10) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York (1969).
11) M. L. Bender and T. M. Marshall, J. Am. Chem. Soc., 90, 201 (1968).

(Received September 14, 1987)