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Reactions of Amino Acid Decyl Esters with Nucleophiles Catalyzed by Polymer-Supported Amine–Metal Complexes

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The reactions of alanine decyl ester (AlaODc) with nucleophiles were catalyzed by a crosslinked polystyrene-supported ethylenediamine–copper(II) ion complex (Cu en-PS) under toluene/resin two-phase conditions or toluene/aqueous buffer/resin three-phase conditions. In the two-phase reactions with octylamine, the rate was increased with a decreasing metal content of the resin. The catalytic efficiency was also dependent on other factors, that is, metal ion, ligand structure, and substrate structure. In the three-phase reactions with water, the hydrolysis was very fast when acetate ions were present in the aqueous phase. It has been suggested that the reactions proceed via a substrate-coordinated intermediate complex under both conditions.

Polymer-supported catalysts have potential merits for synthetic purposes.[1—3] Compared with the corresponding soluble catalysts, they often show an improved stability and a preferable activity. They are easily separated from reaction mixtures and are reusable. We have studied polymer-supported quaternary salts and have clarified the relationship between the state and the nucleophilic reactivity of the immobilized onium salts under two-phase conditions.[4—6] The hydrophobic–hydrophilic balance and other structural factors have been supposed to be very important for triphase catalysis of these catalyst polymers.[7—10]

On the other hand, there have been much research on polymer-supported metal complexes,[11] most of which concern the catalytic activity for oxidation–reduction reactions or organometallic reactions.[12] However, little attention has been given to their catalytic activity as Lewis acids. It is well-known that certain metalloenzymes such as carboxypeptidase have a coordinated metal ion at the active site, which is often surrounded by a hydrophobic environment.[13] Therefore, it is of interest to investigate the catalytic efficiency of metal ions as Lewis acids when the ions are supported by hydrophobic polymers in the form of metal complexes.

In this article, we study the reactions of water-insoluble amino acid decyl esters with some nucleophiles, such as alkylamines, using crosslinked polystyrene-supported diamine–metal complexes as immobilized Lewis catalysts. The reactions were done under organic/resinous two-phase conditions or under organic/aqueous/resinous three-phase conditions; the latter conditions were usually used for conventional triphase catalytic reactions. We show that the polymer complexes have good to excellent catalytic activity, depending on the reactions and on the catalyst structure. The factors determining the catalytic activity are examined in detail.

Experimental

Materials and Equipment: All the materials, unless otherwise indicated, were obtained commercially (guaranteed reagent grade) and used without further purification. Organic solvents were used after distillation. Whatman Co., Ltd., LK-5F silica gel-coated glass plates were used for TLC analyses. The gas chromatogram was obtained by Hitachi 263-30 gas chromatogram equipment with an FID detector. IR spectra were measured with a JASCO IRA-1 spectrometer. NMR spectra were recorded at 40 °C using a JEOL EX-270 spectrometer.

Synthesis of Polystyrene-Supported Ethylenediamine (en-PS): To 2 g of commercial chloromethylated polystyrene beads (1.00 mmol Cl/g resin, 1% crosslinked by divinylbenzene, 200—400 mesh, Eastman Kodak Co., Ltd.), placed in a 50-ml screw-capped test tube, 10 ml of distilled 1,4-dioxane was added and left for 30 min at 90 °C. 1,4-Dioxane solution of ethylenediamine (4.5 mmol in 10 ml 1, 4-dioxane) was then added and left for at least 50 h at 90 °C in a nitrogen atmosphere. The product en-PS was filtered and washed with 1,4-dioxane (3 times), methanol (3 times), deionized water (3 times), and methanol (3 times). The resin was dried under reduced pressure. The degree of ring substitution was measured by pH titration of unreacted ethylenediamine in the filtrate of the reaction mixture and elemental analyses of the resin. Resins containing diethylenetriamine (dien-PS), tetramethylenediamne (ten-PS), or hexamethylenediamine (hen-PS) were synthesized in the same manner. Characterizations of these resins are summarized in Table 1.

Synthesis of Polystyrene-Supported Cu(II)–Eth-

Table 1. Characteristics of Polymer Complexes

Catalysts	Nitrogen content mmol g^{-1}	Metal content[c)] mmol g^{-1}	Color of dry resin	N/M^{2+} ratio
Cu en-PS	2.0[a)]	0.43	Green	4.7
Cu dien-PS	2.9[b)]	1.14	Deep green	2.5
Cu ten-PS	2.0[a)]	0.53	Pale green	3.8
Co en-PS	2.3[b)]	0.38	Greenish blue	6.0
Co dien-PS	2.6[b)]	0.71	Deep blue	3.7
Zn en-PS	2.5[b)]	1.08	White	2.3
Zn dien-PS	2.5[b)]	1.16	White	2.2

a) Determined by amine titration. b) By elemental analyses. c) By EDTA titration.

ylenediamine Complex (Cu en-PS): To 200 mg of en-PS swollen with 10 ml of 1,4-dioxane, was added copper(II) chloride dihydrate (0.68 g, 2.0 mmol) dissolved in 10 ml of methanol. The reaction mixture was left at room temperature overnight. The resin was filtered and washed with 1,4-dioxane (3 times), methanol (3 times), deionized water (3 times), and methanol (3 times). The resin was dried under reduced pressure. The degree of metal ion content of the resin was measured by EDTA titration of the copper(II) ion remaining in the reaction solution. Copper(II) complex of dien-PS or ten-PS (Cu dien-PS or Cu ten-PS, respectively) was prepared in the same procedure. Cobalt(II) complex of en-PS or dien-PS (Co en-PS or Co dien-PS) was synthesized from the corresponding resin and cobalt(II) chloride hexahydrate. Zinc(II) complex of en-PS or dien-PS (Zn en-PS or Zn dien-PS) was prepared from the corresponding resin and anhydrous zinc(II) chloride. Characterizations of these complexes are also summarized in Table 1.

Synthesis of Alanine Decyl Ester (AlaODc): To 30 ml of benzene in a 100-ml round bottom flask, were added 1.78 g (20 mmol) of DL-alanine, 3.17 g (20 mmol) of distilled 1-decanol, and 5.17 g (30 mmol) of *p*-toluenesulfonic acid monohydrate. The flask was equipped with a Telfon® plug-sealed mechanical stirrer and with a Dean–Stark trap. The reaction mixture was refluxed with vigorous stirring. The mixture turned into a homogeneous solution after 8 h. The solvent was evaporated under reduced pressure and the residue was suspended in about 100 ml of hexane. The suspension was left at 4 °C overnight and the solid product was filtered out. *p*-Toluenesulfonate of alanine decyl ester was isolated as a white solid. The salt was washed several times with hexane to remove unreacted 1-decanol. It was then dissolved in toluene and washed with dilute aqueous sodium hydrogencarbonate (3 times) and water (3 times). During this treatment an emulsion was formed. The washing was separated by adding sodium chloride. The organic phase was then dried with $MgSO_4$ and the solvent was removed under reduced pressure. Alanine decyl ester was obtained as a colorless oil. The structure was confirmed by spectroscopic methods.

IR (neat); 3300 (ν_{N-H}), 2920 (ν_{C-H}), 1720 ($\nu_{C=O}$) cm^{-1}. ^{1}HNMR (270 MHz, $CDCl_3$) $\delta=0.85$ (t, 3H), 1.2—1.4 (m, 19H), 2.6 (t, 2H), 3.55 (q, 1H), 4.1 (m, 2H).

Decyl esters of glycine, 2-aminopropionic acid (β-alanine), 3-aminobutyric acid, and 6-aminohexanoic acid were also synthesized by a similar method.

The Reaction of Alanine Decyl Ester with Amines Catalyzed by Polymer Complexes (Two-Phase Reactions): To a 50-ml screw-capped test tube, a polymer catalyst containing 25 µmol of metal ion was added and swollen with 1 ml of toluene containing AlaODc (100 µmol/1 ml) and pentadecane, as a GC internal standard. The reaction mixture was stirred at 90 °C for 30 min and to this mixture 1 ml of toluene solution of reactant amine was added. Conversion of AlaODc was measured by monitoring the formation of 1-decanol using GC; column, PEG-20M 5 mmϕ × 2 m, column temperature 170 °C, injection temperature 250 °C, detector FID.

The Reactions of AlaODc in Organic/Aqueous/Resin Three-Phase Conditions (Three-Phase Reactions): To a 50-ml screw-capped test tube was added a polymer catalyst containing 25 µmol metal ion and this was swollen with 1 ml of toluene containing pentadecane. To this mixture, 2 ml of an aqueous buffer solution was added and stirred at 90 °C for 30 min. The hydrolysis reaction was started by adding AlaODc toluene solution (100 µmol/1 ml). The conversion of AlaODc was measured by monitoring the formation of 1-decanol by GC.

Results

Two-Phase Reactions: Nitrogen contents, metal ion contents, and colors of typical catalyst resins are summarized in Table 1. The contents of Zn(II) were higher. Dien-PS resin tended to support more metal ions than en-PS resins.

At first we examined the catalytic activity of Cu en-PS under two-phase conditions. The catalytic efficiency was evaluated for the ester-amide exchanges of AlaODc with three amines. The reactions were started by adding a toluene solution of an amine to the suspension of the catalyst resin which was pre-swollen by a toluene solution of AlaODc. The mixing of AlaODc solution with Cu en-PS induced color change of the resin from green to blue, while no 1-decanol was formed. The formation of 1-decanol was observed only after the addition of an amine. The results are shown in Table 2.

The reactions did not take place without Cu en-PS. The reaction rates depended on the structure of amines, octylamine > butylamine > 3,3-dimethyl-2-butanamine. However, the reactions did not follow either pseudo-first-order or second-order kinetics, as

Table 2. Catalytic Activity of Cu en-PS for the Reactions of AlaODc with Alkylamines and Alcohols under Two-Phase Conditions[a)]

Nucleophiles	Conversion (%)[b)]
None	0
Octylamine	74(5)
Butylamine	45(1)
3,3-Dimethyl-2-butanamine	0(0)
1-Octanol	3(0)
Benzyl alcohol	6(0)

a) Reaction conditions: catalyst; Cu en-PS 25 μmol as amount of Cu, substrate; AlaODc 100 μmol, nucleophiles 600 μmol, solvent; toluene 2 ml, GC internal standard; pentadecane 0.1 mmol, reaction temperature 90 °C. b) After 4 h. Values in parentheses represent the conversions with no resin.

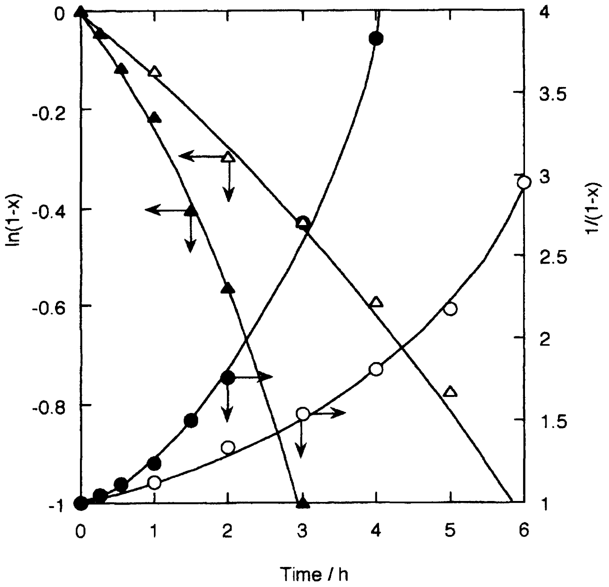


Fig. 1. The reactions of AlaODc with octylamine and butylamine. Pseudo-first-order and second-order kinetics plot. △, ○, octylamine, ▲, ●, butylamine, x, conversion of AlaODc.

shown in Fig. 1. Thus the reaction rate constants could not be calculated. The product amides were not isolated, but the formation of an amide bond was confirmed by the IR spectrum (1650 cm^{-1}) of the product mixture.

The effects of metal content of Cu en-PS are shown in Table 3. The metal content of Cu en-PS was controlled by changing the concentration of a $\mathrm{CuCl_2}$ solution reacted with en-PS. The reaction rate increased inversely with the content. Table 3 also shows the effect of ligand structure. The resin with tetramethylenediamine (Cu ten-PS) afforded a bigger rate than Cu en-PS. The metal loading of Cu ten-PS was 0.53 mmol/g-resin, which was almost the same as that of Cu en-PS (0.57 mmol/g-resin). Therefore the activity difference between Cu en-PS and Cu ten-PS is mainly due to the effect of ligand structure.

The ester-amide exchange reaction of decyl acetate with octylamine did not take place under these conditions. The conversion was only 2% even after 24 h. *N*-Acetylglycine decyl ester was found to be a little reactive (2% conversion at 4 h reaction), but its reactivity was much smaller than glycine decyl ester (61% at 4 h), the reactivity of which is comparable to that of alanine decyl ester. This indicates that a free amino group of amino acid esters is important in these catalytic reactions.

Catalytic reactions of AlaODc with alcohols were also examined. The results are also shown in Table 2. While all the reactions were very slow, Cu en-PS did catalyze the ester-exchange reaction. This is clear if compared with the reactions in the absence of catalyst. The reaction with benzyl alcohol was slightly faster than the reaction with 1-octanol.

Three-Phase Reactions: The results of two-phase reactions indicate the good catalytic activity of Cu en-PS, suggesting Cu en-PS is capable of catalyzing the hydrolysis of AlaODc. Therefore, three-phase reactions were done under toluene/aqueous buffer/resin conditions.

In the absence of metal ions, the hydrolysis did not take place even if metal-free en-PS was present. Interestingly, the rate of the reaction catalyzed by Cu en-PS increased greatly when 0.1 mol $\mathrm{dm^{-3}}$ acetic acid–sodium acetate buffer, instead of deionized water, was used as the aqueous phase; the conversion at 4 h of reaction time increased from 4 to 41% (Fig. 2).

The effects of other water-soluble compounds are also shown in Figs. 2 and 3. Figure 2 represents the effects of simple salts. The fastest reaction was observed when acetic acid–sodium acetate buffer was used as an aqueous phase, which was followed by sodium acetate solution. These results could not be explained by the difference of pH, indicating the kind of anion existing in the aqueous phase being important.

The hydrolysis did not take place when citric acid–sodium citrate buffer or oxalic acid–sodium oxalate buffer was used instead of acetic acid–sodium acetate

Table 3. Effects of Metal Content and Ligand Structure on the Reaction of AlaODc with Octylamine under Two-Phase Conditions[a)]

Catalyst	Metal content	Conversion
	mmol $\mathrm{g^{-1}}$	%
Cu en-PS	0.23	57
	0.43	45
	0.57	24
Cu ten-PS	0.53	80

a) Reaction conditions: catalyst; 25 μmol as amount of Cu, substrate; AlaODc 100 μmol, octylamine 600 μmol, solvent; toluene 2 ml, GC internal standard; pentadecane 100 μmol, reaction temperature 90 °C.

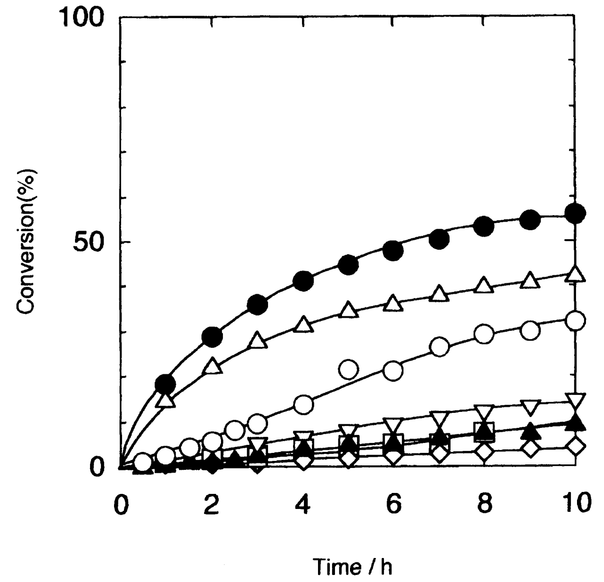


Fig. 2. Effect of aqueous phase composition for the reactions of AlaODc in three-phase reactions. Reaction conditions: catalyst; Cu en-PS containing 25 μmol Cu, substrate; AlaODc 100 μmol, organic phase; toluene 2 ml, reaction temperature; 90 °C. Aqueous phase: ●; NaOAc–AcOH buffer (pH 5), □; $NaHCO_3$–Na_2CO_3 buffer (pH 9), △; NaOAc solution (pH 8), ○; $NaNO_3$ solution (pH 6), ◇; Na_2SO_4 solution (pH 6), ▽; NaCl solution (pH 5.5), ▲; deionized water. Salt concentrations: 0.1 mol dm^{-3}.

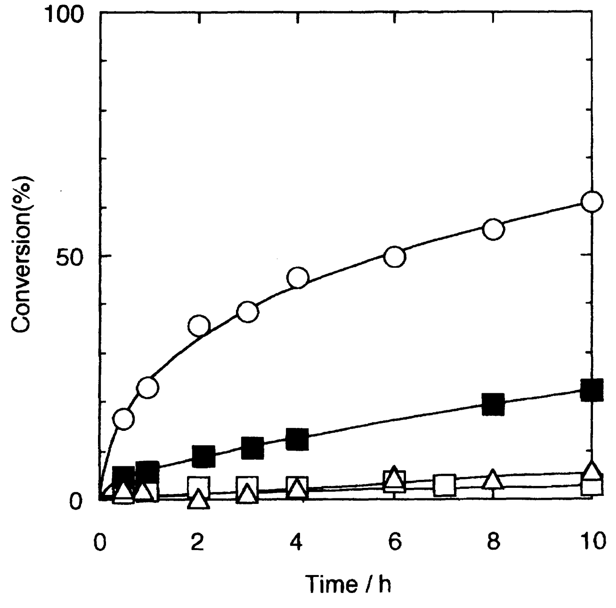


Fig. 3. The effect of the kind of carboxylates in aqueous phase. Reaction conditions: catalyst; Cu en-PS containing 25 μmol Cu, substrate; AlaODc 100 μmol, organic phase; toluene 2 ml, reaction temperature; 90 °C. Aqueous phase: ○; acetic acid–sodium acetate buffer 2 ml, △; oxalic acid–sodium oxalate buffer 2 ml, □; citric acid–sodium citrate buffer. Concentration: 0.1 mol dm^{-3} as [COOH], pH 5 (at 20 °C). ■; 0.1 mol dm^{-3} acetic acid–sodium acetate buffer (2 ml) containing 2 mmol alanine.

buffer (Fig. 3). Those did not enhance the reaction, though the pH of the aqueous phase and concentration of buffer reagent (as carboxyl group content) are the same as those of acetic acid–sodium acetate buffer. In the reactions catalyzed by Cu en-PS, the color of the resin turned from green to blue on contact with the acetic acid–sodium acetate buffer before the addition of AlaODc solution. However, the color of Cu en-PS was not changed by contact with those aqueous buffers even after 30 min, but it turned blue as soon as AlaODc was added. Figure 3 also presents the effects of alanine addition to the reaction mixture. It was found that alanine retarded the reaction in spite of the presence of acetic acid-sodium acetate buffer.

Figure 4 displays catalytic activities of Cu en-PS, Cu dien-PS, Co en-PS, Co dien-PS, Zn en-PS, and Zn dien-PS using 0.1 mol dm^{-3} acetic acid/sodium acetate buffer (pH 5.0 at 25 °C) as an aqueous phase. It was found that the catalytic activity was strongly dependent on the kind of metal ion in the resin. Cu en-PS had an activity superior to other polymer complexes, which was followed by Cu dien-PS. Co en-PS and Co dien-PS also catalyzed the reaction, but activities of these resins were apparently smaller than those of Cu(II)-containing resins. In the reaction with Co en-PS or Co dien-PS, it was found that side reactions, probably oxidations, also proceeded and both the resin and the organic phase turned brown. On the other hand, with Zn en-PS or Zn dien-PS, the reactions were very slow.

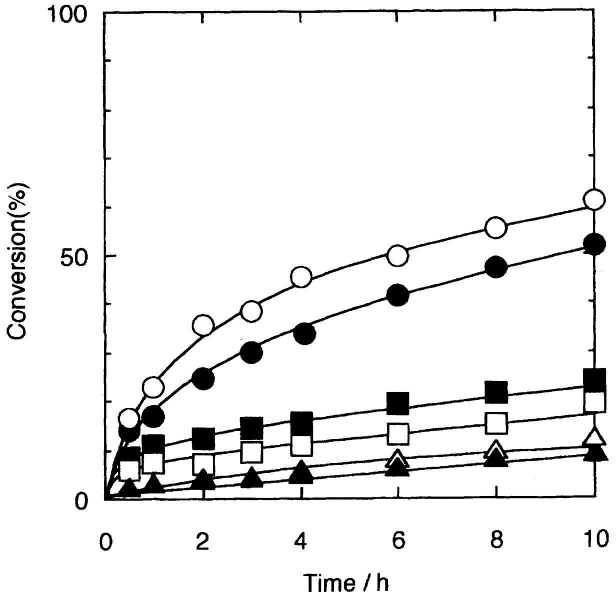


Fig. 4. Reactions of AlaODc catalyzed by polystyrene-supported metal complexes under three-phase conditions. Reaction conditions: catalyst 25 μmol as metal ion, substrate; AlaODc 100 μmol, organic phase; toluene 2 ml, aqueous phase; 0.1 mol dm^{-3} acetic acid–sodium acetate buffer 2 ml, reaction temperature; 90 °C. ○; Cu en-PS, ●; Cu dien-PS, □; Co en-PS, ■; Co dien-PS, △; Zn en-PS, ▲; Zn dien-PS.

Table 4. Effects of Metal Content and Ligand Structure on the Three-Phase Hydrolysis of AlaODc[a)]

Catalyst	Metal content	Conversion[b)]
	mmol g^{-1}	%
Cu en-PS	0.23	52
	0.27	48
	0.43	41
Cu ten-PS	0.53	56
Cu hen-PS	0.45	54

a) Reaction conditions: catalyst; 25 µmol as Cu, substrate; AlaODc 100 µmol, octylamine 600 µmol. Organic phase; toluene 2 ml, GC internal standard; pentadecane 100 µmol. Aqueous phase, 0.1 mol dm^{-3} acetic acid–sodium acetate buffer (pH 5.0 at 25 °C) 2 ml, reaction temperature 90 °C. b) Conversion after 4 h.

As shown in Table 4, the reaction rate slightly increased as the metal loadings of Cu en-PS decreased. Ligand structure effect was also examined and it was found that Cu ten-PS had a bigger rate than Cu en-PS. However, these effects were rather small compared with those in two-phase reactions, which were already shown in Table 3.

The effects of the substrate structure are shown in Fig. 5. A smaller reaction rate was clearly observed for decyl 3-aminopropionate (β-alanine decyl ester). However, decyl 4-aminobutyrate and decyl 6-aminohexanoate were reactive even in the absence of catalyst and readily reacted to produce 1-decanol. Therefore catalytic activity of Cu en-PS to these two esters was not clarified.

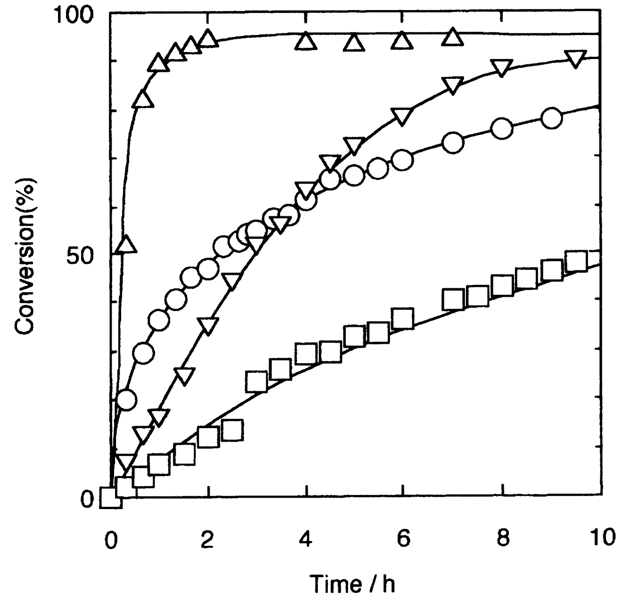


Fig. 5. The reactions of amino acid decyl esters catalyzed by Cu en-PS under three-phase conditions. Reaction conditions: catalyst; Cu en-PS containing 25 µmol Cu, organic phase; toluene 2 ml, aqueous phase; 0.1 mol dm^{-3} acetic acid–sodium acetate buffer 2 ml, reaction temperature; 90 °C. substrate: ○; Glycine decyl ester, □; Decyl 3-aminopropionate, △; Decyl 4-aminonbutyrate, ▽; Decyl 6-aminohexanoate.

Discussion

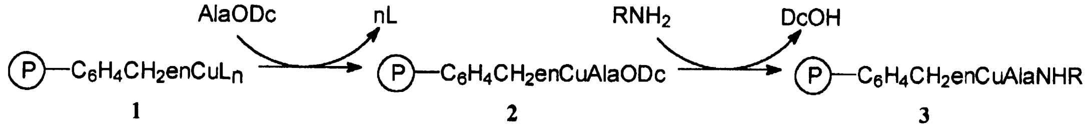
From the results described in the previous section, AlaODc was found to react to produce 1-decanol in the presence of Cu en-PS and amines. There are three possible nucleophiles in the two-phase reaction system, that is, reagent amines, other AlaODc molecules, and ligand amino groups. They should give, as a reaction product, alaninamide, alanylalanine decyl ester, and polymer-bound alaninamide, respectively. The smooth production of 1-decanol was observed only after a reagent amine was added to the organic phase. This suggests that the nucleophile of this two-phase reaction is the reagent amines and the nucleophilic attack of other nucleophiles are negligible, even if they occur.

The presence of a free amino group of a substrate is essential to the two-phase catalytic reactions, but it never acts as a nucleophile. The color changes of polymer complex on addition of AlaODc also suggest the formation of Cu(II)–AlaODc complex. Thus the reactions are supposed to proceed via a metal–ester complex form. A possible reaction mechanism for the two-phase reactions is shown in Scheme 1. Cu(II) ions are assumed to exist as ethylenediamine complex (**1**) in the dry resin, where L is the ethylenediamine moiety, chloride ion, or solvents that were used in the preparation of Cu en-PS. On the addition of AlaODc, it coordinates to the Cu(II) ion at its amino group and presumably at its ester carbonyl group to form Cu(II)–AlaODc chelate complex (**2**).

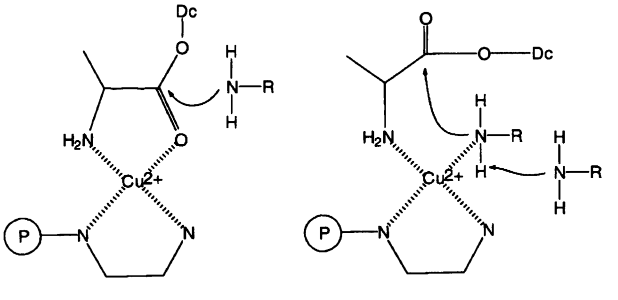
There are two possible pathways for the aminolysis of the complex **2**.[14)] The one is the direct attack of a free alkylamine onto the electron-deficient carbonyl carbon of the coordinated ester substrate, as shown in **2a** (Scheme 2). The metal ion functions as a Lewis acid in this pathway.[13,15)] In the other pathway, an alkylamine coordinates to Cu^{2+} ion via ligand-exchange and then an intracomplex reaction between the coordinated ester substrate and the metal-bound amine takes place. Another free amine may serve as a general base to assist the intracomplex displacement, as shown in **2b**. The function of the Cu^{2+} ion is to serve as a template for the intracomplex reaction of complex **2b**.[13,16)]

These two pathways are difficult to distinguish kinetically. However, the rate difference depending on the kind of nucleophiles (Table 2) indicates the rate-limiting step is the reaction of **2a** or **2b** in Scheme 2. Therefore, a favorable equilibrium toward **2a** or **2b** would enhance the overall reaction rates.

Decyl acetate and *N*-acetylglycine decyl ester, both of which have no free amino group, had little reactivities probably due to their weak complexability to Cu(II) ions. The effect of ligand structure (Table 3) are a little complicated but it may be explained as follows. The



Scheme 1. Schematic representation of reaction mechanism.



2a **2b**

Scheme 2. Possible intermediates for aminolysis of AlaODc.

most likely reason is the stability of the original Cu complex **1**. In Cu ten-PS, having tetramethylenediamine unit, the complex Cu(ten)$_x$ is thought to be less stable than Cu(en)$_x$ in Cu en-PS. This would lead to a favorable equilibrium toward ester complex **2a** or **2b**. On the other hand, metal content effects may be related to the amount of free amino groups, the total content of ionic species, and the amount of stable Cu complex, all of which probably affect the equilibrium between the complexes as well as the microenvironment around the complexes.

The fact, shown in Fig. 5, that β-alanine decyl ester had a smaller rate than glycine decyl ester suggests the existence of a substrate-metal coordinated intermediate in three-phase reactions. The first step of the three-phase reactions would be a coordination of substrates to Cu(II) ion. The hydrolysis reaction is thought to proceed in the same manner as two-phase reaction, which is already shown in Scheme 1. As with two-phase reactions, however, the fundamental question in three-phase reactions is what is a nucleophile. There are four possible nucleophiles, that is, water in the aqueous phase, amino groups of AlaODc and of the polystyrene support, and the buffer agent in the aqueous phase. The two amino groups can be counted out, because the reaction did not proceed without nucleophilic reagents under two-phase reaction conditions.

Figures 2 and 3 indicate that the reaction proceeds smoothly when acetate ions exist in aqueous phase. If acetate ion is a nucleophile toward **2a** in Scheme 2, the products will be 1-decanol and alanine-acetic acid anhydride. However, the acid anhydride reacts readily with water to produce acetic acid and alanine. If water is a nucleophile to attack AlaODc as **2b** (Scheme 2) with an assistance of acetate ion as a general base, it will also produce 1-decanol and alanine. We are unable to make a conclusive decision.

Compared with two-phase reactions (Table 3), the effects of ligand structure and metal content (Table 4) seem to be less dominant in three-phase reactions. This may suggest less of a difference in the feasibility of the ester complex formation under the three-phase reactions.

The inhibition by alanine in acetic acid/sodium acetate buffer (Fig. 3) can be explained by the formation of a stable complex with alanine. We have not attained to a definite conclusion for the reason why oxalate or citrate ion did not enhance the activity of Cu en-PS (Fig. 3). Either their small solubilities to toluene or the formation of stable copper-acid complex may be responsible for their little influence. The reasons why the reaction rates were influenced by simple ionic species other than acetate ion still remain unclarified.

As shown in Fig. 4, the decreased rates were observed when Co(II) or Zn(II) was used instead of Cu(II). The activity order (Cu(II)>Co(II)>Zn(II)) is the same as the stability order of their alanine complexes or ethylenediamine complexes.[17] Therefore it may be suggested that the concentration of the ester complex **2a** or **2b** is a more important factor than the Lewis acidity of metal ions.

One reason why the reaction did not follow simple kinetics may be the accumulation of stable alanine–metal complex, as is indicated by the retardation due to the alanine present in aqueous phase (Fig. 3). However, there may be other reasons, for example, the elution of Cu ion from the resin to the bulk aqueous phase or the deactivation of catalyst due to metal ion-catalyzed oxidation, etc.

In conclusion, polystyrene-supported ethylenediamine coordinated copper(II) complex (Cu en-PS) is a good catalyst for the ester-amide exchange of alanine decyl ester (AlaODc) in toluene. Cu en-PS greatly accelerates the hydrolysis of AlaODc under toluene/acetate ion-containing aqueous phase/resin three-phase conditions. The catalytic mechanism is not completely clear, but it is clear that the reaction proceeded via a metal-substrate coordinated intermediate.

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