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ENANTIOSELECTIVELY CATALYZED OXIDATION OF 3,4-DIHYDROXY-L-PHENYLALANINE BY N-LAUROYL L OR D-HISTIDINE-Cu(II) COMPLEX IN CTABr MICELLES.

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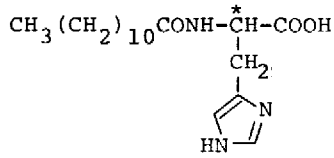
Summary: In order to investigate the enzyme model reaction the oxidation of 3,4-dihydroxy-L-phenylalanine(L-DOPA) was carried out using optically active catalyst, N-lauroyl L or D-histidine-Cu(II) complex(L or D-LauHis-Cu(II)), showing appreciable enantioselectivity in the presence of the mixed micelles with CTABr.

Our previous papers have reported the enantioselectively catalyzed hydrolysis of p-nitrophenyl esters in the presence of CTABr micelles, emphasizing following three requirements for the enantioselective enzyme model.[1,2]

1) Asymmetric center and active site must exist closely in the reaction system.
2) Strong interactions must exist among reagents.
3) The catalyzed hydrolysis must occur in hydrophobic field in order to avoid the reaction with non-selective hydroxide ion.

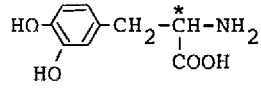
In this work we directed our attention to the enantioselective oxidation in micellar system using L-DOPA as a substrate and L or D-LauHis-Cu(II) complex as

(Ligand in Catalyst)



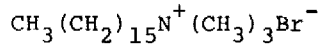
L or D-LauHis

(Substrate)



L-DOPA

(Surfactant)



CTABr

catalysts. In spite of the distinguished enantioselectivities in micellar systems, difficulties are often encountered in the isolation of the products from the reaction mixtures, restricting synthetic application of the reactions. It is worth noticing that DOPA yields on oxidation an o-quinone like compound which can be easily isolated from the reaction mixtures. Hatano et al. have reported the catalytic activity of a poly-L-lysine-Cu(II) complex on the oxidation of DOPA with enantioselective rate ratio D/L of 1.5.[3,4] No study has so far been undertaken on enantioselectively catalyzed oxidation in micellar system.

Materials were all guaranteed reagents except L or D-LauHis which were prepared by the standared method.[5] The experiments were carried out 2×10^{-4} M. of DOPA in air saturated 10.0 v/v% MeOH-H_2O containing 1×10^{-4} M. of LauHis, 1×10^{-5} M. of cupric sulphate, 1×10^{-2} M. of CTABr, while pH was controlled with using buffer solutions. The temperature was kept at 30°C unless otherwise specified. The reaction was followed spectrophotometrically using the absorption of the product(λ 340 nm[3,4]), whose increase in intensity obeyed a good pseudo-first order kinetic up to 40% conversion.

Histidine is well known to form a stable Cu(II) complex. The complexation of the present L or D-LauHis with Cu(II) ion was as well indicated by the characteristic absorption at 644 nm.[6,7,8] Without the catalyst DOPA was oxidized very slowly with a rate constant less than 10^{-7} sec^{-1}, whereas the

Table I. Catalyzed oxidation rates of DOPA.

pH	NaOH(M)	$k_{obs.}$ ($10^{-5}sec^{-1}$)		L/D
		L-LauHis-Cu(II)	D-LauHis-Cu(II)	
6.90[a)]	0.024	10.95	7.69	1.42
7.90[b)]	0.004	8.76	6.30	1.39
8.90[b)]	0.021	5.09	4.52	1.13
9.90[b)]	0.044	1.20	1.17	1.03

a) 0.05 M. KH_2PO_4 buffer

b) 0.05 M. H_3BO_3 buffer

catalyst accelerated the reaction remarkably, giving rate constant $k_{obs.}$ as shown in Table I. The catalyst also gave rise to a distinguished enantioselectivity: the rate ratio L/D of 1.42 was obtained between the reactions catalyzed by L and D-LuaHis-Cu(II) in KH_2PO_4-NaOH buffer. The value of $k_{obs.}$ as well as L/D decreased with an increasing order of pH. This pH dependencies are likely related to the dissociation of DOPA, which has pK_a of 8.71 and 9.74.[9] With using citric acid buffer no acceleration of the reaction was observed at pH 4.90-6.90, perhaps because of the higher stability of the complexation of citric acid with Cu(II) ion than that of L or D-LauHis.

In order to see the effect of ionic strength, the oxidation was examined with various concentration of KH_2PO_4-NaOH buffer at pH 6.90. As shown in Table II, the rate and enantioselectivity increased with increasing concentration of buffer.

Table II. Effect of concentration of KH_2PO_4-NaOH buffer.

Conc(M)	cmc(10^{-5}M)[a]	$k_{obs.}$ ($10^{-5}sec^{-1}$)		L/D
		L-LauHis-Cu(II)	D-LauHis-Cu(II)	
0.01	9.5	9.67	7.38	1.31
0.05	8.2	10.95	7.69	1.42
0.10	7.4	12.35	8.57	1.44

a) The value was obtained for the solution without the substrate.

This could be ascribed to the enhanced tightness of micelles as evidenced by the decrease in cmc.

Cu(II) ion itself displayed without LauHis a catalytic activity as much as half LauHis-Cu(II) did.

By lowering the reaction temperature to 10°C, the L/D value of L and D-LauHis-Cu(II) increased up to 2.50(Table III.). This is presumably ascribed to the increased tightness of the hydrogen bonding among the reagents or to the structural change of micelles. Similar phenomena were observed in the enantioselectively catalyzed hydrolysis in micellar system.[2]

A measurement was undertaken in the absence of CTABr with 60% MeOH as the solvent for a solubility. The reaction proceeded with a rate tenfold smaller

Table III. Effect of temperature.

Temp(°C)	$k_{obs.}$ ($10^{-5}sec^{-1}$)		D/L
	L-LauHis-Cu(II)	D-LauHis-Cu(II)	
30	10.95	7.69	1.42
20	4.63	2.50	1.85
10	1.25	0.50	2.50

than the original value, indicating a marked cooperative function of the micelles with the catalyst.

When the catalyst was replaced by a histidine-Cu(II) complex, no acceleration of the reaction was observed either in the presence or absence of the micelles.

Catalytic activities of the L or D-LauHis complex with Co(II) or Ni(II) in micellar system were also examined. But they gave rise to no acceleration of the reaction.

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