CHEMISTRY LETTERS, pp. 785-788, 1981.

STEREOSELECTIVE DEACYLATION OF LONG-CHAIN p-NITROPHENYL N-ACYLPHENYLALANATES BY PALMITOYL-L-HISTIDINE IN A BILAYER SYSTEM

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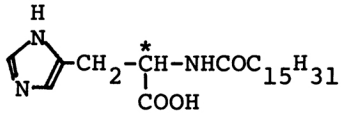
In the stereoselective deacylation of H-$[CH_2]_{n-1}$-$CONHCH(CH_2Ph)CO_2$-$C_6H_4NO_2$-p (n=10 and 16), the bilayer catalytic systems of palmitoyl-L-histidine and double-chain surfactants ($[C_mH_{2m+1}]_2N[CH_3]_2Br$; m=12 and 14) offered the relatively higher enantiomer rate ratios (k^L_{cat}/k^D_{cat}=3.7-5.6) as compared with those (k^L_{cat}/k^D_{cat}=3.5-3.6) obtained with the comicellar system of palmitoyl-L-histidine and octadecyltrimethylammonium chloride.

The stereoselective deacylation of N-protected amino acid p-nitrophenyl esters has already been performed with functionalized surfactants[1] or comicelles of N-acyl-L-histidine and hexadecyltrimethylammonium bromide[2-4], and the relatively high stereoselectivity was attained in the deacylation of diastereomeric dipeptide substrates with the thiol-functionalized surfactant[5,6] or in the deacylation of N-acylamino acid esters with the dipeptide-type L-histidine derivative and the chiral surfactant[7]. However, there has been no report dealing with the stereoselective deacylation of amino acid esters catalyzed by a chiral nucleophile in the presence of the aqueous bilayer membrane of double-chain surfactants, though the rate enhancement of ester hydrolysis by the achiral bilayer membrane system has recently received considerable attention[8,9].

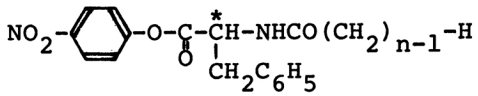
In this paper, we wish to report the stereoselective deacylation of p-nitrophenyl N-acylphenylalanates (S_n; n=2-16) by bilayer catalytic systems of palmitoyl-L-histidine (PalHis) and double-chain surfactants ($2C_mN2C_1Br$; m=12-18).

Nucleophile



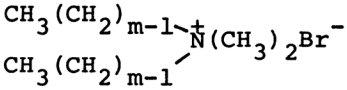
PalHis

Substrate

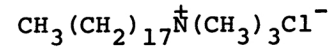


S_n (n=2,10, and 16)

Surfactant



$2C_mN2C_1Br$ (m=12,14, and 18)



OTAC

Since the reaction rates of S_n (1×10^{-5} M; 1 M=1 moldm^{-3}) deacylation with PalHis (5×10^{-5} M) came to be maximum in the presence of ca. 1×10^{-3} M $2C_mN2C_1Br$ (or octadecyltrimethylammonium chloride (OTAC)), the relative activity of different catalytic systems will be discussed in the stereoselective deacylation of S_n (n=2-16) with the said concentrations of the nucleophile and surfactants. From the observed deacylation rates and stereoselectivity (reflected in k^L_{cat}/k^D_{cat}) shown in Table 1, some characteristic features of the present reactions are recognized as follows:

Table 1 The Deacylation Rates (k_{cat}, sec^{-1}M^{-1}) and Stereoselectivity (k^L_{cat}/k^D_{cat})

Catalytic system	S_2			S_{10}			S_{16}		
	k^L_{cat}	k^D_{cat}	$\frac{k^L_{cat}}{k^D_{cat}}$	k^L_{cat}	k^D_{cat}	$\frac{k^L_{cat}}{k^D_{cat}}$	k^L_{cat}	k^D_{cat}	$\frac{k^L_{cat}}{k^D_{cat}}$
PalHis + $2C_{12}N2C_1Br$[b]	316	210	1.5	1511	411	3.7	537	109	4.9
	(452)	(330)	(1.4)	(2236)	(708)	(3.2)	-	-	-
PalHis + $2C_{14}N2C_1Br$[b]	492	262	1.9	2661	648	4.1	1094	197	5.6
PalHis + $2C_{18}N2C_1Br$[b]	(107)	(80)	(1.3)	(896)	(442)	(2.0)	-	-	-
PalHis + OTAC	221	123	1.8	1720	480	3.6	526	152	3.5

Values in the parentheses are those under the condition of 0.01 M tris(hydroxylmethyl)aminomethane (Tris) buffer (0.01 M KCl).

a) At 25 °C in 0.083 M Tris buffer (0.083 M KCl); solvent, (3:97 v/v) CH_3CN-H_2O; 1.0×10^{-5} M of ester, 5.0×10^{-5} M of nucleophile, 1.0×10^{-3} M of surfactant. k_{cat} values were evaluated from $(k_{total}-k_{spont})/[PalHis]_0$, where k_{total} and k_{spont} denote the first-order rate constants in the presence and absence of PalHis, respectively.

b) The stock solutions were prepared by dissolving the nucleophile and the surfactant in Tris-KCl buffer by sonication (Bransonic 12, Yamato Scientific Co.) at 50 °C for 1 hr.

(a) the bilayer membrane system (PalHis+$2C_mN2C_1Br$ (m=12 or 14)) tends to offer the larger deacylation rate of S_n (n=2-16) as compared with the micellar one (PalHis+OTAC) with some exceptions, and the deacylation rate of S_{10} possessing an appropriately long (not too short and not too long) N-acyl chain was found to be largest in the both catalytic systems, (b) the increase in the N-acyl chain length (n) of S_n from n=2 to n=10-16 enhanced the enantiomer rate ratio more remarkably in the bilayer system (PalHis+$2C_mN2C_1Br$ (m=12 or 14)) rather than in the micellar one, though the stereoselectivity of the S_2 deacylation was in almost at the same extent in the both systems, (c) the liquid crystalline bilayer systems (PalHis+$2C_mN2C_1Br$ (m=12 and 14))[10] resulted in the larger deacylation rate and stereoselectivity than the crystalline one (PalHis+$2C_{18}N2C_1Br$)[10], and the double-chain $2C_{14}N2C_1Br$ surfactant forms more efficient bilayer catalytic system with PalHis than $2C_{12}N2C_1Br$, and (d) the catalytic activity of the crystalline bilayer system ($2C_{18}N2C_1Br$) was

Table 2 Kinetic Parameters for the Deacylation of S_n (n= 2 or 10)

Catalytic system	Kinetic Parameter	S_2 L	S_2 D	S_{10} L	S_{10} D
PalHis+2C_{12}N2C_1Br[b]	$K_b/N(M^{-1})$	560	490	18700	15600
	$10^2k_m(sec^{-1})$	5.12	3.96	10.14	3.78
	k_m^L/k_m^D	1.3		2.7	
PalHis+2C_{18}N2C_1Br[c]	$K_b/N(M^{-1})$	250	200	2510	2260
	$10^2k_m(sec^{-1})$	5.66	3.26	9.76	7.25
	k_m^L/k_m^D	1.7		1.3	
PalHis+OTAC[b]	$K_b/N(M^{-1})$	530	640	3900	6330
	$10^2k_m(sec^{-1})$	2.49	1.49	11.16	4.32
	k_m^L/k_m^D	1.7		2.6	

a) At 25 °C; solvent, (3:97 v/v) CH_3CN-H_2O; 1.0×10^{-5} M of ester, $(3.0\text{-}7.5)\times10^{-5}$ M of nucleophile, $(0.6\text{-}1.5)\times10^{-3}$ M of surfactant, [Surfactant]/[Nucleophile]=20. K_b/N (K_b=association constant, and N=aggregation number) and k_m values for a simplified reaction ($M + S_n \underset{}{\overset{K_b}{\rightleftharpoons}} MS_n \xrightarrow{k_m} P$; M, MS_n, and P stand for a aggregate composed of nucleophile and surfactant, a aggregate-substrate complex, and p-nitrophenol, respectively) were obtained by means of the previous technique[12]. The stock solutions (PalHis+2C_mN2C_1Br (m=12 and 18)) were prepared according to the same way described in Table 1.

b) 0.083 M Tris buffer (0.083 M KCl).

c) 0.01 M Tris buffer (0.01 M KCl).

inferior to that of the micellar PalHis+OTAC system. At any rate, the highest enantiomer rate ratio (k_{cat}^L/k_{cat}^D=5.6) was observed in the S_{16} deacylation with the PalHis+2C_{14}N2C_1Br system, and is 1.6 fold with respect to the ratio (k_{cat}^L/k_{cat}^D=3.5) obtained in the S_{16} deacylation with the PalHis+OTAC system.

The notable aspects of the present reaction are also reflected in the kinetic parameters listed in Table 2. Although the difference in the microenvironment of the spherical micellar (PalHis+OTAC) and bilayer membrane (PalHis+2C_mN2C_1Br) systems offered a different relative order of the binding efficiency (K_b/N)[11] between the L- and D-enantiomers, the K_b/N values of the long-chain substrate (S_{10}) were fairly large as compared with those of the short-chain substrate (S_2) in all the reaction systems; the relative order of K_b/N values reflects that of reaction rates (k_{cat}) in the identical catalytic systems. The predominant deacylation of the L-enantiomers by the present catalytic system is in harmony with the larger k_m^L value with respect to the k_m^D one, and the relative order of k_m^L/k_m^D values in the S_n (n=2 or 10) deacylation with three different catalytic systems is well reflected in the relative order of the enantiomer rate ratios. Thus, the liquid crystalline bilayer phase of

PalHis+2C_mN2C_1Br (m=12 or 14) is so effective for the stereoselective deacylation of long-chain amino acid ester substrates that it results in the relatively large numbers of K_b/N and k_m^L/k_m^D.

References and Notes

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10) The phase transition (crystalline-liquid crystalline) temperature was determined for the aqueous solutions of 2C_mN2C_1Br by using a differential scanning calorimeter described in Y. Okahata, S. Tanamachi, and T. Kunitake, Nippon Kagaku Kaishi, 1980, 442 and are as follows: 2C_{12}N2C_1Br, 5-10 °C; 2C_{14}N2C_1Br, 16 °C; 2C_{18}N2C_1Br, 45 °C.
11) The binding efficiency was evaluated by using the K_b/N values since the N values for surfactants could not be determined in this study.
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(Received March 28, 1981)