Enantioselective Catalysis of Deacylation of *p*-Nitrophenyl *N*-Acylphenylalanates by Mixed Micelles composed of N^{α}-Hexadecanoyl-L-histidine and a Cationic Surfactant

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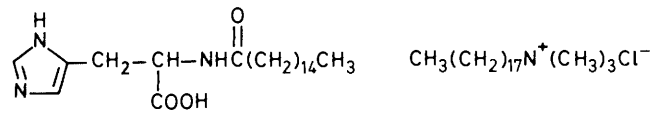
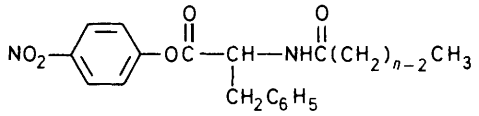
The deacylation of *p*-nitrophenyl *N*-acyl-L- and -D-phenylalanates (acyl = acetyl, decanoyl, and hexadecanoyl) with the co-micellar system composed of N^{α}-hexadecanoyl-L-histidine and octadecyltrimethylammonium chloride was investigated for the 20—35 °C range in CH_3CN–H_2O (3:97 v/v). The enantioselective properties of the co-micellar system effective for the deacylation of such substrates were investigated in the light of substrate-binding properties, activation parameters, and kinetic salt and organic co-solvent effects. Kinetic enantioselectivity is exclusively favoured for the L-substrates, even though the binding constants for the D-isomers are greater than those for the corresponding L-isomers in most cases. The highest enantioselectivity in terms of the apparent second-order rate ratio ($k^{L}_{a,obs}/k^{D}_{a,obs}$) is 4.7 as observed for the deacylation of *p*-nitrophenyl *N*-decanoyl-L- and -D-phenylalanate at 20 °C and pH 7.6.

Recently, the enantioselective deacylation of *N*-acylamino-acid esters, catalysed by micellar surfactants functionalized with amino-acid residues [1–5] and mixed micelles of hydrophobic N^{α}-acylhistidine and hexadecyltrimethylammonium bromide (CTAB),[6–8] has been rather extensively investigated. However, stereoselective catalysis of mixed micelles composed of a nucleophile with various structural modifications and a surfactant in the deacylation of amino-acid esters bearing a long *N*-acyl chain has not been investigated systematically. Therefore, we have examined the stereoselective deacylation of amino-acid esters bearing a series of *N*-acyl chains with *N*-acyl-L-histidines mixed with various cationic surfactants,[9–11] and the following kinetic results have been obtained. (i) The reaction rate and stereoselectivity were enhanced in the deacylation by co-micelles formed with an N^{α}-acyl-L-histidine bearing a long acyl chain (*N*-dodecanoyl or *N*-hexadecanoyl) and a cationic surfactant having either a C_{16} or C_{18} alkyl chain. (ii) The highest stereoselectivity was observed in the deacylation of *p*-nitrophenyl *N*-decanoylphenylalanate which has an adequate acyl chain length for hydrophobic interaction with the co-micelle components. (iii) Co-micelles composed of chiral nucleophiles and chiral surfactants act to enhance the enantioselectivity toward substrates having long chain segments.

In order to examine the kinetic origin of such enantioselectivity in the light of substrate-binding properties, activation parameters, and kinetic salt and organic co-solvent effects, we investigated the deacylation of *p*-nitrophenyl *N*-acylphenylalanates (L- and D-S_n) catalysed by the co-micellar system composed of N^{α}-hexadecanoyl-L-histidine (PalHis) and octadecyltrimethylammonium chloride (OTAC).



PalHis OTAC



L- and D-S_n (n = 2, 10, and 16)

Experimental

Materials.—*p*-Nitrophenyl *N*-acyl-L- and -D-phenylalanates (L- and D-S_n; n = 2, 10, and 16) were prepared from *N*-benzyloxycarbonyl-L- and -D-phenylalanine, which was obtained by acylation of L- and D-phenylalanine with benzyloxycarbonyl chloride, by esterification of the carboxy-group with *p*-nitrophenol and acylation of the amino-group after removal of the amino-protecting group upon treatment with 30% HBr in acetic acid in the manner described previously.[12]

L-S_2 had m.p. 137.5—138.0 °C (lit.,[12] 140.0—140.5 °C); $[\alpha]_D^{25}$ −17.6° (*c* 2.0, $CHCl_3$) {lit.,[12] $[\alpha]_D^{20}$ −18.6° (*c* 2.0, $CHCl_3$)} (Found: C, 61.95; H, 5.0; N, 8.65. $C_{17}H_{16}N_2O_5$ requires C, 62.2; H, 4.9; N, 8.55%).

D-S_2 had m.p. 133.5—134.0 °C (lit.,[12] 135—137 °C); $[\alpha]_D^{25}$ +18.2° (*c* 2.0, $CHCl_3$) {lit.,[12] $[\alpha]_D^{20}$ +17.4° (*c* 2.0, $CHCl_3$)} (Found: C, 62.05; H, 4.85; N, 8.65%).

L-S_{10} had m.p. 100.0—100.5 °C; $[\alpha]_D^{25}$ −13.0° (*c* 2.0, $CHCl_3$) (Found: C, 68.3; H, 7.4; N, 6.2. $C_{25}H_{32}N_2O_5$ requires C, 68.15; H, 7.3; N, 6.35%).

D-S_{10} had m.p. 99.5—100.0 °C; $[\alpha]_D^{25}$ +12.3° (*c* 2.0, $CHCl_3$) (Found: C, 68.35; H, 7.5; N, 6.2%).

L-S_{16} had m.p. 101.0—101.5 °C; $[\alpha]_D^{25}$ −10.0° (*c* 2.0, $CHCl_3$) (Found: C, 70.8; H, 8.45; N, 5.35. $C_{31}H_{44}N_2O_5$ requires C, 70.95; H, 8.45; N, 5.35%).

D-S_{16} had m.p. 100.5—101.0 °C; $[\alpha]_D^{25}$ +11.6° (*c* 2.0, $CHCl_3$) (Found: C, 70.35; H, 8.4; N, 5.25%).

N^{α}-Hexadecanoyl-L-histidine (PalHis) was obtained by reaction of L-histidine with hexadecanoyl chloride,[13] m.p. 153—155 °C; $[\alpha]_D^{22}$ +15.1° (*c* 1.0, CH_3OH) (Found: C, 67.15; H, 10.2; N, 10.35. $C_{22}H_{39}N_3O_3$ requires C, 67.15; H, 10.0; N, 10.7%).

Octadecyltrimethylammonium chloride (OTAC) was obtained from Tokyo Chemical Industries and used after recrystallization from dry ethanol–ether.

Kinetic Measurements.—Rates of *p*-nitrophenol liberation from *p*-nitrophenyl *N*-acylphenylalanates were measured at 317 (pH < 7) or 400 nm (pH ≥ 7) with a Shimadzu UV-200

Table 1. Apparent second-order rate constants and enantioselectivity parameters for deacylation of *p*-nitrophenyl *N*-acylphenylalanates [a]

T/°C	Substrate	$k_{a,obs}$/dm^3 mol^{-1} s^{-1}	$k^L_{a,obs}/k^D_{a,obs}$ [b]
20	L-S_2	51	2.2 (2.1—2.5)
	D-S_2	23	
	L-S_{10}	1 600	4.7 (4.3—4.7)
	D-S_{10}	340	
	L-S_{16}	560	1.6 (1.2—1.6)
	D-S_{16}	340	
25	L-S_2	160	1.8 (1.8—2.0)
	D-S_2	89	
	L-S_{10}	2 300	3.0 (3.0—3.6)
	D-S_{10}	760	
	L-S_{16}	750	3.9 (3.2—3.9)
	D-S_{16}	190	
30	L-S_2	320	2.0 (1.8—2.0)
	D-S_2	160	
	L-S_{10}	3 500	3.2 (3.2—3.9)
	D-S_{10}	1 100	
	L-S_{16}	1 500	3.3 (3.0—3.6)
	D-S_{16}	450	
35	L-S_2	300	1.5 (1.4—2.1)
	D-S_2	200	
	L-S_{10}	3 500	2.5 (2.4—3.4)
	D-S_{10}	1 400	
	L-S_{16}	1 700	1.4 (1.0—1.4)
	D-S_{16}	1 200	

[a] Measured at pH 7.6 (0.083 mol dm^{-3} Tris buffer) in CH_3CN-H_2O (3 : 97 v/v) containing 0.083 mol dm^{-3} KCl. Concentrations: PalHis, 3.0×10^{-5} mol dm^{-3}; OTAC, 6.0×10^{-4} mol dm^{-3}; substrate, 1.0×10^{-5} mol dm^{-3}. [b] Catalyst concentrations for the values in parentheses: PalHis, (2—4) $\times 10^{-5}$ mol dm^{-3}; OTAC, (4—8) $\times 10^{-4}$ mol dm^{-3}; [OTAC]/[PalHis] 20.

spectrophotometer. Each run was in general initiated by adding an acetonitrile solution (0.1 ml) of an ester substrate to a reaction medium which contained both nucleophile and surfactant in a molar ratio of *ca.* 1 : 20 in tris(hydroxymethyl)-methylamine (Tris) buffer (3.4 ml). The reaction followed apparent first-order kinetics up to *ca.* 80% conversion of substrate. An apparent second-order rate constant ($k_{a,obs}$) for the deacylation was evaluated by equation (1). Here, k_t and k_s

$$k_{a,obs} = (k_t - k_s)/[\text{nucleophile}]_0 \quad (1)$$

refer to observed first-order rate constants for the deacylation of S_n with and without the nucleophile (PalHis), respectively; $[\text{nucleophile}]_0$ stands for initial nucleophile concentration.

Determination of Critical Micelle Concentration (C.m.c.).—The c.m.c. value for OTAC was evaluated from its kinetic behaviour in deacylation, referred to a break-point observed in the plot of observed rate constant *versus* OTAC concentration. The c.m.c. value thus obtained is 1.0×10^{-4} mol dm^{-3} at 25 °C and pH 7.6 in CH_3CN-H_2O (3 : 97 v/v) containing 0.083 mol dm^{-3} Tris buffer and 0.083 mol dm^{-3} KCl. The value was observed to remain constant for the temperature range 20—40 °C (with 2% deviation) and was not affected by incorporation of PalHis at [OTAC]/[PalHis] 20.

Results and Discussion

The deacylation of S_n (n = 2, 10, and 16; 1.0×10^{-5} mol dm^{-3}) with PalHis (3.0×10^{-5} mol dm^{-3}) incorporated into OTAC micelles (6.0×10^{-4} mol dm^{-3}) was investigated for the 20—35 °C range and pH 7.6 in CH_3CN-H_2O (3 : 97 v/v) containing 0.083 mol dm^{-3} Tris buffer and 0.083 mol dm^{-3} KCl. The apparent second-order rate constants ($k_{a,obs}$) are listed in Table 1 along with the enantioselectivity parameters ($k^L_{a,obs}/k^D_{a,obs}$).

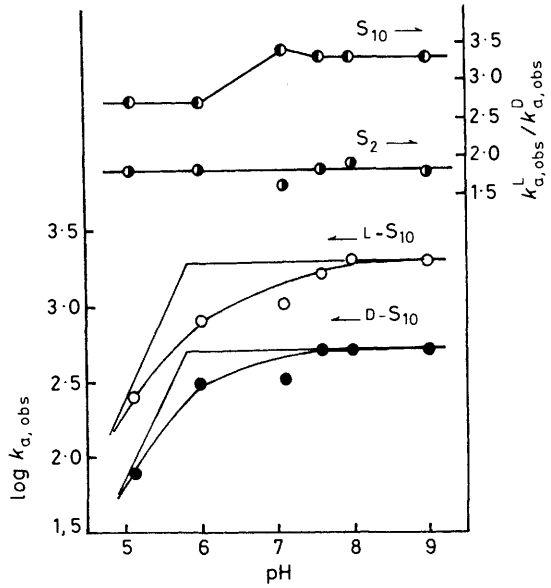


Figure 1. Correlations of apparent second-order rate constants and enantioselectivity parameters with pH for the deacylation of *p*-nitrophenyl *N*-acylphenylalanates at 25 °C in CH_3CN-H_2O (3 : 97 v/v) containing 0.083 mol dm^{-3} KCl; pH values were adjusted with acetate buffer (pH ≦6) and Tris buffer (pH ≧7). Initial concentrations: OTAC, 1.0×10^{-3} mol dm^{-3}; PalHis, 5.0×10^{-5} mol dm^{-3}; substrate, 1.0×10^{-5} mol dm^{-3}

The reaction of PalHis with S_2 and S_{10} in the presence of OTAC was further investigated over the pH range 5.0—9.0. As can be seen from the correlations of log $k_{a,obs}$ with pH in Figure 1, the reaction rates appear to reach saturation levels as the pH increases. The acid dissociation constant (K_a) for the imidazolium group was determined by plotting $1/k_{a,obs}$ against $[H^+]$ on the basis of equation (2),[14,15] where k_a is the second-order rate constant for the neutral imidazolyl

$$1/k_{a,obs} = 1/k_a + [H^+]/k_aK_a \quad (2)$$

group. The pK_a value of PalHis (5.8) in the presence of OTAC micelles is in a fair agreement with the apparent pK_a value (6.2) of N^{α}-myristoyl-L-histidine in the presence of CTAB micelles.[13] In the light of the pK_a value obtained here, PalHis which has a neutral imidazolyl group, acts as a real nucleophile in the present reaction.

Effects of Ionic Strength and Organic Co-solvent.—The reactivity of PalHis in the presence of OTAC micelles was examined at various ionic strengths [μ 0—0.3 (KCl)] as shown in Figure 2. The $k_{a,obs}$ values for deacylation of S_2 and S_{10} are practically constant up to [KCl] 0.2 mol dm^{-3} and then decrease gradually. Since the chloride ion tends to act as a structure-breaking factor,[16] the micellar aggregate would be somewhat disturbed as the salt concentration is raised. On the other hand, the enantioselectivity parameters remain constant over the whole KCl concentration range examined (Figure 2).

The reaction of PalHis with S_2 and S_{10} in the presence of OTAC micelles was investigated at various acetonitrile concentrations [3—20 (v/v)%] while nucleophile and OTAC concentrations as well as ionic strength were maintained

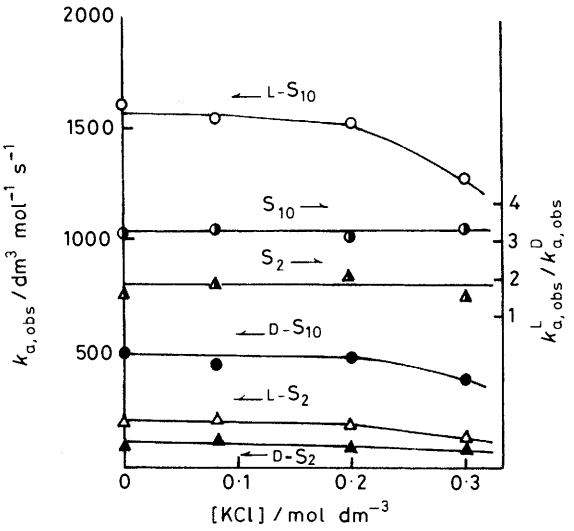


Figure 2. Correlations of apparent second-order rate constants and enantioselectivity parameters with KCl concentration for the deacylation of *p*-nitrophenyl *N*-acylphenylalanates at 25 °C and pH 7.6 (0.083 mol dm^{-3} Tris buffer) in CH_3CN–H_2O (3 : 97 v/v). Initial concentrations: OTAC, 1.0×10^{-3} mol dm^{-3}; PalHis, 5.0×10^{-5} mol dm^{-3}; substrate, 1.0×10^{-5} mol dm^{-3}

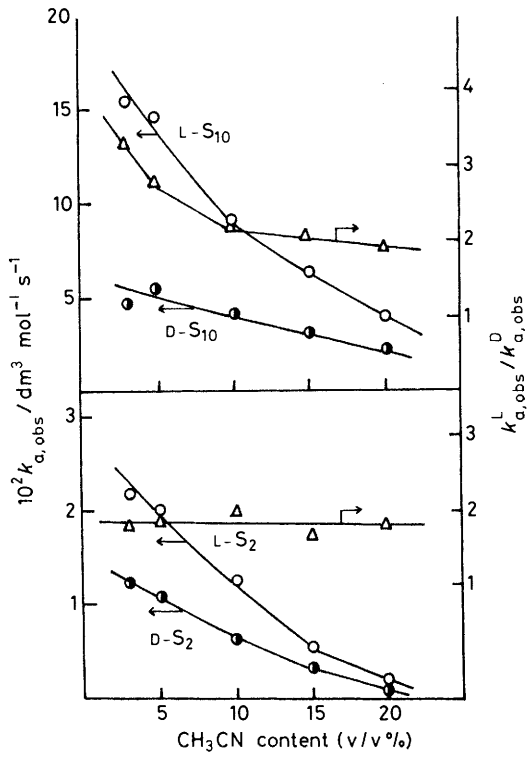


Figure 3. Correlations of apparent second-order rate constants and enantioselectivity parameters with CH_3CN content for the deacylation of *p*-nitrophenyl *N*-acylphenylalanates at 25 °C and pH 7.6 (0.083 mol dm^{-3} Tris buffer; 0.083 mol dm^{-3} KCl). Initial concentrations: OTAC, 1.0×10^{-3} mol dm^{-3}; PalHis, 5.0×10^{-5} mol dm^{-3}; substrate, 1.0×10^{-5} mol dm^{-3}

constant. The $k_{a,obs}$ values for deacylation of S_2 and S_{10} decrease markedly along with the increase in acetonitrile content as shown in Figure 3. On the other hand, the enantioselectivity parameter for deacylation of S_{10} decreases as the acetonitrile content increases, while that for deacylation of S_2 is almost constant irrespective of the acetonitrile content. The result indicates that the higher enantioselectivity for S_{10} is brought about by its strong hydrophobic entanglement with the micellar components and, consequently, the enantioselectivity parameter is subjected to change more drastically than that for S_2 by the nature of hydrophobic microenvironment.

Substrate-binding Property.—The present micellar reaction is consistent with equations (3) and (4) in the light of its saturation-type kinetic behaviour.[17] Here, M is a co-micelle

$$S + M \underset{}{\overset{K_b}{\rightleftharpoons}} MS \xrightarrow{k_m} P \qquad (3)$$

$$S \xrightarrow{k_s} P' \qquad (4)$$

constructed by OTAC and PalHis, S is an ester substrate, MS stands for a micelle–substrate complex, and P and P′ refer to reaction products; K_b is a binding constant for the formation of a micelle–substrate complex, and k_s and k_m refer to rate constants for product formation in the bulk phase and in the co-micellar phase, respectively.

In the present study, the kinetic runs were carried out under the following stoicheiometric conditions: [OTAC] > c.m.c. (1.0×10^{-4} mol dm^{-3}), [OTAC] > [PalHis] > [S_n], [OTAC]/[PalHis] 20. An apparent first-order rate constant (k_t) and other related kinetic parameters in equations (3) and (4) are inter-related by equation (5), where [M] refers to [PalHis] + [OTAC] − $[OTAC]_{c.m.c.}$ and N is an aggregation number for micelle formation. The c.m.c. value of the co-micellar system is practically identical with that of OTAC alone under the present experimental conditions. Linear correlations between

$$1/(k_t - k_s) = N/\{K_b(k_m - k_s)[M]\} + 1/(k_m - k_s) \qquad (5)$$

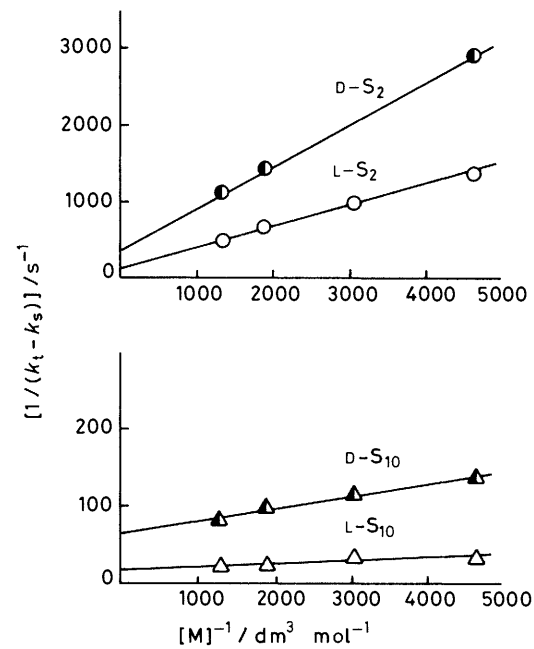


Figure 4. Linear correlations between reciprocal values of $(k_t - k_s)$ and [M] [based on equation (5)] for the deacylation of *p*-nitrophenyl *N*-acylphenylalanates at 25 °C and pH 7.6 (0.083 mol dm^{-3} Tris buffer, 0.083 mol dm^{-3} KCl) in CH_3CN–H_2O (3 : 97 v/v). Initial concentrations: substrate, 1.0×10^{-5} mol dm^{-3}; OTAC, (3.0—15.0) $\times 10^{-4}$ mol dm^{-3}; PalHis, (1.5—7.5) $\times 10^{-5}$ mol dm^{-3}; [OTAC]/[PalHis] 20

Table 2. Kinetic parameters for deacylation of *p*-nitrophenyl *N*-acylphenylalanates in the micellar phase [a]

T/°C	Kinetic parameters	L-S_2	D-S_2	L-S_{10}	D-S_{10}	L-S_{16}	D-S_{16}
20	K_b/N (mol^{-1} dm^3)	470	690	3 800	4 200		
	10^2 k_m (s^{-1})	1.03	0.50	7.29	2.34		
	k_m^L/k_m^D	2.1		3.1			
25	K_b/N (mol^{-1} dm^3)	530	640	3 900	6 300	810	2 100
	10^2 k_m (s^{-1})	2.49	1.49	11.2	4.32	7.94	1.85
	k_m^L/k_m^D	1.7		2.6		4.3	
30	K_b/N (mol^{-1} dm^3)	1 200	1 500	6 400	12 000	6 000	14 000
	10^2 k_m (s^{-1})	3.76	2.34	16.9	7.29	8.33	3.86
	k_m^L/k_m^D	1.6		2.3		2.2	
35	K_b/N (mol^{-1} dm^3)	340	470	3 000	14 000	1 500	1 500
	10^2 k_m (s^{-1})	8.90	5.07	24.8	12.0	14.1	13.4
	k_m^L/k_m^D	1.8		2.1		1.1	

[a] Measured at pH 7.6 (0.083 mol dm^{-3} Tris buffer) in CH_3CN–H_2O (3 : 97 v/v) containing 0.083 mol dm^{-3} KCl. Concentrations: PalHis, (1.5—7.5) × 10^{-5} mol dm^{-3}; OTAC, (3.0—15.0) × 10^{-4} mol dm^{-3}; substrate, 1.0 × 10^{-5} mol dm^{-3}; [OTAC]/[PalHis] 20.

Table 3. Activation parameters for deacylation of *p*-nitrophenyl *N*-acylphenylalanates in the micellar phase (based on k_m values) [a]

Substrate	$\Delta G^{\ddagger}_{298}$/kcal mol^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/ cal mol^{-1} K^{-1}
L-S_2	19.6 ± 0.07	24.0 ± 0.7	14.4 ± 2.3
D-S_2	19.9 ± 0.04	25.7 ± 0.9	19.0 ± 3.0
L-S_{10}	18.7 ± 0.01	14.7 ± 0.2	−13.6 ± 0.5
D-S_{10}	19.3 ± 0.01	18.9 ± 0.2	−1.4 ± 0.6
L-S_{16}	19.0 ± 0.06	10.1 ± 1.3	−30.0 ± 4.3
D-S_{16}	19.8 ± 0.01	35.7 ± 2.0	53.0 ± 6.4

[a] Based on the data obtained at 20—35 °C, pH 7.6 (0.083 mol dm^{-3} Tris buffer) in CH_3CN–H_2O (3 : 97 v/v) containing 0.083 mol dm^{-3} KCl with concentrations: PalHis, (1.5—7.5) × 10^{-5} mol dm^{-3}; OTAC, (3—15) × 10^{-4} mol dm^{-3} at [OTAC]/[PalHis] 20; substrate, 1.0 × 10^{-5} mol dm^{-3}.

reciprocal values of ($k_t - k_s$) and [M] were observed, consistent with equation (5), as shown in Figure 4. The kinetic parameters thus evaluated are summarized in Table 2.

Enantiomer-selective recognition is not exercised in the binding process with less hydrophobic substrates as observed for the deacylation of *p*-nitrophenyl *N*-acylphenylalanates with an N^{α}-acyl-L-histidine surfactant [1] and mixed micelles containing N^{α}-acyl-L-histidine [6] at 25 °C and neutral pH. It needs to be noted, however, that the binding property of the PalHis–OTAC co-micelles observed in this study is significantly different from the previous results. As regards the deacylation of S_2, the K_b/N values for the D-substrate are slightly larger than those for L-species, and the ratio of K_b/N values for D and L remains almost constant over the temperature range of 20—35 °C (1.2—1.5). On the other hand, a different trend was observed as regards the deacylation of S_{10}; the ratio increases as temperature is raised; it is 1.1 at 20 °C and 4.6 at 35 °C. For the deacylation of S_{16} which has the longest acyl chain, the temperature dependence of the K_b/N ratio is in the opposite order. The ratio decreases as temperature is raised; it is 2.6 at 25 °C and 1.0 at 35 °C.

The rate constants in the micellar phase (k_m) for the deacylation of all the substrates increase as the temperature is raised, and the largest rate enhancement is noted with L-S_{10} over the whole temperature range. The enantioselectivity parameters in the micellar phase (k_m^L/k_m^D) are comparable to the corresponding values of $k^L_{a,obs}/k^D_{a,obs}$.

Activation Parameters.—The enantioselective deacylation of S_n (n = 2, 10, and 16) was carried out at pH 7.6 in the temperature range of 20—35 °C in order to obtain the activation parameters according to equation (6). The activation parameters thus obtained are summarized in Table 3. An isokinetic relationship appears to hold for the deacylation of S_n

$$\Delta G^{\ddagger} = 2.303RT\log(kT/hk_m) = \Delta H^{\ddagger} - T\Delta S^{\ddagger} \quad (6)$$

(n = 2, 10, and 16) with the co-micelles of PalHis and OTAC (Figure 5). This means all the deacylation reactions dealt with in this work proceed through the same mechanistic pathway. Furthermore, the isokinetic temperature (β) evaluated on the basis of equation (7) [18] is 313 K. Thus, for the temperature

$$\Delta H^{\ddagger} = \Delta H_0^{\ddagger} + \beta\Delta S^{\ddagger} \quad (7)$$

range of the present study the deacylation primarily goes through an enthalpy-controlled process.

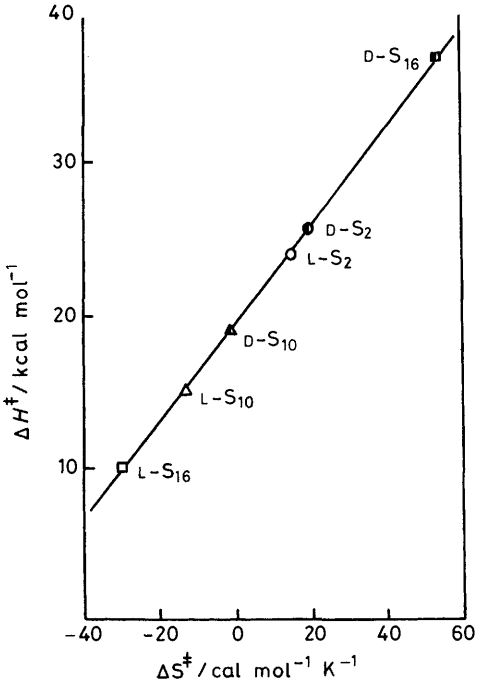


Figure 5. Isokinetic relationship for the deacylation of *p*-nitrophenyl *N*-acylphenylalanates as catalysed by co-micelles of OTAC and PalHis (refer to Table 3)

Enantioselectivity.—An enantioselectivity parameter ($k^{L}_{a,obs}/k^{D}_{a,obs}$) for the deacylation of S_{10} increases sharply from 2.8 to 3.4 as pH goes up from 6 to 7 (Figure 1), though such an enhancement is not observed for the deacylation of S_2.

The deacylation and enantioselective abilities of the co-micelles formed with PalHis and OTAC for S_n (n = 2, 10, and 16) have been examined as listed in Table 1. The deacylation activity of PalHis, as measured by $k_{a,obs}$, increased as temperature was raised. A remarkable rate enhancement was observed for the deacylation of L-S_{10} at each temperature, accompanied with the highest enantioselectivity for S_{10} in most cases. In addition, marked rate enhancement was attained for the deacylation of S_{10} species over the whole temperature range examined. Comparable hydrophobic chain lengths are needed for substrate and micellar components, so that optimal hydrophobic interaction is assured between a chiral nucleophile and a chiral substrate in the micellar phase. This is undoubtedly the cause of efficient catalytic activity and enantioselectivity observed in the deacylation of S_{10} in the present study.

Conclusions.—The remarkable enantioselectivity for L-isomers was found in the deacylation of *p*-nitrophenyl *N*-acylphenylalanates bearing a long hydrophobic acyl chain catalysed by the co-micellar system composed of N^{α}-hexadecanoyl-L-histidine and octadecyltrimethylammoniun chloride. The highest enantioselectivity parameters for the deacylation of S_{10} and S_{16} are 4.7 and 3.9, respectively, even though the binding constants for all the L-isomers are generally smaller than those for the corresponding D-isomers.

Acknowledgements

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References

1 J. M. Brown and C. A. Bunton, *J. Chem. Soc., Chem. Commun.*, 1974, 969.
2 J. M. Brown, C. A. Bunton, and S. Diaz, *J. Chem. Soc., Chem. Commun.*, 1974, 971.
3 R. A. Moss, T. J. Lukas, and R. C. Nahas, *Tetrahedron Lett.*, 1977, 3851.
4 R. A. Moss, R. C. Nahas, and T. J. Lukas, *Tetrahedron Lett.*, 1978, 507.
5 R. A. Moss, Y.-S. Lee, and T. J. Lukas, *J. Am. Chem. Soc.*, 1979, **101**, 2499.
6 Y. Ihara, *J. Chem. Soc., Chem. Commun.*, 1978, 984.
7 K. Yamada, H. Shosenji, and H. Ihara, *Chem. Lett.*, 1979, 491.
8 K. Yamada, H. Shosenji, H. Ihara, and Y. Otsubo, *Tetrahedron Lett.*, 1979, 2529.
9 R. Ueoka, T. Terao, and K. Ohkubo, *Nippon Kagaku Kaishi*, 1980, 462.
10 K. Ohkubo, K. Sugahara, K. Yoshinaga, and R. Ueoka, *J. Chem. Soc., Chem. Commun.*, 1980, 637.
11 K. Ohkubo, K. Sugahara, H. Ohta, K. Tokuda, and R. Ueoka, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 576.
12 D. W. Ingles and J. R. Knowles, *Biochem. J.*, 1967, **104**, 369.
13 C. Gitler and A. Ochoa-Solano, *J. Am. Chem. Soc.*, 1968, **90**, 5004.
14 Y. Murakami, A. Nakano, K. Matsumoto, and K. Iwamoto, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 3573.
15 Y. Okahata, R. Ando, and T. Kunitake, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 3647.
16 W. B. Danklicker and V. A. de Saussure, in ' The Chemistry of Biosurfaces,' ed. M. L. Hair, Marcel Dekker, New York, 1971, vol. 1, ch. 1.
17 J. H. Fendler and E. J. Fendler, ' Catalysis in Micellar and Macromolecular Systems,' Academic Press, New York, 1975, p. 87.
18 J. F. Leffler, *J. Org. Chem.*, 1955, **20**, 1202.

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