Tetrahedron Letters No. 27, pp 2529 - 2532. 0040-4039/79/0701-2529$02.00/0

ENANTIOSELECTIVELY CATALYZED HYDROLYSIS OF p-NITROPHENYL ESTERS OF N-PROTECTED L-AMINO ACIDS BY N-LAUROYL L OR D-HISTIDINE IN CTABr MICELLES.

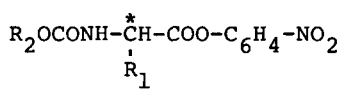
Kimiho YAMADA*, Hideto SHOSENJI, Hirotaka IHARA and Yonejiro OTSUBO

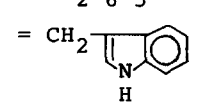
Department of Synthetic Chemistry, Faculty of Engineering,
Kumamoto University, Kumamoto 860, Japan

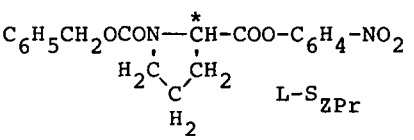
Summary: Remarkable dependencies of the rate constants and enantioselectivities on the substituents and protecting groups were demonstrated by the catalyzed hydrolysis of p-nitrophenyl esters of various N-protected L-amino acids by L or D-LauHis in the presence of mixed micelles with CTABr.

Our previous reports have described the effective enantioselectivities of N-lauroyl L or D-histidine (L or D-LauHis) toward the catalyzed hydrolysis of p-nitrophenyl esters of N-carboethoxy L or D-phenylalanine (L or D-S_{EP}) in the presence of cationic micelles.[1,2] In this work we studied the catalyzed hydrolysis of the following esters in order to investigate the relationship between

(Substrate)

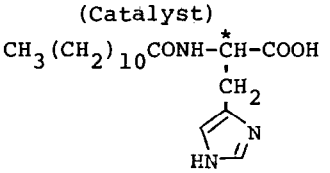


R_1	R_2	
= H	= $C_6H_5CH_2$	S_{ZG}
= CH_3	= "	L-S_{ZA}
= $CH(CH_3)_2$	= "	L-S_{ZV}
= $CH_2CH(CH_3)_2$	= "	L-S_{ZL}
= $CH_2C_6H_5$	= "	L or D-S_{ZP}
= 	= "	L-S_{ZT}
= $CH_2C_6H_5$	= CH_3CH_2	L or D-S_{EP}
= "	= $(CH_3)_3C$	L-S_{BP}



L-S_{ZPr}

(Catalyst)



L or D-LauHis

(Surfactant)

$CH_3(CH_2)_{15}N(CH_3)_3Br$

CTABr

the enantioselectivity and the structure of the substrate, especially focussing on the effects of the substituents (R_1) and the protecting groups (R_2).

The preparation of L or D-LauHis have been described eleswhere.[2,3] The substrates employed in this work were prepared in usual manners[4]: S_{ZG}, mp. 126.5-127.0°C(ref[5] 124-125°C); L-S_{ZA}, mp. 80.5-81.5°C(ref[6] 79.0-79.5°C); L-S_{ZV}, mp. 65.0-66.5°C(ref[5] 63°C); L-S_{ZL}, mp. 95.5-96.5°C(ref[7] 94-95°C); L-S_{ZP}, mp. 124.5-126.0°C(ref[8] 126-126.5°C); D-S_{ZP}, mp. 125.5-126.5°C; L-S_{ZT}, mp. 102.0-103.5°C(ref[7] 102.0-103.5°C); L-S_{EP}, mp. 120.5-121.0°C; D-S_{EP}, mp. 120.0-120.5°C; L-S_{BP}, mp. 126.5-127.5°C; L-S_{ZPr}, mp. 97.0-98.0°C(ref[4] 94-96°C)

The structures and the purities of these compounds were confirmed by the elementary analyses, IR and NMR spectra. The hydrolysis was followed spectrophotometrically at 25°C, pH 7.4 in 0.05M. Tris. buffer, 0.2M. KCl.

As given by Table I the hydrolysis of the substrate protected by N-carbo-

Table I. Hydrolysis of various esters.

Sub	$k_{a,obs}$ ($M^{-1}sec^{-1}$) L-LauHis	D-LauHis	L/D
S_{ZG}	37.4	37.4	1.00
L-S_{ZA}	50.8	33.8	1.50
L-S_{ZV}	12.2	6.51	1.87
L-S_{ZL}	92.2	39.9	2.31
L-S_{ZP}	149.6	68.0	2.20
D-S_{ZP}	65.4	—	—
L-S_{ZT}	21.4	17.4	1.25
L-S_{ZPr}	3.57	2.40	1.49

[CTABr]= 4 x 10^{-3}M, [Cat]= 1 x 10^{-4}M, [Sub]= 4 x 10^{-5}M, 10.0-6.67v/v%CH_3OH-CH_3CN-H_2O, $k_{a,obs} = k_{obs}/[Cat]$

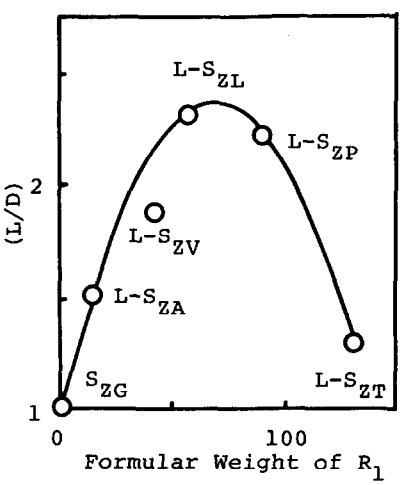


Fig.I. The relationship between (R_1) and (L/D).

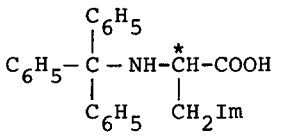
benzoxy function showed remarkable dependency of the rate constant and the enantioselectivity on the substituent (R_1) of the substrate. L-S_{ZV} and L-S_{ZPr} gave the rate constants smaller than the other substrates, implying steric hindrance of R_1 to the estercarbonyl carbon. Fig. I shows the plots of the selectivity (L/D) against the formular weight of R_1 which can be a measure of the size. The figure displays a bell shaped curvature with a maximum around R_1 of isobutyl and benzyl, indicating hydrophobic or steric fitness with these substituents.

Table II. Effect of protected groups (R_2).

Sub	R_2	$k_{a,obs}$ ($M^{-1}sec^{-1}$) L-LauHis	$k_{a,obs}$ ($M^{-1}sec^{-1}$) D-LauHis	L/D
L-S_{EP}	CH_3CH_2	73.2	43.9	1.67
L-S_{BP}	$(CH_3)_3C$	65.8	56.0	1.18
L-D_{ZP}	$C_6H_5CH_2$	149.6	68.0	2.20

[CTABr] = 4 x 10^{-3} M, [Cat] = 1 x 10^{-4} M, [Sub] = 4 x 10^{-5} M, 10.0-6.67v/v%CH_3OH-CH_3CN-H_2O.

Table II summarizes the results of the hydrolysis of the phenylalanine esters with three types of protecting groups. Obviously the selectivity depends so much on the structure of the protecting group as well. Benzyl type protecting group (carbobenzoxy group) afforded the largest selectivity, suggesting the hydrophobic fitness with the catalyst. As to D-LauHis the rate constant increased linearly with the size (or hydrophobicity) of the protecting group (R_2), whereas in the L-LauHis system t-butyl group afforded the least rate constant and the least enantioselectivity. The sterically bulky group appears to have a negative influence on the hydrogen bonding between the reagents, which, as Brown has mantioned[9], is one of the most essential factors to the enantioselectivity. In fact a small selectivity (L/D=1.07) was obtained from the catalyzed hydrolysis of L or D-S_{ZP} by N-trityl-L-histidine (L-TH) which has a sterically bulky trityl function.



N-trityl-L-histidine

(Im:1midazolyl)

By lowering the reaction temperature to 10°C the L/D value of the catalyzed hydrolysis of L and D-S_{ZP} by L-LauHis increased up to 2.75 (Table III). This is considered to arise from the increased tightness of the hydrogen bonding among the reagents or from the structural change of micelles.

Table III. Effect of temperature.

Temp (°C)	$k_{a,obs}$ ($M^{-1}sec^{-1}$) L-S_{ZP}	D-S_{ZP}	L/D
35.0	179.4	86.8	2.07
25.0	145.0	65.0	2.23
15.0	117.0	44.9	2.61
10.0	94.1	34.2	2.75

[CTABr]=4×10^{-3}M, [L-LauHis]=1×10^{-4}M, [Sub]=4×10^{-5}M, pH7.3

REFERENCES

1. H. Ihara, H. Shosenji, K. Yamada, The 15th Chemical Congress of Kyushu Branch of Japan Chemical Society (Fukuoka, 1978.7.14); Abstract, p.40.
2. K. Yamada, H. Shosenji, H. Ihara, Chem. Lett., in press.
3. T. Inoue, K. Nomura, H. Kimizuka, Bull. Chem. Soc. Jpn., 49, 719 (1976).
4. M. Bodanszky, V. du Vigneaud, J, Am. Chem. Soc., 81, 5688 (1959).
5. B. M. Iselin, Helv. Chim. Acta., 40, 373 (1957).
6. G. Goodman, J. Am. Chem. Soc., 81, 3980 (1959).
7. D. W. Ingles, J. R. Knowles, Biochem. J., 104, 369 (1967).
8. M. Bodanszky, V. du Vigneaud, J. Am. Chem. Soc., 81, 6072 (1959).
9. J. M. Brown, C. A. Bunton, J. Chem. Soc., Chem. Comm., 969 (1974).
10. G. C. Stelakatos, D. M. Teodoropoulos, L. Zervas, J. Am. Chem. Soc., 81, 2854 (1958).

(Received in Japan 24 March 1979)