Enantioselectivity in the Hydrolysis of Esters Catalyzed by Polyelectrolyte Surfactant Complexes

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Abstract. A cationic surfactant enhances the enantioselectivity of imidazole containing polymers of isocyanides in the hydrolysis of amino acid 4-nitro-phenyl esters.

Considerable efforts have been directed towards the construction of macromolecular model systems which mimic the high activity of esterolytic enzymes. The success achieved in this field contrasts sharply with the moderate progress made as to regio- and enantioselectivity of these systems. No or very small enantioselectivities have been reported in the hydrolysis of amino acid esters by imidazole containing chiral macromolecules. In the preceding communication we showed that complexation of imidazole containing poly(iminomethylene) polymers, \( \text{I} \) (Table), with cationic surfactants enhances the catalytic activity in the hydrolysis of the ester dinitrophenyl acetate. In the present paper we report that these systems also show enhanced enantioselectivity.

Poly(iminomethylene) \( \text{I} \) have chiral side chains with different absolute configurations. In addition, they possess a chiral main chain. This main chain has a rigid helical configuration which is either right-handed \( \text{P} \) or left-handed \( \text{M} \). The enantioselectivity of polymers \( \text{I} \) was tested in the hydrolysis of \( \text{N} \)-acetyl-(L or D)-alanine 4-nitrophenyl ester (Ac-Ala-ONP) and \( \text{N} \)-acetyl-(L or D)-phenylalanine 4-nitrophenyl ester (Ac-Phe-ONP). Reactions were performed at 23.00°C in the presence of \( 15.8 \times 10^{-4} \) mol/dm\(^3\) 1-cetylpyridinium chloride and also without this surfactant. Acetate or phosphate buffers were used, and the ionic strength was kept constant at 0.2 mol/dm\(^3\). The rates of hydrolysis were determined by following the increase in absorbance of 4-nitrophenolate at 360 nm.

All reactions obeyed first order kinetics. The second order rate constants \( k_{\text{cat}} \) were calculated from experiments with catalyst \( (k_{\text{obsd}}) \) and without catalyst \( (k_{\text{blank}}) \),

\[
 k_{\text{cat}} = (k_{\text{obsd}} - k_{\text{blank}})/[\text{Im}],
\]

in which \([\text{Im}]\) is the molar concentration of imidazolyl groups. The rates in the presence of surfactants are presented in the Table. Without surfactant the catalytic activity of the polymers is much lower. Since the blank rate is high, the accuracy of the latter data is low. Within this accuracy there is no enantioselectivity in the hydrolysis of the L- and D-esters.

In the presence of CePy\(^+\)Cl\(^-\) enantioselectivities \( k_{\text{L}}/k_{\text{D}} \) are observed ranging from 0.5 to about 3. These selectivities are the highest known to date for polymeric enzyme models. Two factors may be responsible for the observed enantioselectivities. First, a preferential solubility of one of the enantiomeric ester molecules in the chiral pseudophase of the polymer-surfactant complex and, secondly, a difference in Gibbs function of the diastereomeric transition states of hydrolysis by the chiral polymers. Both factors probably are important. With respect to the latter factor it is of interest to note that the highest selectivities are found at the lower pH-values. In a previous paper we have shown that during catalysis the protonated carboxylic acid functions and the unprotonated imidazole functions of our polymers act in a cooperative manner during catalysis. The carboxylic acid functions protonate the ester carbonyl function which favours attack by imidazole. The carboxylic acid functions might protonate the L and D ester carbonyl functions to a different extent which would cause a difference in reactivity and stereoselectivity.

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Table Catalytic rate constants $k_L$ and $k_D$ (dm$^3$.mol$^{-1}$.s$^{-1}$) of complexes of poly(iminomethylenes) and 1-cetylpyridinium chloride in the hydrolysis of chiral amino acid nitrophenyl esters.$^a$

<table>
<thead>
<tr>
<th>$R$ in ($R$-H-C)$_n$</th>
<th>Screw Sense</th>
<th>Substrate$^c$</th>
<th>pH 5.6</th>
<th>pH 6.2</th>
<th>pH 7.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>hp(A$_H$L)</td>
<td>M</td>
<td>2a</td>
<td>4.20</td>
<td>0.32</td>
<td>1.68</td>
</tr>
<tr>
<td>cp(A$_S$L)$_1$(A$_H$L)$_2$</td>
<td>M</td>
<td>2a</td>
<td>0.39</td>
<td>0.50</td>
<td>1.36</td>
</tr>
<tr>
<td>cp(A$_S$L)$_1$(A$_H$L)$_1$</td>
<td>M</td>
<td>2a</td>
<td>2.58</td>
<td>1.52</td>
<td>4.33</td>
</tr>
<tr>
<td>hp(A$_H$L)</td>
<td>P</td>
<td>2a</td>
<td>1.83</td>
<td>0.70</td>
<td>0.37</td>
</tr>
<tr>
<td>hp(A$_D$L)</td>
<td>P</td>
<td>2a</td>
<td>1.52</td>
<td>0.75</td>
<td>0.37</td>
</tr>
</tbody>
</table>

$a$ In water at 23.00°C; 0.2 mol/dm$^3$ acetate (pH 5.6) and phosphate buffer (pH 6.2 and 7.0); [I] $10^{-4}$ mol repeating units/ [Cepy$^+$Cl$^-$] $15.8 \times 10^{-4}$ mol/dm$^3$. All experiments were performed in duplicate or triplicate.

$b$ hp = Homopolymer; cp = copolymer; A, H and S stand for alanyl, histidinyl and serinyl residues, respectively; subscripts indicate the ratio of residues in the copolymer.

$c$ 2a = (Ac-Ala-ONP), 2b = (Ac-Phe-ONP).

References


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