

Letter

Catalytic activities of novel L-histidyl group-introduced polymers imprinted by a transition state analogue in the hydrolysis of amino acid esters

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Received 1 May 1995; accepted 26 May 1995

Abstract

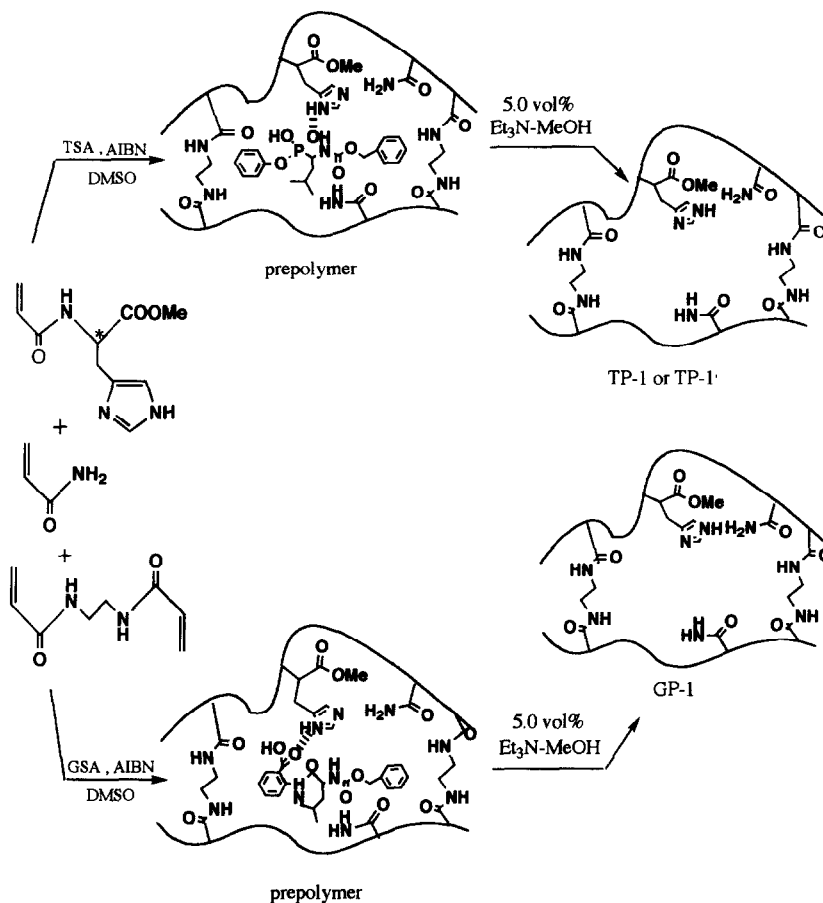
The catalytic activities of L-histidyl group-introduced, cross-linked polymers imprinted by a transition-state analogue (phenyl 1-benzyloxycarbonylamino-3-methylpentylphosphonate) or a ground-state one (*N*-(*N*-benzyloxycarbonyl-L-leucinoyl)anthranilic acid) for the esterolysis of a marked substrate of *p*-nitrophenyl *N*-benzyloxycarbonyl-L-leucinate were examined in the hydrolysis of amino acid esters; a transition-state analogue recorded polymer possessing a low cross-linker content (8.7%) exhibited the highest catalytic activity for the marked substrate hydrolysis with the positively largest activation entropy and the smallest activation free energy.

Keywords: Hydrolysis; Molecular imprinting; Polymer catalyst; Transition state analogue

Although the polymers prepared by the 'molecular imprinting' technique for creating a new kind of catalyst, so-called 'plastic enzyme', have recently received the attention of many chemists [1], the transition state analogue (TSA)-recorded polymer catalysts have hitherto been the subject of only limited investigation; there are only three reports on the esterolytic catalysis of the imidazole- or L-histidine-containing cross-linked polymers imprinted with *p*-nitrophenol methylphosphonate (TSA for the hydrolysis of *p*-nitrophenol acetate) [2-4]. Therefore, further

investigations of novel TSA-imprinted polymer catalysts seem of interest and significant to design efficient 'plastic enzymes'. This paper deals with the catalytic activities of newly synthesized TSA- or GSA (ground state analogue)-recorded cross-linked polymers possessing the catalytic site of L-histidyl group for the selective esterolysis of a marked substrate in the hydrolysis of amino acid esters; Phenyl 1-benzyloxycarbonylamino-3-methylpentylphosphonate or *N*-(*N*-benzyloxycarbonyl-L-leucinoyl)anthranilic acid was respectively selected as a template molecule of TSA or GSA for the following hydrolysis of a marked substrate, *p*-nitrophenyl *N*-benzyloxycarbonyl-L-leucinate (*Z*-L-Leu-PNP) (Scheme 1).

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constants obtained with and without the polymer catalyst, respectively, and $[\text{His}]$ denotes the catalytically active L-histidyl group concentration (determined by the $^1\text{H-NMR}$ spectra) in the polymer catalyst.

In Table 1 are listed the rate constant ratio ($k_{\text{cat}}/k_{\text{uncat}}$) and $k_{\text{cat}}^{\text{APP}}$ values for the hydrolysis of Z-L-Leu-PNP by *N*-acryloyl-L-histidinate

monomer (His), GP-1, TP-1, and TP-1' at 303 K. As the $k_{\text{cat}}/k_{\text{uncat}}$ and $k_{\text{cat}}^{\text{APP}}$ values in Table 1 indicate, the catalytic activities of the template-imprinted polymers followed the order of (None) < (His) < GP-1 < TP-1 < TP-1'. Thus, the catalytic activities of the TSA-imprinted polymers (TP-1 and TP-1') were appreciably higher than that of the GSA-recorded one (GP-1). TP-

Table 1
Kinetic parameters for hydrolysis of Z-L-Leu-PNP by TSA-or GSA-imprinted polymer catalysts at 303 K^a

Catalyst	$10^3 k_{\text{cat}}^{\text{APP}}$ min^{-1}	$k_{\text{cat}}/k_{\text{uncat}}$	$10^3 k_{\text{cat}}^{\text{APP}}$ $\text{mol}^{-1} \text{dm}^3 \text{min}^{-1}$	ΔH^\ddagger kcal mol^{-1}	ΔS^\ddagger $\text{cal mol}^{-1} \text{K}^{-1}$	ΔG^\ddagger kcal mol^{-1}
GP-1	4.78	2.0	12.3	21.8	10.6	18.6
TP-1	5.22	2.2	66.8	19.2	5.3	17.6
TP-1'	8.79	3.7	98.2	31.2	45.2	17.5
His	3.44	1.4	10.4	4.5	-47.1	18.8
None	2.40			22.6	-4.35	23.9

^a Reaction conditions are given in the text.

1' possessing a larger cavity compared with that of TP-1 was found most effective among the polymer catalysts tested. The catalytic activities of these imprinted polymers are also reflected in the activation parameters determined by the temperature dependency of $k_{\text{cat}}^{\text{app}}$ values. The increased values of activation enthalpy (ΔH^\ddagger) for GP-1, TP-2 and TP-1' compared with that for His imply that the reaction of the polymer catalysts with the substrate in their template-shape recorded cavities is energetically impaired by the somewhat restricted proximity between the catalytically active L-histidine imidazole group of the polymers and the susceptible carbonyl group of the substrate. However, the positively enhanced values of activation entropy (ΔS^\ddagger) for GP-1, TP-2 and TP-1', which probably demonstrates the efficient substrate inclusion by the polymer catalysts through their hydrophobic interaction with the substrate, decreased the values of the activation free energy (ΔG^\ddagger) in the same activity order of None < His < GP-1 < TP-1 \leq TP-1'. Therefore, the entropic factor rather than the enthalpic one played an important role in the esterolytic catalysis of the present template-imprinted polymer catalysts. Thus, the TP-1' polymer catalyst having

the low-cross linker content (8.7%) exhibited the highest activity with the rate constant ratio of $k_{\text{cat}}/k_{\text{uncat}} = 3.7$ for the Z-L-Leu-PNP hydrolysis, but it indicated the lower activity for the hydrolysis of other amino acid *p*-nitrophenyl esters such as Z-L-Phe-PNP possessing a more hydrophobic but sterically-hindered side chain and Z-L-Ala-PNP having a more sterically facilitated side chain; the observed $k_{\text{cat}}/k_{\text{uncat}}$ ratios were 1.8 for Z-L-Phe-PNP and 2.2 for Z-L-Ala-PNP. Hence, the TP-1' catalyst was also capable of exhibiting an efficient molecular recognition ability in its esterolytic catalysis.

The further investigation of the TSA-imprinted polymer catalysts improved by changing their frameworks, TSA, and so on for the enhancement of their catalytic abilities are now in progress.

References

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