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Abstract
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The enantioselective synthesis of (S)-Naproxen piperazinylalkyl ester prodrugs via Candida rugosa lipase had high enzyme activity and enantioselectivity. To obtain best reaction conditions, the selection of reaction medium and different preparations of immobilized lipases containing different water activity were studied. Effects of alkyl chain length of piperazinylalkyl alcohols on enzyme activity and enantioselectivity had also been discussed.

The results show that the hydrophobicity of reaction medium has great impact on the activity and enantioselectivity of lipases, and isooctane was the best reaction medium. The best acyl acceptor was 4-(4-methyl-1-piperazinyl)-butanol with the high enzyme activity (VS = 0.12 (mM g-1 h-1) and enantioselectivity (E = 143.5).

The isopropanol dehydration treament of immobilized lipase has good enantioselectivity and the best enzyme activity. The 4-(4-methyl-1-piperazinyl)-butanol still acts as an enzyme inhibitor at higher alcohol concentration and its optimal alcohol concentrations were around 1.5 mM. The enantioselectivity of the esterification increased with the increase of alcohol concentration and excessed 100. Water activity for enzyme activity and enantioselectivity was evaluated with the lipase-catalyzed esterification piperazinylalkyl alcohols with (R,S)-Naproxen. The different preprations of lipase expressed maximal activity at aw = 0.53 and the highest enantioselectivity at aw = 0.33 under different piperazinylalkyl alcohol, respectively.
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