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Abstract
The enantioselective synthesis of (S)-Naproxen morpholinoalkyl ester prodrugs via Candida rugosa lipase had high enzyme activity and enantioselectivity. To obtain best reaction conditions, the selection of reaction medium and immobilized lipases containing different water content were studied. Effects of alkyl chain length of hydroxyalkyl morpholines on enzyme activity had also been discussed. The stability of heat and operation for immobilized lipases protreated with isopropyl alcohol (IPA-dried lipases) were further investigated.

The results show that the hydrophobicity of reaction medium has great impact on the activity and enantioselectivity of lipases, and isooctane and cyclohexane were best reaction medium. Increasing the alkyl carbon chain length of hydroalkyl morpholine decreases the lipase activity and enantioselectivity in enantioselective esterification processes. The use of IPA-dried lipase could improve the enzyme activity and greatly enhance the enantioselectivity with the value more than 100.

The optimum alcohol concentrations for hydroxypropyl morpholine and hydroxybutyl morpholine were found around 10 mM and 5 mM, respectively. The enzymatically enantioselective transesterification procedure for the synthesis of (S)-Naproxen morpholinoalkyl ester prodrugs from racemic 2,2,2-trifluoroethyl Naproxen can improve the enzyme activity and enantioselectivity. An optimum reaction temperature around 37℃ was obtained by using IPA-dried lipases
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