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Abstract
A lipase-catalyzed enantioselective esterification process in organic solvents was developed for the synthesis of (S)-naproxen hydroxyalkyl ester and (S)-ketoprofen hydroxyalkyl ester. With the selection of lipase (Candida rugosa lipase and Lipase MY) and reaction medium (isooctane and cyclohexane), a high enantiomeric ratio of >100 for the enzyme were obtained for the synthesis of (S)-Naproxen hydroxyalkyl ester. 1,4-Butanediol was the best acyl acceptor. The carbon chain length of the alcohol had a major effect on the enzyme activity and enantioselectivity of lipase-catalyzed esterification. For the synthesis of (S)-Ketoprofen hydroxyalkyl ester with the same reaction condition, a low enantiomeric ratio and the enzyme activity for the lipase was obtained. The functional group of (R,S)-2-arylpropionic acids have a major effect on the enantioselectivity and activity of lipase.

Because of a low enantiomeric ratio and the enzyme activity for the enzyme were obtained for the synthesis of (S)-Ketoprofen hydroxyalkyl esters. The propanol dried enzyme preparations of lipases are found to improvement the enantioselectivity and enhance the enzyme activity in the synthesis of (S)-Ketoprofen (or Naproxen) hydroxyalkyl esters. The value of enantiomeric ration of lipase-catalyzed esterification of (R,S)-Ketoprofen with 1,4-butanediol can reach 37 with IPA-dried lipase in the temperature around 27°C.

To solve the limitation of solubility of alcohols using silica gel-adsorbed alcohols was established in lipase-catalyzed esterification reactions. The presence of silica gel-adsorbed alcohols can reduce the inhibition of high alcohols concentration and increase the equilibrium conversion in the system.
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