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Abstract
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A lipase-catalyzed enantioselective dynamic kinetic resolution thiotransesterification in organic solvents was developed for the synthesis of (S)-naproxen morpholinoalkyl ester produrg. With the selection of lipase (Lipase MY) and reaction medium (isooctane), the increase of the alkyl carbon chain length of hydroxyalkyl morpholine increased the lipase activity and enantioselectivity in the lipase-catalized enantioselective thiotransesterification. The optimum temperature and enantioselectivity for the preparation of isopropanol-dried immobilized lipase (IPA-dried IM lipase) was found around 4℃ and 5℃.

The reactions were carried out at lower initial control of water activity that can effectively reduce the degree of the side reaction of hydrolysis. IPA-dried IM lipase expressed the highest thiotransesterification / hydrolysis ratio at the aw = 0.06 , the highest initial rate of thiotransesterification at aw = 0.11 and the highest enantioselectivity for (S)-Naproxen morpholinoalkyl ester produrgs at aw = 0.75 . The constant control of aw was more effective than the initial control of aw for reducing the side reaction of hydrolysis.

The hydroxyalkyl morpholines still acted as an enzyme inhibitor and exited an optimum of the naproxen trifluoroethyl thioester / hydroxybutyl morpholine ratio (SR) at SR = 1/3 for the initial rate of thiotransesterification of (S)-Naproxen trifluoroethyl thioester (VS,Q).
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