Kinetic resolution of 4-phenyl-2-azetidinone in supercritical carbon dioxide

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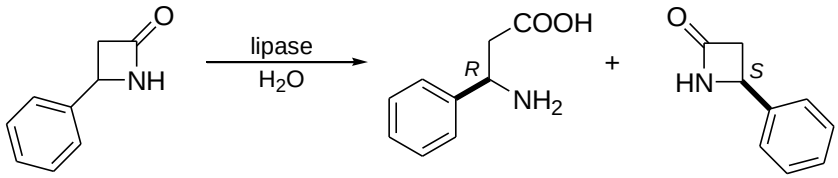
There are continuous efforts in the synthesis of enantiopure β-lactam derivatives and β-amino acids. These compounds are efficiently used in modern medical practice (as antibiotics, antitumor drugs) and are promising candidates in further drug developments [1, 2]. Ring opening reactions of β-lactams by commercially available lipases are viable [3-5]. Lipases can be stable in supercritical carbon dioxide ($scCO_2$) as well [6-8]. Using $scCO_2$ has some advantage over other non-aqueous mediums such as increased mass transfer or solvent-free products obtained after the depressurisation.

Lipase-catalysed kinetic resolution of *rac*-4-phenyl-2-azetidinone using water as nucleophilic donor was investigated in $scCO_2$ in a batch reactor (inner volume: 30 mL).



Lipolase (lipase B from *Candida antarctica*) was used in 1:1 mass ratio with the substrate. The samples were analysed by GC. Reaction kinetics, pressure and temperature effects were studied in details. This enzymatic resolution is performed with full conversion obtaining enantiomerically pure (*R*)-β-amino acid (*ee* > 99%) and (*S*)-β-lactam (*ee* > 99%) at once. The optimal pressure and temperature of the reaction are 150 bar and 70°C. The products could be easily separated by supercritical carbon dioxide extraction of the (*S*)-β-lactam and subsequent washing of the enzyme by water to recover the amino-acid.

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