

N°770 / OC

TOPIC(s) : (Chemo)enzymatic strategies / Biocatalytic cascade reactions

Enhancement of enzymatic kinetic resolution by a new chemoenzymatic cascade strategy

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PURPOSE OF THE ABSTRACT

Aldehydes are common byproducts in enzymatic kinetic resolution (EKR) and enzymatic dynamic kinetic resolution reactions. Due to their high reactivity, physical properties and explosive character they are hardly tolerated in organic laboratories especially in large scale experiments. The most volatile acetaldehyde **4** is formed as byproducts in enzymatic esterification of alcohols, amines or thiols when ethyl acetate is used as an acyl group donor. Hydrolysis of epoxyesters also led to formation of aryl and alkyl aldehyde which are very often very effective enzyme inhibitors. To overcome this common issue in EKR processes we propose a new strategy based on combination of enzyme catalyzed reaction with subsequent aldol reaction into a one-step chemoenzymatic cascade process. In order to eliminate aldehyde's presence in reaction mixture and push the equilibrium towards product formation addition of dimedone **5** into reaction mixture is crucial. This lead to cascade of chemical reaction in which aldehyde **4** the byproduct from enzyme catalyzed reaction immediately reacts with dimedone **5** to form respective aldol product **6** in almost quantitative yield. Elimination of aldehydes presence in reaction mixture makes the process environmentally friendly, and greatly eliminates the enzyme inhibition what is crucial for successful experiments. The validity of the concept on selected examples will be presented and discussed.

ACKNOWLEDGMENT

The project was supported by the Polish National Science Center project No. OPUS No. 2019/33/B/ST4/01118 and COST action COZYME CA21162.

FIGURES

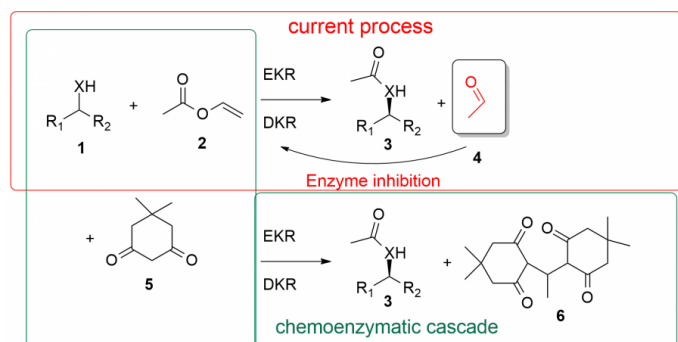


FIGURE 1

Figure 1

General synthetic concept

FIGURE 2

KEYWORDS

Kinetic resolution | chemoenzymatic cascade | byproduct utilization | enzyme activation

BIBLIOGRAPHY

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