Supporting Information for

Lipase-catalyzed Knoevenagel Condensation Together with Esterification in the Presence of Organic solvents

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General procedure for the Synthesis of products:

1 mmol aromatic aldehydes and 50 mg lipases (purchased from J&K Inc.) in 5 ml solvent was incubated at 40°C at 150 rpm. (orbitally shaken) for 30 min. Then, methyl cyanoacetate (1.5 equiv) was added to initiate the reaction. After 12 h, the reaction was terminated by filtering off the enzyme. The crude product was purified by chromatography on silica gel (petroleum ether-EtOAc), recrystallization can be used to purify most of our product.

The structure of the adducts and position of addition was confirmed by 1H NMR and 13C NMR using CDCl3 as solvent and chemical shifts are expressed in ppm with reference to Me4Si. TLC (silica gel; petroleum–ethyl acetate, 3:1) was used to monitor the reaction.

Screening reactions were performed by using GC-MS every few hours. Initial temperature 60°C, then programed heating to 220°C in a 10/min rates.
The denatured procedure: lipase was put in boiling water in the beaker for 1 hour. Let the solution cool to room temperature. Solvent was evaporated under vacuum to dryness.

Procedure for the lipase catalyzed large scale reaction: Paranitrobenzaldehyde 1 (750mg 5mmol) was dissolved in 25mL of Ethanol. To this homogeneous solution, 1ml water and 300mg lipase were added. Then 1 equiv methyl cyanoacetate was added. The reaction mixture was kept at end-over-end rotator at 150rpm at 60°C. After 12h, cooled down the mixture to room temperature, the enzyme was filtered off. The product was separated by recrystallization in filter liquor directly.

**Data of NMR** (1H-NMR (CDCl3, δ, ppm, 300 MHz)

![NMR spectrum](image)