SUPPLEMENTARY INFORMATION

Materials:

Immobilised *Candida Antarctica* lipase B (Novozym® 435) was from Novozymes©. All conventional and 'green' solvents as well as the reagents were purchased from SigmaAldrich choosing the highest purity available. Water content was determined for each solvent, as supplied, via Karl-Fischer analysis providing the following results:

Solvent	Water [ppm]
Hexane	18.7
p-Cymene	158.9
Limonene	1255.7
CPME	99.0
Toluene	212.2
Di-isopropyl ether	103.4
DCE	179.8
Diethylether	226.9
MeTHF	311.2
Dimethyl carbonate	376.8
Ethylene carbonate	NA
Chloroform	157.9
MEK	NA
Cyclopentanone	NA
Acetonitrile	118.3
Pyridine	NA
Acetone	NA
DMF	1066.9
THF	148.4
Diethyl carbonate	116.2
DMSO	8359.6

Typical experimental procedure:

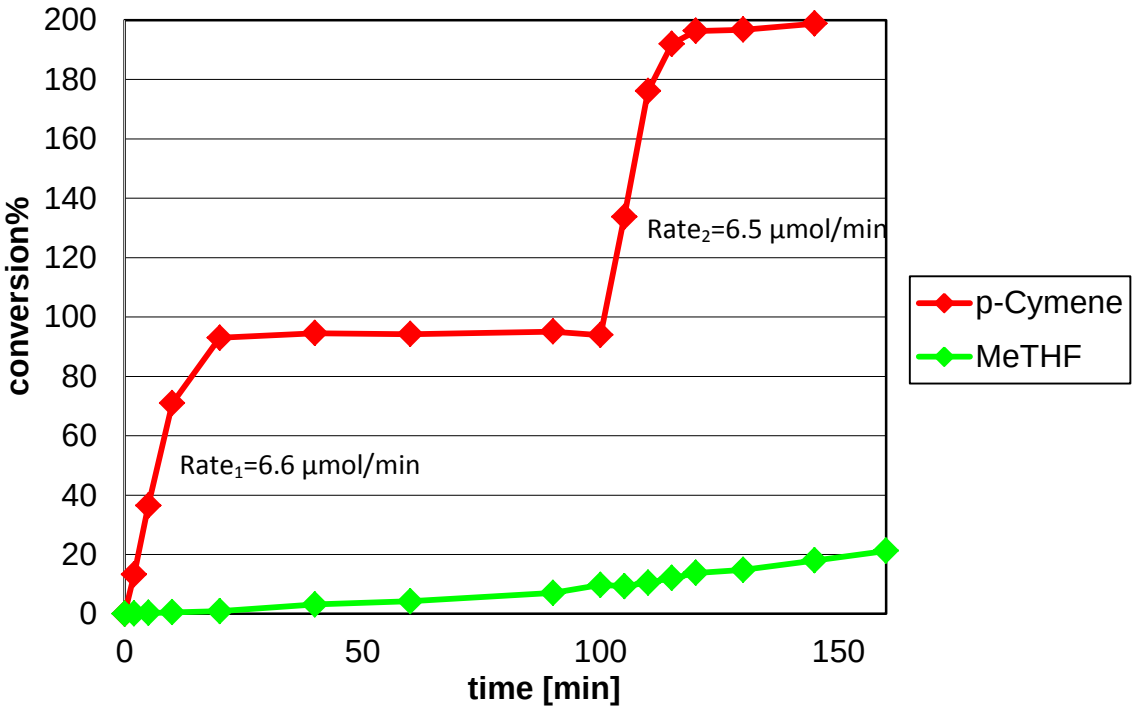
Candida Antarctica lipase B (20mg) was added to 20ml of a solution containing 100mM lauric acid and 5mM internal standard - tetradecane. The reaction vessel was stirred and heated to 40°c on a heating plate for it to reach the desired conditions. The mixture was sampled at t_0 and at frequent intervals after the addition of 250uL (0.2044g, 2mmol) of 1-hexanol. The preparation of each GC sample involved filtration on cotton-wool and dilution with DCM.

GC Method:

Analyses were performed with a Agilent Technologies 6890N Network GC System equipped with FID detector.
Samples were analyzed on a ZB-5HT column (15m X 0.25mm X 0.25mm) and a FID detector in the following conditions: carrier gas (He) at 1 MPa (20 mL/min total flow); temperature programme: 50 ◦C, 9 ◦C/min, 190 ◦C; split ratio 10:1; detector 300 ◦C. The retention times of compounds were confirmed by standards and appeared as follows: hexanol (4.6 min); tetradecane (internal standard, 9.8 min), lauric acid (11.1 min), hexyl laurate (13.5 min).
The percentage yield was defined through a calibration curve.

*a slower/lengthened method (2°C/min) was applied in a few cases in which the solvent signal overlapped with the product peak.

Catalyst reusability:



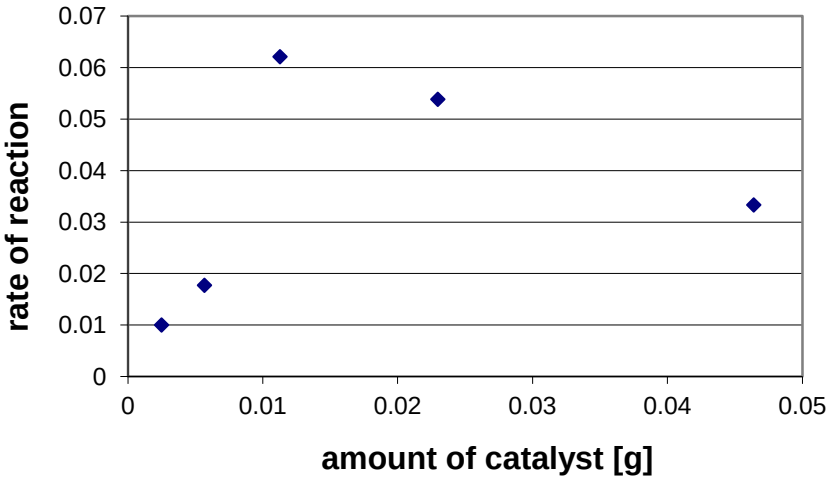
p-Cymene and in 2-methylTHF were chosen as solvents for the catalyst's reusability tests. The first run was performed according to the experimental procedure presented.

As for the reaction in p-cymene, the addition of fresh reagents after 100 minutes of reaction (2mmol lauric acid : 2mmol hexanol) showed approximately 100% retention of the catalyst's activity ($Rate_2/Rate_1$ = 0.98).

Similar observations can be made as for the reusability in 2-MeTHF, however with rather low conversion and reaction rate.

This is especially promising for the application of Novozym435 in continuous flow reactors.

Influence of the amount of catalyst:



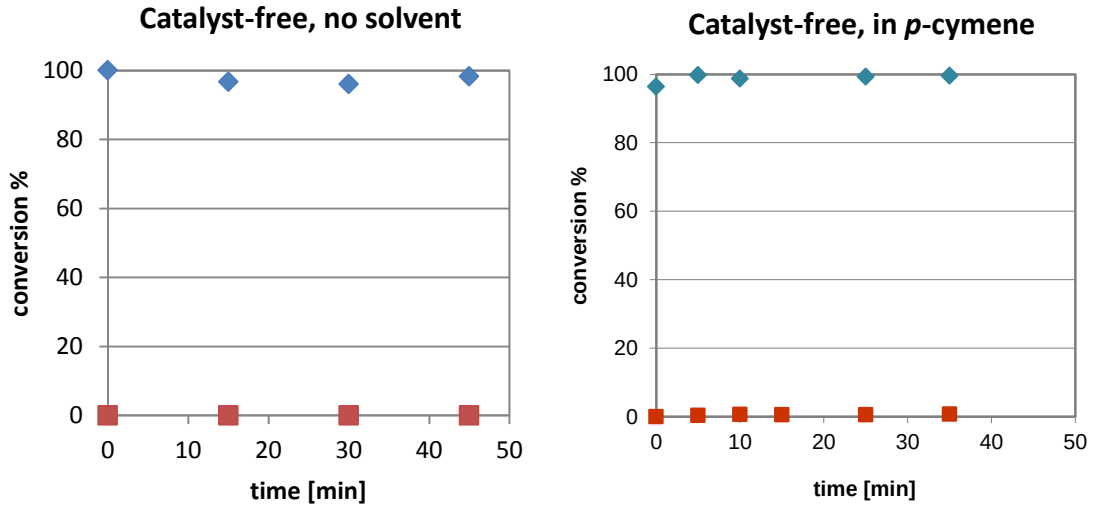
It was found that catalyst load in the range from 10 to 20mg was the most effective for this reaction under the conditions employed.

Scale up

The reaction was performed in 30 grams scale in *p*-cymene with the same procedure described, yielding 98% product.

Catalyst-free tests

Test reactions in solvent-free conditions have been carried out applying the typical experimental protocol, both in presence and absence of the biocatalyst.
The starting material lauric acid represented as blue diamonds; hexyl laurate product represented as red squares.



The biocatalyst has proven to be a crucial component of the synthesis, since no conversion of the starting material into the final product has been observed in absence of the catalyst both in *p*-cymene and in solvent-free conditions.