## Triple Cascade Reaction Leading to TetraSubstituted Cyclohexenes

## Key words



One-pot triple-cascade reaction:
Michael-Michael-Aldol sequence
$20 \mathrm{~mol} \%(R)-1$ or $(S)-1$
toluene, $0^{\circ} \mathrm{C}$ to r.t.
16-24 h, 25-58\%


5


40\% yield
$\mathrm{dr}=3.5: 1$
$>99 \%$ de, ee

$51 \%$ yield
dr = 5.3:1
$>99 \%$ de, ee

ent-5


56\% yield dr $=3.8: 1$
$>99 \%$ de, ee


25\% yield
$\mathrm{dr}=2.1: 1$
$>99 \%$ de, ee


54\% yield dr = 99:1 $99 \%$ de, ee

Significance: A novel 3-component organocatalytic cascade reaction is reported that generates cyclohexene derivatives 5 with four contiguous stereogenic centers in good diastereoselectivities (from 2.1:1 to 99:1) and high enantioselectivities (>99\%). A large variety of substrates can be used: aldehyde $\mathbf{2}$ can be aliphatic or highly functionalized; the $\alpha, \beta$-unsaturated aldehyde $\mathbf{4}$ tolerates aromatics as well as aliphatics. However, nitroolefin $\mathbf{3}$ is limited to aromatic substrates. Surprisingly, the product itself did not react further with the catalyst, possibly due to steric hindrance.

Comment: Construction of several stereogenic centers in complex molecules in a single step is one of the most challenging and desirable processes in synthetic chemistry. Herein the authors present a remarkably broad substrate scope for such a cascade reaction, which allows for building blocks that can be used in natural product synthesis. Moreover, the easy access to both enantiomers of the catalyst gives rise to a large diversity of products. One advantage of this transformation is that it can be employed to combinatorial processes without the need of any protecting groups.

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