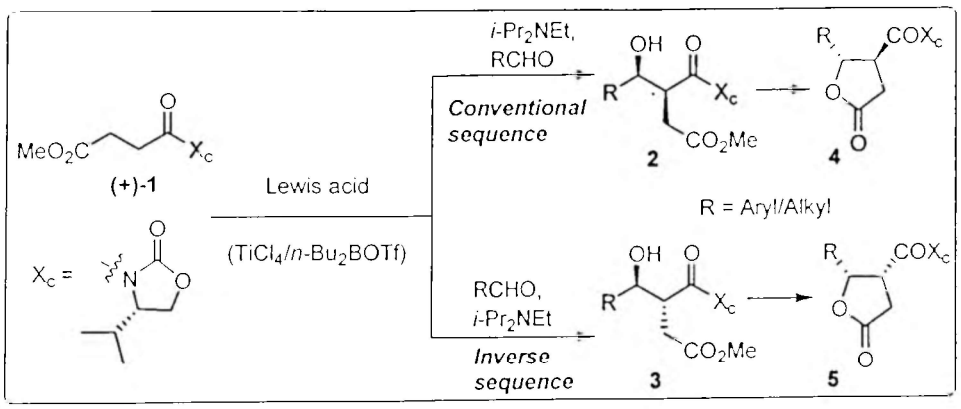
Abstract

Chiral auxiliary based and organocatalyzed aldol reactions have been proved to be very useful methods for the asymmetric synthesis of various natural products. We have developed the strategies using these key reactions and applied them to the synthesis of γ-butyrolactone natural products and analogs.

A highly asymmetric route for the one-pot synthesis of *trans*- and *cis*-4,5-disubstituted-γ-butyrolactones (e.g. **4** and **5**) via reagent sequence controlled *syn*- and *anti*- aldol reactions of *N*-succinyl-2-oxazolidinone **(+)-1** (**Scheme 1**) are described. The details of the work and mechanistic study are also discussed.



Scheme 1. Diastereoselective *syn*- and *anti*-aldol reactions of *N*-succinyl-2-oxazolidinone

Using the same set of reagents and via asymmetric *syn*- and *anti*-aldol reactions of chiral *N*-succinyl-2-oxazolidinones **1**, synthesis of *trans*-paraconic acids like methylenolactocins (**6**), nephrosteranic acids (**7**), roccellaric acids (**8**) and *cis*-paraconic acids like phaseolinic acids (**9**) and chiral intermediates towards nephromopsinic acids (**10**) (**Figure 1**) are accomplished in both of their enantiomeric forms.

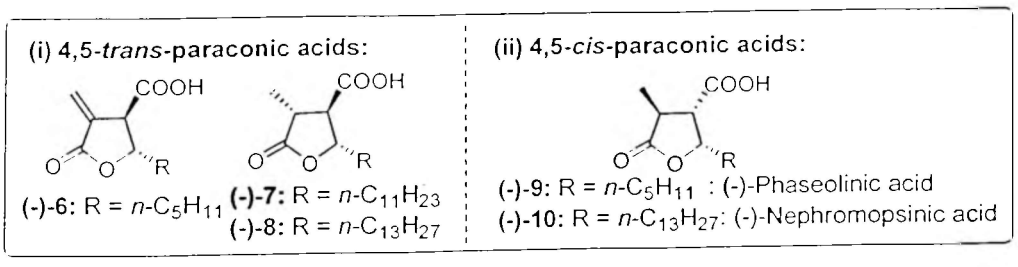
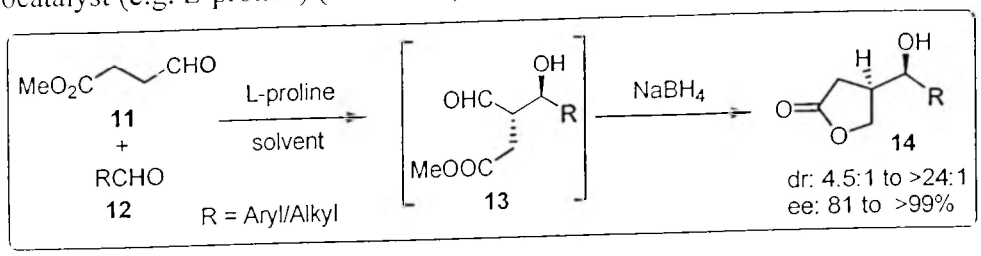


Figure 1. Paraconic acids

We have also developed enantioselective one-pot synthesis of *β*-(hydroxyalkyl)-*γ*-butyrolactones **14** employing cross-aldol (*anti*-aldol) reaction catalyzed by an organocatalyst (e.g. L-proline) (**Scheme 1**).



Scheme 2. Organocatalyzed enantioselective one-pot synthesis of γ-butyrolactones

We have developed an efficient and short route for the asymmetric synthesis of (–)-enterolactone (**15**) and its analog **16** utilizing organocatalytic asymmetric cross-aldol reaction and C-alkylation as the key steps. Similar routes have provided chiral lactones **17** and **18**, which are likely to be useful intermediates for the synthesis of epi-isohydroxymatairesinol and (7*R*)-7-hydroxymatairesinol (**Figure 2**).

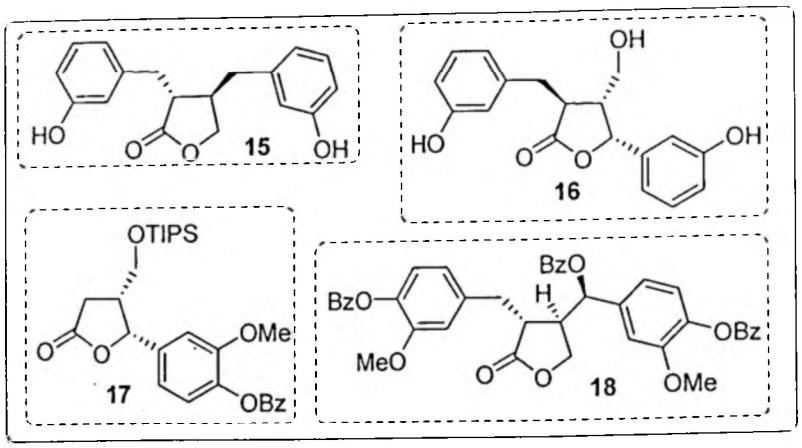


Figure 2. Lignans

Key words: Chiral auxiliary; Organocatalyst; Aldol reaction; Asymmetric synthesis; γ-butyrolactones; Paraconic acids; Lignans.