

### Enantiopure synthesis of (R)- $\gamma$ -valerolactone from levulinic acid by chemoenzymatic method

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Cellulosic biomass is useful in industrial applications because of large-scale availability, low cost and non-food character. Utilization of cellulose, however, is hindered due to the production cost and catalytic power of cellulases. LA is a promising alternative, readily obtainable from cellulosic biomass, and used to synthesize value-added  $\gamma$ -valerolactone (GVL). GVL is a precursor to natural products, bioactive molecules, bio-fuels and carbon-based chemicals. This study has focused on four issues to make GVL synthesis efficient: high enantiopurity, high yield, usage of free form of LA as substrate rather than alkyl ester form, and moderate reaction conditions. A two-step chemoenzymatic strategy for asymmetric synthesis of (R)-GVL from LA was employed. In the first step, LA is converted into 4-hydroxyvaleric acid (4HV) by engineered 3-hydroxybutyrate dehydrogenase (e3HBDH) which was enhanced for catalytic activity on LA. In the second step, the lactonization of 4HV to (R)-GVL is promoted by dehydration with 1 % (v/v) sulfuric acid. The (R)-GVL was successfully produced with nearly 100% yield and high enantiopurity (> 99 % ee) from the free acid form of levulinic acid.