

***Pichia glucozyma*: a powerful biocatalyst for enantioselective reduction of ketones**

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The asymmetric reduction of prochiral ketones using isolated or cell-bound ketoreductases is a well-recognised method for the preparation of chiral alcohols. The major drawback encountered with enzymatic reduction using isolated enzymes is the necessity for cofactor recycling, which can be circumvented by two-enzyme or one-enzyme recycling methodologies. Whole cells exhibit as a major advantage that cofactors are already present and can be intrinsically recycled *via* the oxidation of a second substrate. Beside the easily available *Saccharomyces cerevisiae*, other microbial species have been widely employed for asymmetric reductions or more generally as sources for new selective ketoreductases, since there is still a need for new biocatalysts able to perform stereoselective reductions with different or ameliorated chemo-, regio- and stereoselectivity. Non-conventional yeasts are plentiful sources of different carbonyl reductases and during our past works on enantioselective carbonyl reduction we have found that whole cells of the yeast *Pichia glucozyma* CBS 5766 (now reclassified as *Ogataea glucozyma*) catalysed the stereoselective reduction of different ketones, often showing remarkable results in terms of activity and stereoselectivity. In this work, we have studied the potential of whole cells of *Pichia glucozyma* CBS 5766 for the reduction of various ketones with cells grown under optimised conditions. Enantioselective reduction of aromatic ketoesters and preparation of intermediates for chemo-enzymatic synthesis of steroids and prostaglandins are among the biotransformations studied. Purification and characterization of ketoreductases from *P. glucozyma* are under study.

1) Matsuda, T., Yamanaka, R., & Nakamura, K. **2009**. Recent progress in biocatalysis for asymmetric oxidation and reduction. *Tetrahedron: Asymmetry*, 20(5), 513–557.

2) Hall, M., & Bommarius, A. S. **2011**. Enantioenriched compounds via enzyme-catalyzed redox reactions. *Chemical reviews*, 11(7), 4088–4110.

3) Monti, D., Ottolina, G., Carrea, G., & Riva, S. **2011**. Redox reactions catalyzed by isolated enzymes. *Chemical reviews*, 111(7), 4111–4140.

4) Moore, J. C., Pollard, D. J., Kosjek, B., & Devine, P. N. **2007**. Advances in the Enzymatic Reduction of Ketones. *Accounts of chemical research*, 40(12), 1412–1419.

5) Forzato, C., Gandolfi, R., Molinari, F., Nitti, P., Pitacco, G., & Valentin, E. **2001**. Microbial bioreductions of γ - and δ -ketoacids and their esters. *Tetrahedron: Asymmetry*, 12(7), 1039–1046.

6) Fragnelli, M. C., Hoyos, P., Romano, D., Gandolfi, R., Alcántara, A. R., & Molinari, F. **2012**. Enantioselective reduction and deracemisation using the non-conventional yeast *Pichia glucozyma* in water/organic solvent biphasic systems: preparation of (S)-1,2-diaryl-2-hydroxyethanones (benzoins). *Tetrahedron* 68(2), 523–528.

7) Husain, S. M., Stillger, T., & Dünkelfmann, P. **2011**. Stereoselective Reduction of 2-Hydroxy Ketones towards syn- and anti-1, 2-Diols. *Adv. Synth. Catal.* 353, 2359 – 2362