Preparation of enantiopure secondary alcohols using cells consortia of *Candida albicans* and *Lactobacillus brevis*.

Fábio D. Nasário[1](PG)*, Natalia M. Polidoro[1](IC), J. Augusto R. Rodrigues[1](PQ), Paulo J. S. Moran[1](PQ), Tarcila Cazetta[1] (PG).

[1] Institute of Chemistry, University of Campinas (UNICAMP), 13083-970 Campinas, SP, Brazil.
fabio.nasario@iqm.unicamp.br

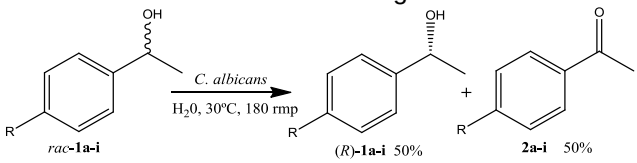
Keywords: *Keywords: Oxidation, kinetic resolution, deracemization*

Introduction

Secondary alcohols are interesting chiral building blocks for the synthesis of natural products, pharmaceutical, and agriculture chemicals. The obtainment of these compounds by kinetic resolution or deracemization catalyzed by whole cells of microorganism is not well studied as reduction of pro-chiral ketones in literature[1,2].

Results and Discussion

1-Phenylethanol and some *p*-substituted 1-phenylethanols were submitted to biocatalysis with whole cells of *C. albicans* (CCT 5847) (Scheme 1) and we observed some interesting results.



Scheme 1. Kinetic resolution of 1-phenylethanols.

The yeast strain was able to oxidize only the (*S*)-enantiomer of the most compounds studied. The Table 1 shows these results, yields, and enantiomeric excess.

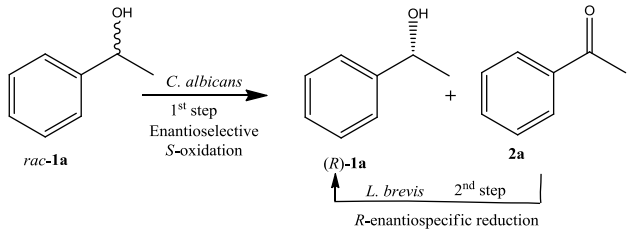
Table 1. Kinetic resolution of *p*-substituted 1-phenylethanols.

R	Time (h)	Yield (%)	*ee* % (*R*)
H (**1a**)	1	35	93
Cl (**1b**)	50	40	87
F (**1c**)	1	49	98
Br (**1d**)	1	46	>99
OH (**1e**)	28	47	>99
CH_3 (**1f**)	44	35	>99
OCH_3 (**1g**)	24	33	>99
NH_2 (**1h**)	48	---	---
NO_2 (**1i**)	8	55	31

We attained a successful kinetic resolution for almost all compounds studied, except for **1h** (totally oxidized) and **1i** (partial selective oxidized). We immobilized *C. albicans* cells in calcium alginate spheres and we could obtained similar results as shown in table 1: 50% of (*R*)-**1a** 93% ee with only 30 minutes of reaction.

In our search to find a microorganism with an anti-Prelog alcohol dehydrogenase (ADH) we made a screening with some yeasts, fungus and bacteria, and we observed that *L. brevis* (ATCC 14869) was able to reduce acetophenone (**2a**) and form (*R*)-**1a** with 99% *ee* in 24 hours of reaction time. Our objective then was use the immobilized cells of *C. albicans* and the free cells of *L. brevis* to make the process of oxidative kinetic resolution be more effective than 50% maximum yield.

After we established the minimum amount of acetone that recycles the NAD^+ used in the oxidative step with *C. albicans;* and the use of 2-propanol or glucose to regenerate the NADH used in reductive step with *L. brevis* we obtained a successful deracemization of **1a** with 17 hours (Scheme 2).



Scheme 2. Deracemization process of **1a**.

Conclusion

We prepared some *p*-substituted (*R*)-1-phenylethanols by oxidative kinetic resolution catalyzed by whole cells of *C. albicans* with regular to good yields (theoretical maximum yield is 50%) with moderate to excellent enantiomeric excesses. We also obtained 99% yield of (*R*)-**1a** 99% *ee* by deracemization in two steps: a oxidative step with immobilized cells of *C. albicans* and a reductive step using *L. brevis* cells in less than 1 day, that is very impressive.

Acknowledgements

To CNPq, FAPESP (process 2014/00108-9), Institute of Chemistry-UNICAMP.

1 Stampfer, W.; Kosjek, B.; Faber, K.; Kroutil, W., Biocatalytic Asymmetric Hydrogen Transfer Employing *Rhodococcus ruber* DSM 44541. *J. Org. Chem.* **2003,** *68* (2), 402-406.

2 Gamenara, D.; Seoane, G. A.; Saenz-Méndez, P.; de María, P. D., Reactions Involving Dehydrogenases. In Redox Biocatalysis, John Wiley & Sons, Inc.: 2012; pp 101-179.