

Influence of microwave irradiation on lipase-catalyzed kinetic resolution of (±)-mandelonitrile

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INTRODUCTION

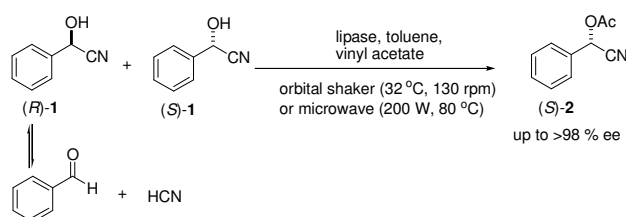
The synthesis of optically pure cyanohydrins is an area of growing interest in synthetic chemistry¹. Microwave irradiation has also attracted considerable interest in recent years because of their advantages, such as reduced chemical reaction time, reduced side reactions, increased yields and improved reproducibility². The objective of this study was investigate the kinetic resolution of (±)-mandelonitrile (**1**) using lipase from *Candida antarctica* under microwave irradiation and conventional conditions.

RESULTS AND DISCUSSION

The kinetic resolution of (±)-mandelonitrile **1** was made with the lipase of *Candida antarctica* (160 mg) using (80 µL, 0.067 mmol) of *rac*-mandelonitrile in toluene (10 mL) and vinyl acetate (500 µL) under microwave irradiation and conventional heating.

Microwave irradiation experiment was performed with Discover System from CEM Corporation: The whole reaction mixture was placed in the microwave oven and irradiated at 80°C, about 200 W. The reaction progress was monitored by collecting samples (2 µL) according to the time indicated in Table 1, which were analyzed by GC-FID with chiral stationary phase, while conventional heating lipase-catalyzed acylation reaction was made in an orbital shaker at 32°C and 130 rpm. The results are summarized in Table 1.

The microwave irradiation showed to be efficient for the enzymatic resolution providing decrease in reaction time and good yield and enantiomeric excess. In addition, the conventional kinetic resolution was performed in 7 days producing (*S*)-mandelonitrile **2** (Table 1). The (*R*)-mandelonitrile (**1**) unreacted, by conventional and microwave reactions, resulted spontaneously in a chemical equilibrium producing the benzaldehyde (Scheme 1).



Scheme 1.

Table 1. Comparison of microwave irradiation and conventional heating on lipase kinetic resolution of (±)-mandelonitrile (**1**).

Time (h)	c (%) 1	c (%) 2	ee (%) 2
Microwave Irradiation			
2	75	25	>98
4	68	32	>98
6	63	38	>98
8	60	40	>98
Conventional Experiment			
48	67	33	>98
72	65	35	>98
120	63	37	>98
168	54	46	>98

CONCLUSION

This study shows the first efficient kinetic resolution of (±)-mandelonitrile (**1**) by lipase from *C. antarctica* under conventional and microwave conditions, producing exclusively the (*S*)-mandelonitrile acetate (**2**) in high selectivity (> 98% ee). The kinetic resolution in toluene proceeded with rate enhancement reducing chemical reaction time in microwave irradiation in comparison with conventional experiment.

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