



Chemoenzymatic resolution of fluorinated compounds by lipase CALB under microwave irradiation

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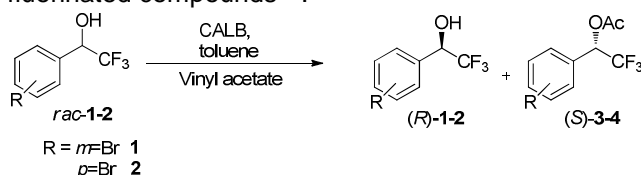
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INTRODUCTION

The synthesis of fluorinated organic compounds has shown an important contribution to the development of pharmaceuticals, agrochemicals and materials, especially due to the electron withdrawing influence of the fluorine groups^{1,2}. This study aimed the investigation of the chemoenzymatic resolution of (±)-1-(3-bromophenyl)-2,2,2-trifluoroethanol **1** and (±)-1-(4-bromophenyl)-2,2,2-trifluoroethanol **2**, using lipase from *Candida antarctica* (CALB) under microwave irradiation and orbital shaker.

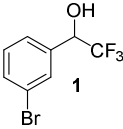
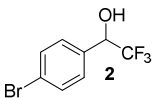
RESULTS AND DISCUSSION

The chemoenzymatic resolution of *rac*-**1** and *rac*-**2** were conducted in orbital shaker or under microwave irradiation, where were used: lipase CALB (160 mg), *rac*-**1** (40 µL, 0.26 mmol), *rac*-**2** (40 µL, 0.26 mmol), toluene (10 mL) and vinyl acetate (500 µL, 5.4 mmol). The reactions were conducted in a microwave reactor Discover CEM (80 °C, 200 W) and in an orbital shaker (32 °C, 130 rpm). The progress of the reaction was monitored by collect of samples (250 µL) in different times, extracted with ethyl acetate (1.5 mL). The analyses were performed by GC-FID with a chiral capillary column model Varian CP-7500 cyclodextrin-β-2,3,6-M-191 (25 m x 0.25 mm x 0,25 µm). For the *rac*-**1** (Table 1) was observed that under microwave irradiation to (S)-**3** (14 h, c=42%, 78% ee) that the reaction time was reduced, when compared to reaction in orbital shaker (144 h, c=49%, 82% ee). Chemoenzymatic resolution yielded the (S)-**4** with better enantioselectivity and conversion in orbital shaker (48 h, c=49%, >99% ee) and microwave irradiation (14 h, c=49%, 98% ee). In the literature, excellent results have been reported by us using microwave irradiation in chemoenzymatic reactions of fluorinated compounds^{3,4}.



Scheme 1

Table 1. Chemoenzymatic resolution of fluorinated compounds **1-2** with CALB.

Substrate	time (h)	c (%)	c (%) 3	ee (%)
	Orbital shaker			
	48	66	34	83
	72	60	40	83
	120	52	48	83
	144	49(36)*	51(34)*	82
	Microwave irradiation			
	1	94	6	83
	6	74	26	81
	12	62	38	81
	14	58	42	78
Substrate	time/h	c (%)	c (%) 4	ee (%)
	Orbital shaker			
	2	95	5	99
	4	94	6	99
	24	65	35	99
	48	51(20)*	49(21)*	99
	Microwave irradiation			
	1	88	12	99
	6	65	35	99
	12	54	46	98
	14	51	49	98

*Isolated yields; enantiomeric excesses of (S)-acetates; c: concentration of unreacted alcohols; c: conversion of acetates determined by GC-FID analyses.

CONCLUSION

The reaction time was significantly reduced using microwave irradiation when compared to reactions in orbital shaker for the enzymatic resolution of fluorinated compounds **1-2** in the presence of CALB.

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