Enzymatic Kinetic Resolution of Hydroxy Furan and Tiophene 2-substituted

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INTRODUCTION

Chiral non racemic secondary alcohols containing 2-Furan and Tiophene rings are widely widespread compounds in the environment and they also play important role in biochemical process.[1] In addition these compounds can be employed as building blocks in the synthesis of bioactive molecules. However, environmentally harmful reagents and many reaction steps are generally assigned to synthetic methodologies that employ it.[2] Here, we propose a chemoenzymatic methodology to prepare enantioenriched secondary alcohols containing furan and tiophene heterocyclic group.

RESULTS AND DISCUSSION

Initially a set of *sec*-alcohols containing furan and tiophene rings **1a**-**h** (Figure 1) were prepared according with the literature[3] in good yields.

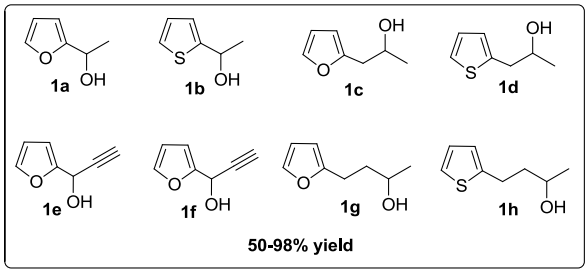
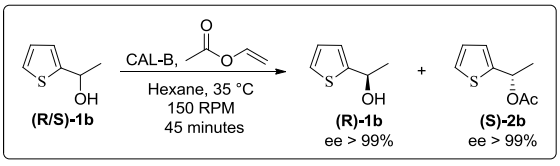


Figure 1. Furan and tiophene derivatives

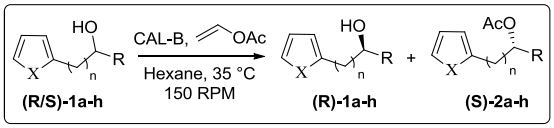
The racemic compound **1b** was submitted to the enzymatic kinetic resolution (EKR) using vinyl acetate as acyl donor, the enzyme *Candida antarctica* lipase (CAL-B) and *n*-hexane as a non-polar organic solvent (Scheme 1).



Scheme 1. Analytical scale EKR of **(R,S)-1b**

The bioresolution of racemic substrate by CAL-B showed an anti Kaslauskas rule preference obtaining the free alcohol **(R)-1b** and ester **(S)-2b** in its enantiomeric pure form (*e.e.* > 99%).

With this, the initial parameters were extended to EKR of the alcohols **1a-h** (Scheme 2 and Table 1).



Scheme 2. Racemic alcohols **1a**-**h** EKR.

Table 1. EKR of the racemic alcohols **1a**-**h**.

Table 1. EKR results of the alcohols **1a**-**h**.

Entry	Substrate	R	n	x	Time (min)	(R)-1a-h (*e.e.*- %)	Yield[a] (%)	(S)-2a-h (*e.e.*- %)	Yield[b] (%)
1	(R/S)-**2a**	-CH_3	0	O	60	> 99	35	79	40
2	(R/S)-**2b**	-CH_3	0	S	45	> 99	49	> 99	40
3	(R/S)-**2c**	-CH_3	1	O	300	> 99	49	80	49
4	(R/S)-**2d**	-CH_3	1	S	270	> 99	46	> 99	45
5	(R/S)-**2e**	-CCH	0	O	30	> 99	49	> 99	30
6	(R/S)-**2f**	-CCH	0	S	120	99	49	68	46
7	(R/S)-**2g**	-CH_3	2	O	10	> 99	45	96	49
8	(R/S)-**2h**	-CH_3	2	S	10	> 99	48	> 99	39

[a] Isolated yield of the alcohols (R)-**1a-h**
[b] Isolated yield of the esters (S)-**1a-h**

As can be seen in the table 1, the chiral non racemic (***S***)-substrates and (***R***)-esters were obtained in an excellent enantioselectivity. Actually the enantiopure compound (***S***)-**1g** has been employed as key intermediate in the enantioselective synthesis of bioactive Pyrenophorine.[4]

CONCLUSION

The alcohols **(R)-1a-h** and esters **(S)-2a-h** have been acquired in high (>99%) and moderated (from 68% to 99%) enantiomeric excess, respectively. The preliminary results have shown that alcohols containing furan and tiophene as heterocyclic compounds could be resolved by CAL-B.

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