Search for an enzymatic approach to achieve the enantiomeric enrichment of β-borylated carboxylic esters

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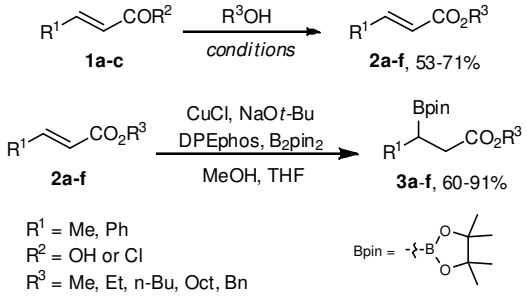
INTRODUCTION

Lipases are the most used enzymes in organic chemistry. Their ability of enantiomers recognition by these biocatalysts represents a useful tool to synthesis of enantiomerically enriched compounds.[1] Additionally, boron-containing compounds have increased the interest of scientists for being important building blocks of bioactive substances.[2] The organoboron compounds are employed mainly in the Suzuki-Miyaura cross-coupling reactions.[3] Herein, we are focused on development of an enzymatic way to enrich enantiomerically boron-containing carboxylic esters, catalyzed by lipases.

RESULTS AND DISCUSSION

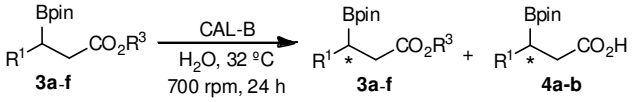
Initially, the carboxylic esters were synthesized from acids or acyl chlorides. β-borylated compounds were synthesized according to the methodology described in the literature.[4] (Scheme 1).



Scheme 1 – Syntheses of β-borylated compounds **3a-f**.

Enzymatic assays were carried out in order to search of lipase for enantioselective hydrolysis of the compound **3a**. Among tested catalysts, CAL-B has shown the highest activity (e.e. 78% for **3a**); PSD-I and PSC-II furnished the ester with low e.e. (<10%). Although the product of hydrolysis is the carboxylic acid **4a-b**, the efficiency of enzymatic assays was measured by e.e. values of compound **2a**. We have also tested to perform the hydrolysis in organic solvents. Water-miscible and water-immiscible solvents were employed; however, no improvement was detected, leading low e.e. values (10-43%) for **3a**. The highest e.e. was obtained when a mixture water:dioxane (9:1) was used as solvent. Our protocol was extended to compounds **3b-f**, which present longer chains / steric hindrance.

Table 1 – Enzymatic hydrolysis of **3a-f**.[a]

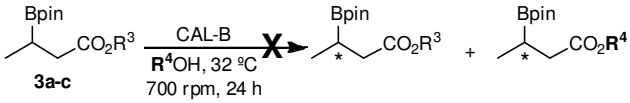


Ester	R^1	R^3	e.e. (%)
3a	Me	Me	78
3b	Me	Et	74
3c	Me	*n*-Bu	<10
3d	Me	Oct	*rac.*
3e	Me	Bn	*rac.*
3f	Ph	Et	*rac.*

[a] Conditions: H_2O (1 mL), CAL-B (10 mg), **3a-f** (0.05 mmol).

We have observed that these structural changes result in a large decrease in e.e. values. (Table 1). In view of achieve the enantiomeric enrichment of the boron compounds by lipase-catalyzed reaction, we turned our attention to transesterification reactions. Thereby, the reactions were carried out with esters **3a-c**, using a set alcohol as solvent and CAL-B as catalyst. Unfortunately, the preliminary tests gave no product from transesterification reaction. (Table 2).

Table 2 – Transesterification reaction of **3a-c**.[a]



Ester	R^3	R^4
3a	Me	Et
3b	Et	Me
3c	*n*-Bu	Me

[a] Conditions: R^4OH (1 mL), CAL-B (10 mg), **3a-c** (0.05 mmol).

CONCLUSION

In summary, we have shown an enzymatic way to achieve the enantiomeric enrichment of β-borylated carboxylic esters. Esters presenting a long carbon chain did not suffer any hydrolysis reaction. The improvement of transesterifications are in progress.

ACKNOWLEDGEMENTS

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