Bioreduction of Morita-Baylis-Hillman Adducts and Derivatives: A New Approach to Asymmetric Chemo-enzymatic Synthesis of Fragrances

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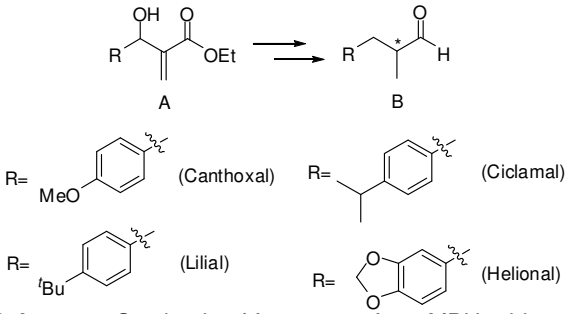
INTRODUCTION

The synthesis of optically active compounds is a highly challenging task for organic chemists, especially if targeted final products possess remarkable applications for the fine chemical industrial sector.[1] It has been extensively demonstrated along recent years that Biocatalysis offers ecological, economic, scalable and straightforward methods for the production of fine chemical with high enantiomeric excess. For all of that, we have focused our attention in the production of chiral fragrances.[1]

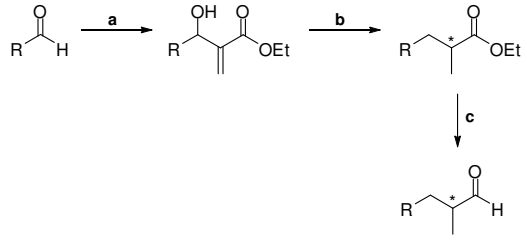
RESULTS AND DISCUSSION

According to the scheme below, the Morita-Baylis-Hillman (MBH) adducts **A** can be employed as versatile substrates to synthesis of the fragrances **B**.



Scheme 1. Synthesis of fragrances from MBH adducts.

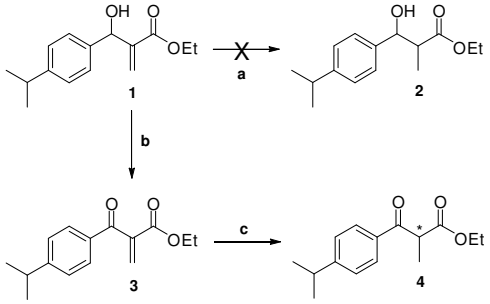
Recently, we have developed a simple and straightforward synthetic strategy for the preparation of 4 fragrances, racemic form, in 3 steps and overall yield of 34-41% (Scheme 2)[2].



(**a**) CH_2CHCO_2Et, DABCO, ultrasound, 75%;
(**b**) Pd/C (10%), Et_3SiH, MeOH, r. t., 10 min., 64%;
(**c**) DIBAL-H (1.1 eq.), CH_2Cl_2, -90°C, 30 min., 80%. (average yields)

Scheme 2. Synthesis of fragrances.

After that, our aim is to establish an asymmetric synthetic strategy to prepare the fragrances **B** because each stereoisomer exerts a different olfactive perception.To the chiral study we have utilized the Biocatalysis as synthetic platform. Firstly, the MBH adduct **1** was treated with baker's yeast in the presence of biphasic system ionic liquid/water at 30 °C and 400 rpm for 24h (Scheme 3)[3]. The desired product **2** not was observed. Next, we have realized the oxidation reaction of the benzylic hydroxyl forming the product **3** in excellent yield. Then, we employed this intermediate at the same reduction conditions and obtained the product **4**, after 9h, in 98% conversion. In this step, we observed a moderate enantiomeric excess of 62% (after 3h) and this value decreases with time due to racemization of compound **4**.



(**a**) baker's yeast, $[bmim]PF_6$/water, 30 °C, 400 rpm, 24h;
(**b**) IBX, acetonitrile, 1h15min, >99%;
(**c**) baker's yeast, $[bmim]PF_6$/water, 30 °C, 400 rpm, 9h, 98%.

Scheme 3. Synthesis of chiral fragrances.

CONCLUSION

In summary, we are developing a new asymmetric approach, *via* Biocatalysis, to prepare 4 available commercially fragrances. Studies are ongoing in our laboratory in order to avoid racemization and to increase the *ee* in step biocatalytic.

ACKNOWLEDGEMENTS

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