Proline and Steroids: An important synergism acting as organocatalyst in enantioselective green aldol reaction

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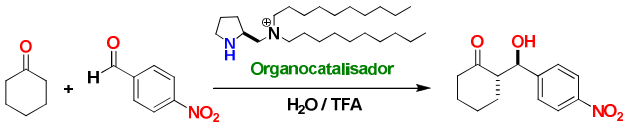
INTRODUCTION

Asymmetric reactions mediated by organocatalysts, has received great attention in recent years and becoming a versatile tool in the synthesis of natural products and active compounds. In this context, the amino acid proline has a key role as mediator of these reactions, which recently has demonstrated great interest in the area of asymmetric catalysis in the development of reactions that can be performed in aqueous media. (Scheme1)[1]



Scheme 1. Aldol reaction organocatalysed in aqueous solution.

The substitution of organic solvents with water minimizes environmental impact; in addition to low cost and have a decrease in operational hazard. However, the use of aqueous solution as reaction solvent is not always efficient because the water often inhibits the activity of the catalyst or changes the enantioselectivity

Herein, we describe the synthesis of new organocatalysts derivatives from amino acid L-proline and D-proline with steroid cholesterol and its applications as organocatalysts in enantioselective aldol reaction with water as the main solvent.

RESULTS AND DISCUSSION

The chiral proline-steroids organocatalysts **2a-c**, were prepared in a few steps reactions. Firstly the coupling of N-Boc proline with the amino cholesterol partner, we chose the method of mixed anhydride (ethyl chloroformate and N-methyl morpholine). Following the deprotection of the boc group.the desired organocatalyst were obtained in good yields (Figure 1).

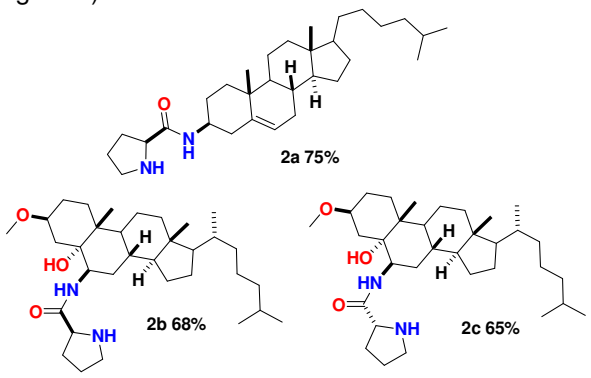
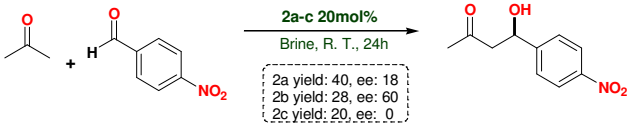


Figure 1. Organocatalysts **2a-c** with overall yields

The organocatalysts **2a-c**, were then evaluated in the aldol addition, between acetone and 4-NO_2-benzaldehyde at room temperature for 24 hours by using brine as solvent. (Scheme 2).



Scheme 2. Aldol reaction between aldehydes and ketones

CONCLUSION

The steroid-peptides derived from proline showed to be efficient organocatalysts, being able to mediate the aldol addition reaction efficiently in green solvent (brine), leading to satisfactory yields and good enantiomeric excess. Studies toward the application of organocatalyst 2b to several aromatic aldehydes are in progress.

ACKNOWLEDGEMENTS

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