

Application of New Organocatalysts on Asymmetric Epoxidation of Chalcones

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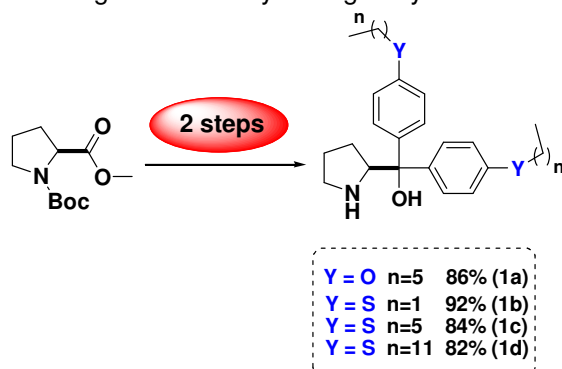
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INTRODUCTION

Optically active epoxy ketones are versatile building blocks for synthesis of several natural products and pharmaceuticals. In this context, the development of efficient methods for the asymmetric epoxidation of α,β -enones is a interesting goal in organic synthesis.¹ In order to achieve these purpose, the enantioselective organocatalysis is an useful tool in the synthesis of building blocks under practical conditions. In this work, we highlight the synthesis and application of a new class of organocatalysts in the enantioselective synthesis of epoxy ketones.

RESULTS AND DISCUSSION

The catalysts were easily prepared from *N*-Boc-proline in 2 steps (Scheme 1). Firstly the addition of Grignard reagent to *N*-Boc-proline ester, followed by deprotection of the Boc group with DMSO/MeOH and KOH gave the catalysts in good yields.

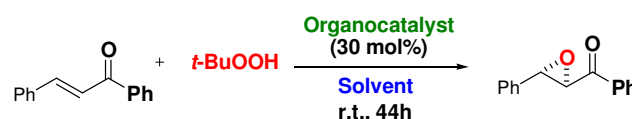


Scheme 1. Synthesis of organocatalysts **1a-d**.

Having these catalysts, we started our studies with the chalcone, using *t*-BuOOH as oxidant reagent, 30 mol% of catalyst and room temperature. The optimization of the reaction conditions are shown in Table 1.

After analyzing the reaction parameters such as solvent, time, temperature and the amount of the organocatalyst, we could observe that the best organocatalyst for this reaction is **1a** (30 mol%), wich gave the product in 88% yield and 82% ee, using hexane as a solvent. After recrystallization the ee was increased to 99% (Entry 2).

Table 1. Epoxidation of chalcones.



Entry	Organo catalyst	Solvent	Yield (%) ^a	ee (%) ^b
1	1a	Hexane	57	64 ^c
2	1a	Hexane	88	82(99^d)
3	1b	Hexane	66	50
4	1c	Hexane	55	50
5	1d	Hexane	45	50
6	1a	H ₂ O	35	58
7	1a	Ethanol	16	34
8	1a	THF	15	50
9	1a	Toluene	32	50
10	1a	PEG	15	48
11	1a	DMSO	2	0
12	1a	Hexane	64	80(98 ^d) ^e
13	1a	Hexane	34	86(100 ^d) ^f
14	1a	Hexane	68	56(94 ^d) ^g
15	1a	Hexane	73	54 ^h

^a After chromatographic column. ^b Determinated by HPLC using chiral column. ^c 24 h. ^d After recrystallization ^e 0°C. ^f -8 °C. ^g -8 °C, 88h. ^h 20 mol% of **1a**.

CONCLUSION

We have developed efficiently a new class of organocatalyst in the enantioselective synthesis of epoxiketones. Our efforts are now focused on the application of the optimized conditions to different α,β -unsaturated ketones.

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REFERENCES

¹ (a) Porter, M. J.; Skidmore, J. *Chem. Commun.* **2000**, 1215. (b) Lauret, C. *Tetrahedron: Asymmetry* **2001**, 12, 2359.