

Design of poly-functionalized catalysts and additives for the Morita-Baylis-Hillman reaction

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Resumo

In this work we developed a new synthetic approach for the preparation of bi-functional catalysts derived from imidazole, without conformational constraints and having a center acting as Lewis base and other as Bronsted acid. These new catalysts were prepared in three steps, in overall yields ranging from 15% to up 48%, using Morita-Baylis-Hillman adducts as building blocks.

Palavras-chave: Morita-Baylis-Hillman, Organocatalysis, Lewis bases.

Introduction

In the present, organocatalysis is a research area of great relevance, since it employs organic molecules to increase rate of organic processes, avoiding the use of metals.¹ This project had as proposal planning, synthesizing and testing new bi-functional organocatalysts (**2**) in organic reactions, using Morita-Baylis-Hillman (MBH) adducts² as building blocks. This work was based on previous results of our laboratory with catalyst **1** (BIA).³

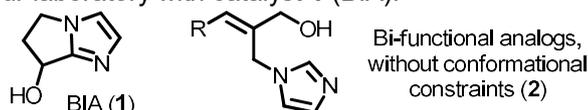
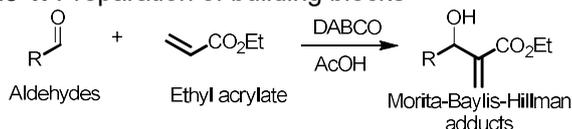


Figure 1: BIA Molecule (**1**) compared with the planned new catalysts (**2**).

Results and Discussion

We began our work by preparing the MBH adducts. The results achieved were summarized in Table 1.

Table 1. Preparation of building blocks



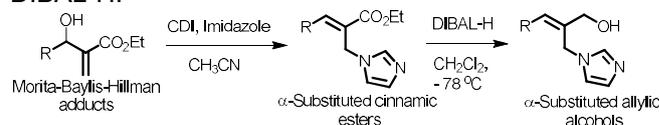
Entry	Aldehyde, R	Time (h)	%
1	C ₆ H ₅	72	64
2	3,5-F ₂ -C ₆ H ₃	120	73
3	3,4(CH ₂ OCH ₂)C ₆ H ₃	168	42
4	2-C ₅ H ₄ N	4	95
5	3-C ₅ H ₄ N	120	54
6	C ₂ H ₅	168	35

All adducts were successfully prepared (Table 1, entries 1-6) in good yields and reasonable reaction times. The spectral data (¹H- e ¹³C NMR) are compatible with the structures proposed for each one.

With the adducts in hands, we followed our synthetic planning. Thus, compounds **1-6** were submitted to the Michael addition conditions to provide the corresponding α -substituted ethyl cinnamates. The results are summarized on Table 2.⁴

The conjugated additions afforded the α -substituted cinnamic esters in good yields. The analysis of spectral data (¹H- and ¹³C-NMR) confirmed the proposed structures for each Michael adduct.

Tabela 2. Michael addition and ester reduction with DIBAL-H.



Imidazole addition – cinnamic esters			
Entry	MBH adducts	Time (h)	%
1	C ₆ H ₅	2	57
2	3,5-F ₂ -C ₆ H ₃	1	70
3	3,4(CH ₂ OCH ₂)C ₆ H ₃	1	56
4	2-C ₅ H ₄ N	2	85
5	3-C ₅ H ₄ N	*	*
6	C ₂ H ₅	*	*
DIBAL-H reduction – allylic alcohols			
Entry	Cinnamic esters	Time (h)	%
7	3,5-F ₂ -C ₆ H ₃	2	57
8	3,4(CH ₂ OCH ₂)C ₆ H ₃	2	62
9	2-C ₅ H ₄ N	2.5	60

* Entries 5 and 6 did not provide the Michael addition products after 4 h.

Following our synthetic planning, the dichloromethane solutions of cinnamic esters were reduced by treatment with DIBAL-H at -78 °C to afford the corresponding allylic alcohols in good yields. The results were summarized in Table 2 (second part).

At this stage of work, we were able to prepare the planned catalyst in three steps in overall yields ranging from 15% to up 48%. The efficiency of these new catalysts will be evaluated in the catalysis of some Morita-Baylis-Hillman reactions and aldolic condensations.

Conclusions

Based on an original synthetic planning we prepared some imidazolic allylic alcohols to be tested as bi-functional organocatalysts in organic reactions. The main features of these new catalysts is its absence of conformational constraints and the presence of basic and acid centers.

Acknowledgements

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¹ Dalko, P. I.; Moisen, L. *Angew. Chem. Int. Ed.* **2004**, *43*, 5138-5175; ² Coelho, F.; Almeida, W. *Quim. Nova* **2000**, *23*, 98-101; ³ Gomes, J. C.; Rodrigues, Jr., M. T.; Moyano, A.; Coelho, F. *Eur. J. Org. Chem.* **2012**, 6861-6866; ⁴ Rodrigues, M.; Santos, M.; Santos, H.; Coelho, F. *Tetrahedron Lett.* **2014**, *55*, 180-183.