A facile three-component one-pot solvent-free synthesis of 2'-aminobenzimidazolomethylnaphtols

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Abstract

A facile, one pot three-component procedure for the efficient synthesis of novel 2'-aminobenzimidazolomethylnaphtols derivatives was developed by the reaction of 2-aminobenzimidazole, 2- naphtol and aromatic aldehydes in the presence of L-proline under grinding and solvent free condition at room temperature.

***Keywords*:** 2'-aminobenzimidazolomethylnaphtols; L-proline; Multicomponent reaction; grinding; solvent free.

Introduction

Benzimidazoles and 2-aminobenzimidazoles are privileged organic compounds due to their interesting biological properties. Many substituted 2-aminobenzimidazole derivatives have found applications in diverse therapeutic areas including antiviral, antifungal, anthelmintic and antihistaminic to name just a few.[1] The pharmaceutical importance of benzimidazole-containing structures has prompted extensive studies for their synthesis.[2]

Today, one of the major goals of synthetic organic chemistry lies in the research, discovery and exploitation of environmentally friendly methods. Recently, several techniques for the efficient use of solvent-free reactions [3] and multi-component reactions have been developed individually but when these two wings of green chemistry can be combined, an excellent green chemistry protocol is expected. Multi-component condensation reactions are a compelling method for the synthesis of organic compounds,

since the products are formed in a single step and diversity can be achieved by simply varying each component.

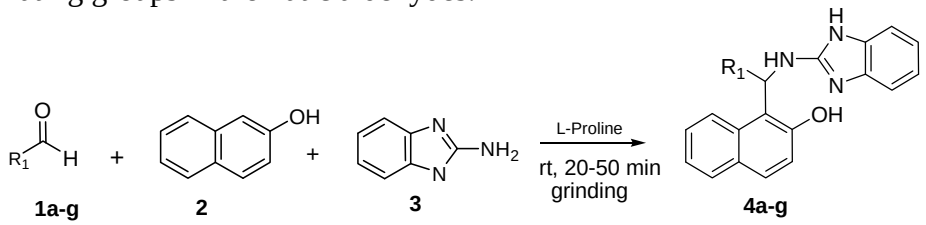
Proline is an efficient bifunctional abundant chiral organocatalyst which is inexpensive and available in both enantiomeric forms. The two functional groups in proline can act as both acid or base and can also facilitate chemical transformations in concert, similar to enzymatic catalysis. It has been extensively used in the synthesis of various heterocycles as well as in aldol, Mannich and Michael reactions.[4,5]

We wish herein to report that L-proline is a very effective, environmentally friendly catalyst for the one pot three component condensation of 2-aminobenzimidazole, 2-naphtol and aromatic aldehydes to form 2'-aminobenzimidazolomethylnaphtols derivatives (**4**) in good to excellent yields (**Scheme 1**).

Results and discussion

The catalyst plays a crucial role in the success of the reaction in terms of the rate and the yields of product. For example, the formation of **4a** did not proceed in the absence of the catalyst L-proline even after refluxing the same reaction mixture for 24 h in solvent. By changing the amount of the catalyst from 5 mol %, 10 mol %, and 15 mol %, the reaction resulted in the formation of **4a** in 72%, 85 %, and 87% yield, respectively. Thus the use of just 10 mol % of L-proline was therefore, chosen as optimal required amount of the catalyst to push the reaction forward with maximum yield of the product. Increase in the mol % of the catalyst has not resulted in any enhancement of the yield of **4a**.

It follows from **Table 1** that the yields of all the products are good to excellent. Aromatic aldehydes carrying electron withdrawing substituent reacted in shorter reaction time with excellent yields to give the desired products compared to the presence of electron donating groups in aromatic aldehydes.



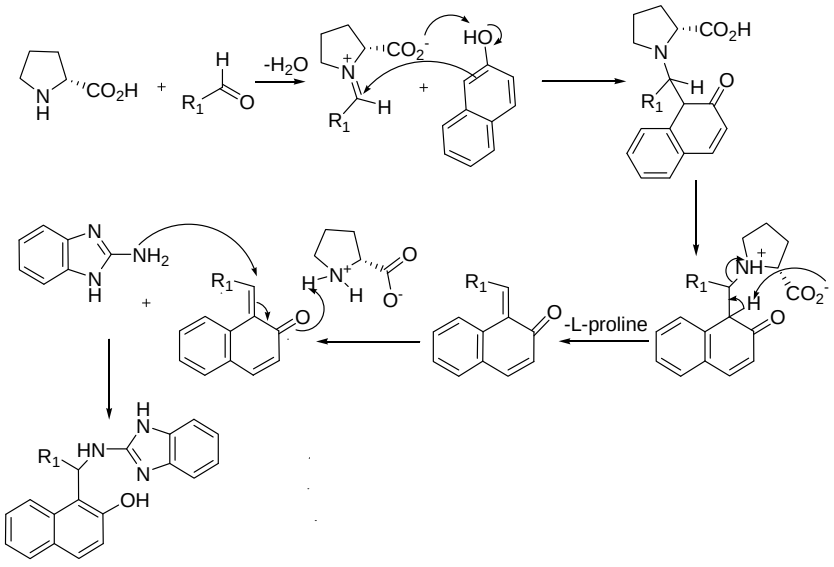
1a-g **2** **3** **4a-g**

Scheme 1. Synthesis of 2'-aminobenzimidazolophenylmethylnaphthols via grinding at room temperature

Table 1. The reaction of 2-aminobenzimidazole, 2-naphthol and aldehydes in the presence of L-proline (10 mol %) under grinding and solvent-free conditions

entry	R_1	time (min)	Yield (%)	Mp (^oC)
4a	$-C_6H_5$	30	85	187-189
4b	$4\text{-}NO_2C_6H_5$	20	95	192-194
4c	$4\text{-}CNC_6H_5$	20	89	157-159
4d	$4\text{-}ClC_6H_5$	30	80	155-157
4e	$4\text{-}BrC_6H_5$	30	78	197-199
4f	$4\text{-}OMeC_6H_5$	50	64	168-169
4g	$4\text{-}OHC_6H_5$	50	70	>300

Finally, we turned our attention to the mechanism of the reaction. A possible reaction mechanism for the formation of 2'-aminobenzimidazolophenylmethylnaphthols was proposed (**Scheme 2**).



Scheme 2. Proposed mechanism for the synthesis of 2'-aminobenzimidazolophenylmethylnaphthols

Conclusion

In conclusion, we have endeavored to present a very efficient methodology for the rapid, high yielding, environmentally friendly preparation of 2'-aminobenzimidazolophenylmethylnaphthols in the presence of L-proline under grinding and solvent free condition at room temperature.

Experimental Section

General

Chemicals were purchased from Fluka, Merck, Riedeldehaen AG and Aldrich chemical companies. All melting points were measured with a Branstead Electrothermal melting point apparatus and uncorrected.

Experimental procedure

A mixture of 2-naphthol (1 mmol), aldehyde (1 mmol) and 2-aminobenzimidazole (1 mmol) in the presence of L-proline 0.012gr (10 mol %) was taken in the mortar and ground with pestle for a specified length of time under solvent free condition at room temperature (**Table 1**)**.** The progress of the reaction was monitored by TLC. On completion of the reaction, the mixture was washed with water and the crude product was purified by recrystallization from ethanol/water.

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