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The Reusable Catalyst-Enabled One-Pot Synthesis of 2-amino-4H-chromenes

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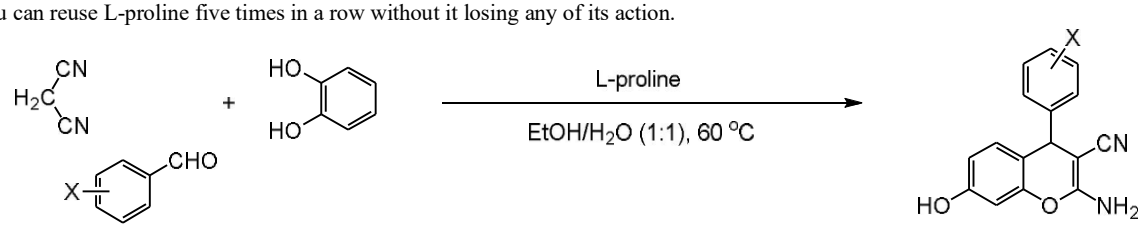
ABS TRACT

Utilizing L-proline as a reusable catalyst, a novel and efficient method for synthesising 2-amino-chromenes is accomplished by a one-pot three-component reaction involving aldehydes, malononitrile, and resorcinol. From the perspective of green chemistry principles, the current process's main benefits are its fast reaction times, high product yields, use of a bioorganic and reusable catalyst, and the use of a green solvent. You can reuse L-proline five times in a row without it losing any of its action.



X: Cl, Br, F, NO_2, OH, OMe, H

88-96%

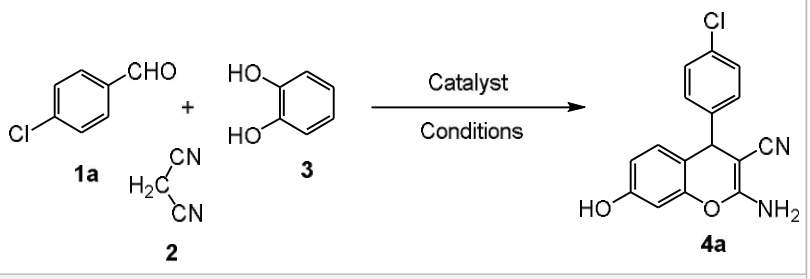
*Keywords:*2-amino-chromenes Three-component reaction, *L*-proline Reusable catalyst Green solvent.

1. Introduction

Antitumor, antibacterial, antifungal, antiviral, antidiabetic, herbicidal, fungicidal, and insecticidal agents are just a few examples of the many biologically active compounds that contain heterocycles. These compounds are present in a wide range of pharmaceuticals, vitamins, natural products, biomolecules, and other biologically active substances. 1-6 They are also often used as building blocks in synthetic agrochemicals and medicines. 1 The medical and pharmaceutical industries have made extensive use of 4H-pyran derivatives because of their significant heterocyclic compounds and their outstanding biological activity. 7The 4H-pyran exhibited hypotensive, antibacterial, antimyopic, antirheumatic, anti-proliferative, and cancer chemopreventive effects. Among the significant 4H-pyran heterocyclic compounds, 2-amino-chrones are the major components of several natural products and have several applications as pigments, possible agro-chemicals, and cosmetics (8–11). 12-14 In response to 2-amino-chromene derivatives' biological activity, scientists have created a plethora of quick and environmentally friendly ways to cook them. There have been multiple reports of protocols for modified techniques including various homogeneous or heterogeneous catalysts for the synthesis of 2-amino-4H-chromenes recently. 14 Because of its high product yields, atom economy, and ease of testing, multicomponent reactions have lately gained a lot of popularity as an approach for discovering new compounds with biological activity. 15-16

2. Result and discussion

Numerous publications have recently reported on the catalytic activity of L-proline for organic reactions. With the help of L-proline, a novel and eco-friendly method for synthesising 2-amino-4H-chromenes is shown here. Various solvent and catalyst amounts were tested in a model reaction including 4-chloro benzaldehyde (1 mmol), malo-nitrile (1 mmol), and resorcinol (1 mmol) (Scheme1) to determine the optimal reaction conditions and achieve the highest catalytic activity. We started by seeing how the model reaction fared with different solvents. Table 1 shows that the optimal reaction conditions were a 1:1 mixture of ethanol and water. After that, the effect of catalyst concentration on Various amounts of catalyst were used to test the reaction. It was noted that when the catalyst concentration rose from As a result of the increased availability of acid sites, the product yield increased significantly from 56% to 96% when the weight of the ingredient was reduced from 0.01 to 0.03 g (Table 1, Entry 8). Consequently, the optimal conditions for catalyst activity were 0.03 g in a 1:1 mixture of ethanol and water at 60 oC. After 120 minutes, the product yielded only 15% when the catalyst was not present. Determining the breadth of the protocol that was developed requires a number of commercially available aldehydes were examined in this transformation under optimized reaction condition (**Scheme 2**), and the results were summarized in **Table 2**. As shown in **Table 2**, aldehydes were found to afford the expected product. In all cases, aromatic aldehydes substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and gave the products in good yields.

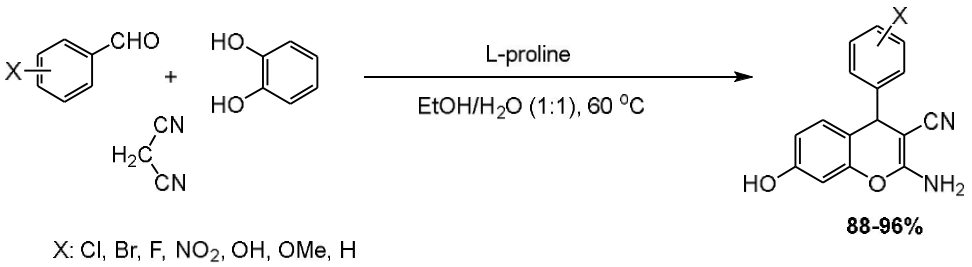


Scheme 1. L-proline catalyzed the model reaction.

Table 1. Optimization of reaction conditions [a]

Entry	Solvent (Tem)	Catalyst amount (g)	Time (min)	Yield (%) [b]
1	CH_3CN (Ref)	0.01	60	68
2	EtOH (Ref)	0.01	60	80
3	H_2O (Ref)	0.01	60	79
4	EtOH/H_2O (1:1) (60 °C)	0.01	60	86
5	1,4-dioxane (Ref)	0.01	60	72
6	THF (Ref)	0.01	60	61
7	EtOH/H_2O (1:1)	0.02	40	91
8	EtOH/H_2O (1:1)	0.03	30	96
9	EtOH/H_2O (1:1)	0.04	30	96
10	EtOH/H_2O (1:1)	---	120	15

[a] Reaction conditions:aldehyde (1 mmol), malononitrile (1 mmol), resorcinol (1 mmol),solvent (10 mL). [b] Isolated yield.



Scheme 2. L-proline catalyzed Synthesis of 2-amino-chromene derivatives.

The reusability of catalyst was tested on the model reaction. As shown in **Fig. 1**, *L*-proline can be reused five consecutive times without a noticeable loss in activity.

3. Conclusion

In summary, we described *L*-proline as a reusable, readily available, inexpensive and efficient catalyst for the one-pot synthesis of 2-amino-chromenes. The methodology offersseveral advantages including increased variations of substituent in the product with high yields, operational simplicity, minimum environmental effects and above all, the ease in purification of products simply by crystallization.

4. Experimental

A mixture of aldehyde (1 mmol), malononitrile (1 mmol), resorcinol (1 mmol) and L-proline (0.03 g) in EtOH:H_2O (1:1)

(10 mL) was stirred at 60 °C. After completion of the reaction (monitored on TLC), ethanol was removed, Ethyl acetate and water were added and the product was extracted. The crude product was obtained recrystallized from ethanol and water.

Next, extracted aqueous layer containing catalyst was washed with 10 ml of dichloromethane twice and was used for four times (**Fig. 1**).

Table 2. Synthesis of 2-amino-chromene derivatives.

Entry	X	Product	Time (min)	Yield (%) [b]	MP (°C)
1	4-Cl	**4a**	30	96	160-162[16]
2	4-OMe	**4b**	50	91	108-111[16]
3	4-NO_2	**4c**	65	88	165-167[16]
4	4-OH	**4d**	80	92	250-252[16]
5	4-Br	**4e**	30	95	221-223[16]
6	4-F	**4f**	30	90	185-188[16]
7	3-NO_2	**4g**	55	91	166-169[16]
8	H	**4h**	35	96	234-237[16]

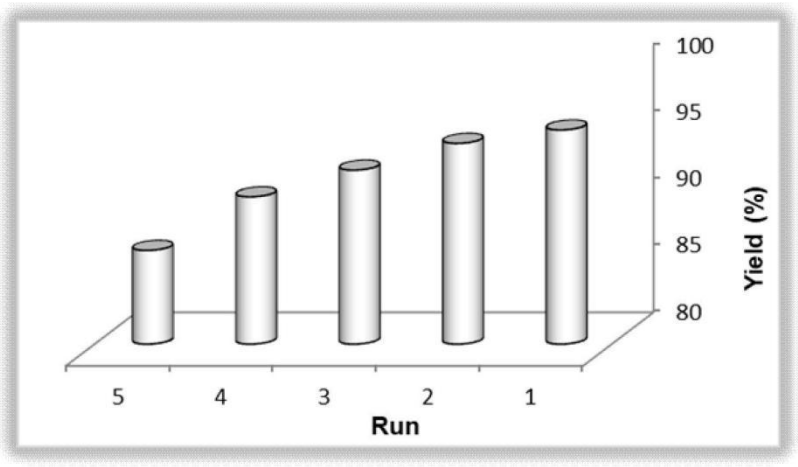


Fig 1. Reusability of L-proline in the model reaction.

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