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**Research Article**

## Investigation of multicomponent synthesis of heterocyclic compounds based on kojic acid reaction

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### ABSTRACT

Multi-component reactions combine to form several synthetic steps without separating the interfaces or changing the conditions to produce the desired synthesis. Hence, such reactions have a special validity in organic and medicinal chemistry. Kojic acid and its derivatives are among the heterocyclic structures that due to their biological and pharmacological importance, research on the synthesis and properties of these compounds is one of the attractive fields of interest to many chemists and has a special place in organic and medicinal chemistry.

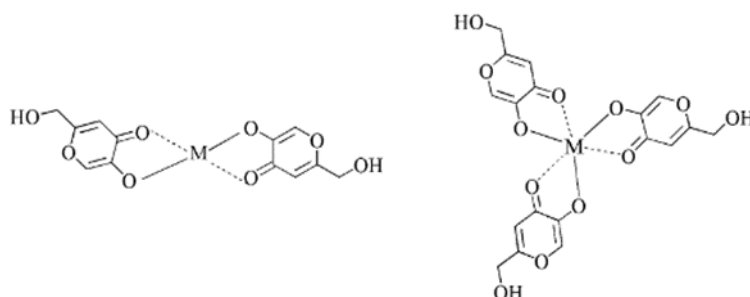
**Keywords:** Multicomponent; Kojic Acid; Heterocyclic compounds

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## 1. Introduction

Kojic acid, the most intensively studied inhibitor of tyrosinase, was discovered by K. Saito in 1907. Since the early twentieth century, it has been known as an additive to prevent browning of food materials such as crab, shrimp, and fresh vegetables in food industry (e.g., as an antioxidant or antibrowning agent) in order to preserve their freshness and to inhibit discoloration. It shows a competitive inhibitory effect on monophenolase activity and a mixed inhibitory effect on the diphenolase activity of mushroom tyrosinase. The ability of kojic acid to chelate copper at the active site of the enzyme may well explain the observed competitive

inhibitory effect. In this article, using the natural and non-toxic catalyst of L-proline, which is one of the essential amino acids in the body.



**Fig.1.** M (kojic acid)  $n$  ( $n = 2,3$ ) metal complex

Much of the research in organic chemistry today is on heterocyclic compounds. These compounds have wide applications, especially in medicinal chemistry, which has accelerated the discovery and development of heterocyclic compounds and their synthesis methods. Heterocycles are cyclic systems containing at least one heteroatom (an atom other than carbon that often contains nitrogen, oxygen, and sulfur). Given the value of heterocyclic compounds, in the past few decades, many efforts have been made to design simple and appropriate methods for the synthesis of these compounds. One of the attractive fields and interests of causal chemists is designing, inventing and performing multi-component reactions in favorable conditions. In general, reactions in which more than two raw materials are involved and all or most of the atoms that make up the raw material are found in the final product are called multi-reactions. Multi-component reactions combine to form several synthetic steps without separating the interfaces or changing the conditions to produce the desired synthesis. Hence, such reactions have a special validity in organic and medicinal chemistry. Kojic acid and its derivatives are among the heterocyclic structures that due to their biological and pharmacological importance, research on the synthesis and properties of these compounds is one of the attractive fields of interest to many chemists and has a special place in organic and medicinal chemistry.

### ***Kojic acid reactions***

Kojic acid has several groups of agents, each of which can be used in appropriate reactions or as an acidic hydrogen donor. For example, become a factor group or other factor groups during processes. The enol group also loses its acidic hydrogen from oxygen or returns a negative charge from oxygen to carbon. The enol becomes a nucleus from this carbon and attacks electrons to produce a variety of products that The following are some of the reactions of kojic acid.

### ***Chemistry of Piran and Croman compounds***

Heterocyclic compounds are of particular importance in the biological sciences and organic chemistry. Some of these compounds, such as chromones, are an important class of heterocycles found in nature that have been considered for their biological activities. Chroman derivatives were first extracted from the Cordia alidora tree, which is a native species of the United States, and used as an anti-inflammatory drug. Croman is an insect repellent in a plant species. The main material of an important group of natural dyes called flavonoids also has a chrome skeleton, which is of special importance.

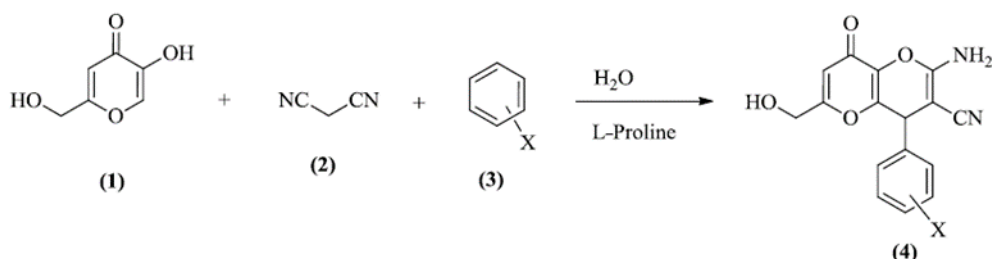
## **2. Experimental**

### ***2.1. General information***

The required chemicals were purchased from Merck and Fluca companies or synthesized in a laboratory. Products are identified by HNMR, CNMR spectra. The HNMR and CNMR nuclear magnetic resonance spectra were prepared with the 250 MHz Avance Bruker at 250 MHz and 250 MHz, respectively.

### ***2.2. Optimization of reaction conditions for the synthesis of dihydropyran compounds (2 and 3 b) by 4 pyrons***

In order to obtain suitable conditions for the synthesis of the desired compounds, the reaction of 1 mmol of benzaldehyde (0.140 g) with 1 mmol of malononitrile (0.066 g) and 1 mmol of kojic acid (0.142 g) was selected as the standard reaction.



**Fig.2.** Kojic acid reaction (1 (with malonitrile) 2 (and benzaldehyde) 3 (as standard reaction)

### 3. Result and discussion

Kojic acid derivatives, aminopiran and pyrano (b 2, 3) pyran are known compounds that due to their biological and pharmacological importance, research on the synthesis and properties of these compounds is of particular importance and has been considered by many chemists. Kojic acid is currently used as tyrosinase inhibitors which are commercially available. Unfortunately, unstability during storage limits its use and new tyrosinase inhibitors of novel kojic acid derivatives are needed in cosmetics industry. More expended studies on this subject will be helpful in designing more suitable tyrosinase inhibitors for human use.

### 4. Conclusion

Considering the importance of kojic acid derivatives, aminopiranes and pyrano (b 2, 3) pyranes, in this paper we tried to derive new derivatives of this class from the three-component and single-step reaction between different aldehyde derivatives, malononitrile and Kojic acid should be prepared. "Green chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products." In our continuing search, a huge number of Mannich bases are being examined as inhibiting mushroom tyrosinase activity at the moment, and few of

them will have confirmed in melanogenesis inhibiting activity in cell or skin models. Mannich bases compounds are more hydrophobic than kojic acid. Therefore, disadvantages of kojic acid might be decreased by increasing skin penetration and stability in formulation. This catalyst is a toxicity and corrosion problem and can be used at high temperatures and pressures. Also easily separated from the product.

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