Title of the project : **A Study on the Synthesis and Biological Evaluation of a few 3(*2H*) - Furanones**

Amount allocated : **Rs. 4,50,000/- (UGC Reference No. F. 1551-MRP/14 15/KLCA009/UGC-SWRO dated 04/02/2015)**

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Summary of the Project

Heterocyclic compounds are compounds having a cyclic structure with at least two different kinds of atoms in the ring, generally one is carbon and the most common hetero atoms present are nitrogen, oxygen and sulfur. The heterocyclic ring may contain one or more than one heteroatom which may be alike or unlike. Heterocyclic compounds may be composed of more than one ring of which at least one must be a heterocyclic ring. There is a rapid increase in the number, diversity as well as applications of heterocyclic compounds. Many known natural drugs as well as synthetic drugs are heterocyclic compounds. Three out of twenty natural amino acids contain heterocyclic ring motifs and many vitamins also contain heterocyclic ring components. A number of materials like dyes, luminophores, pesticides, herbicides, *etc.* useful in everyday life also possess heterocyclic rings.

In view of the incredible potential exhibited by heterocyclic compounds, developing novel synthetic strategies for their construction has immense interest in synthetic chemistry. The diverse methods now available for the synthesis of heterocyclic compounds can be grouped into the following three broad categories:-

1. Heterocyclics *via* the modification of existing carbocyclic rings.

2. Cyclisation process leading to heterocyclic compounds.

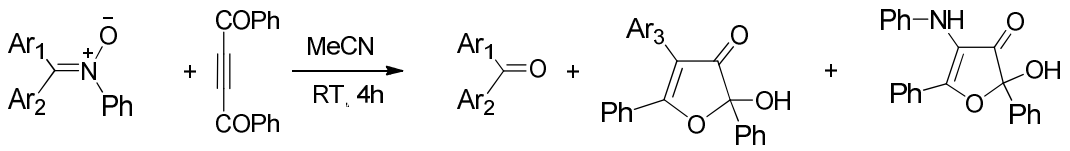
3. Concerted cycloaddition reactions to furnish the heterocyclic compounds.

Among these three methods, cycloaddition reaction involving two simple components appear to be an attractive choice for the synthesis of heterocyclic compounds.

In the present study we selected 1,3-dipolar cycloaddition for the synthesis of heterocyclic system namely 3(2*H*)-Furanones. 3(2*H*)-Furanones is one of the widely distributed heterocyclic systems in Nature and possess unusual range of biological activities. 3(2*H*)-Furanones are promising antitumor drug candidates. Hence the interest in the total synthesis of antitumor agents having 3(2*H*)-furanone ring system as a central structural unit has led to the development of simple and efficient methods for the synthesis of a variety of 3(2*H*)-furanones.

In the present study a novel method based on 1,3-dipolar cycloaddition of nitrones is developed for the synthesis of 3(2*H*)-furanones. 1,3-Dipolar cycloaddition reaction of nitrones is one of the most important methods for the construction of nitrogen and oxygen heterocycles. Nitrones undergo facile cycloaddition reactions with alkenes and alkynes to yield isoxazolidines and isoxazolines respectively. Due to the thermal instability, presumably related to the presence of labile nitrogen-oxygen bond, the isoxazolines thus formed have a tendency to undergo rearrangements to various other products.

1,3-Dipolar cycloaddition reaction between *N*-fluorenylidene-*N*-aryl nitrones and dibenzoylacetylene is conducted in 1:1 molar ratio at RT in dry acetonitrile. The reaction results in the formation of a 1:1 adduct [a 3(2*H*)-furanone], *9*-fluorenone and another 3(2*H*)-furanone.



Scheme 1. Synthesis of 3(2*H*)-furanones

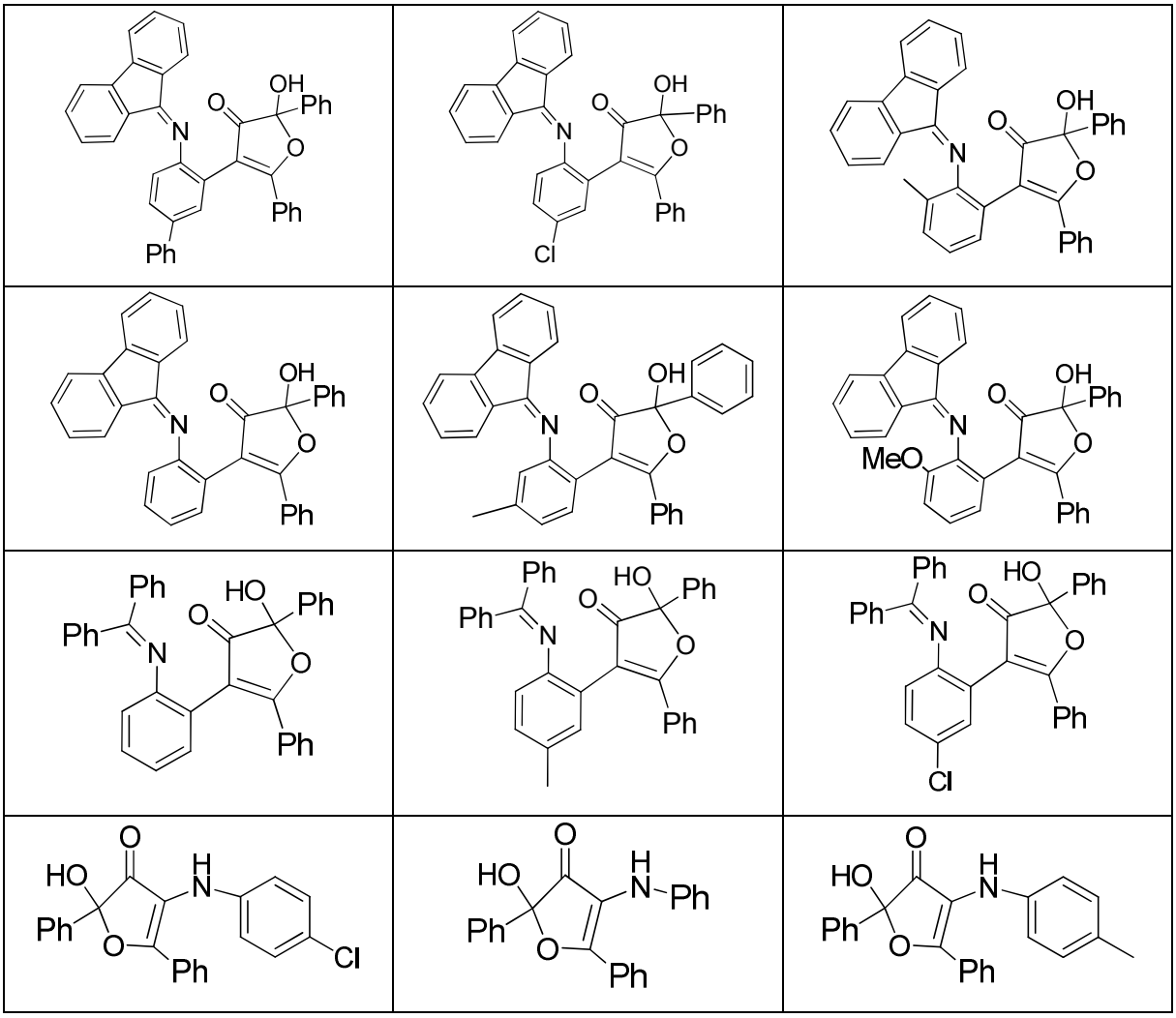
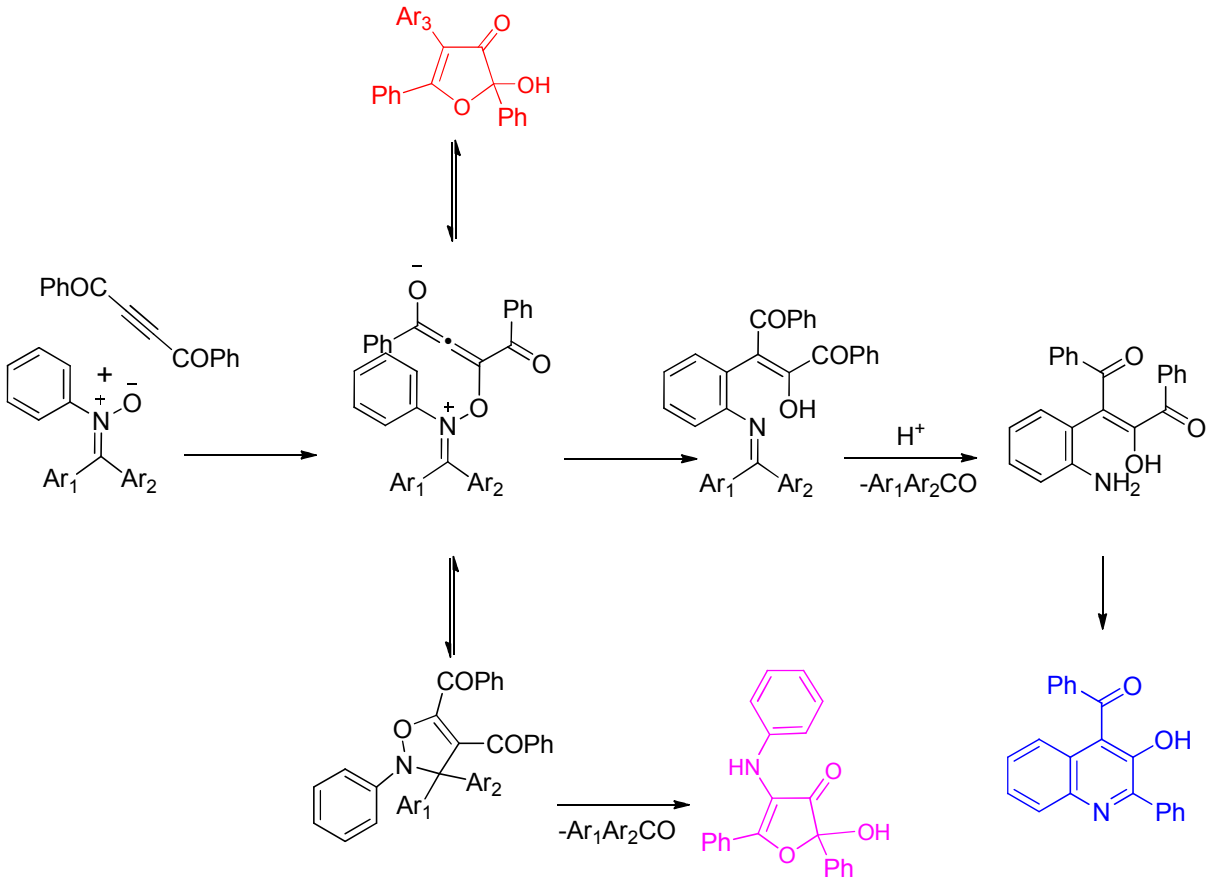


Chart 1. Summary of the 3(2*H*)-furanones synthesized

The following is the mechanism proposed for the formation of 3(2H)-furanones and quinolines.



A close examination of the mechanism proposed for the reaction, reveals that on acid hydrolysis the initially formed 1:1 adduct can be easily converted to a *N*-protected 3-(2-aminophenyl)-prop-2-en-1-one derivative that can undergo deprotection and intramolecular condensation reactions simultaneously to give quinoline in a similar fashion as that of Friedländer quinoline synthesis. Hence we extended our studies to the synthesis of pharmaceutically relevant quinolines and their derivatives.

In short, we have developed a green protocol based on 1,3-dipolar cycloaddition reactions for the synthesis of biologically valuable 3(2H)-furanones and quinolines. The merits of the method are i) simple to conduct the reaction, ii) easily available substrates and reagents, iii) highly atom economic and iv) high conversion

rate. 3(*2H*)-Furanones and quinolines find wide applications in medicinal chemistry. Even though the biological evaluation of synthesised 3(*2H*)-Furanones and quinolines are under examination, the synthetic results will open new realms in the synthesis and transformations of heterocyclics.

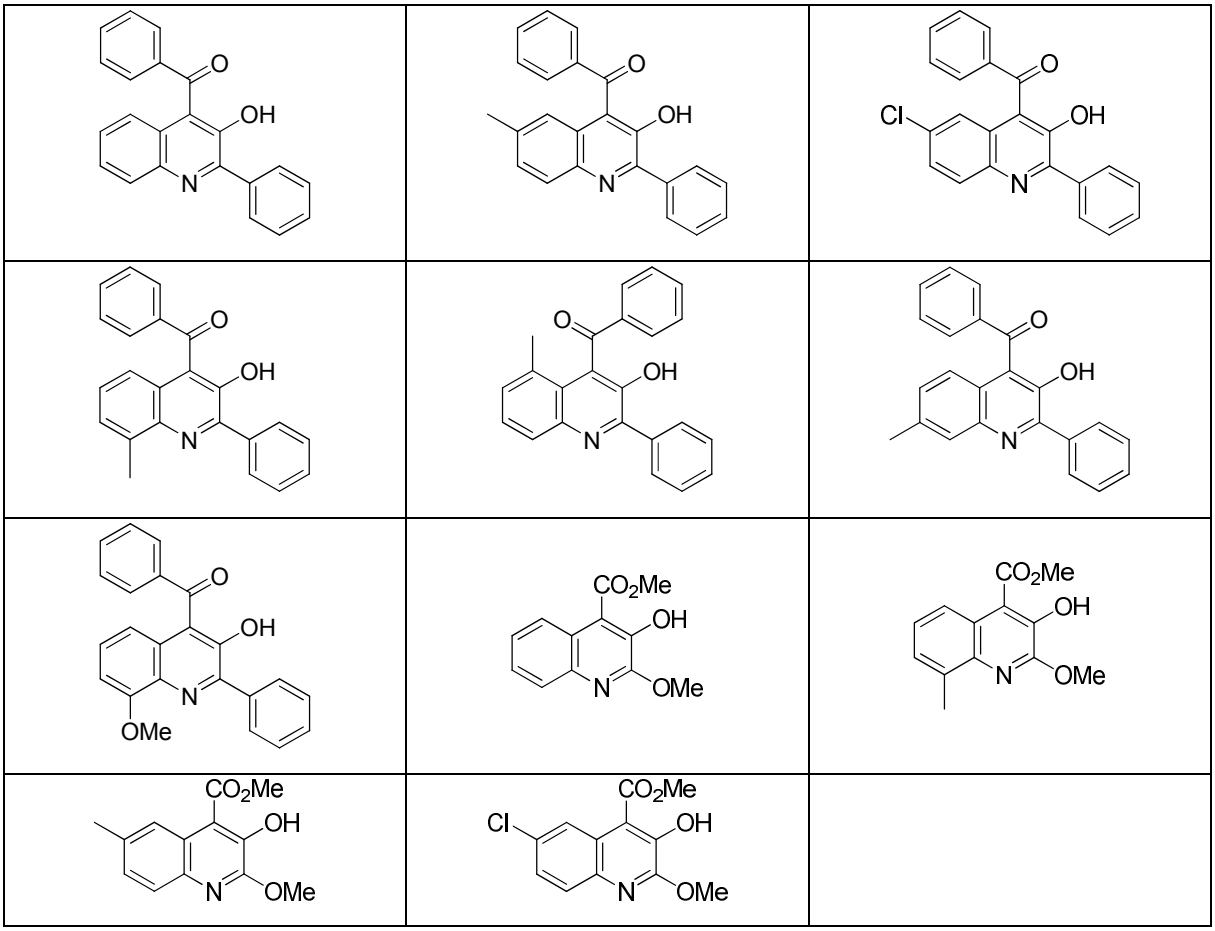


Chart 2. Summary of the quinolines synthesized

The results are published in the conference proceedings of International Conference on Materials for the Millennium, MatCon 2016 [Conference proceedings, ISBN 978-93-80095-738, A Highly Atom Efficient Method for the Synthesis of Quinolines, Vol I, pp 192-195] and in Journal Tetrahedron Letters [Metal free synthesis of highly substituted quinolines under mild conditions, 57(2016), pp 2981-2984].