



STUDY ON THE SYNTHESIS OF QUINOLINE-PYRAZOLOPYRIDINE ANALOGUES

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ABSTRACT

Introduction: The study of matter (both elements and compounds) and the changes that occur to them, as well as the energy that is either created or destroyed in the process.

Aim of the study: the main aim of the study is Study on the Synthesis of Quinoline - pyrazolopyridine Analogues

Material and method: This study set out to answer the question, "What role does active plant-derived molecules with antimalarial properties.

Conclusion: Many of them serve crucial functions in the human body. Furthermore, many chemicals found in nature have pharmaceutical use.

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1. INTRODUCTION

1.1 OVERVIEW

The study of matter (both elements and compounds) and the changes that occur to them, as well as the energy that is either created or destroyed in the process. Every material, whether it was made by nature or by humans, is made up of atoms belonging to one or more of the roughly hundred and eighty different elemental species that we know of. These atoms, which are made up of even smaller particles, are the fundamental components of all chemicals.

Many people in the first two-thirds of the twentieth century thought that chemistry represented the future of science. There seemed to be no end to the ways in which chemical goods might improve people's lives. The intuitions, insights, and experience of pharmaceutical researchers are major drivers of drug design advancement. Attempting to "capture" such sensations by studying the archives of earlier drug design initiatives that were successful can be illuminating. Based on this investigation, we may conclude that interference will be a critical factor in determining the final form of our ongoing and

future endeavours. It is our hope to eventually analyse the structures of many different medications in this area. The finished medicine after extensive research and development. Our ultimate objective is to use this knowledge in the development of new medicines by first simplifying it.

1.1.1 THE FIRST ANTIMICROBIAL DRUGS

For millennia, human societies depended on naturopathic remedies; nevertheless, the first half of the 20th century marked the beginning of the age of strategic drug research. Paul Ehrlich (1854-1915), a German physician and chemist, set out in the early 20th century to find or create chemical substances that might destroy pathogenic germs without injuring the patient. In 1909, Ehrlich's helper SahachiroHata (1873-1938) discovered one such "magic bullet" after testing more than 600 arsenic-containing compounds. Anti-syphilis compound 606 worked by inhibiting the growth of the syphilis-causing bacteria *Treponema pallidum*. After it was discovered that Compound 606 effectively treated syphilis in rabbits, it has been sold as Salvarsan for use in treating the illness in people. The systematic testing of many



compounds, as Ehrlich did, is still a frequent method for finding novel antibiotics.

1.2 HETEROCYCLIC COMPOUNDS

Industrially and physiologically, heterocycles are extremely valuable compounds since they form the biggest of the traditional divisions of organic chemistry. Big additives and modifiers used in manufacturing applications like cosmetics, printing, data storage, and plastics are often heterocyclic, as are the great majority of pharmaceuticals and physiologically active agrochemicals. The ability of heterocycles to spread substituents around a core scaffold within specified 3D representations is a striking structural trait that is being used to great advantage by the medicine industry. Heterocycles have been a primary area of study in organic chemistry for well over a century. Heterocycles have helped contemporary civilization progress from an industrial and biological perspective, as well as to the comprehension of living procedures to increase quality of life. More than two-thirds of the about twenty million chemical compounds predicted to be in use by the turn of the next millennium are either partly or wholly aromatic, and roughly half are heterocyclic. Organic molecules of interest in fields like electronics, pharmacology, optics, biology, materials science, etc. almost universally contain heterocycles. During the many decades of organic synthesis's growth, chemists have maintained an interest in heterocyclic molecules containing either sulphur or nitrogen.

2. LITERATURE REVIEW

Lewńska, Gabriela & Sanetra (2021) Quinoline derivatives have lately acquired appeal as a chemical molecule manufactured for third-generation photovoltaic applications. There are a number of ways in which the compounds may be tested before they can be used in products. Lastly, we show how quinoline derivatives may be used to solar cells. Polymer solar cells and dye-synthesised solar cells were featured, as were their architecture and design, as well as their performance. We've outlined their capabilities

and features. Non-photovoltaic uses for quinoline derivatives have also been discussed.

Elatawy, Mohamed & Hamed (2019) New symmetric and asymmetric 2,3-disubstituted quinoxalines were synthesised by functionalizing 2,3-dichloroquinoxaline (2,3-DCQ) with various sulphur and/or nitrogen nucleophiles. In addition, compounds 3f and 6b shown activity against a wide variety of microorganisms.

B M, Shilpa & N G (2022) Humanity's widespread health problems provide a barrier to the development of new medicines, and the world's growing population only makes the problem more pressing. For the development of anti-infective agents, two methods have been put into practise thus far: either the use of classical antibiotics as a basis for the creation of synthetic analogues with enhanced efficacy, or the screening of natural compounds in addition to synthetic compound libraries for antimicrobial activities. In order to tackle MRSA over the globe, we need to create antimicrobial medicines with a wide enough antimicrobial spectrum to be effective against all strains of the bacteria that cause the condition. It's possible that these cutting-edge methods may be used to lessen the impact of the epidemic and bring the health care crisis under control.

Patil, Sachin & Suryavanshi (2022) Several novel 2,4-disubstituted thiazolyl pyrazole compounds were synthesised in this study using a one-pot method. The desired compounds were obtained by a one-pot reaction involving several types of pyrazoles 4-carbaldehydes, thiosemicarbazide, and -haloketones. One method of synthesis used the standard refluxing in ethanol of pyrazole 4-carbaldehyde, thiosemicarbazide, and -haloketones; the other involved grinding the reaction mixture at room temperature. The reaction rates, product yields, and product purities of the two approaches were evaluated. The antibacterial properties of all produced compounds were examined.

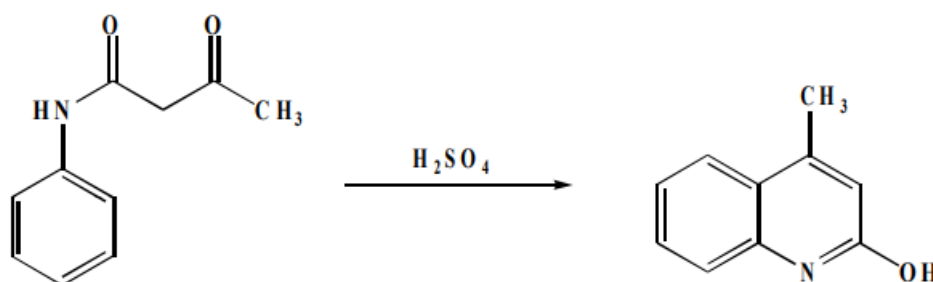
Abdelmonsef, Aboubakr (2022) Here, beginning with 2-cyano-pyrroloanthracen acetamide, we created a sequence of novel derivatives of many heterocyclic compounds

containing the anthracene moiety. Based on the findings, the compounds showed potential antimicrobial action. As a result, the recently synthesised hybrid anthracene compounds may prove to be useful chemical scaffolds for the creation of potentially novel antimicrobial medication candidates.

3. METHODOLOGY

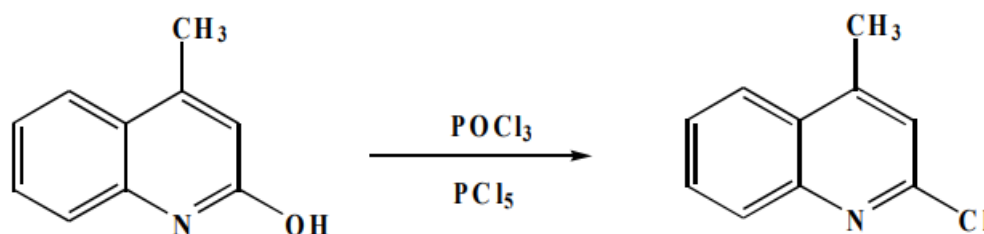
3.1 RATIONALE DESIGNING OF QUINOLINE DERIVATIVES

Following a thorough review of the literature, 20 chemical components with antimalarial potential from plants were chosen for structure-based virtual screening. This study set out to answer the question, "What role does active plant-derived molecules with antimalarial properties. Our work was conducted using the crystal structure of 1U4S.



➤ Step II: Preparation of 2-chloro-4-methylquinoline

It took 2 hrs of refluxing a combination of 2-hydroxy-4-methylquinoline 4.14g (0.026mol), 9.97g (0.065mol), and 5.41g (0.026mol) of phosphorus pentachloride to produce the final product. After cooling, the reaction mixture was put into an ice-water bath and let



➤ Step III: Preparation of 2-hydrazino-4-methylquinoline (1)

At 5- 10 C, the 10g of hydrazine hydrate (200mmol) was slowly added to 10ml of HCl (10ml). Then 40ml of ethylene glycol was

Quinoline's promise as an effective antimalarial moiety was further confirmed by this investigation.

4. RESULTS

4.1. SYNTHESIS OF 2- HYDRAZINO - 4 - METHYLQUINOLINE (1)

➤ Step I: Preparation of 2 - hydroxy - 4 - methylquinoline

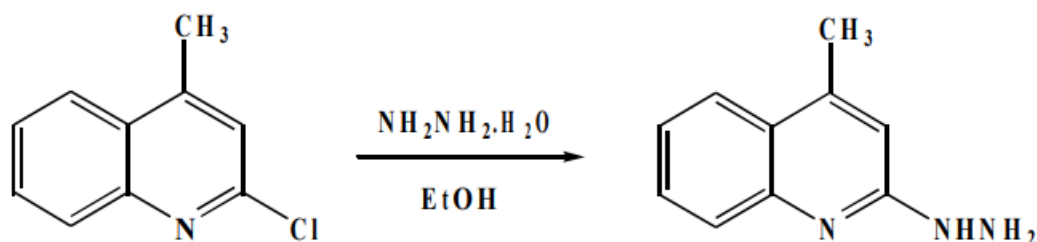
Sulfuric acid (20 ml) was treated with 25 g (0.1425 mol) of acetoacetanilide for 30 minutes at a temperature below 35 °C. Ammonium hydroxide was used to bring the suspension to a neutral pH. The methanol-derived raw material was filtered, cleaned with water, and then crystallised again. In terms of yield, 83% was discovered, and the melting point was between 220-222 °C.

to stand for the night. Acidic NaHCO₃ was used to neutralise the pH. The solid was filtered, water washed, dried, and ethanol was used to recrystallize it. One-seventh of a percent of the yield was discovered, and the melting point ranged from 60-61 degrees Celsius.

added, followed by 8.88g (50 mmol) of 2 - chloro- 4 - methylquinoline, and the mixture was heated under reflux for 2 hours. After cooling, a fine crystalline material separated out, which was then filtered, water washed,

and ethanol crystallised again. The melting point was between 140 and 142°C, with a

yield of 61%.

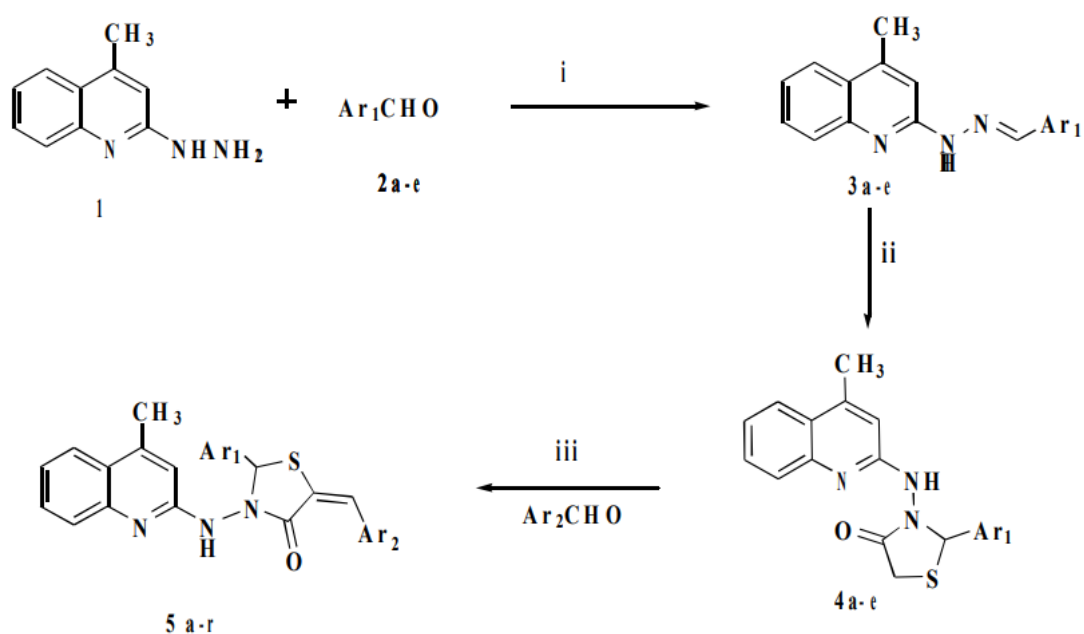


4.2 SYNTHETIC STRATEGIES ADOPTED

Various substances were synthesised in this investigation using the four synthetic techniques listed below:

4.2.1 SERIES 1

Scheme 4.1 depicts the whole series 1 synthetic route, while Table 4.1 provides a list of the produced chemicals.



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Scheme 4.1. Quinoline-thiazolidinone arylidene hybrids: synthesis and characterization (5 ar)

Table 4.1: List of synthesized derivatives of series 1 (5- arylidene - 3 -(4 - methylquinolin - 2 - ylamino) -2 - arylthiazolidin -4 - ones)

S.No	Comp	Ar ₁	Ar ₂
1	5a	C ₆ H ₅	C ₆ H ₅
2	5b	C ₆ H ₅	p-ClC ₆ H ₄
3	5c	C ₆ H ₅	p-CH ₃ C ₆ H ₄
4	5d	C ₆ H ₅	p-ClC ₆ H ₄
5	5e	p-ClC ₆ H ₄	C ₆ H ₅
6	5f	p-ClC ₆ H ₄	p-ClC ₆ H ₄
7	5g	p-ClC ₆ H ₄	p-CH ₃ C ₆ H ₄
8	5h	p-ClC ₆ H ₄	p-OCH ₃ C ₆ H ₄
9	5i	p-CH ₃ C ₆ H ₄	C ₆ H ₅

10	5j	p-CH ₃ C ₆ H ₄	p-ClC ₆ H ₄
11	5k	p-CH ₃ C ₆ H ₄	p-CH ₃ C ₆ H ₄
12	5l	p-CH ₃ C ₆ H ₄	p-OCH ₃ C ₆ H ₄
13	5m	p-OCH ₃ C ₆ H ₄	C ₆ H ₅
14	5n	p-OCH ₃ C ₆ H ₄	p-ClC ₆ H ₄
15	5o	p-OCH ₃ C ₆ H ₄	p-CH ₃ C ₆ H ₄
16	5p	p-OCH ₃ C ₆ H ₄	p-OCH ₃ C ₆ H ₄
17	5q	2-thienyl	C ₆ H ₅
18	5r	2-thienyl	p-CH ₃ C ₆ H ₄

➤ **General experimental procedure for synthesis of 1 - arylidene - 2 -(4 - methylquinolin - 2 - yl)hydrazines (3a - e) :**

Mixture 1, including 2-hydrazino-4-methylquinoline, compound 1, and different aromatic aldehydes in EtOH (20 ml) was refluxed in the presence of glacial acetic acid for 6 hours. Quantitatively, the resultant solution was concentrated by pouring it over ice.

Table 4.2: List of arylaldehyde List of arylaldehydes (2a -e) used

S.No	Compound	Quantity(g)
1	B enaldehyde (2a)	1.17
2	p-chlorobenzaldehyde (2b)	1.55
3	p-methylbenzaldehyde (2c)	1.32
4	p-methoxybenzaldehyde (2d)	1.50
5	Thiophene-2-cabaldehyde (2e)	1.23

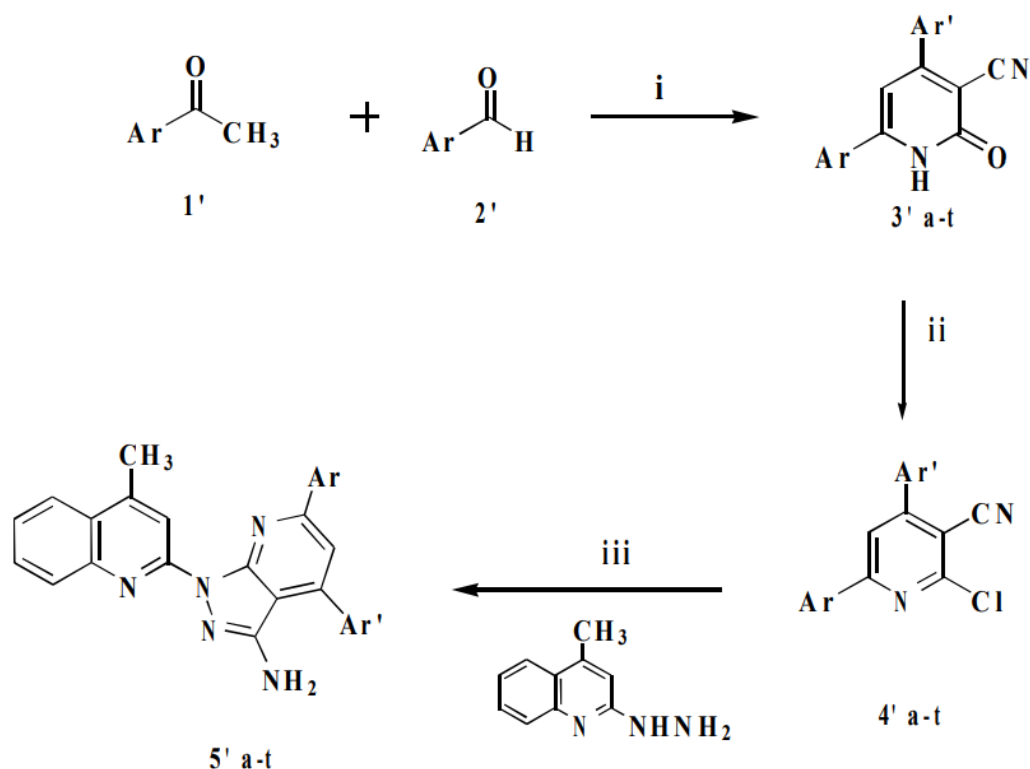
➤ **General experimental procedure for synthesis of 3 - (4- methylquinolin -2 - ylamino)- 2 - aryl thiazolidin - 4 - ones (4 a-e)**

Mercapto ac etic acid (0.003 mol) and a small quantity of anhydrous ZnCl 2 were added to a solution of compound (3) (0.002 mol) in 1,4 dioxane (50 ml). Sodium bicarbonate solution was used to neutralise the mixture after it had been refluxed for 10 to 12 hours. The surplus solvent had been distilled off and the mixture had been cooled. Cold water was used to wash the solid material after it had been filtered. Re-crystallization of the resultant solid in ethanol was carried out (99 percent). Following a 12-hour reflux process, the solution was emptied into a container filled with ice-cold water and the resulting named compounds were analysed. Recrystallization from dioxane was used to purify the final product, which was then further purified using the same method.

The synthesis of thiazolidinone and its arylidene derivatives was carried out satisfactorily according to the prescribed process. Conversion of 2-hydrazino-4-methylquinoline with various aromatic aldehydes under acidic circumstances yielded compounds (3a -e). The thioglycolic acid reaction in dioxane was used to convert the hydrazine intermediates to thiazolidinone (4a -e). After a long process of reaction in Glacial acetic acid, the desired chemicals (Z) - 5-Arylidene - 3- (4-methylquinolin -2-ylamino)- 2- arylthiazolidin - 4 were produced.

4.2.2 SERIES 2

Scheme 4.2 outlines the whole series 2 synthetic method, and the list of chemicals created is provided in Table 4.2.



Scheme 4.2. Synthesis of Quinoline - pyrazolopyridine Analogues

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5. CONCLUSION

Any of a class of organic compounds in which the molecular structure includes one or more rings of atoms in which at least one atom (the heteroatom) is a chemical element other than carbon, most often oxygen, nitrogen, or sulfur. Heterocycles play a crucial role in the natural world and are required for all forms of life to exist. Approximately fifty percent of all natural compounds are heterocyclic. The structural variety offered by heterocyclic compounds is impressive, and these compounds have been shown to be both widely and economically effective as medicinal agents.

Many of them serve crucial functions in the human body. Furthermore, many chemicals found in nature have pharmaceutical use. Most synthesized heterocyclic compounds have several applications in pharmaceuticals, healthcare, plastics, polymers, agriculture, and many other areas. They may be used as antimicrobials, antimalarials, anticancer drugs, antitubercular drugs, antihypertensive drugs, antioxidants, analeptics, and analgesics for the treatment of infectious disorders.

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