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Antimicrobial Evaluation of Quinoline-Conjugated Chalcone Derivatives

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ABSTRACT

Introduction: *Quinoline 1or 1-azanaphthalene or benzo[b] The molecular weight of pyridine, an aromatic nitrogen heterocyclic molecule with the chemical formula C9H7N, is 129.16 Daltons.*

Aim of the study: *the main aim of the study is Antimicrobial Evaluation Of Quinoline-Conjugated Chalcone Derivatives*

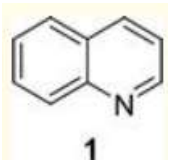
Material and method: *This study set out to answer the question, "What role does active plant-derived molecules with antimalarial properties.*

Conclusion: *Most heterocycles also have significant material science applications, including use as dyes, polymers, brightening agents, fluorescence sensors, and analytical reagents.*

INTRODUCTION

Quinoline Heterocycle: Synthesis and Bioactivity

Quinoline 1or 1-azanaphthalene or benzo[b] The molecular weight of pyridine, an aromatic nitrogen heterocyclic molecule with the chemical formula C9H7N, is 129.16 Daltons. When combined with acids, it creates salts and reacts like benzene and pyridine. Electrophilic as well as nucleophilic substitution reactions are both possible when it is used.



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Many natural chemicals (Cinchona alkaloids) include the quinolone moiety and have been proven to have a wide variety of biological activity because of this moiety's presence. Analgesic, anti-inflammatory, cardiotonic, antifungal, antimalarial, and anthelmintic properties of quinoline have been discovered.

Synthesis

Several well-established methods for synthesising quinolines have been documented in the literature, which may be changed to create a variety of different substituted quinolines. In a nutshell, we may all thank Skraup, Doebner-von Miller, Pfitzinger, Friedlander, Conrad-Limpach, and Combes for their contribution to the synthesis are only a few of the well-known processes that have been used to make the quinoline ring (Figure 1.1).

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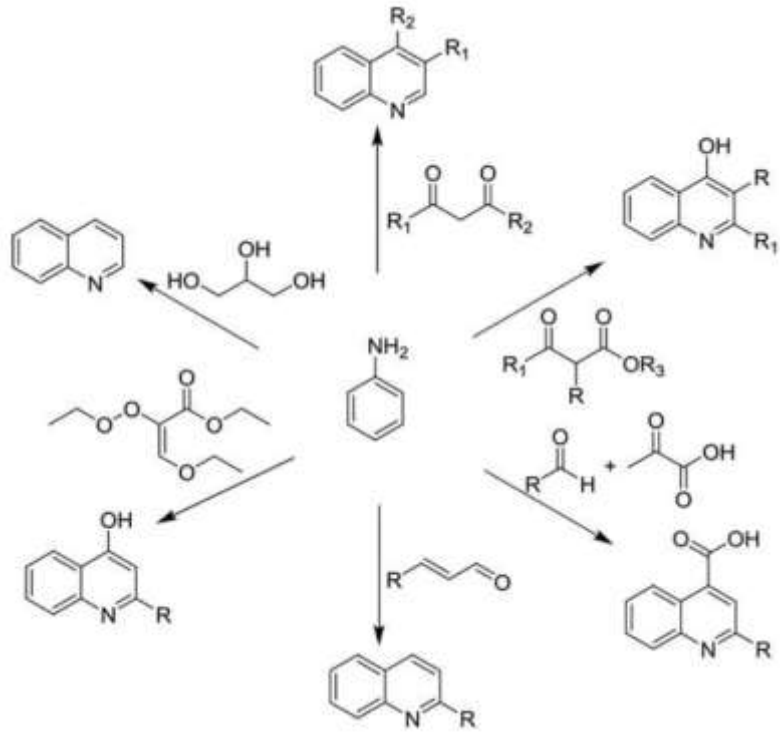
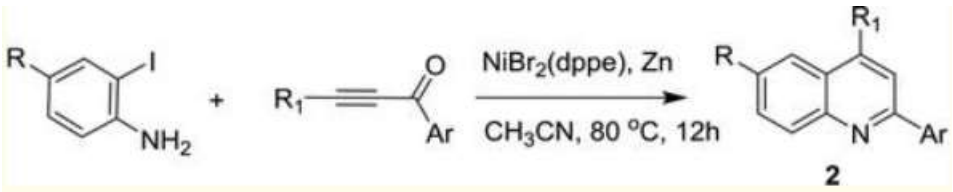
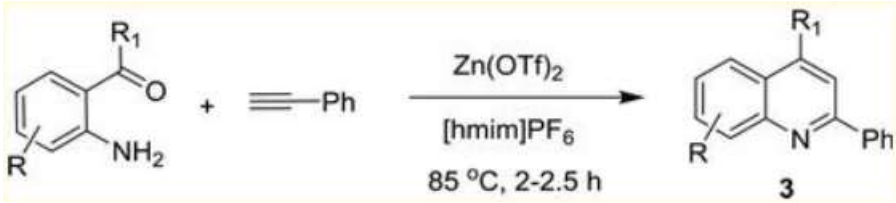


Figure 1.1 Substituted Quinolines may be made using conventional techniques.

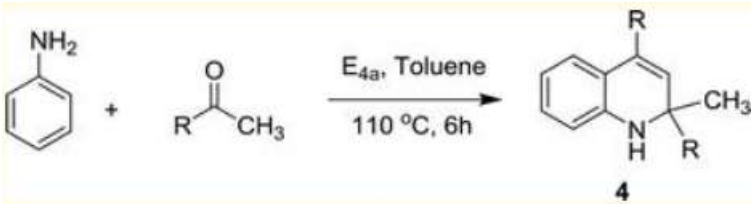
Quinoline and its derivatives may be synthesised using a plethora of new synthetic techniques in addition to the more traditional ones. 2,4-disubstituted quinolines 2 were synthesised by Chen et al. utilising nickel catalyst to condense 2-iodoanilines with alkynyl aryl ketones.



2,4-disubstituted quinolones were produced by cyclizing 2-aminoaryl ketones with phenylacetylenes. In an ionic liquid medium, zinc trifluoromethanesulfonate is employed as a catalyst ([hmim]PF6). Compound In(CF3SO3)3 synthesized by Lekhok et al. under microwave and solvent-free conditions contained catalytic quantities of indium(III) trifluoromethanesulfonate.



"Aniline and acetophenone were first condensed, and then cyclized to get 2,4-diphenyl-2-methyl-1,2-dihydroquinoline, 4. E4a, a zeolite catalyst, aids in the process."



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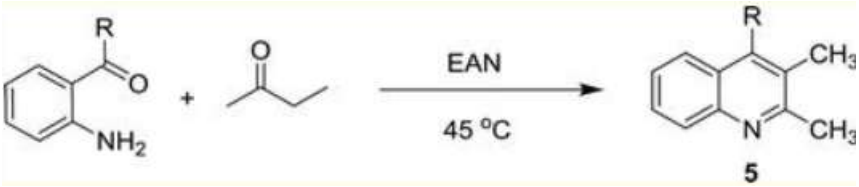
The 5, 2,3,4-trisubstituted quinolines were synthesized via the Friedlander annulation of aromatic ketones and carbonyl compounds in the presence of ethyl ammonium nitrate (EAN).



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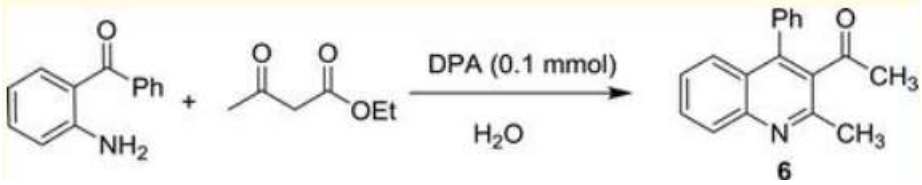
Dodecylphosphonic acid was used to mix 2-aminoaryl ketones with various -methylene ketones to synthesize poly-substituted quinolones, 6. (DPA).



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In the presence of a base, 2-aminobenzyl alcohol interacts with ketones or alcohols, and benzophenone produced poly-substituted quinolones. 7. Benzophenone scavenges hydrides in this instance.

LITERATURE REVIEW

Mandal, Sudip & Dj, Sen & Baidya (2021) For decades, researchers throughout the globe have been fascinated by the N-based heterocyclic molecule known variously as 1-aza-naphthalene, benzo[b]pyridine, and a variety of other names. The reactions of quinoline, a weak tertiary base, resemble those of pyridine and benzene. Quinoline is safe for humans to consume. Antimalarials, antibacterials, antivirals, cardiovascular, analgesics, antidiabetic and other quinoline biological activities are covered in this comprehensive review of quinolines and their bioactivities. Antifungal and other quinoline biological activities are also covered in this comprehensive review of quinolines.

Zinad, Dhafer & Salman (2021) Medical chemistry relies heavily on the use of heterocyclic nuclei as a paradigm for the development of various therapeutic medicines, such as antibiotics with a broad range of activity. Novel quinolone derivatives including triazole and thiadiazole were synthesised in an effort to find a new antibacterial agent. The yields of all the chemicals synthesized ranged from 74% to 79%. Based on the results of molecular docking, just one molecule, 6c, was shown to have the same effect on Gram-negative bacteria in vitro and on silicon. Considering this chemical targets bacteria's Penicillin binding proteins in an ampicillin-like manner, it may have antibiotic potential against Gram-negative bacteria.

Yadav, Kiran & Nandeshwarappa, Belakatte (2021) Heterocyclic compound chemistry has long been a fascinating area of research. For the creation of brand-new medications, heterocyclic molecules are crucial. Anti-inflammatory, analgesic, antibiotic, anticancer, antifungal, antimycobacterial, anticonvulsant, anti-diabetic, and antiviral properties have been attributed to several of these substances. Synthesized heterocyclic compounds with significant biological activity are highlighted in this study.

Sanu, Meenu & Joseph, Jincy & Chacko, Divya (2021) Heterocycles are seen as potential molecules for the creation of new medicinal medicines at the present time. In the field of medicinal chemistry, heterocycle analogues based on nitrogen are in a class of their own. The majority of medications on the market today (over 75%) are nitrogen-containing heterocyclic moieties that have been authorised by the FDA. New medications based on

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nitrogen are expected to account for a disproportionately high percentage of the market in the future decade. The creation of several novel heterocycles based on nitrogen has occurred. New N-heterocyclic moieties with useful physiological characteristics and potential medicinal chemistry applications are constantly being discovered. The purpose of this research is to discuss the pharmacological actions of heterocyclic compounds containing six nitrogen atoms.

Soni, Rinku & Sihag, Monika & Kinger (2021) Inorganic synthesis has benefited greatly from recent developments in the chemistry of water containing hypervalent iodine reagents. Synthesis of various heterocyclic compounds benefits greatly from the established methodologies. To far, we've examined the literature through the year 2020, with an emphasis on studies published in the last five to seven years.

Potapov, Vladimir & Ishigeev, Roman & Amosova, Svetlana (2021) Using commercially available 2-mercaptoquinoline, we show how to make the new compounds 2-quinolinesulfenyl chloride and bromide.

METHODOLOGY

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

RESULTS

1. ANTIMICROBIAL EVALUATION OF QUINOLINE-CONJUGATED CHALCONE DERIVATIVES

In medicinal chemistry, chalcone scaffold is found to be very much interesting moiety. Taking this into consideration, synthesis of versatile design heterocyclic derivatives with better pharmacological properties can be designed. Chalcone possesses reactive chemical structure, easy to make and additionally it shows promising activities.

Heterocycles containing chalcone core are known to possess several biological activities like antiinflammatory, antiviral, anticancer, bactericidal,[7] and insecticidal. **Figure 4.1** shows some potent biologically active chalcone derivatives in clinical use. Medieagenin **AS**, Menchiwanin **AT** and Licochalcone-A **AU** shows *in-vitro* antimalarial, anticancer, antibacterial and antiviral properties.

Figure 4.1: Biologically active chalcones derivatives.

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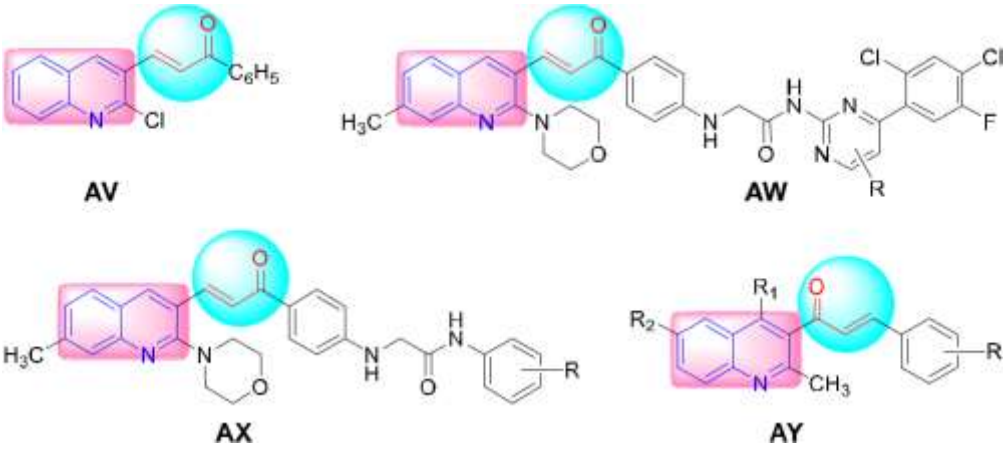


Figure 4.2: Biologically active quinoline-conjugated chalcone derivatives.

The quinoline-derived chalcone derivatives are well acknowledged and found to be fascinating scaffold in drug discovery research.

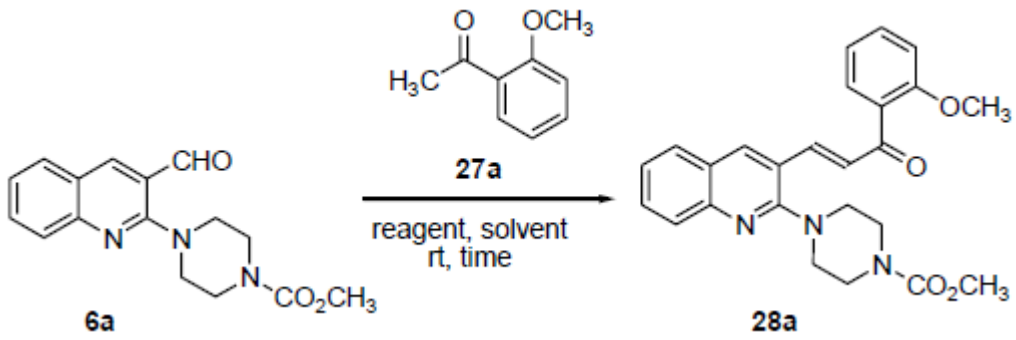
Some biological active quinoline-conjugated chalcone derivatives are represented in **Figure 4.2**. Compound **AV** is reported to possess good antibacterial activity against all strains.[15] Compound **AW** is reported to be highly potent against *B. subtilis*. Further, compound **AX** is reported to be highly active against *E. coli* and *S. aureus* strains respectively.[16] Similarly, the derivatives of compound **AY** are reported to possesses good antimicrobial activity.

From above literature survey it is revealed that, quinoline-derived chalcones need to be extensively studied further to check probability of getting highly potent novel heterocycles.

RESULT AND DISCUSSION

- **Chemistry**

In the current chapter, Compound **6** is considered as a key starting material for synthesis of quinoline-conjugated chalcone derivatives **28**.



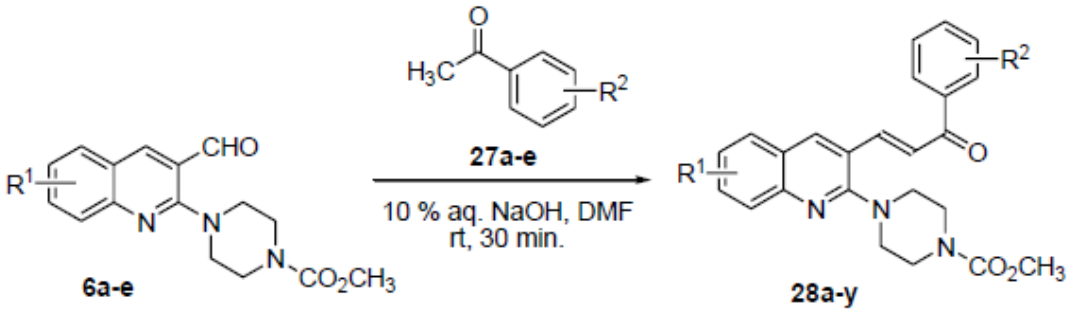
Scheme 4.1: Reaction of compound **6a** with 2-methoxy acetophenones **27a**.

Table 4.1: Optimization conditions for the synthesis of compound **28a**.[a]

Entry	Reagent	Solvent	Temp. (°C)	Reaction time (hr)	% Yield[b]
1	**aq. NaOH**	**DMF**	**rt**	**0.5**	**92**
2	aq. KOH	DMF	rt	0.5	83
3	aq. NaOH	EtOH	rt	5	82
4	aq. NaOH	MeOH	rt	6	83
5	Aq.K_2CO_3	DMF	rt	7	78

[a]All reactions were carried out on 0.668 mmol. of **6a** (1.0 equiv.), 1.05 equiv. of **27c**, 1.5 equiv. of base at rt unless otherwise noted. [b]Isolated yield.

As shown in **Scheme 4.1**, **Table 4.1**, several reaction conditions were screened for the synthesis of quinoline-conjugated chalcone derivatives **28**. The best result was obtained, when synthesis of chalcone was carried out by reaction of compound **6b** and 2-methoxy acetophenone **27a** using aq. sodium hydroxide in presence of DMF at room temperature (entry 1, 92%).



Scheme 4.2: Synthesis of quinoline-conjugated chalcone derivatives **28a-y**.

Table 4.2 Synthesis of quinoline-conjugated chalcone derivatives **28a-y**.

Entry	Comp.	R1	R2	% Yield[a]
1	**28a**	H	2-OCH3	92
2	**28b**	H	2-F	84
3	**28c**	H	4-F	80
4	**28d**	H	2,4-F	77
5	**28e**	H	4-Cl	75
6	**28f**	6-CH3	2-OCH3	88
7	**28g**	6-CH3	2-F	85

8	**28h**	6-CH3	4-F	82
9	**28i**	6-CH3	2,4-F	80
10	**28j**	6-CH3	4-Cl	79
11	**28k**	6-OCH3	2-OCH3	87
12	**28l**	6-OCH3	2-F	85
13	**28m**	6-OCH3	4-F	81
14	**28n**	6-OCH3	2,4-F	83
15	**28o**	6-OCH3	4-Cl	79
16	**28p**	7-F-8-CH3	2-OCH3	84
17	**28q**	7-F-8-CH3	2-F	82
18	**28r**	7-F-8-CH3	4-F	85
19	**28s**	7-F-8-CH3	2,4-F	78
20	**28t**	7-F-8-CH3	4-Cl	74
21	**28u**	7-F	2-OCH3	91
22	**28v**	7-F	2-F	88
23	**28w**	7-F	4-F	87
24	**28x**	7-F	2,4-F	82
25	**28y**	7-F	4-Cl	82

Effect of substitution at quinoline core and at acetophenone for the synthesis of chalcone derivatives was studied in the current chapter. Unsubstituted and 6-CH3, 6-OCH3, 7-F-8-CH3, 7-F substituted quinoline ring along with 2-OCH3, 2-F, 4-F, 2,4-F and 4-Cl substitution at phenyl ring of acetophenones were selected for the synthesis of quinoline-conjugated chalcone derivatives **28**. **Table 4.2** reflects that, good to excellent yield was obtained. As far as the substitution at phenyl ring is concerned, higher yield was obtained with -OCH3 substituent as compared to other substituents. On the other hand, lower yield was obtained in case of Cl substitution. In remaining compounds, comparable yield was obtained.

CONCLUSION

Most heterocycles also have significant material science applications, including use as dyes, polymers, brightening agents, fluorescence sensors, and analytical reagents. Further, they can be used in conjugated polymers and other areas of polymer and supramolecular science.

An alarming rise in the prevalence of bacteria that are resistant to many classes of antibiotics has been documented over the past few decades. Humans and animals alike are suffering from an unprecedented rise in the prevalence of fungal and bacterial illnesses. Serious health risks have resulted from the overuse and subsequent resistance of antibacterial and antifungal medications in the treatment of fungal and bacterial infections.

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These unexpected needs have prompted the study and improvement of novel antifungal and antibacterial medications. This category of medicines represents the 21st century's single most important addition to the field of medicinal chemistry. Research into antimicrobial medicine has received considerable dedication, with an emphasis on the creation of more powerful and effective antimicrobial medicines.

These quinoline analogues were synthesised in four separate series, which are all described in this thesis. The pharmacological and computational antimalarial potential of each of the title compounds was evaluated.

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