

Synthesis and Antimicrobial Evaluation of Quinolinone Derivatives Derived from Substituted Chalcones

Sajid Kausar Shah

Research centre, Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati

M.M.Kodape

Department of Chemistry, Sant, Gadge Baba Amravati University, Amravati

M.A. Kotak

Research centre, Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati

A. B. Gajbhiye

Research centre, Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati

N.D. Gawhale

Department of Chemistry G.S Tompe Arts, Commerce and Science College, Chandur Bazar Dist- Amravati

Abstract

The various structural characteristics and their biological uses of quinolinone derivatives constitute a significant class of nitrogen-containing heterocyclic molecules. The current study used a cyclization technique to create a number of substituted quinolinone derivatives from suitably substituted chalcones. The appropriate quinolinone derivatives were produced in satisfactory yields by purifying the generated compounds under carefully regulated reaction conditions. GC-MS and ^1H NMR spectroscopy were the main methods used to characterize the structures of the produced compounds. Using a suitable *in vitro* screening technique, the produced quinolinone derivatives were then assessed for their antibacterial efficacy against particular bacterial and fungal species. Different levels of antibacterial activity were found in the synthesized derivatives according to the biological evaluation, suggesting that structural substitution on the quinolinone framework affects their biological response. The current study offers initial insight into the antibacterial potential of substituted quinolinone derivatives and illustrates a practical method for their production from chalcone precursors. The produced compounds could be helpful scaffolds for additional structural alteration and biological research.

Keywords: Quinolinone derivatives, Substituted chalcones, Heterocyclic synthesis, ^1H NMR spectroscopy, GC-MS analysis, antimicrobial activity, biological evaluation

Introduction

Several of the derivatives of quinolines, a significant class of heterocyclic compounds, have been shown to have a variety of biological uses, such as bactericidal, anti-inflammatory, and antimalarial properties [1-4]. Ali *et al.* reported an effective synthesis of 2-chloro-3-formylquinolines using Vilsmeier-Haack cyclization [2], while Meth-Cohn *et al.* demonstrated flexible synthetic techniques toward quinoline and similar fused heterocyclic systems [1]. While certain quinoline compounds have shown antimalarial [5] and anti-inflammatory [4] effects, others have shown bactericidal qualities [3].

Due to their wide range of pharmacological uses, many 4-hydroxy-1,2-dihydro-2-quinolinones have also garnered significant interest. There have been reports of various quinolinone derivatives with antitumor [6], anti-HSV [7], anticonvulsant [8], anti-inflammatory [9], bactericidal, fungicidal, and molluscicidal properties [10].

The pharmacological characteristics of a number of 3-substituted quinolin-2(1H)-ones containing electron-withdrawing groups have been studied. Numerous glycine-site NMDA receptor antagonists [11] and endothelin receptor antagonists [12] contain these structural features. Furthermore, several quinolin-2(1H)-ones have been used as intermediates in the production of AMPA/kainate receptor antagonists [15], 5-HT receptor antagonists [14], and HIV-1 reverse transcriptase inhibitors [13]. While Stadlbauer *et al.* studied ring-closure reactions involving quinolin-2-one derivatives [17], Kappe *et al.* reported the synthesis of 3-acetyl-4-hydroxyquinolin-2(1H)-one derivatives [16]. The anticonvulsant properties of 3-acyl-4-hydroxyquinolin-2(1H)-ones have also shown their biological importance.

Another significant class of physiologically active substances is chalcone derivatives. Numerous chalcone derivatives have been shown to have antibacterial, antifungal, antimalarial, and anticancer activities [18-20]. Ibrahim *et al.* described the synthesis of 3-acryloyl-1,2-dihydro-4-hydroxy-1-methyl-2-oxoquinoline derivatives and examined their reactions with nucleophiles [22], whereas Sayed *et al.* reported the synthesis and reactions of substituted 4-

hydroxycarbostyryl derivatives with amines and hydrazines [21]. A significant link between quinoline and chalcone-related structural frameworks was revealed by Rezig *et al.* synthesis of quinolinyl aryl unsaturated ketones [23].

In this article, we have concentrated on quinoline, which has received a lot of attention as an important component in drug development and research. It was thought to be beneficial to synthesis and create specific physiologically active molecules in order to determine the medicinal significance of quinolone hybrids as a potential therapeutic agent.

Material and Methods

All chemicals used in the experiments were of analytical reagent (AR) grade. Analytical thin-layer chromatography (TLC) was carried out on Merck pre-coated silica gel 60 F254 aluminium sheets. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded in CDCl_3 on a 500 MHz spectrometer with tetramethylsilane (TMS) serving as the internal standard.

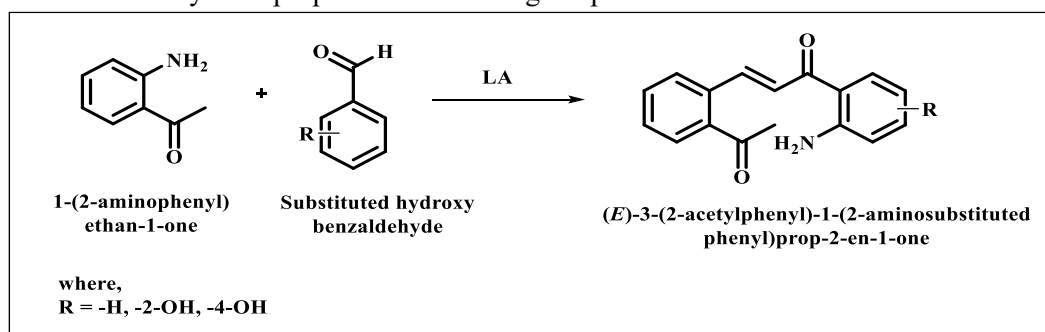
Characterization Techniques

The structure of synthesized compounds was determined by chemical properties elemental analysis and spectral data. ^1H -NMR spectra were recorded on Bruker Avance Neo 500 MHz spectrometer using CDCl_3 solvent and TMS as internal standards at SAIF, Punjab University, Chandigarh (India). Chemical shifts are expressed in ppm. Mass spectrums were recorded on Thermo Scientific TSQ 8000 Gas Chromatogram.

Experimental

General Reaction for synthesis of substituted chalcones

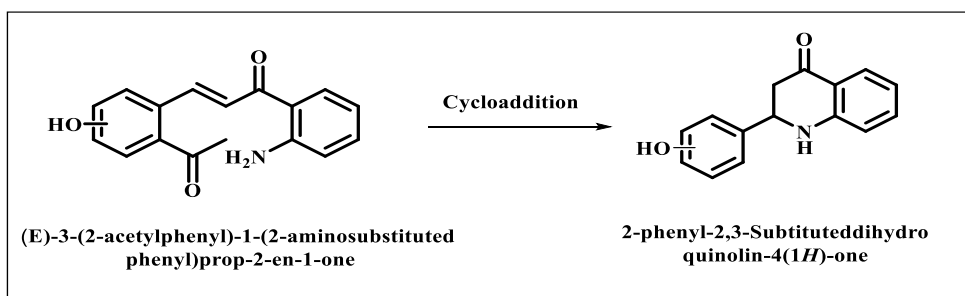
The Claisen-Schmidt condensation is one of the simplest and most effective ways to synthesis the chalcones. In this procedure, LA is reacted with equimolar amounts of acetophenone and derivatives of benzaldehyde. Typically, an alkali content of 10–60% is utilized. The reaction is usually conducted at room temperature for a week or at 55°C for ten to 12 hours. But at these conditions, the Cannizzaro reaction can also occur, reducing the yield of the desired chalcone. to lessen the aldehyde disproportionation during the procedure.



Scheme 1. Synthesis of substituted chalcones

Reaction for synthesis of 2-phenyl-2,3-Substituted dihydroquinolin-4(1H)-one

Several methods, such as using bleaching earth clay as a heterogeneous catalytic medium and PEG-400 as a solvent, are used in the experimental synthesis of quinoline from chalcones. The synthesis begins with the addition of substituted chloroquinoline-3-carbaldehyde. The reaction mixture is acidified with 10% aqueous HCl, the organic material is extracted with dichloromethane, and the mixture is washed with water following ten hours of stirring at 25°C . The product is then dried with anhydrous Na_2SO_4 and concentrated to provide the desired chalcone chemical. The purification process uses a silica gel column in a 9:1 $\text{CHCl}_3:\text{CH}_3\text{OH}$ ratio. The yield of the compounds produced might range from 75% to 85%, depending on the catalyst and reaction circumstances.



Scheme 1. Synthesis of substituted Quinolinone

Table 1. Structural Analysis

Sr. No	Structure of Products	Structural analysis by ¹ HNMR and GCMS
1	 (a)	¹ HNMR(500MHz,CDCl ₃): δ 8.28 (s,1H), 6.70-7.71 (m, 9H), 4.40 (dd,1H), 2.90 (dd,2H) GCMS: Cal m/z: 223.28 Found m/z: 223.24
2	 (b)	¹ HNMR(500MHz,CDCl ₃): δ 9.66 (s,1H), 8.29 (s,1H), 6.71-7.72 (m, 9H), 4.42 (dd,1H), 2.92 (dd,2H) GCMS: Cal m/z: 239.27 Found m/z: 239.25
3	 (c)	¹ HNMR(500MHz,CDCl ₃): δ 9.06 (s,1H), 8.30 (s,1H), 6.74-7.76 (m, 9H), 4.45 (dd,1H), 2.94 (dd,2H) GCMS: Cal m/z: 239.27 Found m/z: 239.22

Biological Investigation

Antimicrobial activity

Important nitrogen-containing heterocyclic molecules with strong antibacterial potential are quinolinone derivatives. The kind and location of substituents on the quinolinone nucleus, which can affect lipophilicity, electrical characteristics, and contact with microbial targets, determine their activity. A number of substituted quinolinones have shown efficacy against certain types of fungus and both Gram-positive and Gram-negative bacteria. Antimicrobial efficacy can be impacted, namely, by structural changes to the 3- and 4-positions. Thus, in order to explore the antibacterial potential of produced quinolinone derivatives and establish first structure–activity connections, they can be evaluated against specific bacterial and fungus strains.

Compound	<i>Staphylococcus aureus</i> (Gram-positive)	<i>Escherichia coli</i> (Gram-negative)	Activity
a	14 mm	12 mm	Moderate
b	18 mm	16 mm	High
c	16 mm	14 mm	Moderate
Standard drug	22 mm	20 mm	High

Conclusion

In the current work, the synthetic series of 2-phenyl-2,3-Substituted dihydroquinolin-4(1H)-one is a promising moiety that can show significant antibacterial activity. Furthermore, the benzo ring

inflection of the structure intentionally includes hydroxyl (ortho-OH) and methoxy (para-OH) groups over the ring. This illustrates the strong and promising biological activity. In conclusion, our results show strong antimicrobial activity and significantly contribute to the formation of a structural moiety and interaction link. this will be useful for designing medications in the future.

Conflict of Interest: Authors have declared that no competing interests exist.

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