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R E S E A E C H A R T I C L E

Synthesis and antimicrobial activity of Schiff base of quinolene-2-ones

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A B S T R A C T

In the present study, we synthesized Schiff bases of quinolene-2-one and their antibacterial activity was evaluated by wells diffusion method. Schiff bases of quinolene-2-one (1 to 3 named as Q2af-Q2ah) were prepared by refluxing with substituted aromatic aldehydes. The final test compounds has purified and characterized by IR, 1HNMR and Mass Spectral studies. M.P. of these compounds was confirmed by open capillary method instrument chemline Cl 725. They have evaluated for antibacterial activity. Compounds were active against Klebsiella pneumonia and Enterococcus faecalis. While ciprofloxacin was used as standards.

Keywords: quinolene-2-one, Schiff base

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

Bacterial infection is one of the most complex global health issues of this century. Klebsiella pneumoniae is a prominent opportunistic pathogen for hospital-acquired and community-acquired infections such as pneumonia, urinary tract infection (UTI) and pyogenic liver abscess (PLA)[1] Enterococci have been known for more than a century for their role as a common cause of endocarditis dates from 1899 and enterococci were subsequently shown to cause a range of infections in the community setting (including pelvic infections, neonatal infections and urinary tract infections (UTIs)), as well as infective endocarditis.[2] The rise of resistant microorganisms is perceived as a serious threat, which aggravates the problem. As a result, increasing efforts have been placed during recent years

towards the search for new antimicrobials [3]. 2-Quinolones are isosteric with coumarins and isomeric to 4-quinolones could become the probable potential candidate for antibacterial activity [4]. A number of biological activities have been associated with quinoline-containing compounds such as antimalarial[5], antitubercular[6], antiallergic[7], anti-inflammatory [8], antibacterial[9],. Quinolin-2-ones or 1-azacoumarins is a part of quinoline alkaloids are known for their diverse biological activity and recently, 6-functionalized 1-aza coumarins are undergoing human clinical trials as an orally active anti-tumor drug in view of its farnesyl protein-inhibiting activity in the Nano molar range [10]. The compounds containing azomethine (-CH=N-) group are known as Schiff bases constitute an important class of compounds for new drug development [11]. In the present study, an attempt was made to synthesize other correlated structures nearing the existing quinolones present in the marketed drugs, to achieve improved biological activities of the parent compounds and a novel series of schiff's bases derived from 7-hydroxy-3-methyl-2-quinolone.

2. Materials and Methods

The chemicals used were of AR grade and LR grade, purchased from Loba Chemicals, Qualigens, S.D Fine Chemicals Ltd. and Merck.

Synthesis of 7-hydroxy-3-methyl-2-quinolone [12] (Q2a). 2.92g of Coumarin dissolved in 30ml of ethanol and 6.4g of hydrazine hydrate was added to the mixture and reflux for 12hours. Cool it and evaporate the solvent at reduced pressure. Then neutral the mixture, the brown color ppt obtained. Reaction confirms by **TLC**

Synthesis of Schiff Base of 7-hydroxy-3-methyl-2-quinolone [12] (Q2aa-Q2ae): Quinolone (Q2a) (10mmol) was dissolved in 2M NaOH (5mL) and to it was added a solution of substituted benzaldehyde (10mmol) in methanol (20mL) drop wise. The mixture was heated under reflux for three hours. After cooling, the mixture was filtered and evaporated under reduced pressure. The product obtained was washed with acetone and dried. In the present study, N-amino quinoline-2-one was allowed to react with aryl aldehydes. (Scheme:1 and Scheme:2)

Spectral Data:

7-hydroxy-1-{[(E)-(2-methoxyphenyl) methylidene] amino} -4-methylquinolin-2(1H)-one (Q_2af): Yield: 47%, MP. 104^0C, colour: yellow, IR (KBr, cm-1): 3361(NH), 2836(CH), 2836(C=O), 1597(C-C ar), 1388(Heterocyclic nitrogen ring skeleton band). 1H NMR δ ppm 8.1(HC=N), 7.57(CH benzene), 6.85(CH benzene (ortho to OCH_3), 6.71(CH benz(ene (adjacent to quinine), 4.96(OH aromatic), 3.75(CH_3). **Mass m/z (%):**294.8 (Molecular ion)

7-hydroxy-1-{[(E)-(4-hydroxy-2-methoxyphenyl) methylidene]amino}-4-methylquinolin-2(1H)-one(Q2ag): Yield: 45%, MP. 110^0C, colour creamish yellow, IR (KBr, cm-1): 3364(NH), 2360(C=C), 1798(N-C=O), 1655(C=O), 1464(N-N), 1868(Overtone of nitrogen heterocyclic). 1H NMR δ ppm 8.1(HC=N), 7.31(CH benzene), 6.71(CH benzene (meta to OCH_3), 6.51(CH benzene (adjacent to quinone), 5.05(OH aromatic), 3.64($CH_{3)}$. Mass m/z (%):310.3 (Molecular ion)

4-methyl-1-{[(1E, 2E)-3-phenylprop-2-en-1-ylidene] amino} quinolin-2(1H)-one (Q2ah):

Yield: 52%, MP. 96^0C, colour: Brisk red, IR (KBr, cm-1): 3392(NH), 3057(CH), 2319(C=C), 1672(C=O), 1597(C-C ar), 1954(Overtone of nitrogen heterocycle). 1H NMR δ ppm 7.6(HC=N), 7.4(CH benzene), 7.18(CH benzene), 6.65(CH ethylene), 6.49(CH benzene (ortho to quinone), 5.7(CH ethylene), 4.98(OH aromatic). **Mass m/z (%):** 292.6(Molecular ion).

Antimicrobial activity

For the studies of antimicrobial effect of synthesized compound, there were 2, microbial successfully procured from Microbial Culture collection, National Centre forcell science, Pune, Maharashtra, India The lyophilized cultures of bacterial strains upon culturing in nutrient broth for 24-48 hours at 37^oC in an incubator resulted into turbid suspension of activated live bacterial cell ready to be used for microbiological study. . The synthesized compound used to suitably dilute up to the concentrations of 100, 50 and 25 µg per ml and applied on to the test organism using well diffusion method **[13].** Results of the experiment are being concluded in the Table2, which clearly shows the anti-microbial activity of synthesized compound of 2 bacteria used in present work.

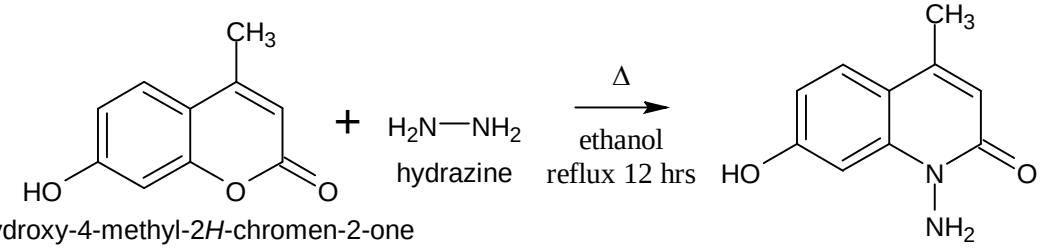
3. Results and Discussions

Chemistry: Schiff bases of 7-hydroxy-3-methyl-2-quinolone (Q_2af-Q_2ah) was synthesised according to literature method [12]. All the compounds were characterized by IR, NMR, and Mass spectral data.

Antimicrobial Activity:

Activity table shows that compound Q2af and Q2ah shows less activity against klebsiella Pneumonia than standard drug while compound Q_2ag has good activity against Eneterococcus faecalis as good as has activity of standard drug.

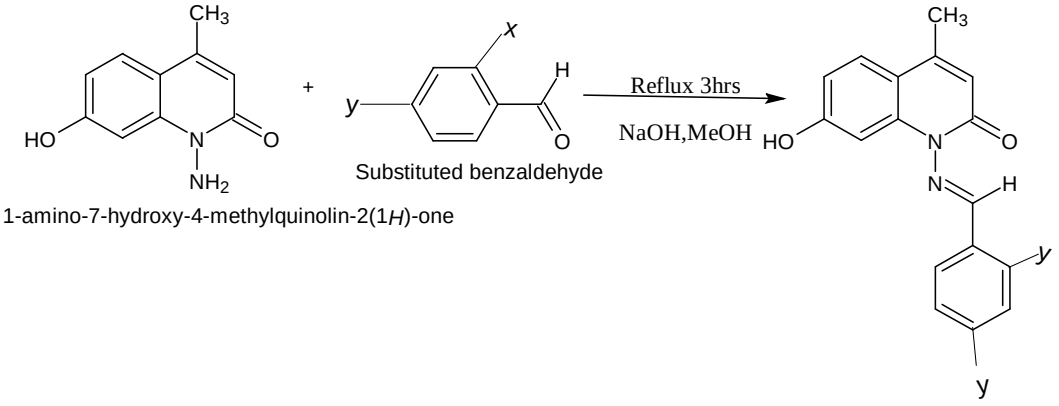
Scheme-1



7-hydroxy-4-methyl-2*H*-chromen-2-one

1-amino-7-hydroxy-4-methylquinolin-2(1*H*)-one

Scheme-1



1-amino-7-hydroxy-4-methylquinolin-2(1*H*)-one

Compound	**X**	**Y**
Q_2af	H	OCH_3
Q_2ag	OH	OCH_3
Q_2ah	H	H

Table 1

S.N	**Name of drug**	**Microbes**	**Zone of inhibition**		
			100 µg/ml	**50 µg/ml**	**25 µg/ml**
1.	**Ciprofloxacin**	***Klebsiella pneumonia***	33±1.5	30±2.88	25±0.57
		Enterococcus faecalis	26±4.04	14±1.15	12±0.57

Table 2

Micro-organism→ Sample↓	***Klebsiella pneumoniae***			***Enterococcus faecalis***		
	In mm Mean			In mm Mean		
	100(µg/ml)	50(µg/ml)	25(µg/ml)	100(µg/ml)	50(µg/ml)	25(µg/ml)
Q_2af	17±0.28	13±0.86	12±0.28	16±0.57	12±0.28	10±0.57
Q_2ag	-	-	-	21±0.86	12±0.28	11±0.57
Q_2ah	19±0.57	12±0.28	10±0.57	-	-	-

4. Conclusion

In the present study, we have synthesized three new derivatives of 7-hydroxy-3-methyl-2-quinolone. The scheme of synthesis is efficient and provides satisfactory yield of the desired compounds. These compounds were confirmed by physical data and spectral studies. The compounds were screened for antimicrobial activity against *Klebsiella pneumonia and Enterococcus faecalis.* One (Q_2ah) out of three compounds (Q_2af, Q2ag and Q_2ah) has good activity against Eneterococcus faecalis as good as has activity of standard drug. Present study shows that there is lots of effort needed to improve their molecular structure to improve their antimicrobial activity compare to drugs already in market having quinolone moiety.

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