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Research Article

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Synthesis of some new analogs of quinoline containing imine bond form the initial composition of aniline

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ABSTRACT

A number of new derivatives quinoline were synthesized using of the Vilsmeier–Haack reagent (DMF+ $POCl_3$). To this end ,the initial composition of aniline after the acquisition of a group methyl- ketone (1) , gave the fused pyridine ring by cyclization and a free aldehyde group is made (2) . Finally , after using aryl-amine derivatives one type, made imine bond connection to the qoinolineis (3) . final products were supported by FTIR, ^1H NMR and Mass spectroscopic measurements and possess moderate to good antibacterial and antifungal activities.

Keywords: quinoline , imine bond , antibacterial

INTRODUCTION

Many derivatives of quinoline have been tudied for the different biological activaty such as Antimicrobia [1-3] , anti-inflammatory[4-5] , ntileishmanial[6-8] , antituberculosis[9] , antimalarial [10-11] , cytotoxicity[12-14] , and HIV-1 Integrase Inhibitors [15-17] .

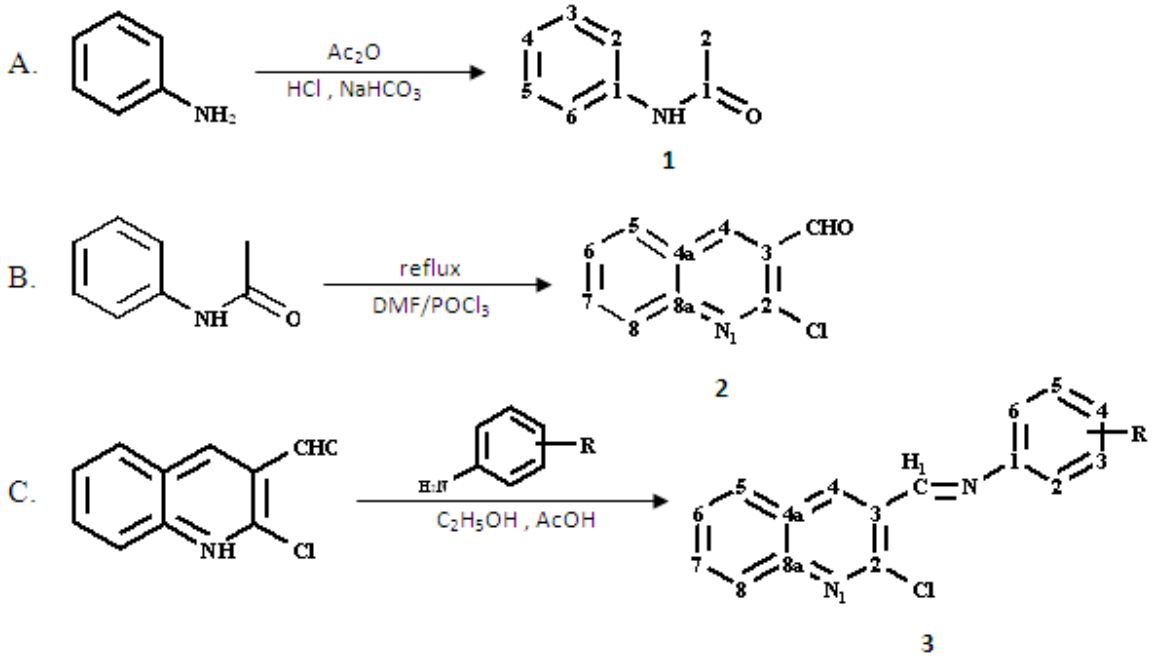
Quinolines and their derivatives are important constituents of several pharmacologically active synthetic compounds[18-19], including biological activities such as DNA binding capability[20], antitumor[21], and DNA-intercalating carrier[22]. The development of general methods for the synthesis and biological evaluation of new agents retaining the ‘core’ quinoline moiety is the subject of considerable synthetic effort. Certain small heterocyclic molecules act as highly functional scaffolds and are known as pharmacophores of a number of biologically active and medicinally useful molecules[23].

Recently,the first quinoline-based structure with very strong antiretroviral activity for HIV treatment has been synthesized . Although some quinoline derivatives has been reported as corrosion inhibitors for steel in sulphuric acid medium [24].

EXPERIMENTAL SECTION

Chemicals and Instrumentation:
The quinoline nucleus was prepared by the method reported in the literature[25-26]. In which the primary aryl amine was taken as starting compound and its acetylation occurs by the treatment with the acetic anhydride.

The resulting aryl acetamide is further cyclized by the treatment with the Vilsmeier–Haack reagent (DMF+ $POCl_3$) which results the quinoline nucleus with primary aldehyde. This aldehyde group is turned to schiff base after the treatment with substituted anilines and gives the various derivatives (scheme 1).



scheme 1

Melting points were determined with open capillary and are uncorrected. Proton NMR spectra were taken in $CDCl_3$ and recorded at 300 MHz in Bruker DRX-300. Chemical shifts (δ) were measured in ppm with respect to TMS. FTIR spectra recorded on instrument simadzu 2100 S and Perkin Elmer BX. MS were obtained on a JEO JMC-300 instrument. Elemental analysis performed on Elementar Vario EL III.

Synthesis of N1-phenylacetamide (1) :

Aniline (10 mmol) was added into the water (50 ml) to produce heterogenous suspension which becomes homogenous after addition of 6N HCl (5 ml) with continuous stirring. The resulting homogenous solution was cooled in an ice bath. In the above solution acetic anhydride (10 mmol) was added followed by the addition of solid sodium bicarbonate until there was no effervescence. The precipitated product filtered and dried and finally dried in a vacuum desicator.

Synthesis of 2-choloro-3-quinolinecarbaldehyde (2) :

The $POCl_3$ (7 ml) was added drop wise to a stirring solution of the acetamide solution (1) in ice cooled DMF (2 ml) and the resulting mixture was heated at 130°C for 2 hrs, the solution was cooled and poured on to ice-water (150 ml) to precipitate synthesized fused pyridine compound.

Synthesis of N-phenyl-2-chloro-3-quinolylmethanimine (3)

Cyclized pyridine compound was dissolved in 30 ml of ethanol containing few drops of glacial acetic acid. The substituted aniline (10 mmol) was added into the above mixture. The reaction mixture was refluxed for 5 hrs at 700C. The reaction mixture was cooled and poured in crushed ice. The solution was filtered and purified by recrystallization from ethanol.

SPECTROSCOPIC DATA OF COMPOUNDS

3a. N-(4-chlorophenyl)-2-chloro-3-quinolylmethanimine :

mp 138-140°C, FTIR (cm^{-1}): 3028. 5 (Ar-C-H), 1503. (Ar C-C), 40.38(Ar C=C), 1541.01(C=N), 936.85(C-N), 764.34(C-Cl), ^1H NMR ($CDCl_3$) : 7.36(d,j=8.5 , 2H) , 7.876(d , j=8.35 Hz ,1H) , 8.22(S , 1H) , 9.23(S , 1H) , Mass (m/z): 301.17(M^+).

3b. 4-[(E)-1-(2-chloro-3-quinolyl)methylideneamino]phenol :
mp 105-108°C, FTIR (cm^{-1}): 3145.45(Ar-C-H), 752.31(C-Cl), 1637.41 (C=C), 966.46(Ar C-C), 1544.54(C=N), 924.81(C-N), 3300.3(O-H), ^1H NMR ($CDCl_3$) :5.11(S , 1H) , 7.119(d , J=8.7 , 2H) , 7.98(d , J=8.7 , 1H) , 8.22(S , 1H) , 9.23(S , 1H) , Mass (m/z): 283.7(M^+).

3c. 4-[(E)-1-(2-chloro-3-quinolyl)methylideneamino]benzoic acid :
mp 128-130°C, FTIR (cm^{-1}): 3135.45(Ar-C-H), 820.31(C-Cl), 1730.31(C=C), 1003.73(Ar C-C), 1710.21(C=N), 971.64(C-N), 1720.31(C=O) , ^1H NMR ($CDCl_3$) :7.26(d , J=7.2 , 2H) , 8.22(S, 1H) , 9.23(S , 1H) , 10.78(S , 1H), Mass (m/z): 310.73(M^+).

3d. 4-[(E)-1-(2-chloro-3-quinolyl)methylideneamino]benzensulfonamide :
mp 140-142°C, FTIR (cm^{-1}): 3272.86(Ar-C-H), 1569.95(C=C), 334.23(Ar C-C), 1538.41(C=N), 1087.34(C-N), 3435.74(-NH). 1168.93(S=O), ^1H NMR ($CDCl_3$):5.9(S , 2H) , 7.454(d , J=8.1 , 2H) , 7.98(d, J=8.73 , 1H) , 8.22(S , 1H) , 9.23 (S , 1H) , Mass (m/z): 345.8(M^+).

3e. N-(4-methoxyphenyl)-2-chloro-3-quinolylmethanimine :
mp 100-104°C, FTIR (cm^{-1}): 3225.15(Ar-C-H), 652.23(C-Cl), 1633.48(C=C), 966.37(Ar C-C), 15245.34(C=N), 924.96(C-N), 1232.46(C-O, OCH3), ^1H NMR ($CDCl_3$) :3.7(S , J=0.23 , 3H) , 7.137(d , J=8.75 , 1H) , 7.87 (d , J=8.35 , 2H) , 8.221(S , 1H) , 9.236(S , 1H) , Mass (m/z): 270(M^+).

3f. N-(4-nitrophenyl)-2-chloro-3-quinolylmethanimine :
mp 112-114°C, FTIR (cm^{-1}): 3144.36(Ar-C-H), 697.75(C-Cl), 1559.65(C=C), 1142.23 (Ar C-C), 15380.91(C=N), 987.34(C-N), 1554.24(N=O, NO2), ^1H NMR ($CDCl_3$) :7.45(d , J=8.2 , 2H) , 7.87(d , J=8.35 , 1H) , 8.22(S , 1H) , 9.23(S , 1H) , Mass (m/z): 311.7(M^+).

RESULTS AND DISCUSSION

Table 1 shows the efficiencies obtained from the derivatives of 3 compound . As can be seen , The highest and lowest yields, respectively, is Pertain to the compounds **3a** and **3c**.

The spectral data of synthesized compounds are evident and showed that all the proposed compounds are synthesized properly and the common mechanism of synthesis of pyridine nucleus can be used to produce quinoline (3). After substitution of schiff base in the heterocyclic nucleus give easier way to compare the antimicrobial activity. The antimicrobial activity of all the synthesized compounds showed that the quinoline compounds are moderately active against all used bacterial strain , except compound **3d** which containing para sulphonamide group in schiff base [27-33]. All the compounds synthesized still not significant against microbes under investigation but the further purification and modification in the synthesized derivatives give scope for further development in the same heterocyclic nucleus.

Table 1 . synthesis of N-phenyl-2-chloro-3-quinolylmethanimine derivatives

Compound	R	Molecular formula	Yield value(%)
3a	4-Cl	$C_{16}H_{10}Cl_2N_2$	87
3b	4-OH	$C_{16}H_{11}ClN_2O$	75
3c	4-COOH	$C_{17}H_{11}ClN_2o_2$	69
3d	4-SO_2NH_2	$C_{16}H_{12}ClN_3O_2S$	79
3e	4-OCH_3	$C_{17}H_{13}ClN_2O$	82
3f	4-NO_2	$C_{16}H_{10}ClN_3O_2$	77

CONCLUSION

In the current research some substituted –N-((2-chloroquinolin-3-yl) methylene) benzenamines (3) have been synthesized . From the above results, it can be conclude that quinoline compounds are moderately active against all used bacterial strain .

Although the compounds synthesized are not much significant against microbes under investigation but the further purification and modification of synthesized derivatives give scope for further development in the same heterocyclic nucleus.

REFERENCES

[1] Joanna godlewska ; wojciech luniewski, Anticancer Res, **2005**, 25(8), 2857 - 2868.
[2] P Shukla , Appl. Envir. Microbiol., **1986**, 51(11), 1332 - 1342.
[3] Ulrike Delling;Martine Raymond; Erwin Schurr , Antimicrob. Agents Chemother., 1**998**, 42(15), 1034 - 1041.
[4] N. P. Dhammika Nanayakkara; Arba L. Ager; Jr Marilyn S. Bartlett;Vanessa Yardley; Simon L. Croft, ; Agents Chemother., **2008**,52(17) , 2130 - 2137.
[5] J. C. Hubbard; Nancy K. Hall; Howard W. Larsh , Antimicrob. Agents Chemother., **1978**,14(22),922 - 923.
[6] Z. Hadidian; T. N. Fredrickson; E. K. Weisburger; J. H. Weisburger; R. M. Glass; N. Mantel , J Natl Cancer Inst, **1968**, 41(3), 985 - 1036.
[7] Aspergillosis; Fusariosis ; Katsura Hata; Takaaki Horii; Mamiko Miyazaki , Antimicrob. Agents Chemother., **2011**, 55(35), 4543 - 4551.
[8] Mamiko Miyazaki; Takaaki Horii; Katsura Hata; Nao-aki Watanabe; Kazutaka Nakamoto, Antimicrob. Agents Chemother., **2011**, 55(8), 4652 - 4658.
[9] Nao-aki Watanabe; Mamiko Miyazaki;Takaaki Horii; Koji Sagane; Kappei Tsukahara; Katsura Hata , Antimicrob. Agents Chemother., **2012**, 56(19), 960 - 971.
[10] Margaret M. T. Hudson , J. Antimicrob. Chemother., **2001**, 48(10), 345 - 350.
[11] Herman Gershon; Raulo Parmegiani; Patricia K. Godfrey , Antimicrob. Agents Chemother., **1972**, 1(8), 373 - 375.
[12] Theodouli Stergiopoulou; Joseph Meletiadis; Tin Sein, Paraskevi Papaioannidou; Ioannis Tsiouris; Emmanuel Roilides, J. Antimicrob. Chemother., **2009**, 63(11), 343 - 348.
[13] Richard D. Cannon;Erwin Lamping; Ann R. Holmes; Kyoko Niimi; Philippe V. Baret, Clin. Microbiol. Rev., **2009**,22(8), 291 - 321.
[14] Patrick Hall-Smith , Br Med J, **1964**, 1(3), 1510.
[15] Ameeta K. Agarwal; Tao Xu, Melissa R. Jacob; Qin Feng, Michael C. Lorenz, Eukaryot. Cell, **2008**, 7(14), 387 - 400.
[16] Shabana I. Khan; Alison C. Nimrod; Mohammed Mehrpooya;John L. Nitiss; Larry A. Walker , Antimicrob. Agents Chemother., **2002**, 46(17), 1785 - 1792.
[17] Ishac Nazi; Adam Scott; Anita Sham; Laura Rossi; Peter R. Williamson; James W. Kronstad, Antimicrob. Agents Chemother., **2007**, 51(13), 1731 - 1736.
[18] Pertti J. Neuvonen; Anders Rane; Mika Valtonen;Hanna Vyyryläinen , Antimicrob. Agents Chemother., **2006**, 50(5), 1967 - 1972.
[19] R J Holt , J. Clin. Pathol., **1975**, 28(6), 767 - 774.
[20] Mark Wainwright , J. Antimicrob. Chemother., **2001**, 47(7),1 - 13.
[21] Br. Med. Bull, J. Antimicrob. Chemother ., **194**4, 2(12), 79 - 84.
[22] J. Bruce-Chwatt , Br Med J., **1964**, 1(3),581 - 586.
[23] Richard Slack , J. Antimicrob. Chemother., **1984**,13(5), 1 - 7.
[24] J. B. Rennie; J. A. Milne; J. Sommerville , Br Med J., **1951**, 1(7), 383 - 388.
[25] Arcivoc , J. Clin. Pathol., **2007**, 11(13), 56-63.
[26] Nicholas White , Tetrahedron Letters., **2006**, 47(16), 7779–7782.
[27] G. A. Grant Peterkin ; Br Med J, J. Clin. Pathol., **1945**,2(5), 1 - 6.
[28] N. J. White , J. Antimicrob. Chemother., **1992**, 30(18), 571 - 585.
[29] Mohammed Mehrpooya, Br Med J, **1964**, 1(7), 825 - 828.
[30] A. M. Geddes , J. Antimicrob. Chemother., **1975**, 1(19), 349 - 350.
[31] D. S. Reeves , J. Antimicrob. Chemother., **1975**, 1(4), 350 - 353.
[32] Nicholas White ; Phil Trans R Soc B, J. Antimicrob. Chemother., **1999**, 354(11), 739 - 749.
[33] Doris McKenzie; Marilyn Stadler; Jane Boothe; J. J. Oleson, Y. Subbarow , J. Immunol., **1948**, 60(2), 283 - 294.