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Synthesis, characterization and antibacterial activity of some new 3-(aryl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one

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Abstract

1-(4-(quinolin-8-ylamino)phenyl)ethanone ***(1)*** *was synthesized from 4-aminoacetophenone and 8-hydroxyquinoline in presence of anhyd. $ZnCl_2$. New chalcones* ***(2)*** *were synthesized from 1-(4-(quinolin-8-ylamino)phenyl)ethanone* ***(1)*** *and aromatic aldehydes under basic conditions via Claisen-Schmidt condensation. The structures of synthetic compounds were established on the basis of analytical* and spectral data. These compounds were screened for their antibacterial activity.

Key Words: 4-aminoacetophenone, 8-hydroxyquinoline, chalcone, antibacterial activity.

INTRODUCTION

Quinolones are extensively investigated as broad spectrum antibacterial [1, 2], antidiabetic [3], anticancer [4], antiviral [5] and anti-HIV [6] agents. Quinoline family compounds are widely used as a parent compound to make drugs (especially antimalarial medicines), fungicides, biocidal. 8-Hydroxyquinoline derivatives are used due to their biological activity as fungicides and antibacterial properties. These properties are closely related with their capability for quelating metallic ions [7].

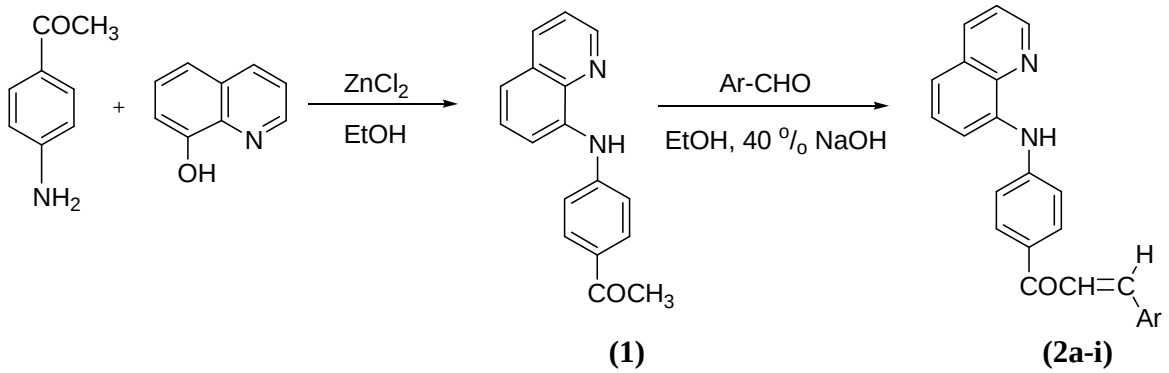
Chalcones are α, β -unsaturated ketones which constitute an important group of natural products that serve as precursors for the synthesis of various heterocyclic compounds like pyrimidines, imidazoles [8], pyrazoles [9], 2-pyrazolines [10, 11], and flavonoids [12, 3]. Chalcones, either natural or synthetic, are known to exhibit various biological activities such as anti-inflammatory

[14, 15], antifungal [16-19], antioxidant [20-23], antimalarial [24-27], antituberculosis [28], analgesic [29], anti-human immunodeficiency virus (HIV) [30], and antitumor activities [31-33]. Some of them act as anticancer [34], antiviral [35] and anti-AIDS agents [36]. Quinoline-based chalcones have been reported to possess antimalarial activity [37]. Chalcones as well as some quinoline derivatives have already been recognized for their antimicrobial [38, 39]. In the present study, the quinoline nucleus and chalcone functionality have been incorporated in a single molecule and deliberated their antibacterial activities with variation of substituents at different positions in the aromatic ring.

Synthesis of the title compounds was based on Claisen–Schmidt condensation [40]. For this purpose, the 8-hydroxyquinoline were condensed with commercially available 4-aminoacetophenone, in the presence of sodium hydroxide. Spectral data (IR, ^{1}H-NMR and MS) of all the newly synthesized chalcones were in full agreement with the proposed structures.

RESULTS AND DISCUSSION

The chalcones i.e. 3-(aryl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one were prepared by the Claisen-Schmidt condensation reaction **(Scheme 1)**.These compounds were prepared by the condensation of 1-(4-(quinolin-8-ylamino)phenyl)ethanone with aromatic aldehydes in basic media under prolonged refluxing condition. The structures of newly synthesized compounds have been confirmed on the basis of elemental analysis and spectral data. From antibacterial screening, it was found that titled compounds exhibited good antibacterial activity against the different bacteria stains.



(1) **(2a-i)**

Scheme 1. 3-(aryl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one

Antibacterial Activity

Antibacterial activities of all the compounds were studied against four different bacterial strains (*E. coil(+ve strain,), B. subtilis, Pseudomonas sp., S.aureus,*) by measuring the zone of inhibition on agar plates. The compounds possess moderate to good activity against all stains in comparison with standard drug (**Table 1**). It can be observed from these results that compounds have shown positive bacterial activity against different bacterial species, which are also known as human pathogenic bacteria. It was also observed that within the synthesized compound extracts, all compounds show good activity against all bacterial strains.

Table 1. Biological activities of 3-(aryl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one.

Bacterial strain	Zone of inhibition in mm along without well diameter (5mm)									
	Chemical compounds									
	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**	**Standard Nystatin**
E. coil (+ve strain)	8	6.5	8.5	-	4.5	3	4	5.5	2.8	9
B. subtilis	4.8	8.3	7	9	6.5	-	5	6	9.9	12
Pseudomonas sp.	6	10	13	11.2	9	7	8	11	7	17
S. aureus	5	-	5.5	6.6	4	4.5	3.3	5.4	2.9	6

"-" represent "not active"

MATERIALS AND METHODS

General: All the chemicals and solvents were obtained from E-Merck, India (AR grade) and were used without further purification. Melting points were taken in an open capillary tube. IR spectra were recorded on a Shimadzu Dr-8031 instrument. Elemental analyses were carried out using a Perkin-Elmer, CHN elemental analyzer model 2400. ^{1}H NMR spectra of the synthesized compounds were recorded on a Bruker-Avance (300 MHz) and Varian-Gemini (200 MHz) spectrophotometer using $CDCl_3$ solvent and TMS as an the internal standard. EI-MS spectra were determined on a LCQ ion trap mass spectrometer (Thermo Fisher, San Jose, CA, USA), equipped with an EI source.

Experimental

Synthesis of 1-(4-(quinolin-8-ylamino)phenyl)ethanone (1).

A mixture of 8-hydroxyquinoline (0.05 mol) and p-aminoacetophenone (0.05mol) in absolute ethanol (50 ml) was heated under reflux in the presence of anhyd. $ZnCl_2$ (0.5 g) for 6 hr. On cooling, a solid mass separated out which was washed with acidified water to remove inorganic materials, then it was filtered off to obtain the product and crystallized from ethanol.

Synthesis of 1-(4-(quinolin-8-ylamino)phenyl)ethanone (1).

Yield: 85 %; m.p. : 110 ^{o}C, IR (KBr): 3588 cm^{-1} (NH-Ar); 1686 (C=O) cm^{-1} ; ^{1}H NMR: δ = 2.50 (s, 3H, Ar-$COCH_3$); 7.40 (s, 1H, Ar-CH); 7.50-7.60 (m, 4H, Ar-CH); 8.00 (d, 2H, Ar-CH); 8.40 (s, 1H, Ar-CH); 8.70 (s, 1H, Ar-CH); 8.80 (s, 1H, Ar-CH); 9.80 (s, 1H, Ar-NH); Anal. Calcd. For $C_{17}H_{14}N_2O$ (262.31) : C, 77.84; H, 5.38; N, 10.68; Found: C, 77.50; H, 5.10; N, 10.30 ; Mass spectra, m/z = 262.00 (100%).

Synthesis of 3-(aryl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2a-i).
Equimolar quantities of 1-(4-(quinolin-8-ylamino)phenyl)ethanone(1) (0.01 mol) and p-aminoacetophenone (0.01 mol) were dissolved in ethanol (15 ml), under stirring and aqueous NaOH (40%, 10 ml) was added dropwise. The reaction mixture was stirred at room temperature and kept for 5-6 hrs.The reaction mixture was diluted with water and acidified with 10% HCl. The separated solid was filtered and recryststallised from aq. ethanol to give compounds.

Synthesis of 3-phenyl-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2a).
Yield: 80 %; m.p. : 150 ^{o}C, IR (KBr): 3588 cm^{-1} (NH-Ar); 1686 cm^{-1} (C=O); 1425 cm^{-1} (C=C); ^{1}H NMR: δ = 7.10 (s, 1H, Ar-CH); 7.30-7.40 (m, 4H, Ar-CH); 7.60-7.70 (m, 9H, Ar-CH); 8.50 (s, 1H, Ar-CH); 8.70 (s, 1H, Ar-CH); 8.80 (s, 1H, Ar-CH); 9.70 (s, 1H, Ar-NH); Anal. Calcd. For $C_{24}H_{18}N_2O$ (350.41) : C, 82.26; H, 5.18; N, 7.99; Found: C, 82.10; H, 5.10; N, 7.40 ; Mass spectra, m/z = 350.10 (100%).

Synthesis of 3-(2-hydroxyphenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2b).
Yield: 76 %; m.p. : 120 ^{o}C, IR (KBr): 3580 cm^{-1} (NH-Ar); 2960 cm^{-1} (Ar-OH); 1670 cm^{-1} (C=O); 1430 cm^{-1} (C=C); ^{1}H NMR: δ = 6.70 (s, 1H, Ar-CH); 6.90 (s, 1H, Ar-CH); 7.20 (s, 1H, Ar-CH); 7.30 (s, 1H, Ar-CH); 7.50-7.70 (m, 9H, Ar-CH); 8.50 (s, 1H, Ar-CH); 8.70 (s, 1H, Ar-CH); 8.90 (s, 1H, Ar-CH); 9.60 (s, 1H, Ar-NH); 9.90 (s, 1H, Ar-OH); Anal. Calcd. For $C_{24}H_{18}N_2O_2$ (366.41) : C, 78.67; H, 4.95; N, 7.65; Found: C, 78.40; H, 4.20; N, 7.30 ; Mass spectra, m/z = 366.10 (100%).

Synthesis of 3-(4-methoxyphenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2c).
Yield: 73 %; m.p. : 170 ^{o}C, IR (KBr): 3570 cm^{-1} (NH-Ar); 1680 cm^{-1} (C=O); 1450 cm^{-1} (C=C); ^{1}H NMR: δ = 3.90 (s, 3H, Ar-OCH_3); 6.90 (d, 2H, Ar-CH); 7.40-7.70 (m, 10H, Ar-CH); 8.00 (s, 1H, C=CH); 8.40 (s, 1H, Ar-CH); 8.70 (s, 1H, Ar-CH); 8.80 (s, 1H, Ar-CH); 9.80 (s, 1H, Ar-NH); Anal. Calcd. For $C_{25}H_{20}N_2O_2$ (380.44) : C, 78.93; H, 5.30; N, 7.36; Found: C, 78.50; H, 5.10; N, 7.20 ; Mass spectra, m/z = 380.10 (100%).

Synthesis of 3-(4-hydroxyphenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2d).
Yield: 68 %; m.p. : 140 ^{o}C, IR (KBr): 3550 cm^{-1} (NH-Ar); 2940 cm^{-1} (Ar-OH); 1690 cm^{-1} (C=O); 1450 cm^{-1} (C=C); ^{1}H NMR: δ = 6.60 (d, 2H, Ar-CH); 7.10 (s, 1H, CO-CH); 7.40 (s, 1H, Ar-CH); 7.50 (s, 1H, C=CH); 7.60-7.70 (m, 8H, Ar-CH); 8.40 (s, 1H, Ar-CH); 8.70(s, 1H, Ar-CH); 8.80(s, 1H, Ar-CH); 9.40 (s, 1H, Ar-NH); 9.80 (s, 1H, Ar-OH); Anal. Calcd. For $C_{24}H_{18}N_2O_2$ (366.41) : C, 78.67; H, 4.95; N, 7.65; Found: C, 78.30; H, 4.50; N, 7.10 ; Mass spectra, m/z = 366.00 (100%).

Synthesis of 3-(4-(dimethylamino)phenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2e).
Yield: 81 %; m.p. : 160 ^{o}C, IR (KBr): 3568 cm^{-1} (NH-Ar); 1655 cm^{-1} (C=O); 1469 cm^{-1} (C=C); ^{1}H NMR: δ = 3.10 (s, 6H, Ar-N$(CH_3)_2$); 6.70 (d, 2H, Ar-CH); 7.10(s, 1H, CO-CH); 7.40-7.60 (m, 9H, Ar-CH); 8.20 (s, 1H, C=CH); 8.50 (s, 1H, Ar-CH); 8.70 (s, 1H, Ar-CH); 8.90 (s, 1H, Ar-CH); 9.60 (s, 1H, Ar-NH); Anal. Calcd. For $C_{26}H_{23}N_3O$ (393.48) : C, 79.36; H, 5.89; N, 10.68; Found: C, 79.10; H, 5.50; N, 10.30 ; Mass spectra, m/z = 393.10 (100%).

Synthesis of 3-(3-nitrophenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2f).
Yield: 79 %; m.p. : 150 ^{o}C, IR (KBr): 3575 cm^{-1} (NH-Ar); 1660 cm^{-1} (C=O); 1470 cm^{-1} (C=C); ^{1}H NMR: δ = 7.30 (s, 1H, CO-CH); 7.40-7.60 (m, 8H, Ar-CH); 7.70 (s, 1H, C=CH); 8.00 (s, 1H, Ar-CH); 8.20 (s, 1H, Ar-CH); 8.30 (s, 1H, Ar-CH); 8.50 (s, 1H, Ar-CH); 8.70 (d, 2H, Ar-CH); 9.80 (s, 1H, Ar-NH); Anal. Calcd. For $C_{24}H_{17}N_3O_3$ (395.41) : C, 72.90; H, 4.33; N, 10.63; Found: C, 72.30; H, 4.10; N, 10.40 ; Mass spectra, m/z = 395.10 (100%).

Synthesis of 3-(2-nitrophenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2g).
Yield: 77 %; m.p. : 160 ^{o}C, IR (KBr): 3570 cm^{-1} (NH-Ar); 1640 cm^{-1} (C=O); 1480 cm^{-1} (C=C); ^{1}H NMR: δ = 7.10 (s, 1H, CO-CH); 7.30-7.60 (m, 8H, Ar-CH); 7.80 (s, 1H, C=CH); 8.10 (s, 1H, Ar-CH); 8.30 (s, 1H, Ar-CH); 8.40 (s, 1H, Ar-CH); 8.60 (s, 1H, Ar-CH); 8.90 (d, 2H, Ar-CH); 9.60 (s, 1H, Ar-NH); Anal. Calcd. For $C_{24}H_{17}N_3O_3$ (395.41) : C, 72.90; H, 4.33; N, 10.63; Found: C, 72.50; H, 3.90; N, 10.10 ; Mass spectra, m/z = 395.00 (100%).

Synthesis of 3-(4-chlorophenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2h).
Yield: 75 %; m.p. : 170 ^{o}C, IR (KBr): 3590 cm^{-1} (NH-Ar); 1620 cm^{-1} (C=O); 1450 cm^{-1} (C=C); ^{1}H NMR: δ = 7.20 (s, 1H, CO-CH); 7.40 (t, 3H, Ar-CH); 7.50-7.60 (m, 8H, Ar-CH); 7.90 (s, 1H, C=CH); 8.40 (s, 1H, Ar-CH); 8.70 (s, 1H, Ar-CH); 8.80 (s, 1H, Ar-CH); 9.90 (s, 1H, Ar-NH); Anal. Calcd. For $C_{24}H_{17}N_2OCl$ (384.86) : C, 74.90; H, 4.45; N, 7.28; Found: C, 74.60; H, 4.10; N, 7.15 ; Mass spectra, m/z = 384.00 (100%).

Synthesis of 3-(2-chlorophenyl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-one (2i).
Yield: 81 %; m.p. : 180 ^{o}C, IR (KBr): 3610 cm^{-1} (NH-Ar); 1660 cm^{-1} (C=O); 1470 cm^{-1} (C=C); ^{1}H NMR: δ = 7.30 (s, 1H, CO-CH); 7.50 (t, 3H, Ar-CH); 7.70-7.90 (m, 8H, Ar-CH); 8.10 (s, 1H, C=CH); 8.50 (s, 1H, Ar-CH); 8.80 (s, 1H, Ar-CH); 8.90 (s, 1H, Ar-CH); 9.50 (s, 1H, Ar-NH); Anal. Calcd. For $C_{24}H_{17}N_2OCl$ (384.86) : C, 74.90; H, 4.45; N, 7.28; Found: C, 74.30; H, 4.20; N, 7.05 ; Mass spectra, m/z = 384.10 (100%).

CONCLUSION

In summary, we have synthesized some bioactive chalcones having 8-hydroxyquinoline moiety. The antibacterial study reveals that synthesized compounds possess good to moderate activity as compared with standard drug. Hence, it can be concluded that these bioactive chalcones can be used in the development of synthesis of new antibiotic drugs.

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