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SYNTHESIS, SPECTRAL STUDIES AND ANTIMICROBIAL SCREENING OF SOME NEWCHALCONE AND QUINOLINE DERIVATIVES

Dhruva U. Dave*, Neha C. Bhoraniya, Heena C. Patel, Priyanka Pankhaniya and D. M. Purohit*

Student A-202, Sanidhya 253, Nr. Spedwell Party Plot, Rajkot, Gujarat- Rajkot Gujarat India.

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***Corresponding Author**
Dhruva U. Dave
Student A-202, Sanidhya 253, Nr. Spedwell Party Plot, Rajkot, Gujarat- Rajkot Gujarat India.

ABSTRACT

(E)-3-(2'-amino-3',5'-dibromophenyl)-1-(aryl) prop-2-en-1-ones (1a-1l) and 2-aryl- 6,8-dibromoquinolines (2a-2l) were synthesized. The synthesized structures were validated through spectral analysis including IR, Mass, and ^{1}H-NMR. The antimicrobial activity of compounds (1a-1l) and (2a-2l) was assessed against Gram positive bacteria (*Bacillus subtilis, Staphylococcus aureus*), Gram negative bacteria (*Escherichia coli, Pseudomonas aeruginosa*) and Fungi *Aspergillus Niger*.

KEYWORDS: Heterocyclic compounds, quinolines, chalcones, antimicrobial activity, spectralstudies.

I. INTRODUCTION

Quinolines, a group of heterocyclic organic compounds, have a bicyclic structure consisting of a benzene ring fused with pyridine ring, quinolines showcase exceptional versatility, playing pivotal roles as foundational components in pharmaceuticals, agrochemicals, and materials science.[1]

These heterocyclic compounds have displayed potent pharmacological effects across various therapeutic domains. Among the notable applications of quinolines is their role in combating malaria as antimalarials. Moreover, quinolines demonstrate antimicrobial activity, with some derivatives showing efficacy against a range of microorganisms including bacteria,fungi, and viruses.[2] Additionally, quinolines have been studied for their anti-inflammatory,[3] antioxidant,[4] and analgesic properties,[5] indicating their potential in managing conditions

such as inflammation, oxidative stress-related disorders, and pain. Furthermore, quinolines exhibit anti-cancer properties, and certain drugs based on them have been investigated for their potential in treatment of disorders like Alzheimer's and Parkinson's diseases.[6]

Chalcones are a class of compounds consisting of two aromatic rings linked by a three-carbon α,β-unsaturated carbonyl system.[7] They are widely distributed in nature, found in various plants, and are also synthesized in the laboratory for their diverse biological activities.[8] Because of their wide range of biological activities, chalcones play a crucial role as primary compounds in the process of drug discovery and development. It possesses various biological activities such as anti-oxidant,[9] anti-inflammatory,[10] antimicrobial,[11] antidiabetic,[12] antiangiogenic,[13] antiviral,[14] and analgesic properties.[15]

Our research work mainly focuses on the synthesis of chalcone derivatives with 2- amino-3,5-dibromo benzaldehyde (1a-1l) with various aromatic acetophenones and the quinoline derivatives[16][17] (2a-2l) of have been synthesized by the reaction of (1a-1l) with 10% aq. NaOH solution. After confirming the structure with spectral studies of synthesized compounds, the antimicrobial activity of newly synthesized compounds was evaluated and compared with the standard drugs using the cup-plate method.[18][19]

II. MATERIALS AND METHOD

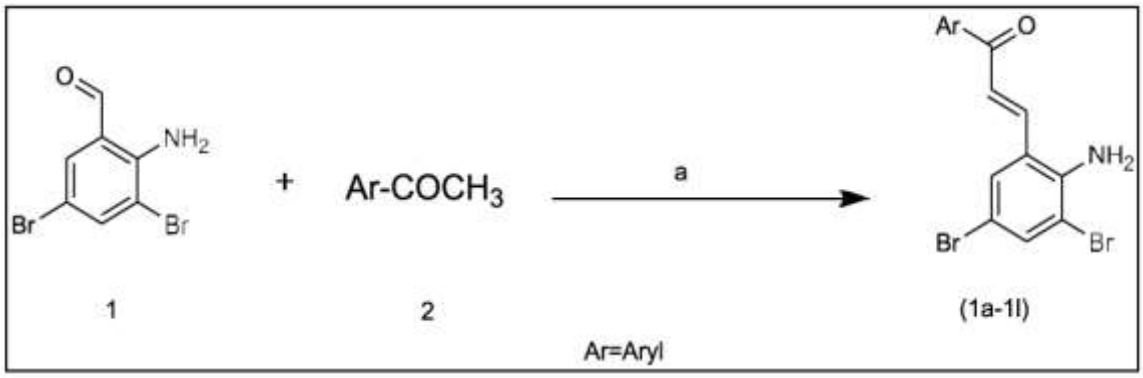
We employed analytical grade (AR) chemicals obtained from Merck, Finar and Loba Chemie for the synthesis process, utilizing them without any further purification. The purityof the synthesized compounds was observed using TLC with silica gel 60 F254 (Merck) and the solvent system ethylacetate: hexane. The TLC plates were visualized under UV chamberat 254 nm. Characterization of the compounds was performed through spectral analysis, like Mass Spectrometry, IR, and ^{1}H-NMR. Mass spectra were recorded using a water Mass spectrometer. Infrared spectroscopy was conducted using KBr pellet on a Shimadzu IR Affinity FT-IR spectrophotometer. ^{1}H-NMR spectra were recorded on a Bruker 400MHz spectrometer in DMSO-d6 and $CDCl_3$ solvent with TMS as an internal standard. Melting points of the synthesized compounds were determined in open glass capillary tubes and are uncorrected. The antimicrobial activities, of the synthesized compounds **(1a-1l), (2a-2l)** have been taken by the Cup plate method, with known standard drugs utilized for comparison.

General method for preparation of compounds (E)-3-(2'-amino-3',5'-Dibromophenyl)-1-(4''-methoxyphenyl) prop-2-ene-1-one. (1j)

The synthesis process involves adding 4-methoxy acetophenone (0.01mole) to 20 mL Methanol, to this solution 2-amino-3,5-dibromobenzaldehyde (0.01 mole) is added and catalytic amount of aq. 40% NaOH solution. Then this solution was stirred continuously for 24 hours at room temperature. With the help of TLC, the progress of reaction was monitored. After the completion of the reaction the mixture was kept overnight, the reaction mixture was poured into crushed ice. The product was filtered, dried, crystallized in methanol. Melting point-156℃, % Yield = 75.4 %. The structure was confirmed by spectral data.

The spectral analysis: IR data: 3333 (N-H str.), 2970 (C-H asym. Str. Alkane), 2839 (C-H str. Sym. Alkane), 1735 (C=O str. Ketone), 1604 (C=C str.), 1481(C-H bending asym. Alkane), 1381 (C-H sym. Bending alkane), 1257(C-O-C, ether), 655 (C-Br str.). ^{1}H-NMR data (400 MHz, CDCl3): 8.2 (Doublet, 2H aromatic), 8.1 (Multiplet, 2H aromatic), 7.12 (doublet,2H vinyl proton), 3.85 (Singlet 3H, methoxy), 3.36 (Singlet, 2H amine). M.S.: 507,498,459.9,411.

Reaction scheme 1



Reaction condition: (a) 40% aq. NaOH, Methanol, Room temperature, 24 hours

Table 1: Physical data for compounds (E)-3-(2'-amino-3',5'-Dibromophenyl)-1-(aryl) prop-2-ene-1-ones (1a-1l).

SeriesCode	Aryl	MolecularFormula	m/z Value	MeltingPoint	%yield
1a	3-Br-C6H4-	C15H10Br3NO	454.83	134	70.3
1b	2-Cl-C6H4-	C15H10Br2ClNO	410.88	122	66.5
1c	4-Cl-C6H4-	C15H10Br2ClNO	410.88	146	81.5
1d	2,4-(Cl)2C6H3-	C15H9Br2Cl2NO	444.84	218	75.2
1e	2-OH-C6H4-	C15H11Br2NO2	392.92	168	65.3
1f	3-OH-C6H4-	C15H11Br2NO2	392.92	128	71.0

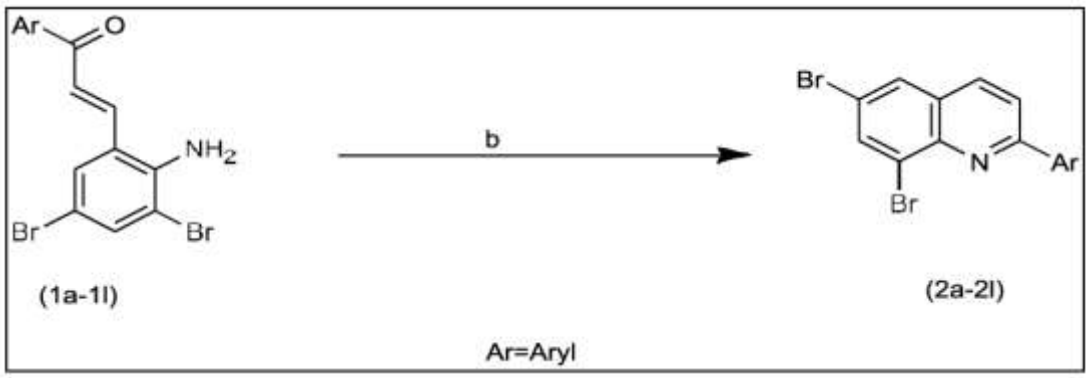
1g	4-OH-C_6H_4-	$C_{15}H_{11}Br_2NO_2$	392.92	140	66.7
1h	2,4-$(OH)_2$-C_6H_3-	$C_{15}H_{11}Br_2NO_3$	408.91	116	66.8
1i	4-OH,3-OMe-C_6H_3-	$C_{16}H_{13}Br_2NO_3$	422.93	138	66.0
1j	4-OMe-C_6H_4-	$C_{16}H_{13}Br_2NO_2$	411.09	156	75.4
1k	4-Me-C_6H_4-	$C_{16}H_{13}Br_2NO$	390.94	116	82.5
1l	3-NO_2-C_6H_4-	$C_{15}H_{10}Br_2N_2O_3$	421.91	206	84.8

General method for preparation of compounds 2-(4'-methylphenyl)-6,8-dibromoquiolines (2k)

Compound 2k has been synthesized by the reaction of the chalcone prepared (E)-3- (2'-amino-3',5' dibromophenyl)-1-(4'-methylphenyl) prop-2-ene-1-one (1k) (0.01 mole) was taken and dissolved in 1,4-dioxane. Catalytic quantity of 10% aq. NaOH was added and the mixture was refluxed for 8 hours at 120°C. Then after completion of reaction, the reaction mixture was poured into crushed ice. Filtered it, dried it and crystallized in methanol. The structure was confirmed by spectral data.

Spectral analysis: IR data: 3063 (C-N), 2908 (C-H asym. Str. Alkane), 2854 (C-H str. Sym. Alkane), 1589 (C=C str.), 1473 (C-H bending asym. Alkane), 1319 (C-H sym. Bending alkane), 655 (C-Br str.). ^{1}H-NMR data (400 MHz, $CDCl_3$): 8.4 (Doublet, 1H aromatic), 8.2 (Multiplet, 5H aromatic), 7.4 (Doublet, 2H aromatic), 2.39 (Singlet, 3H methyl). M.S. :379.9, 376.9, 376.1, 333.7, 209.1, 158.7.

Reaction scheme 2



Reaction condition (b) 10% aq. NaOH, 1,4-Dioxane solvent, 8 hours, 120°C

Table 2: Physical data for compounds 2-(aryl)-6,8-dibromoquiolines (2a-2l).

Series Code	Aryl	Molecular Formula	m/z Value	Melting Point	%yield
2a	3-Br-C_6H_4-	$C_{15}H_8Br_3N$	438.82	111	88.8

2b	2-Cl-C6H4-	C15H8Br2ClN	394.87	122	98.0
2c	4-Cl-C6H4-	C15H8Br2ClN	394.87	148	67.3
2d	2,4-(Cl)2C6H3-	C15H7Br2Cl2N	428.83	200	72.3
2e	2-OH-C6H4-	C15H9Br2NO	376.91	184	86.3
2f	3-OH-C6H4-	C15H9Br2NO	376.91	136	71.9
2g	4-OH-C6H4-	C15H9Br2NO	376.91	134	76.7
2h	2,4-(OH)2-C6H3-	C15H9Br2NO2	392.9	126	62.5
2i	4-OH,3- OMe- C6H3-	C16H11Br2NO2	406.92	130	64.9
2j	4-OMe- C6H4-	C16H11Br2NO	392.2	128	57.8
2k	4-Me-C6H4-	C16H11Br2N	376.92	130	96.4
2l	3-NO2-C6H4-	C15H8Br2N2O2	407.89	204	72.5

III. RESULT AND DISCUSSION

Scheme 1 shows the reaction for synthesis of Chalcone derivatives (1a-1l) and their corresponding quinoline derivatives (2a-2l). The chalcone derivatives were synthesized by condensation of various aromatic acetophenones with 2-amino-3,5-dibromobenzaldehyde in presence of catalytic quantity of 40% aq. NaOH at room temperature for 24 hours. All chalcones obtained gave 65-84% yield. The quinoline derivatives (2a-2l) were synthesized by condensation of chalcones (1a-1l) in presence of 10% aq. NaOH in 1,4-Dioxane at 120°C for 8 hours. The compounds so synthesized gave a yield of 62-98%. The structures of newly synthesized compounds were confirmed by spectral analysis.

Antimicrobial activity

The antimicrobial activity was assessed using cup plate method with 100µg/mL concentration of both the standard drugs and the compounds synthesized. The activity was taken against Gram positive bacteria (*Bacillus subtilis, Staphylococcus aureus*), Gram negative bacteria (*Escherichia coli, Pseudomonas aeruginosa*) and Fungi like *Aspergillus Niger* using DMF as a solvent. The zone of inhibition was measured in mm. The standard drugs used were Gentamycin, Ampicillin for anti-bacterial activity. Nystatin for anti-fungal activity. The results for the same are shown in Table 3 and Table 4. The comparison with standard drugs isshown in Table 5.

Table 4: Antimicrobial activity of (E)-3-(2'-amino-3',5'-Dibromophenyl)-1-(aryl)prop-2-ene-1-ones (1a-1l).

Compound	Ar-	Antibacterial Activity				Anti-fungal activity
		Gram +ve bacteria		Gram -ve bacteria		
		B.subtilis	*S.aureus*	*E.coli*	*P.aeruginosa*	*A.niger*
1a	3-Br-C6H4-	8	-	2	7	-

1b	2-Cl-C6H4-	14	-	2	6	2
1c	4-Cl-C6H4-	5	7	3	7	-
1d	2,4-(Cl)2C6H3-	-	10	2	6	-
1e	2-OH-C6H4-	12	4	3	4	2
1f	3-OH-C6H4-	9	12	1	4	12
1g	4-OH-C6H4-	13	5	2	5	-
1h	2,4-(OH)2-C6H3-	10	9	3	2	-
1i	4-OH,3-OCH3-C6H3-	8	-	2	6	-
1j	4-OCH3-C6H4-	3	2	2	3	-
1k	4-CH3-C6H4-	5	3	5	3	-
1l	3-NO2-C6H4-	2	-	3	5	-
Zone of Inhibition measured in mm						

Table 5: Antimicrobial activity of 2-(aryl)-6,8-Dibromoquiolines (2a-2l).

Compound	**Ar-**	**Antibacterial Activity**				**Anti-fungal activity**
		Gram +ve bacteria		**Gram -ve bacteria**		
		B.subtilis	***S.aureus***	***E.coli***	***P.aeruginosa***	***A.niger***
2a	3-Br-C6H4-	11	-	3	7	9
2b	2-Cl-C6H4-	9	2	3	6	6
2c	4-Cl-C6H4-	2	3	-	6	6
2d	2,4-(Cl)2C6H3-	5	2	4	6	6
2e	2-OH-C6H4-	4	-	5	2	8
2f	3-OH-C6H4-	7	4	4	3	5
2g	4-OH-C6H4-	7	2	4	4	5
2h	2,4-(OH)2-C6H3-	5	2	3	3	4
2i	4-OH,3-OCH3-C6H3-	5	-	3	7	8
2j	4-OCH3-C6H4-	9	4	2	6	6
2k	4-CH3-C6H4-	3	2	5	5	9
2l	3-NO2-C6H4-	5	2	4	4	10
Zone of Inhibition measured in mm						

Table 5: Synthesized compounds (1a-1l) and (2a-2l) showing antimicrobial activity and it's comparison with standard drugs.

Compound	**Antibacterial Activity**				**Anti-fungal activity**
	Gram +ve bacteria		**Gram -ve bacteria**		
	B.subtilis	***S.aureus***	***E.coli***	***P.aeruginosa***	***A.niger***
(1a-1l)	1a,1b,1e,1f,1g ,1h,1i	1c,1d,1f,1h	1k	1a,1b,1c,1d,1i	1b,1e,1f
(2a-2l)	2a,2b,2f,2g,2j	2f,2j	2e,2k	2a,2b,2c,2d,2i ,2j	2a,2e,2i,2k, 2l
Activity of known standard drugs					
Gentamycin (100µg/mL)	30	20	14	16	-

Ampicilin (100µg/mL)	24	22	-	-	-
Nystatin (100µg/mL)	-	-	-	-	22
Zone of Inhibition measured in mm					

CONCLUSION

To conclude we have synthesized (E)-3-(2'-amino-3',5'-dibromophenyl)-1-(aryl) prop-2-ene-1-ones (1a-1l) and 2-(aryl)-6,8-dibromoquiolines (2a-2l) and characterized them on the basis of their physical and spectral data. Most of the synthesized compounds showed presence of antimicrobial activity although some of the compounds from (1a-1l) like 1a,1b, 1c,1d,1e,1f,1g,1h,1i,1k showed presence of anti-bacterial activity while 1b,1e,1f showed anti-fungal activity. Compounds like 2a,2b,2c,2d,2e,2f,2g,2i,2j,2k showed presence of antibacterial activity while 2a,2e,2i,2k,2l showed anti-fungal activity. This activity is compared with standard drugs like gentamycin, ampicillin and nystatin at concentration 100µg/mL as represented in Table 5.

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