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"SYNTHESIS, SPECTRAL AND MICROBIAL STUDIES OF QUINAZOLIN-4-ONE BASED SOME NEW CHALCONES DERIVATIVES."

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ABSTRACT

Chalcones and their analogs have been an area of great interest in recent years. Therefore it is very important to develop the latest strategies in the synthesis of chalcone. Therefore in present research study, a series of 6, 8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one have been synthesized by the condensation of 3-(4-acetylphenyl)-6,8-dibromo-2-phenylquinazolin-4-one with various aldehydes in presence of ethanol. The intermediate 3-(4-acetylphenyl)-6,8-dibromo-2-phenylquinazolin-4-one synthesized by fusion of 6,8-dibromo-2-phenyl-3,1-benzoxazin-4-one with 1-(4-aminophenyl) ethanone. These newly synthesized compounds are screened for antibacterial and antifungal activity by Agar Cup method .The structure of the synthesized compounds are characterized by the IR , ^{1}H-NMR and elemental analysis.

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INTODUCTION

Heterocyclic compounds are widely distributed in nature and are obtained synthetically and play an important role in regulating biological process. Chalcone (1,3-phenyl-2-propene-1-one) is a compound that contain two aromatic rings linked by an unsaturated α, β –ketone, with various substituents on the two rings.

The existence of the α,β-unsaturated ketone moiety in chalcones is a common part found in a large number of biological active compounds. Chalcone and their derivatives have been reported to possess antimicrobial[1], anti-inflammatory[2], antimalerial[3] and anti-tubercular[4], Anticancer[5], antiparasitic[6], Antibacterial[7], Antiviral[8], Cardiovascular[9], Germicidal [10], Herbicidal [11] , Antioxidant [12] activity. In the view of the various biological and pharmacological applications of some new heterocyclic derivatives of Chalcone, So we have decided to synthesize a new series of 6,8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one.

MATERIALS AND METHODS

All reagents were of analytical reagent grade and were used without further purification, Melting points were taken in open capillary tube. The IR spectra were recorded on Bruker Model; Alpha, Laser Class1, Made in Germany and Brooker instrument was used for NMR Spectroscopy and $(CH_3)_4Si$ (tetramethylsilane) used as internal standard and DMSO was used as a solvent. Purity of the compounds was checked by TLC on silica- G plates. Antimicrobial activities were tested by Agar Cup method. Standard drugs like Stretomycin and Fluconozole were used for the comparison purpose.

RESULT AND DISCUSSION

Preparation of 6,8-dibromo-2-phenyl-3,1-benzoxazin-4-one (KS-1).

2-amino-3,5-dibromobenzoic acid (0.01M) in 30 ml pyridine was added benzoylchloride (0.02M) and the mixture was shaken for 5 min and then kept aside room temperature for further 25 minutes with occasional shaking. The reaction mixture was treated with 15 ml 5% $NaHCO_3$. The product separated as solid mass. The yield of the product was 91% and the product melts at 153^0C.

IR(KBr) ; KS-01 (cm^{-1}): 3068 (=C-H), 1699 (>C=O Stretching), 1604 (>C=N stretching), 1572 (>C=C< Aromatic), 1286 (C-N), 1252 (C-O-C) , 558 (C-Br). **^{1}HNMR (DMSO) ; (KS-01) : δ ppm** 7.616-8.488 ,Multiplet (7H) (Ar-H). **Composition found:** C(44.12%) H(1.81%) N(3.64%). **Composition Calculated for $C_{14}H_7Br_2NO_2$:** C(44.13%) H(1.85%) N(3.68%).

Preparation of 3-(4-acetylphenyl)-6,8-dibromo-2-phenylquinazolin-4-one (KS-2).

In a conical flask, a mixure of 6,8-dibromo-2-phenyl-3,1-benzoxazin-4-one (3.8gm,0.01 mole) and 1-(4-aminophenyl)ethanone (1.35gm , 0.01mole) was heated together upon fusion at 150^0C on sand bath for 2 hour. After cooling , the crude mass was crystallized twice from ethanol. The yield of the product was 75% and the product melts at 240^0C.

IR(KBr) ; KS-2 (cm^{-1}): 3063 (=C-H), 2982 (-C-H Stretching), 1683 (>C=O Stretching), 1584 (>C=N stretching) , 1560 (>C=C< Aromatic), 1429 (-CH_3), 1311 (C-N) , 568 (C-Br).

^{1}HNMR (DMSO) ; (KS-02) : δ ppm 2.543, Singlet (3H) (-$COCH_3$), 7.260-8.277, Multiplet (11H) (Ar-H). **Composition found:** C(53.03%) H(2.82%) N(5.62%).

Composition Calculated for $C_{22}H_{14}Br_2N_2O_2$: C(53.04%) H(2.83%) N(5.62%).

Preparation of 6,8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one (KS-3a-3j).

To the solution of 3-(4-acetylphenyl)-6,8-dibromo-2-phenylquinazolin-4-one (0.01M) in absolute ethanol (50 ml), substitutedbenzaldehyde (0.01M) and 2% NaOH (10 ml) were added and refluxed for 10 hours. After refluxing the reaction mixture was concentrated, cooled, filtered and neutralized with dil. HCl. The solid residue thus obtained was crystallized by absolute ethanol.

IR(KBr) ; 3e (cm^{-1}): 6,8-dibromo-3-{4-[3-(2-hydroxyphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one 3230 (-OH), 3065 (=C-H), 1679 (>C=O Stretching), 1584 (>C=N stretching), 1552 (>C=C< Aromatic), 1317 (C-N), 536 (C-Br).

IR(KBr) ; 3h (cm^{-1}): 6,8-dibromo-3-{4-[3-(4-dimethylaminophenyl)prop-2-enoyl]phenyl}-2-phenyl quinazolin-4-one 3051 (=C-H), 2965 (-C-H Stretching), 1679 (>C=O Stretching), 1585 (>C=N stretching), 1515 (>C=C< Aromatic), 1445 (-CH_3), 1312 (C-N), 546 (C-Br)

^{1}HNMR (DMSO); 3h :6,8-dibromo-3-{4-[3-(4-dimethylaminophenyl)prop-2-enoyl]phenyl}-2-phenyl quinazolin-4-one δ ppm 2.827, Singlet (6H) (-$N(CH_3)_2$) 7.942 , Doublet (2H) (-CH=CH-), 7.170 - 8.247 , Multiplet (15H) (Ar-H).

^{1}HNMR (DMSO) ; 3i : 6,8-dibromo-3-{4-[3-(4-methoxyphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one δ ppm 3.867, Singlet (3H) (-OCH_3), 7.858 , Doublet (2H) (-CH=CH-), 7.009 - 8.251 , Multiplet (15H) (Ar-H)

Reaction Scheme

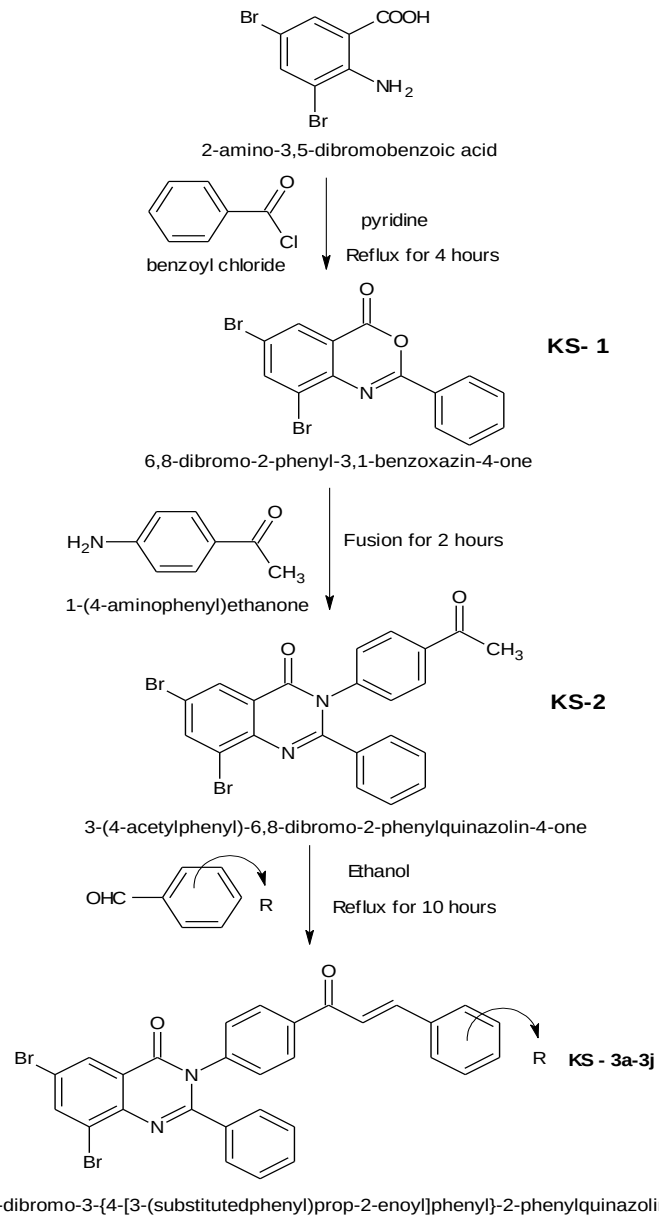

Table 1: Physical constant of of 6,8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one.

Sr. No	Sub. No.	R	M.F.	Mol. Wt (g/mole)	Yield %	M.P. °C	% Carbon		%Nitrogen		% Hydrogen	
							Found	Calcd	Found	Calcd	Found	Calcd
1	KS-3a	-2-Cl	$C_{29}H_{17}Br_2ClN_2O_2$	620.71	80	120	56.10	56.11	4.50	4.51	2.73	2.76
2	KS-3b	-4-Cl	$C_{29}H_{17}Br_2ClN_2O_2$	620.71	70	120	56.10	56.11	4.51	4.51	2.75	2.76
3	KS-3c	-3,4-$(OCH_3)_2$	$C_{31}H_{22}Br_2N_2O_4$	646.32	82	130	57.59	57.61	4.32	4.33	3.40	3.43
4	KS-3d	-H	$C_{29}H_{18}Br_2N_2O_2$	586.27	72	190	59.40	59.41	4.74	4.78	3.05	3.09
5	KS-3e	-2-OH	$C_{29}H_{18}Br_2N_2O_3$	602.27	79	>320	57.82	57.83	4.61	4.65	3.01	3.01
6	KS-3f	-4-OH-3-OCH_3	$C_{30}H_{21}BrN_2O_4$	632.29	73	220	56.97	56.99	4.42	4.43	3.14	3.19
7	KS-3g	-4-OH	$C_{29}H_{18}Br_2N_2O_3$	602.27	69	215	57.82	57.83	4.61	4.65	3.01	3.01
8	KS-3h	-4-N$(CH_3)_2$	$C_{31}H_{24}BrN75_3O_2$	629.34	78	190	59.15	59.16	6.64	6.68	3.63	3.68
9	KS-3i	-4-OCH_3	$C_{30}H_{21}BrN_2O_3$	616.29	75	218	58.43	58.47	4.50	4.55	3.22	3.27
10	KS-3j	-3-NO_2	$C_{23}H_{14}BrN_3O_4$	631.27	82	158	55.17	55.18	6.65	6.66	2.70	2.71

Table 2: Antimicrobial activity of 6,8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one.

SR. NO.	COMP. NO.	R	Zone of Inhibitions in mm			
			S. aureus	E.coli	Aspergillue niger	Saccharomyces
1	3a	2-Cl	25	25	18	21
2	3b	4-Cl	16	16	16	20
3	3c	-3,4-$(OCH_3)_2$	26	25	20	16
4	3d	-H	23	27	NA	15
5	3e	-2-OH	30	26	19	18
6	3f	-4-OH-3-OCH_3	25	NA	20	19
7	3g	-4-OH	30	25	19	NA
8	3h	-4-N$(CH_3)_2$	23	29	17	20
9	3i	-4-OCH_3	25	28	15	19
10	3j	-3-NO_2	23	25	18	15
11	Streptomycin	-	30	30	-	-
12	Fluconozole	-	-	-	20	21

Antibacterial activity:

The Present investigation revealed the maximum antibacterial activity was shown by the compounds 3e , 3g against aureus and 3h against E.coli . Poor antibacterial activity was shown by the compounds 3b against S. aureus. All the synthesized compounds(3b,3d,3h,3j,3a,3f,3i,3c,3e,3g) shows moderate to excellent antibacterial activity against aureus. 3f was inactive against E.coil.

Antifungal activity

From screening results, compound 3c and 3f possesses maximum antifungal activity against Aspergillue niger and Saccharomyces respectively. 3d and 3g were inactive against Aspergillue niger and Saccharomyces respectively. Remaining other synthesized compounds shows very good antifungal activity.

CONCLUSION

The Main objective of present research work was to synthesize, characterize and evaluated antimicrobial activities of the newly synthesized compounds with the help of analytical data such as IR and ^{1}H-NMR. In conclusion, in present we prepared a series of 6,8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-2-phenylquinazolin-4-one based derivatives. Most of all synthesized compounds shows good biological activity.

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