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Synthesis, Spectral Studies and Biological Evoluation of 3-[4-(1-Acetyl-5-(Substitutedphenyl)-4,5-Dihydro-Pyrazol-3-yl)Phenyl]-6,8-Dibromo-2-Methylquinazolin-4-One Derivatives

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ABSTRACT

Synthesis of new series of 3-[4-(1-acetyl-5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl)phenyl]-6,8-dibromo-2-methylquinazolin-4-one has been achieved by the refluxation of 6,8-dibromo-3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-methyl quinazolin-4-one with Glycial acetic acid for three hours. The intermediate have been synthesized by refluxation of 6,8-dibromo-3-{4-[3-(substitutedphenyl)prop-2-enoyl] phenyl}-2-methylquinazolin-4-one (0.01M) and 99% hydrazine hydrate (0.015M) by using ethanol (50ml) as a solvent with various aldehydes. The chemical structures of synthesized acetyl pyrazoline derivatives were characterized by their physical constants and spectral data. The new acetyl pyrazoline derivatives were screened for their antimicrobial activities against several bacterial and fungal species.

1. Introduction

Heterocyclic compounds are widely distributed in nature and have proved to be of an immense significance to life. Nitrogen containing heterocycles play an important role, not only for life science industry but also in many other industrial fields related to special and fine chemical industries. Among them, Recently, substituted pyrazole derivatives have significant interest due to their roles in medicine and agriculture industries [1-5]. In recent years there has been an increasing interest in the chemistry of Pyrazoline because of their biological signifance. Many of them show anticancer [6], cytotoxic [7], antifungal [8], antitubercular [9], anti-inflammatory activity, antioxidant [10]. So it was planned to synthesize some new substituted acetyl pyrazoles with the hope that they may possess better antimicrobial activities.

2. Materials and Methods

All reagents were of analytical reagent grade and were used without further purification. All the product were synthesized and characterized by their spectral analysis.

All Melting points were determine by open capillary tube and are uncorrected. The IR spectra have been recorded on Bruker Model; Alpha, Laser Class1, Made in Germany and ^{1}H-NMR spectra have been recorded on Brooker instrument by using tetramethylsilane as an internal standard. 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.

3. Result and Discussion

Preparation of 6, 8-dibromo-3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-methyl quinazolin-4-one (KS-1a-1j).

A mixture of 6,8-dibromo-3-{4-[3-(substitutedphenyl) prop-2-enoyl]phenyl}-2-methylquinazolin-4-one (0.01M) and 99% hydrazine hydrate (0.015M) in ethanol (50ml) refluxed gently for 3 hours. Then the mixture was concentrated and allowed to cool. The resulting solid was filtered, washed with ethanol and recrystallised from ethanol. **^{1}HNMR (DMSO); (KS-1a):** δ ppm 2.507, Singlet (3H) (-CH_3), 3.368, Doublet(2H) (-CH_2), 3.942 Triplet (1H) (-CH<), 7.377, Singlet (1H) (-NH), 7.277-8.340, Multiplet (10H) (Ar-H). **^{1}HNMR (DMSO) ; (KS-1g) :** δ ppm 2.505, Singlet (3H) (-CH_3), 3.355, Doublet(2H) (-CH_2), 3.959 Triplet (1H) (-CH<), 7.379, Singlet (1H) (-NH), 7.379-8.411, Multiplet (10H) (Ar-H), 9.659, Singlet(1H) (-OH). **IR(KBr) ; KS-1f (cm^{-1}):** 3379 (>NH-), 3269 (-OH), 3029 (=C-H), 2965 (-C-H Stretching), 1671 (>C=O Streching), 1587 (>C=N stretching) , 1503 (>C=C< Aromatic), 1442 (-CH_2 bending) , 1402 (-CH_3), 1304 (C-N), 1264 (N-N) , 1169 (C-O-C) , 535 (C-Br). **IR(KBr) ; KS-1i (cm^{-1}):** 3357 (>NH-), 3087 (=C-H), 2906 (-C-H Stretching), 1662 (>C=O Streching), 1587 (>C=N stretching) , 1507 (>C=C< Aromatic), 1443 (-CH_2 bending) , 1420 (-CH_3), 1294 (C-N), 1249 (N-N) , 1168 (C-O-C) , 548 (C-Br).

Preparation of 3-[4-(1-acetyl-5-(substitutedphenyl) - 4,5-dihydro-pyrazol-3-yl)phenyl]-6,8-dibromo-2-methylquinazolin-4-one (2a-2j).

A mixture of 6,8-dibromo-3-{4-[5-(2-substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-2-methylquinazolin-4-one (0.001M) and acetic acid (10ml) refluxed for 3 hours. The solution was then concentrated, on cooling, the resulting solid was filtered, washed with water and recrystallised from absolute ethanol.

^{1}HNMR (DMSO) ; (KS-2b) : δ ppm 2.070, Singlet (3H) (-$COCH_3$), 2.509, Singlet (3H) (-CH_3), 3.381 , Doublet(2H) (-CH_2) , 3.951, Triplet (1H) (-CH<), 7.202-8.409, Multiplet

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(10H) (Ar-H). **^{1}HNMR (DMSO); (KS-2f) :** δ ppm 2.157, Singlet (3H) (-$COCH_3$), 2.506, Singlet (3H) (-CH_3), 3.367, Doublet(2H) (-CH_2), 3.719, Singlet (3H) (-OCH_3), 3.937,Triplet (1H) (-CH<), 7.499-8.411, Multiplet (9H) (Ar-H), 9.699, Singlet(1H) (-OH).

IR(KBr); KS-2g (cm^{-1}): 3062 (=C-H), 2907(-C-H Stretching), 1677 (>C=OStretching), 1586 (>C=N stretching), 1504 (>C=C< Aromatic), 1444 (-CH_2 bending), 1405 (-CH_3), 1307 (C-N), 1261 (N-N) , 546 (C-Br).

IR(KBr); KS-2i (cm^{-1}): 3056 (=C-H), 2903 (-C-H Stretching), 1669 (>C=OStretching), 1581 (>C=N stretching), 1507 (>C=C< Aromatic), 1439 (-CH_2 bending), 1403 (-CH_3), 1305 (C-N), 1247 (N-N), 1170 (C-O-C), 529 (C-Br).

Reaction Scheme

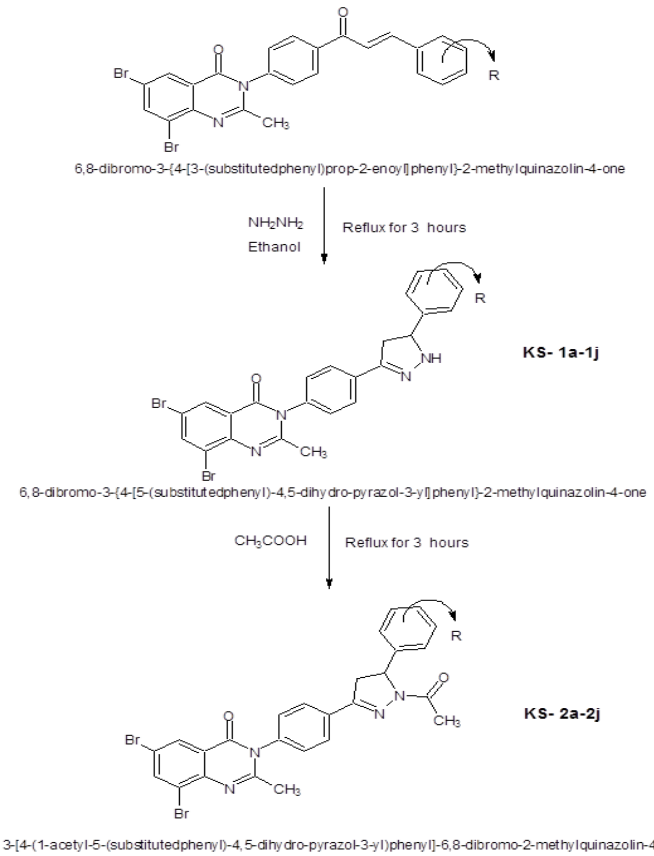

Table No.1 Physical constant of of 3-[4-(1-acetyl-5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl)phenyl]-6,8-dibromo-2-methylquinazolin-4-one.

Sr.No	Sub.No.	R	M.F.	Mol.Wt (g/m)	Yield%	M.P. °C	% Carbon		% Nitrogen		% Hydrogen	
							Found	Calcd	Found	Calcd	Found	Calcd
1	KS-2a	-2-Cl	$C_{26}H_{19}Br_2ClN_4O_2$	614.71	70	145	50.80	50.80	9.10	9.11	3.11	3.12
2	KS-2b	-4-Cl	$C_{26}H_{19}Br_2ClN_4O_2$	614.71	69	168	50.80	50.80	9.10	9.11	3.12	3.12
3	KS-2c	-3,4-$(OCH_3)_2$	$C_{28}H_{24}Br_2N_4O_4$	640.32	78	170	52.51	52.52	8.73	8.75	3.74	3.78
4	KS-2d	-H	$C_{26}H_{20}Br_2N_4O_2$	580.27	80	183	53.82	53.82	9.65	9.66	3.46	3.47
5	KS-2e	-2-OH	$C_{26}H_{20}Br_2N_4O_3$	596.27	65	135	52.33	52.37	9.40	9.40	3.36	3.38
6	KS-2f	-4-OH-3-OCH_3	$C_{27}H_{22}Br_2N_4O_4$	626.29	70	134	51.75	51.78	8.92	8.95	3.54	3.54
7	KS-2g	-4-OH	$C_{26}H_{20}Br_2N_4O_3$	596.27	63	167	51.74	52.37	9.40	9.40	3.37	3.38
8	KS-2h	-4-$N(CH_3)_2$	$C_{28}H_{25}Br_2N_5O_2$	623.33	78	175	53.92	53.95	11.23	11.24	4.02	4.04
9	KS-2i	-4-OCH_3	$C_{27}H_{22}Br_2N_4O_3$	610.29	85	180	53.10	53.14	9.15	9.18	3.61	3.63
10	KS-2j	-3-NO_2	$C_{26}H_{19}Br_2N_5O_4$	625.26	76	203	49.94	49.94	11.20	11.20	3.04	3.06

Table No.2 Antimicrobial activity of 3-[4-(1-acetyl-5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl)phenyl]-6,8-dibromo-2-methylquinazolin-4-one

SR No	COMP NO	R	Zone of inhibition in mm			
			ANTIBACTERIAL ACTIVITY		ANTIFUNGAL ACTIVITY	
			S. aureus	E.coil	Aspergillue niger	Saccharomyces
1	KS-2a	2-Cl	24	28	16	20
2	KS-2b	4-Cl	26	32	19	NA
3	KS-2c	-3,4-$(OCH_3)_2$	24	NA	20	17
4	KS-2d	-H	NA	24	10	15
5	KS-2e	-2-OH	28	27	19	16
6	KS-2f	-4-OH-3-OCH_3	32	28	20	18
7	KS-2g	-4-OH	30	30	16	16
8	KS-2h	-4-$N(CH_3)_2$	29	28	19	18
9	KS-2i	-4-OCH_3	20	30	24	16
10	KS-2j	-3-NO_2	26	31	18	23

Antibacterial activity

Biological evaluation of present investigation revealed maximum antibacterial activity was shown by the compound 2f against Staphylococcus aureus and 2j against Eschirichia coli which showed good anti-bacterial activity than the respective standard test-drug also. Minimum antibacterial activity was shown by the compounds 2i against S. aureus and 2d against E.coil. KS-2d and 2c were found to be inactive against S. aureus and E. Coli respectively.

Antifungal activity

From screening results, compound 2i and 2j were found to possess maximum antifungal activity against Aspergillue niger and Saccharomyces respectively. The minimum antifungal activity was shown by the compound KS-2d for both Aspergillue niger and Saccharomyces. 2b was found to be inactive against Saccharomyces.

4. Conclusion

The Main objective of present research work was to synthesize, characterize and evaluate antimicrobial activities of the newly synthesized compounds with the help of analytical data such as Proton NMR and IR. In conclusion, in present we prepared a series of 3-[4-(1-acetyl-5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl)phenyl]-6,8-di bromo-2-methylquinazolin-4-one. Over all evaluation of the synthesized (2a-2j) compounds suggests that most of them were found to show good to moderate antibacterial and antifungal activity as compared to the standard drugs like Streptomycin and Fluconozole respectively.

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