International Journal for Pharmaceutical Research Scholars (IJPRS)
ISSN No: 2277-7873
RESEARCH ARTICLE
V-1, I-2, 2012

Synthesis, Spectral Studies and Biological Activities of Quinazolin-4-One Based Some New Pyrazolines Derivatives

Shah RM[1], Prajapati NK[2], Patel PS*[1]

[1]*Department of Chemistry, Sheth L.H. Science College, Mansa, India.*

[2]*Department of Chemistry, M. N. College, Visnagar, India.*

Manuscript No: IJPRS/V1/I2/00117, Received On: 15/06/2012, Accepted On: 17/06/2012

ABSTRACT

3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one have been prepared by the refluxation for three hours of 3-{4-[3-substitutedphenyl)prop-2-enoyl]phenyl}-6-iodo-2-thioxo-2,3 dihydroquinazolin -4-one in presence of ethanol & hydrazine hydrate. After Synthesis Compounds Were Characterized by Chemical as Instrumental Methods. Like Elemental, IR and NMR. All the synthesized products were evaluated for their antimicrobial activity. All the compounds were tested for their antibacterial and antifungal activities by broth dilution method.

KEYWORDS

Hydrazine hydrate. Ethanol, IR, NMR, Antimicrobial activity.

INTRODUCTION

The chemistry of heterocycles lies at the heart of drug discovery. The chemistry and pharmacology of quinazolinone have been of great interest to medicinal chemistry. In recent years there has been an increasing interest in the chemistry of 4(3*H*)-quinazolinones because of their biological significance[1,2]. Many of them show antibacterial[3,4], antifungal[5], anti-inflammatory[6], analgesic and anti-inflammatory[7], antitubercular[8].

Pyrazolines are the reduced form of pyrazoles and are well known nitrogen containing heterocyclic compounds. Literature review reveals that pyrazoline derivatives possess of new anticonvulsant[9], antibacterial[10], antimicrobial, antitubercular, antihypertensive and antidiabetic agents and it is justified because more organisms being resistance to the present available drugs in the market.

***Address for Correspondence:**
Dr. Pankaj S. Patel
Department of Chemistry,
Sheth L. H. Science College, Mansa, India.
E-Mail Id: pspatel_mansa@yahoo.co.in

EXPERIMENTAL

Melting points were taken in open capillary tube and were uncorrected. IR spectra were recorded on I.R. Spectrophotometer of Bruker scientific Model No. Alpha E and instrument used for NMR Spectroscopy was 500 MHz and tetra methyl silane used as internal standard. Solvent used were DMSO. Purity of the compounds were checked by TLC on silica- G plates. Anti-microbial activities are taken from Broth Dilution Methods.

Preparation of 3-{4-[3-(substituted phenyl) prop-2-enoyl]phenyl}-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one (1a-1j)

To the solution of 3-(4-acetylphenyl)-6-iodo-2-thioxo-2,3-dihydro quinazolin-4-one (0.01M) in absolute ethanol (50 ml), substitutedaldehyde (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; 1-i (Cm^{-1}): 3465(>N-H of sec. amine), 3356(-OH), 3065(=C-H), 2865(-C-H stretch), 1704(>C=O stretch), 1559 (>C=C< aromatic), 1413(-CH_3 bend), 1303(C-N), 1107(-C-O), 1062(C-O-C), 1219(>C=S), 522(C-I).,

^{1}H NMR (DMSO); 1-i: 3.839 (Singlet)(3H),(-OCH_3), 4.247(Singlet) (1H), (-NH-), 7.776(Doublet) (2H), (-CH=CH-Ar), 6.644-8.185 (Multiplate) (10H), (Ar-H), 9.798(Singlet) (1H), (-OH).

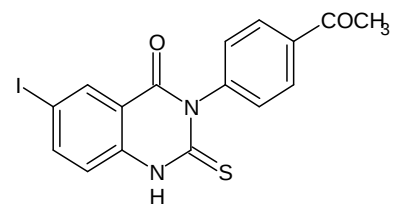
Preparation of 3-{4-[5-(substituted phenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one. (2a-2j)

A mixture of 3-{4-[3-(Substituted)prop-2-enoyl]phenyl}-6-iodo-2-thioxo-2,3 dihydroquinazolin-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 to give a pale brown solid.

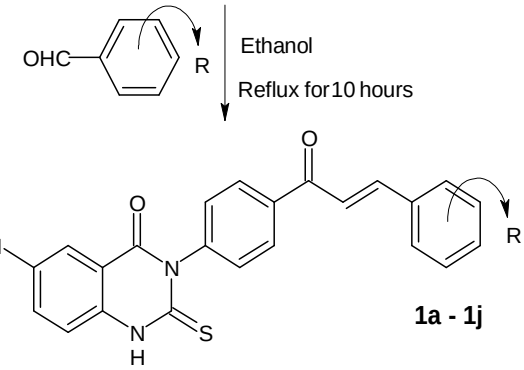
***IR; 2-a ;* (Cm^{-1}) :** 3386(>N-H of sec. amine), 3310(-OH), 3043(=C-H), 1710(>C=O, Stretch), 1648(>C=N-, Stretch), 1491(>C=C<Aromatic), 1444(-CH_2-) (bend), 1179(C-N), 1230(N-N), 1088(-C-O), 1230(>C=S), 525(C-I),

^{1}H NMR (DMSO) 2-e ; 3.819 Doublet (2H), (-CH_2), 3.839 Triplet (1H)(-CH<), 3.898, Singlet (1H), (-NH-), 6.623-7.976 Multiplate (12H)(Ar-H, -NH-)

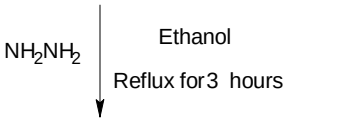
Reaction Scheme

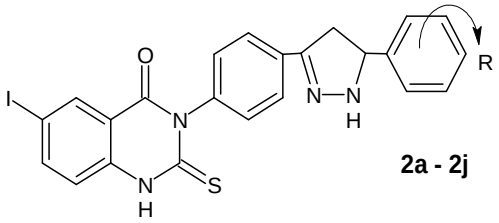


3-(4-acetylphenyl)-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one



3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}
-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one





3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}
-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one

RESULTS AND DISCUSSION

Antimicrobial Activity

The MICs of synthesized compounds were carried out by broth micro dilution method as described by Ratan (2000). The invitro antimicrobial activity of test compounds were assessed against 24 hr cultures of several selected bacteria and fungi. The bacteria used were *E.coli, S.aureus, P. aeruginosa*, and *S. pyogenus*; the fungi used were *C albicans, A. niger, andA.clavatus.*

The antimicrobial activity was performed by broth dilution method in DMSO. Gentamycin, Ampicilin, Chloramphenicol, Ciprofloxacin, Norfloxacin, Nystatin and Greseofulvin were used as standard for the evaluation of antibacterial and antifungal activities respectively. The activity was reported by Minimal Inhibition Concentration. The results are summarized in Table-2.

Table 1: Physical constant of 3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-6-iodo-2-thioxo-2,3- ydroquinazolin-4-one

No.	Sub. No.	R	Molecular Formula	Mol. Wt. (g/m)	Yield (%)	M. P. ^{0}C	Carbon (%)		Hydrogen (%)		Nitrogen (%)	
							Found	required	Found	required	Found	required
1	2a	-2-OH	$C_{23}H_{17}IN_4O_2S$	540.38	75	205	51.10	51.12	3.15	3.17	10.35	10.37
2	2b	-4-Cl	$C_{23}H_{16}C_lIN_4OS$	558.82	74	211	49.43	49.43	2.89	2.89	10.03	10.03
3	2c	-3,4-$(OCH_3)_2$	$C_{25}H_{21}IN_4O_3S$	584.43	73	191	51.36	51.38	3.60	3.62	9.57	9.59
4	2d	-3-NO_2	$C_{23}H_{16}IN_5O_3S$	569.37	74	197	48.52	48.52	2.83	2.83	12.30	12.30
5	2e	-2-Cl	$C_{23}H_{16}C_lIN_4OS$	558.82	72	180	49.41	49.43	2.87	2.89	10.01	10.03
6	2f	-4-OCH_3	$C_{24}H_{19}IN_4O_2S$	554.40	75	220	51.97	51.99	3.43	3.45	10.09	10.11
7	2g	-4-OH	$C_{23}H_{17}IN_4O_2S$	540.38	74	250	51.10	51.12	3.15	3.17	10.35	10.37
8	2h	-4-$N(CH_3)_2$	$C_{25}H_{22}IN_5OS$	567.44	71	257	52.90	52.92	3.89	3.91	12.32	12.34
9	2i	-4-OH-3-OCH_3	$C_{24}H_{19}IN_4O_3S$	570.40	73	241	50.52	50.54	3.34	3.36	9.80	9.82
10	2j	-3,4,5-$(OCH_3)_3$	$C_{26}H_{23}IN_4O_4S$	614.45	73	254	50.80	52.68	3.75	3.27	9.10	10.68

Table-2 Antimicrobial Activity: Minimal Inhibition Concentration

Sr. No.	**Comp. No.**	**R**	**Antibacterial activity Minimal Inhibition Concentration**				**Antifungal activity Minimal Inhibition Concentration**		
			E. Coli	**P.Aeruginosa**	**S. Aureus**	**S. Pyogenus**	**C. Albicans**	**A. Niger**	**A. Clavatus**
			MTCC 443	**MTCC 1688**	**MTCC 96**	**MTCC 442**	**MTCC 227**	**MTCC 282**	**MTCC 1323**
1	2a	–2-OH	125	125	100	100	1000	>1000	>1000
2	2b	-4-CI	250	100	125	125	500	500	500
3	2c	-3,4-$(OCH_3)_2$	100	500	500	62.5	100	200	1000
4	2d	-3-NO_2	125	200	62.5	500	1000	500	100
5	2e	-2-Cl	500	250	125	62.5	500	1000	250
6	2f	-4-OCH_3	62.5	125	100	500	250	>1000	1000
7	2g	-4-OH	500	500	200	100	200	>1000	100
8	2h	-4-$N(CH_3)_2$	200	200	250	250	500	200	250
9	2i	-4-OH-3OCH_3	250	125	500	500	1000	500	1000
10	2j	-3,4,5-$(OCH_3)_3$	100	100	62.5	200	250	500	>1000

Table 3: Antibacterial Activity: Minimal Inhibition Concentration (The Standard Drugs)

Drug	**E. Coli**	**P. Aeruginosa**	**S. Aureus**	**S. Pyogenus**
-	**MTCC 443**	**MTCC 1688**	**MTCC 96**	**MTCC 442**
(Microgramme/ml)				
Gentamycin	0.05	1	0.25	0.5
Ampicillin	100	--	250	100
Chloramphenicol	50	50	50	50
Ciprofloxacin	25	25	50	50
Norfloxacin	10	10	10	10

Table 4: Antifungal Activity: Minimal Inhibition Concentration (The Standard Drugs)

Drug	**C. Albicans**	**A. Niger**	**A. Clavatus**
	MTCC 227	**MTCC 282**	**MTCC 1323**
(Microgramme/ml)			
Nystatin	100	100	100
Greseofulvin	500	100	100

Biological screening result of activities 3-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-6-iodo-2-thioxo-2,3 dihydroquinazolin-4-one based derivatives shows that compound 2g have shown better activity against E. coli. Compound 2d, 2f, and 2i shows good to very good activity against S. pyogenus, while rest of all compound possessed good activity against S.aureus in the range of 62.5-225 mg/ml. Compound 2a is found to be very good antifungal activity against C. albicans, against standard drugs Greseofulvin. While rest of all derivatives are good against A. Niger, and A.clavatus.

ACKNOWLEDGEMENTS

The authors are thankful to the Sheth L.H. Science College, Mansa for providing research facilities.

REFFERENCES

1. Gangawal NA, Narasimhan B, Mourya VK and Dhake AS, “Synthesis and QSAR studies of substituted-4-(1H)-quinazolinones”. Indian. J. Heterocycl.Chem., 2003, 12, 201.
2. Padam K and Saksena RK, “Synthesis and antimicrobial activity of some new2-phenyl-3-p-(2'-methyl-3'-aryl-4'-oxo-thiazolin-2'-yl)phenylquinazolin-4-ones and 2-phenyl-3-p-(1'-aryl-3-phthlimido-4'-

methyllazetidin-2'-one-2'-yl)phenyl-quinazolin -4-ones". Indian J. Heterocycl. Chem., 2003, 12, 315.

3. Udapi FH, Ramesh B, and Bhat AK, (1999) "Synthesis and Biological activity of some quinazolinones derivatives", Indian. J. Heterocycl. Chem., 1999, 8, 301.
4. Abdel-Hamid SG, "Synthesis of some New Heterocyclic Systems Bearing 2- Phenyl-6-iodo-4-(3H)-quinazolinon-3-yl Moiety as Antibacterial Agents", J. Ind. Chem. Soc., 1997, 74, 613-618.
5. Bartroli J, Turmo E, Alguero M, Boncompte E, Vericat ML, Coute L, Ramis J, Merlos M, Garcia-Rafanell J and Forn J, "Synthesis and Antifungal Activity of 3-Substituted-4(3H)-quinazolinones", J. Med. Chem., 1998, 41, 1869–1882.
6. Rani P, Archana SVK, and Kumar A, "Synthesis and anti-inflammatory activity of some new 2,3-disubstituted-6-monosubstituted-quinazolin-4(3H)-ones", Indian. J. Chem., 2002, 41B, 2642.
7. Srinivasa RP, Venugopala KN, Rao GK and Sanjay Pai PN, "Synthesis of some substituted quinazolinones as analgesic and anti-inflammatory agents". Indian J. Heterocycl. Chem., 2007, 16, 243.
8. Nandy P, Vishlakshi MT and Bhat AR, "Synthesis and antitubercular activity of mannich bases of 2-methyl-3H-quinazolin-4-ones". Indian J. Heterocycl. Chem., 2006, 15, 293.
9. Kumar A, Archana, Srivastava VK, Chandra R, "Synthesis of potential quinazolinonyl pyrazolines and quinazolinyl isoxazolines as anticonvulsant agents". Ind J Chem., 2002, 41B, 2371-2375.
10. Mogilaiah K, Sudhakar GR, "Synthesis of pyrazoline, pyrimidine and 1,5-benzodiazepine derivatives of 1,8-naphthyridine and evalution of antibacterial activity". Ind J Chem, 2003, 42B, 636-640.

