

SYNTHESIS, CHARACTERIZATION AND ANTIFUNGAL ACTIVITY OF SOME QUINAZOLIN-4-ONE DERIVATIVES

Dr. Naresh K. Prajapati¹ and Dr. Shailesh P. Prajapati²

¹Department of Chemistry, M.N. College, Visnagar-384315, Gujarat, India.

²Department of Chemistry, Gujarat Arts and Science College, Ahmedabad -380006, India.

Article Received on 01/11/2016

Article Revised on 20/11/2016

Article Accepted on 12/12/2016

***Corresponding Author**

Dr. Naresh K. Prajapati

Department of Chemistry,
M.N. College, Visnagar-
384315, Gujarat, India.

ABSTRACT

A new series from some quinazolin-4-one derivatives have been synthesized by reacting 3-(4-acetyl phenyl)-6-iodo-2-thioxo-2,3-dihydro quinazolin-4-one with different aromatic aldehydes in presence of sodium hydroxide and ethanol at room temperature. The

synthesized compounds were characterized by means of their IR, ¹H-NMR spectral data and elemental analysis. All the compounds were tested for their antifungal activities by broth dilution method.

KEYWORDS: Ethanol, quinazolin-4-one, IR, NMR. Antifungal activity.

INTRODUCTION

The unique heterocyclic nitrogen compounds especially quinazolinone derivatives are employed in many biological processes and as synthetic drugs.^[1] Quinazoline are known to possess good biological and pharmacological activities.^[2-4] It possess CNS depressant activity,^[5] as well as antispermatogenic and antiadjuvant^[6], antibacterial^[7-8], antifungal^[9-10] etc. So we have decided to synthesis 3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl} -6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one derivatives.

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, Chemicals sodium hydroxide, and various aldehyde were purchased from S.D.fine chemicals (India).

Melting points were taken in open capillary tube. IR spectra (KBr) were recorded on Shimadzu-PerkinElmer F.T I.R. Spectrophotometer Gx and Brooker instrument used for NMR Spectroscopy was 500 MHz and tetramethylsilane used as internal standard. Solvent used were DMSO. Purity of the compounds were checked by TLC on silica- G plates.

EXPERIMENTAL

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

To the solution of 3-(4-acetylphenyl)-6-iodo-2-thioxo-2,3-dihydro quinazolin-4-one in absolute ethanol, substituted benzaldehyde and 2% NaOH 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: The characteristic bands of (>NH-) $3460-3360\text{ cm}^{-1}$, (-OH) $3356-3330\text{ cm}^{-1}$, (-C=S) $1240-1220\text{ cm}^{-1}$, (-C-N-) $1303-1280\text{ cm}^{-1}$ were obtained for stretching. The stretching vibrations (-C-O-C-) group showed in the finger print region of $1170-1062\text{ cm}^{-1}$ while (-C-Cl-) stretching signal was obtained at $700-690\text{ cm}^{-1}$. while (-C-I-) stretching signal was obtained at $530-510\text{ cm}^{-1}$ It gives aromatic (-C-H-) stretching frequencies between $3070-2865\text{ cm}^{-1}$ and ring skeleton (-C=C-) stretching at $1600-1560\text{ cm}^{-1}$, C-H stretching frequencies for methyl and methylene group were obtained near $3065-3020\text{ cm}^{-1}$, $1413-1400\text{ cm}^{-1}$.

$^1\text{H NMR (DMSO): (2j):}$ 3.78, singlet (1H) (-NH-), 7.76, Doublet (2H) (-CH=CH-), 6.64-8.31, multiplet (11H) (Ar-H).

RESULTS AND DISCUSSION

Physical constant of 3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one shown in Table-I.

Antifungal activity: The MICs of synthesized compounds were carried out by broth micro dilution method. Each synthesized drug was diluted obtaining 2000 microgram /ml concentration, as a stock solution.^[11-13] The invitro antimicrobial activity of test compounds were assessed against 24 hr cultures of several selected fungi. The fungi used were *C. albicans*, *A. niger*, and *A.clavatus*. The antifungal activity was performed by broth dilution method in DMSO. Nystatin and Griseofulvin were used as standard for the evaluation of antifungal activities respectively. The results are summarized in Table-II. The antifungal activity of minimal inhibition concentration with standard drugs shown in Table:III.

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

No.	Sub No.	R	Molecular Formula	Mol.Wt. (gm)	Yield (%)	M.P. \C	Carbon(%)		Hydrogen(%)		Nitrogen(%)	
							Found	required	Found	required	Found	required
1	2a	- 2- OH	C ₂₃ H ₁₅ IN ₂ O ₃ S	526.35	65	180	52.30	52.48	2.84	2.87	5.28	5.32
2	2b	- 4-Cl	C ₂₃ H ₁₄ ClIN ₂ O ₂ S	544.80	63	162	50.35	50.71	2.56	2.59	5.10	5.14
3	2c	- 3,4-OCH ₃ ,	C ₂₅ H ₁₉ IN ₂ O ₄ S	570.40	69	156	52.23	52.64	3.33	3.36	4.88	4.91
4	2d	- 3- NO ₂	C ₂₃ H ₁₄ IN ₃ O ₄ S	555.34	68	212	49.55	49.74	2.52	2.54	7.54	7.57
5	2e	- 2-Cl	C ₂₃ H ₁₄ ClIN ₂ O ₂ S	544.80	62	184	50.65	50.71	2.55	2.59	5.11	5.14
6	2f	- 4-OCH ₃	C ₂₄ H ₁₇ IN ₂ O ₃ S	540.37	65	225	53.18	53.34	3.14	3.17	5.12	5.18
7	2g	- 4-OH	C ₂₃ H ₁₅ IN ₂ O ₃ S	526.35	66	198	52.38	52.48	2.85	2.87	5.25	5.32
8	2h	- 4-N(CH ₃) ₂	C ₂₅ H ₂₀ IN ₃ O ₂ S	553.41	67	215	52.22	54.26	3.60	3.64	7.55	7.59
9	2i	- 4-OH , -3-OCH ₃	C ₂₄ H ₁₇ IN ₂ O ₄ S	556.37	68	148	51.78	51.81	3.00	3.08	5.00	5.04
10	2j	- 3,4,5-(OCH ₃) ₃	C ₂₆ H ₂₁ IN ₂ O ₅ S	600.42	75	210	52.00	52.01	3.50	3.53	4.61	4.67

Table II: Antifungal activities of 3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one.

Sr. No.	Comp. No.	R	Antifungal Activity		
			Minimal Inhibition Concentration (μ gm/ml)		
			Fungus		
			C.Albicans	A.Niger	A.Clavatus
			MTCC 227	MTCC 282	MTCC 1323
1	2a	- 2- OH	500	500	1000
2	2b	- 4-Cl	500	1000	1000
3	2c	- 3,4-OCH ₃ ,	1000	1000	1000
4	2d	- 3- NO ₂	1000	250	250
5	2e	- 2-Cl	250	1000	1000
6	2f	- 4-OCH ₃	250	500	500
7	2g	- 4-OH	250	>1000	>1000
8	2h	- 4-N(CH ₃) ₂	1000	200	200
9	2i	- 4-OH ,-3-OCH ₃	200	500	500
10	2j	- 3,4,5-(OCH ₃) ₃	1000	250	250

Table III: 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

ANTIFUNGAL ACTIVITY

Against *Candida albicans* (MTCC 227): The present investigation revealed the maximum antifungal activity was shown by the compounds 2c, 2d, 2h and 2j (1000gm/ml) very good activity against *C.albicans* (MTCC 227) compared with standard drugs of nystatin and greseofulvin, the minimum antifungal activity was shown by the compounds 2i (200gm/ml). While Compound 2i was shown poor activity against *C.albicans* compared with standard drug greseofulvin. The remaining compound good to moderate activity against *Candida albicans* with the standard drugs.

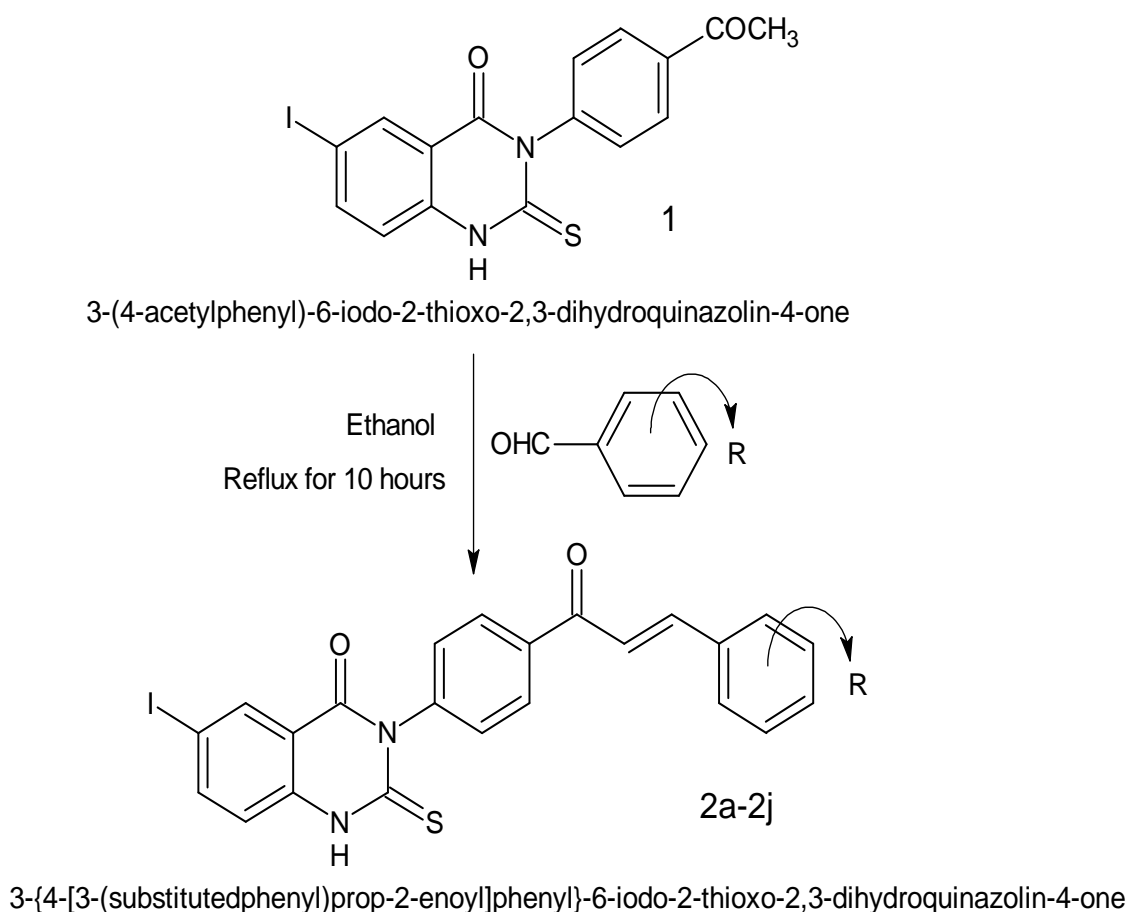
Against *Aspergillus Niger* (MTCC 282): The present investigation revealed the maximum anti fungal activity was shown by the compounds 2g (>1000gm/ml) and the minimum antifungal activity was shown by the compounds 2h (200gm/ml). The compounds 2d and 2j (250gm/ml) was shown poor activity against *Aspergillus Niger* (MTCC 282) with compared

standard drug greseofulvin. The remaining compound good to moderate activity against *Aspergillus Niger* with the standard drugs nystatin and greseofulvin.

Against *Aspergillus clavatus* (MTCC 1323): The present investigation revealed the maximum anti fungal activity was shown by the compounds 2g (>1000gm/ml) and the minimum antifungal activity was shown by the compounds 2h (200gm/ml). The compounds 2d and 2j (250gm/ml) poor activity against *Aspergillus Clavatus* (MTCC 1323) with compared standard drug greseofulvin. The remaining compound good to moderate activity against *Aspergillus Clavatus* with the standard drugs nystatin and greseofulvin.

In future 3-{4-[3-(substitutedphenyl)prop-2-enoyl]phenyl}-6-iodo-2-thioxo-2,3-dihydroquinazolin-4-one derivatives will be used for further development of new antifungal agent.

Reaction Scheme



CONCLUSION

The Main focus of this research work was to synthesize, characterize and evaluate anti fungal activities of the newly synthesized compounds were confirmed and characterized with the help of analytical data's such as IR and ¹H-NMR. Biological screening result of activities 3-{4-[3-(substituted phenyl) prop-2-enoyl]phenyl} -6-iodo-2-thioxo-2,3-dihydro quinazolin-4-one derivatives as above.

REFERENCES

1. Patel N.B. and Chaudhari R.C., Quinazolin-4(3H)-ones of 2-[2-(2,6-dichlorophenyl) amino] phenyl acetic acid with substituted aryl acetamide and their microbial studies., J.Indian Chem. Soc., 2006; 83: 838-841.
2. Mattner P. G. and Salmond W. G., Fr. Patent 2174828, 1973.
3. Bogert M. T. and co-workers, The synthesis of 5-nitro-4-ketodihydroquinazolines from 6-nitro-2-aminobenzoic acid, 6-nitro-2-acetylaminobenzoic acid, and from the corresponding nitro acetylanthranil., J. Amer. Chem. Soc. 1905; **27**: 649.
4. Jawetz R. and Steinder S. H., The synthesis of 7-nitro-2-alkyl-4-ketodihydro quinazolines from 4-nitroacetamthranilic acid, and from 4-nitro-aceranthranil., J. Amer. Chem. Soc., 1905; 27: 1327.
5. Aguire Ormaza V., Spanish Pat., 549881, 1980, C.A., 107, 236726, 1987.
6. Gerimmel H. W. and Guenther A., A New Synthesis of 4-Quinazolones, J. Amer. Chem. Soc., 1946; 68: 542-543.
7. Naik N. M. AND Desai K. R., Ind. Chem. Soc., 1990; 67: 210.
8. Dalal M. M. and Desai K. R., Saudi. Chem. Soc., 1995; 1: 55.
9. Malankar U.V. and Desai K.R., Orient. J. Chem., 1994; 10: 167.
10. Desai T. R. and Desai K.R., Orient. J. Chem., 1995; 13: 65.
11. Penumaka Nagababu P., Pallavi, S. Harish, and S. Satyanarayana, Studies on antimicrobial activity of cobalt(III) ethylenediamine complexes, Can. J. Microbiol., 2006; 52(12): 1247–1254.
12. Flamini G., Cioni P.L., Puleio R., Morelli I. and Panizzi L., Antimicrobial activity of the essential oil of calamintha nepeta and its constituent pulegone against bacteria and fungi, Phytotherap. Res., 1999; 13: 349-351.
13. Jandden A.M., Sheffer J.J. and Vendsen S.B., Antimicrobial activity of essential oils: A 1976-1985 literature review. Aspects on test method, Plant Medica, 1987; 53: 395-508.