Chem Sci Trans., 2013, **2(4)**, 1089-1093
DOI:10.7598/cst2013.301

Chemical Science Transactions
ISSN/E-ISSN: 2278-3458/2278-3318

RESEARCH ARTICLE

Design, Synthesis and Pharmacological Evaluation of New Series of Pyrazolines Based Thiazolidin-4-one Derivatives

PINKA PATEL, DEEPA GOR and P. S. PATEL*

K. K Shah Jarodwala Maninagar Science College, Ahmedabad-8, India
*Department of Chemistry, Sheth L. H. Science College, Mansa-382845, India
pinkapatel59@yahoo.in

Received 11 July 2012 / Accepted 16 August 2012

Abstract: We have prepared 2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substituted phenyl)-1,3-thiazolidin-4-one form *N*-[{4-[2-{5-(4-chloro-phenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}methylene] substituted aniline and thioglycolic acid. Compound having an excellent properties regarding as per as anti cancer and HIV as compared to this compound. Physical properties of pure crystallized substance of 2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(subs-tituted-phenyl)-1,3-thiazolidin-4-one substituted aniline like M.P elementary analysis and spectral data of compound and such as IR and NMR will be evaluated and confirm the structure of compound. 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: Synthesis, Pyrazoline, Chalcones, Schiff base, DMSO, Antimicrobial activity

Introduction

Thiazolidinones are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds containing sulfur and nitrogen in a five member ring. 4-Thiazolidinones[1] have attracted considerable attention as they are endowed with wide range of pharmaceutical activities. The nucleus is also known as wonder nucleus because it gives out different derivatives with all different types of biological activities. One of the main objectives of organic and medicinal chemistry is the design, synthesis and production of molecules having value as human therapeutic agents. During the past decade development in the field of combinatorial chemistry has provided access to chemical libraries based on privileged structures[2]. 4-Thiazolidinones are associated with anticancer[3] and versatile pharmacological activities[4,5] like anti-tubercular[6] anti–inflammatory[7] antimicrobial[8], anti –

HIV[9], antioxidant[10], *etc*. Some thiazolidines are reported as analgesic and ulcerogenic[11]. Moreover anils are reported to have significant anticancer[12] and antibacterial[13] activity. All these observations and important role of anils and 4-thiazolidinones in certain biological reactions prompted us to synthesize some 4-thiazolidinones incorporating styryl moiety and to study their antibacterial activity. The constitution of all the products has been characterized using elemental analyses, IR, ^{1}H NMR and mass spectral study. All the compounds were screened for their *in vitro* antimicrobial activity against different strains of bacteria.

Experimental

Melting points were taken in open capillary tube and were uncorrected. IR spectra were recorded on I.R. spectrophotometer of Buck scientific Model No. 500 and instrument used for NMR spectroscopy was Bruker Advance II 400 and DMSO used as internal standard. Solvent used were $CDCl_3$ and DMSO. Purity of the compounds was checked by TLC on silica-G plates. All the compounds were tested for their antibacterial and antifungal activities by broth dilution method

*Preparation of N-[{4-[2-(5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl}methylene]substitutedaniline (**1a-j**)*

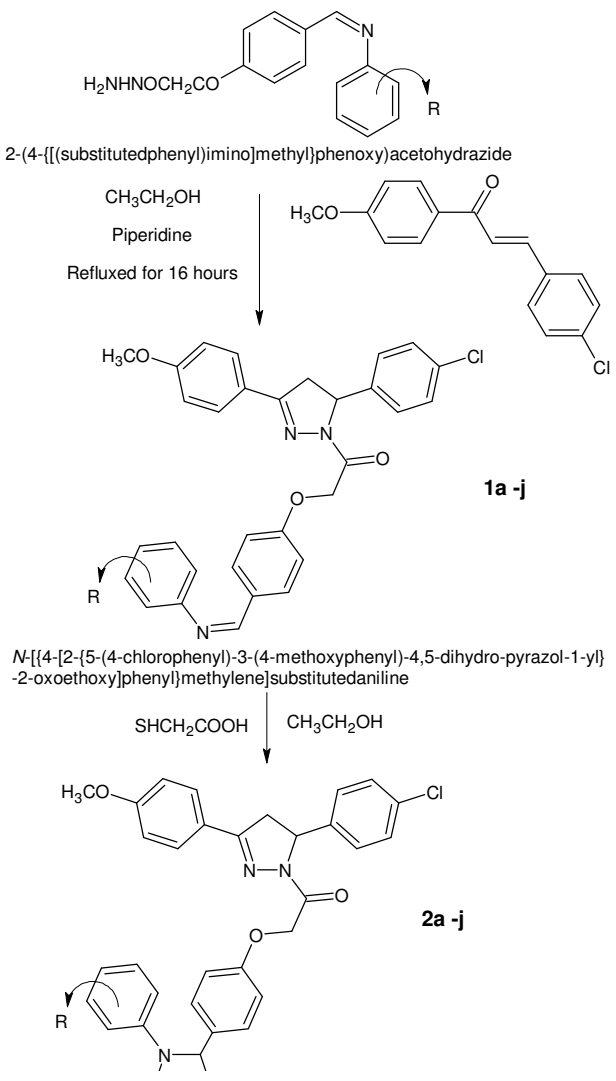
A mixture of 2-(4-{[(2-chlorophenyl)imino]methyl}phenoxy)acetohydrazide (0.1 M), ethanol (25 mL) and 3-(4-chlorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (0.1 M) with piperidine (1 mL) was refluxed for 16 hours. The resulting mixture was concentrated, cooled and poured into cold water containing 6 to 8 drops of HCl, when orange coloured product separated. It was filtered, washed with water and crystallized from methanol-petroleum ether mixture .

IR; 3-d (cm^{-1}): 3011(=CH-), 2933 (-CH-), 1710 (>C=O) ,1665 (C=N-), 1606(>C=C<), 1449 (-CH_2-), 1392(-CH_3-), 1268 (C-N) 1223 (-N-N-), 1167(-C-O-) 1107(-C-O-C). ^{1}H NMR (DMSO); 3-e: 2.5675, doudlet (2H) (CH_2 -cyclic), 3.8489, singlet (3H) (-OCH_3-), 4.5719, singlate (2H) (-CH_2-),5.0906 triplet (1H) (-CH<) 8.5267, singlet (1H) (Ar-CH=N-), 6.6093-8.0824 multiplate (16H) (Ar-H).

*Preparation of 2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin -4-one(**2a-j**)*

A solution of compound *N*-[{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-xoethoxy]phenyl}methylene] naphthalen-1-aniline (0.01 M), thioglycolic acid (0.01 M) and anhydrous zinc chloride (2 g) in absolute ethanol (60 mL) was refluxed for 8 hours, concentrated, cooled and poured into the crushed ice and the filtered. The product obtained was purifed by recrystallization from acetone (Scheme 1).

IR; 2-d (cm^{-1})**:** 3012(=CH-), 2928 (-CH-), 1723 (>C=O), 1640 (C=N-), 1594(>C=C<), 1426 (-CH_2-), 1361(-CH_3-), 1263 (C-N) 1220 (-N-N-), 1166(-C-O-) 1120(-C-O-C). ^{1}H NMR (DMSO); 2-f: 2.5537, doudlet (2H) (CH_2 -cyclic), 3.3800, singlet (2H) (-CH_2-), 3.7405, singlate (3H) (-OCH_3-), 4.8450, singlet (2H) (-CH_2-), 4.9918 triplet (1H) (-CH_2-) 5.9131, singlet (1H) (-CH-N<), 6.8194-8.1245 multiplate (16H) (Ar-H).



Scheme 1

Results and Discussion

Antimicrobial activity

The MICs of synthesized compounds were carried out by broth micro dilution method. The *in vitro* antimicrobial activity of test compounds were assessed against 24 h 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, and A.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 2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one (**2a-j**)

S No	Sample No	R	Molecular formula	Molecular weight	Malting weight	Yield	%C		%H		%N	
							Found	Required	found	Required	found	Required
1	**2a**	1-Phenyl	$C_{33}H_{28}ClN_3O_4S$	598.11	90	70	66.24	66.27	4.69	4.72	7	7.03
2	**2b**	1-amino	$C_{37}H_{30}ClN_3O_4S$	648.17	101	73	68.52	68.56	4.64	4.67	6.45	6.48
3	**2c**	4-CH_3	$C_{34}H_{30}ClN_3O_4S$	612.14	115	68	66.68	66.71	4.91	4.94	6.84	6.86
4	**2d**	3-CH_3	$C_{34}H_{30}ClN_3O_4S$	612.14	100	65	66.69	66.71	4.9	4.94	6.82	6.86
5	**2e**	2-NO_2	$C_{33}H_{27}ClN_3O_4S$	643.11	98	72	61.61	61.63	4.2	4.23	8.67	8.71
6	**2f**	3- NO_2	$C_{33}H_{27}ClN_3O_4S$	643.11	105	78	61.6	61.63	4.21	4.23	8.68	8.71
7	**2g**	4- NO_2	$C_{33}H_{27}ClN_3O_4S$	643.11	120	65	61.59	61.63	4.19	4.23	8.69	8.71
8	**2h**	2-Cl	$C_{33}H_{27}Cl_2N_3O_4S$	632.56	109	71	62.64	62.66	4.28	4.3	6.6	6.64
9	**2i**	3-Cl	$C_{33}H_{27}Cl_2N_3O_4S$	632.56	95	74	62.61	62.66	4.26	4.3	6.59	6.64
10	**2j**	4-Cl	$C_{33}H_{27}Cl_2N_3O_4S$	632.56	123	69	62.63	62.66	4.27	4.3	6.61	6.64

Table 2. Antimicrobial activity of 2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one

S.No	Compd No	R	Antibacterial activity minimal inhibition concentration				Antifungal activity minimal inhibition concentration, µg/mL		
			Gram negative bacteria		Gram positive bacteria		fungus		
			E.coli	*P.Aeruginosa*	*S.Aureus*	*S,pvogenus*	*C.Albicans*	*Aniger*	*Aclavatus*
			MTCC 443	MTCC 1688	MTCC%	MTCC 442	MTCC 227	MTCC 282	MTCC 1323
1	**2a**	1-Phenyl	250	175	200	150	1000	900	800
2	**2b**	1-Napthyl	150	250	225	125	900	700	700
3	**2c**	-4-CH_3	125	100	200	200	500	600	>1000
4	**2d**	-3-CH_3	175	225	250	225	700	>1000	500
5	**2e**	-2-NO_2	200	250	150	200	600	500	700
6	**2f**	-3- NO_2	150	200	175	150	500	800	800
7	**2g**	-4- NO_2	125	150	125	175	800	700	500
8	**2h**	-2-Cl	175	100	200	150	700	900	600
9	**2i**	-3-Cl	250	200	125	125	600	600	700
10	**2j**	-4-Cl	200	150	150	200	1000	500	>1000

Biological screening result of 2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxy phenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one based derivatives shows that compound (**2c** and **2g**) have shown better activity against *E. coli, S. aureus*, while rest of all compound possessed good activity against *S.aureus* in the range of 125-250 µg/mL. Compounds with substitution 4-hydroxy (**2b** and **2i**), shown good antibacterial activity against *S.pyogenus*, while rest of all derivatives possessed good activity against *S.pyogenus* in the range of 100-250 µg/mL. Compound (**2c)** and (**2f)** is found to be significant antifungal activity against *C.albicans*, while rest of all derivatives are poor against *A.niger* and *A.clavatus***.**

Conclusion

The main focus of this research work was to synthesize, characterize and evaluate antimicrobial activities of the newly synthesized chalcone derivatives, structures of synthesized compounds were confirmed and characterized with the help of analytical data's such as IR and ^{1}H-NMR. In summary, we have described the synthesis and antimicrobial activity of novel2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one substituted aniline MIC values revealed that amongst newly synthesized compound having 4-chlorophenyl type linkage has shown good activity against the bacterial strains. Rest of all compounds exhibit moderate improvement in activity against some of the pathogenic strains.

Acknowledgement

The authors are thankful to the Principal Dr. Rutesh R. Shah and Management of K.K.Shah Jarodwala Maninagar Science Colledge, Ahmedabad for providing research Facilities.

References

1. Solankee A, Solankee P and Patel H, *Int J Chem Sci.,* 2008, **6(2),** 1017.
2. Metzger J V, Comprehensive Heterocyclic Chemistry, Katritzky A R and Rees C W, Eds, Pergamon: Oxford, 1984, **6**, 236-330.
3. Pawar R P, Andurkar N M and Vibhute Y B, *J Indian Chem Soc*., 1999, **76,** 271.
4. Thore S N, Shinde D B, Mane D V, Bhawsar S B and Shingareet M S, *Asian J Chem*., 1996, **8(2),** 204-206.
5. Jaish L and Srivastava S K, *J Sci Ind Res*., 2001, **60**, 33.
6. Babaoglu K, M. A. Page M A and Lee R E, *Bioorg Med Chem*., 2003, **13(3),** 227.
7. Kumar A, Verma S, Shetty B, Nikam L B, Misra R P, Bhati S K, Kumar P, Rajput C S, Singh V, Rani P, Rani S, Yashowardhan, Singh S, *Orient J Chem*., 2006, **22(2),** 259.
8. Solankee, Patel A G and Solankee S, *Orient J Chem*., 2008, **25(1)**, 245.
9. Abdel Rehman R M, *Boll Chim Fama*., 2001, **140(6),** 401.
10. Sinh M H and Ke F Y, *Bioorg Med Chem*., 2004, **12,** 4633.
11. Modi D, Sabia S S and Deliwati C V, *J Med Chem.,* 1970, **3,** 935.
12. Raman N, Thalamuthu S and Benerjee S, *J Chill Chem Soc*., 2008, **53,** 1450.