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Synthesis, characterization and antimicrobial activities of N-[{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-yl}-2-oxoethoxy]phenyl}methylene] substituted aniline

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ABSTRACT

Heterocyclic Compounds having a valuable place in a Heterocyclic Chemistry and Heterocyclic Compounds having a excellent properties such as drugs, dyes etc, This compounds are showing anti microbial , anti fungal , anti bacterial ,anti inflammatory ,anti diabetic ,anti hypertensive etc. properties. In present investigation, we have prepared N-[{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl} methyl ene] substituted aniline from chalcon of 1,3-bis(4- methoxyphenyl) prop-2-en-1-one and Schiff base of 2-(4-{[(substituted phenyl)imino]methyl} phenoxy)acetohydrazide. Compound having a excellent properties regarding as per as anti cancer and HIV as compare to this compound. Physical properties of pure crystallized substance N-[{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-oxoethoxy]phenyl}methylene] 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 compounds were tested for their antibacterial and antifungal activities by broth dilution method.

Key Words : synthesis, pyrazoline, chalcones, substituted aniline, Schiff base, Antimicrobial activity.

INTRODUCTION

The pyrazole ring is a prominent structural motif found innumerous pharmaceutically active compounds. Pyrazole and pyrazolone ring systems represent an important class of compounds not only for their theoretical interest but also for their anti-inflammatory, postmenopausal, osteoporosis,angiotension, antagonists, and anticoagulant activities [1-3]. This is mainly due to the ease preparation and theimportant biological activity. Pyrazole framework plays an essential role in biologically active compounds andtherefore represents an interesting template for combinatorial as well as medicinal chemistry [4-5]. Such as antibacterial [6], antifungal [7], antiviral [8], antitubercular [9], antioxidant [10], antiandrogenic [11] etc. Some ofthese compounds have also exhibited antidiabetic [12], herbicidal activity [13], analgesic [14] and antiparasitic [15]properties. Many pyrazoles have been found to be luminescent and fluorescent [16,17] agents. In addition pyrazoleshave played a crucial role in the development of theory in heterocyclic chemistry and also used extensively as usefulsynthon in organic synthesis [18-22]. It is interesting to note that fused bis-pyrazoles are reported as well known pharmacophores. [23, 24] These compounds were also screened for their antimicrobial activity.

MATERIALS AND METHODS

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 (4-{[(substitutedphenyl)imino]methyl}phenoxy)acetic acid (1a-1j)

A mixture of (4-formylphenoxy) acetic acid (0.01M), substitutedaniline (0.01M) and methanol (30ml) was heated for about 5 min. in a beaker (250 ml) to get a clear solution. The solution was kept overnight at room temperature to get the respective crude solid which was recrystalized from ethanol to obtain the pure crystals of (4-{[(substitutedphenyl)imino] methyl}phenoxy)acetic acid respectively.

IR ; 1-d (Cm^{-1}) 3050(C-H,aromatic), 2920(C-H, aliphatic ring), 2580(-OH,carboxylic), 1720(>C=O), 1660(>C=N-), 1580(>C=C<, aromatic ring), 1480(-CH_2-, band.), 1375(-CH_3, band.), 1285(C-N), 1165(-C-O), 1110(C-O-C).

^{1}H NMR (DMSO); 1-g: 4.6911, singlate (2H) (-CH_2-), 8.3424, singlate (1H) (Ar-CH=N-), 6.8918-8.3976, multiplate (8H) (Ar-H), 9.7746, singlate (1H) (-OH).

Preparation of 2-(4-{[(substitutedphenyl)imino]methyl}phenoxy)acetohydrazide(2a-2j)

(4-{[(substitutedphenyl)imino]methyl}phenoxy)aceticacid(0.01M) dissolved in absolute ethanol. Hydrazine hydrate (99%, 0.02M) and few drops of conc. Sulphuricacid were added. The reaction mixture was refluxed for 6 hours. The resulting solid obtained was filtered, dried and crystallized from hot water.

IR; 2-a (Cm^{-1}): 33400(>NH), 3030(=C-H, aromatic), 2930(C-H, stretch), 1720(>C=O), 1620(>C=N-), 1590(>C=C<, aromatic ring), 1450(-CH_2-, band.), 1260(-CN), 1110(C-O-C).

^{1}H NMR (DMSO); 2-f: 2.5662, singlate (2H) (–NH_2) 4.6669, singlate (2H) (-CH_2-), 7.6755, singlate (1H)(-NH), 8.5347,singlet (1H) (Ar-CH=N), 6.8757-8.5615, multiplate (8H)(Ar-H)

Table-1 Physical constant of N-[{4-[2-(3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl}methylene] substitutedaniline

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	3a	1-Phenyl	$C_{32}H_{29}N_3O_4$	519.59036	71	138	73.94	73.97	5.60	5.63	8.05	8.09
2	3b	1-Naphthyl	$C_{36}H_{31}N_3O_4$	569.64904	73	210	75.86	75.90	5.44	5.49	7.34	7.38
3	3c	-4-CH_3	$C_{33}H_{31}N_3O_4$	533.61694	75	140	74.24	74.28	5.84	5.86	7.83	7.87
4	3d	-3-CH_3	$C_{33}H_{31}N_3O_4$	533.61694	70	148	74.24	74.28	5.84	5.86	7.83	7.87
5	3e	-2-NO_2	$C_{32}H_{28}N_4O_6$	564.58792	72	162	68.05	68.07	4.97	5.00	9.89	9.92
6	3f	-3-NO_2	$C_{32}H_{28}N_4O_6$	564.58792	78	192	68.05	68.07	4.97	5.00	9.89	9.92
7	3g	-4-NO_2	$C_{32}H_{28}N_4O_6$	564.58792	69	155	68.05	68.07	4.97	5.00	9.89	9.92
8	3h	-2-Cl	$C_{32}H_{28}ClN_3O_4$	554.03542	74	163	69.35	69.37	5.06	5.09	7.56	7.58
9	3i	-3-Cl	$C_{32}H_{28}ClN_3O_4$	554.03542	76	157	69.35	69.37	5.06	5.09	7.56	7.58
10	3j	-4-Cl	$C_{32}H_{28}ClN_3O_4$	554.03542	68	168	69.35	69.37	5.06	5.09	7.56	7.58

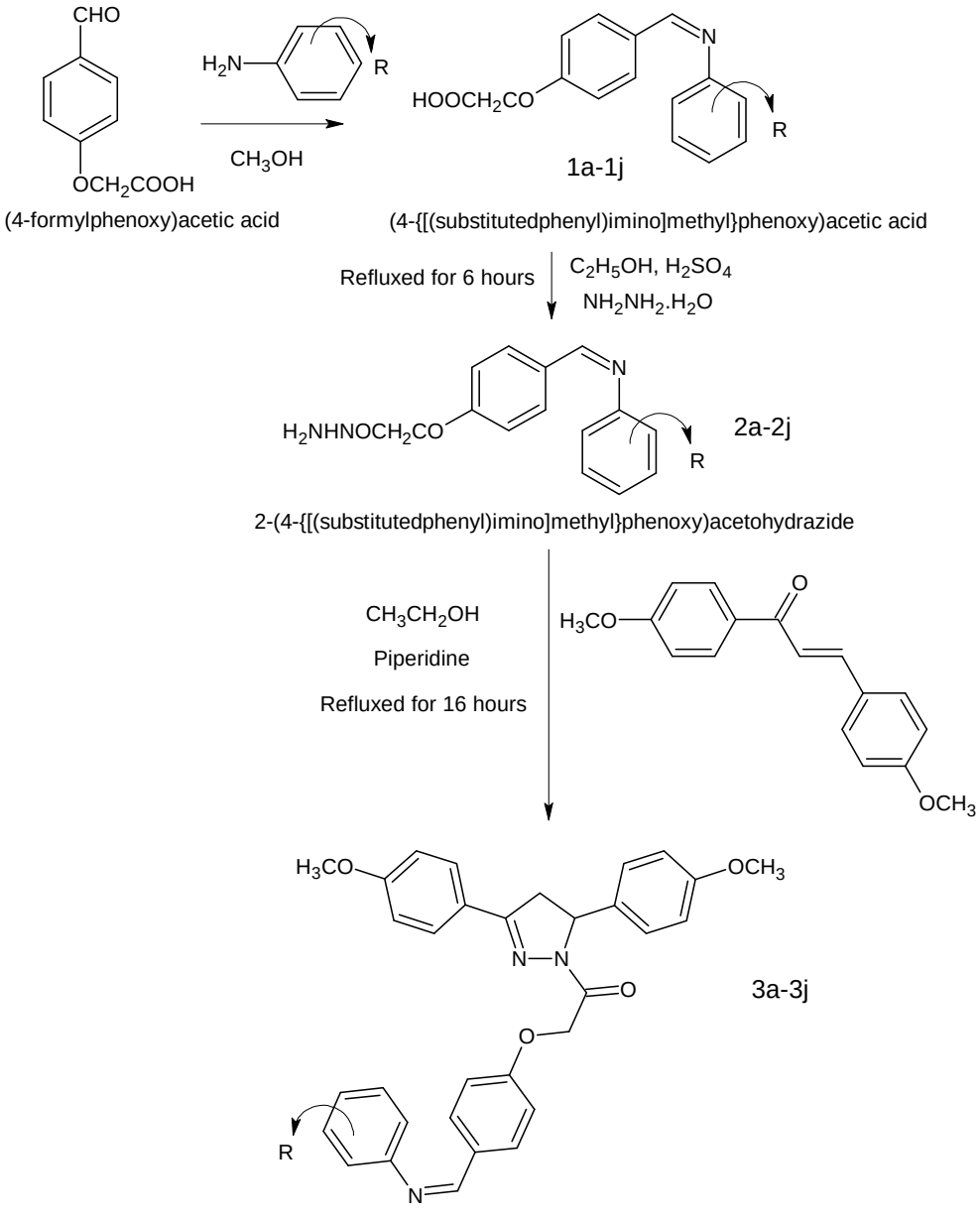
Preparation of *N*-[{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}methylene] substituted aniline (3a-3j)

A mixture of 2-{4-[(phenylimino)methyl]phenoxy} acetohydrazide (0.1M), ethanol (25 ml) and 1,3-bis(4-methoxyphenyl)prop-2-en-1-one (0.1M) with piperidine (1ml) 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-c (Cm^{-1}): 3014 (=CH-), 2940(-CH), 1720 (>C=O), 1655(>C=N), 1592(>C=C<, aromatic ring), 1441(-CH_2-), 1385(-CH_3), 1250(C-N) , 1215(N-N), 1170(C-O)

^{1}H NMR (DMSO); 3-a: 2.5695,doublet(2H)(>CH_2, cyclic), 3.7853,singlet(6H)(-OCH_3), 4.6809,singlet(2H)(-CH_2), 4.9323,triplet(1H)(-CH<), 8.5208,singlet(1H)(Ar-CH=N-), 6.8607 -8.0707, multiplate, (17H) (Ar-H)

Reaction Scheme



N-[{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}methylene]substitutedaniline

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, 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 byMinimal Inhibition Concentration. The results are summarized in Table-2.

Tabel-2 Antimicrobial activity of N-[{4-[2-(3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl}methylene] substitutedaniline

SR. NO.	COMP. NO.	R	ANTIBACTERIAL ACTIVITY Minimal Inhibition Concentration(g/ml)				ANTIFUNGAL ACTIVITY Minimal Inhibition Concen	
			Gram negative bacteria		Gram positive bacteria		Fungus	
			E.COLI	P.AERUGINOSA	S.AUREUS	S.PYOGENUS	C.ALBICANS	A.NIGER
			MTCC 443	MTCC 1688	MTCC 96	MTCC 442	MTCC 227	MTCC 282
1	3a	1-Phenyl	150	100	150	125	500	800
2	3b	1- Napthyl	100	172.5	175	150	600	500
3	3c	-4-CH_3	200	150	175	125	800	>1000
4	3d	-3-CH_3	150	125	275	100	700	600
5	3e	-2-NO_2	175	100	250	150	900	700
6	3f	-3-NO_2	150	150	225	175	>1000	600
7	3g	-4-NO_2	200	150	300	125	900	900
8	3h	-2-Cl	175	125	150	150	>1000	600
9	3i	-3-Cl	150	150	200	150	700	700
10	3j	-4-Cl	175	125	275	100	600	>1000

Biological screening result of N-[{4-[2-(3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl} methylene]substituted aniline based derivatives shows that compound (3b) 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-chloro (3d and 3j), shown good antibacterial activity against S. pyogenus , while rest of all derivatives possessed good activity against S. pyogenus in the range of 150-250 µg/ml. Compound (3f) and (3h) 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 1H-NMR. In summary, we have described the synthesis and antimicrobial activity of novel N-[{4-[2-(3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy] phenyl}methylene] 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.

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.REFERENCES

[1] P Francisco; AMO deRetana; PA Jaiore, *Tetrahedron.*, **1999**, 55, 14451.
[2] KY Lee; JM Kim; JN Kim, *Tetrahedron Lett.***, 2003**, 44, 6737.
[3] J Jiaz; Y Wu; W. Hung; P. Zhang; Y. Song; J. Woolfrey; U.Sinha; AE Arfsten; ST Edwards; A Hutchaleelaha; SJ Hollennbach; JL Lambing; RM Scarborough; BY Zhu, *Bioorg med chem Lett.*, **2004,** 14, 1229.
[4] DP Thomas; K Albert; BC Barbara; AR Mark; LB Mark; W Yaping; DV Tiffany; E Wayne; BF Mary; KF Sandra, *Bioorg Med Chem Lett.***, 2006**, 16, 3156.
[5] V Manuela; P Valeria; V Paola; C Alexander; C Marina; M Ciro, *Bioorg Med Chem Lett.*, **2006**, 16, 1084.
[6] SG Roelfvan; C Arnold; K Wellnga, *J Agric Food Chem.***, 1979**, 84, 406.
[7] Rajendra; Krushanji Wanare, *J. Chem.Pharm.Res*., **2011**, 3(5): 136-144.
[8] Meghasham; Narayanrao Narule, *J. Chem. Pharm. Res.*, **2011**, 3(3):38-47
[9] HZ Katri; SA Vunii, *J Indian Chem Soc***., 1981,** 58, 168.
[10] Singarave; Mohan; Sarkkarai ;Ananthan, *J. Chem. Pharm. Res.*, 2011, 3(1):402-413
[11] G Amr Ael; NA Abdel-Lalif; MM. Abdalla, *Bioorg Med Chem.*, **2006**, 14(2), 373.
[12] HG Garge; Chandraprakash, *J Pharm Sc.*, 1971, 14, 649.
[13] HA Regaila; AK El-Bayonk; M Hammad. Egypt *J Chem.*, **1979**, 197,20.

[14] Bharat Parashar; Sudhir; Bhardwaj; Sharda Sharma; G. D. Gupta; V. K. Sharma; P. B. Punjabi, *J. Chem.Pharm. Res*., **2010**, 2(3):33-42
[15] B Chai; X Qian; S Cao; H Liu; G Song, *Arkivoc*., **2003**, (ii), 141.
[16] A Singh; S Rathod; BN Berad; SD Patil; AG Dosh. *Orient J Chem.*, **2000**, 16,315.
[17] VY Vernon; D William; EI Richard. *International Minerals and Chemical Corpo*, US 4221791 (C1-424-248).
[18] Y Ura; G Sakata; KO Makmo. [Nessam Chemicals Industries Ltd], *Eur Pat Appl EP* 46467 (C1 C07 D241/14).
[19] YV Tomilovi; GP Okonnishnikova; EV Shulishov; OM. Nefedov, *Russ Chem Bt.*, **1995**, 44, 211.
[20] EI Klimova; M Marcos; TB Klimova; AT Cecilio; AT Ruben; RR Lena, J Organometallic Chem., **1999**, 106,585.
[21] D Bhaskarreddy; A Padmaja; PV Ramanareddy; B Seenaiah. *Sulfur Lett.*, **1993**, 16, 227.
[22] D Bhaskarreddy; BN Chandrasekhar; V Padmavathi; RD Sumathi. *Synthesis*, **1998**, 491.
[23] U Hartfiel; G Dorfmeister; H Franke; J Geisler; G Johann; R Rees. *US Patent*, **1995**, 5,405.22] V Padmavathi; RP Sumathi; BN Chandrasekhar; D Bhaskarreddy. *J Chem Research.*, **1999**, 610.