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Research Article

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"Synthesis, Characterization and Antimicrobial Activity of N-[{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl) -4, 5-dihydro-pyrazol-1-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-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy] phenyl} methylene] substituted aniline from chalcon of 3-(4-Chlorophenyl)-1-(4- methoxy phenyl)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-{5-(4-chlorophenyl)-3-(methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxo ethoxy] 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 synthesized products were evaluated for their antimicrobial activity. All the compounds were tested for their antibacterial and antifungal activities by broth dilution method.

Key Words : synthesis, pyrazoline, chalcones, substituted aniline, Schiff base,Hydrazine hydrate, DMSO, Antimicrobial activity

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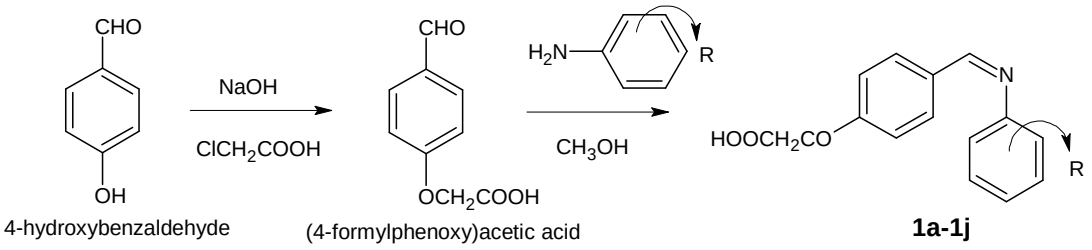
INTRODUCTION

Among the wide variety of heterocycles that have explored for the developing pharmaceutical important molecules. In the family of heterocyclic compounds, nitrogen containing heterocycles with a sulphur atom are an important class of compounds in medicinal chemistry. Pyrazole compounds have practical application in the medicinal and agrochemical field [1, 2].The pyrazole ring has shown to be the basic moiety for a number of dyes and drugs [3,4].Several pyrazoles with antimicrobial, antiviral and anticancer properties have been reported [5].Certain allyl pyrazoles have shown significant antiallergic, anti-inflammatory, and antiarthritic properties [6,7]Many pyrazole-fused heterocyclic compounds have been to exhibit biological activity widely used in pesticides and medicine [8,9]. Pyrazoline derivatives have also been reported in the literature to exhibit various pharmacological activities such as anti-inflammatory [10], antihypertensive [11] and antimicrobial. On the other hand thiazoles and their derivatives have attracted continuing interest over the years because of their biological activities [12,13]recently found application in the drug development for the treatment of allergies [14]hypertensive [15] bacterial[16] to identify new class that may be value in designing new potentantimicrobial agents. Our continuation work on heterocycles [17-21] that having potent biological activities, these assets prompted us to prepare some new pyrazolo [3,4-c] pyrazolthiazolone derivatives with potent biological activity by using polyethylene glycol-400 as greenand

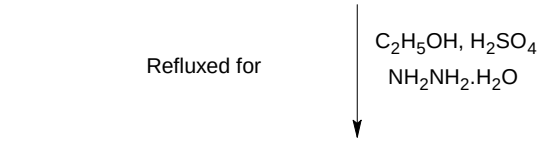
recyclable solvent. we have synthesized Preparation of *N*-[{4-[2-(5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl} methylene]aniline.

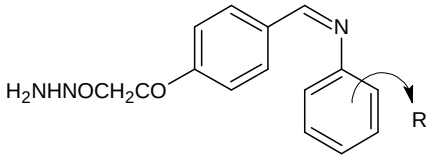
Reaction Scheme



4-hydroxybenzaldehyde (4-formylphenoxy)acetic acid **1a-1j**

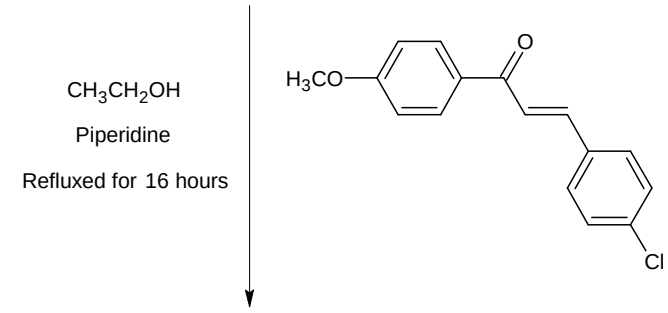
(4-{[(substitutedphenyl)imino]methyl}phenoxy)acetic acid

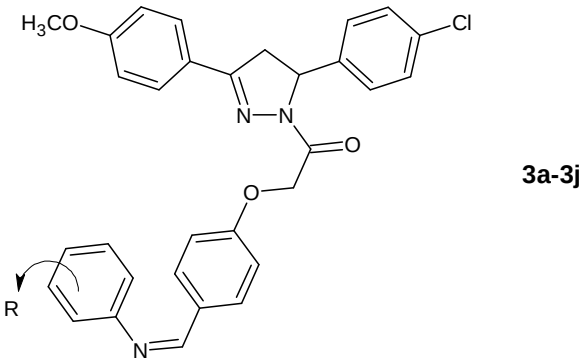




2a-2j

2-(4-{[(substitutedphenyl)imino]methyl}phenoxy)acetohydrazide





3a-3j

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

EXPERIMENTAL SECTION

Melting points were taken in open capillary tube and were uncorrected. IR spectra (KBr) 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 were 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-formylphenoxy)acetic acid (1-a).
To a mixture of 5 gm of 4-hydroxy benzaldehyde, 4gm of chloroacetic acid and 30 ml of water contained in a 250 ml round bottomed flask. add slowly a solution of 3.3 gm of sodium hydroxide in 87.5 ml of water. Heat the mixture to boiling with stirring and reflex for 3 hours the solution acquires a red brown colour Cool and acidity the solution with 7.5 ml. of con. HCl .the solid crystals appear in the solution. The yield of the product was 70% and the product melts at 155^{o}C. Found: C(59.98%) H(4.45%), Calcd. for $C_9H_8O_4$: C(60.00%) H(4.48%)

Preparation of {4-[(phenylimino)methyl]phenoxy}acetic acid (1a-1j)
A mixture of (4-formylphenoxy)acetic acid(0.01M), aniline(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-[(phenylimino)methyl] phenoxy}acetic acid respectively.

IR(KBr); 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).

^{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) aceto hydrazide (2a-2j)
(4-{[(substitutedphenyl)imino]methyl}phenoxy)acetic acid (0.01M) dissolved in absolute ethanol. Hydrazine hydrate (99%, 0.02M) and few drops of conc. Sulphuric acid were added. The reaction mixture was refluxed for 6 hours. The resulting solid obtained was filtered, dried and crystallized from hot water.

IR (KBr); 2-a (cm^{-1}): 3340(>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-(5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl}methylene]substituted aniline (3a-3j)

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	$C_{31}H_{26}ClN_3O_3$	524.0094	71	125	71.03	71.05	4.97	5.00	8.00	8.02
2	3b	1-Naphthyl	$C_{35}H_{28}ClN_3O_3$	574.06812	68	114	73.20	73.23	4.88	4.92	7.29	7.32
3	3c	-4-CH_3	$C_{32}H_{28}ClN_3O_3$	538.03602	74	98	71.10	71.43	5.21	5.25	7.78	7.81
4	3d	-3-CH_3	$C_{32}H_{28}ClN_3O_3$	538.03602	70	110	71.10	71.43	5.21	5.25	7.78	7.81
5	3e	-2-NO_2	$C_{31}H_{25}ClN_4O_5$	569.007	62	105	65.41	65.44	4.40	4.43	9.81	9.85
6	3f	-3-NO_2	$C_{31}H_{25}ClN_4O_5$	569.007	69	90	65.41	65.44	4.40	4.43	9.81	9.85
7	3g	-4-NO_2	$C_{31}H_{25}ClN_4O_5$	569.007	60	99	65.41	65.44	4.40	4.43	9.81	9.85
8	3h	-2-Cl	$C_{31}H_{25}Cl_2N_3O_3$	558.4545	72	101	66.64	66.67	4.47	4.51	7.49	7.52
9	3i	-3-Cl	$C_{31}H_{25}Cl_2N_3O_3$	558.4545	73	111	66.64	66.67	4.47	4.51	7.49	7.52
10	3j	-4-Cl	$C_{31}H_{25}Cl_2N_3O_3$	558.4545	66	103	66.64	66.67	4.47	4.51	7.49	7.52

Preparation of *N*-[{4-[2-(5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol -1-yl)-2-oxoethoxy]phenyl}methylene] substituted aniline (3a-3j)
A mixture of 2-(4-{[(2-chlorophenyl)imino]methyl}phenoxy) acetohydrazide (0.1M), ethanol (25ml) and 3-(4-chlorophenyl)-1-(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 (KBr); 3-d (cm^{-1})**:** 1667(>C=O), 1581(>C=C<, aromatic ring), 1513 (-N=CH-), 1375(-C-N=).
^{1}H NMR (DMSO);3-e: 2.5675 (2H)Doublet(CH_2) 3.8489 singlate (3H) (-OCH_3), 4.5719, singlate (2H) (-CH_2-), 5.0906, triplet (1H) (-CH_2), 8.5267(1H) singlet(Ar-CH=N-).6.6093-8.0824 multiplate (16H) (Ar-H)

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.

Table: 2 Antimicrobial activity of N-[{4-[2-(5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl}methylene]substituted aniline (PA-21-30)

SR. NO.	COMP. NO.	R	ANTIBACTERIAL ACTIVITY Minimal Inhibition Concentration(□g/ml)				ANTIFUNGAL ACTIVITY Minimal Inhibition Concentration (□g/ml)		
			Gram negative bacteria		Gram positive bacteria		Fungus		
			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	3a	1-Phenyl	100	150	175	125	800	500	700
2	3b	1- Napthyl	125	162.5	175	125	600	600	700
3	3c	-4-CH_3	175	125	150	150	600	>1000	700
4	3d	-3-CH_3	150	150	175	125	700	600	800
5	3e	-2-NO_2	200	150	275	100	900	600	800
6	3f	-3-NO_2	175	125	275	150	900	700	600
7	3g	-4-NO_2	200	150	250	175	>1000	900	800
8	3h	-2-Cl	175	100	225	150	700	600	700
9	3i	-3-Cl	200	125	200	125	900	600	>1000
10	3j	-4-Cl	150	150	300	150	>1000	>1000	700

Biological screening result of N-[{4-[2-(5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl)-2-oxoethoxy]phenyl}methylene]substituted aniline based derivatives shows that compound (**3e**) 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 (**3c** and **3g**), 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 (**3a)** 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-(5-(4-chlorophenyl)-3-(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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