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Original Article

SYNTHESIS, *IN VITRO* ANTIMICROBIAL ACTIVITY OF SCHIFF'S BASE, AZETIDINONES AND THIAZOLIDINONES

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ABSTRACT

Objective: The objective of the present study is to synthesize 3-Chloro-4-[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl]-1-(substituted) azetidin-2-one [4a-n] and 2-[3-(2,4-Dichloro-5-fluoro phenyl)-1H-pyraol-4-yl]-3-(substituted phenyl)-1,3-thiazolidin-4-one [5a-n]. The structure of all synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectral studies.

Methods: The titled compounds 3-Chloro-4-[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl]-1-(substituted) azetidin-2-one [4a-n] and 2-[3-(2,4-Dichloro-5-fluoro phenyl)-1H-pyraol-4-yl]-3-(substituted phenyl)-1,3-thiazolidin-4-one [5a-n] were synthesized by the reaction of N-{[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyraol-4-yl] methylene } substituted anilin [3a-n] with chloro acetyl chloride and thioglycolic acid respectively. Compounds N-{[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyraol-4-yl] methylene} substituted aniline [3a-n] were synthesized by the reaction of 3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-carbaldehyde [2] with primary aromatic amine in alcohol. All compounds were evaluated for their antimicrobial activity.

Results: Compounds 3a,3b,3d,3j,3l,4d,4e,4j,4l,4m,5e,5g,5h,5n exhibited excellent to good antibacterial activity as compared to reference drugs.

Conclusion: In summary, N-{[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyraol-4-yl] methylene } substituted anilin [3a-n], 3-Chloro-4-[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl]-1-(substituted) azetidin-2-one [4a-n] and 2-[3-(2,4-Dichloro-5-fluoro phenyl)-1H-pyraol-4-yl]-3-(substituted phenyl)-1,3-thiazolidin-4-one [5a-n] derivatives have been synthesized and characterized. *In vitro* antimicrobial testing of the compounds was carried out by microdilution Method. Amongst the synthesised compounds, many of them had proven their antimicrobial potency which varies from good to excellent.

Keywords: Schiff's base, 2-Azetidinone, 4-Thiazolidinone, Antimicrobial activity

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INTRODUCTION

Heteroaromatic compounds have attracted considerable attention in the design of biologically active molecules and advanced organic materials. Heterocycles containing nitrogen atoms in the core structure shows a number of pharmacologically and biologically active compounds. Hence, a practical method for the preparation of such compounds is of great interest in synthetic organic chemistry. Structurally, a Schiff's base (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group has been replaced by an imine or azomethine group. Schiff's bases of pyrazole aldehydes and aromatic amines exhibit a wide range of biological activities such as antifungal [1], antibacterial [2] and antitubercular [3] etc. The biological significance of this class of compounds impelled us to continue working on the synthesis of new schiff's bases of pyrazole derivatives.

β-Lactam containing antibacterial agents has become an integral part of chemotherapeutic arsenal available to today's medical practitioners. Although the number of existing agents are quite extensive, but the search for better and more effective drug is still going on. Azetidinones are the very important class of compounds possessing a wide range of biological activities such as antibacterial [4], anti-inflammatory [5], antihyperlipidemic [6], anticancer [7], antimicrobial [8], antitumor [9], antitubercular [10] etc. Furthermore, thiazolidinone derivatives found to possess a wide spectrum of biological activities [11-17].

MATERIALS AND METHODS

Melting points were determined by open capillaries and are uncorrected. The progress of the reaction was checked on aluminium coated TLC plates (E. Merck) using various solvent systems as mobile phase and visualised under iodine vapour. IR-spectra (cm^{-1}) were recorded on a Shimadzu FT-IR spectrophotometer using KBr pellet method. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-300 NMR instrument, using $CDCl_3$ as solvent and TMS as an internal reference (chemical shifts in δ, ppm). Mass spectra were obtained on an Agilent 6520 (Q-TOF) Mass spectrometer.

Synthesis of (1E)-1-(2,4-Dichloro-5-fluorophenyl) ethanone hydrazone [1]

A mixture of 2,4-dichloro-5-fluoro acetophenone (0.01 mol) and hydrazine hydrate (0.012 mol) was refluxed in round bottom flask containing absolute alcohol (30 ml) for 2 h in the presence of few drops of acetic acid. The content of the flask was cooled to give a solid product which was filtered, washed with water, dried and recrystallized from ethanol as a yellow crystalline solid.

Synthesis of 3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-carbaldehyde [2]

To a cold solution of (1E)-1-(2,4-Dichloro-5-fluoro phenyl)ethanone hydrazone (0.015 mol) in DMF (25 ml) was added $POCl_3$ (0.0395 mol) and resulting mixture was stirred at 55-60 °C for 5-6 h [18]. Then the mixture was cooled to room temperature and poured into ice cold water.

A saturated solution of bicarbonate was added to neutralise the solution. The precipitate so formed was filtered, washed with water, dried and recrystallized from ethanol as a yellowish white crystalline solid.

General procedure for the synthesis of N-{[3-(2, 4-dichloro-5-fluoro phenyl)-1H-pyraol-4-yl] methylene} substituted anilin [3a-n]

A mixture of 3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-carbaldehyde (0.01 mol), various primary aromatic amine (0.01 mol) and few drops of gla. Acetic acid was refluxed in methanol for six hours. Then the refluxed content was cooled to room

temperature and solid separated was filtered, washed with water and recrystallized from acetone.

[3d] IR (KBr cm^{-1}): 3389.81 (-NH), 1567.08 (C=N), 807.10 (C-Cl), 1094.22 (C-F), 1201.49 (-C-N) ^1H NMR ($CdCl_3$) δ: 6.972 (-NH), 5.996 (-CH), 7.361-7.572 (Ar-H), 7.696 (CH-Cl), 7.701 (CH-F), 9.747 (-CH=N). ^{13}C NMR: 161.38(C1), 120.09(C2), 129.69(C3), 129.08(C4), 139.48(C5), 115.4(C6), 139.85(C7), 110.05(C8), 133.45(C9), 160.00(C10), 150.02(C11), 122.99(C12), 125.85(C13), 131.88(C14), 125.85(C15), 122.99(C16). Mass (m/z): 368.5 (M), 374.5 (M+6), 257, 230, 205, 164, 138.

[3m] IR (KBr cm^{-1}): 1567.20 (C=N), 807.32 (C-Cl), 1095.34 (C-F), 1023.0 (-OCH_3), 1202.57 (-C-N). ^1H NMR ($CdCl_3$) δ: 6.996 (-NH), 5.877 (-CH), 7.328-7.535 (Ar-H), 7.697 (CH-Cl), 7.702 (CH-F), 9.750 (-CH=N), 3.800 (-OCH_3). ^{13}C NMR: 161.45(C1), 119.99(C2), 129.78(C3), 129.59(C4), 139.45(C5), 114.44(C6), 139.95(C7), 110.05(C8), 134.55(C9), 159.97(C10), 139.45(C11), 123.25(C12), 122.25(C13), 128.08(C14), 115.50 (C15), 153.67(C16).

Mass (m/z): 364 (M), 368 (M+4), 257, 230, 200, 164, 134.

General procedure for the synthesis of 3-Chloro-4-[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl]-1-(substituted) azetidin-2-one [4a-n]

Compound N-{[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl] methylene}substituted anilin (0.01 mol) was dissolved in 1,4-dioxan (50 ml). To this solution chloro acetyl chloride (0.012 mol) was added drop wise with constant stirring maintaining the temperature below 10 °C and then tri ethyl amine (0.02 mol) was added to it. The mixture was stirred for 2 h. The reacrtion mixture was then refluxed for 9-10 h. The resulting solution was then poured into crushed ice and the product thus obtained was filtered, washed with water and recrystallized from ethyl acetate.

[4a] IR (KBr cm^{-1}): 1730 (C=O), 1203 (CH-N), 760 (C-Cl), 1062 (C-F). ^1H NMR ($CdCl_3$) δ: 6.930 (-NH pyrazol), 5.958 (-CH pyrazol), 5.103 (CH-N), 3.885 (CH-Cl), 7.307-7.960 (Ar-H). ^{13}C NMR: 161.79(C1), 120.0(C2), 131.69(C3), 129.31C4), 138.60(C5), 117.17(C6), 143.12(C7), 114.3(C8), 133.18(C9), 60.5(C10), 62.0(C11), 162.08(C12), 140.75(C13), 119.77(C14), 130.69(C15), 123.05(C16), 129.31(C17), 117.17(C18). Mass (m/z): 409 (M), 415 (M+6), 333.5, 246.5, 230, 164, 141.5.

[4j] IR (KBr cm^{-1}): 1712 (C=O), 1205 (CH-N), 758 (C-Cl), 1070 (C-F), 2919 (-CH_3). ^1H NMR ($CdCl_3$) δ: 6.931 (-NH pyrazol), 5.961 (-CH pyrazol), 5.105 (CH-N), 3.940 (CH-Cl), 7.305-8.049 (Ar-H), 2.529 (-CH_3). ^{13}C NMR: 161.59(C1), 120.0(C2), 130.69(C3), 129.5(C4), 139.97(C5), 117.29(C6), 144.15(C7), 114.39(C8), 133.19(C9), 60.05(C10), 62.0(C11), 162.0(C12), 138.0(C13), 120.48(C14), 129.31(C15), 133.38(C16), 129.31(C17), 120.48(C18). Mass (m/z): 424.5 (M), 430.5 (M+6), 333.5, 307, 259, 196, 164.

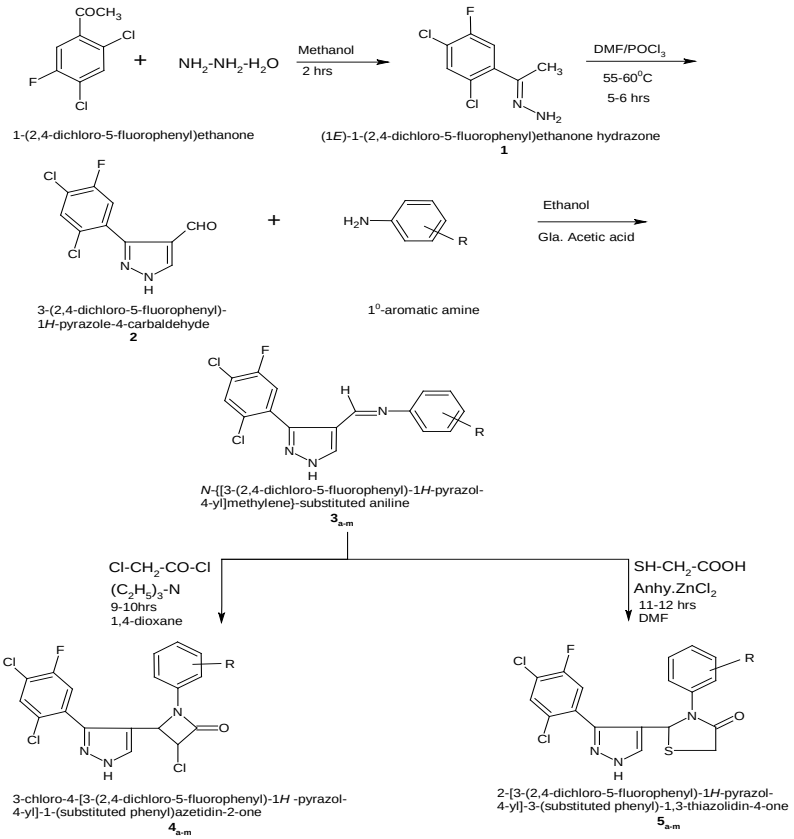
General procedure for the synthesis of 2-[3-(2,4-Dichloro-5-fluoro phenyl)-1H-pyraol-4-yl]-3-(substituted phenyl)-1,3-thiazolidin-4-one [5a-n]

A mixture of N-{[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl] methylene}substituted anilin (0.01 mol), thio glycolic acid (0.01 mol) and anhydrous zinc chloride (0.01 mol) in DMF was refluxed for 11-12 h. The resulting solution was then poured into crushed ice and the product thus obtained was filtered, washed with cold water and recrystallized from methanol.

[5a] IR (KBr cm^{-1}): 1720.20 (C=O), 1260.70 (CH-N), 760.26 (-Cl), 1066.12 (-F).

^1H NMR ($CdCl_3$) δ: 6.927 (-NH pyrazol), 5.959 (-CH pyrazol), 5.871 (CH-N), 4.01 (CH_2-S), 7.324-7.704 (Ar-H). ^{13}C NMR: 161.41(C1), 119.99(C2), 131.91(C3), 129.70(C4), 139.82(C5), 117.18(C6), 144.65(C7), 108.74(C8), 135.82(C9), 66.1(C10), 34.0(C11), 171.1(C12), 141.75(C13), 126.4(C14), 131.82(C15), 129.30(C16), 131.82(C17), 126.4(C18). Mass (m/z): 408(M), 412 (M+4), 380, 331, 245, 230, 164.

[5e] IR (KBr cm^{-1}): 1733.35 (C=O), 1256.46 (CH-N), 766.17 (-Cl), 1063.31 (-F), 1345.04 (-NO_2). ^1H NMR ($CdCl_3$) δ: 6.927 (-NH pyrazol), 5.959 (-CH pyrazol), 5.923 (CH-N), 3.975 (CH_2-S), 7.323-7.703 (Ar-H). ^{13}C NMR: 161.48(C1), 119.99(C2), 131.91(C3), 129.67(C4), 140.05(C5), 117.18(C6), 144.75(C7), 108.74(C8), 135.82(C9), 66.16(C10), 42.36(C11), 171.2(C12), 131.82(C13), 108.74(C14), 131.91(C15), 119.76(C16), 126.44(C17), 141.75(C18). Mass (m/z): 453 (M), 457 (M+4), 421, 331, 289, 230, 212, 164, 122.



Scheme

Table 1: Physical, characterization data of compound (3a-n), (4a-n) and (5a-n)

S. No.	R	Mol. formula	Mol. Wt. gm/mol	M. P. °C	Yield %
3a	H	$C_{16}H_{10}N_3Cl_2F$	334	120	68
3b	2-Cl	$C_{16}H_9N_3Cl_3F$	368.5	140	64
3c	3-Cl	$C_{16}H_9N_3Cl_3F$	368.5	120	62
3d	4-Cl	$C_{16}H_9N_3Cl_3F$	368.5	156	65
3e	2-NO_2	$C_{16}H_9O_2N_4Cl_2F$	379	152	54
3f	3-NO_2	$C_{16}H_9O_2N_4Cl_2F$	379	140	50
3g	4-NO_2	$C_{16}H_9O_2N_4Cl_2F$	379	148	56
3h	2-CH_3	$C_{17}H_{12}N_3Cl_2F$	348	180	0
3i	3-CH_3	$C_{17}H_{12}N_3Cl_2F$	348	182	58
3j	4-CH_3	$C_{17}H_{12}N_3Cl_2F$	348	180	60
3k	2-OCH_3	$C_{17}H_{12}ON_3Cl_2F$	364	210	66
3l	3-OCH_3	$C_{17}H_{12}ON_3Cl_2F$	364	190	60
3m	4-OCH_3	$C_{17}H_{12}ON_3Cl_2F$	364	204	64
3n	$C_{10}H_7$ (naphthyl)	$C_{20}H_{12}N_3Cl_2F$	384	180	56
4a	H	$C_{18}H_{11}ON_3Cl_3F$	410.5	130	58
4b	2-Cl	$C_{18}H_{10}ON_3Cl_4F$	445	170	54
4c	3-Cl	$C_{18}H_{10}ON_3Cl_4F$	445	186	51
4d	4-Cl	$C_{18}H_{10}ON_3Cl_4F$	445	200	5
4e	2-NO_2	$C_{18}H_{10}O_3N_4Cl_3F$	455.5	160	47
4f	3-NO_2	$C_{18}H_{10}O_3N_4Cl_3F$	455.5	120	46
4g	4-NO_2	$C_{18}H_{10}O_3N_4Cl_3F$	455.5	166	49
4h	2-CH_3	$C_{19}H_{13}ON_3Cl_3F$	424.5	196	54
4i	3-CH_3	$C_{19}H_{13}ON_3Cl_3F$	424.5	132	42
4j	4-CH_3	$C_{19}H_{13}ON_3Cl_3F$	424.5	100	51
4k	2-OCH_3	$C_{19}H_{13}O_2N_3Cl_3F$	440.5	220	44
4l	3-OCH_3	$C_{19}H_{13}O_2N_3Cl_3F$	440.5	202	40
4m	4-OCH_3	$C_{19}H_{13}O_2N_3Cl_3F$	440.5	176	42
4n	$C_{10}H_7$ (naphthyl)	$C_{22}H_{13}ON_3Cl_3F$	460.5	190	40
5a	H	$C_{18}H_{12}ON_3Cl_2FS$	408	127	56
5b	2-Cl	$C_{18}H_{11}ON_3Cl_3FS$	442.5	152	48
5c	3-Cl	$C_{18}H_{11}ON_3Cl_3FS$	442.5	173	47
5d	4-Cl	$C_{18}H_{11}ON_3Cl_3FS$	442.5	200	50
5e	2-NO_2	$C_{18}H_{11}O_3N_4Cl_2FS$	453	160	51
5f	3-NO_2	$C_{18}H_{11}O_3N_4Cl_2FS$	453	120	48
5g	4-NO_2	$C_{18}H_{11}O_3N_4Cl_2FS$	453	186	50
5h	2-CH_3	$C_{19}H_{14}ON_3Cl_2FS$	422	120	58
5i	3-CH_3	$C_{19}H_{14}ON_3Cl_2FS$	422	142	56
5j	4-CH_3	$C_{19}H_{14}ON_3Cl_2FS$	422	168	60
5k	2-OCH_3	$C_{19}H_{14}O_2N_3Cl_2FS$	438	260	52
5l	3-OCH_3	$C_{19}H_{14}O_2N_3Cl_2FS$	438	210	50
5m	4-OCH_3	$C_{19}H_{14}O_2N_3Cl_2FS$	438	224	52
5n	$C_{10}H_7$ (naphthyl)	$C_{22}H_{14}ON_3Cl_2FS$	458	230	42

Antimicrobial activity

Following common standard strains were used for screening of antibacterial and antifungal activities: *E. Coli* (MTCC 442), *P. Aeruginosa* (MTCC 441), *S. Aureus* (MTCC 96), *S. Pyogenus* (MTCC 443), *C. Albicans* (MTCC 227), *A. Niger* (MTCC 282), *A. Clavatus* (MTCC 1323). The strains were procured from Institute of Microbial Technology, Chandigarh. DMSO was used as diluents/vehicle to get desired concentration of drugs to test upon standard bacterial strains. Each synthesised drug was diluted for obtaining 2000 microgram/ml concentration, as a stock solution. In primary screening 1000 microgram/ml, 500 microgram/ml, and 250 microgram/ml concentrations of the synthesised drugs were taken. The actively synthesised drugs found in this primary screening were further tested in the second set of dilution against all microorganisms. The drugs found active in primary screening were similarly diluted to obtain 200 microgram/ml, 100 microgram/ml, 50 microgram/ml, 25 microgram/ml, 12.5 microgram/ml and 6.250 microgram/ml concentrations. The highest dilution showing at least 99 % inhibition zone is taken as MIC. The result of this is much affected by the size of the inoculums. Gentamycin, Ampicillin, Chloramphenicol, Ciprofloxacin, Norfloxacin, Nystatin and Griseofulvin were used as a standard. The Comparative activities of the newly synthesised compounds and the control antibiotics on bacterial and fungal strains respectively were summarised in table 2 and table 3.

Excellent to good activity was observed in compounds 4d (against *E. Coli, P. Aeruginosa, S. Aureus, S. Pyogenus*), compounds 3g, 4e, 5g, 5n (against *E. Coli, S. Aureus, S. Pyogenus*), compounds 3a, 3b, 3j, 3l, 4j, 4l, 4m, 5e, 5h (against *E. Coli, S. Aureus*) as well as compounds 3a, 3c, 3f, 3g, 3h, 3j, 3k, 3l, 4c, 4e, 4f, 4g, 4h, 4k, 4l, 4m, 5b, 5e, 5f, 5g, 5i, 5j, 5l, 5m (against *C. Albicans*). The remaining compounds were found effective at a much higher concentration as compared to the standard drugs.

Table 2: Antibacterial activity of compounds 3a-n, 4a-n and 5a-n

Code	*E. Coli*	*P. Aeruginosa*	*S. Aureus*	*S. Pyogenus*
No.	***MTCC 442***	***MTCC 441***	***MTCC 96***	***MTCC 443***
3a	100	200	250	125
3b	62.5	100	125	200
3c	200	125	250	62.5
3d	250	200	200	200

3e	200	125	250	125
3f	125	125	250	62.5
3g	62.5	200	100	100
3h	200	250	250	250
3i	250	250	500	100
3j	100	200	250	125
3k	250	200	100	125
3l	100	125	100	250
3m	62.5	250	500	500
3n	200	125	250	500
4a	200	250	500	500
4b	100	200	500	250
4c	125	100	250	500
4d	62.5	50	100	100
4e	100	125	250	100
4f	250	100	200	200
4g	500	500	100	200
4h	250	250	500	500
4i	200	200	200	250
4j	62.5	100	200	250
4k	200	250	250	250
4l	100	62.5	62.5	125
4m	62.5	100	200	200
4n	125	100	250	250
5a	200	125	100	125
5b	125	62.5	100	100
5c	200	62.5	100	250
5d	200	250	250	250
5e	100	125	250	500
5f	200	250	200	250
5g	62.5	100	100	62.5
5h	62.5	125	250	250
5i	250	250	250	500
5j	100	125	500	500
5k	250	250	125	100
5l	250	500	500	500
5m	500	250	500	500
5n	100	125	250	100
Ampicillin	100	--	250	100
Chloramphenicol	50	50	50	50
Ciprofloxacin	25	25	50	50
Norfloxacin	10	10	10	10

Table 3: Antifungal activity of compounds 3a-n, 4a-n and 5a-n

Code	***C. albicans***	***A. niger***	***A. clavatus***
No.	***MTCC 227***	***MTCC 282***	***MTCC 1323***
3a	500	250	250
3b	1000	1000	>1000
3c	250	1000	1000
3d	>1000	1000	1000
3e	>1000	1000	1000
3f	500	500	500
3g	500	500	1000
3h	250	500	500
3i	>1000	1000	1000
3j	100	>1000	>1000
3k	500	1000	1000
3l	500	>1000	>1000
3m	1000	500	500
3n	>1000	500	500
4a	>1000	500	500
4b	>1000	500	500
4c	500	1000	1000
4d	1000	1000	500
4e	500	>1000	>1000
4f	500	200	500
4g	250	1000	1000
4h	500	1000	1000
4i	1000	500	500
4j	1000	1000	1000
4k	250	1000	>1000
4l	500	500	1000

4m	500	250	500
4n	1000	>1000	>1000
5a	1000	500	500
5b	500	500	500
5c	1000	1000	1000
5d	>1000	>1000	>1000
5e	500	500	500
5f	250	500	500
5g	500	>1000	>1000
5h	1000	500	>1000
5i	250	>1000	>1000
5j	250	1000	>1000
5k	1000	>1000	>1000
5l	500	500	500
5m	200	500	1000
5n	>1000	500	500
Nystatin	100	100	100
Greseofulvin	500	100	100

RESULTS AND DISCUSSION

The compounds were synthesised as per scheme

Compound (1E)-1-(2,4-Dichloro-5-fluorophenyl) ethanone hydrazone 1 were synthesized from 1-(2,4-dichloro-5-fluorophenyl) ethanone, which upon reaction with DMF/POCl3 yields 3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-carbaldehyde 2. Compounds N-{[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyraol-4-yl] methylene } substituted anilin [3a-n] were synthesized from 3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-carbaldehyde 2 and various aromatic amine, which upon cyclization with chloro acetyl chloride and thioglycolic acid yields 3-Chloro-4-[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl]-1-(substituted) azetidin -2-one [4a-n] and 2-[3-(2,4-Dichloro-5-fluoro phenyl)-1H-pyraol-4-yl]-3-(substituted phenyl)-1,3-thiazolidin-4-one [5a-n] respectively. The proposed structures of all the synthesised compounds were well supported by IR, 1H NMR, ^{13}C NMR and mass spectral data. The formation of compounds 3a-n was confirmed by the appearance of singlet signal at δ 9.747-9.750 for CH=N system. The 1H NMR spectrum also displayed signals at δ 5.103-5.105 for CH-N of azetidine ring and at δ 4.01-3.975 for CH2-S of thiazolidinone ring system respectively. Aromatic protons were observed in the usual region as multiplet between δ 7.328-7.535, δ 7.305-8.049, δ 7.323-7.703.

CONCLUSION

In summary, N-{[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyraol-4-yl] methylene } substituted anilin [3a-n], 3-Chloro-4-[3-(2,4-dichloro-5-fluoro phenyl)-1H-pyrazol-4-yl]-1-(substituted) azetidin-2-one [4a-n] and 2-[3-(2,4-Dichloro-5-fluoro phenyl)-1H-pyraol-4-yl]-3-(substituted phenyl)-1,3-thiazolidin-4-one [5a-n] derivatives have been synthesized and characterized. *In vitro* antimicrobial testing of the compounds was carried out by microdilution Method. Amongst the synthesised compounds, many of them had proven their antimicrobial potency which varies from good to excellent. Excellent to good activity was observed in compounds 4d (against *E. Coli, P. Aeruginosa, S. Aureus, S. Pyogenus*), compounds 3g, 4e, 5g, 5n (against *E. Coli, S. Aureus, S. Pyogenus*), compounds 3a, 3b, 3j, 3l, 4j, 4l, 4m, 5e, 5h (against *E. Coli, S. Aureus*) as well as compounds 3a, 3c, 3f, 3g, 3h, 3j, 3k, 3l, 4c, 4e, 4f, 4g, 4h, 4k, 4l, 4m, 5b, 5e, 5f, 5g, 5i, 5j, 5l, 5m (against *C. Albicans*). The remaining compounds were found effective at a much higher concentration as compared to the standard drugs.

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CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Akhaja T. 1,3-dihydro-2H-indol-2-ones derivatives: Design, Synthesis, *in vitro* antibacterial, antifungal and antitubercular study. Eur J Med Chem 2011;46:5573-9.
2. Pandey V, Chawla V, Saraf S. Comparative study of the conventional and microwave-assisted synthesis of some Schiff bases and their potential as antimicrobial agents. Med Chem Res 2011;21:4500-12.
3. Masunari A. A new class of nifuroxazide analogues: synthesis of 5-nitrophene derivatives with antimicrobial activity against multidrug-resistant *Staphylococcus aureus.* Bioorg Med Chem 2007;15:4229-36.
4. Chavan AA, Pai NR. Synthesis and biological activity of N-Substituted-3-chloro-2-azetidinones. Molecules 2007;12:2467-77.
5. Kumar A, Rajput CS. Synthesis and anti-inflammatory activity of newer quinazolin-4-one derivatives. Eur J Med Chem 2009;44:83-90.
6. Leach CA, Deirdre MB. Lipoprotein-associated PLA2 inhibition-a novel, non-lipid lowering strategy for atherosclerosis therapy. II Farmaco 2001;56:45-50.
7. Banik BK, Banik I, Becker FF. Stereocontrolled synthesis of anticancer β-lactams via the Staudinger reaction. Bioorg Med Chem 2005;13:3611-22.
8. Patel KH, Mehta AG. Synthesis and antifungal activity of azetidines and thiazolidinediones derivative of 2-amino-6-(2-naphthalenyl) thiazolo [3, 2-d] thiadiazole. E J Chem 2006;3:267-73.
9. Veinberg G, Shestakova I, Vorona M, Kanepe I, Lukevics E. Synthesis of antitumor 6-alkylidenepenicillanate sulfones and related 3-alkylidene-2-azetidinones. Bioorg Med Chem Lett 2004;14:147-50.
10. Narute AS, Khedekar PB, Bhusari KP. QSAR studies on 4-thiazolidinoes and 2-azetidinones bearing benzothiophene nucleus as potential anti-tubercular agents. Indian J Chem 2008;47B:586-91.
11. Datta NJ, Khunt RC, Parikh AR. Synthesis of some new 4-thiazolidinones as biologically potent agents. Indian J Chem 2002;41B:433-5.
12. Patel KD, Mistry BD, Desai KR. Synthesis and biological screening of 2-thiazolidinones and 4-thiazolidinones. J Indian Chem Soc 2004;81:783-5.
13. Yadav R, Srivastava SD, Srivastava SK. Synthesis, antimicrobial and anti-inflammatory activities of 4-oxothiazolidines and their 5-arylidines. Indian J Chem 2005;44B:1262-6.
14. Mistry K, Desai KR. Microwave assisted rapid and efficient synthesis of nitrogen and sulphur containing heterocyclic compounds and their pharmacological evaluation. Indian J Chem 2006;45(B):1762-6.
15. Gurupadyya BM, Gopal M, Padmashali B, Manohara YN. Synthesis and pharmacological evaluation of azetidin-2-ones and thiazolidin-4-ones encompassing benzothiazole. Indian J Pharm Sci 2008;70:572-7.
16. Milan C, Maja M, Nela D. Design and synthesis of some thiazolidin-4-ones based on (7-Hydroxy-2-oxo-2*H*-chromen-4-yl) acetic acid. Molecule 2009;14:2501-13.
17. Omar K, Geronikaki A, Zoumpoulakis P, Camoutsis C, Sokovic M, Ciric A, *et al*. Novel 4-thiazolidinone derivatives as potential

antifungal and antibacterial drugs. Bioorg Med Chem 2010;18:426-32.

18. Goel N, Drabu S, Bawa S. Antimicrobial screening and one-pot synthesis of 4-(substituted-aminomethyl)-3-(2-naphthyl)-1-phenyl-1H-pyrazole derivatives. J Pharm Bioallied Sci 2014;6:253-9.

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