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Synthesis of bioactive molecule fluoro benzothiazole comprising quinazolinyl oxadiazoles derivative for biological and pharmacological screening

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ABSTRACT

Various substituted 3-{6-fluoro-7-(substituted)-1,3-benzothiazol-2-yl-1-[(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]-2-thioxo-2,3-dihydroquinazoline-4 (1H) -one and 3-{(6-fluoro –7- (substituted) - 1,3 -benzothiazol-2-yl-1-({4-acetyl-5-[4-(dimethylamino)phenyl]-4,5-dihydro-1,3,4-oxadiazol-2-yl}methyl) -2- thioxo -2,3- dihydroquinazolin –4 (1H)-one. containing different functional groups have been synthesized by condensing anthranilic acids with substituted 2-aminobenzothiazoles in dry pyridine and then by condensing with ethylchloroacetate in presence dry acetone and K_2CO_3. The identity of compounds were confirmed on the basis of their spectral (UV, IR, ^{1}H NMR and MASS) data. Further, they have been screened for their antimicrobial activities.

Key words: Fluorine, benzothiazole, quinazoline (Cyclo addition reaction) Oxadizole (Schiff base).

INTRODUCTION

The chemistry and pharmacology of quinazoline have been of great interest because quinazoline derivatives possess various biological activities. This include antimicrobial[1-5], anticonvulsant[6-7], antineoplastic, analgesic and antiinflammatory[8] etc.

Therefore in present work we have prepared quinazoline incorporate with fluoro substituted benzothiazole.

The oxadiazole drugs were the first effective chemotherapeutic agents to be employed systematically for the prevention and cure of bacterial infection in human beings. Benzothiazole with oxadiazole groups were reported to possess various pharmacological activity of clinical importance.

Oxadiazole derivatives are well known to have number of biological and antimicrobial[9-12] activities, this also having antiinflammatory[13], anthelmentic and anticonvulsant activities.

MATERIAL AND METHODS

Melting point was determined by open capillary tube method and are uncorrected. T.L.C was run on silica gel G plates using butanol, ethyl acetate and chloroform (1:2:1) as developing solvent for the purity of the compounds. I.R. Spectra were recorded on Shimadzu FTIR Spectrophotometer by using NUJOL MULL technique.

All the compounds synthesized were screened for antibacterial and antifungal activities at two different concentrations (50µg/ml, 100µg/ml) against *Staphylococcus aureus*, *Streptococci, Escherchia coli, Ps. aureus* and *Candida albicans*,

Aspergillus niger by cup plate method using Procaine Penicillin, Streptomycin and Griseoflavin respectively as standards. The compounds showed considerable activity against all species tested at 50µg/ml, 100µg/ml. Fluoro substituted benzothiazoles series was tested for antibacterial activity. Were calculated which are shown in the table. The compounds showing activity index more than 0.7 were considered to be significantly active.

General synthesis of 2-amino-*N*-(7-chloro-6-fluoro-1,3-benzothiazol-2-yl)benzamide

Anthranilic acid (4.0 g, 0.029 mol) and 2-amino-benzothiazole (5.22 g, 0.026 mol), were dissolved in dry pyridine (20 ml, 0.25 mol). The solution was refluxed for 8 hr. The solution was cooled and poured in water. The separated mass was filtered, washed with water and dried. The product was recrystallized using ethanol.

General synthesis of 3-(7-chloro-6-fluoro-1,3-benzothiazol-2-yl)-2-thioxo-2,3-dihydroquinazolin- 4(1*H*)-one

To an ice cold solution of potassium hydroxide (0.1 g, 0.02 mol) in dry ethanol (50 ml), 2-amino-N-(2'-benzothiazolyl 6'-fluoro-7'-chloro) benzamide (2.6 g, 0.008 mol) and carbon disulphide (6.0 ml, 0.078 mol) was added with stirring. The solution was refluxed for 10 hr and cooled. The quantity of solvents was reduced by distillation. The separated solid was filtered, washed with dry ether and dried. The product was recrystallized from ethanol.

General synthesis of ethyl [3-(7-chloro-6-fluoro-1,3-benzothiazol-2-yl)-4-oxo-2-thioxo-3,4-dihydroquinazolin-1(2*H*)-yl]acetate

A mixture of step III (0.01 mole), ethyl chloro acetate (0.1 mole) and potassium carbonate (0.15 mole) in absolute alcohol (120 ml) was refluxed for 7-8 hours on water bath. The reaction mixture was filtered hot and the excess solvent was distilled off from the filtrate. The crude ester IV thus obtained was purified by recrystallisation from ethanol, yield 84%.

Table 1: Analytical data

S No.	Comp. code	M.P./ B.P^{0}C	% yield	Mol. Form	M.Wt.	C%	H%	N%
1	AP_1	242-244	81%	$C_{33}H_{24}O_5S_2N_7F$	681	58.1	3.5	14.4
2	AP_2	225-227	79%	$C_{33}H_{24}O_5S_2N_7F$	681	58.1	3.5	14.4
3	AP_3	235-237	68%	$C_{33}H_{24}O_5S_2N_7F$	681	58.1	3.5	14.4
4	AP_4	230-232	70%	$C_{33}H_{24}O_3S_2N_6FCl$	670.5	59.1	4.1	12.5
5	AP_5	239-241	80%	$C_{33}H_{24}O_3S_2N_6FCl$	670.5	59.1	4.1	12.5
6	AP_6	228-230	77%	$C_{33}H_{24}O_3S_2N_6FCl$	670.5	59.1	4.1	12.5
7	AP_7	233-235	78%	$C_{31}H_{27}O_4S_2N_6F$	630	59.1	4.3	13.3
8	AP_8	224-226	75%	$C_{34}H_{27}O_3S_2N_6F$	651	62.7	4.1	12.9
9	AP_9	232-234	77%	$C_{31}H_{28}O_3S_2N_7F$	629	59.1	4.4	15.6
10	AP_{10}	222-224	83%	$C_{34}H_{25}O_5S_2N_6F$	680	60.0	3.7	12.3
11	BZ_1	225-227	77%	$C_{34}H_{23}O_5S_2N_8F$	706	57.8	3.2	15.8
12	BZ_2	219-221	75%	$C_{34}H_{23}O_5S_2N_8F$	706	57.8	3.2	15.8
13	BZ_3	225-227	84%	$C_{34}H_{23}O_5S_2N_8F$	706	57.8	3.2	15.8
14	BZ_4	222-224	79%	$C_{34}H_{23}O_3S_2N_7FCl$	695.5	58.7	3.3	14.1
15	BZ_5	221-223	81%	$C_{34}H_{23}O_3S_2N_7FCl$	695.5	58.7	3.3	14.1
16	BZ_6	215-217	82%	$C_{34}H_{23}O_3S_2N_7FCl$	695.5	58.7	3.3	14.1
17	BZ_7	217-219	77%	$C_{34}H_{22}O_3S_2N_7FCl_2$	731	55.9	3.0	13.4
18	BZ_8	225-227	76%	$C_{34}H_{22}O_3S_2N_7FCl_2$	731	55.9	3.0	13.4
19	BZ_9	222-224	83%	$C_{35}H_{26}O_4S_2N_7F$	691	60.7	3.7	14.1
20	BZ_{10}	224-226	81%	$C_{35}H_{24}O_5S_2N_7F$	705	59.6	3.4	13.9

Table 2: Characteristics IR absorption bands of similar compounds (AP_1 to AP_{10} and BZ_1 to BZ_{10}) are tabulated below

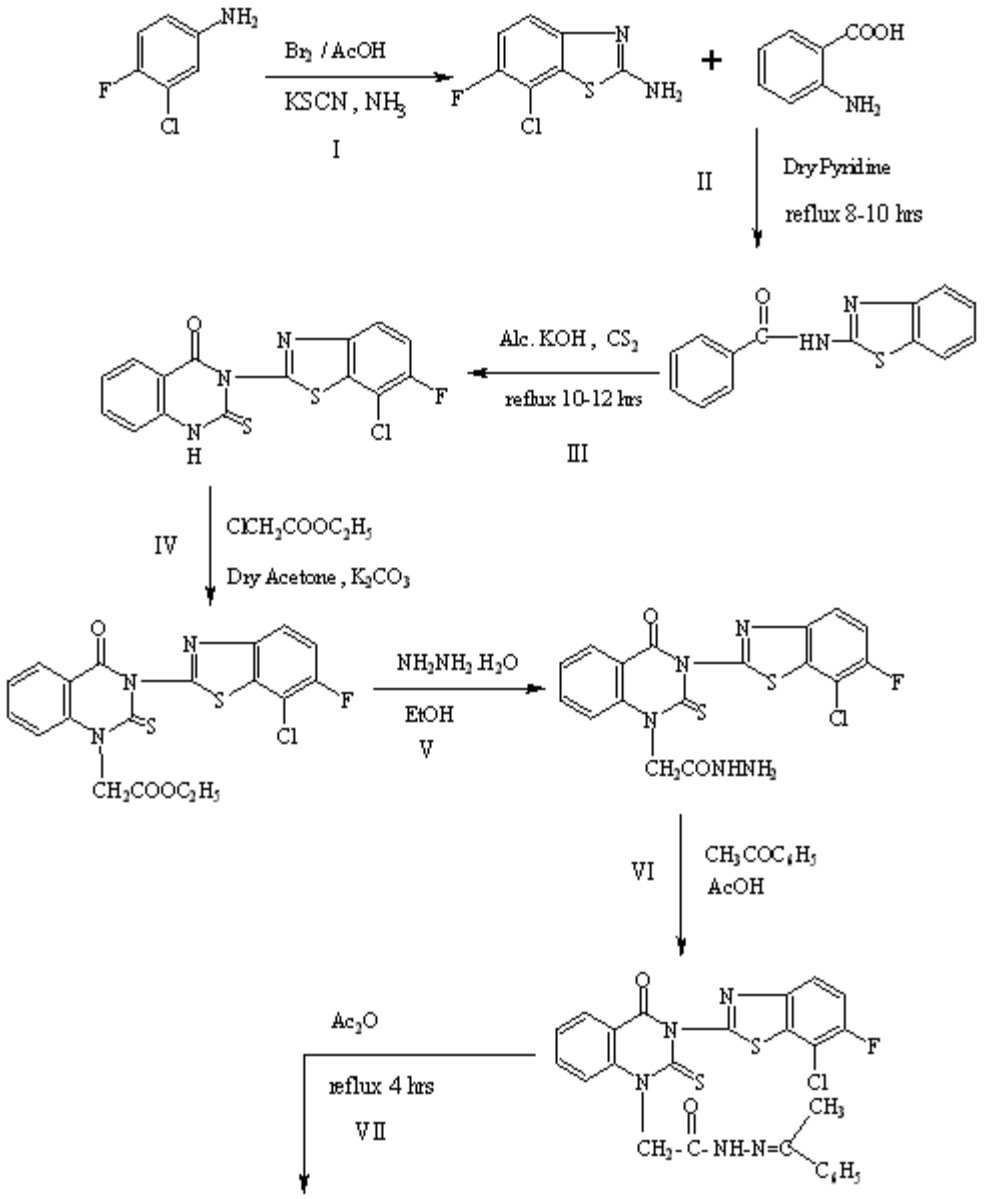
S No.	Spec No.	Compound code	Ar-NH stertcm^{-1}	ArC=C cm^{-1}	C=N cm^{-1}	C-F cm^{-1}	C=O cm^{-1}	C=S cm^{-1}	C-C cm^{-1}	NO_2 cm^{-1}	CH_3 cm^{-1}	C-O-C cm^{-1}
1.	03	CFA	3433	1494	-	1259	-	-	762	-	-	-
2.	04	2AB	3479	1460	1646	1193			685	-	-	-
3.	05	AP	3238	1485	1610	1180	1670	1540	755	-	1075	1035
4.	06	BZ	3220	1450	1580	1115	1590	1570	725	-	1078	1045
5.	07	AP1	3240	1480	1612	1170	1680	1535	-	745	1075	1035
6.	08	AP2	3245	1475	1605	1155	1675	1546	-	760	1078	1030
7.	09	AP3	3248	1475	1610	1165	1670	1540	-	755	1072	1030
8.	10	AP4	3245	1480	1605	1167	1675	1544	760	-	1075	1035
9.	11	AP5	3240	1482	1614	1164	1672	1530	753	-	1070	1040
10.	12	AP6	3240	1480	1605	1175	1670	1540	770	-	1073	1025
11.	13	AP7	3235	1485	1605	1170	1675	1545	-	-	1075	1032
12.	14	AP8	3240	1475	1610	1165	1660	1540	-	-	1092	1035
13.	15	AP9	3233	1480	1605	1168	1675	1540	-	-	1083	1042
14.	16	AP10	3245	1480	1607	1170	1670	1545	-	-	1080	1046
15.	17	BZ1	3240	1475	1603	1180	1670	1575	-	725	1075	1040
16.	18	BZ2	3235	1475	1601	1165	1675	1565	-	715	1060	1035
17.	19	BZ3	3242	1470	1600	1168	1675	1570	-	723	1070	1038
18.	20	BZ4	3240	1465	1602	1175	1670	1575	720	-	1065	1030
19.	21	BZ5	3235	1480	1604	1170	1660	1575	715	-	1075	1025
20.	22	BZ6	3240	1490	1605	1170	1670	1560	710	-	1085	1020
21.	23	BZ7	3233	1490	1605	1175	1675	1570	740	-	1090	1030
22.	24	BZ8	3235	1484	1603	1165	1660	1565	745	-	1085	1035
23.	25	BZ9	3238	1480	1602	1165	1672	1575	-	-	1080	1033
24.	26	BZ10	3235	1485	1603	1175	1665	1568	-	-	1082	1030

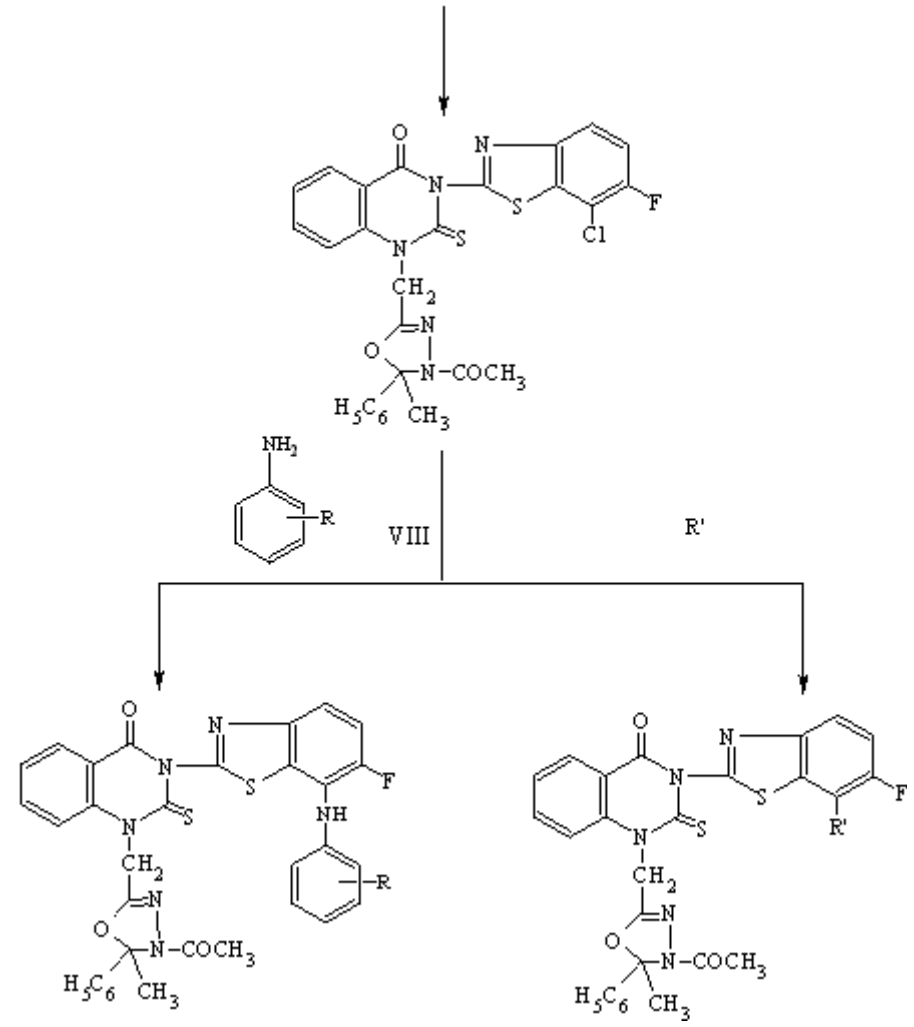
General synthesis of 2-[3-(7-chloro-6-fluoro-1,3-benzothiazol-2-yl)-4-oxo-2-thioxo-3,4-dihydroquinazolin-1(2*H*)-yl]acetohydrazide

A mixture of step IV (0.01 mole) and hydrazine hydrate (4 ml) in absolute alcohol (30 ml) was refluxed for 5 hours on water bath. Cool the solution at room temperature and filter it then recrystallised from ethanol, yield 54%.

General synthesis of 3- (7- chloro – 6 – fluoro - 1,3- benzothiazole-2-yl)-N-(1-phenylethylidene) - 4-oxo- 2-thioxo-3,4-dihydroquinazolin-1(2*H*)-carbohydrazide

A mixture of step V (0.01 mole), and acetophenone (0.01 mole) in glacial acetic acid (20 ml), was refluxed for 1 hour on an oil bath. Distilled off excess solvent and the cooled reaction mixture was poured into ice cold water and the solid was filtered. The dried solid was recrystallised from ethanol-DMF.





R = o, m, p- nitro (AP_1 - AP_3)
= o, m, p- chloro ((AP_4 - AP_6)
= p-toludine (AP_8)

R' = morpholine (AP_7)
= piperazine (AP_9)
= PABA (AP_{10})

Scheme 1

General synthesis of 3-(7-chloro-6-fluoro-1,3-benzothiazol-2-yl)-1-[(4-acetyl-5-methyl -5-phenyl -4,5- dihydro -1,3,4- oxadiazol -2- yl) methyl] -2- thioxo -2,3-dihydroquinazoline-4(1H)-one

A mixture of step VI (0.005 mole) and acetic anhydride (10ml) was refluxed for 4 hours. The excess acetic anhydride was distilled off and the residue was poured into ice cold water. The solid was filtered and recrystallised from ethanol-DMF.

General synthesis of 3-{6-fluoro-7-(substituted)-1,3-benzothiazol-2-yl}-1-[(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]-2-thioxo-2,3-dihydroquinazoline-4(1H)-one

The Product of step VII (0.002 mole) was treated with equimolar quantity (0.002 mole) of various substituted aromatic anilines like nitro

aniline, chloro aniline, PABA, morpholine, piperazine etc. in presence of DMF (dimethyl formamide, 30 ml) and refluxed for 2 hours on an oil bath. The reaction mixture was cooled and then poured into crushed ice. The solid separated was filter off, dried and recrystallised from benzene and absolute alcohol (1:1).

Scheme II

General synthesis of 3- (7- chloro -6 – fluoro - 1,3- benzothiazole-2-yl) -N - [(1-dimethylamino) benzylidene] -4- oxo -2- thioxo -3,4 – dihydroquinazolin -1 (2*H*)-carbohydrazide

A mixture of step V (0.01 mole), and 4-dimethylaminobenzaldehyde (0.01 mole) in glacial acetic acid (20 ml), was refluxed for 1 hour on an oil bath. Distilled off excess solvent and then cooled the reaction mixture was poured into ice cold water and the solid was filtered. The dried solid was recrystallised from ethanol-DMF.

Table 3: NMR Spectral Data of Compounds AP_3, AP_6, AP_7, AP_9, BZ_2, BZ_7, BZ_9, BZ_{10}.

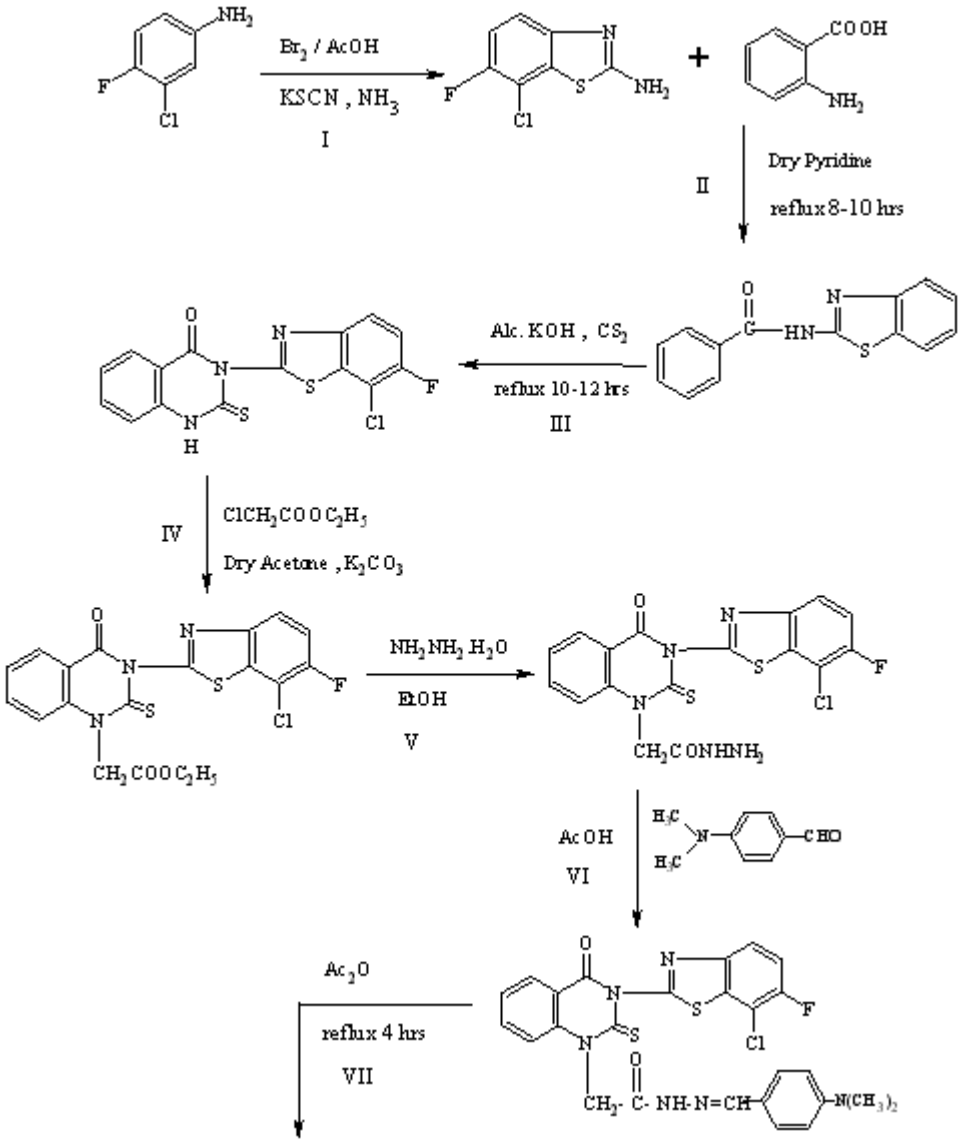
S No.	Spectra no.	Compound code	Hydrogen	δ (ppm)	Multiplity	Solvent
1	27	AP_3	-10H-Ar-H	6.6-8.0	Multiplet	DMSO
			-3H-CH_3	2.1	Singlet	
			-3H-$COCH_3$	2.9	Singlet	
			-H-NH	5.5	Singlet	
2	28	AP_6	-10H-Ar-H	7.2-7.7	Multiplet	DMSO
			-H-CH_3	2.2	Singlet	
			-H-$COCH_3$	2.9	Singlet	
3	29	AP_7	-6H-Ar-H	7.2-7.7	Multiplet	DMSO
			-H-CH_3	2.2	Singlet	
			-H-$COCH_3$	2.8	Singlet	
4	30	AP_9	-6H-Ar-H	7.2-7.7	Multiplet	DMSO
			-H-CH_3	2.1	Singlet	
			-H-$COCH_3$	2.9	Singlet	
5	31	BZ_2	-10H-Ar-H	6.6-8.3	Multiplet	$CDCl_3$
			-H-CH_3	2.2	Singlet	
			-H-$COCH_3$	2.8	Singlet	
6	32	BZ_7	-6H-Ar-H	6.6-7.7	Multiplet	$CDCl_3$
			-H-CH_3	2.2	Singlet	
			-H-$COCH_3$	3.0	Singlet	
7	33	BZ_9	-10H-Ar-H	7.2-7.7	Multiplet	$CDCl_3$
			-H-CH_3	2.2	Singlet	
			-H-$COCH_3$	3.2	Singlet	
8	34	BZ_{10}	-10H-Ar-H	6.6-7.7	Multiplet	$CDCl_3$
			-H-CH_3	2.2	Singlet	
			-H-$COCH_3$	3.0	Singlet	
			-H-COOH	9.7	Singlet	

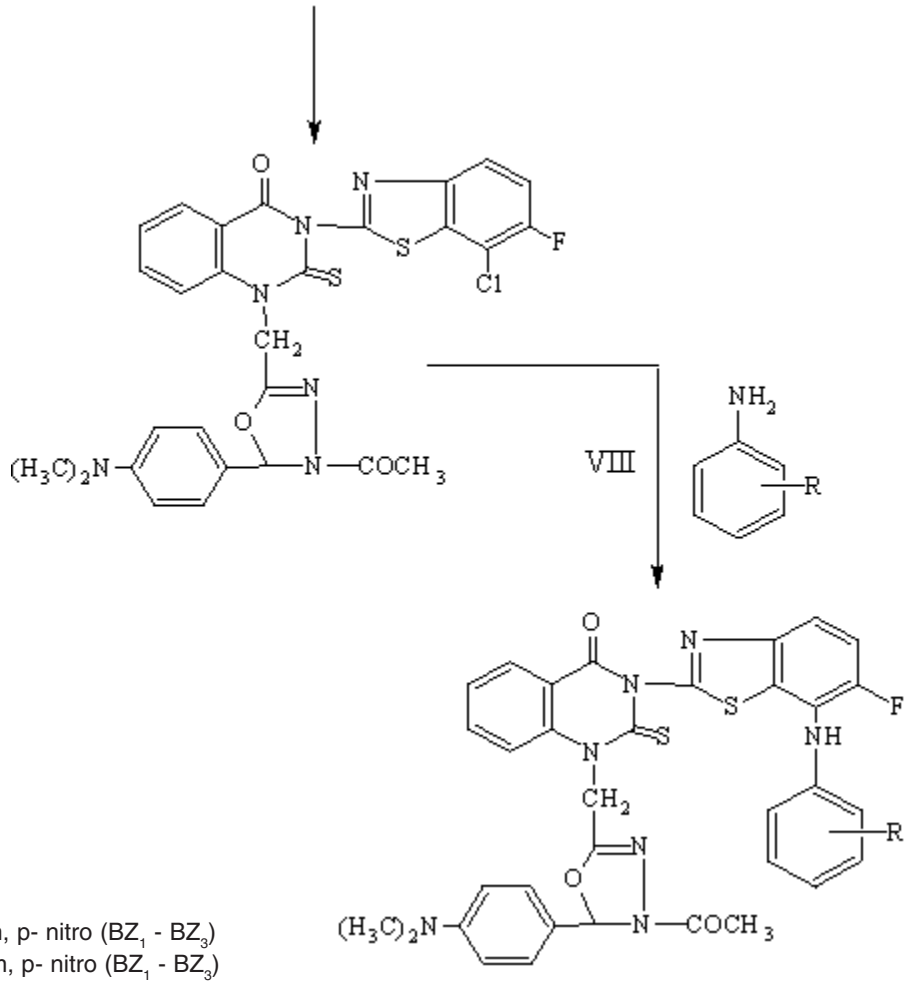
General synthesis of 3-(7-chloro-6-fluoro-1,3-benzothiazol-2-yl)-1-({4-acetyl-5-[4-(dimethylamino)phenyl]-4,5-dihydro-1,3,4-oxadiazol-2-yl}methyl)-2-thioxo-2,3-dihydroquinazoline-4(1H)-one

A mixture of step VI (0.005 mole) and acetic anhydride (10ml) was refluxed for 4 hours. The excess acetic anhydride was distilled off and the residue was poured into ice cold water. The solid was filtered and recrystallised from ethanol-DMF.

General synthesis of 3- { (6- fluoro -7-(substituted) -1,3- benzothiazole -2-yl}-1-({4-acetyl-5-[4-(dimethylamino)phenyl]-4,5-dihydro-1,3,4-oxadiazol-2-yl}methyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one

The Product of step VII (0.003 mole) was treated with equimolar quantity (0.003 mole) of various substituted aromatic anilines like nitro aniline, chloro aniline, PABA, anisidine etc. in presence of DMF (dimethyl formamide, 30 ml) and refluxed for 2 hours on an oil bath. The reaction





R = o, m, p- nitro (BZ_1 - BZ_3)
= o, m, p- nitro (BZ_1 - BZ_3)
= 2,3 -dichloro (BZ_7)
= 3,4- dichloro (BZ_8)
= o- anisidine (BZ_9)
= PABA (BZ_{10})

Scheme 2

mixture was cooled and then poured into crushed ice. The solid separated was filter off, dried and recrystallised from benzene and absolute alcohol (1:1).

RESULTS AND DISCUSSION

Anti-bacterial activity

Synthesis and Pharmacological screening of 3-{6-fluoro-7-(substituted)-1,3-benzothiazol -2-yl}-1-[(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl]-2-thioxo-2,3-dihydroquinazolin-4(1H)-one and 3-{(6- fluoro-7-(substituted) -1,3-benzothiazol-2-yl}-1-({4-acetyl-5-[4-(dimethylamino)phenyl]-4,5-dihydro-1,3,4-oxadiazol-2-yl}methyl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one were tested for the antibacterial activity against following bacterias;

a) (i) *S.aureus*,
   (ii) *Streptococci* (gram +ve*)* and
b) (iii) *E.coli*,
   (iv) *Pseudomonas aureus* (gram –ve).

The test compounds AP_3, AP_4, AP_7, AP_{10} and BZ_1, BZ_4, BZ_7, BZ_9 showed moderate antibacterial activity against *S.aureus* (gram +ve) compare to standard drug Procaine Penicillin.

Compounds AP_1, AP_2, AP_5, and BZ_4, BZ_8, BZ_9 showed promising antibacterial activity against, *E. coli* (gram –ve) compared to standard drugs and streptomycin.

Compounds AP_1, AP_3, AP_6, AP_9, and BZ_3, BZ_5, BZ_7, BZ_8 showed promising antibacterial activity against, gram +ve (*Streptococci*) at both lower and higher concentration (50 µg/ml and 100 µg/ml).

Compound AP_4, AP_6 AP_7, AP_{10} and BZ_2, BZ_4 BZ_5 showed moderate activity against gm –ve (*Pseudomonas aureus*) at both lower and higher concentration compare to standard drug Streptomycin.

Table 4: Antibacterial activity

S. No.	Name of the compounds	Mean zone of inhibition (in mm)*			
		Staphylococcus aureus		*Escherichia coli*	
		50µg	100µg	50µg	100µg
1.	Procaine penicillin	20	24	-	-
2.	Streptomycin	-	-	20	25
3.	AP_1	13 (0.65)	16 (0.66)	14 (0.70)	18 (0.72)
4.	AP_2	14 (0.70)	15 (0.62)	14 (0.70)	17 (0.68)
5.	AP_3	14 (0.70)	19 (0.79)	13 (0.65)	16 (0.64)
6.	AP_4	17 (0.85)	18 (0.75)	12 (0.60)	15 (0.60)
7.	AP_5	12 (0.60)	17 (0.70)	15 (0.75)	18 (0.72)
8.	AP_6	14 (0.70)	17 (0.70)	13 (0.65)	15 (0.60)
9.	AP_7	15 (0.75)	19 (0.79)	12 (0.60)	16 (0.64)
10.	AP_8	13 (0.65)	16 (0.66)	12 (0.60)	15 (0.60)
11.	AP_9	15 (0.75)	18 (0.75)	14 (0.70)	15 (0.60)
12.	AP_{10}	16 (0.80)	18 (0.75)	13 (0.65)	16 (0.64)
13.	BZ_1	14 (0.70)	18 (0.75)	13 (0.65)	16 (0.64)
14.	BZ_2	12 (0.60)	16 (0.66)	12 (0.60)	17 (0.68)
15.	BZ_3	14 (0.70)	17 (0.70)	13 (0.65)	15 (0.60)
16.	BZ_4	16 (0.80)	16 (0.66)	14 (0.70)	16 (0.64)
17.	BZ_5	14 (0.70)	18 (0.75)	11 (0.55)	15 (0.60)
18.	BZ_6	15 (0.75)	17 (0.70)	13 (0.65)	16 (0.64)
19.	BZ_7	14 (0.70)	19 (0.79)	11 (0.55)	15 (0.60)
20.	BZ_8	15 (0.75)	17 (0.70)	13 (0.65)	18 (0.72)
21.	BZ_9	17 (0.85)	17 (0.70)	14 (0.70)	17 (0.68)
22.	BZ_{10}	13 (0.65)	18 (0.75)	12 (0.60)	15 (0.60)

$$^{*}\text{Activity Index} = \frac{\text{Test Compound}}{\text{Standard Compound}}$$

Anti-fungal activity

The above screened compounds were tested for antifungal activity against *Candida albicans* and *Aspergillus niger*.

Among the compounds tested; AP_2, AP_5, AP_9 and BZ_2, BZ_3 showed good activity against *Candida albicans* at both concentrations compare to standard Griseofulvin.

AP_4, AP_5, AP_7, AP_{10}, and BZ_5, BZ_7, BZ_9 showed significant activity against *Aspergillus niger* compared to standard Griseofulvin.

Table 5: Antibacterial activity

S. No.	Name of the compounds	Mean zone of inhibition (in mm)* *Streptococci*		*Pseudomonas aureus*	
		50µg	100µg	50µg	100µg
1.	Procaine penicillin	20	24	-	-
2.	Streptomycin	-	-	20	23
3.	AP_1	13 (0.65)	18 (0.75)	14 (0.70)	16 (0.69)
4.	AP_2	14 (0.70)	15 (0.62)	13 (0.65)	16 (0.69)
5.	AP_3	16 (0.80)	17 (0.70)	14 (0.70)	17 (0.73)
6.	AP_4	13 (0.65)	16 (0.66)	15 (0.75)	19 (0.79)
7.	AP_5	14 (0.70)	16 (0.66)	13 (0.65)	15 (0.65)
8.	AP_6	13 (0.65)	19 (0.79)	16 (0.80)	17 (0.73)
9.	AP_7	12 (0.60)	15 (0.62)	13 (0.65)	18 (0.78)
10.	AP_8	14 (0.70)	17 (0.70)	13 (0.65)	16 (0.69)
11.	AP_9	15 (0.75)	18 (0.75)	14 (0.70)	16 (0.69)
12.	AP_{10}	13 (0.65)	15 (0.62)	15 (0.75)	18 (0.78)
13.	BZ_1	14 (0.70)	17 (0.70)	12 (0.60)	16 (0.69)
14.	BZ_2	14 (0.70)	17 (0.70)	15 (0.75)	18 (0.78)
15.	BZ_3	16 (0.80)	19 (0.79)	14 (0.70)	17 (0.73)
16.	BZ_4	13 (0.65)	16 (0.66)	16 (0.80)	15 (0.65)
17.	BZ_5	13 (0.65)	18 (0.75)	15 (0.75)	19 (0.79)
18.	BZ_6	14 (0.70)	18 (0.75)	13 (0.65)	17 (0.73)
19.	BZ_7	16 (0.80)	16 (0.66)	13 (0.65)	16 (0.69)
20.	BZ_8	15 (0.75)	16 (0.64)	14 (0.70)	15 (0.65)
21.	BZ_9	13 (0.65)	17 (0.70)	13 (0.65)	15 (0.65)
22.	BZ_{10}	11 (0.55)	15 (0.62)	13 (0.65)	16 (0.69)

$$*\text{Activity Index} = \frac{\text{Test Compound}}{\text{Standard Compound}}$$

Table 6: Antifungal activity

S No.	Name of the coompounds	Mean zone of inhibition (in mm)*			
		Candida albicans		*Aspergillus niger*	
		50µg	100µg	50µg	100µg
1.	Griseofulvin	20	25	20	25
2.	AP_1	12 (0.60)	15 (0.60)	11 (0.55)	15 (0.60)
3.	AP_2	14 (0.70)	18 (0.72)	13 (0.65)	16 (0.64)
4.	AP_3	13 (0.65)	17 (0.68)	12 (0.60)	15 (0.60)
5.	AP_4	13 (0.65)	17 (0.68)	14 (0.70)	19 (0.76)
6.	AP_5	15 (0.75)	16 (0.64)	15 (0.75)	18 (0.72)
7.	AP_6	12 (0.60)	15 (0.60)	12 (0.60)	17 (0.68)
8.	AP_7	10 (0.50)	14 (0.56)	16 (0.80)	16 (0.64)
9.	AP_8	11 (0.55)	13 (0.52)	13 (0.65)	19 (0.76)
10.	AP_9	11 (0.55)	14 (0.56)	12 (0.60)	16 (0.64)
11.	AP_{10}	13 (0.65)	15 (0.60)	15 (0.75)	14 (0.56)
12.	BZ_1	12 (0.60)	16 (0.64)	11 (0.55)	16 (0.64)
13.	BZ_2	14 (0.70)	17 (0.68)	12 (0.60)	13 (0.52)
14.	BZ_3	14 (0.70)	18 (0.72)	12 (0.60)	16 (0.64)
15.	BZ_4	10 (0.50)	15 (0.60)	14 (0.70)	15 (0.60)
16.	BZ_5	12 (0.60)	13 (0.52)	13 (0.65)	19 (0.76)
17.	BZ_6	11 (0.55)	14 (0.56)	14 (0.70)	15 (0.60)
18.	BZ_7	13 (0.65)	16 (0.64)	10 (0.50)	18 (0.72)
19.	BZ_8	13 (0.65)	15 (0.60)	11 (0.55)	15 (0.60)
20.	BZ_9	10 (0.50)	13 (0.52)	15 (0.75)	18 (0.72)
21.	BZ_{10}	12 (0.60)	14 (0.56)	13 (0.65)	17 (0.68)

$$*\text{Activity Index} = \frac{\text{Test Compound}}{\text{Standard Compound}}$$

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