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Synthesis and antimicrobial activity of pyrazolyl-quinazolin-4(3*H*)ones

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Abstract

A series of 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-(5-substituted phenyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino)-6-iodoquinazolin-4(3*H*)ones 6a-m were synthesized from 2-[2-(2,6-dichlorophenyl)amino]phenyl acetyl chloride 1 by literature procedure, involved various steps. Acid chloride 1 on cyclization reaction with 5-iodoanthranilic acid yielded 2-[2-(2,6-dichlorophenyl)amino]benzyl-6-iodo-3,1-benzoxazin-4(3*H*)one 2, which on reaction with hydrazine hydrate and then with acetyl chloride afforded 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-acetamido-6-iodoquinazolin-4(3*H*)one 4. The chalcones 5a-m were synthesized by the condensation of compound 4 with different substituted aromatic aldehydes. Finally the reaction of chalcones 5a-m with phenyl hydrazine yielded the title compounds 6a-m. The structures of these compounds have been elucidated by elemental analyses, IR and NMR spectral data. The title compounds pyrazolyl-quinazolin-4(3*H*)ones 6a-m were evaluated for their antibacterial and antifungal activities.

Keywords: Quinazolin-4(3*H*)one, chalcone, pyrazole, antimicrobial activity.

Introduction

Quinazolinone derivatives substituted by different heterocyclic moieties at 3rd position of this heterocyclic system have attracted the attention of medicinal chemists due to their wide range of biological activities as antibacterial, antifungal, analgesic, anti-inflammatory, anthelminthic, anticonvulsant, anti HIV, antitubercular, antiviral, CNS depressant, diuretic and hypolipidemic [1-11]. Pyrazoline system are known to be biologically active and are important constituents of many pharmacological and agrochemical products. These compounds are known for their antibacterial, antifungal, anti-inflammatory, analgesic, antitumor, insecticidal, anti-arthritic, antidepressant, muscle relaxant and anticonvulsant properties [12-20]. In the present work, we have synthesize a series of pyrazolyl-quinazolin-4(3*H*)ones **6a-m** for antimicrobial screening and calculates its potency [21]. The potency of compounds **6a-m** was compared with standard drugs to study the strength of compounds **6a-m**, with a hope to get a better antimicrobial agent.

Results and Discussion

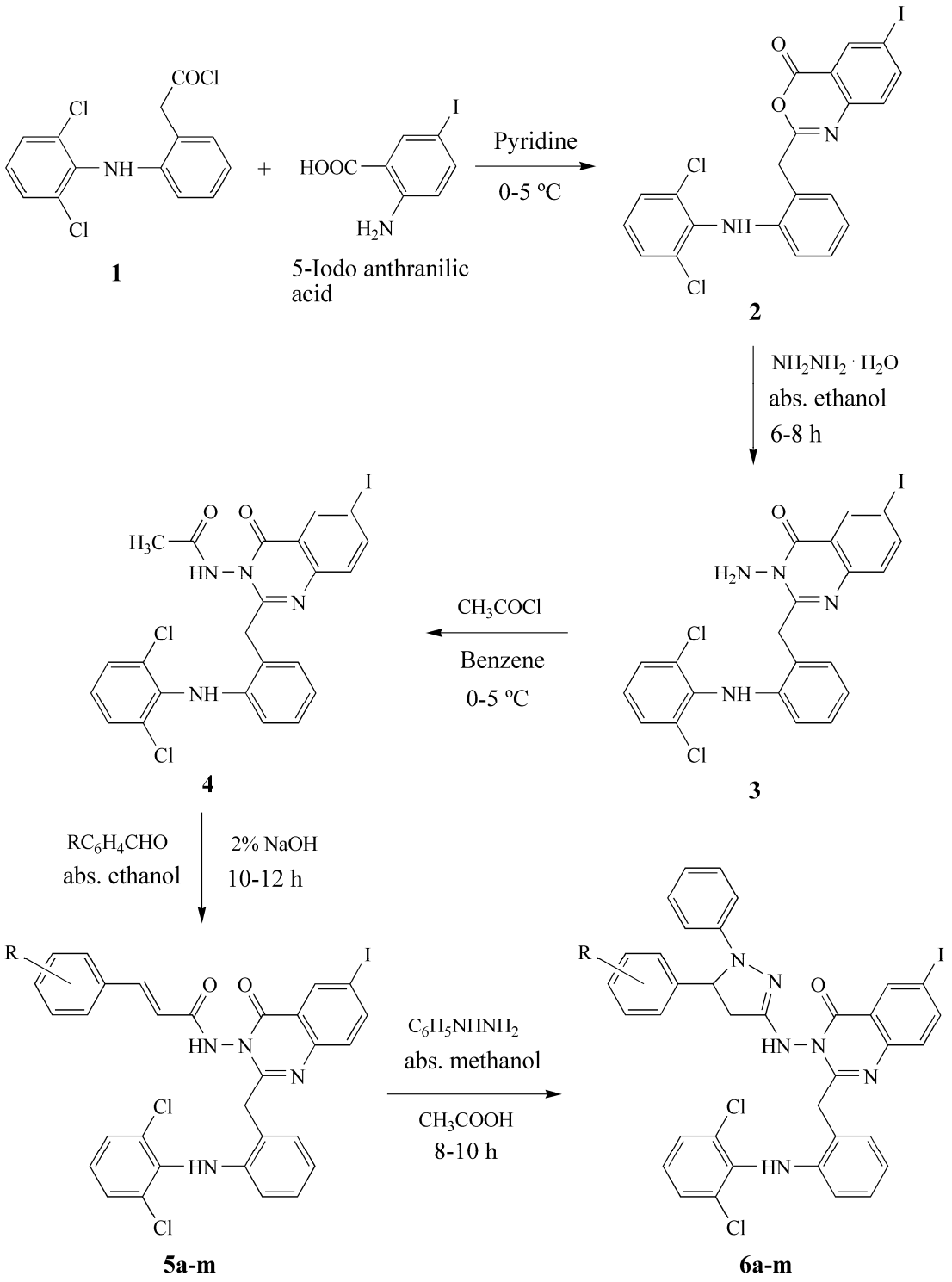
The title compounds 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-(5-substituted phenyl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl-amino)-6-iodoquinazolin-4(3*H*)ones **6a-m** were synthesized according to described process in **Scheme I**. The structures attributed to the compounds **2**, **3**, **4** and **5a-m** were supported by the elemental analysis as well as the IR and NMR spectra. IR spectra showed strong C=O and C=N stretching of quinazolinone at around 1720 cm^{-1} and 1610 cm^{-1}. The ^{1}H NMR spectra of pyrazolines **6a-m** showed the three characteristic signals due to diasteriotopic protons Ha, Hb and Hx. The Ha proton which is *cis* to Hx resonates upfield in the range δ 3.02-3.07 as a double of doublet while Hb, the other proton which is *trans* to Hx resonates downfield in the range δ 3.42-3.51 as a double of doublet. The Hx proton which is vicinal to two methylene protons (Ha and Hb) resonates as a double of doublet in the range δ 5.43-5.53. In ^{13}C NMR spectrum, signals at around δ 35, δ 55 and δ 161 confirms the presence of CH_2, CH and C=N of pyrazoline ring respectively, whereas C=O and C=N signals of quinazolinone ring are appear at around δ 162 and δ 168 respectively.

The results of *in vitro* antibacterial activity of compounds **6a-m** are shown in Table 1. Compound **6a** showed good activity against two gram positive bacteria, *S. aureus* and *B. subtilis* having 62.76 % and 65.85 % potency as compared to penicillin-G. Compound **6i** displayed good activity against two gram negative bacteria, *E. coli* and *Certium* having 69.87 % and 74.50 % potency as compared to penicillin-G. On the other hand compounds **6a** and **6g** were found inactive towards both gram negative bacteria. The remaining compounds possessed moderate activities against both gram positive as well as gram negative bacteria.

Table 1: Antibacterial activity of compounds 6a-m

Comd.	R	Zone of inhibition (mm)											
		S. aureus			*B. subtilis*			*E. coli*			*Certium*		
		C_H	C_L	Pot. %	C_H	C_L	Pot. %	C_H	C_L	Pot. %	C_H	C_L	Pot. %
6a	H	18	14	62.76	18	15	65.85	07	0	0	07	0	0
6b	2-OH	10	08	38.14	10	08	39.04	12	10	40.09	11	09	41.94
6c	3-OH	13	11	44.59	13	11	47.13	14	12	44.64	13	11	46.91
6d	4-OH	11	09	40.18	11	09	41.58	11	09	38.01	10	08	39.66
6e	2-Cl	09	07	36.20	10	08	39.04	11	09	38.01	10	08	39.66
6f	3-Cl	09	07	36.20	09	07	36.67	10	08	35.99	09	07	37.50
6g	4-Cl	10	08	38.14	10	08	39.04	06	0	0	07	0	0
6h	2-NO_2	16	13	55.29	15	12	55.69	16	13	52.46	15	13	52.48
6i	3-NO_2	14	12	46.97	13	11	47.13	22	19	69.87	21	18	74.50
6j	4-NO_2	15	12	52.82	15	12	55.69	15	13	47.11	14	12	49.63
6k	4-$N(CH_3)_2$	10	08	38.14	10	08	39.04	10	08	35.99	10	08	39.66
6l	2-OCH_3	12	10	42.33	12	10	44.26	16	13	52.46	15	13	52.48
6m	4-OCH_3	12	10	42.33	13	11	47.13	16	13	52.46	15	13	52.48
Penicillin		30	25	100	27	21	100	31	25	100	28	23	100

C_H = Zone of inhibition at 100 µg/ml, C_L = Zone of inhibition at 50 µg/ml, Pot. = Potency in %



R = H, 2-OH, 3-OH, 4-OH, 2-Cl, 3-Cl, 4-Cl, 2-NO_2, 3-NO_2, 4-NO_2, 4-$N(CH_3)_2$, 2-OCH_3, 4-OCH_3

Scheme I: Synthetic route for pyrazolyl-quinazolin-4(3*H*)ones 6a-m

The in *vitro* antifungal screening results of compounds **6a-m** are shown in Table 2. Compound **6e** showed good activity against *C. albicans* and *A. niger* having 68.82 % and 61.80 % potency respectively, when compared with fluconazole. In addition compound **6a** showed 61.86 % potency against *C. albicans* as compared to fluconazole. **6m** was found inactive against *C. albicans* and *A. niger*. The remaining compounds of the series showed moderate activities towards both fungal species *C. albicans* and *A. niger*.

Table 2: Antifungal activity of compounds 6a-m

Comd.	R	Zone of inhibition (mm)					
		C. albicans			*A. niger*		
		C_H	C_L	Pot. %	C_H	C_L	Pot. %
6a	H	16	13	61.86	15	12	54.08
6b	2-OH	12	10	46.68	11	09	40.53
6c	3-OH	10	08	41.30	09	07	35.96
6d	4-OH	11	09	43.89	10	08	38.19
6e	2-Cl	18	15	68.82	17	13	61.80
6f	3-Cl	14	12	52.71	13	11	45.75
6g	4-Cl	15	12	54.34	14	12	48.59
6h	2-NO_2	14	12	52.71	13	11	45.75
6i	3-NO_2	12	10	46.68	11	09	40.53
6j	4-NO_2	13	11	49.60	12	10	43.08
6k	4-$N(CH_3)_2$	14	12	52.71	13	11	45.75
6l	2-OCH_3	09	07	38.86	08	06	33.87
6m	4-OCH_3	07	0	0	07	0	0
Fluconazole		26	21	100	28	22	100

C_H = Zone of inhibition at 20µg/ml, C_L = Zone of inhibition at 10µg/ml, Pot. = Potency in %

Material and Methods

Chemistry

The Melting points were determined in open capillary tubes and are uncorrected. The IR spectra of the synthesized compounds were recorded on Perkin Elmer 1300 FTIR spectrometer using KBr pellets and frequencies are recorded in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker Avance II 400 NMR spectrometer using $CDCl_3$ as a solvent. The chemical shifts are reported in δ (ppm) downfield from tetramethylsilane (TMS). All the compounds gave satisfactory chemical analysis. The purities of all the compounds were checked by TLC on Merck silica gel 60 F254 using toluene:ethylacetate (8:2) as mobile phase and spots were visualized under UV radiation. 2-[(2,6-Dichlorophenyl)amino]phenyl acetyl chloride **1** was synthesized by the literature procedure [22].

*Synthesis of 2-[2-(2,6-dichlorophenyl)amino]benzyl-6-iodo-3,1-benzoxazin-4(H)one **2**.*

A mixture of 2-[(2,6-dichlorophenyl)amino]phenyl acetyl chloride (0.01 moles) **1** and 5-iodo anthranilic acid (0.01 moles) in 20ml pyridine was stirred at 0-5 ºC for 1 h, further stirred for 1 h at room temperature. After completion of reaction, a pasty mass obtained, was washed thoroughly with sodium bicarbonate (5 % w/v) to remove unreacted acid. A solid separated was filtered, dried and recrystallized from methanol.

Yield: 58 %. m.p. 189-193 °C. IR (KBr) cm^{-1}: 3450 (NH), 2923, 2848 (CH_2), 1745 (C=O), 1617 (C=N), 1148 (C-O), 747 (C-Cl), 620 (C-I); ^1H NMR ($CDCl_3$): 3.53 (s, 2H, CH_2), 6.40-

8.48 (m, 10H, Ar-H), 9.10 (bs, 1H, NH); Anal. found: C, 48.25; H, 2.46; N, 5.32%; Calc. for $C_{21}H_{13}Cl_2IN_2O_2$, C, 48.21; H, 2.50; N, 5.35%.

*Synthesis of 3-amino-2-[2-(2,6-dichlorophenyl)amino]benzyl-6-iodoquinazolin-4(3H)one **3**.*
A mixture of 2-[2-(2,6-dichlorophenyl)amino]benzyl-6-iodo-3,1-benzoxazine-4(*H*)one (0.01 moles) **2** and hydrazine hydrate (0.01 moles) in 25ml absolute ethanol was refluxed on water bath for 6-8 h. After completion of the reaction, it was slowly poured onto crushed ice cold water with continuous stirring. The solid thus obtained was filtered and washed several times with cold water. The crude product was dried and recrystallized from ethanol.
Yield: 71 %. m.p. 132-134 °C. IR (KBr) cm^{-1}: 3505-3403 (NH and NH_2), 2926, 2851 (CH_2), 1719 (C=O), 1613 (C=N), 752 (C-Cl), 615 (C-I); ^{1}H NMR ($CDCl_3$): 3.51 (s, 2H, CH_2), 5.72 (bs, 2H, NH_2), 6.38-8.32 (m, 10H, Ar-H), 9.18 (s, 1H, NH); Anal. found: C, 46.86; H, 2.85; N, 10.38%; Calc. for $C_{21}H_{15}Cl_2IN_4O$, C, 46.95; H, 2.81; N, 10.43%.

*Synthesis of 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-acetamido-6-iodoquinazolin-4(3H)one **4**.*
To the solution of 3-amino-2-[2-(2,6-dichlorophenyl)amino]benzyl-6-iodoquinazolin-4(3*H*)one (0.01 moles) **3** in 50ml dry benzene, acetyl chloride (0.01 moles) was added drop by drop at 0-5 °C over the period of 1 h with continuous shaking. After completion of the addition, the reaction mixture kept over night. The excess of solvent was distilled off under reduced pressure and then poured onto ice and shake well, the solid thus obtained was filtered and recrystallized from methanol.
Yield: 71 %. m.p. 181-183 °C. IR (KBr) cm^{-1}: 3444 (NH), 2931, 2852 (CH_2), 1723 (C=O), 1634 (C=O of amide), 1611 (C=N), 749 (C-Cl), 607 (C-I); ^{1}H NMR ($CDCl_3$): 2.19 (s, 3H, CH_3), 3.52 (s, 2H, CH_2), 6.41-8.37 (m, 10H, Ar-H), 9.15 (bs, 1H, NH), 10.27 (bs, 1H, NH); Anal. found: C, 47.62; H, 2.93; N, 9.71%; Calc. for $C_{23}H_{17}Cl_2IN_4O_2$, C, 47.69; H, 2.96; N, 9.67%.

General procedure for the synthesis of 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-(substituted phenylacrylamido)-6-iodoquinazolin-4(3H)ones 5a-m.
To the solution of 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-acetamido-6-iodoquinazolin-4(3*H*)one (0.01 moles) **4** in 50ml absolute ethanol, benzaldehyde (0.01 moles) in 2% NaOH was added and refluxed for 10-12 h. After completed the reaction, it was concentrated, cooled and poured onto ice. The solid thus obtained was filtered, washed with water and recrystallized from methanol. The remaining compounds **5b-m** were synthesized by using the same procedure.

*2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(phenylacrylamido)-6-iodoquinazolin-4(3H)one **a***: Yield: 69 %. m.p. 148-150 °C. IR (KBr) cm^{-1}: 3451 (NH), 2934, 2859 (CH_2), 1713 (C=O), 1612 (C=N), 1582 (CH=CH), 747 (C-Cl), 609 (C-I); ^{1}H NMR ($CDCl_3$): 3.52 (s, 2H, CH_2), 6.37-8.30 (m, 15H, Ar-H), 6.81 (d, 1H, =CHCO, J = 16.2 Hz), 7.61 (d, 1H, =CH-Ar, J = 16.2 Hz), 8.82 (bs, 1H, NH), 9.19 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.53 (CH_2), 109.37-143.53 (26C, CH=CH and Ar-C), 161.94 (C=O), 168.37 (C=N), 173.15 (CONH); Anal. found: C, 53.99; H, 3.15; N, 8.41%; Calc. for $C_{30}H_{21}Cl_2IN_4O_2$, C, 53.99; H, 3.17; N, 8.40%.

*2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(2-hydroxyphenylacrylamido)-6-iodoquinazolin-4(3H)one **5b***: Yield: 71 %. m.p. 183-185 °C. IR (KBr) cm^{-1}: 3547 (OH), 3443 (NH), 2929, 2855 (CH_2), 1721 (C=O), 1607 (C=N), 1569 (CH=CH), 745 (C-Cl), 610 (C-I); ^{1}H NMR ($CDCl_3$): 3.57 (s, 2H, CH_2), 6.38-8.34 (m, 14H, Ar-H), 6.79 (d, 1H, =CHCO, J = 16 Hz), 7.58 (d, 1H, =CH-Ar, J = 16 Hz), 8.81 (bs, 1H, NH), 9.18 (bs, 1H, NH), 10.37 (bs, 1H, OH); ^{13}C NMR ($CDCl_3$): 30.61 (CH_2), 109.23-155.68 (26C, CH=CH and Ar-C), 161.72 (C=O), 168.42

(C=N), 173.23 (CONH); Anal. found: C, 52.71; H, 3.09; N, 8.21%; Calc. for $C_{30}H_{21}Cl_2IN_4O_3$, C, 52.73; H, 3.10; N, 8.20%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(3-hydroxyphenylacrylamido)-6-iodoquinazolin-4(3H)one ***5c***: Yield: 68 %. m.p. 201-203 °C. IR (KBr) cm^{-1}: 3541 (OH), 3453 (NH), 2931, 2854 (CH_2), 1729 (C=O), 1611 (C=N), 1579 (CH=CH), 750 (C-Cl), 606 (C-I); ^{1}H NMR ($CDCl_3$): 3.52 (s, 2H, CH_2), 5.56 (bs, 1H, OH), 6.37-8.31 (m, 14H, Ar-H), 6.80 (d, 1H, =CHCO, *J* = 16.4 Hz), 7.62 (d, 1H, =CH-Ar, *J* = 16.4 Hz), 8.85 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.65 (CH_2), 109.18-159.32 (26C, CH=CH and Ar-C), 162.14 (C=O), 167.67 (C=N), 172.92 (CONH); Anal. found: C, 52.69; H, 3.08; N, 8.22%; Calc. for $C_{30}H_{21}Cl_2IN_4O_3$, C, 52.73; H, 3.10; N, 8.20%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(4-hydroxyphenylacrylamido)-6-iodoquinazolin-4(3H)one ***5d***: Yield: 73 %. m.p. 217-219 °C. IR (KBr) cm^{-1}: 3545 (OH), 3447 (NH), 2935, 2854 (CH_2), 1718 (C=O), 1608 (C=N), 1580 (CH=CH), 750 (C-Cl), 611 (C-I); ^{1}H NMR ($CDCl_3$): 3.53 (s, 2H, CH_2), 5.57 (bs, 1H, OH), 6.39-8.32 (m, 14H, Ar-H), 6.82 (d, 1H, =CHCO, *J* = 16.4 Hz), 7.61 (d, 1H, =CH-Ar, *J* = 16.4 Hz), 8.78 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.48 (CH_2), 109.26-157.35 (26C, CH=CH and Ar-C), 161.96 (C=O), 167.98 (C=N), 173.48 (CONH); Anal. found: C, 52.72; H, 3.09; N, 8.21%; Calc. for $C_{30}H_{21}Cl_2IN_4O_3$, C, 52.73; H, 3.10; N, 8.20%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(2-chlorophenylacrylamido)-6-iodoquinazolin-4(3H)one ***5e***: Yield: 74 %. m.p. 153-155 °C. IR (KBr) cm^{-1}: 3446 (NH), 2932, 2855 (CH_2), 1719 (C=O), 1613 (C=N), 1583 (CH=CH), 748 (C-Cl), 613 (C-I); ^{1}H NMR ($CDCl_3$): 3.56 (s, 2H, CH_2), 6.38-8.29 (m, 14H, Ar-H), 6.79 (d, 1H, =CHCO, *J* = 16.2 Hz), 7.60 (d, 1H, =CH-Ar, *J* = 16.2 Hz), 8.83 (bs, 1H, NH), 9.15 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 29.82 (CH_2), 108.85-143.34 (26C, CH=CH and Ar-C), 162.09 (C=O), 168.11 (C=N), 173.32 (CONH); Anal. found: C, 51.33; H, 2.87; N, 7.99%; Calc. for $C_{30}H_{20}Cl_3IN_4O_2$, C, 51.34; H, 2.87; N, 7.98%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(3-chlorophenylacrylamido)-6-iodoquinazolin-4(3H)one ***5f***: Yield: 67 %. m.p. 169-171 °C. IR (KBr) cm^{-1}: 3453 (NH), 2925, 2847 (CH_2), 1716 (C=O), 1610 (C=N), 1579 (CH=CH), 749 (C-Cl), 610 (C-I); ^{1}H NMR ($CDCl_3$): 3.53 (s, 2H, CH_2), 6.37-8.32 (m, 14H, Ar-H), 6.84 (d, 1H, =CHCO, *J* = 16 Hz), 7.63 (d, 1H, =CH-Ar, *J* = 16 Hz), 8.81 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 31.18 (CH_2), 109.06-143.45 (26C, CH=CH and Ar-C), 162.05 (C=O), 168.14 (C=N), 173.26 (CONH); Anal. found: C, 51.31; H, 2.86; N, 8.00%; Calc. for $C_{30}H_{20}Cl_3IN_4O_2$, C, 51.34; H, 2.87; N, 7.98%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(4-chlorophenylacrylamido)-6-iodoquinazolin-4(3H)one ***5g***: Yield: 70 %. m.p. 177-179 °C. IR (KBr) cm^{-1}: 3449 (NH), 2931, 2857 (CH_2), 1711 (C=O), 1608 (C=N), 1582 (CH=CH), 741 (C-Cl), 611 (C-I); ^{1}H NMR ($CDCl_3$): 3.55 (s, 2H, CH_2), 6.36-8.30 (m, 14H, Ar-H), 6.79 (d, 1H, =CHCO, *J* = 16.2 Hz), 7.58 (d, 1H, =CH-Ar, *J* = 16.2 Hz), 8.81 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.57 (CH_2), 109.12-143.52 (26C, CH=CH and Ar-C), 162.23 (C=O), 167.68 (C=N), 172.86 (CONH); Anal. found: C, 51.32; H, 2.87; N, 7.99%; Calc. for $C_{30}H_{20}Cl_3IN_4O_2$, C, 51.34; H, 2.87; N, 7.98%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(2-nitrophenylacrylamido)-6-iodoquinazolin-4(3H)one ***5h***: Yield: 72 %. m.p. 191-193 °C. IR (KBr) cm^{-1}: 3456 (NH), 2934, 2857 (CH_2), 1726 (C=O), 1612 (C=N), 1578 (CH=CH), 1547, 1363 (NO_2), 748 (C-Cl), 607 (C-I); ^{1}H NMR ($CDCl_3$): 3.56 (s, 2H, CH_2), 6.39-8.32 (m, 14H, Ar-H), 6.81 (d, 1H, =CHCO, *J* = 16.4 Hz), 7.60 (d, 1H, =CH-Ar, *J* = 16.4 Hz), 8.84 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$):

30.41 (CH_2), 109.12-148.23 (26C, CH=CH and Ar-C), 162.10 (C=O), 167.97 (C=N), 172.97 (CONH); Anal. found: C, 50.58; H, 2.82; N, 9.85%; Calc. for $C_{30}H_{20}Cl_2IN_5O_4$, C, 50.58; H, 2.83; N, 9.83%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(3-nitrophenylacrylamido)-6-iodoquinazolin-4(3H)one ***5i***: Yield: 69 %. m.p. 211-213 °C. IR (KBr) cm^{-1}: 3451 (NH), 2928, 2853 (CH_2), 1728 (C=O), 1607 (C=N), 1579 (CH=CH), 1540, 1357 (NO_2), 748 (C-Cl), 613 (C-I); ^{1}H NMR ($CDCl_3$): 3.51 (s, 2H, CH_2), 6.36-8.39 (m, 14H, Ar-H), 6.84 (d, 1H, =CHCO, *J* = 16.2 Hz), 7.63 (d, 1H, =CH-Ar, *J* = 16.2 Hz), 8.85 (bs, 1H, NH), 9.19 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.36 (CH_2), 109.21-148.42 (26C, CH=CH and Ar-C), 161.93 (C=O), 168.69 (C=N), 172.89 (CONH); Anal. found: C, 50.55; H, 2.81; N, 9.84%; Calc. for $C_{30}H_{20}Cl_2IN_5O_4$, C, 50.58; H, 2.83; N, 9.83%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(4-nitrophenylacrylamido)-6-iodoquinazolin-4(3H)one ***5j***: Yield: 66 %. m.p. 237-239 °C. IR (KBr) cm^{-1}: 3448 (NH), 2934, 2858 (CH_2), 1725 (C=O), 1605 (C=N), 1582 (CH=CH), 1541, 1360 (NO_2), 751 (C-Cl), 612 (C-I); ^{1}H NMR ($CDCl_3$): 3.57 (s, 2H, CH_2), 6.38-8.34 (m, 14H, Ar-H), 6.81 (d, 1H, =CHCO, *J* = 16.4 Hz), 7.62 (d, 1H, =CH-Ar, *J* = 16.4 Hz), 8.81 (bs, 1H, NH), 9.16 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.54 (CH_2), 109.17-146.26 (26C, CH=CH and Ar-C), 162.25 (C=O), 167.98 (C=N), 173.15 (CONH); Anal. found: C, 50.57; H, 2.81; N, 9.84%; Calc. for $C_{30}H_{20}Cl_2IN_5O_4$, C, 50.58; H, 2.83; N, 9.83%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(4-dimethylaminophenylacrylamido)-6-iodoquinazolin-4(3H)one ***5k***: Yield: 69 %. m.p. 173-176°C. IR (KBr) cm^{-1}: 3447 (NH), 2932, 2857 (CH_2), 1717 (C=O), 1611 (C=N), 1578 (CH=CH), 751 (C-Cl), 613 (C-I); ^{1}H NMR ($CDCl_3$): 2.82 (s, 6H, $N(CH_3)_2$), 3.53 (s, 2H, CH_2), 6.36-8.31 (m, 14H, Ar-H), 6.79 (d, 1H, =CHCO, *J* = 16.2 Hz), 7.58 (d, 1H, =CH-Ar, *J* = 16.2 Hz), 8.79 (bs, 1H, NH), 9.14 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.38 (CH_2), 46.57 (N-(CH_3)$_2$), 109.02-148.12 (26C, CH=CH and Ar-C), 162.23 (C=O), 168.08 (C=N), 173.24 (CONH); Anal. found: C, 54.09; H, 3.67; N, 9.87%; Calc. for $C_{32}H_{26}Cl_2IN_5O_2$, C, 54.10; H, 3.69; N, 9.86%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(2-methoxyphenylacrylamido)-6-iodoquinazolin-4(3H)one ***5l***: Yield: 65 %. m.p. 166-168 °C. IR (KBr) cm^{-1}: 3451 (NH), 2926, 2849 (CH_2), 1721 (C=O), 1614 (C=N), 1579 (CH=CH), 1243, 1106 (C-O-C), 750, (C-Cl), 605 (C-I); ^{1}H NMR ($CDCl_3$): 3.54 (s, 2H, CH_2), 3.67 (s, 3H, OCH_3), 6.37-8.29 (m, 14H, Ar-H), 6.83 (d, 1H, =CHCO, *J* = 16 Hz), 7.64 (d, 1H, =CH-Ar, *J* = 16 Hz), 8.81 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 31.62 (CH_2), 61.06 (OCH_3), 109.22-156.17 (26C, CH=CH and Ar-C), 162.20 (C=O), 167.61 (C=N), 173.32 (CONH); Anal. found: C, 53.38; H, 3.31; N, 8.04%; Calc. for $C_{31}H_{23}Cl_2IN_4O_3$, C, 53.39; H, 3.32; N, 8.03%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(4-methoxyphenylacrylamido)-6-iodoquinazolin-4(3H)one ***5m***: Yield: 69 %. m.p. 182-184 °C. IR (KBr) cm^{-1}: 3443 (NH), 2924, 2850 (CH_2), 1711 (C=O), 1612 (C=N), 1582 (CH=CH), 1240, 1105 (C-O-C), 748 (C-Cl), 609 (C-I); ^{1}H NMR ($CDCl_3$): 3.52 (s, 2H, CH_2), 3.64 (s, 3H, OCH_3), 6.36-8.31 (m, 14H, Ar-H), 6.81 (d, 1H, =CHCO, *J* = 16.2 Hz), 7.59 (d, 1H, =CH-Ar, *J* = 16.2 Hz), 8.78 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.65 (CH_2), 59.34 (OCH_3), 109.19-158.24 (26C, CH=CH and Ar-C), 162.17 (C=O), 168.23 (C=N), 173.28 (CONH); Anal. found: C, 53.39; H, 3.30; N, 8.05%; Calc. for $C_{31}H_{23}Cl_2IN_4O_3$, C, 53.39; H, 3.32; N, 8.03%.

General procedure for the synthesis of 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-(5-substituted-phenyl-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino)-6-iodoquinazolin-(3H)ones 6a-m.

A mixture of 2-[2-(2,6-dichlorophenyl)amino]benzyl-3-(phenylacrylamido)-6-iodoquinazolin-4(3*H*)one (0.01moles) **5a**, phenyl hydrazine (0.01 moles) in 30ml absolute methanol was added few drops of glacial acetic acid and refluxed for 8-10 h. After completion of the reaction, excess of solvent was distilled off; the separated solid was filtered, washed with water and recrystallized from methanol. Similarly other pyrazolyl derivatives **6b-m** were synthesized.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-(1,5-diphenyl-4,5-dihydro-1H-pyrazol-3-yl-amino)-6-iodoquinazolin-4(3H)one ***6a***: Yield: 65 %. m.p. 110-112 °C. IR (KBr) cm^{-1}: 3449 (NH), 2933, 2857 (CH_2), 1715 (C=O), 1604 (C=N), 751 (C-Cl), 602 (C-I); ^{1}H NMR ($CDCl_3$): 3.05 (dd, 1H, Ha, $J_{a,b}$ = 17.5 Hz, J_{ax} = 5.4 Hz), 3.46 (dd, 1H, Hb, J_{ba} = 17.5 Hz, J_{bx} = 12 Hz), 3.59 (s, 2H, CH_2), 5.51 (dd, 1H, Hx, J_{xb} = 12 Hz, J_{xa} = 5.4 Hz), 6.38-8.29 (m, 20H, Ar-H), 8.34 (bs, 1H, NH), 9.19 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.53 (CH_2), 36.45 (CH_2 of pyrazole), 55.6 (CH of pyrazole), 109.32-143.49 (30C, Ar-C), 161.13 (C=N of pyrazole), 162.17 (C=O), 168.48 (C=N); Anal. found: C, 57.06; H, 3.58; N, 11.11%; Calc. for $C_{36}H_{27}Cl_2IN_6O$, C, 57.08; H, 3.59; N, 11.10%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(2-hydroxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6b***: Yield: 64 %. m.p. 141-143 °C. IR (KBr) cm^{-1}: 3546 (OH), 3450 (NH), 2931, 2856 (CH_2), 1729 (C=O), 1604 (C=N), 741 (C-Cl), 611 (C-I); ^{1}H NMR ($CDCl_3$): 3.03 (dd, 1H, Ha, $J_{a,b}$ = 17.4 Hz, J_{ax} = 5.4 Hz), 3.42 (dd, 1H, Hb, J_{ba} = 17.4 Hz, J_{bx} = 11.8 Hz), 3.60 (s, 2H, CH_2), 5.47 (dd, 1H, Hx, J_{xb} = 11.8 Hz, J_{xa} = 5.4 Hz), 6.40-8.32 (m, 19H, Ar-H), 8.37 (bs, 1H, NH), 9.17 (bs, 1H, NH), 10.35 (bs, 1H, OH); ^{13}C NMR ($CDCl_3$): 30.48 (CH_2), 35.47 (CH_2 of pyrazole), 55.58 (CH of pyrazole), 109.13-155.63 (30C, Ar-C), 161.23 (C=N of pyrazole), 162.12 (C=O), 168.34 (C=N); Anal. found: C, 55.88; H, 3.50; N, 10.85%; Calc. for $C_{36}H_{27}Cl_2IN_6O_2$, C, 55.90; H, 3.52; N, 10.87%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(3-hydroxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6c***: Yield: 67 %. m.p. 153-155 °C. IR (KBr) cm^{-1}: 3537 (OH), 3451 (NH), 2933, 2857 (CH_2), 1730 (C=O), 1601 (C=N), 751 (C-Cl), 611 (C-I); ^{1}H NMR ($CDCl_3$): 3.07 (dd, 1H, Ha, $J_{a,b}$ = 17.7 Hz, J_{ax} = 5.5 Hz), 3.48 (dd, 1H, Hb, J_{ba} = 17.7 Hz, J_{bx} = 12 Hz), 3.53 (s, 2H, CH_2), 5.49 (dd, 1H, Hx, J_{xb} = 12 Hz, J_{xa} = 5.5 Hz), 5.58 (bs, 1H, OH), 6.36-8.30 (m, 19H, Ar-H), 8.38 (bs, 1H, NH), 9.16 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 31.28 (CH_2), 36.52 (CH_2 of pyrazole), 54.91 (CH of pyrazole), 109.26-159.15 (30C, Ar-C), 161.15 (C=N of pyrazole), 162.39 (C=O), 167.98 (C=N); Anal. found: C, 55.94; H, 3.54; N, 10.84%; Calc. for $C_{36}H_{27}Cl_2IN_6O_2$, C, 55.90; H, 3.52; N, 10.87%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(4-hydroxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6d***: Yield: 69 %. m.p. 168-170 °C. IR (KBr) cm^{-1}: 3542 (OH), 3449 (NH), 2937, 2852 (CH_2), 1727 (C=O), 1603 (C=N), 751 (C-Cl), 616 (C-I); ^{1}H NMR ($CDCl_3$): 3.06 (dd, 1H, Ha, $J_{a,b}$ = 17.5 Hz, J_{ax} = 5.5 Hz), 3.45 (dd, 1H, Hb, J_{ba} = 17.5 Hz, J_{bx} = 11.7 Hz), 3.51 (s, 2H, CH_2), 5.48 (dd, 1H, Hx, J_{xb} = 11.7 Hz, J_{xa} = 5.5 Hz), 5.59 (bs, 1H, OH), 6.38-8.29 (m, 19H, Ar-H), 8.35 (bs, 1H, NH), 9.19 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.63 (CH_2), 36.55 (CH_2 of pyrazole), 55.69 (CH of pyrazole), 109.17-157.13 (30C, Ar-C), 161.32 (C=N of pyrazole), 162.14 (C=O), 168.19 (C=N); Anal. found: C, 55.87; H, 3.51; N, 10.89%; Calc. for $C_{36}H_{27}Cl_2IN_6O_2$, C, 55.90; H, 3.52; N, 10.87%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(2-chlorophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6e***: Yield: 72 %. m.p. 119-120 °C. IR (KBr) cm^{-1}: 3449 (NH), 2933, 2857(CH_2), 1715 (C=O), 1604 (C=N), 751 (C-Cl), 602 (C-I); ^{1}H NMR ($CDCl_3$): 3.05 (dd, 1H, Ha, $J_{a,b}$ = 17.7 Hz, J_{ax} = 5.6 Hz), 3.48 (dd, 1H, Hb, J_{ba} = 17.7 Hz, J_{bx} = 11.9 Hz), 3.56 (s, 2H, CH_2), 5.47 (dd, 1H, Hx, J_{xb} = 11.9 Hz, J_{xa} = 5.6 Hz), 6.40-8.31 (m, 19H, Ar-H), 8.38 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 29.95 (CH_2), 36.26 (CH_2 of pyrazole), 56.51 (CH of pyrazole), 108.92-143.25 (30C, Ar-C), 160.96 (C=N of pyrazole), 162.33 (C=O), 168.24 (C=N); Anal. found: C, 54.56; H, 3.29; N, 10.57%; Calc. for $C_{36}H_{26}Cl_3IN_6O$, C, 54.60; H, 3.31; N, 10.61%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(3-chlorophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6f***: Yield: 67 %. m.p. 127-129 °C. IR (KBr) cm^{-1}: 3450 (NH), 2925, 2850 (CH_2), 1717 (C=O), 1607 (C=N), 748 (C-Cl), 611 (C-I); ^{1}H NMR ($CDCl_3$): 3.06 (dd, 1H, Ha, $J_{a,b}$ = 17.7 Hz, J_{ax} = 5.5 Hz), 3.47 (dd, 1H, Hb, J_{ba} = 17.7 Hz, J_{bx} = 12 Hz), 3.54 (s, 2H, CH_2), 5.53 (dd, 1H, Hx, J_{xb} = 12 Hz, J_{xa} = 5.5 Hz), 6.39-8.30 (m, 19H, Ar-H), 8.37 (bs, 1H, NH), 9.19 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 31.29 (CH_2), 36.45 (CH_2 of pyrazole), 55.16 (CH of pyrazole), 109.13-143.38 (30C, Ar-C), 161.28 (C=N of pyrazole), 162.25 (C=O), 168.31 (C=N); Anal. found: C, 54.55; H, 3.34; N, 10.65%; Calc. for $C_{36}H_{26}Cl_3IN_6O$, C, 54.60; H, 3.31; N, 10.61%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(4-chlorophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6g***: Yield: 72 %. m.p. 146-148 °C. IR (KBr) cm^{-1}: 3448 (NH), 2930, 2856 (CH_2), 1714 (C=O), 1605 (C=N), 747 (C-Cl), 607 (C-I); ^{1}H NMR ($CDCl_3$): 3.07 (dd, 1H, Ha, $J_{a,b}$ = 17.6 Hz, J_{ax} = 5.6 Hz), 3.48 (dd, 1H, Hb, J_{ba} = 17.6 Hz, J_{bx} = 11.8 Hz), 3.57 (s, 2H, CH_2), 5.51 (dd, 1H, Hx, J_{xb} = 11.8 Hz, J_{xa} = 5.6 Hz), 6.37-8.31 (m, 19H, Ar-H), 8.36 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.73 (CH_2), 36.24 (CH_2 of pyrazole), 55.71 (CH of pyrazole), 109.17-143.46 (30C, Ar-C), 161.22 (C=N of pyrazole), 162.34 (C=O), 167.83 (C=N); Anal. found: C, 54.58; H, 3.28; N, 10.57%; Calc. for $C_{36}H_{26}Cl_3IN_6O$, C, 54.60; H, 3.31; N, 10.61%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(2-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6h***: Yield: 69 %. m.p. 149-151 °C. IR (KBr) cm^{-1}: 3450 (NH), 2924, 2851 (CH_2), 1728 (C=O), 1603 (C=N), 1545, 1359 (NO_2), 751 (C-Cl), 610 (C-I); ^{1}H NMR ($CDCl_3$): 3.05 (dd, 1H, Ha, $J_{a,b}$ = 17.7 Hz, J_{ax} = 5.5 Hz), 3.49 (dd, 1H, Hb, J_{ba} = 17.7 Hz, J_{bx} = 12 Hz), 3.57 (s, 2H, CH_2), 5.49 (dd, 1H, Hx, J_{xb} = 12 Hz, J_{xa} = 5.5 Hz), 6.41-8.30 (m, 19H, Ar-H), 8.37 (bs, 1H, NH), 9.19 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.57 (CH_2), 36.42 (CH_2 of pyrazole), 56.29 (CH of pyrazole), 108.91-148.11 (30C, Ar-C), 161.53 (C=N of pyrazole), 162.19 (C=O), 168.16 (C=N); Anal. found: C, 53.81; H, 3.25; N, 12.23%; Calc. for $C_{36}H_{26}Cl_2IN_7O_3$, C, 53.88; H, 3.27; N, 12.22%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(3-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6i***: Yield: 75 %. m.p. 163-165 °C. IR (KBr) cm^{-1}: 3447 (NH), 2928, 2856 (CH_2), 1731 (C=O), 1604 (C=N), 1542, 1361 (NO_2), 749 (C-Cl), 606 (C-I); ^{1}H NMR ($CDCl_3$): 3.03 (dd, 1H, Ha, $J_{a,b}$ = 17.5 Hz, J_{ax} = 5.5 Hz), 3.50 (dd, 1H, Hb, J_{ba} = 17.5 Hz, J_{bx} = 11.8 Hz), 3.58 (s, 2H, CH_2), 5.45 (dd, 1H, Hx, J_{xb} = 11.8 Hz, J_{xa} = 5.5 Hz), 6.37-8.41 (m, 19H, Ar-H), 8.34 (bs, 1H, NH), 9.15 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.48 (CH_2), 36.12 (CH_2 of pyrazole), 55.53 (CH of pyrazole), 109.13-148.54 (30C, Ar-C), 160.93 (C=N of pyrazole), 162.12 (C=O), 168.86 (C=N); Anal. found: C, 53.91; H, 3.29; N, 12.18%; Calc. for $C_{36}H_{26}Cl_2IN_7O_3$, C, 53.88; H, 3.27; N, 12.22%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6j***: Yield: 66 %. m.p. 181-183 °C. IR (KBr) cm^{-1}: 3445 (NH), 2932, 2857 (CH_2), 1730 (C=O), 1605 (C=N), 1543, 1361 (NO_2), 748 (C-Cl), 603 (C-I); ^{1}H NMR ($CDCl_3$): 3.05 (dd, 1H, Ha, $J_{a,b}$ = 17.7 Hz, J_{ax} = 5.6 Hz), 3.47 (dd, 1H, Hb, J_{ba} = 17.7 Hz, J_{bx} = 12 Hz), 3.53 (s, 2H, CH_2), 5.52 (dd, 1H, Hx, J_{xb} = 12 Hz, J_{xa} = 5.6 Hz), 6.40-8.33 (m, 19H, Ar-H), 8.36 (bs, 1H, NH), 9.14 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.66 (CH_2), 36.17 (CH_2 of pyrazole), 55.70 (CH of pyrazole), 109.21-146.11 (30C, Ar-C), 161.21 (C=N of pyrazole), 162.32 (C=O), 168.18 (C=N); Anal. found: C, 53.84; H, 3.25; N, 12.21%; Calc. for $C_{36}H_{26}Cl_2IN_7O_3$, C, 53.88; H, 3.27; N, 12.22%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(4-dimethylaminophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6k***: Yield: 71 %. m.p. 137-139 °C. IR (KBr) cm^{-1}: 3446 (NH), 2922, 2847 (CH_2), 1720 (C=O), 1607 (C=N), 753 (C-Cl), 611 (C-I); ^{1}H NMR ($CDCl_3$): 2.83 (s, 6H, $N(CH_3)_2$), 3.04 (dd, 1H, Ha, $J_{a,b}$ = 17.4 Hz, J_{ax} = 5.4 Hz), 3.50 (dd, 1H, Hb, J_{ba} = 17.4 Hz, J_{bx} = 11.7 Hz), 3.56 (s, 2H, CH_2), 5.53 (dd, 1H, Hx, J_{xb} = 11.7 Hz, J_{xa} = 5.4 Hz), 6.37-8.29 (m, 19H, Ar-H), 8.37 (bs, 1H, NH), 9.16 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.56 (CH_2), 36.23 (CH_2 of pyrazole), 46.43 (N-$(CH_3)_2$), 56.57 (CH of pyrazole), 108.89-147.95 (30C, Ar-C), 161.27 (C=N of pyrazole), 162.31 (C=O), 168.24 (C=N); Anal. found: C, 56.96; H, 4.07; N, 12.21%; Calc. for $C_{38}H_{32}Cl_2IN_7O$, C, 57.01; H, 4.03; N, 12.25%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(2-methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6l***: Yield: 65 %. m.p. 129-131 °C. IR (KBr) cm^{-1}: 3455 (NH), 2927, 2854 (CH_2), 1719 (C=O), 1608 (C=N), 1241, 1109 (C-O-C), 751 (C-Cl), 616 (C-I); ^{1}H NMR ($CDCl_3$): 3.02 (dd, 1H, Ha, $J_{a,b}$ = 17.5 Hz, J_{ax} = 5.5 Hz), 3.45 (dd, 1H, Hb, J_{ba} = 17.5 Hz, J_{bx} = 11.7 Hz), 3.53 (s, 2H, CH_2), 3.66 (s, 3H, OCH_3), 5.43 (dd, 1H, Hx, J_{xb} = 11.7 Hz, J_{xa} = 5.5 Hz), 6.38-8.30 (m, 19H, Ar-H), 8.34 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 31.77 (CH_2), 35.32 (CH_2 of pyrazole), 55.43 (CH of pyrazole), 109.14-156.13 (30C, Ar-C), 161.13 (C=N of pyrazole), 162.36 (C=O), 167.76 (C=N), 61.13 (OCH_3); Anal. found: C, 56.45; H, 3.75; N, 10.65%; Calc. for $C_{37}H_{29}Cl_2IN_6O_2$, C, 56.43; H, 3.71; N, 10.67%.

2-[2-(2,6-Dichlorophenyl)amino]benzyl-3-[5-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino]-6-iodoquinazolin-4(3H)one ***6m***: Yield: 69 %. m.p. 141-143 °C. IR (KBr) cm^{-1}: 3445 (NH), 2925, 2852(C-H), 1715 (C=O), 1603 (C=N), 1237, 1106 (C-O-C), 747 (C-Cl), 607 (C-I); ^{1}H NMR ($CDCl_3$): 3.06 (dd, 1H, Ha, $J_{a,b}$ = 17.7 Hz, J_{ax} = 5.7 Hz), 3.51 (dd, 1H, Hb, J_{ba} = 17.7 Hz, J_{bx} = 12 Hz), 3.57 (s, 2H, CH_2), 3.68 (s, 3H, OCH_3), 5.53 (dd, 1H, Hx, J_{xb} = 12 Hz, J_{xa} = 5.7 Hz), 6.38-8.28 (m, 19H, Ar-H), 8.33 (bs, 1H, NH), 9.15 (bs, 1H, NH); ^{13}C NMR ($CDCl_3$): 30.82 (CH_2), 36.47 (CH_2 of pyrazole), 55.56 (CH of pyrazole), 59.29 (OCH_3), 109.12-158.15 (30C, Ar-C), 161.28 (C=N of pyrazole), 162.25 (C=O), 168.27 (C=N); Anal. found: C, 56.40; H, 3.68; N, 10.71%; Calc. for $C_{37}H_{29}Cl_2IN_6O_2$, C, 56.43; H, 3.71; N, 10.67%.

Antimicrobial activity

The *in vitro* antimicrobial activities of compounds **6a-m** were carried out by cup-plate method [23]. Antibacterial activity was screened against two gram positive bacteria (*S. aureus* and *B. subtilis*) and two gram negative bacteria (*E. coli* and *certium*), by measuring the zone of inhibition on agar plates at two different concentrations 100 µg/ml and 50 µg/ml. While antifungal activity was tested by measuring the zone of inhibition on agar plates with two fungal species *C. albicans* and *A. niger* at two different concentrations 20 µg/ml and 10 µg/ml. Penicillin-G was used as a standard antibacterial agent whereas fluconazole was used as a standard antifungal agent.

Conclusion

The screening results revealed that almost all the compounds showed moderate activities towards bacteria and fungi. The compound **6a** (R = H) exhibited good activity against gram positive bacteria while compound **6i** (R = 3-NO_2) showed good activity against gram negative bacteria. Whereas compound **6e** (R = 2-Cl) displayed good activity against fungi.

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