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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

In vitro evaluation of the antibacterial and antifungal activity of some new pyrazolyl-quinazolin-4(3*H*)-one derivatives

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Abstract Several pyrazolyl-quinazolin-4(3*H*)-ones **6a–m** were synthesized by the cyclization of acrylamides **5a–m** with hydrazine hydrate. The overall reaction was carried out by multi step process. The base-catalyzed cyclization of acid chloride **1** with 5-iodo anthranilic acid yielded benzoxazinone **2**, which on reaction with hydrazine hydrate afforded amino quinazolin-4(3*H*)-one **3**. The acrylamides **5a–m** were easily synthesized by acetylation and then condensation with aromatic aldehyde of quinazolin-4(3*H*)-one **3**. The structural confirmation of the synthesized compounds was carried out on the basis of elemental analyses as well as IR and NMR spectral results. The title compound **6a–m** was evaluated for antibacterial and antifungal activity in vitro.

Keywords Acrylamide · Antimicrobial activity · Pyrazole · Quinazolin-4(3*H*)-one

Introduction

The heterocyclic compounds have great importance due to their widespread application in medicinal chemistry. In the family of heterocyclic compounds, nitrogen-containing heterocycles are considered to be an important class of compounds because of their interesting diversified biological properties. One of the most frequently encountered heterocycles in medicinal chemistry is quinazolin-4(3*H*)-one with widespread applications as antibacterial (Gupta *et al.*, 2008), antifungal (Bartroli *et al.*, 1998), analgesic, anti-inflammatory (Alafeefy *et al.*, 2008), antitubercular, anticancer (Raghavendra *et al.*, 2007), antiviral (Selvam *et al.*,2008), anticonvulsant (Micale *et al.*, 2006), CNS depressant (Kashaw *et al.*, 2009), and antihyperglycemic (Ram *et al.*, 2003) therapeutic agent. Among different heterocyclic systems five-member heterocycles represent a class of compounds of biological significance. Pyrazoline is a five-member heterocyclic system known to be a biologically active scaffold and an important constituent of many pharmacological products. These compounds possess antibacterial (Ozdemir *et al.*, 2007), antifungal, antimycobacterial (Zampieri *et al.*, 2008), analgesic (Oruc *et al.*, 2006), anti-inflammatory (Bekhit and Abdel-Aziem 2004), antitumor (Zsoldos-Mady *et al.*, 2006), antiamoebic (Abid and Azam 2005), molluscicidal (Barsoum *et al.*, 2006), antidepressant, anticonvulsant (Ozdemir *et al.*, 2008), and hypotensive (Turan-Zitouni *et al.*, 2000) activities.

In this study, we have synthesized quinazolin-4(3*H*)-one incorporating pyrazoline at 3rd position of quinazolin-4(3*H*)-one and studied its antibacterial and antifungal activities. The potency (Edwin and Marion 1945) of these compounds are calculated and compared with standard drugs to observe the strength of these compounds.

Results and discussion

Chemistry

The title compound pyrazolyl-quinazolin-4(3*H*)-ones **6a–m** was synthesized according to the described process

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in Scheme 1. Base-catalyzed cyclization of acid chloride **1** with 5-iodo anthranilic acid in pyridine at 0–5°C yielded benzoxazinone **2** which showed strong C=O stretching at 1745 cm^{-1}. The benzoxazinone **2** on condensation reaction with hydrazine hydrate and then acetylation with acetyl chloride afforded acetamido quinazolin-4(3*H*)-one **4**. The IR spectra showing strong stretching vibrations at 1727 and 1651 cm^{-1} indicate the presence of C=O group of quinazolinone and acetamide, respectively. This was further confirmed by ^{1}H NMR spectra which showed singlet at δ 2.24 ppm equivalent to three protons of acetamide group. The acetamido quinazolin-4(3*H*)-one **4** on base-catalyzed condensation with aromatic aldehydes yielded acrylamides **5a–m** which showed CH=CH stretching at around 1580 cm^{-1} in IR spectrum while ^{1}H NMR spectra showed doublet of these protons at around δ 6.8 ppm and δ 7.6 ppm with coupling constant $J = 16.0$–16.6 Hz. Further cyclization of acrylamides **5a–m** with hydrazine hydrate yielded the desired compounds pyrazolyl-quinazolin-4(3*H*)-ones **6a–m**. The IR spectra of compounds **6a–m** showed

Scheme 1 Synthesis of pyrazolyl-quinazolin-4(3*H*)-ones **6a–6m**

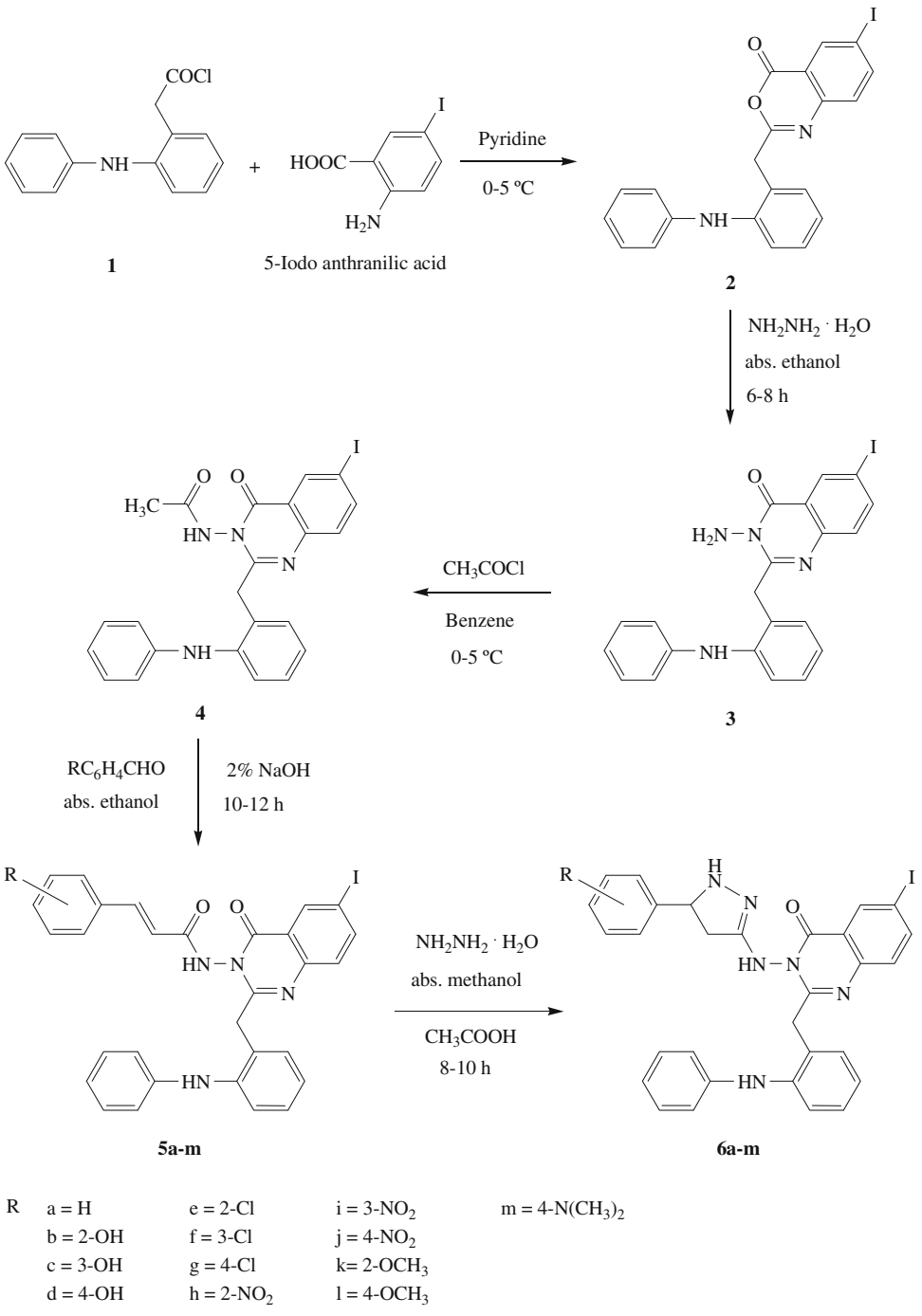

Table 1 Antibacterial activity of compounds **6a–m**

C6aompound	Zone of inhibition (mm)											
	S. aureus ATCC 9144			*B. subtilis* ATCC 6633			*E. coli* ATCC 25922			*P. aeruginosa* ATCC 9027		
	C_H	C_L	Pot %	C_H	C_L	Pot %	C_H	C_L	Pot %	C_H	C_L	Pot %
6a	21	17	70.87	22	18	81.79	6	0	40.81	7	0	48.61
6b	10	8	38.15	11	9	41.49	9	7	34.11	10	8	39.56
6c	12	10	42.34	13	11	47.05	9	7	34.11	10	8	39.56
6d	10	8	38.15	11	9	41.49	8	6	32.33	9	7	37.40
6e	6	0	44.39	7	0	45.27	7	0	44.45	7	0	48.61
6f	6	0	44.39	6	0	41.49	6	0	40.81	6	0	44.72
6g	6	0	44.39	6	0	41.49	6	0	40.81	7	0	48.61
6h	16	13	55.29	17	13	63.61	14	11	47.67	15	12	55.43
6i	15	12	52.83	14	11	52.61	19	15	62.30	19	16	67.47
6j	15	11	55.57	16	13	58.83	16	12	54.75	17	14	61.15
6k	9	7	36.21	10	8	38.97	16	13	52.45	17	13	63.19
6l	10	8	38.15	11	9	41.49	18	15	57.71	19	15	68.97
6m	7	0	48.23	7	0	45.27	6	0	40.81	7	0	48.61
Penicillin-G	30	25	100	27	21	100	31	25	100	28	23	100

C_H Zone of inhibition at concentration 100 μg/ml, *C_L* zone of inhibition at concentration 50 μg/ml, *Pot* potency of compound (%) as compared to penicillin-G

C=O and C=N stretchings of quinazolinone at around 1720 and 1610 cm^{-1}, respectively. The ^1H NMR spectra of compounds **6a–m** indicated that the $-CH_2$ protons of the pyrazoline ring resonated as a pair of doublet of doublets (Ha and Hb) because of geminal and vicinal coupling. The CH proton appeared as a doublet of doublet (Hx) because of vicinal coupling with the two magnetically nonequivalent protons of methylene group at position 4 of pyrazoline ring. The Ha proton which is *cis* to Hx resonates upfield in the range δ 3.01–3.08 ppm as a doublet of doublet while Hb, the other proton which is *trans* to Hx resonates downfield in the range δ 3.45c3.51 ppm as a doublet of doublet. The Hx proton which is vicinal to two methylene protons (Ha and Hb) resonates as a doublet of doublet in the range δ 5.45–5.52 ppm. In ^{13}C NMR spectra, signals at around δ 36 ppm, δ 55 ppm, and δ 161 ppm 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 ppm and δ 168 ppm, respectively.

Antimicrobial Activity

The in vitro antibacterial and antifungal activity results of compounds **6a–m** are shown in Tables 1 and 2, respectively. The potency of these compounds are calculated and compared with standard antibacterial drug penicillin-G and antifungal drug fluconazole. The results shows that compounds **6a** (R=H), **6 h** (R=2-NO_2), **6i** (R=3-NO_2), and **6j** (R=4-NO_2) showed very good activities against gram positive bacteria in which compound **6a** (R=H) possessed higher activity with potency of 70.87% and 81.79% compared with *S. aureus* and

Table 2 Antifungal activity of compounds **6a–m**

Compound	Zone of inhibition (mm)					
	C. albicans ATCC 10231			*A. Niger* ATCC 6275		
	C_H	C_L	Pot %	C_H	C_L	Pot %
6a	18	15	68.81	17	15	58.12
6b	12	9	49.95	10	8	38.11
6c	7	0	49.07	7	0	45.04
6d	15	13	56.01	14	11	51.18
6e	20	17	76.62	19	16	66.90
6f	16	14	59.53	15	12	53.99
6g	18	16	67.26	17	15	58.12
6h	18	15	68.81	17	15	58.12
6i	15	13	56.01	14	11	51.18
6j	16	14	59.53	15	13	51.52
6k	6	0	45.11	6	0	41.30
6l	7	0	49.07	7	0	45.04
6m	18	15	68.81	17	14	60.10
Fluconazole	26	21	100	28	22	100

C_H zone of inhibition at concentration 20 μg/ml, *C_L* zone of inhibition at concentration 10 μg/ml, *Pot* potency of compound (%) as compared to fluconazole

B. subtilis, respectively. On the other hand, compounds **6i** (R=3-NO_2), **6j** (R=4-NO_2), **6k** (R=2-OCH_3), and **6l** (R=4-OCH_3) exhibited very good activities against gram negative bacteria. The compound **6i** (R=3-NO_2) was found to be active against both gram positive as well as gram negative bacteria. Compound **6a** (R=H) showed excellent activity against gram positive bacteria *S. aureus* and *B. subtilis* while compound **6l** (R=4-OCH_3) displayed very good activity against gram negative bacteria *P. aeruginosa*. The remaining compounds possessed moderate activity against gram positive as well as gram negative bacteria as compared to standard drug penicillin-G. The most of the compounds showed good antifungal activity as compared to fluconazole except compounds **6b** (R=2-OH), **6c** (R=3-OH), **6k** (R=2-OCH_3), and **6l** (R=4-OCH_3) which displayed moderate antifungal activity against *C. albicans* ans *A. niger*. Compound **6e** (R=2-Cl) showed excellent activity against both fungi along with compounds **6a** (R=H), **6g** (R=4-Cl), **6h** (R=2-NO_2), and **6m** (R=4-$N(CH_3)_2$) which also showed very good activities.

Conclusion

The title compound pyrazolyl-quinazolin-4(3*H*)-ones **6a**–**m** were comprehensively synthesized by well-organized methods. In addition, some of the compounds possessed good antibacterial as well as antifungal activity in vitro. Phenyl group-containing compound showed very good activity against gram positive bacteria. Nitro group-containing compounds also showed good activity against gram positive bacteria in which *ortho*- and *para* nitro group-containing compound was found to be active as compared to *meta* nitro-containing compound. On the other hand, *meta* nitro group-containing compound displayed higher activity than *ortho*- and *para* nitro-containing compounds against gram negative bacteria. Methoxy group-containing compounds also possessed good activity against gram negative bacteria in which *para*-methoxy-substituted compound exhibited higher activity than *ortho*-substituted compound. Hydroxy- and methoxy-substituted compounds exhibited lower antifungal activity as compared to others. Chloro- and nitro group-containing compounds showed good antifungal activity when they are present at *ortho* position. Therefore, these results will give some idea about further research on this molecule.

Experimental

General

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 deutero $CDCl_3$ as a solvent. The chemical shifts are reported in (δ ppm) downfield from tetramethylsilane (TMS). Elemental analyses of newly synthesized compounds were carried out on Carlo Erba 1108 analyzer. 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-(Phenylamino) phenyl]acetyl chloride **1** was synthesized by the literature procedure (Furniss *et al.*, 1989).

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

A mixture of 2-[2-(phenylamino)phenyl]acetyl chloride (**1**) (0.01 mol) and 5-iodo anthranilic acid (0.01 mol) in dry pyridine (20 ml) was stirred at 0–5°C for 1 h, and further stirred for 1 h at room temperature. After completion of reaction, a pasty mass was obtained, which was washed thoroughly with sodium bicarbonate (5% w/v) to remove unreacted acid. A solid separated was filtered, dried, and recrystallized from methanol. Yield = 65%, m.p. 287–290°C; IR (KBr) cm^{-1}: 3441 (NH), 2926, 2854 (CH_2), 1745 (C=O), 1613 (C=N), 1145 (C–O), 617 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.54 (s, 2H, CH_2), 6.37–8.18 (m, 12H, Ar–H), 9.15 (bs, 1H, NH); *Anal*. Calcd. for $C_{21}H_{15}IN_2O_2$: C, 55.52; H, 3.33; N, 6.17. Found: C, 55.38; H, 3.26; N, 6.05.

Synthesis of 3-amino-6-iodo-2-[2-(phenylamino)benzyl]quinazolin-4(3*H*)-one (**3**)

A mixture of compound (**2**) (0.01 mol) and hydrazine hydrate (0.02 mol) in absolute ethanol (25 ml) 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 = 73%, m.p. 152–155°C; IR (KBr) cm^{-1}: 3512–3394 (NH and NH_2), 2932, 2856 (CH_2), 1724 (C=O), 1610 (C=N), 612 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.55 (s, 2H, CH_2), 5.74 (bs, 2H, NH_2), 6.38–8.18 (m, 12H, Ar–H), 9.16 (bs, 1H, NH); *Anal*. Calcd. for $C_{21}H_{17}IN_4O$: C, 53.86; H, 3.66; N, 11.96. Found: C, 53.74; H, 3.57; N, 11.85.

Synthesis of N-{6-iodo-4-oxo-2-[2-(phenylamino)benzyl]quinazolin-3(4H)-yl} acetamide (**4**)

To the solution of compound (**3**) (0.01 mol) in dry benzene (50 ml), acetyl chloride (0.01 mol) 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 was kept over night. The excess of solvent was distilled off under reduced pressure and then poured onto ice and shaken well, the solid thus obtained was filtered and recrystallized from methanol. Yield = 70%, m.p. 185–188°C; IR (KBr) cm^{-1}: 3452 (NH), 2929, 2851 (CH_2), 1727 (C=O), 1651 (C=O of amide), 1615 (C=N), 619 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H, CH_3), 3.54 (s, 2H, CH_2), 6.37–8.18 (m, 12H, Ar–H), 9.15 (bs, 1H, NH), 10.35 (bs, 1H, NH); *Anal*. Calcd for $C_{23}H_{19}IN_4O_2$: C, 54.13; H, 3.75; N, 10.98. Found: C, 54.02; H, 3.68; N, 10.86.

General procedure for the synthesis of acrylamides (**5a**–**m**)

To the solution of compound (**4**) (0.01 mol) in absolute ethanol (50 ml), substituted aromatic aldehyde (0.01 mol) 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.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(phenylacrylamido)-quinazolin-4(3H)-one (**5a**)*

Yield = 72%, m.p. 176–178°C; IR (KBr) cm^{-1}: 3437 (NH), 2918, 2849 (CH_2), 1719 (C=O), 1664 (C=O), 1613 (C=N), 1576 (CH=CH), 623 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.55 (s, 2H, CH_2), 6.37–8.18 (m, 17H, Ar–H), 6.77 (d, 1H, J = 16.6 Hz, =CHCO), 7.62 (d, 1H, J = 16.6 Hz, =CH–Ar), 8.85 (bs, 1H, CONH), 9.17 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.57 (CH_2), 112.52–148.64 (26C, CH=CH and Ar–C), 162.14 (C=O), 168.11 (C=N), 173.24 (CONH); *Anal*. Calcd for $C_{30}H_{23}IN_4O_2$: C, 60.21; H, 3.87; N, 9.36. Found: C, 60.07; H, 3.78; N, 9.23.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(2-hydroxyphenylacrylamido)-quinazolin-4(3H)-one (**5b**)*

Yield = 66%, m.p. 164–167°C; IR (KBr) cm^{-1}: 3546 (OH), 3442 (NH), 2924, 2850 (CH_2), 1722 (C=O), 1658 (C=O), 1615 (C=N), 1568 (CH=CH), 620 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.54 (s, 2H, CH_2), 6.36–8.17 (m, 16H, Ar–H), 6.79 (d, 1H, J = 16.2 Hz, =CHCO), 7.57 (d, 1H, J = 16.2 Hz, =CH–Ar), 8.82 (bs, 1H, CONH), 9.16 (bs, 1H, NH), 10.36 (bs, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.43 (CH_2), 112.17–155.69 (26C, CH=CH and Ar–C), 161.76 (C=O), 168.42 (C=N), 173.34 (CONH); *Anal*. Calcd for $C_{30}H_{23}IN_4O_3$: C, 58.64; H, 3.77; N, 9.12. Found: C, 58.55; H, 3.69; N, 9.18.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(3-hydroxyphenylacrylamido)-quinazolin-4(3H)-one (**5c**)*

Yield = 71%, m.p. 178–181°C; IR (KBr) cm^{-1}: 3539 (OH), 3454 (NH), 2932, 2856 (CH_2), 1725 (C=O), 1662 (C=O), 1616 (C=N), 1577 (CH=CH), 617 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.56 (s, 2H, CH_2), 5.57 (bs, 1H, OH), 6.37–8.18 (m, 16H, Ar–H), 6.78 (d, 1H, J = 16.4 Hz, =CHCO), 7.60 (d, 1H, J = 16.4 Hz, =CH–Ar), 8.84 (bs, 1H, CONH), 9.17 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.76 (CH_2), 112.08–159.27 (26C, CH=CH and Ar–C), 162.18 (C=O), 168.26 (C=N), 172.88 (CONH); *Anal*. Calcd for $C_{30}H_{23}IN_4O_3$: C, 58.64; H, 3.77; N, 9.12. Found: C, 58.77; H, 3.85; N, 9.05.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(4-hydroxyphenylacrylamido)-quinazolin-4(3H)-one (**5d**)*

Yield = 78%, m.p. 193–196°C; IR (KBr) cm^{-1}: 3552 (OH), 3445 (NH), 2934, 2853 (CH_2), 1720 (C=O), 1655 (C=O), 1609 (C=N), 1569 (CH=CH), 625 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.58 (s, 2H, CH_2), 5.59 (bs, 1H, OH), 6.36–8.16 (m, 16H, Ar–H), 6.81 (d, 1H, J = 16.6 Hz, =CHCO), 7.62 (d, 1H, J = 16.6 Hz, =CH–Ar), 8.82 (bs, 1H, CONH), 9.16 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.36 (CH_2), 112.31–157.29 (26C, CH=CH and Ar–C), 161.98 (C=O), 167.93 (C=N), 173.22 (CONH); *Anal*. Calcd for $C_{30}H_{23}IN_4O_3$: C, 58.64; H, 3.77; N, 9.12. Found: C, 58.56; H, 3.71; N, 9.23.

*6-Iodo-3-(2-chlorophenylacrylamido)-2-[2-(phenylamino)benzyl]quinazolin-4(3H)-one (**5e**)*

Yield = 63%, m.p. 159–162°C; IR (KBr) cm^{-1}: 3440 (NH), 2921, 2846 (CH_2), 1726 (C=O), 1653 (C=O), 1611 (C=N), 1581 (CH=CH), 742 (C–Cl), 618 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.57 (s, 2H, CH_2), 6.37–8.17 (m, 16H, Ar–H), 6.78 (d, 1H, J = 16.4 Hz, =CHCO), 7.59 (d, 1H, J = 16.4 Hz, =CH–Ar), 8.79 (bs, 1H, CONH), 9.14 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.18 (CH_2), 111.91–148.59 (26C, CH=CH and Ar–C), 162.06 (C=O), 168.35 (C=N), 173.42 (CONH); *Anal*. Calcd for $C_{30}H_{22}ClIN_4O_2$: C, 56.93; H, 3.50; N, 8.85. Found: C, 56.79; H, 3.62; N, 8.73.

*6-Iodo-3-(3-chlorophenylacrylamido)-2-[2-(phenylamino)benzyl]quinazolin-4(3H)-one (**5f**)*

Yield = 61%, m.p. 171–174°C; IR (KBr) cm^{-1}: 3454 (NH), 2928, 2853 (CH_2), 1718 (C=O), 1660 (C=O), 1607 (C=N), 1575 (CH=CH), 755 (C–Cl), 612 (C–I); ^1H NMR (400 MHz, $CDCl_3$): δ 3.54 (s, 2H, CH_2), 6.36–8.18 (m, 16H, Ar–H), 6.82

(d, 1H, $J = 16.4$ Hz, =CHCO), 7.62 (d, 1H, $J = 16.4$ Hz, =CH–Ar), 8.77 (bs, 1H, CONH), 9.15 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.36 (CH_2), 112.24–148.25 (26C, CH=CH and Ar–C), 161.76 (C=O), 167.86 (C=N), 173.21 (CONH); *Anal*. Calcd for $C_{30}H_{22}ClIN_4O_2$: C, 56.93; H, 3.50; N, 8.85. Found: C, 56.81; H, 3.42; N, 8.97.

*6-Iodo-3-(4-chlorophenylacrylamido)-2-[2-(phenylamino)benzyl]quinazolin-4(3H)-one (**5g**)*

Yield = 68%, m.p. 195–197°C; IR (KBr) cm^{-1}: 3444 (NH), 2930, 2856 (CH_2), 1716 (C=O), 1663 (C=O), 1611 (C=N), 1573 (CH=CH), 738 (C–Cl), 622 (C–I); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.57 (s, 2H, CH_2), 6.37–8.18 (m, 16H, Ar–H), 6.85 (d, 1H, $J = 16.2$ Hz, =CHCO), 7.60 (d, 1H, $J = 16.2$ Hz, =CH–Ar), 8.81 (bs, 1H, CONH), 9.17 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.54 (CH_2), 112.32–148.57 (26C, CH=CH and Ar–C), 162.16 (C=O), 167.89 (C=N), 173.33 (CONH); *Anal*. Calcd for $C_{30}H_{22}ClIN_4O_2$: C, 56.93; H, 3.50; N, 8.85. Found: C, 57.08; H, 3.38; N, 8.69.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(2-nitrophenylacrylamido)-quinazolin-4(3H)-one (**5h**)*

Yield = 76%, m.p. 205–210°C; IR (KBr) cm^{-1}: 3452 (NH), 2933, 2855 (CH_2), 1724 (C=O), 1659 (C=O), 1614 (C=N), 1580 (CH=CH), 1544, 1357 (NO_2), 619 (C–I); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.56 (s, 2H, CH_2), 6.38–8.19 (m, 16H, Ar–H), 6.83 (d, 1H, $J = 16$ Hz, =CHCO), 7.62 (d, 1H, $J = 16$ Hz, =CH–Ar), 8.84 (bs, 1H, CONH), 9.16 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.32 (CH_2), 111.82–150.48 (26C, CH=CH and Ar–C), 162.29 (C=O), 168.06 (C=N), 172.94 (CONH); *Anal*. Calcd for $C_{30}H_{22}IN_5O_4$: C, 56.00; H, 3.45; N, 10.88. Found: C, 55.86; H, 3.56; N, 10.75.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(3-nitrophenylacrylamido)-quinazolin-4(3H)-one (**5i**)*

Yield = 67%, m.p. 225–228°C; IR (KBr) cm^{-1}: 3457 (NH), 2928, 2850 (CH_2), 1729 (C=O), 1654 (C=O), 1612 (C=N), 1578 (CH=CH), 1535, 1353 (NO_2), 611 (C–I); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.53 (s, 2H, CH_2), 6.37–8.40 (m, 16H, Ar–H), 6.82 (d, 1H, $J = 16.2$ Hz, =CHCO), 7.65 (d, 1H, $J = 16.2$ Hz, =CH–Ar), 8.86 (bs, 1H, CONH), 9.17 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.24 (CH_2), 112.17–150.58 (26C, CH=CH and Ar–C), 161.87 (C=O), 168.15 (C=N), 173.06 (CONH); *Anal*. Calcd for $C_{30}H_{22}IN_5O_4$: C, 56.00; H, 3.45; N, 10.88. Found: C, 56.17; H, 3.52; N, 10.81.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(4-nitrophenylacrylamido)-quinazolin-4(3H)-one (**5j**)*

Yield = 65%, m.p. 243–245°C; IR (KBr) cm^{-1}: 3443 (NH), 2927, 2852 (CH_2), 1722 (C=O), 1659 (C=O), 1608 (C=N), 1582 (CH=CH), 1540, 1361 (NO_2), 614 (C–I); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.55 (s, 2H, CH_2), 6.36–8.17 (m, 16H, Ar–H), 6.80 (d, 1H, $J = 16.4$ Hz, =CHCO), 7.61 (d, 1H, $J = 16.4$ Hz, =CH–Ar), 8.83 (bs, 1H, CONH), 9.18 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.56 (CH_2), 112.27–148.32 (26C, CH=CH and Ar–C), 162.25 (C=O), 168.03 (C=N), 173.24 (CONH); *Anal*. Calcd for $C_{30}H_{22}IN_5O_4$: C, 56.00; H, 3.45; N, 10.88. Found: C, 55.89; H, 3.38; N, 10.96.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(2-methoxyphenylacrylamido)-quinazolin-4(3H)-one (**5k**)*

Yield = 67%, m.p. 155–158°C; IR (KBr) cm^{-1}: 3454 (NH), 2926, 2847 (CH_2), 1725 (C=O), 1661 (C=O), 1612 (C=N), 1584 (CH=CH), 1249, 1103 (C–O–C), 625 (C–I); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.54 (s, 2H, CH_2), 3.66 (s, 3H, OCH_3), 6.37–8.17 (m, 16H, Ar–H), 6.82 (d, 1H, $J = 16$ Hz, =CHCO), 7.64 (d, 1H, $J = 16$ Hz, =CH–Ar), 8.78 (bs, 1H, CONH), 9.14 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.46 (CH_2), 61.23 (OCH_3), 112.12–156.44 (26C, CH=CH and Ar–C), 162.38 (C=O), 167.89 (C=N), 173.32 (CONH); *Anal*. Calcd for $C_{31}H_{25}IN_4O_3$: C, 59.25; H, 4.01; N, 8.91. Found: C, 59.17; H, 3.96; N, 8.83.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(4-methoxyphenylacrylamido)-quinazolin-4(3H)-one (**5l**)*

Yield = 70%, m.p. 170–174°C; IR (KBr) cm^{-1}: 3443 (NH), 2924, 2853 (CH_2), 1715 (C=O), 1655 (C=O), 1614 (C=N), 1582 (CH=CH), 1241, 1105 (C–O–C), 617 (C–I); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.55 (s, 2H, CH_2), 3.64 (s, 3H, OCH_3), 6.37–8.18 (m, 16H, Ar–H), 6.79 (d, 1H, $J = 16.4$ Hz, =CHCO), 7.58 (d, 1H, $J = 16.4$ Hz, =CH–Ar), 8.76 (bs, 1H, CONH), 9.15 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.62 (CH_2), 59.56 (OCH_3), 111.76–158.45 (26C, CH=CH and Ar–C), 161.82 (C=O), 167.88 (C=N), 173.19 (CONH); *Anal*. Calcd for $C_{31}H_{25}IN_4O_3$: C, 59.25; H, 4.01; N, 8.91. Found: C, 59.12; H, 4.11; N, 8.85.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(4-dimethylaminophenylacrylamido)-quinazolin-4(3H)-one (**5m**)*

Yield = 72%, m.p. 144–148°C; IR (KBr) cm^{-1}: 3448 (NH), 2935, 2860 (CH_2), 1717 (C=O), 1662 (C=O), 1618 (C=N),

1585 (CH=CH), 611 (C–I); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.86 (s, 6H, $N(CH_3)_2$), 3.56 (s, 2H, CH_2), 6.38–8.18 (m, 16H, Ar–H), 6.81 (d, 1H, $J = 16.6$ Hz, =CHCO), 7.62 (d, 1H, $J = 16.6$ Hz, =CH–Ar), 8.78 (bs, 1H, CONH), 9.16 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.45 (CH_2), 46.72 (N-$(CH_3)_2$), 111.92–150.22 (26C, CH=CH and Ar–C), 162.17 (C=O), 168.27 (C=N), 172.86 (CONH); *Anal*. Calcd for $C_{32}H_{28}IN_5O_2$: C, 59.91; H, 4.40; N, 10.92. Found: C, 59.76; H, 4.28; N, 10.78.

General procedure for the synthesis of pyrazolyl-quinazolin-4(3H)-ones (**6a**–**m**)

To a mixture of compound (**5a**) (0.01 mol) and hydrazine hydrate (0.02 mol) in absolute methanol (30 ml) was added a 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.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-(5-phenyl-4,5-dihydro-1H-pyrazol-3-yl-amino)quinazolin-4(3H)-one (**6a**)*

Yield: 66%, m.p. 112–115°C; IR (KBr): 3446 (NH), 2925, 2853 (CH_2), 1729 (C=O), 1615 (C=N), 617 (C–I) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.03 (dd, 1H, $J_{ab} = 17.6$ Hz, $J_{ax} = 5.4$ Hz, Ha), 3.48 (dd, 1H, $J_{ba} = 17.6$ Hz, $J_{bx} = 12.4$ Hz, Hb), 3.54 (s, 2H, CH_2), 5.49 (dd, 1H, $J_{xb} = 12.4$ Hz, $J_{xa} = 5.4$ Hz, Hx), 6.37–8.19 (m, 18H, NH and Ar–H), 8.35 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.42 (CH_2), 36.32 (CH_2 of pyrazole), 55.64 (CH of pyrazole), 112.37–148.76 (24C, Ar–C), 161.12 (C=N of pyrazole), 162.19 (C=O), 168.27 (C=N); Anal. Calcd for $C_{30}H_{25}IN_6O$: C, 58.83; H, 4.11; N, 13.72. Found: C, 58.69; H, 4.18; N, 13.63.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(2-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6b**)*

Yield: 71%, m.p. 153–157°C; IR (KBr): 3546 (OH), 3440 (NH), 2921, 2848 (CH_2), 1723 (C=O), 1611 (C=N), 622 (C–I) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.01 (dd, 1H, $J_{ab} = 17.4$ Hz, $J_{ax} = 5.6$ Hz, Ha), 3.45 (dd, 1H, $J_{ba} = 17.4$ Hz, $J_{bx} = 12$ Hz, Hb), 3.55 (s, 2H, CH_2), 5.52 (dd, 1H, $J_{xb} = 12$ Hz, $J_{xa} = 5.6$ Hz, Hx), 6.37–8.18 (m, 17H, NH and Ar–H), 8.41 (bs, 1H, NH), 9.15 (bs, 1H, NH), 10.34 (bs, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.67 (CH_2), 35.53 (CH_2 of pyrazole), 55.84 (CH of pyrazole), 111.86–155.78 (24C, Ar–C), 161.34 (C=N of pyrazole), 161.95 (C=O), 168.42 (C=N); Anal. Calcd for $C_{30}H_{25}IN_6O_2$: C, 57.33; H, 4.01; N, 13.37. Found: C, 57.24; H, 3.96; N, 13.46.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(3-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6c**)*

Yield: 66%, m.p. 167–170°C; IR (KBr): 3550 (OH), 3452 (NH), 2927, 2855 (CH_2), 1734 (C=O), 1618 (C=N), 619 (C–I) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.04 (dd, 1H, $J_{ab} = 17.6$ Hz, $J_{ax} = 5.6$ Hz, Ha), 3.50 (dd, 1H, $J_{ba} = 17.6$ Hz, $J_{bx} = 12.6$ Hz, Hb), 3.54 (s, 2H, CH_2), 5.51 (dd, 1H, $J_{xb} = 12.6$ Hz, $J_{xa} = 5.6$ Hz, Hx), 5.57 (bs, 1H, OH), 6.37–8.19 (m, 17H, NH and Ar–H), 8.39 (bs, 1H, NH), 9.15 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.46 (CH_2), 36.14 (CH_2 of pyrazole), 54.98 (CH of pyrazole), 112.28–159.51 (24C, Ar–C), 161.12 (C=N of pyrazole), 162.24 (C=O), 168.13 (C=N); Anal. Calcd for $C_{30}H_{25}IN_6O_2$: C, 57.33; H, 4.01; N, 13.37. Found: C, 57.48; H, 4.08; N, 13.29.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6d**)*

Yield: 64%, m.p. 181–184°C; IR (KBr): 3542 (OH), 3445 (NH), 2932, 2851 (CH_2), 1721 (C=O), 1612 (C=N), 612 (C–I) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.08 (dd, 1H, $J_{ab} = 17.8$ Hz, $J_{ax} = 5.6$ Hz, Ha), 3.51 (dd, 1H, $J_{ba} = 17.8$ Hz, $J_{bx} = 12.2$ Hz, Hb), 3.59 (s, 2H, CH_2), 5.50 (dd, 1H, $J_{xb} = 12.2$ Hz, $J_{xa} = 5.6$ Hz, Hx), 5.58 (bs, 1H, OH), 6.37–8.17 (m, 17H, NH and Ar–H), 8.37 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.31 (CH_2), 36.48 (CH_2 of pyrazole), 55.26 (CH of pyrazole), 111.92–157.37 (24C, Ar–C), 161.33 (C=N of pyrazole), 162.06 (C=O), 167.86 (C=N); Anal. Calcd for $C_{30}H_{25}IN_6O_2$: C, 57.33; H, 4.01; N, 13.37. Found: C, 57.25; H, 4.05; N, 13.28.

*6-Iodo-3-[5-(2-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]-2-[2-(phenylamino)benzyl]quinazolin-4(3H)-one (**6e**)*

Yield: 69%, m.p. 123–125°C; IR (KBr): 3432 (NH), 2917, 2845 (CH_2), 1714 (C=O), 1617 (C=N), 748 (C–Cl), 629 (C–I) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.03 (dd, 1H, $J_{ab} = 17.4$ Hz, $J_{ax} = 5.4$ Hz, Ha), 3.47 (dd, 1H, $J_{ba} = 17.4$ Hz, $J_{bx} = 12.2$ Hz, Hb), 3.56 (s, 2H, CH_2), 5.48 (dd, 1H, $J_{xb} = 12.2$ Hz, $J_{xa} = 5.4$ Hz, Hx), 6.36–8.19 (m, 17H, NH and Ar–H), 8.42 (bs, 1H, NH), 9.15 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.14 (CH_2), 36.31 (CH_2 of pyrazole), 55.58 (CH of pyrazole), 112.27–148.89 (24C, Ar–C), 161.18 (C=N of pyrazole), 162.21 (C=O), 168.24 (C=N); Anal. Calcd for $C_{30}H_{24}ClIN_6O$: C, 55.70; H, 3.74; N, 12.99. Found: C, 55.53; H, 3.67; N, 12.88.

*6-Iodo-3-[5-(3-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]-2-[2-(phenylamino)benzyl]quinazolin-4(3H)-one (**6f**)*

Yield: 67%, m.p. 136–140°C; IR (KBr): 3453 (NH), 2926, 2852 (CH_2), 1722 (C=O), 1613 (C=N), 759 (C–Cl), 620 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.01 (dd, 1H, $J_{ab} = 17.8$ Hz, $J_{ax} = 5.6$ Hz, Ha), 3.46 (dd, 1H, $J_{ba} = 17.8$ Hz, $J_{bx} = 11.8$ Hz, Hb), 3.55 (s, 2H, CH_2), 5.45 (dd, 1H, $J_{xb} = 11.8$ Hz, $J_{xa} = 5.6$ Hz, Hx), 6.37–8.18 (m, 17H, NH and Ar–H), 8.38 (bs, 1H, NH), 9.16 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.26 (CH_2), 36.49 (CH_2 of pyrazole), 55.78 (CH of pyrazole), 112.45–148.86 (24C, Ar–C), 161.32 (C=N of pyrazole), 162.38 (C=O), 167.97 (C=N); Anal. Calcd for $C_{30}H_{24}ClIN_6O$: C, 55.70; H, 3.74; N, 12.99. Found: C, 55.48; H, 3.86; N, 13.07.

*6-Iodo-3-[5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]-2-[2-(phenylamino)benzyl]quinazolin-4(3H)-one (**6g**)*

Yield: 65%, m.p. 151–156°C; IR (KBr): 3441 (NH), 2920, 2849 (CH_2), 1724 (C=O), 1608 (C=N), 736 (C–Cl), 605 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.04 (dd, 1H, $J_{ab} = 17.8$ Hz, $J_{ax} = 5.8$ Hz, Ha), 3.45 (dd, 1H, $J_{ba} = 17.8$ Hz, $J_{bx} = 12.2$ Hz, Hb), 3.56 (s, 2H, CH_2), 5.49 (dd, 1H, $J_{xb} = 12.2$ Hz, $J_{xa} = 5.8$ Hz, Hx), 6.37–8.19 (m, 17H, NH and Ar–H), 8.36 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.55 (CH_2), 36.22 (CH_2 of pyrazole), 55.57 (CH of pyrazole), 111.83–148.66 (24C, Ar–C), 161.49 (C=N of pyrazole), 162.53 (C=O), 168.19 (C=N); Anal. Calcd for $C_{30}H_{24}ClIN_6O$: C, 55.70; H, 3.74; N, 12.99. Found: C, 55.84; H, 3.82; N, 12.87.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(2-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6h**)*

Yield: 70%, m.p. 171–173°C; IR (KBr): 3457 (NH), 2929, 2855 (CH_2), 1732 (C=O), 1616 (C=N), 1548, 1362 (NO_2), 618 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.02 (dd, 1H, $J_{ab} = 17.2$ Hz, $J_{ax} = 5.2$ Hz, Ha), 3.47 (dd, 1H, $J_{ba} = 17.2$ Hz, $J_{bx} = 11.8$ Hz, Hb), 3.55 (s, 2H, CH_2), 5.47 (dd, 1H, $J_{xb} = 11.8$ Hz, $J_{xa} = 5.2$ Hz, Hx), 6.37–8.18 (m, 17H, NH and Ar–H), 8.43 (bs, 1H, NH), 9.15 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.72 (CH_2), 36.68 (CH_2 of pyrazole), 55.76 (CH of pyrazole), 112.15–150.56 (24C, Ar–C), 161.33 (C=N of pyrazole), 162.18 (C=O), 168.31 (C=N); Anal. Calcd for $C_{30}H_{24}IN_7O_3$: C, 54.80; H, 3.68; N, 14.91. Found: C, 54.62; H, 3.59; N, 14.78.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(3-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6i**)*

Yield: 72%, m.p. 183–186°C; IR (KBr): 3455 (NH), 2930, 2854 (CH_2), 1728 (C=O), 1606 (C=N), 1543, 1356 (NO_2), 612 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.01 (dd, 1H, $J_{ab} = 17.4$ Hz, $J_{ax} = 5.4$ Hz, Ha), 3.48 (dd, 1H, $J_{ba} = 17.4$ Hz, $J_{bx} = 12$ Hz, Hb), 3.54 (s, 2H, CH_2), 5.49 (dd, 1H, $J_{xb} = 12$ Hz, $J_{xa} = 5.4$ Hz, Hx), 6.36–8.40 (m, 17H, NH and Ar–H), 8.40 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.23 (CH_2), 36.44 (CH_2 of pyrazole), 55.54 (CH of pyrazole), 112.36–150.83 (24C, Ar–C), 161.12 (C=N of pyrazole), 161.93 (C=O), 168.16 (C=N); Anal. Calcd for $C_{30}H_{24}IN_7O_3$: C, 54.80; H, 3.68; N, 14.91. Found: C, 54.66; H, 3.76; N, 14.82.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6j**)*

Yield: 67%, m.p. 188–193°C; IR (KBr): 3438 (NH), 2923, 2854 (CH_2), 1726 (C=O), 1619 (C=N), 1553, 1365 (NO_2), 615 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.05 (dd, 1H, $J_{ab} = 17.2$ Hz, $J_{ax} = 5.4$ Hz, Ha), 3.49 (dd, 1H, $J_{ba} = 17.2$ Hz, $J_{bx} = 11.8$ Hz, Hb), 3.56 (s, 2H, CH_2), 5.52 (dd, 1H, $J_{xb} = 11.8$ Hz, $J_{xa} = 5.4$ Hz, Hx), 6.36–8.18 (m, 17H, NH and Ar–H), 8.41 (bs, 1H, NH), 9.17 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.41 (CH_2), 36.59 (CH_2 of pyrazole), 55.75 (CH of pyrazole), 112.26–148.53 (24C, Ar–C), 161.25 (C=N of pyrazole), 162.47 (C=O), 168.39 (C=N); Anal. Calcd for $C_{30}H_{24}IN_7O_3$: C, 54.80; H, 3.68; N, 14.91. Found: C, 54.93; H, 3.61; N, 14.83.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(2-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6k**)*

Yield: 69%, m.p. 139–143°C; IR (KBr): 3448 (NH), 2925, 2853 (CH_2), 1719 (C=O), 1608 (C=N), 1246, 1106 (C–O–C), 619 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.06 (dd, 1H, $J_{ab} = 18.2$ Hz, $J_{ax} = 5.8$ Hz, Ha), 3.50 (dd, 1H, $J_{ba} = 18.2$ Hz, $J_{bx} = 12.4$ Hz, Hb), 3.55 (s, 2H, CH_2), 3.65 (s, 3H, OCH_3), 5.48 (dd, 1H, $J_{xb} = 12.4$ Hz, $J_{xa} = 5.8$ Hz, Hx), 6.38–8.18 (m, 17H, NH and Ar–H), 8.45 (bs, 1H, NH), 9.16 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.23 (CH_2), 36.34 (CH_2 of pyrazole), 55.48 (CH of pyrazole), 111.79–156.36 (24C, Ar–C), 161.08 (C=N of pyrazole), 162.20 (C=O), 167.76 (C=N); Anal. Calcd for $C_{31}H_{27}IN_6O_2$: C, 57.95; H, 4.24; N, 13.08. Found: C, 57.74; H, 4.12; N, 13.22.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6l**)*

Yield: 70%, m.p. 153–155°C; IR (KBr): 3437 (NH), 2921, 2850 (CH_2), 1720 (C=O), 1614 (C=N), 1248, 1115 (C–O–C), 626 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.08 (dd, 1H, $J_{ab} = 17.8$ Hz, $J_{ax} = 5.4$ Hz, Ha), 3.48 (dd, 1H, $J_{ba} = 17.8$ Hz, $J_{bx} = 11.6$ Hz, Hb), 3.57 (s, 2H, CH_2), 3.64 (s, 3H, OCH_3), 5.52 (dd, 1H, $J_{xb} = 11.6$ Hz, $J_{xa} = 5.4$ Hz, Hx), 6.36–8.17 (m, 17H, NH and Ar–H), 8.43 (bs, 1H, NH), 9.14 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.81 (CH_2), 36.73 (CH_2 of pyrazole), 55.27 (CH of pyrazole), 111.82–158.44 (24C, Ar–C), 160.91 (C=N of pyrazole), 162.14 (C=O), 168.16 (C=N); Anal. Calcd for $C_{31}H_{27}IN_6O_2$: C, 57.95; H, 4.24; N, 13.08. Found: C, 57.79; H, 4.19; N, 13.17.

*6-Iodo-2-[2-(phenylamino)benzyl]-3-[5-(4-dimethylaminophenyl)-4,5-dihydro-1H-pyrazol-3-yl-amino]quinazolin-4(3H)-one (**6m**)*

Yield: 65%, m.p. 162–166°C; IR (KBr): 3458 (NH), 2936, 2855 (CH_2), 1732 (C=O), 1618 (C=N), 618 (C–I) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.85 (s, 6H, $N(CH_3)_2$), 3.08 (dd, 1H, $J_{ab} = 17.4$ Hz, $J_{ax} = 5.6$ Hz, Ha), 3.48 (dd, 1H, $J_{ba} = 17.4$ Hz, $J_{bx} = 12.2$ Hz, Hb), 3.58 (s, 2H, CH_2), 5.52 (dd, 1H, $J_{xb} = 12.2$ Hz, $J_{xa} = 5.6$ Hz, Hx), 6.37–8.19 (m, 17H, NH and Ar–H), 8.41 (bs, 1H, NH), 9.18 (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.35 (CH_2), 36.53 (CH_2 of pyrazole), 55.62 (CH of pyrazole), 111.79–150.34 (24C, Ar–C), 161.13 (C=N of pyrazole), 162.39 (C=O), 168.43 (C=N); Anal. Calcd for $C_{32}H_{30}IN_7O$: C, 58.63; H, 4.61; N, 14.96. Found: C, 58.44; H, 4.45; N, 14.82.

Antimicrobial Activity

The in vitro antimicrobial activity of compounds **6a**–**m** was carried out by cup–plate method (Barry 1976). Antibacterial activity was screened against two gram positive bacteria (*Staphylococcus aureus* ATCC 9144 and *Bacillus subtilis* ATCC 6633) and two gram negative bacteria (*Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 9027), by measuring the zone of inhibition on agar plates at two different concentrations 100 and 50 μg/ml, whereas antifungal activity was tested by measuring the zone of inhibition on agar plates with two fungal species, *Candida albicans* ATCC 10231 and *Aspergillus niger* ATCC 6275, at two different concentrations 20 μg/ml and 10 μg/ml. Penicillin-G and fluconazole were used as standard drugs.

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