Section II

Chapter 5: Experimental

5. Experimental

The experimental work carried out in the thesis is discussed under two heads:

5.1 Chemical work

5.2 Biological activities

5.1 Chemical Work

Melting points were measured using VEEGO multi-programmable melting point apparatus and are uncorrected. IR spectra were recorded on FT-IR system-2000 Bruker spectrometer on KBr pellets or neat samples. ^{1}H-NMR spectra were recorded on Bruker Avance II 400 MHz FT-NMR spectrometer in $CDCl_3$ unless stated. Chemical shifts are expressed in δ units relative to tetramethylsilane (TMS) signal as internal reference. The following abbreviations are used in reporting NMR data: s, singlet; bs, broad singlet; b, broad; d, doublet; t, triplet; q, quartet; dq, doublet of quartet; dd, doublet of doublet and m, mutiplet. Mass spectra were recorded on Thermo Scientific DSQ-II Mass analyzer. Elemental analyses were performed on ThermoFisher FLASH 2000 organic elemental analyzer.

The chemical work carried out has been discussed under the following heads:

5.1.1 Synthesis of different *N*-substituted isatoic anhydrides **(1-7)**

5.1.2 Synthesis of substituted 2-aminobenzamides **(8-49)**

5.1.3 Synthesis of 1,3-disubstituted 2-imino-2,3-dihydro-4-quinazolinones **(50-91)**

5.1.1 Synthesis of different *N*-substituted isatoic anhydride (1-7)

In a 250 ml round-bottomed flask, isatoic anhydride (10 g, 61.3 mmol) was dissolved in DMA (25 ml) and DiPEA (26.15 ml, 153.25 mmol) was added into it. An alkyl halide (73.6 mmol, quantity as mentioned in Table 5.1) was added and the mixture was stirred for 2-4 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into diethyl ether with continuous stirring. The precipitated white coloured solid was filtered, washed with a little quantity of ether and used for the next step without purification.

Table 5.1 Synthesis of different *N*-substituted isatoic anhydrides (**1-7**)

Compound	**Aryl/alkyl halide used**	**Quantity of halide (73.6 mmol)**	**Reaction Conditions (Temp. / Time)**
1	4-Bromobenzyl Bromide	18 g	RT / 2-3 hrs
2	4-Methoxybenzyl Chloride	10 ml	80-100^{0}C / 2-3hrs
3	Phenylethyl Bromide	9.9 ml	80-100^{0}C / 2-3hrs
4	Methyl Iodide	4.6 ml	RT / 3-4 hrs
5	Ethyl Iodide	6 ml	80-100^{0}C / 2-3hrs
6	Allyl Bromide	7.8 ml	RT / 2-3 hrs
7	Benzyl Bromide	9.0 ml	RT / 3-4 hrs

All the synthesized intermediate was confirmed by their reported melting points and IR spectra. The yield, m.p., R_f value and IR values are given in Table 5.2.

Table 5.2 Analytical data of different *N*-substituted isatoic anhydrides (**1-7**)

Compound	**Name**	**Yield (%)**	**m.p. (^{o}C)**	**R_f (40% Hexane: EtOAc)**	**IR (KBr, cm^{-1})**
1	1-(4-Bromobenzyl)-1*H*-benzo[*d*][1,3]oxazine-2,4-dione	94.3	124-126	0.6	1777 and 1719, 1324, 839, 755
2	1-(4-Methoxybenzyl)-1*H*-benzo[*d*][1,3]oxazine-2,4-dione	92.1	117-119	0.55	1777 and 1717, 1310, 835, 759
3	1-(Phenylethyl)-1*H*-benzo[*d*][1,3]oxazine-2,4-dione	92.4	114-116	0.75	1776 and 1722 1317, 1022, 758, 681
4	1-(Methyl)-1*H*-benzo[*d*][1,3]oxazine-2,4-dione	91.7	118-121	0.4	1777 and 1719, 1324, 1067, 1028, 839, 755
5	1-(Ethyl)-1*H*-benzo[*d*][1,3]oxazine-2,4-dione	90.6	122-125	0.5	1773 and 1726, 1323, 1050, 745
6	1-(allyl)-1*H*-	89.3	107-109	0.625	1771 and

	benzo[*d*][1,3]oxazine-2,4-dione				1723, 1318, 1055, 760
7	1-(Benzyl)-1*H*-benzo[*d*][1,3]oxazine-2,4-dione	93.8	106-108	0.675	1779 and 1719, 1317, 1027, 758, 742, 681

5.1.2 Synthesis of substituted 2-aminobenzamides (8-49)

For the synthesis of compounds **(8-16)**, the starting substrate *N*-(4-bromobenzyl)isatoic anhydride was used. In a round-bottomed flask, *N*-(4-bromobenzyl)isatoic anhydride (0.5 g, 1.51 mmol) was dissolved in DMF (2 ml) and anhydrous K_2CO_3 (0.84 gm, 6.04 mmol) was added to it. Sufficient quantity of an alkyl amine (1.81 mmol) (given in Table 5.3) was added to the reaction flask. The mixture was stirred at 45°C for 45 min. Completion of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water. The precipitated off-white solid was filtered, washed with water, dried and recrystalised from methanol. TLC was performed with 30% hexane:EtOAc as the mobile phase under visualization with UV or I_2 vapours.

Table 5.3 Synthesis of *N*-substituted 2-(4-bromobenzylamino)benzamides (**8-16**)

Compound	**Primary Amine Used**	**Quantity of Amine (1.81 mmol) (ml)**
8	Phenylethylamine	0.23
9	Isobutylamine	0.18
10	Butylamine	0.18
11	4-Methylbenzylamine	0.19
12	Isopropylamine	0.13
13	Propylamine	0.13
14	Cyclopropylamine	0.11
15	Benzylamine	0.2
16	2-Chlorobenzylamine	0.18

Table 5.4 Analytical data of *N*-substituted 2-(4-bromobenzylamino)benzamides (**8-16**)

Compo	**Name**	**Yield**	**m.p.**	**R_f (30%**	

und		(%)	(^{o}C)	Hexane: EtOAc)	IR (KBr, cm^{-1})
8	2-(4-Bromobenzylamino)-*N*-phenethylbenzamide	89.3	118-120	0.61	3378, 1629, 1515, 814, 747, 700
9	2-(4-Bromobenzylamino)-*N*-isobutylbenzamide	89.5	114-117	0.58	3287, 1627, 1577,1552, 812, 753
10	2-(4-Bromobenzylamino)-*N*-butylbenzamide	89.3	100-104	0.58	3300, 1623, 1578, 1544, 813, 753
11	2-(4-Bromobenzylamino)-*N*-(4-methylbenzyl)benzamide	88.2	140-142	0.56	3287, 1623, 1578, 1512, 802, 745, 692
12	2-(4-Bromobenzylamino)-*N*-isopropylbenzamide	89.4	125-129	0.56	3254, 1625, 1578, 1538, 1509, 1284, 811, 750
13	2-(4-Bromobenzylamino)-*N*-propylbenzamide	89.6	103-106	0.56	3323, 1628, 1531, 1516, 1272, 803, 743
14	2-(4-Bromobenzylamino)-*N*-cyclopropylbenzamide	88.4	122-124	0.57	3310, 1628, 1577, 1529, 1288, 811, 751
15	2-(4-Bromobenzylamino)-*N*-benzylbenzamide	88.6	160-162	0.58	3248, 1625, 1578, 1545, 1287, 813, 754, 700
16	2-(4-Bromobenzylamino)-*N*-(2-chlorobenzyl)benzamide	89.3	137-141	0.55	3324, 1629, 1577, 1544, 1287, 812, 754

For the synthesis of compound (**17-25**), the starting substrate *N*-(4-methoxybenzyl)isatoic anhydride was used. In a round-bottomed flask, *N*-(4-methoxybenzyl)isatoic anhydride (0.5 g, 1.77 mmol) was dissolved in DMF (2 ml) and anhydrous K_2CO_3 (0.98 gm, 7.07 mmol) was added to it. Suitable quantity of an alkyl amine (2.12 mmol) (given in Table 5.5) was added to the reaction flask. The mixture was stirred at 45^0C for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water. The precipitated off-white solid was filtered,

washed with water, dried and was used for the next step. TLC was performed with 30% hexane:EtOAc as the mobile phase under visualization with UV or I_2 vapours.

Table 5.5 Synthesis of *N*-substituted 2-(4-methoxybenzylamino)benzamides (**17-25**)

Compound	**Primary Amine Used**	**Quantity of Amine (2.12 mmol) (ml)**
17	Phenylethylamine	0.23
18	Isobutylamine	0.18
19	Butylamine	0.18
20	4-Methylbenzylamine	0.23
21	Isopropylamine	0.15
22	Benzylamine	0.195
23	4-Methoxybenzylamine	0.23
24	2-Chlorobenzylamine	0.22
25	2-Furylmethylamine	0.17

Table 5.6 Analytical data of *N*-substituted 2-(4-methoxybenzylamino)benzamides (**17-25**)

Compound	**Name**	**Yield (%)**	**m.p. (^oC)**	**R_f(30% Hexane: EtOAc)**	**IR (KBr, cm^{-1})**
17	2-(4-Methoxy benzylamino)-*N*-phenethylbenzamide	90.5	99-102	0.48	3330, 1623, 1533, 824, 749, 699
18	2-(4-Methoxy benzylamino)-*N*-isobutylbenzamide	87.3	98-102	0.47	3291, 1616, 1538, 1328, 1251, 813, 755
19	2-(4-Methoxy benzylamino)-*N*-butylbenzamide	88.2	100-104	0.47	3325, 1624, 1534, 1511, 1246, 821, 749
20	2-(4-Methoxy-benzylamino)-*N*-(4-methylbenzyl)benzamide	89.5	108-111	0.46	3332, 1624, 1512, 1245, 821, 748
21	2-(4-Methoxy benzylamino)-*N*-isopropylbenzamide	88.1	100-107	0.46	3325, 1622, 1533, 1512, 1245, 823, 748
22	2-(4-Methoxy benzylamino)-*N*-	89.7	115-118	0.46	3339, 1625, 1535, 1510, 1243, 826,

	benzylbenzamide				751, 701
23	2-(4-Methoxy benzylamino)-*N*-(4-methoxybenzyl) benzamide	90.5	110-113	0.45	3389, 1612, 1511, 1246 and 1028, 823, 751
24	2-(4-Methoxy benzylamino)-*N*-(2-chlorobenzyl)benzamide	88.3	98-102	0.44	3354, 1627, 1531, 1511, 1246, 824, 751
25	2-(4-Methoxy benzylamino)-*N*-furfurylbenzamide	88.7	105-110	0.45	3346, 1627, 1512, 821, 748

For the synthesis of compound (**26-33**), the starting substrate *N*-phenylethylisatoic anhydride was used. In a round-bottomed flask, *N*-phenylethylisatoic anhydride (0.5 gm, 1.87 mmol) was dissolved in DMF (2 ml) and anhydrous K_2CO_3 (1.03 gm, 7.5 mmol) was added to it. Suitable quantity of an alkyl amine (2.24 mmol) (given in Table 5.7) was added to the reaction flask. The mixture was stirred at 45^0C for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water. The precipitated off-white solid was filtered, washed with water, dried and was used for the next step. TLC was performed with 30% hexane:EtOAc as the mobile phase under visualization with UV or I_2 vapours.

Table 5.7 Synthesis of different *N*-substituted 2-(phenylethylamino)benzamides (**26-33**)

Compound	**Primary Amine Used**	**Quantity of Amine (2.24 mmol) (ml)**
26	Phenylethylamine	0.24
27	Isobutylamine	0.19
28	Butylamine	0.19
29	4-Methylbenzylamine	0.24
30	propylamine	0.16
31	Benzylamine	0.21
32	4-Methoxybenzylamine	0.25
33	2-Chlorobenzylamine	0.23

Table 5.8 Analytical data of different *N*-substituted 2-(phenylethylamino)benzamides (**26-33**)

Compound	Name	Yield (%)	m.p. (^oC)	R_f (30% Hexane: EtOAc)	IR (KBr, cm^{-1})
26	*N*-Phenethyl-2-phenyl ethylaminobenzamide	90.3	94-96	0.58	3317, 1624, 1516, 747,697
27	*N*-Isobutyl-2-phenethylamino benzamide	88.2	92-94	0.56	3338, 1628, 1515, 744, 696
28	*N*-Butyl-2-phenethylamino benzamide	89.4	85-87	0.56	3353, 1628, 1537, 1513, 1239, 746, 700
29	*N*-(4-Methylbenzyl)-2-phenethylamino benzamide	88.8	107-110	0.55	3290, 1625, 1517, 1250, 799, 741, 695
30	*N*-Propyl-2-phenethylamino benzamide	88.1	65-68	0.54	3330, 1628, 1541, 1514, 1242, 747, 700
31	*N*-Benzyl-2-phenethylamino benzamide	88.3	107-110	0.55	3279, 1628, 1545, 1514, 1285, 743, 699
32	*N*-(4-Methoxybenzyl)-2-phenethylamino benzamide	87.6	88-90	0.53	3275, 1626, 1539, 1512, 1246, 827, 750, 697
33	*N*-(2-Chlorobenzyl) -2-phenethylamino benzamide	91.3	114-118	0.52	3338, 1630, 1519, 1245, 746, 693

For the synthesis of compound (**34-38**), the starting substrate *N*-methylisatoic anhydride was used. In a round-bottomed flask, *N*-methylisatoic anhydride (0.5 gm, 2.82 mmol) was dissolved in DMF (2 ml) and anhydrous K_2CO_3 (1.56 gm, 11.3 mmol) was added to it. Suitable quantity of an alkyl amine (3.39 mmol) (given in Table 5.9) was added to the reaction flask. The mixture was stirred at 45^0C for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water. The precipitated off-white solid was filtered, washed with water, dried and was used for the next step. TLC was performed with 30% hexane:EtOAc as the mobile phase under visualization with UV or I_2 vapours.

Table 5.9 Synthesis of different *N*-substituted 2-methylaminobenzamides (**34-38**)

Compound	**Primary Amine Used**	**Quantity of Amine (3.39 mmol) (ml)**
34	Phenylethylamine	0.43
35	Isobutylamine	0.28
36	4-Methylbenzylamine	0.36
37	Propylamine	0.24
38	2-Chlorobenzylamine	0.34

Table 5.10 Analytical data of different *N*-substituted 2-methylaminobenzamides (**34-38**)

Compound	**Name**	**Yield (%)**	**m.p. (^oC)**	**R_f (30% Hexane: EtOAc)**	**IR (KBr, cm^{-1})**
34	2-Methylamino-*N*-phenethylbenzamide	91.3	177-180	0.52	3320, 1624, 1538, 1512, 1277, 747, 698
35	2-Methylamino-*N*-isobutylbenzamide	88.5	143-146	0.50	3266, 1632, 1544, 1517, 1285, 754
36	2-Methylamino-*N*-(4-methylbenzyl)benzamide	91.3	178-180	0.50	3302, 1621, 1514, 1270, 817, 744
37	2-Methylamino-*N*-propylbenzamide	89.3	149-151	0.49	3305, 1628, 1545, 1520, 1285, 746
38	2-Methylamino-*N*-(2-chlorobenzyl)benzamide	87.9	>200	0.46	3314, 1627, 1515, 745

For the synthesis of compound (**39**), in a round-bottomed flask, *N*-ethylisatoic anhydride (0.5 gm, 2.62 mmol) was dissolved in DMF (2 ml) and anhydrous K_2CO_3 (1.44 gm, 10.5 mmol) was added to it. 4-methylbenzylamine (0.34 ml, 3.14 mmol) was added to the reaction flask. The mixture was stirred at 45^0C for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water. The precipitated off-white solid was filtered, washed with water, dried and was used for the next

step. TLC was performed with 30% hexane:EtOAc as the mobile phase under visualization with UV or I_2 vapours.

Table 5.11 Analytical data of *N*-(4-methylbenzyl)-2-ethylaminobenzamide (**39**)

Compound	Name	Yield (%)	m.p. (^oC)	R_f (30% Hexane: EtOAc)	IR (KBr, cm^{-1})
39	2-Ethylamino-*N*-(4-methylbenzyl)benzamide	91.5	100-102	0.61	3302, 1621, 1512, 810, 743

For the synthesis of compound (**40-44**), the starting substrate *N*-allylisatoic anhydride was used. In a round-bottomed flask, *N*-allylisatoic anhydride (0.5 gm, 2.46 mmol) was dissolved in DMF (2 ml) and anhydrous K_2CO_3 (1.03 gm, 9.85 mmol) was added to it. Suitable quantity of an alkyl amine (2.95 mmol) (given in Table 5.12) was added to the reaction flask. The mixture was stirred at 45^0C for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water. The precipitated off-white solid was filtered, washed with water, dried and was used for the next step. TLC was performed with 30% hexane:EtOAc as the mobile phase under visualization with UV or I_2 vapours.

Table 5.12 Synthesis of different *N*-substituted 2-allylaminobenzamides (**40-44**)

Compound	Primary Amine Used	Quantity of Amine (2.95 mmol) (ml)
40	Isobutylamine	0.25
41	Isopropylamine	0.2
42	Cyclopropylamine	0.17
43	Benzylamine	0.25
44	2-Chlorobenzylamine	0.3

Table 5.13 Analytical data of *N*-substituted 2-allylaminobenzamides (**40-44**)

Compound	Name	Yield (%)	m.p. (^oC)	R_f (30% Hexane: EtOAc)	IR (KBr, cm^{-1})
40	2-Allylamino-*N*-	87.5	145-147	0.68	3294, 1638,

	isobutylbenzamide				1599, 1537, 1332, 758
41	2-Allylamino-*N*-isopropylbenzamide	91.1	146-148	0.66	3308, 1624, 1539, 1516, 1275, 744
42	2-Allylamino-*N*-cyclopropylbenzamide	89.3	164-167	0.67	3269, 1627, 1516, 745
43	2-Allylamino-*N*-benzylbenzamide	88.5	177-179	0.67	3224, 1634, 1535, 1329, 753, 697
44	2-Allylamino-*N*-(2-chlorobenzyl)benzamide	90.3	>200	0.65	3339, 1629, 1518, 1280, 749

For the synthesis of compound (**45-49**), the starting substrate *N*-benzylisatoic anhydride was used. In a round-bottomed flask, *N*-benzylisatoic anhydride (0.5 gm, 1.98 mmol) was dissolved in DMF (2 ml) and anhydrous K_2CO_3 (1.1 gm, 7.91 mmol) was added to it. Suitable quantity of an alkyl amine (2.37 mmol) (given in Table 5.14) was added to the reaction flask. The mixture was stirred at 45^0C for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into water. The precipitated off-white solid was filtered, washed with water, dried and was used for the next step. TLC was performed with 30% hexane:EtOAc as the mobile phase under visualization with UV or I_2 vapours.

Table 5.14 Synthesis of different *N*-substituted 2-benzylaminobenzamides (**45-49**)

Compound	**Primary Amine Used**	**Quantity of Amine (2.37 mmol) (ml)**
45	Isobutylamine	0.2
46	4-Methylbenzylamine	0.25
47	Propylamine	0.17
48	Benzylamine	0.26
49	2-Chlorobenzylamine	0.24

Table 5.15 Analytical data of different *N*-substituted 2-benzylaminobenzamides (**45-49**)

Compound	**Name**	**Yield (%)**	**m.p. (^{o}C)**	**R_f (30% Hexane:**	**IR**

				EtOAc)	(KBr, cm^{-1})
45	2-Benzylamino-*N*-isobutylbenzamide	89.1	160-163	0.67	3266, 1624, 1549, 1512, 1276, 752, 695
46	2-Benzylamino-*N*-(4-methylbenzyl)benzamide	89.2	112-115	0.65	3363, 1630, 1512, 1274, 786, 749, 696
47	2-Benzylamino-*N*-propylbenzamide	89.5	108-112	0.64	3325, 1623, 1540, 1514, 1279, 749, 701
48	2-Benzylamino-*N*-benzylbenzamide	86.6	186-188	0.64	3374, 1632, 1514, 1272, 746, 694
49	2-Benzylamino-*N*-(2-chlorobenzyl)benzamide	89.3	>200	0.60	3280, 1625, 1544, 1520, 1282, 744, 692

5.1.3 General procedure for synthesis of 1,3-disubstituted 2-imino-2,3-dihydro-4-quinazolinones (50-91)

In a round-bottomed flask, substituted 2-aminobenzamides and cyanogen bromide were dissolved in DMSO:KCl (10:1) (3 ml). The mixture was stirred at 100^{o}C for 2- 3 hr. Progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into ice-cold water with continuous stirring. The precipitated white solid was filtered, washed with water, dried and purified by column chromatography using silica (100-200 mesh) as stationary phase and hexane-ethyl acetate as eluent.

1-(4-Bromobenzyl)-3-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (50)

It was synthesized from 2-(4-bromobenzylamino)-*N*-phenethylbenzamide (1.22 mmol, 0.5 g) and cyanogen bromide (1.83 mmol, 0.19 g) by the above general procedure. Yield: 83.65 %, m.p.: 240-242 ^{o}C

Anal.:

TLC : R_f 0.36

IR (cm^{-1}) : 3296, 1603, 1553, 1536, 1446, 1336, 809, 756 and 697

^{1}H-NMR : 8.46 (s, 1H, C=N*H*), 8.10-7.10 (m, 13H, Ar*H*), 5.33 (s, 2H, NCH_2Ar), 3.82-3.77 (m, 2H, NCH_2CH_2) and 3.01 (t, 2H, ArCH_2CH_2)

MS (m/z) : 434 (M+) and 436 (M+2)

1-(4-Bromobenzyl)-3-isobutyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (51)

It was synthesized from 2-(4-bromobenzylamino)-*N*-isobutylbenzamide (1.38 mmol, 0.5 g) and cyanogen bromide (2.08 mmol, 0.22 g) by the above general procedure. Yield: 81.2 %, m.p.: 177-180 ^{o}C

Anal.:

TLC : R_f 0.47

IR (cm^{-1}) : 3287, 1617, 1602, 1537, 1333, 811 and 758

^{1}H-NMR : 7.55-6.83 (m, 8H, Ar*H*), 5.84 (s, 1H, C=N*H*), 5.45 (s, 2H, NCH_2Ar), 3.57 (d, 2H, NCH_2CH), 2.07-2.00 (m, 1H, CH_2C*H*(CH_3)$_2$) and 1.04 (d, 6H, CH(CH_3)$_2$)

MS (m/z) : 386 (M+) and 388 (M+2)

1-(4-Bromobenzyl)-3-butyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (52)

It was synthesized from 2-(4-bromobenzylamino)-*N*-butylbenzamide (1.38 mmol, 0.5 g) and cyanogen bromide (2.08 mmol, 0.22 g) by the above general procedure. Yield: 76.2 %, m.p.: 202-205 ^{o}C

Anal.:

TLC : R_f 0.44

IR (cm^{-1}) : 3283, 1620, 1604, 1541, 1334, 805, 757 and 697

1-(4-Bromobenzyl)-3-(4-methylbenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (53)

It was synthesized from *N*-(4-methylbenzyl)-2-(4-bromobenzylamino)benzamide (1.22 mmol, 0.5 g) and cyanogen bromide (1.83 mmol, 0.19 g) by the above general procedure. Yield: 80.2 %, m.p.: 208-212 ^{o}C

Anal.:

TLC : R_f 0.52

IR (cm^{-1}) : 3257, 1639, 1595, 1536, 1326, 828 and 752

^{1}H-NMR : 7.56-7.07 (m, 12H, Ar*H*), 5.37 (s, 1H, C=N*H*), 4.88 (s, 2H, ArNCH_2Ar),

4.47-4.39 (m, 2H, CONCH_2Ar) and 2.34 (s, 3H, ArCH_3)

MS (m/z) : 434 (M+) and 436 (M+2)

1-(4-Bromobenzyl)-3-isopropyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (54):

It was synthesized from 2-(4-bromobenzylamino)-*N*-isopropylbenzamide (1.44 mmol, 0.5 g) and cyanogen bromide (2.16 mmol, 0.23 g) by the above general procedure. Yield: 75.2 %, m.p.: 257-260 ^oC

Anal.:

TLC : R_f 0.36

IR (cm^{-1}) : 3301, 1617, 1595, 1534, 1333 and 755

1-(4-Bromobenzyl)-3-propyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (55)

It was synthesized from 2-(4-bromobenzylamino)-*N*-propylbenzamide (1.44 mmol, 0.5 g) and cyanogen bromide (2.16 mmol, 0.23 g) by the above general procedure. Yield: 77.4 %, m.p.: 180-183 ^oC

Anal.:

TLC : R_f 0.34

IR (cm^{-1}) : 3277, 1616, 1599, 1537, 1329, 792 and 755

1-(4-Bromobenzyl)-3-cyclopropyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (56)

It was synthesized from 2-(4-bromobenzylamino)-*N*-cyclopropylbenzamide (1.45 mmol, 0.5 g) and cyanogen bromide (2.17 mmol, 0.23 g) by the above general procedure. Yield: 76.6 %, m.p.: 266-269 ^{o}C

Anal.:

TLC : R_f 0.17

IR (cm^{-1}) : 3265, 1615, 1595, 1533, 1452, 1332, 817 and 756

^{1}H-NMR : 7.61-7.04 (m, 8H, Ar*H*), 5.38 (s, 2H, NCH_2Ar), 3.20-3.16 (m, 1H, C*H*(CH_2)$_2$), 1.01-0.96 (m, 2H, NCHCH_2) and 0.73-0.71 (m, 2H, NCHCH_2)

1-(4-Bromobenzyl)-3-benzyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (57)

It was synthesized from 2-(4-bromobenzylamino)-*N*-benzylbenzamide (1.26 mmol, 0.5 g) and cyanogen bromide (1.9 mmol, 0.2 g) by the above general procedure. Yield: 77.1 %, m.p.: 190-193 ^{o}C

Anal.:

TLC : R_f 0.53

IR (cm^{-1}) : 3271, 1615, 1596, 1538, 1331, 829, 749 and 697

1-(4-Bromobenzyl)-3-(2-chlorobenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (58)

It was synthesized from *N*-(2-chlorobenzyl)-2-(4-bromobenzylamino)benzamide (1.16 mmol, 0.5 g) and cyanogen bromide (1.75 mmol, 0.18 g) by the above general procedure. Yield: 78.5 %, m.p.: 213-216 ^{o}C

Anal.:

TLC : R_f 0.59

IR (cm^{-1}) : 3299, 1617, 1597, 1536, 1323, 797 and 742

^{1}H-NMR : 7.63-6.93 (m, 12H, Ar*H*), 6.21 (s, 1H, C=N*H*), 5.39 (s, 2H, ArNCH_2Ar)
and 5.03-4.99 (m, 2H, CONCH_2Ar)

1-(4-Methoxybenzyl)-3-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (59)

It was synthesized from 2-(4-methoxybenzylamino)-*N*-phenethylbenzamide (1.39 mmol, 0.5 g) and cyanogen bromide (2.08 mmol, 0.22 g) by the above general procedure. Yield: 79.1 %, m.p.: 201-203 ^{o}C

Anal.:

TLC : R_f 0.42

IR (cm^{-1}) : 3290, 1635, 1600, 1537, 1322, 1249, 811, 752 and 698

^{1}H-NMR : 7.51-6.72 (m, 13H, Ar*H*), 5.28 (s, 2H, NCH_2Ar), 3.93 (t, 2H, NCH_2CH_2),
3.68 (s, 3H, OCH_3) and 2.97 (t, 2H, CH_2CH_2Ar)

MS (m/z) : 386.1 (M+1)

3-Isobutyl-1-(4-methoxybenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (60)

It was synthesized from 2-(4-methoxybenzylamino)-*N*-isobutylbenzamide (1.6 mmol, 0.5 g) and cyanogen bromide (2.4 mmol, 0.25 g) by the above general procedure. Yield: 78.4 %, m.p.: 180-182 ^{o}C

Anal.:

TLC : R_f 0.39

IR (cm^{-1}) : 3291, 1616, 1599, 1538, 1328, 1251, 813 and 755

^{1}H-NMR : 7.51-6.72 (m, 8H, Ar*H*), 5.89 (s, 1H, C=N*H*), 5.30 (s, 2H, NCH_2Ar), 3.68 (s, 3H, OCH_3), 3.49 (m, 2H, NCH_2CH), 2.00-1.93 (m, 1H, CH_2C*H*(CH_3)$_2$) and 0.95 (d, 6H, CH(CH_3)$_2$)

MS (m/z) : 338.4 (M+1)

3-Butyl-1-(4-Methoxybenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (61)

It was synthesized from 2-(4-methoxybenzylamino)-*N*-butylbenzamide (1.6 mmol, 0.5 g) and cyanogen bromide (2.4 mmol, 0.25 g) by the above general procedure. Yield: 75.4 %, m.p.: 164-166 ^{o}C

Anal.:

TLC : R_f 0.41

IR (cm^{-1}) : 3274, 1618, 1602, 1542, 1324, 1249, 808 and 752

1-(4-Methoxybenzyl)-3-(4-methylbenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (62)

It was synthesized from *N*-(4-methylbenzyl)-2-(4-methoxybenzylamino)benzamide (1.39 mmol, 0.5 g) and cyanogen bromide (2.08 mmol, 0.22 g) by the above general procedure. Yield: 79.1 %, m.p.: 201-204^{o}C

Anal.:

TLC : R_f 0.48

IR (cm^{-1}) : 3260, 1617, 1596, 1536, 1332 and 751

^{1}H-NMR : 7.51-6.81 (m, 12H, Ar*H*), 5.88 (s, 1H, C=N*H*), 5.40 (s, 2H, ArNCH_2 Ar), 4.86-4.84 (m, 2H, CONCH_2Ar), 3.76 (s, 3H, OCH_3) and 2.36 (s, 3H, ArCH_3)

MS (m/z) : 386.5 (M+1)

3-Isopropyl-1-(4-methoxybenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (63)

It was synthesized from 2-(4-methoxybenzylamino)-*N*-isopropylbenzamide (1.68 mmol, 0.5 g) and cyanogen bromide (2.51 mmol, 0.27 g) by the above general procedure. Yield: 79.5 %, m.p.: 185-187 ^{o}C

Anal.:

TLC : R_f 0.24

IR (cm^{-1}) : 3274, 1614, 1594, 1534, 1328, 1247, 812 and 751

^{1}H-NMR : 7.58-6.79 (m, 8H, Ar*H*), 5.73 (s, 1H, C=N*H*), 5.37 (s, 2H, NCH_2Ar), 4.74-4.72 (m, 1H, NC*H*(CH_3)$_2$), 3.75 (s, 3H, OCH_3) and 1.33 (d, 6H, CH(CH_3)$_2$)

MS (m/z) : 324.1 (M+1)

3-Benzyl-1-(4-methoxybenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (64)

It was synthesized from 2-(4-methoxybenzylamino)-*N*-benzylbenzamide (1.44 mmol, 0.5 g) and cyanogen bromide (2.17 mmol, 0.23 g) by the above general procedure. Yield: 78.2 %, m.p.: 214-216 ^{o}C

Anal.:

TLC : R_f 0.47

IR (cm^{-1}) : 3271, 1639, 1600, 1539, 1324, 1248, 810, 750 and 697

^{1}H-NMR : 7.52-6.82 (m, 13H, Ar*H*), 5.93 (s, 1H, C=N*H*), 5.40 (s, 2H, ArNCH_2Ar), 4.90 (s, 2H, CONCH_2Ar) and 3.79 (s, 3H, OCH_3)

1,3-bis(4-Methoxybenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (65)

It was synthesized from *N*-(4-methoxybenzyl)-2-(4-methoxybenzylamino) benzamide (1.33 mmol, 0.5 g) and cyanogen bromide (1.99 mmol, 0.21 g) by the above general procedure. Yield: 80.3 %, m.p.: 190-193 ^{o}C

Anal.:

TLC : R_f 0.3

IR (cm^{-1}) : 3253, 1616, 1597, 1535, 1449, 1332, 813 and 753

^{1}H-NMR : 7.65-6.81 (m, 12H, Ar*H*), 5.37 (s, 2H, ArNCH_2Ar), 4.83 (s, 2H, CONCH_2Ar), 3.80 (s, 3H, ArOCH_3) and 3.76 (s, 3H, ArOCH_3)

3-(2-Chlorobenzyl)-1-(4-methoxybenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (66)

It was synthesized from *N*-(2-chlorobenzyl)-2-(4-methoxybenzylamino)benzamide (1.31mmol, 0.5 g) and cyanogen bromide (1.97 mmol, 0.21 g) by the above general procedure. Yield: 81.5 %, m.p.: 169-172 ^{o}C

Anal.:

TLC : R_f 0.47

IR (cm^{-1}) : 3276, 1617, 1597, 1537, 1328, 1248, 810 and 749

^{1}H-NMR : 7.58-6.89 (m, 12H, Ar*H*), 6.29 (s, 1H, C=N*H*), 5.37 (s, 2H, ArNCH_2Ar), 5.02-4.98 (m, 2H, CONCH_2Ar) and 3.75 (s, 3H, OCH_3)

3-(Furan-2-yl)methyl-1-(4-methoxybenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (67)

It was synthesized from *N*-(4-methoxybenzyl)-2-(4-methoxybenzylamino) benzamide (1.33 mmol, 0.5 g) and cyanogen bromide (1.99 mmol, 0.21 g) by the above general procedure. Yield: 79.2 %, m.p.: 203-205^{o}C

Anal.:

TLC : R_f 0.46

IR (cm^{-1}) : 3278, 1617, 1595, 1538, 1325, 1251, 813 and 749

1,3-Diphenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (68)

It was synthesized from *N*-phenethyl-2-(phenethylamino) benzamide (1.45 mmol, 0.5 g) and cyanogen bromide (2.18 mmol, 0.23 g) by the above general procedure. Yield: 81.4 %, m.p.: 184-186 ^{o}C

Anal.:

TLC : R_f 0.5

IR (cm^{-1}) : 3329, 1615, 1595, 1533, 1332 and 756

^{1}H-NMR : 7.58 (t, 1H, Ar*H*), 7.48 (d, 1H, Ar*H*), 7.34-7.20 (m, 11H, Ar*H*), 7.09 (t, 1H, Ar*H*), 6.10 (br, 1H, C=N*H),* 4.39-4.35(m, 2H, NCH_2CH_2), 3.98-3.93 (m, 2H, NCH_2CH_2) and 3.04-2.99 (m, 4H, ArCH_2CH_2, ArCH_2CH_2)

MS (m/z) : 370 (M+1)

3-Isobutyl-1-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (69)

It was synthesized from, *N*-isobutyl-2-(phenethylamino)benzamide (1.69 mmol, 0.5 g) and cyanogen bromide (2.53 mmol, 0.27 g) by the above general procedure. Yield: 76.6 %, m.p.: 192-194 ^{0}C

Anal.:

TLC : R_f 0.39

IR (cm^{-1}) : 3274, 1620, 1603, 1540, 1457, 1334, 757 and 697

^{1}H-NMR : 7.67-7.59 (m, 2H, Ar*H*), 7.34-7.15 (m, 7H, Ar*H*), 6.21 (br, 1H, C=N*H),* 4.39-4.35 (m, 2H, NCH_2CH_2), 3.54 (d, 2H, NCH_2CH), 3.04-3.00 (m, 2H, ArCH_2CH_2), 2.11-2.02 (m, 1H, CH_2C*H*(CH_3)$_2$) and 1.02 (d, 6H, CH(CH_3)$_2$)

MS (m/z) : 322.1 (M+1)

3-Butyl-1-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (70)

It was synthesized from *N*-butyl-2-(phenethylamino) benzamide (1.69 mmol, 0.5 g) and cyanogen bromide (2.53 mmol, 0.27 g) by the above general procedure. Yield: 77.4 %, m.p.: 162-164 ^{o}C

Anal.:

TLC : R_f 0.45

IR (cm^{-1}) : 3327, 3280, 1638, 1603, 1541, 1452, 747 and 696

^{1}H-NMR : 7.71-7.14 (m, 9H, Ar*H*), 6.24 (bs, 1H, C=N*H*), 4.39-4.35 (m, 2H, NC$H_2$$CH_2$Ar), 3.68 (t, 2H, NC$H_2$$CH_2$$CH_2$), 3.02 (t, 2H, ArC$H_2$$CH_2$), 1.72-1.65 (m, 2H, NCH_2C$H_2$$CH_2$), 1.45-1.40 (m, 2H, NCH_2CH_2CH_2) and 0.94 (t, 3H, CH_2CH_3)

MS (m/z) : 322.4 (M+1)

3-(4-Methylbenzyl)-1-phenylethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (71)

It was synthesized from *N*-(4,methylbenzyl)-2-(phenylethylamino)benzamide (1.45 mmol, 0.5 g) and cyanogen bromide (2.17 mmol, 0.23 g) by the above general procedure. Yield: 81.3 %, m.p.: 211-213 ^oC

Anal.:

TLC : R_f 0.45

IR (cm^{-1}) : 3257, 1622, 1594, 1536, 1334, 792, 750 and 697

^{1}H-NMR : 7.65-7.04 (m, 13H, Ar*H*), 5.86 (s, 1H, C=N*H*), 4.82 (s, 2H, CONCH_2Ar),

4.37 (t, 2H, ArNC$H_2$$CH_2$), 3.03 (t, 2H, NCH_2CH_2Ar) and 2.36 (s, 3H, ArCH_3)

MS (m/z) : 370.1 (M+1)

1-Phenethyl-3-propyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (72)

It was synthesized from 2-(phenethylamino)-*N*-propylbenzamide (1.77 mmol, 0.5 g) and cyanogen bromide (2.66 mmol, 0.28 g) by the above general procedure. Yield: 79.5 %, m.p.: 208-211 ^oC

Anal.:

TLC : R_f 0.31

IR (cm^{-1}) : 3274, 1638, 1605, 1542, 1330, 749 and 696

^{1}H-NMR : 7.72-7.10 (m, 9H, Ar*H*), 6.48 (s, 1H, C=N*H*), 4.30 (t, 2H, NCH_2CH$_2$Ar),
3.61 (t, 2H, NCH_2CH$_2$CH$_3$), 2.95 (t, 2H, CH$_2$CH_2Ar), 1.73-1.65 (m, 2H, CH$_2$CH_2CH$_3$) and 0.94 (t, 3H, CH$_2$CH_3)

MS (m/z) : 308.4 (M+1)

3-Benzyl-1-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (73)

It was synthesized from *N*-benzyl-2-(phenethylamino)benzamide (1.51 mmol, 0.5 g) and cyanogen bromide (2.27 mmol, 0.24 g) by the above general procedure. Yield: 77.4 %, m.p.: 195-197 ^{o}C

Anal.:

TLC : R_f 0.54

IR (cm^{-1}) : 3257, 1622, 1593, 1537, 1335, 750 and 697

^{1}H-NMR : 7.63-7.11 (m, 14H, Ar*H*), 5.94 (s, 1H, C=N*H*), 4.88-4.87 (d, 2H, NCH_2Ar), 4.39 (t, 2H, NCH_2CH$_2$) and 3.04 (t, 2H, CH$_2$CH_2Ar)

MS (m/z) : 356.4 (M+1)

3-(4-Methoxybenzyl)-1-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (74)

It was synthesized from *N*-(4-methoxybenzyl)-2-(phenethylamino)benzamide (1.39 mmol, 0.5 g) and cyanogen bromide (2.08 mmol, 0.22 g) by the above general procedure. Yield: 77.9 %, m.p.: 172-174 ^{o}C

Anal.:

TLC : R_f 0.45

IR (cm^{-1}) : 3255, 1627, 1595, 1538, 1335, 805, 750 and 696

^{1}H-NMR : 7.77-6.80 (m, 13H, Ar*H*), 4.76 (s, 2H, NCH_2Ar), 4.3 (t, 2H, NCH_2CH$_2$),
3.62 (s, 3H, OCH_3) and 2.96 (t, 2H, CH$_2$CH_2Ar)

3-(2-Chlorobenzyl)-1-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (75)

It was synthesized from *N*-(2-chlorobenzyl)-2-(phenethylamino) benzamide (1.37 mmol, 0.5 g) and cyanogen bromide (2.06 mmol, 0.22 g) by the above general procedure. Yield: 79.1 %, m.p.: 154-157 ^{o}C

Anal.:

TLC : R_f 0.64

IR (cm^{-1}) : 3218, 1621, 1594, 1535, 1334, 751 and 698

^{1}H-NMR : 7.63-7.13 (m, 13H, Ar*H*), 6.27 (s, 1H, C=N*H*), 4.98 (s, 2H, NCH_2Ar), 4.37 (t, 2H, NCH_2CH_2) and 3.02 (t, 2H, CH_2CH_2Ar)

MS (m/z) : 390.4 (M+1)

1-Methyl-3-phenethyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (76)

It was synthesized from 2-(methylamino)-*N*-phenethylbenzamide (1.97 mmol, 0.5 g) and cyanogen bromide (2.95 mmol, 0.31 g) by the above given general procedure. Yield: 76.5 %, m.p.: 203-205 ^{o}C

Anal.:

TLC : R_f 0.17

IR (cm^{-1}) : 3259, 1622, 1599, 1538, 1325, 749 and 696

MS (m/z) : 280.2 (M+1)

3-Isobutyl-1-methyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (77)

It was synthesized from *N*-isobutyl-2-(methylamino) benzamide (2.42 mmol, 0.5 g) and cyanogen bromide (3.64 mmol, 0.39 g) by the above general procedure. Yield: 79.2 %, m.p.: 208-211 ^{o}C

Anal.:

TLC : R_f 0.17

IR (cm^{-1}) : 3269, 1620, 1597, 1536, 1327 and 753

1-Methyl-3-(4-methylbenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (78)

It was synthesized from *N*-(4-methylbenzyl)-2-(methylamino) benzamide (1.97 mmol, 0.5 g) and cyanogen bromide (2.95 mmol, 0.31 g) by the above general procedure. Yield: 76.1 %, m.p.: 156-158 ^{o}C

Anal.:

TLC : R_f 0.18

IR (cm^{-1}) : 3328, 1618, 1597, 1535, 1450, 1328, 808 and 748

^{1}H-NMR : 7.67-7.14 (m, 8H, Ar*H*), 4.81 (s, 2H, NCH_2Ar), 3.62 (s, 3H, NCH_3) and

2.33 (s, 3H, ArCH_3)

MS (m/z) : 280.3 (M+1)

1-Methyl-3-propyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (79)

It was synthesized from 2-(methylamino)-*N*-propylbenzamide (2.6 mmol, 0.5 g) and cyanogen bromide (3.9 mmol, 0.41 g) by the above general procedure. Yield: 79.7 %, m.p.: 224-227^{o}C

Anal.:

TLC : R_f 0.13

IR (cm^{-1}) : 3287, 1620, 1595, 1537, 1326 and 749

3-(2-Chlorobenzyl)-1-methyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (80)

It was synthesized from *N*-(2-chlorobenzyl)-2-(methylamino) benzamide (1.82 mmol, 0.5 g) and cyanogen bromide (2.73 mmol, 0.29 g) by the above general procedure. Yield: 77.2 %, m.p.: 211-213 ^{o}C

Anal.:

TLC : R_f 0.17

IR (cm^{-1}) : 3259, 1623, 1599, 1539, 1454, 1324 and 748

^{1}H-NMR : 7.65-7.10 (m, 8H, Ar*H*), 5.77 (s, 1H, C=N*H*), 3.98-3.94 (m, 2H, NCH_2Ar) and 3.62 (s, 3H, NCH_3)

1-Ethyl-3(4-methylbenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (81)

It was synthesized from *N*-(4-methylbenzyl)-2-(ethylamino) benzamide (1.86 mmol, 0.5 g) and cyanogen bromide (2.79 mmol, 0.3 g) by the above general procedure. Yield: 76.7 %, m.p.: 210-212 ^oC

Anal.:

TLC : R_f 0.25

IR (cm^{-1}) : 3222, 1623, 1597, 1540, 1446, 1336, 811 and 752

^{1}H-NMR : 7.66-7.12 (m, 8H, Ar*H*), 6.30 (bs, 1H, C=N*H*), 4.80 (s, 2H, NCH_2Ar), 4.24 (q, 2H, NCH_2CH_3), 2.33 (s, 3H, ArCH_3) and 1.33 (t, 3H, CH_2CH_3)

MS (m/z) : 294.3 (M+1)

1-Allyl-3-isobutyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (82)

It was synthesized from 2-(allylamino)-*N*-isobutylbenzamide (2.15 mmol, 0.5 g) and cyanogen bromide (3.23 mmol, 0.34 g) by the above general procedure. Yield: 76.5 %, m.p.: 176-178 ^oC

Anal.:

TLC : R_f 0.33

IR (cm^{-1}) : 3294, 1638, 1599, 1537, 1332 and 758

^{1}H-NMR : 7.55-7.07 (m, 4H, Ar*H*), 5.91 (br, 1H, C=N*H*), 5.90-5.82 (m, 1H, CH_2C*H*=CH_2), 5.15-5.10 (m, 2H, CH=CH_2), 4.77-4.75 (m, 2H, NCH_2CH=CH_2), 3.45 (t, NCH_2CH(CH_3)$_2$), 1.98-1.91 (m, 1H, CH_2C*H*(CH_3)$_2$) and 0.93 (d, 6H, CH(CH_3)$_2$)

MS (m/z) : 258.2 (M+1)

1-Allyl-3-isopropyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (83)

It was synthesized from 2-(allylamino)-*N*-isopropylbenzamide (2.29 mmol, 0.5 g) and cyanogen bromide (3.44 mmol, 0.36 g) by the above general procedure. Yield: 80.5 %, m.p.: 174-176 ^{o}C

Anal.:

TLC : R_f 0.27

IR (cm^{-1}) : 3307, 1615, 1597, 1534, 1330 and 753

^{1}H-NMR : 7.64-7.13 (m, 4H, Ar*H*), 5.98-5.89 (m, 1H, CH_2CH=CH_2), 5.82 (bs, 1H, C=N*H*), 5.21-5.12 (m, 2H, CH=CH_2), 4.83 (d, 2H, NCH_2CH), 4.72-4.67 (m, 1H, NC*H*$(CH_3)_2$) and 1.30 (d, 6H, CH(C$H_3)_2$)

MS (m/z) : 244.3 (M+1)

1-Allyl-3-cyclopropyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (84)

It was synthesized from 2-(allylamino)-*N*-cyclopropylbenzamide (2.31 mmol, 0.5 g) and cyanogen bromide (3.47 mmol, 0.37 g) by the above general procedure. Yield: 81.1 %, m.p.: 162-164 ^{o}C

Anal.:

TLC : R_f 0.24

IR (cm^{-1}) : 3245, 1654, 1613, 1532, 1326 and 756

1-Allyl-3-benzyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (85)

It was synthesized from 2-(allylamino)-*N*-benzylbenzamide (1.88 mmol, 0.5 g) and cyanogen bromide (2.82 mmol, 0.3 g) by the above general procedure. Yield: 79.3 %, m.p.: 205-208 ^{o}C

Anal.:

TLC : R_f 0.38

IR (cm^{-1}) : 3224, 1634, 1595, 1535, 1329, 753 and 697

^{1}H-NMR : 7.62-7.12 (m, 9H, Ar*H*), 5.99-5.92 (m, 2H, C=N*H*, $CH_2C\mathit{H}=CH_2$), 5.23-5.14 (m, 2H, CH=CH_2) and 4.88-4.85 (m, 4H, NCH_2 and NCH_2Ar)

1-Allyl-3-(2-chlorobenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (86)

It was synthesized from *N*-(2-chlorobenzyl)-2-(allylamino) benzamide (1.67 mmol, 0.5 g) and cyanogen bromide (2.51 mmol, 0.26 g) by the above general procedure. Yield: 75.4 %, m.p.: 189-192 ^oC

Anal.:

TLC : R_f 0.42

IR (cm^{-1}) : 3265, 1632, 1599, 1540, 1333 and 750

^{1}H-NMR : 7.62-7.13 (m, 8H, Ar*H*), 6.20 (s, 1H, C=N*H*), 5.98-5.89 (m, 1H, $CH_2C\mathit{H}=CH_2$), 5.22-5.17 (m, 2H, CH=CH_2), 4.99 (d, 2H, NCH_2) and 4.84-4.83 (m, 2H, NCH_2Ar)

1-Benzyl-3-isobutyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (87)

It was synthesized from 2-(benzylamino)-*N*-isobutylbenzamide (1.77 mmol, 0.5 g) and cyanogen bromide (2.66 mmol, 0.28 g) by the above general procedure. Yield: 76.2 %, m.p.: 152-155 ^oC

Anal.:

TLC : R_f 0.44

IR (cm^{-1}) : 3322, 1637, 1594, 1538, 1331, 756 and 698

1-Benzyl-3-(4-methylbenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (88)

It was synthesized from *N*-(4-methylbenzyl)-2-(benzylamino) benzamide (1.51 mmol, 0.5 g) and cyanogen bromide (2.27 mmol, 0.24 g) by the above general procedure. Yield: 80.1 %, m.p.: 150-153 ^{o}C

Anal.:

TLC : R_f 0.52

IR (cm^{-1}) : 3267, 1617, 1596, 1535, 1330, 803, 751 and 695

^{1}H-NMR : 7.51-7.06 (m, 13H, Ar*H*), 5.94 (s, 1H, C=N*H*), 5.46 (s, 2H, ArNCH_2Ar), 4.87-4.85 (m, 2H, CONCH_2Ar) and 2.36 (s, 3H, ArCH_3)

MS (m/z) : 356.4 (M+1)

1-Benzyl-3-propyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (89)

It was synthesized from 2-(benzylamino)-*N*-propylbenzamide (1.86 mmol, 0.5 g) and cyanogen bromide (2.79 mmol, 0.3 g) by the above general procedure. Yield: 77.6 %, m.p.: 202-205 ^{o}C

Anal.:

TLC : R_f 0.28

IR (cm^{-1}) : 3276, 1638, 1602, 1540, 1332, 757 and 698

^{1}H-NMR : 7.76-7.12 (m, 9H, Ar*H*), 6.56 (s, 1H, C=N*H*), 5.44 (s, 2H, NCH_2Ar), 3.70(t, 2H, NCH_2CH_2), 1.81-1.72 (m, 2H, CH_2CH_2CH_3) and 1.02 (t, 3H, CH_2CH_3)

MS (m/z) : 294.3 (M+1)

1,3-Dibenzyl-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (90)

It was synthesized from *N*-benzyl-2-(benzylamino) benzamide (1.58 mmol, 0.5 g) and cyanogen bromide (2.37 mmol, 0.25 g) by the above general procedure. Yield: 76.5 %, m.p.: 160-163 ^{o}C

Anal.:

TLC : R_f 0.5

IR (cm^{-1}) : 3270, 1647, 1602, 1540, 1328, 748 and 697

1-Benzyl-3-(2-chlorobenzyl)-2-imino-2,3-dihydroquinazolin-4(1*H*)-one (91)

It was synthesized from *N*-(2-chlorobenzyl)-2-(benzylamino) benzamide (1.43 mmol, 0.5 g) and cyanogen bromide (2.14 mmol, 0.23 g) by the above general procedure. Yield: 81.2 %, m.p.: >250^oC

Anal.:

TLC : R_f 0.61

IR (cm^{-1}) : 3304, 1641, 1598, 1540, 1327, 754 and 696

^{1}H-NMR : 7.61-7.09 (m, 13H, Ar*H*), 6.21 (br, 1H, C=N*H*), 5.45 (s, 2H, NCH_2 *o*-ClC_6H_4) and 5.03 (s, 2H, NC$H_2C_6H_5$)

5.2 Biological activities:

The biological activity of the synthesized compounds has been carried out by the researchers of the pharmacology section and not by the candidate himself.

5.2.1 *In vitro* AChE and BuChE inhibition assays

The assays were performed according to the method described by Ellman *et al*.[151] AChE from human erythrocytes and BuChE from equine serum, 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB-Ellman's reagent), acetylthiocholine iodide (ATCI) and butyrylthiocholine iodide (BTCI) were purchased from Sigma. Tacrine and donepezil were used as reference compounds (Sigma). All the experiments were conducted in 50 mM Tris-HCl buffer at *p*H 8. Five different concentrations (0.001–100 μM) of each compound were used to determine the enzyme inhibition activity. Briefly, 50 μl of AChE (0.22 U/ml) or 50 μl of BuChE (0.06 U/ml) and 10 μl of the test or standard compound were incubated in 96-well plates at room

temperature for 30 min. Further, 30 µl of the substrate viz. ATCI (15 mM) or BTCI (15 mM) was added and incubated for additional 30 min. Finally, 160 µl of DTNB (1.5 mM) was added and the absorbance was measured at 415 nm wavelength using microplate reader 680 XR (BIO-RAD, India). The IC_{50} values were calculated from the absorbance changes. IC_{50} value depicts the concentration of the drug resulting in 50 % inhibition of the enzyme activity. All the determinations were performed in triplicate and at least in three independent runs.

5.2.2 Thioflavin T (ThT) assay for determining $A\beta_{1-42}$ aggregation inhibitory activity of the test compounds

In order to identify multi-target-directed ligands, $A\beta_{1-42}$ aggregation inhibitory activity was determined using the thioflavin T (ThT) fluorescence assay for the most promising test compounds obtained from the *in vitro* MTT assay, as per the earlier described method.[100] $A\beta_{1-42}$ (Sigma) dissolved in phosphate buffer saline (PBS) was further diluted with 0.215 M sodium phosphate buffer (*p*H 8) to get the final concentration of 20 µM. The test compounds were dissolved in DMSO and diluted with 0.215 M sodium phosphate buffer (*p*H 8). To determine $A\beta_{1-42}$ aggregation, the solution containing 20 µM of $A\beta_{1-42}$ or $A\beta_{1-42}$ plus the test compound (10 µM) in 0.215 M sodium phosphate buffer was incubated at room temperature for 24 hr. After incubation, 20 µM ThT (prepared in 50 mM glycine-NaOH buffer; *p*H 8.5) was added to the above solution. Finally, the fluorescence intensity was read at 442 nm excitation and 490 nm emission wavelengths using spectrofluorometer (RF-5301 PC, Shimadzu). The percentage inhibition of $A\beta_{1-42}$ aggregation was calculated using the formula: 100-(IFi/IFo×100), where IFi and IFo are fluorescence intensities in the presence and absence of the test compound respectively. Each assay was run in triplicate.

5.2.3 Congo red (CR) binding assay for determining $A\beta_{1-42}$ aggregation inhibitory activity of the test compounds

$A\beta_{1-42}$ Aggregation inhibitory potential of the potent test compounds was assessed using Congo red (CR) binding assay. CR (Hi-Media) solution prepared in PBS (*p*H 7.4) was diluted to get a final concentration of 5 µM. $A\beta_{1-42}$ (Sigma) prepared in PBS was diluted to get a final concentration of 20 µM. Briefly, 20 µM of $A\beta_{1-42}$ was incubated with or without the test compound (10 µM) for 6 hr at 37°C. Later on, the mixture was incubated with 5µM of

CR for 30 min at room temperature. Following incubation, CR spectra were measured using a UVspectrophotometer (UV-1700, Shimadzu) at 480 nm and 540 nm wavelengths. CR binding was calculated using the following formula: CB (M) = (OD at 540 nm/25,295) - (OD at 480 nm/46,306); where, CB (M) is the amount of CR bound with β sheets of $A\beta_{1-42}$ and OD is the optical density.[152,153]

5.2.4 Determination of cell viability and neuroprotection against H_2O_2 insult using SH-SY5Y cells

The SH-SY5Y cells (National Centre for Cell Science, Pune) were cultured in Dulbecco's Modified Eagle Medium DMEM) supplemented with (10 % v/v) fetal bovine serum (FBS), 100 U/ml penicillin and 100 U/ml streptomycin at 37 ºC and 5 % CO_2. The cells, cultured in 75 cm2 flasks, were seeded in 96 well plates and incubated for 24 hr. To determine the cytotoxicity of the selected test compounds, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was performed. SH-SY5Y cells were seeded in 96-well plate at a density of 5×104 cells per well. After 24 hr, the medium was replaced with two different concentrations of the test compounds (40 μM and 80 μM) for another 24 hr at 37°C. After incubation period, the cell viability was determined using MTT assay. In another set of experiment, the test compounds were assessed for their ability to protect SH-SY5Y cells against oxidative damage induced by H_2O_2.[144,145] The cells were exposed to the test compounds at relatively lower concentrations (5 μM, 10 μM and 20 μM) and incubated for 2 hr.

After the incubation period, the test compounds were replaced with a media containing the cytotoxic insult, i.e. H_2O_2 (100 μM)[144] which was left for an additional 24 hr period. Thereafter, cell viability was assessed using MTT assay. Briefly, the medium was replaced with 80 μl of fresh medium and 20 μl of MTT (0.5 mg/ml, final concentration; Sigma) in PBS. After 4 hr, MTT was removed and crystals of the formazan were dissolved in DMSO. Formazan concentrations were quantified at 570 nm with 630 nm reference wavelengths using a microplate reader 680 XR (BIO-RAD, India). Percentage protection against H_2O_2 insult was calculated by considering the absorbance of control cells as 100 % of the cell viability.

5.2.5 2,2-Diphenyl-1-picrylhydrazyl radical (DPPH) assay to determine free radical scavenging ability of the test compounds

The 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) assay is based on the reduction of DPPH, a purple colored stable free radical. DPPH gets paired off and reduced to yellow colored diphenylpicrylhydrazine by antioxidants. Thus the assay measures an electron (or hydrogen atom) donating activity and hence provides assessment of antioxidant activity of a compound which may be attributed to its free radical scavenging ability.[146,154] The spectrophotometric DPPH assay was carried out according to the earlier described reports.[155] Concentrations at which the selected test derivatives showed promising neuroprotective effects against H_2O_2 insult were selected for the DPPH assay. In brief, 10 µl of a test compound (10 and 20 µM, in Tris-HCl buffer-*p*H 7.4) was mixed with 20 µl of DPPH (from 10 mM stock, in methanol) (Hi-Media) in a 96 well plate. Finally, the volume was adjusted to 200 µl using methanol. After 30 sec incubation at room temperature and protection from light, the absorbance was read at 520 nm wavelength using a microplate reader 680 XR (BIO-RAD, India). The free radical scavenging activity was determined as the reduction percentage (RP) of DPPH using the equation: $RP= 100[(A0 - AC)/Ao]$, where *A0* is the untreated DPPH absorbance and *AC* is the absorbance value for added sample concentration *C*. Ascorbic acid was used as a standard antioxidant.

5.2.6 Morris water maze test for assessing spatial learning ability

The spatial learning ability of the animals was assessed using Morris water maze (MWM) test. The test was performed during the last five days of the treatment period. Time required to reach the hidden platform (i.e. escape latency time-ELT) and number of crossings over the platform area were recorded during 2 min of training session to determine spatial learning ability.[156]

5.2.7 Y maze test for assessing immediate working memory

Immediate working memory was evaluated using Y-maze test.[157] The Y-maze test was also carried out during the last five days of the treatment period. Each animal was placed at the end of any one arm of the maze and allowed to explore all the three arms. The sequence

and the number of arm entries were recorded visually over a period of 5 min. An actual "alteration" was defined as entries in all three arms in consecutive choices (i.e. ABC, BCA or CAB but not BAB). Repeat arm entry was considered as a sign of memory impairment. The number of arm entries indicated locomotor activity. The "alteration score" for each rat was calculated using the equation:

% Alternation = [(Number of alternations) / (Total arm entries−2)] × 100.

5.2.8 ROS scavenging activity of test compounds

The ROS scavenging activity of the potent test compounds was determined using 2′,7′-dichlorofluorescin diacetate (DCFH-DA) assay.[158] Briefly, primary rat hippocampal neuronal cells were seeded in 96 well plates. Cells were exposed to the test compounds (10-40 μM) for 2 hr, followed by $A\beta_{1-42}$ (10 μM) insult for 24 hr. After the incubation period, the hippocampal cells were loaded with 10 μM DCFH-DA (Sigma) at 37 °C for 30 min. Fluorescence intensity was determined using the Synergy HTX multi-mode microplate reader with excitation wavelength of 492 nm and emission of 495 nm. The fluorescence intensities in the presence and absence of the inhibitors were compared using appropriate control and the percentage inhibition of ROS was calculated for individual inhibitors.

5.2.9 Statistical analysis

The observed data were analysed using GraphPad Prism (version 5) software. The data are expressed as mean ± SEM. Significant difference between the experimental groups was determined using two way ANOVA (MWM and Y maze test) and one way ANOVA followed by Bonferroni test. Images were visualized and captured using a Carl-Zeiss confocal microscope. While capturing images, all parameters such as gain, contrast, brightness, the positions, and types of filters were set to standard parameters, such that the signals were not saturated and all images could be quantified and compared to one another. Captured images were analysed using ZEN 2012 imaging software. For statistical analysis, a minimum of 30 randomly chosen cells per condition were analysed (n=4 independent experiments with 3-4 replicates). A value of $p<0.05$ was considered significant. * and # indicated the level of significance.