Experimental

All the reagents and solvents required for synthesis were purified by general laboratory techniques before use. Compounds were purified by passing them through silica gel H (100-200 mesh) purifying column using mixture of chloroform and methanol or chloroform alone as eluent. Melting points were determined using a Veego make silicon oil bath-type melting point apparatus and are uncorrected. Purity of the compounds and completion of reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F_{254}; Merck), visualizing with ultraviolet light or iodine vapors. The yields reported here are un-optimized. The IR spectra were recorded using KBr disc method on a Bruker FT-IR, model alpha. The ^{1}H-NMR spectra (on a Bruker 300/400 MHz spectrometer) were recorded in DMSO-d_6 (chemical shifts in δ ppm) or otherwise stated. The assignment of exchangeable protons was confirmed by the D_2O exchange studies wherever required. Mass spectral data were obtained on a Thermo Scientific mass spectrometer (DSQ II). Microwave reactions were performed in CEM-Discovery, USA microwave reactor.

5.1 Chemical work

5.1.1 Synthesis of starting materials and intermediates

- **Synthesis of 6-nitroveratric acid (4)**

Veratraldehyde (2)

In a three-neck round bottom (Rb) flask (100 mL) equipped with two dropping funnels, vanillin (**1**) (1.0 g, 6.57 mmol) was fused at 100 °C. Addition of an aqueous solution of potassium hydroxide (0.55 g, 9.81 mmol in 0.8 ml water) was started at a rate of 1-2 drops per second while the external heating was continued. After about one-fourth of potassium hydroxide solution was added, addition of dimethyl sulfate (DMS) (1.03 g, 8.61 mmol) was started at the same rate as that of potassium hydroxide solution. The *p*H of the solution was always maintained basic by adjusting the rate of addition of the two reagents. The external heating was switched off after 5 min of the start of the addition and the solution was allowed to reflux by the heat of the reaction. Yellow colored oil separated out in the reaction mixture at the end of the addition. The solution was stirred for another 30 min after the addition of both of the reagents was completed. The reaction mixture was kept at 10-12 °C for 18 h. The solid mass so obtained was triturated with cold water, filtered, washed with water and dried under vacuum to give white colored veratraldehyde (**2**) (0.9 g, 82 %) m.p. 44-46 °C (lit.[370]43-44.5 °C).

Anal.:

TLC : R_f 0.45 (Benzene)

IR : 1683, 1590, 1512, 1272, 1138 and 1019 cm^{-1}

6-Nitroveratraldehyde (3)

In an Rb flask (50 mL), concentrated nitric acid (5.0 mL) was cooled to 5 °C and veratraldehyde (**2**) (1.0 g, 6.02 mmol) was added to it portion-wise over a period of 10 min, keeping the temperature of the reaction mixture between 5-10 °C. The reaction mixture was stirred at RT for another 2 h and quenched into crushed ice (30 g). As the product is light sensitive, enough care was taken to prevent the product from light exposure from this point onwards. The solid so formed was filtered, washed with cold water and dried under vacuum to get compound (**3**) as yellow colored solid (0.88 g, 70 %) m.p. 128-29 °C (lit.[371]129-31 °C).

Anal.:

TLC : R_f 0.75 (Benzene)

IR : 1686, 1523, 1336, 1288, 1227 and 1060 cm^{-1}

6-Nitroveratric acid (4)

6-Nitroveratraldehyde (**3**) (5.0 g, 23.69 mmol) was dissolved in aldehyde-free acetone (25 mL) in an Rb flask (250 mL). An aqueous solution of potassium permanganate (15.0 g, 94.78 mmol in 25 ml water) was added drop-wise to the above solution through a pressure equalizing dropping funnel (PEDF) over a period of 20 min. The reaction mixture was stirred at RT for another 2 h, filtered through filtering aid (hiflosupercel) and washed with hot water. The filtrate was concentrated to remove acetone and acidified with dilute sulfuric acid (5 %). The precipitated material so obtained was filtered, washed with cold water and dried under vacuum to give compound (**4**) as yellow colored solid (3.76 g, 70 %) m.p. 193-95 °C (lit.[380] 192-95 °C).

Anal.:

TLC : R_f 0.1 (Chloroform: Methanol, 18:2)

IR : 3300, 2854, 1703, 1599, 1530, 1419, 1364, 1286, 1219 and 1054 cm^{-1}

- **Synthesis of 2-amino-4,5-dimethoxybenzonitrile (8)**

3,4-Dimethoxybenzaldoxime (5)

Method A: Veratraldehyde (5 g, 30.08 mmol) (**2**) was dissolved in warm methanol (10 mL) in an Rb flask (100 mL). An aqueous solution of hydroxylamine hydrochloride (2.51g, 36.10 moles in 5ml water) was added and mixed thoroughly. A solution of sodium hydroxide (1.8 g, 45.13 mmol in 5ml water) was added drop-wise through dropping funnel with constant stirring. The reaction mixture was allowed to stand for 2.5 h and quenched into crushed ice (25 g).The solution was saturated with CO_2. Aldoxime was separated as oil. The mixture was allowed to stand for 12-24 h in refrigerator. When the oil was solidified, crystalline aldoxime was filtered off through vaccume pumpand dried in air (5.2 g, 95 %) m.p. 88-90 °C.

Anal:

TLC : R_f 0.24 (Chloroform: Methanol, 19:1)

IR : 3458, 1584, 1511, 1460, 1337, 1267, 1141, 1020, 970, 905, 860 and 757 cm^{-1}

3,4-Dimethoxybenzonitrile (6)

Method B: 3,4-Dimethoxybenzaldoxime (**5**) (5 g, 27.62 mmol) was dissolved in diethyl ether (20 mL) in an Rb flask (100 mL). Thionyl chloride (5 mL) was added dropwise through dropping funnel with constant stirring. Hydrogen chloride gas produced during reaction was trapped through sodium hydroxide trap. The reaction mixture was allowed to stirr for 2 h and poured drop-wise into ice-cold water.The precipitates so obtained were filtered, washed with cold water and dried under vacuum to obtain the product (3.8 g, 85 %) m.p. 65-67 °C (lit.[374] 67 °C).

Anal:

TLC : R_f 0.8 (Chloroform: methanol, 19:1)

IR : 2221, 1598, 1514, 1269, 1243, 1137, 1017, 875, 810 and 762 cm^{-1}

4,5-Dimethoxy-2-nitrobenzonitrile (7)

In an Rb flask (50 mL), concentrated nitric acid (10 mL) was cooled to 10 °C and 3,4-dimethoxybenzonitrile (**6**) (5 g, 30.66 mmol) was added to it portion-wise. After complete addition, the mixture was allowed to stir for 1 h and then quenched into ice cold water. The solid product so formed was filtered, washed with saturated solution of sodium bicarbonate and followed by ice cold water to remove excess nitric acid.The solid was dried under vacuum to obtain the desired product (7) (5.98 g, 94.62 %) m. p. 164-66 °C (lit.[375]164-66 °C).

Anal:

TLC : R_f 0.41(Chloroform: methanol, 19:1)

IR : 2226, 1570, 1523, 1458, 1397, 1292, 1229, 1058, 978 and 886 cm^{-1}

MS : m/z 208.06 (M^+ peak)

2-Amino-4,5-dimethoxybenzonitrile (8)

4,5-Dimethoxy-2-nitrobenzonitrile (7) (5 g, 24 mmol) was taken in an Rb flask (250 mL). Concentrated hydrochloric acid (30 mL) and granulated tin (4.25 g, 36 mmol) were added into it. The reaction mixture was allowed to reflux for 2 h. The reaction mixture was poured in ice-cold water (50 mL) and basified with sodium hydroxide until the precipitated tin oxide residue got dissolved. Thereaction mixture was filtered and washed with water.The solid thus obtained was recrystallized from methanol to get 2-amino-4,5-dimethoxybenzonitrile(**8**) (2.2g, 51.28 %) m.p. 96-99°C (lit.[376] 96-101°C).

Anal:

TLC : R_f 0.24(Chloroform: methanol, 19:1)

IR : 3452, 3230, 2210, 1658, 1621, 1581, 1513, 1464, 1268, 1132, 1003 and 838 cm^{-1}

MS : m/z 178 (M^+ peak)

- **Synthesis of substituted amines**

Methyl 3-aminobenzoate

Method C: 3-Aminobenzoic acid (5 g) was dissolved in methanol (50 mL) saturated initially with dry hydrogen chloride gas. The solution was refluxed under anhydrous conditions on water bath for 2 h and the reaction mixture was concentrated to half of its original volume. The solution was quenched into cold water (50 mL) to get a clear solution which was neutralized with solid sodium bicarbonate to get a precipitate which was filtered, washed with cold water and dried to obtain the desired compound as white colored solid (4.9 g, 89.0 %) m.p. 49-50 °C (lit.[381]50-54°C).

Anal:

TLC : R_f 0.58 (Chloroform: Methanol, 19:1)

IR : 3415, 3131, 1723, 1619, 1401, 1090 and 745 cm^{-1}

Methyl 4-aminobenzoate

Following **Method C**, butusing 4-aminobenzoic acid (5 g), the desired compound methyl 4-aminobenzoate was obtained as a solid (4.7 g, 84.7 %) m.p. 111-13 °C (lit.[382] 110-113 °C).

Anal:

TLC : R_f 0.58 (Chloroform: Methanol 19:1)

IR : 3416, 3120, 1714, 1608, 1400, 1113 and 857 cm^{-1}

3-Acetamidoaniline

3-Acetamidonitrobenzene

Method D: 3-Nitroaniline (5.0 g, 36.0 mmol) was dissolved in glacial acetic acid (15 mL) and acetic anhydride (6.85 mL, 72.4 mmol) was added to it. The reaction mixture was refluxed under anhydrous conditions on an oil bath for 1 h and quenched into crushed ice (30 g). The precipitate was filtered, washed with cold water and dried to afford3-acetamidonitrobenzene (5.8 g, 89.2 %), m.p. 151-53 °C. (lit.[383] 151-53 °C).

Anal:

TLC : R_f 0.35 (Chloroform: Methanol 19:1)

3-Acetamidoaniline

Method E: A solution of 3-acetamidonitrobenzene (5.0 g, 27.5 mmol) in methanol (50 mL) was refluxed on a water bath. Iron powder (12 g, 220 mmol) and a solution of ammonium chloride (11.7 g, 220 mmol) in water (15 mL) were added portion-wise (in 4 parts at an interval of 45 min) to the refluxing solution. Refluxing was continued for 7-8 h and the solution was filtered through filtering aid and washed with hot methanol (2 x 10 mL). The filtrate was concentrated under reduced pressure to remove excess of methanol and the resulting aqueous solution was diluted with water (25 mL), basified with sodium bicarbonate (10 % aq solution) and extracted with chloroform (3 x 50 mL). The combined chloroform layer was dried and concentrated to get brown colored residue which was dried under vacuum to afford 3-acetamidoaniline (3.0 g, 72 %) m.p. 84-86 °C (lit.[384] 86-88 °C).

Anal:

TLC : R_f 0.16 (Chloroform: Methanol, 19:1)

IR : 3413, 1674, 1611, 1370, 1259, 1163 and 850 cm^{-1}

4-Acetamidoaniline

4-Acetamidonitrobenzene

Following **Method D**, but using 4-nitroaniline (5.0 g, 36.0 mmol), 4-acetamidonitrobenzene was obtained as a solid (5.8 g, 89.2 %) m.p. 215-17 °C (lit.[385] 215-17 °C).

Anal.:

TLC : R_f 0.35 (Chloroform: Methanol 19:1)

4-Acetamidoaniline

4-Acetamidonitrobenzene (5.0 g, 27.5 mmol) was reduced with iron powder and sodium chloride in aqueous methanol using **Method E** to afford 4-acetamidoaniline (0.45 g, 54.2 %) m.p. 164-67 °C (lit.[386] 164-67 °C).

Anal.:

TLC : R_f 0.12 (Chloroform: Methanol 19:1)

IR : 3370, 1664, 1512, 1265, 1089 and 827 cm^{-1}

3-Methanesulfonamidoaniline

3-Methanesulfonamidonitrobenzene

Method F: A solution of 3-nitroaniline (1.0 g, 7.24 mmol) in dry pyridine (4 mL) in a two-neck Rb flask (50 mL) was cooled to 0 °C. Methanesulfonyl chloride (0.84 mL, 10.86 mmol) was added to it drop-wise over a period of 10 min maintaining the temperature at 0-5 °C. The reaction mixture was stirred at RT for another 1 h and quenched into a mixture of hydrochloric acid (5 mL) and ice (50 g). The solid so formed was filtered, washed with cold water and dried to give 3-methanesulfonamido-nitrobenzene (1.38 g, 88.0 %) m.p. 136-38 °C.

Anal.:

TLC : R_f 0.23 (Chloroform: Methanol 19:1)

3-Methanesulfonamidoaniline

3-Methanesulfonamidonitrobenzene (0.1 g, 0.54 mmol) as obtained above was reduced with iron powder and aq. ammonium chloride in methanol using **Method E** to provide 3-methanesulfonamidoaniline (0.06 g, 73.2 %) m.p. 122-24 °C.

Anal:

TLC : R_f 0.44 (Chloroform: Methanol 19:1)

IR : 3406, 3337. 3118, 1607, 1401, 1317, 1147, 987 and 876 cm^{-1}

4-Methanesulfonamidoaniline

4-Methanesulfonamidonitrobenzene

Following **Method F**, but using 4-nitroaniline (1.0 g, 7.24 mmol), 4-methanesulfonamidonitrobenzene was obtained as a solid (1.34 g, 85.7 %) m.p. 166-68 °C.

Anal.:

TLC : R_f 0.35 (Chloroform: Methanol, 19:1)

4-Methanesulfonamidoaniline

4-Methanesulfonamidonitrobenzene (0.1 g, 0.54 mmol) was reduced with iron powder and aq. ammonium chloride in methanol using **Method E** to provide 4-methanesulfonamidoaniline (0.05 g, 68.8 %) m.p. 118-20 °C.

Anal.:

TLC : R_f 0.51 (Chloroform: Methanol, 19:1)

IR : 3414, 3256, 1634, 1512, 1397, 1279, 1146 and 1017 cm^{-1}

5-(3-Aminophenyl)-1*H*-tetrazole

3-Nitrobenzaldoxime

Following **Method A**, but using 3-nitrobenaldehyde (5 g, 33.11 mmol), 3-nitrobenzaldoxime was obtained as a solid (4.94 g, 90 %) m.p.119-21°C (lit[387] 123-25 °C).

Anal.:

TLC : R_f 0.33 (Chloroform: Methanol, 19:1)

3-Nitrobenzonitrile

3-Nitrobenzaldoxime (4 g, 24.09 mmol) was converted to 3-nitrobenzonitrile using **Method B** (3.1 g, 87 %) m.p. 114-16 °C (lit[388] 115-19 °C).

Anal.:

TLC : R_f 0.73 (Chloroform: Methanol, 19:1)

IR : 2236, 1619, 1534, 1356, 1200 and 1101 cm^{-1}

5-(3-Nitrophenyl)-1*H*-tetrazole

Method G: In an Rb flask (10 mL) equipped with a guard tube, 3-nitrobenzonitrile (2 g, 13.51 mmol), was dissolved in DMF (1 mL). Sodium azide (2.63 g, 40.57 mmol) and ammonium chloride (3.58 g, 67.5 mmol) were added to the above solution and the reaction mixture was heated at 100 °C with stirring for 6 h. The reaction mixture was quenched with water and acidified with dilute hydrochloric acid. The precipitate so formed was filtered, washed with water and dried (1.6 g, 62 %) m.p. 210 dec.

Anal.:

TLC : R_f 0. 21 (Chloroform: Methanol, 19:1)

5-(3-Aminophenyl)-1*H*-tetrazole

5-(3-Nitrophenyl)-1*H*-tetrazole (1 g, 0.54 mmol) as obtained above was reduced with iron powder and aq. ammonium chloride in methanol using **Method E** (0.6 g, 71 %) m.p. 197-99 dec. (lit [389] 202-05 dec.).

Anal.:

TLC :R_f 0. 15 (Chloroform: Methanol 19:1)

IR : 3119, 1628, 1523, 1399, 1056 and 1006 cm^{-1}

5-(4-Aminophenyl)-1*H*-tetrazole

4-Nitrobenzaldoxime

Following **Method A**, but using 4-nitrobenaldehyde (5 g, 33.11 mmol), 4-nitrobenzaldoxime was obtained as a solid (4.83 g, 88%) m.p. 122-24 °C (lit[390] 126-31 °C).

Anal.:

TLC : R_f 0. 33(Chloroform: Methanol, 19:1)

4-Nitrobenzonitrile

4-Nitrobenzaldoxime (4 g, 24.09 mmol) was converted to 4-nitrobenzonitrile using **Method B** (3.15 g, 88 %) m.p. 144-47 °C (lit[391] 146-49 °C).

Anal.:

TLC : R_f 0. 69 (Chloroform: Methanol, 19:1)

IR : 2232, 1603, 1527, 1349, 1293 and 1104 cm^{-1}

5-(4-Nitrophenyl)-1*H*-tetrazole

5-(4-Nitrophenyl)-1*H*-tetrazole was prepared from 4-nitrobenzonitrile (2 g, 13.51 mmol) by following **Method G** (1.75 g, 67 %) m.p. 218 °C dec (lit[392] 223 dec.).

Anal.:

TLC : R_f 0. 21 (Chloroform: Methanol 19:1)

5-(4-Aminophenyl)-1*H*-tetrazole

5-(4-Nitrophenyl)-1*H*-tetrazole (1 g, 0.54 mmol) as obtained above was reduced with iron powder and aq. ammonium chloride in methanol using **Method E** (0.67 g, 79 %) m.p. 272-74 °C (lit[393] 275-77 °C).

Anal.:

TLC : R_f 0. 15 (Chloroform: Methanol 19:1)

IR : 3129, 1620, 1500, 1400 and 1263 cm^{-1}

- **Synthesis of substituted benzyl bromides**

3-Cyanobenzyl bromide

Method H: 3-Tolunitrile (2 mL, 1.7 mmol), *N*-bromosuccinimide (3.65 g, 2.04 mmol) and benzoyl peroxide (0.1 g) in dichloromethane (DCM) were taken in an Rb flask (50 mL). The reaction mixture was refluxed on water bath. The orange color disappeared after 2-3 h. Reaction was monitored by TLC. After completion of the reaction, the mixture was cooled to get precipitate of the*N*-succinimide. The reaction mixture was filtered and the filtrate was concentrated to get solid compound (1.49 g, 45 %) m.p. 90-92 °C (lit.[394]93-96 °C).

Anal.:

TLC : R_f 0.60 (Hexane: Ethyl acetate, 18:2)

IR : 3060, 2227, 1713, 1449, 1268, 1178 and 1025 cm^{-1}

3-Nitrobenzyl bromide

Following **Method H,** but using 3-nitrotoluene (2 mL), compound 3-nitrobenzyl bromide was obtained as a solid (1.68 g, 54 %) m.p. 54-56 °C (lit.[395]58-59 °C).

Anal.:

TLC : R_f 0.56 (Hexane: Ethyl acetate, 18:2)

IR : 1528, 1350, 1224 and 808 cm^{-1}

Methyl 3-(bromomethyl)benzoate

Following **Method H,** but using methyl 3-toluate (2 mL), the desired compound methyl 3-(bromomethyl)benzoate was obtained as a solid (1.66 g, 55 %) m.p. 44-46 °C (lit.[396] 46-47 °C).

Anal.:

TLC : R_f 0.53 (Hexane: Ethyl acetate, 18:2)

IR : 1723, 1605, 1433, 1289, 1203, 1107 and 987 cm^{-1}

Methyl 4-(bromomethyl)benzoate

Following **Method H**, but using methyl 4-toluate (2 mL), the desired compound methyl 4-(bromomethyl)benzoate was obtained as a solid (1.84 g, 61 %) m.p. 54-56 °C (lit.[397] 56-58 °C).

Anal.:

TLC : R_f 0.53 (Hexane: Ethyl acetate, 18:2)

IR : 1726, 1610, 1435, 1280, 1111, 1018 and 859 cm^{-1}

5.1.2 Synthesis of 3-*n*.butyl-2-chloromethyl-6,7-dimethoxyquinazolin-4(3*H*)-one (12)

2-Nitro-*N*-*n*.butyl-4,5-dimethoxybenzamide (9)

Method I: A mixture of 6-nitroveratric acid (**4**) (5.0 g, 22.0 mmol) and thionyl chloride (10 mL) was refluxed under anhydrous conditions for 2 h. Excess of thionyl chloride was removed under reduced pressure and the residue was dissolved in anhydrous tetrahydrofuran (THF, 10 mL). In a separate two-neck Rb flask (100 mL) a solution of *n*.butylamine (2.6 mL, 26.4 mmol) and triethylamine (TEA, 9.2 mL, 66.0 mmol) in THF (15 mL) was cooled to 0-5 °C. The acid chloride solution prepared above was added drop-wise to this solution over a period of 10 min, maintaining the temperature below 10 °C. The reaction mixture was stirred for further 2 h at RT and quenched in cold water (75 mL). The precipitate so formed was filtered, washed with cold water and dried. The solid thus obtained was recrystallized from methanol to get yellow colored crystals for 2-nitro-*N*-*n*.butyl-4,5-dimethoxybenzamide (**9**) (4.8 g, 77.4 %) m.p. 130-32 °C.

Anal.:

TLC : R_f 0.38 (Chloroform: methanol, 19:1)

IR : 3270, 1640, 1519, 1349, 1277, 1224, 1077 and 1036 cm^{-1}

2-Amino-*N*-*n*.butyl-4,5-dimethoxybenzamide (10)

2-Nitro-*N*-*n*.butyl-4,5-dimethoxybenzamide (**9**) (1.0 g, 3.5 mmol) was reduced with iron powder and sodium chloride in aqueous methanol using **Method E** to afford 2-amino-*N*-*n*.butyl-4,5-dimethoxybenzamide (**10**) (0.84 g, 95.0 %) m.p. 110-11 °C.

Anal.:

TLC : R_f 0.35 (Chloroform: methanol, 19:1)

IR : 3409, 3317, 1637, 1512, 1462, 1260, 1220, 1178 and 860 cm^{-1}

2-(2-Chloroacetamido)-*N*-*n*.butyl-4,5-dimethoxybenzamide (11)

In a two neck Rb flask (150 mL), 2-amino-*N*-*n*.butyl-4,5-dimethoxybenzamide (**10**) (5 g, 19.84 mmol) and TEA (2.40 mL, 23.80 mmol) were dissolved in dry THF and cooled to 5-10°C. Chloroacetyl chloride (1.88 ml, 23.80 mmol) was added drop-wise to this solution through pressure equalizing funnel, while maintaining the temperature of the reaction mixture between 5-10 °C and allowed the reaction mixture to stir for 1 h at RT. The reaction mixture was then poured in the ice cold water (50 mL). The precipitate so formed was filtered, washed with water and dried to get the compound **(11)** (4.6 g, 70%) m.p. 130-32 °C.

Anal:

TLC : R_f 0.31 (Chloroform: Methanol, 9:1)

IR : 3404, 3298, 1666, 1604, 1527, 1460, 1113 and 1034 cm^{-1}

MS : m/z 329 (M^+ peak)

3-*n*.Butyl-2-(chloromethyl)-6,7-dimethoxyquinazolin-4(3*H*)-one (12)

2-(2-Chloroacetamido)-*N*-*n*.butyl-4,5-dimethoxybenzamide (**7**) (3 g, 9.12 mmol) and sodium *t*.butoxide (1.75 g, 18.24 mmol) was dissolved in ethylene glycol (10 mL). The reaction mixture was stirred for 1 h and quenched in cold water (50 mL). The reaction mixture was extracted several times with chloroform (3 × 25 mL). The organic layer was collected and dried over sodium sulphate to remove traces of water andremoved to afford the compound **(12)** (2 g, 72 %) m.p. 128-30 °C.

Anal:

TLC .: R_f 0.36 (Chloroform: Methanol, 9:1)

IR : 1669, 1503, 1260, 1039 and 792 cm^{-1}

MS : m/z 311 (M^+ peak)

- **Synthesis of 3-*n*.butyl-6,7-dimethoxy-2-[(4-substituted piperazin-1-ylmethyl]) quinazolin-4(3*H*)-ones (Series I)**

3-*n*.Butyl-6,7-dimethoxy-2-[(4-methylpiperazin-1-yl)methyl]quinazolin-4(3*H*)-one (I-1)

Method J: 3-*n*.Butyl-2-(chloromethyl)-6,7-dimethoxyquinazolin-4(3*H*)-one **(12)** (0.15 g, 0.48 mmol), *N*-methylpiperazine (0.08 mL, 0.72 mmol), flame dried potassium carbonate (0.28 g, 2.41 mmol) and dry DMF (1 mL) were taken in an Rb flask (50 mL). The reaction mixture was stirred overnight at 60° C and poured in ice cold water (20 mL) and precipitates so obtained were washed several times with water and filtered. The solid thus obtained was recrystallized from DCM-methanol to afford compound **(I-1)** (0.12 g, 65 %) m.p. 153-55 °C.

Anal.:

TLC : R_f 0.5 (DCM: methanol, 19:1)

IR : 1662, 1501, 1242, 1160, 1012 and 836 cm^{-1}

3-*n*.Butyl-2-[(4-ethylpiperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4(3*H*)-one (I-2)

Compound **(I-2)** was prepared by reacting *N*-ethylpiperazine (0.093 mL, 0.72 mmol) with compound **(12)** (0.15 g, 0.48 mmol) following **Method J** (0.12 g, 64 %) m.p.157-59 °C.

Anal.:

TLC : R_f 0.53 (DCM: methanol, 19:1)

IR : 1663, 1500, 1266, 1162, 1019 and 837 cm^{-1}

3-*n*.Butyl-6,7-dimethoxy-2-[(4-phenylpiperazin-1-yl)methyl]quinazolin-4(3*H*)-one (I-3)

Compound **(I-3)** was prepared by reacting *N*-phenylpiperazine (0.11 mL, 0.72 mmol) with compound **(12)** (0.15 g, 0.48 mmol) following **Method J** (0.15, 72 %) m.p. 162-64 °C.

Anal.:

TLC : R_f 0.43 (Hexane: ethyl acetate, 10:10)

IR : 1667, 1606, 1498, 1266, 1235, 1139, 1053 and 1009 cm^{-1}

NMR : δ 7.43 (s, 1H, Ar-*H*), 7.22-7.15 (m, 3H, Ar-*H*), 6.93-6.91 (m, 2H, Ar-*H*), 6.79-6.75 (m, 1H, Ar-*H*), 4.15-4.11 (t, 2H, CH_2), 3.90 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.69 (s, 2H, CH_2), 3.12 (b, 4H, 2 × CH_2), 2.63 (b, 4H, 2 ×CH_2), 1.72-1.69 (m, 2H, CH_2), 1.41-1.35 (m, 2H, CH_2) and 0.94-0.92 (t, 3H, CH_3)

3-*n*.Butyl-2-[(4-cyclohexylpiperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4(3*H*)-one (I-4)

Reaction of *N*-cyclohexylpiperazine (0.12 g, 0.72 mmol) and compound **(12)** (0.15 g, 0.48 mmol) under the set of conditions described in **Method J** afforded compound **(I-4)** (0.19 g, 60 %) m.p. 154-56 °C.

Anal.:

TLC : R_f 0.1 (Hexane: ethyl acetate, 10:10)

IR : 1660, 1611, 1502, 1400, 1341, 1271, 1160, 1051 and 1019 cm^{-1}

2-[4-((3-*n*.Butyl-3,4-dihydro-6,7-dimethoxy-4-oxoquinazolin-2-yl)methyl)piperazin-1-yl]benzonitrile (I-5)

Reaction of 1-(2-cyanophenyl)piperazine (0.12 mL, 0.72 mmol) and compound **(12)** (0.15 g, 0.48 mmol) under a set of conditions described in **Method J** afforded compound **(I-5)** (0.15 g, 66 %) m.p. 171-73°C.

Anal.:

TLC : R_f 0.5 (Hexane: ethyl acetate, 10:10)

IR : 2220, 1669, 1593, 1496, 1265, 1237, 1053, 1016 and 759 cm^{-1}

NMR : δ 7.72-7.69 (m, 1H, Ar-*H*), 7.62-7.57 (m, 1H, Ar-*H*), 7.44 (s, 1H, Ar-*H*), 7.17 (s, 1H, Ar-*H*), 7.14-7.08 (m, 2H, Ar-*H*), 4.16-4.12 (t, 3H, N-CH_2), 3.90 (s, 3H, O-CH_3), 3.87 (s, 3H, O-CH_3), 3.71 (s,2H, CH_2), 3.14 (b, 4H, CH_2), 2.68 (b, 4H, CH_2), 1.73-1.69 (m, 2H,CH_2), 1.42-1.37 (m, 2H, CH_2) and 0.96-0.93 (t, 3H, CH_3)

3-*n*.Butyl-6,7-dimethoxy-2-[(4-(2-methoxyphenyl)piperazin-1-yl)methyl]quinazolin-4(3*H*)-one (I-6)

Compound (**I-6**) was obtained by the reaction of 1-(2-methoxyphenyl)piperazine (0.12 mL, 0.72 mmol) and compound (**12**) (0.15 g, 0.48 mmol) as per general **Method J** (0.17 g, 75 %) m.p. 160-62 °C.

Anal.:

TLC : R_f 0.26 (Hexane: ethyl acetate, 10:10)

IR : 1669, 1607, 1500, 1458, 1238, 1053, 1022 and 749 cm^{-1}

NMR : δ 7.42 (s, 1H, Ar-*H*), 7.14 (s, 1H, Ar-*H*), 6.92-6.85 (m, 4H, Ar-*H*), 4.13 (m, 2H, N-CH_2), 3.90 (s, 3H, O-CH_3), 3.86 (s, 3H, O-CH_3), 3.76(s, 3H, O-CH_3),3.68 (s, 2H, -CH_2), 2.95 (b, 4H, CH_2), 2.61(b, 4H,CH_2), 1.73 (m, 2H, CH_2), 1.39-1.37 (m, 2H, CH_2) and 0.95-0.92 (t, 3H, CH_3)

MS : m/z 467.43 (M^+ peak)

3-*n*.Butyl-2-[(4-(2-fluorophenyl)piperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4(3*H*)-one (I-7)

Compound (**I-7**) was prepared by reacting 1-(2-flurophenyl)piperazine (0.09 mL, 0.72 mmol) with compound (**12**) (0.15, 0.48 mmol) following **Method J** (0.15 g, 68 %) m.p. 189-91 °C.

Anal.:

TLC : R_f 0.5 (Hexane: ethyl acetate, 10:10)

IR : 1666, 1613, 1500, 1456, 1237, 1138, 1052, 1018 and 757 cm^{-1}

NMR : δ 7.42 (s, 1H, Ar-*H*), 7.15 (s,1H,Ar-*H*), 7.13-7.07 (m, 2H, Ar-*H*), 7.03-6.95 (m, 2H, Ar-*H*), 4.15-4.11 (m, 3H, N-CH_2), 3.90 (s, 3H, O-CH_3), 3.87 (s, 3H, O-CH_3), 3.69 (s, 2H,CH_2), 3.00 (s, 4H,CH_2), 2.65 (b, 4H, CH_2), 1.73-1.69 (m, 2H, CH_2), 1.44-1.34 (m, 2H, CH_2) and 0.98-0.94 (t, 3H, CH_3)

3-*n*.Butyl-6,7-dimethoxy-2-[(4-(pyridin-2-yl)piperazin-1-yl)methyl]quinazolin-4(3*H*)-one (I-8)

1-(2-Pyridyl)piperazine(0.11 mL, 0.72 mmol) was reacted with compound **(12)** (0.15 g, 0.48 mmol) as per **Method J** to get compound **(I-8)** (0.14 g, 64 %) m.p. 186-88 °C.

Anal.:

TLC : R_f 0.23 (Hexane: ethyl acetate, 10:10)

IR : 1668, 1638, 1500, 1268, 1244, 1166, 1052 and 1013 cm^{-1}

NMR : δ 8.1 (m, 1H, Ar-*H*), 7.55-7.50 (m, 1H, Ar-*H*), 7.43 (s, 1H, Ar-*H*), 7.15 (s, 1H, Ar-*H*), 6.82-6.80 (m, 1H, Ar-*H*), 6.66-6.63 (m, 1H, Ar-*H*), 4.17- 4.13 (t, 2H, CH_2), 3.90 (s, 3H, O-CH_3),3.87 (s, 3H, OCH_3), 3.68 (s, 2H, CH_2), 3.46 (b, 4H, 2 × CH_2), 2.57 (b, 4H, 2 × CH_2), 1.73-1.69 (m, 2H, CH_2), 1.42- 1.35 (m, 2H, CH_2) and 0.95 (t, 3H, CH_3)

3-*n*.Butyl-2-[(4-(4-hydroxyphenyl)piperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4(3*H*)-one (I-9)

Reaction of 1-(4-hydroxyphenyl)piperazine (0.12 g, 0.72 mmol) and compound **(12)** (0.15 g, 0.48 mmol) under a set of conditions described in **Method J**afforded compound (0.15 g, 66 %) m.p. 204-06 °C.

Anal.:

TLC : R_f 0.13 (Hexane: ethyl acetate, 10:10)

IR : 3146, 1660, 1614, 1501, 1406, 1272, 1179, 1020 and 836 cm^{-1}

NMR : δ 8.85 (s, 1H, O*H*), 7.43 (s, 1H, Ar-H_c), 7.15 (s, 1H, Ar-H_d), 6.77-6.75 (d, 2H, Ar-*H*), 6.64-6.62 (d, 2H, Ar-*H*), 4.14-4.10 (t, 2H, N-CH_2), 3.90 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.67 (s, 2H, CH_2), 2.95 (bs, 4H, 2 × CH_2), 2.60 (bs, 4H, 2 × CH_2), 1.72-1.68 (m, 2H, CH_2), 1.40- 1.33 (m, 2H, CH_2) and 0.94-0.90 (t, 3H, CH_3).

2-[(4-Benzhydrylpiperazin-1-yl)methyl]-3-*n*.butyl-6,7-dimethoxyquinazolin-4(3*H*)-one (I-10)

Compound **(I-10)** was prepared by reacting 1-benzhydrylpiperazine (0.15 g, 0.72

mmol) with compound (**12**) (0.15 g, 0.48 mmol) following **Method J** (0.18 g, 72 %) m.p. 130-32°C.

Anal.:

TLC : R_f 0.5 (Hexane: ethyl acetate, 10:10)

IR : 1668, 1603, 1498, 1459, 1400, 1268, 1139, 1005 and 704 cm^{-1}

NMR : δ 7.40-7.10 (m, 12H, Ar-*H*), 4.07-4.04 (t, 2H, N-CH_2), 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.68 (s, 2H, CH_2), 2.69 (b, 4H, 2 × CH_2), 2.08 (b, 4H, 2 × CH_2), 1.67 (b, 2H, CH_2), 1.36-1.33 (m, 2H, CH_2) and 0.92-0.88 (t, 3H, CH_3).

- **Synthesis of 2-[(3/4-substituted phenylamino)methyl)-3-*n*.butyl-6,7-dimethoxy-quinazoline-4(3*H*)-ones (Series II)**

3-[(3-*n*.Butyl-3,4-dihydro-6,7-dimethoxy-4-oxoquinazolin-2yl)methylamino)benzoic acid (II-1)

Method K: 3-*n*.Butyl-2-(chloromethyl)-6,7-dimethoxyquinazolin-4(3*H*)-one (**12**) (0.2 g, 0.64 mmol), 3-aminobenzoic acid (0.13 g, 0.96 mmol), flame dried cesium carbonate (0.31 g, 0.64 mmol) and dry DMF (10 mL) were taken in Rb flak (50 mL). The reaction mixture was stirred overnight and poured in ice cold water (20 mL). The precipitates so obtained were washed several times with water and filtered. The solid residue was recrystallized from methanol to afford compound (**II-1**) (0.16 g, 60 %) m.p. 192-94°C.

Anal.:

TLC : R_f 0.52 (Chloroform: Methanol, 19:1)

IR : 3455, 3360, 1717, 1662, 1503, 1226 and 1098 cm^{-1}

NMR : δ 7.61 (s, 1H, Ar-*H*), 7.49-7.47 (m, 1H, Ar-*H*), 7.39-7.38 (m, 1H, Ar-*H*), 7.28-7.21 (m, 1H, Ar-*H*), 7.08 (s, 1H, Ar-*H*), 6.91-6.88 (m, 1H, Ar-*H*), 5.39 (s, 2H, CH_2), 4.12-4.08 (t, 2H, N-CH_2), 4.01 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 1.78-1.72 (m, 2H, CH_2), 1.43-1.37 (m, 2H, CH_2) and 0.93-0.89 (t, 3H, CH_3).

MS : m/z 410.90 (M^+ peak)

4-[(3-*n*.Butyl-3,4-dihydro-6,7-dimethoxy-4-oxoquinazolin-2-yl)methylamino]benzoic acid (II-2)

Compound **(II-2)** was prepared by reacting 4-aminobenzoic acid (0.13 g, 0.96 mmol) with compound **(12)** (0.2 g, 0.64 mmol) as per **Method K** (0.17 g, 68 %) m.p. 122-24°C.

Anal.:

TLC : R_f 0. 33(Chloroform: Methanol, 19:1)

IR : 3466, 3352, 1700, 1657, 1604, 1503, 1272, 1111 and 1028 cm^{-1}

NMR : δ 7.91-7.89 (d, 2H, Ar-*H*), 7.61 (s, 3H, Ar-*H*), 7.09 (s, 3H, Ar-*H*), 6.66 6.64 (d, 2H, Ar-*H*), 5.37 (s, 2H, CH_2), 4.14-4.08 (m, 2H, N-CH_2), 4.00 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 1.77-1.74 (m, 2H, CH_2), 1.42-1.36 (m, 2H, CH_2) and 0.91-0.88 (t, 3H,CH_3).

MS : m/z 410.96 (M^+ peak)

2-[(3-Aminophenylamino)methyl]-3-*n*.butyl-6,7-dimethoxyquinazolin-4(3*H*)-one (II-3)

Compound **(II-3)** was prepared by reacting 3-phenylenediamine (0.10 g, 0.96 mmol) with compound **(12)** (0.2 g, 0.64 mmol) as per **Method K** (0.18 g, 69 %) m.p. 98-102 °C.

Anal.:

TLC : R_f 0.59 (Chloroform: Methanol, 9:1)

IR : 3131, 1663, 1608, 1499, 1400, 1210 and 1167 cm^{-1}

MS : m/z 382.13 (M^+ peak)

2-[(4-Aminophenylamino)methyl]-3-*n*.butyl-6,7-dimethoxyquinazolin-4(3*H*)-one (II-4)

4-Phenylenediamine (0.10 g, 0.96 mmol) was reacted with compound **(12)** (0.2 g, 0.64 mmol) as per the **Method K** to get compound **(II-4)** (0.16 g, 65 %) m.p. 135-38 °C.

Anal.:

TLC : R_f 0.56 (Chloroform: Methanol, 19:1)

IR : 3127, 1668, 1608, 1504, 1447, 1261, 1095 and 801 cm^{-1}

MS : m/z 381.20 (M^+ peak)

_N_-[3-[(3-_n_.Butyl-3,4-dihydro-6,7-dimethoxy-4-oxoquinazolin-2yl)methylamino] phenyl]methanesulfonamide (II-5)

Reaction of 3-methanesulfonamidoaniline (0.179 g, 0.96 mmol) and compound (**12**) (0.2 g, 0.64 mmol) under a set of conditions described in **Method K** afforded compound (**II-5**) (0.17 g, 60 %) m.p. 160 °C dec.

Anal.:

TLC : R_f 0.39 (Chloroform: Methanol, 19:1)

IR : 3444, 3361, 1678, 1607, 1501, 1331, 1272, 1147 and 1082 cm^{-1}

NMR : δ 7.57 (s, 1H, Ar-*H*), 7.13-7.09 (m, 1H, Ar-*H*), 6.93 (s, 1H, Ar-*H*), 6.92-6.88 (m, 2H, Ar-*H*), 6.60-6.58 (m, 1H, Ar-*H*), 4.99 (s, 2H, CH_2), 4.14-4.11 (t, 2H, N-CH_2), 3.98 (s, 6H, 2 × OCH_3), 3.73 (b, 1H, N*H*), 3.23 (s, 3H, CH_3), 1.71-1.66 (m, 2H, CH_2), 1.47-1.41 (m, 2H, CH_2) and 0.99-0.95 (t, 3H, CH_3)

MS : m/z 460.10 (M^+ peak)

_N_-[4-[(3-_n_.Butyl-3,4-dihydro-6,7-dimethoxy-4-oxoquinazoline-2yl)methylamino]-_N_-phenyl]methanesulfonamide (II-6)

Reaction of 4-methanesulfonamidoaniline (0.179 g, 0.96 mmol) and compound (**12**) (0.2 g, 0.64 mmol) under a set of conditions described in **Method K** afforded compound (**II-6**) (0.17 g, 62 %) m.p. 172 °C dec.

Anal.:

TLC : R_f 0.37 (Chloroform: Methanol, 19:1)

IR : 3462, 3366, 1655, 1607, 1508, 1338, 1272, 1145 and 1078 cm^{-1}

NMR : δ 7.56 (s, 1H, Ar-*H*), 7.31-7.28 (d, 2H, Ar-*H*), 6.94 (s, 1H, Ar-H_d), 6.60-6.58 (d, 2H, Ar-*H*), 4.96 (s, 2H, CH_2), 4.16-4.12 (t, 2H, N-CH_2), 3.99 (s, 3H, OCH_3), 3.98 (s, 3H, OCH_3), 3.16 (s, 3H, CH_3), 1.68-1.61 (m, 2H, CH_2), 1.46-1.41 (m, 2H, CH_2) and 0.99-0.95 (t, 3H, CH_3).

MS : m/z 460.09 (M^+ peak)

5-[3-((3-*n*.Butyl-3,4-dihydro-6,7-dimethoxy-4-oxoquinazolin-2yl)methylamino)-phenyl]-1*H*-tetrazole (II-7)

Compound (**II-7**) was prepared by reacting 5-(3-aminophenyl)-1*H*-tetrazole (0.19 g, 0.96 mmol) with compound (**12**) (0.2 g, 0.64 mmol) as per **Method K** (0.13 g, 46 %) m.p. 167-70 °C.

Anal.:

TLC : R_f 0.78(Chloroform: Methanol, 18:2)

IR : 3416, 1665, 1611, 1501, 1400, 1262, 1210, 1171, 1038 and 788 cm^{-1}

NMR : δ 7.52 (s, 1H, Ar-*H*), 7.45 (s, 1H, Ar-*H*), 7.40-7.38 (m, 1H, Ar-*H*), 7.22-7.18 (m, 1H, Ar-*H*), 6.91 (s, 1H, Ar-*H*), 6.78-6.77 (m, 1H, Ar-*H*), 6.14 (s, 2H, N-CH_2), 4.21-4.13 (t, 2H, N-CH_2), 3.95 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 1.66-1.59 (m, 2H, CH_2), 1.51-1.43 (m, 2H, CH_2) and 0.88-0.85 (t, 3H, CH_3)

MS : m/z 434.98 (M+ peak)

5-[4-((3-*n*.Butyl-3,4-dihydro-6,7-dimethoxy-4-oxoquinazolin-2yl)methylamino)-phenyl]-1*H*-tetrazole (II-8)

Compound (**II-8**) was prepared by reacting 5-(4-aminophenyl)-1*H*-tetrazole (0.19 g, 0.96 mmol) with compound (**12**) (0.2 g, 0.64 mmol) as per **Method K** (0.12 g, 44 %) m.p. 90-92 °C.

Anal.:

TLC : R_f0.78 (Chloroform: Methanol, 18:2)

IR : 3359, 3133, 1664, 1611, 1502, 1465, 1270, 1207, 1174 and 1037 cm^{-1}

NMR : δ 7.80-7.78 (d, 2H, Ar-*H*), 7.49 (s, 1H, Ar-*H*), 6.89 (s, 3H, Ar-*H*), 6.72-6.69 (d, 2H, Ar-*H*), 6.14 (s, 2H, CH_2), 4.19-4.15 (t, 2H, N-CH_2), 3.98 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 1.62-1.55 (m, 2H, CH_2), 1.48-1.42 (m, 2H, CH_2) and 0.99-0.84 (t, 3H, CH_3)

MS : m/z 435.17 (M^+ peak)

5.1.3 Synthesis of 3-(3/4-substituted benzyl)-2-*n*.butyl-6,7-dimethoxyquinzolin-4(3*H*)-ones (Series III)

4,5-Dimethoxyanthranilic acid (13)

Method L: 6-Nitroveratric acid (**4**) (5 g) was dissolved in methanol (50 mL) in a three-neck Rb flask (100 mL) equipped with a hydrogen balloon. Palladium-charcoal (0.1 g, 10 %) was added to the above solution and the reaction mixture was stirred under an atmosphere of hydrogen gas for 4 h. The reaction mixture was filtered through filtering aid, washed with hot methanol and the filtrate was concentrated under reduced pressure to afford 4,5-dimethoxyanthranilic acid (**13**) as brown colored solid (3.6 g, 85 %), m.p. 154-56 °C (lit[398] 155-58 °C).

Anal.:

TLC : R_f 0.2 (Chloroform: Methanol, 18:2)

IR : 3487, 3373, 1705, 1652, 1550, 1386, 1180 and 1033 cm^{-1}

2-*n*.Butyl-6,7-dimethoxyquinazolin-4(3*H*)-one (14)

In a Rb flask (10 mL), a solution of 4,5-dimethoxyanthranilic acid (**13**) (1 g, 5.1 mmol), *n*.valeroyl chloride (1.4 mL, 11.16 mmol) in DMF (2 mL) was taken and heated on an oil bath for 2 h under anhydrous conditions. Few dropsof acetic anhydride wereadded in order to complete the reaction.The black colored sticky residue thus obtained was triturated with hexane to give free flowing solid which was filtered and dried to afford 2-*n*.butyl-6,7-dimethoxybenz[1,3-*d*]-4*H*-oxazin-4-one (1.0 g, 89.3 %) m.p. 182-84 °C.

Anal.:

TLC : R_f 0.73 (Chloroform: Methanol, 17:3)

IR : 1746, 1605, 1509, 1459, 1260, 1093, 1024 and 801cm^{-1}

2-*n*.Butyl-6,7-dimethoxy-4*H*-benz[1,3-*d*]oxazin-4-one prepared as above was treated with ammonium acetate and the reaction mixture heated at 100°C until the reaction completed. The reaction mixture was poured in ice-cold water (20 mL), filtered and washed several times with water. The dried residue was recrystallized from DCM and methanol to afford the desired product.

Anal.:

TLC : R_f 0.36 (Chloroform: Methanol, 17:3)

IR : 3157, 3057, 1670, 1614, 1496, 1393, 1260, 1217, 995 and 864 cm^{-1}

MS : 262.06 (M^+ peak)

Methyl 3-[(2-*n*.butyl-6,7-dimethoxy-4-oxoquinazolin-3(4*H*)-yl)methyl]benzoate (III-1)

Method M: Compound **(14)** (0.2 g, 0.76 mmol), methyl 3-(bromomethyl)benzoate (0.35 g, 1.52 mmol) and K_2CO_3 (0.21 g, 1.52 mmol) were taken in dry acetone. The reaction mixture was stirred at RT and monitored by TLC. After completion of the reaction, it was poured in ice-cold water (20 mL). The precipitate so formed were filtered and washed several times with water. The residue was recrystallized from DCM-methanol to afford the solid compound **(III-1)** (0.18 g, 57 %) m.p. 178-80 °C.

Anal.:

TLC : R_f 0.5 (Hexane: ethyl acetate, 12:8)

IR : 1669, 1611, 1500, 1403, 1273, 1168, 1138, 1032 and 870 cm^{-1}

Methyl4-[(2-*n*.butyl-6,7-dimethoxy-4-oxoquinazolin-3(4*H*)-yl)methyl]benzoate (III-2)

Compound **(III-2)** was obtained by the reaction of methyl 4-(bromomethyl)benzoate (0.35 g, 1.52 mmol) and compound **(14)** (0.2 g, 0.76 mmol) as per general **Method M** (0.17 g, 55 %) m.p. 186-89 °C.

Anal.:

TLC : R_f 0.46 (Hexane: ethyl acetate 12:8)

IR : 1720, 1654, 1611, 1503, 1435, 1283, 1059, 1012 and749 cm^{-1}

NMR : δ 7.94- 7.92 (d, 2h, Ar-*H*), 7.46 (s, 1H, Ar-*H*), 7.29-7.27 (d, 2H, Ar-*H*), 7.11 (s, 1H, Ar-*H*), 5.46 (s, 2H, CH_2), 3.92 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 2.68-2.65 (t, 2H, CH_2),1.67-1.59 (m, 2H, CH_2), 1.33-1.24 (m, 2H, CH_2) and 0.82-0.79 (t, 3H, CH_3)

3-[(2-*n*.Butyl-6,7-dimethoxy-4-oxoquinazolin-3(4*H*)-yl)methyl]benzoic acid (III-3)

Method N: Compound **(III-1)** (0.1 g, 0.23 mmol) was suspended in methanol (5 mL) in an Rb flask (10 mL) and aq sodium hydroxide solution (30 %, 0.5 mL) was added to it. The reaction mixture was refluxed for 30 min and excess of methanol was recovered. The residue was quenched in cold water (20 mL) and carefully neutralized (*p*H 5.5-6.0) with dilute hydrochloric acid. The precipitate so formed was filtered under suction, washed with cold water and dried. The solid thus obtained was subjected to recrystallization from a mixture of chloroform and methanol to afford compound **(III-3)** (0.067 g, 70 %) m.p. 198-200 °C.

Anal.:

TLC : R_f 0.2 (Hexane: ethyl acetate 12:8)

IR : 3130, 1703, 1660, 1617, 1506, 1400, 1288, 1167 and 1003cm^{-1}

NMR : δ 7.86-7.84 (d, 1H, Ar-*H*), 7.68 (s, 1H, Ar-*H*), 7.51-7.43 (m, 3H, Ar-*H*), 7.11 (s, 1H, Ar-*H*), 5.77 (s, 2H, N-CH_2), 3.92 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 2.71-2.67 (m, 2H, CH_2), 1.64-1.60 (m, 2H, CH_2), 1.31-1.27 (m, 2H, CH_2) and 0.84-0.77 (t, 3H, CH_3)

4-[(2-*n*.Butyl-6,7-dimethoxy-4-oxoquinazolin-3(4*H*)-yl)methyl]benzoic acid (III-4)

Compound **(III-4)** was obtained from compound **(III-2)** (0.1 g, 0.23 mmol) as per general **Method N** (0.071g, 74 %) m.p. 240-42 °C dec.

Anal.:

TLC : R_f 0.18 (Hexane: ethyl acetate, 12:8)

IR : 3413, 1670, 1638, 1616, 1502, 1402. 1348, 1254, 1058 and 1013 cm^{-1}

NMR : *δ* 8.23-8.21 (d, 2H, Ar-*H*), 7.46 (s, 1H, Ar-*H*), 7.44-7.41 (d, 2H, Ar-*H*), 7.12 (s, 1H, Ar-*H*), 5.51 (s, 2H, CH_2), 3.93 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 2.70-2.66 (m, 2H, CH_2), 1.69-1.62 (m, 2H, CH_2), 1.35-1.23 (m, 2H, CH_2) and 0.87-0.83 (t, 3H, CH_3)

2-*n*.Butyl-6,7-dimethoxy-3-(3-nitrobenzyl)quinazolin-4(3*H*)-one (III-5)

Compound **(III-5)** was prepared by reacting 3-nitrobenzyl bromide (0.33 g, 1.52 mmol) with compound **(14)** (0.2 g, 0.76 mmol) as per **Method M** (0.18 g, 61 %) m.p. 160-62 °C.

Anal.:

TLC : R_f 0.33 (Hexane: ethyl acetate, 12:8)

IR : 1664, 1612, 1571, 1530, 1443, 1351, 1228, 1000 and 780 cm^{-1}

2-*n*.Butyl-6,7-dimethoxy-3-(4-nitrobenzyl)quinazolin-4(3*H*)-one (III-6)

Compound **(III-6)** was prepared by reacting 4-nitrobenzyl bromide (0.33 g, 1.52 mmol) with compound **(14)** (0.2 g, 0.76 mmol) as per **Method M** (0.19 g, 63 %) m.p. 178-80 °C.

Anal.:

TLC : R_f 0.36 (Hexane: ethyl acetate, 12:8)

IR : 1657, 1610, 1520, 1501, 1401, 1345, 1230, 1002, 850 and 733 cm^{-1}

NMR : δ 8.20-8.18 (d, 2H, Ar-*H*), 7.50 (s, 1H, Ar-*H*), 7.44-7.41 (d, 2H, Ar-*H*), 7.10 (s, 1H, Ar-H), 5.29 (s, 3H, N-CH_2), 3.97 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 2.71-2.67(t, 2H, N-CH_2), 1.73-1.67 (m, 2H, CH_2), 1.39-1.33 (m, 2H, CH_2) and 0.90-0.86 (t, 3H, CH_3)

3-(3-Aminobenzyl)-2-*n*.butyl-6,7-dimethoxyquinazolin-4(3*H*)-one (III-7)

Compound **(III-7)** was prepared from compound **(III-5)** (0.15 g, 0.37 mmol) with iron powder and ammonium chloride by following **Method E** (0.11 g, 76 %) m.p. 224-26 °C.

Anal:

TLC : R_f 0.2 (Hexane: ethyl acetate, 12:8)

IR : 3413, 3115, 1664, 1614, 1530, 1503, 1400, 1351, 1271, 1208, 999 and 780 cm^{-1}

3-(4-Aminobenzyl)-2-*n*.butyl-6,7-dimethoxyquinazolin-4(3*H*)-one (III-8)

Compound **(III-8)** was prepared from compound **(III-6)** (0.15 g, 0.37 mmol) with iron powder and ammonium chloride by following **Method E** (0.11, 80 %) m.p. > 280°C.

Anal.:

TLC : R_f 0.23 (Hexane: ethyl acetate, 12:8)

IR : 3413, 3159, 3006, 1658, 1614, 1496, 1400, 1266, 1138 and 1001 cm^{-1}

***N*-[4-((2-*n*.Butyl-6,7-dimethoxy-4-oxoquinazolin-3(4*H*)-yl)methyl)phenyl]methane sulfonamide (III-9)**

Compound (**III-9**) was prepared by methylsulfonation of compound (**III-8**) (0.1 g, 0.27 mmol) by following **Method F** (0.083 g, 69 %) m.p. 154-56 °C.

Anal.:

TLC : R_f 0.26 (Hexane: ethyl acetate, 12:8)

IR : 3414, 3143, 1659, 1612, 1500, 1401, 1335, 1247, 1210, 1152, 1013 and 781cm^{-1}

3-[(2-*n*.Butyl-6,7-dimethoxy-4-oxoquinazolin-3(4*H*)-yl)methyl]benzonitrile (III-10)

Reaction of 3-(bromomethyl)benzonitrile (0.30 g, 1.52 mmol) and compound (**14**) (0.2 g, 0.76 mmol) under a set of conditions described in **Method M** afforded compound (**III-10**) (0.16 g, 58 %) m.p. 215-17 °C.

Anal.:

TLC : R_f 0.56 (Hexane: ethyl acetate, 12:8)

IR : 2230, 1660, 1611, 1501, 1400, 1269, 1245, 1141 and 1012 cm^{-1}

NMR : δ 7.63-7.62 (m, 1H, Ar-*H*), 7.56-7.51 (m, 4H, Ar-H), 7.20 (s, 1H, Ar-*H*), 5.46 (s, 2H, N-CH_2), 4.00 (s, 3H. O-CH_3), 3.97 (s, 3H, O-CH_3), 2.81-2.77 (t, 2H, N-CH_2), 1.74-1.68 (m, 2H, CH_2), 1.43-1.38 (m, 2H, CH_2) and 0.92-0.88 (t, 3H, CH_3)

MS : m/z 377.90 (M^+ peak)

4-[(2-*n*.Butyl-6,7-dimethoxy-4-oxoquinazolin-3(4*H*)-yl)methyl]benzonitrile (III-11)

Reaction of 4-(bromomethyl)benzonitrile (0.30 g, 1.52 mmol) and compound (**14**) (0.2 g, 0.76 mmol) under a set of conditions described in **Method M** afforded compound (**III-11**) (0.17 g, 60 %) m.p. 214-16 °C.

Anal.:

TLC : R_f 0.56 (Hexane: ethyl acetate, 12:8)

IR : 2228, 1658, 1610, 1502, 1402, 1245, 1232, 1013, 846 and 784 cm^{-1}

2-*n*.Butyl-6,7-dimethoxy-3-[3-(1*H*-tetrazol-5-yl)benzyl]quinazolin-4(3*H*)-one (III-12)

Compound **III-12** was prepared from compound **(III-10)** (0.12 g, 0.32 mmol) by following **Method G** (0.073 g, 55 %) m.p. 260 °C dec.

Anal.:

TLC : R_f0.2 (Hexane: ethyl acetate, 12:8)

IR : 3132, 1638, 1608, 1501, 1403, 1294, 1245, 1212, 1173, 1024 and 860 cm^{-1}

NMR : δ 7.96-7.94 (d, 1H, Ar-*H*), 7.82 (s, 1H, Ar-*H*), 7.61-7.57 (t, 1H, Ar-*H*), 7.48(s, 1H, Ar-*H*), 7.42-7.40 (d, 1H, Ar-*H*), 7.12 (s, 1H, Ar-*H*), 5.48 (s, 2H, CH_2), 3.92 (s, 3H, O-CH_3), 3.88 (s, 3H, O-CH_3), 2.74-2.71 (t, 2H, CH_2), 1.69-1.61 (m, 2H, CH_2), 1.32-1.26 (m, 2H, CH_2) and 0.82 (t, 3H, CH_3)

2-*n*.Butyl-6,7-dimethoxy-3-[4-(1*H*-tetrazol-5-yl)benzyl]quinazolin-4(3*H*)-one (III-13)

Compound **(III-13)** was obtained from compound **(III-11)** (0.12 g, 0.32 mmol) as per general **Method G** (0.076 g, 57 %). m.p. 195-97 °C.

Anal.:

TLC : R_f0.17 (Hexane: ethyl acetate 12:8)

IR : 3148, 1649, 1613, 1502, 1403, 1292, 1252, 1167, 1067 and 999 cm^{-1}

5.1.4 Synthesis of 2-chloro-6,7-dimethoxyquinazolin-4-amine (19)

3,4-Dimethoxy-6-nitrobenzamide (15)

A solution of 6-nitroverateric acid (**4**) (5.0 g, 22.0 mmol) in thionyl chloride (10 mL) was refluxed under anhydrous conditions for 2 h in an Rb flask (50 mL). The excess of thionyl chloride was removed under reduced pressure. The residue so obtained was dissolved in anhydrous tetrahydrofuran (THF) (25 mL) and cooled to 5 °C. Aqueous ammonia (15 mL) was added to this solution drop-wise over a period of 15 min, keeping the temperature of the reaction mixture between 5-10 °C. The reaction mixture was stirred for further 2 h at RT and quenched in cold water (100 mL). The precipitate thus formed was filtered, washed with cold water and dried. The solid so obtained was recrystallized from methanol to get yellow colored crystals of 3,4-dimethoxy-6-nitrobenzamide (**15**) (3.0 g, 60.2 %), m.p. 192-95 °C (lit.[399] 192-95 °C).

Anal.:

TLC : R_f 0.5 (Chloroform: methanol, 18:2)

IR : 3423, 1663, 1576, 1525, 1512, 1343, 1276, 1226 and 1050 cm^{-1}

2-Amino-4,5-dimethoxybenzamide (16)

Compound (**16**) was prepared from compound (**15**) (1.0 g, 4.4 mmol) with iron powder and ammonium chloride by following **Method E** (0.45 g, 51.9 %), m.p. 144-46 °C (lit.[400] 145-47 °C).

Anal.:

TLC : R_f 0.45 (Chloroform: methanol, 18:2)

IR : 3450, 3341, 1671, 1631, 1548, 1394, 1258, 1178 and 1078 cm^{-1}

6,7-Dimethoxy-1,2,3,4-tetrahydroquinazoline-2,4-dione (17)

Compound (**16**) (1.0 g, 5.10 mmol) was dissolved in pyridine (3 mL) in an Rb flask (10 mL) and to the clear solution urea (0.06 g, 10.20 mmol) and 2 drops of dilute hydrochloric acid were added. The reaction mixture was refluxed with stirring for 8 h, cooled to RT and the precipitate so formed was filtered, washed with diethyl ether and dried. The solid thus obtained was subjected to recrystallization from a mixture of chloroform and methanol to afford 6,7-dimethoxy-1,2,3,4-tetrahydroquinazoline-2,4-dione (**17**) (0.60 g, 57 %) m.p. > 280 °C.

Anal.:

TLC : R_f 0.13 (Chloroform: methanol, 18:2)

IR : 3176, 1706, 1657, 1625, 1509, 1426, 1264, 1101 and 1039 cm^{-1}

2,4-Dichloro-6,7-dimethoxyquinazoline (18)

A mixture of 6,7-dimethoxy-1,2,3,4-tetrahydroquinazoline-2,4-dione (**17**) (1.0 g, 4.50 mmol), phosphorus oxychloride (3.0 mL) and *N,N*-dimethylaniline (2 drops) was refluxed with stirring in an Rb flask (10 mL) for 16 h. The reaction mixture was cooled to RT and cautiously quenched in crushed ice (50 g) with vigorous stirring. The precipitate so formed was filtered and immediately dissolved in chloroform (25 mL) which was dried and concentrated to give yellow colored solid of 2,4-dichloro-6,7-dimethoxyquinazoline (**18**), which was immediately used as such for the next step (0.52 g, 44.5 %) m.p. > 280 °C.

Anal.:

TLC : R_f 0.88 (Chloroform: methanol, 18:2)

IR : 1612, 1543, 1480, 1445, 1372, 1340, 1268, 1153 and 1110 cm^{-1}

4-Amino-2-chloro-6,7-dimethoxyquinazoline (19)

2,4-Dichloro-6,7-dimethoxyquinazoline (**18**) (1.0 g, 3.86 mmol) was dissolved in THF (15 mL) and dry ammonia gas was bubbled through this solution for 36 h. The solid precipitate formed was filtered after every 16 h and at the end of the reaction the reaction mixture was concentrated to get an additional crop. The solid thus obtained was recrystallized from a mixture of chloroform and methanol to afford 4-amino-2-chloro-6,7-dimethoxyquinazoline (**19**).(0.27 g, 30 %) m.p. 260-62 °C dec. (lit.[401] 262-66 °C dec.).

Anal.:

TLC : R_f 0.18 (Hexane: ethyl acetate, 10:10)

IR : 3409, 3326, 1658, 1585, 1498, 1279, 1250, 1087 and 1026 cm^{-1}

MS : m/z 240 $(M + 1)^+$

- **Synthesis of 6,7-dimethoxy-2-(4-substituted piperazin-1-yl)quinazolin-4-amine (Series IV)**

6,7-Dimethoxy-2-(4-methylpiperazin-1-yl)quinazolin-4-amine (IV-1)

Method O: Potassium carbonate was flame dried under vacuum. To a solution of 4-amino-2-chloro-6,7-dimethoxyquinazoline (**19**) (0.1 g, 0.41 mmol) and *N*-methyl piperazine (0.139 mL, 1.25 mmol) potassium carbonate in dry DMF was added. The reaction mixture was stirred overnight at 120°C in sealed tube. The reaction mixture was poured in ice cold water and the precipitates so obtained were filtered and washed with water. The residue was recrystallized from DCM-methanol to afford the desired compound (**IV-1**) (0.07 g, 58 %) m.p. 132-34°C.[402]

Anal.:

TLC : R_f 0.9 (DCM: methanol, 19:1)

IR : 3555, 3334, 1644, 1485, 1443, 1374, 1280, 1244, 1143, 1002 and 836 cm^{-1}

NMR : δ 7.40 (s, 1H, Ar-*H*), 7.09 (b, 2H, NH_2), 6.70 (s, 1H, Ar-*H*), 3.82 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.68 (b, 4H, 2 × CH_2), 2.33 (b, 4H, 2× CH_2) and 2.19 (s, 3H, CH_3)

2-(4-Ethylpiperazin-1-yl)-6,7-dimethoxyquinazolin-4-amine (IV-2)

Reaction of *N*-ethylpiperazine (0.15 mL, 1.25 mmol) and compound (**19**) (0.1 g, 0.41 mmol) under a set of conditions described in **Method O** afforded compound (**IV-2**) (0.08 g, 60%) m.p. 187-89 °C.

Anal.:

TLC : R_f 0.33 (DCM: methanol, 19:1)

IR : 3291, 3086, 1666, 1580, 1494, 1382, 1294, 1248, 1212, 1180, 993 and 844 cm^{-1}

6,7-Dimethoxy-2-(4-phenylpiperazin-1-yl)quinazolin-4-amine (IV-3)

Reaction of *N*-phenylpiperazine (0.19 mL, 1.25 mmol) and compound (**19**) (0.1g, 0.41 mmol) as per **Method O** afforded compound (**IV-3**) (0.1 g, 70%) m.p. 230-32 °C.[403]

Anal.:

TLC : R_f 0.36 (Hexane: ethyl acetate, 15:5)

IR : 3456, 3362, 1628, 1570, 1440, 1379, 1288, 1235, 1166, 1103, 1033 988 and 840 cm^{-1}

NMR : δ 7.42 (s, 1H, Ar-*H*), 7.25-7.21 (m, 2H, Ar-*H*), 7.15 (b, 2H, NH_2), 7.01-6.99 (d, 2H, Ar-*H*), 6.82-6.78 (m, 1H, Ar-*H*), 6.74 (s, 1H, Ar-H), 3.83 (s, 6H, 2 × OCH_3), 3.17-3.15 (m, 8H, 4 × CH_2).

2-[4-(4-Amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl]benzonitrile (IV-4)

1-(2-Cyanophenyl)piperazine (0.20 mL, 1.25 mmol) was reacted with compound

(19) (0.1g, 0.41 mmol) as per **Method O** to get compound **(IV-4)** (0.1 g, 65%) m.p. 127-29 °C.

Anal.:

TLC : R_f 0.46 (Hexane: ethyl acetate, 15:5)

IR : 3491, 3321, 2218, 1638, 1571, 1485, 1379, 1284, 1253, 1217, 1149, 1106, 1034, 995 and 850 cm^{-1}

NMR : δ 7.75-7.73 (dd, 1H, Ar-*H*), 7.73-7.60 (m, 1H, Ar-*H*), 7.43 (s, 1H,Ar-*H*), 7.23-7.06 (m, 4H, Ar-*H* and NH_2), 6.75 (s, 1H, Ar-*H*), 3.90-3.88 (m, 4H, 2× CH_2), 3.84 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3) and 3.19-3.17 (m, 4H, 2× CH_2)

MS : m/z 390.21 (M^+ peak)

6,7-Dimethoxy-2-[4-(2-methoxyphenyl)piperazin-1-yl]quinazolin-4-amine (IV-5)

Compound **(IV-5)** was prepared by reacting 1-(2-methoxyphenyl)piperazine (0.22 mL, 1.25 mmol) with compound **(19)** (0.1g, 0.41 mmol) as per **Method O** (0.11 g, 72%) m.p. 122-24 °C.[404]

Anal.:

TLC : R_f 0.3 (Hexane: ethyl acetate, 15:5)

IR : 3412, 3211, 1639, 1557, 1501, 1442, 1404, 1291, 1247, 1146, 1112, 1028, 846 and 750 cm^{-1}

NMR : δ 7.42 (s, 1H, Ar-*H*), 7.13 (b, 2H, NH_2), 6.97-6.85 (m, 4H, Ar- *H*), 6.73 (s, 1H, Ar-*H*), 3.85-3.83 (bs, 7H, 2 × CH_2 and OCH_3), 3.80 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3) and 2.98-2.96 (t, 4H, 2 × CH_2)

2-[4-(2-Fluorophenyl)piperazin-1-yl]-6,7-dimethoxyquinazolin-4-amine (IV-6)

Reaction of 1-(2-flurophenyl)piperazine (0.19, 1.25 mmol) and compound **(19)** (0.1g, 0.41 mmol) under a set of conditions described in **Method O** afforded compound **(IV-6)** (0.1 g, 62 %) m.p. 202-04 °C.

Anal.:

TLC : R_f 0.53(Hexane: ethyl acetate, 15:5)

IR : 3484, 3371, 1626, 1573, 1435, 1371, 1281, 1235, 1168, 1098, 1033, 993, 839 and 745 cm^{-1}

NMR : δ 7.42 (s, 1H, Ar-*H*), 7.18-6.98 (m, 6H, Ar-*H* and NH_2), 6.74 (s, 1H, Ar-H), 3.88-3.86 (t, 4H, 2 × CH_2), 3.83 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3) and 3.04-3.02 (t, 4H, 2 × CH_2)

6,7-Dimethoxy-2-[4-(pyridin-2-yl)piperazin-1-yl]quinazolin-4-amine (IV-7)

Reaction of 1-(2-pyridyl)piperazine (0.19 mL, 1.25 mmol) and compound **(19)** (0.1 g, 0.41 mmol) under conditions described in **Method O** afforded compound **(IV-7)** (0.08 g, 52%) m.p. 226 °C dec.

Anal.:

TLC : R_f 0.3 (Hexane: ethyl acetate 15:5)

IR : 3433, 3189, 1646, 1562, 1490, 1436, 1374, 1277, 1235, 1165, 1099, 1033, 982, 836 and 773 cm^{-1}

NMR : δ 8.13-8.12 (dd, 1H, Ar-*H*), 7.57-7.53 (m, 1H, Ar-*H*), 7.42 (s, 1H, Ar-*H*), 7.18 (b, 2H, NH_2), 6.89-6.87 (d, 1H, Ar-*H*), 6.76 (s, 1H, Ar-*H*),6.67-6.64 (m, 1H, Ar-*H*), 3.83-3.78 (m, 10H, 2 × CH_2 and 2 × OCH_3) and3.55-3.52 (t, 4H, 2 × CH_2)

4-[4-(4-Amino-6,7-dimethoxyquinazolin-2-yl)piperazin-1-yl]phenol (IV-8)

Compound **(IV-8)** was prepared by reacting 1-(4-hydroxyphenyl)piperazine (0.22 g, 1.25 mmol) and compound **(19)** (0.1g, 0.41 mmol) using **Method O** (0.09 g, 56%) m.p. > 280 °C (lit[405])

Anal.:

TLC : R_f 0.2 (Hexane: ethyl acetate 15:5)

IR : 3357, 3145, 1631, 1510, 1279, 1230, 1176 and 1031 cm^{-1}

2-(4-Benzhydrylpiperazin-1-yl)-6,7-dimethoxyquinazolin-4-amine (IV-9)

Compound **(IV-9)** was obtained by the reaction of benzhydryl piperazine (0.26 g, 1.25 mmol) and compound **(19)** (0.1g, 0.41 mmol) as per general **Method O** (0.12 g, 68 %) m.p. 270-72 °C (lit[406] 273-74 °C).

Anal.:

TLC : R_f 0.46 (Hexane: ethyl acetate 15:5)

IR : 3438, 3330, 1654, 1562, 1490, 1441, 1277, 1239, 1146, 1107, 1030, 997, 850 and 749 cm^{-1}

NMR : δ 7.46-7.09 (m, 13H, 11 Ar-*H* and NH_2), 6.68 (s, 1H, Ar-*H*), 4.30 (s, 1H, C*H*), 3.80 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.70 (b, 4H, 2 × CH_2) and 2.36-2.33 (b, 4H, 2× CH_2)

5.1.5 Synthesis of 2-(chloromethyl)-6,7-dimethoxyquinazolin-4-amine

2-(Chloromethyl)-6,7-dimethoxyquinazolin-4-amine (20)

Chloroacetonitrile (0.42 ml, 6.74 mmol) and dioxane (5 mL) saturated with dry HCl gas (0.82 g, 22.47 mmol) were taken in Rb flask (50 mL) and allowed to stir for half an hour. 2-Amino-4,5-dimethoxybenzonitrile (**8**) (1 g, 5.61 mmol) was dissolved in dry dioxane and addedto the above reaction mixture. The reaction mixture was allowed to stir for 24 hour. The reaction mixture was quenched in ice cold water (15 mL). The suspension so formed was filtered and the precipitate rejected. The filtrate was basified with ammonia solution. The precipitates so obtained were filtered and dried under vaccum to obtain the product (**20**) (0.9g, 63.38%) m.p. 250 °C dec.

Anal.:

TLC : R_f 0.21(Ethyl acetate: hexane, 14:6)

IR : 3479, 3330, 3136, 1657, 1583, 1508, 1434, 1254, 1216, 1170, 1001 and 841 cm^{-1}

MS : m/z 252.98 (M^+ peak), 254.99 $(M + 2)^+$

- **Synthesis of 6,7-dimethoxy-2-(4-substituted piperazin-1-yl)quinazolin-4-amine (Series V)**

6,7-Dimethoxy-2-[(4-methylpiperazin-1-yl)methyl]quinazolin-4-amine (V-1)

Reaction of *N*-methylpiperazine (0.26 mL, 2.37 mmol) and compound (**20**) (0.2 g, 0.79 mmol) under a set of conditions described in **Method J** afforded compound (**V-1**) (0.16 g, 63%) m.p. 253-55 °C.

Anal.:

TLC : R_f 0.1 (DCM: Methanol, 18:2)

IR : 3131, 1672, 1582, 1489, 14011261, 1225 and 1142 cm^{-1}

NMR : δ 7.53 (s, 1H, Ar-*H*), 7.41 (b, 2H, NH_2), 7.07 (s, 1H, Ar-*H*), 3.87 (s, 3H, OCH_3), 3.84(s, 3H, OCH_3), 3.40 (s, 2H, CH_2), 2.50 (b, 4H), 2.28 (b, 4H, CH_2) and 2.12 (s, 3H)

2-[(4-Ethylpiperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4-amine (V-2)

Reaction of *N*-ethylpiperazine (0.3 mL, 2.37 mmol) and compound **(20)** (0.2 g, 0.79 mmol) under the conditions described in **Method J** afforded compound **(V-2)** (0.17 g, 64%) m.p. 241-43 °C.

Anal.:

TLC : R_f 0.1 (DCM: Methanol, 18:2)

IR : 3306, 3146, 1666, 1580, 1491, 1279, 1248, 1165, 1016 and 869 cm^{-1}

6,7-Dimethoxy-2-[(4-phenylpiperazin-1-yl)methyl]quinazolin-4-amine (V-3)

Compound **(V-3)** was prepared by reacting *N*-phenylpiperazine (0.36 mL, 2.371 mmol) with compound **(20)** (0.2 g, 0.79 mmol) as per **MethodJ** (0.22 g, 74%) m.p. 230-32 °C.

Anal.:

TLC : R_f 0.73 (DCM: Methanol, 18:2)

IR : 3313, 3151, 1666, 1579, 1323, 1281, 1222, 1133, 1015 and 862 cm^{-1}

NMR : δ 7.55 (s, 1H, Ar-*H*), 7.44 (b, 2H, NH_2), 7.21-7.17 (t, 2H, Ar-*H*), 7.09 (s, 1H, Ar-*H*), 6.92-6.90 (d, 2H, Ar-*H*), 6.77-6.73 (t, 1H, Ar-*H*), 3.88(s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.49 (s, 2H, CH_2), 3.10-3.09 (t, 4H, CH_2) and 2.64-2.62 (t, 4H, CH_2)

2-[(4-Cyclohexylpiperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4-amine (V-4)

Compound **(V-4)** was obtained by the reaction of *N*-cyclohexylpiperazine (0.39 g, 2.371 mmol) and compound **(20)** (0.2 g, 0.79 mmol) as per general **Method J** (0.18, 60 %) m.p. 234-36 °C.

Anal.:

TLC : R_f 0.1 (DCM: Methanol, 19:1)

IR : 3387, 3171, 1647, 1511, 1401, 1259, 1223, 1171, 1017 and 993 cm^{-1}

2-[4-((4-Amino-6,7-dimethoxyquinazolin-2-yl)methyl)piperazin-1-yl]benzonitrile (V-5)

Reaction of 1-(2-cyanophenyl)piperazine (0.40 mL, 2.371 mmol) and compound (**20**) (0.2 g, 0.79 mmol) under conditions as described in **Method J** afforded compound (**V-5**) (0.21 g, 68 %) m.p. 137-39 °C.

Anal.:

TLC : R_f 0.76 (DCM: Methanol, 18:2)

IR : 3382, 3132, 2223, 1630, 1513, 1481, 1400, 1265, 1221 and 773 cm^{-1}

NMR : δ 7.57-7.50 (m, 3H, Ar-*H*), 7.19 (b, 2H, NH_2), 7.13 (s, 1H, Ar-*H*), 7.07-7.00 (m, 2H, Ar-*H*), 3.93 (s, 6H, 2 × OCH_3), 3.63 (s, 2H, CH_2), 3.24 (b,4H, CH_2) and 2.77 (b, 4H, CH_2)

MS : m/z 404.8 (M^+ peak)

6,7-Dimethoxy-2-[(4-(2-methoxyphenyl)piperazin-1-yl)methyl]quinazolin-4-amine (V-6)

Compound (**V-6**) was obtained by the reaction of 1-(2 methoxyphenyl)piperazine (0.41 mL, 0.2371 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.22 g, 71 %) m.p. 236-38 °C.

Anal.:

TLC : R_f 0.73 (DCM: Methanol, 19:1)

IR : 3299, 3145, 1661, 1581, 1507, 1334, 1275, 1241, 1138, 1017 and 744 cm^{-1}

NMR : δ 7.58 (s, 1H, Ar-*H*), 7.17 (s, 1H, Ar-*H*), 6.95-6.84(m, 4H, Ar-*H*), 3.96 (s, 6H, OCH_3), 3.83 (s, 3H, OCH_3), 3.67 (s, 2H, CH_2), 3.10 (b, 4H, CH_2) and 2.79 (b, 4H, CH_2)

2-[(4-(2-Fluorophenyl)piperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4-amine (V-7)

Compound **(V-7)** was obtained by the reaction of 1-(2-fluorophenyl)piperazine (0.39 mL, 2.371 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.21 g, 70%) m.p. 217-20 °C dec.

Anal.:

TLC : R_f 0.8 (DCM: Methanol, 18:2)

IR : 3324, 3161, 1654, 1577, 1506, 1408, 1279, 1233, 1134, 1014, 854 and 757 cm^{-1}

NMR : δ 7.59 (s, 3H, Ar-*H* and N*H*$_2$), 7.27 (s, 1H, Ar-*H*), 7.07-6.89 (m, 4H, Ar-*H*), 4.00 (s, 6H, 2 × OC*H*$_3$), 3.74 (s, 2H, C*H*$_2$), 3.17 (b, 4H, C*H*$_2$) and 2.81 (b, 4H, C*H*$_2$).

6,7-Dimethoxy-2-[(4-(pyridin-2-yl)piperazin-1-yl)methyl]quinazolin-4-amine (V-8)

1-(2-pyridyl)piperazine (0.36 mL, 2.371 mmol) was reacted with compound **(20)** (0.2 g, 0.79 mmol) under set of reaction conditions as described in **Method J** to yield compound **(V-8)** (0.19g, 64%) m.p. > 280 °C.

Anal.:

TLC : R_f 0.53 (DCM: Methanol, 18:2)

IR : 3008, 1603, 1553, 1432, 1272, 1240, 1166, 990 and 731 cm^{-1}

4-[4-((4-Amino-6,7-dimethoxyquinazolin-2-yl)methyl)piperazin-1-yl]phenol (V-9)

Reaction of 1-(4-hydroxyphenyl)piperazine (0.42g, 2.371 mmol) and compound **(20)** (0.2 g, 0.79 mmol) under a set of conditions described in **Method J** afforded compound **(V-9)** (0.2 g, 63%) m.p. > 280 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 18:2)

IR : 3419, 3190, 1638, 1583, 1510, 1401, 1328, 1255, 1226, 1135 and 987 cm^{-1}

2-[(4-Benzhydrylpiperazin-1-yl)methyl]-6,7-dimethoxyquinazolin-4-amine (V-10)

Compound (**V-10**) was obtained by the reaction of benzhydrylpiperazine (0.5 g, 2.371 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.28, 78%) m.p. 246-48 °C.

Anal.:

TLC : R_f0.4 (DCM: Methanol, 18:2)

IR : 3490, 3297, 1646, 1572, 1480, 1279, 1252, 1163, 1078, 1001, 856 and 702 cm^{-1}

NMR : δ 7.55 (s, 1H, Ar-*H*), 7.41-7.22 (m, 9H, Ar-*H*), 7.16-7.11 (m, 4H,Ar-*H* and NH_2), 4.22 (s, 1H, C*H*), 3.93 (s, 6H, OCH_3), 3.59 (s, 2H, CH_2),2.64 (b, 4H, CH_2) and 2.42 (b, 4H, CH_2)

Sodium 2-[4-((4-amino-6,7-dimethoxyquinazolin-2-yl)methyl)piperazin-1-y]benzoate (V-11)

Compound (**V-5**) (0.1 g, 0.24 mmol) and aq. solution of conc. H_2SO_4 (5 mL, 60%) were taken in an Rb flask (10 mL). The reaction mixture was heated on water bath. The reaction was monitored by TLC. The reaction mixture was poured in water and basified with sodium hydroxide to get its sodium salt. In order to get the precipitated salt, the reaction mixture was mixed with acetone. The precipitated salt was filtered. The solid residue was then refluxed in methanol. The solution was filtered and filtrate was concentrated to obtain solid compound.m. p. > 280 °C.

Anal.:

TLC : R_f0.56 (DCM: Methanol, 18:2)

MS : m/z 423.48 (M^+ peak)

NMR : δ 7.44 (s, 1H, Ar-*H*), 7.24-7.21 (m, 2H, Ar-*H*), 7.13 (s, 1H, Ar-*H*), 7.05-6.90 (m, 4H, Ar-*H* and NH_2), 3.95 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.55 (s, 2H, CH_2), 3.02 (b, 4H, 2 × CH_2) and 2.61 (b, 4H, 2 × CH_2).

- **Synthesis of 2-[(aryl(alky)amino/heteroaryl)methyl]-6,7-dimethoxyquinazo-lin-4-amine (Series VI)**

***N*-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methyl]aniline (VI-1)**

Compound (**V1-1**) was obtained by the reaction of aniline (0.32 mL, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.16 g, 65 %) m.p. 181-83 °C.

Anal.:

TLC : R_f 0.53 (DCM: Methanol, 19:1)

IR : 3384, 3126, 1665, 1579, 1510, 1483, 1404, 1254, 1216, 867 and 745 cm^{-1}

NMR : δ 7.57 (s, 1H, Ar-*H*), 7.37 (b, 2H, NH_2), 7.10-7.07 (m, 3H, Ar-*H*), 6.67-6.65 (m, 2H, Ar-*H*), 6.58-6.54 (m, 1H, Ar-*H*), 5.69 (b, 1H, N*H*), 4.21-4.20 (d, 2H, CH_2),3.93 (s, 3H, OCH_3)and3.91 (s, 3H, OCH_3)

MS : m/z 310.5 (M^+ peak)

2-[(3-Toluidino)-*N*-methyl]-6,7-dimethoxyquinazolin-4-amine (VI-2)

3-Toluidine (0.54 g, 3.95 mmol) was reacted with compound (**20**) (0.2 g, 0.79 mmol) under set of reaction conditions described in **Method J** to yield compound (**VI-2**) (0.16 g, 64 %) m.p. 160-62 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 19:1)

IR : 3396, 3119, 1644, 1615, 1578, 1506, 1477, 1402, 1270, 1242, 1168, 1132 and 848 cm^{-1}

NMR : δ 7.52 (s, 1H, Ar-*H*), 7.28 (b, 2H, NH_2), 7.03 (s, 1H, Ar-*H*), 6.93-6.89 (m, 1H, Ar-*H*), 6.43-6.39 (m, 2H, Ar-*H*), 6.34-6.32 (m, 1H, Ar-*H*), 5.52 (b, 1H, N*H*), 4.13-4.12 (d, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3) and 2.16 (s, 3H, CH_3)

2-[(4-Toluidino)-*N*-methyl]-6,7-dimethoxyquinazolin-4-amine (VI-3)

4-Toluidine (0.54 g, 3.95 mmol) was reacted with compound (**20**) (0.2 g, 0.79 mmol) under set of reaction conditions described in **Method J** to yield compound (**VI-3**) (0.17 g, 68%) m.p. 204-207 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 19:1)

IR : 3414, 3126, 1668, 1620, 1580, 1518, 1486, 1401, 1254, 1222, 1173, 1014 and 803 cm^{-1}

NMR : δ 7.58 (s, 1H, Ar-*H*), 7.47 (b, 2H, Ar-*H*), 7.11 (s, 1H, Ar-H), 6.91-6.88 (d,2H, Ar-*H*), 6.59-6.57 (d, 2H, Ar-H), 5.57 (s, 1H, N*H*), 4.18 (s, 2H, CH_2), 3.93 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3) and 2.17 (s, 3H, CH_3)

MS : m/z 324.9 (M^+ peak)

6,7-Dimethoxy-2-[(4-methoxyphenylamino)methyl]quinazolin-4-amine (VI-4)

Reaction of 4-anisidine (1.48 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) under set of conditions described in **Method J** afforded compound (**VI-4**) (0.19 g, 72 %) m.p.173-75 °C.

Anal.:

TLC : R_f 0.44 (DCM: Methanol, 19:1)

IR : 3444, 3124, 1659, 1624, 1509, 1402, 1250, 1127, 1030 and 851 cm^{-1}

NMR : δ 7.97-7.97 (b, 2H, NH_2), 7.69-7.67 (d, 2H, Ar-*H*), 7.53 (s, 1H, Ar-*H*), 7.05 (s, 1H, Ar-*H*), 6.63-6.60 (d, 2H, Ar-*H*), 6.50 (b, 1H, N*H*), 4.25- 4.24 (d, 2H, CH_2), 3.89 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3) and 3.71(s, 3H, OCH_3)

3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]benzoic acid (VI-5)

Compound (**V1-5**) was obtained by the reaction of 3-aminobenzoic acid (0.54 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.17 g, 62%) m.p. 249-52 °C.

Anal.:

TLC : R_f 0.2 (DCM: Methanol, 19:1)

IR : 3444, 3322, 3122, 1705, 1662, 1584, 1490, 1279, 1235, 1110, 982, 861 and 749 cm^{-1}

NMR : δ 7.56 (s, 1H, Ar-*H*), 7.35-7.27 (m, 4H, Ar-*H* and NH_2), 7.15-7.11 (m, 1H, Ar-*H*), 7.01 (s, 3H, Ar-*H*), 6.85-6.83 (m, 1H, Ar-*H*), 5.23 (s, 2H, CH_2), 4.92 (b, 1H, N*H*) and 3.93 (s, 6H, 2 × OCH_3)

4-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]benzoic acid (VI-6)

Compound (**V1-6**) was obtained by the reaction of 4-aminobenzoic acid (0.54 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.18 g, 64%) m.p. 275-80 °C.

Anal.:

TLC : R_f 0.18 (DCM: Methanol, 19:1)

IR : 3425, 3369, 3120, 1673, 1607, 1516, 1493, 1279, 1218, 1169, 1114, 1081, 1018, 873 and 769 cm^{-1}

NMR : δ 7.75-7.73 (d, 2H, Ar-*H*), 7.57 (s, 1H, Ar-*H*), 7.39 (b, 2H, NH_2), 7.04(s, 1H, Ar-*H*), 6.61-6.58 (d, 2H, Ar-*H*), 5.69 (b, 2H, N*H* and O*H*), 5.16 (s, 2H, CH_2) and 3.93 (s, 6H, 2 × OCH_3)

MS : m/z 354.8 (M^+ peak)

Methyl 3-[(4-amino-6,7-dimethoxyquinazolin-2-yl)methylamino]benzoate (VI-7)

Methyl 3-aminobenzoate (0.5 g, 3.95 mmol) was reacted with compound (**20**) (0.2 g, 0.79 mmol) under set of reaction conditions described in **Method J** to yield compound (**VI-7**) (0.20 g, 69 %) m.p. 146-49 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 19:1)

IR : 3343, 3204, 1715, 1650, 1588, 1546, 1511, 1445, 1293, 1228, 1031 and 752 cm^{-1}

NMR : δ 7.52 (s, 1H, Ar-H_d), 7.35 (b, 2H, NH_2), 7.03 (s, 1H, Ar-H), 6.99-6.95 (m, 1H, Ar-H_j), 6.60 (s, 1H, Ar-*H*), 6.54-6.52 (m, 1H, Ar- *H*), 6.46-6.44 (m, 1H, Ar-*H*), 6.08 (b, 1H, N*H*) 4.14 (b, 2H, CH_2), 3.86 (s, 3H, OCH_3) and 3.84(s, 3H, $COOCH_3$).

Methyl 4-[(4-amino-6,7-dimethoxyquinazolin-2-yl)methylamino]benzoate (VI-8)

Methyl4-aminobenzoate (0.5 g, 3.95 mmol) was reacted with compound **(20)** (0.2 g, 0.79 mmol) under reaction conditions as described in **Method J** to yield compound **(VI-8)** (0.20 g, 69 %). m.p. 148-50 °C.

Anal.:

TLC : R_f0.56 (DCM: Methanol, 19:1)

IR : 3419, 3133, 1684, 1669, 1603, 1513, 1406, 1321, 1276, 1227, 1175, 1111 and 774 cm^{-1}

NMR : δ 7.51 (s, 1H, Ar-*H*), 7.28-7.18 (b, 2H, NH_2), 7.03 (s, 1H, Ar-H), 6.68-6.65(d, 2H, Ar-*H*), 6.60-6.56 (d, 2H, Ar-*H*), 5.20 (b, 1H, N*H*), 4.11 (s, 2H, CH_2), 3.90 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3) and 3.61 (s, 3H, COOCH_3)

2-[(3-Nitrophenylamino)methyl]-6,7-dimethoxyquinazolin-4-amine (VI-9)

Reaction of 3-nitroaniline (0.54 g, 3.95 mmol) and compound **(20)** (0.2 g, 0.79 mmol) under the conditions as described in **Method J** afforded compound **(VI-9)** (0.14g, 52 %) m.p. 223-25 °C.

Anal.:

TLC : R_f0.53 (DCM: Methanol, 19:1)

IR : 3374, 3125, 1624, 1518, 1400, 1347, 1244 and 1127 cm^{-1}

NMR : δ 7.54 (s, 1H, Ar-*H*), 7.45 (s, 1H, Ar-*H*), 7.33-7.31(m, 3H, Ar-*H* and NH_2), 7.26-7.22 (m, 1H, Ar-*H*), 7.05 (s, 1H, Ar-*H*), 7.04-7.01 (m, 1H, Ar-*H*), 6.57-6.55 (t, 1H, N*H*), 4.26-4.25 (d, 2H, CH_2), 3.90 (s, 3H, OCH_3) and 3.84 (s, 3H, OCH_3)

2-[(4-Nitrophenylamino)methyl]-6,7-dimethoxyquinazolin-4-amine (VI-10)

Reaction of 4-nitroaniline (0.54 g, 3.95 mmol) and compound **(20)** (0.2 g, 0.79 mmol) under the conditions described in **Method J** afforded compound **(VI-10)** (0.15 g, 54 %) m.p. 214 °C dec.

Anal.:

TLC : R_f0.53 (DCM: Methanol, 19:1)

IR : 3367, 3128, 1623, 1527, 1481, 1405, 1345, 1247, 1168, 990 and 852 cm^{-1}

_N_-[3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]phenyl]methane sulfonamide (VI-11)

Compound **(VI-11)** was prepared by reacting 3-methanesulfonamidoaniline (0.73 g, 3.95 mmol) with compound **(20)** (0.2 g, 0.79 mmol) as per **Method J** (0.18 g, 59 %) m.p. > 280 °C.

Anal.:

TLC : R_f 0.28 (DCM: Methanol, 19:1)

IR : 3450, 3361, 3045, 1673, 1624, 1584, 1489, 1319, 1249, 1147, 1031, 857 and 779 cm^{-1}

NMR : δ 7.57 (s, 1H, Ar-*H*), 7.39 (b, 2H,NH_2), 7.01 (s, 1H, Ar-*H*), 6.93-6.89 (m, 1H, Ar-*H*), 6.75-6.74 (t, 1H, Ar-*H*), 6.58-6.56 (dd, 1H, Ar-*H*), 6.46-6.44 (dd, 1H, Ar-*H*), 4.95-4.93 (d, 2H, 2 × N*H*), 4.76 (s, 2H, CH_2), 3.92 (s,6H, 2 × OCH_3) and 3.30 (s, 3H, CH_3)

MS : m/z 403.8 (M+ peak)

_N_-[4-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]phenyl]methane sulfonamide (VI-12)

Compound **(VI-12)** was prepared by reacting 4-methanesulfonamidoaniline (0.73 g, 3.95 mmol) with compound **(20)** (0.2 g, 0.79 mmol) as per **Method J** (0.18 g, 59 %) m.p. 206-09 °C.

Anal.:

TLC : R_f 0.31 (DCM: Methanol, 19:1)

IR : 3417, 3144, 1637, 1512, 1401, 1320 and 1153 cm^{-1}

NMR : δ 7.57 (s, 1H, Ar-*H*), 7.40 (b, 2H, NH_2), 7.05 (s, 1H,Ar-*H*), 7.03-7.01 (d, 2H, Ar-*H*), 6.47-6.45 (d,2H, Ar-*H*), 4.90 (b, 2H, 2 × N*H*), 4.69(s, 2H,), 3.92 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3) and 3.28 (s, 3H, CH_3)

MS : m/z 403.4 (M^+ peak)

***N*-[3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]phenyl]acetamide (VI-13)**

Compound (**VI-13**) was obtained by the reaction of 3-acetamidoaniline (0.65 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.15 g, 54 %) m.p. 235-37 °C.

Anal.:

TLC : R_f 0.46 (DCM: Methanol, 19:1)

IR : 3450, 3396, 3124, 1663, 1616, 1511, 1480, 1334, 1276, 1248, 1167, 1032 and 990 cm^{-1}

NMR : δ 7.54 (s, 1H, Ar-*H*), 7.34 (b, 2H, NH_2), 7.07 (s, 2H, Ar-H), 6.97-6.93 (t, 1H, Ar-*H*), 6.70-6.68 (m, 1H, Ar-*H*), 6.33-6.31 (m, 1H, Ar-*H*), 5.62 (b, 1H, N*H*), 4.16 (s, 2H, CH_2), 3.93 (s, 3H, OCH_3)3.90 (s, 3H, OCH_3)and 2.00 (s, 3H, CH_3)

***N*-[4-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]phenyl]acetamide (VI-14)**

Compound (**VI-14**) was obtained by the reaction of 4-acetamidoaniline (0.65 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.16 g, 57 %) m.p. 239 °C dec.

Anal.:

TLC : R_f0.46 (DCM: Methanol, 19:1)

IR : 3362, 3131, 1656, 1622, 1515, 1401, 1373, 1312, 1239, 1165, 1028 and 850 cm^{-1}

NMR : δ 9.39 (b, 1H, N*H*), 7.54 (s, 1H, Ar-*H*), 7.32-7.25 (m, 4H, Ar-H and NH_2), 7.06 (s, 1H, Ar-*H*), 6.58-6.56 (d, 2H, Ar-H), 5.49 (b, 1H, N*H*), 4.15 (s, 2H, CH_2), 3.90(s, 3H, OCH_3), 3.88 (s, 3H,OCH_3) and 1.96 (s, 3H, CH_3)

2-[(3-Chlorophenylamino)methyl]-6,7-dimethoxyquinazolin-4-amine (VI-15)

4-Chloroaniline (0.41 mL, 3.95 mmol) was reacted with compound (**20**) (0.2 g, 0.79 mmol) under set of reaction conditions described in **Method J** to yield compound **(VI-15)** (0.17 g, 63 %) m.p. 219-21 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 19:1)

IR : 3502, 3388, 3321, 1657, 1583, 1509, 1482, 1313, 1258, 1211, 1126 and 864 cm^{-1}

NMR : δ 10.61 (b, 1H, N*H*), 8.39 (s, 1H, Ar-*H*), 8.09-8.07 (m, 1H, Ar-*H*), 7.69-7.67 (m, 2H, Ar-*H*), 7.64 (s, 1H, Ar-*H*), 7.44-7.40 (t, 1H, Ar-*H*), 7.27 (s, 1H, Ar-*H*), 3.92 (s, 3H, OCH_3) 3.91 (s, 3H, OCH_3) and 3.84 (s, 2H, CH_2)

2-[(4-Chlorophenylamino)methyl]-6,7-dimethoxyquinazolin-4-amine (VI-16)

4-Chloroaniline (0.5 g, 3.95 mmol) was reacted with compound **(20)** (0.2 g, 0.79 mmol) under set of reaction conditions described in **Method J** to yield compound **(VI-16)** (0.18 g, 66 %) m.p. 230-32 °C.

Anal.:

TLC : R_f0.56 (DCM: Methanol, 19:1)

IR : 3482, 3389, 3316, 1653, 1578, 1507, 1402, 1314, 1256, 1216, 1171, 1091and 1013 cm^{-1}

NMR : δ 7.51 (s, 1H, Ar-*H*), 7.29 (b, 2H, NH_2), 7.03 (s, 1H, Ar-H), 7.02-6.99 (d, 2H, Ar-*H*),6.60-6.58 (d, 2H, Ar-*H*), 5.84 (b, 1H, N*H*), 4.14-4.13 (d, 2H, CH_2), 3.87 (s, 3H, OCH_3) and 3.85 (s, 3H, OCH_3).

3-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]bromobenzene (VI-17)

Compound **(VI-17)** was obtained by the reaction of 3-bromoaniline (0.41 mL, 3.95 mmol) and compound **(20)** (0.2 g, 0.79 mmol) as per general **Method J** (0.184 g, 60 %) m.p. 234-36 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 19:1)

IR : 3421, 3122, 1656, 1611, 1502, 1400, 1344, 1289, 1229, 1167 and 1055 cm^{-1}

NMR : 7.57 (s, 1H, Ar-*H*), 7.47 (s, 2H, NH_2), 7.07 (s, 1H, Ar-*H*), 7.69-7.67 (t, 1H, Ar-*H*), 6.80-6.79 (t, 1H, Ar-*H*), 6.65-6.61 (m, 2H, Ar-*H*), 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3) and 3.17 (s, 2H, CH_2).

4-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]bromobenzene (VI-18)

Compound (**VI-18**) was obtained by the reaction of 4-bromoaniline (0.67 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.18 g, 58 %) m.p. 217-19 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 19:1)

IR : 3380, 3127, 1672, 1588, 1493, 1371, 1239, 1168, 1022 and857 cm^{-1}

4-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]fluorobenzene (VI-19)

Reaction of 4-fluoroaniline (0.44 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) under the conditions as described in **Method J** afforded compound (**VI-19**) (0.14 g, 56 %) m.p. 214 °C dec.

Anal.:

TLC : R_f 0.50 (DCM: Methanol, 19:1)

IR : 3383, 3123, 1606, 1506, 1402, 1247, 1214, 992 and 856 cm^{-1}

NMR : δ 7.53 (s, 1H, Ar-*H*), 7.27 (b, 2H, NH_2), 7.05 (s, 1H, Ar-*H*), 6.84- 6.79 (m, 2H, Ar-*H*), 6.63-6.58 (m, 2H, Ar-*H*), 5.54 (b, 1H, N*H*), 4.14 (s, 2H, CH_2), 3.90 (s, 3H, OCH_3) and 3.88 (d, 3H, OCH_3)

1-[(4-Amino-6,7-dimethoxyquinazolin-2-yl)methylamino]naphthalene (VI-20)

1-Naphthylamine (0.56 g, 3.95 mmol) was reacted with compound (**20**) (0.2 g, 0.79 mmol) under reaction conditions as described in **Method J** to yield compound (**VI-20**) (0.22 g, 80 %) m.p. 235-37 °C.

Anal.:

TLC : R_f 0.40 (DCM: Methanol, 19:1)

IR : 3390, 3129, 1659, 1580, 1510, 1405, 1245, 1167, 1131 and 768 cm^{-1}

NMR : δ 8.16-8.14 (d, 1H, Ar-*H* and N*H*), 7.76-7.75 (d, 1H, Ar-*H*), 7.60 (s, 1H, Ar-*H*), 7.49-7.41 (m, 2H, Ar-*H*), 7.30-7.26 (t, 1H, Ar-*H*), 7.15-7.11 (m, 2H, Ar-*H*), 6.56-6.54 (m, 2H, NH_2), 4.40-4.39 (d, 2H, CH_2), 3.98 (s, 3H, OCH_3) and 3.93 (s, 3H, OCH_3)

MS : m/z 360.6 (M^+ peak)

6,7-Dimethoxy-2-[(pyridin-2-ylamino)methyl]quinazolin-4-amine (VI-21)

Compound **(VI-21)** was obtained by the reaction of 2-aminopyridine (0.37 g, 3.95 mmol) and compound **(20)** (0.2 g, 0.79 mmol) as per general **Method J** (0.13 g, 52 %) m.p. 210-14 °C dec.

Anal.:

TLC : R_f 0.13 (DCM: Methanol, 19:1)

IR : 3343, 3134, 1673, 1586, 1516, 1486, 1435, 1249, 1207, 1170, 1034, 866 and 775 cm^{-1}

NMR : δ 7.97 (b, 1H), 7.74 (b, 2H), 7.59 (s, 1H, Ar-*H*), 6.99-6.96 (d, 1H, Ar-*H*), 6.85 (s, 1H, Ar-*H*), 6.72 (s, 1H), 5.31 (s, 2H, CH_2) and 3.85 (s, 6H, 2 × OCH_3).

6,7-Dimethoxy-2-[(pyridin-3-ylamino)methyl]quinazolin-4-amine (VI-22)

Compound **(VI-22)** was obtained by the reaction of 3-aminopyridine (0.37 g, 3.95 mmol) and compound **(20)** (0.2 g, 0.79 mmol) as per general **Method J** (0.10 g, 44 %) m.p. 220-24 °C dec.

Anal.:

TLC : R_f 0.13 (DCM: Methanol, 19:1)

IR : 3339, 3190, 1635, 1585, 1511, 1403, 1250, 1208, 1118 and1028 cm^{-1}

6,7-Dimethoxy-2-[(pyridin-4-ylamino)methyl]quinazolin-4-amine (VI-23)

Compound **(VI-23)** was obtained by the reaction of 4-aminopyridine (0.37 g, 3.95 mmol) and compound **(20)** (0.2 g, 0.79 mmol) as per general **Method J** (0.15 g, 56 %) m.p. > 280 °C.

Anal.:

TLC : R_f 0.13 (DCM: Methanol, 19:1)

IR : 3221, 3110, 1675, 1587, 1514, 1481, 1395, 1256, 1216, 1094, 995 and 849 cm^{-1}

NMR : δ 8.16-8.14 (m, 2H, Ar-*H*), 7.59 (s, 1H, Ar-*H*), 6.93 (m, 3H, Ar-*H*), 5.32 (s, 2H, CH_2), 3.90 (d, 6H, 2 ×OCH_3) and 3.33 (b, 3H, N*H* and NH_2)

6,7-Dimethoxy-2-(4-morpholinomethyl)quinazolin-4-amine (VI-24)

Reaction of morpholine (0.31 mL, 3.95mmol) and compound **(20)** (0.2 g, 0.79 mmol) under the conditions as described in **Method J** afforded compound **(VI-24)** (0.17 g, 72 %) m.p. 231-33 °C.

Anal.:

TLC : R_f 0.56 (DCM: Methanol, 19:1)

IR : 3310, 3132, 1670, 1620, 1482, 1323, 1249, 1211, 1113 and 852 cm^{-1}

NMR : δ 7.86 (s, 1H, Ar-*H*), 7.14 (s, 1H, Ar-*H*), 7.05 (b, 2H, NH_2), 3.95 (s, 6H, 2 × OCH_3), 3.71-3.69 (t, 4H, CH_2), 3.57 (s, 2H, CH_2) and 2.58-2.57 (b, 4H, 2 × CH_2)

6,7-Dimethoxy-2-[(piperidin-1-yl)methyl]quinazolin-4-amine (VI-25)

Reaction of piperidine (0.39 mL, 3.9 mmol) and compound **(20)** (0.2 g, 0.79 mmol) under the conditions as described in **Method J** afforded compound **(VI-25)** (0.16 g, 67 %) m.p. 232-34 °C.

Anal.:

TLC : R_f 0.16 (DCM: Methanol, 19:1)

IR : 3316, 3133, 1670, 1579, 1508, 1433, 1244, 1209, 1167, 1115, 860 and 781 cm^{-1}

6,7-Dimethoxy-2-[(1*H*-1,2,4-triazol-1-yl)methyl]quinazolin-4-amine (VI-26)

Compound **(VI-26)** was obtained by the reaction of 1,2,4-triazole (0.27 g, 3.95

mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.13 g, 56 %) m.p. 235-40 °C.

Anal.:

TLC : R_f0.56 (DCM: Methanol, 19:1)

IR : 3401, 3338, 1671, 1588, 1492, 1422, 1266, 1233, 1215, 1036 and 846 cm^{-1}

NMR : δ 8.52 (s, 1H, Ar-*H*), 7.89 (s, 1H, Ar-*H*), 7.62 (s, 1H, Ar-*H*), 7.10 (s, 1H, Ar-*H*), 5.45 (s, 2H, CH_2), 3.97 (s, 3H, OCH_3) and 3.95 (s, 3H, OCH_3)

6,7-Dimethoxy-2-[(pyrrolidin-1-yl)methyl]quinazolin-4-amine (VI-27)

Compound (**VI27**) was obtained by the reaction of pyrrolidine (0.28 g, 3.95 mmol) and compound (**20**) (0.2 g, 0.79 mmol) as per general **Method J** (0.13 g, 56 %) m.p. 201-03 °C.

Anal.:

TLC : R_f0.23 (DCM: Methanol, 19:1)

IR : 1685, 1562, 1510, 1415, 1340, 1245, 1163 and 1130 cm^{-1}

NMR : δ 7.53 (s, 1H, Ar-*H*), 7.37 (b, 2H, NH_2), 7.06 (s, 1H, Ar-*H*), 3.87(s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.54 (s, 2H, CH_2), 2.51-2.50 (m, 4H, CH_2) and 1.67-1.64 (m, 4H, CH_2)

2-[(1*H*-Benzimidazol-1-yl)methyl]-6,7-dimethoxyquinazolin-4-amine(VI-28)

Benzimidazole (0.46 g, 3.95 mmol) was reacted with compound (**20**) (0.2 g, 0.79 mmol) under set of reaction conditions described in **Method J** to yield compound (**VI-28**) (0.14 g, 54 %) m.p. 234-36 °C.

Anal.:

TLC : R_f0.56 (DCM: Methanol, 19:1)

IR : 3295, 3122, 1680, 1585, 1495, 1416, 1256, 1203, 997, 868 and 742 cm^{-1}

NMR : δ 8.33 (s, 1H, Ar-H), 7.68-7.66 (m, 3H, Ar-*H* and NH_2), 7.59 (s, 1H, Ar-*H*), 7.49-7.46 (m, 1H, Ar-H), 7.21-7.19 (m, 2H, Ar-*H*), 7.05 (s, 1H, Ar-*H*), 5.46 (s, 2H, CH_2), 3.93 (s, 3H, OCH_3)and3.90(s, 3H, OCH_3)

5.2 Biological work

General

The study was conducted on healthy wistar rats of either sex weighing 200-250 g. The animals were housed in an air-conditioned room (22±2°C) in polypropylene cages in groups of 3 each. The animals were maintained on commercial pelleted rat chow and tapwater *ad libitum*. They were housed in 12 hr light/12 hr dark cycle. The study protocol was approved by the Institutional Animal Ethics Committee of the Pharmacy Dept., The Maharaja Sayajirao University of Baroda. All the experiments were carried out in accordance with the guidelines provided by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), New Delhi, India. The work has been carried out in the pharmacology section of the department and not by the candidate himself.

In vitro study

Animals were sacrificed by cervical dislocation.Descending thoracic aortas were removed immediately and placed in ice-cold Kreb's bicarbonate solution of the following composition (mM): NaCl 112, $NaHCO_3$ 12, glucose 11.1, KCl 5.0, $MgSO_4$ 1.2, KH_2PO_4 1.0 and $CaCl_2$ 2.5. The tissue was aerated with 95% O_2 and 5% CO_2. Peri-adventitious tissue was removed, taking care not to stretch the tissue. A spinal needle was inserted in the tissue and rotated gently to denude the endothelium. Following this, the tissue was cut spirally into a helical strip (20 mm × 3 mm) using a surgical blade. The strip was tied at both ends using a cotton thread and suspended in a 25 ml organ tube under an initial resting tension of 2 g. The *p*H of the Kreb's solution was 7.4 and maintained at 37°C using a thermostat. The Kreb's solution in the organ tube was changed every 10 mins during an equilibration period of about 90 mins. Denudation of the endothelium was confirmed by observing the "absence of relaxation" on strips precontracted with phenylephrine. Isometric contractions were recorded using a force transducer (UGO BASILE, Italy) coupled to a Gemini 7070 recorder (UGO BASILE, Italy).Contractions were induced in rat aortic strips with graded, cumulative concentrations of phenylephrine or ang II. Test compounds (10 μM) or vehicle were added to the organ tubes atleast 30 mins prior to the addition of either phenylephrine or ang II. pA_2 Values were calculated by the method described by Arunlakshana and Schild, 1959.[407]