Supplementary Material (ESI) for Organic & Biomolecular Chemistry

SUPPORTING INFORMATION

Convergent Assembly of Structurally Diverse Quinazolines

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General Information

Chemistry: Commercially available starting materials, reagents and solvents were purchased (Sigma-Aldrich) and used without further purification. When necessary, solvents were dried by standard techniques and distilled. After extraction from aqueous phases, the organic solvents were dried over anhydrous sodium sulphate. The reactions were monitored by thin-layer chromatography (TLC) with 2.5 mm Merck silica gel GF 254 strips, and the purified compounds each showed a single spot; unless stated otherwise, UV light and/or iodine vapour were used for detection of compounds. Purification of isolated products was carried out by column chromatography (Kieselgel 0.040-0.063 mm, E. Merck) or by using an ISCO Combiflash system that employs pre-packed silica gel columns and then recrystallised. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected.

All compounds described were characterised by spectroscopic and analytical data. IR spectra were measured on a Perkin-Elmer 1640 FTIR spectrophotometer with samples as potassium bromide pellets, only noteworthy IR absortions are listed (cm^{-1}). The NMR spectra were recorded on Bruker AM300 and XM500 spectrometers. Chemical shifts are given as δ values against tetramethylsilane as internal standard and *J* values are given in Hz. Mass spectra were obtained on a Varian MAT-711 instrument. High resolution mass spectra were obtained on an Autospec Micromass spectrometer. Elemental analyses were performed on a Perkin-Elmer 240B apparatus at the Microanalysis Service of the University of Santiago de Compostela, the elemental composition of the new compounds agreed to within ±0.4% of the calculated value.

Representative procedure for the synthesis of quinazoline derivatives 6 and 13 and 20. To a solution of the corresponding 5-acetyl-6-methylpyrimidine derivative (**1** or **9**) (10 mmol) in dimethylformamide (10 mL) was added freshly distilled phosphoryl oxychloride (40 mmol) and the reaction mixture stirred at room temperature. Once the reaction was complete the mixture was quenched by addition of water and evaporated in vacuo. The oily residue was added to ice and the aqueous layer was extracted with dichloromethane (3 × 25 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (2 × 20 mL), brine (2 × 20 mL) and dried over Na_2SO_4. The extracts were filtered through a pad of Celite and the solvent was removed on a rotary evaporator to give an oily residue, which was purified by chromatography on silica gel.

Representative procedure for the synthesis of quinazoline derivatives 6, 10, 11, 12, 19 and 21. To a solution of the corresponding 5-acetyl-6-methylpyrimidine derivative (**1**, **9 or 18**) (10 mmol) in dimethylformamide (10 mL) was added freshly distilled phosphoryl oxychloride (40 mmol) and the reaction mixture stirred at 60ºC. Once the reaction was complete, the mixture was allowed to reach room temperature, quenched by addition of water and evaporated in vacuo. The oily residue was added to ice and the aqueous layer was extracted with dichloromethane (3 × 25 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (2 × 20 mL), brine (2 × 20 mL) and dried over Na_2SO_4. The extracts were filtered through a pad of Celite and the solvent was removed on a rotary evaporator to give an oily residue, which was purified by chromatography on silica gel.

Representative procedure for the synthesis of quinazoline derivatives 7 and 22. To a solution of the corresponding 5-acetyl-6-methylpyrimidine derivative (**1**) (10 mmol) in dimethylformamide (10 mL) was added freshly distilled phosphoryl oxybromide (30 mmol) and the reaction mixture stirred at 90ºC. Once the reaction was complete, the mixture was allowed to reach room temperature, quenched by addition of water and evaporated in vacuo. The oily residue was added to ice and the aqueous layer was extracted with dichloromethane (3 × 25 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (2 × 20 mL), brine (2 × 20 mL) and dried over Na_2SO_4. The extracts were filtered through a pad of Celite and the solvent was removed on a rotary evaporator to give an oily residue, which was purified by chromatography on silica gel.

Spectroscopic and analytical data of described compounds.

5-chloro-1,2-dihydro-2-oxo-4-phenylquinazoline-8-carbaldehyde (5a). Purification by column chromatography on silica gel using AcOEt/hexane (1:3) as eluent. yield 88%. M.p.: 246-247 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1706, 1667, 1581. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.75 (s, 1H), 10.07 (s, 1H), 7.99 (d, *J*= 8.1 Hz, 1H), 7.45-7.53 (m, 5H), 7.38 (d, *J*=8.2 Hz, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 192.8 (C=O), 175.2 (C=O), 163.0 (C), 153.5 (C), 145.5 (C), 142.4 (C), 141.2 (CH), 138.9 (CH), 131.0 (CH), 128.9 (CH), 128.7 (CH), 125.7 (CH), 118.8 (C). MS (70 eV) *m*/*z* (%): 286 [M^+] (14), 284 [M^+] (42). HRMS (EI) *m*/*z* calcd for $C_{15}H_9N_2O_2Cl$ (M^+), 284.0353, found 284.0339.

5-chloro-1,2-dihydro-4-(4-methoxyphenyl)-2-oxoquinazoline-8-carbaldehyde (5b). Purification by column chromatography on silica gel using AcOEt/hexane (1:3) as eluent. yield 65%. M.p.: 220-221 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1678, 1581. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.66 (s, 1H), 10.07 (s, 1H), 7.96 (d, *J*= 8.2 Hz, 1H), 7.54 (d, *J*= 8.7 Hz, 2H), 7.38 (d, *J*=8.2 Hz, 1H), 6.97 (d, *J*= 8.7 Hz, 2H), 3.88 (s,3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 192.7 (C=O), 177.0 (C=O), 162.6 (C), 153.7 (C), 145.6 (C), 142.4 (C), 140.9 (CH), 131.4 (CH), 131.0 (C), 125.5 (CH), 118.8 (C), 114.1 (CH), 114.0 (C), 59.9 (CH_3). MS (70 eV) *m*/*z* (%): 316 [M^+] (19), 314 [M^+] (66). HRMS (EI) *m*/*z* calcd for $C_{16}H_{11}N_2O_3Cl$ (M^+), 314.0458, found 314.0449.

5-chloro-4-(4-chlorophenyl)-1,2-dihydro-2-oxoquinazoline-8-carbaldehyde (5c). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 50%. M.p.: 266-267 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1674, 1580. ^{1}H-NMR (DMSO-d_6 300 MHz), δ (ppm): 10.25 (s, 1H), 10.02 (s, 1H), 8.32-8.38 (m, 1H), 7.89 (d, *J*=8.2 Hz, 1H), 7.54-7.56 (m, 1H), 7.32-7.38 (m, 2H), 7.14 (d, *J*=8.2 Hz, 1H). ^{13}C-NMR (DMSO-d_6 75 MHz), δ (ppm): 195.7 (C=O), 174.5 (C=O), 148.2 (C), 145.0 (C), 140.3 (C), 139.4 (C), 137.4 (CH), 132.2 (C), 128.4 (CH), 128.0 (CH), 124.3 (C), 121.8 (C), 117.4 (C). MS (70 eV) *m*/*z* (%): 320 [M^+] (29), 318 [M^+] (46). HRMS (EI) *m*/*z* calcd for $C_{15}H_8N_2O_2Cl_2$ (M^+), 317.9963, found 317.9951.

4-(4-bromophenyl)-5-chloro-1,2-dihydro-2-oxoquinazoline-8-carbaldehyde (5d). Purification by column chromatography on silica gel using AcOEt/hexane (1:1) as eluent. yield 53%. M.p.: 252-253 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1677, 1580. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.77 (s, 1H), 10.08 (s, 1H), 8.00 (d, *J*=8.0 Hz, 1H), 7.61 (d, *J*=8.5 Hz, 2H), 7.38-7.42 (m, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 192.7 (C=O), 174.2 (C=O), 153.1 (C), 145.5 (C), 142.1 (C), 141.4 (CH), 132.0 (CH), 131.7 (C), 130.6 (CH), 126.9 (C), 125.8 (C), 125.7 (CH), 118.9 (C). MS (70 eV) *m*/*z* (%): 366 [M^+] (8), 364 [M^+] (40), 362 [M^+] (34). HRMS (EI) *m*/*z* calcd for $C_{15}H_8N_2O_2ClBr$ (M^+), 361.9458, found 361.9464.

5-chloro-1-methyl-4-phenylquinazolin-2(1*H*)-one (6a). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 56%. M.p.: 210-211 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1654, 1595, 1535. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 7.63-7.68 (m, 1H), 7.44-7.56 (m, 5H), 7.29-7.34 (m, 2H), 3.76 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 173.5 (C=O), 155.1 (C), 146.4 (C), 139.5 (C), 135.2 (C), 135.1 (CH), 130.5 (CH), 129.2 (C), 129.1 (CH), 128.5 (CH), 125.8 (CH), 113.3 (CH), 32.2 (CH_3). MS (70 eV) *m*/*z* (%): 272 [M^+] (20), 270 [M^+] (64). HRMS (EI) *m*/*z* calcd for $C_{15}H_{11}N_2OCl$ (M^+), 270.0560, found 270.0550.

1-benzyl-5-chloro-4-phenylquinazolin-2(1*H*)-one (6b). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 47%. M.p.: 192-193 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1648, 1593. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 7.60-7.20 (m, 13H), 5.54 (s, 2H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 173.5 (C=O), 145.5 (C), 143.5 (C) 139.1 (C), 135.4(C), 134.6 (CH), 134.5 (C), 130.2 (CH), 129.0 (CH), 128.7 (CH), 128.6(C), 128.1 (CH), 127.7 (CH), 126.8 (CH), 125.5 (CH), 113.9 (CH), 48.3 (CH_2). MS (70 eV) *m*/*z* (%): 348 [M^+] (61), 346 [M^+] (93). HRMS (EI) *m*/*z* calcd for $C_{21}H_{15}N_2OCl$ (M^+), 346.0873, found 346.0874.

5-chloro-4-(4-methoxyphenyl)-1-methylquinazolin-2(1*H*)-one (6c). Purification by column chromatography on silica gel using AcOEt/hexane (1:1) as eluent. yield 46%. M.p.: 190-191 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1658, 1597. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 7.61-7.66 (m, 1H), 7.55 (d, *J*=8.7 Hz, 2H), 7.26-7.31 (m, 2H), 6.96 (d, *J*=8.7 Hz, 2H), 3.88 (s, 3H), 3.73 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 172.6 (C=O), 162.1 (C), 146.5 (C), 135.0 (C), 134.9 (CH), 131.7 (C), 131.3 (CH), 125.6 (CH), 114.8 (C), 113.9 (CH), 113.2 (CH), 94.1 (C), 55.8 (CH_3), 32.1 (CH_3). MS (70 eV) *m*/*z* (%): 302 [M^+] (13), 300 [M^+] (37). HRMS (EI) *m*/*z* calcd for $C_{16}H_{13}N_2O_2Cl$ (M^+), 300.0666, found 300.0664.

5-chloro-4-(4-chlorophenyl)-1-methylquinazolin-2(1*H*)-one (6d). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 53%. M.p.: 191-192 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1660, 1596, 1538. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 7.63-7.68 (m, 1H), 7.48 (d, *J*=8.6 Hz, 2H), 7.40 (d, *J*=8.7 Hz, 2H), 7.26-7.34 (m, 2H), 3.74 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 172.2 (C=O), 154.9 (C), 146.5 (C), 137.9 (C), 136.9 (C), 135.4 (CH), 134.8 (C), 130.5 (CH), 128.8 (CH), 125.9 (CH), 114.6 (C), 113.5 (CH), 32.2 (CH_3). MS (70 eV) *m*/*z* (%): 308 [M^+] (1), 306 [M^+] (9), 304 [M^+] (13). HRMS (EI) *m*/*z* calcd for $C_{15}H_{10}N_2OCl_2$ (M^+), 304.0170, found 304.0160.

4-(4-bromophenyl)-5-chloro-1-methylquinazolin-2(1*H*)-one (6e). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 50%. M.p.: 207-208 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1659, 1595. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 7.63-7.68 (m, 1H), 7.57 (d, *J*=8.5 Hz, 2H), 7.41 (d, *J*=8.5 Hz, 2H), 7.26-7.34 (m, 2H), 3.74 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 172.3 (C=O), 154.9 (C), 146.5 (C), 138.4 (C), 135.4 (CH), 134.8 (C), 131.7 (CH), 130.7 (CH), 125.9 (CH), 125.2 (C), 114.5 (C), 113.5 (CH), 32.2 (CH_3). MS (70 eV) *m*/*z* (%): 350 [M^+] (21), 348 [M^+] (16). HRMS (EI) *m*/*z* calcd for $C_{15}H_{10}N_2OClBr$ (M^+), 347.9665, found 347.9667.

2,5-dichloro-4-phenylquinazoline-8-carbaldehyde (7a). Purification by column chromatography on silica gel using AcOEt/hexane (1:1) as eluent. yield 76%. M.p.: 152-153 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1689, 1552, 1515. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.22 (s, 1H), 8.43 (d, *J*= 7.9 Hz, 1H), 7.78 (d, *J*= 7.9 Hz,1H), 7.48-7.59 (m, 5H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 190.2 (C=O), 172.3 (C), 157.4 (C), 154.3 (C), 139.1 (C), 138.5 (C), 134.3 (CH), 130.9 (CH), 130.8 (CH), 130.2 (C), 129.7 (CH), 128.7 (CH), 120.5 (C). MS (70 eV) *m*/*z* (%): 302 [M^+] (26). HRMS (EI) *m*/*z* calcd for $C_{15}H_8N_2OCl_2$ (M^+), 302.0014, found 302.0028.

2,5-dichloro-4-(4-methoxyphenyl)quinazoline-8-carbaldehyde (7b). Purification by column chromatography on silica gel using AcOEt/hexane (1:10) as eluent. yield 58%. M.p.: 143-144 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1684, 1604, 1553, 1512. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.19 (s, 1H), 8.40 (d, *J*= 7.9 Hz, 1H), 7.75 (d, *J*= 7.9 Hz,1H), 7.55 (d, *J*=8.7 Hz, 2H), 7.02 (d, *J*=8.7 Hz, 2H), 3.90 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 190.3 (C=O), 171.5 (C), 162.5 (C), 157.2 (C), 154.6 (C), 139.0 (C), 134.0 (CH), 132.1 (CH), 130.7 (C), 130.6 (CH), 130.0 (C), 120.4 (C), 114.2 (CH), 55.9 (CH_3). MS (70 eV) *m*/*z* (%): 332 [M^+] (26). HRMS (EI) *m*/*z* calcd for $C_{16}H_{10}N_2O_2Cl_2$ (M^+), 332.0119, found 332.0113.

2,5-dichloro-4-(4-chlorophenyl)quinazoline-8-carbaldehyde (7c). Purification by column chromatography on silica gel using AcOEt/hexane (1:3) as eluent. yield 63%. M.p.: 171-172 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1691, 1590, 1555, 1520. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.20 (s, 1H), 8.44 (d, *J*= 7.9 Hz, 1H), 7.79 (d, *J*= 7.9 Hz, 1H), 7.47 (m, 4H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 190.1 (C=O), 171.0 (C), 157.4 (C), 154.4 (C), 138.6 (C), 137.5 (C), 136.9 (C), 134.4 (CH), 131.2 (CH), 131.0 (CH), 130.3 (C), 129.0 (CH), 120.4 (C). MS (70 eV) *m*/*z* (%): 336 [M^+] (55). HRMS (EI) *m*/*z* calcd for $C_{15}H_7N_2OCl_3$ (M^+), 335.9624, found 335.9622.

4-(4-bromophenyl)-2,5-dichloroquinazoline-8-carbaldehyde (7d). Purification by column chromatography on silica gel using AcOEt/hexane (1:1) as eluent. yield 85%. M.p.: 158-159 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1695, 1556. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.20 (s, 1H), 8.44 (d, *J*= 7.9 Hz, 1H), 7.79 (d, *J*= 7.9 Hz,1H), 7.66 (d, *J*=8.4 Hz, 2H), 7.43 (d, *J*=8.4 Hz, 2H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 190.1 (C=O), 171.0 (C), 157.4 (C), 154.4 (C), 138.6 (C), 137.4 (C), 134.5 (CH), 132.0 (CH), 131.4 (CH), 131.0 (CH), 130.3 (C), 125.8 (C), 120.3 (C). MS (70 eV) *m*/*z* (%): 387 [M^+] (16), 385 [M^+] (58), 383 [M^+] (100), 381 [M^+] (83). HRMS (CI) *m*/*z* calcd for $C_{15}H_7N_2OCl_2Br$ (MH^+), 380.9197, found 380.9198.

5-chloro-4-phenylquinazolin-2(1*H*)-one (8). Purification by column chromatography on silica gel using AcOEt/hexane (1:1) as eluent. yield 74%. M.p.: 306°C. IR (KBr): ν_{max}/cm^{-1} 1655, 1585. ^{1}H-NMR (DMSO-d_6 300 MHz), δ (ppm): 12.15 (s, 1H), 7.70-7.65 (m, 1H), 7.50-7.25 (m, 7H). ^{13}C-NMR (DMSO-d_6 75 MHz), δ (ppm): 174.1 (C=O), 154.2 (C), 146.1 (C), 140.0(C), 135.8 (CH), 132.4 (C), 129.9 (CH), 128.5 (CH), 128.4 (CH), 127.8 (C), 126.4 (C), 125.6 (CH), 115.6 (CH). MS (70 eV) *m*/*z* (%): 258 [M^+] (25), 256 [M^+] (76). HRMS (EI) *m*/*z* calcd for $C_{16}H_{11}N_2O_3Br$ (M^+), 357.9953, found 357.9947. HRMS (EI) *m*/*z* calcd for $C_{14}H_9N_2OCl$ (M^+), 256.0403, found 256.0406.

5-chloro-1,2-dihydro-2-oxo-4-phenylquinazoline-3,8(4*H*)-dicarbaldehyde (10a). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 56%. M.p.: 147-148 °C. IR (KBr): ν_{max}/cm^{-1} 1690, 1588. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 10.54 (s, 1H), 9.99 (s, 1H), 9.37 (s, 1H), 7.66 (d, *J*=8.3 Hz, 1H), 7.30 (m, 5H), 7.27 (d, *J*=8.3 Hz, 1H), 6.85 (s, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 193.6 (C=O), 161.4 (C=O), 150.6 (C=O), 140.0 (C), 138.1 (C), 137.9 (C), 135.9 (CH), 129.4 (CH), 129.3 (CH), 128.0 (CH), 124.8 (CH), 121.8 (C), 118.7 (C), 53.5 (CH). MS (70 eV) *m*/*z* (%): 316 [M^+] (8), 314 [M^+] 23). HRMS (ESI) *m*/*z* calcd for $C_{16}H_{11}N_2O_3Cl$ (MH^+), 315.0458, found 315.0525.

5-chloro-1,2-dihydro-4-(4-methoxyphenyl)-2-oxoquinazoline-3,8(4*H*)-dicarbaldehyde (10b). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 53%. M.p.: 99-100 °C. IR (KBr): ν_{max}/cm^{-1} 1719, 1675, 1605, 1511. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 10.52 (s, 1H), 9.98 (s, 1H), 9.35 (s, 1H), 7.65 (d, *J*=8.3 Hz, 1H), 7.25 (d, *J*=8.3 Hz, 1H), 7.23 (d, *J*=8.6 Hz, 2H), 6.80 (d, *J*=8.6 Hz, 2H), 5.30 (s, 1H), 3.75 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 193.6 (C=O), 161.5 (C=O), 160.3 (C=O), 150.6 (C), 140.0 (C), 138.0 (C), 135.8 (CH), 130.1 (C), 129.4 (CH), 124.8 (CH), 122.0 (C), 118.7 (C), 114.6 (CH), 55.7(CH_3), 53.0 (CH). MS (70 eV) *m*/*z* (%): 346 [M^+] (9), 344 [M^+] (27). HRMS (EI) *m*/*z* calcd for $C_{17}H_{13}N_2O_4Cl$ (M^+), 344.0564, found 334.0568.

5-chloro-4-(4-chlorophenyl)-1,2-dihydro-2-oxoquinazoline-3,8(4*H*)-dicarbaldehyde (10c). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 60%. M.p.: 187-188 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1723, 1675, 1602. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 10.55 (s, 1H), 9.99 (s, 1H), 9.35 (s, 1H), 7.68 (d, *J*=8.3 Hz, 1H), 7.29 (m, 5H), 6.80 (s, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 193.6 (C=O), 161.5 (C=O), 150.3 (C=O), 140.0 (C), 138.0 (C), 136.4 (C), 136.1 (CH), 135.4 (C), 129.6 (CH), 129.5 (CH), 124.9 (CH), 121.2 (C), 118.8 (C), 53.0 (CH). MS (70 eV) *m*/*z* (%): 352 [M$^+$] (2), 350 [M$^+$] (13), 348 [M$^+$] (20). HRMS (EI) *m*/*z* calcd for $C_{16}H_{10}N_2O_3Cl_2$ (M$^+$), 348.0068, found 348.0062.

4-(4-bromophenyl)-5-chloro-1,2-dihydro-2-oxoquinazoline-3,8(4*H*)-dicarbaldehyde (10d). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 57%. M.p.: 165-166 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1723, 1675, 1602. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 10.55 (s, 1H), 9.99 (s, 1H), 9.35 (s, 1H), 7.68 (d, *J*=8.4 Hz, 1H), 7.42 (d, *J*=8.4Hz, 2H), 7.27 (d, *J*=8.4 Hz, 1H), 7.19 (d, *J*=8.4 Hz, 2H), 6.79 (s, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 193.6 (C=O), 161.5 (C=O), 150.3 (C=O), 140.0 (C), 138.0 (C), 136.9 (C), 136.1 (CH), 132.6 (CH), 129.8 (CH), 124.9 (CH), 123.6 (C), 121.2 (C), 118.8 (C), 53.0 (CH). MS (70 eV) *m*/*z* (%): 396 [M$^+$] (5), 395 [M$^+$] (4), 392 [M$^+$] (16). HRMS (EI) *m*/*z* calcd for $C_{16}H_{10}N_2O_3BrCl$ (M$^+$), 391.9563, found 391.9566.

5-chloro-1,2-dihydro-2-oxo-4-phenylquinazoline-3(4*H*)-carbaldehyde (11a). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 62%. M.p.: 184-185 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1700, 1589. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.40 (s, 1H), 8.85 (s, 1H), 7.29 (m, 6H), 7.12 (d, *J*=8.9 Hz, 1H), 6.89 (d, J=8.9 Hz, 1H), 6.85 (s, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 161.5 (C=O), 152.7 (C=O), 138.4 (C), 136.0 (C), 133.3 (C), 130.4 (CH), 129.2 (CH), 129.0 (CH), 128.1 (CH), 125.4 (CH), 120.6 (C), 114.0 (CH), 53.6 (CH). MS (70 eV) *m*/*z* (%): 288 [M$^+$] (12), 286 [M$^+$] (35). HRMS (EI) *m*/*z* calcd for $C_{15}H_{11}N_2O_2Cl$ (M$^+$), 286.0509, found 286.0499.

5-chloro-1,2-dihydro-4-(4-methoxyphenyl)-2-oxoquinazoline-3(4*H*)-carbaldehyde (11b). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 55%. M.p.: 233-234 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1690, 1588. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.36 (s, 1H), 8.55 (s, 1H), 7.28 (m, 3H), 7.11 (d, *J*=7.3 Hz, 1H), 6.78-6.88 (m, 3H), 6.63 (s, 1H), 3.75 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 161.6 (C=O), 152.6 (C=O), 138.4 (C), 136.0 (C), 133.2 (C), 130.7 (C), 130.2 (CH), 129.5 (CH), 127.7 (CH), 125.3 (CH), 120.8 (C), 114.5 (CH), 55.6 (CH_3), 53.2 (CH). MS (70 eV) *m*/*z* (%): 318 [M^+] (9), 316 [M^+] (28). HRMS (EI) *m*/*z* calcd for $C_{16}H_{13}N_2O_3Cl$ (M^+), 316.0615, found 316.0613.

5-chloro-4-(4-chlorophenyl)-1,2-dihydro-2-oxoquinazoline-3(4*H*)-carbaldehyde (11c). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 67%. M.p.: 234-235 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1698, 1586. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.37 (s, 1H), 8.49 (s, 1H), 7.27-7.30 (m, 5H), 7.13 (d, *J*=7.9 Hz, 1H), 6.88 (d, *J*=7.9 Hz, 1H), 6.80 (s, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 161.5 (C=O), 152.4 (C=O), 136.9 (C), 135.9 (C), 135.0 (C), 133.2 (C), 130.6 (CH), 129.6 (CH), 129.5 (CH), 125.5 (CH), 120.1 (C), 114.1 (CH), 53.1 (CH). MS (70 eV) *m*/*z* (%): 322 [M^+] (7), 320 [M^+] (10). HRMS (EI) *m*/*z* calcd for $C_{15}H_{10}N_2O_2Cl_2$ (M^+), 320.0119, found 320.0115.

4-(4-bromophenyl)-5-chloro-1,2-dihydro-2-oxoquinazoline-3(4*H*)-carbaldehyde (11d). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 62%. M.p.: 157-158 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1703, 1690, 1595. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.38 (s, 1H), 8.85 (s, 1H), 7.42 (d, *J*=8.5 Hz, 2H), 7.18-7.30 (m, 1H), 7.13 (d, *J*=8.5 Hz, 2H), 6.89 (d, *J*=8.9 Hz, 1H), 6.87 (d, *J*=8.0 Hz, 1H), 6.79 (s, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 161.5 (C=O), 152.4 (C=O), 137.4 (C), 135.9 (C), 133.2 (C), 132.4 (CH), 130.6 (CH), 129.9 (CH), 125.5 (C), 123.3 (C), 120.0 (C), 114.1 (CH), 53.2 (CH). MS (70 eV) *m*/*z* (%): 368 [M^+] (6), 366 [M^+] (24), 364 [M^+] (18). HRMS (EI) *m*/*z* calcd for $C_{15}H_{10}N_2O_2ClBr$ (M^+), 363.9614, found 335.9608.

5-chloro-1,2-dihydro-1-methyl-2-oxo-4-phenylquinazoline-3(4*H*)-carbaldehyde (12a). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 59%. M.p.: 158-159 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1707, 1691, 1592. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.34 (s, 1H), 7.27 (m, 7H), 7.01 (d, *J*=8.1 Hz, 1H), 6.91 (s, 1H), 3.43 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 162.0 (C=O), 152.1 (C=O), 139.3 (C), 137.9 (C), 133.2 (C), 130.1 (CH), 129.2 (CH), 128.9 (CH), 127.6 (CH), 125.2 (CH), 122.5 (C), 113.2 (CH), 51.8 (CH), 31.5 (CH_3). MS (70 eV) *m*/*z* (%): 302 [M^+] (6), 300 [M^+] (19). HRMS (EI) *m*/*z* calcd for $C_{16}H_{13}N_2O_2Cl$ (M^+), 300.0666, found, 300.0657.

1-benzyl-5-chloro-2-oxo-4-phenyl-1,2-dihydroquinazoline-3(4*H*)-carbaldehyde (12b). Purification by column chromatography on silica gel using AcOEt/hexane (1:3) as eluent. yield 66%. M.p.: 129-130^{o}C. IR (KBr): ν_{max}/cm^{-1} 1705, 1682,1590. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.26 (s, 1H), 7.13-6.93 (m, 12H), 6.82 (s, 1H), 6.77 (d, *J*=7.7 Hz, 1H), 5.03 (c, *J*=16.3Hz ,2H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 161.6 (C=O), 151.9 (C=O), 137.8 (C), 137.2 (C), 135.3 (C), 132.7 (C), 129.6 (CH), 128.7 (CH), 128.4 (CH), 127.5 (CH), 127.2 (CH), 126.6(CH), 124.7(CH), 122.3 (C), 113.9 (CH), 110.4 (CH), 51.1 (CH), 47.2 (CH_2). MS (70 eV) *m*/*z* (%): 378 [M^+] (22), 376 [M^+] (61). HRMS (EI) *m*/*z* calcd for $C_{22}H_{17}N_2O_2Cl$ (M^+), 376.0979, found 376.0971.

5-chloro-1,2-dihydro-4-(4-methoxyphenyl)-1-methyl-2-oxoquinazoline-3(4*H*)-carbaldehyde (12c). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 53%. M.p.: 132-133 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1707, 1691, 1592. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.32 (s, 1H), 7.31 (m, 1H), 7.17 (m, 1H), 7.11 (d, *J*=8.8 Hz, 2H), 7.00 (d, *J*=8.0 Hz, 1H), 6.84 (s, 1H), 6.78 (d, *J*=8.8 Hz, 2H), 3.74 (s, 3H), 3.42 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 162.1 (C=O), 160.0 (C=O), 152.1 (C), 139.2 (C), 133.0 (C), 130.2 (C), 130.1 (CH), 129.0 (CH), 125.1 (CH), 122.6 (C), 114.5 (CH), 113.3 (CH), 55.6 (CH_3), 51.4 (CH), 31.5 (CH_3). MS (70 eV) *m*/*z* (%): 332 [M^+] 9), 330 [M^+] (26). HRMS (EI) *m*/*z* calcd for $C_{17}H_{15}N_2O_3Cl$ (M^+), 330.0771, found 330.0762.

5-chloro-4-(4-chlorophenyl)-1,2-dihydro-1-methyl-2-oxoquinazoline-3(4*H*)-carbaldehyde (12d). Purification by column chromatography on silica gel using

AcOEt/hexane (1:2) as eluent. yield 58%. M.p.: 127-128 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1708, 1691, 1590. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.33 (s, 1H), 7.25 (m, 6H), 7.02 (d, *J*=8.2 Hz, 1H), 6.86 (s, 1H), 3.43 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 162.0 (C=O), 151.9 (C=O), 139.2 (C), 136.5 (C), 134.9 (C), 133.2 (C), 130.4 (CH), 129.5 (CH), 129.2 (CH), 125.3 (CH), 121.9 (C), 113.3 (CH), 51.2 (CH), 31.5 (CH_3). MS (70 eV) *m*/*z* (%): 338 [M^+] (4), 336 [M^+] (28), 334 [M^+] (43). HRMS (EI) *m*/*z* calcd for $C_{16}H_{12}N_2O_2Cl_2$ (M^+), 334.0276, found 334.0285.

4-(4-bromophenyl)-5-chloro-1,2-dihydro-1-methyl-2-oxoquinazoline-3(4*H*)-carbaldehyde (12e). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 49%. M.p.: 137-138 ^{o}C. IR (KBr): ν_{max}/cm^{-1} 1707, 1591. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.32 (s, 1H), 7.31 (m, 3H), 7.19 (d, *J*=8.2 Hz, 1H), 7.04 (m, 3H), 6.85 (s, 1H), 3.43 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 162.0 (C=O), 151.9 (C=O), 139.2 (C), 137.0 (C), 133.1 (C), 132.4 (CH), 130.4 (C), 129.5 (CH), 125.3 (CH), 123.1 (C), 121.8 (C), 113.3 (CH), 51.3 (CH), 31.5 (CH_3). MS (70 eV) *m*/*z* (%): 382 [M^+] (2), 380 [M^+] (9), 378 [M^+] (7). HRMS (EI) *m*/*z* calcd for $C_{16}H_{12}N_2O_2ClBr$ (M^+), 377.9771, found 377.9769.

4-phenyl-3,4-dihydro-1-methylquinazolin-2(1*H*)-one (13). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 53%. M.p.: 222-223 ^{o}C.^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.23 (s, 1H), 8.31 (d, *J*=7.8 Hz, 1H), 8.04 (d, *J*=7.8 Hz, 1H), 7.53 (m, 6H), 5.72 (d, *J*= 3.1Hz, 1H), 3.34 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 154.2 (C=O), 140.3 (C), 140.1 (C), 133.9 (C), 132.2 (C), 129.5 (CH), 129.0 (CH), 127.9 (CH), 123.4 (CH), 121.1 (C), 112.1 (CH), 54.1 (CH), 30.0 (CH_3). MS (70 eV) *m*/*z* (%): 272 [M^+] (21). HRMS (EI) *m*/*z* calcd for $C_{15}H_{13}N_2OCl$ (M^+), 272.0716, found 272.0713.

5-chloro-2-(methylthio)-4-phenylquinazoline-8-carbaldehyde (19). Purification by column chromatography on silica gel using AcOEt/hexane (1:8) as eluent. yield 52%. M.p.: 160°C. IR (KBr): ν_{max}/cm^{-1} 1672, 1594. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 8.98 (s, 1H), 7.72-7.61 (m, 3H), 7.46-7.41 (m, 2H), 7.40-7.31 (m, 2H), 1.97 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 159.4 (C=O), 144.4 (C), 140.7 (C), 140.0 (C), 136.8 (CH), 133.7 (CH), 129.3 (CH), 128.6 (CH), 127.6 (CH), 109.2 (C), 100.0 (C), 99.0 (C), 13.9 (CH_3). MS (70 eV) *m*/*z* (%): 316 [M^+] (14), 314 [M^+] (40). HRMS (EI) *m*/*z* calcd for $C_{16}H_{11}N_2OSCl$ (M^+), 314.0281, found 314.0295.

5-bromo-2-oxo-4-phenyl-1,2-dihydroquinazoline-8-carbaldehyde (20a). Purification by column chromatography on silica gel using AcOEt/hexane (1:4) as eluent. yield 52%. M.p.: 241-242 °C. IR (KBr): ν_{max}/cm^{-1} 1714, 1692, 1599. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.97 (s, 1H), 8.63 (s, 1H), 7.61-7.48 (m, 7H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 192.6 (C=O), 157.9 (C=O), 157.8 (C), 150.1 (C), 150.0 (C), 130.6 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.1(CH), 128.9(C), 128.8(C), 114.5 (C). MS (70 eV) *m*/*z* (%): 328 [M^+] (17). HRMS (EI) *m*/*z* calcd for $C_{15}H_9N_2O_2Br$ (M^+), 327.9847, found 327.9851.

5-bromo-2-oxo-4-phenyl-1,2-dihydroquinazoline-3(4*H*)-carbaldehyde (21a). Purification by column chromatography on silica gel using AcOEt/hexane (1:5) as eluent. yield 45%. M.p.: 239°C. IR (KBr): ν_{max}/cm^{-1} 1697, 1604, 1585. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 9.19 (s, 1H), 7.74 (s, 1H), 7.17-6.99 (m, 7H), 6.73 (dd, *J*=7.7Hz), 6.67 (s, 1H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 161.1 (C=O), 151.9 (C), 137.7 (C), 135.6 (C), 130.2 (CH), 128.8 (CH), 128.6 (CH), 128.2 (CH), 127.9 (CH), 122.8 (C), 121.9 (C), 114.2 (CH), 55.1 (CH). MS (70 eV) *m*/*z* (%): 330 [M^+] (21). HRMS (EI) *m*/*z* calcd for $C_{15}H_{11}N_2O_2Br$ (M^+), 330.0004, found 330.0017.

5-bromo-2-oxo-4-phenyl-1,2-dihydroquinazoline-3,8(4*H*)-dicarbaldehyde (21b). Purification by column chromatography on silica gel using AcOEt/hexane (1:5) as eluent. yield 19%. M.p.: 184°C. IR (KBr): ν_{max}/cm^{-1} 1716, 1701, 1665, 1596. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 10.37 (s, 1H), 9.83 (s, 1H), 9.19 (s, 1H), 7.36 (dd, *J*=8.3Hz, 2H)7.13-7.09 (m, 5H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 193.3 (C=O), 161.0 (C=O), 150.2(C), 137.5 (C), 137.2 (C), 135.4 (CH), 130.4(C), 129.1 (C), 128.9 (CH), 127.8 (CH), 127.6 (CH), 123.1 (C), 118.8 (C), 55.0 (CH). MS (70 eV) *m*/*z* (%): 360 [M^+] (31), 358 [M^+] (32). HRMS (EI) *m*/*z* calcd for $C_{16}H_{11}N_2O_3Br$ (M^+), 357.9953, found 357.9947.

5-bromo-1-methyl-2-oxo-4-phenyl-1,2-dihydroquinazoline-3(4*H*)-carbaldehyde (21c). Purification by column chromatography on silica gel using AcOEt/hexane (1:5) as eluent. yield 50%. M.p.: 181°C. IR (KBr): ν_{max}/cm^{-1} 1710, 1686. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 8.98 (s, 1H), 7.72-7.31 (m, 8H), 6.90 (s, 1H), 1.97 (s, 3H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 161.6 (C=O), 138.8 (C=O), 137.3 (C), 130.1(CH), 128.9 (CH), 128.6 (CH), 128.1 (CH), 127.5 (CH), 123.8 (C), 122.9 (C), 113.5 (CH), 53.5(CH), 31.1(CH_3). MS (70 eV) *m*/*z* (%): 345 [M^+] (69), 343 [M^+] (46). HRMS (EI) *m*/*z* calcd for $C_{16}H_{13}N_2O_2Br$ (M^+), 344.0160, found 344.0159.

2,5-dibromo-4-phenylquinazoline-8-carbaldehyde (22). Purification by column chromatography on silica gel using AcOEt/hexane (1:2) as eluent. yield 63%. M.p.: 162-163 °C. IR (KBr): ν_{max}/cm^{-1} 1689, 1548, 1511. ^{1}H-NMR ($CDCl_3$ 300 MHz), δ (ppm): 11.23 (s, 1H), 8.31 (d, *J*=7.8 Hz, 1H), 8.04 (d, *J*=7.8 Hz, 1H), 7.53 (m, 5H). ^{13}C-NMR ($CDCl_3$ 75 MHz), δ (ppm): 190.5 (C=O), 164.9 (C), 152.1 (C), 140.3 (CH), 135.7 (CH), 135.1 (C), 134.1 (C), 131.8 (CH), 131.1 (C), 130.5 (CH), 129.0 (CH), 127.6 (C), 124.0 (C). MS (70 eV) *m*/*z* (%): 395 [M^+] (71), 393 [M^+] (100), 392 [M^+] (71). HRMS (CI) *m*/*z* calcd for $C_{15}H_8N_2OBr_2$ (MH^+), 390.9082, found 390.9089.