Electronic supplementary Information

3-Diarylethyne quinazolinones: A new class of senescence inducers

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Contents

General. (**A**) **Chemistry:**All chemicals and reagents were obtained from Aldrich (Sigma–Aldrich, St. Louis, MO, USA), Lancaster (Alfa Aesar, Johnson Matthey Company, Ward Hill, MA, USA) or Spectrochem Pvt. Ltd (Mumbai, India) and were used without further purification. Reactions were monitored by TLC, performed on silica gel glass plates containing 60 GF-254, and visualization on TLC was achieved by UV light or iodine indicator. Column chromatography was performed with Merck 60–120 mesh silica gel. ^{1}H spectra were recorded on Bruker UXNMR/XWIN-NMR (300 MHz) or Inova Varian-VXR-unity (400, 500 MHz) instruments. Chemical shifts (δ) are reported in ppm downfield from internal TMS standard. ESI spectra were recorded on Micro mass, Quattro LC using ESI+ software with capillary voltage 3.98 kV and ESI mode positive ion trap detector. High-resolution mass spectra (HRMS) were recorded on QSTAR XL Hybrid MS/MS mass spectrometer. Melting points were determined with an Electro thermal melting point apparatus, and are uncorrected.

(**B**) **Biology:**(**a**) **Cell culture.** Human breast cancer cell line MCF-7 cells, Colon cancer cell line Colo-205 cells, Breast adenocarcinoma (MDA-MB-231), A549 lung cancer cells, Pancreatic carcinoma cells MIA PaCa were purchased from American Type culture collection were maintained in Dulbecco's modified Eagle's medium (DMEM) and RPMI (Invitrogen), supplemented with 2 mM glutamax (Invitrogen), 10% fetal calf serum and 100 U/ml Pencillin and 100 mg/ml streptomycin sulfate (Sigma). The cell line was maintained at 37 °C in a humidified atmosphere containing 5% CO_2 in the incubator.

(b) MTT assay:Cell viability was assessed by MTT assay, a mitochondrial function assay. It is based on the ability of viable cells to reduce the MTT to insoluble formazan crystals by mitochondrial dehydrogenase. MCF-7 cells were seeded in a 96-well plate at a density of 10,000 cells/well. After overnight incubation, cells were treated with compounds **4a-ad** at 1, 2, 4 and 8 µM concentration and incubated for 48h. Medium was then discarded and replaced with 10 µL MTT dye. Plates were incubated at 37 °C for 2 h. The resulting formazan crystals were solubilised in 100 µL extraction buffer. The optical density (O.D) was read at 570 nm with micro plate reader (Multi-mode Varioskan instrument-Themo Scientific). The same experiment was conducted in Colo-205, MDA-MB-231, A549 and MIAPaCa cells with effective compounds **4i, 4p, 4q, 4s** and **4w** at 1, 2, 4 and 8 µM concentrations for 48 h.

(c) Cell cycle analysis: 5×10^5 MCF-7 cells were seeded in 60 mm dish and were allowed to grow for 24 h. Compounds **4a-ad** were added at a final concentration of 4 μM to the culture media, and the cells were incubated for an additional 24 h. Cells were harvested with Trypsin-EDTA, fixed with ice-cold 70% ethanol at 4 °C for 30 min, washed with PBS and incubated with 1 mg/ml RNase A solution (Sigma) at 37°C for 30 min. Cells were collected by centrifugation at 2000 rpm for 5 min and further stained with 250 μL of DNA staining solution [10 mg of Propidium Iodide (PI), 0.1 mg of trisodium citrate, and 0.03 mL of Triton X-100 were dissolved in 100 mL of sterile MilliQ water at room temperature for 30 min in the dark]. The DNA contents of 20,000 events were measured by flow cytometer (DAKO CYTOMATION, Beckman Coulter, Brea, CA). Histograms were analyzed using Summit Software.

(d) BrdU cell proliferation assay: This assay was carried out by using the 5-Bromo-2-deoxyuridine (BrdU) cell proliferation assay kit (Millipore) to assess the effect of compounds **4i**, **4p**, **4q**, **4s, 4w** and **Doxo** on proliferation of MCF-7 cells. 1×10^4cells were seeded and allowed to grow for 24 h. BrdU was added and allowed to incorporate for 5 h followed by the addition of test compounds **4i**, **4p**, **4q**, **4s, 4w** and **Doxo** at 4μM concentration for 24 h. Fixation was done for 30 min at room temperature. The cells were then washed, anti-BrdU antibody was added which binds to BrdU that was incorporated in the cells. After 1 h incubation, 100 μl anti-BrdU goat anti-mouse horse raddish peroxidise (HRP)-conjugated secondary antibody (1:2000) was added and incubated for 30 min. Washing procedures were followed according to the manufacturer's instructions. TMB substrate (100 μL) was added, incubated for another 30 min at room temperature and O.D values were taken at a wave length of 450 nm. Lower O.D values reflect lower BrdU concentrations in the sample and thus an indirect depiction of a low cell proliferation rate.

(e) TRAPeze XL Telomerase assay: This detection kit (Millipore) is a sensitive as well as rapid PCR based fluorescent assay for detecting telomerase activity in cell extracts. Treatments were given for 24h with compounds **4i**, **4p**, **4q**, **4s, 4w** and **Doxo** at a concentration of 4 μM. Lysis of cells was carried out using CHAPS buffer. The extracts were further used for PCR reaction. Heat inactivated control untreated MCF-7 cell

extract, which lost the telomerase activity is a negative control. Here the telomerase master mix which contains fluoro labelled primers designed both for Telomerase as well as internal control TSK2 template was used along with cell extract and Taq polymerase enzyme. The telomerase activity was measured with green fluorescence (F). Internal control amplification pattern was indicated by sulforhodamine (R), which gives red colour. The ratio of F and R gives the actual telomerase activity. PCR reaction conditions were followed according to the manufacturer's recommendation.

(f) Protein extraction and Western blot analysis: Total cell lysates from cultured MCF-7 cells treated with compounds **4i**, **4p**, **4q**, **4s, 4w** and **Doxo** at 4 µM for 24 h were obtained by lysing the cells in ice-cold RIPA buffer (1XPBS, 1% NP-40, 0.5% sodium deoxycholate and 0.1% SDS) and containing 100 mg/mL PMSF, 5 mg/mL Aprotinin, 5 mg/mL leupeptin, 5 mg/mL pepstatin and 100 mg/mL NaF. After centrifugation at 12,000 rpm for 10 min, the protein in supernatant was quantified by Bradford method (BIO-RAD) using Multimode varioskan instrument (Thermo-Fischer Scientifics). Seventy five micrograms of protein per lane was applied in 12% SDS-polyacrylamide gel. After electrophoresis, the protein was transferred to polyvinylidine difluoride (PVDF) membrane (GE Biosciences). The membrane was blocked at room temperature for 2 h in TBS + 0.1% Tween20 (TBST) containing 5% blocking powder (Santacruz). The membrane was washed with TBST for 5 min, primary antibody was added and incubated at 4°C overnight (O/N). p53 (53 KDa), β-actin (38 KDa) were purchased from Imgenex, USA. TRF2 (66KDa), p21(21 KDa), p16 (16 KDa) and Tankyrase-1 antibodies were purchased from Millipore Company. POT1 and TRF1 (50 KDa) were purchased from Abbiotec company. The membrane was incubated with corresponding horseradish peroxidase-labeled secondary antibody (1:2000) (Santa Cruz) at room temperature for 1 h. Membranes were washed with TBST three times for 15 min and the blots were visualized with chemiluminescence reagent (Thermo Fischer Scientifics Ltd.). The X-ray films were developed with developer and fixed with fixer solution (Kodak Company Ltd).

(g) p53 ELISA: Enzyme-linked immunorsorbent assays (ELISA) for p53 was conducted with the p53 ELISA kit obtained from Alexis Biochemical. MCF-7 cells were treated

with compounds **4i**, **4p**, **4q**, **4s, 4w** and **Doxo** at 4 µM concentration for 24 h. Cell lysates were isolated and added to micro plate wells containing p53 antibody. Biotin conjugated anti-human p53 monoclonal antibody (100 µL) was then added. After the incubation period and washing steps, bound p53 was detected by using streptavidin–HRP secondary antibody (150 µL). The coloured product obtained was detected by measuring OD at 450 nm. OD is directly proportional to the amount of p53 protein present in the sample.

(h) Senescence associated β-gal assay: MCF-7 cells were taken at density of $0.1x\ 10^{5}$ in chamber slide. Treatments were carried out with effective compounds **4s** and **4w** along with standard Doxorubicin (**Doxo**) for 72h at 4 µM concentrations. Cells were fixed in 3% para formaldehyde and then incubated 10 min at room temperature. After thorough PBS wash the cells were again fixed in methanol for 20 min at 4 ^{o}C. This is followed by incubation in sodium phosphate buffer containing 2mg X-gal, $K_4Fe(CN)_6.3H_20$, $K_3Fe(CN)_6$, 1mM $MgCl_2$, 2M NaCl, 0.1 M citric acid for 24 h. The Cells were then subjected to microscopy studies for the visualisation of blue colour formation, which is the indication of cells undergoing senescence.

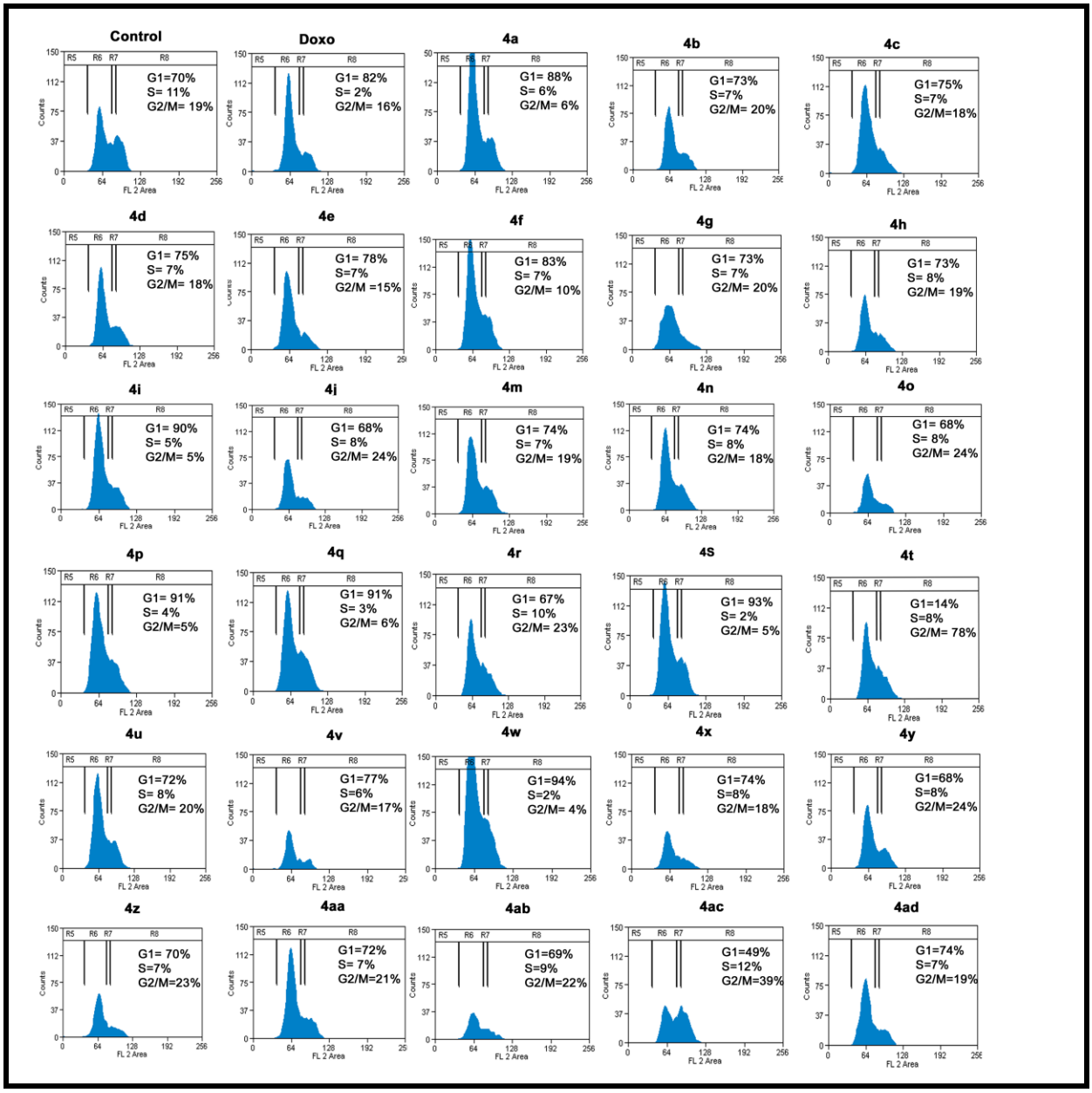

Figure 1. Fluorescent activated cell sorting (FACS) analysis of compounds **4a-ad** at 4 μM concentration.

Table 1. Effect of compounds on cell viability in MCF-7 breast carcinoma cells at 2 and 4 µM concentration for 48h

	OD values	
Compound	2 µM	4 µM
Control	1.01	0.89
4a	0.78	0.51
4b	0.75	0.61
4c	0.74	0.48
4d	0.87	0.58
4e	0.84	0.73
4f	0.92	0.73
4g	0.90	0.51
4h	0.93	0.61
4i	0.47	0.27
4j	0.97	0.43
4k	0.88	0.37
4l	0.71	0.59
4m	0.71	0.52
4n	0.60	0.43
40	0.54	0.25
4p	0.84	0.27
4q	0.41	0.27
4r	0.67	0.52
4s	0.77	0.39
4t	0.74	0.55
4u	0.92	0.61
4v	0.70	0.40
4w	0.59	0.24
4x	0.67	0.57
4y	0.77	0.63
4z	0.70	0.60
4aa	0.57	0.58
4ab	0.81	0.46
4ac	0.66	0.58
4ad	0.76	0.50

Table 2. Cell cycle distribution of compounds **4a-ad** treated MCF-7 cells at 4 µM concentration for 24 h

Compound	**Cell cycle distribution (%)**		
	G1	**S**	**G2/M**
Control	70	11	19
Doxorubicin(Doxo)	82	2	16
4a	88	6	6
4b	73	7	20
4c	75	7	18
4d	75	7	18
4e	78	7	15
4f	83	7	10
4g	73	7	20
4h	73	8	19
4i	90	5	5
4j	68	8	24
4m	74	7	19
4n	74	8	18
4o	68	8	24
4p	91	4	5
4q	91	3	6
4r	67	10	23
4s	93	2	5
4t	14	8	78
4u	72	8	20
4v	77	6	17
4w	94	2	4
4x	74	8	18
4y	68	8	24
4z	70	7	23
4aa	72	7	21
4ab	69	9	22
4ac	49	12	39
4ad	74	7	19

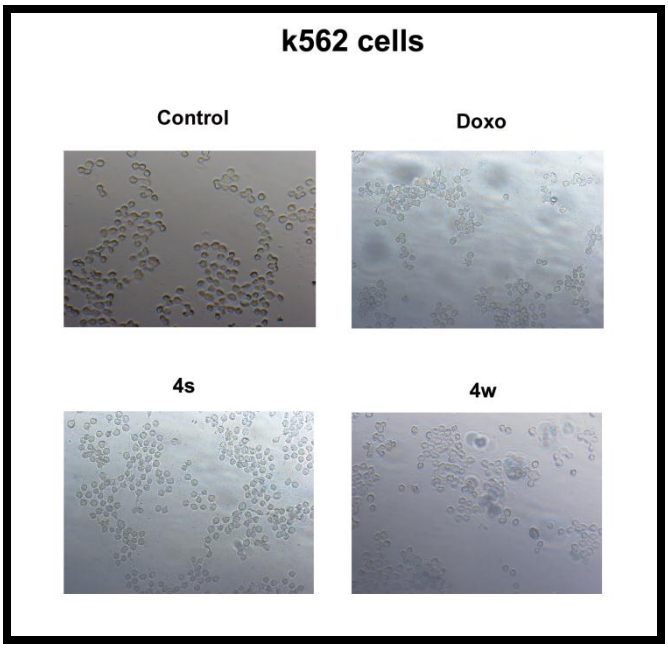

Figure 2: Effect of compounds **4s** and **4w** at 4 µM concentration at 72 h on senescence in K562 cells. Control cells works as negative control and doxorubicin works as positive control.

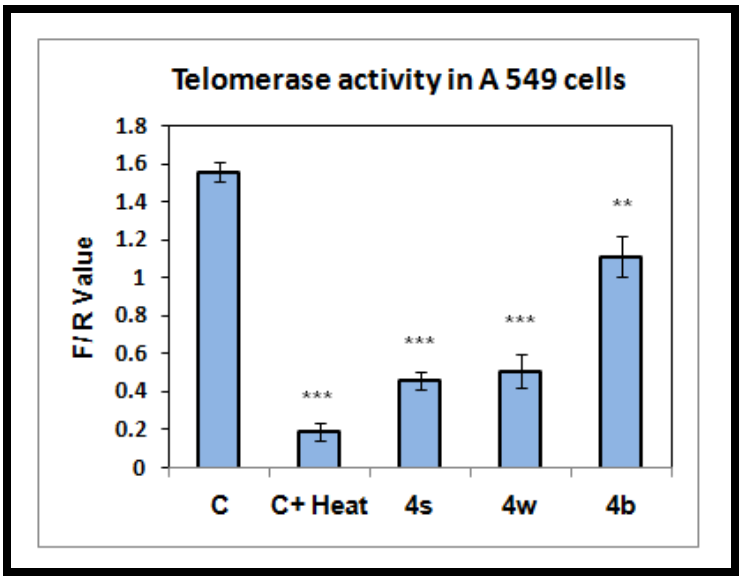

Figure 3. The telomerase activity was examined in A549 cancer cell line on effective compounds **4s** and **4w**. We have taken compound **4b** as a control compound as it has not much senescence as well G1 arrest activity. Control cells works as negative control and C+Heat works as positive control.

Spectral Data and Procedure of Compounds (7a–c, 9, 10 a–c and **7a–ad).**

2-Methyl-4-(phenylethynyl)benzenamine (7a): 4-Iodo-2-methyl-benzenamine (**5**, 233 mg, 1 mmol) was dissolved in ether, to this tetrakis triphenyl phosphine palladium (138 mg, 0.12 mmol) was added, stirred at rt for 30 min. Phenyl acetylene (**6a**, 0.1 ml, 1 mmol) dissolved in ether, to this CuI (11 mg, 0.06 mmol), butyl amine (0.25 ml, 3 mmol) were added, followed by addition of this solution to benzamine. Resulting reaction mixture stirred at room temparature for 6h. After completion of the reaction as indicated by TLC, reaction mixture quenched with NH_4Cl solution, extracted with ethyl acetate, combined organic layer dried over anhydrous sodium sulfate and concentrated under vacuum, crude mass purified by column chromatography by using (8:2) hexane, ethyl acetate as eluent to afford compound **7a** as white solid. Yield 92%; mp 105-106 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.50-7.47 (m, 2H, Ar**H**), 7.34-7.21 (m, 5H, Ar**H**), 6.61 (d, 1H, *J* = 8.1 Hz, Ar**H**), 4.10-3.61 (br, 2H, N**H**), 2.15 (s, 3H, -C**H**$_3$); MS (ESI): *m/z* 208 $(M+1)^+$.

4-((4-*tert*-Butylphenyl)ethynyl)-2-methylbenzenamine (7b): 4-Iodo-2-methylbenzenamine (**5**, 233mg, 1 mmol) was dissolved in ether, to this tetrakistriphenylphosphinepalladium (138 mg, 0.12 mmol) was added, stirred at rt 30 min. 1-*tert*-butyl-4-ethynylbenzene (**6b**, 0.1 mL, 1 mmol) dissolved in ether, to this CuI (11 mg, 0.06 mmol), butyl amine (0.25 mL, 3 mmol) were added, followed by addition of this solution to benzamine. Resulting reaction mixture stirred at rt for 6h. After completion of the reaction as indicated by TLC, reaction mixture quenched with NH_4Cl solution, extracted with ethyl acetate, combined organic layer dried over anhydrous sodium sulfate and concentrated under vacuum, crude mass purified by column chromatography by using (8:2) hexane, ethyl acetate as eluent to afford compound **7b** as white solid, yield 95%; mp 108-109 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.43 (s, 1H, Ar**H**), 7.41-7.40 (m, 1H, Ar**H**), 7.36-7.32 (m, 2H, Ar**H**), 7.30 (d, 1H, *J* = 2.2 Hz, , Ar**H**), 7.26 (d, 1H, *J* = 2.2 Hz, Ar**H**), 7.72-7.19 (m, 1H, Ar**H**), 3.80-3.60 (br, 2H, N**H**), 2.10 (s, 3H, -C**H**$_3$), 1.13 (s, 9H, *t*-butyl-**H**); MS (ESI): *m/z* 264 $(M+1)^+$.

4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylbenzenamine (7c): 4-Iodo-2-methyl-benzenamine (**5**, 233 mg, 1 mmol) was dissolved in ether, to this tetrakistriphenyl

phosphinepalladium (138 mg, 0.12 mmol) was added, stirred at rt 30 min. 2-ethynyl-6-methoxynaphthalene (**6c**, 182 mg, 1 mmol) dissolved in ether, to this CuI (11 mg, 0.06 mmol), butyl amine (0.25 mL, 3 mmol) were added, followed by addition of this solution to benzamine. Resulting reaction mixture stirred at rt for 6h. After completion of the reaction as indicated by TLC, reaction mixture quenched with NH_4Cl solution, extracted with ethyl acetate, combined organic layer dried over anhydrous sodium sulfate and concentrated under vacuum, crude mass purified by column chromatography by using (8:2) hexane, ethyl acetate as eluent to afford compound **7c** as solid, yield: 94%; mp 105-106 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.92 (s, 1H, Ar**H**), 7.73-7.65 (m, 2H, Ar**H**), 7.53-(dd, 1H, *J* = 1.5, 2.2 Hz, Ar**H**), 7.31-7.24 (m, 2H, Ar**H**), 7.18-7.10 (m, 2H, Ar**H**), 6.64 (d, 1H, *J* = 7.5 Hz, Ar**H**), 3.92 (s, 3H, -OC**H**$_3$), 2.16 (s, 3H, -C**H**$_3$); MS (ESI): *m/z* 288 $(M+1)^+$.

2-Methyl-4*H*-benzo[*d*][1,3]oxazin-4-one (9): Anthranilic acid **(8**, 1.6 g, 10 mmol) was dissolved in acetic anhydride (10 mL), resulting mixture refluxed for 15 min, after completion of the reaction water was added, quenched with saturated $NaHCO_3$ solution, resulting reaction mixture extracted with ethyl acetate. Organic organic layer dried over anhydrous sodium sulfate and concentrated under vacuum to yield desired product, yield 93%; mp 80-81^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.19 (dd, 1H, *J* = 1.1, 7.9 Hz , Ar**H**), 7.77-7.84 (m, 1H, Ar**H**), 7.55 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.49 (d, 1H, *J* = 7.5 Hz, Ar**H**), 2.48 (s, 3H, -C**H**$_3$); MS (ESI): *m/z* 162 $(M+1)^+$.

2-Methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (10a): 2-Methyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**9**, 1.61 g, 1 mmol) was dissolved in acetic acid, to this 2-methyl-4-(phenylethynyl)benzenamine (**7a**, 207 mg, 1 mmol) was added, resulting mixture was stirred at reflux for 6h and poured into ice water. The mixture was neutralized by the addition of $NaHCO_3$ solution. Reaction mixture extracted with ethyl acetate, combined organic layer dried over anhydrous sodium sulfate and concentrated under vacuum under vacuum, crude mass purified by column chromatography by using (7:3) hexane, ethyl acetate as eluent to afford compound **10a** as white solid, yield 85%; mp 117-118 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.28 (d, 1H, *J* = 7.9 Hz, Ar**H**), 7.80-7.76 (m, 2H, Ar**H**), 7.71-7.68 (m, 2H, Ar**H**), 7.59 (s, 1H, Ar**H**), 7.56-7.52 (m, 2H, Ar**H**),

7.37-7.35 (m, 2H, Ar**H**), 7.15 (d, 1H, *J* = 7.9 Hz, Ar**H**), 6.89 (d, 1H, *J* = 7.9 Hz, Ar**H**), 2.78 (s, 3H, -C**H**$_3$), 2.19 (s, 3H, -C**H**$_3$); MS (ESI): *m/z* 351 $(M+1)^+$.

3-(4-((4-*tert*-Butylphenyl)ethynyl)-2-methylphenyl)-2-methyl-quinazolin-4(3H)-one (10b): 2-methyl-4*H*-benzo[*d*][1,3]oxazin-4-one (**9**, 1.61 g, 1mmol) was dissolved in acetic acid, to this 4-((4-*tert*-butylphenyl)ethynyl)-2-methylbenzenamine (**7b**, 263 mg, 1 mmol) was added, resulting mixture was stirred at reflux for 6h. After completion of the reaction as indicated by TLC reaction mixture poured into ice water. The mixture was neutralized by the addition of saturated $NaHCO_3$ solution. Reaction mixture extracted with ethyl acetate, combined organic layer dried under anhydrous sodium sulfate and concentrated over vacuum, crude mass purified by column chromatography by using (7:3) hexane, ethyl acetate as eluent to afford compound **10b** as white solid, yield 87%; mp 114-115 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.91(d, 1H, *J* = 8.4 Hz, Ar**H**), 7.80-7.65 (m, 5H, Ar**H**), 7.50 (d, 1H, *J* = 8.4 Hz, Ar**H**), 7.31(d, 2H, *J* = 8.3 Hz, Ar**H**), 7.20 (d, 2H, *J* = 8.3 Hz, Ar**H**), 2.76 (s, 3H, -C**H**$_3$), 2.18 (s, 3H, -C**H**$_3$), 1.29 (s, 9H, *tert*butyl **H**); MS (ESI): *m/z* 407 $(M+1)^+$.

3-(4-((6-Methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3H)-one (10c): 2-methyl-4H-benzo[d][1,3]-oxazin-4-one (**9**, 1.61 g, 1 mmol) was dissolved in acetic acid, to this 4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylbenzenamine (**7c**, 287 mg, 1 mmol) was added, resulting mixture was stirred at reflux for 12h and poured into ice water. The mixture was neutralized by the addition of $NaHCO_3$ solution. Reaction mixture extracted with ethyl acetate, combined organic layer dried under anhydrous sodium sulfate and concentrated over vacuum, crude mass purified by column chromatography by using (7:3) hexane, ethyl acetate as eluent to afford compound **10c** as white solid, yield 87%; mp 100-101 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.28 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.98 (s, 1H, Ar**H**), 7.81-7.74 (m, 1H, Ar**H**), 7.73-7.67 (m, 1H, Ar**H**), 7.6 (s, 1H, Ar**H**), 7.56-7.53 (s, 2H, Ar**H**), 7.50-7.45 (m, 1H, Ar**H**), 7.71 (s, 1H, Ar**H**), 7.14 (s, 1H, Ar**H**), 7.11(s, 1H, Ar**H**), 3.93 (s, 3H, -OC**H**$_3$), 2.80 (s, 3H, -C**H**$_3$), 2.20 (s, 3H, -C**H**$_3$); MS (ESI): *m/z* 431 $(M+1)^+$.

(*E*)-2-(2-Methylstyryl)-3-(4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (4a): 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) was dissolved in acetic acid, to this 2-methylbenzaldehyde (120 mg, 1 mmol) was added, resulting mixture was stirred at reflux for 12h and poured into ice water. The mixture was neutralized by the addition of saturated $NaHCO_3$ solution. Reaction mixture extracted with ethyl acetate, combined organic layer dried under anhydrous sodium sulfate and concentrated over vacuum, crude mass purified by column chromatography by using (7:3) hexane, ethyl acetate as eluent to afford the compound **4a** as white solid, yield 90 %; mp 135-136 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.29 (d, 1H, *J* = 7.5 Hz, Ar**H**), 8.27 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 7.78-7.76 (m, 2H, Ar**H**), 7.55 (s, 1H, Ar**H**), 7.56-7.48 (m, 3H, Ar**H**), 7.47-7.43 (m, 1H, Ar**H**), 7.34-7.32 (m, 3H, Ar**H**), 7.24-7.18 (m, 2H, Ar**H**), 7.16-7.08 (m, 3H, Ar**H**), 6.22 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 2.47 (s, 3H, -C**H**$_3$), 2.15 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.7, 147.9, 138.4, 137.4, 136.2, 134.6, 134.4, 131.6, 130.7, 129.5, 128.7, 128.5, 128.3, 127.4, 127.16 126.6, 126.2, 122.8. 120.7, 120.0, 90.5, 19.5, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1551, 1684, 1605, 1626, 2922, 3062, 3433. MS (ESI): *m/z* 453 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{32}H_{25}N_2O$, calcd 453.1966, found 453.1984 [M + H]); HPLC purity: t_R 10.25 min (98.1 %).

(*E*)-2-(4-Fluorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (4b): The title compound was prepared according to the method described for compound **4a** employing compound 2- methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 4-fluorobenzaldehyde (124 mg, 1 mmol) to obtain the pure product **4b** as white solid. Yield 92 %; mp 138-139 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.27 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.97 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.78-7.74 (m, 2H, Ar**H**), 7.61 (s, 1H, Ar**H**), 7.58-7.44 (m, 4H, Ar**H**), 7.35-7.20 (m, 4H, Ar**H**), 7.18-7.15 (m, 1H, Ar**H**), 7.11 (d, 1H, *J* = 7.6 Hz, Ar**H**), 7.01-6.92 (m, 2H, Ar**H**), 6.27 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 2.14 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.5, 150.96, 147.7, 139.4, 137.3, 136.8, 136.3, 135.7, 134.7, 131.6, 130.7, 130.3, 128.7, 127.4, 126.8, 124.9, 123.6, 122.7, 120.8, 120.0, 119.9, 116.7, 114.2, 113.9, 90.7, 88.3, 17.4 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1502, 1549, 1607, 1582, 1637, 3334; MS (ESI): *m/z* 457$(M+1)^+$; HRMS (ESI *m/z*) for $C_{31}H_{22}N_2OF$, calcd 457.1716, found 457.1733 [M + H]; HPLC purity: t_R 11.96 min (97.3 %).

(*E*)-2-(4-Chlorostyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (4c): The title compound was prepared according to the method described for compound **4a** employing compound 2- methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 4-chlorobenzaldehyde (140 mg, 1 mmol) to obtained the pure product **4c** as white solid. Yield 95 %; mp 140-141 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.29 (d, 1H, *J* = 7.6 Hz, Ar**H**), 7.92 (d, 1H, *J* = 15.9 Hz, *Trans*-**H**), 7.81-7.71 (m, 3H, Ar**H**), 7.61 (s, 1H, Ar**H**), 7.58-7.49 (m, 2H, Ar**H**), 7.46 (d, 1H, *J* = 8.3 Hz, Ar**H**), 7.38-7.28 (m, 4H, Ar**H**), 7.27-7.22 (m, 2H, Ar**H**), 7.20-7.17 (m, 2H, Ar**H**), 6.28 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 2.14 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.5, 150.9, 147.7, 140.4, 139.1, 136.9, 136.8, 135.7, 134.7, 134.5, 131.6, 130.7, 130.2, 130.04, 129.6, 128.7, 128.5, 128.8, 127.4, 127.1, 126.8, 125.6, 120.1, 88.4, 87.9, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1501, 1548, 1577, 1605, 1682, 1634, 3439; MS (ESI): *m/z* 473 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{31}H_{22}N_2OCl$, calcd 473.1420, found 473.1432 [M + H]; HPLC purity: t_R 5.65 min (96.5 %).

(*E*)-2-(4-Hydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (4d): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 4-hydroxy benzaldehyde (122 mg, 1 mmol) to obtained the pure product **4d** as white solid. Yield 85 %; mp 161-162 ^{o}C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 300 MHz): δ 8.24 (d, 1H, J = 7.5 Hz, Ar**H**), 7.95 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 7.80-7.68 (m, 2H, Ar**H**), 7.60-7.46 (m, 2H, Ar**H**), 7.42 (s, 1H, Ar**H**), 7.37-7.30 (m, 2H, Ar**H**), 7.27-7.15 (m, 6H, Ar**H**), 6.78-6.68 (m, 2H, Ar**H**), 6.12 (d, 1H, *J* = 15.3 Hz, *Trans*-H), 5.69 (s, 1H, O**H**), 2.16 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$+DMSO-d_6, 75 MHz) 160.3, 158.9, 150.6, 146.9, 139.9, 139.7, 135.3, 135.1, 133.5,133.2, 133.0, 130.4, 129.4, 128.4, 127.8, 126.1, 125.6, 125.1, 125.0, 123.2, 121.5, 119.2, 114.9, 113.8, 89.4, 87.4, 17.2 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1500, 1514, 1544, 1654, 1604, 1636, 1575, 1686, 2360, 2342, 3410, 3854; MS (ESI): *m/z* 455 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{31}H_{23}N_2O_2$, calcd 455.1759, found 455.1743 [M + H]; HPLC purity: t_R 4.66 min (95.3 %).

(*E*)-2-(4-Methoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (4e): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 4-methoxybenzaldehyde (136 mg, 1 mmol) to obtained the pure product **4e** as white solid. Yield 92%; mp 143-144 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.30 (d, 1H, *J* = 7.2 Hz, Ar**H**), 8.01 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.81-7.78 (m, 2H, Ar**H**), 7.61 (s, 1H, Ar**H**), 7.58-7.56 (m, 3H, Ar**H**), 7.49-7.44 (m, 1H, Ar**H**), 7.40-7.35 (m, 2H, Ar**H**), 7.32-7.25 (m, 3H, Ar**H**), 7.20 (d, 1H, *J* = 7.2 Hz, Ar**H**), 6.85-6.83 (m, 2H, Ar**H**), 6.19 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 3.80 (s, 3H, -OC**H**$_3$), 2.13 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.73, 160.0, 148.0, 140.38 136.4, 136.9, 134.6, 134.4, 131.6, 130.6, 129.45, 128.7, 128.5, 128.4, 127.8, 127.2, 127.15 126.3, 124.6, 122.8, 120.6, 116.9, 114.6, 90.5, 88.5, 55.3, 29.6, 17.5 ppm: IR (KBr) (ν_{max}/cm^{-1}): 1509. 1544, 1572, 1673, 2924, 3427; MS (ESI): *m/z* 469 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{32}H_{25}N_2O_2$ calcd 469.1916, found 469.1902 [M + H]; HPLC purity: t_R 6.15 min (98.9 %).

(*E*)-2-(3,5-Dihydroxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (4f): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 3,5 -dihydroxybenzaldehyde (138 mg, 1 mmol) to obtained the pure product **4f** as white solid. Yield 84 %; mp 170-171 ^{o}C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 300 MHz): δ 8.24 (d, 1H, *J* = 7.6 Hz, Ar**H**), 8.02 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 7.80-7.72 (m, 2H, Ar**H**), 7.02-7.61 (m, 2H, Ar**H**), 7.58-7.43 (m, 5H, Ar**H**), 7.38-7.29 (m, 3H, Ar**H**), 7.17 (s, 1H, Ar**H**), 7.13 (d, 1H, *J* =7.6 Hz, Ar**H**), 6.59 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 2.83 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$+DMSO-d_6, 75 MHz) 160.3, 150.9, 148.9, 148.9, 146.9, 136.2, 135.3, 135.3, 133.4, 132.9, 130.3, 129.3, 127.9, 127.6, 127.4, 126.2, 125.5, 125.0, 122.9, 121.3, 121.0, 119.2, 117.4, 117.1, 115.8, 113.1, 89.4, 87.5, 28.34, 16.2 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1470, 1500, 1596, 1608.5, 1658; 3320: MS (ESI): *m/z* 471 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{31}H_{23}N_2O_3$ calcd 471.1708, found 471.1722 [M + H]; HPLC purity: t_R 5.06 min (96.4 %).

(*E*)-2-(4-Hydroxy-3-nitrostyryl)-3-(2-methyl-4-(phenylethynyl)-phenyl)quinazolin-4(3*H*)-one (4g): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 4 hydroxy-3-nitrobenzaldehyde (167 mg, 1 mmol) to obtained the pure product **4g** as yellow solid. Yield 90 %; mp 108-109 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.70 (s, O**H**), 8.30 (d, 1H, J = 7.5 Hz, Ar**H**), 8.11 (s, 1H, Ar**H**), 7.97 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 7.62 (s, 1H, Ar**H**), 7.85-7.74 (m, 3H, Ar**H**), 7.59-7.48 (m, 5H, Ar**H**), 7.39-7.35 (m, 3H, Ar**H**), 7.19 (d, 1H, *J* = 8.3 Hz, Ar**H**), 7.13 (d, 1H, *J* = 8.3 Hz, Ar**H**), 6.27 (d, 1H, *J* = 15.8 Hz, *Trans*-**H**), 2.14 (s, 3H, C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.4, 155.7, 150.7, 147.6, 137.4, 136.3, 135.6, 135.0, 134.7, 134.4, 133.7, 133.4, 131.6, 130.76 128.7, 128.6, 128.3, 127.4, 127.2, 127.1, 126.8, 125.9, 124.9, 120.7, 119.8, 119.5, 90.8, 88.1, 17.4 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1425, 1470, 1546.2, 1574, 1605, 1678, 2922, 3427; MS (ESI): *m/z* 500 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{31}H_{21}N_2O_4$ calcd 500.1052, found 500.1058 [M + H]. Anal. ($C_{31}H_{21}N_2O_4$); HPLC purity: t_R 5.54 min (98.6 %).

(*E*)-2-(3,5-Dimethoxystyryl)-3-(2-methyl-4-(phenylethynyl)phenyl)-quinazolin-4(3*H*)-one (4h): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl)quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 3,5-dimethoxybenzaldehyde (166 mg, 1 mmol) to obtained the pure product **4h** as white solid. Yield 89%; mp 153-154 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.24 (d, 1H, *J* = 7.9 Hz, Ar**H**), 7.95 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 7.81-7.74 (m, 2H, Ar**H**), 7.61-7.53 (m, 4H, Ar**H**), 7.48-7.43 (m, 1H, Ar**H**), 7.39-7.35 (m, 3H, Ar**H**), 7.25-7.7.20 (m, 1H, Ar**H**), 6.94 (d, 1H, *J* = 7.5 Ar**H**), 6.80-6.78 (m, 2H, Ar**H**), 6.14 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 3.86 (s, 3H, -OC**H**$_3$), 3.83 (s, 3H, -OC**H**$_3$), 2.14 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.6, 151.6, 150.6, 149.9, 147.9, 140.4, 136.4, 136.0, 134.6, 134.3, 131.6, 130.5, 128.8, 128.5, 128.3, 128.3, 127.8, 127.2, 127.0, 126.3, 124.9, 120.6, 122.8, 121.1, 116.8, 111.1, 110.5, 90.5, 88.4, 55.9, 55.1, 30.8, 17.2 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1605, 1577, 1630, 1678, 2361, 2923, 3424, 3569, 3588, 3855; MS (ESI): *m/z* 499 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{33}H_{27}N_2O_3$, calcd 499.2021, found 499.2015 [M + H]; HPLC purity: t_R 6.44 min (97.2 %).

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(3,4,5-trimethoxy-styryl)quinazolin-4(3*H*)-one (4i): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 3,4,5-trimethoxybenzaldehyde (196 mg, 1 mmol) to obtained the pure product **4i** as white solid. Yield 93%; mp 175-176 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.29 (d, 1H, *J* = 7.8 Hz, Ar**H**), 7.87 (d, 1H, *J* = 15.6 Hz, *Trans*-**H**), 7.78-7.72 (m, 2H, Ar**H**), 7.60 (s, 1H, Ar**H**), 7.56 (d, 1H, *J* = 7.8 Hz, Ar**H**), 7.52-7.51 (m, 2H, Ar**H**), 7.47-7.44 (m, 1H, Ar**H**), 7.37-7.34 (m, 3H, Ar**H**), 7.25-7.21 (m, 1H, Ar**H**), 6.47-6.43 (m, 2H, Ar**H**), 6.10 (d, 1H, *J* = 15.6 Hz, *Trans*-**H**), 3.79 (s, 9H, 3 × OC**H**$_3$), 2.15 (s, 3H, C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 153.3, 151.3, 147.9, 140.3, 136.4, 136.0, 134.7, 134.33, 133.6, 130.7, 130.5, 128.8, 128.6, 128.4, 127.3, 127.1, 126.1, 124.7, 122.7, 120.7, 118.5, 104.5, 90.6, 88.3, 60.9, 56.0, 17.3 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1462, 1503, 1548, 1581, 1631, 1676. 2931, 3824; MS (ESI): *m/z* 529 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{34}H_{29}N_2O_4$ calcd 529.2127, found 529.2133 [M + H]; HPLC purity: t_R 6.51 min (95.0 %).

(*E*)-3-(2-Methyl-4-(phenylethynyl)phenyl)-2-(2-(naphthalen-2-l)vinyl)quinazolin-4(3*H*)-one (4j): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)phenyl) quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 2-naphthaldehyde (156 mg, 1 mmol) to obtained the pure product **4j** as white solid. Yield 90%; mp 120-121 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.32 (d, 1H, *J* = 8.2 Hz, Ar**H**), 8.13 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.86-7.82 (m, 5H, Ar**H**), 7.80-7.76 (m, 2H, Ar**H**), 7.73 (d, 1H, *J* = 8.2 Hz, Ar**H**), 7.64 (s, 1H, Ar**H**), 7.60-7.57 (m, 2H, Ar**H**), 7.51-7.47 (m, 3H, Ar**H**), 7.40-7.34 (m, 3H, Ar**H**), 7.25 (s, 1H, Ar**H**), 6.44 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 2.14 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 159.6, 151.5, 147.9, 144.4, 140.3, 136.6, 136.0, 132.6, 134.5, 130.5, 129.5,128.5, 128.4, .27.4, 127.2, 127.0, 123.2, 120.7, 90.8, 90.6, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1467, 1499, 1540, 1571, 1604, 1628, 2357, 2851, 2921, 3048, 3431, 3629, 3658; MS (ESI): *m/z* 489 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{35}H_{25}N_2O$ calcd 489.1866, found 489.1949 [M + H]; HPLC purity: t_R 12.23 min (95.7 %).

(*E*)-3-(2-Methyl-4-(2-phenylethynyl)phenyl)-2-(2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (4k): The title compound was prepared according to the method described for compound **4a** employing compound 2-methyl-3-(2-methyl-4-(phenylethynyl)-phenyl)quinazolin-4(3*H*)-one (**10a**, 350 mg, 1 mmol) and 5-nitrofuran-2-carbaldehyde (141 mg, 1 mmol) to obtained the pure product **4k** as yellow solid. Yield 92%; mp 131-132 ^{o}C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.30 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.79 (d, 1H, *J* = 14.5 Hz, *Trans*-**H**), 7.82-7.79 (m, 2H, Ar**H**), 7.62-7.52 (m, 5H, Ar**H**), 7.36-7.28 (m, 3H, Ar**H**), 7.28 (s, 1H, Ar**H**), 7.18 (s, 1H, Ar**H**), 6.67 (s, 1H, Ar**H**), 6.51 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 2.12 (s, 3H, C**H**$_3$); ^{13}C NMR ($CDCl_3$+DMSO-d_6, 75 MHz) : 159.5, 159.4, 151.1, 150.3, 148.3, 148.20, 145.98 ,138.75, 137.0, 135.3, 135.0, 134.1, 132.8, 130.5, 129.2, 127.6, 127.3, 127.1, 126.2, 125.8, 125.4, 123.7, 121.1, 121.1, 125.4, 123.7, 123.2, 121.9, 121.1, 119.42, 114.3, 114.2, 112.5, 89.3, 86.9, 29.9, 28.6, 28.0, 15.9 ppm; IR (KBr) (ν_{max}/cm^{-1}1500, 1518, 1542, 1570, 1692, 2922, 3427; MS (ESI): *m/z* 474 $(M+1)^+$; HRMS (ESI *m/z*) for $C_{29}H_{20}N_3O_4$ calcd 474.1453, found 474.1459 [M + H]; HPLC purity: t_R 11.58 min (95.3 %).

3-(4-(2-(4-*tert*-Butylphenyl)ethynyl)phenyl)-2-((*E*)-2-(4-chlorophenyl)prop-1-enyl)quinazolin-4(3*H*)-one (4l): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 4-chloro benzaldehyde (140 mg, 1 mmol) to obtained the pure product **4l** as white solid. Yield 86%; Mp 164-165 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.27 (d, 1H, *J* = 8.6 Hz, Ar**H**), 7.83 (d, 1H, *J* = 15.4 Hz, *Trans*-**H**), 7.81-7.73 (m, 2H, Ar**H**), 7.61 (s, 1H, Ar**H**), 7.55 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.48-7.44 (m, 3H, Ar**H**), 7.37-7.35 (m, 2H, Ar**H**), 7.31 (s, 1H, Ar**H**), 7.26-7.22 (m, 2H, Ar**H**), 7.18-7.16 (m, 2H, Ar**H**), 6.32 (d, 1H, *J* = 15.4 Hz, *Trans*-**H**), 2.14 (s, 3H, -C**H**$_3$), 1.35 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.5, 151.88, 150.9, 147.7, 140.4, 139.0, 135.5, 134.7, 134.4, 131.3, 130.7, 130.0, 129.5, 128.6, 127.8, 127.4, 127.1, 126.8, 125.6, 125.3, 120.8, 120.1, 90.9, 87.7, 31.0, 17.4 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1544, 1631, 1690, 2962, 3430, 3650; MS (ESI): *m/z* 529$(M+1)^+$; HRMS (ESI *m/z*) $C_{35}H_{30}N_2OCl$ calcd 529.2046, found 529.2024 [M + H]; HPLC purity: t_R 15.48 min (94.8 %).

2-(4-Hydroxystyryl)-3-(4-(2-(4-*tert*-butylphenyl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (4m): The title compound was prepared according to the method described for compound **4a** employing compound **3**-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 4-hydroxy benzaldehyde (122 mg, 1 mmol) to obtained the pure product **4m** as white solid. Yield 84%; mp 119-120 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.28 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.91 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.78-7.73 (m, 2H, Ar**H**), 7.56-7.39 (m, 5H, Ar**H**), 7.34-7.31 (m, 2H, Ar**H**), 7.15-7.08 (m, 2H, Ar**H**), 6.82 (d, 1H, *J* = 7.7 Hz, Ar**H**), 6.59-6.49 (s, 2H, Ar**H**), 6.25 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 2.11 (s, 3H, -C**H**$_3$), 1.34 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.9, 156.4, 151.5, 147.8, 141.0, 140.8, 140.3, 136.3, 136.1, 134.8, 134.4, 131.3, 130.7, 129.8, 128.5, 127.2, 127.1, 126.7, 125.3, 120.4, 120.0, 118.6, 117.1, 114.4, 90.9, 87.7, 34.7, 31.0, 17.4 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1491, 1507, 1549, 1595, 2360, 2960., 3398; MS (ESI): *m/z* 511(M+1)$^{+}$; HRMS (ESI *m/z*) for $C_{35}H_{31}N_2O_2$, calcd 511.2385, found 511.2395 [M + H]; HPLC purity: t_R 19.30min (97.7 %).

2-(3,5-Dihydroxystyryl)-3-(4-(2-(4-*tert*-butylphenyl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one(4n): The title compound was prepared according to the method described for compound 4a employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 3,5-dihydroxybenzaldehyde (138 mg, 1 mmol) to obtained the pure product **4n** as white solid. Yield 80%; mp 93-94 ^{o}C; ^{1}H NMR ($CDCl_3$+DMSO-d_6, 300 MHz): δ 8.25 (d, 1H, *J* = 7.5 Hz, Ar**H**), 8.23 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.82-7.64 (m, 2H, Ar**H**), 7.54-7.34 (m, 6H, Ar**H**), 7.25 (s, 1H, Ar**H**), 7.04 (d, 1H, *J* = 8.3 Hz, Ar**H**), 6.89 (d, 1H, *J* = 8.3 Hz, Ar**H**), 6.21 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 6.17 (s, 2H, Ar**H**), 2.05 (s, 3H, -C**H**$_3$), 1.25 (s, 9H, *Tert* butyl -**H**); ^{13}C NMR ($CDCl_3$+DMSO-d_6, 75 MHz): 162.4, 158.9, 158.7, 154.6, 151.1, 150.0, 149.0, 147.2, 145.5, 140.6, 140.4, 139.5, 139.0, 136.7, 138.6, 131.4, 133.2, 134.3, 134.5, 130.6, 129.8, 127.7, 126.3, 125.4, 122.2, 123.1. 123.7, 119.7, 114.4, 112.6, 109.4, 108.5, 96.8, 96.0, 31.1, 29.6, 27.6, 22.6, 17.4 ppm: IR (KBr) (ν_{max}/cm^{-1}): 1468, 1540, 1618, 1642, 1655, 2359, 2852, 2923, 2954, 3427, 3588, 3568, 3629, 3854; MS (ESI): *m/z* 527(M+1)$^{+}$; HRMS (ESI *m/z*) for $C_{35}H_{31}N_2O_3$ calcd 527.2334, found 527.2336 [M + H]; HPLC purity: t_R 11.19 min (96.1 %).

(*E*)-3-(4-((4-*tert*-Butylphenyl)ethynyl)-2-methylphenyl)-2-(2-(5-nitrothiophen-2-yl)vinyl)quinazolin-4(3*H*)-one (4o): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 5-nitrothiophene-2-carbaldehyde (157 mg, 1mmol) to obtained the pure product **4o** as yellow solid. Yield 85%; Mp 160-161 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.23 (d, 1H, *J* = 7.9 Hz, Ar**H**), 7.97 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 7.78-7.66 (m, 3H, Ar**H**), 7.55-7.39 (m, 5H, Ar**H**), 7.53-7.30 (m, 3H, Ar**H**), 7.09 (d, 1H, *J* =7.9 Hz, Ar**H**), 7.01-6.99 (m, 1H, Ar**H**), 6.25 (d, 1H, J = 15.3 Hz, *Trans*-**H**), 2.05 (s, 3H, -C**H**$_3$), 1.26 (s, 9H, *Tert* butyl -**H**): C^{13} NMR ($CDCl_3$, 75 MHz): 161.2, 151.9, 151.4, 149.7, 147.4, 146.5, 136.1, 134.9, 134.8, 134.5, 131.4, 131.3, 131.0, 130.7, 129.1, 128.5, 127.9, 127.5, 127.3, 127.2, 125.2, 125.3, 122.6, 121.0, 119.6, 91.2, 87.6, 34.7, 31.1, 29.6, 17.4 ppm; IR (KBr) (ν_{max}/cm^{-1}); 1469, 1544, 1624, 2923, 3434; MS (ESI): *m/z* 546(M+1)$^{+}$; HRMS (ESI *m/z*) for $C_{33}H_{28}N_3O_3S$ calcd 546.1851, found 546.1856 [M + H]. HPLC purity: t_R 14.19 min (95.1 %).

2-(3-Hydroxy-4-methoxystyryl)-3-(4-(2-(4-*tert*-butylphenyl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (4p): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)-ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 3-hydroxy-4-methoxybenzaldehyde (152 mg, 1 mmol) to obtained the pure product **4p** as white solid. Yield 85%; mp 144-145 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.25 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.90 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.78 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.75-7.70 (m, 2H, Ar**H**), 7.59 (s, 1H, Ar**H**), 7.56 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.46-7.33 (m, 4H, Ar**H**), 7.21 (d, 1H, *J* = 8.1 Hz, Ar**H**), 6.91-6.87 (m, 1H, Ar**H**), 6.14 (s, 1H, O**H**), 6.84-6.80 (m, 1H, Ar**H**), 6.75-6.73 (m, 1H, Ar**H**), 6.10 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 3.87 (s, 3H, -OC**H**$_3$), 2.14 (s, 3H, -C**H**$_3$), 1.34 (s, 9H, *Tert* butyl-**H**);^{13}C NMR ($CDCl_3$, 75 MHz): 161.2, 151.4, 151.3, 148.1, 147.6, 147.0, 140.5, 135.9, 135.5, 134.2, 133.7, 130.9, 130.0, 128.3, 126.7, 126.6, 126.5, 125.7, 124.9, 124.5, 121.0, 120.0, 119.5, 115.3, 115.19 110.7, 90.3, 87.3, 55.4, 34.3, 30.70 29.1, 17.0 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1472, 1517, 147, 1577, 1603, 1676, 2961, 3499, 3629; MS (ESI): *m/z* 541(M+1)$^{+}$; HRMS

(ESI *m/z*) for $C_{36}H_{33}N_2O_3$, calcd 541.2491, found 541.2512 [M + H]; HPLC purity: t_R 13.40 min (95.7 %).

2-(3,4-Dimethoxystyryl)-3-(4-(2-(4-*tert*-butylphenyl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (4q): The title compound was prepared according to the method described for compound **4a** employing compound **3**-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 3,4-dimethoxybenzaldehyde (166 mg, 1 mmol) to obtained the pure product **4q** as white solid. Yield 90%; mp 92-93 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.28 (d, 1H, *J* = 7.4 Hz, Ar**H**), 7.94 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.79-7.67 (m, 2H, Ar**H**), 7.60 (s, 1H, Ar**H**), 7.56 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.46-7.42 (m, 3H, Ar**H**), 7.37-7.34 (m, 2H, Ar**H**), 7.25-7.18 (m, 1H, Ar**H**), 6.94-6.89 (m, 1H, Ar**H**), 6.79-6.75 (m,2H, Ar**H**), 6.121 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 3.85 (s, 3H, -OC**H**$_3$), 3.82 (s, 3H, -OC**H**$_3$), 2.15 (s, 3H, -C**H**$_3$), 1.35 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 151.9, 150.5, 148.9, 140.3, 136.9, 136.3, 135.8, 134.6, 134.2, 131.3, 130.6, 130.5, 130.3, 128.7, 128.1, 127.1, 126.8, 126.7, 126.3, 125.3, 124.8, 123.9, 121.1, 120.5, 119.7, 116.7, 110.0, 110.4, 90.3, 87.7, 55.7, 31.0, 17.4 ppm; ; IR (KBr) (ν_{max}/cm^{-1}): 1470, 1540, 1609, 1654, 2853, 2924, 3429; MS (ESI): *m/z* 555(M+1)$^+$; HRMS (ESI *m/z*) for $C_{37}H_{35}N_2O_3$ calcd 555.2647, found 555.2642 [M + H]; HPLC purity: t_R 16.75 min (97.2 %).

3-(4-(2-(4-*tert*-Butylphenyl)ethynyl)-2-methylphenyl)-2-((*E*)-2-(benzo[d][1,3]dioxol-5-yl)vinyl)quinazolin-4(3*H*)-one (4r): The title compound was prepared according to the method described for compound **4**a employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and benzo[*d*][1,3]dioxole-5-carbaldehyde (150 mg, 1 mmol) to obtained the pure product **4r** as white solid. Yield 82%; mp 205-206 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.25 (d, 1H, *J* = 7.8 Hz, Ar**H**), 7.93 (d, 1H, *J* = 15.6 Hz, *Trans*-**H**), 7.78-7.71 (m, 2H, Ar**H**), 7.59 (s, 1H, Ar**H**), 7.55 (d, 1H, *J* = 7.8 Hz, Ar**H**), 7.45-7.41 (m, 3H, Ar**H**), 7.36-7.35 (m, 2H, Ar**H**), 7.18 (d, 1H, *J* =7.8 Hz, Ar**H**), 6.87 (d, 1H, *J* = 7.8 Hz, Ar**H**), 6.77-6.72 (m, 2H, Ar**H**), 6.13 (d, 1H, *J* = 15.6 Hz, *Trans*-**H**), 5.94 (s, 2H, O-C**H**$_2$-O), 2.13 (s, 3H, -C**H**$_3$), 1.34 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.2, 151.5, 151.1, 148.8, 147.8, 141.5, 140.0, 135.9, 135.4, 134.3, 133.9, 131.0, 130.2, 129.1, 128.3, 126.9,

126.6, 126.0, 125.0, 123.7, 124.5, 120.2, 119.3, 116.3, 108.1, 105.8, 101.1, 90.2, 87.5, 34.4, 30.7, 17.0 ppm; IR (KBr) (ν_{max}/cm^{-}): 1445, 1488, 1504, 1542, 1682, 1630, 1604, 2957, 3423; MS (ESI): *m/z* 539(M+1)$^{+}$; HRMS (ESI *m/z* $C_{35}H_{27}N_2O_4O$ calcd 539.1970, found 539.1979 [M + H]; HPLC purity: t_R 7.06 min (95.3%).

2-(2,6-Dichlorostyryl)-3-(4-(2-(4-*tert*-butylphenyl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (4s): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 2,6-dichloro benzaldehyde (175 mg, 1 mmol) to obtained the pure product **4s** as white solid. Yield 86%; mp 186-186 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.28 (d, 1H, *J* = 7.4 Hz, Ar**H**), 8.06 (d, 1H, *J* = 15.7 Hz, *Trans*-**H**), 7.83-7.75 (m, 2H, Ar**H**), 7.56-7.41 (m, 5H, Ar**H**), 7.35-7.25 (m, 4H, Ar**H**), 7.13 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.11 (m, 1H, Ar**H**), 6.55 (d, 1H, *J* = 15.7 Hz, *Trans*-**H**), 2.15 (s, 3H, -C**H**$_3$), 1.34 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 166.9, 156.5, 156.4, 153.0, 146.7, 135.5, 134.4, 132.1, 129.8, 128.67, 123.1, 119.5, 117.5, 112.3, 118.8, 105.8, 103.3, 91.37, 9.10, 88.3, 70.4, 60.94 56.1, 55.9, 29.6, 17.3 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1429, 1507, 1682, 1637. 2360, 2956, 3447; MS (ESI): *m/z* 563(M+1)$^{+}$; HRMS (ESI *m/z*) for $C_{35}H_{29}N_2OCl_2$ calcd 563.1656, found 563.1645 [M + H]; HPLC purity: t_R 12.40 min (95.6 %).

2-(3,4,5-Trimethoxystyryl)-3-(4-(2-(4-*tert*-butylphenyl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (4t): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 3,4,5-trimethoxybenzaldehyde (196 mg, 1 mmol) to obtained the pure product **4t** as white solid. Yield 94%; Mp 142-143 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.29 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.89 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 7.80-7.71 (m, 2H, Ar**H**), 7.60 (s, 1H, Ar**H**), 7.47-7.42 (m, 3H, Ar**H**), 7.37-7.35 (m, 2H, Ar**H**), 7.25-7.19 (m, 1H, Ar**H**), 7.54 (d, 1H, *J* = 7.9 Hz, Ar**H**), 6.47 (s, 2H, Ar**H**), 6.11 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 3.80 (s, 9H, 3 × 0C**H**$_3$), 2.15 (s, 3H, -C**H**$_3$), 1.35 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 153.3, 151.7, 151.2, 147.9, 140.3, 136.4, 134.5, 134.2, 131.4, 130.7, 130.4, 128.9, 127.3, 126.4, 125.5, 125.0, 120.8, 119.8, 118.4, 104.9, 96.1, 90.4, 87.7, 60.7, 55.9, 31.2,

17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1463, 1503, 1546, 1636, 1604, 2658, 3433, 3568; MS (ESI): *m/z* 585(M+1)$^{+}$; HRMS (ESI *m/z*) for $C_{38}H_{37}N_2O_4$, calcd 585.2753, found 585.2749 [M + H]; HPLC purity: t_R 8.65 min (95.8 %).

3-(4-(2-(4-*tert*-Butylphenyl)ethynyl)-2-methylphenyl)-2-((*E*)-2-(naphthalen-2-yl)vinyl)quinazolin-4(3*H*)-one (4u): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 2-naphthaldehyde (156 mg, 1 mmol) to obtained the pure product **4u** as white solid. Yield 90%; Mp 156-157 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.27 (d, 1H, *J* = 7.7 Hz, Ar**H**), 8.19 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.83-7.70 (m, 6H, Ar**H**), 7.65 (s, 1H, Ar**H**), 7.56 (d, 1H, *J* = 7.7 Hz, Ar**H**), 7.47-7.41 (m, 5H, Ar**H**), 7.37-7.32 (m, 3H, Ar**H**), 7.24-7.20 (m, 1H, Ar**H**), 6.39 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 2.16 (s, 3H, -C**H**$_3$), 1.35 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.6, 151.8, 151.5, 147.3, 140.7, 136.3, 135.7, 134.4, 133.9, 133.2, 132.59 131.4, 130.7, 129.6, 128.5, 128.4, 127.7, 127.3, 127.1, 127.0, 126.6, 125.4, 125.0, 123.2, 120.8, 119.8, 118.9, 90.8, 87.9, 34.8, 31.1, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1545, 1571, 1602, 1632, 1670, 2957, 3422; MS (ESI): *m/z* 545(M+1)$^{+}$; HRMS (ESI *m/z* $C_{39}H_{33}N_2O$ calcd 545.2592, found 545.2585 [M + H]; HPLC purity: t_R 13.06 min (94.5%).

3-(4-(2-(4-*tert*-Butylphenyl)ethynyl)-2-methylphenyl)-2-((*E*)-2-(5-nitrofuran-2-yl)vinyl) quinazolin-4(3*H*)-one (4v): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and 5-nitrofuran-2-carbaldehyde (141 mg, 1 mmol) to obtained the pure product **4v** as yellow solid. Yield 85%; mp 170-171 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.31 (d, 1H, *J* = 7.2 Hz, Ar**H**), 7.83 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 7.85-7.76 (m, 2H, Ar**H**), 7.62 (s, 1H, Ar**H**), 7.59-7.48 (m, 3H, Ar**H**), 7.40-7.37 (m, 2H, Ar**H**), 7.34-7.26 (m, 2H, Ar**H**), 7.16 (d, 1H, *J* = 8.1 Hz, Ar**H**), 6.69-6.70 (m, 1H, Ar**H**), 6.52 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 2.13 (s, 3H, -C**H**$_3$), 1.34 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 178.2, 161.3, 153.2, 151.9, 143.9, 147.4, 136.17 134.9, 134.8, 134.5, 131.4, 130.8, 128.5, 127.6, 127.3, 127.2, 125.4, 125.37, 124.94, 123.23, 121.03, 119.73, 118.64, 114.52, 113.21,

111.60, 91.141, 87.70, 34.7, 31.1, 17.4 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1481, 1547, 1571, 1544, 2959, 3434, 3629, 3855; MS (ESI): *m/z* 530$(M+1)^+$; HRMS (ESI *m/z*) for $C_{33}H_{28}N_3O_4$ calcd 530.2079, found 530.2060 [M + H]; HPLC purity: t_R 6.57 min (95.1 %).

3-(4-(2-(4-*tert*-Butylphenyl)ethynyl)-2-methylphenyl)-2-((*E*)-2-(quinolin-4-yl)vinyl) quinazolin-4(3*H*)-one (4w): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((4-tert-butylphenyl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10b**, 406 mg, 1 mmol) and quinoline-4-carbaldehyde (157 mg, 1 mmol) to obtained the pure product **4w** as white solid. Yield 86%; mp 143-144 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.81 (d, 1H, *J* = 4.5 Hz, Ar**H**), 8.68 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 8.32 (d, 1H, *J* = 7.5 Hz, Ar**H**), 8.16 (d, 1H, *J* = 9.0 Hz, Ar**H**), 8.08 (d, 1H, *J* = 8.3 Hz, Ar**H**), 7.85-7.80 (m, 2H, Ar**H**), 7.75-7.69 (m, 1H, Ar**H**), 7.61-7.49 (m, 4H, Ar**H**), 7.49-7.34 (m, 4H, Ar**H**), 7.25 (d, 1H, *J* = 4.5 Hz, Ar**H**), 7.20-7.16 (m, 1H, Ar**H**), 6.54 (d, 1H, *J* = 15.9 Hz, *Trans*-**H**), 2.17 (s, 3H, -C**H**$_3$), 1.35 (s, 9H, *Tert* butyl-**H**); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.4, 151.9, 150.4, 150.0, 148.5, 147.6, 140.6, 136.2, 135.4, 134.8, 134.8, 134.5, 131.4, 130.7, 130.0, 129.6, 127.7, 127.2, 127.1, 126.0, 125.3, 125.3, 125.39 123.4, 121.0, 119.6, 117.8, 91.4, 87.6, 34.8, 31.1, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1468, 1506, 1547, 1604, 1580, 1629, 1688, 2864, 2959, 3064, 3432; MS (ESI): *m/z* 546$(M+1)^+$; HRMS (ESI *m/z*) for $C_{38}H_{32}N_3O$ calcd 546.2545, found 546.2572 [M + H]; HPLC purity: t_R 8.66 min (95.8 %).

2-(4-Fluorostyryl)-3-(4-(2-(2-methoxynaphthalen-6-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (4x): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10c**, 430 mg, 1 mmol) and 4-fluorobenzaldehyde (124 mg, 1 mmol) to obtained the pure product **4x** as white solid. Yield 82%; mp 180-181 ^oC; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.30 (d, 1H *J* = 7.5 Hz, Ar**H**), 7.97 (s, 1H, Ar**H**), 7.94 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**), 7.81-7.74 (m, 2H, Ar**H**), 7.60-7.52 (m, 1H, Ar**H**), 7.50-7.45 (m, 2H, Ar**H**), 7.31-7.27 (m, 1H, Ar**H**), 7.18 (d, 1H, *J* = 7.5 Hz, Ar**H**), 7.15-7.07 (m, 3H, Ar**H**), 7.01-6.95 (m, 2H, Ar**H**), 6.32 (d, *J* = 15.9 Hz, *Trans*-**H**), 3.93 (s,3H, -OC**H**$_3$), 2.16 (s, 3H. –C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 164.1, 158.4,

147.7, 139.2, 137.3, 136.3, 135.5, 134.7, 134.4, 134.5, 131.5, 130.7, 130.3, 130.2, 129.3, 128.9, 128.7, 127.4, 127.2, 126.8, 125.1, 123.6, 120.8, 120.1, 119.4, 116.7, 116.4, 114.3, 114.0, 105.7, 91.4, 88.1, 55.3, 29.6, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1470, 1481, 1499, 1546, 1604, 1582. 1629, 2204, 2917, 3423; MS (ESI): *m/z* 537 $(M+1)^+$; HRMS (ESI *m/z* $C_{36}H_{26}N_2O_2F$ calcd 537.1978, found 537.1962 [M + H]; HPLC purity: t_R 13.70 min (98.6 %).

2-(2,6-Dichlorostyryl)-3-(4-(2-(2-methoxynaphthalen-6-yl)ethynyl)-2-methylphenyl) quinazolin-4(3*H*)-one (4y): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10c**, 430 mg, 1 mmol) and 2,6-dichlorobenzaldehyde (175 mg, 1 mmol) to obtained the pure product **4y** as white solid. Yield 84%; mp 119-120 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.31 (d, 1H, *J* = 8.3 Hz, Ar**H**), 8.06 (d, 1H, *J* = 15.9 Hz, *Trans*-**H**), 7.98 (s, 1H, Ar**H**), 7.83 (s, 1H, Ar**H**), 7.81 (d, 1H, *J* = 8.3 Hz, Ar**H**), 7.73-7.68 (m, 2H, Ar**H**), 7.60 (s, 1H, Ar**H**),7.57-7.4 (m, 3H, Ar**H**), 7.30-7.38 (m, 6H, Napthyl-**H**), 6.56 (d, 1H, *J* = 15.9 Hz, *Trans*-**H**), 3.93 (s, 3H, -OC**H**$_3$), 2.16 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.6, 158.4, 147.7, 135.6, 134.90, 134.6, 134.3, 134.2, 133.7, 132.6, 131.4, 130.6, 129.3, 128.9, 128.7, 128.4, 127.8, 127.6, 127.1, 126.9, 126.8, 125.3, 121.0, 119.4, 105.7, 96.0, 88.1, 55.3, 29.6, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1469, 1482, 1499, 157, 1604, 1553, 1628, 1685, 2341, 2359, 3435; MS (ESI): *m/z* 587 $(M+1)^+$; HRMS (ESI *m/z* $C_{36}H_{25}N_2O_2Cl_2$ calcd 587.1293, found 587.1315 [M + H]; HPLC purity: t_R 6.57 min (95.10 %).

2-(3,4-Dimethoxystyryl)-3-(4-(2-(2-methoxynaphthalen-6-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (4z): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10c**, 430 mg, 1 mmol) and 3,4-dimethoxybenzaldehyde (166 mg, 1 mmol) to obtained the pure product **4z** as white solid. Yield 88%; mp 124-125 ^oC; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.29 (d, 1H, *J* = 7.5 Hz, Ar**H**), 8.07 (d, 1H, *J* = 15.9 Hz, *Trans*-**H**), 7.83-7.75 (m, 2H, Ar**H**), 7.63-7.54 (m, 3H, Ar**H**), 7.49-7.43 (m, 1H, Ar**H**), 7.27(d, 1H, *J* = 7.5 Hz, Ar**H**), 7.18-7.12 (m, 2H, Ar**H**), 6.81-6.73 (m, 3H, Ar**H**), 6.62 (d, 1H, *J* = 15.1 Hz, *Trans*-**H**),

3.39 (s, 3H, -OC**H**$_3$), 3.73 (s, 3H, -OC**H**$_3$), 3.70 (s,3H, -OC**H**$_3$), 2.15 (s, 3H, -OC**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 158.4, 155.0, 153.97, 153.2, 152.1, 147.6, 142.3, 136.3, 136.2, 135.7, 134.5, 134.3, 131.4, 130.6, 129.3, 128.9, 128.8, 128.4, 128.1, 127.1, 126.8, 126.7, 126.2, 125.0, 124.6, 120.6, 119.5, 107.3, 91.5, 88.2, 60.80, 60.6, 55.8, 55.36 23.8, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1468, 1548, 1571, 1604, 1629, 1673, 2924, 3422, 3650; MS (ESI): *m/z* 579(M+1)$^+$; HRMS (ESI *m/z* $C_{38}H_{31}N_2O_4$ calcd 579.2283, found 579.2294 [M + H]; HPLC purity: t_R 12.40 min (95.6 %).

2-(3,4,5-Trimethoxystyryl)-3-(4-(2-(2-methoxynaphthalen-6-yl)ethynyl)-2-methylphenyl)quinazolin-4(3*H*)-one (4aa): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10c**, 430 mg, 1 mmol) and 3,4,5-trimethoxybenzaldehyde (196 mg, 1 mmol) to obtained the pure product **4aa** as white solid. Yield 90%; mp 130-131 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.27 (d, 1H, *J* = 8.4 Hz, Ar**H**), 7.87 (d, 1H, *J* = 15.5 Hz, *Trans*-**H**), 7.69 (s, 1H, Ar**H**), 7.80-7.62 (m, 4H, Ar**H**), 7.59-7.44 (m, 4H, Ar**H**), 7.24 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.17-7.11 (m, 2H, Ar**H**), 7.07 (s, 1H, Ar**H**), 6.49 (s, 1H, Ar**H**), 6.14 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 3.93 (s, 3H, -OC**H**$_3$), 3.81 (s, 9H, 3 × -OC**H**$_3$), 2.11 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.5, 158.41, 153.9, 151.4, 147.2, 140.3, 139.7, 136.4, 135.6, 134.6, 134.4, 134.2, 134.7, 130.7, 130.7, 129.3, 128.8, 127.0, 127.1, 126.9, 126.8, 126.8, 126.6, 119.5, 119.47, 118.5, 117.6, 105.8, 89.2, 87.9, 60.9, 55.3, 23.7, 17.2 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1501, 1574, 1547, 1628, 184, 2927, 3429, 3650; MS (ESI): *m/z* 609(M+1)$^+$; HRMS (ESI *m/z* $C_{39}H_{33}N_2O_5$ calcd 609.2389, found 609.2409 [M + H]; HPLC purity: t_R 9.29 min (98.1 %).

3-(4-(2-(2-Methoxynaphthalen-6-yl)ethynyl)-2-methylphenyl)-2-((*E*)-2-(naphthalen-2-yl)vinyl)quinazolin-4(3*H*)-one (4ab): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10c**, 430 mg, 1 mmol) and 2-naphthaldehyde (156 mg, 1 mmol) to obtained the pure product **4ab** as white solid. Yield 85%; Mp 170-171 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.31 (d, 1H, *J* = 7.5 Hz, Ar**H**), 8.20 (d, 1H, *J* = 15.3 Hz, *Trans*-**H**), 8.20 (s, 1H, Ar**H**), 7.85-7.78

(m, 4H, Ar**H**), 7.76-7.66 (m, 3H, Ar**H**), 7.63-7.53 (m, 3H, Ar**H**), 7.51-7.45 (m, 3H, Ar**H**), 7.37 (d, 1H, *J* = 8.3 Hz, Ar**H**), 7.26-7.24 (m, 2H, Ar**H**), 7.18-7.09 (m, 2H, Ar**H**), 6.47 (d, 1H, *J* = 15.4 Hz, *Trans*-**H**), 3.94 (s, 3H, -OC**H**$_3$), 2.17 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 158.4, 151.4, 140.8, 135.9, 134.6, 134.4, 133.9, 132.6, 131.5, 130.7, 129.7, 129.3, 128.9, 128.5, 127.4, 127.27, 127.0, 126.9, 126.5, 123.2, 119.5, 118.9, 105.8, 96.1, 55.30, 29.7, 17.02 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1480, 1544, 1629, 1603, 1684, 2360. 2922, 3429. 3630; MS (ESI): *m/z* 579 $(M+1)^+$; HRMS (ESI *m/z* $C_{38}H_{31}N_2O_4$ calcd 579.2283, found 579.2308 [M + H]; HPLC purity: t_R 10.67 min (96.2 %).

3-(4-(2-(2-Methoxynaphthalen-6-yl)ethynyl)-2-methylphenyl)-2-((*E*)-2-(5-nitrofuran-2-yl)vinyl)quinazolin-4(3*H*)-one (4ac): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10c**, 430 mg, 1 mmol) and 5-nitrofuran-2-carbaldehyde (141 mg, 1 mmol) to obtained the pure product **4ac** as yellow solid. Yield 85%; mp 128-129 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.30 (d, 1H, *J* = 7.5 Hz, Ar**H**), 8.01 (s, 1H, Ar**H**), 7.79 (d, 1H, *J* = 15.9 Hz, *Trans*-**H**), 7.82-7.78 (m, 2H, Ar**H**), 7.75-7.65 (m, 2H, Ar**H**), 7.65 (s, 1H, Ar**H**), 7.61-7.48 (m, 3H, Ar**H**), 7.28 (d, 1H, *J* = 3.7 Hz, Furan-**H**), 7.25-7.17 (m, 2H), 7.17 (d, *J* = 7.5 Hz, 1H), 6.65 (d, *J* = 3.7 Hz, Furan-**H**), 6.53 (d, 1H, *J* = 15.9 Hz, *Trans*-**H**), 3.93 (s,3H, -OC**H**$_3$), 2.14 ppm (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.3, 158.4, 153.2, 149.9, 147.4, 136.2, 135.0, 134.8, 134.6, 134, 131.5, 130.8, 129.4, 128.9, 128.4, 127.6, 127.4, 127.3, 126.8, 125.5, 124.9, 123.2, 121.1, 119.4, 117.7, 114.4, 133.1, 105.8, 96.1, 91.6, 88.0, 55.3, 29.7, 17.5 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1480, 1544, 1604, 1629, 1685, 2359, 3436; MS (ESI): *m/z* 554$(M+1)^+$; HRMS (ESI *m/z* $C_{32}H_{25}N_3O_5$ calcd 554.1619, found 554.1683 [M + H]; HPLC purity: t_R 13.94 min (97.5 %).

3-(4-(2-(2-Methoxynaphthalen-6-yl)ethynyl)-2-methylphenyl)-2-((E)-2-(quinolin-4-yl)vinyl)quinazolin-4(3*H*)-one (4ad): The title compound was prepared according to the method described for compound **4a** employing compound 3-(4-((6-methoxynaphthalen-2-yl)ethynyl)-2-methylphenyl)-2-methylquinazolin-4(3*H*)-one (**10c**, 430 mg, 1 mmol) and quinoline-4-carbaldehyde (157 mg, 1 mmol) to obtained the pure product **4ad** as solid. Yield 87%; mp 140-141 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.82 (d, 1H, *J* = 4.4

Hz, Ar**H**), 8.67 (d, 1H, *J* = 15.4 Hz, *Trans*-**H**), 8.33 (d, 1H, *J* = 7.3 Hz, Ar**H**), 8.20 (d, 1H, *J* = 8.1 Hz, Ar**H**), 8.08 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.96 (s, 1H, Ar**H**), 7.86-7.81 (m, 2H, Ar**H**), 7.74-7.58 (m, 6H, Napthyl-**H**), 7.54-7.51 (m, 2H, Ar**H**), 7.25 (d, 1H, *J* = 8.1 Hz, Ar**H**), 7.16 (d, 1H, *J* = 4.4 Hz, Ar**H**), 7.14-7.15 (m, 1H, Ar**H**), 7.06 (s, 1H, Ar**H**), 6.57 (d, 1H, *J* = 15.4 Hz, *Trans*-**H**), 3.93 (s, 3H, -OC**H**$_3$), 2.19 (s, 3H, -C**H**$_3$); ^{13}C NMR ($CDCl_3$, 75 MHz): 161.43, 158.40, 150.40, 149.99, 148.51, 147.58, 140.57, 136.26, 135.42, 134.81, 134.22, 131.46, 130.73, 130.06, 129.63, 128.81, 128.70, 128.35, 127.68, 127.21, 126.86, 125.18, 123.37, 119.45, 117.79, 105.72, 91.55, 87.91, 55.27, 29.61, 17.51 ppm; IR (KBr) (ν_{max}/cm^{-1}): 1480.5, 1550.5, 1580.2, 1629.5, 1690.6, 2207.8, 2357.1, 2919.2, 3050.5, 3412.6; MS (ESI): *m/z* 570 $(M+1)^+$; HRMS (ESI *m/z* $C_{31}H_{23}N_2O_2$ calcd 570.1751, found 570.1743 [M + H]; HPLC purity: t_R 18.28 min (97.8 %).