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Synthesis of novel quinazolinone-1,2,3-triazole conjugates

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ABSTRACT

Hybrid compounds of 2-styryl quinazolinone and 1,2,3-triazoles were synthesized via 1,3-dipolar azide-alkyne cycloaddition reaction from 3-(2-azidoethyl)quinazolinones and various alkynes, followed by Knoevenagel reaction between 2-methylquinazolinone-1,2,3-triazole conjugates and aromatic aldehydes. All quinazolinone-1,2,3-triazole hybrid compounds were tested for their antiradical and antibacterial activity, but did not show any significant activity.

Key words: 2-Styryl quinazolinone-1,2,3-triazole conjugate, Huisgen reaction, Knoevenagel condition, antiradical activity, antibacterial activity

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INTRODUCTION

Both quinazolinones and 1,2,3-triazoles possess wide range of biological activity. In the last years an attention is devoted to the studies of compounds containing quinazolin-4-one moiety as antibacterial [[1]-[3]] and antiradical agents [[1], [2]]. Some examples of biologically active compounds containing quinazolinone moiety are listed below. Quinazolinone alkaloid isolated from *Dichroa febrifuga* roots, known as Febrifugine and its analogues demonstrate strong antimalarial activity [[5], [6]]. Halofuginone acts as an agent for reducing fibrosis [[6]]. Raltitrexed is used in cancer therapy as an alternative to 5-fluorouracil and capecitabine [[7]]. Afloqualone is a muscle relaxant [[8]]; however, it can cause dermatitis through photosensitization [[9]]. On the other hand, compounds containing 1,2,3-triazole moiety exhibit anticancer, antituberculosis, antifungal, antibacterial, miscellaneous [[10], [11]], anti-inflammatory, antileishmanial, antimicrobial [[11]], antiviral [[11], [12]], antimalarian [[12]], citotoxic and antioxidant activity [[13]]. They can also act as HIV protease inhibitors [[10]]. Some compounds containing both quinazolinone and 1,2,4-triazole moiety are used in medicine, e. g., albaconazole is used as an antifungal drug [[14]].

EXPERIMENTAL SECTION

^{1}H (300 MHz) and ^{13}C (75.5 MHz) NMR spectra were recorded on Bruker Avance 300 spectrometer; the samples were dissolved in $CDCl_3$ or DMSO–d_6 and the spectra were calibrated to the residue of $CHCl_3$ or DMSO. IR spectra were recorded on Perkin Elmer spectrometer (model: Spectrum BX, FT-IR system) for solid sample in KBr disc. Melting points were measured with Fisher Digital Melting Point Analyzer (model 355). Microanalysis was done with Carlo-Erba Instruments element analyzer (model: EA1108). High resolution mass spectra were recorded on Agilent 1290 Infinity series UPLC chromatograph equipped with Agilent 6230 TOF LC/MS masspectrometer.

Compound **1** [[18]] was obtained according to the known procedure from anthranilic acid, triethyl orto-formate and ethanolamine [[19]]. Compound **2** was obtained by known methods through cyclization of anthranilic acid followed by treatment with ethanolamine [[21]-[22]]. Compounds **3** and **4** were obtained analogously to the method described previously [[23], 24].

2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)ethyl 4-methylbenzenesulfonate (**4**): DMAP (0.40 g, 3.3 mmol) and Et_3N (5.1 mL, 36 mmol) was added to a solution of 3-(2-hydroxyethyl)-2-methylquinazolin-4(3*H*)-one (**1**) (7.0 g, 34 mmol) in DCM (68 mL). The mixture was stirred, cooled to 0 °C and *p*-TsCl (6.95 g, 36 mmol) was added portion-wise. The resulting solution was stirred at 0 °C for 1 h, followed with mixing at room temperature (TLC control). The solution was washed with water (3 × 20 mL), saturated aqueous solution of $NaHCO_3$ (3 × 20 mL) and brine (3 × 20 mL). Organic phase was separated and dried over Na_2SO_4, filtrated and evaporated. The solid residue was recrystallized from the mixture of DCM and MTBE. The compound was obtained as white crystals (7.6 g, 62%) with mp 128-130°C. IR (KBr) ν, cm^{-1}: 3774, 1672, 1593, 1382, 1300, 1198, 1165, 979, 894, 769, 700. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.20 (d, 1H, *J* = 7.4 Hz, C(6)H), 7.82-7.60 (m, 5H, C(7,8,9)H, 2 × C^{Ts}H), 7.52-7.40 (m, 2H, 2 × C^{Ts}H), 4.42 (t, 2H, *J* = 6.2 Hz, C(12)H_2), 3.89 (t, 2H, *J* = 6.2 Hz, C(11)H_2), 2.74 (s, 3H, CH_3), 2.32 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz), δ, ppm: 162.2, 154.7, 147.2, 143.0, 140.4, 135.4, 134.8, 129.0, 127.3, 126.9, 126.8, 120.7, 60.2, 41.0, 23.9, 22.3. HRMS calcd. for $C_{18}H_{18}N_2O_4S$ $[M+H]^+$ *m/z*: 359.4191; found *m/z*: 359.4210.

3-(2-Azidoethyl)quinazolin-4(3*H*)-one (**5**). NaN_3 (2.6 g, 40 mmol) was added to the solution of compound **3** (2.8 g, 8 mmol) in DMF (30 mL) and heated at 60°C 1 h, followed by addition of MTBE (300 mL) and washing with brine (10 × 20 mL). The organic layer was separated, dried over Na_2SO_4, filtrated and evaporated. The solid residue (1.7 g, 99%) was used for further transformations without additional purification. Mp 63-64 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.32 (d, 1H, *J* = 7.9 Hz, C(6)H), 8.05 (broad s., 1H, C(2)H), 7.69 (m, 2H, C(8,9)H), 7.53 (t, 1H, *J* = 6.8 Hz, C(7)H), 4.13 (t, 2H, *J* = 5.7 Hz, C(11)H_2), 3.77 (t, 2H, *J* = 5.7 Hz, C(12)H_2). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm:161.2, 148.2, 146.7, 134.6, 127.7, 127.6, 126.7, 122.1, 49.6, 46.5. Elemental analysis calcd. for $C_{10}H_9N_5O$: C 55.81, H 4.22, N 32.54; found:C 55.55, H 4.24, N 32.50.

3-(2-Azidoethyl)-2-methylquinazolin-4(3*H*)-one (**6**). NaN_3 (6.92 g, 83 mmol) was added to the solution of quinazolinone **4** (7.62 g, 21 mmol) in DMF (78 mL) and the resulting mixture was heated at 80°C 1 h. Then it was filtered, and evaporated. The compound **6** was obtained as white crystals (3.6 g, 73%) with mp 91-92°C after recrystallization from MTBE. IR (KBr) ν, cm^{-1}: 3774, 3011, 2968, 2129, 2091, 1669, 1598, 1388, 1340, 1282, 1210, 1171, 1008, 771, 703. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.27 (d, 1H, *J* = 8.0 Hz, C(6)H), 7.76 (t, 1H, *J* = 8.0 Hz, C(8)H), 7.70 (d, 1H, *J* = 8.0 Hz, C(9)H), 7.49 (t, 1H, *J* = 8.0 Hz, C(7)H), 4.28 (t, 2H, *J* = 5.8 Hz, C(11)H_2), 3.82 (t, 2H, *J* = 5.8 Hz, C(12)H_2), 2.75 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 159.3, 146.8, 134.7, 126.9, 126.8, 126.8, 120.3, 104.9, 49.4, 44.2, 23.8. Elemental analysis calcd. for $C_{11}H_{11}N_5O$: C 57.63, H 4.84, N 30.55; found: C 57.58, H 4.84, N 30.55.

Hybrid compounds **8** and **9** of quinazolin-4-ones and 1,2,3-triazoles.

Method I. (Compounds **8a**,**c-e**,**j**,**k**. General procedure.) Alkyne **7** (1.2 equiv.), sodium ascorbate (0.2 equiv.) solution in water (0.3 mmol/0.1 mL) and $CuSO_4 \cdot 5H_2O$ (0.1 equiv.) solution in water (0.15 mmol/0.1 mL) were added to the solution of 3-(2-azidoethyl)quinolin-4(3*H*)-one **5** (1.0 equiv.) in acetone (1.5 mmol/5 mL). The resulting solution was stirred and refluxed for 1-7 h (TLC control). When the reaction was completed, acetone was evaporated, the solid residue was dissolved in DCM (20 mL) and washed with brine (3 × 10 mL). Organic layer was dried over Na_2SO_4, filtrated and evaporated. The solid residue was crystallized from a mixture of DCM and hexanes (1:3). Compounds **8a**,**c-e**,**j**,**k** were obtained as white crystals.

3-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8a). Yield - 200 mg (42%). Mp 198-201°C. IR (KBr) ν, cm^{-1}: 3774, 1679, 1600, 1293, 1026, 765, 700. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.60 (broad s., 1H, C(2)H), 8.17 (dd, 1H, ^2J = 7.9 Hz, ^3J = 1.2 Hz, C(6)H), 7.97 (broad s., 1H, C(13)H), 7.87-7.76 (m, 3H, C(7,8,9)H), 7.66-7.53 (m, 2H, 2 × C^{Ph}H), 7.48-7.40 (m, 2H, 2 × C^{Ph}H), 7.37-7.29 (m, 1H, C^{Ph}H), 4.84 (t, 2H, *J* = 5.7 Hz, C(12)H_2), 4.50 (t, 2H, *J* = 5.7 Hz, C(11)H_2). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 160.3, 147.9, 147.4, 146.5, 134.6, 130.7, 128.9 (2C), 128.0, 127.2 (2C), 127.1, 126.1, 125.1, 122.0, 121.4, 47.8, 46.2. Elemental analysis calcd. for $C_{18}H_{15}N_5O \cdot 0.5H_2O$: C 66.24, H 4.63, N 21.46; found: C 66.10, H 4.58, N 21.40.

3-(2-(4-Pentyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8c). Yield - 196 mg (42%). Mp 108-109 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.32 (d, 1H, *J* = 7.5 Hz, C(6)H), 7.81-7.74 (m, 2H, C(8,9H), 7.71 (broad s., 1H, C(2)H), 7.52 (t, 1H, *J* = 7.7 Hz, C(7)H), 7.19 (broad s., 1H, C(13)H), 4.79 (t, 2H, *J* = 6.1 Hz, C(12)H_2), 4.56 (t, 2H, *J* = 6.1Hz, C(11)H_2), 2.71-2.56 (m, 2H, CH_2), 1.63-1.51 (m, 2H, CH_2), 1.35-1.19 (m, 4H, 2 × CH_2), 0.85 (t, 3H, *J* = 6.6 Hz, CH_3). Elemental analysis calcd. for $C_{17}H_{21}N_5O$: C 65.58, H 6.80, N 22.49; found: C 65.19, H 6.78, N 22.31.

3-(2-(4-Hexyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8d). Yield – 283 mg (58%). Mp 116-117 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.32 (d, 1H, *J* = 7.3 Hz, C(6)H), 7.78 (t, 1H, *J* = 8.1 Hz, C(8H), 7.68 (d, 1H, *J* = 8.1 Hz, C(9)H), 7.57 (broad s., 1H, C(2)H), 7.54 (t, 1H, *J* = 7.3 Hz, C(7)H), 7.09 (broad s., 1H, C(13)H), 4.76 (t, 2H, *J* = 5.8 Hz, C(12)H_2), 4.53 (t, 2H, *J* = 5.8 Hz, C(11)H_2), 2.63 (t, 2H, *J* = 7.5 Hz, CH_2), 1.66-1.48 (m, 2H, CH_2), 1.29-

1.19 (m, 6H, 3 × CH_2), 0.85 (t, 3H, *J* = 6.4 Hz, CH_3). Elemental analysis calcd. for $C_{18}H_{23}N_5O$: C 66.44, H 7.12, N 21.52; found: C 66.14, H 7.14, N 21.48.

3-(2-(4-(2-Hydroxyethyl)-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8e). Yield – 325 mg (76%). Mp 153-154 C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.17 (d, 1H, *J* = 7.3 Hz, C(6)H), 7.90 (broad s., 1H, C(2)H), 7.88 (broad s., 1H, C(13)H), 7.84 (t, 1H, *J* = 7.9 Hz, C(8)H), 7.65 (d, 1H, *J* = 7.3 Hz, C(9)H), 7.57 (t, 1H, *J* = 7.9 Hz, C(7)H), 4.73 (t, 2H, *J* = 5.4 Hz, C(12)H_2), 4.68 (t, 1H, *J* = 5.4 Hz, OH), 4.42 (t, 2H, *J* = 5.4 Hz, C(11)H_2), 3.57 (q., 2H, *J* = 6.8 Hz, CH_2), 2.73 (t, 2H, *J* = 6.8 Hz, CH_2). Elemental analysis calcd. for $C_{14}H_{15}N_5O_2$: C 58.94, H 5.30, N 24.55; found: C 58.94, H 5.23, N 24.46.

3-(2-(4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8j). Yield – 256 mg (63%). Mp 196-197 C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.15 (d, 1H, *J* = 8.1 Hz, C(6)H), 8.03 (broad s., 1H, C(2)H), 7.89 (broad s., 1H, C(13)H), 7.82 (t, 1H, *J* = 7.2 Hz, C(8)H), 7.68 (d, 1H, *J* = 8.1 Hz, C(9)H), 7.55 (t, 1H, *J* = 7.2 Hz, C(7)H), 5.23 (t, 2H, *J* = 5.3 Hz, C(12)H_2), 4.77 (t, 2H, *J* = 5.3 Hz, C(11)H_2), 4.49 (t, 1H, *J* = 8.2 Hz, OH), 4.46 (d, 2H, *J* = 8.2 Hz, CH_2). Elemental analysis calcd. for $C_{13}H_{13}N_5O_2$: C 57.55, H 4.83, N 25.82; found: C 57.21, H 4.70, N 25.80.

3-(2-(4-(2-Hydroxypropan-2-yl)-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8k). Yield – 292 mg (65%). Mp 171-173°C. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.17 (d, 1H, *J* = 8.1 Hz, C(6)H), 7.91 (broad s., 1H, C(2)H), 7.89 (broad s., 1H, C(13)H), 7.82 (t, 1H, *J* = 7.3 Hz, C(8)H), 7.64 (d, 1H, *J* = 8.1Hz, C(9)H), 7.55 (t, 1H, *J* = 7.3 Hz, C(7)H), 5.11 (s, 1H, OH), 4.74 (t, 2H, *J* = 5.6 Hz, C(12)H_2), 4.46 (t, 2H, *J* = 5.6 Hz, C(11)H_2), 1.41 (s, 6H, 2 × CH_3). Elemental analysis calcd. for $C_{15}H_{17}N_5O_2$: C 60.19, H 5.72, N 23.40; found: C 59.89, H 5.65, N 23.01.

Method II. (Compounds **8b**,**g-i** and **9a-g**,**l**,**m**. General procedure.) CuI (0.25 equiv.), DIPEA (0.26 equiv.) and alkyne **7** were added to the solution of derivative of quinazolin-4-one **5** or **6** (1 equiv.) in THF (2.18 mmol of comp. **5** or **6** in 20 mL). The solution was stirred and heated at 70°C for 1-12 h (TLC control). The resulted precipitate was centrifuged and the supernatant was evaporated. The solid residue was dissolved in DCM (20 mL), washed with 5% trilon B buffer (7 × 2 mL) and brine (3 × 5 mL). Organic layer was dried over Na_2SO_4, filtered, evaporated and recrystalized from a mixture of DCM and hexanes (1:3). Compounds **8b**,**g-i** and **9a-g**,**l**,**m** was obtained as white crystals.

3-(2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8b). Yield - 286 mg (64%). Mp 126-129 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.31 (d, 1H, *J* = 8.1 Hz, C(6)H), 7.78 (t, 1H, *J* = 7.7 Hz, C(8)H), 7.68 (d, 1H, *J* = 8.1 Hz, C(9)H), 7.57 (broad s., 1H, C(2)H), 7.53 (t, 1H, *J* = 7.7 Hz, C(7)H), 7.10 (broad s., 1H, C(13)H), 4.76 (t, 2H, *J* = 5.8 Hz, C(12)H_2), 4.52 (t, 2H, *J* = 5.8 Hz, C(11)H_2), 2.64 (t, 2H, *J* = 7.5 Hz, CH_2), 1.54 (q., 2H, *J* = 7.5 Hz, CH_2), 1.26 (sextet., 2H, *J* = 7.5 Hz, CH_2), 0.86 (t, 3H, *J* = 7.5 Hz, CH_3). Elemental analysis calcd. for $C_{16}H_{19}N_5O$: C 64.63, H 6.44, N 23.55; found: C 64.24, H 6.29, N 23.39.

3-(2-(4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8g). Yield – 312 mg (74%). Mp 171-173°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.24 (d, 1H, *J* = 8.1 Hz, C(6)H), 7.73 (t, 1H, *J* = 7.2 Hz, C(8)H), 7.65 (d, 1H, *J* = 8.1 Hz, C(9)H), 7.60 (broad s., 1H, C(2)H), 7.48 (t, 1H, *J* = 7.2 Hz, C(7)H), 7.08 (broad. s., 1H, C(13)H), 4.70 (t, 2H, *J* = 5.7 Hz, C(12)H_2), 4.48 (t, 2H, *J* = 5.7 Hz, C(11)H_2), 1.84 (m, 1H, $C^{c\text{-}Pr}H$), 0.86 (t, 2H, *J* = 7.2 Hz, $C^{c\text{-}Pr}H_2$), 0.73-0.66 (m, 2H, $C^{c\text{-}Pr}H_2$). Elemental analysis calcd. for $C_{15}H_{15}N_5O$: C 64.04, H 5.37, N 24.89; found: C 63.86, H 5.11, N 24.59.

3-(2-(4-(1-Hydroxycyclohexyl)-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (8h). Yield – 331 mg (65%). Mp 158-160 C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.27 (d, 1H, *J* = 7.9 Hz, C(6)H), 7.75 (t, 1H, *J* = 7.4 Hz, C(8)H), 7.62 (d, 1H, *J* = 7.9 Hz, C(9)H), 7.56 (broad s., 1H, C(2)H), 7.50 (t, 1H, *J* = 7.4 Hz, C(7)H), 7.31 (broad s., 1H, C(13)H), 4.76 (t, 2H, *J* = 5.8 Hz, C(12)H_2), 4.50 (t, 2H, *J* = 5.8 Hz, C(11)H_2), 2.77 (s, 1H, OH), 1.97-1.17 (m, 10H, 5 × $C^{c\text{-}Hex}H_2$). Elemental analysis calcd. for $C_{18}H_{21}N_5O_2$: C 63.70, H 6.24, N 20.63; found: C 63.49, H 6.17, N 20.44.

3,3'-((4,4'-(Butan-1,4-diyl)bis(1*H*-1,2,3-triazol-1,1-diyl))bis(etan-2,1-diyl))bis(quinazolin-4(3*H*)-one) (8i). Yield – 378 mg (47%). Mp 215-217°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.27 (d, 2H, *J* = 8.2 Hz, C(6,6')H), 7.73 (t, 2H, *J* = 7.7 Hz, C(8,8')H), 7.62 (d, 2H, *J* = 8.2 Hz, C(9,9')H), 7.57 (broad. s., 2H, C(2,2')H), 7.51 (t, 2H, *J* = 7.7 Hz, C(7,7')H), 7.16 (broad. s., 2H, C(13,13')H), 4.74 (t, 4H, *J* = 6.2 Hz, C(12,12')H_2), 4.51 (t, 4H, *J* = 6.2 Hz, C(11,11')H_2), 2.67-2.55 (m, 4H, 2 × CH_2), 1.61-1.51 (m, 4H, 2 × CH_2). Elemental analysis calcd. $C_{28}H_{28}N_{10}O_2$: C 62.67, H 5.27, N 26.10; found: C 62.27, H 5.22, N 25.81.

3-(2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9a). Yield – 524 mg (72%). Mp 172-175°C. IR (KBr) ν, cm^{-1}: 3774, 3136, 1670, 1595, 1342, 1229, 1199, 766, 699. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.29 (dd, 1H, ^2J = 8.0 Hz, ^3J = 1.2 Hz, C(6)H), 7.80-7.72 (m, 3H, C(13)H, and 2 × $C^{Ph}H$), 7.68-7.60 (m, 2H,

C(8,9)H), 7.51 (t, 1H, *J* = 7.0 Hz, C(7)H), 7.46-7.30 (m, 3 × C^{Ph}H), 4.87 (t, 2H, *J* = 6.1 Hz, C(12)H_2), 4.64 (t, 2H, *J* = 6.1 Hz, C(11)H_2), 2.33 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.4, 153.9, 148.5, 134.9, 130.2, 129.0, 128.6, 127.1, 127.0, 126.7, 125.9, 120.7, 120.2, 47.8, 45.5, 22.9. HRMS calcd. for $C_{19}H_{17}N_5O$ $[M+H]^+$ *m/z*: 332.1506; found *m/z*: 332.1502.

3-(2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9b). Yield – 409 mg (60%). Mp 145-146°C. IR (KBr) ν, cm^{-1}: 3774, 2965, 2862, 1671, 1594, 1387, 1344, 772, 701. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.29 (dd, 1H, ^2J = 8.0 Hz, ^3J = 1.2 Hz, C(6H), 7.78 (t, 1H, *J* = 8.0 Hz, C(8)H), 7.65 (d, 1H, *J* = 8.0 Hz, C(9)H), 7.52 (t, 1H, *J* = 7.0 Hz, C(7)H), 7.09 (s, 1H, C(13)H), 4.79 (t, 2H, *J* = 5.9 Hz, C(12)H_2), 4.57 (t, 2H, *J* = 5.9 Hz, C(11)H_2), 2.67 (t, 2H, *J* = 7.6 Hz, CH_2), 2.23 (s, 3H, CH_3), 1.58 (q, 2H, *J* = 7.6 Hz, CH_2), 1.31 (sextet, 2H, *J* = 7.6 Hz, CH_2), 0.90 (t, 3H, *J* = 7.6 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.6, 155.6, 146.5, 134.5, 126.6, 126.6, 126.0, 120.0, 47.4, 45.6, 31.5, 29.3, 22.6, 23.8, 14.1. Elemental analysis calcd. for $C_{17}H_{21}N_5O \cdot 0.35H_2O$: C 64.27, H 6.66, N 22.04; found: C 64.66, H 6.69, N 22.27.

2-Methyl-3-(2-(4-Pentyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (9c). Yield – 155 mg (35%). Mp 108-110°C. IR (KBr) ν, cm^{-1}: 3774, 3124, 3072, 2931, 2857, 1675, 1595, 1388, 1333, 1249, 1146, 773, 702. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.28 (d, 1H, *J* = 7.7 Hz, C(6)H), 7.78 (t, 1H, *J* = 7.7 Hz, C(8)H), 7.68 (d, 1H, *J* = 7.7 Hz, C(9)H), 7.51 (t, 1H, *J* = 7.7 Hz, C(7)H), 7.14 (s, 1H, C(13)H), 4.79 (t, 2H, *J* = 6.0 Hz, C(12)H_2), 4.58(t, 2H, *J* = 6.0 Hz, C(11)H_2), 2.56-2.77 (m, 2H, CH_2), 2.25 (s, 3H, CH_3), 1.70-1.49 (m, 2H, CH_2), 1.41-1.17 (m, 4H, 2 × CH_2), 0.87 (t, 3H, *J* = 6.2 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.1, 154.7, 146,7, 135.0, 127.1, 126.8, 126.7, 121.3, 120.0, 47.5, 45.6, 31.4, 29.2, 25.5, 22.7, 22.5, 14.0. Elemental analysis calcd. for $C_{18}H_{23}N_5O \cdot 0.3H_2O$: C 65.35, H 7.01, N 21.17; found: C 65.72, H 7.01, N 21.18.

3-(2-(4-Hexyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9d). Yield – 450 mg (61%). Mp 111-113 C. IR (KBr) ν, cm^{-1}: 3774, 2856, 1673, 1594, 1343, 1221, 1141, 772. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.28 (d, 1H, *J* = 8.1 Hz, C(6)H), 7.78 (t, 1H, *J* = 8.1 Hz, C(8)H), 7.64 (d, 1H, *J* = 8.1 Hz, C(9)H), 7.51 (t, 1H, *J* = 8.1 Hz, C(7)H), 7.09 (s, 1H, C(13)H), 4.79 (t, 2H, *J* = 5.8 Hz, C(12)H_2), 4.56 (t, 2H, *J* = 5.8 Hz, C(11)H_2), 2.66 (t, 2H, *J* = 7.5 Hz, CH_2), 2.22 (s, 3H, CH_3), 1.68-1.50 (m, 2H, CH_2), 1.37-1.18 (m, 6H, 3 × CH_2), 0.88 (t, 3H, *J* = 5.9 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.2, 154.2, 146.6, 135.0, 127.1, 126.9, 126.8, 120.1, 47.5, 45.6, 31.6, 29.5, 28.9, 25.6, 22.7 (2C), 14.2. Elemental analysis calcd. for $C_{19}H_{25}N_5O \cdot 0.25H_2O$: C 66.35, H 7.33, N 20.36; found: C 66.75, H 7.46, N 20.16.

3-(2-(4-(2-Hydroxyethyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9e). Yield - 19 mg (15%). Mp 159-162 C. IR (KBr) ν, cm^{-1}: 3694, 2715, 1673, 1593, 1386, 1219, 1056, 776, 702. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.23 (d, 1H, *J* = 7.8 Hz, C(6)H), 7.75 (t, 1H, *J* = 7.2 Hz, C(8)H), 7.62 (d, 1H, *J* = 7.8 Hz, C(9)H), 7.48 (t, 1H, *J* = 7.2 Hz, C(7)H), 7.33 (broad s., 1H, C(13)H), 4.84-4.72 (m, 2H, C(12)H_2), 4.55 (t, 2H, *J* = 7.5 Hz, C(11)H_2), 3.90 (broad s., 1H, OH), 2.97-2.47 (m, 4H, 2 × CH_2), 2.23 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.1, 154.1, 146.9, 135.1, 131.4, 127.2, 126.8 (2C), 123.0, 120.0, 61.8, 48.0, 45.7, 28.8, 23.1. HRMS calcd. for $C_{15}H_{17}N_5O_2$ $[M+H]^+$ *m/z* 300.1455; found *m/z*: 300.1465.

3-(2-(4-(3-Hydroxypropyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9f). Yield – 304 mg (45%). Mp 155-158°C. IR (KBr) ν, cm^{-1}: 3774, 3294, 2949, 2866, 1673, 1593, 1342, 1252, 1057, 783. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.28 (d, 1H, *J* = 8.0 Hz, C(6)H), 7.79 (t, 1H, *J* = 7.8 Hz, C(8)H), 7.69 (d, 1H, *J* = 8.0 Hz, C(9)H), 7.53 (t, 1H, *J* = 7.8 Hz, C(7)H), 7.15 (s, 1H, C(13)H), 4.81 (t, 2H, *J* = 5.7 Hz, C(12)H_2), 4.58 (t, 2H, *J* = 5.7 Hz, C(11)H_2), 3.65 (t, 2H, *J* = 6.0 Hz, CH_2), 2.78 (t, 2H, *J* = 7.1 Hz, CH_2), 2.64-2.45 (m, 1H, OH), 2.26 (s, 3H, CH_3), 1.96-1.80 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 161.9, 154.5, 146.5, 135.2, 127.3, 126.8, 126.6, 120.0, 61.7, 47.5, 45.5, 31.9, 22.5, 22.0. HRMS calcd. for $C_{16}H_{19}N_5O_2$ $[M+H]^+$ *m/z*: 314.1612; found *m/z*: 314.1590.

3-(2-(4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9g). Yield – 547 mg (85%). Mp 192-195°C. IR (KBr) ν, cm^{-1}: 3774, 3091, 1669, 1595, 1221, 1167, 1029, 777. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.27 (d, 1H, *J* = 7.8 Hz, C(6)H), 7.78 (t, 1H, *J* = 7.2 Hz, C(8)H), 7.65 (d, 1H, *J* = 7.8 Hz, C(9)H), 7.50 (t, 1H, *J* = 7.2 Hz, C(7)H), 7.12 (broad s., 1H, C(13)H), 4.76 (t, 2H, *J* = 5.6 Hz, C(12)H_2), 4.55 (t, 2H, *J* = 5.6 Hz, C(11)H_2), 2.24 (s, 3H, CH_3), 1.90 (s, 1H, $C^{c\text{-}Pr}$H), 1.22-0.88 (m, 2H, $C^{c\text{-}Pr}H_2$), 0.80-0.68 (m, 2H, $C^{c\text{-}Pr}H_2$). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.1, 154.4, 146.7, 146.4, 135.0, 127.2, 126.8, 126.7, 120.0, 47.6, 45.5, 22.6, 7.9 (2C), 6.7. HRMS calcd. $C_{16}H_{17}N_5O$ $[M+H]^+$ *m/z*: 296.1506; found 296.1515.

3-(2-(4-(3-Chlorophenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9l). Yield – 69 mg (43%). Mp 180-182°C. IS (KBr) ν, cm^{-1}: 3774, 3135, 1675, 1598, 1387, 1234, 1084, 789, 767. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.28 (d, 1H, *J* = 7.2 Hz, C(6)H), 7.82-7.73 (m, 2H, C(8,9)H), 7.70-7.59 (m, 3H, C(13)H, 2 × C^{Ar}H), 7.51 (t, 1H, *J* = 7.5 Hz, C(7)H), 7.39-7.25 (m, 2H, 2 × C^{Ar}H), 4.87 (t, 2H, *J* = 6.1 Hz, C(12)H_2), 4.63 (t, 2H, *J* = 6.1 Hz, C(11)H_2), 2.33 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.4, 159.9, 153.6, 147.4, 147.1, 135.0, 131.9,

130.3, 128.6, 127.1, 126.7, 125.9, 123.9, 121.1, 120.2, 47.9, 45.4, 23.0. Elemental analysis calcd. for $C_{19}H_{16}ClN_5O$: C 62.38, H 4.41, N 19.14; found: C 62.23, H 4.41, N 19.19.

3-(2-(4-(2-Fluorophenyl)-1*H*-1,2,3-triazol-1-yl)ethyl)-2-methylquinazolin-4(3*H*)-one (9m). Yield - 179 mg (39%). Mp 175-176 C. IR (KBr) ν, cm^{-1}: 3167, 2885, 1673, 1596, 1386, 1342, 1232, 1218, 1052, 818, 772, 702. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.36 (d, 1H, *J* = 8.0 Hz, C (6)H), 7.93-7.10 (m, 8H, C(7,8,9,13)H, 4 × C^{Ar}H), 4.95-4.80 (m, 2H, C(12)H_2), 4.71-4.55 (m, 2H, C(11)H_2), 2.31 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz), δ, ppm: 162.3, 160.5, 153.6, 147.2, 141.6, 134.7, 129.6, 127.8, 126.9, 126.8, 126.5, 124.6, 123.7, 120.1, 115.8, 47.7, 45.2, 22.8. HRMS calcd. for $C_{19}H_{16}FN_5O$ $[M+H]^+$ *m/z*: 350.1412; found *m/z*: 350.1410.

2-Styryl quinazolin-4(3*H*)-ones **11**. (General procedure).
A mixture of 2-methyl quinazolin-4(3*H*)-one **9** (1 equiv.) and aromatic aldehyde **10** (2 equiv.) was refluxed in 10% Ac_2O/AcOH (0.3 mmol of comp. **6**/1 mL AcOH) for 5-12 h (TLC control). Then the reaction mixture was cooled to room temperature and poured into cold water. The resulting precipitate was centrifuged, washed with water, dried and recrystallized from a mixture of DCM and hexanes (1:2).

(*E*)-3-(2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (11aa). Light yellow crystals. Yield - 84.7 mg (55%). MP 160-163°C. IR (KBr) ν, cm^{-1}: 2696, 1676, 1583, 1342, 1126, 971, 773. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.22 (d, 1H, *J* = 8.1 Hz, C(6)H), 7.73-7.50 (m, 7H, C(8,9,13,14,15)H, 2 × C^{Ph}H), 7.42 (t, 1H, *J* = 8.1 Hz, C(7)H), 7.28-7.19 (m, 3H, 3 × C^{Ph}H), 6.70 (s, 2H, C(17,21)H), 4.82 (m, 2H, C(12)H_2), 4.72 (m, 2H, C(11)H_2), 3.90 (s, 6H, 2 × OCH_3), 3.82 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 153.3, 148.4 (2C), 139.8 (2C), 134.9, 130.0, 128.7, 128.3 (4C), 126.8 (2C), 125.7, 121.0, 105.3, 60.9, 56.4 (2C), 48.6, 45.0. HRMS calcd. for $C_{29}H_{27}N_5O_4$ $[M+H]^+$ *m/z*: 510.2136; found *m/z*: 510.2154.

(*E*)-2-(4-Methoxystyryl)-3-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (11af). Light yellow crystals. Yield – 53 mg (39%). Mp 239-241°C. IR (KBr) ν, cm^{-1}: 2884, 1659, 1536, 1257, 1147, 975, 768, 695. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.11 (d, 1H, *J* = 8.0 Hz, C(6)H), 7.80 (t, 1H, *J* = 7.8 Hz, C(8)H), 7.68-7.60 (m, 4H, C(7,9,13,15)H), 7.59-7.25 (m, 7H, C(17,21)H, 5 × C^{Ph}H), 6.83 (s, 2H, C(18,20)H), 6.60 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.85-4.71 (m, 4H, C (11,12)H_2), 3.77 (s, 3H, OCH_3). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 163.2, 153.4, 152.7, 146.9, 140.7, 134.9, 131.0, 130.1, 129.2 (2C), 128.3, 127.5 (2C), 126.7 (2C), 125.6, 122.7, 120.1, 116.3, 114.6, 55.7, 48.5, 43.9. HRMS calcd. for $C_{27}H_{23}N_5O_2$ $[M+H]^+$ *m/z*: 450.1952; found *m/z*: 450.1925.

(*E*)-3-(2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (11ba). Light yellow crystals. Yield - 68.6 mg (44%). Mp 131-134°C. IR (KBr) ν, cm^{-1}: 2928, 1659, 1583, 1311, 1126, 930, 774. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.15 (d, 1H, *J* = 8.0 Hz, C(6)H), 7.97-7.77 (m, 2H, C(8,15)H), 7.70-7.67 (m, 2H, C(9,13)H), 7.51 (t, 1H, *J* = 7.6 Hz, C(7)H), 6.99 (s, 2H, C(17,21)H), 6.57 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.77-4.70 (m, 4H, C(11,12)H_2), 3.91 (s, 6H, 2 × OCH_3), 3.71 (s, 3H, OCH_3), 2.32 (t, 2H, *J* = 7.6 Hz, CH_2), 1.35-1.23 (m, 2H, CH_2), 1.12 (sextet, 2H, *J* = 7.3 Hz, CH_2), 0.72 (t, 3H, *J* = 7.2 Hz, CH_3). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 161.5, 152.9, 152.1, 147.2, 140.5, 140.0, 134.5, 130.7, 126.9 (3C), 126.3, 122.8, 119.8, 117.4, 105.6, 60.0, 56.1 (2C), 47.7, 43.6, 30.8, 24.5, 21.5, 13.5. HRMS calcd. for $C_{27}H_{31}N_5O_4$ $[M+H]^+$ *m/z*: 490.2449; found *m/z*: 490.2450.

(*E*)-3-(2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(2,5-dimethoxystyryl)quinazolin-4(3*H*)-one (11bb). Bright yellow crystals. Yield – 60 mg (41%). Mp 114-117°C. IR (KBr) ν, cm^{-1}: 2927, 1667, 1579, 1378, 1221, 1066, 970, 767. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.26 (dd, 1H, ^{2}*J* = 7.7 Hz, ^{3}*J* = 1.3 Hz, C(9)H), 8.12 (d, 1H, *J* = 15.2 Hz, C(15)H), 7.88-7.73 (m, 2H, C(7,8)H), 7.48 (t, 1H, *J* = 7.4 Hz, C(6)H), 7.20 (s, 1H, C(21)H), 7.09 (s, 1H, C(13)H), 7.01-6.89 (m, 2H, C(17,19)H), 6.82 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.79 (m, 2H, C(12)H), 4.72 (m, 2H, C(11)H), 3.91 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 2.57 (t, 2H, *J* = 7.7 Hz, CH_2), 1.49 (quintet, 2H, *J* = 7.7 Hz, CH_2), 1.27 (sextet, 2H, *J* = 7.4 Hz, CH_2), 0.83 (t, 3H, *J* = 7.4 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz), δ, ppm: 153.6, 153.1, 149.0, 134.8, 126.8, 126.7, 124.1, 121.7, 119.7, 117.7, 113.3, 112.3, 56.1 (2C), 47.8, 44.7, 31.3, 25.2, 22.2, 13.7. HRMS calcd. for $C_{26}H_{29}N_5O_3$ $[M+H]^+$ *m/z*: 460.2343; found *m/z* 460.2327.

(*E*)-3-(2-(4-Butyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(2,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (11bc). Dark yellow crystals. Yield - 76.1 mg (49%). Mp 118-121 C. IR (KBr) ν, cm^{-1}: 2962, 1665, 1541, 1286, 1213, 844, 763. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.12 (d, 1H, *J* = 7.9 Hz, C(6)H), 8.00 (d, 1H, *J* = 15.2 Hz, C(15)H), 7.88-7.76 (m, 2H, C(8,13)H), 7.66 (d, 1H, *J* = 7.9 Hz, C(9)H), 7.48 (t, 1H, *J* = 7.5 Hz, C(7)H), 7.23 (s, 1H, C(21)H), 6.73 (s, 1H, C(18)H), 6.53 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.81-4.66 (m, 4H, C(11,12)H_2), 3.94-3.84 (m, 9H, 3 × OCH_3), 2.35 (t, 2H, *J* = 7.5 Hz, CH_2), 1.29 (quintet, 2H, *J* = 7.5 Hz, CH_2), 1.13 (sextet, 2H, *J* = 7.5 Hz, CH_2), 0.73 (t, 3H, *J* = 7.3 Hz, CH_3). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 161.4, 153.1, 152.6, 151.9, 147.3, 147.1, 143.0, 134.8, 134.5, 126.9, 126.2, 125.9, 122.8, 119.6, 115.1, 114.8, 110.8, 97.5, 56.4, 56.3, 55.8, 47.6, 43.5, 30.8, 24.5, 21.6, 13.6. HRMS calcd. for $C_{27}H_{31}N_5O_4$ $[M+H]^+$ *m/z*: 490.2449; found *m/z*: 490.2443.

(*E*)-2-(4-Bromostyryl)-3-(2-(4-butyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (11bd). Light yellow crystals. Yield - 82.8 mg (54%). Mp 161-164°C. IR (KBr) ν, cm^{-1}: 3059, 1663, 1545, 1257, 1138, 813, 772. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.15 (d, 1H, *J* = 7.9 Hz, C(6)H), 7.88-7.79 (m, 2H, C(8,15)H), 7.71-7.57 (m, 6H, C(9,13,17,18,20,21)H), 7.51 (m, 1H, C(7)H), 6.84 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.79-4.65 (m, 4H, C(11,12)H_2), 2.29 (t, 2H, *J* = 7.4 Hz, CH_2), 1.25 (quintet, 2H, *J* = 7.4 Hz, CH_2), 1.12 (sextet, 2H, *J* = 7.4 Hz, CH_2), 0.74 (t, 3H, *J* = 7.4 Hz, CH_3). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 161.2, 151.8, 150.0, 138.7, 134.6, 131.6 (2C), 130.0, 127.0, 126.5, 126.3, 122.9, 119.8, 119.3, 47.6, 43.3, 30.7, 24.5, 21.5, 13.5. HRMS calcd. for $C_{24}H_{24}BrN_5O$ $[M+H]^+$ *m/z*: 478.1237; found *m/z*: 478.1223.

(*E*)-3-(2-(4-Hexyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(3,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (11da). Light yellow crystals. Yield - 58.7 mg (39%). Mp 123-125°C. IR (KBr) ν, cm^{-1}: 2883, 1658, 1532, 1126, 814, 774. ^{1}H NMR ($CDCl_3$, 300 MHz) δ, ppm: 8.29 (d, 1H, *J* = 8.2 Hz, C(6)H), 7.81-7.73 (m, 2H, C(8,15)H), 7.70 (d, 1H, *J* = 8.2 Hz, C(9)H), 7.47 (t, 1H, *J* = 7.5 Hz, C(7)H), 7.11 (s, 1H, C(13)H), 6.79 (s, 2H, C(17,21)H), 6.16 (d, 1H, *J* = 15.0 Hz, C(14)H), 4.83 (t, 2H, *J* =5.8 Hz, C(12)H_2), 4.67 (t, 2H, *J* =5.8 Hz, C(11)H_2), 4.01 (s, 6H, 2 × OCH_3), 3.90 (s, 3H, OCH_3), 2.57 (t, 2H, *J* =7.6 Hz, CH_2), 1.48 (quintet, 2H, *J* =7.6 Hz, CH_2), 1.28-1.10 (m, 6H, 3 × CH_2), 0.8172 (t, 3H, *J* = 7.6 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ, ppm: 162.5, 153.4, 149.2, 147.6, 142.3, 139.8, 134.7, 130.6, 127.4, 126.7, 126.6, 122.2, 120.0, 116.4, 105.2, 60.9, 56.4 (2C), 48.3, 45.1, 31.5, 29.3, 28.7, 25.5, 22.4, 14.0. HRMS calcd. for $C_{29}H_{35}N_5O_4$ $[M+H]^+$ *m/z*: 518.2762; found *m/z*: 518.2763.

(*E*)-2-(3-Fluorostyryl)-3-(2-(4-hexyl-1*H*-1,2,3-triazol-1-yl)ethyl)quinazolin-4(3*H*)-one (11de). Light yellow crystals. Yield - 64.5 mg (49%). Mp 178-181°C. IR (KBr) ν, cm^{-1}: 2857, 1664, 1547, 1379, 1158, 971, 779, 697. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.14 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz, C(6)H), 7.92-7.79 (m, 2H, C(8,15)H), 7.70-7.57 (m, 3H, C(9,13,17)H), 7.56-7.42 (m, 3H, C(19,20,21)H), 7.23 (m, 1H, C(7)H), 6.81 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.76-4.69 (m, 4H, C(11,12)H_2), 2.30 (t, 2H, *J* = 7.4 Hz, CH_2), 1.36-1.04 (m, 8H, 4 × CH_2), 0.81 (t, 3H, *J* = 7.4 Hz, CH_3). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 161.2, 160.8, 151.6, 146.9, 138.6, 137.6, 134.6, 130.7, 130.6, 127.0, 126.5, 126.3, 124.8, 124.7, 120.0, 116.1, 113.9, 113.7, 47.6, 43.4, 30.9, 28.5, 28.1, 24.8, 21.9, 13.9. Elemental analysis calcd. for $C_{26}H_{28}FN_5O \cdot H_2O$: C 67.37, H 6.09, N 15.11; found: C 67.34, H 5.94, N 14.94.

(*E*)-3-(2-(4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(2,4,5-trimethoxystyryl)quinazolin-4(3*H*)-one (11gc). Dark yellow crystals. Yield - 102.5 mg (64%). Mp 178-180°C. IR (KBr) ν, cm^{-1}: 2861, 1668, 1541, 1350, 1284, 1217, 1035, 978, 763, 702. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 8.10 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz, C(6)H), 8.00 (d, 1H, *J* = 15.2 Hz, C(15)H), 7.88-7.74 (m, 2H, C(8,13)H, 7.63 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz, C(9)H), 7.45 (t, 1H, *J* = 7.1 Hz, C(7)H), 7.19 (s, 1H, C(21)H), 6.71 (s, 1H, C(20)H), 6.45 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.73-4.60 (m, 4H, C(11,12)H_2), 3.86 (s, 9H, 3 × OCH_3), 1.69 (tt, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz, $C^{c\text{-}Pr}H$), 0.72-0.58 (m, 2H, $C^{c\text{-}Pr}H_2$), 0.50-0.39 (m, 2H, $C^{c\text{-}Pr}H_2$). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 161.9, 153.6, 153.0, 149.5, 143.4, 135.3, 135.0, 127.4, 126.7, 126.4, 122.4, 120.0, 115.3 (2C), 111.2, 98.0, 56.8, 56.7, 56.2, 48.1, 44.0, 7.7, 6.7. HRMS calcd. for $C_{26}H_{27}N_5O_4$ $[M+H]^+$ *m/z*: 474.2136; found *m/z*: 474.2138.

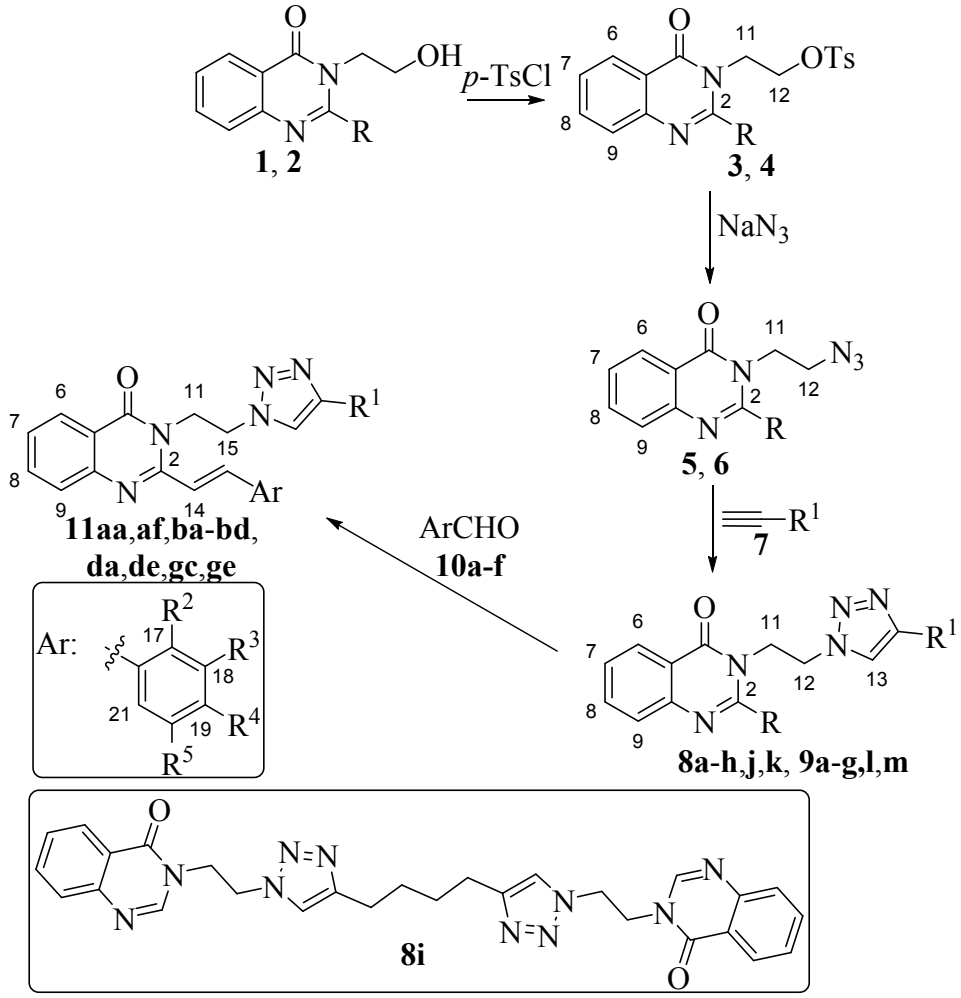
(*E*)-3-(2-(4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)ethyl)-2-(3-fluorostyryl)quinazolin-4(3*H*)-one (11ge). Yellow crystals. Yield - 41.8 mg (31%). Mp 245-247 C. IR (KBr) ν, cm^{-1}: 2873, 1672, 1550, 1381, 1245, 966, 772, 699. ^{1}H NMR (DMSO-d_6, 300 MHz) δ, ppm: 7.73 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz, C(6)H), 7.48-7.34 (m, 2H, C(8,15)H), 7.30-7.01 (m, 6H, C(9,13,17,19,20,21)H, 6.83 (t, 1H, *J* = 7.2 Hz, C(7)H), 6.36 (d, 1H, *J* = 15.2 Hz, C(14)H), 4.34-4.24 (m, 4H, C(11,12)H_2), 1.27 (tt, 1H, *J* = 8.6 Hz, *J* = 5.0 Hz, $C^{c\text{-}Pr}H$), 0.31-0.21 (m, 2H, $C^{c\text{-}Pr}H_2$), 0.15-0.10 (m, 2H, $C^{c\text{-}Pr}H_2$). ^{13}C NMR (DMSO-d_6, 75 MHz) δ, ppm: 161.7, 154.2, 147.4, 143.1, 135.1, 131.2, 127.6, 127.0, 126.8, 125.3, 122.2, 120.5, 120.3, 114.5, 52.2, 48.2, 43.9, 7.8, 6.7. HRMS calcd. for $C_{23}H_{20}FN_5O$ $[M+H]^+$ *m/z*: 402.1725; found *m/z*: 402.1713.

Antiradical and antibacterial activity was determined according to the test methods described previously [[4]].

RESULTS AND DISCUSSION

Previously, we have studied synthesis, antiradical and antibacterial activity of quinazolinone-oxadiazole conjugates [[4]]. Herein we are continuing our studies devoted to quinazolinones with heterocyclic substituent in the side chain. This work is devoted to the synthesis and properties of quinazolinone-1,2,3-triazole conjugates with a focus to their antiradical and antibacterial activities. According to the introduction section, compounds with incorporated quinazolinone and 1,2,3-triazole moieties should demonstrate new or modified biological activity. Nevertheless such hybrid compounds till now are not well explored in the scientific literature. Quinazolinones with 1,2,3-triazole scaffold in side chain at N-3 are synthesized from alkynyl quinazolinone and various azides through Cu(I) catalyzed "click" reaction [[15], [16]]. Some quinazolinone-1,2,3-triazole conjugates are obtained from quinazolinones with azide group in the side chain at C-2 and dimethyl acetylenedicarboxylate [[17]].

In order to synthesize hybrid compounds of quinazolinones and 1,2,3-triazoles we provide the following scheme:



Compounds **1**, **3**, **5** and **8**: R = H.

Compounds **2**, **4**, **6** and **9**: R = Me.

Compounds **7**, **8** and **9**: **a** R^1 = phenyl; **b** R^1 = butyl; **c** R^1= pentyl; **d** R^1 = hexyl;

e R^1 = 2-hydroxyetyl; **f** R^1 = 3-hydroxypropyl; **g** R^1 = cyclopropyl.

Compounds **7** and **8**: **h** R^1 = 1-hydroxycyclohexyl; **i** R^1 = hex-5-yn-1-yl;

j R^1 = hydroxymethyl; **k** R^1 = 2-hydroxy-propan-2-yl.

Compounds **7** and **9 11**: **l** R^1 = 3-chlorophenyl; **m** R^1 = 2-fluorophenyl.

Compounds **10**: **a** R^2 = H, R^3 = R^4 = R^5 = OMe; **b** R^2 = R^5 = OMe, R^3 = R^4 = H;

c R^2 = R^4 = R^5 = OMe, R^3 = H; **d** R^2 = R^3 = R^5 = H, R^4 = Br;

e R^2 = R^4 = R^5 = H, R^3 = F; **f** R^2 = R^3 = R^5 = H, R^4 = OMe .

Abbreviations of compounds **11**:

the first letter represents analoguos substituents R^1 in compound **9**,

the second letter - analoguos substituents R^2-R^5 in aldehyde **10**.

Starting compounds **1** and **2** were converted to the corresponding tosylates **3** and **4** in the reaction with *p*-toluenesulfonyl chloride. Further the tosyl group was substituted with azido group. The obtained 3-(2-azidoethyl)quinazolin-4(3*H*)-ones **5** and **6** were treated with acetylenes **7** *via* Cu (I) catalyzed alkyne 1,3-cycloaddition. Both CuI and $CuSO_4 \cdot H_2O$/sodium ascorbate as the reductant were used as the source of Cu(I). The yield of resulting triazoles was similar in both cases and varied from medium to high. Compounds **9** were converted to styryl compounds **11** in the Knoevenagel reaction with various aromatic aldehydes **10**. Various reaction conditions were tried for this conversion. For example, heating (130 °C) under basic conditions (Py:DMF, 2:1 [[25]]) was

unsuccessful – even after 16 h the conversion was negligible, but the increase of the reaction temperature to 180 °C resulted in the formation of a mixture of products. Better results were obtained when Knoevenagel reaction was carried out in acetic acid. The yields of the products were even higher when the process was carried out in the mixture Ac_2O:AcOH (1:10).

It was observed that the styryl derivatives were light sensitive and their *cis*-/*trans*- isomerisation occurred. For example, a freshly obtained compound **11bc** revealed the *E*/*Z* ratio 9:1 (^{1}H NMR), but after 24 h on the bench at ambient temperature the *E*/*Z* ratio was already 4:6 (^{1}H NMR). Such light-induced isomerisation is observed also with other compounds containing styryl moiety [[26], [27]], but to the best our knowledge, in the series of quinazolinones it is reported for the first time.

Synthesized compounds **8**, **9** and **11** were tested for their antiradical and antibacterial activity. The reaction of compounds **8a**, **9g** and **11ab**,**bb**-**be**,**gc** and 1,1-diphenyl-2-picrylhidrazyl (DPPH) was carried out in ethanol solution at room temperature for 30 min. Unfortunately, the tested compounds did not demonstrate any considerable antiradical activity (inhibition of DPPH varied in the range of 0-3%). Thus, the antiradical activity of other compounds **8**, **9** or **11** was not determined. The compounds **8a-h**,**j**,**k**, **9a-g**,**l**,**m** or **11aa**,**af**,**ba-bd**,**da**,**de**,**gc**,**ge** did not inhibited also the growth of selected Gram negative (*Escherichia coli* and *Pseudomonas aeruginosa*) and Gram positive (Staphylococcus aureus, *Staphylococcus epidermidis* and *Lactobacillus reuteri*) bacteria, although various quinazolin-4-one derivatives containing styryl functionality demonstrate antibacterial activity [[28], [29]].

CONCLUSION

In summary a convenient, user-friendly synthesis of novel type of 2-styryl quinazolinone-1,2,3-triazole conjugates is presented. An unusual light-induced izomerization of double bound is observed in the series of 2-styrylquinazolione derivatives. This work is a valuable addition to the structure-activity relationship studies, revealing that activity is lost, when three structural moieties with potential antibacterial activity are introduced into one structure.

REFERENCES

[1] R Subramaniam; G Rao; S Pai; GK Virya, GS Sodhi, *J. Chem. Pharm. Res*., **2010**, 2, 462-468.
[2] S Rajasekaran; G Rao; PN Sanjay Pai; GS Sodhi, *J. Chem. Pharm. Res*., **2010**, 2, 482-488.
[3] AA El-Sawy; SK Mohamed; AE-MMF Eissa; AH Tantawy; YA Issac, *J. Chem. Pharm. Res*., **2012**, 4, 2755-2762.
[4] D Zicane; Z Tetere; I Mierina; M Turks; I Ravina; A Leonciks, *J. Chem. Pharm. Res.*, **2014**, 6(4), 1153-1158.
[5] H Kikuchi; S Horoiwa; R Kasahara; N Hariguchi; M Matsumoto; Y Oshima, *Eur. J. Med. Chem*., **2014**, 76, 10-19.
[6] NP McLaughlin; P Evans; M Pines, *Bioorg. Med. Chem*., **2014**, 22(7), 1993-2004.
[7] C Kelly; N Bhuva; M Harrison; A Buckley; M Saunders, *Eur. J. Cancer*, **2013**, 49(10), 2303-2310.
[8] T Ochiai; R Ishida, *Jpn. J. Pharmacol.*, **1982**, 32(3), 427-438.
[9] Y Tokura, *Expert Rev. Dermatol*., **2009**, 4(3), 263-270.
[10] SG Agalave; SR Maujan; VS Pore, *Chem. Asian J*., **2011**, 6, 2696-2718.
[11] S Haider; MS Alam; H Hamid, *Inflammation & Cell signaling*, **2014**, 1, e95.
[12] J Sharma; S Ahmad; M Shamsher Alam, *J. Chem. Pharm. Res*., **2012**, 4, 5157-5164.
[13] Nithinchandra; BalakrishnaKalluraya; ShobhithaShelty; M. Babu, *J. Chem. Pharm. Res.*, **2013**, 5, 307-313.
[14] C Girmenia; E Finolezzi, *Clin. Invest*., **2011**, 1(11), 1577-1594.
[15] R. Karuturi; RA Al-Horani; SC Mehta; D Gailani; UR Desai, *J. Med. Chem*., **2013**, 56(6), 2415-2428.
[16] PM Chandrika; T Yakaiah; G Gayatri; KP Kumar; B Narsaiah; USN Murthy; AR Ram Rao, *Eur. J. Med. Chem.*, **2010**, 45, 78-84.
[17] A Komaraiah; K Ramakrishna; B Sailu; PSN Reddy, *Arkivoc*, **2007**, (xiv), 110-116.
[18] P Punthasee; A Vanitcha; S Wacharasindhu, T*etrahedron Lett.*, **2010**, 51(13), 1713-1716.
[19] TRV Feire; RE Mannochio de Souza, Int. Pat. Appl. 2012037634, Mar 29, **2012**.
[20] MI Bogert; HA Soil, *J. Am. Chem. Soc*., **1907**, 29, 517-536.
[21] MT Hassan Khan; R Khan; Y Wuxiuer; M Arfan; M Ahmed; I Sylte, *Bioorg. Med. Chem.*, **2010**, 18, 4317-4327.
[22] J Jampilek; R Musiol; J Finster; M Pesko; J Carroll; K Kralova; M Vejsova; J O'Mahony; A Coffey; J Dohnal; J Polanski, *Molecules*, **2009**, 14, 4246-4265.
[23] CE Jamookeeah; CD Beadle; RFW Jackson; JPA Harrity, *J. Org. Chem.*, **2008**, 73, 1128-1130.
[24] BK Baker; MV Querry; AF Kadish; JH Williams, *J. Org. Chem*., **1952**, 17, 35-51.
[25] CL Jagani; NA Sojitra; SF Vanparia; TS Patel; RB Dixit; BC Dixit, *J. Saudi Chem. Soc.*, **2012**, 16, 363-369.
[26] LB Feringa, *J. Org. Chem.*, **2007**, 18, 6635-6652.
[27] Y Imanishi; ML Batten; DW Piston; W Baehr; K Palczewski, *Cell Biol.*, **2004**, 164, 373-383.
[28] C Sowjanya; V RamaBharathi; G Kalpana Devi; G Rajitha, *J. Chem. Pharm. Res*., **2011**, 3, 212-216.

[29] RP Modh; AC Patel; DH Mahajan; C Pannecouque; E De Clercq; KH Chikhalia, *Arch. Pharm*., **2012**, 345, 964-972.