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Substituted 2-(2-Arylethenyl)quinazolines. Synthesis and Structure

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Abstract—The reaction of 2-methyl-4*H*-3,1-benzoxazin-4-one and its 6-iodo derivatives with a number of amines in polyphosphoric acid afforded 3- and 3,6-substituted 2-methylquinazolin-4(3*H*)-ones. The latter reacted with aromatic and heterocyclic aldehydes under solvent-free conditions to give 2-[(*E*)-2-arylethenyl]-quinazolin-4(3*H*)-ones. The structure of the synthesized compounds was confirmed by two-dimensional ^{1}H–^{1}H NOESY data and X-ray analysis.

Keywords: 2-methyl-4*H*-3,1-benzoxazin-4-one, pharmacophoric amines, 3- and 6-substituted (unsubstituted) 2-methylquinazolin-4(3*H*)-ones, aryl(hetaryl)carbaldehydes, 2-[(*E*)-2-arylethenyl]quinazolin-4(3*H*)-ones.

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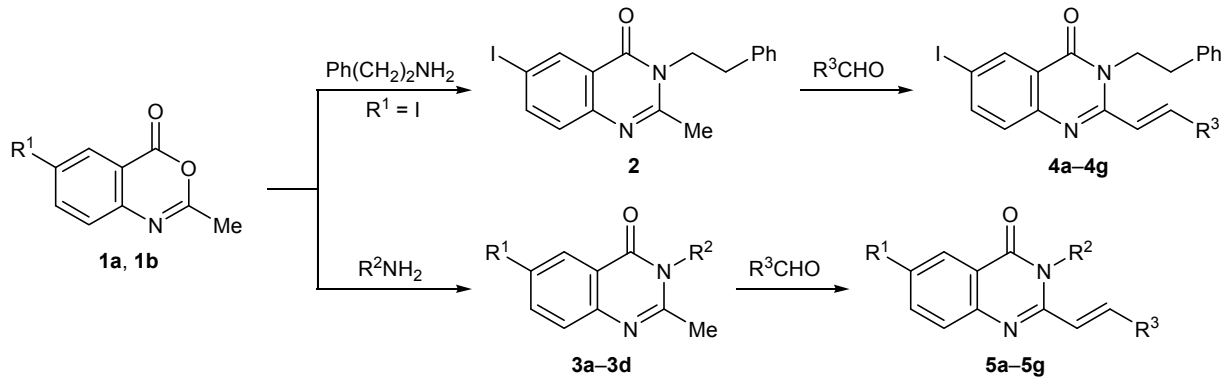
Taking into account high biological activity of quinazoline derivatives [1], the goal of the present work was to synthesize a series of new quinazolines containing substituents in both aromatic and dihydropyrimidine fragments. Initial compounds were synthesized by a classical method for the construction of quinazoline ring system, which is based on the reaction of 2-methyl-4*H*-3,1-benzoxazin-4-one derivatives with amines [2]. Broad synthetic potential of this method makes it possible to obtain large series of quinazolines by using 2-methyl-4*H*-3,1-benzoxazin-4-ones both substituted and unsubstituted in the aromatic ring, as well as various amines which give rise to a substituent group in the 3-position of the resulting quinazoline molecule. Furthermore, the methyl group on C^2 is activated due to effect of π-deficient pyrimidine ring and is capable of reacting with aromatic and heterocyclic aldehydes to produce 2-[(*E*)-2-arylvinyl]quinazolin-4(3*H*)-ones; this further extends the series of quinazoline derivatives necessary for applied studies [3].

We used as starting compounds both unsubstituted 2-methyl-4*H*-3,1-benzoxazin-4-one (**1a**) and its 6-iodo-substituted analog **1b** [3]. Introduction of a iodine atom into the 6-position of the quinazoline system seemed to be reasonable from the viewpoints of both potential biological activity of target compounds and possibility of further functionalization via transition metal-catalyzed cross-couplings. The set of amines determining the substituent in the 3-position was chosen with account taken of the recent concept of hybrid molecules, i.e., compounds with a combination of two and more pharmacoporic fragments in a single molecule. In particular, the amine series included 2-phenylethan-1-amine, *N*,*N*-dimethylbenzene-1,4-diamine, 3-methyl-1-phenyl-1*H*-pyrazol-5-amine, and 4-aminobenzenesulfonamide. These amines or their parent structures are structural units of biologically active compounds. In addition, it was interesting to couple 2-styrylquinazolines with compounds possessing pronounced antibacterial properties, such as 4-aminobenzenesulfonamide (sulfanilamide) and 5-nitrofurfural, with the goal of obtaining more active compounds with a broad spectrum of antibacterial effect [4, 5].

3-Alkyl(aryl)quinazolines **2** and **3a**–**3d** were synthesized in good yields by heating 2-methyl-4*H*-3,1-benzoxazin-4-ones **1a** and **1b** with the corresponding amines at 160–170°C under solvent-free conditions (Scheme 1). The reactions with 3-methyl-1-phenyl-1*H*-pyrazol-5-amine were carried out in polyphosphoric

Scheme 1.



1, R^1 = H (**a**), I (**b**); **3**, R^1 = H, R^2 = 4-$Me_2NC_6H_4$ (**a**), 4-$H_2NSO_2C_6H_4$ (**b**), 3-methyl-1-phenyl-1*H*-pyrazol-5-yl (**c**); R^1 = I, R^2 = 4-ClC_6H_4 (**d**); **4**, R^3 = Ph (**a**), 4-ClC_6H_4 (**b**), 2,4-$Cl_2C_6H_3$ (**c**), 4-$Me_2NC_6H_4$ (**d**), 4-$O_2NC_6H_4$ (**e**), 4-*i*-PrC_6H_4 (**f**), 1-methyl-1*H*-indol-3-yl (**g**); **5**, R^1 = H, R^2 = 4-$Me_2NC_6H_4$, R^3 = 4-ClC_6H_4 (**a**), 2,4-$Cl_2C_6H_3$ (**b**); R^2 = 3-methyl-1-phenyl-1*H*-pyrazol-5-yl, R^3 = 4-ClC_6H_4 (**c**), 2,4-$Cl_2C_6H_3$ (**d**); R^2 = 4-$H_2NSO_2C_6H_4$, R^3 = 3-$O_2NC_6H_4$ (**e**); R^1 = I, R^2 = 4-ClC_6H_4, R^3 = 5-nitrofuran-2-yl (**f**), PhCH=CH (**g**).

acid. Compounds **2** and **3a**–**3c** reacted with a number of aromatic and heterocyclic aldehydes on heating in the absence of a catalyst to afford 2-[2-aryl(hetaryl)-ethenyl] derivatives **4a**–**4g**, **5a**–**5e**, and **5g**. The condensation of quinazoline **3d** with 5-nitrofuran-2-carbaldehyde to obtain compound **5f** was carried out by heating the reactants in acetic anhydride at 100°C.

The structures of quinazolines **3c** and **4a** were studied by X-ray analysis (Figs. 1, 2). According to the X-ray diffraction data, the exocyclic double bond in molecule **4a** has *E* configuration (Fig. 2). All cyclic fragments in molecules **3c** and **4a** are planar (the maximum deviations of atoms from the corresponding mean-square planes do not exceed 0.02 Å). Three-dimensional crystal packings of **3c** and **4a** are determined mainly by van der Waals interactions.

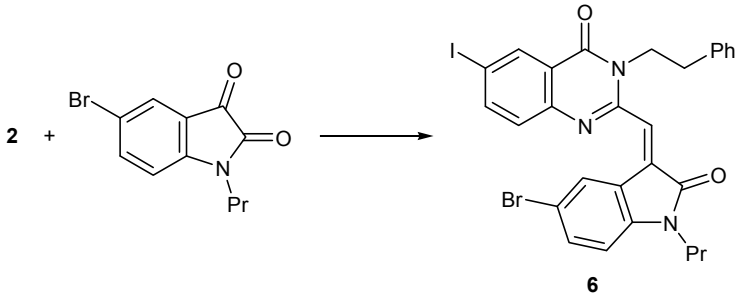
The condensation of 3-(2-phenylethyl)quinazoline **2** with 5-bromo-1-propylindole-2,3(1*H*)-dione gave only one of the possible isomeric products (compound **6**; Scheme 2) whose structure was proved by ^1H–^1H NOESY data. The exocyclic double bond in **6** was assigned *E* configuration taking into account the absence of NOE between the =CH proton and proton in the 4-position of the indole ring and the presence of NOE between the latter and 8-H of the quinazoline ring. The reverse pattern should be expected for alternative *Z* isomer.

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Avatar 330 spectrometer from samples dispersed in mineral oil. The ^1H and ^{13}C NMR spectra were measured on a Varian Mercury-300 VX spectrometer at 300.8 and 75.46 MHz, respectively, using DMSO-d_6–CCl_4 (1:3) as solvent and tetramethylsilane as internal standard. Analytical thin-layer chromatography was performed on Silufol UV-254 plates using acetone–hexane (1:3) as eluent; spots were visualized by treatment with iodine vapor.

The X-ray diffraction data for single crystals of **3c** and **4a** were obtained at room temperature on an Enraf–Nonius CAD-4 automated diffractometer (Mo K_α radiation, graphite monochromator, θ/2θ scan-

Scheme 2.



ning). The structures were solved by the direct method. The positions of hydrogen atoms in structure **3c** were determined from the difference Fourier maps and were refined independently. The hydrogen atoms in structure **4a** were placed in geometrically calculated positions which were refined according to the riding model with the following constraints: C–H bond length 0.93–0.97 Å, U_{iso}(H) =1.2 U_{eq}(C). A correction for absorption by the crystal of **4a** was applied by the psi-scan method. The structures were refined by the full-matrix least-squares method in anisotropic approximation for non-hydrogen atoms and isotropic approximation for hydrogen atoms. All calculations were performed using SHELXTL package [6]. The crystallographic data were deposited to the Cambridge Crystallographic Data Centre (Table 1).

Quinazolines 2 and 3a–3d (*general procedure*). A mixture of 0.01 mol of 2-methyl-4*H*-3,1-benzoxazin-4-one **1a** or **1b** and 0.01 mol of the corresponding amine was heated for 4 h at 160–170°C on a metal bath. When the reaction was complete, the product was cooled and dissolved on heating in 30 mL of ethanol. After cooling, the precipitate was filtered off and dried. In the synthesis of quinazoline **3c**, a mixture 0.01 mol of **1b** and 0.01 mol of 3-methyl-1-phenyl-1*H*-pyrazol-5-amine in 5 g of polyphosphoric acid was heated for 4 h at 160–170°C. After cooling, the mixture was neutralized with dilute aqueous ammonia (until weakly alkaline reaction), and the precipitate was filtered off, dried, and recrystallized from ethanol.

6-Iodo-2-methyl-3-(2-phenylethyl)quinazolin-4(3*H*)-one (2) was synthesized by reaction of 2-methyl-4*H*-3,1-benzoxazin-4-one (**1b**) with 2-phenylethanamine. Yield 48.3%, mp 122–123°C, R_f 0.5. IR spectrum, ν, sm^{-1}: 1655 (C=O), 1595 (C=C–C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.45 s (3H, CH_3), 2.94–3.00 m (2H, CH_2), 4.19–4.25 m (2H, NCH_2), 7.21–7.34 m (5H, C_6H_5), 7.37 d (1H, *J* = 8.6), 8.06 d.d (1H, *J* = 8.6, 2.1), and 8.39 d (1H, *J* = 2.1) (5-H, 7-H, 8-H). ^{13}C NMR spectrum, δ_C, ppm: 22.7 (CH_3), 33.3 (CH_2), 45.7 (CH_2), 90.8, 121.7, 128.5 (2C, CH), 128.7 (3C, CH), 134.3, 138.1, 142.5, 146.3, 155.7, 159.7. Found, %: C 52.23; H 3.74; N 7.12. $C_{17}H_{15}IN_2O$. Calculated, %: C 52.33; H 3.87; N 7.18.

3-(4-Dimethylaminophenyl)-2-methylquinazolin-4(3*H*)-one (3a). Yield 60.5%, mp 228–230°C, R_f 0.47. IR spectrum, ν, cm^{-1}: 1683 (C= O), 1610 (C=C-C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.15 s (3H, CH_3), 2.97 s (6H, NMe_2), 6.79–6.84 m (2H, $C_6\mathbf{H}_4NMe_2$), 7.14–7.19 m (2H, $C_6\mathbf{H}_4NMe_2$); 7.49 d.d.d (1H, *J* = 8.0, 7.1, 1.0), 7.63 br.d (1H, *J* = 8.1), and 7.81 d.d.d (1H, *J* = 8.0, 7.1, 1.3) (6-H, 7-H, 8-H); 8.08 d.d (1H, *J* = 8.1, 1.6, 5-H). ^{13}C NMR spectrum, δ_C, ppm: 24.0 (CH_3), 40.0 (NMe_2), 112.3 (2C, CH), 120.5, 126.0, 126.1 (CH), 126.2 (CH), 126.5 (CH), 128.5 (2C, CH), 134.3 (CH), 147.2, 150.1, 155.4, 161.6. Found, %: C 71.98; H 4.98; N 17.68. $C_{17}H_{17}N_3O$. Calculated, %: C 72.13; H 5.10; N 17.71.

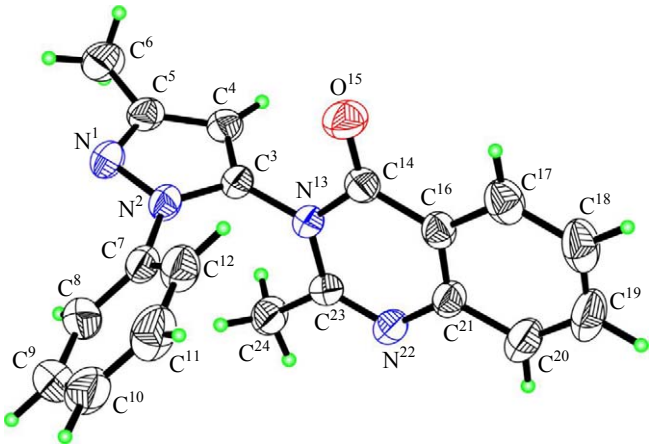


Fig. 1. Structure of the molecule of 2-methyl-3-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)quinazolin-4(3*H*)-one (**3c**) with arbitrary atom numbering according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

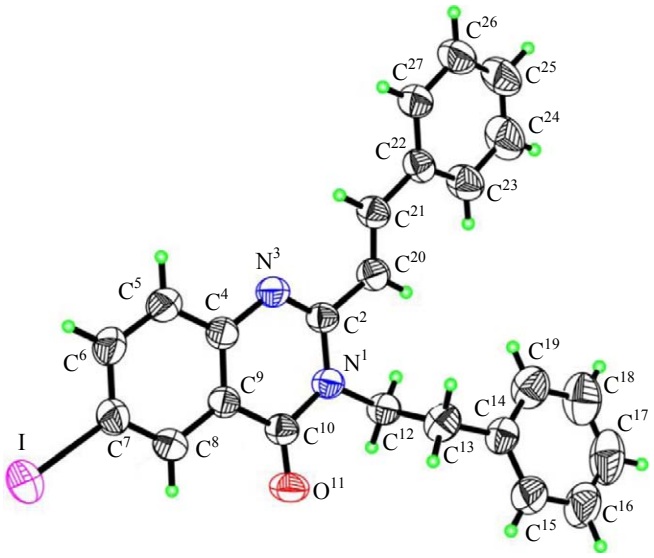


Fig. 2. Structure of the molecule of 6-iodo-2-phenyl-2-[(*E*)-2-phenylethenyl]-3-(phenylethyl)quinazolin-4(3*H*)-one (**4a**) with arbitrary atom numbering according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

4-(2-Methyl-4-oxo-3,4-dihydroquinazolin-3-yl)-benzenesulfonamide (3b). Yield 45.8%, mp 264–

Table 1. Principal crystallographic data and parameters of X-ray diffraction experiments for compounds **3c** and **4a**

Parameter	**3c**	**4a**
CCDC entry no.	1904995	1882015
Formula	$C_{19}H_{16}N_4O$	$C_{24}H_{19}N_2OI$
Molecular weight	316.36	478.31
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
a, Å	10.525(2)	13.873(3)
b, Å	16.149(3)	9.5118(19)
c, Å	9.822(2)	15.799(3)
β, deg	103.80(3)	91.03(3)
V, Å^3	1621.2(6)	2084.5(7)
Z	4	4
d_{calc}, g/cm^3	1.296	1.524
μ(MoK_α), mm^{-1},	0.084	1.552
T_{min}	–	0.22659
T_{max}	–	0.26966
F(000)	664	952
Crystal dimensions, mm	0.38×0.26×0.22	0.30×0.32×0.42
Temperature, K	293	293
Radiation wavelength, Å	0.71073	0.71073
θ_{min}, θ_{max}, deg	2.0, 30.0	1.5, 30.0
Scan range (hkl)	$-14 \le h \le 14$	$0 \le h \le 19$
	$-22 \le k \le 0$	$0 \le k \le 13$
	$0 \le l \le 13$	$-22 \le l \le 22$
Total number of reflections	4981	6290
Number of reflections with $I > 2.0\sigma(I)$	3199	3767
Number of independent reflections	4729	6064
Number of variables	281	253
R, wR_2	0.0461, 0.1376	0.0398, 0.1089
Goodness of fit S	1.03	1.02

266°C, R_f 0.50. IR spectrum, ν, cm^{-1}: 3279 (NH_2), 1668 (C=O), 1654 (C=C–C=N). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.20 s (3H, CH_3), 7.30 br.s (2H, NH_2), 7.45 d.d.d (1H, H_{arom}, J = 7.9, 7.2, 1.0), 7.50–7.55 m (2H, $C_6H_4SO_2$), 7.61 br.d (1H, H_{arom}, J = 8.2), 7.76 d.d.d (1H, H_{arom}, J = 8.2, 7.2, 1.5), 8.03–8.08 m (2H, $C_6H_4SO_2$), 8.12 br.d (1H, H_{arom}, J = 7.9). ^{13}C NMR spectrum, δ_C, ppm: 23.7 (CH_3), 120.3, 125.7, 126.1, 126.4, 127.1 (2C, CH), 128.5 (2C, CH), 133.7, 140.1, 144.7, 147.1, 152.9, 160.8. Found, %: C 57.01; H 4.08; N 13.28. $C_{15}H_{13}N_3O_3S$. Calculated, %: C 57.13; H 4.16; N 13.33.

2-Methyl-3-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)quinazolin-4(3*H*)-one (3c). Yield 55.3%, mp 158–160°C, R_f 0.48. IR spectrum, ν, cm^{-1}: 1691 (C=O), 1610 (C=C–C=N). ^{1}H NMR spectrum, δ, ppm (J, Hz): 2.23 s (3H, 2-CH_3), 2.50 d (3H, 3′-CH_3, J = 0.4), 6.45 q (1H, 4′-H, J = 0.4), 7.35–7.48 m (5H, Ph); 7.58 d.d.d (1H, J = 7.9, 7.2, 1.2), 7.65 d.d.d (1H, J = 8.2, 1.2, 0.6), 7.87 d.d.d (1H, J = 8.2, 7.2, 1.6), and 8.25 d.d.d (1H, J = 7.9, 1.6, 0.6) (5-H, 6-H, 7-H, 8-H). ^{13}C NMR spectrum, δ_C, ppm: 13.6, 22.3, 105.6, 119.4, 122.4, 126.3, 126.4, 126.6, 127.3, 128.7, 134.2, 134.3, 137.6, 146.7, 148.4, 152.6, 160.6. Found, %: C 72.01; H 4.98; N 1.68. $C_{19}H_{16}N_4O$. Calculated, %: C 72.13; H 5.10; N 17.71.

3-(4-Chlorophenyl)-6-iodo-2-methylquinazolin-4(3*H*)-one (3d). Yield 60.3%, mp 158–160°C, R_f 0.59.

IR spectrum, ν, cm^{-1}: 1681 (C=O), 1601 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.17 s (3H, CH_3), 7.33–7.38 m (2H, C_6H_4), 7.38 d.d (1H, 8-H, *J* = 8.6, 0.4), 7.53–7.58 m (2H, C_6H_4), 8.01 d.d (1H, 7-H, *J* = 8.6, 2.1), 8.40 d.d (1H, 5-H, *J* = 2.1, 0.4). ^{13}C NMR spectrum, δ_C, ppm: 23.7 (CH_3), 89.9, 122.1, 128.5 (CH), 129.3 (2C, CH), 129.6 (2C, CH), 134.1, 134.7 (CH), 135.8, 142.2 (CH), 146.4, 154.1, 159.4. Found, %: C 45.38; H 2.46; N 6.98. $C_{15}H_{10}ClIN_2O$. Calculated, %: C 45.43; H 2.54; N 7.06.

General procedure for the synthesis of 2-(2-arylethynyl)quinazolin-4(3*H*)-ones 4a–4g, 5a–5f, and 6. A mixture of 0.01 mol of quinazoline **2** or **3a–3d** and 0.01 mol of the corresponding aldehyde was heated for 1 h at 170–180°C on a metal bath. After cooling, the mixture was triturated with ethanol, and the precipitate was filtered off, dried, and recrystallized from DMF.

6-Iodo-2-phenyl-2-[(*E*)-2-phenylethenyl]-3-(2-phenylethyl)quinazolin-4(3*H*)-one (4a) was synthesized from quinazoline **2** and benzaldehyde. Yield 58.3%, mp 160–162°C, R_f 0.55. IR spectrum, ν, cm^{-1}: 1661 (C=O), 1630 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.03 br.t (2H, CH_2, *J* = 7.5), 4.48 br.t (2H, NCH_2, *J* = 7.5), 7.08 d (1H, CH=CH, *J* = 15.2), 7.13–7.28 m (5H, C_6H_5), 7.39 d (1H, H_{arom}, *J* = 8.6), 7.58 m (2H, C_6H_5), 7.82 d (1H, CH=CH, *J* = 15.2), 7.97 d.d (1H, H_{arom}, *J* = 8.6, 2.1), 8.46 d (1H, H_{arom}, *J* = 2.1). ^{13}C NMR spectrum, δ_C, ppm: 34.4, 44.2, 89.6, 118.6, 121.7, 126.1, 127.5 (2C), 128.0 (2C), 128.2 (2C), 128.4 (2C), 128.7, 129.0, 134.8, 134.9, 137.5, 140.5, 141.9, 146.3, 152.1, 159.3. Found, %: C 60.16; H 3.88; N 5.78. $C_{24}H_{19}IN_2O$. Calculated, %: C 60.26; H 4.00; N 5.86.

2-[(*E*)-2-(4-Chlorophenyl)ethenyl]-6-iodo-3-(2-phenylethyl)quinazolin-4(3*H*)-one (4b) was synthesized from quinazoline **2** and 4-chlorobenzaldehyde. Yield 55.2%, mp 202–203°C, R_f 0.59. IR spectrum, ν, cm^{-1}: 1669 (C=O), 1560 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.96–3.02 m (2H, CH_2), 4.47–4.53 m (2H, NCH_2), 7.10 d (1H, =CH, *J* = 15.2), 7.12–7.27 m (5H, C_6H_5), 7.38 d (1H, H_{arom}, *J* = 8.6), 7.36–7.41 m (2H, C_6H_4), 7.59–7.64 m (2H, C_6H_4), 7.76 d (1H, =CH, *J* = 15.2), 7.97 d.d (1H, H_{arom}, *J* = 8.6, 2.1), 8.46 d (1H, H_{arom}, *J* = 2.1). ^{13}C NMR spectrum, δ_C, ppm: 34.3 (CH_2), 44.1 (CH_2), 90.1, 119.6 (CH), 121.6, 126.1 (CH), 128.0 (2C, CH), 128.4 (2C, CH), 128.6 (2C, CH), 128.8 (CH), 129.2 (2C, CH), 133.7, 134.2, 134.7 (CH), 137.6, 138.9 (CH), 142.1 (CH), 146.2, 152.1, 159.4. Found, %: C 56.13; H 3.44; N 5.32. $C_{24}H_{18}ClIN_2O$. Calculated, %: C 56.22; H 3.54; N 5.46.

2-[(*E*)-2-(2,4-Dichlorophenyl)ethenyl]-6-iodo-3-(2-phenylethyl)quinazolin-4(3*H*)-one (4c) was synthesized from quinazoline **2** and 2,4-dichlorobenzaldehyde. Yield 53.8%, mp 168–170°C, R_f 0.52. IR spectrum, ν, cm^{-1}: 1687 (C=O), 1626 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.98–3.94 m (2H, CH_2), 4.47–5.53 m (2H, NCH_2), 7.14 d (1H, =CH, *J* = 15.2), 7.12–7.23 m (5H, C_6H_5), 7.37 d.d.d (1H, $C_6H_3Cl_2$, *J* = 8.5, 2.2, 0.5), 7.44 d.d (1H, H_{arom}, *J* = 8.6, 0.4), 7.47 d (1H, $C_6H_3Cl_2$, *J* = 2.2), 7.86 d (1H, $C_6H_3Cl_2$, *J* = 8.5), 7.99 d.d (1H, H_{arom}, *J* = 8.6, 2.1), 8.04 br.d (1H, =CH, *J* = 15.2), 8.48 d.d (1H, H_{arom}, *J* = 2.1, 0.4). ^{13}C NMR spectrum, δ_C, ppm: 34.3 (2C, CH_2), 44.2, 90.0, 121.8, 122.0, 126.1, 127.0, 127.9 (2C), 128.5 (2C), 128.8, 128.9, 131.8, 134.3, 134.4, 134.5, 134.8, 137.5, 141.9, 146.1, 151.7, 159.2. Found, %: C 52.58; H 3.04; N 5.02. $C_{24}H_{17}Cl_2IN_2O$. Calculated, %: C 52.68; H 3.13; N 5.12.

2-[(*E*)-2-(4-Dimethylaminophenyl)ethenyl]-6-iodo-3-(2-phenylethyl)quinazolin-4(3*H*)-one (4d) was synthesized by reaction of quinazoline **2** with 4-dimethylaminobenzaldehyde. Yield 46.5%, mp 214–215°C, R_f 0.49. IR spectrum, ν, cm^{-1}: 1670 (C=O), 1624 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.00–3.05 m (2H, CH_2), 3.07 s (6H, NMe_2), 4.41–4.47 m (2H, NCH_2), 6.66–6.72 m (2H, C_6H_4), 6.80 d (1H, =CH, *J* = 15.0), 7.16–7.30 m (5H, C_6H_5), 7.36 d (1H, H_{arom}, *J* = 8.6), 7.43–7.48 m (2H, C_6H_4), 7.85 d (1H, =CH, *J* = 15.0), 7.93 d.d (1H, H_{arom}, *J* = 8.6, 2.2), 8.42 d (1H, H_{arom}, *J* = 2.2). Found, %: C 59.83; H 4.54; N 7.92. $C_{26}H_{24}IN_3O$. Calculated, %: C 59.89; H 4.64; N 8.06.

6-Iodo-2-[(*E*)-2-(4-nitrophenyl)ethenyl]-3-(2-phenylethenyl)quinazolin-4(3*H*)-one (4e) was synthesized by reaction of quinazoline **2** with 4-nitrobenzaldehyde. Yield 56.1%, mp 238–240°C, R_f 0.55. IR spectrum, ν, cm^{-1}: 1671 (C=O), 1592 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.02 t (2H, $CH_2C_6H_5$, *J* = 7.3), 4.54 t (2H, NCH_2, *J* = 7.3), 7.09–7.15 m (1H) and 7.18–7.25 m (4H) (C_6H_5), 7.33 d (1H, CH=CH, *J* = 15.2), 7.41 d (1H, H_{arom}, *J* = 8.6), 7.81 d (1H, CH=CH, *J* = 15.2), 7.86–7.91 m (2H, C_6H_4), 8.00 d.d (1H, H_{arom}, *J* = 8.6, 2.1), 8.23–8.28 m (2H, C_6H_4), 8.49 (1H, H_{arom}, *J* = 2.1). Found, %: C 54.96; H 3.38; N 7.88. $C_{24}H_{18}IN_3O_3$. Calculated, %: C 55.08; H 3.47; N 8.03.

6-Iodo-3-(2-phenylethyl)-2-{(*E*)-2-[4-(propan-2-yl)phenyl]ethenyl}quinazolin-4(3*H*)-one (4f) was synthesized by reaction of quinazoline **2** with 4-(propan-2-yl)benzaldehyde. Yield 45.3%, mp 158–

160°C, R_f 0.62. IR spectrum, ν, cm^{-1}: 1672 (C=O), 1631 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.30 d (6H, CH_3, *J* = 6.9), 2.95 sept (1H, CH, *J* = 6.9), 2.99–3.06 m (2H, C**H**$_2C_6H_5$), 4.43–4.50 m (2H, NCH_2), 7.02 d (1H, =CH, *J* = 15.2), 7.15–7.29 m (7H, H_{arom}), 7.39 d.d (1H, =CH, *J* = 8.6, 0.3), 7.50–7.54 m (2H, C_6H_4), 7.83 d (1H, =CH, *J* = 15.2), 7.97 d.d (1H, =CH, *J* = 8.6, 2.1), 8.45 d.d (1H, =CH, *J* = 2.1, 0.6). Found, %: C 62.23; H 4.64; N 5.22. $C_{27}H_{25}IN_2O$. Calculated, %: C 62.31; H 4.84; N 5.38.

6-Iodo-2-[(*E*)-2-(1-methyl-1*H*-indol-3-yl)-ethenyl]-3-(2-phenylethyl)quinazolin-4(3*H*)-one (4g) was synthesized by reaction of quinazoline **2** with 1-methyl-1*H*-indole-3-carbaldehyde. Yield 50.2%, mp 198–200°C, R_f 0.48. IR spectrum, ν, cm^{-1}: 1665 (C=O), 1621 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.06–3.11 m (2H, CH_2), 3.91 s (3H, CH_3), 4.45–4.50 m (2H, NCH_2), 7.01 d (1H, =CH, *J* = 15.0), 7.17–7.44 m (9H, H_{arom}), 7.75 s (1H, =CHN), 7.85–7.88 m (1H, H_{arom}), 7.93 d.d (1H, H_{arom}, *J* = 8.6, 2.2), 8.20 d (1H, =CH, *J* = 15.0), 8.43 d (1H, H_{arom}, *J* = 2.2). Found, %: C 60.96; H 4.08; N 7.82. $C_{27}H_{22}IN_3O$. Calculated, %: C 61.03; H 4.17; N 7.91.

2-[(*E*)-2-(4-Chlorophenyl)ethenyl]-3-[4-(dimethylamino)phenyl]quinazolin-4(3*H*)-one (5a) was synthesized by reaction of quinazoline **3a** with 4-chlorobenzaldehyde. Yield 52.4%, mp 210–212°C, R_f 0.51. IR spectrum, ν, cm^{-1}: 1678 (C=O), 1633 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.09 s (6H, NCH_3), 6.44 d (1H, =CH, *J* = 15.5), 6.80–6.85 m (2H, C_6**H**$_4NMe_2$), 7.05–7.10 m (2H, C_6**H**$_4NMe_2$), 7.29–7.36 m (4H, C_6H_4Cl), 7.43 d.d.d (1H, H_{arom}, *J* = 7.9, 7.0, 1.3), 7.68 br.d (1H, H_{arom}, *J* = 8.2), 7.76 d.d.d (1H, H_{arom}, *J* = 8.2, 7.0, 1.5), 7.87 d (1H, =CH, *J* = 15.5), 8.14 d.d (1H, H_{arom}, *J* = 7.9, 1.5). ^{13}C NMR spectrum, δ_C, ppm: 39.8 (2C, NMe_2), 111.9, 120.5, 120.6, 124.5, 125.5, 126.3, 126.7, 128.4 (2C, CH), 128.4 (2C, CH), 128.6 (2C, CH), 133.5, 133.6, 134.2, 137.1, 147.2, 149.8, 151.4, 161.0. Found, %: C 71.68; H 4.98; N 10.38. $C_{24}H_{20}ClN_3O$. Calculated, %: C 71.73; H 5.02; N 10.46.

2-[(*E*)-2-(2,4-Dichlorophenyl)ethenyl]-3-[(4-dimethylamino)phenyl]quinazolin-4(3*H*)-one (5b) was synthesized by reaction of quinazoline **3a** with 2,4-dichlorobenzaldehyde. Yield 51.8%, mp 242–244°C, R_f 0.53. IR spectrum, ν, cm^{-1}: 1682 (C=O), 1630 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.08 s (6H, NCH_3), 6.49 d (1H, =CH, *J* = 15.5), 6.79–6.84 m (2H, C_6**H**$_4NMe_2$), 7.06–7.11 m (2H, C_6**H**$_4NMe_2$), 7.24 d.d (1H, $C_6H_3Cl_2$, *J* = 8.5, 2.0), 7.29 d (1H, $C_6H_3Cl_2$, *J* = 8.5), 7.44 d (1H, $C_6H_3Cl_2$, *J* = 2.0), 7.45 d.d.d (1H, H_{arom}, *J* = 8.0, 6.7, 1.6), 7.71–7.80 m (2H, H_{arom}), 8.12 d (1H, =CH, *J* = 15.5), 8.15 d.d (1H, H_{arom}, *J* = 8.0, 1.2). ^{13}C NMR spectrum, δ_C, ppm: 39.8 (2C, NMe_2), 111.9, 120.7, 123.4, 124.4, 125.8, 126.3, 127.0, 127.1, 127.9, 128.6, 129.0, 132.0, 132.8, 133.5, 134.2, 134.4, 147.0, 149.8, 151.0, 161.0. Found %: C 65.98; H 4.28; N 9.58. $C_{24}H_{19}Cl_2N_3O$. Calculated, %: C 66.06; H 4.39; N 9.63.

2-[(*E*)-2-(4-Chlorophenyl)ethenyl]-3-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)quinazolin-4(3*H*)-one (5c) was synthesized by reaction of quinazoline **3c** with 4-chlorobenzaldehyde. Yield 50.5%, mp 216–218°C, R_f 0.51. IR spectrum, ν, cm^{-1}: 1682 (C=O), 1636 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.46 s (3H, CH_3), 6.35 d (1H, =CH, *J* = 15.4), 6.39 br.s (1H, 4′-H), 7.22–7.30 m (5H, C_6H_5), 7.34–7.43 m (4H, C_6H_4Cl), 7.48 d.d.d (1H, H_{arom}, *J* = 7.9, 7.2, 1.1), 7.66 br.d (1H, H_{arom}, *J* = 8.1), 7.80 d.d.d (1H, H_{arom}, *J* = 8.1, 7.2, 1.5), 7.81 d (1H. =CH, *J* = 15.4), 8.14 d.d (1H, H_{arom}, *J* = 7.9, 1.5). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 106.3, 118.1, 119.5, 122.7, 126.4, 126.6, 127.1, 127.3, 128.6, 128.6, 128.7, 133.1, 133.4, 134.5, 134.7, 137.5, 139.0, 146.8, 148.5, 150.0, 160.3. Found, %: C 71.04; H 4.28; N 12.68. $C_{26}H_{19}ClN_4O$. Calculated, %: C 71.15; H 4.36; N 12.77.

2-[(*E*)-2-(2,4-Dichlorophenyl)ethenyl]-3-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)quinazolin-4(3*H*)-one (5d) was synthesized by reaction of quinazoline **3c** with 2,4-dichlorobenzaldehyde. Yield 49.7%, mp 206–208°C, R_f 0.43. IR spectrum, ν, cm^{-1}: 1694 (C=O), 1631 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.44 s (3H, CH_3), 6.40 s (1H, 4′-H), 6.43 d (1H, =CH, *J* = 15.4), 7.22–7.34 m (6H, H_{arom}), 7.44–7.53 m (3H, H_{arom}), 7.70 br.d (1H, H_{arom}, *J* = 8.1), 7.81 br.d.d.d (1H, H_{arom}, *J* = 8.1, 7.1, 1.4), 8.06 d (1H, =CH, *J* = 15.4), 8.15 br.d (1H, H_{arom}, *J* = 7.9). ^{13}C NMR spectrum, δ_C, ppm: 13.7, 106.3, 119.6, 121.0, 122.8, 126.7, 127.3, 127.4, 128.5, 129.1, 131.4, 133.2, 134.3, 134.4, 134.6, 134.9, 137.5, 146.6, 148.5, 149.6, 160.2. Found, %: C 65.91; H 3.78; N 11.78. $C_{26}H_{18}Cl_2N_4O$. Calculated, %: C 65.97; H 3.83; N 11.84.

4-{2-[(*E*)-2-(3-Nitrophenyl)ethenyl]-4-oxo-3,4-dihydroquinazolin-3-yl}benzenesulfonamide (5e) was synthesized by reaction of quinazoline **3b** with 3-nitrobenzaldehyde. Yield 45.5%, mp 310–312°C, R_f 0.45. IR spectrum, ν, cm^{-1}: 3310 (NH_2), 1655 (C=O), 1604 (C=C–C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 6.52 d (1H, CH=CH, *J* = 15.5), 7.33 br.s (2H, NH_2), 7.50 d.d.d (1H, C_6H_4, *J* = 8.1, 7.1, 1.2), 7.52–7.57 m (2H, $C_6H_4SO_2$), 7.61 t (1H, 5′-H, *J* = 7.9), 7.72–7.78 m

(2H, H_{arom}), 7.83 d.d.d (1H, H_{arom}, J = 8.1, 7.1, 1.5), 8.00 d (1H, CH=CH, J = 15.3), 8.08–8.13 m (2H, $C_6H_4SO_2$), 8.12–8.19 m (2H, H_{arom}), 8.23 t (1H, 2′-H, J = 1.8). ^{13}C NMR spectrum, δ_C, ppm: 120.5, 122.2, 122.4, 123.3, 126.2, 126.3, 127.0, 127.1 (2C, CH), 129.0 (2C, CH), 129.9, 132.3, 134.0, 136.4, 136.8, 138.9, 144.9, 147.0, 148.1, 149.9, 160.6. Found, %: C 58.81; H 3.55; N 12.38. $C_{22}H_{16}N_4O_5S$. Calculated, %: C 58.92; H 3.60; N 12.49.

3-(4-Chlorophenyl)-6-iodo-2-[(*E*)-2-(5-nitrofuran-2-yl)ethenyl]quinazolin-4(3*H*)-one (5f) was synthesized by reaction of quinazoline **3d** with 5-nitrofuran-2-carbaldehyde. Yield 70.5%, mp 268–270°C, R_f 0.52. IR spectrum, ν, cm^{-1}: 1682 (C=O), 1631 (C=C–C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.47 d.d (1H, CH=CH, J = 15.3, 0.4), 7.04 d.t (1H, 4′-H, J = 3.9, 0.4), 7.36–7.41 m (2H, C_6H_4), 7.49 d.d (1H, H_{arom}, J = 8.5, 0.4), 7.49 d (1H, 3′-H, J = 3.9), 7.61–7.66 m (2H, C_6H_4), 7.79 d (1H, CH=CH, J = 15.3), 8.07 91 d.d (1H, H_{arom}, J = 8.5, 2.1), 8.46 d.d (1H, H_{arom}, J = 2.1, 0.4). ^{13}C NMR spectrum, δ_C, ppm: 90.9, 113.4, 115.5, 122.3, 122.6, 124.7, 129.0, 129.5, 130.1, 134.5, 135.0, 142.6, 146.1, 150.1, 152.5, 159.1. Found, %: C 46.18; H 2.01; N 7.98. $C_{20}H_{11}ClN_3O_4$. Calculated, %: C 46.22; H 2.13; N 8.09.

3-(4-Chlorophenyl)-6-iodo-2-[(1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl]quinazolin-4(3*H*)-one (5g) was synthesized by reaction of quinazoline **3d** with (*E*)-3-phenylprop-2-enal. Yield 67.3%, mp 261–263°C, R_f 0.57. IR spectrum, ν, cm^{-1}: 1697 (C=O), 1621 (C=C–C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 5.89 br.d (1H, 1′-H, J = 14.6), 6.85 d.d.d (1H, 3′-H, J = 15.5, 10.6, 0.5), 6.95 d (1H, 4′-H, J = 15.5), 7.21–7.32 m (3H, *m*-H, *p*-H), 7.30–7.35 m (2H, C_6H_4Cl), 7.42–7.46 m (2H, *o*-H), 7.44 d (1H, 8-H, J = 8.6), 7.57–7.62 m (2H, C_6H_4Cl), 7.78 d.d (1H, 2′-H, J = 14.6, 10.6), 8.03 d.d (1H, 7-H, J = 8.6, 2.1), 8.42 d (1H, 5-H, J = 2.1). ^{13}C NMR spectrum, δ_C, ppm: 89.7, 122.0, 126.6 (2C, CH), 126.9 (CH), 128.1 (2C, CH), 128.2 (CH), 128.8 (CH), 129.4 (2C, CH), 130.0 (2C, CH), 134.2, 134.9, 135.0, 135.7 (CH), 139.0 (CH), 140.7 (CH), 142.4 (CH), 146.6, 151.3, 159.3. Found, %: C 56.67; H 2.95; N 5.67. $C_{24}H_{16}ClN_2O$. Calculated, %: C 56.44; H 3.6; N 5.48.

2-(*E*)-(5-Bromo-2-oxo-1-propyl-2,3-dihydro-1*H*-indol-3-ylidenemethyl)-6-iodo-3-(2-phenylethyl)-quinazolin-4(3*H*)-one (6). Yield 49.2%, mp 248–250°C, R_f 0.46. IR spectrum, ν, cm^{-1}: 1707 (C=O), 1664 (C=C–C=N). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.02 t (3H, CH_3, J = 7.4), 1.66–1.79 m (2H, C**H**$_2$CH$_3$), 3.00–3.07 m (2H, C**H**$_2$C$_6$H$_5$), 3.71 t (2H, NCH_2), 4.42 m (2H, NCH_2), 6.89 d (1H, =CH, J = 8.4), 6.96–7.03 m (1H, H_{arom}), 7.11–7.21 m (4H, H_{arom}), 7.36 s (1H, =CH), 7.44 d.d (1H, =CH, J = 8.4, 2.1), 7.45 d (1H, =CH, J = 8.5), 8.11 d.d (1H, =CH, J = 8.5, 2.1), 8.43 d (1H, =CH, J = 2.1), 8.58 d (1H, =CH, J = 2.1). Found, %: C 52.26; H 3.84; N 6.42. $C_{27}H_{25}IN_2O$. Calculated, %: C 52.36; H 3.92; N 6.54.

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CONFLICT OF INTERESTS

The authors declare the absence of conflict of interests.

REFERENCES

1. Ajani, O.O., Audu, O.Y., Aderohunmu, D.V., Owolabi, E.O., and Olomieja, A.O., *Am. J. Drug Discovery Dev.*, 2017, vol. 7, p. 1. doi 10.3923/ajdd.2017.1.24
2. Anschütz, R., Schmidt, O., and Greiffenberg, A., *Ber.*, 1902, vol. 35, p. 3482.
3. Agbo, E.N., Makhafola, T.J., Choong, Y.S., Mphahlele, M.J., and Ramasami, P.R., *Molecules*, 2016, vol. 21, p. 28. doi 10.3390/molecules21010028
4. Harutyunyan, A.A., Ghukasyan, G.T., and Danagulyan, G.G., *Org. Med. Chem. Int. J.*, 2018, vol. 7, p. 1. doi 10.19080/OMCIJ.2018.07.555718
5. Arutyunyan, A.A., Gukasyan, G.T., Panosyan, G.A., and Danagulyan, G.G., *Khim. Zh. Arm.*, 2018, vol. 71, p. 249.
6. Sheldrick, G.M., *Acta Crystallogr., Sect. C*, 2015, vol. 71, p. 3.