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3-Aryl(alkyl)quinazoline-2,4(1*H*,3*H*)-diones and Their Alkyl Derivatives

A. S. Shestakov[a], O. E. Sidorenko[a], I. S. Bushmarinov[b], Kh. S. Shikhaliev[a], and M. Yu. Antipin[b]

[a]*Voronezh State University, Voronezh, 394006 Russia*
e-mail: chocd261@chem.vsu.ru
[b]*Nesmeyanov Institute of Organoelemental Compounds, Russian Academy of Sciences*

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Abstract—Two-stage reaction of methyl anthranilate with aryl(alkyl) isocyanates in keeping with the quantum-chemical calculations and XRD analysis resulted in 3-aryl(alkyl)quinazoline-2,4(1*H*,3*H*)-diones that by treatment with alkyl halides, phenacyl bromides, esters and amides of chloroacetic acid were converted into the corresponding 1-alkyl derivatives.

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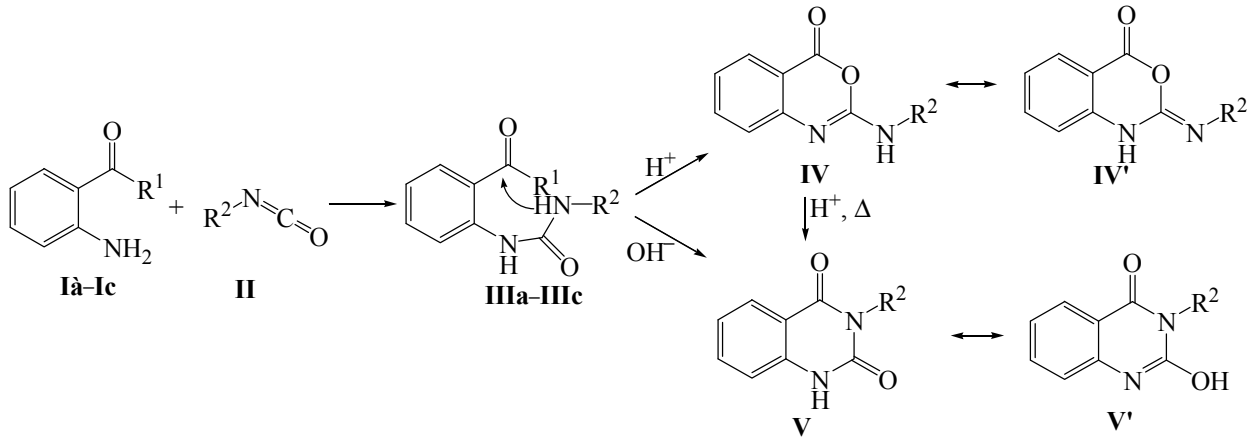
Compounds containing a fragment of a quinazoline-2,4(1*H*,3*H*)-dione may be regarded as analogs of methylxanthines and purine nucleotides and therefore they might exhibit high biological activity. Some among them are under investigation as antidiabetic [1] and antitumor drugs [1–3]. The target of the present study was the development of synthesis methods for preparation of combinatorial library with the use of quinazolinediones. Formerly a building up was described of analogous library of sulfamides containing a fragment of 1,3-dimethyl-1*H*-quinazoline-2,4-dione [1].

One of the preparation procedures for 3-R-quinazoline-2,4(1*H*,3*H*)-diones **V** is underlain by the application of isocyanates **II** and anthranilic acid (**Ia**), and also its ester **Ib**, amide **Ic**, or nitrile (Scheme 1) [2–7]. In the first stage carbamide **III** is formed whose further cyclization is catalyzed both by acids and bases. The acid catalysis under mild conditions leads to the formation of isomeric 2-(R-amino)-4*H*-benzo[*d*][1,3]-oxazin-4-ones **IV** that under more stringent conditions

Scheme 1.



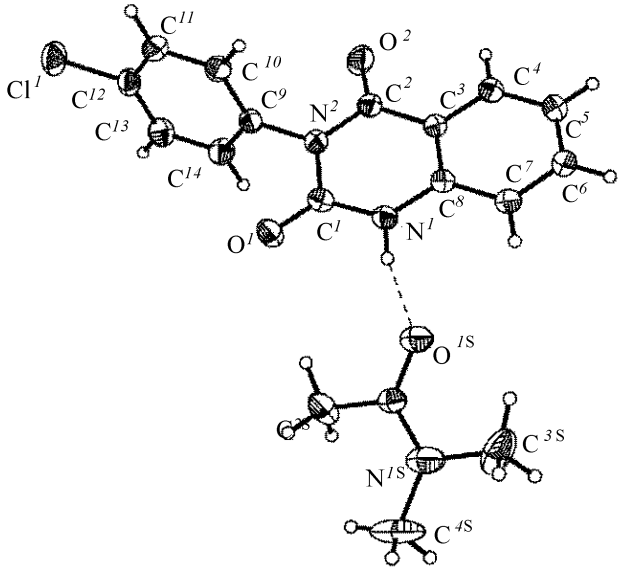
R^1 = OH (**a**), OMe (**b**), NH_2 (**c**); R^2 = 4-ClC_6H_4

are converted into target compounds **V**. Under the basic catalysis or the hard acid treatment 3-R-quinazoline-2,4(1*H*,3*H*)-diones **V** formed from the carbamides.

We performed quantum-chemical calculations of geometrical parameters and electronic structure of compounds **IV** and **V** employing program package GAUSSIAN 03 [8]. The calculations were carried out by the density functional method B3LYP. The full optimization of the molecules geometry and the calculation of the electronic structure were performed in the basis 6-31G**.

The comparison of energy of isolated molecules of regioisomers **IV** and **V** and their tautomers **IV'** and **V'** shows that the lowest energy corresponds to compound **V**. The energy difference between compounds **IV** and **V** amounts to 54.4 kJ mol^{-1}. The tautomeric forms **IV** and **V** are more feasible than **IV'**and **V'** (energy difference equals 26.0 and 54.4 kJ mol^{-1} respectively). Thus compound **V** is thermodynamically more stable in agreement with the published data [2, 4–6].

The structure of compounds **V** is not planar according to the calculations. The torsion angle between the planes of the benzene ring and the heterocycle is 63 deg. The rotation of the aromatic ring into the plane of the heterocyclic fragment requires 38.9 kJ mol^{-1} that is considerably more than the insurmountable barrier to the rotation around the carbon-carbon bond (~12 kJ mol^{-1}).



General appearance of the molecule of 3-(4-chlorophenyl)-quinazoline-2,4(1*H*,3*H*)-dione **Vc** with atoms represented by thermal ellipsoids. The solvent is disordered by two positions with the ratio of occupancy 0.65 : 0.35, the position with lesser occupancy is not shown in the figure.

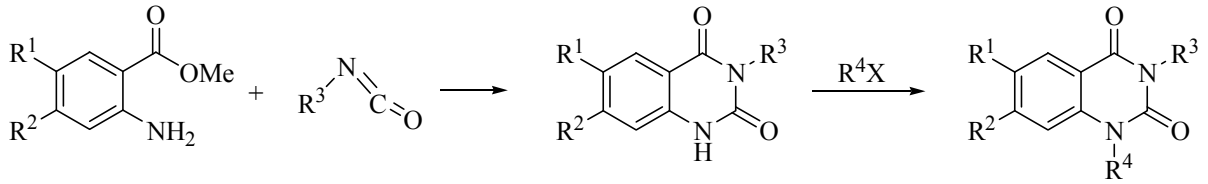
In keeping with Scheme 1 we prepared a number of quinazolinediones **V** with diverse substituents in positions *3*, *6*, and *7* (Scheme 2). The heating of anthranilates with the isocyanate resulted in the formation of carbamides **III** that after isolation were subjected to cyclization into the corresponding quinazolinediones by boiling in alcohol solution of KOH. The potassium hydroxide (sodium hydroxide and alcoholate are also suitable) operates as a catalyst that reacting with the intermediate carbamide causes of the deprotonation of the nitrogen atoms thus in-creasing their nucleophilicity. At the use of aryl isocyanates *N,N*'-di-arylcarbamides are formed where the proton elimination from any of the two nitrogen atoms is equally probable. With alkyl isocyanates *N*-aryl-, *N*'-alkylcarbamides are formed. In these compounds the nitrogen linked to the alkyl substituent and playing the part of the nucleophilic site during the cyclization is less "acidic", and this apparently is the reason of lower yields in the synthesis of 3-alkylquinazoline-2,4(1*H*,3*H*)-diones.

The quantum-chemical calculation of the electronic structure of compound **III** shows that the energy difference between the lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO) is small and equals 0.1617 eV. In the anionic form of carbamide **III** where the attacking nitrogen atom (Scheme 1) is negatively charged this difference is even smaller and amounts to 0.0317 eV thus suggesting the orbital control of the reaction. The form of the frontier orbitals in compound **III** both in the neutral molecule and anion is favorable for the formation just of compound **V**.

The proof that the cyclization of carbamides **III** resulted just in 3-R-quinazoline-2,4(1*H*,3*H*)-diones **V** and not in their isomers, 2-(R-amino)-4*H*-benzo[*d*][1,3]oxazin-4-ones **IV**, was obtained by XRD analysis of compound **Vc** (see the figure).

Compound **Vc** crystallizes with one molecule of dimethylacetamide and exists in the amide tautomeric form in full agreement with the calculated and published data (see the figure). The plane of the ring of the *para*-chlorophenyl substituent is orthogonal to the plane of the heterocycle with the angle of rotation of 81.2(2)°. The bond distances and bond angles in molecule **Vc** are close to the respective values in the 3-phenylquinazoline-2,4(1*H*,3*H*)-dione [9]. The analysis of intermolecular interactions showed that the amide hydrogen formed a strong hydrogen bond with the oxygen atom of the solvent N^{1}–H^{1N}···O^{1S} (distance N···O 2.757(2) Å, angle NH···O 166°). The other intermolecular contacts in the crystal

Scheme 2.



IIa–IIf **Va–Vk** **VIa–VIk**

II, R^3 = Ph (**a**), 3-ClC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 3,4-$Cl_2C_6H_3$ (**d**), Et (**e**), cyclohexyl (**f**); **V**, $R^1 = R^2$ = H, R^3 = Ph (**a**), 3-ClC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 3,4-$Cl_2C_6H_3$ (**d**), Et (**e**), cyclohexyl (**f**); R^1 = Br, R^2 = H, R^3 = Ph (**g**), Et (**h**), cyclohexyl (**i**); $R^1 = R^2$ = MeO, R^3 = Et (**j**), cyclohexyl (**k**); **VI**, $R^1 = R^2$ = H: R^3 = Ph, R^4 = 2,5-$(MeO)_2C_6H_3NHCOCH_2$ (**a**); R^3 = 3-ClC_6H_4, R^4 = MeAc (**b**); R^3 = 4-ClC_6H_4, R^4 = 3,4-$(MeO)_2C_6H_3COCH_2$ (**c**); R^3 = 3,4-$Cl_2C_6H_3$, R^4 = 3-ClBn (**d**); R^3 = Et, R^4 = 4-TolNHCOCH$_2$ (**e**); R^3 = cyclohexyl, R^4 = 4-TolCOCH$_2$ (**f**); R^1 = Br, R^2 = H: R^3 = Ph, R^4 = 4-ClBn (**g**); R^3 = Et, R^4 = Me (**h**); R^3 = cyclohexyl, R^4 = All (**i**); $R^1 = R^2$ = MeO: $R^3 = R^4$ = Et (**j**), R^3 = cyclohexyl, R^4 = 4-$MeOC_6H_4COCH_2$ (**k**); X = Cl, Br, I.

correspond to the common van der Waals interactions.

As follows from the XRD findings, in quinazolinediones **V** a mobile amide hydrogen atom is present in the position *1*. These compounds are relatively strong acids ($pK_a \approx 10$ [10, 11]) which easily form the correspondins salts. This fact provides a possibility to involve compound **V** into alkylation reactions. By treating with 1M solution of sodium methylate compound **V** was converted into the sodium salt. On removing methanol the salt was dissolved in DMF and treated with the alkyl halide solution. A short heating resulted in the formation of the alkyl derivative. The developed procedure makes it possible to prepare quickly and is good yields a number of 1-alkyl-3-aryl-(alkyl)quinazoline-2,4(1*H*,3*H*)-diones.

EXPERIMENTAL

The monitoring of reaction progress and checking of homogeneity of compounds obtained was performed by TLC on Merck UV-254 plates, eluent chloroform–methanol, 20:1. ^{1}H NMR spectra were registered on a spectrometer Bruker AC-300 (300 MHz), internal reference TMS.

Colorless crystals of compound **Vc** ($C_{18}H_{18}ClN_3O_3$) were grown from a solution in dimethylacetamide. Crystals monoclinic, space group $P2_1/n$, a 9.1792(6), b 14.5533(9), c 13.3453(8) Å, β 93.5898(13)°, V 1779.27(19) Å^3, Z 4 (Z' 1), d_{calc} 1.343 g/cm^{-3}, μ(MoK_α) 0.237 cm^{-1}, F(000) 752. The intensities of 20334 reflections were measured at 120 K on a diffractometer Bruker SMART 1000 CCD [λ(MoK_α) 0.71073 Å, ш-scanning, 2θ < 60°], 5162 independent reflections (R_{int} 0.0247) were used in further refining.

The structure was solved by the direct method and by successive syntheses of the electron density. Positions of hydrogen atoms were revealed from the difference Fourier syntheses. The refinement was performed for F^2_{hkl} in anisotropic approximation for nonhydrogen atoms except for $C^{1S'}$ (see below). The hydrogen atoms were refined in isotropic approximation in the *rider* model. The solvent molecule in the crystal is disordered by two positions with the common O^{1S} atom. The refinement of the occupancy of the positions at fixed thermal parameters gave 0.65 : 0.35 ratio. The atom $C^{1S'}$ of the minor component is located at a distance 0.36 Å from the atom C^{1S} of the main component, and it is refined in the isotropic approximation for solving the problem of instability of the least squares method.

The final values of divergence factors**:** R_1 0.0518 [calculated for F_{hkl} of 3935 reflections with $I > 2\sigma(I)$], wR_2 0.1464 (calculated for F^2_{hkl} of all 5162 reflections), the number of refined parameters 266, *GOF* 1.001. The calculations were carried out using program package SHELXTL 5.10 [12].

3-Phenylquinazoline-2,4(1*H*,3*H*)-dione (Va). In anhydrous dioxane 1.51 g (10 mmol) of ester **Ib** and 1.19 g (10 mmol) of isocyanate **IIa** was heated at 70°C for 5 h, the reaction mixture was poured into 100 ml of water, the precipitate was filtered off, washed with 2-propanol and placed into a solution of 0.5 g (9 mmol) of potassium hydroxide in 20 ml of methanol. The solution obtained was boiled for 4 h. The reaction mixture was poured into 100 ml of water and acidified till weak acid reaction. The precipitate was filtered off, washed with water, and recrystallized from a mixture 2-propanol–DMF. Yield 2.32 g (85%), mp 281–282°C (280–282 [4],

281 [5], 272 [3], 274–275°C [13]). ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 7.18–7.29 m ($4H_{arom}$), 7.40–7.52 m ($3H_{arom}$), 7.66 t ($1H_{arom}$, *J* 7 Hz), 7.95 d ($1H_{arom}$, *J* 8 Hz), 11.51 s (1H, NH). Found, %: C 70.39; H 4.17; N 11.86. $C_{14}H_{10}N_2O_2$. Calculated, % C 70.58; H 4.23; N 11.76.

Quinazolinediones **Vb–Vk** were similarly prepared.

3-(3-Chlorophenyl)quinazoline-2,4(1*H*,3*H*)-dione (Vb). Yield 2.26 g (83%), mp 261–262°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 7.30 d ($1H_{arom}$, *J* 7 Hz), 7.38 t ($1H_{arom}$, *J* 7 Hz), 7.45 s ($1H_{arom}$), 7.54 d ($1H_{arom}$, *J* 7 Hz), 7.62–7.78 m ($2H_{arom}$), 7.81 t ($1H_{arom}$, *J* 8 Hz), 8.19 d ($1H_{arom}$, *J* 7 Hz) 11.34 s (1H, NH). Found, %: C 61.69; H 3.21; N 10.16. $C_{14}H_9ClN_2O_2$. Calculated, %: C 61.66; H 3.33; N 10.27.

3-(4-Chlorophenyl)quinazoline-2,4(1*H*,3*H*)-dione (Vc). Yield 2.24 g (82%), mp 281–282°C (295°C [3]). ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 7.22 t ($1H_{arom}$, *J* 7 Hz), 7.39 d ($1H_{arom}$, *J* 7 Hz), 7.55 d $2H_{arom}$, *J* 8 Hz), 7.69 t ($1H_{arom}$, *J* 8 Hz), 7.86 d ($2H_{arom}$, *J* 8 Hz), 8.08 d ($1H_{arom}$, *J* 7 Hz), 11.28 s (1H, NH). Found, %: C 61.57; H 3.30; N 10.32. $C_{14}H_9ClN_2O_2$. Calculated, %: C 61.66; H 3.33; N 10.27.

3-(3,4-Dichlorophenyl)quinazoline-2,4(1*H*,3*H*)-dione (Vd). Yield 2.64 g (86%), mp 282–283°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 7.29–7.36 m ($2H_{arom}$), 7.58 d ($1H_{arom}$, *J* 8 Hz), 7.74 t ($1H_{arom}$, *J* 7 Hz), 7.95 d ($1H_{arom}$, *J* 8 Hz), 8.10 d ($1H_{arom}$, *J* 7 Hz), 8.26 s ($1H_{arom}$), 11.37 s (1H, NH). Found, %: C 54.68; H 2.61; N 9.16. $C_{14}H_8Cl_2N_2O_2$. Calculated, %: C 54.75; H 2.63; N 9.12.

3-Ethylquinazoline-2,4(1*H*,3*H*)-dione (Ve). Yield 1.05 g (55%), mp 196–197°C (198°C [14], 194–196°C [15]). ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 1.19 t (3H, CH_2CH_3, *J* 8 Hz), 3.98 q (2H, CH_2CH_3, *J* 7 Hz), 7.14–7.19 m ($2H_{arom}$), 7.59 t ($1H_{arom}$, *J* 7 Hz), 7.93 d ($1H_{arom}$, *J* 8 Hz), 11.28 s (1H, NH). Found, %: C 61.69; H 3.21; N 10.16. $C_{10}H_{10}N_2O_2$. Calculated, %: C 63.15; H 5.30; N 14.73.

3-Cyclohexylquinazoline-2,4(1*H*,3*H*)-dione (Vf). Yield 1.25 g (51%), mp 271–272°C (270–271° C [4, 14]). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.21–1.46 m ($3H_{aliph}$), 1.57–1.72 m ($3H_{aliph}$), 1.80–1.96 m ($2H_{aliph}$), 2.36–2.45 m ($2H_{aliph}$), 4.67–4.75 m ($1H_{aliph}$), 7.30 t ($1H_{arom}$, *J* 7 Hz), 7.39 d ($1H_{arom}$, *J* 7 Hz), 7.72 t ($1H_{arom}$, *J* 7 Hz), 8.06 d ($1H_{arom}$, *J* 8 Hz), 11.16 s (1H, NH). Found, %: C 68.78; H 6.61; N 11.46. $C_{14}H_{16}N_2O_2$. Calculated, %: C 68.83; H 6.60; N 11.47.

6-Bromo-3-phenylquinazoline-2,4(1*H*,3*H*)-dione (Vg). Yield 2.21 g (87%), mp 254–255°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 7.07–7.21 m ($3H_{arom}$), 7.39–7.50 m ($2H_{arom}$), 7.78 d ($1H_{arom}$, *J* 8 Hz), 8.10 d ($1H_{arom}$, *J* 8 Hz), 8.18 s ($1H_{arom}$), 11.47 s (1H, NH). Found, %: C 52.94; H 2.91; N 8.77. $C_{14}H_9BrN_2O_2$. Calculated, %: C 53.02; H 2.86; N 8.83.

6-Bromo-3-ethylquinazoline-2,4(1*H*,3*H*)-dione (Vh). Yield 1.40 g (52%), mp 218–219°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.20 t (3H, CH_2CH_3, *J* 8 Hz), 3.84 q (2H, CH_2CH_3, *J* 7 Hz), 7.82 d ($1H_{arom}$, *J* 8 Hz), 8.06 d ($1H_{arom}$, *J* 8 Hz), 8.14 s ($1H_{arom}$), 11.52 s (1H, NH). Found, %: C 44.69; H 3.30; N 10.36. $C_{10}H_9BrN_2O_2$. Calculated, %: C 44.63; H 3.37; N 10.41.

6-Bromo-3-cyclohexylquinazoline-2,4(1*H*,3*H*)-dione (Vi). Yield 1.81 g (56%), mp 230–231°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 1.15–1.40 m ($3H_{aliph}$), 1.54–1.76 m ($3H_{aliph}$), 1.85–1.96 m ($2H_{aliph}$), 2.28–2.37 m ($2H_{aliph}$), 4.70–4.79 m ($1H_{aliph}$), 7.76 d ($1H_{arom}$, *J* 8 Hz), 8.00 d ($1H_{arom}$, *J* 8 Hz), 8.12 s ($1H_{arom}$), 11.34 s (1H, NH). Found, %: C 57.59; H 5.53; N 11.28. $C_{14}H_{15}BrN_2O_2$. Calculated, %: C 52.03; H 4.68; N 8.67.

6,7-Dimethoxy-3-ethylquinazoline-2,4(1*H*,3*H*)-dione (Vj). Yield 1.60 g (64%), mp 287–288°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 1.26 t (3H, CH_2CH_3, *J* 8 Hz), 3.79 s (3H, OCH_3), 3.86 s (3H, OCH_3), 4.07 q (2H, CH_2CH_3, *J* 7 Hz), 6.56 s ($1H_{arom}$), 7.26 s ($1H_{arom}$), 10.97 s (1H, NH). Found, %: C 57.59; H 5.53; N 11.28. $C_{12}H_{14}N_2O_4$. Calculated, %: C 57.59; H 5.64; N 11.19.

6,7-Dimethoxy-3-cyclohexylquinazoline-2,4(1*H*,3*H*)-dione (Vk). Yield 1.70 g (56%), mp 288–290°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.28–1.51 m ($3H_{aliph}$), 1.61–1.74 m ($3H_{aliph}$), 1.80–1.97 m ($2H_{aliph}$), 2.29–2.41 m ($2H_{aliph}$), 3.80 s (3H, OCH_3), 3.88 s (3H, OCH_3), 4.70–4.80 m ($1H_{aliph}$), 6.62 s ($1H_{arom}$), 7.28 s ($1H_{arom}$), 11.09 sC (1H, NH). Found, %: C 63.09; H 6.60; N 9.11. $C_{16}H_{20}N_2O_4$. Calculated, %: C 63.14; H 6.62; N 9.20.

***N*-(2,5-Dimethoxyphenyl)-2-[2,4-dioxo-3-phenyl-3,4-dihydroquinazolin-1(2*H*)-yl]acetamide (VIa).** In 5 ml of 1M solution of sodium methylate in methanol (that was prepared by dissolving sodium in methanol with subsequent checking of the concentration by titration) was dissolved 1.19 g (5 mmol) of reagent **Va**. The solution was evaporated on a rotary evaporator, the residue was dissolved in anhydrous DMF, and a solution of 1.15 g (5 mmol) of 2-chloro-*N*-(2,5-dimethoxy-phenyl)acetamide

in anhydrous DMF was added. The solution obtained was heated for 10 min at 100°C and on cooling was poured into 50 ml of water. The precipitate was filtered off and recrystallized from a mixture 2-propanol–DMF. Yield 1.92 g (89%), mp 228–230°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.66 s (3H, OCH_3), 3.82 s (3H, OCH_3), 5.21 s (2H, CH_2), 6.64 d (1H$_{arom}$, *J* 10 Hz), 6.99 d (1H$_{arom}$, *J* 10 Hz), 7.63–7.74 m (3H$_{arom}$), 7.43 d (1H$_{arom}$, *J* 7 Hz), 7.48 d (1H$_{arom}$, *J* 7 Hz), 7.53 t (2H$_{arom}$, *J* 7 Hz), 7.39 s (1H$_{arom}$), 7.62 t (1H$_{arom}$, *J* 8 Hz), 8.21 d (1H$_{arom}$, *J* 8 Hz), 9.69 s (1H, NH). Found, %: C 66.74; H 4.88; N 9.71. $C_{24}H_{21}N_3O_5$. Calculated, %: C 66.81; H 4.91; N 9.74.

The alkylated derivatives of quinazolinediones **VIb–VIk** were obtained in a similar way.

Methyl 2-[2,4-dioxo-3-(3-chlorophenyl)-3,4-dihydroquinazolin-1(2*H*)-yl]acetate (VIb). Into a solution of 5 mmol of sodium salt **Vb** in anhydrous DMF was added 0.88 ml (10 mmol) of methyl 2-chloroacetate, the precipitate was recrystallized from 2-propanol. Yield 0.85 g (49%), mp 157–158°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 3.76 s (3H, OCH_3), 5.00 s (2H, CH_2), 7.28 d (1H$_{arom}$, *J* 6 Hz), 7.34 t (1H$_{arom}$, *J* 7 Hz), 7.41 s (1H$_{arom}$), 7.43 d (1H$_{arom}$, *J* 7 Hz), 7.47–7.53 m (2H$_{arom}$), 7.77 t (1H$_{arom}$, *J* 8 Hz), 8.11 d (1H$_{arom}$, *J* 7 Hz). Found, %: C 59.28; H 3.72; N 8.22. $C_{17}H_{13}ClN_2O_4$. Calculated, %: C 59.23; H 3.80; N 8.13.

1-[2-(3,4-Dimethoxyphenyl)-2-oxoethyl]-3-(4-chlorophenyl)quinazoline-2,4(1*H*,3*H*)-dione (VIc). Yield 1.31 g (58%), mp 160–162°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 3.76 s (3H, OCH_3), 3.81 s (3H, OCH_3), 5.34 s (2H, CH_2), 6.63 d (1H$_{arom}$, *J* 8 Hz), 7.08 s (1H$_{arom}$), 7.16–7.28 m (2H$_{arom}$), 7.46 d (1H$_{arom}$, *J* 8 Hz), 7.58 d (1H$_{arom}$, *J* 8 Hz), 7.86 d (2H$_{arom}$, *J* 8 Hz), 7.91 t (2H$_{arom}$, *J* 7 Hz), 8.08 d (1H$_{arom}$, *J* 7 Hz). Found, %: C 63.99; H 4.26; N 6.17. $C_{24}H_{19}ClN_2O_5$. Calculated, %: C 63.93; H 4.25; N 6.21.

3-(3,4-Dichlorophenyl)-1-(3-chlorobenzyl)-quinazoline-2,4(1*H*,3*H*)-dione (VId). Yield 1.96 g (91%), mp 183–185°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 4.82 s (2H, CH_2), 7.12–7.23 m (3H$_{arom}$), 7.30–7.39 m (3H$_{arom}$), 7.60 d (1H$_{arom}$, *J* 8 Hz), 7.79 t (1H$_{arom}$, *J* 7 Hz), 7.94 d (1H$_{arom}$, *J* 8 Hz), 8.08 d (1H$_{arom}$, *J* 7 Hz), 8.25 s (1H$_{arom}$). Found, %: C 58.35; H 2.98; N 6.58. $C_{21}H_{13}Cl_3N_2O_2$. Calculated, %: C 58.43; H 3.04; N 6.49.

***N*-*p*-Tolyl-2-[(2,4-dioxo-3-ethyl-3,4-dihydroquinazolin-1(2*H*)-yl]acetamide (VIe)**. Yield 1.33 g (79%), mp 232–233°C (2-propanol). ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 1.19 t (3H, CH_2CH_3, *J* 7 Hz), 2.22 s (3H, CH_3), 4.01 q (2H, CH_2CH_3, *J* 7 Hz), 4.95 s (2H, CH_2), 7.11 d (2H$_{arom}$, *J* 7 Hz), 7.32 t (1H$_{arom}$, *J* 7 Hz), 7.36 d (1H$_{arom}$, *J* 7 Hz), 7.42 d (2H$_{arom}$, *J* 7 Hz), 7.74 t (1H$_{arom}$, *J* 8 Hz), 8.10 d (1H$_{arom}$, *J* 7 Hz), 10.23 s (1H, NH). Found, %: C 67.60; H 5.60; N 12.33. $C_{19}H_{19}N_3O_3$. Calculated, %: C 67.64; H 5.68; N 12.45.

3-Cyclohexyl-1-[2-oxo-2-(*p*-tolyl)ethyl]quinazoline-2,4(1*H*,3*H*)-dione (VIf). To ensure dissolution of 3-cyclohexylquinazoline-2,4(1*H*,3*H*)-dione (**Vf**) to 5 ml of 1M sodium methylate solution was added 1 ml of anhydrous DMF. Yield 1.38 g (79%), mp 147–148°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.19–1.49 m (3H$_{aliph}$), 1.60–1.73 m (3H$_{aliph}$), 1.82–1.93 m (2H$_{aliph}$), 2.41–2.52 m (2H$_{aliph}$), 4.73–4.89 m (1H$_{aliph}$), 5.61 s (2H, CH_2), 7.09 d (1H$_{arom}$, *J* 7 Hz), 7.21 t (1H$_{arom}$, *J* 7 Hz), 7.38 d (2H$_{arom}$, *J* 8 Hz), 7.57 t (1H$_{arom}$, *J* 7 Hz), 7.99 d (2H$_{arom}$, *J* 8 Hz), 8.10 d (1H$_{arom}$, *J* 7 Hz). Found, %: C 75.74; H 6.86; N 7.97. $C_{22}H_{24}N_2O_2$. Calculated, %: C 75.83; H 6.94; N 8.04.

6-Bromo-3-phenyl-1-(4-chlorobenzyl)quinazoline-2,4(1*H*,3*H*)-dione (VIg). Yield 1.24 g (56%), mp 169–171°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 4.80 s (2H, CH_2), 7.05–7.20 m (3H$_{arom}$), 7.26 d (2H$_{arom}$, *J* 8 Hz), 7.39–7.50 m (2H$_{arom}$), 7.67 d (2H$_{arom}$, *J* 8 Hz), 7.81 d (1H$_{arom}$, *J* 8 Hz), 8.11 d (1H$_{arom}$, *J* 8 Hz), 8.18 s (1H$_{arom}$). Found, %: C 57.02; H 3.24; N 6.28. $C_{21}H_{14}BrClN_2O_2$. Calculated, %: C 57.10; H 3.19; N 6.34.

6-Bromo-1-methyl-3-ethylquinazoline-2,4(1*H*,3*H*)-dione (VIh). To a solution of sodium salt **Vh** in anhydrous DMF was added 0.94 ml (15 mmol) of methyl iodide. Yield 1.08 g (76%), mp 140–142°C (2-propanol). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.20 t (3H, CH_2CH_3, *J* 8 Hz), 3.57 s (3H, CH_3), 3.84 q (2H, CH_2CH_3, *J* 7 Hz), 7.82 d (1H$_{arom}$, *J* 8 Hz), 8.06 d (1H$_{arom}$, *J* 8 Hz), 8.14 s (1H$_{arom}$). Found, %: C 46.67; H 3.84; N 9.93. $C_{11}H_{11}BrN_2O_2$. Calculated, %: C 46.67; H 3.92; N 9.89.

1-Allyl-6-bromo-3-cyclohexylquinazoline-2,4(2*H*,3*H*)-dione (VIi). To ensure dissolution of dione **VI** to 5 ml of 1M sodium methylate solution was added 1 ml of anhydrous DMF. Into a solution of 5 mmol of sodium salt in DMF obtained by evaporation of methanol was added 0.82 ml (10 mmol) of allyl chloride. Yield 1.62 g (89%), mp 90–91°C (2-propanol). ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 1.15–1.40 m (3H$_{aliph}$), 1.54–1.76 m (3H$_{aliph}$), 1.85–1.96 m (2H$_{aliph}$), 2.28–2.37 m (2H$_{aliph}$), 4.48 d.d (2H, CH_2, ^2J 3, ^3J 8 Hz),

4.70–4.79 m (1H_{aliph}), 5.38 d.d (1H, =CH_2, ^2J 3, ^3J 9 Hz), 5.66 d.d (1H, =CH_2, ^2J 4, ^3J 18 Hz), 6.48–6.56 m (1H, –CH=CH_2), 7.76 d (1H_{arom}, J 8 Hz), 8.00 d (1H_{arom}, J 8 Hz), 8.12 s (1H_{arom}), 11.34 s (1H, NH). Found, %: C 56.14; H 5.27; N 7.74. $C_{17}H_{19}BrN_2O_2$. Calculated, %: C 56.21; H 5.27; N 7.71.

6,7-Dimethoxy-1,3-diethylquinazoline-2,4(1*H*,3*H*)-dione (VIj). To a solution of 5 mmol of sodium salt of dione **Vj** in anhydrous DMF was added 0.75 ml (10 mmol) of ethyl bromide. Yield 1.07 g (77%), mp 149–151°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 1.11 t (3H, CH_2CH_3, J 8 Hz), 1.24 t (3H, CH_2CH_3, J 8 Hz), 3.80 s (3H, OCH_3), 3.89 s (3H, OCH_3), 4.07 q (2H, CH_2CH_3, J 7 Hz), 4.19 q (2H, CH_2CH_3, J 7 Hz), 6.62 s (1H_{arom}), 7.24 s (1H_{arom}). Found, %: C 60.42; H 6.60; N 10.10. $C_{14}H_{18}N_2O_4$. Calculated, %: C 60.42; H 6.52; N 10.07.

6,7-Dimethoxy-1-[2-(4-methoxyphenyl)-2-oxoethyl)-3-cyclohexylquinazoline-2,4(1*H*,3*H*)-dione (VIk). To ensure dissolution of dione **Vk** to 5 ml of 1M sodium methylate solution was added 2 ml of anhydrous DMF. Yield 1.11 g (49%), mp 185–186°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4), δ, ppm: 1.16–1.48 m (3H_{aliph}), 1.53–1.72 m (3H_{aliph}), 1.80–1.91 m (2H_{aliph}), 2.36–2.50 m (2H_{aliph}), 3.77 s (3H, OCH_3), 3.84 s (3H, OCH_3), 3.91 s (3H, OCH_3), 4.69–4.85 m (1H_{aliph}), 5.60 s (2H, CH_2), 6.70 s (1H_{arom}), 7.03 d (2H_{arom}, J 8 Hz), 7.41 s (1H_{arom}), 8.08 d (2H_{arom}, J 8 Hz). Found, %: C 66.42; H 6.28; N 6.17. $C_{25}H_{28}N_2O_6$. Calculated, %: C 66.36; H 6.24; N 6.19.

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