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Dedicated to the Full Member of the Russian Academy of Sciences V.A.Tartakovsky on occasion of his 75th birthday

Synthesis of Substituted 4-([1,2,4]Triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)quinolines

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Abstract—4-Amino-5-R^1-4*H*-1,2,4-triazole-3-thiols react with 2-R^2-6-R^3-quinoline-4-carboxylic acids in phosphoryl chloride to give 2-R^2-6-R^3-4-(3-R^1-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)quinolines.

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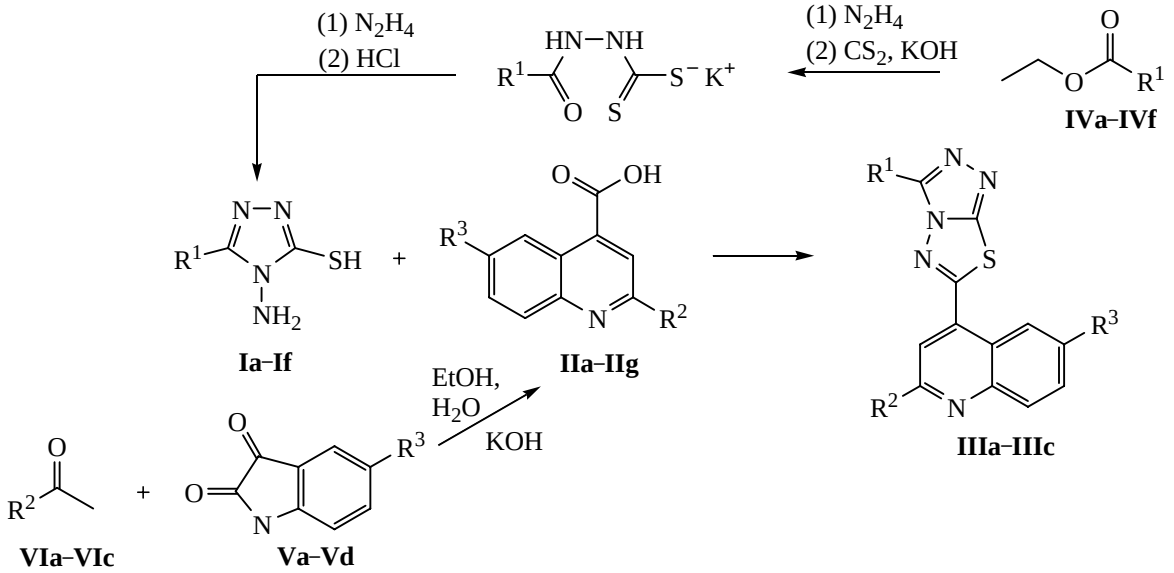
1,2,4-Triazole derivatives exhibit a broad spectrum of biological activity, including anticarcinogenic [1], antimicrobial [2], antiphlogistic [3], fungicidal [4], and antiviral [5]; some compounds of this series are used in medical practice [6]. In this connection, the fused [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole system seems to be promising [7–9], and both methods for preparation [10–14] and properties [15, 16] of these compounds have been extensively studied in the recent years. As follows from the data of [10–16], the most convenient procedure for the synthesis of [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazole derivatives is based on the reaction of 5-substituted 4-amino-4*H*-1,2,4-triazole-3-thiols with carboxylic acids. Biological activity is also intrinsic to compounds containing a quinoline fragment, and numerous quinoline derivatives are used as medical agents [17].

In the present work we made an attempt to combine the above pharmacophoric fragments in a single molecule. For this purpose we synthesized 1,2,4-triazoles **Ia**–**If** and quinoline-4-carboxylic acids **IIa**–**IIg** and examined reactions between these reagents in $POCl_3$. The reactions involved closure of 1,3,4-thiadiazole ring, and the products were 2-R^2-6-R^3-4-(3-R^1-[1,2,4]triazolo-[3,4-*b*][1,3,4]thiadiazol-6-yl)quinolines **IIIa**–**IIIq** (Scheme 1). 5-Substituted 4-amino-4*H*-1,2,4-triazole-3-thiols **Ia**–**If** were synthesized from carboxylic acid esters **IVa**–**IVf** [7, 18] as shown in Scheme 1. Cinchoninic acids **IIa**–**IIg** were prepared in one step according to Pfitzinger [19] from 5-substituted isatins **Va**–**Vd** and ketones **VIa**–**VIc** (Scheme 1).

The cyclizations of compounds **Ia**–**If** with **IIa**–**IIg** took 10–18 h. More prolonged heating of the reaction mixture resulted in tarring. The first reaction step is the transformation of acids **IIa**–**IIg** into the corresponding acyl chlorides which rapidly react with triazoles **Ia**–**If** at the amino group. In some cases, a solid material separated from the reaction mixture and dissolved before the reaction was complete (hydrogen chloride no longer evolved). Standard treatment of the reaction mixture (hydrolysis of excess $POCl_3$, followed by neutralization) often gave the products as dark viscous materials which were difficult to purify. We found that the more effective procedure is hydrolysis of the reaction mixture with a 5 N solution of sodium hydroxide on cooling. When preliminarily prepared quinoline-4-carbonyl chlorides were used, no tarring was observed, and the yields of **IIIa**–**IIIq** were larger. These data indicate that quinolin-4-carboxylic acids are not very reactive in the cyclizations with triazoles **Ia**–**If**. 1,2,3,4-Tetrahydroacridine-9-carboxylic acid (**IIh**) failed to react with 4-amino-5-R^1-4*H*-1,2,4-triazole-3-thiols **Ia**–**Id** (Scheme 2).

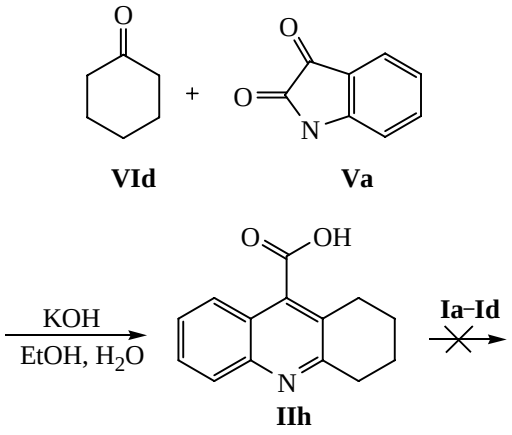
To conclude, we have shown that reactions of 5-substituted 4-amino-4*H*-1,2,4-triazole-3-thioles with quinoline-4-carboxylic acids on heating in phosphoryl chloride involve cyclization with formation of 1,3,4-thiadiazole ring. This reaction may be useful for combinatorial syntheses of type **III** compounds having various R^1–R^3 substituents with a view to test them for biological activity.

Scheme 1.



I, IV, R^1 = Et (**a**), Pr (**b**), 2-furyl (**c**), Ph (**d**), $PhCH_2$ (**e**), 4-$MeOC_6H_4CH_2$ (**f**); **II**, R^2 = Me, R^3 = H (**a**), Cl (**b**), Br (**c**); R^2 = Ph, R^3 = H (**d**), Me (**e**), Br (**f**); R^2 = 4-MeC_6H_4, R^3 = H (**g**); **III**, R^1 = Et: R^2 = Me, R^3 = Cl (**a**), Br (**b**); R^2 = Ph, R^3 = H (**c**), Me (**d**), Br (**e**); R^1 = Pr, R^2 = Ph, R^3 = Me (**f**), Br (**g**); R^1 = 2-furyl: R^2 = Me, R^3 = H (**h**); R^2 = Ph, R^3 = H (**i**), Br (**j**); R^1 = Ph: R^2 = Me, R^3 = H (**k**); R^2 = Ph, R^3 = Me (**l**), Br (**m**); R^2 = 4-MeC_6H_4, R^3 = H (**n**); R^1 = $PhCH_2$, R^2 = Ph, R^3 = Me (**o**), Br (**p**); R^1 = 4-$MeOC_6H_4CH_2$, R^2 = Ph, R^3 = Br (**r**); **V**, R^3 = H (**a**), Me (**b**), Cl (**c**), Br (**d**); **VI**, R^2 = Me (**a**), Ph (**b**), 4-MeC_6H_4 (**c**).

Scheme 2.



EXPERIMENTAL

The ^1H NMR spectra were recorded on a Varian Mercury spectrometer at 400 MHz from solutions in DMSO-d_6–CCl_4; the chemical shifts were measured relative to the solvent signal (DMSO-d_5, δ 2.50 ppm).

Compounds **Ia**–**If** were synthesized according to the procedures reported in [7, 18] (the yields were calculated on the initial carboxylic acid ester **IVa**–**IVf**): **Ia**, yield 67%, mp 159–160°C (from water); **Ib**, yield 58%, mp 112–113°C (from aqueous ethanol); **Ic**, yield 61%, mp 205–206°C (from aqueous ethanol); **Id**, yield 76%, mp 206–208°C (from aqueous ethanol); **Ie**, yield 62%, mp 180°C (from ethanol); **If**, yield 55%, mp 199–200°C (from benzene). Quinoline-4-carboxylic acids **IIa**–**IIg** were prepared as described in [20] and were purified by recrystallization from aqueous alcohol: **IIa**, yield 84%, mp 183.5–184°C; **IIb**, yield 76%, mp 213°C; **IIc**, yield 92%, mp 229–230°C; **IId**, yield 84%, mp 233.5–234°C; **IIe**, yield 74%, mp 275°C; **IIf**, yield 81%, mp >300°C; **IIg**, yield 89%, mp 242°C; **IIh**, yield 88%, mp 284–285°C.

2,6-Substituted 4-(3-R-[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)quinolines IIIa–IIIq (*general procedure*). Phosphoryl chloride, 10 ml, was added to a mixture of 5 mmol of 5-substituted 4-amino-4*H*-1,2,4-triazole-3-thiol **Ia**–**If** and 5 mmol of acid **IIa**–**IIg**, and the mixture was heated under reflux until hydrogen chloride no longer evolved. The mixture was cooled to room temperature, and the viscous material thus formed was added in small portions to a mixture of 20 g of sodium hydroxide, 50 ml of water, and 50 g of ice using a cooling bath. The mixture was kept for 0.5 h at room temperature and adjusted to pH 8 (if necessary) by adding a 2 M

solution of sodium hydroxide. The precipitate was filtered off, washed on a filter with a 2 M solution of sodium hydroxide (up to 15 ml) and warm water (up to 500 ml), dried in air, and recrystallized from appropriate solvent (if necessary, with addition of charcoal).

6-Chloro-4-(3-ethyl[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)-2-methylquinoline (IIIa). Yield 64%, mp 214.5°C. ^{1}H NMR spectrum, δ, ppm: 1.50 t (3H, Me, ^3J = 7.6Hz), 2.78 s (3H, Me), 3.18 q (2H, CH_2, ^3J = 7.6 Hz), 7.76 d.d (1H, 7-H, ^4J = 2.4, ^3J = 9.2 Hz), 7.84 s (1H, 3-H), 8.03 d (1H, 8-H, ^3J = 8.8 Hz), 8.66 d (1H, 5-H, ^4J = 2.4 Hz). Found, %: C 54.42; H 3.58; N 21.14; S 9.58. $C_{15}H_{12}ClN_5S$. Calculated, %: C 54.63; H 3.67; N 21.23; S 9.72.

6-Bromo-4-(3-ethyl[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)-2-methylquinoline (IIIb). Yield 71%, mp 210°C. ^{1}H NMR spectrum, δ, ppm: 1.50 t (3H, Me, ^3J = 7.6 Hz), 2.78 s (3H, Me), 3.17 q (2H, CH_2, ^3J = 7.6 Hz), 7.84 s (1H, 3-H), 7.88 d.d (1H, 7-H, ^4J = 1.6, ^3J = 8.8 Hz), 7.96 d (1H, 8-H, ^3J = 8.8 Hz), 8.83 d (1H, 5-H, ^4J = 1.6 Hz). Found, %: C 48.28; H 3.08; N 18.56; S 8.41. $C_{15}H_{12}BrN_5S$. Calculated, %: C 48.14; H 3.23; N 18.71; S 8.57.

4-(3-Ethyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)-6-phenylquinoline (IIIc). Yield 78%, mp 172°C. ^{1}H NMR spectrum, δ, ppm: 1.50 t (3H, Me, ^3J = 7.6 Hz), 3.18 q (2H, CH_2, ^3J = 7.6 Hz), 7.50–7.59 m (3H, Ph), 7.71 t (1H, 7-H, ^3J = 8.8 Hz), 7.88 t (1H, 6-H, ^3J = 8.8 Hz), 8.20 d (1H, 8-H, ^3J = 8.8 Hz), 8.28–8.36 m (3H, Ph, 3-H), 8.58 d (1H, 5-H, ^3J = 8.4 Hz). Found, %: C 66.98; H 4.28; N 19.56; S 8.85. $C_{20}H_{15}N_5S$. Calculated, %: C 67.21; H 4.23; N 19.59; S 8.97.

4-(3-Ethyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)-6-methyl-2-phenylquinoline (IIId). Yield 56%, mp 205°C. ^{1}H NMR spectrum, δ, ppm: 1.51 t (3H, Me, ^3J = 7.6 Hz), 2.58 s (3H, Me), 3.18 q (2H, CH_2, ^3J = 7.6 Hz), 7.43–7.58 m (3H, Ph), 7.69 d (1H, 7-H, ^3J = 8.4 Hz), 8.08 d (1H, 8-H, ^3J = 8.8 Hz), 8.24–8.33 m (4H, Ph, 3-H, 5-H). Found, %: C 67.83; H 4.69; N 18.78; S 8.53. $C_{21}H_{17}N_5S$. Calculated, %: C 67.90; H 4.61; N 18.85; S 8.63.

6-Bromo-4-(3-ethyl[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)-2-phenylquinoline (IIIe). Yield 84%, mp 266°C. ^{1}H NMR spectrum, δ, ppm: 1.52 t (3H, Me, ^3J = 7.6 Hz), 3.18 q (2H, CH_2, ^3J = 7.6 Hz), 7.50–7.61 m (3H, Ph), 7.96 d.d (1H, 7-H, ^4J = 2.0, ^3J = 9.0 Hz), 8.12 d (1H, 8-H, ^3J = 9.0 Hz), 8.31 d (2H, Ph, ^3J = 7.4 Hz), 8.39 s (1H, 3-H), 8.82 d (1H, 5-H, ^4J = 2.0 Hz). Found, %: C 54.76; H 3.17; N 16.07; S 7.25. $C_{20}H_{14}BrN_5S$. Calculated, %: C 55.05; H 3.23; N 16.05; S 7.35.

6-Methyl-4-(3-propyl[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)-2-phenylquinoline (IIIf). Yield 43%, mp 186°C. ^{1}H NMR spectrum, δ, ppm: 1.10 t (3H, Me, ^3J = 7.2 Hz), 1.90–2.01 m (2H, CH_2), 2.57 s (3H, Me), 3.13 t (2H, CH_2, ^3J = 7.2 Hz), 7.45–7.57 m (3H, Ph), 7.69 d (1H, 7-H, ^3J = 8.7 Hz), 8.08 d (1H, 8-H, ^3J = 8.7 Hz), 8.24–8.32 m (4H, Ph, 3-H, 5-H). Found, %: C 68.61; H 4.89; N 18.20; S 8.14. $C_{22}H_{19}N_5S$. Calculated, %: C 68.55; H 4.97; N 18.17; S 8.32.

6-Bromo-4-(3-propyl[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)-2-phenylquinoline (IIIg). Yield 55%, mp 253°C. ^{1}H NMR spectrum, δ, ppm: 1.12 t (3H, Me, ^3J = 7.2 Hz), 1.92–2.01 m (2H, CH_2), 3.14 t (2H, CH_2, ^3J = 7.2 Hz), 7.51–7.58 m (3H, Ph), 7.96 d.d (1H, 7-H, ^4J = 1.6, ^3J = 8.8 Hz), 8.12 d (1H, 8-H, ^3J = 8.8 Hz), 8.31 d (2H, Ph, ^3J = 7.6 Hz), 8.38 s (1H, 3-H), 8.81 br.s (1H, 5-H). Found, %: C 55.92; H 3.51; N 15.68; S 7.20. $C_{21}H_{16}BrN_5S$. Calculated, %: C 56.01; H 3.58; N 15.55; S 7.12.

4-{3-(2-Furyl)[1,2,4]triazolo[3,4-*b*][1,3,4]-thiadiazol-6-yl}-2-methylquinoline (IIIh). Yield 61%, mp 214°C. ^{1}H NMR spectrum, δ, ppm: 3.10 s (3H, Me), 6.73 d.d (1H, 42 -H, ^3J = 1.6, ^3J = 3.4 Hz), 7.28 d (1H, 3'-H, ^3J = 3.4 Hz), 7.69 pseudotriplet (1H, 7-H), 7.82 pseudotriplet (2H, 6-H), 7.83 s (1H, 3-H), 7.92 br.s (1H, 5'-H), 8.05 d (1H, 8-H, ^3J = 8.4 Hz), 8.62 d (1H, 5-H, ^3J = 8.4 Hz). Found, %: C 60.97; H 3.29; N 21.09; S 9.49. $C_{17}H_{11}N_5OS$. Calculated, %: C 61.25; H 3.33; N 21.01; S 9.62.

4-{3-(2-Furyl)[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl}-2-phenylquinoline (IIIi). Yield 71%, mp 208°C. ^{1}H NMR spectrum, δ, ppm: 6.72 d.d (1H, 4'-H, ^3J = 1.6, 3.2 Hz), 7.30 d (1H, 3'-H, ^3J = 3.2 Hz), 7.47–7.59 m (3H, Ph), 7.74 pseudotriplet (1H, 7-H), 7.88 pseudotriplet (2H, 6-H), 7.92 d (1H, 52 -H, ^3J = 1.6 Hz), 8.20 d (1H, 8-H, ^3J = 8.4 Hz), 8.32 d (2H, Ph, ^3J = 7.2 Hz), 8.39 s (1H, 3-H), 8.61 d (1H, 5-H, ^3J = 8.4 Hz). Found, %: C 66.71; H 3.25; N 17.60; S 8.21. $C_{22}H_{13}N_5OS$. Calculated, %: C 66.82; H 3.31; N 17.71; S 8.11.

6-Bromo-4-{3-(2-furyl)[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl}-2-phenylquinoline (IIIj). Yield 78%, mp 302°C. ^{1}H NMR spectrum, δ, ppm: 6.74 br.s (1H, 4'-H), 7.30 br.s (1H, 3'-H), 7.51–7.60 m (3H, Ph), 7.92 br.s (1H, 5'-H), 7.95–8.01 m (1H, 7-H), 8.11–

8.17 m (1H, 8-H), 8.30–8.36 m (2H, Ph), 8.46 s (1H, 3-H), 8.96 s (1H, 5-H). Found, %: C 55.56; H 2.48; N 14.70; S 6.81. $C_{22}H_{12}BrN_5OS$. Calculated, %: C 55.71; H 2.55; N 14.76; S 6.76.

2-Methyl-4-(3-phenyl[1,2,4]triazolo[3,4-*b*]-[1,3,4]thiadiazol-6-yl)quinoline (IIIk). Yield 64%, mp 218.5°C. ^{1}H NMR spectrum, δ, ppm: 2.82 s (3H, Me), 7.51–7.60 m (3H, Ph), 7.69 pseudotriplet (1H, 7-H), 7.84 pseudotriplet (1H, 6-H), 7.85 s (1H, 3-H), 8.08 d (1H, 8-H, ^3J = 8.0 Hz), 8.28–8.32 m (2H, Ph), 8.60 d (1H, 5-H, ^3J = 8.0 Hz). Found, %: C 66.56; H 3.69; N 20.27; S 9.26. $C_{19}H_{13}N_5S$. Calculated, %: C 66.45; H 3.82; N 20.39; S 9.34.

6-Methyl-2-phenyl-4-(3-phenyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)quinoline (IIIl). Yield 52%, mp 238°C. ^{1}H NMR spectrum, δ, ppm: 2.57 s (3H, Me), 7.45–7.60 m (6H, Ph), 7.68 d (1H, 7-H, ^3J = 8.2 Hz), 8.08 d (1H, 8-H, ^3J = 8.2 Hz), 8.24–8.35 m (5H, Ph, 5-H), 8.40 s (1H, 3-H). Found, %: C 71.51; H 3.96; N 16.74; S 7.55. $C_{25}H_{17}N_5S$. Calculated, %: C 71.58; H 4.08; N 16.69; S 7.64.

6-Bromo-2-phenyl-4-(3-phenyl[1,2,4]triazolo-[3,4-*b*][1,3,4]thiadiazol-6-yl)quinoline (IIIm). Yield 69%, mp 277.5°C. ^{1}H NMR spectrum, δ, ppm: 7.50–7.63 m (6H, Ph), 7.96 d.d (1H, 7-H, ^4J = 1.6, ^3J = 8.8 Hz), 8.13 d (1H, 8-H, ^3J = 8.8 Hz), 8.30–8.38 m (4H, Ph), 8.45 s (1H, 3-H), 8.99 br.s (1H, 5-H). Found, %: C 59.38; H 2.94; N 14.31; S 6.58. $C_{24}H_{14}BrN_5S$. Calculated, %: C 59.51; H 2.91; N 14.46; S 6.62.

2-(4-Methylphenyl)-4-(3-phenyl[1,2,4]triazolo-[3,4-*b*][1,3,4]thiadiazol-6-yl)quinoline (IIIn). Yield 67%, mp 239°C. ^{1}H NMR spectrum, δ, ppm: 2.44 s (3H, Me), 7.35 d (2H, C_6H_4, ^3J = 8.0 Hz), 7.50–7.60 m (3H, Ph), 7.70 pseudotriplet (1H, 7-H), 7.87 pseudotriplet (1H, 6-H), 8.19 d (1H, 8-H, ^3J = 8.8 Hz), 8.22 d (2H, C_6H_4, ^3J = 8.0 Hz), 8.30–8.34 m (2H, Ph), 8.37 s (1H, 3-H), 8.56 d (1H, 5-H, ^3J = 8.4 Hz). Found, %: C 71.68; H 3.99; N 16.42; S 7.61. $C_{25}H_{17}N_5S$. Calculated, %: C 71.58; H 4.08; N 16.69; S 7.64.

4-(3-Benzyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)-6-methyl-2-phenylquinoline (IIIo). Yield 54%, mp 247°C. ^{1}H NMR spectrum, δ, ppm: 2.54 s (3H, Me), 4.52 s (2H, CH_2), 7.26 t (1H, Ph, ^3J = 7.4 Hz), 7.34 t (2H, Ph, ^3J = 7.4 Hz), 7.43 d (2H, Ph, ^3J = 7.4 Hz), 7.46–7.57 m (3H, Ph), 7.67 d (1H, 7-H, ^3J = 8.8 Hz), 8.05 d (1H, 8-H, ^3J = 8.8 Hz), 8.20 s (1H, 5-H), 8.24 s (1H, 3-H), 8.25 d (3H, Ph, ^3J = 7.6 Hz). Found, %: C 71.80; H 4.36; N 16.04; S 7.46. $C_{26}H_{19}N_5S$. Calculated, %: C 72.03; H 4.42; N 16.15; S 7.37.

4-(3-Benzyl[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl)-6-bromo-2-phenylquinoline (IIIp). Yield 58%, mp 251°C. ^{1}H NMR spectrum, δ, ppm: 4.53 s (2H, CH_2), 7.21–7.58 m (8H, Ph), 7.90–8.00 m (1H, 7-H), 8.05–8.14 m (1H, 8-H), 8.25–8.38 m (3H, Ph, 3-H), 8.80 s (1H, 5-H). Found, %: C 60.19; H 3.31; N 14.11; S 6.30. $C_{25}H_{16}BrN_5S$. Calculated, %: C 60.25; H 3.24; N 14.05; S 6.43.

6-Bromo-4-{3-(4-methoxybenzyl)[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazol-6-yl}-2-phenylquinoline (IIIq). Yield 61%, mp 229.5°C. ^{1}H NMR spectrum, δ, ppm: 3.73 s (3H, MeO), 4.43 s (2H, CH_2), 6.88 d (2H, C_6H_4, ^3J = 8.8 Hz), 7.36 d (2H, C_6H_4, ^3J = 8.8 Hz), 7.50–7.57 m (3H, Ph), 7.96 d.d (1H, 7-H, ^4J = 1.8, ^3J = 9.2 Hz), 8.10 d (1H, 8-H, ^3J = 9.2 Hz), 8.29 d (2H, Ph, ^3J = 7.6 Hz), 8.36 s (1H, 3-H), 8.96 d (1H, 5-H, ^4J = 1.8 Hz). Found, %: C 58.78; H 3.38; N 13.18; S 6.12. $C_{26}H_{18}BrN_5OS$. Calculated, %: C 59.10; H 3.43; N 13.25; S 6.07.

REFERENCES

1. Al-Soud, Y.A., Al-Masoudi, N.A., and Ferwanah, A.E.-R.S., *Bioorg. Med. Chem*., 2003, vol. 11, p. 1701; Holla, B.S., Veerendra, V., Shivananda, M.K., and Poojary, B., *Eur. J. Med. Chem*., 2003, vol. 38, p. 759; Turan-Zitouni, G., Sivaci, M., Kilic, F.S., and Erol, K., *Eur. J. Med. Chem*., 2001, vol. 36, p. 685; Bekircan, O., Kuxuk, M., Kahveci, B., and Kolayl, S., *Arch. Pharm*., 2005, vol. 338, p. 365.
2. Malbec, F., Milcent, R., Vicart, P., and Bure, A.M., *J. Heterocycl. Chem*., 1984, vol. 21, p. 1769; Gulerman, N., Rollas, S., Kiraz, M., Ekinci, A.C., and Vidin, A., *Farmaco*, 1997, vol. 52, p. 691.
3. Wade, P.C., Vogt, B.R., Kissick, T.P., Simpkins, L.M., Palmer, D.M., and Millonig, R.C., *J. Med. Chem*., 1982, vol. 25, p. 331; Modzelewska, V. and Kalabun, J., *Pharmazie*, 1999, vol. 54, p. 503.
4. Rollas, S., Kalyoncuoglu, N., Sur-Altiner, D., and Yegenoglu, Y., *Pharmazie*, 1993, vol. 48, p. 308; Murabayashi, A., Masuko, M., Niikawa, M., Shirane, N., Futura, T., Hayashi, Y., and Makisumi, Y., *J. Pestic. Sci*., 1991, vol. 16, p. 419.
5. Farghaly, A.-R., De Clercq, E., and El-Kashef, H., *Arkivoc*, 2006, part (x), p. 137.
6. Clemons, M., Coleman, R.E., and Verma, S., *Cancer Treat. Rev*., 2004, vol. 30, p. 325; Johnston, G.A.R., *Curr. Top. Med. Chem*., 2002, vol. 2, p. 903; Shujuan, S., Hongxiang, L., Gao, Y., Fan, P., Ma, V., Ge, W., and Wang, X., *J. Pharm. Biomed. Anal*., 2004, vol. 34, p. 1117; Bekircan, O. and Bektas, H., *Molecules*, 2006, vol. 11, p. 469.
7. Zhang, L.-X., Zhang, A.-J., Chen, X.-X., Lei, X.-X., Nan,

X.-Y., Chen, D.-Y., and Zhang, Z.-Y., *Molecules*, 2002, vol. 7, p. 681.
8. Gupta, R., Sudan, S., Mengi, V., and Kachroo, P.L., *Indian J. Chem., Sect. B*, 1996, vol. 35, p. 621.
9. Zhang, Q., Pan, J., Zheng, R.-L., and Wang, Q., *Pharmazie*, 2005, vol. 60, p. 378.
10. Li, D., Long, D., and Fu, H., *Phosphorus, Sulfur Silicon Relat. Elem*., 2006, vol. 181, p. 519.
11. Bhat, K.S., Prasad, D.J., Poojary, B., and Holla, B.S., *Phosphorus, Sulfur Silicon Relat. Elem*., 2004, vol. 179, p. 1595.
12. Dong, H.-S. and Wang, B., *J. Chin. Chem. Soc*., 2005, vol. 52, p. 103.
13. Xu, P.F., Zhang, Z.H., Hui, X.P., Zhang, Z.Y., and Zheng, R.L., *J. Chin. Chem. Soc*., 2004, vol. 51, p. 315.
14. Li, D., Long, D., and Fu, H., *Synth. Commun*., 2005, vol. 35, p. 2495.
15. Spaliñska, K., Foks, H., Kedzia, A., Wierzbowska, M., Kwapisz, E., Gebska, A., and Zilkó³wska-Klinkosz, M., *Phosphorus, Sulfur Silicon Relat. Elem*., 2006, vol. 181, p. 609.
16. Demirbas, N., Demirbas, A., Karaoglu, S.A., and Zelik, E., *Arkivoc*, 2005, part (i), p. 75.
17. Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Moscow: Novaya Volna, 2000, vols. 1, 2.
18. *Sint. Geterotsikl. Soedin*. (Erevan), 1960, vol. 5, p. 9.
19. Hassner, A. and Stumer, C., *Organic Syntheses Based on Name Reactions and Unnamed Reactions*, Oxford: Pergamon, 1994, p. 297.
20. Tietze, L.-F. and Eicher, T., *Reactions and Syntheses in the Organic Chemistry Laboratory*, Mill Valley, California: University Science Books, 1989. Translated under the title *Preparativnaya organicheskaya khimiya*, Moscow: Mir, 1999, p. 384.