DOI 10.1007/s10593-018-2351-6

Chemistry of Heterocyclic Compounds **2018**, *54*(8), 784–788

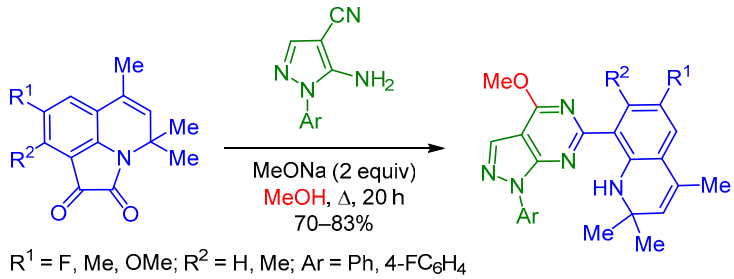
Efficient synthesis of substituted 8-(pyrazolo[3,4-*d*]pyrimidin-6-yl)-1,2-dihydroquinolines

Svetlana M. Medvedeva[1], Yevgeniya A. Kosheleva[1], Mariya A. Berdnikova[1], Khidmet S. Shikhaliev[1]*

[1] *Voronezh State University, 1 Universitetskaya Sq., Voronezh 394018, Russia; e-mail: chocd261@chem.vsu.ru*

Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2018, *54*(8), 784–788

Submitted June 29, 2018
Accepted September 17, 2018



An effective method for the synthesis of 8-(1-aryl-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl)-2,2,4-trimethyl-1,2-dihydroquinolines was developed on the basis of a three-component reaction between substituted 4,4,6-trimethyl-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-diones and 5-amino-1-aryl-1*H*-pyrazole-4-carbonitriles in refluxing methanol in the presence of an excess of sodium methoxide. HPLC-MS analysis showed that the cascade process started by addition of methanol molecule to the nitrile group of aminopyrazolecarbonitrile.

Keywords: 5-aminopyrazole-4-carbonitrile, pyrazolo[3,4-*d*]pyrimidine, 8-(1*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl)-1,2-dihydroquinoline, pyrrolo[3,2,1-*ij*]quinoline-1,2-dione, 2,2,4-trimethyl-1,2-dihydroquinoline, hybrid molecules.

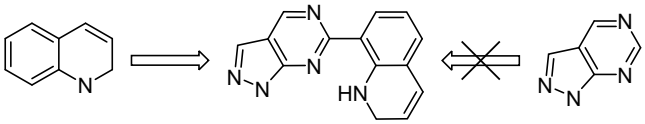
The concept of hybrid drug molecules is gaining importance in medicinal chemistry, as the combination of structural features with different pharmacological profiles in one molecule may be necessary for the minimization of side effects, enhancing the therapeutic efficacy or reducing the resistance to it, as well for expanding the range of therapeutic use. The design of such drugs is based on assembling multifunctional hybrid molecules by covalently linking together several active pharmaceutical compounds.[1–4] The design of hybrid molecules with structures containing several pharmacophoric moieties represents one of the rapidly developing directions in contemporary organic synthesis. Recently there has been a significant interest in hybrid molecules containing a quinoline ring system linked in linear sequence with various heterocycles,[5–8] for example, a pyrimidine ring.[8] Fused pyrimidines, especially pyrazolo[3,4-*d*]pyrimidines, exhibit a broad spectrum of biological effects (antitumor, antidiabetic, anti-inflammatory, antiviral, antimicrobial, tuberculostatic, and antifungal activity).[9] For these reasons, it is important to synthesize hybrid molecules combining the structural motifs of hydroquinoline and pyrazolo[3,4-*d*]pyrimidine.

A key task for synthetic organic chemistry is the development of simple and robust procedures for the preparation of heavily functionalized fused heterocyclic compounds. Therefore, we were interested in approaches requiring as few steps as possible that would provide new hybrid heterocyclic systems in preparative yields.

The goal of this work was to develop an effective strategy for the synthesis of a hybrid heterocyclic system containing a linear sequence of hydroquinoline and pyrazolo[3,4-*d*]pyrimidine rings. The most preferred approach to this problem is based on the annulation of pyrazolopyrimidine system to an existing hydroquinoline ring (Scheme 1), due to the variety and relative simplicity of the methods available for synthesis of the latter.[9]

Among the multiple known routes for the synthesis of pyrazolo[3,4-*d*]pyrimidine system,[9] which have been described in recent years, we were particularly interested in a method on the basis of reaction between 5-amino-1-aryl-

Scheme 1

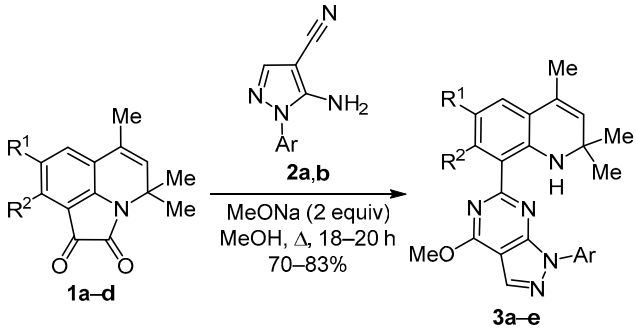


1*H*-pyrazole-4-carbonitriles and carbonyl compounds[10,11] in alcohol medium in the presence of bases. It has been reported in the literature[10,11] that the alcohol used in this reaction not only serves as a solvent, but also participates in the process as reactant. A probable mechanism has been proposed[10] for this reaction, in which the alcohol molecule adds to the imine intermediate formed by condensation of aldehyde with the amino group of aminopyrazole-carbonitrile, forming an amidine. The amidine intermediate subsequently undergoes cyclization and aromatization, resulting in substituted pyrazolo[3,4-*d*]pyrimidine. Besides that, another probable route has been discussed in the literature,[11] which uses an intramolecular Pinner reaction (involving the product from amino group addition to carbonyl group). The imino-1,3-oxazine obtained by this route was recyclized, giving the respective pyrimidinone, which was then aromatized and underwent nucleophilic attack by an alcohol molecule, resulting in the formation of the final product.

We have recently demonstrated[12] that a cascade reaction occurred between 5-amino-1-phenyl-1*H*-pyrazole-4-carbonitrile and *N*-substituted isatins in alcohol medium in the presence of sodium methoxide, resulting in the formation of substituted pyrazolo[3,4-*d*]pyrimidines. While proposing a likely mechanism for this process, we similarly to the authors of earlier studies[10,11] assumed that the first step of this cascade consists of a nucleophilic attack by pyrazole amino group on the β-carbonyl group of isatin. This step is followed by alcoholysis of nitrile group in the condensation product and cyclization to a spiro compound, and, finally, pyrrole ring opening.[12]

We had established earlier that the isatin ring system in substituted pyrrolo[3,2,1-*ij*]quinoline-1,2-diones was still reactive toward bisnucleophiles,[13,14] and the pyrrole-1,2-dione ring showed selective activity – cyclocondensation proceeded at the β-carbonyl group (counting from the nitrogen atom). We have also shown that, similarly to isatin, the pyrrole-1,2-dione moiety in pyrrolo[3,2,1-*ij*]-quinoline-1,2-diones underwent ring opening by the action of hydrogen peroxide in the presence of alkali, followed by decarboxylation. This led to the formation of hydroquinoline-8-carboxylic acids.[15] Thus it could be expected that the interaction of substituted 4,4,6-trimethyl-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-diones **1a**–**d** with 5-amino-1-aryl-1*H*-pyrazole-4-carbonitriles **2a**,**b** should proceed as a cascade reaction with pyrrole ring opening, similarly to the reaction of isatins,[12] and should result in the formation of pyrazolo[3,4-*d*]pyrimidinyl moiety at the C-8 position of 2,2,4-trimethyl-1,2-dihydroquinoline ring. The reaction was performed by refluxing equimolar amounts of the respective compounds **1a**–**d** and **2a**,**b** in MeOH in the presence of 2 equiv of sodium methoxide. It was found that the reaction was complete in 18–20 h and resulted in precipitation of product as yellow fine-grained solid. The reaction products were characterized by NMR spectroscopy and mass spectrometry and were identified as 8-(1-aryl-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl)-2,2,4-trimethyl-1,2-dihydroquinolines **3a**–**e** (Scheme 2).

Scheme 2



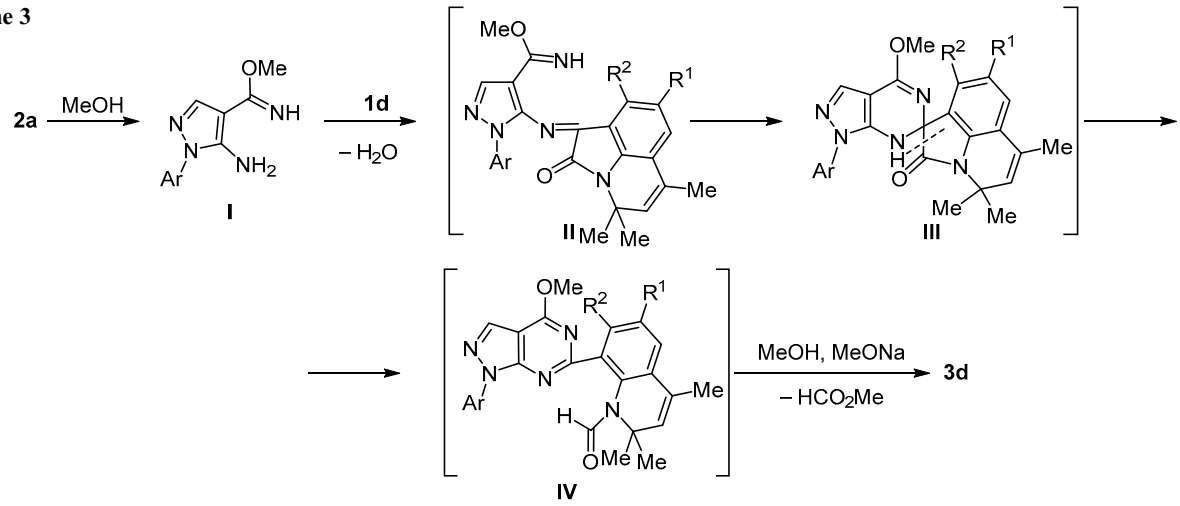
1a, **3a** R^1 = F; **1b**, **3b**,**c** R^1 = Me; **1d**, **3d**,**e** R^1 = OMe
1a,**b**,**d**, **3a**,**b**,**d**,**e** R^2 = H; **1c**, **3c** R^2 = Me
2a, **3a**–**d** Ar = Ph; **2b**, **3e** Ar = 4-FC_6H_4

It was established that the cycloaddition reaction duration and product yields were not significantly affected by the presence of a substituent at the C-7 position and the electronic properties of substituent at the C-6 position of hydroquinoline ring in compounds **1a**–**d**. Besides that, the reaction proceeded equally smoothly when there were no substituents in the aromatic ring (compound **2a**) and in the case of 4-fluoro-substituted aminopyrazolecarbonitrile **2b**.

The isolation of intermediate products – spiro[indole-3,6'-pyrazolo[3,4-*d*]pyrimidin]-2(1*H*)-ones from the reaction of 5-amino-1-phenyl-1*H*-pyrazole-4-carbonitrile with *N*-substituted isatins allowed our group to propose a likely mechanism for this cascade reaction.[12] However, we have also described a probable mechanism for such cascade cyclocondensation in another publication[16] that was deduced without isolation of intermediate products, instead using mass spectral monitoring (with electrospray ionization) in combination with liquid chromatography. That approach allowed us to analyze the composition of intermediates and formed products in the mixtures of reactions proceeding in liquid phase.[16]

In the current work, our purpose was to determine the reaction mechanism of the studied cascade reaction, and thus HPLC-MS analysis was performed for the mixture obtained during reaction of pyrroloquinolinedione **1d** with aminopyrazolecarbonitrile **2a** in MeOH. The reaction mixture was sampled 10–15 min, 20–25 min, and 4 h after the start of the reaction. After 15 min, the reaction mixture contained not only the starting pyrroloquinolinedione **1d** (*m*/*z* for $[M+H]^+$: calculated 258.1126 / found 258.1123) and aminopyrazolecarbonitrile **2a** (*m*/*z* 185.0822 / 185.0820), but also a compound with *m*/*z* 217.1082, which matched the molecular ion of product expected from the addition of MeOH molecule to the nitrile functional group of compound **2a** (compound **I**, *m*/*z* 217.1084) (Scheme 3). Besides that, the reaction mixture contained a compound with *m*/*z* 456.2019. Such *m*/*z* value matched the spiro product (*m*/*z* 456.2031) arising from cyclocondensation of

Scheme 3



pyrroloquinolinedione **1d** with intermediate **I**. In a relatively short time (25 min), the starting compound **1d** had disappeared from the reaction mixture, but the spiro product also disappeared after 4 h and the final product **3d** appeared (*m*/*z* 428.2082 / 428.2105). The reaction mixture also contained byproducts with *m*/*z* 276.1229 and 262.1428, corresponding to the molecular ions of compound formed by hydration of pyrroloquinolinedione **1d** (*m*/*z* 276.1231) and the methyl ester of 6-methoxy-2,2,4-trimethyl-1,2-dihydroquinoline-8-carboxylic acid (*m*/*z* 456.2031), generated during the decyclization of pyrroledione ring of the starting compound **1d** in the presence of MeONa in MeOH.

On the basis of the obtained data, it can be proposed that this cascade process probably occurred according to the mechanism shown in Scheme 3. Obviously, the first step involved the cyclization of β-carbonyl group of pyrroloquinolinedione **1d**, but not with the amino group of the starting compound **2a** (as assumed earlier by authors of publications[10,11] and previously proposed by our group[12]), but rather with the amino group of intermediate **I**. The condensation product **II** that was thus formed was converted to the spiro product **III**. The further transformation of spiro product **III** proceeded, as previously described by our group[12] (similarly to the spiroindole-3,2'-quinazoline in the presence of a base[17]) through pyrrole ring opening, which in our opinion led to the unstable intermediate **IV**. Alcoholysis of the amide group of intermediate **IV** in the presence of base resulted in the final product **3d**.

^{1}H NMR spectra of all compounds **3a**–**e** exhibited the signals of pyrazole ring methine proton and methoxy group protons as singlets in the characteristic regions of 8.38–8.55 and 4.13–4.24 ppm, respectively.[10,12] A characteristic spectral feature of products **3a**,**b**,**d**,**e** containing one substituent in the aromatic quinoline ring was the unusual downfield chemical shift (8.75–8.93 ppm) of the NH signals from hydroquinoline moiety, while for disubstituted product **3c** the signal of this proton was observed in the typical region at 5.27–5.29 ppm.[18,19] A similar change in the chemical shift of amino group proton signals was previously observed by our group in ^{1}H NMR spectra of hydroquinoline-8-carboxylic acids.[15] Apparently, this observation can be explained by the presence of an intramolecular hydrogen bond between the amino group hydrogen atom of hydroquinoline ring in compounds **3a**,**b**,**d**,**e** and the nitrogen atom at the C-7 position of the pyrazolopyrimidine moiety. It should be noted that X-ray structural analysis of one of the disubstituted products (compound **3d**) unequivocally confirmed the presence of an intramolecular hydrogen bond (Fig. 1, the hydrogen bond shown by dotted line). Intramolecular hydrogen bond was not present in compound **3c**, apparently due to the disrupted coplanarity in the molecule caused by the steric influence from the substituent at the C-7 position of the hydroquinoline ring.

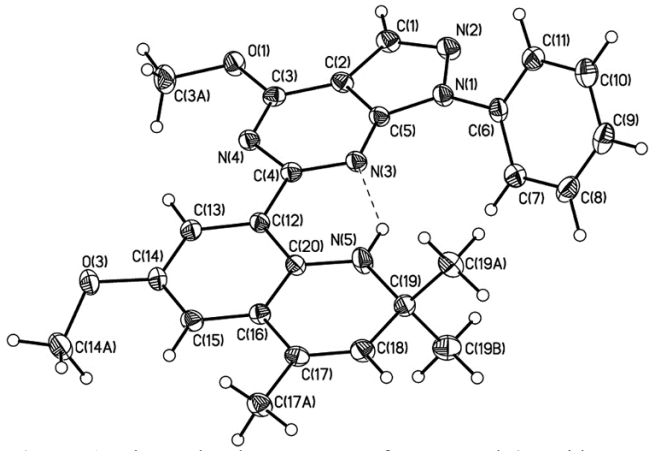


Figure 1. The molecular structure of compound **3d** with non-hydrogen atoms represented by thermal vibration ellipsoids of 50% probability.

Thus, in this work we have proposed a simple and convenient one-pot method for the synthesis of previously unknown 8-(1-aryl-4-methoxy-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl)-2,2,4-trimethyl-1,2-dihydroquinolines by cascade reaction of substituted 4,4,6-trimethyl-4*H*-pyrrolo[3,2,1-*ij*]quinoline-1,2-diones with 5-amino-1-aryl-1*H*-pyrazole-4-carbonitriles.

Experimental

^{1}H and ^{13}C NMR spectra were acquired on a Bruker DRX-500 instrument (500 and 125 MHz, respectively) in

DMSO-d_6. Residual solvent signals were used as internal standard (2.50 and 39.5 ppm for ^{1}H and ^{13}C nuclei, respectively). HPLC–MS analyses were performed on an Agilent Infinity 1260 liquid chromatograph equipped with an Agilent 6230 TOF mass selective detector. The conditions of chromatographic separation were the following: mobile phase 0.1% formic acid in MeCN (eluent A) / 0.1% formic acid in water (eluent B), gradient 0–100%: A, 3.5 min, 50%; A, 1.5 min, 50–100%; B, 3.5 min, 50%; B, 1.5 min, 50–0%; flow rate 0.4 ml/min, column – Poroshell 120 EC-C_{18} (4.6 × 50 mm, 2.7 μm), thermostat at 28°C, electrospray ionization (capillary voltage –3.5 kV; fragmentor voltage +191 V; OctRF +66 V – positive polarity). Melting points were determined on a PTP-M apparatus. The reaction progress and purity of the obtained compounds were determined by TLC on Merck TLC Silica gel 60 F_{254} plates using $CHCl_3$–MeOH, 10:1 mobile phase (visualization under UV light).

Commercially available reagents from Lancaster were used in the syntheses. The starting compounds **1a**–**d**[20] and **2a**,**b**[21] were synthesized according to literature procedures. The solvents were purified according to standard methods.

Synthesis of compounds 3a–e (General method). A mixture of the appropriate aminopyrazolecarbonitrile **2a**,**b** (2.5 mmol) and pyrroloquinolinedione **1a**–**d** (2.5 mmol) in MeOH (15–20 ml) was treated with 2 M sodium methoxide solution in MeOH (2.5 ml, 5 mmol), and the reaction mixture was refluxed for 18–20 h (control by TLC). The mixture was cooled and the precipitate that formed was filtered off, followed by recrystallization from *i*-PrOH.

6-Fluoro-8-(4-methoxy-1-phenyl-1*H*-pyrazolo[3,4-*d*]-pyrimidin-6-yl)-2,2,4-trimethyl-1,2-dihydroquinoline (3a). Yield 861 mg (83%), bright-yellow powder, mp 135–136°C (*i*-PrOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (6H, s, $2CH_3$); 1.95 (3H, s, CH_3); 4.22 (3H, s, OCH_3); 5.54 (1H, s, H-3 quinoline); 7.00 (1H, dd, *J* = 9.2, *J* = 3.0, H quinoline); 7.48 (1H, t, *J* = 7.4, H Ph); 7.63 (2H, t, *J* = 7.8, H Ph); 7.99 (2H, d, *J* = 7.6, H Ph); 8.09 (1H, dd, *J* = 9.7, *J* = 3.1, H quinoline); 8.47 (1H, s, H pyrazole); 8.98 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 18.7; 31.6; 51.3; 54.1; 101.1; 113.8 (d, *J* = 24.3); 114.9 (d, *J* = 24.4); 115.1 (d, *J* = 8.1); 116.2; 121.9; 123.3 (d, *J* = 6.6); 126.8; 127.1; 129.4; 129.7; 129.9; 133.1; 138.3; 141.9; 151.8; 153.6 (d, *J* = 22.9); 158.5 (d, *J* = 38.9); 161.5; 162.2. Found, *m*/*z*: 416.1883 $[M+H]^+$. $C_{24}H_{23}FN_5O$. Calculated, *m*/*z*: 416.1882.

8-(4-Methoxy-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl)-2,2,4,6-tetramethyl-1,2-dihydroquinoline (3b). Yield 719 mg (70%), bright-yellow powder, mp 121–122°C (*i*-PrOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.21 (6H, s, $2CH_3$); 1.95 (3H, s, CH_3); 2.23 (3H, s, CH_3); 4.20 (3H, s, OCH_3); 5.41 (1H, s, H-3 quinoline); 7.00 (1H, s, H quinoline); 7.60 (1H, t, *J* = 7.4, H Ph); 7.63 (2H, t, *J* = 7.8, H Ph); 8.01 (2H, d, *J* = 7.8, H Ph); 8.17 (1H, s, H quinoline); 8.38 (1H, s, H pyrazole); 8.93 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 19.0; 20.6; 31.8; 51.1; 54.1; 100.1; 115.2; 121.9; 122.2; 124.2; 127.1; 127.4; 127.7; 127.9; 128.5; 129.6; 130.7; 133.2; 138.4; 143.2; 154.1; 162.2; 162.7. Found, *m*/*z*: 412.2058 $[M+H]^+$. $C_{25}H_{26}N_5O$. Calculated, *m*/*z*: 412.2133.

8-(4-Methoxy-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidin-6-yl)-2,2,4,6,7-pentamethyl-1,2-dihydroquinoline (3c). Yield 807 mg (76%), bright-yellow powder, mp 186–187°C (*i*-PrOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.15 (6H, s, $2CH_3$); 1.94 (3H, s, CH_3); 1.96 (3H, s, CH_3); 2.16 (3H, s, CH_3); 4.13 (3H, s, OCH_3); 5.27 (1H, s, H-3 quinoline (NH)); 5.29 (1H, s, NH(H-3 quinoline)); 6.90 (1H, s, H quinoline); 7.38 (1H, t, *J* = 7.4, H Ph); 7.56 (2H, t, *J* = 7.6, H Ph); 8.21 (2H, d, *J* = 7.6, H Ph); 8.55 (1H, s, H pyrazole). ^{13}C NMR spectrum, δ, ppm: 17.3; 18.6; 19.6; 25.5; 30.6; 51.3; 54.4; 102.1; 119.0; 121.0; 122.9; 123.1; 125.2; 126.7; 127.4; 128.3; 129.3; 133.1; 134.4; 138.6; 140.1; 155.3; 163.6; 163.8. Found, *m*/*z*: 426.2381 $[M+H]^+$. $C_{26}H_{28}N_5O$. Calculated, *m*/*z*: 426.2290.

6-Methoxy-8-(4-methoxy-1-phenyl-1*H*-pyrazolo[3,4-*d*]-pyrimidin-6-yl)-2,2,4-trimethyl-1,2-dihydroquinoline (3d). Yield 769 mg (72%), bright-yellow powder, mp 135–136°C (*i*-PrOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (6H, s, $2CH_3$); 1.96 (3H, s, CH_3); 3.76 (3H, s, OCH_3); 4.24 (3H, s, OCH_3); 5.51 (1H, s, H-3 quinoline); 6.84 (1H, s, H quinoline); 7.48 (1H, t, *J* = 7.4, H Ph); 7.63 (2H, t, *J* = 7.8, H Ph); 8.00 (1H, s, H quinoline); 8.05 (2H, d, *J* = 7.8, H Ph); 8.47 (1H, s, H pyrazole); 8.80 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 18.9; 31.5; 39.8; 51.1; 54.1; 55.2; 100.1; 113.4; 115.2; 115.4; 121.9; 123.3; 127.1; 127.3; 129.5; 129.7; 133.2; 138.4; 140.4; 148.8; 154.1; 162.2; 162.3. Found, *m*/*z*: 428.2105 $[M+H]^+$. $C_{25}H_{26}N_5O_2$. Calculated, *m*/*z*: 428.2082.

8-[1-(4-Fluorophenyl)-4-methoxy-1*H*-pyrazolo[3,4-*d*]-pyrimidin-6-yl]-6-methoxy-2,2,4-trimethyl-1,2-dihydro-quinoline (3e). Yield 879 mg (79%), bright-yellow powder, mp 138–139°C (*i*-PrOH). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.20 (6H, s, $2CH_3$); 1.96 (3H, s, CH_3); 3.76 (3H, s, OCH_3); 4.24 (3H, s, OCH_3); 5.51 (1H, s, H-3 quinoline); 6.84 (1H, d, *J* = 3.0, H quinoline); 7.46–7.50 (2H, m, H Ar); 7.98 (1H, d, *J* = 3.0, H quinoline); 8.04–8.08 (2H, m, H Ar); 8.47 (1H, s, H pyrazole); 8.75 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 18.9; 31.5; 39.8; 40.0; 51.1; 54.2; 55.2; 100.8; 113.3; 115.2; 115.4; 116.3 (d, *J* = 22.9); 123.4; 124.1 (d, *J* = 8.5); 127.4; 129.7; 133.2; 134.8; 140.3; 148.8; 154.1; 159.6; 161.5; 162.3 (d, *J* = 11.9). Found, *m*/*z*: 446.2081 $[M+H]^+$. $C_{25}H_{25}FN_5O_2$. Calculated, *m*/*z*: 446.1988.

X-ray structural analysis of compound 3d was performed on an APEX II CCD diffractometer (MoKα radiation, graphite monochromator, ω-scanning). Suitable monoclinic, bright-yellow crystals of compound **3d** were grown from DMF ($C_{25}H_{25}N_5O_2$, *M* 427.50). At 120 K: *a* 37.8970(3), *b* 12.1033(10), *c* 9.3678(7) Å; β 101.7150(2)°; *V* 4207.30(6) Å^3; d_{calc} 1.350 g/cm^3; space group *C*2/*c*; *Z* 8. The final probability factor *R* 0.0661, maximum Bragg angle $2\Theta_{max}$ 60°. A total of 26922 reflections were collected, of which 6235 were independent. The structure was solved by direct method and refined by method of least squares in anisotropic full-matrix approximation by F_{hkl}^2. The positions of all hydrogen atoms were revealed from difference Fourier synthesis of residual electron density and refined in isotropic approximation. All calculations were performed using the SHELXTL PLUS software

suite.[22] The X-ray structural analysis dataset was deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1503754).

The Supplementary information file containing ^{1}H and ^{13}C NMR spectra and mass spectra of compounds **3a**–**e**, as well as the results of HPLC-MS analyses of reaction mixture during the synthesis of compound **3d** is available at the journal website at http://link.springer.com/journal/10593.

This work received financial support from the Ministry of Education and Science Russian Federation within the framework of State Contract with universities regarding scientific research during years 2017–2019 (project No. 4.3633.2017/4.6).

References

1. Meunier, B. *Acc. Chem. Res.* **2008**, *1*, 69.
2. Morphy, R.; Rankovic, Z. *J. Med. Chem.* **2005**, *48*, 6523.
3. Tietze, L. F.; Bell, H. P.; Chandrasekh, S. *Angew. Chem*., *Int. Ed.* **2003**, *42*, 3996.
4. Gademann, K. *Chimia* **2006**, *60*, 841.
5. Nqoro, X.; Tobeka, N.; Aderibigbe, B. A. *Molecules* **2017**, *12*, 2268.
6. Desai, N. C.; Rajpara, K. M.; Joshi, V. V.; Vaghani, H. V.; Satodiya, H. M. *J. Chem. Sci.* **2013**, *2*, 321.
7. Burgess, S. J.; Selzer, A.; Kelly, J. X.; Smilkstein, M. J.; Riscoe, M. K.; Peyton, D. H. *J. Med. Chem.* **2006**, *49*, 5623.
8. Rajpara, K.; Patel, Kh.; Jadeja, U. *Synthesis and Antimicrobial Screening of Hybrid Molecules of Quinoline*; Scholars' Press, 2017, p. 72.
9. Chauhan, M.; Kumar, R. *Bioorg. Med. Chem.* **2013**, *21*, 5657.
10. Liu, J.; Zhang, X.-w.; Wang, Y.; Chen, Y.; Zhang, M.-r.; Cai, Z.-q.; Zhou, Y.-p.; Xu, L.-f. *Synth. Commun.* **2015**, *45*, 1009.
11. Liu, M.; Li, J.; Chai, H.; Zhang, K.; Yang, D.; Zhang, Q.; Shi, D. *Beilstein J. Org. Chem.* **2015**, *11*, 2125.
12. Kosheleva, Y. A.; Medvedeva, S. M.; Shikhaliev, Kh. S.; Zubkov, F. I.; Ryzhkova, E. A.; Prezent, M. A. *Chem. Heterocycl. Compd.* **2016**, *52*, 578. [*Khim. Geterotsikl. Soedin.* **2016**, *52*, 578.]
13. Medvedeva, S. M.; Krysin, M. Yu.; Zubkov, F. I.; Nikitina, E. V.; Shikhaliev, Kh. S. *Chem. Heterocycl. Compd.* **2014**, *50*, 1280. [*Khim. Geterotsikl. Soedin.* **2014**, 1388.]
14. Medvedeva, S. M.; Sabynin, A. L.; Shikhaliev, Kh. S. *Russ. Chem. Bull*., *Int. Ed.* **2014**, *63*, 2693. [*Izv. Akad. Nauk*, *Ser. Khim.* **2014**, 2693.]
15. Medvedeva, S. M.; Plaksina, M. E.; Shikhaliev, Kh. S. *Zh. Org. Farm. Khim.* **2015**, *13*, 21.
16. Medvedeva, S. M.; Shikhaliev, Kh. S.; Krysin, M. Yu.; Gotsak, I. V. *Chem. Heterocycl. Compd.* **2016**, *52*, 309. [*Khim. Geterotsikl. Soedin.* **2016**, 309.]
17. Bergman, J.; Arewång, C.-J.; Svensson, P. H. *J. Org. Chem.* **2014**, *79*, 9065.
18. Rosowsky, A.; Modest, E. J. *J. Org. Chem.* **1965**, *30*, 1832.
19. Tung, C. C. *Tetrahedron* **1963**, *19*, 1685.
20. Santos, M. S.; Bernardino, A. M. R.; Pinheiro, L. C. S.; Canto-Cavalheiro, M. M.; Leon, L. L. *J. Heterocycl. Chem.* **2012**, *49*, 1425.
21. Leshcheva, E. V.; Medvedeva, S. M.; Shikhaliev, Kh. S. *Zh. Org. Farm. Khim.* **2014**, *12*, 15.
22. Sheldrick, G. M. *Acta Crystallogr.*, *Sect. A: Found Crystallogr.* **2008**, *A64*, 112.