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Synthesis of pyrazolo- and [1,2,4]triazolo-[1,5-*a*]quinolin-9-ols by cycloaddition to 8-hydroxyquinoline *N*-imide

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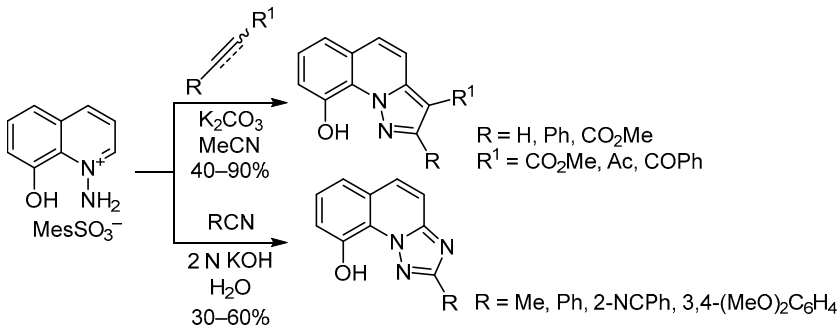


The reaction of 1-amino-8-hydroxyquinolinium mesitylenesulfonate with alkenes and alkynes containing electron-withdrawing substituents was performed in MeCN–K_2CO_3 system and gave the respective 9-hydroxypyrazolo[1,5-*a*]quinolines. The reaction with acetonitrile and aromatic nitriles in aqueous 2 N KOH solution gave the respective 2-substituted 9-hydroxy[1,2,4]triazolo[1,5-*a*]quinolines.

Keywords: 8-hydroxyquinoline, *N*-imines, pyrazolo[1,5-*a*]quinoline, [1,2,4]triazolo[1,5-*a*]quinoline, 1,3-dipolar cycloaddition.

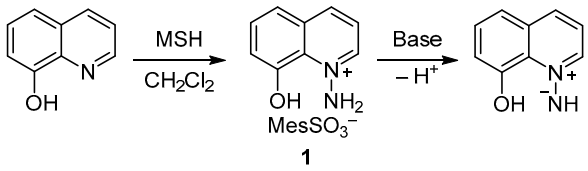
8-Hydroxyquinoline (quinolin-8-ol) ring system provides a promising structural motif for the design of new pharmaceutical compounds.[1] For example, a series of 8-hydroxyquinoline derivatives have been characterized with regard to their antimicrobial,[2] antiviral,[3] and anticancer[4] activity. Clioquinol (5-chloro-7-iodoquinolin-8-ol) is used as active pharmaceutical ingredient in topical medications for the treatment of bacterial and fungal skin infections.[5] It is known that the ions of certain metals (iron, copper, zinc, aluminum) play an important role in the development of neurodegenerative conditions.[6] The development of such diseases can be slowed by using chelate-forming molecules, in particular 8-hydroxyquinoline derivatives.[7] Coordination compounds of 8-hydroxyquinoline and its derivatives, for example, aluminum 8-hydroxyquinolinate, are widely used in the design of devices on the basis of organic light-emitting diodes (OLED).[8] A traditional application of 8-hydroxyquinoline and some of its substituted analogs has been in analytical chemistry for qualitative and quantitative determination of various metal ions.[9] Compounds of such structure are also commonly used in the design of fluorescent and colorimetric chemical sensors.[10] The wide range of practical applications show that there is a substantial need for developing new methods for the modification of 8-hydroxyquinoline ring system.

In the current work, we propose an approach that relies of the *N*-amination of 8-hydroxyquinoline, followed by modification of cation in *N*-aminoquinolinium salt **1** (Scheme 1). A convenient *N*-aminating reagent for this purpose is *O*-(mesitylenesulfonyl)hydroxylamine (MSH).[11] The *N*-amino cations formed by amination of azines are deprotonated at the NH group even in the presence of a weak base, giving the respective *N*-imides (azanides), which actively participate in 1,3-dipolar cycloaddition

reactions. Suitable dipolarophiles include alkynes bearing electron-withdrawing groups, as well as alkenes or nitriles.[12]

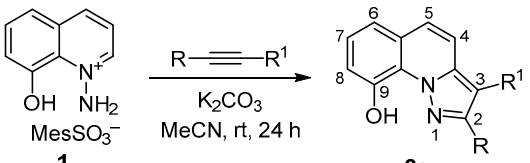
At the first stage of our work, we studied the reaction of mesitylenesulfonate **1** with acetylenes containing electron-withdrawing substituents in the presence of a base (Scheme 1). Such reactions have been thoroughly studied for pyridine *N*-imides and can be used to obtain pyrazolo-[1,5-*a*]pyridines in moderate to good yields.[12,13] The reactions of quinoline and isoquinoline *N*-amino derivatives, as well as other benzo-fused azines with alkynes resulted in only moderate yields of the respective pyrazolo[1,5-*a*]azines.[14]

Scheme 1



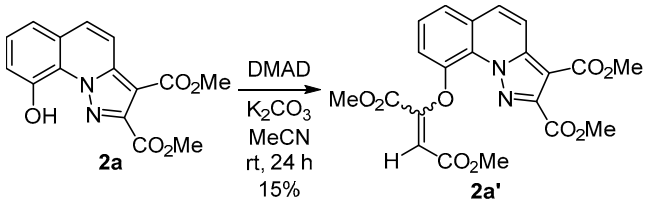
The reactions of *N*-amino-8-hydroxyquinolinium salt **1** with acetylenes containing electron-withdrawing substituents gave high yields of products **2b**,**c** (Scheme 2). The best results were achieved by using K_2CO_3 as a base and MeCN as a solvent. However, the preparation of product **2a** was complicated by a side reaction where dimethyl acetylenedicarboxylate (DMAD) added at the hydroxy group, resulting in the formation of product **2a'** in 15% yield (Scheme 3). This observation can be explained by the substantially higher electrophilicity of DMAD compared to other acetylenes. The double bond geometry (*E* or *Z*) of compound **2a'** was not established, since it was found to be unstable. The structure was proposed on the basis of ^{1}H NMR and high-resolution mass spectral data.

Scheme 2



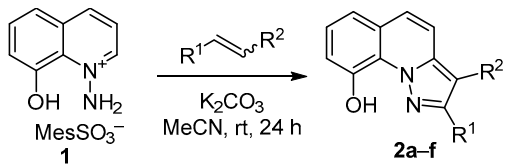
a R, R^1 = CO_2Me (50%)
b R = H, R^1 = CO_2Et (77%)
c R = Ph, R^1 = CO_2Me (92%)

Scheme 3



A research group from India has previously demonstrated that alkenes containing a carbonyl or carboxy group at the double bond effectively reacted with pyridine *N*-imides in *N*-methylpyrrolidone (NMP) medium in the absence of a base, resulting in the formation of pyrazolo-[1,5-*a*]pyridines in high yields.[15] Taking into account the fact that alkenes containing electron-withdrawing groups are affordable and readily available compounds, we decided to apply this method for the preparation of pyrazolo[1,5-*a*]quinolin-9-ols. However, performing the reaction of mesitylenesulfonate **1** with benzalacetone in NMP did not result in the formation of product in even trace amounts, with only the starting ketone recovered. The addition of a base (K_2CO_3 or DBU) led to the formation of product **2d** in small amounts (Scheme 4). Further optimization of reaction conditions allowed to establish that our previously used K_2CO_3–MeCN system was the most effective option.

Scheme 4

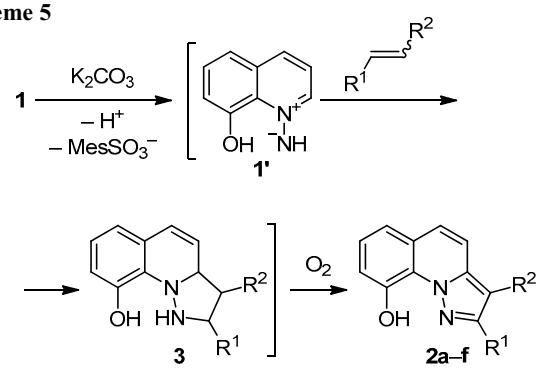


a R^1 = R^2 = CO_2Me (55%); **b** R^1 = H, R^2 = CO_2Et (63%);
c R^1 = Ph, R^2 = CO_2Me (51%); **d** R^1 = Ph, R^2 = Ac (88%);
e R^1 = H, R^2 = Ac (85%); **f** R^1 = Ph, R^2 = COPh (91%)

Reactions with dimethyl fumarate or maleate gave product **2a** in equal yields. Ethyl acrylate and methyl cinnamate led to the formation of pyrazoloquinolines **2b**,**c**, respectively, in moderate yields that were lower than obtained from reactions of salt **1** with the respective acetylenes. Remarkably, performing this reaction with alkenes containing a carbonyl group led to substantially higher yields (Scheme 4, products **2d**–**f**). This could be explained by the stronger electron-withdrawing effect of carbonyl group compared to a carboxy group.

The reaction mechanism apparently included deprotonation of mesitylenesulfonate **1** with the formation of *N*-imide **1'**, which further participated in 1,3-cycloaddition reaction with alkenes containing electron-withdrawing groups (Scheme 5). The subsequent oxidation of cycloadduct **3** with air oxygen led to the reaction

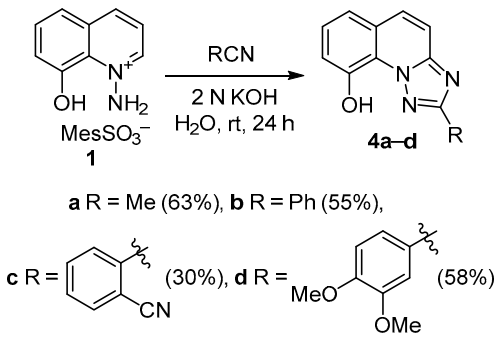
Scheme 5



products **2a**–**f**. Studying the reaction mixtures with ^{1}H NMR spectroscopy did not reveal the signals of hydrogenated derivatives **3**, indicating that the oxidation reaction occurred rapidly. The addition of oxidants such as chloranil or DDQ had no significant effect on the yields of products **2a**–**f** (Scheme 5).

It is known that nitriles also participate in cycloaddition reactions with pyridinium *N*-imines, resulting in the formation of [1,2,4]triazolo[1,5-*a*]pyridines.[12,16] We have previously used the reaction of salt **1** with 2-cyanopyridine for the synthesis of 2-(2-pyridyl)[1,2,4]triazolo[1,5-*a*]-quinolin-9-ol that was characterized regarding its ability to coordinate with rhenium.[17] In this work, we set out to study the reaction of mesitylenesulfonate **1** with aliphatic and aromatic nitriles. The reaction with an excess of MeCN in 2 N KOH solution produced 2-methylpyrazoloquinoline **4a** (Scheme 6). However, the attempts to perform this reaction with other aliphatic nitriles, such as propionitrile, butyronitrile, isobutyronitrile, and pivalonitrile, were not successful. It is also interesting to note that, although the reaction of salt **1** with acetonitrile readily occurred in aqueous alkali solutions, this reaction did not proceed in pure acetonitrile.

Scheme 6



The reactions with benzonitrile, phthalodinitrile, and 3,4-dimethoxybenzonitrile gave moderate yields of products **4b**–**d**, respectively. However, 4-hydroxy-3-methoxybenzonitrile did not participate in the reaction, apparently due to the deprotonation of OH group, which markedly reduced the reactivity of this dipolarophile.

The molecular structures of the obtained compounds were confirmed by data of ^{1}H and ^{13}C NMR spectroscopy. For all of the described compounds, ^{1}H NMR spectra featured an OH signal in the chemical shift range of 10.5–12.0 ppm. The characteristic signals of AB system consisting of H-4,5 protons were also present, with coupling constants of 9.4–9.5 Hz. It should be noted that the value of spin-spin coupling constant did not differ depending on the presence of pyrazole or triazole ring fused with the quinoline nucleus. The spectra of all compounds contained signals of ABC system consisting of H-6,7,8 protons with the characteristic spin-spin coupling constants of 7.8–7.9 Hz between vicinal protons, while in some cases also coupling between the H-6 and H-8 protons was observed, with spin-spin coupling constants of 1.3–1.4 Hz.

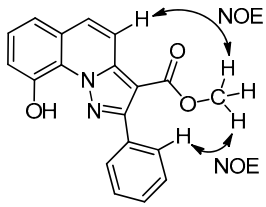


Figure 1. The observed NOE signals in the molecule of compound **2c**.

The spin-spin coupling constant between H-5 and H-6 protons in the spectrum of compound **4b** was 0.4 Hz, which was used for the assignment of signals. The positions of substituents in the molecule of compound **2c** were determined from NOE signals that were observed between the protons of OCH_3 group and the H-4 and H-2',6' Ph protons (Fig. 1).

IR spectra of all obtained compounds featured an absorption band due to the stretching vibrations of O–H group. The spectra of compounds **2a**–**c** contained a C=O absorption band in the range of 1709–1714 cm^{-1}, which is characteristic for the ester groups. In the case of products **2d**–**f**, the C=O absorption band was observed in the range of 1637–1671 cm^{-1}, as expected for ketone carbonyl groups. Furthermore, IR spectrum of compound **4c** showed an abosorption band at 2220 cm^{-1}, corresponding to CN group. Mass spectra of all compounds showed molecular ion peaks that matched the calculated values. Purity was confirmed by the results of elemental analysis.

Thus, we have studied the reactions of 1-amino-8-hydroxyquinolinium mesitylenesulfonate in the presence of base with various types of dipolarophiles: alkynes and alkenes containing electron-withdrawing groups, as well as with nitriles. Both the reactions with alkynes and alkenes led to the formation of the respective pyrazolo[1,5-*a*]-quinolin-9-ol derivatives in moderate to good yields. It was shown that suitable electron-withdrawing substituents in the alkene molecule included CO_2R, COMe, and COPh groups. We also demonstrated that 2-substituted [1,2,4]triazolo[1,5-*a*]quinolin-9-ols can be obtained by reactions of 1-amino-8-hydroxyquinolinium salt with acetonitrile and aromatic nitriles. At the same time, other aliphatic nitriles did not participate in similar reactions.

Experimental

IR spectra were recorded on a Bruker Vector 22 FT-IR spectrometer for samples in KBr pellets. ^{1}H NMR spectra were acquired on a Bruker AV-400 instrument (400 MHz), ^{13}C NMR spectra – on a Bruker AV-300 instrument (75 MHz). The residual signals of $CDCl_3$ solvent were used as internal standard (7.26 ppm for ^{1}H nuclei and 77.16 ppm for ^{13}C nuclei). High-resolution mass spectra were recorded on a DFS Thermo Electron instrument, using EI ionization (70 eV). Melting points were determined on a Kofler bench. Column chromatography was performed on neutral alumina (Reakhim, pure grade, specification (TU) 6-09-3916-75) or silica gel 60 from Macherey–Nagel (0.040–0.060 mm). The reaction progress was controlled by TLC on Sorbfil silica gel plates, visualization under UV light.

8-Hydroxyquinoline, nitriles, acetylenes, and alkenes were purchased from commercial sources and were used without additional purification. 1-Amino-8-hydroxyquinolinium mesitylenesulfonate was obtained from *O*-mesitylenesulfonylhydroxylamine[10] according to previously reported procedures.[15] MeCN was distilled from P_2O_5 and stored over 4 Å molecular sieves.

Dimethyl 9-hydroxypyrazolo[1,5-*a*]quinoline-2,3-dicarboxylate (2a). A solution of DMAD (44 mg, 0.31 mmol) in MeCN (4 ml) was added to a solution of salt **1** (112 mg, 0.31 mmol) in MeCN (2 ml). The stirred solution was then treated by adding K_2CO_3 (1.55 mmol) in a single portion. The obtained mixture was further stirred for 24 h, then diluted with water (20 ml), adjusted with 2 N HCl to neutral pH, and extracted with CH_2Cl_2 (3×10 ml). The extract was dried over anhydrous Na_2SO_4, and the solvent was removed by evaporation on a rotary evaporator. The obtained mixture was separated by silica gel column chromatography, using CH_2Cl_2 as eluent, R_f 0.62. Yield 47 mg (50%), pale-yellow crystals, mp 149–150°C (EtOH). IR spectrum, ν, cm^{-1}: 3430 (OH), 1714 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.93 (3H, s, OCH_3); 4.02 (3H, s, OCH_3); 7.24 (1H, dm, *J* = 8.0, H-6(8)); 7.29 (1H, dm, *J* = 7.9, H-8(6)); 7.41 (1H, t, *J* = 8.0, H-7); 7.68 (1H, d, *J* = 9.5, H-4(5)); 7.93 (1H, d, *J* = 9.5, H-5(4)); 11.15 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 52.1 (CH_3); 53.3 (CH_3); 104.5; 116.4; 117.3; 118.9; 121.8; 125.9; 127.7; 130.5; 139.5; 144.0; 148.8; 162.6 (2CO). Found, *m*/*z*: 300.0744 $[M]^+$. $C_{15}H_{12}N_2O_5$. Calculated, *m*/*z*: 300.0741. Found, %: C 60.25; H 3.91; N 9.30. $C_{15}H_{12}N_2O_5$. Calculated, %: C 60.00; H 4.03; N 9.33.

Compound **2a** was also obtained under analogous conditions from dimethyl fumarate or dimethyl maleate (45 mg, 0.31 mmol). Yield 52 mg (55%).

Further elution yielded a compound that was identified as **dimethyl 9-[(1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)-oxy]pyrazolo[1,5-*a*]quinoline-2,3-dicarboxylate (2a')**. R_f 0.19. Yield 20 mg (15%), yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.59 (3H, s, OCH_3); 3.92 (3H, s, OCH_3); 3.96 (3H, s, OCH_3); 4.01 (3H, s, OCH_3); 4.83 (1H, s, CH); 7.51 (1H, dd, *J* = 7.9, *J* =1.5, H-6(8)); 7.57 (1H, t, *J* = 7.8, H-7); 7.72 (1H, d, *J* = 9.4, H-4(5)); 7.79 (1H, dd, *J* = 7.8, *J* = 1.5, H-8(6)); 8.13 (1H, d, *J* = 9.4, H-5(4)). Found, *m*/*z*: 442.1009 $[M]^+$. $C_{21}H_{18}N_2O_9$. Calculated, *m*/*z*: 442.1007.

Ethyl 9-hydroxypyrazolo[1,5-*a*]quinoline-3-carboxylate (2b) was obtained analogously to the procedure for the preparation of compound **2a** from ethyl propiolate (31 mg, 0.31 mmol). R_f 0.68 on silica gel sorbent with CH_2Cl_2 as eluent. Yield 61 mg (77%), beige crystals, mp 214–215°C (EtOH). IR spectrum, ν, cm^{-1}: 3432 (OH), 1709 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.43 (3H, t, *J* = 7.8, CH_3); 4.40 (2H, q, *J* = 7.8, CH_2); 7.24 (1H, dm, *J* = 7.9, H-6(8)); 7.29 (1H, dm, *J* = 7.9, H-6(8)); 7.39 (1H, t, *J* = 7.9, H-7); 7.67 (1H, d, *J* = 9.4, H-4(5)); 8.00 (1H, d, *J* = 9.4, H-5(4)); 8.36 (1H, s, H-2); 11.70 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 14.6; 60.5; 105.7; 116.4; 116.7; 118.6; 122.4; 125.5; 126.9; 129.7; 138.7; 141.1; 148.9; 163.3. Found, *m*/*z*: 256.0847 $[M]^+$. $C_{14}H_{12}N_2O_3$. Calculated, *m*/*z*: 256.0842. Found, %: C 65.87; H 4.68; N 10.99. $C_{14}H_{12}N_2O_3$. Calculated, %: C 65.62; H 4.72; N 10.93.

Compound **2b** was also obtained under analogous conditions from ethyl acrylate (32 mg, 0.31 mmol). Yield 50 mg (63%).

Methyl 9-hydroxy-2-phenylpyrazolo[1,5-*a*]quinoline-3-carboxylate (2c) was obtained from methyl 3-phenylpropiolate (54 mg, 0.31 mmol) analogously to the procedure for the preparation of compound **2a**. R_f 0.60 on silica gel sorbent with CH_2Cl_2 as eluent. Yield 91 mg (92%), beige crystals, mp 172–173°C (EtOH). IR spectrum, ν, cm^{-1}: 3432 (OH), 1714 (CO). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.86 (3H, s, OCH_3); 7.24 (1H, dm, *J* = 7.9, H-6(8)); 7.30 (1H, dm, *J* = 7.9, H-8(6)); 7.40 (1H, t, *J* = 7.9, H-7); 7.46–7.51 (3H, m, H-3,4,5 Ph); 7.68 (1H, d, *J* = 9.5, H-4(5)); 7.77–7.82 (2H, m, H-2,6 Ph); 8.05 (1H, d, *J* = 9.5, H-5(4)); 11.83 (1H, br. s, OH). ^{13}C NMR spectrum δ, ppm: 51.5; 102.4; 116.7; 116.9; 118.6; 122.1; 125.5; 126.9; 128.1; 129.4; 129.6; 130.0; 131.7; 140.5; 148.9; 153.5; 163.9. Found, *m*/*z*: 318.1006 $[M]^+$. $C_{19}H_{14}N_2O_3$. Calculated, *m*/*z*: 318.0999. Found, %: C 71.85; H 4.40; N 8.85. $C_{19}H_{14}N_2O_3$. Calculated, %: C 71.69; H 4.43; N 8.80.

Compound **2c** was also obtained under analogous conditions from methyl cinnamate (55 mg, 0.31 mmol). Yield 51 mg (51%).

1-(9-Hydroxy-2-phenylpyrazolo[1,5-*a*]quinolin-3-yl)ethan-1-one (2d) was obtained analogously to the procedure for the preparation of compound **2a** from benzalacetone (46 mg, 0.31 mmol). R_f 0.65 on silica gel sorbent with CH_2Cl_2 as eluent. Yield 83 mg (88%), white crystals, mp 134–135°C (EtOH). IR spectrum, ν, cm^{-1}: 3431 (OH), 1651 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.18 (3H, s, CH_3); 7.27 (1H, dm, *J* = 7.7, H-6(8)); 7.36 (1H, dm, *J* = 7.8, H-8(6)); 7.45 (1H, t, *J* = 7.8, H-7); 7.52–7.60 (3H, m, H-3,4,5 Ph); 7.60–7.67 (2H, m, H-2,6 Ph); 7.75 (1H, d, *J* = 9.4, H-4(5)); 8.27 (1H, d, *J* = 9.5, H-5(4)); 11.80 (1H, br. s, OH). ^{13}C NMR spectrum δ, ppm (*J*, Hz): 30.6; 112.9; 116.7; 117.3; 118.6; 121.9; 126.0; 127.0; 128.7; 129.7; 130.0; 130.5; 132.6; 139.8; 148.9; 153.1; 194.4. Found, *m*/*z*: 302.1049 $[M]^+$. $C_{19}H_{14}N_2O_2$. Calculated, *m*/*z*: 302.1050. Found, %: C 75.61; H 4.55; N 9.20. $C_{19}H_{14}N_2O_2$. Calculated, %: C 75.48; H 4.67; N 9.27.

1-(9-Hydroxypyrazolo[1,5-*a*]quinolin-3-yl)ethan-1-one (2e) was obtained analogously to the procedure for the preparation of compound **2a** from methyl vinyl ketone (22 mg, 0.31 mmol). R_f 0.61 on silica gel sorbent with $CHCl_3$ as eluent. Yield 60 mg (85%), white crystals, mp 145–146°C (EtOH). IR spectrum, ν, cm^{-1}: 3430 (OH), 1671 (C=O). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.58 (3H, s, CH_3); 7.23 (1H, d, *J* = 7.9, H-6(8)); 7.28 (1H, d, *J* = 7.9, H-8(6)); 7.40 (1H, t, *J* = 7.9, H-7); 7.68 (1H, d, *J* = 9.4, H-4(5)); 8.15 (1H, d, *J* = 9.5, H-5(4)); 8.28 (1H, s, H-2); 11.64 (1H, s, OH). ^{13}C NMR spectrum δ, ppm: 28.4; 114.1; 116.7; 116.9, 118.6; 122.1; 125.8; 127.1; 130.5; 138.0; 140.8; 148.9; 192.2. Found, *m*/*z*: 226.0744 $[M]^+$. $C_{13}H_{10}N_2O_2$. Calculated, *m*/*z*: 226.0737. Found, %: C 69.31; H 4.50; N 12.27. $C_{13}H_{10}N_2O_2$. Calculated, %: C 69.02; H 4.46; N 12.38.

(9-Hydroxy-2-phenylpyrazolo[1,5-*a*]pyridin-3-yl)(phenyl)-methanone (2f) was obtained analogously to the procedure

for the preparation of compound **2a** from benzalacetophenone (65 mg, 0.31 mmol). R_f 0.63 on silica gel sorbent $CHCl_3$ as eluent. Yield 103 mg (91%), white crystals, mp 131–132°C (EtOH). IR spectrum, ν, cm^{-1}: 3435 (OH), 1637 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.16–7.25 (7H, m, H Ar); 7.30–7.37 (2H, m, H Ar); 7.45–7.49 (2H, m, H Ar); 7.56 (1H, d, *J* = 9.4, H-4(5)); 7.62–7.66 (2H, m, H Ar); 7.68 (1H, d, *J* = 9.4, H 5(4)); 11.85 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 110.8; 116.2; 116.5; 118.5; 121.9; 125.5; 126.7; 128.1; 128.2; 128.8; 129.3; 129.5; 129.6; 131.4; 132.3; 138.6; 140.5; 148.7; 152.4; 191.0. Found, *m/z*: 364.1210 $[M]^+$. $C_{24}H_{16}N_2O_2$. Calculated, *m/z*: 364.1206. Found, %: C 79.26; H 4.39; N 7.74. Calculated, %: C 79.11; H 4.43; N 7.69.

2-Methyl[1,2,4]triazolo[1,5-*a*]quinolin-9-ol (4a). Salt **1** (100 mg, 0.28 mmol) was dissolved in aqueous 2 N KOH solution (5 ml). MeCN (0.5 ml) was added to the obtained mixture, and stirring was continued until the yellow color faded. The mixture was then neutralized with 2 N HCl solution and extracted with $CHCl_3$ (3×10 ml). The extract was dried over anhydrous Na_2SO_4 and evaporated. The product was purified by column chromatography on alumina, using 100:1 CH_2Cl_2–MeOH mixture as eluent, R_f 0.71. Yield 35 mg (63%), yellowish crystals, mp 133–135°C (EtOH–hexane, 1:2). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.64 (3H, s, CH_3); 7.22 (1H, dm, *J* = 7.8, H-6(8)); 7.30 (1H, dm, *J* = 7.9, H-8(6)); 7.32–7.44 (1H, m, *J* = 7.9, H-7); 7.50 (1H, d, *J* = 9.5, H-4(5)); 7.76 (1H, d, *J* = 9.5, H-5(4)); 10.90 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm: 14.5; 114.4; 116.3; 118.9; 122.0; 124.8; 126.8; 131.8; 147.7; 149.2; 161.2. Found, *m/z*: 199.0743 $[M]^+$. $C_{11}H_9N_3O$. Calculated, *m/z*: 199.0740. Found, %: C 66.00; H 4.56; N 21.09. $C_{11}H_9N_3O$. Calculated, %: C 66.32; H 4.55; N 21.09.

2-Phenyl[1,2,4]triazolo[1,5-*a*]quinolin-9-ol (4b). Salt **1** (200 mg, 0.56 mmol) was dissolved in aqueous 2 N KOH solution (5 ml). The obtained mixture was treated with a solution of benzonitrile (57 mg, 0.56 mmol) in EtOH (0.5 ml), and stirring was continued until the yellow color faded (approximately 24 h). The mixture was then neutralized with 2 N HCl solution and extracted with $CHCl_3$ (3×10 ml). The extract was dried over anhydrous Na_2SO_4 and evaporated. The product was purified by column chromatography on alumina, using CH_2Cl_2 as eluent, R_f 0.65. Yield 81 mg (55%), pale-yellow crystals, mp 153–154°C (EtOH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.30 (1H, ddd, *J* = 7.8, *J* = 1.3, *J* = 0.4, H-6); 7.38 (1H, dd, *J* = 7.9, *J* = 1.3, H-8); 7.45 (1H, t, *J* = 7.9, H-7); 7.46–7.55 (3H, m, H Ph); 7.65 (1H, d, *J* = 9.4, H-4); 7.84 (1H, dd, *J* = 9.4, *J* = 0.4, H-5); 8.25–8.29 (2H, m, H Ph); 11.06 (1H, s, OH). ^{13}C NMR spectrum δ, ppm: 114.7; 116.5; 119.1; 122.1; 125.0; 127.1; 127.4; 129.0; 130.0; 130.5; 132.2; 147.9; 149.8; 161.8. Found, *m/z*: 261.0905 $[M]^+$. $C_{16}H_{11}N_3O$. Calculated, *m/z*: 261.0897. Found, %: C 73.21; H 3.98; N 16.25. $C_{16}H_{11}N_3O$. Calculated, %: C 73.55; H 4.24; N 16.08.

2-(9-Hydroxy[1,2,4]triazolo[1,5-*a*]quinolin-2-yl)benzonitrile (4c) was obtained from phthalodinitrile (72 mg, 0.56 mmol) analogously to the procedure for the preparation of compound **4b**. R_f 0.32 on silica gel sorbent, using CH_2Cl_2 as eluent. Yield 48 mg (30%), beige crystals, mp 235–236°C (EtOH). IR spectrum, ν, cm^{-1}: 3211 (OH); 2220 (C≡N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.34 (1H, dd, *J* = 7.9, *J* = 1.2, H-8(9)); 7.38 (1H, dd, *J* = 7.8, *J* = 1.2, H-9(8)); 7.47 (1H, t, *J* = 7.9, H-7); 7.57 (1H, td, *J* = 7.6, *J* = 1.1, H Ar); 7.66 (1H, d, *J* = 9.4, H-4(5)); 7.72–7.78 (1H, m, H Ar); 7.83–7.92 (2H, m, H Ar, H-5(4)); 8.49 (1H, dd, *J* = 8.0, *J* = 1.1, H Ar); 10.78 (1H, br. s, OH). ^{13}C NMR spectrum, δ, ppm: 110.5; 114.5; 117.3; 119.2 (2C); 122.0; 125.2; 127.7; 129.7; 130.3; 132.1; 133.0; 133.2; 135.0; 147.9; 149.3; 158.8. Found, *m/z*: 286.0849 $[M]^+$. $C_{17}H_{10}N_4O$. Calculated, *m/z*: 286.0849. Found, %: C 71.03; H 3.66; N 19.61. $C_{17}H_{10}N_4O$. Calculated, %: C 71.32; H 3.52; N 19.57.

2-(3,4-Dimethoxyphenyl)[1,2,4]triazolo[1,5-*a*]quinolin-9-ol (4d) was obtained from 3,4-dimethoxybenzonitrile (91 mg, 0.56 mmol) analogously to the procedure for preparation of compound **4b**. R_f 0.62 on silica gel sorbent using 100:1 $CHCl_3$–MeOH mixture as eluent. Yield 104 mg (58%), white crystals, mp 185–187°C (EtOH). ^1H NMR spectrum, δ, ppm (*J*, Hz): 6.98 (1H, d, *J* = 8.4, H-5' Ar); 7.28 (1H, dd, *J* = 7.9, *J* = 1.4, H Ar); 7.37 (1H, dd, *J* = 8.0, *J* = 1.4, H Ar); 7.43 (1H, t, *J* = 7.9, H Ar); 7.62 (1H, d, *J* = 9.4, H-4(5)); 7.75 (1H, d, *J* = 2.0, H-2' Ar); 7.82 (1H, d, *J* = 9.4, H-5(4)); 7.85 (1H, dd, *J* = 8.4, *J* = 2.0, H-6' Ar); 11.09 (1H, s, OH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 56.2; 56.3; 110.3; 111.4; 114.6; 116.4; 119.1; 120.5; 122.2; 122.8; 125.0; 127.0; 132.0; 147.8; 149.5; 149.7; 151.2; 161.8. Found, *m/z*: 286.1109 $[M]^+$. $C_{18}H_{15}N_3O_3$. Calculated, *m/z*: 321.1108. Found, %: C 67.45; H 4.77; N 13.01. $C_{18}H_{15}N_3O_3$. Calculated, %: C 67.28; H 4.71; N 13.08.

Supplementary information file containing ^1H and ^{13}C NMR spectra of the obtained compounds is available at the journal website at http://link.springer.com/journal/10593.

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