Synthesis, crystal structures, and properties of 5-(het)aryl-3-cyano-1-ethyl-2(1*H*)-pyrazinones

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A simple method for the synthesis of 5-(het)aryl-3-cyano-1-ethyl-2(1*H*)-pyrazinones was proposed. The method is based on the hydrolysis of the corresponding 2,3-dicyanopyrazinium salts. The spectral properties of pyrazinones were studied and their crystallographic investigation was carried out. The possibility of introduction of 5-(het)aryl-3-cyano-1-ethyl-2(1*H*)-pyrazinones into the [2+4] cycloaddition under the microwave activation conditions was shown.

Key words: pyrazinium salts, 5-aryl-3-cyano-2(1*H*)-pyrazinones, 1,2-dihydropyrazines, microwave irradiation, cycloaddition reactions.

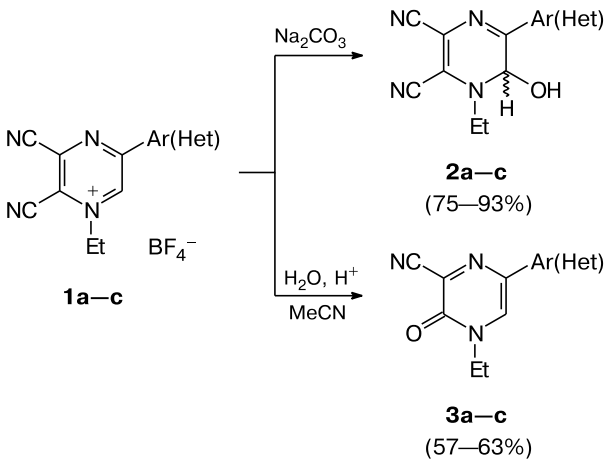
2(1*H*)-Pyrazinones are known as substances widely used in syntheses of biologically active compounds,[1—9] since the 2(1*H*)-pyrazinone fragment makes it possible to introduce into molecules a whole series of pharmacologically active groups capable of purposefully interacting with biological targets.[10—13]

The traditional method for the synthesis of 2(1*H*)-pyrazinones is the condensation of α-aminocarboxamides with 1,2-dicarbonyl compounds; however, the formation of a mixture of regioisomers is a substantial drawback of this method.[14] Multicomponent reactions involving primary amines, aldehydes, and cyanide are also used for the synthesis of pyrazinones. These reactions lead to α-aminonitriles, whose subsequent cyclization affords the corresponding pyrazinones.[3,4,10] A possibility of preparing 3-cyano-1-ethyl-2(1*H*)-pyrazinone by the reaction of 2,3-dicyano-1-ethylpyrazinium tetrafluoroborate with water was shown.[15] However, the reactions of salts of 5-(het)aryl-2,3-dicyano-1-ethylpyrazinium **1a—c** with water under the basic catalysis conditions lead to comparatively stable 6-hydroxyadducts **2a—c** (Scheme 1).[16]

In the present work, we show that the hydrolysis of salts **1** in an acidic medium (reflux in a mixture of MeCN—H_2O—HCl(conc.), 5 : 10 : 1) affords 6-(het)aryl-4-ethyl-3-oxo-3,4-dihydropyrazine-2-carbonitriles **3a—c** (see Scheme 1) in high yields. Their structures were determined by X-ray diffraction analysis for compounds **3a**,**c** as an example (Figs 1 and 2).

Attempts of oxidative aromatization of 6-hydroxyadducts **2a—c** to pyrazinones **4a—c** under the action of oxidants (such as air oxygen and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone) were unsuccessful. The reactions with the Barluenga reagent (bis(pyridinium)iodonium tetrafluoroborate[17,18]) afforded 6-(het)aryl-4-ethyl-3-oxo-3,4-dihydropyrazine-2-carbonitriles **3a—c** (Scheme 2).

Scheme 1



1—3: Ar = Ph (**a**), 4-FC_6H_4 (**b**); Het = thiophen-3-yl (**c**)

The reaction of compound **3c** with molecular bromine gives 6-(2,5-dibromothiophen-3-yl)-4-ethyl-3-oxo-3,4-dihydropyrazine-2-carbonitrile (**5**) (Scheme 3), whose structure was unambiguously proved by X-ray diffraction analysis (Fig. 3). Note that the obtained bifunctional dibromothiophene **5** can be interesting as a component for copolycondensation and synthesis of polythiophenes with specified optical properties.

Spectral studies of 2(1*H*)-pyrazinones. The synthesized pyrazinones **3a—c** have extended π-conjugation and an intramolecular system of chromophores. Due to this, compounds **3a—c** possess yellow-green fluorescence both

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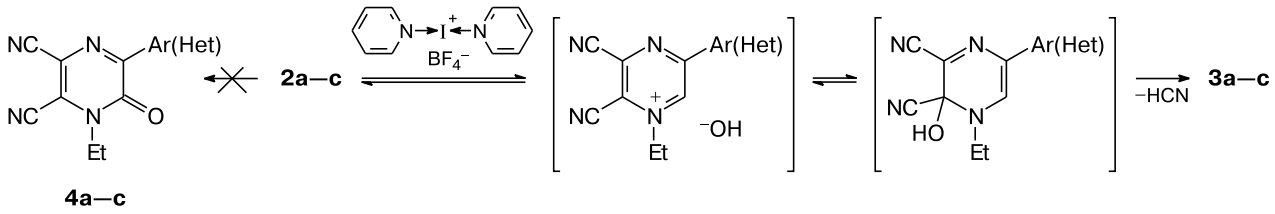
Scheme 2



Ar = Ph (**a**), 4-FC_6H_4 (**b**); Het = thiophen-3-yl (**c**)

in solutions and in the solid state. At the same time, 2(1*H*)-pyrazinone **5**, having a large Stokes shift, exhibits weak yellow luminescence, which can be caused by both a change in the electronic structure and changes in its crystal packing due to the presence of two bromine atoms. The results of spectral studies of compounds **3a—c** and **5** are given in Table 1.

X-ray diffraction study of 2(1*H*)-pyrazinones. Crystals of compound **3a** are formed by two crystallographically independent molecules of close configurations (I and II), which crystallize in the centrosymmetric space group $P\bar{1}$ of the triclinic crystal system. The general view of the

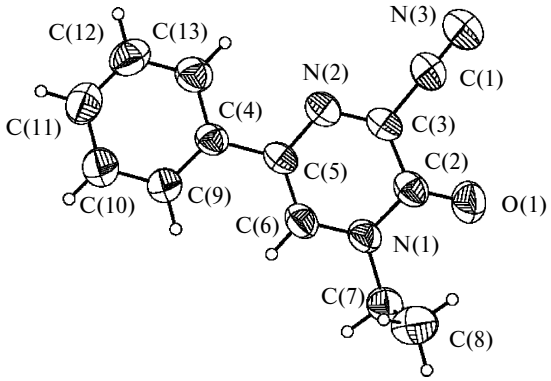


Fig. 1. X-ray crystal structure of compound **3a**.

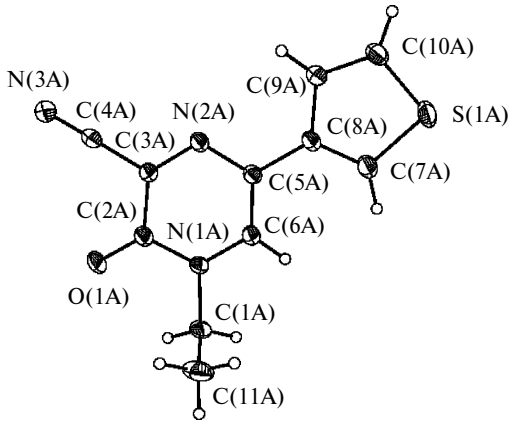
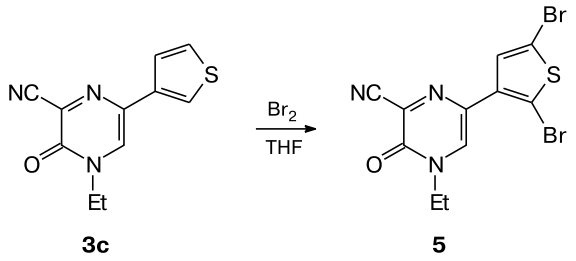


Fig. 2. X-ray crystal structure of compound **3c**.

Scheme 3



structure and the atomic numbering scheme in the X-ray diffraction experiment are presented in Fig. 1 for molecule I as an example; atoms of molecule II are marked with additional index "A." The corresponding bond lengths and bond angles in the both molecules are close, but there are some differences in their conformations. For example, the phenyl substituent of molecule I lies almost in the pyrazine ring plane and the deviation of atoms through the root-mean-square plane drawn through the atoms of these cycles is <0.03 Å, whereas the substituent in molecule II is unfolded relatively to the pyrazine cycle at an angle of 13.3°. The bond lengths in the pyrazine cycle are equalized to a considerable extent and are close in value to the bond lengths in aromatic systems. The exception is the bond C(2)—C(3) equal to 1.446(3) Å (C(2A)—C(3A), 1.460(3) Å), whose length more corresponds to the ordinary bond length in the system of conjugation of multiple

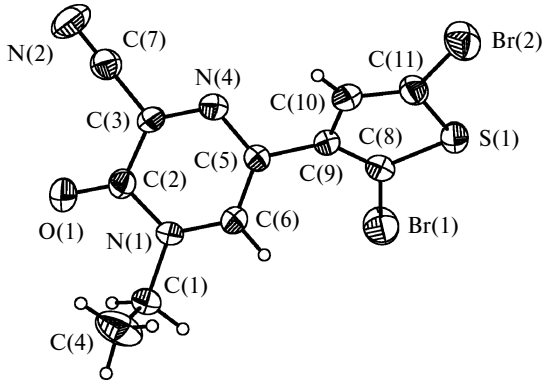


Fig. 3. X-ray crystal structure of compound **5**.

Table 1. Data of the IR, UV, and fluorescence spectra of compounds **3a—c** and **5**

Compound	IR,[a] ν/cm^{-1}	UV, λ_{max}/nm (ε)		F_{max}^{MeCN} [b]	*SS*[c]
		MeCN	solid state	nm	
3a	693 (C—H arom., C—Carom.), 767 (C—H arom., C—C arom.), 780 (C—H arom.), 1596 (C—C arom.), 1653 (C=O), 2227 (C≡N), 3073 (C—H arom.)	400 (8060), 272 (24060), 216 (15200), 206 (13960)	401, 269	465	65
3b	779 (C—H arom., C—C arom.), 821 (C—H arom., C—C arom.), 853 (C—H arom., C—C arom.), 1515 (C—C arom.), 1652 (C=O), 2230 (C≡N), 3062 (C—H arom.)	400 (9600), 270 (29000)	407, 277	466	66
3c	795 (C—H of thiophene), 1451 (thiophene cycle), 1534 (thiophene cycle), 1652 (C=O), 2232 (C≡N), 3073 (C—H of thiophene), 3088 (C—H of thiophene)	410 (8460), 277 (28460), 231 (11760), 210 (14540)	411, 277	491	81
5	781, 841, 851 (C—H of thiophene), 1066 (C_{Het}—Br), 1442, 1475 (thiophene cycle), 1540 (thiophene cycle), 1668 (C=O), 2234 (C≡N), 3064 (C—H of thiophene)	391 (5800), 280 (12300), 248 (21200), 208 (15900)	396, 251	479	88

[a] The bands were assigned on the basis of the published data.[19]
[b] Fluorescence maximum at λ_{max}^{MeCN}.
[c] Stokes shift, $SS = \lambda_{max}^{MeCN} - F_{max}^{MeCN}$.

bonds. It is most likely this is related to the influence of the electron-withdrawing substituents (conjugated carbonyl and cyano groups). In the molecular packing molecules I form piles oriented along the axis *a*. Molecules II are arranged at an angle between the pile to form rather loosened structure. No shortened intermolecular π—π-contacts are observed in the packing, but there is the strongly shortened intermolecular contact C—H...O=C close in value to the intermolecular hydrogen bond: *d*(C(6)...O(1A) [*x*, −1 + *y*, *z*]) = 3.159 Å, *d*(C(6A)...O(1)) = 3.188 Å (by 0.061 and 0.032 Å shorter than the sum of van der Waals radii), *d*(H(6A)...O(1A) [*x*, −1 + *y*, *z*]) = 2.271 Å, *d*(O(1)...H(6AA)) = 2.309 Å (by 0.449 and 0.411 Å shorter than the sum of van der Waals radii). Taking into account these contacts, the molecular packing takes the shape of convex ribbons oriented along the axis *b* and formed by alternating molecules I and II.

The crystals of compound **3c** are formed by two crystallographically independent molecules (I and II), which crystallize in the centrosymmetric space group $P\bar{1}$ of triclinic crystal system, and the unit cell parameters determined by the molecular crystal packing differ sharply from the unit cell parameters of compound **3a**. The general view of molecules I and II and the atomic numbering scheme in the X-ray diffraction experiment are presented in Fig. 2, and the corresponding atoms of molecule II are marked by additional index "A." The corresponding bond lengths and bond angles in the both molecules are close between each other, and the differences are observed in the orientation of the thienyl substituent relatively to the atoms of the pyrazine cycle: the torsional angle N(2)—C(5)—C(8)—C(7) is 0.0° and N(2A)—C(5A)—C(8A)—C(7A) is 175.5°. In the both cases, the thienyl substituent lies almost in the pyrazine cycle plane, and the deviation of atoms from the root-mean-square plane drawn through the atoms of these cycles for molecule I is <0.015 Å and that for molecule II is <0.05 Å. The bond length distribution in pyrazine cycle **3c** is analogous to the bond length distribution in molecules **3a**, in particular, *d*(C(2)—C(3)) = 1.456(3) Å, *d*(C(2A)—C(3A)) = 1.449(3) Å.

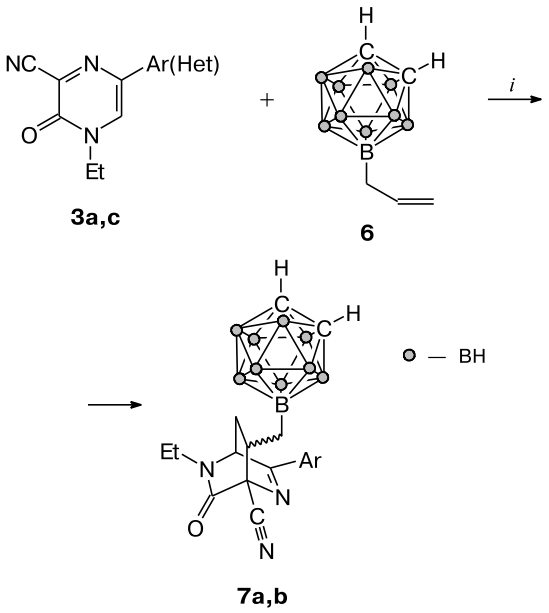
The molecular packing is layered, and the planes of the layers are parallel to the crystallographic plane [110]. The interlayer shortened π—π-contacts are observed for the pyrazine and thiophene cycles. The distances between the centroids of the pyrazine cycle of molecule II and the thiophene cycle of molecule I is 3.456 Å, whereas that between the centroids of the pyrazine cycle of molecule I and the thiophene cycle of molecule II is 3.578 Å. Thus, in molecular packing **3c** the conjugation of the thiophene cycle with the pyrazine ring is a rigidly fixed system of intermolecular contacts, which probably favors the enhancement of luminescence properties of the compound due to a decrease in energy losses on thermal vibrations.

The crystals of compound **5** are triclinic, and the substance crystallizes in the centrosymmetric space group $P\bar{1}$. The general view of the molecule and the atomic numbering scheme in the X-ray diffraction experiment are shown in Fig. 3. The thienyl substituent is unfolded relatively to the pyrazine plane at an angle of 44.25°. The bond length between the cyano and keto groups of the pyrazine cycle

(d(C(2)—C(3)) = 1.446(3) Å) coincides with the corresponding bond lengths in compounds **3a**,**c**. The molecular packing has no a pronounced geometric motive. The shortened π—π-contact between the carbon atoms of the pyrazine cycle bearing the CN group (d(C(3)...C(3) [$-x$, $2-y$, $3-z$]) = 3.324 Å) should be mentioned.

Transformation of 2(1*H*)-pyrazinones. It has earlier[20,21] been shown that 2(1*H*)-pyrazinones **3a**,**c** undergo the [4+2] cycloaddition reaction with 9-allylcarborane (**6**), yielding the corresponding cyclic adducts **7a**,**b** (Scheme 4).

Scheme 4



Ar = Ph (**3a**, **7a**); Het = thiophen-3-yl (**3c**, **7b**)

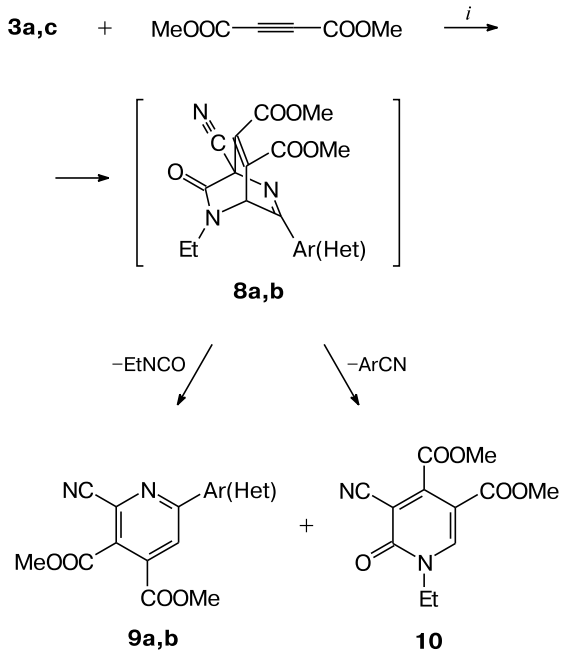
i. MW, 195 °C, 250 W, 300 min, 1,2-dichlorobenzene.

In this work, the reactions of cycloaddition of B 2(1*H*)-pyrazinones **3a,c** with acetylenic dienophiles attracted our attention. These Diels—Alder reactions were shown to give a mixture of pyridines **9a,b** and pyridone **10** because of the competitive routes of retrodecomposition of primarily formed bicyclic adducts **8a,b** (Scheme 5).

Using 2(1*H*)-pyrazinone precursors **3a,c** as model substrates, we studied the cycloaddition of dimethyl acetylenedicarboxylate under the microwave (MW) irradiation conditions and the use of 1-butyl-3-methylimidazolium hexafluorophosphate (bmimPF_6) as the ionic liquid (see Scheme 5). For comparison the same reactions were carried out under thermal conditions on reflux (178—180 °C, 100 min) in 1,2-dichlorobenzene in the absence of additives. The results are given in Table 2.

The results (see Table 2) indicate that the yield and the ratio of products are close regardless of the reaction conditions. In this case, advantages of microwave synthesis are in the acceleration of the reaction by

Scheme 5



Ar = Ph (**3a**, **8a**, **9a**); Het = thiophen-3-yl (**3c**, **8b**, **9b**)

i. MW, 195 °C, 200 W, 15 min, bmimPF_6, 1,2-dichlorobenzene.

5—7 times and a decrease in the amount of resinification products.

The GLC/MS study of the reaction mixtures also indicates that the reaction is accelerated at the same duration (15 min) and the formation of 2(1*H*)-pyridone **10** is preferential. The results of studying the cycloaddition reaction by GLC/MS are generalized in Table 3.

The synthesized dimethyl 6-(het)aryl-2-cyanopyridine-3,4-dicarboxylate **9a,b** and dimethyl 5-cyano-1-ethyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (**10**) were isolated using preparative HPLC. The structure of the latter was unambiguously established on the basis of X-ray diffraction data (Fig. 4).

Table 2. Conditions of the reaction of 2(1*H*)-pyrazinones **3a**,**c** with dimethyl acetylenedicarboxylate and their influence of the yields of pyridines **9a**,**b** and pyridone **10**

Initial compound	Reaction conditions	Yield of products (%)	
		9	**10**
3a	MW*, 195 °C, 15 min	5 (**9a**)	83
	Reflux**, 178—180 °C, 100 min	3 (**9a**)	74
3c	MW*, 195 °C, 15 min	6 (**9b**)	88
	Reflux**, 178—180 °C, 70 min	4 (**9b**)	78

* Microwave irradiation.

** With reflux condenser.

Table 3. Ratio of products in the reactions of 2(1*H*)-pyrazinones **3a,c** with dimethyl acetylenedicarboxylate (according to the GLC/MS data)

Initial pyrazinone	Reaction conditions	Ratio of products (%)
3a	MW, 195 °C	85 : 11 : 4 (**10** : **9a** : **3a**)
	Reflux, 178—180 °C	57 : 11 : 32 (**10** : **9a** : **3a**)
3c	MW, 195 °C	79 : 7 : 14 (**10** : **9b** : **3c**)
	Reflux, 178—180 °C	83 : 6 : 11 (**10** : **9b** : **3c**)

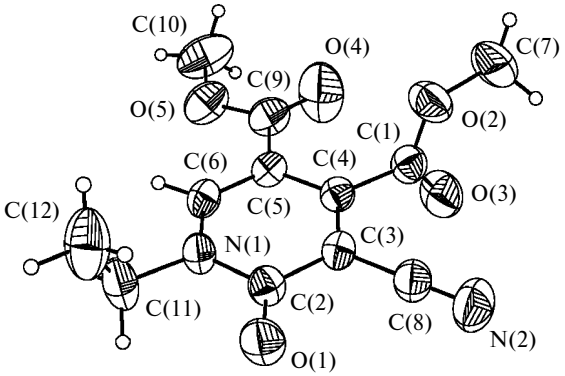


Fig. 4. X-ray crystal structure of compound **10**.

Thus, the simple method for the synthesis of 5-(het)aryl-3-cyano-1-ethyl-2(1*H*)-pyrazinones was proposed in the work. 5-(Het)aryl-3-cyano-1-ethyl-2(1*H*)-pyrazinones exhibit pronounced luminescence properties and can be used as the initial compounds in cycloaddition reactions.

Experimental

Solvents and reagents were dried and purified according to described procedures.[22] Compounds **1a—c** were synthesized according to the known procedure,[16] and bis(pyridinium)iodonium tetrafluoroborate was synthesized according to the published procedure.[17]

^{1}H NMR spectra were recorded on a Bruker DRX-400 instrument (400 MHz) using Me_4Si as an internal standard. Elemental analysis was carried on a Perkin—Elmer PE-2400 automated analyzer. IR spectra were recorded on an FT-IR Spectrometer Spectrum One instrument (Perkin—Elmer) in Nujol. UV spectra were measured on a UV-2401 PC instrument (Shimadzu) for solutions of the compounds in acetonitrile with a concentration of 10^{-5} mol L^{-1}. UV spectra in the solid state were obtained by mixing a sample of compound **3a—c** with $BaSO_4$ using the "integrating sphere" attachment. Emission spectra were recorded on a Varian Cary Eclipse spectrofluorimeter for solutions of the compounds in acetonitrile with a concentration of 10^{-5} mol L^{-1}. Melting points were determined on Boetius combined heating stages and were not corrected. Preparative HPLC was carried out using an Agilent 1200 Series semi-preparative liquid chromatograph (Agilent Technologies, USA). The instrument is equipped with an autosampler (900 μL), a diode-matrix detector (chosen analytical wavelength 280 nm), and a collector of fractions; column: ZORBAX Eclipse XDB-C18 PrepHT (21.2 mm × 150 mm), particle size 5 μm (Agilent Technologies, USA), room temperature of the column. An acetonitrile—water (50 : 50) mixture was used as a mobile phase, the flow rate of the mobile phase was 20 mL min^{-1}, and the elution regime was isocratic.

The GLC/MS analysis of all samples was carried out using an Agilent GC 7890A MS 5975C Inert XL EI/CI GC/MS spectrometer with a quadrupole mass-spectrometric detector with electron ionization (70 eV) and scan over the total ionic current in the range m/z 20—1000 and a quartz capillary column HP-5MS (30 m × 0.25 mm, film thickness 0.25 μm). Helium served as a carrier gas, the split ratio of the flow was 1 : 50, and the consumption through the column was 1.0 mL min^{-1}; the initial temperature of the column was 40 °C (storage 3 min), programming rate was 10 °C min^{-1} to 290 °C (storage 20 min), the temperature of the evaporator was 250 °C, the temperature of the source was 230 °C, the temperature of the quadrupole was 150 °C, and the temperature of the transition chamber was 280 °C. Solutions of the samples with a concentration of 3—4 mg mL^{-1} were prepared in acetonitrile. Samples of 1 μL of the obtained solutions were analyzed.

Flash chromatography was carried out using silica gel Lancaster 0.040—0.063 mm (230—400 mesh).

The reaction course and purity of the products were monitored by TLC on plates Sorbfil (UV development).

All microwave experiments were carried out in a CEM-Discover monomode microwave apparatus (USA) operating at a frequency of 2.45 GHz and with continuous irradiation power from 0 to 300 W. with utilization of the standard absorbance level of 200 W maximum power. The reactions were carried out in microwave process vials (10 mL) with sealed Teflon crimp top, which can be exposed to 250 °C and 20 bar external pressure. The temperature was measured with an IR sensor on the outer surface of the process vial.

Synthesis of 6-(het)aryl-4-ethyl-3-oxo-3,4-dihydropyrazine-2-carbonitriles 3a—c from 5-(het)aryl-2,3-dicyano-1-ethylpyrazinium tetrafluoroborates 1a—c (general procedure). Salt **1a—c** (1 mmol) was dissolved in MeCN (5 mL), and H_2O (10 mL) and concentrated hydrochloric acid (1 mL) were added to the obtained solution. The reaction mixture was refluxed for 0.5 h, the solvent was distilled off *in vacuo*, and the residue was separated on silica gel eluting with an ethyl acetate—hexane (1 : 3) mixture. The obtained product was recrystallized from MeOH.

4-Ethyl-3-oxo-6-phenyl-3,4-dihydropyrazine-2-carbonitrile (3a). Yellow crystalline powder. The yield was 61%, m.p. 191—193 °C. ^{1}H NMR (CD_3CN), δ: 1.39 (t, 3 H, Me, J = 7.2 Hz); 4.08 (q, 2 H, NCH_2, J = 7.2 Hz); 7.40—7.42 (m, 1 H, Ph); 7.46—7.50 (m, 2 H, Ph); 7.78—7.81 (m, 2 H, Ph); 8.23 (s, 1 H, C(5)H). Found (%): C, 69.29; H, 5.02; N, 18.68. $C_{13}H_{11}N_3O$. Calculated (%): C, 69.32; H, 4.92; N, 18.66. GLC: t_R = 25.465 min. MS (EI, 70 eV), m/z (I_{rel} (%)): 225 $[M]^+$ (100).

4-Ethyl-6-(4-fluorophenyl)-3-oxo-3,4-dihydropyrazine-2-carbonitrile (3b). Yellow crystalline powder. The yield was 60%, m.p. 219—220 °C. ^{1}H NMR (CD_3CN), δ: 1.39 (t, 3 H, Me, J = 7.2 Hz); 4.07 (q, 2 H, NCH_2, J = 7.2 Hz); 7.20—7.24 (m, 2 H, Ph); 7.79—7.83 (m, 2 H, Ph); 8.20 (s, 1 H, C(5)H). Found (%): C, 64.00; H, 4.36; N, 17.48. $C_{13}H_{10}FN_3O$. Calculated (%): C, 64.19; H, 4.14; N, 17.28.

4-Ethyl-3-oxo-6-(thiophen-3-yl)-3,4-dihydropyrazine-2-carbonitrile (3c). Yellow crystalline powder. The yield was 57%, m.p. 166—167 °C. ^{1}H NMR (CD_3CN), δ: 1.38 (t, 3 H, Me, J = 7.2); 4.05 (q, 2 H, NCH_2, J = 7.2 Hz); 7.46 (dd, 1 H, H(4′) of thiophen-3-yl, J = 5.2 Hz, J = 1.2 Hz); 7.52 (dd, 1 H, H(5′) of thiophen-3-yl, J = 5.2 Hz, J = 3.2 Hz); 7.73 (dd, 1 H, H(2′) of thiophen-3-yl, J = 3.2 Hz, J = 1.2 Hz); 8.16 (s, 1 H, C(5)H). Found (%): C, 57.309; H, 4.12; N, 18.43. $C_{11}H_9N_3OS$. Calculated (%): C, 57.13; H, 3.92; N, 18.17. GLC: t_R = 25.714 min. MS (EI, 70 eV), m/z (I_{rel} (%)): 231 $[M]^+$ (100).

6-(2,5-Dibromothiophen-3-yl)-4-ethyl-3-oxo-3,4-dihydropyrazine-2-carbonitrile (5). Bromine Br_2 (153 μL, 3 mmol) was added to a solution of compound **3c** (231 mg, 1 mmol) in anhydrous THF (5 mL). The reaction mixture was stirred for 30 min at room temperature, the solvent was distilled off *in vacuo*, and the residue was treated with an aqueous solution of Na_2CO_3 and extracted with 10—20 mL of $CHCl_3$. The extract was dried with anhydrous Na_2SO_4, the solvent was distilled off *in vacuo*, and the residue was separated on silica gel eluting with an ethyl acetate—hexane (1 : 1) mixture. The obtained product was recrystallized from EtOH. The yield was 230 mg (59%), m.p. 145—147 °C. Yellow crystalline powder. ^{1}H NMR (CD_3CN), δ: 1.37 (t, 3 H, Me, J = 7.2 Hz); 4.05 (q, 2 H, NCH_2, J = 7.2 Hz); 7.10 (s, 1 H, H(4′) of thiophen-3-yl); 8.20 (s, 1 H, C(5)H). Found (%): C, 33.80; H, 1.64; Br, 40.82; N, 10.68. $C_{11}H_7Br_2N_3OS$. Calculated (%): C, 33.96; H, 1.82; Br, 41.07; N, 10.80.

Synthesis of dimethyl 6-(het)aryl-2-cyanopyridine-3,4-dicarboxylates 9a,b and dimethyl 5-cyano-1-ethyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (10) (general procedure *A*). A solution of 2(1*H*)-pyrazinone **3a,c** (0.60 mmol), dimethyl acetylenedicarboxylate (0.72 mmol), and bmimPF_6 (15 μL, 0.15 mmol) in 1,2-dichlorobenzene (3 mL) was irradiated with microwave radiation (250 W) at 195 °C for 15 min, the solvent was distilled off *in vacuo*, and the residue was separated on silica gel eluting with an ethyl acetate—hexane (1 : 1) mixture or was isolated by HPLC. The yields of the products and reaction conditions are given in Table 2.

General procedure *B*. A solution of 2(1*H*)-pyrazinone **3a**,**c** (0.60 mmol) and dimethyl acetylenedicarboxylate (0.72 mmol) in 1,2-dichlorobenzene (3 mL) was refluxed with a reflux condenser until the initial pyrazinone disappeared (TLC monitoring), the solvent was distilled off *in vacuo*, and the residue was separated on silica gel eluting with an ethyl acetate—hexane (1 : 1) mixture or was isolated by preparative HPLC.

Table 4. Selected parameters of X-ray diffraction experiments for compounds **3a,c**, **5**, and **10**

Compound	**3a**	**3c**	**5**	**10**
Formula	$C_{13}H_{11}N_3O$	$C_{11}H_9N_3OS$	$C_{11}H_7Br_2N_3OS$	$C_{12}H_{12}N_2O_5$
Molecular weight	225.25	231.27	389.08	264.24
T/K	295(2)	130(2)	295(2)	295(2)
Crystal system	Triclinic	Triclinic	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$	$C2/c$
a/Å	7.3234(11)	10.0725(7)	8.5161(7)	17.5631(16)
b/Å	11.818(3)	10.4250(9)	9.5480(7)	12.7613(12)
c/Å	13.626(3)	10.7356(4)	10.0678(7)	11.6843(11)
α/deg	89.900(17)	110.186(7)	106.279(7)	90
β/deg	81.249(14)	91.764(6)	105.992(7)	98.960(8)
γ/deg	88.071(14)	94.049(7)	109.823(7)	90
V/Å^3	1164.8(4)	1053.58(12)	674.14(9)	2586.8(4)
Z	4	4	2	8
d_{calc}/g cm^{-3}	1.284	1.458	1.917	1.357
μ/mm^{-1}	0.085	0.287	6.157	0.107
Scan range on θ/deg	2.82 < θ < 26.37	2.78 < θ < 29.13	2.60 < θ < 28.28	2.77 < θ < 28.28
Number of measured reflections	8159	10107	3694	5833
Number of independent reflections (R_{int})	4526 (0.0356)	5569 (0.0175)	3259 (0.0218)	3167 (0.0193)
Number of reflection with $I > 2\sigma(I)$	1611	3980	1649	1539
Completeness of experiment (%) (for θ/deg)	95.5 (26.00)	98.7 (26.00)	97.5 (28.28)	99.3 (26.00)
Number of refined parameters	307	321	164	180
S	1.000	1.002	1.003	1.006
R_1 (on $I > 2\sigma(I)$)	0.0433	0.0337	0.0301	0.0378
wR_2 (on $I > 2\sigma(I)$)	0.0917	0.0901	0.0479	0.0884
R_1 (on all reflections)	0.1295	0.0511	0.0703	0.0849
wR_2 (on all reflections)	0.0972	0.0948	0.0495	0.0945
Δe/e Å^{-3}	0.177/−0.173	0.364/−0.226	0.367/−0.458	0.197/−0.174

The yields of the products and reaction conditions are given in Table 2.

Dimethyl 2-cyanopyridine-6-phenyl-3,4-dicarboxylate (9a). Yellow oil. ^{1}H NMR ($CDCl_3$), δ: 3.98 (s, 3 H, COOMe); 4.07 (s, 3 H, COOMe); 7.53—7.56 (m, 3 H, Ph); 8.09—8.11 (m, 2 H, Ph); 8.34 (s, 1 H, C(5)H). Found (%): C, 64.75; H, 4.05; N, 9.66. $C_{16}H_{12}N_2O_4$. Calculated (%): C, 64.86; H, 4.08; N, 9.45. R_f 0.60 (Sorbfil, ethyl acetate—hexane, 1 : 1). HPLC: t_R 8.5—9.5 min. GLC: t_R 25.389 min. MS (EI, 70 eV), m/z (I_{rel} (%)): 296 $[M]^+$ (100).

Dimethyl 2-cyanopyridine-6-(thiophen-3-yl)-3,4-dicarboxylate (9b). Yellow oil. ^{1}H NMR ($CDCl_3$), δ: 3.99 (s, 3 H, COOMe); 4.06 (s, 3 H, COOMe); 7.47 (dd, 1 H, H(5′) of thiophen-3-yl, J = 5.1 Hz, J = 3.0 Hz); 7.73 (dd, 1 H, H(4′) of thiophen-3-yl, J = 5.1 Hz, J = 1.3 Hz); 8.14 (dd, 1 H, H(2′) of thiophen-3-yl, J = 1.4 Hz, J = 3.0 Hz); 8.15 (s, 1 H, C(5)H). Found (%): C, 55.75; H, 3.37; N, 9.15. $C_{14}H_{10}N_2O_4S$. Calculated (%): C, 55.62; H, 3.33; N, 9.27. R_f 0.63 (Sorbfil, ethyl acetate—hexane, 1 : 1). GLC: t_R 25.725 min. MS (EI, 70 eV), m/z (I_{rel} (%)): 302 $[M]^+$ (100).

Dimethyl 5-cyano-1-ethyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (10). Light yellow crystalline powder. M.p. 183—184 °C. ^{1}H NMR ($CDCl_3$), δ: 1.44 (t, 3 H, Me, J = 7.2 Hz); 3.87 (s, 3 H, COOMe); 4.03 (s, 3 H, COOMe); 4.11 (q, 2 H, NCH_2, J = 7.2 Hz); 8.40 (s, 1 H, C(2)H). Found (%): C, 54.48; H, 4.33; N, 10.57. $C_{12}H_{12}N_2O_5$. Calculated (%): C, 54.55; H, 4.58; N, 10.60. R_f 0.25 (Sorbfil, ethyl acetate—hexane, 1 : 1). HPLC: t_R 1.7—3.0 min. GLC: t_R 24.326 min. MS (EI, 70 eV), m/z (I_{rel} (%)): 264 $[M]^+$ (100).

X-ray diffraction experiments were carried out on an Xcalibur-3 X-ray diffractometer with a CCD detector according to a standard procedure (λ(Mo-Kα), graphite monochromator, ω scan mode). Pieces of yellow crystals 0.51 × 0.39 × 0.23 mm (**3a**), 0.49 × 0.41 × 0.35 mm (**3c**), 0.33 × 0.21 × 0.05 (**5**), and 0.25 × 0.12 × 0.08 mm (**10**) in size were used for analysis. The data were collected and processed using the CrysAlis program package.[23] No absorption correction was applied for samples **3a**,**c** and for sample **5** a correction was applied analytically by the crystal model.[24] The structures of all compounds were determined by a direct method using the SHELXS-97 program and refined using the SHELXL-97 program[25] in the anisotropic (isotropic for hydrogen atoms) approximation. Hydrogen atoms were partially resolved and refined independently and were partially included into refinement in the riding model with dependent thermal parameters. Selected crystallographic parameters and the results of X-ray diffraction experiments are presented in Table 4.

The results of X-ray diffraction study were deposited with the Cambridge Crystallographic Data Centre (CCDC Nos 817 258 (**3a**), 817 259 (**3c**), 817 260 (**5**), and 817 261 (**10**)). These materials are available free of charge and can be requested at www.ccdc.cam.ac.uk/data_request/cif.

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