Chemistry of Heterocyclic Compounds, Vol. 45, No. 12, 2009

INTERACTION OF 2-CHLOROQUINOLINE-3-CARBALDEHYDES WITH 2-HETARYL-ACETONITRILES

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The interaction of 2-chloroquinoline-3-carbaldehydes with 1H-benzimidazol-2-ylacetonitriles and 1-benzyl-1H-imidazol-2-ylacetonitrile has been studied. It was shown that products of condensation at the methylene group are formed under mild conditions. Carrying out the reaction under more forcing conditions leads to an intramolecular nucleophilic substitution of the chlorine atom and the formation of cyclic ionic compounds (in the case of N-substituted hetarylacetonitriles), which are subsequently dealkylated.

Keywords: (1-benzyl-1H-imidazol-2-yl)acetonitrile, 2-(1-benzyl-1H-imidazol-2-yl)-3-(2-chloroquinolin-3-yl)acrylonitrile, benzimidazo[1,2-*a*]benzo[*g*]-1,8-naphthyridine-6-carbonitriles, 1H-benzimidazol-2-ylacetonitriles, benzo[*g*]imidazo[1,2-*a*]-1,8-naphthyridine-4-carbonitriles, 2-(1H-benzimidazol-2-yl)-3-(2-chloroquinolin-3-yl)acrylonitriles, 5-alkyl-6-cyanobenzimidazo[1,2-*a*]benzo[*g*]-1,8-naphthyridinium chlorides, 2-chloroquinoline-3-carbaldehydes.

We showed previously [1-4] that the interaction of (het)aromatic 2-haloaldehydes with hetaryl-acetonitriles leads at the first stage to a condensation product of a type of Knoevenagel reaction, but subsequently nucleophilic substitution of the halogen atom is accompanied by intramolecular cyclization with the formation of new heterocyclic compounds.

In the present work we have studied the interaction of 2-chloroquinoline-3-carbaldehydes **1** with 1H-benzimidazol-2-ylacetonitriles **2** and 1-benzyl-1H-imidazol-2-ylacetonitrile **6**. Only one example is known of the reaction of 2-chloro-7-methylquinoline-3-carbaldehyde with 1H-benzimidazol-2-ylacetonitrile [5], as a result of which a cyclic product possessing fluorescent properties was formed.

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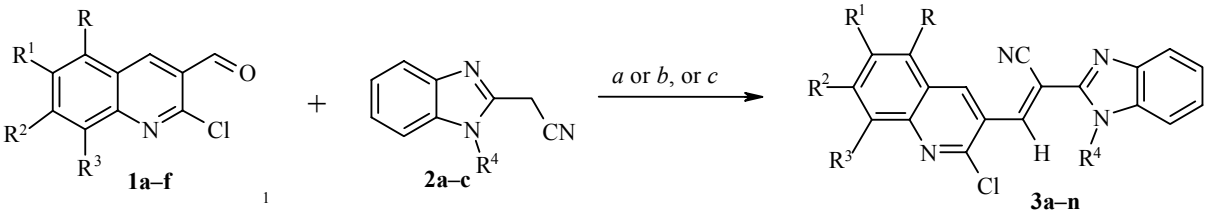
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1847-1863, December, 2009. Original article submitted April 30, 2009.

The reaction of 2-chloroquinoline-3-carbaldehydes **1** with 1H-benzimidazol-2-ylacetonitriles **2** under mild conditions (heating in DMF at 90-95°C or boiling in 2-propanol) leads to condensation products at the methylene group, 2-(1H-benzimidazol-2-yl)-3-(2-chloroquinolin-3-yl)acrylonitriles **3** (Table 1). The exception



a DMF, 90–95 °C, 1–2 h 30 min; *b* 2-PrOH, boiling, 10 min – 3 h; *c* MeOH, boiling, 10–20 min.
1 a–c R = R^1 = H; **a** R^2 = R^3 = H, **b** R^2 = Me, R^3 = H; **c** R^2 = R^3 = Me, **d** R = R^3 = Me, R^1 = R^2 = H; **e** R = R^2 = R^3 = H, R^1 = OMe; **f** R = R^1 = R^2 = H, R^3 = OMe; **2 a** R^4 = H, **b** R^4 = Me, **c** R^4 = Bn; **3 a–g** R^1 = H, **a** R = R^2 = R^3 = R^4 = H, **b** R = R^4 = H, R^2 = R^3 = Me, **c** R^2 = R^4 = H, R = R^3 = Me, **d** R = R^2 = R^4 = H, R^3 = OMe, **e** R = R^2 = R^3 = H, R^4 = Me, **f** R = H, R^2 = R^3 = R^4 = Me, **g** R^2 = H, R = R^3 = R^4 = Me, **h–n** R = H, **h** R^1 = OMe, R^2 = R^3 = H, R^4 = Me, **i** R^1 = R^2 = H, R^3 = OMe, R^4 = Me, **j** R^1 = R^2 = R^3 = H, R^4 = Bn, **k** R^1 = R^3 = H, R^2 = Me, R^4 = Bn, **l** R^1 = H, R^2 = R^3 = Me, R^4 = Bn, **m** R^1 = OMe, R^2 = R^3 = H; R^4 = Bn, **n** R^1 = R^2 = H, R^3 = OMe, R^4 = Bn

TABLE 1. Characteristics of Acrylonitriles **3**

Compound	Empirical formula	Found, % / Calculated, %		mp, °C*	Yield, %
		Cl	N		
3a	$C_{19}H_{11}ClN_4$	10.73 / 10.72	17.02 / 16.94	208	80
3b	$C_{21}H_{15}ClN_4$	9.79 / 9.88	15.70 / 15.61	> 300	86
3c	$C_{21}H_{15}ClN_4$	9.82 / 9.88	15.54 / 15.61	> 300	91
3d	$C_{20}H_{13}ClN_4O$	9.87 / 9.83	15.55 / 15.53	> 300	87
3e	$C_{20}H_{13}ClN_4$	10.21 / 10.28	16.29 / 16.25	221	84
3f	$C_{22}H_{17}ClN_4$	9.57 / 9.51	15.10 / 15.03	230	79
3g	$C_{22}H_{17}ClN_4$	9.45 / 9.51	15.09 / 15.03	204	71
3h	$C_{21}H_{15}ClN_4O$	9.39 / 9.46	15.01 / 14.95	227	80
3i	$C_{21}H_{15}ClN_4O$	9.43 / 9.46	15.04 / 14.95	237	75
3j	$C_{26}H_{17}ClN_4$	8.40 / 8.42	13.37 / 13.31	212	72
3k	$C_{27}H_{19}ClN_4$	8.14 / 8.15	12.93 / 12.88	189	71
3l	$C_{28}H_{21}ClN_4$	7.93 / 7.90	12.54 / 12.48	163	74
3m	$C_{27}H_{19}ClN_4O$	7.81 / 7.86	12.38 / 12.43	204	75
3n	$C_{27}H_{19}ClN_4O$	7.89 / 7.86	12.44 / 12.43	186	79

*A heterocyclization reaction may occur on heating.

was aldehyde **1a**, the products of condensation of which **3a,e,j** were obtained only on brief boiling in alcohol (**3a** in methanol and **3e,j** in 2-propanol). Carrying out the reaction in DMF involving aldehyde **1a** gave a mixture of condensation products and cyclic products.

The structure of compounds **3** is confirmed by the presence in the ^{1}H NMR spectra (in DMSO-d_6) of a singlet for the H-4 proton of the quinoline nucleus at 8.88-9.29 and the styryl CH proton singlet at 8.12-8.62 ppm. In the case of compounds **3a-d** a signal for the NH proton was also present with a chemical shift of 13.18-13.21 ppm. Assignment of the signals in the spectra of compounds **3** was made with the aid of experiments on homonuclear (COSY, NOESY-1D) and heteronuclear (HMQC and HMBC) correlations using product **3m** as example (Fig. 1). A complete list of the heteronuclear correlations found is given in Table 2. In the IR spectra of compounds **3** stretching vibrations were observed for the nitrile group in the 2207-2241 region, and for the NH group at 3249-3317 cm^{-1} for compounds **3a-d** (Table 3).

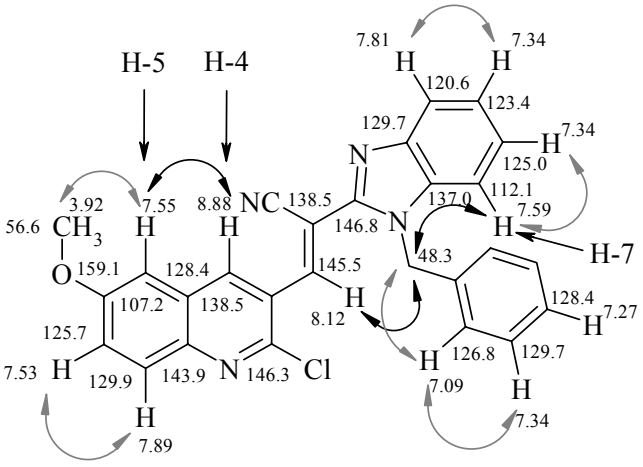


Fig. 1. Assignment of signals and Overhauser effects for compound **3m**.

TABLE 2. Heteronuclear Correlations for Compound **3m** (DMSO-d_6)

Proton signals, δ, ppm	Chemical shifts of carbon signals with which there are correlations, δ, ppm	
	HMQC	HMBC
8.88	138.5	146.3; 143.9; 107.2; 145.5
8.12	145.5	146.8; 146.3; 138.5; 116.1
7.89	129.9	159.1; 128.4
7.81	120.6	125.0
7.59	112.1	124.0
7.55	107.2	159.1
7.53	125.7	159.1
7.34	129.7	126.8;
	125.0	137.0; 120.6
	123.4	129.7; 112.1
7.27	128.4	126.8
7.09	126.8	48.3; 128.4
5.83	48.3	146.8; 137.0; 126.8
3.92	56.6	159.1

TABLE 3. IR and ^{1}H NMR Spectra of Compounds **3**

Compound	IR, spectrum ν_{CN} (ν_{NH}), cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)*		
		Characteristic signals	CH=CCN (1H, s)	H-4 quinoline (1H, s)
1	2	3	4	5
3a	2230 (3249)	7.24-7.29 (2H, m, H-5,6 benzimidazole); 7.50-7.52 (1H, m, H-7 benzimidazole); 7.70-7.73 (2H, m, H-6 quinoline, H-4 benzimidazole); 7.89 (1H, t, *J* = 7.2, H-7 quinoline); 8.01 (1H, d, *J* = 8.4, H-5 quinoline); 8.16 (1H, d, *J* = 8.0, H-8 quinoline); 13.21 (1H, s, NH)	8.60	9.09
3b	2241 (3277)	2.50 (3H, s, C-CH$_3$); 2.68 (3H, s, C-CH$_3$); 7.23 (2H, m, H-5,6 benzimidazole); 7.52 (2H, d, *J* = 8.0, H-6 quinoline, H-7 benzimidazole); 7.68 (1H, d, *J* = 7.2, H-4 benzimidazole); 7.85 (1H, d, *J* = 8.4, H-5 quinoline); 13.18 (1H, s, NH)	8.58	8.99
3c	2224 (3317)	2.68 (3H, s, C-CH$_3$); 2.74 (3H, s, C-CH$_3$); 7.23-7.28 (2H, m, H-5,6 benzimidazole); 7.40 (1H, d, *J* = 7.2); 7.53 (1H, d, *J* = 7.2); 7.58 (1H, d, *J* = 7.2); 7.68 (1H, d, *J* = 8.0, H-7 quinoline); 13.20 (1H, s, NH)	8.62	9.29
3d	2234 (3303)	4.04 (3H, s, O-CH$_3$); 7.24-7.26 (2H, m, H-5,6 benzimidazole); 7.31 (1H, d, *J* = 7.2, H-7 quinoline); 7.56-7.67 (4H, m, H-5,6 quinoline, H-4,7 benzimidazole); 13.21 (1H, s, NH)	8.57	9.00
3e	2227	4.11 (3H, s, N-CH$_3$); 7.28-7.35 (2H, m, H-5,6 benzimidazole); 7.61 (1H, d, *J* = 7.2, H-7 benzimidazole); 7.70-7.74 (2H, m, H-6 quinoline, H-4 benzimidazole); 7.90 (1H, t, *J* = 7.2, H-7 quinoline); 8.00 (1H, d, *J* = 7.6, H-5 quinoline); 8.16 (1H, d, *J* = 7.2, H-8 quinoline)	8.39	9.12
3f	2231, 2204	2.56 (3H, s, C-CH$_3$); 2.68 (3H, s, C-CH$_3$); 4.11 (3H, s, N-CH$_3$); 7.27 (1H, t, *J* = 7.6, benzimidazole); 7.33 (1H, t, *J* = 7.6, benzimidazole); 7.53 (1H, d, *J* = 8.0, H-7 benzimidazole); 7.60 (1H, d, *J* = 8.4, H-6 quinoline); 7.69 (1H, d, *J* = 8.0, H-4 benzimidazole); 7.86 (1H, d, *J* = 8.4, H-5 quinoline)	8.41	9.02
3g	2207	2.95 (3H, s, C-CH$_3$); 3.04 (3H, s, C-CH$_3$); 4.45 (3H, s, N-CH$_3$); 7.90-8.00 (5H, m, H-6 quinoline, H-4,5,6,7 benzimidazole); 8.18 (1H, d, *J* = 7.2, H-7 quinoline)	8.78	10.32
3h	2230	4.12 (3H, s, N-CH$_3$); 4.39 (3H, s, O-CH$_3$); 7.83-7.94 (5H, m, H-5 quinoline, H-4,5,6,7 benzimidazole); 8.01 (1H, d, *J* = 9.6, H-7 quinoline); 8.22 (1H, d, *J* = 9.6, H-8 quinoline)	8.68	9.82
3i	2231	4.04 (3H, s, N-CH$_3$); 4.11 (3H, s, O-CH$_3$); 7.28-7.37 (3H, m, H-7 quinoline, H-5,6 benzimidazole); 7.60-7.67 (3H, m, H-6 quinoline, H-4,7 benzimidazole); 7.70 (1H, d, *J* = 8.0, H-5 quinoline)	8.39	9.04
3j	2237	5.81 (2H, s, CH$_2$Ph); 7.12 (2H, d, *J* = 7.2, H-2,6 Ph); 7.26-7.35 (5H, m, H-5,6 benzimidazole, H-3,4,5 Ph); 7.49-7.51 (1H, m, H-7 benzimidazole); 7.69 (1H, t, *J* = 7.2, H-6 quinoline); 7.76-7.78 (1H, m, H-4 benzimidazole); 7.87 (1H, t, *J* = 7.2, H-7 quinoline); 7.96 (1H, d, *J* = 8.0, H-5 quinoline); 8.11 (1H, d, *J* = 8.4, H-8 quinoline)	8.14	9.00

TABLE 3 (continued)

1	2	3	4	5
3k	2234	2.61 (3H, s, C-CH_3); 5.77 (2H, s, CH_2Ph); 7.12 (2H, d, *J* = 7.2, H-2,6 Ph); 7.26-7.36 (5H, m, H-5,6 benzimidazole, H-3,4,5 Ph); 7.49-7.52 (1H, m, H-7 benzimidazole); 7.54 (1H, d, *J* = 8.4, H-6 quinoline); 7.77-7.79 (2H, m, H-8 quinoline, H-4 benzimidazole); 8.01 (1H, d, *J* = 8.4, H-5 quinoline)	8.14	8.96
3l	2230	2.54 (3H, s, C-CH_3); 2.65 (3H, s, C-CH_3); 5.81 (2H, s, CH_2Ph); 7.12 (2H, d, *J* = 7.2, H-2,6 Ph); 7.28-7.35 (5H, m, H-5,6 benzimidazole, H-3,4,5 Ph); 7.48-7.52 (2H, m, H-6 quinoline, H-7 benzimidazole); 7.76-7.78 (1H, m, H-4 benzimidazole); 7.81 (1H, d, *J* = 8.0, H-5 quinoline)	8.17	8.91
3m	2232	3.92 (3H, s, O-CH_3); 5.83 (2H, s, CH_2Ph); 7.09 (1H, d, *J* = 7.2, H-2,6 Ph); 7.27-7.36 (5H, m, H-5,6 benzimidazole, H-3,4,5 Ph); 7.53-7.60 (3H, m, H-5,7 quinoline, H-7 benzimidazole); 7.81-7.82 (1H, m, H-4 benzimidazole); 7.89 (1H, d, *J* = 8.8, H-8 quinoline)	8.12	8.88
3n	2230	4.02 (3H, s, O-CH_3); 5.82 (2H, s, CH_2Ph); 7.12 (2H, d, *J* = 7.2, H-2,6 Ph); 7.28-7.35 (6H, m, H-6 quinoline, H-5,6 benzimidazole, H-3,4,5 Ph); 7.48-7.50 (1H, m, H-7 benzimidazole); 7.59-7.61 (2H, m, H-5,7 quinoline); 7.77-7.79 (1H, m, H-4 benzimidazole)	8.14	8.91

*The ^{1}H NMR spectra were taken in DMSO-d_6 (compounds **3a-f,i-n**) and in deuterated trifluoroacetic acid (compounds **3g,h**).

Data of X-ray structural analysis of compound **3i** indicate the formation of only one of the possible isomers, just the *E*-isomer (Fig. 2).

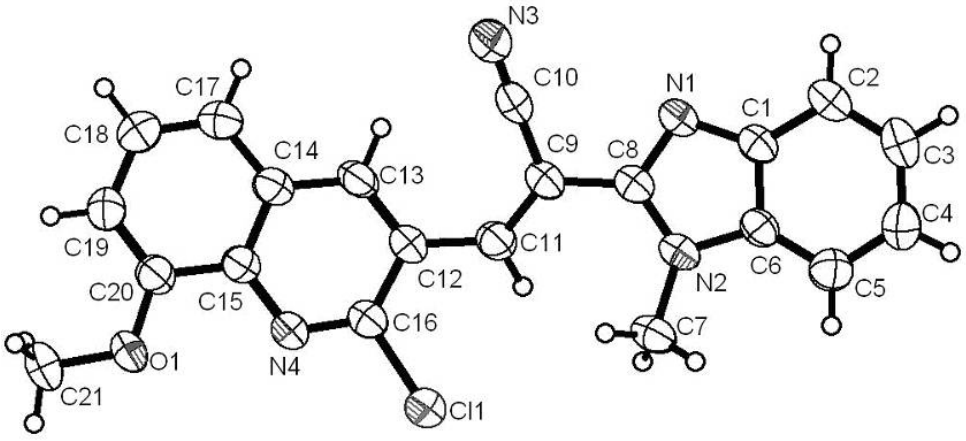


Fig. 2. Molecular structure of compound **3i** according to data of XSA. Ellipses of the thermal vibrations of nonhydrogen atoms are shown at the 50% probability level.

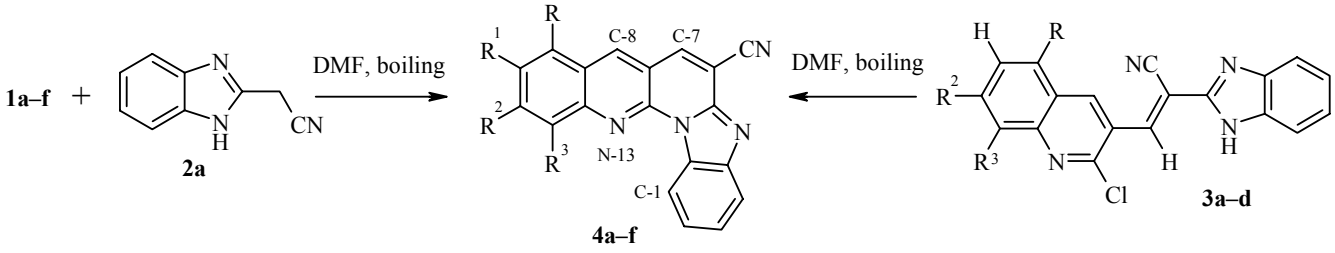
TABLE 4. Benzimidazo[1,2-*a*]benzo[*g*]-1,8-naphthyridine-6-carbonitriles **4**

Compound	Empirical formula	Found, % / Calculated, % N	IR spectrum, ν_{CN}, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)* Characteristic signals	H-7 (1H, s), H-8 (1H, s)	H-1 (1H, d)	mp, °C	Yield, %*[2]
4a	$C_{19}H_{10}N_4$	19.01 / 19.04	2232	7.59-7.65 (2H, m, H-2,3); 7.71 (1H, t, *J* = 7.6, H-10); 8.00-8.04 (2H, m, H-4,11); 8.24-8.28 (2H, m, H-12, 9)	8.85, 9.13	9.25 (*J* = 7.2)	297	86
4b	$C_{20}H_{12}N_4$	18.21 / 18.17	2227	2.86 (3H, s, C–CH_3); 7.86 (1H, d, *J* = 8.8, H-10); 8.04-8.14 (3H, m, H-2,3,4); 8.26 (1H, d, *J* = 8.8, H-9); 8.41 (1H, s, H-12)	9.26, 9.32	9.92 (*J* = 7.6)	> 300	83
4c	$C_{21}H_{14}N_4$	17.33 / 17.38	2230	2.84 (3H, s, C–CH_3); 3.16 (3H, s, C–CH_3); 7.86 (1H, d, *J* = 8.4, H-10); 8.05-8.16 (4H, m, H-2,3,4,9)	9.27, 9.30	9.91 (*J* = 8.0)	> 300	85
4d	$C_{21}H_{14}N_4$	17.40 / 17.38	2227	2.98 (3H, s, C–CH_3); 3.16 (3H, s, C–CH_3); 7.75 (1H, d, *J* = 6.8, H-10); 8.06-8.18 (4H, m, H-2,3,4,11)	9.36, 9.59	9.90 (*J* = 8.0)	> 300	82
4e	$C_{20}H_{12}N_4O$	17.26 / 17.27	2235	3.99 (3H, s, O–CH_3); 7.55-7.63 (4H, m, H-2,3,9,11); 7.95 (1H, d, *J* = 8.0, H-4); 8.15 (1H, d, *J* = 8.8, H-12)	8.81, 8.99	9.28 (*J* = 7.2)	> 300	86
4f	$C_{20}H_{12}N_4O$	17.21 / 17.27	2230	4.16 (3H, s, O–CH_3); 7.51 (1H, d, *J* = 7.2, H-11); 7.62-7.71 (3H, m, H-2,3,10); 7.82 (1H, d, *J* = 8.4, H-4); 8.03 (1H, d, *J* = 7.6, H-9)	8.92, 9.16	9.37 (*J* = 8.0)	> 300	88

* The ^{1}H NMR spectra were taken in DMSO-d_6 (compounds **4a,e,f**) and deuterated trifluoroacetic acid (compounds **4b-d**).
*[2] Method A.

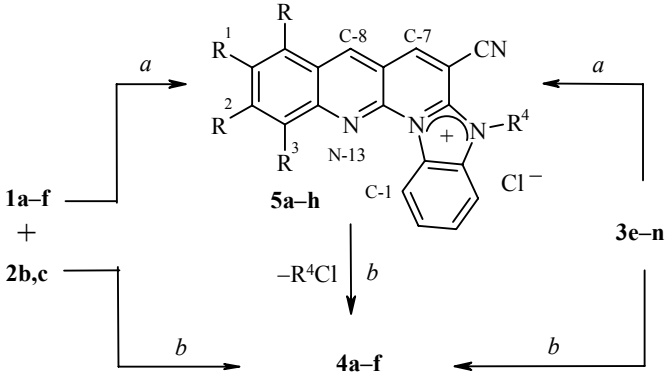
The marked steric strain of the **3i** molecule should be noted, linked with the presence of bulky substituents at the central C=C double bond. This is indicated by the highly shortened intramolecular contacts at C(7)···H(11) 2.55 and C(10)···H(14) 2.44 Å with the sum of the van der Waals radii at 2.87 Å [6], which lead to distortion of the molecule [torsion angles N(2)–C(8)–C(9)–C(11) -24.0(3)° and C(9)–C(11)–C(12)–C(13) 22.6(4)°], and also to an increase of the valence angles C(11)–C(9)–C(10) 122.6(2)° and C(8)–N(2)–C(7) 129.85(18)° in comparison with the analogous angles C(10)–C(9)–C(8) 112.59(17)° and C(6)–N(2)–C(7) 123.04(18)° respectively.

The cyclic compounds **4** (Table 4), which we considered as models in subsequent investigations, were synthesized from 2-chloroquinoline-3-carbaldehydes **1** and N-unsubstituted 1H-benzimidazol-2-ylacetonitrile **2a** under more forcing conditions (boiling in DMF). Compounds **4** (Table 4) may also be obtained in high yield from the corresponding condensation products **3a-d**. As mentioned above compound **4b** was synthesized previously in [5]. All the remaining products **4a,c-f** are new substances.



4 a–d R^1 = H, **a** R = R^2 = R^3 = H, **b** R = R^3 = H, R^2 = Me, **c** R = H, R^2 = R^3 = Me,
d R = R^3 = Me, R^2 = H, **e, f** R = R^2 = H, **e** R^1 = OMe, R^3 = H, **f** R^1 = H, R^3 = OMe

A doublet for H-1 was observed at very low field in the ^{1}H NMR spectra of compounds **4**, the anomalous chemical shift of which at 9.25-9.37 (DMSO-d_6) or 9.90-9.92 ppm (TFA) is explained by the effect of the electron pair of the N-13 atom. Singlets for H-7 and H-8 are frequently drawn together and are observed at low field in the 8.81-9.16 (DMSO-d_6) or 9.26-9.59 ppm (TFA) regions. In the IR spectra of products **4** an intense band for the stretching vibrations of the CN group at 2227-2235 cm^{-1} was characteristic.



a – DMF, boiling, 20 min – 1h 30 min; *b* – DMF, boiling, 3-12 h.
5 a-c R = R^1 = H, **a** R^2 = R^3 = H, R^4 = Me, **b** R^2 = R^4 = Me, R^3 = H,
c R^2 = R^3 = R^4 = Me, **d** R = R^3 = R^4 = Me, R^1 = R^2 = H, **e–h** R = H,
e R^1 = OMe, R^2 = R^3 = H, R^4 = Me, **f** R^1 = R^2 = H, R^3 = OMe, R^4 = Me,
g R^1 = R^3 = H, R^2 = Me, R^4 = Bn, **h** R^1 = OMe, R^2 = R^3 = H, R^4 = Bn

On brief boiling of 2-chloroquinoline-3-carbaldehydes **1** with N-substituted 1H-benzamidazol-2-ylacetonitriles **2b,c** in DMF the ionic compounds **5** were obtained (Table 5) with the positive charge centered on the nitrogen atoms and with Cl^- anion as counter ion. Under similar conditions product **5** may also be obtained with the same good yields from the appropriate compounds **3**.

TABLE 5. 5-Alkyl-6-cyanobenzimidazo[1,2-*a*]benzo[*g*]-1,8-naphthyridinium Chlorides **5** and 2-(1-Benzyl-1H-imidazol-2-yl)-3-(1-chloroquinolin-3-yl)acrylonitriles **7**

Compound	Empirical formula	Found, % / Calculated, %		mp, °C*	Yield, %*[2]
		Cl	N		
5a	$C_{20}H_{13}ClN_4$	10.23 / 10.28	16.32 / 16.25	164	79
5b	$C_{21}H_{15}ClN_4$	9.95 / 9.88	15.57 / 15.61	232	77
5c	$C_{22}H_{17}ClN_4$	9.45 / 9.51	15.06 / 15.03	275	80
5d	$C_{22}H_{17}ClN_4$	9.49 / 9.51	14.97 / 15.03	> 300	75
5e	$C_{21}H_{15}ClN_4O$	9.47 / 9.46	15.01 / 14.95	> 300	77
5f	$C_{21}H_{15}ClN_4O$	9.53 / 9.46	14.99 / 14.95	238	78
5g	$C_{27}H_{19}ClN_4$	8.18 / 8.15	12.95 / 12.88	247	72
5h	$C_{27}H_{19}ClN_4O$	7.80 / 7.86	12.52 / 12.43	251	74
7a	$C_{22}H_{15}ClN_4$	15.15 / 15.11	9.62 / 9.56	162	83
7b	$C_{23}H_{17}ClN_4$	14.59 / 14.56	9.13 / 9.21	157	79
7c	$C_{24}H_{19}ClN_4$	14.08 / 14.05	8.96 / 9.89	145	86
7d	$C_{23}H_{17}ClN_4O$	14.04 / 13.98	8.78 / 8.84	158	85
7e	$C_{23}H_{17}ClN_4O$	14.01 / 13.98	8.90 / 8.84	129	89

*Heterocyclization may occur on heating compounds **7a-e**.
*[2]The yield of compounds **5a-h** is given for method A.

The disposition of the characteristic signals in the ^{1}H NMR spectra of products **5** (Table 6) is analogous to that in the spectra of cyclic compounds **4**. However the H-1 doublet is displaced insignificantly towards low field at 10.01-10.20 ppm (TFA). The H-7 and H-8 singlets were found in the 9.26-9.57 ppm (TFA) region and in individual cases ran together into one signal. The presence of signals for the methyl (4.80-4.98 ppm) or benzyl substituent (6.48 ppm for the CH_2 group) at the N-5 atom is characteristic of the spectra of compounds **5**. The band for the stretching vibrations of the nitrile group was observed at 2207-2246 cm^{-1}.

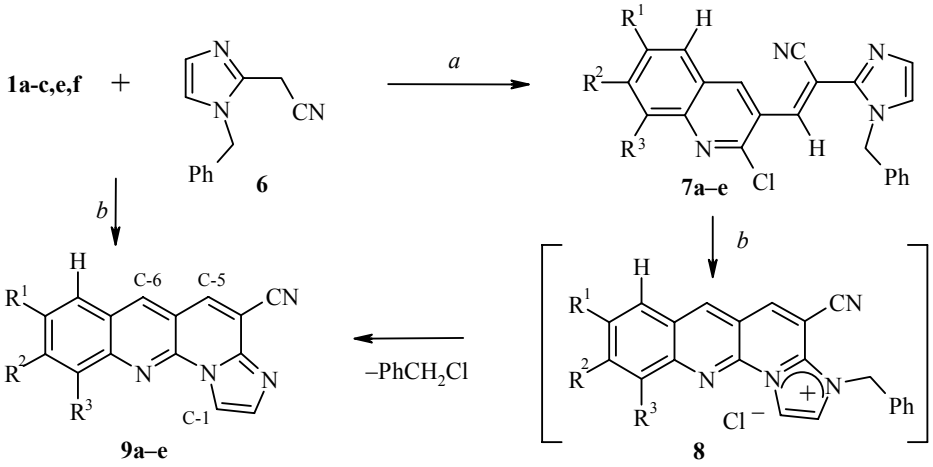
Subsequent investigations showed that as a result of the extended boiling of ionic compounds **5** in DMF elimination of the substituent at atom N-5 occurs, as a result of which cyclic products are formed, the ^{1}H NMR spectra of which were identical to the spectra of model compounds **4**.

We also proposed that in the elimination reactions the best leaving group is the benzyl substituent by virtue of the greater stability of the benzyl cation. Confirmation of this is served by the shorter time needed to carry out the elimination reaction and also the impossibility of isolating ionic compounds **5** in a pure state in many stages in reactions with 1-benzyl-1H-benzimidazol-2-ylacetonitrile **2c.**

TABLE 6. IR and ^{1}H NMR Spectra of Compounds **5**

Compound	IR spectrum, ν_{CN}, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)*		
		Characteristic signals	H-7 (1H, s), H-8 (1H, s)	H-1 (1H, d)
5a	2246	4.80 (3H, s, N–CH_3); 8.00 (1H, t, *J* = 7.2, H-10); 8.12-8.15 (3H, m, H-2,3,4); 8.31 (1H, t, *J* = 8.0, H-11); 8.37 (1H, d, *J* = 8.4, H-9); 8.60 (1H, d, *J* = 8.4, H-12)	9.34, 9.39	10.05 (*J* = 8.0)
5b	2231	2.91 (3H, s, C–CH_3); 4.84 (3H, s, N–CH_3); 7.92 (1H, d, *J* = 8.4, H-10); 8.12-8.17 (3H, m, H-2,3,4); 8.31 (1H, d, *J* = 8.8, H-9); 8.46 (1H, s, H-12)	9.36,	10.10 (*J* = 7.6)
5c	2230	2.84 (3H, s, C–CH_3); 3.16 (3H, s, C–CH_3); 4.80 (3H, s, N–CH_3); 7.87 (1H, d, *J* = 8.4, H-10); 8.10-8.16 (4H, m, H-2,3,4,9)	9.29, 9.32	10.04 (*J* = 7.6)
5d	2207	2.98 (3H, s, C–CH_3); 3.15 (3H, s, C–CH_3); 4.80 (3H, s, N–CH_3); 7.74 (1H, d, *J* = 7.2, H-10); 8.08-8.14 (4H, m, H-2,3,4,11)	9.40, 9.57	10.01 (*J* = 7.2)
5e	2235	4.38 (3H, s, OCH_3); 4.98 (3H, s, N–CH_3); 7.83 (1H, s, H-9); 8.19 (1H, d, *J* = 9.2, H-11); 8.30-8.33 (3H, m, H-2,3,4); 8.69 (1H, d, *J* = 9.2, H-12)	9.44, 9.50	10.20 (*J* = 6.8)
5f	2231	4.45 (3H, s, OCH_3); 4.83 (3H, s, N–CH_3); 7.77 (1H, d, *J* = 8.4, H-11); 7.94-8.02 (2H, m, H-9,10); 8.15-8.19 (3H, m, H-2,3,4)	9.37, 9.40	10.12 (*J* = 6.8)
5g	2230	2.87 (3H, s, C–CH_3); 6.48 (2H, s, CH_2Ph); 7.31 (2H, m, H-2,6 Ph); 7.45 (3H, m, H-3,4,5 Ph); 7.88 (1H, d, *J* = 8.4, H-10); 8.09-8.14 (3H, m, H-2,3,4); 8.27 (1H, d, *J* = 8.8, H-9); 8.44 (1H, s, H-12)	9.33,	10.12 (*J* = 8.4)
5h	2232	4.18 (3H, s, OCH_3); 6.48 (2H, s, CH_2Ph); 7.28-7.30 (2H, m, H-2,6 Ph); 7.43-7.45 (3H, m, H-3,4,5 Ph); 7.64 (1H, s, H-9); 8.02–8.15 (4H, m, H-2,3,4,11); 8.52 (1H, d, *J* = 9.2, H-12)	9.26, 9.33	10.08 (*J* = 8.4)

*The ^{1}H NMR spectra were taken in deuterated trifluoroacetic acid.



a – 2-PrOH, boiling, 30 min – 2h; *b* – DMF, boiling, 30 min – 1h;
7, 9 a $R^1 = R^2 = R^3 = H$, **b** $R^1 = R^3 = H$, $R^2 = Me$, **c** $R^1 = H$, $R^2 = R^3 = Me$,
d $R^2 = R^3 = H$, $R^1 = OMe$, **e** $R^1 = R^2 = H$, $R^3 = OMe$

We continued to study the processes of heterocyclization and elimination using the example of reactions of 2-chloroquinoline-3-carbaldehydes **1** with 1-benzyl-1H-imidazol-2-ylacetonitrile **6**.

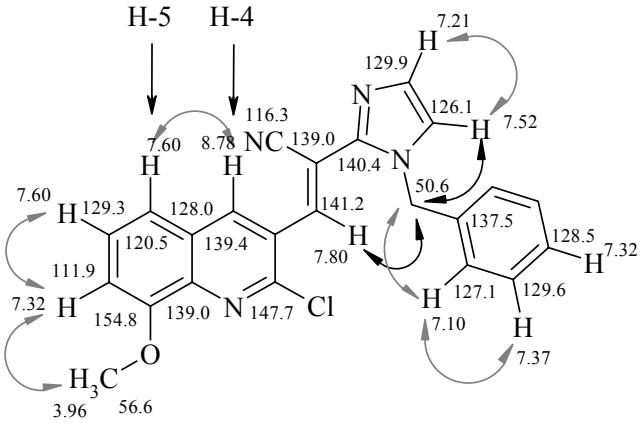


Fig. 3. Assignment of signals and Overhauser effect for compound **7e**.

TABLE 7. IR and ^{1}H NMR Spectra of Compounds **7**

Com-pound	IR spectrum, ν_{CN}, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)*		
		Characteristic signals	CH=CCN (1H, s)	H-4 quinoline (1H, s)
7a	2230	5.56 (2H, s, C<u>H</u>$_2$–Ph); 7.13-7.15 (3H, m, H-2,6 Ph, H-4 imidazole); 7.29–7.40 (4H, m, H-3,4,5 Ph, H-5 imidazole); 7.69 (1H, t, *J* = 7.6, H-6 quinoline); 7.84 (1H, t, *J* = 7.6, H-7 quinoline); 7.94 (1H, d, *J* = 8.0, H-5 quinoline); 8.07 (1H, d, *J* = 8.0, H-8 quinoline)	7.88	8.85
7b	2227	2.59 (3H, s, CH$_3$); 5.55 (2H, s, C<u>H</u>$_2$–Ph); 7.11-7.17 (3H, m, H-2,6 Ph, H-4 imidazole); 7.28-7.39 (4H, m, H-3,4,5 Ph, H-5 imidazole); 7.51 (1H, d, *J* = 7.6, H-6 quinoline); 7.73 (1H, s, H-8 quinoline); 7.95 (1H, d, *J* = 8.0, H-5 quinoline)	7.86	8.80
7c	2224	2.51 (3H, s, CH$_3$); 2.63 (3H, s, CH$_3$); 5.55 (2H, s, C<u>H</u>$_2$–Ph); 7.12-7.15 (3H, m, H-2,6 Ph, H-4 imidazole); 7.27-7.39 (4H, m, H-3,4,5 Ph, H-5 imidazole); 7.48 (1H, d, *J* = 8.4, H-6 quinoline); 7.77 (1H, d, *J* = 8.4, H-5 quinoline)	7.87	8.75
7d	2227	3.94 (3H, s, CH$_3$); 5.56 (2H, s, C<u>H</u>$_2$–Ph); 7.13-7.15 (3H, m, H-2,6 Ph, H-4 imidazole); 7.30-7.43 (6H, m, H-5,7 quinoline, H-3,4,5 Ph, H-5 imidazole); 7.82-7.84 (1H, m, H-8 quinoline)	7.86	8.73
7e	2224	3.96 (3H, s, CH$_3$); 5.57 (2H, s, C<u>H</u>$_2$–Ph); 7.10 (2H, d, *J* = 8.4, H-2,6 Ph); 7.21 (1H, s, H-4 imidazole); 7.29-7.38 (4H, m, H-3,4,5 Ph, H-7 quinoline); 7.52 (1H, s, H-5 imidazole); 7.60-7.63 (2H, m, H-5,6 quinoline)	7.80	8.78

*The ^{1}H NMR spectra were taken in DMSO-d$_6$

TABLE 8. Heteronuclear Correlations for Compound **7e** (DMSO-d_6)

Proton signals, δ, ppm	Chemical shifts of carbon signals with which there are correlations	
	HMQC	HMBC
8.78	139.4	154.8; 147.7; 141.2; 139.0; 120.5
7.80	141.2	147.7; 140.4; 139.0; 116.3; 120.5
7.61	129.3	154.8; 128.0
	120.5	139.0
7.52	126.1	140.4; 129.9
7.37	129.6	137.5; 129.6; 127.1
7.32	111.9	139.0; 154.8; 120.5
	128.5	127.1
7.21	129.9	140.4
7.10	127.1	129.6; 128.5; 127.1
5.57	50.6	140.4; 137.5; 127.1; 126.1
3.96	56.6	154.8

The condensation products **7** (Tables 5, 7) were obtained on interacting the initial compounds in boiling 2-propanol or on heating in DMF (90-95°C). In the ^{1}H NMR spectra of these compounds the singlet of H-4 of the quinoline nucleus, as in the spectra of condensation products **3**, is observed at lowest field at 8.73-8.85 ppm.

The singlet of the styryl proton is found at lower field at 7.80-7.88 ppm. All assignments of signals were carried out on the basis of investigations on homonuclear (COSY, NOESY-1D) and heteronuclear (HMQS and HMBC) correlations using compound **7e** as example (Fig. 3, Table 8).

In difference to reactions with 1H-benzimidazol-2-ylacetonitriles **2b,c**, no ionic compounds **8** were isolated even on brief boiling of the initial compounds **1** and **6** in DMF, since cyclic products **9** are formed at once (Table 9) as a result of elimination of the benzyl substituent, and are derivatives of a new heterocyclic system, *viz.* benzo[*g*]imidazo[1,2-*a*]-1,8-naphthyridine. Compounds **9** under analogous conditions were also obtained from the appropriate products **7**.

A characteristic of the ^{1}H NMR spectra of the cyclic compounds **9** is the presence of three singlets in the low field region corresponding to H-5 (8.50-8.62), H-1 (8.56-8.66), and H-6 (9.00-9.21 ppm) (Fig. 4). The position of the characteristic signals was determined with the aid of experiments on homonuclear and heteronuclear correlations using compound **9e** as example (Table 10). In the IR spectra the band of the CN group of the cyclic products **9** was observed at 2227-2235 cm^{-1} and was more intense than the band of the CN group of condensation products **7** at 2224-2230 cm^{-1}.

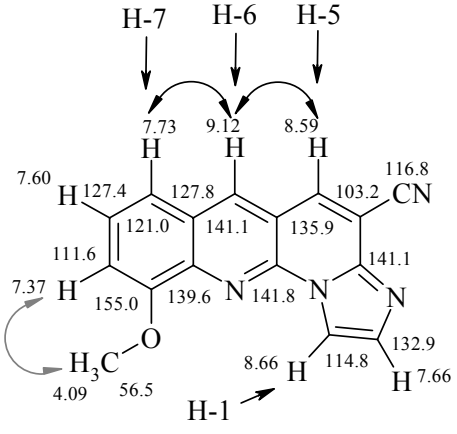


Fig. 4. Assignment of signals and Overhauser effect for compound **9e.**

TABLE 9. Benzo[*g*]imidazo[1,2-*a*]-1,8-naphthyridine-4-carbonitriles **9**

Compound	Empirical formula	Found, % / Calculated, %	IR spectrum, ν_{CN}, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)*				mp, °C	Yield, %*[2]
		N		Characteristic signals	H-5 (1H, s)	H-1 (1H, s)	H-6 (1H, s)		
9a	$C_{15}H_8N_4$	23.02 / 22.94	2227	7.67 (1H, s, H-2); 7.72 (1H, t, *J* = 7.6, H-8); 7.96 (1H, t, *J* = 7.6, H-9); 8.15 (1H, d, *J* = 8.4, H-7); 8.23 (1H, d, *J* = 8.4, H-10)	8.62	8.65	9.21	> 300	94
9b	$C_{16}H_{10}N_4$	21.65 / 21.69	2235	2.77 (3H, s, CH_3); 7.50 (1H, d, *J* = 8.4, H-8); 7.64 (1H, s, H-2); 7.88 (1H, s, H-10); 8.05 (1H, d, *J* = 8.4, H-7)	8.53	8.56	9.05	276	95
9c	$C_{17}H_{12}N_4$	20.49 / 20.58	2230	2.58 (3H, s, CH_3); 2.78 (3H, s, CH_3); 7.48 (1H, d, *J* = 8.8, H-8); 7.65 (1H, s, H-2); 7.89 (1H, d, *J* = 8.8, H-7)	8.50	8.62	9.00	> 300	91
9d	$C_{16}H_{10}N_4O$	20.47 / 20.43	2232	3.98 (3H, s, CH_3); 7.56-7.61 (2H, m, H-7, 9); 7. 65 (1H, s, H-2); 8.05 (1H, d, *J* = 9.2, H-10)	8.61	8.61	9.03	297	94
9e	$C_{16}H_{10}N_4O$	20.35 / 20.43	2230	4.09 (3H, s, CH_3); 7.37 (1H, d, *J* = 8.0, H-9); 7.60 (1H, t, *J* = 8.0, H-8); 7.66 (1H, s, H-2); 7.73 (1H, d, *J* = 8.4, H-7)	8.59	8.66	9.12	282	96

*The ^{1}H NMR spectra were taken in DMSO-d_6.

*[2]Method A.

TABLE 10. Heteronuclear Correlations for Compound **9e** (DMSO-d_6)

Signals of protons, δ, ppm	Chemical shifts of carbon signals with which there are correlations	
	HMQC	HMBC
9.12	141.1	155.0; 141.8; 139.6; 127.8; 121.0
8.66	114.8	141.1; 132.9
8.59	135.9	141.1; 141.8; 116.8; 115.4; 103.2
7.73	121.0	141.1; 139.6
7.66	132.9	141.1
7.60	127.4	155.0; 127.8
7.37	111.6	155.0
4.09	56.5	155.5

EXPERIMENTAL

The IR spectra were recorded on a Perkin-Elmer Spectrum BX instrument in KBr disks. The ^{1}H NMR spectra were measured on a Varian Mercury 400 spectrometer (400 MHz), in DMSO-d_6 or deuterated trifluoroacetic acid, internal standard was TMS. Experiments on NOE were carried out by the NOESY-1D method, blending time 500 msec. The HMQC spectra were obtained for 128 experiments on 32 accumulations at increments with spectral range of 4 kHz for protons and 21 kHz for carbon. Blending time corresponded to $^1J_{CH}$ = 140 Hz. The HMBC spctra were obtained for 400 increments at 32 accumulations at increments of spectral range 4 kHz for protons and 21 kHz for carbon. Blending time corresponded to $^{2\text{-}3}J_{CH}$ = 8 Hz. Melting points were measured on a microhot-stage of Boetius type with a PNMK 05 VEB Analytik eyepiece. A check on the progress of reactions and the purity of the synthesized compounds was carried by TLC on Silufol UV 254 plates in the system chloroform–methanol, 9:1.

X-Ray Structural Investigation of Compound 3i. Crystals of compound **3i** were monoclinic, obtained by slow crystallization from a hot solution of substance **3i** in DMF. $C_{21}H_{15}ClN_4O$, at 20°C: a = 11.6324(4), b = 19.8026(9), c = 7.5798 (4) Å, β = 101.298(4)°, V = 1712.18(13) Å^3, M_r = 374.82, Z = 4, space group $P2_1/c$, d_{calc} = 1.454 g/cm^3, μ(MoKα) = 0.24 mm^{-1}, F(000) = 776. The parameters of the unit cell and the intensities of 16867 reflections (2921 independent, R_{int} = 0.046) were measured on an Xcalibur 3 automatic four-circle diffractometer (MoKα, graphite monochromator, CCD detector, ω scanning, $2\theta_{max}$ = 50°). The structure was solved by the direct method with the SHELX97 set of programs[7]. The positions of the hydrogen atoms were made apparent from an electron density difference synthesis and refined with a rider model with $U_{iso} = nU_{eq}$ (n = 1.5 for hydrogen atoms of methyl groups and n = 1.2 for the remaining hydrogen atoms). The structure was refined on F^2 by the full matrix least-squares method in an anisotropic approximation for the non-hydrogen atoms to wR_2 = 0.092 at 2921 reflections (R_1 = 0.040 for 1907 reflections with $F > 4\sigma(F)$, S = 1.01). The crystallographic data have been deposited in the Cambridge structural data bank (CCDC 726718).

Synthesis of 2-(1H-Benzimidazol-2-yl)-3-(2-chloroquinolin-3-yl)acrylonitriles 3f-i,k-n (General Method). 2-Chloroquinoline-3-carbaldehyde **1b-f** (2 mmol) was added to a solution of 1H-benzimidazol-2-ylacetonitrile **2b,c** (2 mmol) in DMF (2-3 ml) or in 2-propanol (5-7 ml) and the mixture heated on a boiling water bath for 1 h to 2 h 30 min (in the case of 2-propanol boiled for 40 min to 3 h). The reaction mixture was then cooled, the resulting solid was filtered off, washed with acetone, and dried.

Synthesis of 2-(1H-Benzimidazol-2-yl)-3-(2-chloroquinolin-3-yl)acrylonitriles 3a-e,j (General Method). Compound **1** (2 mmol) was added to a solution of 1H-benzimidazol-2-ylacetonitrile **2a-c** (2 mmol) in 2-propanol (5-7 ml), or in methanol (5-7 ml) for compound **3a,** and the mixture boiled for 10-20 min (in the case of compounds **3a-d**) or 30 min to 1 h (in the case of compounds **3e,j**). The reaction mixture was then cooled, the resulting solid was filtered off, washed with acetone, and dried.

Synthesis of Benzimidazo[1,2-*a*]benzo[*g*]-1,8-naphthyridine-6-carbonitriles 4a-f (General Method). A. 2-Chloroquinoline-3-carbaldehyde **1** (2 mmol) was added to a solution of 1H-benzimidazol-2-ylacetonitrile **2a** (2 mmol) in DMF (2-3 ml) and the mixture boiled for 30 min to 1 h 30 min. The reaction mixture was then cooled, the resulting solid was filtered off, washed with acetone, and dried.

B. The appropriate product **3a-d** (2 mmol) was dissolved in DMF (2-3 ml) and the solution boiled for 20 min to 1 h 30 min, then cooled. The resulting solid was filtered off, washed with acetone, and dried.

C. The appropriate 2-chloroquinoline-3-carbaldehyde **1** (2 mmol) was added to a solution of 1H-benzimidazol-2-ylacetonitrile **2b,c** (2 mmol) in DMF (2-3 ml) and the mixture boiled for 3 to 12 h. The mixture was then cooled, the resulting solid was filtered off, washed with acetone, and dried.

D. The appropriate product **3e-n** (2 mmol) was dissolved in DMF (2-3 ml), and the mixture boiled for 3-12 h. After cooling, the resulting solid was filtered off, washed with acetone, and dried.

E. The appropriate product **5a-h** (2 mmol) was dissolved in DMF (2-3 ml) and the mixture boiled for 3 to 12 h. After cooling, the resulting solid was filtered off, washed with acetone, and dried.

Synthesis of 5-Alkyl-6-cyanobenzimidazo[1,2-*a*]benzo[*g*]1,8-naphthyridinium Chlorides 5a-h (General Method). A. The appropriate 2-chloroquinoline-3-carbaldehyde **1** (2 mmol) was added to a solution of 1H-benzimidazol-2-ylacetonitrile **2b,c** (2 mmol) in DMF (2-3 ml) and the mixture boiled for 20 min to 1 h 30 min (in the case of compound **5a** the reaction mixture was heated for 1-2 h on a boiling water bath). The mixture was then cooled, the resulting solid was filtered off, washed with acetone, and dried.

B. The appropriate product **3** (2 mmol) was boiled in DMF (2-3 ml) for 20 min to 1 h 30 min (in the case of compound **5a** the reaction mixture was heated on a boiling water bath for 1-2 h). The reaction mixture was then cooled, the resulting solid was filtered off, washed with acetone, and dried.

Synthesis of 2-(1-Benzyl-1H-imidazol-2-yl)-3-(2-chloroquinolin-3-yl)acrylonitriles 7a-e (General Method). 2-Chloroquinoline-3-carbaldehyde **1** (2 mmol) was added to a solution of 1-benzyl-1H-imidazol-2-ylacetonitrile **6** (2 mmol) in 2-propanol (5-7 ml) or in DMF (2-3 ml) and the mixture boiled for 30 min to 2 h or in the case of DMF heated on a boiling water bath for 1 h to 1 h 30 min. After cooling the resulting solid was filtered off, washed with acetone, and dried.

Synthesis of Benzo[*g*]imidazo[1,2-*a*]-1,8-naphthyridine-4-carbonitriles 9a-e (General Method). A. The appropriate 2-chloroquinoline-3-carbaldehyde **1** (2 mmol) was added to a solution of compound **6** (2 mmol) in DMF (2-3 ml) and the mixture boiled for 30 min to 1 h. The reaction mixture was cooled, and the resulting solid filtered off, washed with acetone, and dried.

B. The appropriate product **7** (2 mmol) was dissolved in DMF (2-3 ml) and boiled for 30 min to 1 h. The reaction mixture was then cooled, the resulting solid was filtered off, washed with acetone, and dried.

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