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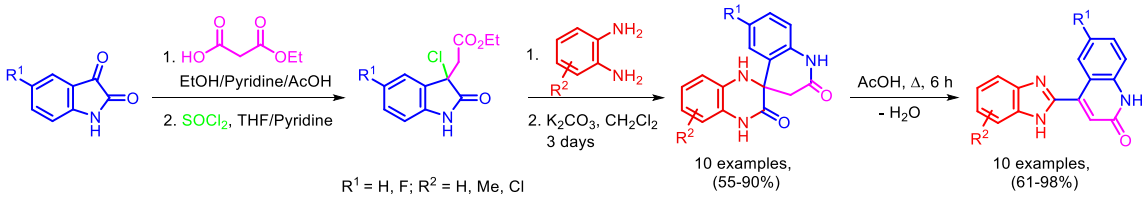
Sequential rearrangements of ethyl 2-(3-chloro-2-oxoindolin-3-yl)acetates and 1*H*,1′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′ (3*H*,4′*H*)-diones for the efficient synthesis of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones

Vakhid A. Mamedov[1]*, Elena A. Khafizova[1], Victor V. Syakaev[1]
Aida I. Samigullina[1], Nataliya E. Algaeva[1], Aidar T. Gubaidullin[1]

[1]Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of RAS, Kazan, Russian Federation



Abstract. A new and highly efficient method for the synthesis of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones via the sequential rearrangements of ethyl 2-(3-chloro-2-oxoindolin-3-yl)acetates and 1*H*,1′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*,4′*H*)-diones in moderate-to-excellent yields has been developed. The rearrangement represents a facile approach to medicinally important biheterocyclic compounds. Compared to other methods, the present protocol has a number of advantages such as – cost-effectiveness, avoidance of difficult of access quinolin-2-one and benzimidazole derivatives as reaction partners, and easy accessibility of starting materials, making it a highly practical approach to access various 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones.

Keywords: *Spiroquinoxalinones, Rearrangements, Benzimidazoles, Quinolin-2(1H)-ones.*

Corresponding Author: *Prof. Vakhid A. Mamedov, Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center of RAS, 420088, Arbuzova str., 8, Kazan, Russian Federation, e-mail: mamedov@iopc.ru*

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1. Introduction

Benzimidazole and its derivatives occupy an important place in pharmaceutical and medicinal chemistry due to their synthetic utility and diversified biological activities.[1a-c] They are the key structural intermediate in the synthesis of a variety of bioactive compounds such as albendazole (anthelmintic), astemizole (antihistaminic), telmisartan (antihypertensive), omeprazole (antiulcer), RAF265 (CHIR-265) (antitumor), Benomyl (antifungal), etc. that contain benzimidazole as a core template (Figure 1).[1d-h] These moieties serve as important intermediates in numerous organic reactions[2] and are used as important ligands for transition metals in various organic transformations.[3] Owing to such a broad utility including a wide range of biological activities, constant efforts have been made by different research groups and numerous methods have been published to improve the synthesis of substituted benzimidazoles.[4]

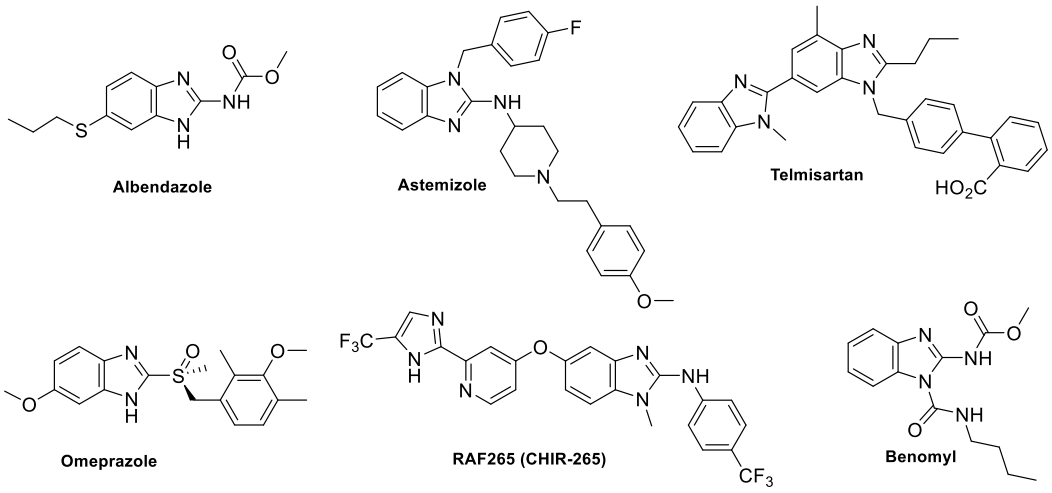


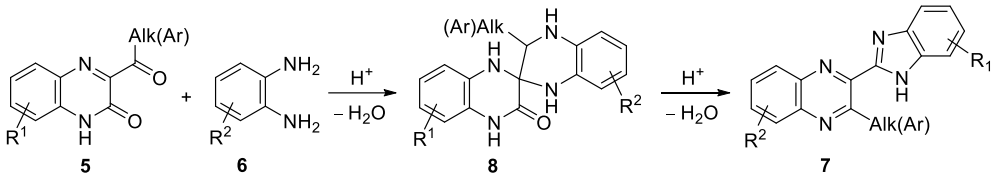
Figure 1. Biologically potent benzimidazole derivatives

There are two classical methods for benzimidazole synthesis, i.e. the coupling of 1,2-diaminobenzenes (1,2-DABs) with carboxylic acids,[5] or their derivatives (e.g., nitriles, imidates, or orthoesters)[5a-b,6] and of 1,2-DABs with aldehydes and ketones (the Phillips-Ladenburg and the Weidenhagen reactions, respectively).[7] The classical versions of these reactions are limited by the use of high temperatures including microwave irradiation,[8] strong acidic conditions and the low yields of products.[9] Actually, all the methods of benzimidazole synthesis which currently exist represent modifications of the reactions mentioned.[10] Recently various catalytic systems have been established for the synthesis of benzimidazole derivatives from 1,2-DAB and aldehydes such as $PhI(OAc)_2$,[11a] DDQ,[11b] heteropoly acids,[11c] Zn-proline,[11d] MnO_2,[11e] H_2O_2/HCl,[11f] H_2O_2/CAN,[11g] oxone,[11h] $NaHSO_3$,[11i] $Na_2S_2O_5$,[11j] sulfamic acid,[11k] $FeCl_3 \cdot 6H_2O$,[11l] $KHSO_4$,[11m] $ZrCl_4$,[11n] $In(OTf)_3$,[11o] $Yb(OTf)_3$,[11p] $Sc(OTf)_3$,[11q] $Cu(OTf)_2$,[11r] *p*-TSA,[11s] polymer-supported hypervalent iodine,[11t] cobalt(II) chloride hexahydrate,[11u] $Sm(OTf)_3$,[11v] thiamine hydrochloride,[11w] $FeCl_3$-doped polyaniline nanoparticles,[11x] a mixture of Ti(IV) isopropoxide and cumene hydroperoxide,[11y] animal bone meal,[11z] nano ceria,[12a] cobalt (II) hydroxide and oxide,[12b] Zn^{2+}-K10-clay,[12c] laccase,[12d] 4-methoxy TEMPO,[12e] CuO nano-particles supported silica[12f] and sodium perborate.[12h] The direct synthesis of these heterocycles by C–X bond activation[13] and from 2-nitro aniline in combination with benzyl amine/benzyl alcohol by redox reaction[14] are also well known in literature. Despite the merits of the methods for the synthesis of benzimidazoles, most of these reported methods have one or more drawbacks such as drastic reaction conditions, longer reaction times, high temperatures, low yields, generation of toxic side products, use of expensive and/or toxic catalysts, hazardous solvent and work-up difficulties, which makes them undesirable in the aspect of green chemistry, sustainable development, and industrial applications.

The analysis of the data published has shown that the main shortcoming of these methods involve the impossibility to use them for synthesizing various types of benzimidazole derivatives. For example, it is no easy task to enter any given heterocycle in position 2 of benzimidazole ring and vice versa to enter a benzimidazole ring for any given heterocycle using any of these methods. In addition to the methods mentioned, examples of the formation of benzimidazole derivatives by rearrangement of

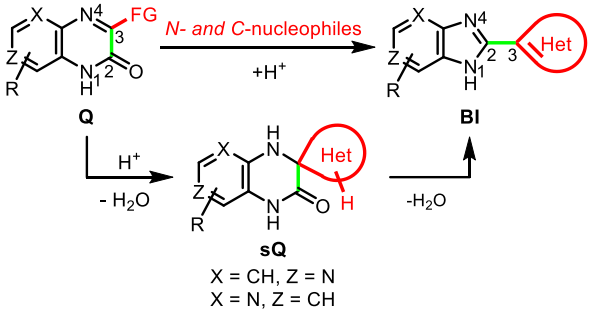
heterocyclic systems have been documented.[15,16] Despite the fact that the publications on these reactions are much fewer as compared with the Phillips-Ladenburg and Weidenhagen reactions, they are more diverse but unfortunately not general.

As part of our ongoing interest in the synthesis and utilization of nitrogen-containing heterocyclic and heteroaromatic compounds,[17] we had a cause to explore the chemistry of quinoxalin-2(1*H*)-ones **5**. We have recently reported a new method for the synthesis of the 2-(benzimidazol-2-yl)quinoxalines via the reaction of alkanoyl(aroyl)quinoxalin-2(1*H*)-ones **5** and 1,2-diaminobenzenes **6** (Scheme 1).[18] The key step in this transformation involves a novel acid catalyzed rearrangement of an intermediate spiro-quinoxalin-2(1*H*)-one derivatives **8** with the contraction of the pyrazine ring of the quinoxalin-2(1*H*)-one fragment.



Scheme 1. Ring transformation of quinoxalin-2(1*H*)-ones towards benzimidazoles

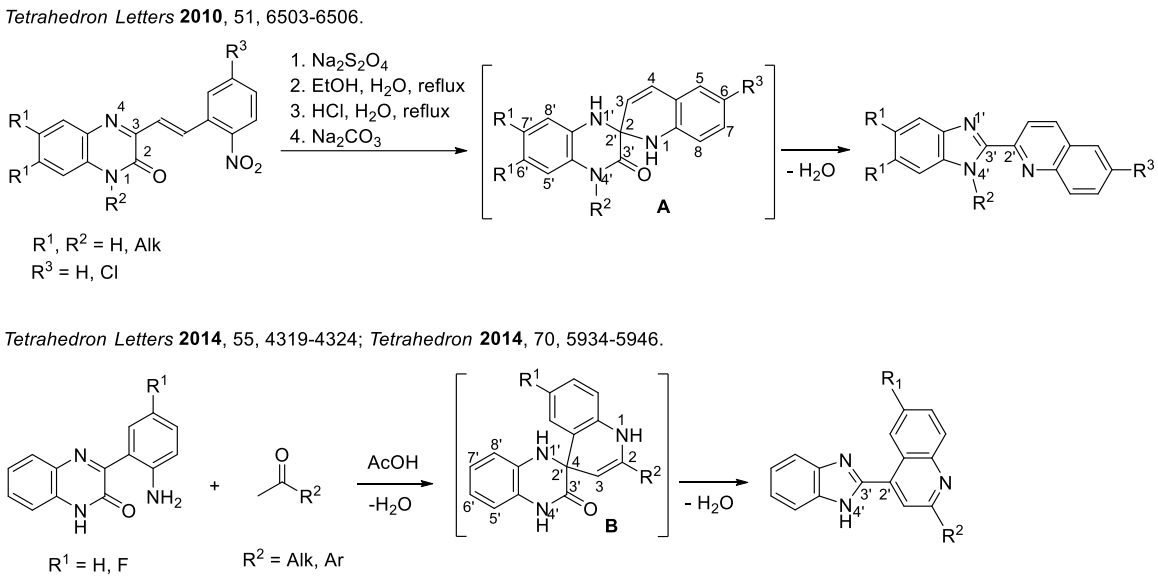
We also showed that the scope of this rearrangement could be extended to the use of other functionalized quinoxalinones (**Q**) and *N*-nucleophiles for synthesizing various 2-(hetero)aryl-substituted benzimidazoles (**BI**),[19] which proceeds via spiro-quinoxalinones (**sQ**). On the basis of these results we have proposed[20] and shown,[15] that "any of the spiro-derivatives of 1,2,3,4-tetrahydroquinoxalin-3-one with at least one mobile hydrogen atom in their spiro-forming component are on their way to the benzimidazole derivative with the spiro-forming component in position 2" (Scheme 2).[19e,20] It should be pointed out that these results were recognized by Hassner and Namboothiri as the Mamedov heterocycle rearrangement,[21] which is applicable for the synthesis of aza-analogues of **BI**.



Scheme 2. A schematic presentation of the quinoxalinones when exposed to *N*-, *C*-nucleophiles.

Based on this Scheme, we have synthesized a series of 2-(heteroaryl)benzimidazoles, including 2- and 4-(benzimidazole-2-yl)quinolines,[19c,22] by the rearrangement of the corresponding quinoxalin-2(1*H*)one derivatives. At the same time in some cases spiro-derivatives of quinoxalin-2-ones have been isolated and characterized,[19b,19d,20] and in other cases including when 2- and 4-(benzimidazole-2-

yl)quinolines were synthesized,[19c,22] the formation of corresponding spiroquinoxalinones **A** and **B** under the reaction conditions was assumed (Scheme 3).



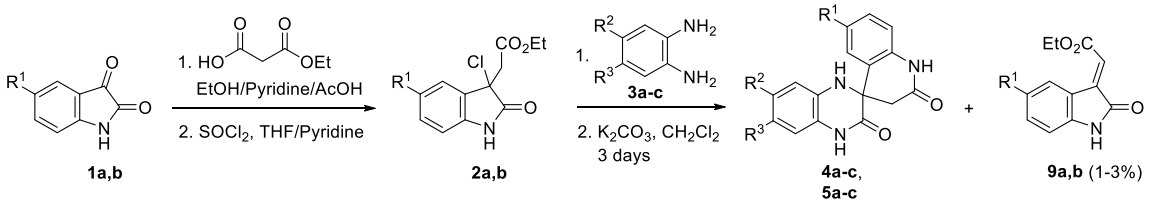
Scheme 3. Our previous works

2. Results and discussion

As can be seen from the schematic presentation of the quinoxalinone → benzimidazole rearrangement (Scheme 2), the introduction of heterocyclic system as a spiro-fragment in position 3 of quinoxalinones via the reaction of functionally substituted derivatives of quinoxalinones with the appropriate nucleophilic reagents was necessary in all cases for its implementation. The question arises whether it is possible to synthesize spiro-derivatives of quinoxalinones on the basis of other heterocyclic systems, besides quinoxalinones. The reply has significantly expanded the possibility of the quinoxalinone → benzimidazole rearrangement, because of the wide variety of heterocyclic systems. We started our investigations in this direction with an isatine considering that are known for this heterocycle the methods of the synthesizing its infinite number of spiroderivatives[23] including spiroquinoxalinones **4**.[24] The latter **4** are synthesized under mild conditions via the condensation of chlorooxoindolines **2a,b** and benzene-1,2-diamines **3**. Chlorooxoindolines **2** in their turn were synthesized via the condensation of substituted isatins **1a,b** with mono-ethyl malonate followed by chlorination with thionyl chloride (Table 1).[24] Following a similar approach, we synthesized a series of new spiroquinoxalinones **4, 5** with the use of symmetrical di- (**3b,c**) and unsymmetrical mono- (**3d,e**) substituted benzene-1,2-diamines. It should be pointed out that in the second stage of the process K_2CO_3 was used as a base instead of Cs_2CO_3, which as a result of the dehydrochlorination of the initial 3-chlorooxindolines **2** with the main desired reaction products **4** and **5** contributed to the formation of the side products; *i.e.* compounds **9a,b** with 1-3% yields. An additional point to emphasize is that to complete the reaction in the case of the use of unsubstituted benzene-1,2-diamine **3a** and its monosubstituted derivatives **3d,e** three days are sufficient, but in the cases of

4,5-dimethylbenzene-1,2-diamine **3b** and pyridine-2,3-diamine **3f** up to 5 days are neccesary. However, in the case of 4,5-dichlorobenzene-1,2-diamine **3c**, it takes three days to complete the reaction.

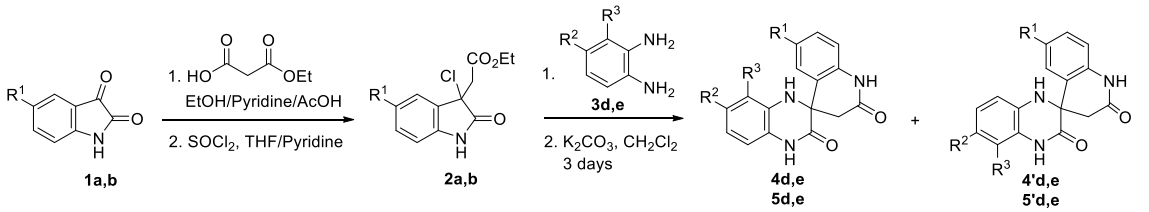
Table 1. Synthesis of 3-chlorooxoindoles and spiroquinoxalinones



entry	compound	R^1	R^2	R^3	yield, %
1	**4a**	H	H	H	65 (62)[24]
2	**5a**	F	H	H	73 (70)[24]
3	**4b**	H	CH_3	CH_3	90
4	**5b**	F	CH_3	CH_3	86
5	**4c**	H	Cl	Cl	70
6	**5c**	F	Cl	Cl	82

The reaction of chlorooxoindolines **2a,b** with monosubstituted benzene-1,2-diamines **3d,e** proceeds with the formation of regioisomeric spiroquinoxalinones **4d,e, 5d,e** and **4′d,e**, **5′d,e**. As can be seen from the data in Table 2, a significant difference in the ratio of regioisomers has been manifested only in the case of benzene-1,2-diamine **3e**. In this case the methyl group is adjacent to the amino group, which spatially hinders the formation of regioisomeric **4e**.

Table 2. Synthesis of spiroquinoxalinones



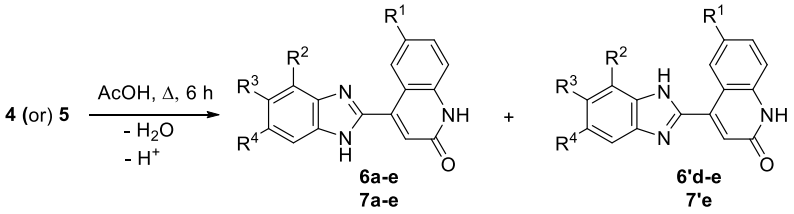
entry	compound	R^1	R^2	R^3	overall yield, (**4**/**4′** and **5**/**5′**)[a,b]
1	**4d** + **4′d**	H	Cl	H	68%, 45:55
2	**5d** + **5′d**	F	Cl	H	85%, 33:67
3	**4e** + **4′e**	H	H	CH_3	89%, 9:91
4	**5e** + **5′e**	F	CH_3	H	84%, 45:55

[a]Ratio determined by the ^{1}H NMR of the crude products.
[b]Compounds **8a,b**, which are formed as by-products in 1-3% yields are not presented.

There have been a variety of different 1*H*,1′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*,4′*H*)-diones at our disposal, we have investigated their properties in boiling acetic acid (under conditions of our rearrangements)[15,21,25] **4a-c** for synthesizing 4-(benzimidazol-2-yl)quinoline-2-ones **6** and **7**. The reaction has been completed within 6

hours and formed the desired products **6** and **7** with medium and high yields. It should be noted that the reactions proceeded successfully not only with individual spiro-compounds **4a-c** and **5a-c** obtained from the unsubstituted benzene-1,2-diamine **3a** and its symmetrically disubstituted derivatives **3b**,**c,** but also with regioisomeric mixtures of spiro- compounds **4d**,**e**, **5d**,**e** and **4′d**,**e**, **5′d**,**e,** obtained from the mono-substituted benzene-1,2-diamines **3d,e**. They were completed with the formation of the expected 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones **6a-d** and **7a-e** (**Table 3**). In the case of the spiro-derivative **4d** (with the monochlorosubstituted on the benzene ring quinoxaline-2(1*H*)-one fragment), the formation of the only product **7d** is observed regardless of the precursor's ratio (**Table 3**).The reason is the benzimidazoletautomerism. However, the same reason explains a whole series of regioisimeric compounds **6e, 7d**,**e** and **6′e, 7′d**,**e** formed with approximately the same ratio in the case of thespiro-derivatives **4e**, **5d**,**e** and **4′e, 5′d**,**e** (with the monosubstituted on the benzene ring quinoxaline-2(1*H*)-one fragments), regardless of the components ratio in their original mixtures (**Table 3**).

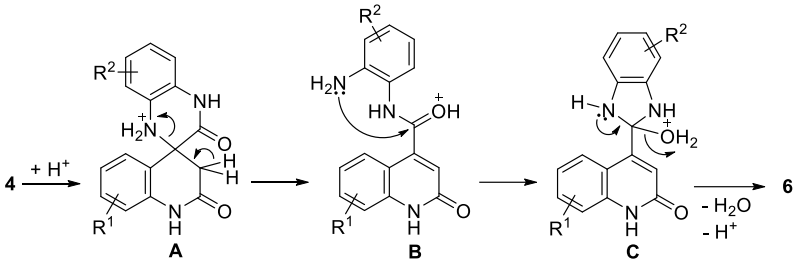
Table 3. Synthesis of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones via the rearrangement of 6-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*,4′*H*)-diones



№	compound[a]	R^1	R^2	R^3	R^4	yield, %
1	**6a**	H	H	H	H	98
2	**7a**	F	H	H	H	75
3	**6b**	H	H	CH_3	CH_3	61
4	**7b**	F	H	CH_3	CH_3	66
5	**6c**	H	H	Cl	Cl	67
6	**7c**	F	H	Cl	Cl	56
7	**6d + 6′d**	H	H	Cl	H	96
8	**7d**	F	H	Cl	H	81
9	**6e + 6′e**	H	CH_3	H	H	89
10	**7e + 7′e**	F	H	CH_3	H	52

[a] The ratios of regioisomers **6d/6′d**, **6e/6′e** and **7e/7′e** are given in Experimental part.

Based on the known chemistry of amines,[26] amides,[25] quinoxalinones,[15,16,25] and the previous reports[18-20,28] a plausible mechanism for the reaction of the formation of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones **6** has been proposed (Scheme 5). The rearrangement of the spiro-quinoxalinone **4** is assumed to occur according to Scheme 5, which proceeds by cascade reactions involving: a) the ring-opening with the cleavage of the C3-N4 bond in the spiro-compound **A** with the intermediate formation of the quinoline derivative **B**, b) the intramolecular nucleophilic attack by the amino group on the carbonyl group with the intermediate formation of the hydroxy-derivative **C**, and c) the elimination of water leading to the formation of the final product **6**. All the stages of the reaction include acid-catalyzed processes.



Scheme 5. A plausible mechanism for the formation of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones.

The structures of all synthesized compounds were established by a variety of NMR methods. The complete assignment of the signals in the ^{1}H, ^{13}C and ^{15}N NMR spectra was accomplished using 2D NMR techniques (COSY, HSQC, HMBC).

Futhermore, the structure of the 4-(benzimidazol-2-yl)quinolin-2(1*H*)-one **6a** and 4-(5,6-dimethylbenzimidazol-2-yl)quinolin-2(1*H*)-one **6b** were confirmed by X-ray crystallographic analysis (Figures 2-8). The colorless prismatic crystals of **6a** suitable for X-ray analysis were obtained by the crystallization from DMSO. The compound crystallized in monoclinic unit cell with DMSO molecules in a ratio of 1:1 (Figure 2). The **6a** molecule is located in the unit cell at the general position, so that only the pair of molecules **6a** and DMSO turn out to be in its independent part.

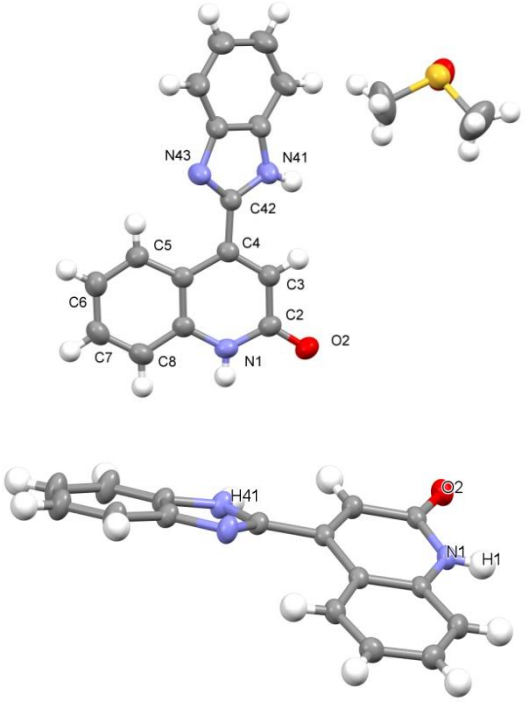


Figure 2. Two projections of ORTEP view of molecules in the crystal of **6a** and partial numbering scheme. Non-hydrogen atoms are represented by probability ellipsoids of thermal vibrations (p = 50%), hydrogen atoms – by spheres of arbitrary radii.

The benzimidazole and quinoline fragments of the molecule of **6a** are flat within the experimental errors of 0.025(3)Å and 0.020(1)Å, respectively. With the exception of the double bond C42-N43 (1.322(2)Å), all other single bonds in benzimidazole fragment are sufficiently aligned and are distributed in the range of 1.360(2) - 1.394(3)Å, in the quinoline fragment all bonds are distributed in a wider range of values

- from 1.356(2) up to 1.444(2)Å.

The plane of the benzimidazole moiety of the molecule **6a** is slightly turned relative to the plane of the quinoline system - dihedral angle between two planes is equal 23.93(6)°. However, this reversal of the fragments does not prevent the formation of intramolecular C-H···N type hydrogen bonds (the interaction parameters are given in Table 4), which apparently stabilizes the conformation of the molecule and prevents significant vibrations of its fragments, as can be seen from the ellipsoids of thermal oscillations of the atoms.

The characteristic feature of the supramolecular structure of **6a** is the formation of centrosymmetric H-dimers in the crystals due to the presence of amino groups and the formation of classical N-H···O hydrogen bonds (Figure 3). Solvate DMSO molecules also participate in the hydrogen bonds with 4-(benzimidazol-2-yl)quinolin-2(1*H*)-one molecules and are located around these H-dimers. The hydrogen bonds parameters are presented in Table 4.

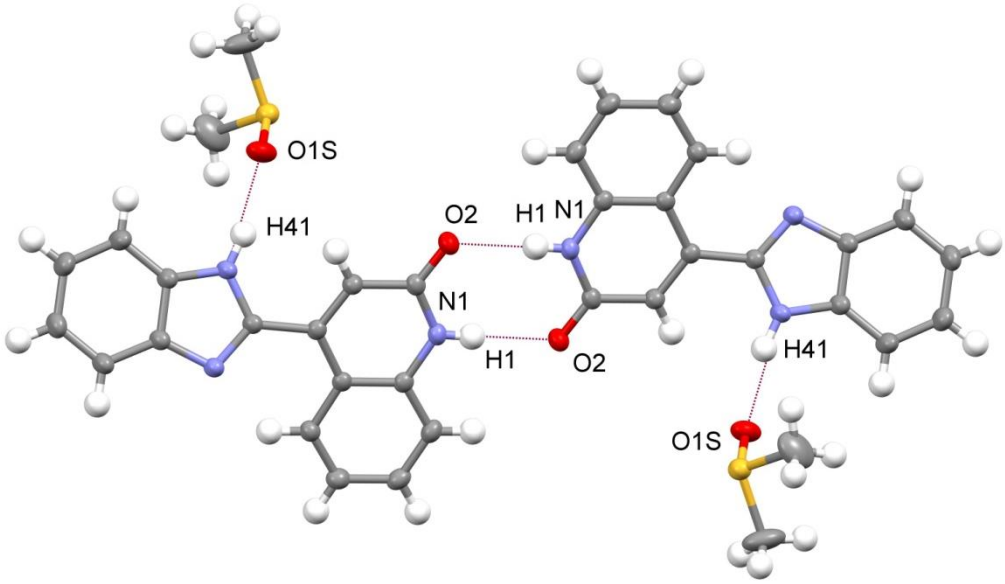


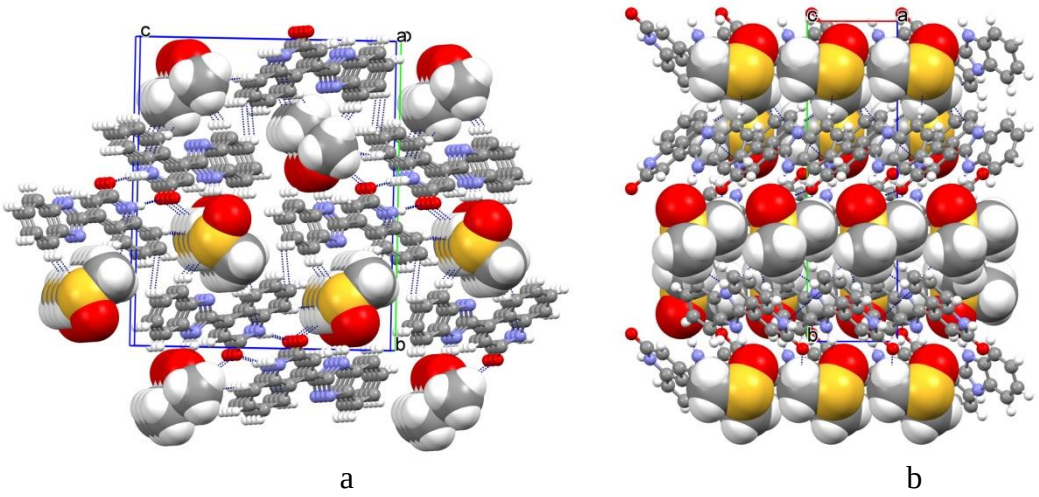
Figure 3. H-dimer of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-one molecules and two H-bounded solvate DMSO molecules in the crystal of **6a**. H-bonds are shown by red dashed-lines.

Table 4. Hydrogen bonds parameters in the crystal of **6a**.

Contact, D–H···A	d(D–H),Å	d(H···A), Å	d(D···A), Å	∠(D–H···A), °	Symmetry operation
N1-H1···O2*	0.80(3)	2.02(3)	2.817(2)	177(2)	-x,-y,1-z
N41-H41···O1S**	0.89(3)	1.92(3)	2.784(2)	165(2)	1-x,-1/2+y,1/2-z
C3-H3···N41	0.93	2.54	2.868(2)	101	intra
N5-H5···N43	0.93	2.32	2.958(3)	126	intra

1D- inclined stack (or column) of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-one molecules along *0a* axis formed through the π…π contacts between aromatic benzimidazole and quinoline fragments may be considered as the second structure-forming motif in the crystal of **6a** (Figure 4). The dihedral angles between aromatic fragments of contacting molecules in 1D-stack are in the range 0 - 23.3(1)°, the

distances between the centers of aromatic cycles is 3.995(1) - 4.473(1)Å and the shortest distances between contacting molecular planes are in the range 3.0910(8) - 3.9278(7)Å. Parallel tetragonal-type packing of such 1D-stacks along crystallographic directions *0b* and *0c* (Figure 4) forms 3D structure of the **6a** crystals. Referring to Figure 7, it will be seen that **6a** crystal packing contains the open-ended channels. Solvate DMSO molecules are located in these channels formed by 1D-stack of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-one **6a** molecules. The low packing index (equal to 68.2%) points on the loose nature of the crystal packing as well.



a b

Figure 4. Two projections of **6a** crystal packing. Sovate DMSO molecules are shown in space-filling model, H-bonds and π···π contacts are shown by blue dashed lines. View near *0a* axis (a) and along *0c* axis (b).

In addition, the molecular structure of compound **6b** was also determined by the X-Ray diffraction method (Figure 5). As well as the previously studied compound **6a**, benzimidazole-quinolinone **6b** does not crystallize individually, but forms monoclinic crystals of crystal solvate with acetic acid molecules in the ratio 1:2. The benzimidazole and quinoline fragments are flat within the experimental errors of 0.034(2) and 0.038(2) Å, respectively. The plane of the benzimidazole fragment is turned relative to the plane of the quinoline fragment by an angle of 35.10°, which is slightly larger than in compound **6a**. Additionally the geometry of the molecule is also stabilized by the intramolecular interaction of the C-H···N type.

As conserned of molecular interactions in the crystal of **6b**, it should be noted that both intramolecular interactions that stabilize the geometry of the molecule and intermolecular interactions of various types are observed. An important remark should be noted. The molecule of compound **6b**, as well as the previous compound **6a**, contains two proton-donor centers - aminocarbonyl and imidazole moieties. Earlier we have shown,[29] that in the crystals of most heterocyclic compounds with a carbamoyl group, centrosymmetric H-dimers are formed from the molecules of the compound due to the formation of paired classical NH···O hydrogen bonds, provided that this compound crystallizes in an individual form. But in the case of crystallization with solvate molecules, a different situation is observed: there is a competition between solvate molecules and the molecules of the compound. Solvate molecules with active proton-donor and proton-acceptor centers can participate in the formation of intermolecular

interactions with the aminocarbonyl moiety, thus blocking it and preventing the formation of a centrosymmetric H-dimer. However, if the number of independent solvate molecules is small, the possibility of H-dimer formation persists, as was observed in the case of the crystal of compound **6a**.

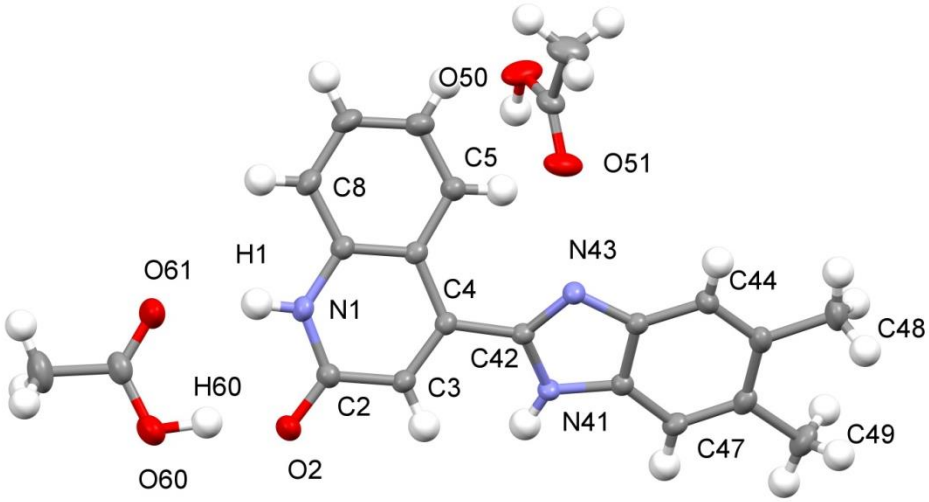


Figure 5. Geometry of molecules in a crystal **6b** and partial numbering scheme. Displacement ellipsoids are drawn at the 50% probability level, hydrogen atoms are represented as fixed-size spheres.

In the case of 4-(5,6-dimethylbenzimidazol-2-yl)quinolin-2(1*H*)-one **6b**, there are two solvate molecules per one independent molecule of the heterocyclic system. One molecule of acetic acid binds to the aminocarbonyl fragment due to the classical hydrogen bonds N-H···O and O-H···O type (Figure 6), forming a pseudo H-dimer. In this case, the molecules of the solvent prevent the formation of a centrosymmetric H-dimer. The parameters of all the interactions are shown in the Table 5.

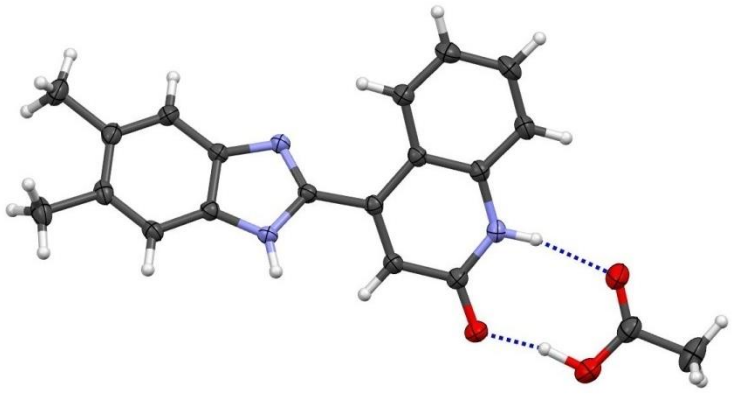


Figure 6. Pseudo H-dimer formed with the participation of the aminocarbonyl moiety of the molecule of the compound **6b** and one acetic acid molecule.

The second molecule of acetic acid is a bridging molecule, connecting two molecules of the compound **6b** together and participating in the formation of a 1D-supramolecular structure along *0a* axis (corresponding to the shortest parameter of unit cell) due to the classical N-H···O and O-H···N hydrogen bonds (Figure 7). The one-dimensional H-chain is additionally stabilized by π···π c**o**ntacts between benzoimidazole and quinolinone aromatic systems. The contact parameters: the shortest

distance between electronic systems is 3.447Å, the dihedral angle is equal to 5.56° (symmetry operation 3/2-x, -1 / 2 + y, 1/2-z).

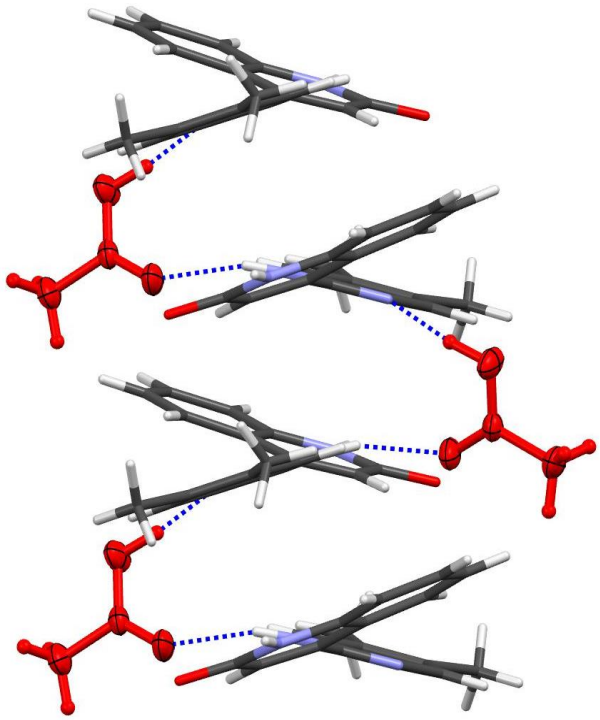


Figure 7. 1D-chain of H-bounded (blue dashed-lines) molecules of compound **6b** and the second solvent molecules (marked with red color)

Table 5. Hydrogen bonds parameters in the crystal of **6b**

D–H···A	D–H, Å	H···A, Å	D···A, Å	∠ DHA, °	Symmetry operation
C5-H5···N43	0.93	2.43	3.026(2)	122	-
N1-H1···O61	0.88(2)	1.98(2)	2.839(2)	166(2)	1/2+x,3/2-y,1/2+z
O60-H60···O2	1.06(3)	1.55(3)	2.593(2)	168(3)	-1/2+x,3/2-y,-1/2+z
N41-H41···O51	0.86(2)	1.96(2)	2.777(2)	159(2)	3/2-x,1/2+y,1/2-z
O50-H50···N43	1.00(3)	1.67(3)	2.666(2)	173(3)	x,-1+y,z

Analyzing the three-dimensional crystal structure, it should be noted that the solvent molecules are located in two-dimensional regions (Figure 8). Such layered arrangement of solvate molecules should lead to instability of the crystal outside the mother solvate medium. Meanwhile, in air crystals are stable, and their destruction is not observed. This behavior can be associated with the participation of solvate molecules in the classical hydrogen bonds with the molecules of the compound **6b**, which are the strongest intermolecular interactions.

However, such a mutual arrangement of molecules does not lead to a densest packing of molecules in the crystal - the calculated packing coefficient of molecules in crystal at 293K for compound is 66.9%, which is closer to the lower boundary of the limits typical for crystals of organic compounds (65-75%).

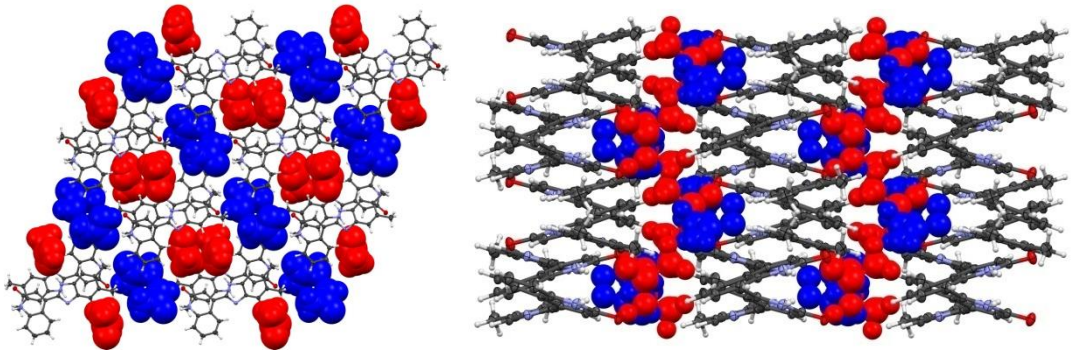
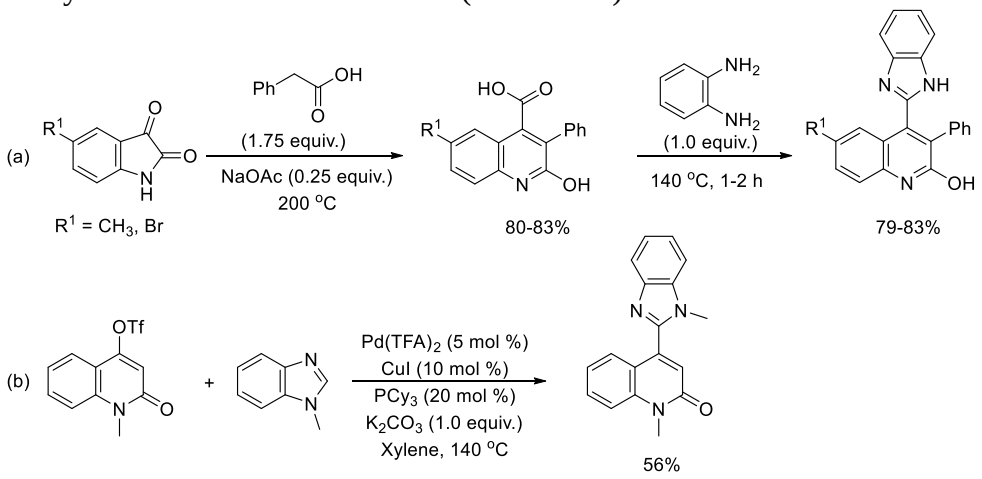


Figure 8. Two projections of **6b** crystal packing. Two independent sovate molecules are shown in space-filling model by red and blue color. View along *0b* axis (a) and along a*0c* diagonal (b).

It should be pointed out that only two cases of the synthetic methods for 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones are known.[30,31] The first is traditional and based on the condensation of corresponding quinolin-2(1*H*)-one-4-carboxylic acid derivatives with benzene-1,2-diamine under the Phillips–Ladenburg reaction condition (Scheme 6a).[5,30] Synthesis of the substituted quinolin-2(1*H*)-one-4-carboxylic acid derivatives, which are the starting compounds for this method was achieved through Pfitzinger reaction by heating isatins with phenylacetic acid in an aqueous/alcoholic KOH solution.[32] Isatins that are not commercially available can be prepared from anilines via the Sandmeyer isatin synthesis[33] or *o*-lithiation and cyclization,[34] but these resulting additional steps inevitably reduce the overall yield of the desired products. The second method is the palladium/copper-catalyzed coupling reactions between 4-quinolinonyl triflates with benzimidazole (Scheme 6b).[31]



Scheme 6. The known methods for the synthesis of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones

Synthesis of the 4-quinolinonyl triflate, which is the starting compound for this method was prepared with a two-stage process involving the cyclization of the corresponding anthranilic acids with acetic anhydride in acetic acid with the formation of *N*-methyl-4-hydroxy-2-quinolin-2(1*H*)-one[35] and the synthesis of its triflate derivative.[31] Only one compound was synthesized by this method and it cannot be used for the synthesis of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones derivatives with non-protected NH groups of

heterocycles. The overall yields of the target products according to these methods seldom exceeded 20%. The method proposed by us appears preferable to the above mentioned one and makes it more simple to synthesize 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones with a variety of substituents in both benzimidazole and quinolin-2(1*H*)-one ring systems and with the free positions 1 of heterocycles into which any substituent, in particular any alkyl group can be introduced.

In conclusion, we have developed a new practical and efficient approach for the direct synthesis of 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones via the Mamedov rearrangement of 1*H*,1′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*,4′*H*)-diones. The substrate scope was broad, permitting the construction of a variety of spiroquinoxalinones. The procedure described here has the advantage that the reaction is performed under mild and metal-free condition. Using this established method, the 4-(benzimidazol-2-yl)quinolin-2(1*H*)-ones and their aza analogues are accessible for further biological evaluation as a new class of bi-heterocyclic compounds.

3. Experimental section

General Information

NMR experiments were performed on a Bruker Avance 500 spectrometer equipped with broadband z-grad probes. The temperature for all measurements was set to 303 K. Chemical shifts (δ in ppm) are given from internal solvent, DMSO-*d*6 2.49 for ^{1}H and 39.5 for ^{13}C, external references CD_3NO_2 (380.2 ppm) were used for ^{15}N. Typical parameters for ^{1}H-NMR spectra were spectral width 12020 Hz, pulse width (π/3) 3.7 μs, acquisition time 2 s and relaxation delay 2 s. Typical parameters for ^{13}C-NMR spectra were spectral width 27 kHz, pulse width (π/3) 3.2 μs, acquisition time 1 s and relaxation delay 4 s; WALTZ-16 was used for broadband proton decoupling; the FIDs were multiplied by an exponential weighting (lb = 2 Hz) before Fourier transformation. 2D NMR spectra were acquired and processed using standard Bruker NMR software. Selected parameters for (^{1}H-^{13}C) gs-HSQC and gs-HMBC spectra were spectral width 8000 Hz for 1H and 25 kHz for ^{13}C, 4024 × 256 data set, number of scans 8 (gs-HSQC) or 16 (gs-HMBC) and relaxation delay 3 s. Selected parameters for 2D (^{1}H-^{15}N) spectra were spectral width 8000 Hz for ^{1}H and 10.5 kHz for gs-HSQC(^{15}N), 28 kHz for gs-HMBC(^{15}N), number of scans 8 (gs-HSQC) or 32 (gs-HMBC) and relaxation delay 3 s. In the gs-HSQC experiments, GARP modulation of X-nuclear was used for decoupling. The FIDs were processed using zero filling in both domain and a sine squared window function in both dimensions was applied prior to Fourier transformation.

IR spectra in the range of 4000–400 cm–1 were recorded for KBr pellets on a Bruker Tensor 27 spectrometer with optical resolution of 4 cm–1 and accumulation of 64 scans.

Melting points were determined in glass capillaries on an Electrothermal IA9200 apparatus.

X-ray Crystallographic Details for Compound **6a** and **6b**.

The X-ray diffraction data for the crystal of **6a** and **6b** were collected on a Bruker Kappa Apex II CCD diffractometer in the ω and φ-scan modes using graphite monochromated Mo K_α (λ = 0.71073 Å) radiation at 296(2) K. Data were corrected for the absorption effect using SADABS program.[36] The structures were solved by direct method and refined by the full matrix least-squares using SHELXTL[37] and WinGX[37]

programs. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were inserted at calculated positions and refined using a "riding" models atoms except the hydrogen atoms H41, H1 of NH groups of both compounds and H50, H60 of OH groups in **6b**, which were located from difference maps and refined isotropically. During data collections the images were indexed, integrated, and scaled using the APEX2 data reduction package.[38] Analysis of the intermolecular interactions was performed using the program PLATON.[39] Mercury program[40] package was used for figures preparation.

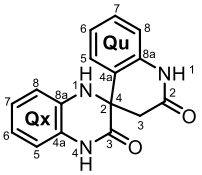
Crystallographic data for **6a**: $C_{16}H_{11}N_3O{*}C_2H_6OS$ ($C_{18}H_{17}N_3O_2S$), colorless prism, size 0.14x0.24x0.32 mm^3, M = 339.40, monoclinic, a = 5.3582(12) Å, b = 19.064(4) Å, c = 16.176(4) Å, β = 91.033(3)°, V = 1652.1(6) Å^3, T = 296(2) K, space group P $2_1/c$, Z = 4, μ(Mo K$_\alpha$) = 0.211 mm^{-1}, ρ_{calc} = 1.365 g·cm^{-3}, F(000) = 712, theta range for data collection 1.65 to 29.64°, 22638 reflections measured, 4392 independent reflections (R_{int} = 0.0301), 227 parameters, 0 restraints. Final indices: R_1 = 0.0504, wR_2 = 0.1287 (4392 reflections with $I > 2\sigma_I$), R_1 = 0.0785, wR_2 = 0.1479 (all data), GoF = 1.026, largest difference in peak and hole (0.445 and -0.398 eÅ^{-3}).

Crystallographic data for **6b**: $C_{18}H_{15}N_3O{*}2(C_2H_4O_2)$ ($C_{22}H_{23}N_3O_5$), colorless needle, size 0.10x0.19x0.90 mm^3, M = 409.43, monoclinic, a = 16.975(3)Å, b = 7.168(1)Å, c = 18.219(3)Å, β = 109.549(4)°, V = 2089.0(5)Å^3, T = 296(2) K, space group P $2_1/n$, Z = 4, μ(Mo K$_\alpha$)= 0.094 mm^{-1}, ρ_{calc} = 1.302 g·cm^{-3}, F(000) = 864, theta range for data collection 3.65 to 28.00°, 26064 reflections measured, 5026 independent reflections (R_{int}= 0.0589), 291 parameters, 0 restraints. Final indices: R_1= 0.0490, wR_2= 0.1122 (3070 reflections with $I > 2\sigma_I$), R_1= 0.0939, wR_2= 0.1360 (all data), GoF = 1.020, largest difference in peak and hole (0.201 and -0.248 eÅ^{-3}).

Ethyl 2-(3-chloro-2-oxoindolin-3-yl)acetate **2a** and ethyl 2-(3-chloro-5-fluoro-2-oxoindolin-3-yl)acetate **2b** were prepared according to a literature procedure.[24]

Typical experimental procedure for the preparation of spiroquinolinones 4, 5 and 4′, 5′. A mixture of diamines **3** (2.0 mmol) and K_2CO_3 (5.0 mmol) in CH_2Cl_2 (5 mL) were stirred at rt for 10 min before a solution of 3-chlorooxindolines **2** (1.0 mmol) in CH_2Cl_2 (5 mL) was added dropwise. The resultant mixture was stirred at room temperature for 3 days (in the case of mixture of **4f** was stirred at room temperature for 5 days). The reaction mixture was concentrated in vacuo and the residue purified by column chromatography on silica gel (eluant: hexane/ethyl acetate V/V=20:1→2:1) to afford pure spiroquinolinone as a solid (major product) and ethyl 2-(2-oxoindolin-3-ylidene)acetate **8a** and ethyl 2-(5-fluoro-2-oxoindolin-3-ylidene)acetate **8b** (minor products) as by products in 1-3% yields.

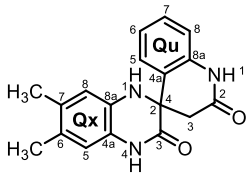
1′,4′-Dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 4a.



Yield 182 mg (65%); pinkish solid; R_f (EtOAc) 0.47; mp 289-291 °C (263-264 °C[24]); ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.68, 2.93 (AB, J = 16.1 Hz, 2H, H3-Qu), 6.64 (ddd, J = 7.5 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H, H6-Qx), 6.73 (dd, J = 7.5 Hz, J = 1.4 Hz, 1H,

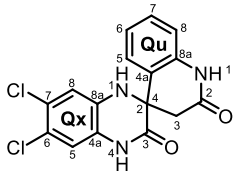
H8-Qx), 6.76 (s, 1H, NH1-Qx), 6.80 (brd, *J* ~ 7.5 Hz, 1H, H5-Qx), 6.81 (ddd, *J* = 8.2 Hz, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H7-Qx), 6.85 (ddd, *J* = 8.2 Hz, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H6-Qu), 6.91 (dd, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H8-Qu), 7.14 (dd, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H5-Qu), 7.19 (ddd, *J* = 8.2 Hz, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H7-Qu), 10.15 (s, 1H, NH1-Qu), 10.54 (s, 1H, NH4-Qx). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz) δ 167.2 (C2-Qu), 166.1 (C3-Qx), 137.1 (C8a-Qu), 133.1 (C8a-Qx), 129.0 (C7-Qu), 125.8 (C4a-Qu), 125.2 (C4a-Qx), 124.9 (C5-Qu), 123.2 (C7-Qx), 122.0 (C6-Qu), 117.8 (C6-Qx), 115.7 (C8-Qu), 114.6 (C5-Qx), 113.1 (C8-Qx), 58.4 (C2-Qx/C4-Qu), 41.1 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 74.5 (N1-Qx), 130.0 (N4-Qx), 133.8 (N1-Qu). ν_{max} (KBr) ν 3329, 3190, 3053, 2919, 1698, 1684, 1611, 1594, 1504, 1491, 1376, 1319, 1254, 750, 739 cm^{-1};
Anal. Calcd for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.77; H, 4.71; N, 15.15%.

6′,7′-Dimethyl-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 4b.



Yield 277 mg (90%); light-brown solid; R_f (EtOAc) 0.39; mp 193-195 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.07 (s, 6H, CH_3-Qx), 2.64, 2.91 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.48 (s, 1H, NH1-Qx), 6.53 (s, 1H, H8-Qx), 6.57 (s, 1H, H5-Qx), 6.85 (ddd, *J* = 7.8 Hz, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H, H6-Qu), 6.90 (dd, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H, H8-Qu), 7.13 (dd, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H, H5-Qu), 7.16 (ddd, *J* = 7.8 Hz, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H, H7-Qu), 10.12 (s, 1H, NH1-Qu), 10.39 (s, 1H, NH4-Qx). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz) δ 167.3 (C2-Qu), 166.1 (C3-Qx), 137.1 (C8a-Qu), 130.8 (C8a-Qx), 130.5 (C7-Qx), 128.9 (C7-Qu), 125.9 (C4a-Qu), 125.2 (C5-Qu), 125.1 (C6-Qx), 122.9 (C4a-Qx), 121.9 (C6-Qu), 115.8 (C5-Qx), 115.6 (C8-Qu), 114.6 (C8-Qx), 58.4 (C2-Qx/C4-Qu), 41.1 (C3-Qu), 19.0 (CH_3-C7-Qx), 18.6 (CH_3-C6-Qx). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 73.2 (N1-Qx), 129.8 (N4-Qx), 134.9 (N1-Qu). ν_{max} (KBr) ν 3369, 2967, 2929, 1707, 1685, 1610, 1594, 1489, 1461, 1392, 1372, 1300, 1240, 1020, 870, 753 cm^{-1}; Anal. Calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.19; H, 5.51; N, 13.60%.

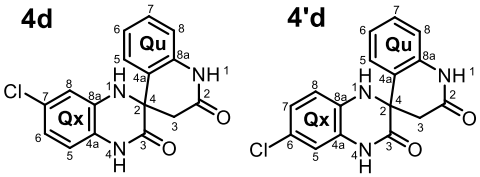
6′,7′-Dichloro-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 4c.



Yield 243 mg (70%); orange solid; R_f (EtOAc) 0.38; mp 151-153 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.68, 2.99 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.91 (s, 1H, H8-Qx), 6.91 (ddd, *J* = 7.6 Hz, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H, H6-Qu), 6.93 (dd, *J* = 7.8 Hz, *J* = 1.0 Hz, 1H, H8-Qu), 6.95 (s, 1H, H5-Qx), 7.09 (dd, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H, H5-Qu), 7.22 (s, 1H, NH1-Qx), 7.22 (ddd, *J* = 8.0 Hz, *J* = 7.8 Hz, *J* = 1.5 Hz, 1H, H7-Qu), 10.23

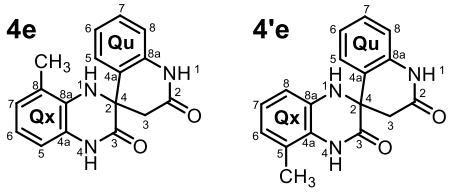
(s, 1H, NH1-Qu), 10.84 (s, 1H, NH4-Qx). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz) δ 166.8 (C2-Qu), 165.7 (C3-Qx), 137.1 (C8a-Qu), 133.3 (C8a-Qx), 129.3 (C7-Qu), 125.3 (C6-Qx), 125.1 (C4a-Qu), 125.0 (C5-Qu), 124.3 (C7-Qx), 122.2 (C6-Qu), 118.5 (C4a-Qx), 115.9 (C8-Qu), 115.5 (C5-Qx), 113.7 (C8-Qx), 58.3 (C2-Qx/C4-Qu), 41.0 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 77.3 (N1-Qx), 129.7 (N4-Qx), 135.3 (N1-Qu). ν_{max} (KBr) ν 3393, 3358, 3324, 3057, 1713, 1687, 1630, 1498, 1400, 1365, 1278, 1217, 1130, 865, 783, 754, 681 cm^{-1}; Anal. Calcd for $C_{16}H_{11}Cl_2N_3O_2$: C, 55.19; H, 3.18; N, 12.07. Found: C, 55.08; H, 3.15; N, 12.06%.

7′-Chloro-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 4d and 6′-chloro-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 4′d were characterized as the mixture of regioisomers in percentage ratio 45:55.



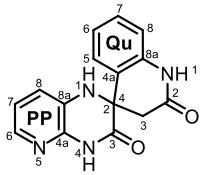
Yield 213 mg (68%); brownish-red solid; R_f (EtOAc) 0.42; mp 261-263 °C; (**4d**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.67, 2.97 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.67 (dd, *J* = 8.3 Hz, *J* = 2.3 Hz, 1H, H6-Qx), 6.75 (d, *J* = 2.3 Hz, 1H, H8-Qx), 6.75 (d, *J* = 8.3 Hz, 1H, H5-Qx), 6.87-6.88 (m, 1H, H6-Qu), 6.91-6.93 (m, 1H, H8-Qu), 7.05 (s, 1H, NH1-Qx), 7.07 (dd, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H, H5-Qu), 7.21 (ddd, *J* = 8.0 Hz, *J* = 7.5 Hz, *J* = 1.5 Hz, 1H, H7-Qu), 10.20 (s, 1H, NH1-Qu), 10.70 (s, 1H, NH4-Qx). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz) δ 166.9 (C2-Qu), 165.7 (C3-Qx), 137.1 (C8a-Qu), 134.4 (C8a-Qx), 129.2 (C7-Qu), 126.8 (C7-Qx), 125.3 (C4a-Qu), 125.1 (C5-Qu), 124.0 (C4a-Qx), 122.1 (C6-Qu), 117.3 (C6-Qx), 115.8 (C8-Qu and C5-Qx), 112.4 (C8-Qx), 58.3 (C2-Qx/C4-Qu), 41.1 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 77.3 (N1-Qx), 129.9 (N4-Qx), 135.1 (N1-Qu). (**4′d**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.67, 2.96 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.74 (d, *J* = 8.4 Hz, 1H, H8-Qx), 6.82 (d, *J* = 2.4 Hz, 1H, H5-Qx), 6.84 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H, H7-Qx), 6.87-6.89 (m, 1H, H6-Qu), 6.91-6.92 (m, 1H, H8-Qu), 6.97 (s, 1H, NH1-Qx), 7.10 (dd, *J* = 7.8 Hz, *J* = 1.1 Hz, 1H, H5-Qu), 7.21 (ddd, *J* = 8.0 Hz, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H, H7-Qu), 10.19 (s, 1H, NH1-Qu), 10.70 (s, 1H, NH4-Qx). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz) δ 167.0 (C2-Qu), 166.0 (C3-Qx), 137.1 (C8a-Qu), 132.1 (C8a-Qx), 129.2 (C7-Qu), 126.2 (C4a-Qx), 125.4 (C4a-Qu), 125.1 (C5-Qu), 122.7 (C7-Qx), 122.1 (C6-Qu), 121.0 (C6-Qx), 115.8 (C8-Qu), 114.3 (C5-Qx), 114.1 (C8-Qx), 58.3 (C2-Qx/C4-Qu), 41.1 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 75.7 (N1-Qx), 130.1 (N4-Qx), 135.3 (N1-Qu). ν_{max} (KBr) ν 3361, 3271, 2991, 1715, 1687, 1605, 1505, 1489, 1360, 1244, 1086, 872, 799, 769, 751 cm^{-1}; Anal. Calcd for $C_{16}H_{12}ClN_3O_2$: C, 61.25; H, 3.86; N, 13.39. Found: C, 61.12; H, 3.82; N, 13.41%.

8′-Methyl-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 4e and 5′-methyl-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 4′e.



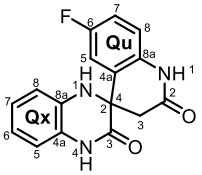
Yield 261 mg (89%); light-brown solid; R_f (EtOAc) 0.35; mp 241-243 °C; **4e**+**4′e (9:91)**. The spectra of the predominant product **4′e** are given. ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.21 (s, 3H, CH_3-Qx), 2.67, 2.98 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.51 (d, *J* = 7.3 Hz, 1H, H6-Qx), 6.63 (d, *J* = 7.3 Hz, 1H, H8-Qx), 6.72 (dd, *J* = 7.3 Hz, *J* = 7.3 Hz, 1H, H7-Qx), 6.73 (s, 1H, NH1-Qx), 6.85 (ddd, *J* = 7.6 Hz, *J* = 7.6 Hz, *J* = 1.1 Hz, 1H, H6-Qu), 6.92 (d, *J* = 7.6 Hz, 1H, H8-Qu), 7.12 (d, *J* = 7.6 Hz, 1H, H5-Qu), 7.19 (ddd, *J* = 7.6 Hz, *J* = 7.6 Hz, *J* = 1.1 Hz, 1H, H7-Qu), 10.07 (s, 1H, NH4-Qx), 10.19 (s, 1H, NH1-Qu). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 167.3 (C2-Qu), 166.6 (C3-Qx), 137.2 (C8a-Qu), 133.4 (C8a-Qx), 129.0 (C7-Qu), 125.5 (C4a-Qu), 125.2 (C5-Qu), 123.3 (C5-Qx and C4a-Qx), 122.9 (C7-Qx), 122.0 (C6-Qu), 120.0 (C6-Qx), 115.7 (C8-Qu), 111.5 (C8-Qx), 58.1 (C2-Qx/C4-Qu), 40.9 (C3-Qu), 17.0 (CH_3-Qx). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 75.4 (N1-Qx), 127.4 (N4-Qx), 135.4 (N1-Qu). ν_{max} (KBr) ν 3382, 3231, 2977, 1712, 1674, 1605, 1592, 1486, 1419, 1364, 1311, 1248, 1150. 833, 800, 757, 723 cm^{-1}; Anal. Calcd for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.57; H, 5.13; N, 14.35%.

1,4-Dihydro-1′*H*,3*H*-spiro[pyrido[2,3-*b*]pyrazine-2,4′-quinoline]-2′,3(3′*H*)-dione 4f or 1,4-dihydro-1′*H*,2*H*-spiro[pyrido[2,3-*b*]pyrazine-3,4′-quinoline]-2,2′(3′*H*)-dione 4f.



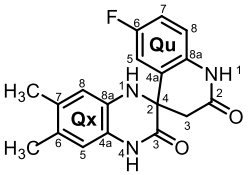
Yield 148 mg (53%); dark purple solid; R_f (EtOAc) 0.27; mp 293-296 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.71, 2.98 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.86 (dd, *J* = 7.5 Hz, *J* = 5.2 Hz, 1H, H7-PP), 6.88 (ddd, *J* = 7.6 Hz, *J* = 7.6 Hz, *J* = 1.1 Hz, 1H, H6-Qu), 6.93 (dd, *J* = 7.6 Hz, *J* = 1.1 Hz, 1H, H8-Qu), 7.02 (s, 1H, NH1-PP), 7.06 (dd, *J* = 7.5, *J* = 1.5, 1H, H8-PP), 7.08 (dd, *J* = 7.6 Hz, *J* = 1.1 Hz, 1H, H5-Qu), 7.21 (ddd, *J* = 7.6 Hz, *J* = 7.6 Hz, *J* = 1.1 Hz, 1H, H7-Qu), 7.63 (dd, *J* = 5.2, *J* = 1.5, 1H, H6-PP), 10.22 (s, 1H, NH1-Qu), 11.03 (s, 1H, NH4-PP). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 167.0 (C2-Qu and C3-PP), 139.3 (C4a-PP), 137.1 (C8a-Qu), 136.4 (C6-PP), 129.3 (C7-Qu), 128.9 (C8a-PP), 125.4 (C4a-Qu), 125.0 (C5-Qu), 122.1 (C6-Qu), 119.2 (C7-PP), 118.9 (C8-Qu), 115.9 (C8-PP), 58.7 (C2-PP/C4-Qu), 41.2 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 73.1 (N1-PP), 135.1 (N1-Qu), 140.5 (N4-PP), 278.2 (N5-PP). ν_{max} (KBr) ν 3370, 3209, 3065, 2917, 1687, 1600, 1521, 1483, 1466, 1363, 1292, 1235, 866, 784, 751 cm^{-1}; Anal. Calcd for $C_{15}H_{12}N_4O_2$: C, 64.28; H, 4.32; N, 19.99. Found: C, 64.22; H, 4.29; N, 19.96%.

6-Fluoro-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 5a.



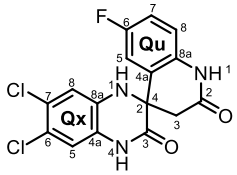
Yield 217 mg (73%); dark brown solid; R_f (EtOAc) 0.45; mp 274-275 °C (273-274 °C[24]); ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.67, 2.89 (AB, J = 16.1 Hz, 2H, H3-Qu), 6.68 (ddd, J = 7.5 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H, H6-Qx), 6.78 (dd, J = 7.5 Hz, J = 1.4 Hz, 1H, H8-Qx), 6.81 (s, 1H, NH1-Qx), 6.82 (dd, J = 7.5 Hz, J = 1.4 Hz, 1H, H5-Qx), 6.84 (ddd, J = 7.5 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H, H7-Qx), 6.89 (dd, J_{HF} = 9.5 Hz, J = 2.9 Hz, 1H, H5-Qu), 6.93 (dd, J = 8.8. Hz, J_{HF} = 5.0 Hz, 1H, H8-Qu), 7.09 (ddd, J = 8.8. Hz, J_{HF} = 8.6 Hz, J = 2.9 Hz, 1H, H7-Qu), 10.21 (s, 1H, NH1-Qu), 10.60 (s, 1H, NH4-Qx). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 166.9 (C2-Qu), 165.6 (C3-Qx), 157.3 (d, J_{CF} = 236.3 Hz, C6-Qu), 133.9 (d, J_{CF} = 2.1 Hz, C8a-Qu), 132.7 (C8a-Qx), 127.5 (d, J_{CF} = 6.4 Hz, C4a-Qu), 124.9 (C4a-Qx), 123.4 (C7-Qx), 118.3 (C6-Qx), 117.2 (d, J_{CF} = 8.0 Hz, C8-Qu), 115.8 (d, J_{CF} = 22.6 Hz, C7-Qu), 114.8 (C5-Qx), 113.4 (C8-Qx), 111.8 (d, J_{CF} = 24.1 Hz, C5-Qu), 58.3 (C2-Qx/C4-Qu), 40.6 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 74.4 (N1-Qx), 129.9 (N4-Qx), 133.5 (N1-Qu). ν_{max} (KBr) ν 3338, 3196, 3070, 1698, 1685, 1612, 1504, 1375, 1317, 1256, 1104, 1078, 874, 819, 737 cm^{-1}; Anal. Calcd for $C_{16}H_{12}FN_3O_2$: C, 64.64; H, 4.07; N, 14.13. Found: C, 64.50; H, 4.08; N, 14.09%.

6-Fluoro-6′,7′-dimethyl-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 5b.



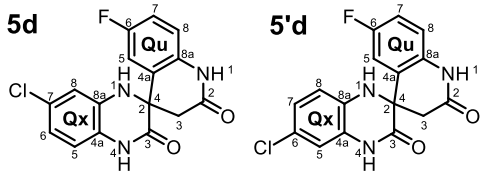
Yield 280 mg (86%); light brown solid; R_f (EtOAc) 0.44; mp 286-287 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.08 (s, 6H, CH_3-Qx), 2.62, 2.86 (AB, J = 16.1 Hz, 2H, H3-Qu), 6.54 (s, 1H, NH1-Qx), 6.56 (s, 1H, H8-Qx), 6.59 (s, 1H, H5-Qx), 6.88 (dd, J_{HF} = 9.5 Hz, J = 2.9 Hz, 1H, H5-Qu),
6.92 (dd, J = 8.8. Hz, J_{HF} = 5.0 Hz, 1H, H8-Qu), 7.08 (ddd, J = 8.8 Hz, J_{HF} = 8.7 Hz, J = 2.9 Hz, 1H, H7-Qu), 10.18 (s, 1H, NH1-Qu), 10.46 (s, 1H, NH4-Qx). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 167.0 (C2-Qu), 165.6 (C3-Qx), 157.2 (d, J_{CF} = 238.2 Hz, C6-Qu), 133.9 (d, J_{CF} = 2.1 Hz, C8a-Qu), 130.8 (C7-Qx), 130.4 (C8a-Qx), 127.5 (d, J_{CF} = 6.4, C4a-Qu), 125.6 (C6-Qx), 122.8 (C4a-Qx), 117.1 (d, J_{CF} = 7.8 Hz, C8-Qu), 115.9 (C5-Qx), 115.7 (d, J_{CF} = 22.6 Hz, C7-Qu), 114.8 (C8-Qx), 111.9 (d, J_{CF} = 24.2 Hz, C5-Qu), 58.4 (C2-Qx /C4-Qu), 40.5 (C3-Qu), 19.0 (CH_3(C7-Qx), 18.6 (CH_3(C6-Qx). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 72.2 (N1-Qx), 129.0 (N4-Qx), 133.5 (N1-Qu). ν_{max} (KBr) ν 3379, 3191, 3083, 2977, 1707, 1683, 1629, 1518, 1499, 1396, 1373, 1358, 1269, 1256, 1163, 1017, 873, 827, 725 cm^{-1}; Anal. Calcd for $C_{18}H_{16}FN_3O_2$: C, 66.45; H, 4.96; N, 12.92. Found: C, 66.32; H, 4.92; N, 12.88%.

6′,7′-Dichloro-6-fluoro-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 5c.



Yield 300 mg (82%); light brown solid; R_f (EtOAc) 0.41; mp 168-170 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.68, 2.95 (AB, J = 16.1 Hz, 2H, H3-Qu), 6.87 (dd, J_{HF} = 9.3 Hz, J = 2.9 Hz, 1H, H5-Qu), 6.93 (s, 1H, H8-Qx), 6.96 (dd, J = 8.5 Hz, J_{HF} = 4.9 Hz, 1H, H8-Qu), 6.97 (s, 1H, H5-Qx), 7.13 (ddd, J_{HF} = 8.6 Hz, J = 8.5 Hz, J = 2.7 Hz, 1H, H7-Qu), 7.24 (s, 1H, NH1-Qx), 10.29 (s, 1H, NH1-Qu), 10.89 (s, 1H, NH4-Qx). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 166.4 (C2-Qu), 165.1 (C3-Qx), 157.3 (d, J_{CF} = 238.9 Hz, C6-Qu), 134.0 (d, J_{CF} = 2.1 Hz, C8a-Qu), 132.9 (C8a-Qx), 126.5 (d, J_{CF} = 6.3 Hz, C4a-Qu), 125.1 (C4a-Qx), 124.5 (C6-Qx), 118.9 (C7-Qx), 117.4 (d, J_{CF} = 7.8 Hz, C8-Qu), 116.3 (d, J_{CF} = 22.8 Hz, C7-Qu), 115.7 (C5-Qx), 114.0 (C8-Qx), 111.8 (d, J_{CF} = 24.2 Hz, C5-Qu), 58.3 (C2-Qx/C4-Qu), 40.5 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 76.1 (N1-Qx), 129.7 (N4-Qx), 133.7 (N1-Qu). ν_{max} (KBr) ν 3346, 3203, 3079, 2981, 1727, 1715, 1688, 1631, 1617, 1498, 1376, 1344, 1272, 1218, 1196, 1126, 1019, 867, 825 cm^{-1}; Anal. Calcd for $C_{16}H_{10}Cl_2FN_3O_2$: C, 52.48; H, 2.75; N, 11.48. Found: C, 52.41; H, 2.76; N, 11.45%.

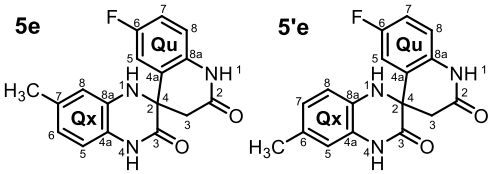
7′-Chloro-6-fluoro-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 5d and 6′-chloro-6-fluoro-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 5′d were characterized as the mixture of regioisomers in percentage ratio 33:67.



Yield 281 mg (85%); brownish-red solid; R_f (EtOAc) 0.36; mp 285-286 °C; (**5d**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.67, 2.93 (AB, J = 16.1 Hz, 2H, H3-Qu), 6.70 (dd, J = 8.3 Hz, J = 2.3 Hz, 1H, H6-Qx), 6.78 (d, J = 2.3 Hz, 1H, H8-Qx), 6.81 (d, J = 8.3 Hz, 1H, H5-Qx), 6.86-6.89 (m, 1H, H5-Qu), 6.93-6.97 (m, 1H, H8-Qu), 7.09 (s, 1H, NH1-Qx), 7.09-7.12 (m, 1H, H7-Qu), 10.26 (s, 1H, NH1-Qu), 10.77 (s, 1H, NH4-Qx). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 166.5 (C2-Qu), 165.1 (C3-Qx), 157.2 (d, J_{CF} = 238.7 Hz, C6-Qu), 133.9 (d, J_{CF} = 2.4 Hz, C8a-Qu), 126.9 (d, J_{CF} = 3.7 Hz, C4a-Qu), 126.9 (C7-Qx), 123.9 (C4a-Qx), 117.7 (C6-Qx), 117.2 (d, J_{CF} = 7.7 Hz, C8-Qu), 116.0 (C5-Qx), 115.9 (d, J_{CF} = 22.2 Hz, C7-Qu), 112.7 (C8-Qx), 111.8 (d, J_{CF} = 24.3 Hz, C5-Qu), 58.3 (C2-Qx/C4-Qu), 40.5 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 76.4 (N1-Qx), 129.7 (N4-Qx), 133.6 (N1-Qu). (**5′d**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.67, 2.91 (AB, J = 16.1 Hz, 2H, H3-Qu), 6.77 (d, J = 8.4 Hz, 1H, H8-Qx), 6.84 (d, J = 2.3 Hz, 1H, H5-Qx), 6.86-6.89 (m, 2H, H7-Qx 5′d H5-Qu), 6.93-6.97 (m, 1H, H8-Qu), 7.02 (s, 1H, NH1-Qx), 7.09-7.12 (m, 1H, H7-Qu), 10.24 (s, 1H, NH1-Qu), 10.76 (s, 1H, NH4-Qx), ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 166.6 (C2-Qu), 165.4 (C3-Qx), 157.2 (d, J_{CF} = 238.7 Hz, C6-Qu), 133.9 (d, J_{CF} = 2.4 Hz, C8a-Qu), 131.6 (C8a-Qx),

126.9 (d, J_{CF} = 3.7 Hz, C4a-Qu), 126.1 (C6-Qx), 122.8 (C7-Qx), 121.4 (C4a-Qx), 117.2 (d, J_{CF} = 7.7 Hz, C8-Qu), 115.9 (d, J_{CF} = 22.2 Hz, C7-Qu), 114.5 (C8-Qx), 114.2 (C5-Qx), 111.8 (d, J_{CF} = 24.3 Hz, C5-Qu), 58.3 (C2-Qx/C4-Qu), 40.4 (C3-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 74.6 (N1-Qx), 130.2 (N4-Qx), 133.6 (N1-Qu). ν_{max} (KBr) ν 3402, 3369, 2976, 1712, 1683, 1628, 1590, 1503, 1410, 1372, 1276, 1240, 1158, 1087, 855, 831, 806, 703 cm^{-1}; Anal. Calcd for $C_{16}H_{11}ClFN_3O_2$: C, 57.93; H, 3.34; N, 12.67. Found: C, 57.97; H, 3.30; N, 12.59%.

6-Fluoro-7′-methyl-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 5e and 6-fluoro-6′-methyl-1′,4′-dihydro-1*H*,3′*H*-spiro[quinoline-4,2′-quinoxaline]-2,3′(3*H*)-dione 5′e were characterized as the mixture of regioisomers in percentage ratio 45:55.

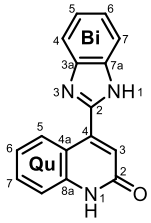


Yield 261 mg (84%); dark brown solid; R_f (EtOAc) 0.40; mp 141-143 °C; (**5e**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.17 (s, 3H, CH_3-Qx), 2.65, 2.88 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.85 (dd, *J* = 8.1, *J* = 0.9 Hz, 1H, H6-Qx), 6.58 (d, *J* = 0.9 Hz, 1H, H8-Qx), 6.70 (d, *J* = 8.1 Hz, 1H, H5-Qx), 6.72 (s, 1H, NH1-Qx), 6.89 (dd, J_{HF} = 9.5 Hz, *J* = 2.8 Hz, 1H, H5-Qu), 6.93 (dd, *J* = 8.7 Hz, J_{HF} = 5.0 Hz, 1H, H8-Qu), 7.06-7.10 (m, 1H, H7-Qu), 10.19 (s, 1H, NH1-Qu), 10.52 (s, 1H, NH4-Qx). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 166.8 (C2-Qu), 166.4 (C3-Qx), 157.2 (d, J_{CF} = 236.1 Hz, C6-Qu), 133.9 (d, J_{CF} = 2.6 Hz, C8a-Qu), 132.3 (C7-Qx), 127.4 (d, J_{CF} = 4.4 Hz, C4a-Qu), 127.0 (C8a-Qx), 122.6 (C4a-Qx), 118.8 (C6-Qx), 117.1 (d, J_{CF} = 7.9 Hz, C8-Qu), 115.7 (d, J_{CF} = 23.0 Hz, C7-Qu), 114.7 (C5-Qx), 113.8 (C8-Qx), 111.8 (d, J_{CF} = 24.0 Hz, C5-Qu), 58.3 (C2-Qx/C4-Qu), 40.4 (C3-Qu), 20.7 (CH_3-Qx). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 74.2 (N1-Qx), 130.3 (N4-Qx), 133.5 (N1-Qu). (**5′e**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.18 (s, 3H, CH_3-Qx), 2.64, 2.88 (AB, *J* = 16.1 Hz, 2H, H3-Qu), 6.64 (d, *J* = 1.0 Hz, 1H, H5-Qx), 6.64 (s, 1H, NH1-Qx), 6.64 (dd, *J* = 8.0 Hz, *J* = 1.0 Hz, 1H, H7-Qx), 6.66 (d, *J* = 8.0 Hz, 1H, H8-Qx), 6.89 (dd, J_{HF} = 9.5 Hz, *J* = 2.8 Hz, 1H, H5-Qu), 6.93 (dd, *J* = 8.7 Hz, J_{HF} = 5.0 Hz, 1H, H8-Qu), 7.06-7.10 (m, 1H, H7-Qu), 10.19 (s, 1H, NH1-Qu), 10.56 (s, 1H, NH4-Qx). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 166.9 (C2-Qu), 165.7 (C3-Qx), 157.2 (d, J_{CF} = 236.1 Hz, C6-Qu), 133.9 (d, J_{CF} = 2.6 Hz, C8a-Qu), 132.5 (C6-Qx), 130.3 (C4a-Qx), 127.4 (d, J_{CF} = 4.4 Hz, C4a-Qu), 124.9 (C8a-Qx), 123.8 (C7-Qx), 117.1 (d, J_{CF} = 7.9 Hz, C8-Qu), 115.7 (d, J_{CF} = 23.0 Hz, C7-Qu), 115.2 (C5-Qx), 113.4 (C8-Qx), 111.8 (d, J_{CF} = 24.0 Hz, C5-Qu), 58.3 (C2-Qx/C4-Qu), 40.5 (C3-Qu), 20.7 (CH_3-Qx). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 72.8 (N1-Qx), 130.2 (N4-Qx), 133.5 (N1-Qu). ν_{max} (KBr) ν 3375, 2918, 2865, 171709, 1681, 1629, 1520, 1499, 1372, 1292, 1269, 1247, 1166, 873, 809, 711 cm^{-1}; Anal. Calcd for $C_{17}H_{14}FN_3O_2$: C, 65.59; H, 4.53; N, 13.50. Found: C, 65.46; H, 4.48; N, 13.39%.

Typical experimental procedure for the preparation of 6 or 7. A solution of spiroquinoxalinone **4** or **5** (0.7 mmol) in acetic acid (10 mL) was heated at reflux for 6 h. The reaction mixture was allowed to cool to room temperature and a white precipitate was removed by filtration to afford analytically pure samples of **6** or **7**. The filtrate was

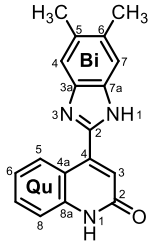
evaporated in vacuum to dryness and the residue was treated with water (10 mL), the precipitate was washed with water (2×5 mL), filtered, air-dried and the additional portions of **6** or **7** were obtained.

4-(1*H*-Benzimidazol-2-yl)quinolin-2(1*H*)-one 6a.



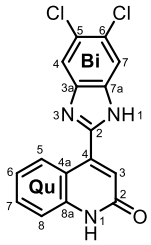
Yield 183 mg (98%); light brown solid; mp 144-146 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.07 (s, 1H, H3-Qu), 7.28 (ddd, *J* = 8.2 Hz, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H6-Qu), 7.27-7.31 (m, 2H, H5-Bi and H6-Bi), 7.43 (d, *J* = 8.2 Hz, 1H, H8-Qu), 7.58 (ddd, *J* = 8.2 Hz, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H7-Qu), 7.71 (brs, 2H, H4-Bi and H7-Bi), 8.95 (dd, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, H5-Qu),
12.03 (s, 1H, NH-Qu), 13.09 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 161.0 (C2-Qu), 148.2 (C2-Bi), 139.6 (C8a-Qu), 138.8 (C4-Qu), 130.8 (C7-Qu), 127.6 (C5-Qu), 122.9 (C5-Bi and C6-Bi), 122.3 (C3-Qu), 122.0 (C6-Qu), 116.7 (C4a-Qu), 115.7 (C8-Qu), n/d/ (C3a-Bi), (C4-Bi), (C7-Bi), (C7a-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 151.8 (N1-Qu), n/d/ (N3-Bi), n/d/ (N1-Bi). ν_{max} (KBr) 3314, 2993, 1715, 1652, 1548, 1504, 1418, 1356, 1266, 1156, 1042, 932, 876, 745, 727 cm^{-1}; Anal. Calcd for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.43; H, 4.27; N, 16.00%.

4-(5,6-Dichlorobenimidazol-2-yl)quinolin-2(1*H*)-one 6c.



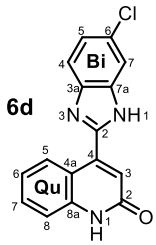
Yield 115 mg (61%); orange solid; mp 177-178 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.35 (s, 3H, CH_3-Bi), 2.37 (s, 3H, CH_3-Bi), 7.03 (s, 1H, H3-Qu), 7.27 (dd, *J* = 7.9 Hz, *J* = 7.9 Hz, 1H, H6-Qu), 7.35 (brs, 1H, H7-Bi), 7.41 (d, *J* = 7.9 Hz, 1H, H8-Qu), 7.57 (dd, *J* = 7.9 Hz, *J* = 7.9 Hz, 1H, H7-Qu), 7.57 (brs, 1H, H4-Bi), 9.00 (d, *J* = 7.9 Hz, 1H, H5-Qu), 11.95 (s, 1H, NH-Qu), 12.87 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 161.1 (C2-Qu), 147.2 (C2-Bi), 142.5 (C3a-Bi), 139.6 (C8a-Qu), 138.9 (C4-Qu), 132.7 (C5-Bi and C6-Bi), 130.8 (C7a-Bi), 130.7 (C7-Qu), 127.7 (C5-Qu), 121.9 (C6-Qu), 121.6 (C3-Qu), 119.4 (C4-Bi), 116.8 (C4a-Qu), 115.6 (C8-Qu), 111.8 (C7-Bi), 20.0 (both CH_3-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 151.8 (N1-Qu), n/d/ (N3-Bi), n/d/ (N1-Bi). ν_{max} (KBr) 3381, 3136, 2859, 1707, 1663, 1605, 1551, 1431, 1379, 1331, 1269, 1022, 1000, 864, 754 cm^{-1}; Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52. Found: C, 74.59; H, 5.18; N, 14.46%.

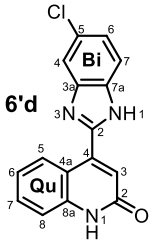
4-(5,6-Dichloro-1*H*-benzo[*d*]imidazol-2-yl)quinolin-2(1*H*)-one 6c.



Yield 127 mg (67%); beige solid; mp >350°C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.06 (s, 1H, H3-Qu), 7.26 (ddd, *J* = 7.7 Hz, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H, H6-Qu), 7.42 (d, *J* = 8.2 Hz, 1H, H8-Qu), 7.59 (ddd, *J* = 7.7 Hz, *J* = 7.7 Hz, *J* = 1.4 Hz, 1H, H7-Qu), 7.86 (brs, 1H, H7-Bi), 8.09 (brs, 1H, H4-Bi), 8.78 (dd, *J* = 8.3 Hz, *J* = 1.2 Hz, 1H, H5-Qu), 12.05 (s, 1H, NH-Qu), 13.49 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 160.9 (C2-Qu), 150.8 (C2-Bi), 139.7 (C8a-Qu), 138.3 (C4-Qu), 138.1 (C3a-Bi and C7a-Bi), 131.0 (C7-Qu), 127.3 (C5-Qu), 123.7 (C5-Bi and C6-Bi), 123.0 (C3-Qu), 122.2 (C6-Qu), 116.5 (C4a-Qu), 115.8 (C8-Qu), 115.6 (C4-Bi and C7-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 151.8 (N1-Qu), n/d/ (N3-Bi), n/d/ (N1-Bi). ν_{max} (KBr) 3273, 3096, 2994, 1712, 1652, 1548, 1536, 1449, 1372, 1324, 1268, 1098, 1021, 952, 861, 796, 763 cm^{-1}; Anal. Calcd for $C_{16}H_9Cl_2N_3O$: C, 58.21; H, 2.75; N, 12.73. Found: C, 58.10; H, 2.71; N, 12.69%.

4-(6-Chlorobenzimidazol-2-yl)quinolin-2(1*H*)-one 6d and 4-(5-Chlorobenzimidazol-2-yl)quinolin-2(1*H*)-one 6′d were characterized as the mixture of regioisomers in percentage ratio 60:40.

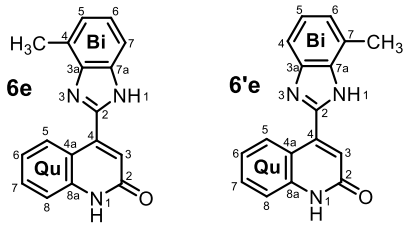




Yield 181 mg (96%); dark brown solid; mp 189-190 °C; (**6d**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.06 (s, 1H, H3-Qu), 7.26 (ddd, *J* = 7.9 Hz, *J* = 7.9 Hz, *J* = 0.9 Hz, 1H, H6-Qu), 7.32-7.36 (m, 1H, H5-Bi), 7.42 (d, *J* = 7.9 Hz, 1H, H8-Qu), 7.58 (ddd, *J* = 7.9 Hz, *J* = 7.9 Hz, *J* = 0.9 Hz, 1H, H7-Qu), 7.60-7.64 (m, 1H, H4-Bi), 7.86-7.90 (m, 1H, H7-Bi), 8.81-8.87 (m, 1H, H5-Qu), 12.01 (s, 1H, NH-Qu), 13.36 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 160.9 (C2-Qu), 149.7 (C2-Bi), 144.4 (C7a-Bi), 139.6 (C8a-Qu), 138.4 (C4-Qu), 132.9 (C3a-Bi), 130.8 (C7-Qu), 127.4 (C5-Qu), 126.5 (C6-Bi), 123.8 (C5-Bi), 122.6 (C3-Qu), 122.0 (C6-Qu), 119.0 (C7-Bi), 116.5 (C4a-Qu), 115.7 (C8-Qu), 111.4 (C4-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 153.8 (N1-Qu), n/d/ (N3-Bi), n/d/ (N1-Bi). (**6′d**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.06 (s, 1H, H3-Qu), 7.26 (ddd, *J* = 7.9 Hz, *J* = 7.9 Hz, *J* = 0.9 Hz, 1H, H6-Qu), 7.26-7.30 (m, 1H, H7-Bi), 7.42 (d, *J* = 7.9 Hz, 1H, H8-Qu), 7.58 (ddd, *J* = 7.9 Hz, *J* = 7.9 Hz, *J* = 0.9 Hz, 1H, H7-Qu), 7.56-7.60 (m, 1H, H4-Bi), 7.78-7.82 (m, 1H, H6-Bi), 8.81-8.87 (m, 1H, H5-Qu), 12.01 (s, 1H, NH-Qu), 13.36 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 160.9 (C2-Qu), 149.3 (C2-Bi), 142.4 (C3a-Bi), 139.6 (C8a-Qu), 138.4 (C4-Qu), 134.8 (C7a-Bi), 130.8 (C7-Qu), 128.1 (C5-Bi), 127.4 (C5-Qu), 122.6 (C7-Bi), 122.6 (C3-Qu),

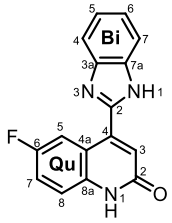
122.0 (C6-Qu), 120.9 (C6-Bi), 116.5 (C4a-Qu), 115.7 (C8-Qu), 113.1 (C4-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 153.8 (N1-Qu), n/d/ (N3-Bi), n/d/ (N1-Bi). ν_{max} (KBr) 3070, 2871, 1699, 1661, 1619, 1604, 1516, 1412, 1337, 1298, 1268, 1239, 1061, 1044, 1029, 933, 890, 843, 811, 791, 760, 689 cm^{-1};
Anal. Calcd for $C_{16}H_{10}ClN_3O$: C, 64.98; H, 3.41; N, 14.21. Found: C, 64.90; H, 3.36; N, 14.12%.

4-(4-Methylbenzimidazol-2-yl)quinolin-2(1*H*)-one 6e and 4-(7-Methylbenzimidazol-2-yl)quinolin-2(1*H*)-one 6′e were characterized as the mixture of regioisomers in percentage ratio 55:45.



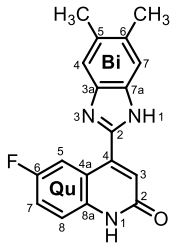
Yield 167 mg (89%); light brown solid; mp 189-191 °C; (**6e**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.64 (s, 3H, CH_3-Bi), 7.07 (d, *J* = 8.0 Hz, 1H, H5-Bi), 7.15 (s, 1H, H3-Qu), 7.20 (dd, *J* = 8.0 Hz, *J* = 8.0 Hz, 1H, H6-Bi), 7.25-7.29 (m, 1H, H6-Qu), 7.40 (d, *J* = 8.0 Hz, 1H, H7-Bi), 7.43 (d, *J* = 8.2 Hz, 1H, H8-Qu), 7.58 (d, *J* = 8.2 Hz, 1H, H7-Qu), 8.98 (d, *J* = 8.2 Hz, 1H, H5-Qu), 12.00 (s, 2H, NH-Qu), 13.07 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 161.1 (C2-Qu), 147.3 (C2-Bi), 143.2 (C3a-Bi), 139.6 (C4-Qu), 138.9 (C8a-Qu), 133.7 (C7a-Bi), 130.6 (C7-Qu), 129.1 (C4-Bi), 127.5 (C5-Qu), 123.6 (C6-Bi), 122.5 (C3-Qu), 122.1 (C5-Bi), 122.0 (C6-Qu), 116.8 (C4a-Qu), 115.7 (C8-Qu), 109.1 (C7-Bi), 16.5 (CH_3-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 150.9 (N1-Bi), 151.6 (N1-Qu), n/d/ (N3-Bi). (**6'e**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.57 (s, 3H, CH_3-Bi), 7.04 (s, 1H, H3-Qu), 7.10 (d, *J* = 8.0 Hz, 1H, H4-Bi), 7.17 (dd, *J* = 8.0 Hz, *J* = 8.0 Hz, 1H, H5-Bi), 7.25-7.29 (m, 1H, H6-Qu), 7.43 (d, *J* = 8.2 Hz, 1H, H8-Qu), 7.58 (d, *J* = 8.2 Hz, 1H, H7-Qu), 7.61 (d, *J* = 8.0 Hz, 1H, H6-Bi), 8.90 (d, *J* = 8.2 Hz, 1H, H5-Qu), 12.00 (s, 1H, NH-Qu), 12.94 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 161.0 (C2-Qu), 148.0 (C2-Bi), 143.4 (C3a-Bi), 139.5 (C4-Qu), 139.0 (C8a-Qu), 133.8 (C7a-Bi), 130.7 (C7-Qu), 127.6 (C5-Qu), 124.0 (C4-Bi), 122.2 (C5-Bi), 122.0 (C6-Qu), 121.9 (C3-Qu), 121.8 (C7-Bi), 116.9 (C6-Bi), 116.8 (C4a-Qu), 115.7 (C8-Qu), 17.0 (CH_3-Bi), ^{15}N NMR (DMSO-d_6, 51 MHz) δ 149.2 (N1-Bi), 151.6 (N1-Qu), n/d/ (N3-Bi). ν_{max} (KBr) 3160, 3017, 2853, 1661, 1616, 1552, 1429, 1351, 1267, 1157, 870, 771, 749 cm^{-1}; Anal. Calcd for $C_{17}H_{13}N_3O$: C, 74.17; H, 4.76; N, 15.26. Found: C, 74.05; H, 4.70; N, 15.23%.

4-(Benzimidazol-2-yl)-6-fluoroquinolin-2(1*H*)-one 7a.



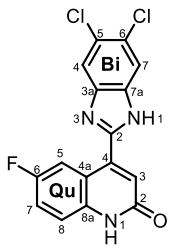
Yield 141 mg (75%); yellow solid; mp 166-168 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.20 (s, 1H, H3-Qu), 7.30-7.33 (m, 2H, H5-Bi and H6-Bi), 7.44 (dd, J = 9.0 Hz, J_{HF} = 5.3 Hz, 1H, H8-Qu), 7.50 (ddd, J = 9.0 Hz, J_{HF} = 8.0 Hz, J = 2.8 Hz, 1H, H7-Qu), 7.70-7.73 (m, 2H, H7-Bi and H4-Bi), 8.97 (dd, J_{HF} = 11.0 Hz, J = 2.8 Hz, 1H, H5-Qu), 12.10 (s, 1H, NH-Qu), 13.21 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 160.8 (C2-Qu), 157.3 (d, J_{CF} = 236.8 Hz, C6-Qu), 147.9 (C2-Bi), 143.5 (C3a-Bi), 137.4 (d, J_{CF} = 3.3 Hz, C4-Qu), 136.4 (C8a-Qu), 134.0 (C7a-Bi), 123.9 (C6-Bi), 123.0 (C3-Qu), 122.2 (C5-Bi), 119.7 (C4-Bi), 118.9 (d, J_{CF} = 24.7 Hz, C7-Qu), 117.4 (d, J_{CF} = 8.5 Hz, C8-Qu), 117.3 (d, J_{CF} = 9.6 Hz, C4a-Qu), 112.7 (d, J_{CF} = 25.6 Hz, C5-Qu), 111.7 (C7-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 151.1 (N1-Qu), 151.2 (N1-Bi), n/d/ (N3-Bi). ν_{max} (KBr) 3433, 3009, 2872, 1681, 1649, 1601, 1465, 1377, 1336, 1279, 1187, 1142, 1095, 1009, 876, 828, 803 cm^{-1}; Anal. Calcd for $C_{16}H_{10}FN_3O$: C, 68.81; H, 3.61; N, 15.05. Found: C, 68.74; H, 3.56; N, 15.01%.

4-(5,6-Dimethylbenzimidazol-2-yl)-6-fluoroquinolin-2(1*H*)-one 7b.



Yield 115 mg (66%); orange solid; mp 181-182 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.35 (s, 6H, CH_3-Bi), 7.17 (s, 1H, H3-Qu), 7.35 (brs, 1H, H7-Bi), 7.42 (dd, J = 8.9 Hz, J_{HF} = 5.2 Hz, 1H, H8-Qu), 7.48 (ddd, J = 8.9 Hz, J_{HF} = 8.0 Hz, J = 2.9 Hz, 1H, H7-Qu), 7.57 (brs, 1H, H4-Bi), 9.07 (dd, J_{HF} = 11.2 Hz, J = 2.6 Hz, 1H, H5-Qu), 12.00 (s, 1H, NH-Qu), 12.93 (s, 1H, NH-Bi). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 160.8 (C2-Qu), 157.0 (d, J_{CF} =236.5 Hz, C6-Qu), 146.9 (C2-Bi), 142.3 (C3a-Bi), 137.4 (d, J_{CF} =3.6 Hz, C4-Qu), 136.4 (C8a-Qu), 132.8 (C5-Bi and C6-Bi), 130.8 (C7a-Bi), 122.3 (C3-Qu), 119.6 (C4-Bi), 118.7 (d, J_{CF} = 24.7 Hz, C7-Qu), 117.4 (d, J_{CF} = 8.4 Hz, C8-Qu), 117.3 (d, J_{CF} = 9.7 Hz, C4a-Qu), 112.9 (d, J_{CF} = 25.9 Hz, C5-Qu), 111.5 (C7-Bi), 20.0 (CH_3-Bi), 19.9 (CH_3-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 150.7 (N1-Qu), n/d/ (N1-Bi), n/d/ (N3-Bi). ν_{max} (KBr) 3188, 2855, 2729, 1701, 1661, 1607, 1503, 1436, 1403, 1369, 1335, 1256, 1219, 1142, 1121, 997, 901, 883, 848, 823 cm^{-1}; Anal. Calcd for $C_{18}H_{14}FN_3O$: C, 70.35; H, 4.59; N, 13.67. Found: C, 70.25; H, 4.54; N, 13.62%.

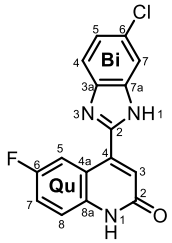
4-(5,6-Dichlorobenzimidazol-2-yl)-6-fluoroquinolin-2(1*H*)-one 7c.



Yield 106 mg (56%); beige solid; mp >350 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.19 (s, 1H, H3-Qu), 7.43 (dd, J = 9.0 Hz, J_{HF} = 5.3 Hz, 1H, H8-Qu), 7.50 (ddd, J = 9.0 Hz, J_{HF} = 8.2 Hz, J = 2.7 Hz, 1H, H7-Qu), 7.82 (brs, 1H, H7-Bi), 8.12 (brs, 1H, H4-Bi),

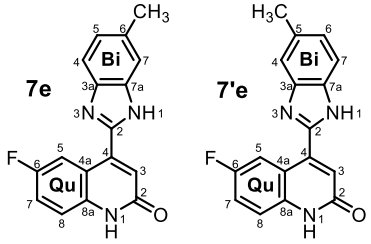
8.81 (dd, *J* = 11.0 Hz, *J* = 2.7 Hz, 1H, H5-Qu), 12.07 (s, 1H, NH-Qu), 13.52 (s, 1H, NH-Bi). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz) δ 160.6 (C2-Qu), 157.0 (d, J_{CF} = 237.0 Hz, C6-Qu), 150.4 (C2-Bi), 143.0 (C3a-Bi), 136.7 (C4-Qu), 136.4 (C8a-Qu), 133.5 (C7a-Bi), 123.3 (C6-Bi), 124.8 (C5-Bi), 123.8 (C3-Qu), 120.9 (C4-Bi), 119.0 (d, J_{CF} = 24.6 Hz, C7-Qu), 117.5 (d, J_{CF} = 8.3 Hz, C8-Qu), 116.9 (d, J_{CF} = 9.6 Hz, C4a-Qu), 113.1 (C7-Bi), 112.4 (d, J_{CF} = 25.7 Hz, C5-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 151.1 (N1-Qu), 151.2 (N1-Bi), n/d/ (N3-Bi). ν_{max} (KBr) 3290, 3082, 1717, 1657, 1625, 1504, 1433, 1388, 1369, 1313, 1261, 1225, 1121, 1096, 1023, 972, 889, 870, 842 cm^{-1}; Anal. Calcd for $C_{16}H_8Cl_2FN_3O$: C, 55.20; H, 2.32; N, 12.07. Found: C, 55.06; H, 2.29; N, 12.01%.

4-(5(6)-Chlorobenzimidazol-2-yl)-6-fluoroquinolin-2(1*H*)-one 7d.



Yield 153 mg (81%); brown solid; mp 275-276 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.19 (s, 1H, H3-Qu), 7.32 (brd, *J* ~ 8.0 Hz, 1H, H5(6)-Bi), 7.45 (dd, *J* = 8.4 Hz, J_{HF} = 5.3 Hz, 1H, H8-Qu), 7.50 (ddd, *J* = 8.4 Hz, J_{HF} = 8.3 Hz, *J*= 1.9 Hz, 1H, H7-Qu), 7.73 (brs, 2H, H4-Bi and H7-Bi), 8.89 (dd, J_{HF} = 11.6 Hz, *J* = 1.9 Hz, 1H, H5-Qu), 12.11 (s, 1H, NH-Qu), 13.39 (s, 1H, NH-Bi). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126 MHz) δ 160.7 (C2-Qu), 157.0 (d, J_{CF} = 236.9 Hz, C6-Qu), 149.2 (C2-Bi), n/d/ (C3a-Bi), 137.1 (d, J_{CF} = 2.3 Hz, C4-Qu), 136.4 (C8a-Qu), n/d/ (C7a-Bi), n/d/ (C6-Bi), 123.6 (C5-Bi), 123.5 (C3-Qu), n/d/ (C4-Bi), 118.9 (d, J_{CF} = 24.7 Hz, C7-Qu), 117.5 (d, J_{CF} = 8.4 Hz, C8-Qu), 117.1 (d, J_{CF} = 9.6 Hz, C4a-Qu), n/d/ (C7-Bi), 112.5 (d, J_{CF} = 25.7 Hz, C5-Qu). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 150.9 (N1-Qu), n/d/ (N1-Bi), n/d/ (N3-Bi). ν_{max} (KBr) 3293, 3088, 1721, 1702, 1656, 1621, 1608, 1504, 1436, 1398, 1360, 1256, 1121, 1024, 929, 888, 818, 802, 719 cm^{-1}; Anal. Calcd for $C_{16}H_9ClFN_3O$: C, 61.26; H, 2.89; N, 13.39. ound: C, 61.19; H, 2.82; N, 13.33%.

6-Fluoro-4-(6-methylbenzimidazol-2-yl)quinolin-2(1*H*)-one 7e and 6-fluoro-4-(5-methylbenzimidazol-2-yl)quinolin-2(1*H*)-one 7′e were characterized as the mixture of regioisomers in percentage ratio 60:40.



Yield 98 mg (52%); light brown solid; mp 163-165 °C; (**7e**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.46 (s, 3H, CH_3-Bi), 7.15 (brs, 1H, H5-Bi), 7.19 (s, 1H, H3-Qu), 7.44 (dd, *J* = 9.0 Hz, J_{HF} = 7.8 Hz, 1H, H8-Qu), 7.49 (brs, 1H, H4-Bi), 7.50 (ddd, *J* = 9.0 Hz, J_{HF} = 5.1 Hz, *J* = 2.8 Hz, 1H, H7-Qu), 7.70 (m, 1H, H7-Bi), 9.03 (brd, J_{HF} ~ 9.1 Hz, 1H, H5-Qu), 12.06 (s, 1H, NH-Bi), 13.04 (s, 1H, NH-Qu). $^{13}C\{^{1}H\}$ NMR (DMSO-d_6, 126

MHz) δ 160.8 (C2-Qu), 157.0 (d, J_{CF} = 236.6 Hz, C6-Qu), 147.7 (C2-Bi), 143.9 (C7a-Bi), 137.4 (d, J_{CF} = 1.9 Hz, C4-Qu), 136.4 (C8a-Qu), 133.6 (C3a-Bi), 126.5 (C6-Bi), 124.0 (C5-Bi), 122.7 (C3-Qu), 119.3 (C7-Bi), 118.8 (d, J_{CF} = 24.6 Hz, C7-Qu), 117.4 (d, J_{CF} = 8.4 Hz, C8-Qu), 117.3 (d, J_{CF} = 9.7 Hz, C4a-Qu), 112.8 (d, J_{CF} = 25.8 Hz, C5-Qu), 111.2 (C4-Bi), 21.3 (CH_3-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 148.8 (N1-Bi), 150.1 (N1-Qu), n/d/ (N3-Bi). (**7′e**): ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.46 (s, 3H, CH_3-Bi), 7.11 (brs, 1H, H7-Bi), 7.19 (s, 1H, H3-Qu), 7.37 (brs, 1H, H4-Bi), 7.44 (dd, J = 9.0 Hz, J_{HF} = 7.8 Hz, 1H, H8-Qu), 7.50 (ddd, J = 9.0 Hz, J_{HF} = 5.1 Hz, J = 2.8 Hz, 1H, H7-Qu), 7.62 (m, 1H, H6-Bi), 9.03 (brd, J_{HF} ~ 9.1 Hz, 1H, H5-Qu), 12.06 (s, 1H, NH-Bi), 13.04 (s, 1H, NH-Qu). ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz) δ 160.8 (C2-Qu), 157.0 (d, J_{CF} = 236.6 Hz, C6-Qu), 147.4 (C2-Bi), 141.9 (C3a-Bi), 137.4 (d, J_{CF} = 1.9 Hz, C4-Qu), 136.4 (C8a-Qu), 134.3 (C7a-Bi), 126.5 (C5-Bi), 124.0 (C7-Bi), 122.7 (C3-Qu), 119.3 (C6-Bi), 118.8 (d, J_{CF} = 24.6 Hz, C7-Qu), 117.4 (d, J_{CF} = 8.4 Hz, C8-Qu), 117.3 (d, J_{CF} = 9.7 Hz, C4a-Qu), 112.8 (d, J_{CF} = 25.8 Hz, C5-Qu), 111.2 (C4-Bi), 21.3 (CH_3-Bi). ^{15}N NMR (DMSO-d_6, 51 MHz) δ 148.8 (N1-Bi), 150.1 (N1-Qu), n/d/ (N3-Bi). ν_{max} (KBr) 3173, 3080, 2920, 1666, 1626, 1608, 1504, 1432, 1403, 1338, 1258, 1220, 1121, 1028, 892, 802, 758 cm^{-1}; Anal. Calcd for $C_{17}H_{12}FN_3O_2$: C, 69.62; H, 4.12; N, 14.33. Found: C, 69.53; H, 4.09; N, 14.39%.

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