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# Molecular rearrangement of pyrazino[2,3-*c*]quinolin-5(6*H*)-ones during their reaction with isocyanic acid.

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## Abstract

A new tetrahydropyrazino[2,3-*c*]quinolin-5(6*H*)-ones were prepared from 3-chloroquinoline-2,4(1*H*,3*H*)-diones and ethylene diamine. In their reaction with HNCO, an unprecedented molecular rearrangement produced new types of hydantoin derivatives. All prepared compounds are characterized using their $^{1}H$, $^{13}C$, and $^{15}N$ NMR spectra and the results of the X-ray analysis are also presented. A proposed mechanism of rearrangement is discussed in this essay.

## Key words

3-(3-Acylureido)-2,3-dihydro-1*H*-indol-2-ones; 4-alkylidene-1´*H*-spiro[imidazolidine-5,3´-indole]-2,2´-diones; imidazo[1,5-*c*]quinazoline-3,5-diones; $^{1}H$, $^{13}C$ and $^{15}N$ NMR; spiro-linked imidazoline-2-thiones; X-ray

## Introduction

The presence of an amino group is common in many biologically active compounds. The group of reactive compounds including an amino group (especially α-aminoketones with respect to their easily conversion) belongs to various heterocycles [1]. Suitable compounds of this type are 3-aminoquinoline-2,4-diones, which is our particular area of interest [2]. Even if the occurrence of these compounds in the relevant literature was early rather than rare [3,4], we managed to prepare 3-aminoderivatives using 3-chloroquinolinediones and ammonium salts or primary amines [2a]. Later, we proved that these compounds may also be prepared from 3-hydroxyquinoline-2,4-diones in reaction with ammonia or ammonium salts [2n].

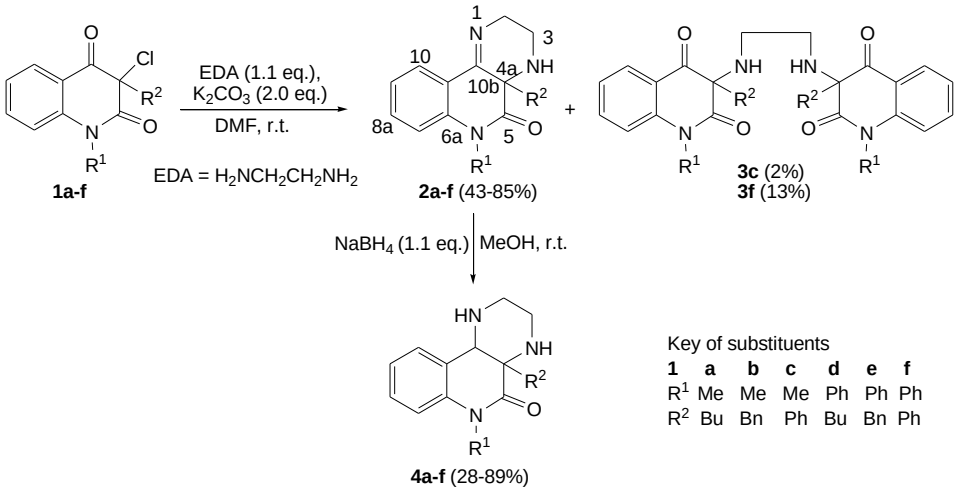
The biological activity of some 3-aminoquinoline-2,4-diones was described. 3-Amino-3-(4-fluorophenyl)-1*H*-quinoline-2,4-dione was demonstrated as effective against oxidative stress-related diseases [5]. It also suppressing the reactive oxygen species [6,7]. A similar effect was exhibited by 3-amino-6-fluoro-3-(4-fluorophenyl)-1*H*-quinoline-2,4-dione [5].

We found, that 3-aminoquinoline-2,4-diones are subject to molecular rearrangements by their reaction with urea, nitrourea, isocyanates, isothiocyanates, isothiocyanic acid, and isocyanic acid [2], creating a broad palette of new heterocyclic compounds, *e.g.*, imidazo[1,5-*c*]quinazoline-3,5-diones, 3-(3-acylureido)-2,3-dihydro-1*H*-indol-2-ones, 4-alkylidene-1´*H*-spiro[imidazolidine-5,3´-indole]-,2´-diones and spiro-linked imidazoline-2-thiones [2].

We also examined the reaction of 3-chloroquinolin-2,4-diones **1** with ethanolamine and found, that the results are similar to those of the reaction of **1** with simple aliphatic amines [2] and 3-(2-hydroxyethylamino)quinoline-2,4-diones were obtained. Their reaction with isocyanic acid presented rearranged products that are structurally analogous to those listed above. However, their reaction with isothiocyanic acid proceeded differently and resulted in mainly non-rearranged compounds [2o].

Considering these results, we decided to study the reactions of the 3-chloroquinoline-2,4-diones **1** with 1,2-diamines. In the literature, most of the reactions reported are of α-haloketones with *o*-phenylenediamines. Surprisingly, reactions of tertiary α-chloroketones with aliphatic 1,2-diamines were only described in one article [8].

In our previous paper [2p] we described the reaction of N-1 unsubstituted 3-chloroquinolinediones with ethylene diamine. The results of this reaction were remarkable because we obtained two types of new quinazoline derivatives that did not react with isocyanic and isothiocyanic acids.




**Scheme 1.** The preparation and reduction of pyrazino[2,3-*c*]quinolin-5(6*H*)-ones **2**.

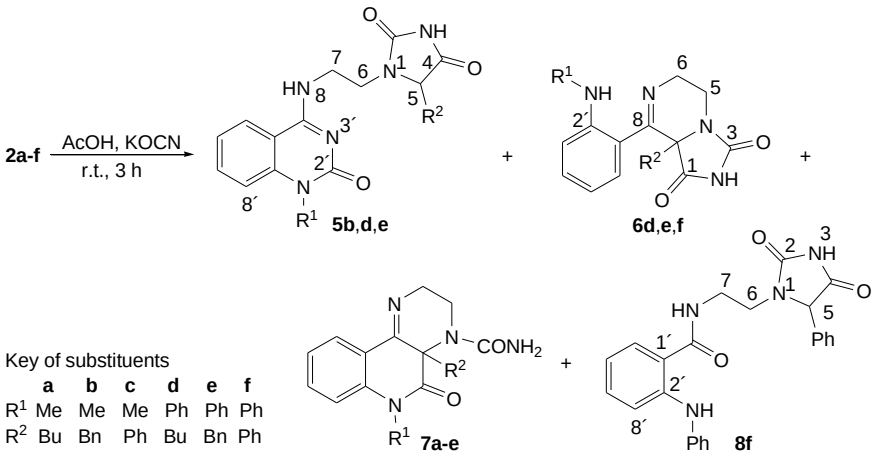
In this paper we would like to show that the reaction of ethylene diamine with N-1 substituted 3-chloroquinoline-2,4-diones proceeds smoothly without rearrangement to result in pyrazino[2,3-*c*]quinolin-5(6*H*)-ones **2**, whose reduction and the reaction with isocyanic acid will be described.

## Results and discussion

Our purpose was the detailed study of the reaction connected with isolation a large quantity of minority compounds to clarifying of the reaction mechanism. The reactions of 3-chloroquinolin-2,4-diones **1a-f** with ethylene diamine were performed in DMF in the presence of powdered potassium carbonate. In a good yield, novel tricyclic pyrazino[2,3-*c*]quinolin-5(6*H*)-ones **2** were obtained (Scheme 1). In just two cases, a small quantity of dimeric compound **3c** and **3f** was produced *via* double alkylation of ethylene diamine with chloroderivative **1c** and **1f**. Their $^{1}$H and $^{13}$C NMR spectra exhibit two sets of signals according to the presence of two observable diastereoisomers. Reaction of compounds **2** with sodium

borohydride confirmed the presence of the imine group in their molecule and leads to the expected dihydroderivatives **4** (Scheme 1). Even if ethylene diamine is strong base, we do not observe the formation of other compounds, that would be products of the rearrangement analogous to rearrangement of 3-aminoquinolinediones.[2] The NMR spectra of isolated compounds **2**, **3** and **4** are presented in SI 0(Figures S1–S15). The reactions of compound **2** with potassium cyanate were carried out in the molar ratio 1:1.6 in a solution of acetic acid (Scheme 2, Table 1). Our first look to the IR and NMR spectra of the reaction products shows that compounds of at least three types arise. However, we were not able to determine the structure of isolated compounds from their NMR spectra. Only a few isolated fragments were found, but it was impossible to determine how they interconnected. Fortunately, after more unsuccessful experimentation, we managed to prepare a single crystal of the compound acquired from compound **2d**. The structure of this compound (**5d**) was established by X-ray diffraction analysis (Figure 1). Although the crystal structures of imidazolidine-2,4-dione (also a part of **5d** skeleton), derivatives had been described crystallographically more than 170 times, the derivatives with a longer hydrocarbon chain are absent from the literature. Moreover, the second part of the **5d** molecule, 1,2-dihydroquinazolin-2-one fragment, is scarcely reported [9,10].

In **5d** (Figure 1), the planes of the imidazolidine-2,4-dione and 1,2-dihydroquinazolin-2-one parts, that are separated by the iminoethane bridge exhibit the interplanar angle of 26.16(9)°. Two molecules are interconnected by C=O**…**H–N bridges (see Figure S29 in SI).




**Scheme 2.** Reaction of compounds **2** with potassium cyanate.

**Table 1.** Results of the reactions of compounds **2**, **6** and **7**

| Starting compoud | Molar ratio of **2** to KOCN | Product, (yield, %) | | | |
|---|---|---|---|---|---|
| | | **5** | **6** | **7** | **8** |
| **2a** | 1 : 1.6 | | | **7a** (47) | |
| **2a** | 1 : 4.0 | | | **7a** (57) | |
| **2b** | 1 : 1.6 | **5b** (18) | | **7b** (63) | |
| **2c** | 1 : 1.6 | | | **7c** (32) | |
| **2c** | 1 : 4.0 | | | **7c** (68) | |
| **2d** | 1 : 1.6 | **5d** (17) | **6d** (13) | **7d** (38) | |
| **2d** | 1 : 3.0 | **5d** (17) | **6d** (8) | **7d** (31) | |
| **2e** | 1 : 1.6 | **5e** (22) | **6e** (14) | **7e** (49) | |
| **2e** | 1 : 4.0 | **5e** (50) | **6e** (6) | **7e** (29) | |
| **2f** | 1 : 3.0 | | **6f** (20) | | **8f** (18) |
| **6d** | 1 : 3.0 | **5d** (57) | | | |
| **7d** | 1 : 3.0 | **5d** (33) | | | |

The structure of **5d** is surprising, because its creation requires the scission of the C(2)–C(3) bond in starting compound **2d**. We did not observe such a reaction at any time. The transformation of quinolinedione to a quinazolinedione skeleton was observed only in cases, where the starting compound was N-unsubstituted, allowing the formation of a useful isocyanate intermediate [2p].

Compound **5d** consists of two bioactive moieties: 4-iminoquinazolin-2-one and substituted hydantoin. Several methods exist for the preparation of closely related quinazolinediones [11]. These compounds exhibit significant antihypertensive, antineoplastic, antidepressant and antipsychotic activities. Hydantoins are compounds that play an important role in the purine catabolic pathway. They have pharmacological properties and are used to treat many human diseases. For example, 5,5-diphenylhydantoin has been used for decades to treat epilepsy, but different substituted hydantoins also exhibit further pharmacological properties, *e.g*., fungicidal, herbicidal, antitumor, anti-inflammatory, anti-HIV, hypolipidemic, antiarrhythmic and antihypertensive activities have also been identified [12] Several marketed drugs having hydantoin core are recognized and many methods for their synthesis are described [13]. However, none of them are remotely similar to the presented transformation. It must be point out here that the reaction of compounds **2** with HNCO was carried out in molar ratio 1:1.6, because we did not anticipate initially the reaction of compound **2** with more than one mole of isocyanic acid. Therefore, it is impossible looked forward to the completely conversion of compounds **2** to **5**, but only formation of mixtures of the products can proceed (Table 1). Using the

excess of KNCO, the composition of the reaction products changes (Table 1), but at no time was the full conversion of **2** to **5** achieved.

Compounds **5b** and **5e** belong to the group of compounds produced by the reaction of **2** with two equivalents of HNCO and exhibiting an absorption band at *ca.* 1770 $cm^{-1}$ in the IR spectrum, characteristic of hydantoins [14]. All their NMR data (Table 2) are in the agreement with the proposed structure.

In addition to compound **5d**, the next product was obtained from compound **2d**. From ESI-MS and elemental analysis it was determined that only one mole of HNCO was consumed. Its IR spectrum exhibits an absorption band at 1776 $cm^{-1}$, indicative of the presence of the hydantoin ring [14]. In the $^{1}H$ NMR spectrum of isolated compounds, a singlet at 11.2 ppm appeared, pertaining to the NH proton in position 2 of hydantoin moiety [15]. The fragment Ar–NH–Ph was also found, what bear witness to the opening of the quinolinone ring in **2d**.

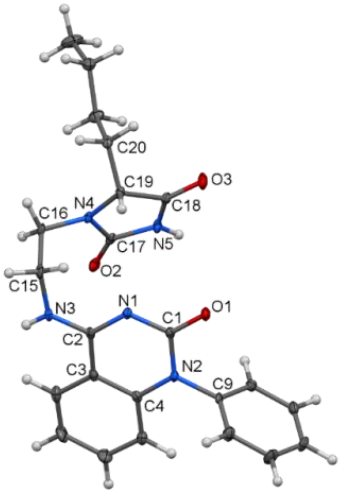



**Figure 1.** Molecular structure of **5d** - *ORTEP view, 40% probability level.*

Compound **6d** represents the second structural group of products produced from the reaction of **2** with only one mole of isocyanic acid and exhibiting an IR absorption band at *ca* 1760 $cm^{-1}$. Compounds **6e** and **6f** also pertains to this group. All these compounds display their absorption band at *ca* 1760 $cm^{-1}$ in the IR spectrum and their broad signal at *ca* 11.1 ppm in the $^{1}H$ NMR spectrum. In their $^{13}C$ NMR spectrum (Table 3), the quaternary carbons signals appeared at *ca* 68.9 ppm and, in the $^{15}N$ NMR spectrum, the signal adherent to the C=N group can be seen, much like that in the starting compound

**2**. Four nitrogen atoms are present in forename compounds. One of them belongs to C=N group, the second is imidic and the third pertains to the tertiary amino group. Therefore, the fourth nitrogen atom, exhibiting a singlet at *ca* 8 ppm in its $^{1}$H NMR spectrum, must be part of Ar–NH–R$^{1}$ grouping.

The third product of the reaction of **2d** with HCNO was a compound that did not have any IR absorption around 1760 cm$^{-1}$ and, therefore, does not contain the hydantoin ring. From the $^{1}$H and $^{13}$C NMR spectra (see SI) that are similar to **2d**, but exhibited the presence of the $CONH_2$ group results suggest the structure of **7d**. The reaction of this compound with the excess of HNCO (Table 1) provided compound **5d**, indicating that **7d** is the first intermediate in the molecular rearrangement of **2d**. It was found, that compound **7** results from all compounds **2** except of **2f**.

**Table 2.** $^{1}$H, $^{13}$C and $^{15}$N chemical shifts and $^{1}J(^{15}N, ^{1}H)$ coupling constants of compounds **5** in DMSO-$d_6$

| Position | **5b** | | **5d** | | **5e** | |
|---|---|---|---|---|---|---|
| | δ(H) | δ(C) | δ(H) | δ(C) | δ(H) | δ(C) |
| 1N | - | -286.8[a] | - | -286.4[a] | - | -287.6[a] |
| 2 | - | 156.5 | - | 156.9 | - | 156.6 |
| 3 | 10.53 | n.o. | 10.78 | n.o. | 10.58 | 232.2[a] |
| | | 95.2 [b] | | 90.8 [b] | | 94.6 [b] |
| 4 | - | 173.8 | - | 174.6 | - | 173.8 |
| 5 | 4.55 | 60.6 | 4.26 | 59.9 | 4.60 | 60.6 |
| 6 | 3.61 | 38.7 | 3.67 | 38.8 | 3.69 | 38.8 |
| 7 | 3.85 | 38.1 | 3.82 | 38.6 | 3.82 | 38.2 |
| | 3.17 | | 3.24 | | 3.20 | |
| 8 | 8.37 | -286.8[a] | 8.58 | -285.0[a] | 8.56 | -285.0[a] |
| | | 88.5 [b] | | 92.4 [b] | | 92.7 [b] |
| 1´ | - | -262.9[a] | - | -241.2[a] | - | -241.1[a] |
| 2´ | - | 155.2 | - | 154.6 | - | 154.5 |
| 3´ | - | -171.2[a] | - | -171.4[a] | - | -171.7[a] |
| 4´ | - | 160.0 | - | 160.6 | - | 160.6 |
| 4a´ | - | 109.8 | - | 109.4 | - | 109.4 |
| 5´ | 7.95 | 123.7 | 8.04 | 123.7 | 8.02 | 123.6 |
| 6´ | 7.20 | 121.0 | 7.19 | 121.4 | 7.21 | 121.3 |
| 7´ | 7.67 | 133.9 | 7.45 | 133.6 | 7.49 | 133.5 |
| 8´ | 7.34 | 114.4 | 6.40 | 115.0 | 6.41 | 115.0 |
| 8a´ | - | 142.8 | - | 143.7 | - | 143.7 |
| 1´(R$^{1}$) | 3.43 | 30.0 | - | 138.2 | - | 138.2 |
| 2´(R$^{1}$) | - | - | 7.26 | 128.3 | 7.24 | 128.2 |
| 3´(R$^{1}$) | - | - | 7.58 | 129.9 | 7.59 | 129.9 |
| 4´(R$^{1}$) | - | - | 7.49 | 128.3 | 7.50 | 128.2 |
| 1´(R$^{2}$) | 3.14 | 33.4 | 1.76 | 27.4 | 3.20 | 30.9 |
| | 3.01 | | 1.73 | | 3.05 | |
| 2´(R$^{2}$) | - | 135.4 | 1.20 | 25.0 | - | 135.4 |
| | | | 1.04 | | | |
| 3´(R$^{2}$) | 7.10 | 128.2 | 1.20 | 21.9 | 7.14 | 128.2 |
| 4´(R$^{2}$) | 7.20 | 129.4 | 0.79 | 13.8 | 7.28 | 129.4 |
| 5(R$^{2}$) | 7.20 | 126.7 | - | - | 7.22 | 126.7 |

[a] δ $^{15}$N) [b] $^{1}J(^{15}N, ^{1}H)$

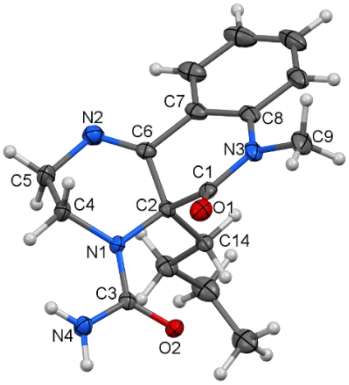



**Figure 2.** Molecular structure of **7a** - *ORTEP view, 40% probability level.*

Their structure was proven by the X-ray analysis of compound **7a** (Figure 2) and **7b** (Figure 3). The structures of **7a** and **7b** are characterized by the presence of substituted tricyclic systems where the π-electron conjugation is interrupted by the presence of the stereogenic center at C-2 (**7a**) and or C-11 (**7b**) atoms as well as the ethylene bridge. The constitution of the tricyclic system in **7a** is totally unknown. On the other hand, the characteristic interatomic distances and angles in both compounds, that crystallize in achiral space groups $P2_1/c$ and $P\text{-}1$, respectively, are essentially the same to the previously known structures with the same type of functional groups and atom hybridization [16,17].

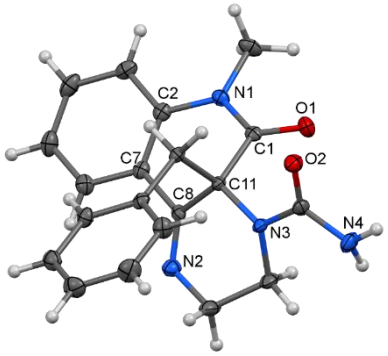



**Figure 3.** Molecular structure of **7b** - *ORTEP view, 40% probability level.*

**Table 3.** $^{1}H$, $^{13}C$ and $^{15}N$ chemical shifts of compounds **6** in DMSO-$d_6$

| Position | **6d** | | **6e** | | **6f** | |
|---|---|---|---|---|---|---|
| | (δH) | (δC) | (δH) | (δC) | (δH) | (δC) |
| 2 | 11.01 | n.o. [a] | 10.68 | n.o. [a] | 11.05 | n.o. [a] |
| 3 | - | 156.2 | - | 155.8 | - | 155.4 |
| 4 | - | -290.8[a] | - | -291.4[a] | - | -285.5[a] |
| 5 | 3.82 | 46.4 | 3.93<br>3.86 | 46.6 | 4.03<br>3.55 | 45.5 |
| 6 | 3.82<br>3.15 | 33.9 | 3.78<br>3.42 | 34.0 | 3.48<br>3.34 | 36.2 |
| 7 | - | -53.7[a] | - | -50.6[a] | - | -58.2[a] |
| 8 | - | 163.1 | - | 162.9 | - | 165.0 |
| 8a | - | 68.0 | - | 68.3 | - | 68.9 |
| 1´ | - | 128.3 | - | 128.2 | - | 125.3 |
| 2´ | - | 141.7 | - | 142.1 | - | 138.8 |
| 3´ | 7.10 | 117.9 | 7.12 | 117.7 | 7.19 | 118.9 |
| 4´ | 7.19 | 128.7 | 7.22 | 128.9 | 7.23 | 130.8 |
| 5´ | 6.86 | 119.7 | 6.93 | 120.1 | 6.82 | 119.4 |
| 6´ | 7.10 | 129.3 | 7.22 | 129.4 | 7.25 | 131.6 |
| 2´ | 7.15 | -295.9[a]<br>90.3 [b] | 7.37 | -295.6[a]<br>90.4[b] | 8.85 | -292.2[a]<br>87.2 [b] |
| 1´($R^1$) | - | 143.6 | - | 143.5 | - | 142.8 |
| 2´($R^1$) | 7.02 | 118.6 | 7.02 | 119.1 | 7.01 | 118.9 |
| 3´($R^1$) | 7.19 | 128.7 | 7.21 | 128.7 | 7.22 | 128.9 |
| 4´($R^1$) | 6.83 | 120.3 | 6.83 | 120.5 | 6.89 | 120.9 |
| 1´($R^2$) | 1.94 | 32.7 | 3.26<br>3.36 | 38.5 | - | 137.3 |
| 2´($R^2$) | 1.15<br>0.98 | 24.7 | - | 133.8 | 7.39 | 126.5 |
| 3´($R^2$) | 1.15 | 21.7 | 7.02 | 131.2 | 7.42 | 128.9 |
| 4´($R^2$) | 0.74 | 13.7 | 7.20 | 128.3 | 7.42 | 130.0 |
| 5´($R^2$) | - | - | 7.22 | 127.1 | - | - |

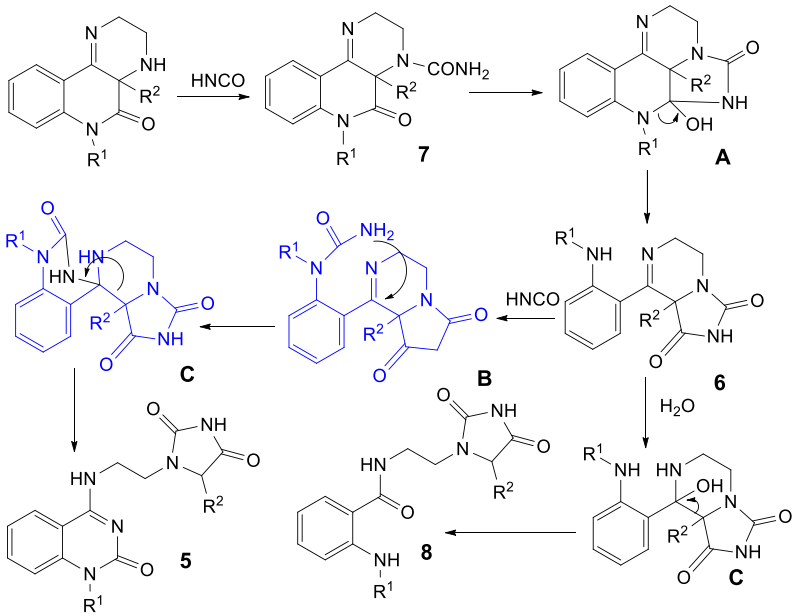
[a] δ $^{15}N$); [b] $^{1}J$($^{15}N$, $^{1}H$); [c] prochiral $NCH_2$ 3.41, 3.43/38.5;

COO -/167.0, $CH_2$ 3.96/61.3, $CH_3$ 1.03/13.8

Three molecules of **7a** co-crystallize with two molecules of water to form an extensive system of H-bridges. In **7b**, both optical isomers are interconnected by an NH**…**O=C bridging motif. Co-crystallized dichloromethane molecules occupy the tunnels formed by the aromatic rings of the molecule. All the geometric parameters of all X-rayed structures are given in SI. The anomalous behavior showed that compounds **7c** and **7d**, whose NMR spectra measured in DMSO-$d_6$, exhibit very broad signals. Therefore, they were measured in $CDCl_3$.

Compound **7** is primarily the product of the reaction between compound **2** and isocyanic acid, and therefore provides the starting compounds of the following molecular rearrangement to compounds **5** and **6**. Our proposal of the reaction mechanism of rearrangement of compounds **2** is illustrated in Scheme 2. We suppose that addition of compound **2** to isocyanic acid produces compound **7** which is subsequently changed to compound **6** *via* the intermediate **A**. The reaction of compound **6** with isocyanic acid affords the intermediate **B**, which is liable to retro-Claisen condensation under the formation of compounds **5**.

One of the isolated products, prepared from **2f**, was different from the compounds mentioned above. The fragment $NCH_2CH_2N$ is present, but the compound does not contain the C=N group and instead of quaternary carbon atom contain the CHR group. The presence of an IR band at 1775 $cm^{-1}$ in the IR spectrum and 11.2 ppm in the $^1H$ NMR spectrum shows that the hydantoin ring must be present. In the molecule that pointed to the structure **8f**, the amide group was found (see figure S27). The origin of this compound can be explained by the addition of water to the compound **6f** and following retro-Claisen condensation through intermediates **B** and **C**. (Scheme 3).




**Scheme 3.** Proposed reaction mechanism.

## Conclusions

In conclusion, the tetrahydropyrazino[2,3-*c*]quinolin-5(6*H*)-ones **2** react with isocyanic acid to give (2-oxo-2,3-dihydroquinazolin-4(*1H*)-ylidene)-amino)ethyl)imidazolidine-2,4-diones **5**, 2-(phenylamino) phenyl)-5,6-dihydroimidazo[1,5-a]pyrazine-diones **6**, and 5-oxo-tetrahydropyrazinoquinoline-4-carboxamides **7**. The structures of compounds **5** and **7** were proven by X-ray analysis. The mechanism of the rearrangement of starting compounds **2** to **5** and **6** is not only of theoretical importance, but enables, through a simple procedure, the targeted preparation of new types of hydantoins that are suitable for biological testing and further study of the transformations. The presented work extends the set of compounds containing a hydantoin structural motif which is a component of compounds that have significant pharmacological properties and are used to treat many human diseases.

## Experimental section

***General:*** Melting points were determined on a Kofler block. IR (KBr) spectra were recorded on a Smart OMNI-Transmission Nicolet iS10 spectrophotometer. The $^{1}$H, $^{13}$C, and $^{15}$N NMR spectra were recorded on a Bruker Avance III HD 500 spectrometer (500.13 MHz for $^{1}$H, 125.76 MHz for $^{13}$C, and 50.68 MHz for $^{15}$N) in DMSO-$d_6$. $^{1}$H and $^{13}$C chemical shifts are given on the $\delta$ scale (ppm) and are referenced to internal TMS ($\delta$ = 0.0). $^{15}$N chemical shifts were referred to external neat $CH_3NO_2$ in a co-axial capillary ($\delta$ = 0.0). All 2D experiments (gradient-selected (gs)-COSY, gs-TOCSY, gs-HMQC, gs-HMQC-RELAY, gs-HMBC) were performed using manufacturer's software. Full-sets of diffraction data for **5d** (yellow) and **7a** and **7b** (colourless) were collected at 150(2)K with a Bruker D8-Venture diffractometer equipped with Cu (Cu/$K_\alpha$ radiation; $\lambda$ =1.54178 Å) or Mo (Mo/$K_\alpha$ radiation; $\lambda$ = 0.71073 Å) microfocus X-ray (IμS) sources, Photon CMOS detector and Oxford Cryosystems cooling device was used for data collection. Experimental details are stated in Supporting Information. The frames were integrated with the Bruker SAINT Software package using a narrow-frame algorithm. Data were corrected for absorption effects using the Multi-Scan method (SADABS). Obtained data were treated by XT-version 2018/1 and SHELXL-2017/1 software implemented in APEX3 v2016.5-0 (Bruker AXS) system [18]. The positive-ion EI mass spectra were measured on a Shimadzu QP-2010 instrument

within the mass range *m/z* = 50–600 using direct inlet probe (DI). Samples were dissolved in dichloromethane (30 μg·mL$^{-1}$) and 10 μL of the solution was evaporated in DI cuvette at 50 °C. The ion source temperature was 200 °C; the energy of electrons was 70 eV. Only signals exceeding relative abundance of 5% are listed. The electrospray mass spectra (ESI-MS) were recorded using an amaZon X ion-trap mass spectrometer (Bruker Daltonics, Bremen, Germany) equipped with an electrospray ion source. All experiments were conducted in both positive and negative polarity mode. Individual samples (with a concentration of 500 ng·mL$^{-1}$) were infused into the ESI source as methanol/water (1/1, v/v) solutions via a syringe pump with a constant flow rate of 3 μL·min$^{-1}$. The other instrumental conditions were as follows: *m/z* range 50–1500, electrospray voltage of ±4.2 kV, capillary exit voltage of ±140 V, drying gas temperature of 220 °C, drying gas flow of 6.0 dm$^3$·min$^{-1}$, nebulizer pressure of 55.16 kPa. Nitrogen was used as the nebulizing and drying gases for all experiments. Tandem mass spectra were collected using collision-induced dissociation (CID) with He as the collision gas after isolating of the required ions. Column chromatography was carried out on silica gel (Merck, grade 60, 70–230 mesh) using successive mixtures of chloroform/ethanol (in ratios from 99:1 to 8:2) (S1) or benzene/ethyl acetate (in ratios from 99:1 to 8:2) (S2). Reactions as well as the course of separation and also the purity of substances were monitored by TLC (elution systems benzene/ethyl acetate (4:1) (S3), chloroform/ethanol (9:1 and 1:1) (S4 and S5), and chloroform/ethyl acetate (7:3) (S6) on Alugram® SIL G/UV$_{254}$ foils (Macherey-Nagel). Elemental analyses (C, H, N) were performed with a EA Flash EA 1112 Elemental Analyzer (Thermo Fisher Scientific).

**General procedure for the reaction of compounds 1 with ethylene diamine**

To the solution of compound **1** (1 mmol) in DMF (9 mL), pulverized potassium carbonate (276 mg, 2 mmol) and ethylene diamine (EDA) (0.1 ml, 1.1 mmol) were added and the mixture was stirred at room temperature. The course of the reaction was monitored with TLC. After fade away of the spot corresponding to compound **1**, the reaction mixture was diluted with water (20 mL). Deposited product was filtered with suction, dried and crystallized from appropriate solvent. In cases where the crude product was oily or waxy, the solution was extracted with chloroform (3 × 20 mL). The collected extracts were dried, evaporated to dryness and the residue was separated by chromatography on silica gel column.

*4a-Butyl-6-methyl-2,3,4,4a-tetrahydro-pyrazino-[2,3-c]quinolin-5(6H)-one (**2a**).* Compound was prepared from **1a** and EDA in 53% yield, reaction time 6 h. White solid, mp 111–113 °C (ethyl acetate/hexane). IR ($cm^{-1}$) ν: 3346, 3042, 2959, 2936, 2872, 2825, 1676, 1645, 1602, 1462, 1431, 1410, 1367, 1347, 1315, 1297, 1279, 1265, 1229, 1192, 1125, 1109, 1056, 1044, 992, 961, 946, 840, 759, 740, 680, 654,627, 579, 532. ESI-MS (pos.) *m/z* (%): 565.2 $[2\cdot M+Na]^+$ (7), 294.1 $[M+K]^+$ (19), 272.1 $[M+Na]^+$ (100), 216.0 $[M+H]^+$ (11). Anal calcd for $C_{16}H_{21}N_3O$ (271.36): C, 70.82, H, 7.80, N, 15.49. Found: C, 70.55, H, 8.00, N, 15.40.

*6-Methyl-4a-benzyl-2,3,4,4a-tetrahydropyrazino[2,3-c]quinolin-5(6H)-one (**2b**).* Compound was prepared from **1b** and EDA in 43% yield. Colourless solid, mp 102–106 °C (benzene/hexane). IR ($cm^{-1}$) ν: 3329, 3066, 3028, 2942, 2905, 2838, 1668, 1633, 1603, 1497, 1472, 1455, 1438, 1416, 1357, 1339, 1298, 1270, 1226, 1202, 1159, 1129, 1076, 1062, 1047, 1010, 958, 903, 763, 699, 656, 620, 535, 504. ESI-MS (pos.) *m/z* (%): 633.2 $[2\cdot M+Na]^+$ (6), 328.0 $[M+Na]^+$ (20), 306.0 $[M+H]^+$ (100), 214.9 $[M+H-C_7H_7]^+$ (10). Anal. calcd for $C_{19}H_{19}N_3O$ (305.37): C, 74.73, H, 6.27, N 13.76. Found: C, 74.63, H, 6.40, N, 13.84.

*6-Methyl-4a-phenyl-2,3,4,4a-tetrahydropyrazino[2,3-c]quinolin-5(6H)-one (**2c**)*. Compound was prepared from **1c** in 54% yield besides **3c**. White solid, mp 178–182 °C (benzene). IR ($cm^{-1}$) ν: 3358, 2933, 2838, 1671, 1638, 1602, 1469, 1446, 1417, 1362, 1297, 1150, 1124, 1080, 991, 896, 845, 763, 744, 706, 692, 661, 625, 569, 536, 506. EI-MS *m/z* (%): 292 (21), 291 ($M^+$, 100), 290 (20), 262 (23), 261 (47), 160 (12), 132 (14), 131 (20), 104 (18), 77 (16). ESI-MS (pos.) *m/z* (%): 605.2 $[2\cdot M+Na]^+$ (42), 583.2 $[2\cdot M+H]^+$ (16), 314.1 $[M+Na]^+$ (18), 292.1 $[M+H]^+$ (100). EA: For $C_{18}H_{17}N_3O$ (291.35) calcd: C, 74.20, H, 5.88, N, 14.42. Found: C, 73.99, H, 5.98, N, 14.24.

*4a-Butyl-6-phenyl-2,3,4,4a-tetrahydropyrazino[2,3-c]quinolin-5(6H)-one (**2d**)*. Compound was prepared from **1d** and EDA in 85% yield. Colourless solid, mp 86–90 °C (hexane). IR ($cm^{-1}$) ν: 3448, 3330, 2954, 2868, 1677, 1642, 1604, 1492, 1456, 1348, 1332, 1314, 1293, 1261, 1222, 1177, 1113, 1072, 999, 770, 697, 682, 656, 648, 610, 491. ESI-MS (pos.) *m/z* (%): 356.1 $[M+Na]^+$ (5), 334.2 $[M+H]^+$ (100), 278.1 $[M+H-C_4H_8]^+$ (3). EI-MS: *m/z* (%) 334 (6), 333 (24), 291 (6), 290 (25), 277 (21), 276 (100), 275 (7), 262 (6), 77 (7), 57 (5). Anal. calcd for $C_{21}H_{23}N_3O$ (333.43):C, 75.65, H, 6.95, N, 12.60. Found: C, 75.82, H, 7.14, N, 12.55.

*4a-Benzyl-6-phenyl-2,3,4,4a-tetrahydropyrazino[2,3-c]quinolin-5(6H)-one* ***(2e).*** Compound was prepared from **1e** and EDA in 51% yield, reaction time 3 h. White solid, mp 161–164 °C (benzene/cyclohexane). IR ($cm^{-1}$) ν: 3354, 2925, 2897, 2836, 1690, 1638, 1600, 1492, 1460, 1351, 1315, 1275, 1214, 1164, 1073, 1003, 959, 877, 782, 766, 741, 702, 657, 632, 598. ESI-MS (pos.) *m/z* (%): 757.3 $[2\cdot M+Na]^+$ (5), 390.1 $[M+Na]^+$ (21), 368.1 $[M+H]^+$ (100), 277.0 $[M+H-C_7H_7]^+$ (5). EI-MS: *m/z* (%): 367 (14), 277 (21), 276 (100), 91 (8), 77 (5). Anal. calcd for $C_{24}H_{21}N_3O$ (367.44): C, 78.45, H, 5.76, N, 11.44. Found: C, 78.41, H, 5.88, N, 11.43.

*4a,6-Diphenyl-2,3,4,4a-tetrahydropyrazino[2,3-c]quinolin-5(6H)-one* ***(2f***). Compound was prepared from **1f** and EDA in 66% yield. Colourless solid, mp 156–160 °C (hexane). IR ($cm^{-1}$) ν: 3442, 2908, 2820, 1681, 1638, 1602, 1493, 1458, 1422, 1355, 1335, 1261, 1261, 1160, 1109, 995, 936, 893, 758, 740, 719, 700, 663, 627, 574, 516. ESI-MS (pos.) *m/z* (%): 354.1 $[M+H]^+$ (100). EI-MS: *m/z* (%): 354 (26), 353 (100), 352 (16), 338 (6), 324 (13), 323 (26), 296 (5), 250 (7), 249 (5), 248 (5), 222 (7), 221 (9), 194 (14), 193 (6), 149 (6), 131 (8), 104 (11), 103 (6), 77 (17), 71 (5), 66 (5), 57 (9), 55 (6), 51 (7), 43 (10). Anal. calcd for $C_{23}H_{19}N_3O$ (353.42): C, 78.16, H, 5.42, N, 11.89: Found: C, 78.06, H, 5.50, N, 11.88.

*3,3´-(Ethane-1,2-diylbis(azanediyl)bis(1-methyl-3-phenylquinoline-2,4(1H,3H)-dione* ***(3c***). Compound was prepared from **1c** in 2% yield besides **2c**. Yellowish solid, mp 198–210 °C (benzene-hexane).IR ($cm^{-1}$) ν: 3333, 3064, 3033, 2946, 2854, 1703, 1666, 1602, 1472, 1417, 1354, 1303, 1254, 1185, 1114, 1034, 994, 911, 864, 764, 699, 684, 637, 600, 533, 495. ESI-MS (pos.) *m/z* (%): 581.2 $[M+Na]^+$ (44), 559.2 $[M+H]^+$ (100). ESI-MS (neg.) *m/z* (%): 575.1 $[M-H+H_2O]^-$ (100), 557.1 $[M-H]^-$ (37). Anal calcd for $C_{34}H_{30}N_4O_4$ (558.63): C, 73.10, H, 5.41, N, 10.03. Found: C, 73.41, H, 5.68, N, 9.95.

*3,3´-(Ethane-1,2-diylbis(azanediyl)bis(1,3-diphenylquinoline-2,4(1H,3H)-dione* ***(3f***). Compound was prepared from **1f** in 13% yield. Colourless solid, mp 262–268 °C (benzene/hexane). IR ($cm^{-1}$) ν: 3442, 3063, 2927, 2858, 1707, 1673, 1600, 1492, 1461, 1337, 1303, 1249, 1192, 1173, 1158, 1113, 1072, 1031, 1002, 981, 902, 820, 762, 747, 719, 703, 650, 609, 576, 539, 516. ESI-MS (pos.) *m/z* (%): 1387.5 $[2\cdot M+Na]^+$ (11), 1365.4 $[2\cdot M+H]^+$ (6), 721.2 $[M+K]^+$ (7), 705.3 $[M+Na]^+$ (31), 683.3 $[M+H]^+$ (100) Anal. calcd for $C_{44}H_{34}N_4O_4$ (682.77):.C, 77.40, H, 5.02, N, 8.21. Found: C, 76.98, H, 5.13, N, 8.36.

**General procedure for the reduction of compounds 2 with $NaBH_4$**

To the solution of compound **2** (1.5 mmol) in methanol (20 mL) was added during 5 min $NaBH_4$ (67 mg, 1.7 mmol). The mixture was stirred for 1.5 – 3 h at room temperature and then poured to 20 mL of crushed ice. Hydrochloric acid (35%, 0.28 ml) and, after 5 min, 5% $NaHCO_3$ were added. The alkaline reaction mixture was extracted with chloroform (3 × 25 mL), the extract was dried and evaporated to dryness. The residue was crystallized from an appropriate solvent.

*4a-Butyl-6-methyl-1,2,3,4,4a,10b-hexahydropyrazino[2,3-c]quinolin-5(6H)-one (**4a**).* Compound was prepared from **2a** in 28% yield. Colourless solid, mp 145–149 °C (hexane). IR ($cm^{-1}$) ν: 3369, 3064, 3040, 2951, 2928, 2862, 2801, 1666, 1601, 1497, 1470, 1443, 1418, 1357, 1294, 1275, 1233, 1203, 1156, 1124, 1040, 983, 958, 887, 874, 847, 824, 758, 684, 632, 593, 548, 537. . ESI-MS (pos.) *m/z* (%): 547.2 $[2\cdot M+H]^+$ (7), 274.1 $[M+H]^+$ (100). Anal. calcd for $C_{16}H_{23}N_3O$ (273.37): C, 70.30, H, 8.48, N, 15.37. Found: C, 70.53, H, 8.34, N, 15.23.

*4a-Benzyl-6-methyl-1,2,3,4,4a,10b-hexahydropyrazino[2,3-c]quinolin-5(6H)-one (**4b**).* Compound was prepared from **2b** in 30% yield. Colourless solid, mp 207–210 °C (ethanol). IR ($cm^{-1}$) ν: 3295, 3070, 3024, 2969, 2940, 2898, 2835, 2814, 2769, 2721, 1665, 1604, 1504, 1479, 1470, 1459, 1422, 1367, 1336, 1318, 1284, 1238, 1145, 1132, 1118, 1082, 1050, 991, 973, 862, 827, 764, 730, 702, 691, 662, 643, 504. ESI-MS (pos.) *m/z* (%): 637.2 $[2\cdot M+Na]^+$ (4), 330.1 $[M+Na]^+$ (9), 308.1 $[M+H]^+$ (100). Anal. calcd for $C_{19}H_{21}N_3O$ (307.39): C, 74.69, H, 6.89, N, 13.69. Found: C, 74.57, H, 7.05, N, 13.61.

*6-Methyl-4a-phenyl-1,2,3,4,4a,10b-hexahydropyrazino[2,3-c]quinolin-5(6H)-one (**4c**).* Compound was prepared from **2c** in 89% yield. Colourless solid, mp 216–218 °C (benzene). IR ($cm^{-1}$) ν: 3067, 2954, 2922, 2802, 1668, 1601, 1495, 1470, 1448, 1412, 1355, 1306, 1271, 1155, 1140, 1117, 1042, 981, 951, 816, 771, 756, 719, 705, 679, 694, 600, 543. ESI-MS (pos.) *m/z* (%): 587.2 $[2\cdot M+H]^+$ (7), 316.0 $[M+Na]^+$ (8), 294.1 $[M+H]^+$ (100). Anal. calcd for $C_{18}H_{19}N_3O$ (293.36): C, 73.69, H, 6.53, N, 14.32. Found: C, 73.60, H, 6.70, N, 14.32.

*4a-Butyl-6-phenyl-1,2,3,4,4a,10b-hexahydropyrazino[2,3-c]quinolin-5(6H)-one (**4d**).* Compound was prepared from **2d** in 62% yield. Colourless solid, mp 120–124 °C (benzene). IR ($cm^{-1}$) ν: 3251, 3206, 3064, 2958, 2932, 2872, 1709, 1666, 1604, 1494, 1461, 1405, 1379, 1353, 1300, 1266, 1201, 1158, 1141, 1105, 1048, 929, 872, 838, 757, 696, 667, 564. ESI-MS (pos.) *m/z* (%): 671.3 $[2\cdot M+H]^+$ (11),

358.1 $[M+Na]^+$ (5), 336.1 $[M+H]^+$ (100). Anal. calcd for $C_{20}H_{21}N_3O$ (335.40): C, 71.62, H, 6.31, N, 12.53. Found: C, 71.79, H, 6.48, N, 12.43.

*4a-Benzyl-6-phenyl-1,2,3,4,4a,10b-hexahydropyrazino[2,3-c]quinolin-5(6H)-one (**4e**).* Compound was prepared from **2e** in 80% yield. Colourless solid, mp 182–184 °C (benzene/hexane). IR ($cm^{-1}$) ν: 3287, 3268, 3059, 3019, 2913, 2851, 1690, 1603, 1489, 1449, 1347, 1335, 1289, 1277, 1233, 1193, 1153, 1123, 1080, 1029, 897, 951, 899, 874, 755, 724, 695, 639, 595, 556. ESI-MS (pos.) *m/z* (%): 761.3 $[2\cdot M+Na]^+$ (5), 739.3 $[2\cdot M+H]^+$ (18), 392.1 $[M+Na]^+$ (10), 370.1 $[M+H]^+$ (100).Anal. calcd for $C_{24}H_{23}N_3O$ (369.46): C, 78.02, H, 6.27, N, 11.37. Found: C, 77.97, H, 6.25, N, 11.28.

*4a,6-Diphenyl-1,2,3,4,4a,10b-hexahydropyrazino[2,3-c]quinolin-5(6H)-one (**4f**).* Compound was prepared from **2f** in 80% yield. Colourless solid, mp 174–179 °C (benzene). IR ($cm^{-1}$) ν: 3261, 2943, 2904, 2851, 1674, 1604, 1467, 1452, 1346, 1291, 1144, 1072, 772, 755, 717, 698, 648, 586, 550. ESI-MS (pos.) *m/z* (%): 356.2 $[M+H]^+$ (100). Anal. calcd for $C_{23}H_{21}N_3O$ (355.43): C, 77.72, H, 5.96, N, 11.82. Found: C, 77.59, H, 6.00, N, 11.69.

**General procedure for the reaction of compounds 2 with isocyanic acid.**

To the solution of **2** (1.5 mmol) in acetic acid (4.5 mL), potassium cyanate (0.195 g, 2.4 mmol) was added and the mixture was stirred for 3 h at room temperature. The mixture was poured onto crushed ice (20 mL) and extracted with chloroform (5 × 15 mL). Collected extracts were dried and evaporated to dryness. The residue was chromatographed on silica gel column.

*5-Benzyl-1-(2-((1-methyl-2-oxo-2,3-dihydroquinazolin-4(1H)-ylidene)amino)ethyl)imidazolidine-2,4-dione (**5b**).* Compound was prepared from **2b** in 18% yield besides **7b**. Colourless solid, mp 209–215 °C (ethyl acetate). IR ($cm^{-1}$) ν: 3400, 3129, 3030, 2939, 2746, 1761, 1709, 1619, 1597, 1565, 1543, 1497, 1456, 1419, 1352, 1329, 1263, 1234, 1173, 1138, 1127, 1095, 1036, 1005, 946, 872, 851, 768, 749, 702, 681, 650, 621, 594, 535. ESI-MS (pos.) *m/z* (%): 805.3 $[2\cdot M+Na]^+$ (8), 430.1 $[M+K]^+$ (5), 414.1 $[M+Na]^+$ (100), 392.1 $[M+H]^+$ (22). ESI-MS (neg.) *m/z* (%): 390.0 $[M-H]^-$ (100). Anal. calcd for $C_{21}H_{21}N_5O_3$ (391.16): C, 64.44, H, 5.41, N, 17.89. Found: C, 64.63, H, 5.70, N, 17.89.

*5-Butyl-1-(2-((2-oxo-1-phenyl-2,3-dihydroquinazolin-4(1H)-ylidene)amino)ethyl)imidazolidine-2,4-dione (**5d**).* Compound was prepared from **2d** in 17% yield besides **6d** and **7d**. Yellowish solid, mp 247–250 °C (benzene/cyclohexane). IR ($cm^{-1}$) ν: 3335, 3063, 2956, 2871, 1771, 1703, 1640, 1599, 1565, 1537, 1492, 1453, 1418, 1390, 1354, 1327, 1263, 1230, 1183, 1156, 1138, 1113, 1086, 1070, 973, 877, 813, 764, 748, 704, 675, 654, 613, 562, 547, 510. ESI-MS (pos.) *m/z* (%): 861.4 $[2\cdot M+Na]^+$ (8), 458.2 $[M+K]^+$ (6), 442.2 $[M+Na]^+$ (100), 420.2 $[M+H]^+$ (11). ESI-MS (neg.) *m/z* (%): 418.0 $[M-H]^-$ (100). Anal. calcd for $C_{23}H_{25}N_5O_3$ (419.48): C, 65.85, H, 6.01, N, 16.70. Found: C, 65.74, H, 6.07, N 16.57. Using the excess of KOCN (3 equiv.), 17% of **5d**, 8% of **6d** and 31% of **7d** was obtained. Using the excess of KOCN (3 equiv.), compound **5d** was prepared in 57% yield from **6d** and in 33% yield from **7d**.

*5-Benzyl-1-(2-((2´-oxo-1´-phenyl-1,2-dihydroquinazolin-4-yl)amino)ethyl)imidazolidine-2,4-dione* (***5e***). Compound was prepared from **2e** in 22% yield besides **6e** and **7e**. Colourless solid, mp 181–192 °C (ethyl acetate). After recrystallization from ethanol, the mp increased to 280–283 °C without any change in its IR spectrum. IR ($cm^{-1}$) ν: 3331, 3065, 2936, 1770, 1712, 1653, 1641, 1615, 1600, 1538, 1488, 1454, 1423, 1355, 1330, 1225, 1184, 1156, 1131, 1084, 1030, 775, 753, 707, 675, 622, 541, 509 $cm^{-1}$. ESI-MS (pos.) *m/z* (%): 929.4 $[2\cdot M+Na]^+$ (4), 492.2 $[M+K]^+$ (11), 476.2 $[M+Na]^+$ (100), 454.2 $[M+H]^+$ (16). ESI-MS (neg.) *m/z* (%): 452.0 $[M-H]^-$ (100). Anal. calcd for $C_{26}H_{23}N_5O_3$ (453.49): C, 68.86, H, 5.11, N, 15.44. Found:C, 68.67, H, 5.56, N 15.22. Using the excess of KOCN (4 equiv.), 50% of **5e**, 6% of **6e** and 29% of **7e** was prepared from **2e**.

*8a-Butyl-8-(2-(phenylamino)phenyl)-5,6-dihydroimidazo[1,5-a]pyrazine-1,3(2H,8aH)-dione (**6d**).* Compound was prepared from **2d** in 13% yield. Colourless solid, mp 187–190 °C (benzene). IR ($cm^{-1}$) ν: 3302, 3046, 2958, 2871, 2732, 1776, 1719, 1640, 1593, 1508, 1455, 1419, 1303, 1127, 1115, 1070, 1021, 912, 890, 859, 756, 699, 678, 627, 578, 534, 499 $cm^{-1}$. ESI-MS (pos.) *m/z* (%): 399.2 $[M+Na]^+$

(12), 377.2 $[M+H]^+$ (100). ESI-MS (neg.) *m/z* (%): 375.0 $[M–H]^–$ (100). Anal. calcd for $C_{22}H_{24}N_4O_2$ (376.45): C, 70.19, H, 6.43, N, 14.88. Found: C, 70.30, H, 6.58, N, 14.53.

*8a-Benzyl-8-(2-(phenylamino)phenyl)-5,6-dihydroimidazo[1,5-a]pyrazine-1,3(2H,8aH)-dione* ***(6e)****.* Compound was prepared from **2e** in 14% yield. Colourless solid, mp 227–230 °C (benzene), IR ($cm^{-1}$) ν: 3323, 3032, 2932, 2731, 1770, 1720, 1645, 1595, 1510, 1496, 1478, 1454, 1411, 1302, 1137, 1067, 1039, 929, 753, 700, 689, 663, 597, 560, 535, 491 $cm^{-1}$. ESI-MS (pos.) *m/z* (%): 433.2 $[M+Na]^+$ (7), 411.2 $[M+H]^+$ (100). ESI-MS (neg.) *m/z* (%): 409.0 $[M–H]^–$ (100). Anal. calcd for $C_{25}H_{22}N_4O_2$ (410.47): C, 73.15, H, 5.40, N, 13.65. Found: C, 73.12, H, 5.55, N, 13.81. Using the excess of KOCN (3 equiv.), 6% of **6e**, 29% of **7e**, and 30% of **5e** was obtained.

*8a-Phenyl-8-(2-(phenylamino)phenyl)-5,6-dihydroimidazo[1,5-a]pyrazine-1,3(2H,8aH)-dione* ***(6f)****.* Compound was prepared from **2f** and KOCN (3 equiv.) in 20% yield besides **8f.** Colourless solid, mp 190–192 °C (ethyl acetate/hexane). IR ($cm^{-1}$) ν: 3181, 3061, 2925, 2849, 2740, 1775, 1718, 1594, 1570, 1497, 1451, 1310, 1220, 1167, 1124, 1070, 1031, 963, 913, 889, 853, 751, 696, 594, 549 $cm^{-1}$. ESI-MS (pos.) *m/z* (%): 815.2 $[2·M+Na]^+$ (4), 419.1 $[M+Na]^+$ (18), 397.1 $[M+H]^+$ (100). ESI-MS (neg.) *m/z* (%): 813.2 $[2·M–2·H+Na]^–$ (33), 395.0 $[M–H]^–$ (100). Anal. calcd for $C_{24}H_{20}N_4O_2$ (396.43): C, 72.71, H, 5.08, N, 14.13. Found: C, 72.29, H, 5.06, N, 14.08.

*4a-Butyl-6-methyl-5-oxo-2,3,5,6-tetrahydropyrazino[2,3-c]quinoline-4(4aH)-carboxamide* ***(7a)****.* Compound was prepared from **2a** and KOCN (1.4 equiv.) in 47% yield. Using the excess of KNCO (4 equiv.), **7a** was prepared in 57% yield. Colourless solid, mp 155–158 °C (ethyl acetate/hexane). IR ($cm^{-1}$) ν: 3350. 3193, 2954, 2856, 1684, 1644, 1621, 1603, 1461, 1402, 1358, 1310, 1255, 1223, 1138, 1059, 1041, 1008, 992, 966, 941, 862, 750, 727, 699, 676, 595, 559 $cm^{-1}$ ESI-MS (pos.) *m/z* (%): 651.3 $[2·M+Na]^+$ (19), 353.0 $[M+K]^+$ (6), 337.1 $[M+Na]^+$ (77), 315.1 $[M+H]^+$ (100), 272.0 $[M+H–HCNO]^+$ (16). ESI-MS (neg.) *m/z* (%): 312.9 $[M–H]^–$ (100). Anal. calcd for $C_{17}H_{22}N_4O_2$ (314.38): C, 64.95, H, 7.05, N, 17.82. Found: C, 64.75, H, 7.22, N, 17.71.

*4a-Benzyl-6-methyl-5-oxo-2,3,5,6-tetrahydropyrazino[2,3-c]quinolone-4-(4aH)-carboxamide* ***(7b)****.* Compound was prepared from **2b** in 63% yield besides **5b**. Colourless solid, mp 146–151 °C (ethyl acetate/hexane). IR ($cm^{-1}$) ν: 3447, 2942, 1686, 1663, 1647, 1602, 1493, 1470, 1430, 1360, 1297, 1270, 1224, 1138, 1059, 1039, 1011, 973, 951, 919, 875, 760, 704, 620, 556, 504 $cm^{-1}$. ESI-MS (pos.)

*m/z* (%): 719.3 $[2\cdot M+Na]^+$ (18), 387.1 $[M+K]^+$ (12), 371.1 $[M+Na]^+$ (85), 349.1 $[M+H]^+$ (100), 306.1 $[M+H–HCNO]^+$ (32). Anal. calcd for C, 68.95, H, 5.73, N, 16.08). Found: C, 68.81, H, 5.92, N, 15.82.

*6-Methyl-5-oxo-4a-phenyl-2,3,5,6-tetrahydropyrazino[2,3-c]quinoline-4(4aH)-carboxamide* ***(7c).*** Compound was prepared from **2c** in 32% yield. Using the excess of KOCN (4 equiv.), **7c** was prepared in 68% yield. Yellowish solid, mp 209–211 °C (chloroform). IR ($cm^{-1}$) ν: 3422, 3352, 3305, 3247, 3197, 3062, 2953, 1689, 1663, 1626, 1601, 1471, 1406, 1361, 1297, 1170, 1127, 1079, 1029, 1010, 933, 903, 886, 821, 762, 696, 633, 554. ESI-MS (pos.) *m/z* (%): 691.2 $[2\cdot M+Na]^+$ (9), 373.0 $[M+K]^+$ (17), 357.0 $[M+Na]^+$ (100), 335.1 $[M+H]^+$ (84), 292.0 $[M+H–HCNO]^+$ (13). Anal. calcd for $C_{19}H_{18}N_4O_2$ (334.37): C, 68.25, H, 5.43, N, 16.76. Found: C, 68.21, H, 5.50, N, 16.79.

*4a-Butyl-5-oxo-6-phenyl-2,3,5,6-tetrahydropyrazino[2,3-c]quinoline-4(4aH)-carboxamide.* ***(7d).*** Compound was prepared from **2d** in 38% yield besides **5d** and **6d**. Colourless solid, mp 144–152 °C (benzene/hexane). IR ($cm^{-1}$) ν: 3434, 3398, 3215, 2955, 2851, 1700, 1662, 1645, 1607, 1489, 1459, 1428, 1350, 1330, 1313, 1301, 1257, 1217, 1173, 1163, 1131, 1052, 1030, 1009, 955, 877, 801, 769, 756, 701, 679, 646, 603, 570, 511, 490. ESI-MS (pos.) *m/z* (%): 775.4 $[2\cdot M+Na]^+$ (8), 415.2 $[M+K]^+$ (10), 399.2 $[M+Na]^+$ (84), 377.2 $[M+H]^+$ (100). ESI-MS (neg.) *m/z* (%): 375.0 $[M–H]^-$ (100).Anal. calcd for $C_{22}H_{24}N_4O_2$ (376.45): C, 70.19, H, 6.43, N, 14.89. Found: C, 70.51, H, 6.41, N, 14.52.

*4a-Benzyl-5-oxo-6-phenyl-2,3,5,6-tetrahydropyrazino[2,3-c]quinoline-4(4aH)-carboxamide* ***(7e).*** Compound was prepared from **2e** in 49 % yield besides **5e** and **6e**. Colourless solid, mp 197–200 °C (benzene/cyclohexane). IR ($cm^{-1}$) ν: 3427, 3196, 3063, 2938, 2850, 1703, 1666, 1602, 1492, 1460, 1420, 1359, 1336, 1310, 1298, 1267, 1217, 1179, 1074, 1046, 1032, 877, 845, 792, 754, 704, 641, 606, 575, 560, 544, 497. ESI-MS (pos.) *m/z* (%): 843.4 $[2\cdot M+Na]^+$ (6), 449.1 $[M+K]^+$ (16), 433.2 $[M+Na]^+$ (85), 411.2 $[M+H]^+$ (100), 368.2 $[M+H–HCNO]^+$ (6). ESI-MS (neg.) *m/z* (%): 409.0 $[M–H]^-$ (100). Anal. calcd for $C_{25}H_{22}N_4O_2$ (410.46): C, 73.15, H, 5.40, N, 13.65. Found: C, 73.28, H, 5.92, N, 13.51.

*N-(2-(2,4-Dioxo-5-phenylimidazolidin-1-yl)ethyl)-2-(phenylamino)benzamide* ***(8f).*** Compound was prepared from **2f** in 18% yield besides **6f**. Colourless solid, mp 160–165 °C (benzene). IR ($cm^{-1}$) ν: 3390, 3353, 3228, 3068, 2939, 2740, 1775, 1722, 1629, 1589, 1512, 1447, 1421, 1383, 1329, 1310, 1282, 1222, 1167, 1157, 1120, 1078, 1053, 1027, 963, 942, 895, 841, 751, 701, 628, 580, 516. ESI-

MS (pos.) *m/z* (%): 851.3 $[2\cdot M+Na]^+$ (11), 453.2 $[M+K]^+$ (26), 437.2 $[M+Na]^+$ (100), 415.2 $[M+H]^+$ (31). ESI-MS (neg.) *m/z* (%): 413.0 $[M-H]^-$ (100). Anal. calcd for $C_{24}H_{22}N_4O_3$ (414.46): C, 69.55, H, 5.35, N, 13.52. Found: C, 69.99, H, 5.78, N, 13.17.

## Supporting information

NMR spectra for all prepared compounds and crystal structure data for compounds **5** and **7** is available as supporting information. Format: Microsoft Word, Size: 7,45 MB.

## Conflicts of interest

The authors declare no competing financial interest.

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