Rearrangement in the series of 3-(2-aryl-2-oxoethyl)-3,4-dihydroquinoxalin-2(1*H*)-ones

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4-Acetyl- and 4-succinyl-3-(2-aryl-2-oxoethyl)-3,4-dihydroquinoxalin-2(1*H*)-ones undergo the rearrangement into (*Z*)-2-(3-arylquinoxalin-2-ylidene)acetic acids accompanied by the elimination of the acyl groups. The nitration of 3-(2-oxo-2-phenylethyl)-3,4-dihydroquinoxalin-2(1*H*)-one affords 5-nitro- and 7-nitro-2-carboxymethylidenequinoxalines. The bromination of quinoxalin-2-ones in AcOH gives 3-aryl-2-carboxymethylidenequinoxalines and the corresponding 7-bromo derivatives, with the former products predominating.

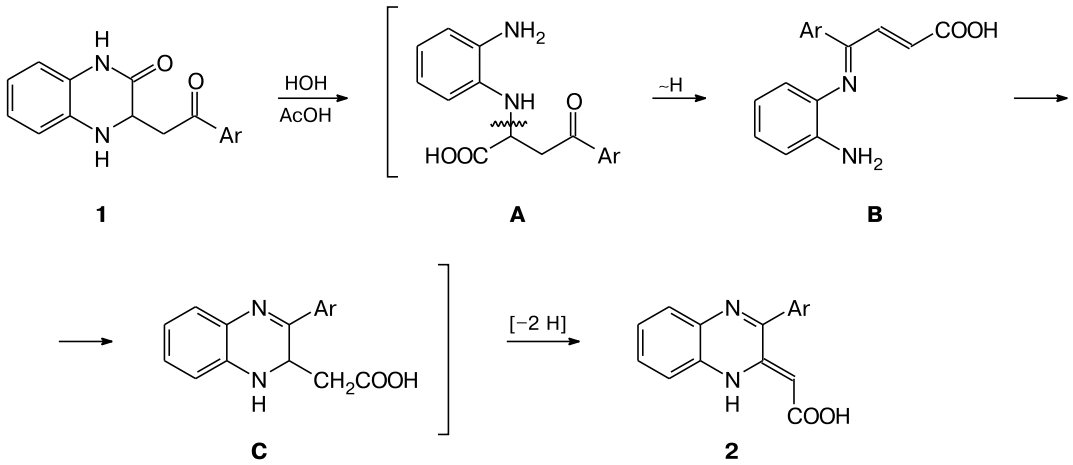
Key words: 3-(2-aryl-2-oxoethyl)-3,4-dihydroquinoxalin-2(1*H*)-ones, nitration, bromination, acylation, rearrangement, (*Z*)-2-(3-arylquinoxalin-2-ylidene)acetic acids, IR spectroscopy, ^{1}H NMR spectroscopy.

Previously,[1] it has been found that 3-(2-aryl-2-oxoethyl)-3,4-dihydroquinoxalin-2(1*H*)-ones **1** are rearranged into 3-aryl-2-carboxymethylidenequinoxalines **2** in low yields (20—37%) upon heating in acetic acid. The proposed mechanism of the rearrangement involves the hydrolysis of the amide bond giving rise to the intermediate **A**, the condensation of the carbonyl and amino groups accompanied by the C—N bond cleavage yielding the intermediate **B**, the nucleophilic addition of the amino group at the activated C=C bond, and the dehydrogenation of the intermediate **C** to form acid **2** (Scheme 1).[2]

Since the rearrangement is the oxidative process, it was suggested that this reaction should be performed in the presence of mild oxidizing agents. Actually, the heating of quinoxalinones **1** in DMF (or in BuOH) in the presence of an equimolar amount of sulfur or iodine made it possible to increase the yield of acids **2** to 80—85% and to perform the rearrangement of quinoxalinones containing electron-withdrawing substituents in the *o*-phenylenediamine fragment.[2,3] Sulfur is involved in the α-thiolation of the methylene group of quinoxalinones **1**,[4] thus facilitating the oxidation of the dihydro structure **C** due to the rapid elimination of the hydrogen sulfide molecule (Scheme 2).

However, we detected no other products except H_2S, which could confirm the above-presented sequence of reaction steps.

Scheme 1



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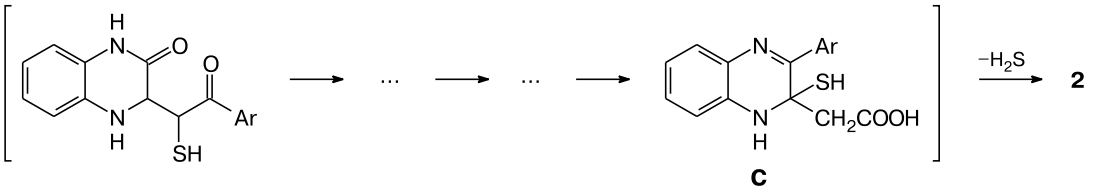
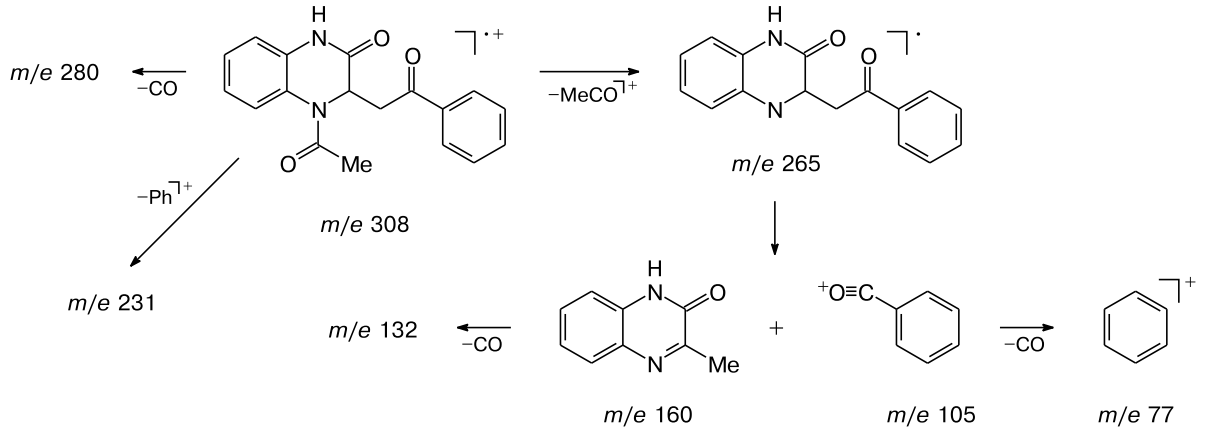
Scheme 2



Scheme 3



In the present study, we investigated the rearrangement of 3-(2-aryl-2-oxoethyl)-3,4-dihydroquinoxalin-2(1*H*)-ones by considering their 4-acylated derivatives and also using the nitration and bromination reactions of the starting quinoxalin-2-ones.

4-Acetyl and 4-succinyl derivatives of quinoxalin-2-one **3a—c** and **4a,b**, respectively, were synthesized according to a known procedure.[5] Under these conditions, we failed to synthesize acyl derivatives of quinoxalinones **1** containing electron-withdrawing substituents (Br and NO_2) in the benzene ring.

The structures of compounds **3** and **4** were confirmed by IR and ^{1}H NMR spectroscopy. The IR spectra (in KBr pellets) of the reaction products show no stretching bands of the secondary amino group at 3340—3380 cm^{-1} characteristic of quinoxalinones **1** and contain a broadened band at 3430—3440 cm^{-1}, which is indicative of the retention of the amide NH group.

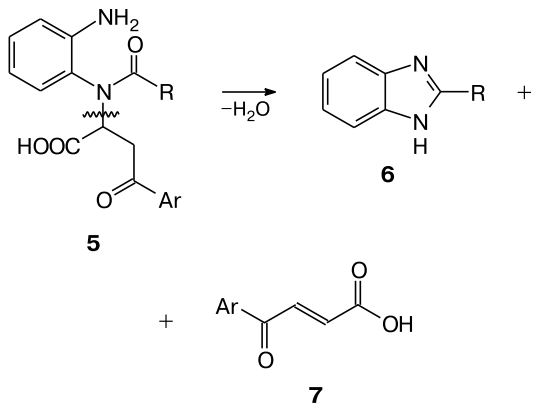
The ^{1}H NMR spectra of compounds **3a—c** show the following signals for the protons of the ABX system: doublets of doublets for the methylene protons A and B, a doublet of doublets for the methine proton, a singlet for the NH proton (amide) at δ 10.74—10.84, and multiplets for aromatic protons. At the same time, the singlet for the proton of the amino group at δ 6.0—6.5 disappears, and a singlet for the methyl protons of the acetyl fragment is observed at δ ~2.10. In addition, the ^{1}H NMR spectra of compounds **4a,b** show triplets for the protons of two methylene groups of the succinyl fragment and a broadened signal at δ 12.0 assigned to the OH group.

The fragmentation in the mass spectrum of acetyl derivative **3a** ($[M]^{\bullet+}$ = 308) is in complete agreement with the suggested structure. The elimination of the acetyl group ($[M - CH_3CO]^+$), the benzoyl fragment ($[M - C_6H_5CO]^+$), and the phenyl cation ($[M - C_6H_5]^+$) are the most characteristic processes (Scheme 3). An analogous fragmentation pattern is observed for acyl derivative **4a**.

The rearrangement of acyl derivatives **3** and **4** was performed by refluxing in DMF in the presence of sulfur. It was expected that the presence of *N*-acyl groups in molecules **3** and **4** would allow us to isolate either the cleavage products of the dihydropyrazine ring in **5** or 2-R-benzimidazole derivatives **6** (as a result of the intramolecular condensation of the acyl and amino groups[6]) and the corresponding β-aroylacrylic acids **7** (Scheme 4), which could be formed in the course of the rearrangement.

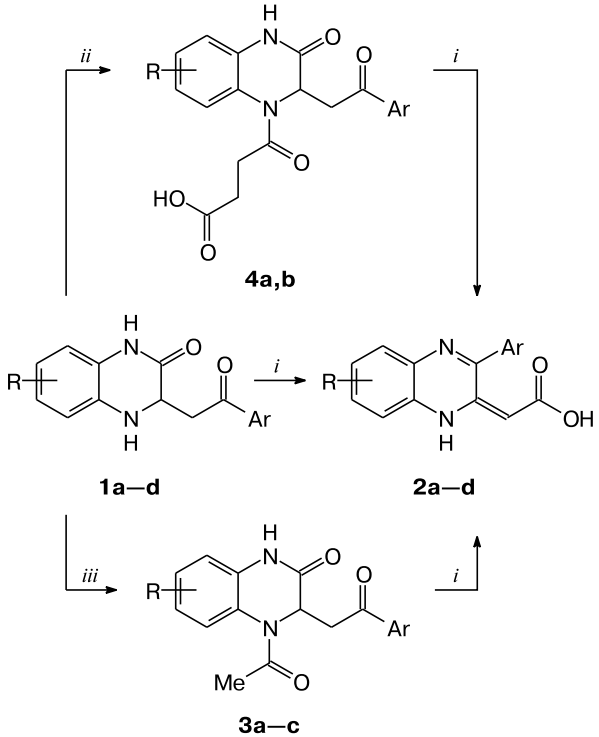
Acids **2a—c** proved to be identical to the products prepared previously by the rearrangement of unacylated quinoxalinones **1** (Scheme 5). An analysis of the mother liquors obtained in the synthesis of acetyl derivatives **3a—c** showed that 2-methylbenzimidazole **6** and β-aroylacrylic acids **7** were absent in these mixtures (TLC analysis with authentic samples), which is indicative of the rapid deacylation under the experimental conditions (see Scheme 5). It should be noted that the yields of com-

Scheme 4



pounds **2a—c** were 53—58%, whereas the corresponding reactions of the unacylated derivatives afforded the products in 85—87% yields.[2]

Scheme 5



Reagents and conditions: *i*. DMF, S. *ii*. $(CH_2CO)_2O$. *iii*. Ac_2O.

1	R	Ar	**2**	R	Ar	**3**	R	Ar
a	H	Ph	**a**	H	Ph	**a**	H	Ph
b	H	4-MeC_6H_4	**b**	H	4-MeC_6H_4	**b**	H	4-MeC_6H_4
c	H	4-BrC_6H_4	**c**	H	4-BrC_6H_4	**c**	H	4-BrC_6H_4
d	7-Me	4-ClC_6H_4	**d**	6-Me	4-ClC_6H_4			

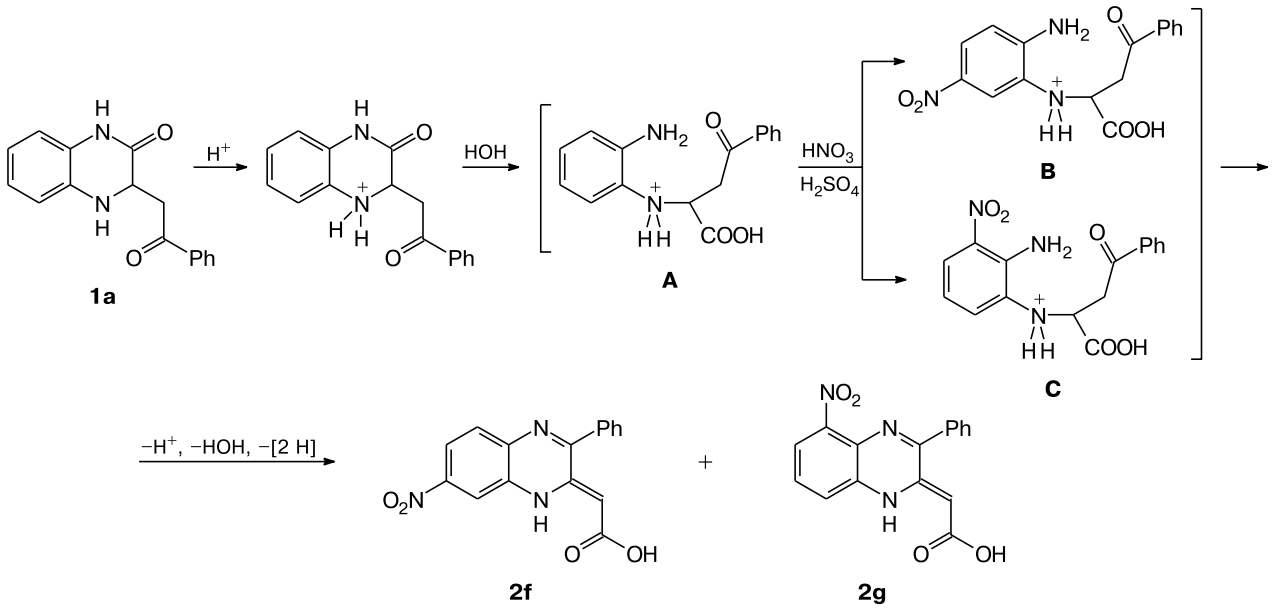
4: R = H, Ar = Ph (**a**); R = 7-Me, Ar = 4-ClC_6H_4 (**b**)

To study the mechanism of the rearrangement in more detail, we performed the nitration of quinoxalinone **1a** according to a known procedure used for the nitration of arenes.[7] This reaction afforded a mixture of colored nitration products, which was studied by HPLC. The starting quinoxalinone **1a**, a mixture of 6(7)-nitro-(2-oxo-2-phenylethyl)-3,4-dihydroquinoxalin-2(1*H*)-ones **1e** + **1f** (possible nitration products of compound **1a** prepared by the reaction of 4-nitro-*o*-phenylenediamine with β-benzoylacrylic acid[8]), and 2-carboxymethylidene-6-nitro-3-phenylquinoxaline (**2e**) (the individual regioisomer isolated after the rearrangement of a mixture of quinoxalinones **1e** + **1f**)[2] served as the reference compounds. An analysis of the results showed that a mixture contained the starting quinoxalinone **1a** and two products, whose signals correspond to none of the above-mentioned reference samples. The mixture of the nitration products was separated by fractional crystallization from MeOH.

The IR spectra of compounds **2f,g** contain bands $\nu_s(NO_2)$ and $\nu_{as}(NO_2)$ at 1340—1350 and 1510—1512 cm^{-1}, respectively. The structures of products **2f,g** were determined by analyzing the ^1H NMR spectra. Thus, the spectrum of compound **2f** shows a doublet at δ 7.12 (J = 2.4 Hz) assigned to the proton H(8) of the annulated benzene ring, a doublet for the proton H(5) at δ 7.75 (J = 7.0 Hz), and a doublet of doublets for the proton H(6) (J = 6.8 Hz) at δ 7.90. The protons of the phenyl group at position 3 appear as a doublet at δ 8.00 and a multiplet at δ 7.51—7.62 with integrated intensities equal to two and three protons, respectively. In addition, the spectrum shows one-proton singlets at δ 6.94, 12.05, and 13.28 assigned to the vinyl, enamine, and carboxyl protons, respectively. The above results suggest that product **2f** has the structure of 2-(7-nitro-3-phenylquinoxalin-2(1*H*)-ylidene)acetic acid. Compound **2g** was assigned to the 5-nitro isomer. The physicochemical characteristics of **2g** appeared to be similar to those of 2-(5-nitro-3-phenylquinoxalin-2(1*H*)-ylidene)acetic acid, which has been synthesized previously[9] by the reaction of 3-nitro-*o*-phenylenediamine with 2,3-dibromo-4-oxo-4-phenylbutanoic acid. The configuration of compounds **2f,g** was established by ^1H NMR and NOE studies. The saturation of the signal for the vinyl proton at δ 6.94 in the spectrum of compound **2f** leads to the response of the protons of the phenyl substituent in the *ortho* position, which is indicative of the *Z* configuration of the rearrangement products.

We failed to nitrate acid **2a** under the conditions used in the known procedure[7] (see the Experimental section). Hence, we suggest the most probable pathway giving rise to nitroquinoxalines **2f,g** under the reaction conditions. The protonation of the amine nitrogen atom N(4) followed by the cleavage of the quinoxalinone ring affords the protonated form **A**, whose nitration gives the intermediates **B** and **C** (the *para* and *ortho* orientations with

Scheme 6



respect to the free amino group). The latter compounds undergo cyclization to acids **2f,g**, which were isolated in a ratio of 5 : 1 (Scheme 6). The formation of regioisomer **2f** as the major product is well consistent with the known data on the nitration of activated arenes.[10]

It should be noted that acid **2g** could be formed also through the rearrangement of 8-nitro isomer **1g** as the nitration product of quinoxalinone **1a**. However, this is unlikely because it is known[1] that 6(7)-nitroquinoxalinones remain intact even upon prolonged refluxing in AcOH. These compounds do not undergo the rearrangement upon the treatment with a nitrating mixture at ~5 °C as well. At the same time, the thermodynamic stability of quinoxalinone **1a** is low. Thus, acid **2a** was detected chromatographically even upon refluxing in methanol for 2—3 h, *i.e.*, the opening of the pyrazine ring in quinoxalinones containing no electron-withdrawing substituents in the annulated moiety proceeds rapidly.

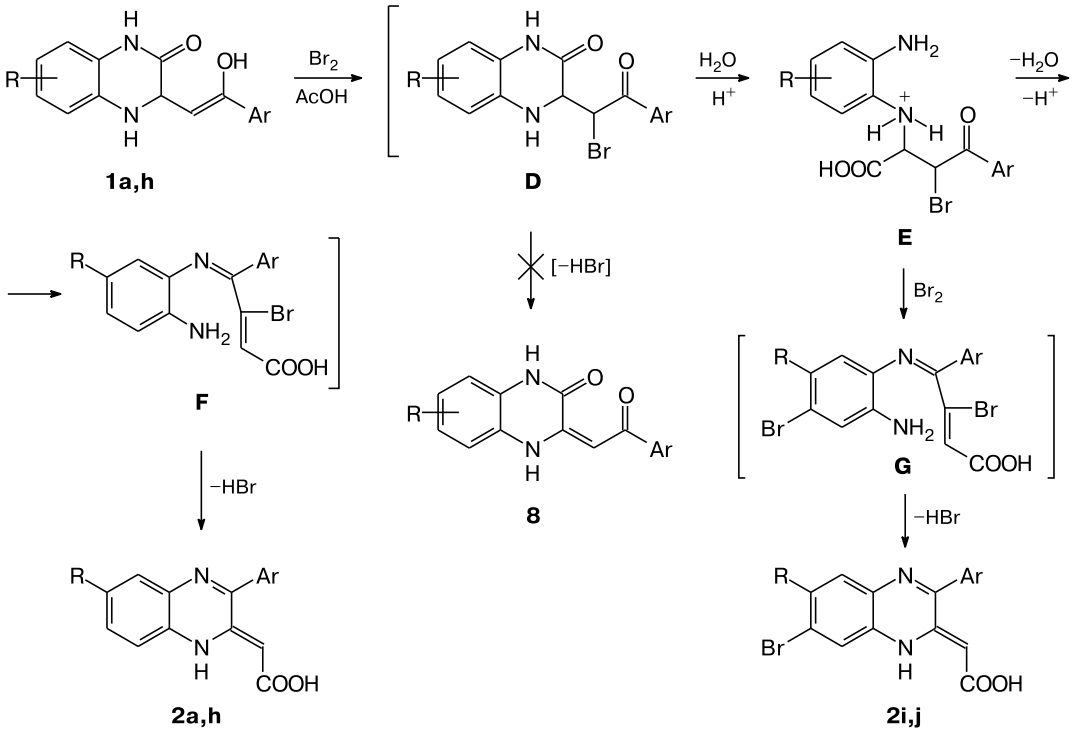
The rearrangement occurs also in the case of the bromination of a 1 : 4 mixture of 6(7)-nitro-3-(2-oxo-2-tolylethyl)-3,4-dihydroquinoxalin-2(1*H*)-ones **1h** + **1i** in AcOH (^{1}H NMR data). After washing off of the unconsumed regioisomer **1i**, the mixture of the reaction products was studied by HPLC. 2-Carboxymethylidene-3-(*p*-methylphenyl)-6-nitroquinoxaline (**2h**), which was synthesized according to a known procedure,[2] served as the reference compound. An analysis of the chromatograms showed that the isolated mixture contained acid **2h** and a new compound in a ratio of 3 : 2. The minor product (^{1}H NMR data) proved to be 7-bromo-2-carboxymethylidene-6-nitroquinoxaline (**2i**).

The fact that the rearrangement occurs more rapidly than the electrophilic aromatic substitution is also evidenced by our attempt to perform the bromination of quinoxalinone **1a**. Thus, acid **2a** and 2-(7-bromo-3-phenylquinoxalin-2(1*H*)-ylidene)acetic acid **2j** were isolated from the reaction mixture in a ratio of 3 : 1.

The fact that the bromination affords 6-nitro isomers as the major products (like in the rearrangement of mixtures of 6(7)-nitroquinoxalinones upon heating in DMF in the presence of sulfur[2]) can be explained as follows (Scheme 7).

The bromination occurs through the enol form to give the intermediate **D**. The protonation of the latter followed by the ring opening affords the intermediate **E**. It is known that the acid-catalyzed hydrolysis of amides is more sensitive to the steric effect of the substituents than to the electronic effect. Thus, only slight changes in the hydrolysis rate were observed for the *m*- and *p*-nitro-substituted benzamides, whereas the hydrolysis rate for the *o*-nitro isomer is substantially lower.[11] Consequently, the hydrolysis rates for 6(7)-nitro isomers **1i** and **1h** are virtually equal. The elimination of the HBr molecule from the intermediate **D** giving rise to phenacylidene derivatives **8** is theoretically possible. However, according to the available data,[12] these compounds are not prone to the rearrangement. The 7-nitro group of quinoxalinones **1** facilitates the formation of the intermediates **F** or **G**. This group accelerates the C—N bond cleavage in the intermediate **E** and assists in the formation of the azomethine bond (the nucleophilicity of the amino group in the *meta* position with respect to the 7-nitro group is higher). However, the cyclization of the intermediates **F** and **G** should occur more slowly (the nucleophilicity of the amino group in the *para* position with respect to the nitro group is lower). Evidently, this step is not rate-

Scheme 7

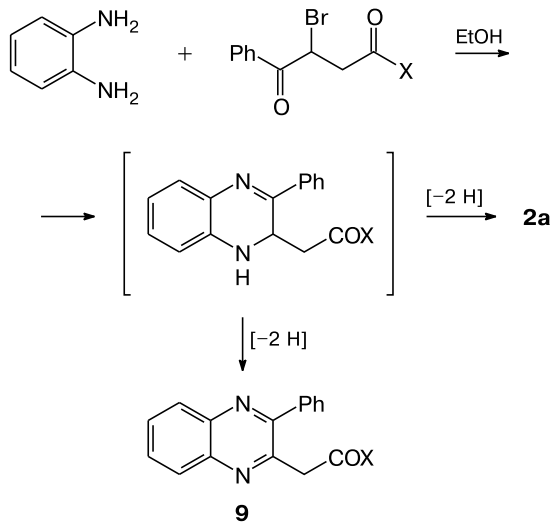


R = H, Ar = Ph (**1a**, **2a,j**); R = NO_2, Ar = 4-MeC_6H_4 (**1h**, **2h,i**)

determining, which accounts for the lower activity of 6-nitro isomer **1i** in the rearrangements and the predominant formation of the 6-nitro isomers of quinoxalines **2h,i**. The synthesis of acid **2i** involves the bromination of the intermediate **E** and correlates well with the results of nitration of quinoxalinone **1a**.

Therefore, the data on the nitration and bromination reactions of quinoxalinones **1** confirm the fact that the quinoxalinone-quinoxaline rearrangement occurs through the cleavage of the amide bond, which is characteristic of quinoxalin-2-one derivatives.[13] We failed to isolate the cleavage products, but the related α-amino adducts of β-aroylacrylic acids have been long known.[14,15] The latter compounds are thermodynamically unstable and are easily decomposed into the starting components upon heating.[8] The transformation of the α-amino adduct into the azomethine intermediate is apparently the rate-determining step and occurs intramolecularly, as evidenced by the fact that only acids **2a,j** were isolated after the rearrangement of a mixture of quinoxalinones **1a,j** (see the Experimental section). The rapid elimination of the HBr molecule (or the H_2S molecule in the reaction in DMF in the presence of sulfur) in the course of the cyclization reaction is the decisive factor in the formation of acids **2** in high yields. In the reaction of 3-bromo-4-oxo-4-phenylbutanoic acid with *o*-phenylenediamine, in which the oxidation occurs slowly, the yield of enamine **2a** stabilized by the conjugation with the electron-withdrawing carboxy group was <20%.[16] Interestingly, the reaction of morpholide of this acid with *o*-phenylenediamine produces quinoxaline **9** rather than dihydro derivative **2** (Scheme 8). This fact can be attributed to the π-electron density delocalization in the amide fragment.

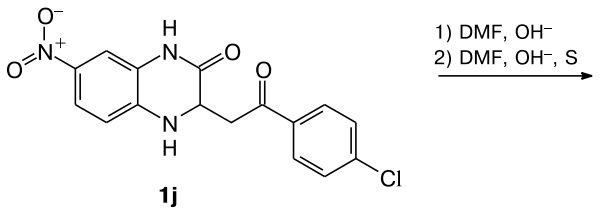
Scheme 8



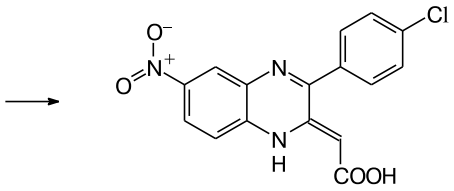
X = OH (**2a**), $N(CH_2)_4O$ (**9**)

It is known[17] that amides undergo hydrolysis in an alkaline medium as well. Hence, we performed the rearrangement of 7-nitroquinoxalinone **1j** by heating in DMF with the addition of a concentrated NaOH solution, as well as in the presence of sulfur. As a result, we isolated 6-nitroquinoxaline **2k** in 25 and 50% yields, respectively (Scheme 9). However, these procedures have drawbacks from the experimental point of view, because these reactions are accompanied by resinification, which hinders the isolation and purification of the target products.

Scheme 9



1j



2k

The quinoxalinone-quinoxaline rearrangement under study is similar to the Pfitzinger reaction. It is known[18,19] that the prolonged boiling of isatins with α-methylenecarbonyl compounds in the presence of an alkali (in some cases, in the presence of an acid) is accompanied by the formation of quinoline-4-carboxylic acids. The mechanism of the Pfitzinger reaction with aryl methyl ketones involves the formation of the phenacylidene derivative of isatin, the amide bond cleavage, and the cyclization to the quinoline ring.

Therefore, the formation of thermodynamically stable aromatic compounds, such as quinoxaline- or quinolinecarboxylic acids, is the driving force for both the quinoxalinone-quinoxaline rearrangement and the Pfitzinger rearrangement.

Experimental

The IR spectra were recorded on a Specord-75 IR spectrometer (in KBr pellets and in solutions in CCl_4). The ^{1}H NMR spectra were measured on a Varian Mercury VX-200 spectrometer (200 MHz) in DMSO-d_6 with Me_4Si as the internal standard. The mass spectra were obtained on a Hewlett-Packard LC/MSD 1100 instrument (EI, 70 eV). The elemental analysis was carried out on a LECO CHNS-900 instrument. The purity of the reaction products was checked by TLC on Silufol UV-254 plates using a 1 : 1 toluene—ethyl acetate mixture as the eluent. The melting points were measured on a Kofler hot stage.

Chromatographic measurements were carried out on a Hewlett Packard chromatograph (Agilent Technologies, Walborn, Germany) consisting of a Series 1050 pump, a variable-wavelength Series 1050 spectrophotometric detector, and a Series 3395 integrator. A Kromasil C18 250S4.6 mm analytical column (Hichrom Limited, Theale, UK) was packed with a sorbent with a particle size of 5 μm; an acetonitrile (for HPLC)—water mixture (40 : 60, v/v) was used as the mobile phase at a flow rate of 1.0 mL min^{-1}; the temperature of the column thermostat was 30.0±0.1 °C; the detection wavelength was 254 nm; the sample volume was 10 μL. The analytes were prepared by dissolving weighed samples in a 1 : 1 methanol—acetonitrile mixture until the solution at a concentration of ~1 mg mL^{-1} was obtained. Some analytes were dissolved in DMSO (1—2 mL) to improve the solubility, and then the solutions were brought to the desired volume with a 1 : 1 methanol—acetonitrile mixture.

Quinoxalinones **1a—d,j** and mixtures of 6(7)-nitroquinoxalinones **1f** + **1e** and **1i** + **1h** were synthesized according to a known procedure[2] by refluxing 4-R-substituted *o*-phenylenediamines and the corresponding β-aroylacrylic acids in ethanol for 1 h.

4-Acetyl-3-(2-oxo-2-phenylethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (3a). A solution of 3-(2-oxo-2-phenylethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (**1a**) (0.27 g, 1 mmol) in acetic anhydride (10 mmol) was heated (60—70 °C) with magnetic stirring until the quinoxalinone was completely dissolved. Then one-two drops of concentrated H_2SO_4 were added. The reaction mixture was kept at this temperature for 5—10 min and then cooled. The precipitate that formed was filtered off and washed with water. Product **3a** was obtained in a yield of 0.23 g (75%), m.p. 184—185 °C (from EtOH). Found (%): C, 70.10; H, 5.27; N, 9.11. $C_{18}H_{16}N_2O_3$. Calculated (%): C, 70.12; H, 5.23; N, 9.09. ^{1}H NMR, δ: 2.12 (s, 3 H, Me); 3.27 (dd, 1 H, H_A, J = 17.2 Hz, J = 6.8 Hz); 3.49 (dd, 1 H, H_B, J = 17.2 Hz, J = 6.8 Hz); 5.62 (t, 1 H, H_X, J = 6.8 Hz, J = 4.2 Hz); 7.01—7.89 (m, 9 H, Ar); 10.82 (s, 1 H, NH). IR (in KBr pellets), ν/cm^{-1}: 3440 (NH), 3150, 3056 (CH arom.), 2983, 2920 (CH aliph.), 1695, 1680 (C=O). MS, m/z (I_{rel} (%)): 308 [M]$^+$ (10), 265 (9), 105 (64), 77 (100).

4-Acetyl-3-[2-oxo-2-(*p*-tolyl)ethyl]-3,4-dihydroquinoxalin-2(1*H*)-one (3b). Analogously to compound **3a**, compound **3b** was synthesized from quinoxalinone **1b** (0.28 g, 1 mmol) in a yield of 0.2 g (61%), m.p. 216—218 °C (from EtOH). Found (%): C, 70.75; H, 5.64; N, 8.71. $C_{19}H_{18}N_2O_3$. Calculated (%): C, 70.79; H, 5.63; N, 8.69. ^{1}H NMR, δ: 2.10 and 2.34 (both s, 3 H each, Me); 2.96 (dd, 1 H, H_A, J = 17.5 Hz, J = 6.7 Hz); 3.13 (dd, 1 H, H_B, J = 17.5 Hz, J = 6.7 Hz); 5.61 (t, 1 H, H_X, J = 6.7 Hz, J = 4.4 Hz); 6.97—7.33 (m, 4 H, H(5), H(6), H(7), H(8)); 7.27 (d, 2 H, *m*-H_{Ar}, J = 7.9 Hz); 7.70 (d, 2 H, *o*-H_{Ar}, J = 7.9 Hz); 10.84 (s, 1 H, NH). IR (in KBr pellets), ν/cm^{-1}: 3430 (NH), 3150, 3056 (CH arom.), 2980, 2920 (CH aliph.), 1690, 1678 (C=O).

4-Acetyl-3-[2-(*p*-bromophenyl)-2-oxoethyl]-3,4-dihydroquinoxalin-2(1*H*)-one (3c). Analogously to compound **3a**, compound **3c** was synthesized from quinoxalinone **1c** (0.34 g, 1 mmol) in a yield of 0.3 g (78%), m.p. 215—217 °C (from EtOH). Found (%): C, 55.81; H, 4.11; N, 7.21. $C_{18}H_{15}BrN_2O_3$. Calculated (%): C, 55.83; H, 3.90; N, 7.23. ^{1}H NMR, δ: 2.11 (s, 3 H, Me); 2.97 (dd, 1 H, H_A, J = 17.6 Hz, J = 6.3 Hz); 3.17 (dd, 1 H,

H_B, J = 17.6 Hz, J = 6.3 Hz); 5.57 (t, 1 H, H_X, J = 6.3 Hz, J = 4.4 Hz); 7.10—7.33 (m, 4 H, H(5), H(6), H(7), H(8)); 7.67 (d, 2 H, *m*-H_{Ar}, J = 8.9 Hz); 7.75 (d, 2 H, *o*-H_{Ar}, J = 8.9 Hz); 10.82 (s, 1 H, NH). IR (in KBr pellets), ν/cm^{-1}: 3440 (NH), 3145, 3060 (CH arom.), 2980, 2920 (CH aliph.), 1692, 1680 (C=O).

3-(2-Oxo-2-phenylethyl)-4-succinyl-3,4-dihydroquinoxalin-2(1*H*)-one (4a). Succinic anhydride (0.1 g, 1 mmol) was added to a solution of quinoxalin-2-one **1a** (0.27 g, 1 mmol) in benzene (10 mL). The reaction mixture was refluxed for 3.5 h and then cooled to room temperature. The precipitate that formed was filtered off, washed with water, and recrystallized from ethanol. Compound **4a** was obtained in a yield of 0.26 g (72%), m.p. 182—183 °C (from EtOH). Found (%): C, 65.61; H, 4.96; N, 7.59. $C_{20}H_{18}N_2O_5$. Calculated (%): C, 65.57; H, 4.95; N, 7.65. ^{1}H NMR, δ: 2.40 and 2.80 (both t, 2 H each, J = 7.0 Hz); 2.90 (dd, 1 H, H_A, J = 6.8 Hz); 3.19 (dd, 1 H, H_B, J = 17.2 Hz, J = 6.8 Hz); 5.57 (t, 1 H, H_X, J = 6.8 Hz, J = 4.2 Hz); 7.01—7.82 (m, 9 H, Ar); 10.43 (s, 1 H, NH); 12.04 (s, 1 H, OH). MS, m/z (I_{rel} (%)): 366 $[M]^+$ (10), 265 (44), 105 (100), 77 (83). IR (in KBr pellets), ν/cm^{-1}: 3435 (NH), 3150, 3065 (CH arom.), 2985, 2925 (CH aliph.), 1715, 1695, 1682 (C=O).

3-[2-(*p*-Chlorophenyl)-2-oxoethyl]-7-methyl-4-succinyl-3,4-dihydroquinoxalin-2(1*H*)-one (4b). Analogously to compound **4a**, compound **4b** was synthesized from quinoxalinone **1d** (0.31 g, 1 mmol) in a yield of 0.22 g (53%), m.p. 190—192 °C (EtOH). Found (%): C, 60.75; H, 4.64; N, 6.73. $C_{21}H_{19}ClN_2O_5$. Calculated (%): C, 60.80; H, 4.62; N, 6.75. ^{1}H NMR, δ: 2.27 (s, 3 H, CH_3); 2.39 and 2.80 (both t, 2 H each, J = 7.0 Hz); 2.92 (dd, 1 H, H_A, J = 17.2 Hz, J = 6.8 Hz); 3.20 (dd, 1 H, H_B, J = 17.2 Hz, J = 6.8 Hz); 5.59 (t, 1 H, H_X, J = 6.8 Hz, J = 4.2 Hz); 6.81—7.23 (m, 3 H, H(5), H(6), H(8)); 7.59 (d, 2 H, *m*-H_{Ar}, J = 8.4 Hz); 7.81 (d, 2 H, *o*-H_{Ar}, J = 8.4 Hz); 10.75 (s, 1 H, NH); 12.04 (s, 1 H, OH). IR (in KBr pellets), ν/cm^{-1}: 3430 (NH), 3150, 3060 (CH arom.), 2985, 2925 (CH aliph.), 1710, 1690, 1678 (C=O).

The rearrangement of acyl derivatives **3** and **4** was carried out according to a procedure described previously.[3]

(*Z*)-2-(3-Phenylquinoxalin-2(1*H*)-ylidene)acetic acid (2a). 4-Acetyl-3-(2-oxo-2-phenylethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (**3a**) (0.31 g, 1 mmol) was added to a solution of sulfur (0.032 g, 1 mmol) in DMF (10 mL). The reaction mixture was refluxed for 6 h. The precipitate that formed was filtered off, washed on the filter with hot ethanol, and dried in air. The yield was 0.15 g (58%), m.p. 240—241 °C (from EtOH) (*cf.* lit. data[9]: m.p. 240—241 °C).

(*Z*)-2-[3-(*p*-Tolyl)quinoxalin-2(1*H*)-ylidene]acetic acid (2b). Analogously to compound **2a**, compound **2b** was synthesized from quinoxalinone **3b** (0.32 g, 1 mmol) in a yield of 0.15 g (53%), m.p. 245 °C (from EtOH) (*cf.* lit. data[9]: m.p. 245 °C).

(*Z*)-2-[3-(*p*-Bromophenyl)quinoxalin-2(1*H*)-ylidene]acetic acid (2c). Analogously to compound **2a**, compound **2c** was synthesized from quinoxalinone **3c** (0.39 g, 1 mmol) in a yield of 0.18 g (54%), m.p. 265 °C (from EtOH) (*cf.* lit. data[9]: m.p. 264—265 °C).

(*Z*)-2-[3-(*p*-Chlorophenyl)-7-methylquinoxalin-2(1*H*)-ylidene]acetic acid (2d). Analogously to compound **2a**, compound **2d** was synthesized from quinoxalinone **4b** (0.41 g, 1 mmol) in a yield of 0.13 g (41%), m.p. 257—259 °C (from EtOH). Found (%): C, 65.26; H, 7.21; N, 8.93. $C_{17}H_{13}ClN_2O_2$. Calculated (%): C, 65.29; H, 7.19; N, 8.96. ^{1}H NMR, δ: 2.28 (s, 3 H, Me); 6.76 (s, 1 H, CH=); 7.55 (d, 2 H, *o*-H_{Ar}, J = 9.2 Hz); 7.97 (d, 2 H, *m*-H_{Ar}, J = 9.2 Hz); 6.93—7.43 (m, 3 H, H(5), H(6), H(8)); 12.04 (s, 1 H, NH); 13.67 (s, 1 H, OH). IR (in KBr pellets), ν/cm^{-1}: 1698 (C=O), 1620 (C=C). IR (CCl_4), ν/cm^{-1}: 3522 (OH), 3400 (NH), 1740, 1702, 1684 (C=O).

Analogously to compound **2a**, acid **2a** (in a yield of 0.20 g, 76%) and acid **2j** (in a yield of 0.24 g, 70%; m.p. >300 °C (from EtOH); *cf.* lit. data[2]: m.p. >300 °C) were isolated from the mixture containing quinoxalinone **1a** (0.27 g, 1 mmol) and quinoxalinone **1j** (0.35 g, 1 mmol).

Nitration of 3-(2-oxo-2-phenylethyl)-3,4-dihydroquinoxalin-2(1*H*)-one (1a). A 2 : 1 mixture of sulfuric acid (0.125 mL) and nitric acid (0.2 mL) was added with cooling and constant stirring to a solution of quinoxalin-2-one **1a** (0.27 g, 1 mmol) in sulfuric acid (0.6 mL, 10 mmol). The reaction solution was stirred at a temperature of no higher than 5 °C for 1 h. Then the mixture was poured into ice water. The precipitate was filtered off, washed with water, and recrystallized from methanol. Poorly soluble 5-nitro isomer **2g** was filtered off. 7-Nitro isomer **2f** was isolated from the filtrate upon cooling. The starting quinoxalinone **1a** was detected in the filtrate (R_f 0.6, a toluene—ethyl acetate mixture as the eluent).

(*Z*)-2-[7-Nitro-3-phenylquinoxalin-2(1*H*)-ylidene]acetic acid (2f). The yield was 0.16 g (52%), m.p. 274—276 °C (from MeOH). Found (%): C, 62.11; H, 3.64; N, 13.62. $C_{16}H_{11}N_3O_4$. Calculated (%): C, 62.14; H, 3.58; N, 13.59. ^{1}H NMR, δ: 6.94 (s, 1 H, CH=); 7.12 (d, 1 H, H(8), J = 2.4 Hz); 7.75 (d, 1 H, H(5), J = 7.0 Hz); 7.51—7.62 (m, 3 H, *m*-H_{Ph} + *p*-H_{Ph}); 8.00 (d, 2 H, *o*-H_{Ph}, J = 7.8 Hz); 7.94 (d, 1 H, H(6), J = 6.8 Hz); 12.05 (s, 1 H, NH); 13.28 (s, 1 H, OH). IR (in KBr pellets), ν/cm^{-1}: 1346, 1512 (NO_2), 1620 (C=C), 1698 (C=O).

(*Z*)-2-[5-Nitro-3-phenylquinoxalin-2(1*H*)-ylidene]acetic acid (2g). The yield was 0.03 g (10%), m.p. 259—260 °C (from MeOH) (*cf.* lit. data[9]: m.p. 259—260 °C). ^{1}H NMR, δ: 6.81 (s, 1 H, CH=); 7.35 (d, 1 H, H(8), J = 7.9 Hz); 7.94 (d, 2 H, *o*-H_{Ph}, J = 6.8 Hz); 7.51—7.76 (m, 5 H, H(6), H(7), *m*-H_{Ph} + *p*-H_{Ph}); 12.14 (s, 1 H, NH); 13.67 (s, 1 H, OH).

A mixture of compound **2g** with 2-[5-nitro-3-phenylquinoxalin-2(1*H*)-ylidene]acetic acid described in the study[9] showed no melting point depression.

The treatment of compound **2a** (0.26 g, 1 mmol) with a nitrating mixture (analogously to compound **1a**) afforded the starting acid **2a** in a yield of 0.24 g (91%).

Bromination of a mixture of quinoxalinones 1h + 1i. A solution of Br_2 (5 mmol) in AcOH (0.3 mL) was added dropwise with constant stirring to a solution of a mixture of quinoxalin-2-ones **1h** + **1i** (1.6 g, 5 mmol) in AcOH (15 mL). The reaction mixture was stirred at room temperature for 1 h and then poured into ice water. The precipitate was filtered off, washed with water, and triturated with hot ethanol (in 10 mL portions). The residue was recrystallized from ethyl acetate. Poorly soluble 7-bromo-6-nitro isomer **2i** was filtered off. 6-Nitro acid **2h** was isolated from the filtrate on cooling. 6-Nitroquinoxalinone **1i** was isolated from the ethanolic solution in a yield of 1.1 g (85%).

6-Nitro-3-[2-oxo-2-(*p*-tolyl)ethyl]-3,4-dihydroquinoxalin-2(1*H*)-one (1i). The yield was 1.1 g (85%), m.p. 196—198 °C (from EtOH). Found (%): C, 62.73; H, 4.64; N, 12.79. $C_{17}H_{15}N_3O_4$. Calculated (%): C, 62.76; H, 4.65; N, 12.92. ^{1}H NMR, δ: 2.35 (s, 3 H, CH_3); 3.36 (dd, 1 H, H_A, J = 17.7 Hz, J = 6.7 Hz); 3.52 (dd, 1 H, H_B, J = 17.7 Hz, J = 6.7 Hz); 4.53 (t, 1 H, H_X, J = 6.7 Hz, J = 4.6 Hz); 6.60 (s, 1 H, NH); 7.33 (d, 2 H, *m*-H_{Ar}, J = 7.9 Hz);

7.49—7.73 (m, 3 H, H(5), H(7), H(8)); 7.88 (d, 2 H, *o*-H_{Ar}, J = 7.9 Hz); 10.93 (s, 1 H, NH).

(*Z*)-2-[7-Bromo-6-nitro-3-(*p*-tolyl)quinoxalin-2(1*H*)-ylidene]-acetic acid (2i). The yield was 0.12 g (29%), m.p. 288—290 °C (from AcOEt). Found (%): C, 70.75; H, 5.64; N, 10.79. $C_{16}H_{10}BrN_3O_4$. Calculated (%): C, 70.79; H, 5.63; N, 10.83. ^{1}H NMR, δ: 2.37 (s, 3 H, Me); 6.98 (s, 1 H, CH=); 7.87 (s, 1 H, H(8)); 8.25 (d, 1 H, H(5), J = 2.2 Hz); 7.34 (d, 2 H, *m*-H_{Ar}, J = 7.6 Hz); 7.92 (d, 2 H, *o*-H_{Ar}, J = 7.6 Hz); 12.38 (s, 1 H, NH); 13.84 (s, 1 H, OH). IR (in KBr pellets), ν/cm^{-1}: 1694 (C=O), 1610 (C=C).

(*Z*)-2-[6-Nitro-3-(*p*-tolyl)quinoxalin-2(1*H*)-ylidene]acetic acid (2h). The yield was 0.15 g (45%), m.p. >300 °C (from AcOEt) (*cf.* lit. data[2]: m.p. >300 °C).

The bromination of compound **1a** (0.27 g, 1 mmol) in acetic acid, like the bromination of a mixture of quinoxalin-2-ones **1h** + **1i**, afforded acid **2a** in a yield of 0.14 g (53%) and acid **2j** in a yield of 0.06 g (18%).

(*Z*)-2-[7-Bromo-3-phenylquinoxalin-2(1*H*)-ylidene]acetic acid (2j). The yield was 0.06 g (18%), m.p. 208—210 °C (from EtOH). Found (%): C, 54.97; H, 3.24; N, 8.13. $C_{16}H_{11}BrN_2O_2$. Calculated (%): C, 56.00; H, 3.23; N, 8.16. ^{1}H NMR, δ: 6.80 (s, 1 H, CH=); 7.87 (d, 1 H, H(8), J = 2.4 Hz); 7.52—7.60 (m, 5 H, Ar); 8.00 (d, 2 H, *o*-H_{Ph}, J = 7.6 Hz); 12.04 (s, 1 H, NH); 13.47 (s, 1 H, OH). IR (in KBr pellets), ν/cm^{-1}: 1692 (C=O), 1618 (C=C). IR (CCl_4), ν/cm^{-1}: 3530 (OH), 3400 (NH), 1750, 1700, 1688 (C=O).

(*Z*)-2-[3-(*p*-Chlorophenyl)-6-nitroquinoxalin-2(1*H*)-ylidene]-acetic acid (2k). A 40% aqueous NaOH solution (2-3 drops) and quinoxalinone **1j** (0.35 g, 1 mmol) were added to a solution of elemental sulfur (0.05 g) in DMF (5 mL). The reaction mixture was refluxed for 5 h and cooled. Then water (20 mL) was added, and the mixture was acidified with 20% HCl. The precipitate that formed was filtered off and recrystallized from ethanol. The yield was 0.17 g (50%). In the absence of sulfur, acid **2k** was obtained in 25% yield.

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