Polycyclic heterocycles with acidic N-H group, VI.[1] The synthesis of some polycyclic heterocyclic compounds related to 3-phenyl-1,2-dihydroquinoxaline-2-one

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Abstract

This work deals with the study of the reactivity of substituted 3-(2-aminophenyl)-1,2-dihydro-quinoxaline-2-ones (**4a, 4b**). 3-(2-Amino-4-fluorophenyl)-1,2-dihydroquinoxaline-2-one (**4a**) was prepared by the reaction of 6-fluoro-N-acetylisatin (**2a**) with 1,2-diaminobenzene and further hydrolysis of the acetyl group. Compound **4b** was prepared directly by the reaction of 7-nitroisatin (**1b**) with 1,2-diaminobenzene. The cyclization reaction of compounds **4a, 4b** in $POCl_3$ afforded indolo[2,3-b]quinoxalines **7a, 7b**. Intramolecular splitting cyclizations of diazonium salts **5a, 5b** led to [1]benzofuro[2,3-b]quinoxalines (**6a, 6b**) and azo-coupling reactions of diazonium salts **5a** with ethyl cyanoacetylcarbamate and malonodinitrile gave arylhydrazones **9a** and **10a**. By the diazotization of amine **4b** we were able to isolate diazotate **8b** in sodium acetate solution. The azo- coupling reactions of diazotate **8b** with ethyl cyanoacetyl carbamate and malonodinitrile gave the arylhydrazones **9b** and **10b**. These arylhydrazones were then transformed into 1,3-diaminopyrazoles (**11a, 11b**) and 6-azauracils (**12a, 12b**).

Keywords: 3-Substituted 1,2-dihydroquinoxaline-2-ones, 1-aryl-6-azauracils, heterocycles with acidic N-H groups

Introduction

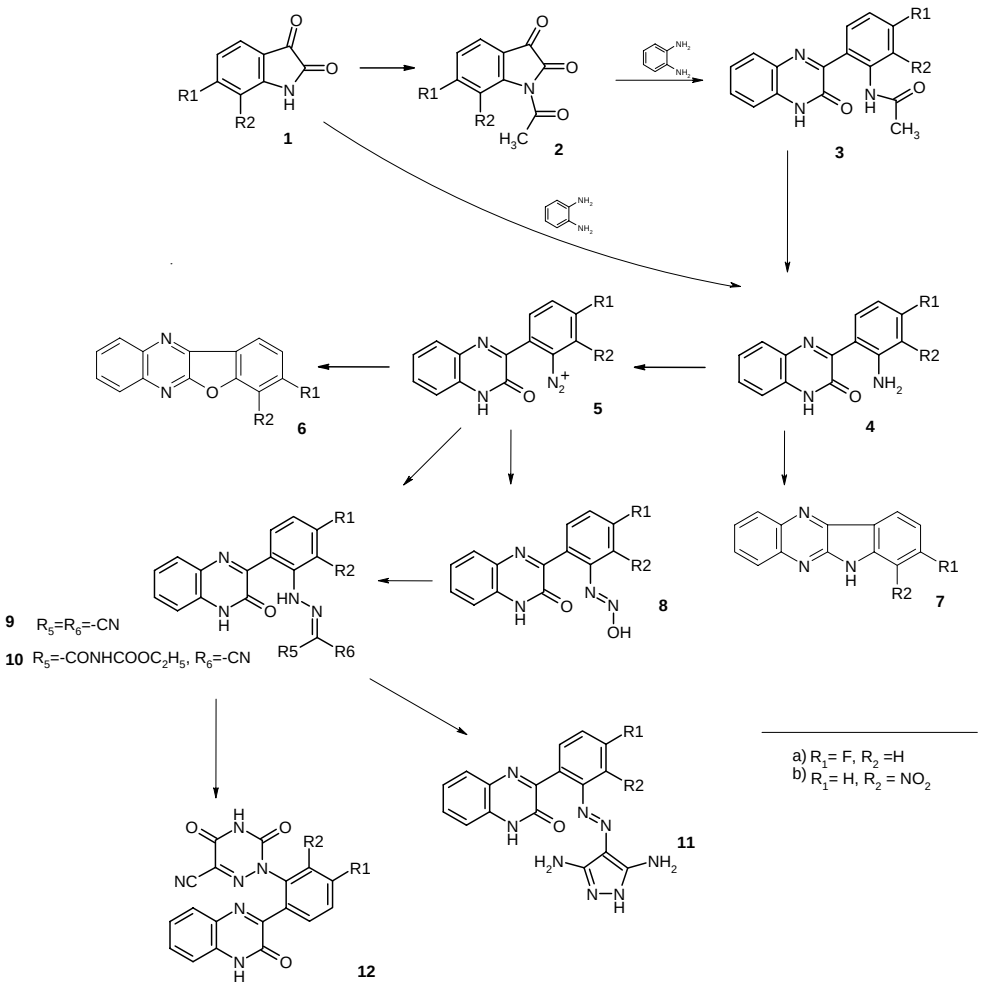
There have been found a large number of biologically active compounds among polycyclic heterocyclic compounds with free rotation of their rings.[2-8] This group of heterocycles includes with surprise some transforming growth factor[9, 10] inhibitors, reverse transcriptase,[11, 12] dihydrofolate reductase[13] and cyclin-dependent kinase inhibitors.[14, 15]

The structure of most cyclin- dependent kinase inhibitors is related to purine,[15] however recently the same activity was found for a few compounds with completely different structure.

This fact inspired us to prepare other polycyclic heterocyclic compounds bearing quinoxaline and [1,2,4]triazine or pyrazole ring in their structure.[16, 17]

Results and Discussion

The target of this work is the study of reactivity of some substituted 3-(2-aminophenyl)-1,2-dihydroquinoxaline-2-ones and their use for preparation of condensed heterocyclic compounds which bear quinoxaline ring as well as non condensed heterocyclic compounds comprising quinoxaline and [1,2,4]-triazine or pyrazole ring.



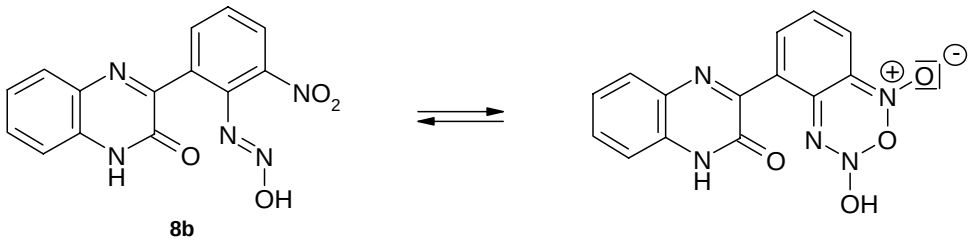
Scheme 1

The key intermediate **4a** was prepared easily in a multistep reaction from the corresponding isatin **1a**.[18,19] The cyclocondensation reaction of isatin **1a** with 1,2-diaminobenzene was not successful; however, the cyclocondensation reaction of the protected N-acetylisatin **2a** proceeded

smoothly to 3-(2-acetylamino-4-fluorophenyl)-1,2-dihydroquinoxaline-2-one (**3a**). The hydrolysis of the acetyl group was then performed in potassium hydroxide solution. On the other hand, it was not necessary to protect 7-nitroisatin [20] (**1b**) by acetylation, and the cyclocondensation reaction of **1b** with 1,2-diaminobenzene afforded the quinoxaline **4b** in one step.

The amino- derivatives **4a, 4b** were cyclized to indolo[2,3-b]quinoxalines (**7a, 7b**) by the action of phosphorous oxychloride with catalytic amount of pyridine. Other transformations of the key amino derivatives **4** are based on the diazotization of the amino group and further intramolecular coupling with the oxo group in position 2- of the quinoxaline ring and coupling reactions on the active methylene groups of ethyl cyanoacetyl carbamate and malonodinitrile.

Because of the low basicity of the amino derivatives **4** we had to use nitrosylsulfuric acid for diazotization reactions. Benzofuro[2,3-b]quinoxalines (**6a, 6b**) were obtained after short heating of corresponding diazonium salts, in high yields and purity. The probable intermediates of coupling reactions seem to be diazohydroxides (**8**) and we were able to isolate diazohydroxide **8b** which is more stable than **8a**. The relatively high stability of diazohydroxide **8b** is probably caused by the influence of a nitro group, which can stabilize it by formation of the benzooxatriazine ring (see Scheme 2).



8b

Scheme 2

Arylhydrazones **9a** and **10a** were prepared by coupling of the diazonium salt **5a** with ethyl cyanoacetylcarbamate and malonodinitrile as precursors for further cyclization reactions. The arylhydrazones **9b** and **10b** were prepared by coupling of diazotate **8b** with ethyl cyanoacetylcarbamate and malonodinitrile as precursors for further cyclization reactions. Arylhydrazones **10a, 10b** were cyclized in sodium carbonate solution to **12a, 12b**, and the action of hydrazine on the dinitriles **9a, 9b** led to the diaminopyrazole derivatives **11a, 11b**.

Experimental Section

General Procedures. Melting points (Boetius) are uncorrected. Infrared spectra were measured as potassium bromide disks and scanned on an ATI Unicam Genesis FTIR instrument. The NMR spectra were measured in DMSO-d_6 solutions on a Bruker AMX-300 spectrometer (300 MHz)

with TMS as internal standard. Mass spectra were measured on a ZAB-EQ (VG Analytical Ltd., England). Elemental analyses were performed using an EA Elemental Analyzer (Fisons Instruments). RT denotes room temperature.

6-Fluoroisatin (1a). Chloral hydrate (18.0 g; 108.8 mmol) and hydroxylamine sulfate (14.0 g; 218.75 mmol) were dissolved in a mixture of water (120 ml) and hydrochloric acid (37 %; 8.0 ml). The solution was stirred at room temperature for 10 min. Then 3-fluoroaniline (10.0 g; 108 mmol) was added and the mixture was heated at 60° for 3 hours. After cooling to RT the mixture was left to stand overnight. The yellow precipitate was collected, washed with water and air-dried. The crude product (0.625 mol) was added portionwise with stirring to concentrated sulfuric acid (100 ml). The mixture was heated at 70 °C for 30 min. After cooling to RT it was poured over crushed ice. The precipitate was collected, washed with water, diethyl ether, and air-dried. Yellow crystals, yield 83.0 %, mp 185-186 °C, IR (KBr) ν: 3181, 3072, 1738, 1620, 1489, 1297, 1194, 847. ^{1}H NMR (DMSO) δ: 7.00 (dd, 1H, J_1 = 2.4, J_2 = 9.3, ArH); 7.19 (dt, 1H, J_1 = 2.1, J_2 = 8.1, ArH); 7.87 (dd, 1H, J_1 = 5.7, J_2 = 8.1, ArH); 11.43 (s, 1H, NH). Anal. Calcd. for $C_8H_4NO_2F$ (165.13): C, 58.19; H, 2.44; N, 8.48. Found: C, 58.12; H, 2.45; N, 8.35.

6-Fluoro-*N*-acetylisatin (2a). A mixture of 6-fluoroisatin (**1a**) (168.4 mg, 1.02 mol) and acetic anhydride (0.347 ml) was refluxed for 4 hours. After cooling to RT it was left to stand overnight. The precipitate was collected, washed with water, diethyl ether, and air-dried. Green crystals, yield 89.9 %, mp 132-133 °C, IR (KBr) ν: 3120, 2998, 2939, 1777, 1742, 1717, 1619, 1592, 1479, 1438, 1376, 1345, 1295, 1231, 1198, 1231, 1159, 1092, 1036, 983, 911, 839, 795. ^{1}H NMR (DMSO) δ: 2.60 (s, 3H, CH_3), 7.23 (dt, 1H, J_1 = 2.1, J_2 = 8.4, ArH), 7.88 (dd, 1H, J_1 = 6.0, J_2 = 8.4, ArH), 8.03 (dd, 1H, J_1 = 2.4, J_2 = 10.8, ArH). Anal. Calcd. for $C_{10}H_6NO_3F$ (207.16): C, 57.98; H, 2.92; N, 6.76. Found: C, 58.01; H, 3.00; N, 6.71.

3-(2-Acetylamino-4-fluorophenyl)-1,2-dihydroquinoxaline-2-one (3a). The 6-fluoro-N-acetylisatin **2** (8.29 g; 40.02 mmol) was dissolved in acetic acid (90 ml), heated to 80°C, and a solution of 1,2-diaminobenzene (4.60 g, 42.54 mmol) in a mixture of water (10 ml) and acetic acid (10 ml) was added with intensive stirring. After a few minutes of stirring, a thick precipitate separated out from the solution. The reaction mixture was stirred for a further 15 minutes and cooled to RT. The precipitate was collected, washed with a small amount of acetic acid, a mixture of acetic acid and water, and finally with water. White crystals, yield 90.9 %, mp 318-319 °C, IR (KBr) ν: 3199, 3098, 3053, 1745, 1683, 1523, 1300, 1215, 1088, 940, 724, 607. ^{1}H NMR (DMSO) δ: 1,97 (s, 3H, CH_3), 7.00 (dt, 1H, J_1 = 2.7, J_2 = 8.7, ArH), 7.34 (d, 2H, J = 7.5, ArH), 7.56 (t, 1H, J = 7.2, ArH), 7.82 (m, 3H, ArH), 10.03 (s, 1H, NH), 12.53 (s, 1H NH). Anal. Calcd. for $C_{16}H_{12}N_3O_2F$ (297.29): C, 64.64; H, 4.07; N, 14.13. Found: C, 64.39; H, 4.03; N, 14.23.

3-(2-Amino-4-fluorophenyl)-1,2-dihydroquinoxaline-2-one (4a). The acetyl derivative (**3a**) (3.76 g; 12.66 mmol) was dissolved in a solution of KOH (6.5 g) in a mixture of ethanol (30 ml) and water (25 ml), and refluxed for a further 5 hours. Ethanol was evaporated from the reaction mixture from a water bath and the solution was acidified with acetic acid to pH 5. The precipitate

was collected, washed with water, and air-dried. Yellow crystals, yield 96.3 %, mp > 320 °C, IR (KBr) ν: 3383, 3100, 2978, 1656, 1624, 1572, 1527, 1432, 1265, 211, 903, 839, 755. ^{1}H NMR (DMSO) δ: 6.63 (t, 1H, J = 8.7, ArH); 6.85 (dd, 1H, J_1 = 2.7, J_2 = 11.7, ArH); 7.19 (s, 2H, NH_2); 7.53 (m, 2H, ArH); 7.78 (m, 1H, ArH); 8.06 (d, 1H, J = 8.1, ArH); 8.57 (m, 1H, ArH); 12.74 (s, 1H, NH). Anal. Calcd. for $C_{14}H_{10}N_3OF$ (255.25): C, 65.88; H, 3.95; N, 16.46. Found: C, 65.78; H, 3.87; N, 16.33.

3-(2-Amino-3-nitrophenyl)-1,2-dihydroquinoxaline-2-one (4b). The 7-nitroisatin[20] (**1b**) (1.5 g; 7.8 mmol) was dissolved in acetic acid (110 ml), heated to 80°C, and a solution of 1,2-diaminobenzene (0.73 g, 6.82 mmol) in acetic acid (5 ml) was added with intensive stirring. After a few minutes of stirring, a thick precipitate separated out from the solution. The reaction mixture was stirred for the next 15 minutes and cooled to RT. The precipitate was collected, washed with a small amount of acetic acid, a mixture of acetic acid and water, and finally with water. Yellow crystals, yield 73.3 %, mp 252-253 °C, IR (KBr) ν: 3476, 3356, 3086, 2990, 2843, 1664, 1621, 1570, 1520, 1439, 1352, 1264, 1030, 896, 749. ^{1}H NMR (DMSO) δ: 6.75 (t, 1H, J = 15.9, ArH), 7.33 (m, 2H, J = 16.2, ArH), 7.57 (m, 1H, ArH), 7.81 (d, 1H, J = 7.5, ArH), 7.87 (s, 2H, NH_2), 7.98 (dd, 1H, J_1 = 1.5, J_2 = 7.5, ArH), 8.15 (dd, 1H, J_1 = 1.5, J_2 = 8.7, ArH). Anal. Calcd. for $C_{14}H_{10}N_4O_3$ (282.26): C, 59.57; H, 3.57; N, 19.85. Found: C, 59.50; H, 3.62; N, 19.53.

Substituted benzofuro[2,3-*b*]quinoxalines (6a, 6b). General procedure

Finely powdered $NaNO_2$ (170.0 mg; 2.4 mmol) was added portionwise to H_2SO_4 (2.6 ml; 98 %) that was pre-cooled to 0 °C. After dissolving the $NaNO_2$ the mixture was left to stand 2 hours at RT and then heated up to 70 °C, and cooled down to 0-5 °C. To this solution the corresponding amine (**4a, 4b**) (2.02 mmol) was added portionwise under stirring, with cooling in an ice-bath. This solution was left to stand at RT for 10 min. Then the mixture was slowly heated on a water bath to 50°C. At this temperature the product started to precipitate from the solution. The temperature of water bath was then elevated to boiling. The reaction mixture was left to stand overnight at RT. The yellow crystalline compounds were collected with suction, washed with water, and air-dried.

3-Fluorobenzofuro[2,3-*b*]quinoxaline (6a). White crystals, yield 83.7 %, mp 187-188 °C, IR (KBr) ν: 3105, 2986, 1670, 1637, 1386, 1310, 1236, 1115, 1008, 890, 827, 620, 493. ^{1}H NMR (DMSO) δ: 10.31 (m, 3H, ArH), 10.52 (t, 1H, J = 8.7, ArH), 10.83 (d, 1H, J = 7.9, ArH), 11.38 (dd, 2H, J_1 = 5.7, J_2 = 9.0, ArH). Anal. Calcd. for $C_{14}H_7N_2OF$ (238.22): C, 70.59; H, 2.96; N, 11.76. Found: C, 70.52; H, 2.89; N, 11.67.

3-Nitrobenzofuro[2,3-*b*]quinoxaline (6b). White crystals, yield 80.6 %, mp 200-201 °C, IR (KBr) ν: 3100, 1680, 1635, 1610, 1548, 1470, 1412, 1325, 840, 692. ^{1}H NMR (DMSO) δ: 7.96 (m, 4H, ArH), 8.35 (d, 1H, J = 8.0, ArH), 8.60 (d, 1H, J = 8.5, ArH), 9.05 (m, 1H, ArH). Anal. Calcd. for $C_{14}H_7N_3O_3$ (265.23): C, 63.40; H, 2.66; N, 15.84. Found: C, 63.32; H, 2.71; N, 15.82.

Substituted 5*H*-indolo[2,3-*b*]quinoxalines (7a,7b) or their 6H-tautomers. General procedure
A mixture of amine (**4a, 4b**) (1.0 mmol) and $POCl_3$ (2 ml) was refluxed for 16 hours. After cooling to RT, the mixture was poured over crushed ice. The next day, the crystalline compound was collected with suction, washed with water, and dried in air.

8-Fluoro-5*H*-indolo[2,3-*b*]quinoxaline (7a). Yellow crystals, yield 96.5 %, mp > 320 °C (toluene), IR (KBr) ν: 3105, 2986, 1670, 1637, 1386, 1310, 1236, 1115, 1008, 890, 827, 620, 493. ^{1}H NMR (DMSO) δ: 10.59 (m, 2H, ArH), 10.73 (dt, 1H, J_1 = 1.5, J2 = 6.9, ArH), 10.79 (dt, 1H, J_1=1.5, J_2 = 6.9, ArH), 11.15 (m. 2H, ArH), 11.23 (dd, 1H, J_1 = 1.8, J_2 = 8.4, ArH), 15.07 (s, 1H, NH). Anal. Calcd. for $C_{14}H_8N_3F$ (237.24): C, 70.88; H, 3.40; N, 17.71. Found: C, 70.89; H, 3.20; N, 17.60.

8-Nitro-5*H*-indolo[2,3-*b*]quinoxalines (7b). Yellow crystals, yield 89.3 %, mp > 320 °C (toluene), IR (KBr) ν: 3100, 1680, 1635, 1610, 1548, 1470, 1412, 1325, 840, 692. ^{1}H NMR (DMSO) δ: 10.55 (d, 1H, J = 8.4, ArH), 10.73 (t, 1H, J = 6.9, ArH), 10.82 (m, 2H, ArH), 11.07 (d, 1H, J = 8.2, ArH), 11.24 (d, 1H, J = 8.4, ArH), 11.46 (d, 1H, J = 2.1, ArH), 15.19 (s, 1H, NH). Anal. Calcd. for $C_{14}H_8N_4O_2$ (264.24): C, 63.64; H, 3.05; N, 21.20. Found: C, 63.51; H, 2.98; N, 21.13.

3-[(2-Hydroxydiazenyl)-3-nitrophenyl]-1,2-dihydroquinoxaline-2-one (8b). Finely powdered $NaNO_2$ (170.0 mg; 2.4 mmol) was added portionwise to H_2SO_4 (2.6 ml; 98 %) pre-cooled to 0 °C. After dissolving the $NaNO_2$ the mixture was left to stand 2 hours at RT and then heated up to 70 °C and cooled down to 0-5 °C. To this solution the amine (**4b**) (570.2 mg; 2.02 mmol) was added portionwise under stirring, with cooling in an ice-bath. The solution was left to stand for 30 min in the ice bath and then was added portionwise during 10 min to a stirred mixture obtained by dissolving CH_3COONa (24 g) in warm water (130 ml), cooling on an ice bath, and adding crushed ice. The next day, a crystalline compound was collected with suction, washed with water, and dried in air. Yellow crystals, yield 97.2 %, mp 215-216 °C, IR (KBr) ν: 3210, 3055, 2922, 1696, 1611, 1530, 1497, 1432, 1347, 1146, 1105, 1041, 818, 749. ^{1}H NMR (DMSO) δ: 7.15 (dd, 1H, J1 = 1.5, J_2 = 1.5, ArH), 7.21 (m, 1H, ArH), 7.30 (m, 1H, ArH), 7.84 (m, 2H, ArH), 8.12 (dd, 1H, J_1=1.5, J_2=1.5, ArH), 8.41 (dd, 1H, J_1=1.5, J_2=1.5, ArH). Anal. Calcd. for $C_{14}H_9N_5O_4$ (311.26): C, 54.02; H, 2.91; N, 22.50. Found: C, 53.96; H, 2.79; N, 22.37. MS (ESI, m/z (rel. %)): 312.1 (100) $(M+1)^+$.

5-Fluoro-2-(3-oxo-3,4-dihydroquinoxaline-2-yl)-phenylhydrazonomalonodinitrile (9a). Finely powdered $NaNO_2$ (170.0 mg; 2.4 mmol) was added portionwise to H_2SO_4 (2.6 ml; 98 %) that was pre-cooled to 0 °C. After dissolving the $NaNO_2$ the mixture was left to stand 2 hours at RT and then heated to 70 °C and cooled down to 0-5 °C. To this solution the amine (**4a**) (515.6 mg; 2.02 mmol) was added portionwise under stirring. The solution was left to stand for 30 min in an ice bath and then was added portionwise during 10 min to a stirred mixture obtained by dissolving malonodinitrile (0.202 g; 2.02 mmol) in warm water (130 ml), cooling on an ice bath, adding CH_3COONa (24.0 g) and crushed ice (5 g). The next day, the crystalline compound was collected with suction, washed with water, and dried in air. Yellow crystals, yield 91.5 %, mp 203-204 °C, IR (KBr) ν: 3005, 2893, 2858, 2228, 1657, 1587, 1474, 1433, 1293, 1246, 1210,

892, 755, 518. ^{1}H NMR (DMSO) δ: 6.59 (m, 1H, ArH), 6.89 (dd, 1H, J_1=2.6, J_2=11.0, ArH), 7.53 (m, 2H, ArH), 7.78 (m, 1H, ArH), 8.10 (d, 1H, J = 8.5, ArH), 8.58 (m, 1H, ArH), 12.85 (s, 1H, NH). Anal. Calcd. for $C_{17}H_9N_6OF$ (332.3): C, 61.45; H, 2.73; N, 25.29. Found: C, 61.33; H, 2.77; N, 25.17.

6-Nitro-2-(3-oxo-3,4-dihydroquinoxaline-2-yl)-phenylhydrazonomalonodinitrile (9b). To the mixture of diazotate (**8b**) (150.0 mg, 0.48 mmol) in a mixture of water:acetonitrile (30 ml; 1:1) ethyl cyanoacetyl carbamate (112.32 mg, 0.72 mmol) was added and the reaction mixture was stirred for a further 24 hours. The next day, the crystalline compound was collected with suction, washed with water, and dried in air. Yellow crystals, yield 87.5 %, mp 240-241 °C, IR (KBr) ν: 3322, 3094, 2843, 2224, 1664, 1580, 1535, 1515, 1356, 1246, 754. ^{1}H NMR (DMSO) δ: 7.34 (m, 2H, ArH), 7.47 (t, 1H, J = 15.9, ArH), 7.56 (m, 1H, ArH), 7.78 (dd, 1H, J_1 = 0.9, J_2 = 8.1, ArH), 7.85 (dd, 1H, J_1 = 1.5, J_2 = 7.8, ArH), 8.01 (dd, 1H, J_1 = 1.5, J_2 = 8.1, ArH), 12.61 (s, 1H, NH). Anal. Calcd. for $C_{17}H_9N_7O_3$ (359.3): C, 56.83; H, 2.52; N, 27.29. Found: C, 56.77; H, 2.44; N, 27.19.

Ethyl 5-fluoro-2-(3-oxo-3,4-dihydroquinoxaline-2-yl)-phenylhydrazonocyanoacetyl carbamate (10a). Finely powdered $NaNO_2$ (170.0 mg; 2.4 mmol) was added portionwise to H_2SO_4 (2.6 ml; 98 %) that was pre-cooled to 0 °C. After dissolving the $NaNO_2$ the mixture was left to stand 2 hours at RT and then heated up to 70 °C and cooled down to 0-5 °C. To this solution, amine (**4a**) (515.6 mg; 2.02 mmol) was added portionwise under stirring. The solution was left to stand for 30 min in an ice bath and then was added portionwise during 10 min to a stirred mixture obtained by dissolving ethyl cyanoacetylcarbamate (0.42 g; 2.691 mmol) in warm water (130 ml), cooling on an ice bath, adding CH_3COONa (24.0 g) and crushed ice (5 g). The next day, a crystalline compound was collected with suction, washed with water, and dried in air. Yellow crystals, yield 92.0 %, mp 195-196 °C, IR (KBr) ν: 3477, 3284, 3088, 3002, 2214, 1773, 1737, 1656, 1617, 1578, 1526, 1483, 1434, 1372, 1301, 1270, 1205, 1167, 1100, 1044, 854. ^{1}H NMR (DMSO) δ: 1.06 (t, 3H, J = 7.2, CH_3), 4.08 (q, 2H, J_1 = 5.7, J_2 = 13.5, CH_2), 7.33 (m, 2H, ArH), 7.57 (m, 2H, ArH), 7.79 (m, 2H, ArH), 8.09 (d, 1H, J = 9.0, ArH), 10.95 (s, 1H, NH), 13.02 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{15}N_6O_4F$ (422.38): C, 56.87; H, 3.58; N, 19.90. Found: C, 56.67; H, 3.59; N, 20.01.

Ethyl 6-nitro-2-(3-oxo-3,4-dihydroquinoxaline-2-yl)-phenylhydrazonocyanoacetyl carbamate (10b). To the mixture of 3-[(2-hydroxydiazenyl)-3-nitrophenyl]-1,2-dihydro-quinoxaline-2-one (**8b**) (150.0 mg, 0.48 mmol) in a mixture of water:acetonitrile (1:1) the malonodinitrile (47.5 mg, 0.72 mmol) was added and the reaction mixture was stirred for a further 24 hours. The next day, the crystalline compound was collected with suction, washed with water and dried in air. Yellow crystals, yield 80.9 %, mp 207-208 °C, IR (KBr) ν: 3360, 3080, 2829, 2214, 1789, 1669, 1533, 1503, 1293, 1188, 1028, 933, 773. ^{1}H NMR (DMSO) δ: 1.10 (t, 3H, J = 7.2, CH_3); 3.81 (q, 2H, J_1 = 6.9, J_2 = 14.1, CH_2); 7.32 (m, 2H, ArH); 7.57 (m, 2H, ArH); 7.81 (dd, 1H, J_1 = 1.2, J_2 = 8.1, ArH); 8.04 (dd, 1H, J_1 = 1.2, J_2 = 7.9, ArH); 8.2 (dd, 1H, J_1 = 1.2, J_2 = 8.1, ArH); 9.31 (s, 1H, NH); 12.69 (s, 1H, NH). Anal. Calcd. for $C_{20}H_{15}N_7O_6$ (449.38): C, 53.46; H, 3.36; N, 21.82. Found: C, 53.38; H, 3.42; N, 21.78.

3-[Substituted-2-(3,5-diamino-pyrazol-4-yl)-azo]-phenyl-1,2-dihydroquinoxalin-2-one (11a, 11b). General procedure

A suspension of the corresponding hydrazone (**9a**, **9b**) (1 mmol), hydrazine hydrate (0.1 ml; 2.0 mmol; 99 %) and methanol (35 ml) was heated for 10 minutes. After cooling to RT the solution was acidified with acetic acid (0.3 ml). The reaction mixture was crystallized with charcoal. The filtrate was evaporated (40 °C; 20 mm Hg) and the solid was mixed with water (20 l). The next day the compounds were collected with suction, washed with water, and dried in air.

3-[4-Fluoro-2-(3,5-diamino-pyrazol-4-yl)-azo]-phenyl-1,2-dihydroquinoxalin-2-one (11a). Yellow crystals, yield 84.9 %, mp 238-239 °C (ethanol), IR (KBr) ν: 3024, 2814, 1761, 1721, 1654, 1537, 1223, 774, 589. ^{1}H NMR (DMSO) δ: 4.12 (s, 2H, NH_2), 5.91 (s, 2H, NH_2), 7.49 (m, 3H, ArH), 7.60 (m, 2H, ArH), 7.70 (d, 1H, J = 9.0, ArH), 7.96 (m, 1H, ArH), 11.58 (s, 1H, NH). Anal. Calcd. for $C_{17}H_{13}N_8OF$ (364.34): C, 56.04; H, 3.60; N, 30.76. Found: C, 55.98; H, 3.51; N, 30.69.

3-[3-Nitro-2-(3,5-diamino-pyrazol-4-yl)-azo]-phenyl-1,2-dihydroquinoxalin-2-one (11b). Yellow crystals, yield 73.9 %, mp 249-250 °C (ethanol), IR (KBr) ν: 3463, 3375, 1674, 1617, 1561, 1522, 1505, 1395, 1303, 1226, 1121, 752. ^{1}H NMR (DMSO) δ: 4.22 (s, 2H, NH_2); 5.99 (s, 2H, NH_2); 7.31 (m, 2H, ArH), 7.42 (t, 1H, J = 15.6, ArH), 7.53 (m, 1H, ArH), 7.66 (dd, 1H, J_1 = 1.2, J_2 = 7.5, ArH), 7.75 (dd, 1H, J1 = 1.2, J_2 = 8.4, ArH), 7.93 (dd, 1H, J_1 = 1.5, J_2 = 7.8, ArH), 11.01 (s, 1H, NH), 12.43 (s, 1H NH). Anal. Calcd. for $C_{17}H_{13}N_9O_3$ (391.35): C, 52.18; H, 3.35; N, 32.21. Found: C, 52.19; H, 3.40; N, 32.17.

2-[Substituted-2-(3-oxo-3,4-dihydroquinoxalin-2-yl)-phenyl]-3,5-dioxo-2,3,4,5-tetrahydro-[1,2,4]-triazine-6-carbonitrile (12a, 12b). General procedure

A mixture of hydrazone (**10a**, **10b**) (1.0 mmol), Na_2CO_3 (120.0 mg) and water (10 ml) was heated on a boiling water bath until a solution was formed and then for an additional 15 minutes. After cooling to RT the solution was allowed to cool down and acidified with HCl (37 %) to pH 1. After several hours, the crystalline solid was collected with suction, washed with a little water, and dried in air.

2-[2-(3-Oxo-3,4-dihydroquinoxalin-2-yl)-5-fluorophenyl]-3,5-dioxo-2,3,4,5-tetrahydro-[1,2,4]-triazine-6-carbonitrile (12a). White crystals, yield 79.7 %, mp 183-184 °C (ethanol), IR (KBr) ν: 3388, 3256, 3098, 2945, 2242, 1640, 1600, 1564, 1500, 1427, 1366, 1259, 1148, 1007, 857, 756, 515. ^{1}H NMR (DMSO) δ: 7.39 (m, 2H, ArH), 7.53 (m, 3H, ArH), 7.60 (d, 1H, J = 8.7, ArH), 7.90 (m, 1H, ArH), 9.86 (s, 1H, NH), 12.70 (s, 1H, NH). Anal. Calcd. for $C_{18}H_9N_6O_3F$ (376.31): C, 57.45; H, 2.41; N, 22.33. Found: C, 57.50; H, 2.43; N, 22.26.

2-[2-(3-Oxo-3,4-dihydroquinoxalin-2-yl)-6-nitrophenyl]-3,5-dioxo-2,3,4,5-tetrahydro-[1,2,4]-triazine-6-carbonitrile (12b). White crystals, yield 80.0 %, mp 240-241 °C (ethanol), IR (KBr) ν: 3455, 3369, 2244, 1699, 1650, 1558, 1390, 1300, 1225, 1121, 748, 500. ^{1}H NMR (DMSO) δ: 7.40 (m, 2H, ArH), 7.56 (t, 1H, J = 7.6, ArH), 7.78 (d, 1H, J = 8.8, ArH), 7.98 (m, 3H, ArH), 12.78 (s, 1H, NH). Anal. Calcd. for $C_{18}H_9N_7O_5$ (403.31): C, 53.61; H, 2.25; N, 24.31. Found: C, 53.49; H, 2.19; N, 24.28.

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