Cyclization Reactions of Hydrazones XXVII*
Synthesis and oxidative cyclization of some formazan-substituted quinoxaline-2-ones

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Abstract

A series of 1,5-diaryl-3-formazylglyoxylic acids **1a-1f** was prepared by azocoupling of diazonium salts with sodium pyruvate. These compounds gave the corresponding 3-(1,5-diaryl-3-formazyl)-1,2-dihydro-quinoxaline-2-ones **2a-2f** by condensation with o-phenylenediamine. Oxidative cyclization of these compounds did not lead to the [1,2,3]triazolo[1,5-a]quinoxaline derivatives **6a-6f**, but to the isomeric 2,3-diaryl-5-(2-oxo-1,2-dihydro-quinoxaline-3-yl)-tetrazolium chlorides **3a-3f**, which were transformed into the less hygroscopic picrates **4a-4f**.

Introduction

The hydrazones of some heterocyclic aldehydes and ketones can be transformed to the condensed heterocyclic compounds by oxidative cyclization.
For example, phenylhydrazone of 2-benzoyl-benzothiazole gives 1,3-diphenyl[1,2,3]-triazolo[5,1-b]benzothiazolium salts in this way (1) and the same reaction of phenylhydrazone of 2-benzoylbenzimidazole leads to the 1,3-diphenyl-[1,2,3]triazolo[1,5-a]benzimidazole (1). The oxidative cyclization of 2-acylpyridine hydrazones to [1,2,3]triazolo[1,5-a]pyridine derivatives is also known (2).

In this connection we were interested in properties of 3-(1,5-diaryl-3-formazyl)-1,2-dihydro-quinoxaline-2-one, for which it was possible to expect two different courses of oxidative cyclization: usual cyclization to the corresponding tetrazolium salts **3**, or oxidative cyclization, which could lead to the isomeric derivatives of [1,2,3]triazolo[1,5-a]-quinoxalinium salts **6**. The isomerization of the Z-hydrazono form **2** into the E-isomer **5** is possible due to azo-hydrazono tautomerism.

Results

Contrary to the series of heterocyclic methyl-derivatives, which gave corresponding formazans by azocoupling with two equivalents of diazonium salts (3), in the case of 3-methyl-1,2-dihydro-quinoxaline-2-one this reaction didn't occur and gave arylhydrazones of 2-oxo-1,2-dihydro-quinoxaline-3-carbaldehyde only (4-9). These arylhydrazones are not able to react with another equivalent of diazonium salts to form formazans (9).

For this reason we had to prepare these 3-(1,5-diaryl-3-formazyl)-1,2-dihydro-quinoxaline-2-ones in a different way. Using modified Bamberger and Müller method (10) we prepared a series of 1,5-diaryl-3-formazylglyoxylic acids **1a-1f** by azocoupling of diazonium salts with sodium pyruvate in alkaline medium. These compounds were condensed with o-phenylenediamine and we received a series of formazanes **2a-2f** mentioned above.

For oxidative cyclization of formazanes we used lead(IV)tetraacetate in a chloroform solution. With respect to the fact that products are nearly colourless crystalline compounds and there is no characteristic band for arylazo group in the visible part of UV-VIS spectrum, it is possible to exclude the structure expressed by formula **6**, so that studied compounds are

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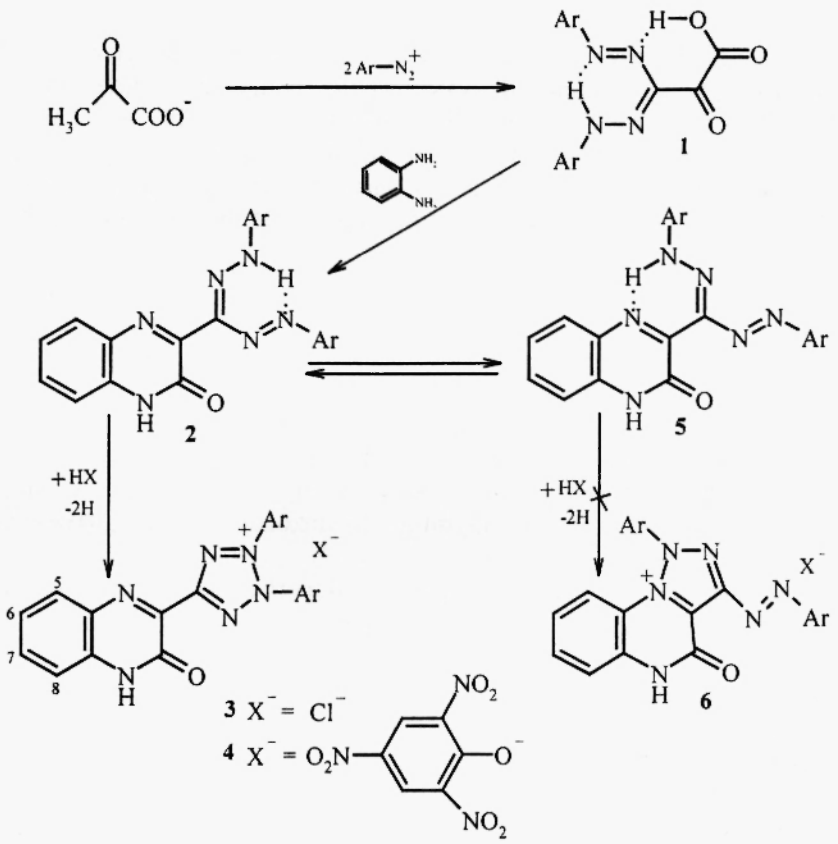
2,3-diaryl-5-(2-oxo-1,2-dihydro-quinoxaline-3-yl)-tetrazolium chlorides **3a-3f**. These compounds are soluble in water, but give after recrystallisation the corresponding hydrates. By the reaction with sodium picrate, the chlorides were transformed to the corresponding picrates **4a-4f**, which aren't hygroscopic. By the reduction with sodium hyposulfite, tetrazolium salts **3** were transformed back to the corresponding formazans **2**.



Apparatus and methods

The melting points were determined on a Boetius apparatus and are uncorrected. The IR spectra were measured using KBr disc technique and scanned on an ATI Unicam Genesis FTIR instrument. Elemental analyses were performed by using an EA 1108 Elemental Analyser (Fison Instrument). NMR spectra were measured on a Bruker AMX-360 spectrometer (360 MHz) in DMSO-d_6 ;the chemical shifts δ are reported in ppm and coupling constants are in Hertz. Electronic spectra were measured in ethanol solutions on a UV-VIS spectrometr Unicam Helios α in 1 cm cuvettes. Concentrations of the samples varied from 0.5-1 $.10^{-5}$ $mol.l^{-1}$.

Experimental

1,5-Diaryl-3-formazylglyoxylic acids **(1a-1f)**
General procedure:

A solution of $NaNO_2$ (1.38g, 20.0 mmol) in ice-cold water (5 ml) was added portionwise under stirring to the solution of corresponding aromatic amine (20.2 mmol) in a mixture of HCl (37%, 10.0 ml) and water (10-20 ml), which was cooled in an ice-bath. The solution was left to stand for 20 min in an ice bath and then was added portionwise during 3 min. under stirring to a pre-cooled solution of sodium pyruvate (4.00 g, 36,35 mmol) and KOH (30g) in water (300 ml). Reaction mixture was left in an ice bath for 20 min. with vigourous stirring. Small amount of separated precipitate of 1,5-diaryl-3-arylazoformazane was filtered off and washed with water. The combined filtrates were acidified under vigorous stirring with HCl (37%) to pH=1. After several hours, the separated red compound was collected with suction, thoroughly washed with water and suspended in a solution of $NaHCO_3$ (1.0 g) in water (30-50 ml). The reaction mixture was stirred for several hours and then filtered after addition of small amount of charcoal. The filtrate was acidified with HCl (37%) to pH=1. Precipitate was collected with suction after several hours, carefully washed with water and dried in air. Obtained compounds were purified by recrystallization from ethanol/water.
For further details see tables 1 and 2.

3-(1,5-Diaryl-3-formazyl)-1,2-dihydro-quinoxaline-2-ones **(2a-2f)**
General procedure:

Formazylglyoxylic acid **1a-1f** (1.0 mmol) was disolved in hot ethanol (10 ml) and o-phenylenediamine (108 mg, 1.0 mmol) was disolved in 1 ml hot ethanol. The mixture of both solutions was refluxed for 15 min. After cooling to 20 °C, the red crystalline compound was separated with suction, washed with water and dried. Obtained compounds were purified by recrystallization from ethanol.
For further details see table 1 and 2.

2,3-Diaryl-5-(2-oxo-1,2-dihydro-quinoxaline-3-yl)-tetrazolium chlorides **(3a-3f)**
General procedure:

Lead(IV)tetraacetate (0.50 g, 1.12 mmol) was added with stirring to a solution prepared from 1,2-dihydro-3-(1,5-diarylformazyl-3-yl-quinoxaline-2-one **2a-2f** (1.00 mmol) and $CHCl_3$ 50-150 ml. The solution was filtered after 3 hours of stirring. The filtrate was evaporated, the residue was dissolved in H_2O (10 ml) and the solution was acidified with HCl (37%) to pH=2. The precipitate was separated with suction and the filtrate was evaporated. The residue was dissolved in methanol (7-10 ml), filtered and evaporated. The

residue was dried over KOH. Compounds **3c**, **3e** and **3f** were used without purifying and for preparation of corresponding picrates.
For further details see tables 1 and 2.

2,3-Diaryl-5-(2-oxo-1,2-dihydro-quinoxaline-3-yl)-tetrazolium picrates **(4a-4f)**
General procedure:

A solution of sodium picrate (251.0 mg. 1.00 mmol) in H_2O (5 ml) was added to the stirred solution prepared from tetrazolium salt **3a-3f** (1 mmol) and H_2O (1-3 ml). The precipitated compound **4a-4f** was collected with suction and dried.
For further details see tables 1 and 2.

Table 1
^{1}H-NMR spectra of compounds 1, 2 and 3a

Compound	^{1}H-NMR spectrum
1a	7.50(t, 2H, J=7.5, H_4); 7.61(t, 4H, J=8.0, H_3); 7.88(d, 4H, J=7.5, H_2); 14.48(s, 1H, NH)
1b	2.43(s, 6H, CH_3); 7.41 (d, 4H, J=8.4, H_3); 7.78(d, 4H, J=8.4, H_2); 14.7(s, 1H, NH)
1c	7.47(t, 4H, J=8.8, H_3); 7.94(dd, 4H, J=3.4, J=5.1, H_2); 14.32(s, 1H, NH)
1d	7.68 (d, 4H, J=8.8, H_3); 7.90(d, 4H, J=8.8, H_2) ; 14.21 (s, 1H, NH)
1e	7.69(d, 4H, J=8.7, H_3); 7.91(d, 4H, J=8.7, H_2); 14.20(s, 1H, NH)
1f	3.89(s, 6H, CH_3) ; 7.16(dd, 4H, J=7.2, J=2.1, H_3); 7.84(dd, 4H, J=7.2, J=2.1, H_2); 14.80(s, 1H, NH)
2a	7.40(t, 4H, J=7.3, ArH); 7.61(t, 4H, J=7.3, ArH); 7.92(d, 6H, J=6.7, ArH), 13.97(s,2H, NH)
2b	2.43(s, 6H, CH_3); 7.40(m, 6H, ArH); 7.87(m, 6H, ArH); 13.92 (Brs, 2H, NH)
2c	7.43(m, 6H, ArH); 7.96(m, 6H, ArH); 13.96(Brs, 2H, NH)
2d	7.60(m, 6H, ArH); 7.88(m, 6H, ArH); 14.06(Brs, 2H NH)
2e	7.65(m, 6H, ArH); 7.93(m, 6H, ArH); 13.94(s,2H,NH)
2f	3.93(s, 6H, CH_3); 7.41(m, 6H, ArH); 7.90(m, 6H, ArH); 13.87(Brs, 2H, NH)
3a	7.48(m, 2H, H_4); 7.78(t, 4H, J=7.7, H_3); 7.86(m, 4H, H_{5-8}); 8.05(d, 4H, J=7.7, H_2)

Table 2
Characteristic data of compounds 1-4

Compound	M.p. (°C) Yield (%)	Formula M.w.	Elemental Analysis (Calcul./Found) % C	% H	% N	ν(C=O)	λ(max)	(logε)
1a	165-167* 68.52	$C_{15}H_{12}N_4O_3$ 296.28	60.80 60.79	4.08 4.01	18.91 17.99	1740	304 nm 439 nm	4.66 4.78
1b	173-174 57.00	$C_{17}H_{16}N_4O_3 \cdot 0.5H_2O$ 333.34	61.25 61.08	5.14 4.89	16,81 16.00	1716	317 nm 448 nm	4.29 4.44
1c	178-179 55.08	$C_{15}H_{10}F_2N_4O_3 \cdot H_2O$ 350.29	51.43 51.45	3.45 3.35	16.00 15.97	1717	308 nm 436 nm	4.44 4.61
1d	174-175 65.44	$C_{15}H_{10}Cl_2N_4O_3$ 365.19	49.33 49.48	2.79 2.95	15.34 15.19	1713	314 nm 444 nm	4.43 4.60
1e	185-187 70.46	$C_{15}H_{10}Br_2N_4O_3$ 454.10	39.67 39.47	2.22 2.34	12.34 11.85	1672	313 nm 447 nm	4.32 4.45
1f	164-165 63.14	$C_{17}H_{16}N_4O_5$ 356.33	57.30 56.96	4.53 4.76	15.72 15.70	1716	310 nm 440 nm	4.53 4.68
2a	218-219 91.3	$C_{21}H_{16}N_6O$ 368.4	68.47 68.55	4.38 4.58	22.81 20.92	1765	322 nm 438 nm	5.10 5.04
2b	222-224 95.4	$C_{25}H_{20}N_6O$ 396.45	69.68 68.99	5.08 4.99	21.20 20.90	1700	327 nm 459 nm	4.41 4.32
2c	221-222 93.5	$C_{21}H_{14}F_2N_6O$ 404.38	62.37 62.05	3.49 3.20	20.78 20.95	1768	325 nm 435 nm	4.40 4.31
2d	223-225 97.0	$C_{21}H_{14}Cl_2N_6O$ 437.38	57.67 57.45	3.23 3.23	19.21 20.50	1768	324 nm 441 nm	4.42 4.36
2e	243-244 90.9	$C_{21}H_{14}Br_2N_6O$ 526.18	47.93 47.55	2.68 2.45	15.97 16.95	1742	330 nm 450 nm	4.11 4.24
2f	218-219 94.2	$C_{23}H_{20}N_6O_3$ 428.45	64.48 64.20	4.70 4.28	19.61 19.90	1786	335 nm 465 nm	4.43 4.23
3a	245-255 69.3	$C_{21}H_{15}ClN_6O \cdot 3.5H_2O$ 465.94	54.13 54.70	4.76 4.25	18.04 18.14	1728	306 nm	4.64
3b	210-212 57.2	$C_{23}H_{19}ClN_6O \cdot 3H_2O$ 484.99	56.96 56.88	5.20 4.56	17.33 16.33	1710	305 nm	4.54
3d	230-235 70.7	$C_{21}H_{13}Cl_3N_6O \cdot 3.5H_2O$ 534.87	47.15 46.89	3.77 3.19	15.71 14.50	1749	308 nm	4.52
4a	127-128 97.9	$C_{27}H_{17}N_9O_8 \cdot 0.5H_2O$ 604.49	53.65 53.78	3.00 3.01	20.85 20.02	1631	307 nm	4.62
4b	129-131 93.04	$C_{29}H_{21}N_9O_8$ 623.54	55.86 55.69	3.39 3.18	20.22 19.11	1634	313 nm	4.70
4c	119-121 96.0	$C_{27}H_{15}F_2N_9O_8$ 631.47	51.36 51.45	2.39 2.22	19.96 18.82	1634	309 nm	4.70
4d	134-135 90.3	$C_{27}H_{15}Cl_2N_9O_8$ 664.47	48.81 49.29	2.28 2.17	18.87 18.01	1698	311 nm	4.64
4e	136-138 96.0	$C_{27}H_{15}Br_2N_9O_8$ 753.27	43.05 43.00	2.01 2.00	16.74 15.66	1700	309 nm	4.65
4f	126-128 93.8	$C_{29}H_{21}N_9O_{10}$ 655.54	53.13 52.89	3.23 3.11	19.23 18.52	1689	307 nm	4.49

* ref. (10): 166 °C

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