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-dihydroquinoxaline-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-d₆ ;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.1⁻¹.

Experimental

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

A solution of NaNO₂ (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 NaHCO₃ (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 CHCI₃ 50-150 ml. The solution was filtered after 3 hours of stirring. The filtrate was evaporated, the residue was dissolved in H₂O (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

¹H-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)
lf	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)	Formula	ElementalAnalysis			(2.0)		
	Yield (%)	M.w.	% C		a) % N	V(C=O)	A(max)	(loge)
	165-167*	C.H.N.O.	60.80	4.08	18.01		204 pm	1 66
1a	68 52	296.28	60.79	4.08	17.99	1740	439 nm	4.00
	173-174	CuHUNO 05HO	61.25	5.14	16.81	12 Dates	317 nm	4.70
1b	57.00	333.34	61.08	4.89	16.00	1716	448 nm	4 44
1c	178-179	CisHipFiNi Oz. HiO	51.43	3.45	16.00	1717	308 nm	4 44
	55.08	350.29	51.45	3.35	15.97		436 nm	4.61
1d	174-175	C15H10Cl2N4 O3	49.33	2.79	15.34	1713	314 nm	4.43
	65.44	365.19	49.48	2.95	15.19		444 nm	4.60
1e	185-187	C15H10Br2N4 O3	39.67	2.22	12.34	1672	313 nm	4.32
	70.46	454.10	39.47	2.34	11.85		447 nm	4.45
1f	164-165	C ₁₇ H ₁₆ N ₄ O ₅	57.30	4.53	15.72	1716	310 nm	4.53
	63.14	356.33	56.96	4.76	15.70		440 nm	4.68
20	218-219	C ₂₁ H ₁₆ N ₆ O	68.47	4.38	22.81	1765	322 nm	5.10
24	91.3	368.4	68.55	4.58	20.92		438 nm	5.04
2h	222-224	C ₂₃ H ₂₀ N ₆ O	69.68	5.08	21.20	1700	327 nm	4.41
20	95.4	396.45	68.99	4.99	20.90		459 nm	4.32
2c	221-222	$C_{21}H_{14}F_{2}N_{6}O$	62.37	3.49	20.78	1768	325 nm	4.40
	93.5	404.38	62.05	3.20	20.95		435 nm	4.31
2d	223-225	$C_{21}H_{14}CI_2N_6O$	57.67	3.23	19.21	1768	324 nm	4.42
	97.0	437.38	57.45	3.23	20.50		441 nm	4.36
2e	243-244	$C_{21}H_{14}Br_2N_6O$	47.93	2.68	15.97	1742	330 nm	4.11
	90.9	<u> </u>	47.33	2.43	10.93		430 mm	4.24
2f	01 7	428 45	64.40	4.70	10 00	1786	465 nm	4.43
3a	245-255	C.H.CIN.O. 15H.O	54.13	4.20	19.90	1728	306 nm	4.64
	69 3	465 94	54 70	4.76	18.04			
3b	210-212	CarHunCINCO 3HaO	56.96	5.20	17.33	1710	305 nm	4.54
	57.2	484.99	56.88	4.56	16.33			
3d	230-235	C21H13Cl3N6O, 3.5H2O	47.15	3.77	15.71	1749	308 nm	4.52
	70.7	534.87	46.89	3.19	14.50			
4 a	127-128	C ₂₇ H ₁₇ N ₉ O ₈ . 0.5H ₂ O	53.65	3.00	20.85	1631	307 nm	4.62
	97.9	604.49	53.78	3.01	20.02			
4b	129-131	C ₂₉ H ₂₁ N ₉ O ₈	55.86	3.39	20.22	1634	313 nm	4.70
	93.04	623.54	55.69	3.18	19.11			
4c	119-121	C27H15F2N9 O8	51.36	2.39	19.96	1634	200 nm	4 70
	96.0	631.47	51.45	2.22	18.82		307 1111	4.70
4d	134-135	C27H15Cl2N9 O8	48.81	2.28	18.87	1698	311 nm	4 64
	90.3	664.47	49.29	2.17	18.01		JITUII	7.07
4 e	136-138	C ₂₇ H ₁₅ Br ₂ N ₉ O ₈	43.05	2.01	16.74	1700	309 nm	4.65
	96.0	753.27	43.00	2.00	15.66		507 mil	
4f	126-128	$C_{29}H_{21}N_9O_{10}$	53.13	3.23	19.23	1689	307 nm	4 49
	93.8	655.54	52.89	3.11	18.52		507 mm	7.77

* ref. (10): 166 °C

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