An anomalous course of the condensation of 1,5-diaryl-3-formazyl glyoxylic acids with o-phenylenediamine. A simple synthesis of some benzimidazole-2-carboxamidarylhydrazones.

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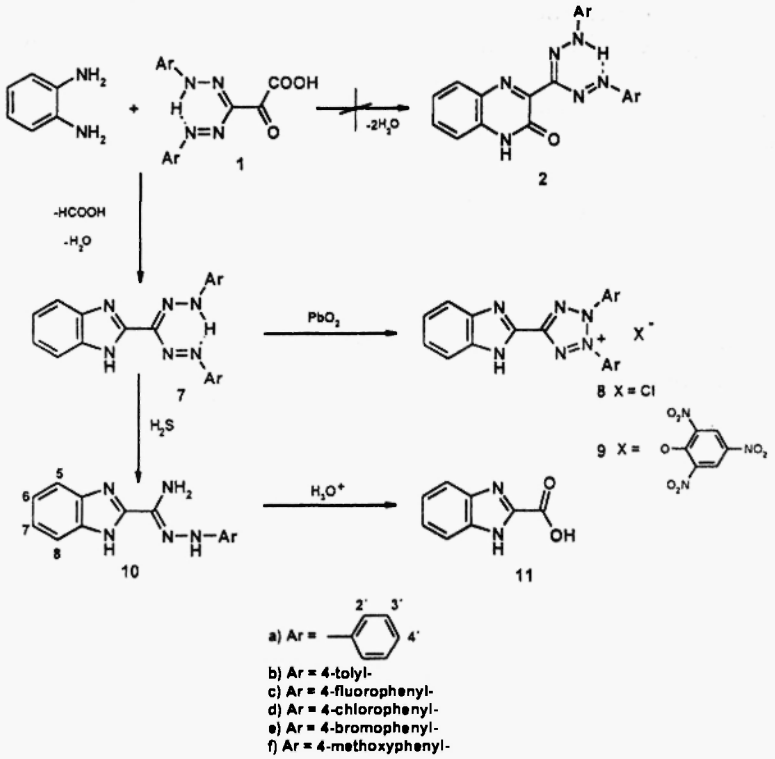
Abstract

The condensation of 1,5-diaryl-3-formazylglyoxylic acids **1** with o-phenylenediamine did not afford 1,2-dihydro-3-(1,5-diaryl-3-formazyl)-chinoxalin-2-ones **2** as it had been described in a previous communication[1] , but actually 1,5-diaryl-3-(2-benzimidazol-2-yl)-formazanes **7** with simultaneous elimination of formic acid. Also tetrazolium chlorides **3** and analogous picrates **4** described in the same communication[1] were not derivatives of 1,2-dihydro-quinoxaline-2-one, but in fact they were 2,3-diaryl-5-(benzimidazol-2-yl)-tetrazolium chlorides **8** and analogous picrates **9**.
Formazans **7** were transformed by reductive splitting into benzimidazol-2-carboxamid arylhydrazones **10**.

Introduction and Results



The subject of our the previous communication[1] was the synthesis of 1,5-diaryl-3-formazylglyoxylic acids **1a-f** and their condensation with o-phenylenediamine.

The reaction of α-ketocarboxylic acids with o-phenylenediamine leading to 1,2-dihydro-quinoxaline-2-ones has already been known for a long time[2]. It is a quite general

method running with high yields and it has been used for the preparation of a great number of substituted quinoxaline derivatives[3-5].

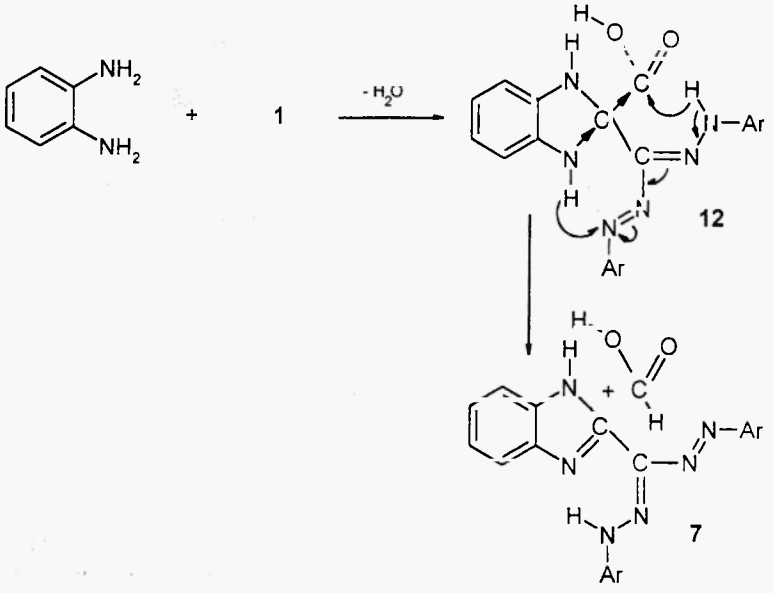
We did not suppose that the reaction of o-phenylenediamine with α-ketocarboxylic acids **1** could proceed in another way and for this reason the new compounds were formulated as 1,2-dihydro-3-(1,5-diaryl-3-formazyl)-quinoxaline-2-ones **2a-f** without more detailed confirmation of their structure[1].

The subject of this communication is a revision of the mentioned structures. We found that in the mentioned reaction of o-phenylenediamine with 1,5-diaryl-3- formazylglyoxylic acids **1a-f** did not arise stated derivatives of chinoxaline **2a-f** but in fact the 1,5-diaryl-3-(benzimidazol-2-yl)-formazans **7a-f**.

This surprising finding came out from the results of ^{13}C NMR and mass spectroscopies. While results of ^{1}H NMR and IR spectroscopies were not in inconsistency with the mentioned structure **2**[1], the results of ^{13}C NMR spectroscopy excluded this structure (the signal C=O group at 160-180 ppm was missing). The results of mass spectroscopy also confirmed the structure **7** with respect to the fact that the molecular ion corresponds exactly to the molecular mass of compounds **7**. Also the course of the reductive splitting of these compounds with H_2S is in agreement with the structure **7** since benzimidazole-2-carboxamid arylhydrazones **10a-f** are formed in good yield. It is interesting, that in this case reaction differs from analogous reaction proceeding at formazans of sacharide family, the result of which are appropriate thiohydrazides[6].

The structure of amidrazones **10** was confirmed both by IR and NMR spectra and by their acid hydrolysis to benzimidazol-2-carboxylic acid **11**.

The mentioned unexpected course of the reaction of o-phenylenediamine with acids **1** can proceed not only under conditions given in our previous work[1] (by boiling in ethanol) but as it was found later the reaction proceeds also at room temperature and even at 0°C. This reaction does not proceed then as with all other α-ketocarboxylic acids e.g. by elimination of 2 mol of water and by formation of 1,2-dihydro-quinoxaline-2-ones, but with elimination of 1 mol of water and 1 mol of formic acid. The eliminated formic acid was identified in the mother liquor after the isolation of formazans **7** by neutralization as HCOONa. It can be supposed that the key intermediates in this anomalous reaction are benzimidazoline derivatives **12** where the easy elimination of formic acid is caused by a cyclic mechanism in cooperation with hydrogen bonds.



It favour of the formation of the intermediate **12** speaks the creation of the similar benzimidazoline derivative by reaction of o-phenylenediamine with sodium mesoxalate[7].

With respect to the fact that formazans described in our previous work[1] have the structure **7** and not the structure **2** it is necessary to revise also the structure of their oxidation products, that are not tetrazolium salts with quinoxaline substituent (presented in ref.[1] as compounds **3** resp. **4**) but are in fact 2,3-diaryl-5-(benzimidazol-2-yl)-tetrazolium chlorides **8** and resp. picrates **9**.

Apparatus and methods

MS spectra were measured on ZAB-EQ (VG Analytical Ltd., England). ^{13}C NMR spectra were measured on AMX-360 BRUKER (360 MHz) spectrometer in DMSO-δ_6 solutions, chemical shifts δ are in ppm. IR spectra were measured using KBr disc technique and scanned on an ATI Unicam Genesis FTIR instrument.

Experimental

1,5-Diaryl-3-(benzimidazol-2-yl)-formazans (7a-f)

1,5-Diaryl-3-(benzimidazol-2-yl)-formazans **(7a-f)** were prepared by the method mentioned in our previous communication[1] for the compounds **2**. New data these compounds are outlined in tables 1-5.

The condensation of 1,5-diphenyl-3-formazylglyoxalic acid (1a) with o-phenylenediamine at low temperature and a following proof of formation formic acid.

Diphenylformazylglyoxylic acid **1a** (2.00 g, 6.75 mmol) was dissolved in ethanol (70 ml) at room temperature and mixed with a solution of o-phenylenediamine (0.729 g, 6.75 mmol) in ethanol (50 ml). Result solution was left to stand until next day. The precipitated solid was collected with suction [yield: 2.136g (93%)]. The filtrate was mixed with a solution of Na_2CO_3 (0,337 mmol) in water (5 ml). The mixture was then evaporated *in vacuo* and the residue was identified as sodium formate using IR spectroscopy where three characteristic absorption bands 1604, 1358, 774 cm^{-1} were found.

Benzimidazole-2-carboxamidarylhydrazones (10a-f)

A solution of corresponding 1,5-diaryl-3-(benzimidazol-2-yl)-formazan (7) (1 mmol) in ethanol (50-150 ml) was saturated with H_2S. The solution was allowed to stand in the closed flask with intermittent stirring for 7 days. Then the reaction mixture was filtered and the filtrate was taken down in vacuo. The solid was mixed with 5 ml water and 3 ml ethanol and after two hours was heated for 10 minutes. The hot reaction mixture was filtered. The filtrate was taken down in vacuo. The product was purified by recrystallisation from ethanol-wather (1:1). Data of compounds **(10)** are outlined in the tables 1-5.

1H-Benzimidazole-2-carboxylic acid (11)

A solution of benzimidazole-2-carboxamidarylhydrazones **(10a)** (1 mmol) in hydrochloric acid (10 %, 3 ml) was stirred for two days. Then the reaction mixture was taken down. The solution was mixed with little water and the precipitated solid was collected with suction, washed with water and dried in air. M.p. = 170-173 °C (ref.[8]: 169-171 °C). m/s (m/z): 162.1.

Table 1
Characteristic data of compounds **7, 8, 9, 10**

Compound	M.p. (°C) Yield (%)	Formula M.w.	Elemental Analysis (Calcul./Found) %C	%H	%N	m/s (m/z) (rel. int.)	λ (max)	(logε)
7a	218-219 93.0	$C_{20}H_{16}N_6$ 340.39	70.57 70.49	4.74 4.68	24.69 24.83	341.3(100)	322 nm 438 nm	5.10 5.04
7b	222-224 88.66	$C_{22}H_{20}N_6$ 368.44	71.72 71.80	5.47 5.49	22.81 22.71	369.3(80), 391.3(40), 759.1(100)	327 nm 459 nm	4.41 4.32
7c	221-222 87.03	$C_{20}H_{14}N_6F_2$ 376.37	63.83 63.80	3.75 3.60	22.33 22.35	377 (100), 399.5(70), 775.3(85)	325 nm 435 nm	4.40 4.31
7d	223-225 90.8	$C_{20}H_{14}N_6Cl_2$ 409.37	58.68 58.45	3.45 3.43	20.53 20.50	409(100)	324 nm 441 nm	4.42 4.36
7e	243-244 86.06	$C_{20}H_{14}N_6Br_2$ 498.17	48.22 48.35	2.83 2.75	16.87 16.95	497.3(100)	330 nm 450 nm	4.11 4.24
7f	218-219 88.04	$C_{22}H_{20}N_6O_2$ 400.44	65.99 65.80	5.03 4.99	20.99 20.79	401.5(55), 423.5(70), 823.3(100)	335 nm 465 nm	4.43 4.23
8a	245-255 65.1	$C_{20}H_{15}N_6Cl.2,5H_2O$ 428.94	57.20 57.30	4.80 4.64	20.01 20.14	339.2(100), 677.1 (40)	306 nm	4.64
8b	210-212 53.9	$C_{22}H_{19}N_6Cl.2,5H_2O$ 456.99	58.98 58.88	5.40 5.49	18.76 18.33	367.2(100), 733.1 (50)	305 nm	4.54
8d	230-235 66.9	$C_{20}H_{13}N_6Cl_3.2,5H_2O$ 497.92	49.13 49.29	3.71 3.79	17.19 17.38	407.1(100)	308 nm	4.52
9a	127-128 93.4	$C_{26}H_{17}N_9O_7.H_2O$ 585.50	53.34 53.68	3.27 3.01	21.53 21.02	339.2(100)	307 nm	4.62
9b	129-131 88.9	$C_{28}H_{21}N_9O_7$ 595.53	56.47 56.69	3.55 3.47	21.17 21.11	367.2 (100)	313 nm	4.70
9c	119-121 91.7	$C_{26}H_{15}N_9O_7F_2$ 603.46	51.75 51.65	2.51 2.42	20.89 20.82	375.1 (100)	309 nm	4.70
9d	134-135 86.5	$C_{26}H_{15}N_9O_7Cl_2$ 636.46	49.07 49.29	2.38 2.27	19.81 19.51	407.1 (100)	311 nm	4.64
9e	136-138 92.4	$C_{26}H_{15}N_9O_7Br_2$ 725.26	43.05 41.00	2.08 2.00	17.38 16.66	495.3(100)	309 nm	4.65
9f	139-140 93.8	$C_{28}H_{21}N_9O_9$ 627.53	53.59 53.69	3.37 3.21	20.09 19.53	399.2(100)	307 nm	4.49
10a	203-205 84.7	$C_{14}H_{13}N_5$ 251.29	66.92 66.85	5.21 5.50	27.87 27.65	252.2(100)	216 nm 280 nm 348 nm	3.34 3.02 3.36
10b	200-201 82.6	$C_{15}H_{15}N_5$ 265.32	67.91 67.80	5.70 5.75	26.40 26.45	266.3(100)	208 nm 296 nm 352 nm	3.47 3.17 3.21
10c	205-207 87.9	$C_{14}H_{12}N_5F$ 269.28	62.45 62.40	4.49 4.45	26.01 26.15	270.2(100)	208 nm 280 nm 348 nm	3.31 2.96 3.24
10d	202-204 85.0	$C_{14}H_{12}N_5Cl$ 285.78	58.84 58.50	4.23 4.25	24.51 24.40	286.1(100)	204 nm 276 nm 352 nm	3.39 3.05 3.32
10e	220-222 79.9	$C_{14}H_{12}N_5Br$ 330.18	50.92 50.90	3.66 3.60	21.21 21.45	330.2(100)	210 nm 282 nm 346 nm	3.33 3.00 3.20
10f	199-201 89.9	$C_{15}H_{15}N_5O$ 281.32	64.04 63.95	5.37 5.20	24.89 25.00	282.3(100)	207 nm 300 nm 366 nm	3.50 3.15 3.20

Table 2
^{1}H-NMR spectra of compounds **7** and **10**

Compound	^{1}H-NMR spectrum
7a	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)
7b	2:43(s, 6H, CH_3); 7.40(m, 6H, ArH); 7.87(m, 6H, ArH); 13.92(br.s, 2H, NH)
7c	7.43(m, 6H, ArH); 7.96(m, 6H, ArH); 13.96(br.s, 2H, NH)
7d	7.60(m, 6H, ArH); 7.88(m, 6H, ArH); 14.06(br.s, 2H, NH)
7e	7.65(m, 6H, ArH); 7.993(m, 6H, ArH); 13.94(s, 2H, NH)
7f	3.93(s, 6H, CH_3); 7.41(m, 6H, ArH); 7.90(m, 6H, ArH); 13.87(br.s, 2H, NH)
8a	7.48(m, 2H, $H_{4'}$); 7.78(t, 4H, J=7.7, H_3); 7.86(m, 4H, $H_{5\text{-}8}$), 8.05(d, 4H, J=7.7, H_2)
10a	6.21 (b, 2H, NH_2), 6.75 (m, 1H, H_4), 7.27 (m, 6H, $H_{2',3',5',8}$), 7.64 (m, 2H, $H_{6,7}$), 8.77 (b, 1H, $N_\delta H$), 12.50 (b, 1H, $N_\alpha H$)
10b	2.45(s, 3H, CH_3); 6.15(s, 2H, NH_2); 7.10(m, 4H, ArH); 7.57(m, 4H, ArH); 8.62(s, 1H, NH); 12.87(s, 1H, NH)
10c	6.15(s, 2H, NH_2); 7.09(m, 2H, ArH); 7.23(m, 4H, ArH); 7.56(d, 1H, J=5.61, ArH); 7.67(d, 1H, J=5.69, ArH), 8.72(s, 1H, NH); 12.50(s, 1H, NH)
10d	6.22(s, 2H, NH_2); 7.26(m, 5H, ArH); 7.48(m, 3H, ArH); 8.91(s, 1H, NH); 12.53(s, 1H, NH)
10e	6.27(s, 2H, NH_2); 7.30(m, 5H, ArH); 7.55(m, 3H, ArH); 8.80(s, 1H, NH); 12.43(s, 1H, NH)
10f	3.90(s, 3H, CH_3); 6.25(s, 2H, NH_2); 7.50(m, 4H, ArH); 7.85(m, 4H, ArH); 9.22(s, 1H, NH); 12.67(s, 1H, NH)

Table 3
^{13}C-NMR spectra of compounds **7**

Compound	^{13}C-NMR spectrum
7a	147.39, 142.92, 138.58, 136.16, 129.49, 127.15, 123.52, 118.88, 115.91
7b	145.411, 143.186, 138.141, 136.891, 136.224, 130.05, 123.621, 118.953, 116.047, 20.86
7c	162.554, 159.852, 144.184, 142.961, 138.519, 136.252, 123.754, 121.002, 120.909, 116.571, 116.316, 116.096
7d	146.216, 142.744, 138.959, 136.229, 131.515, 129.573, 123.813, 120.730, 116.122
7e	146.585, 142.795, 139.54, 136.244, 132.503, 123.847, 121.071, 119.991, 116.139
7f	158.707, 141.512, 136.226, 123.545, 120.452, 116.006, 114.841, 55.605

Table 4
^{13}C-NMR and ^{15}N-NMR spectra of compound **10a**

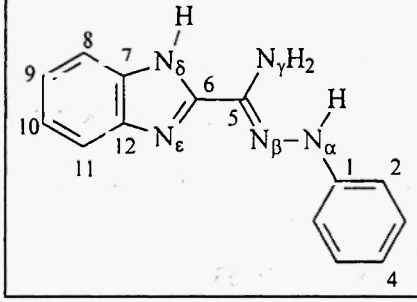
Compound	^{13}C-NMR spectrum and ^{15}N-NMR spectrum
10a 	111.57 (C-11), 112.29 (C-2), 117.95 (C-4), 118.77 (C-8), 121.48 (C-9), 122.91 (C-10), 128.90 (C-3), 134.69 (C-6), 134.98 (C-7), 143.04 (C-12), 146.53 (C-1), 147.81 (C-5).
	-253.64 (N_δ), -136.50 (N_ε), -317. 12 (N_γ). $^{1}J(^{15}N_\gamma, ^{1}H)$ = 86.6 Hz, $^{1}J(^{15}N_\delta, ^{1}H)$ = 91.2 Hz.

Figure 1
^{1}H-^{15}N HMBC spectrum of compound **10a**

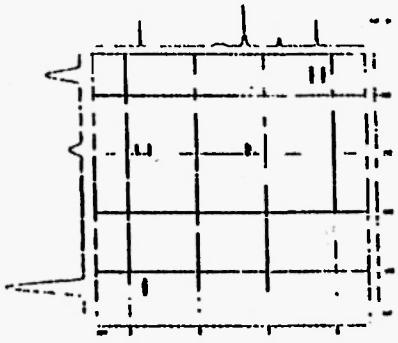


Table 5
IR spectra of compounds **7** and **10**

Compound	IR spectrum
7a	3289, 1600, 1553, 1486, 1414, 1284, 1224, 748, 689, 548
7b	3355, 1615, 1581, 1581, 1458, 1342, 1215, 1163, 1100, 1079, 920, 832, 724, 515, 423
7c	3332, 1631, 1560, 1496, 1434, 1359, 1286, 1286, 1222, 1172, 1143, 1095, 923, 833, 753, 516, 430
7d	3339, 3063, 1593, 1553, 1481, 1428, 1288, 1226, 1090, 826, 723, 506
7e	3330, 1621, 1584, 1491, 1422, 1350, 1235, 1202, 1172, 1105, 1096, 986, 838, 739, 552, 434
7f	3339, 1618, 1532, 1495, 1343,1230, 1170, 1148, 1025, 906, 853, 428
10a	3278, 1626, 1599, 1509, 1496, 1429, 1394, 1335, 1308, 1253, 1143, 1067, 884, 747, 695
10b	3154, 3037, 1638, 1612, 1512, 1437, 1333, 1249, 1172, 812, 715, 631
10c	3432, 1651, 1610, 1503, 1439, 1337, 1252, 1204, 1156, 822, 748, 583
10d	3258, 1658, 1597, 1526, 1493, 1485, 1450, 1392, 1305, 1251, 1157, 1087, 822, 749, 588
10e	3279, 1600, 1590, 1546, 1485, 1432, 1387, 1300, 1157, 1028, 890, 799, 478
10f	3434, 3069, 3000, 1629, 1607, 1579, 1430, 1349, 1272, 1100, 715, 599

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References:

(1) I. Wiedermannová, J. Slouka: Heterocyclic Commun. **7**, 55 (2001)
(2) O. Hinsberg: Liebigs Ann. Chem. **292**, 245 (1896)
(3) J. C. E. Simpson: „Condensed pyridazine and pyrazine rings", A. E.Weissberger, ed. Interscience New York (1953)
(4) Y. T. Pratt: The Quinoxaline – In Heterocyclic Compounds,Vol. 6, Chapter 10, (R.C. Elderfield, ed), Wiley New York (1956)
(5) D. C. Morrison: J. Am. Chem. Soc. **76**, 4483 (1954)
(6) G. Zemplén, L. Mester, A. A. Messmer: Chem. Ber. **86**, 697 (1953)
(7) E. C. Taylor, M. J. Thompson: J. Org. Chem. **26**, 3511 (1961)
(8) R. A. B. Copeland, A. R. Day: J. Am. Chem. Soc. **65**, 1072 (1943)

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