

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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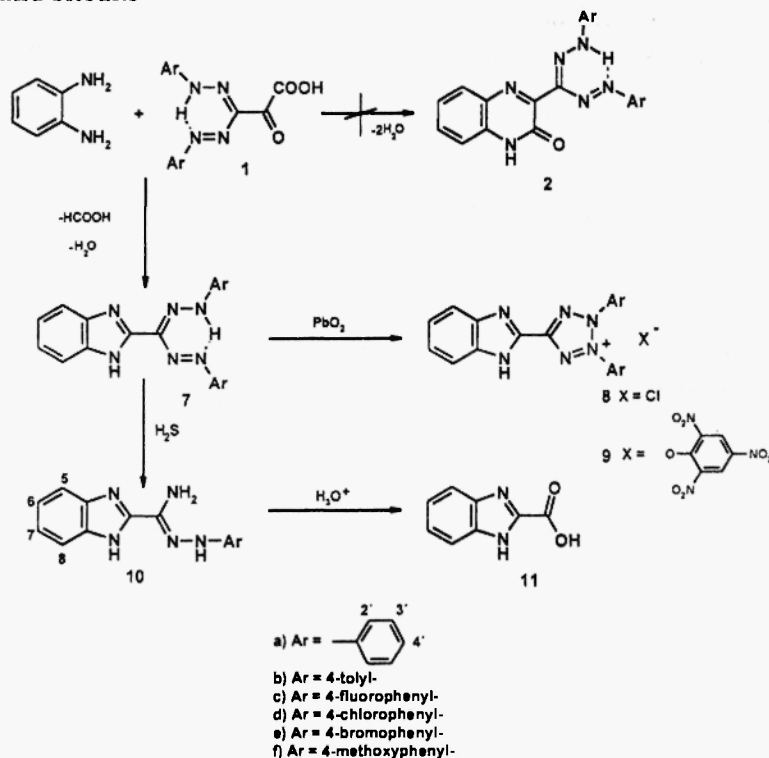
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Abstract

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 communication¹, 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 communication¹ 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-carboxamidarylhydrazones **10**.

Introduction and Results



The subject of our the previous communication¹ 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 time². 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 derivatives³⁻⁵.

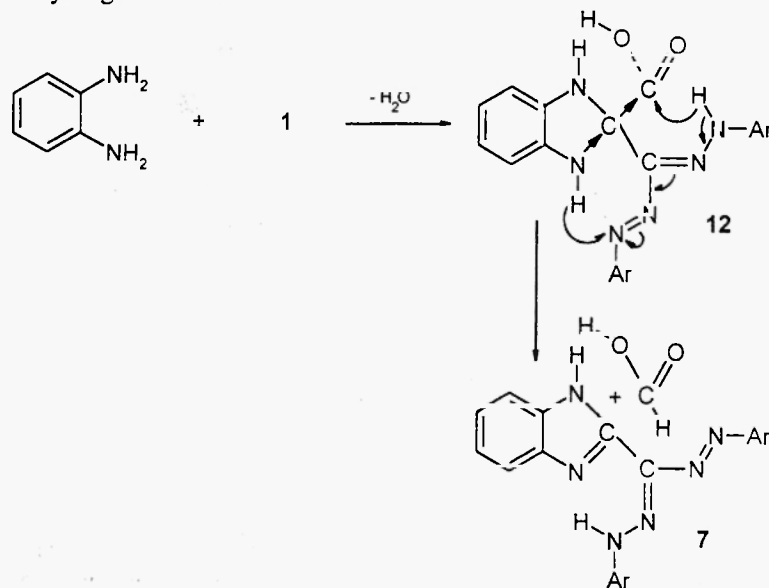
We did not suppose that the reaction of *o*-phenylenediamine with α -ketocarboxylic acids **1** could proceed in another way and for this reason the new compounds were formulated as 1,2-dihydro-3-(1,5-diaryl-3-formazyl)-quinoxaline-2-ones **2a-f** without more detailed confirmation of their structure¹.

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 quinoxaline **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 ¹³C NMR and mass spectroscopies. While results of ¹H NMR and IR spectroscopies were not in inconsistency with the mentioned structure **2**¹, the results of ¹³C 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 H₂S 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 thiohydrazides⁶.

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 work¹ (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 favours the formation of the intermediate **12** speaks the creation of the similar benzimidazoline derivative by reaction of *o*-phenylenediamine with sodium mesoxalate⁷.

With respect to the fact that formazans described in our previous work¹ 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). ¹³C 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 communication¹ for the compounds **2**. New data these compounds are outlined in tables 1-5.

The condensation of 1,5-diphenyl-3-formazylglyoxylic 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 Na₂CO₃ (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-carboxamidarylhyazones (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 H₂S. 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-water (1:1). Data of compounds (**10**) are outlined in the tables 1-5.

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

A solution of benzimidazole-2-carboxamidarylhyazones (**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) | | | m/s (m/z) (rel. int.) | λ (max) | (logε) |
|----------|------------------------|---|---------------------------------------|------|-------|--|---------|--------|
| | | | %C | %H | %N | | | |
| 7a | 218-219 93.0 | C ₂₀ H ₁₆ N ₆ 340.39 | 70.57 | 4.74 | 24.69 | 341.3(100) | 322 nm | 5.10 |
| | | | 70.49 | 4.68 | 24.83 | | 438 nm | 5.04 |
| 7b | 222-224 88.66 | C ₂₂ H ₂₀ N ₆ 368.44 | 71.72 | 5.47 | 22.81 | 369.3(80), 391.3(40), 759.1(100) | 327 nm | 4.41 |
| | | | 71.80 | 5.49 | 22.71 | | 459 nm | 4.32 |
| 7c | 221-222 87.03 | C ₂₀ H ₁₄ N ₆ F ₂ 376.37 | 63.83 | 3.75 | 22.33 | 377 (100), 399.5(70), 775.3(85) | 325 nm | 4.40 |
| | | | 63.80 | 3.60 | 22.35 | | 435 nm | 4.31 |
| 7d | 223-225 90.8 | C ₂₀ H ₁₄ N ₆ Cl ₂ 409.37 | 58.68 | 3.45 | 20.53 | 409(100) | 324 nm | 4.42 |
| | | | 58.45 | 3.43 | 20.50 | | 441 nm | 4.36 |
| 7e | 243-244 86.06 | C ₂₀ H ₁₄ N ₆ Br ₂ 498.17 | 48.22 | 2.83 | 16.87 | 497.3(100) | 330 nm | 4.11 |
| | | | 48.35 | 2.75 | 16.95 | | 450 nm | 4.24 |
| 7f | 218-219 88.04 | C ₂₂ H ₂₀ N ₆ O ₃ 400.44 | 65.99 | 5.03 | 20.99 | 401.5(55), 423.5(70), 823.3(100) | 335 nm | 4.43 |
| | | | 65.80 | 4.99 | 20.79 | | 465 nm | 4.23 |
| 8a | 245-255 65.1 | C ₂₀ H ₁₅ N ₆ Cl ₂ ·2,5H ₂ O 428.94 | 57.20 | 4.80 | 20.01 | 339.2(100), 677.1 (40) | 306 nm | 4.64 |
| | | | 57.30 | 4.64 | 20.14 | | | |
| 8b | 210-212 53.9 | C ₂₂ H ₁₉ N ₆ Cl ₂ ·2,5H ₂ O 456.99 | 58.98 | 5.40 | 18.76 | 367.2(100), 733.1 (50) | 305 nm | 4.54 |
| | | | 58.88 | 5.49 | 18.33 | | | |
| 8d | 230-235 66.9 | C ₂₀ H ₁₃ N ₆ Cl ₃ ·2,5H ₂ O 497.92 | 49.13 | 3.71 | 17.19 | 407.1(100) | 308 nm | 4.52 |
| | | | 49.29 | 3.79 | 17.38 | | | |
| 9a | 127-128 93.4 | C ₂₆ H ₁₇ N ₉ O ₇ ·H ₂ O 585.50 | 53.34 | 3.27 | 21.53 | 339.2(100) | 307 nm | 4.62 |
| | | | 53.68 | 3.01 | 21.02 | | | |
| 9b | 129-131 88.9 | C ₂₈ H ₂₁ N ₉ O ₇ 595.53 | 56.47 | 3.55 | 21.17 | 367.2 (100) | 313 nm | 4.70 |
| | | | 56.69 | 3.47 | 21.11 | | | |
| 9c | 119-121 91.7 | C ₂₆ H ₁₅ N ₉ O ₇ F ₂ 603.46 | 51.75 | 2.51 | 20.89 | 375.1 (100) | 309 nm | 4.70 |
| | | | 51.65 | 2.42 | 20.82 | | | |
| 9d | 134-135 86.5 | C ₂₆ H ₁₅ N ₉ O ₇ Cl ₂ 636.46 | 49.07 | 2.38 | 19.81 | 407.1 (100) | 311 nm | 4.64 |
| | | | 49.29 | 2.27 | 19.51 | | | |
| 9e | 136-138 92.4 | C ₂₆ H ₁₅ N ₉ O ₇ Br ₂ 725.26 | 43.05 | 2.08 | 17.38 | 495.3(100) | 309 nm | 4.65 |
| | | | 41.00 | 2.00 | 16.66 | | | |
| 9f | 139-140 93.8 | C ₂₈ H ₂₁ N ₉ O ₉ 627.53 | 53.59 | 3.37 | 20.09 | 399.2(100) | 307 nm | 4.49 |
| | | | 53.69 | 3.21 | 19.53 | | | |
| 10a | 203-205 84.7 | C ₁₄ H ₁₃ N ₅ 251.29 | 66.92 | 5.21 | 27.87 | 252.2(100) | 216 nm | 3.34 |
| | | | 66.85 | 5.50 | 27.65 | | 280 nm | 3.02 |
| 10b | 200-201 82.6 | C ₁₅ H ₁₃ N ₅ 265.32 | 67.91 | 5.70 | 26.40 | 266.3(100) | 208 nm | 3.47 |
| | | | 67.80 | 5.75 | 26.45 | | 296 nm | 3.17 |
| 10c | 205-207 87.9 | C ₁₄ H ₁₂ N ₅ F 269.28 | 62.45 | 4.49 | 26.01 | 270.2(100) | 208 nm | 3.31 |
| | | | 62.40 | 4.45 | 26.15 | | 280 nm | 2.96 |
| 10d | 202-204 85.0 | C ₁₄ H ₁₂ N ₅ Cl 285.78 | 58.84 | 4.23 | 24.51 | 286.1(100) | 204 nm | 3.39 |
| | | | 58.50 | 4.25 | 24.40 | | 276 nm | 3.05 |
| 10e | 220-222 79.9 | C ₁₄ H ₁₂ N ₅ Br 330.18 | 50.92 | 3.66 | 21.21 | 330.2(100) | 210 nm | 3.33 |
| | | | 50.90 | 3.60 | 21.45 | | 282 nm | 3.00 |
| 10f | 199-201 89.9 | C ₁₅ H ₁₅ N ₅ O 281.32 | 64.04 | 5.37 | 24.89 | 282.3(100) | 207 nm | 3.50 |
| | | | 63.95 | 5.20 | 25.00 | | 300 nm | 3.15 |
| | | | | | | 366 nm | 3.20 | |

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

| Compound | $^1\text{H-NMR}$ 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, $\text{H}_{5,8}$), 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, $\text{H}_2, 3, 5, 8$), 7.64 (m, 2H, $\text{H}_6, 7$), 8.77 (b, 1H, N_δH), 12.50 (b, 1H, N_αH) |
| 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
 $^{13}\text{C-NMR}$ spectra of compounds **7**

| Compound | $^{13}\text{C-NMR}$ 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
 $^{13}\text{C-NMR}$ and $^{15}\text{N-NMR}$ spectra of compound **10a**

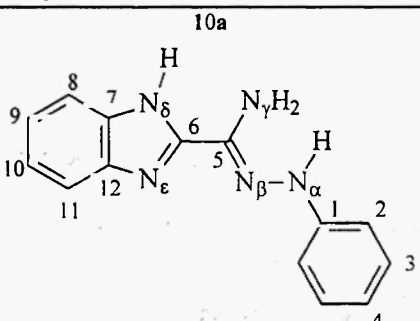
| Compound | $^{13}\text{C-NMR}$ spectrum and $^{15}\text{N-NMR}$ spectrum |
|---|--|
|  | 111.57 (C-11), 112.29 (C-2), 117.95 (C-4), 118.77 (C-8), 121.48 (C-9), 122.91 (C-10), 128.90 (C-3), 134.69 (C-6), 134.98 (C-7), 143.04 (C-12), 146.53 (C-1), 147.81 (C-5). -253.64 (N_δ), -136.50 (N_ϵ), -317.12 (N_γ). $^1J(^{15}\text{N}_\gamma, ^1\text{H}) = 86.6$ Hz, $^1J(^{15}\text{N}_\delta, ^1\text{H}) = 91.2$ Hz. |

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

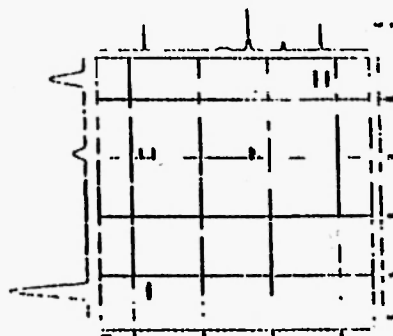


Table 5
 IR spectra of compounds **7** and **10**

| 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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