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Reactions of 3*H*-furan-2-ones and 2*H*-chromen-2-ones with pyrazole-3(5)-diazonium salts

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Abstract: Derivatives of the new heterocyclic system, 6*H*-chromeno[4,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazin-6-one, were obtained by the reaction of pyrazole-3(5)-diazonium salts with 4-hydroxy-2*H*-chromen-2-one. Similar reactions with 5-phenyl-3*H*-furan-2-one followed by intramolecular heterocyclization furnished 6-(4-halophenyl)-7-alkyl-2-phenylfuro[2,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazines.

Keywords: 3*H*-furan-2-one; azo compounds; cyclocondensation; heterocyclic; intramolecular; pyrazolo[5,1-*c*][1,2,4] triazine.

Introduction

The structure and stability of pyrazole-3(5)-diazonium salts are the subject of many research reports [1–8]. However, the reactions of pyrazole-diazonium salts with heterocycles remain poorly studied [9]. The ability of the reaction products to undergo further cyclizations has not been sufficiently investigated. At the same time, the use of methylene-active compounds of heterocyclic series as the azo component in reactions with pyrazole-3(5)-diazonium salts opens up wide opportunities for the synthesis of new promising biologically active polyheterocyclic systems [10–13]. Previously, successful attempts have been made to react pyrazole-3(5)-diazonium salts with several methylene-active heterocyclic compounds including barbituric and thiobarbituric acids, isochromane-1,3-diones, as well as the derivatives of pyridine-2,4-dione, pyran-2,4-dione and pyrimidine-2,4-dione [14–16]. The purpose of this work was to synthesize derivatives of substituted pyrazolotriazines by introducing into their structure oxygen-containing six- and five-membered rings.

Results and discussion

In continuation of our previous research, the pyrazole-3(5)-diazonium salt **1a–c** was allowed to react with 4-hydroxy-2*H*-chromen-2-one (**2**). This reaction furnished colored azo compounds **3a–c** or hydrazones **3′a–c** [17, 18] that were difficult to isolate. Heating under reflux of **3a–c** or **3′a–c** under acid catalysis led to intramolecular cyclocondensation of these compounds due to attack of the endo-cyclic nitrogen atom of pyrazole at the cyclic ketone group. Based on proton nuclear magnetic resonance (^{1}H NMR) spectroscopic data, the products were 6*H*-chromeno[4,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazin-6-ones **4a–c**. These products were obtained in 66–85% yields. Their ^{1}H NMR spectra show no signals of the NH protons of the pyrazole and hydrazone fragments within the typical range of 12–13 ppm, as well as no proton signals of the hydroxyl groups of the salicylic fragment [19, 20].

In contrast to the reaction of Scheme 1, the hydrazones **6b–d**, obtained by coupling of pyrazole-3(5)-diazonium salts **1b–d** with 5-phenyl-3*H*-furan-2-one (**5**), were isolated and characterized (Scheme 2). Under acid catalysis, compounds **6b–d** underwent intramolecular cyclocondensation to new derivatives of phenylfuro[2,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazines **7b–d**. The reaction was carried out under reflux in acetic acid for 6 h.

In summary, the reactions of readily available pyrazole-3(5)-diazonium salts with heterocyclic azo components are convenient ways for obtaining new derivatives of pyrazolo[5,1-*c*][1,2,4]triazine and polyheterocyclic ensembles with their fragments.

Experimental

^{1}H NMR spectra were recorded on a Varian 400 and a Bruker DRX-500 (400 and 500 MHz, respectively) spectrometers at 20°C in hexadeuterated dimethylsulfoxide (DMSO-d_6) in the presence of tetramethylsilane (TMS) as internal standard. Elemental analysis was carried out on a Carlo Erba NA 1500 and a VarioMicroCube devices. Melting

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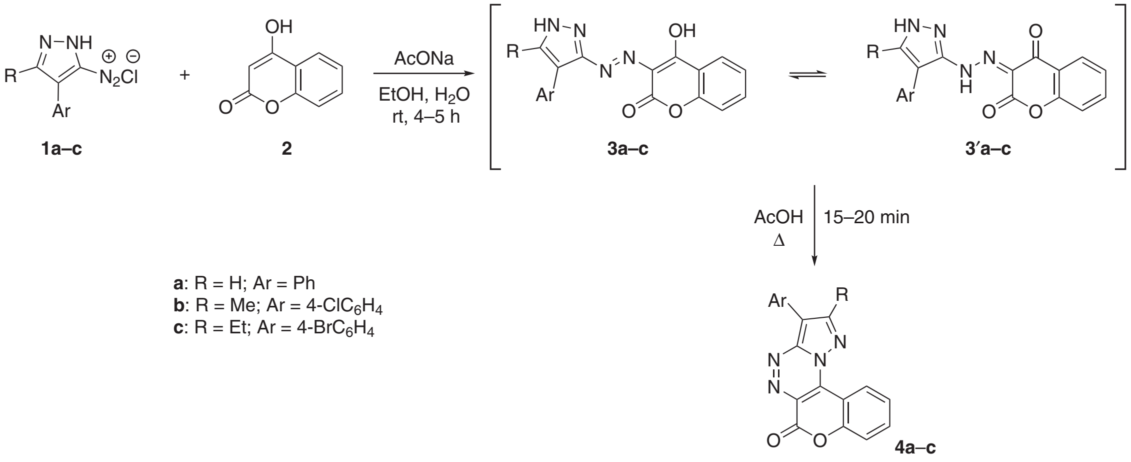
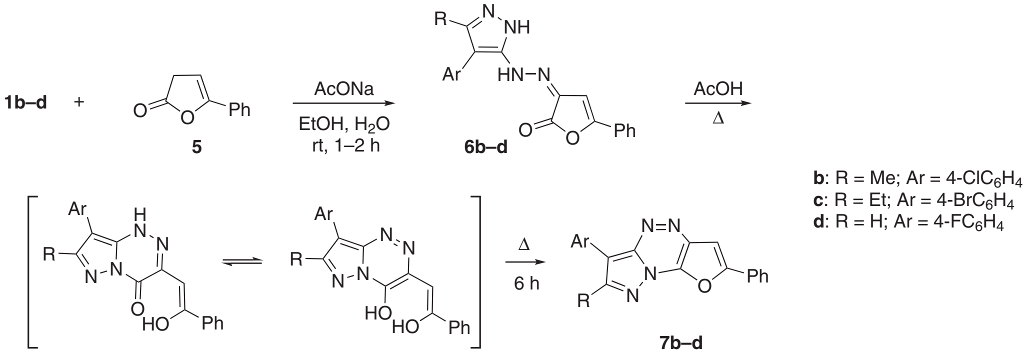


Scheme 1



Scheme 2

points were measured on a Stuart SMP30 instrument. Qualitative analysis of the reaction mixtures was carried out using thin layer chromatography (TLC) on silica gel 60 F245, silufol UV-245 and alugram N/UN$_{245}$ plates, eluting with hexane, ethyl acetate and chloroform or their mixtures. Chromatograms were visualized under UV light or exposure to iodine vapor.

General synthesis of compounds 4a–c, 6b–d and 7b–d

A solution of 10 mmol of a substituted 5-aminopyrazole (10 mmol) in water (15 mL) and hydrochloric acid (30 mL, d = 1.19 g/cm^3) was stirred at 0°C and treated with an aqueous solution of $NaNO_2$ (10 mmol, 10%). After stirring for 10 min at 0°C, the solution of the resultant pyrazole-3(5)-diazonium salt **1a–d** was transferred in portions to a mixture containing compound **2** or **5** (10 mmol), ethanol (10 mL) and a saturated aqueous solution of sodium acetate (7 mL). The mixture was stirred for 4–5 h and then the precipitate of **3a–c** or **6b–d** was filtered off, washed with water and dried at room temperature. A solution of each individual compound in acetic acid (50 mL) was heated under reflux for 20 min for product **4a–c** and for 6 h for product **7b–d**. The solution was cooled slowly, and the resultant crystalline precipitate was filtered off, washed with cold 2-propanol (50 mL), dried and crystallized from acetic acid.

3-Phenyl-6*H*-chromeno[4,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazin-6-one (4a) This compound was obtained from **1a**; red crystals; yield 66%; mp 260–262°C; ^{1}H NMR: δ 7.41 (t, 1H, $^3J = 7.4$ Hz), 7.56–7.64 (m, 4H), 7.92–7.97 (m, 1H), 8.36 (d, 2H, $^3J = 7.6$ Hz), 9.23 (s, 1H), 9.81 (d, 1H, $^3J = 8.3$ Hz). Anal. Calcd for $C_{18}H_{10}N_4O_2$: C, 68.79; H, 3.12; N, 17.83. Found: C, 68.85; H, 3.12; N, 17.90.

3-(4-Chlorophenyl)-2-methyl-6*H*-chromeno[4,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazin-6-one (4b) This compound was obtained from **1b**; red-orange crystals; yield 82%; mp 270–272°C; ^{1}H NMR: δ 1.29 (s, 3H), 7.51 (t, 1H, $^3J = 7.5$ Hz), 7.62–7.67 (m, 2H), 7.87–7.98 (m, 5H, $^3J = 7.6$ Hz), 9.79 (d, 1H, $^3J = 8.1$ Hz). Anal. Calcd for $C_{19}H_{11}ClN_4O_2$: C, 62.91; H, 3.06; N, 15.44. Found: C, 62.85; H, 3.06; N, 15.48.

3-(4-Bromophenyl)-2-ethyl-6*H*-chromeno[4,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazin-6-one (4c) This compound was obtained from **1c**; orange crystals; yield 75%; mp 265–267°C; ^{1}H NMR: δ 1.27 (t, 3H), 2.77 (dd, 2H), 7.13–7.88 (m, 7H), 9.56–9.70 (m, 1H), the sample is paramagnetic. Anal. Calcd for $C_{20}H_{13}BrN_4O_3$: C, 57.02; H, 3.11; N, 13.30. Found: C, 57.10; H, 3.15; N, 13.55.

5-Phenyl-3-(2-(4-(4-chlorophenyl)-3-methyl-1*H*-pyralol-5-yl)hydrazono)-3*H*-furan-2-one (6b) This compound was obtained from **1b**; green-yellow crystals; yield 76%; mp 129–131°C; ^{1}H NMR: δ 1.25 (s, 3H), 6.20 (s, 1H), 7.80–7.89 (dd, 4H, $^3J = 7.8$ Hz), 7.25–7.48

(m, 5H, $^3J=7.4$ Hz), 8.70 (s, 1H), 11.80 (s, 1H). Anal. Calcd for $C_{20}H_{15}ClN_4O_2$: C, 63.49; H, 3.97; N, 14.82. Found: C, 63.12; H, 3.97; N, 14.95. N, 14.82.

5-Phenyl-3-(2-(4-(4-bromophenyl)-3-ethyl-1*H*-pyralol-5-yl) hydrazono)-3*H*-furan-2-one (6c) This compound was obtained from **1c**; orange crystals; yield 73%; mp 140–142°C; ^{1}H NMR: δ 1.25 (t, 3H), 2.65 (dd, 2H), 6.51 (s, 1H), 7.26–7.50 (m, 5H, $^3J=7.4$ Hz), 7.76–7.89 (m, 5H, $^3J=7.8$ Hz), 8.77 (s, 1H), 11.94 (s, 1H). Anal. Calcd for $C_{21}H_{17}BrN_4O_2$: C, 57.67; H, 3.89; N, 12.81. Found: C, 57.61; H, 3.89; N, 12.92.

5-Phenyl-3-(2-(4-(4-fluorophenyl)-1*H*-pyrazol-5-yl)hydrazono)-3*H*-furan-2-one (6d) This compound was obtained from **1d**; red-orange crystals; yield 68%; mp 205–207°C; ^{1}H NMR: δ 6.23 (s, 1H), 7.30–7.37 (m, 4H, $^3J=7.3$ Hz), 7.53–7.70 (m, 4H, $^3J=7.6$ Hz), 7.89 (m, 2H, $^3J=7.8$ Hz), 8.71 (s, 1H), 11.90 (s, 1H). Anal. Calcd for $C_{19}H_{13}FN_4O_2$: C, 65.52; H, 3.74; N, 16.09. Found: C, 65.49; H, 3.74; N, 16.12.

6-(4-Chlorophenyl)-7-methyl-2-phenylfuro[2,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazine (7b) This compound was obtained from **9g**; brown crystals; yield 73%; mp 101–103°C; ^{1}H NMR: δ 2.15 (s, 3H), 7.35–7.46 (m, 5H, $^3J=7.4$ Hz), 7.80–8.06 (m, 4H, $^3J=7.9$ Hz), 8.45 (s, 1H). Anal. Calcd for $C_{20}H_{13}ClN_4O$: C, 66.67; H, 3.61; N, 15.56. Found: C, 66.79; H, 3.61; N, 15.62.

6-(4-Bromophenyl)-7-ethyl-2-phenylfuro[2,3-*e*]pyrazolo[5,1-*c*][1,2,4]triazine (7c) This compound was obtained from **9h**; brown crystals; yield 75%; mp 95–97°C; ^{1}H NMR: δ 1.15 (t, 3H), 1.75 (m, 2H), 7.11–7.53 (m, 5H, $^3J=7.3$ Hz), 7.85–8.19 (m, 4H, $^3J=8.1$ Hz), 8.67 (s, 1H). Anal. Calcd for $C_{21}H_{15}BrN_4O$: C, 60.14; H, 3.58; N, 13.37. Found: C, 60.29; H, 3.58; N, 13.12.

6-(4-Fluorophenyl)-2-phenylfuro[2,3-*e*]pyrazolo[5,1-*c*][1,2,4] triazine (7d) This compound was obtained from **9f**; brown crystals; yield 77%; mp 105–107°C; ^{1}H NMR: δ 6.52 (s, 1H), 7.10–7.50 (m, 5H, $^3J=7.3$ Hz), 8.12–8.26 (m, 5H, $^3J=8.2$ Hz), 8.60 (s, 1H). Anal. Calcd for $C_{19}H_{11}FN_4O$: C, 69.09; H, 3.33; N, 16.97. Found: C, 69.21; H, 3.33; N, 16.52.

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