One-pot Synthesis of Novel Polysubstituted Pyrazole and Pyrrolo[2,1-*b*]benzothiazole Derivatives†

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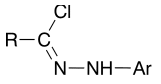
Reaction of hydrazonoyl chlorides **1** and bis-hydrazonoyl chlorides **2** with benzothiazole-2-acetonitrile furnished novel polysubstituted pyrazole and pyrrolo[2,1-*b*]benzothiazole derivatives.

Hydrazonoyl halides are highly versatile intermediates for the synthesis of a variety of heterocyclic systems.[1] In continuation of our interest in the synthesis of novel polyfunctionally substituted heterocycles[2–6] of expected biological importance, we report here a facile, one-pot synthesis of the title compounds *via* reaction of hydrazonoyl chlorides **1** and bis-hydrazonoyl chlorides **2** with benzothiazole-2-acetonitrile.



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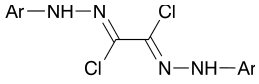
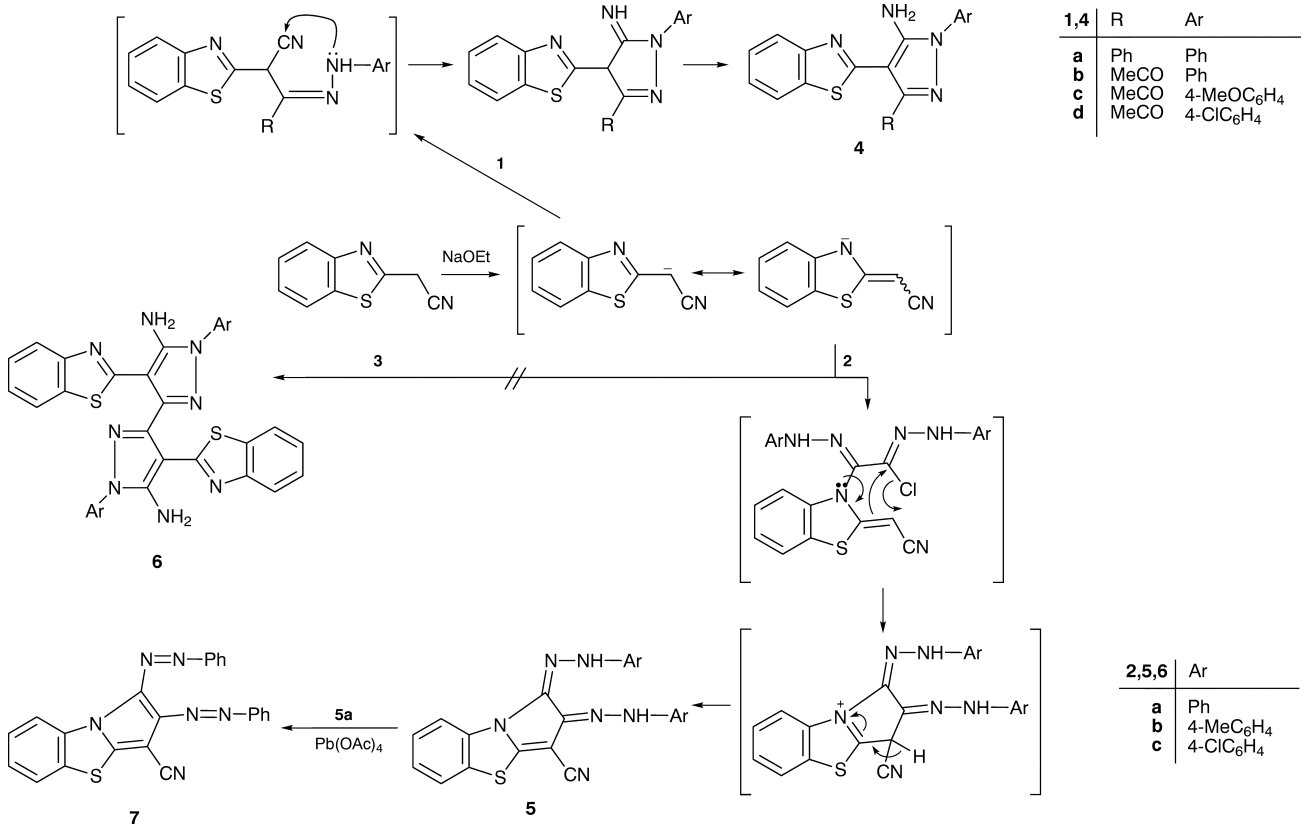


2

Thus, treatment of the hydrazonoyl chlorides **1a–d** with benzothiazole-2-acetonitrile (**3**) in ethanolic sodium ethoxide solution, at room temperature, afforded products identified as 3-substituted 5-amino-1-aryl-4-(benzothiazol-2-yl)pyrazoles **4a–d** (Scheme 1). The appearance for each product of two characteristic IR absorption bands in the region 3450–3200 cm^{-1} and a broad singlet in the NMR spectrum around δ 6.5 due to an amino function provided firm support for structure **4**.

However, when the bis-hydrazonoyl chloride **2a** was treated with 2 mol equivalents of compound **3** under the same reaction conditions, two products were isolated (as examined by TLC). Elemental analyses and spectral data proved that one of these is the unreacted benzothiazole-2-acetonitrile (**3**) (obtained from the mother-liquor after slight acidification). The main product obtained from the reaction mixture was found to be a 1:1 cycloadduct identified as 3-cyano-1,2-diphenylhydrazonopyrrolo[2,1-*b*]benzothiazole-2,3-dione (**5a**). The IR spectrum of **5a** exhibited two absorption bands at 3427 and 3270 cm^{-1} due to two hydrazone NH stretchings as well as a nitrile absorption band at 2218 cm^{-1}, while its ^1H NMR spectrum displayed two D_2O-exchangeable hydrazone NH protons at δ 11.62 besides an aromatic multiplet in the region δ 7.02–8.69. However, all attempts to prepare the 3,3′-bi(5-aminopyrazole) derivative **6a** *via* reaction of **2a** with **3** in a 1:2 molar ratio were unsuccessful. A plausible mechanism for the formation of compounds **3** and **5** is depicted in Scheme 1. Furthermore, the bis(phenyl hydrazone) **5a** was substantiated by its



Scheme 1

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

oxidation with lead tetraacetate in glacial acetic acid at reflux temperature to give 3-cyano-1,2-diphenylazopyrrolo-[2,1-*b*]benzothiazole (**7**). Assignment of structure **7** was made on the basis of its spectral data where its IR spectrum was free of NH absorptions and exhibited only a nitrile absorption band at 2218 cm^{-1}. Prompted by these interesting results and in order to generalize this phenomenon, the reaction of compound **3** with other bis-hydrazonoyl chlorides **2b,c** under the same experimental conditions was examined. The reaction products were found to be 1:1 cycloadducts identified as 3-cyano-1,2-diarylhydrazonopyrrolo[2,1-*b*]-benzothiazole-1,2-diones **5b,c**, respectively.

Experimental

Mps were measured on a Gallenkamp apparatus. IR spectra were recorded for KBr pellets on a Pye–Unicam SP 3-300 infrared spectrophotometer. ^1H NMR spectra were obtained in [^2H]chloroform on a Varian Gemini 200 NMR spectrometer using tetramethylsilane as an internal standard. Mass spectra were recorded on a GCMS-QP 1000 EX mass spectrometer at 70 eV. Microanalyses were carried out at the Microanalytical Center, University of Cairo, Giza, Egypt.

Hydrazonoyl chlorides **1a**[7] and **1b–d**,[8] *N*,*N*′-diarylethanediohydrazonoyl chlorides **2a–c**[9,10] and benzothiazole-2-acetonitrile (**3**)[11] were prepared according to literature procedures.

Synthesis of 5-Aminopyrazoles **4a–d** *and Pyrrolo*[2,1-*b*]*benzothiazoles* **5a–c**. *General procedures*.—Benzothiazole-2-acetonitrile (**3**) (0.348 g, 2 mmol) was added to an ethanolic sodium ethoxide solution [prepared by dissolving sodium metal (46 mg, 2 mmol) in ethanol (25 ml)] with stirring. To the resulting solution was added the appropriate hydrazonoyl chloride **1a–d** (2 mmol) or bis-hydrazonoyl chloride **2a–c** (1 mmol) in portions and the mixture was left to stir overnight. The precipitated product was collected by filtration, washed with water, dried and finally recrystallized from ethanol or *N*,*N*-dimethylformamide–water to afford **4a–d** and **5a–c** in 53–78% and 65–74% yields, respectively. The mother-liquors of **5a–c** were treated with water (10 ml) and concentrated hydrochloric acid (0.5 ml) and the solid product was filtered off and crystallized from ethanol to give, in each case, compound **3**, mp 101–102 °C (lit.,[11] 101–102 °C). **4a** (68%): mp 142–144 °C; ν_{max}/cm^{-1} 3400, 3280 (NH_2), 1600 (C=N); δ_H 6.18 (2 H, s), 7.00–7.90 (14 H, m); *m*/*z* 368 (M^+) (Found: C, 71.51; H, 4.19; N, 15.15; S, 8.73. $C_{22}H_{16}N_4S$ requires C, 71.74; H, 4.34; N, 15.21; S, 8.69%). **4b** (72%): mp 178–180 °C; ν_{max}/cm^{-1} 3409, 3244 (NH_2), 1678 (C=O), 1608 (C=N); δ_H 2.68 (3 H, s), 6.52 (2 H, s), 7.26–7.90 (9 H, m); *m*/*z* 334 (M^+) (Found: C, 64.70; H, 4.16; N, 16.54; S, 9.60. $C_{18}H_{14}N_4OS$ requires C, 64.67; H, 4.19; N, 16.76; S, 9.58%). **4c** (53%): mp 172–174 °C; ν_{max}/cm^{-1} 3444, 3226 (NH_2), 1683 (C=O), 1606 (C=N); δ_H 2.68 (3 H, s), 3.88 (3 H, s), 6.42 (2 H, s), 7.05–7.91 (8 H, M); *m*/*z* 364 (M^+) (Found: C, 62.65; H, 4.31; N, 15.29; S, 8.80. $C_{19}H_{16}N_4O_2S$ requires C, 62.63; H, 4.39; N, 15.38; S, 8.79%). **4d** (78%): mp 187–188 °C; ν_{max}/cm^{-1} 3415, 3225 (NH_2), 1681 (C=O), 1608 (C=N); δ_H 2.68 (3 H, s), 6.53 (2 H, s), 7.20–7.98 (8 H, m); *m*/*z* 368 (M^+) (Found: C, 58.58; H, 3.50; Cl, 9.55; N, 15.21; S, 8.70. $C_{18}H_{13}ClN_4OS$ requires C, 58.61; H, 3.52; Cl, 9.63; N, 15.19; S, 8.68%). **5a** (72%): mp 178–180 °C: ν_{max}/cm^{-1} 3427, 3270 (2 NH), 2218 (C≡N), 1596 (C=N); δ_H 7.02–8.69 (14 H, m), 11.62 (2 H, s); *m*/*z* 408 (M^+) (Found: C, 67.58; H, 3.88; N, 20.42; S, 7.90. $C_{23}H_{16}N_6S$ requires C, 67.64; H, 3.92; N, 20.58; S, 7.84%). **5b** (65%): mp 184–186 °C; ν_{max}/cm^{-1} 3446, 3295 (2 NH), 2214 (C≡N), 1600 (C=N); δ_H 2.46 (6 H, s), 6.91–8.60 (12 H, m), 12.95 (2 H, s); *m*/*z* 436 (M^+) (Found: C, 68.74; H, 4.50; N, 19.30; S, 7.23. $C_{25}H_{20}N_6S$ requires C, 68.80; H, 4.58; N, 19.26; S, 7.34%). **5c** (74%): mp 258–260 °C; ν_{max}/cm^{-1} 3361, 3265 (2 NH), 2218 (C≡N), 1600 (C=N); δ_H 7.10–8.64 (12 H, m), 12.60 (2 H, s); *m*/*z* 477 (M^+) (Found: C, 57.80; H, 2.77; Cl, 14.82; N, 17.65; S, 6.67. $C_{23}H_{14}Cl_2N_6S$ requires C, 57.86; H, 2.93; Cl, 14.88; N, 17.61; S, 6.70%).

Oxidation of **5a**.—A mixture of **5a** (0.408 g, 1 mmol) and lead tetraacetate (0.52 g, 1.2 mmol) in glacial acetic acid was refluxed for 2 h, then cooled. The solid product so formed was collected by filtration, washed with water and dried. Recrystallization from *N*,*N*-dimenthylformamide afforded 3-cyano-1,2-bis(phenylazo)pyrrolo-[2,1-*b*]benzothiazole (**7**) as reddish-brown crystals in 75% yield, mp 233–235 °C; ν_{max}/cm^{-1} 2218 (C≡N), 1625 (C=C); δ_H 7.06–8.55 (m, ArH's); *m.z* 406 (M^+) (Found: C, 67.82; H, 3.39; N, 20.57; S, 7.90. $C_{23}H_{14}N_6S$ requires C, 67.98; H, 3.44; N, 20.68; S, 7.88%).

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