Synthesis and antibacterial activity of 4-arylaazo-1-substituted-3,5-diphenylpyrazoles

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Various 4-arylaazo-1-(2-acetonaphthyl)-3,5-diphenylpyrazoles (2a-g), 4-arylaazo-1-isonicotinyl-3,5-diphenylpyrazoles (3a-g) and 4-arylaazo-1-thiocarbamoyl-3,5-diphenylpyrazoles (4a-g) have been synthesized and evaluated for their antibacterial activity. The compounds show significant antibacterial activity.

In view of the potential biological activities¹ of arylazopyrazoles, we report here the synthesis of some new 4-arylaazo-1-substituted-3,5-diphenylpyrazoles. The synthesis involves treatment of 1,3-diphenylpropane-1,3-dione with different diazonium salts in the presence of sodium acetate to yield 2-arylaazo-1,3-diphenylpropane-1,3-diones. The latter on treatment with 2-naphthylacetic acid hydrazide, isonicotinic acid hydrazide and thiosemicarbazide furnish 4-arylaazo-1-(substituted)-3,5-diphenylpyrazoles (Scheme 1).

Nine pyrazole derivatives (2b, c, f; 3a, b, d; 4e, f, g) were screened for their antibacterial activity against Gram-positive *S. aureus* and Gram-negative *E. coli* applying agar-plate-diffusion technique². The pyrazole derivatives having isonicotinyl group at position-1 showed maximum inhibition (16–20 mm) against *S. aureus* and *E. coli* at 100 $\mu\text{g ml}^{-1}$ concentration. When the isonicotinyl group was replaced by 2-acetonaphthyl or 1-thiocarbamoyl the activity decreased (10–15 mm) except the pyrazole derivatives with 2-acetonaphthyl group at position-1 and having R = *p*-Cl and *o*-COOH in the phenyl ring at position-4 showing no activity against *E. coli*.

Experimental

M.p.s. were determined by open capillary methods and are uncorrected. IR spectra were recorded on a Perkin-Elmer 157 infracord spectrophotometer and ¹H NMR spectra on a Bruker WM-400 (400 MHz FT NMR) spectrometer using TMS as internal reference. Purity of the compounds was checked by TLC on silica gel plates and the spots were visualized by exposure to iodine vapour. 1,3-Diphenylpropane-1,3-dione³ and 2-naphthylacetic acid hydrazide⁴ were prepared as reported.

2-Arylaazo-1,3-diphenylpropane-1,3-dione (1a-g) : Substituted aniline (0.05 mol) dissolved in aq. HCl (40 ml;

1 : 1) was stirred and cooled (0–2°), then a cold solution of sodium nitrite (6.0 g in 15 ml of water) was added to it slowly maintaining the temperature at 0–2°. The cold diazotized solution was added dropwise to a well-cooled and stirred mixture of 1,3-diphenylpropane-1,3-diol (0.05 mol) and sodium acetate (4 g dissolved in 5 ml of 50% ethanol). The stirring was continued for 1.5 h and the crystals separated were washed with water, dried and crystallized from ethanol to yield **1a-g** (43–65%); ν_{max} (KBr) 1510–1550 (N=N), 1620–1660 cm^{-1} (C=O); **1a**, m.p. 58°; **b**, 64°; **c**, 77°; **d**, 59°; **e**, 54°; **f**, 63°, δ (CDCl_3) 1.25 (3H, s, CH_3), 4.61 (1H, s, CH), 6.85–8.0 (14H, m, ArH); **g**, 71°.

4-Arylaazo-1-(2-acetonaphthyl)-3,5-diphenylpyrazole (2a-g) : 2-Arylaazo-1,3-diphenylpropane-1,3-dione (**1a-g**, 0.001 mol) and 2-naphthylacetic acid hydrazide (0.001 mol) were dissolved in glacial acetic acid (10 ml) and the solution was refluxed for 10 h. The resulting solid was purified by washing with acetic acid and crystallized from acetic acid to yield **2a-g** (30–43%); ν_{max} (KBr) 1520–1560 (N=N), 1650–1690 cm^{-1} (C=O); **2a**, m.p. 239°, δ (CDCl_3) 2.84 (2H, s, CH_2), 7.25–8.13 (21H, m, ArH); **b**, 206°; **c**, 204°; **d**, 187°; **e**, 189°; **f**, 152°; **g**, 227°.

4-Arylaazo-1-isonicotinyl-3,5-diphenylpyrazole (3a-g) : 2-Arylaazo-1,3-diphenylpropane-1,3-dione (**1a-g**, 0.001 mol) and 2-isonicotinic acid hydrazide (0.001 mol) were dissolved in glacial acetic acid (10 ml) and the solution was refluxed for 10 h. The reaction mixture was cooled and the solid separated was washed with acetic acid. It was further purified by recrystallization from acetic acid to yield **3a-g** (20–35%); ν_{max} (KBr) 1510–1550 (N=N) and 1630–1660 cm^{-1} (C=O); **3a**, m.p. 231°; **b**, 230°, δ ($\text{DMSO}-d_6$) 7.10–7.70 (14H, m, ArH), 7.85–7.88 (4H, m, pyridyl); **c**, 212°, δ ($\text{DMSO}-d_6$) 6.96–7.43 (14H, m, ArH), 7.44–7.82 (4H, m, pyridyl), 10.10 (1H, s, COOH); **d**, 252°; **e**, 207°; **f**, 288°; **g**, 241°.