Studies on Pyrazolines. Part-III. Preparation and Antimicrobial Activity of 3-(4′-Phenylsulphonamidophenyl)-5-aryl-1-acetyl/phenyl-4,5-dihydropyrazoles

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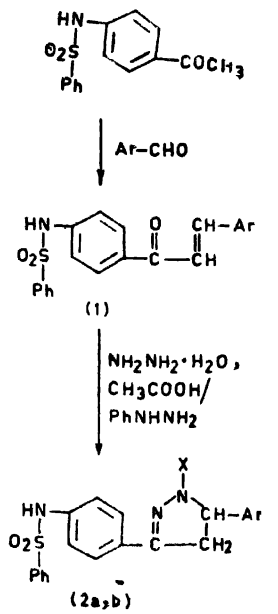
PYRAZOLINES are important nitrogen containing heterocycles, possessing diverse biological activities[1]. In continuation of our work on pyrazoline derivatives, various pyrazolines (**2a, b**) have been synthesised. 4′-Aminoacetophenone was condensed with benzenesulphonyl chloride to get 4-benzenesulphonamidoacetophenone which was then condensed with various aromatic aldehydes to get the chalcones (**1**). The chalcones (**1**) on treatment with hydrazine hydrate and acetic acid and phenyl hydrazine separately gave the pyrazolines (**2a, b** ; Scheme 1). The structures of the compounds have been characterised by elemental analyses, ir, mass and nmr spectral data. The products have been screened for antimicrobial activity.



2a ; X=Acetyl
2b ; X=Phenyl

Scheme 1

Antimicrobial activity : The compounds were screened for antibacterial and antifungal activity using cup-plate method[2] at a concentrations of 50 μg using gram-positive bacteria *Staphylococcus aureus* and *Bacillus megeterium*, gram-negative bacteria *Escherichia coli* and *Pseudomonas flourescens* and

fungi *Candida albicans*. Most of the compounds were found moderately active (12–25 mm zone of inhibition) against different strains of bacteria and fungi which is comparable with known antibiotics norfloxacin, ampicillin and chloromycetin (17–33 mm).

Experimental

All the melting points have been determined in open capillaries and are uncorrected. Ir spectra were taken on a Shimadzu DR-1 435 spectrophotometer, mass spectra on a Jeol JMS-D 300 spectrometer and nmr spectra on a Varian FT-80A spectrometer. All compounds gave satisfactory results for nitrogen analyses.

4'-Phenylsulphonamidochalcones (**1**) : A mixture of *p*-anisaldehyde (0.01 mol, 1.36 g) and 4-benzenesulphonamidoacetophenone (0.01 mol, 2.75 g) in ethanol was stirred for 15 min and then made alkaline, further stirred for 30 min at room temperature, neutralised with HCl, diluted with water and left overnight. The resulting solid was recrystallised from ethanol, (88%), m.p. 180° (Found : C, 67.03 ; H, 4.49 ; N, 3.41. $C_{22}H_{19}NO_4S$ requires : C, 67.17 ; H, 4.83 ; N, 3.56%) ; ν_{max} (KBr) 3 450, 3 250 (NH) and 1 6 0 (C=O), 1 350 and 1 160 cm^{-1} (S=O) ; *m/z* 155, 161, 238, 252, 259, 273, 284 and 393 (M^+) ; δ (DMSO-d_6) 3.6 (3H, s, OCH_3), 6.9–7.01 (2H, d, *J* 9 Hz, =CH–Ar), 8.05–8.19 (2H, d, *J*~11 Hz, =CH–C=O), 10.8 (1H, s, SO_2NH) and 7.2–7.95 (13H, m, ArH).

Similarly, other aldehydes were condensed : Ar=phenyl, m.p. 150° ; 2-methoxyphenyl, 165° ; 3-methoxyphenyl, 145° ; 4-methoxyphenyl, 180° ; 3,4-dimethoxyphenyl, 228° ; 4-aminophenyl, 128° ; 3-aminophenyl, 110° ; 4-hydroxyphenyl, 78° ; 2-hydroxyphenyl, 128° ; 3-hydroxyphenyl, 164° ; 2-nitrophenyl, 114° ; 3-nitrophenyl, 94° ; 2-chlorophenyl, 156° ; 3-chlorophenyl, 148° ; 4-chlorophenyl, 174° ; 3,4-dichlorophenyl, 152° ; 2,4-dichlorophenyl, 108° ; 2-hydroxy-1-naphthyl, 78° ; 3-methoxy-4-hydroxyphenyl, 98° ; 4-(*N,N*)-dimethylaminophenyl, 105°.

3-(4'-Phenylsulphonamido)phenyl-5-(4"-methoxyphenyl)-1-acetyl-4,5-dihydropyrazole (**2a** ; *X=Acetyl*) : A mixture of the chalcone (0.01 mol, 3.93 g) in ethanol (25 ml), hydrazine hydrate (0.01 mol, 0.50 g) and acetic acid (10 ml) was refluxed for 8 h. The mixture was then concentrated, cooled and poured into ice-water. The resulting solid was recrystallised from ethanol, (73%), m.p. 114° (Found : C, 64.09 ; H, 4.9 ; N, 9.17. $C_{24}H_{23}N_3O_4S$ requires : C, 64.14 ; H, 5.12 ; N, 9.35%) ; R=4-methoxyphenyl ν_{max} (KBr) 3 450 (NH), 1 640 (amide C=O), 1 340, 1 160 cm^{-1} (S=O) ; *m/z* 120, 134, 176, 218, 258, 272, 300, 342, 392 and 449 (M^+) ; δ (DMSO-d_6) 3.4 (3H, s, OCH_3), 3.05–3.2 (2H, d, $J_{4,4}$ ~15 Hz, CH_2 of pyrazoline), 3.5–3.9 (1H, t, $J_{4,5}$ 12 Hz, CH of pyrazoline), 2.3 (2H, s, $COCH_3$), 7.2–7.9 (13H, m, ArH) and 10.5 (1H, s, SO_2NH).

Similarly, other compounds were prepared Ar=phenyl, 113° ; 2-methoxyphenyl, 122° ; 3-methoxyphenyl, 96° ; 4-methoxyphenyl, 114° ; 3,4-dimethoxyphenyl, 240° ; 4-aminophenyl, 118° ; 3-aminophenyl, 114° ; 4-hydroxyphenyl, 105° ; 2-hydroxyphenyl, 75° ; 3-hydroxyphenyl, 113° ; 2-nitrophenyl, 155° ; 3-nitrophenyl, 110° ; 2-chlorophenyl, 85° ; 3-chlorophenyl, 99° ; 4-chlorophenyl, 96° ; 3,4-dichlorophenyl, 95° ; 2,4-dichlorophenyl, 127° ; 2-hydroxy-1-naphthyl, 91° ; 3-methoxy-4-hydroxyphenyl, 78° ; 4-(*N,N*)-dimethylaminophenyl, 86°.

3-(4'-Phenylsulphonamido)phenyl-5-(4"-methoxyphenyl)-1-phenyl-4,5-dihydropyrazole (**2b** ; *X-Phenyl*). A mixture of the chalcone (0.01 mol, 3.93 g) in ethanol (25 ml), phenyl hydrazine (0.01 mol, 1.08 g) and piperidine (2 ml) was refluxed for 8–10 h. The mixture was then concentrated, cooled and poured into acidified ice-water. The resulting solid was recrystallised from ethanol, (64%), m.p. 65° (Found : C, 69.35 ; H, 5.08 ; N, 8.42. $C_{28}H_{25}N_3O_3S$ requires : C, 69.56 ; H, 5.17 ; N, 8.70%) ; R=*p*-Methoxyphenyl ν_{max} (KBr) 3 450 (NH), 1 520, 1 500 (pyrazoline) 1 350, 1 160 (S=O sym.) and 1 160 cm^{-1} (S=O asym.); δ (DMSO-d_6) 3.3 (3H, s, OCH_3), 3.7–3.8 (2H, d, $J_{4,4}$ 15 Hz, CH_2 of pyrazoline), 4.01 (1H, t, $J_{4,5}$ 11 Hz, CH of pyrazoline), 10.3 (1H, s, SO_2NH) and 7.2–8.2 (18H, m, ArH).

Similarly, other compounds were prepared : Ar=phenyl, 70° ; 2-methoxyphenyl, 68° ; 3-methoxyphenyl, 83° ; 4-methoxyphenyl, 65° ; 3,4-dimethoxyphenyl, 82° ; 4-aminophenyl, 55° ; 3-aminophenyl, 138° ; 4-hydroxyphenyl, 75° ; 2-hydroxyphenyl, 63° ; 3-hydroxyphenyl, 77° ; 2-nitrophenyl, 80° ; 3-nitrophenyl, 89° ; 2-chlorophenyl, 68° ; 3-chlorophenyl, 87° ; 4-chlorophenyl, 64° ; 3,4-dichlorophenyl, 93° ; 2,4-dichlorophenyl, 98° ; 2-hydroxy-1-naphthyl, 62° ; 3-methoxy-4-hydroxyphenyl, 69° ; 4-(*N,N*)-dimethylaminophenyl, 76°.

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