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Synthesis of 3-[3-(4′-Methyl-benzenesulfonamido)phenyl]-5-(4-substituted phenyl)-1-acetyl-2-pyrazolines

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3-Aminoacetophenone was condensed with 4-toluenesulfonyl chloride to give 3-(4-methylbenzenesulphonamido)acetophenone **(1)** which on treatment with various aromatic aldehydes afforded 3-[3-(4′-methylbenzenesulfonamido)phenyl]-3-(4-substituted phenyl)-2-propene-1-ones **(2a–e).** The compounds **(2a–e)** on cyclization with hydrazine hydrate in glacial acetic acid furnished 3-[3-(4′-methyl-benzenesulfonamido)phenyl]-5-(4-substituted phenyl)-1-acetyl-2-pyrazolines **(3a–e).** The constitution of the products was supported by IR, NMR, mass spectral data and elemental analysis. All the compounds synthesized have been screened for their biological activity.

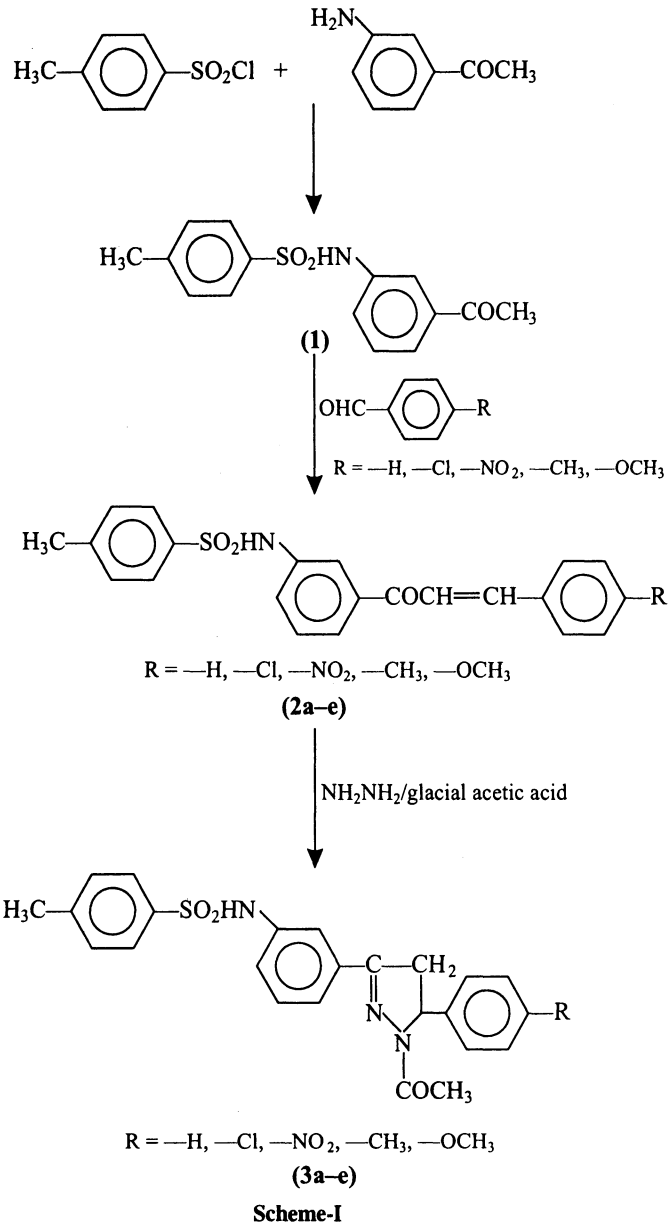
Key Words: Synthesis, Substituted, Pyrazolines.

In view of the fact that many pharmacological activities such as antibacterial[1], antifungal[2], antidiabetic[3] and antitubercular[4] were associated with pyrazoline nucleus, it was thought of interest to synthesize a few substituted pyrazoline derivatives **(3a–e)** and study them for their antibacterial and antifungal activity.

The condensation of 3-aminoacetophenone with 4-toluenesulfonyl chloride in presence of pyridine furnished 3-(4′-methylbenzenesulfonamido) acetophenone **(1)** which on further treatment with various aromatic aldehydes 3-[3-(4′-methylbenzenesulfonamido) phenyl]-3-(4-substituted phenyl)-2-propene-1-ones **(2a–e).** Cyclization of the propene-1-ones **(2a–e)** with hydrazine hydrate in glacial acetic acid yielded 3-[3-(4′-methylbenzenesulfonamido)phenyl]-5-(4-substituted phenyl)-1-acetyl-2-pyrazolines **(3a–e) [Scheme-1].**

The melting points were taken in open capillaries and are uncorrected. IR spectra (KBr, cm^{-1}) were recorded on Shimadzu 8201 PC FTIR spectrophotometer. ^1H NMR spectra were recorded on a Varian VXR-300SH (300 MHz) NMR spectrophotometer using DMSO-d_6 as solvent and TMS as internal standard. The purity of the compounds was monitored by thin layer chromatography.

3-(4′-Methylbenzenesulfonamido)acetophenone (1): 4-Toluenesulfonyl chloride (9.525 g, 0.05 mol) was added slowly to a mixture of 3-amino acetophenone (6.755 g, 0.05 mol) in 60 cm^3 methanol and pyridine (4.8 cm^3, 0.05 mol). The reaction mixture was refluxed for 1 h, then poured into crushed ice and concentrated HCl. The product obtained was filtered, washed with water and crystallized from methanol, yield 11.56 g, 80%; m.p. 225°C. Found: C, 61.19%; H, 5.23; N, 4.79 $C_{15}H_{15}NO_3S$ calculated: C, 62.29; H, 5.18; N, 4.84%.



Scheme-I

3-[3-(4′-Methylbenzenesulfonamido)phenyl]-3-(4-substituted phenyl)-2-propene-1-ones (2a–e): To a mixture of compound **1** (14.45 g, 0.05 mol) in methanol and 20% NaOH (80 cm^3), apropriate aromatic aldehyde (0.05 mol) was added dropwise over a period of half an hour and stirred at 30°C for 3 h. The reaction mixture was then poured into cold water. On acidification with dilute HCl, the compound obtained was filtered, washed with water and crystallized from ethanol. The melting points, yields and analytical data are given in Table-1.

TABLE-1
CHARACTERIZATION DATA 3-[3-(4′-METHYLBENZENESULFONAMIDO) PHENYL]-3-(4-SUBSTITUTED PHENYL)-2-PROPENE-1-ONES (**2a–e**)

Compound	R	m.p. (°C)	Yield (%)	m.f.	Analysis %, N	
					Calculated	Found
2a	H	197	82	$C_{22}H_{19}NO_3S$	3.71	3.57
2b	Cl	185	72	$C_{22}H_{18}ClNO_3S$	3.40	3.24
2c	NO_2	213	65	$C_{22}H_{18}N_1O_5S$	6.63	6.51
2d	CH_3	210	88	$C_{23}H_{21}NO_3S$	3.57	3.41
2e	OCH_3	203	81	$C_{23}H_{21}NO_4S$	3.43	3.29

3-[3-(4′-Methylbenzenesulfonamido)phenyl]-5-(4-substituted phenyl)-1-acetyl-2-pyrazolines (3a–e): The propene-1-one (**2,** 0.01 mol) was dissolved in glacial acetic acid (120 cm^3) and hydrazine hydrate (1.46 cm^3, 0.03 mol) was added. The reaction mixture was refluxed for 5 h and then poured into crushed ice. The resulting solid (**3**) was filtered, washed with water and crystallized from methanol. Other 1-acetyl-2-pyrazolines were obtained in a similar manner. **3e:** IR (KBr, cm^{-1}) 3599 ν(N—H str.), 1631 ν(C=O str.), 1600 ν(C=N str.), 1159, 1340 ν(S=O str.), 1244 ν(C—O—C str.); NMR (DMSO-d_6) δ 2.26 (s, 3H, —CH_3), 2.5 (s, 3H, —$COCH_3$), 3.71 (s, 3H, —OCH_3), 6.8–7.6 (m, 12H, ArH), 2.92–2.98 (dd, 2H, —CH_2), 5.43–5.47 (dd, 1H, —CH), 10.42 (s, 1H, —NH); mass m/z 464 (M + 1), 422, 314, 223, 191, 176, 160, 149, 134, 121, 106, 91(B), 77, 65.

The melting points, yields and analytical data are given in Table-2.

TABLE-2
CHARACTERIZATION DATA OF 3-[3-4′-METHYLBENZENESULFONAMIDO) PHENYL]-5-(4-SUBSTITUTED PHENYL)-1-ACETYL-2-PYRAZOLINES (**3a–e**)

Compound	R	m.p. (°C)	Yield (%)	m.f.	Analysis %, N	
					Calculated	Found
3a	H	210	70	$C_{24}H_{23}N_3O_3S$	9.69	9.42
3b	Cl	228	50	$C_{24}H_{22}ClN_3O_3S$	8.98	8.82
3c	NO_2	241	45	$C_{24}H_{22}N_4O_5S$	11.71	11.42
3d	CH_3	232	55	$C_{25}H_{25}N_3O_3S$	9.39	9.15
3e	OCH_3	222	75	$C_{25}H_{25}N_3O_4S$	9.06	8.95

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