

Synthesis and Antimicrobial Activity of 3-{3-[(4-Chlorophenyl)-sulphonamido]phenyl}-5-aryl- Δ^2 -pyrazolines

V.S. JAMODE†, P.R. BHAGAT* and H.S. CHANDAK‡
Dept. of Chemistry, J. Darda Institute of Engineering and Technology
Lohara, Yavatmal-445 001, India
E-mail: pundlik_bhagat@rediffmail.com

3-(4-Chlorophenyl)sulphonamidoacetophenone and aromatic aldehydes in alcoholic NaOH were condensed to obtain chalcones (1a–h), which on refluxing with 3-chlorophenylhydrazine hydrochloride/semicarbazide hydrochloride in pyridine solvent gave 1-(3-chlorophenyl)/carboxamido-3{3-[(4-chlorophenyl)sulphonamido]phenyl}-5-Aryl- Δ^2 -pyrazolines (2a–h). The structures of these compounds were established by elemental analysis and spectral analysis (IR, NMR).

Key Words: Synthesis, Pyrazolines, Spectral studies.

INTRODUCTION

Pyrazolines with sulphonamidoaryl substituent at 3 position show antidepressant activity¹, hypoglycemic activity² and broad spectrum of biological activity. Pyrazoline derivatives acquire cerebroprotective³ and anti-implantation activity⁴. Due to this vital biological role of pyrazoline derivatives^{5–14}, it was thought of interest to synthesize and study antimicrobial activity by substituting one more chemical functions in the corresponding pyrazolines. Thus we present herein the synthesis of the titled compounds having 3-(4-chlorophenyl) sulphonamidophenyl moiety at 3-position in the pyrazoline nucleus.

It has been observed that substituted prop-2-ones are best starting compounds of the pyrazoline derivatives. The present work deals with the synthesis of some new 3,5-diaryl-pyrazolines and their characterization by elemental analysis, IR, ¹H NMR analysis and for antimicrobial activity.

EXPERIMENTAL

All the melting points were taken in silicon oil bath with open capillary tubes and are uncorrected. Thin layer chromatography on silica gel-G was used to check the purity of the compounds. ¹H NMR spectra were recorded on a Bruker AC300 FNMR spectrometer (300 MHz), using TMS as an internal standard. IR spectra

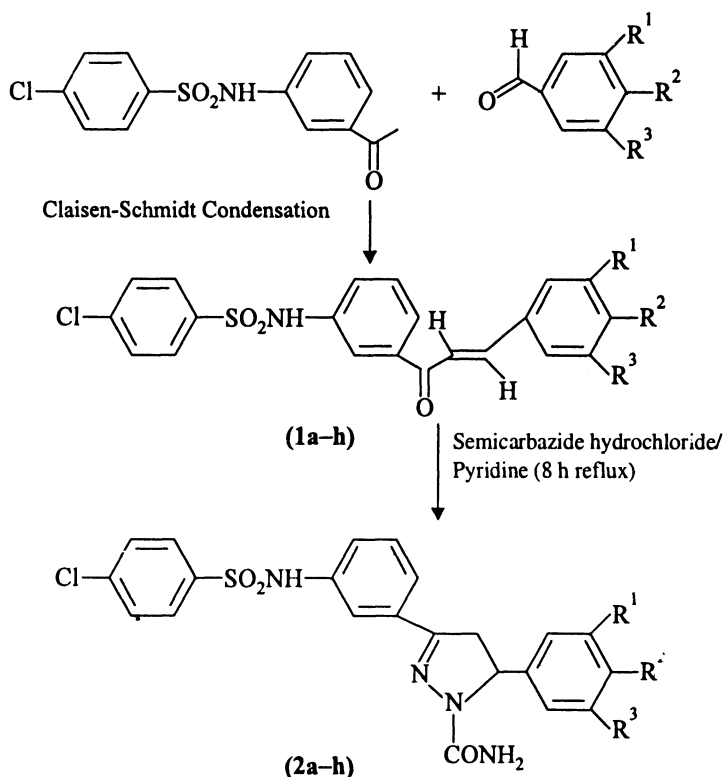
†Pro-Vice-Chancellor, Amravati University, Amravati-444 602, India.

‡Department of Chemistry, Barwale Mahavidyalaya, Aurangabad Road, Jalna-431 203, India.

were recorded on a Nicolet-Impact 400 FT-IR spectrometer. Microanalysis of nitrogen was obtained on Colman 29-N analyzer.

Preparation of 1-{3-[(4-chlorophenyl)sulphonamidophenyl]}-3-(4-methoxyphenyl)-prop-2-one (1a)

3-(4-Chlorophenyl)sulphonamidoacetophenone (3.095 g, 0.01 mol) and 4-methoxy benzaldehyde (1.36 g, 0.01 mol) were dissolved in ethanol at 50°C. To this mixture 40% aq NaOH (6 mL) was added gradually with constant stirring. The yellow solid cake obtained was kept overnight and then acidified with dilute HCl. The resulting solid was filtered and crystallized from ethanol to get compound (1a) (Scheme-1), m.p. 171°C, yield 69%.



where R¹ = H, OCH₃, R² = H, OCH₃, OH, N(CH₃)₂, R³ = H, OCH₃

Scheme-1

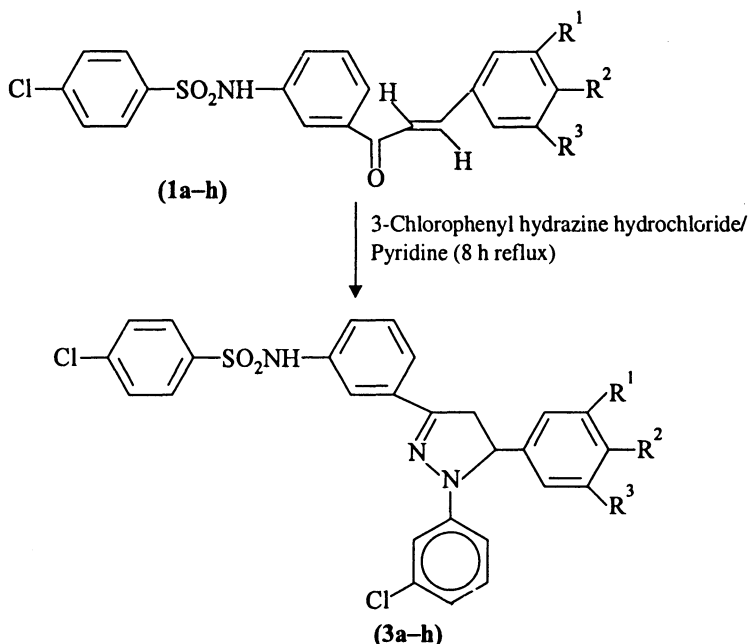
Preparation of 1-carboxamido-3-{3-[(4-chlorophenyl)sulphonamido]-phenyl}-5-(4-methoxyphenyl)-Δ²-pyrazoline (2a)

1-{3-[(4-Chlorophenyl)sulphonamidophenyl]}-3-(4-methoxyphenyl)-prop-2-one (1a) (4.275 g, 0.01 mol) and semicarbazide hydrochloride (2.24 g, 0.02 mol) were refluxed for 6 h in pyridine. The reaction mixture was cooled and dilute

HCl was added to neutralize pyridine. The solid obtained was filtered, washed with water and crystallized from ethanol to get compound (2a) (Scheme-1), m.p. 244°C, yield 61%.

Preparation of 1-(3-(4-chlorophenyl)-3-{3-[(4-chlorophenyl)sulphonamido]phenyl})-5-(4-methoxyphenyl)- Δ^2 -pyrazoline (3a)

1-{3-[(4-Chlorophenyl)sulphonamidophenyl]}-3-(4-methoxyphenyl)-prop-2-one (1a) (4.275 g, 0.01 mol) and 3-chlorophenylhydrazine hydrochloride (1.79 g, 0.01 mol) were refluxed for 6 h in pyridine. The reaction mixture was cooled and dil HCl was added to neutralize pyridine. The solid obtained was isolated and crystallized from ethanol to get compound (3a) (Scheme-2), m.p. 196°C, yield 65%.



where $R^1 = \text{H, OCH}_3$, $R^2 = \text{H, OCH}_3, \text{OH, N(CH}_3)_2$, $R^3 = \text{H, OCH}_3$

Scheme-2

RESULTS AND DISCUSSION

Spectral interpretation of (1a)

IR (ν_{\max}) (cm^{-1}): 3196 $\nu(\text{NH})$, 1648 $\nu(\text{C}=\text{O})$, 1605 $\nu(\text{C}=\text{C})$, 2930 $\nu(\text{C}-\text{H})$, 1159, 1343 $\nu(\text{SO}_2, \text{symm, asymm})$, 1217, $\nu(\text{C}-\text{O}-\text{C})$.

NMR δ ppm: 3.79 (s, 3H, OCH_3), 6.66–7.80 (m, 12Ar-H and $\text{CH}=\text{CH}$), 8 (s, 1H, NH).

Similarly 1-{3-[(4-chlorophenyl)sulphonamidophenyl]}-3-aryl-prop-2-ones (1b-h) were prepared and their physical data is given in Table-1.

Spectral interpretation of (2a)

IR (ν_{\max}) (cm^{-1}): 3731 $\nu(\text{CONH}_2)$, 3447 $\nu(\text{NH})$, 1628 $\nu(\text{C}=\text{N})$, 1329, 1159 $\nu(\text{SO}_2 \text{ asymm, symm})$.

NMR δ ppm: 2.40 (s, 3H, OCH_3), 2.99–3.07 (dd, 1H, H_A), $J_{AB} = 17.81$ Hz, $J_{AX} = 4.66$ Hz; 3.68–3.78 (dd, 1H, H_B), $J_{AB} = 17.81$ Hz, $J_{BX} = 11.87$ Hz; 5.51–5.56 (dd, 1H, H_X), $J_{AX} = 4.66$ Hz, $J_{BX} = 11.87$ Hz; 7.20–7.82 (m, 12Ar—H), 7.4 (s, 2H, NH_2), 10.2 (s, 2H, SO_2NH).

Similarly, pyrazolines (2b–h) were prepared and their physical data is given in Table-1.

TABLE-1
PHYSICAL DATA OF SYNTHESIZED COMPOUNDS

Compound	R ¹	R ²	R ³	m.p. (°C)	Yield (%)	(% N)	
						Found	Calculated
1a	H	OCH ₃	H	171	75	3.22	3.27
1b	OCH ₃	H	H	172	73	3.25	3.27
1c	H	H	H	167	72	3.47	3.52
1d	OCH ₃	OCH ₃	H	180	70	3.16	3.06
1e	OCH ₃	OCH ₃	OCH ₃	195	76	2.79	2.87
1f	OCH ₃	OH	H	157	68	3.10	3.16
1g	H	NMe ₂	H	181	71	6.26	6.36
1h	H	OH	H	160	68	3.27	3.39
2a	H	OCH ₃	H	196	65	7.52	7.61
2b	OCH ₃	H	H	188	60	7.63	7.61
2c	H	H	H	180	61	7.79	8.05
2d	OCH ₃	OCH ₃	H	218	59	7.10	7.22
2e	OCH ₃	OCH ₃	OCH ₃	221	71	6.81	6.88
2f	OCH ₃	OH	H	158	58	7.25	7.39
2g	H	NMe ₂	H	177	73	9.82	9.91
2h	H	OH	H	165	57	7.83	7.81
3a	H	OCH ₃	H	244	61	11.49	11.56
3b	OCH ₃	H	H	201	58	11.58	11.56
3c	H	H	H	214	65	12.11	12.32
3d	OCH ₃	OCH ₃	H	213	70	10.75	10.88
3e	OCH ₃	OCH ₃	OCH ₃	197	72	10.12	10.28
3f	OCH ₃	OH	H	178	55	11.01	11.19
3g	H	NMe ₂	H	220	67	13.98	14.07
3h	H	OH	H	182	59	11.72	11.90

Spectral interpretation of (3a)

IR (ν_{\max}) (cm^{-1}): 3500 $\nu(\text{NH})$, 1668 $\nu(\text{C}=\text{N})$, 1255 $\nu(\text{C}-\text{O}-\text{C})$, 1330, 1159 $\nu(\text{SO}_2 \text{ asym, sym})$.

NMR δ ppm: 3.75 (s, 3H, OCH_3), 2.99–3.06 (dd, 1H, H_A), $J_{AB} = 18.57$ Hz, $J_{AX} = 4.55$ Hz; 3.61–3.71 (dd, 1H, H_B), $J_{AB} = 18.57$ Hz, $J_{BX} = 11.79$ Hz; 5.46–5.51 (dd, 1H, H_X), $J_{AX} = 4.55$ Hz, $J_{BX} = 11.79$ Hz; 7.1–7.8 (m, 16Ar—H), 10.1 (s, 2H, SO_2NH).

Similarly pyrazolines (3b–h) were prepared and their physical data is recorded in Table-1.

Antimicrobial Studies

All pyrazolines have been studied for their antimicrobial activity against *Proteus mirabilis*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The culture of each species was incubated at 37°C and the zone of inhibition was measured after 24 h. Most of these compounds were found active.

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