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NOTE

Synthesis of 1-(3-Aryl/Alkyl-4-formylpyrazole-1-carbonyl)-4-chlorobenzenes

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Condensation of 4-chlorophenyl carboxylic acid hydrazide (**III**) with different acetophenones and acetaldehydes afforded the corresponding acetophenones/acetaldehydes-4 chlorophenyl carbonyl hydrazones **IV'**, **IV** which on Vilsemeir Haack reaction treatment with $POCl_3$ and DMF formylated the compound 1-(3-aryl/alkyl-4-formylpyrazole-1-carbonyl)-4-chlorobenzenes.

Key Words: Synthesis, Formylpyrazole derivatives.

Literature search revealed that pyrazoles[1] exhibits antibacterial[2-4], antifungal[5] and antiinflammentary[6] properties. It was considered worth while to synthesize compounds bearing substituted phenyl nucleus linked to the pyrazole moiety through carbonyl linkage and evaluate their antibacterial activities.

The key intermediate 4-chloro-phenyl carboxylic acid hydrazide (**III**) was prepared by the reaction of hydrazine hydrate with methyl-4-chlorophenyl carboxylate which is turn was obtained by condensation of 4-chloro-benzoic acid with methanol containing catalytic amount of H_2SO_4. The reaction of **III** with different acetophenones and acetaldehydes in methanol with a trace of acetic acid furnished corresponding acetophenones/acetaldehydes-4-chlorobenzene-1-carbonyl hydrazones **IV'**, **IV** which on formylation by Vilsemeir Haack reaction using $POCl_3$ and DMF led to 1-(3-aryl/alkyl-4-formyl pyrazole-1 carbonyl)-4-chlorobenzenes (**V**) as shown in **Scheme-I**.

Melting point were taken in open capillaries and are uncorrected. IR Spectra were recorded on a Perkin-Elmer 283 Spectrophotometer (V_{max}, cm^{-1}). PMR spectra on Varian EM-390 spectrometer using TMS as internal standard.

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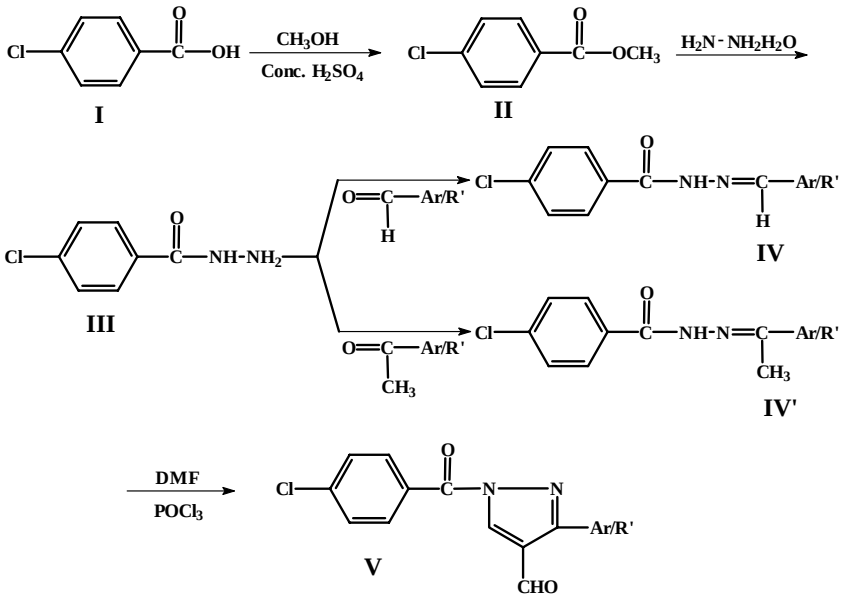
Acetophenone/acetaldehyde-4-chlorophenyl-carbonylhydrazones (IV, IV'): To a solution of **III** (0.01 M) in hot methanol an appropriate amount of acetophenone/acetaldehyde (0.01 M) and a drop of glacial acetic acid were added. The solid that separated on refluxing for 1-2 h was filtered washed with cold methanol and recrystalized from ethanol to give **IV, IV'** (Table-1). IR (KBr, cm^{-1}) (**IV**): 3060 ν(N-H), 1660 ν(C=O) and 1589 ν(C=N).



Scheme-I

Pyrazole-1-carbonyl-4-chlorophenyl (V): To the Vilsemeier-Haack complex prepared from DMF (10 mL) and $POCl_3$ (1.1 mL, 0.012 M) was added the hydrazone **IV, IV'** (0.004 M) and the reaction mixture stirred at 60-70ºC for 4 h and poured into ice cold water. The product which separated on neutralization with $NaHCO_3$ was filtered and recrystallized from methanol-water to give **V** (Table-1).

IR(KBr, cm^{-1}) **Va**: 1691 ν(aldehyde >C=O), 1650 ν(>C=O), 1589 ν(C=N), 2836 ν(C-H, aldehyde); ^{1}H NMR ($CDCl_3$): 9.9 δ(S, 1H, CHO), 7.2 δ(C-H of pyrazole), 7.4 δ(S, 5H, Ar-H), 7.9 δ(q, 4H, C_6H_4Cl).

Antibacterial activity: All the compounds were tested for antibacterial activity by agar-cup plate method[7] against the strains of *S. aureus* and *E. coli*. The testing was carried out 1 mg/mL of sample in DMF. The results are presented in Table-1.

Solvent used for crystallization were methanol for **IV'(a-f)**, **IV(g-j)** and methanol-water for **V(a-j)**.

TABLE-1
CHARACTERIZATION DATA OF COMPOUNDS **IV, IV'** and **V**

Comp.	Ar/R'	m.p. (ºC)	Yield (%)	m.f.	*E. coli*	*S. aureus*
IV'a	Phenyl	175	85.15	$C_{15}H_{13}N_2OCl$	-	-
IV'b	*p*-Methoxy phenyl	250	87.61	$C_{16}H_{15}N_2O_2Cl$	-	+
IV'c	*p*-Hydroxy phenyl	170	85.80	$C_{15}H_{13}N_2O_2Cl$	-	+
IV'd	*p*-Nitro phenyl	225	90.00	$C_{15}H_{12}N_3O_3Cl$	-	-
IV'e	Butanone	111	44.55	$C_{11}H_{13}N_2OCl$	-	-
IV'f	Cyclohexanone	142	55.89	$C_{13}H_{15}N_2OCl$	-	+
IVg	*p*-Methoxy phenyl	174	95.33	$C_{15}H_{13}N_2O_2Cl$	-	+
IVh	*p*-Hydroxy phenyl	290	94.73	$C_{14}H_{11}N_2O_2Cl$	-	+
IVi	*o*-Nitro phenyl	234	72.49	$C_{14}H_{10}N_2O_3Cl$	-	-
IVj	Phenyl	248	96.00	$C_{14}H_{11}N_2OCl$	+	-
Va	Phenyl	126	40.26	$C_{17}H_{11}N_2O_2Cl$	+	+
Vb	*p*-Methoxy phenyl	110	44.00	$C_{18}H_{13}N_2O_3Cl$	+	+
Vc	*p*-Hydroxy phenyl	133	55.30	$C_{17}H_{11}N_2O_3Cl$	+	+
Vd	*p*-Nitro phenyl	98	35.57	$C_{17}H_{10}N_3O_4Cl$	-	+
Ve	Butanone	135	19.00	$C_{13}H_{11}N_2O_2Cl$	-	+
Vf	Cyclohexanone	157	27.73	$C_{17}H_{17}N_2O_2Cl$	+	+
Vg	*p*-Methoxy phenyl	102	56.47	$C_{18}H_{13}N_2O_3Cl$	+	+
Vh	*p*-Hydroxy phenyl	120	30.02	$C_{17}H_{11}N_2O_3Cl$	+	-
Vi	*o*-Nitro phenyl	115	23.91	$C_{17}H_{10}N_3O_4Cl$	+	+
Vj	Phenyl	120	31.40	$C_{17}H_{11}N_2O_2Cl$	-	+

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