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NOTE

Synthesis and Characterization of 1-Isonicotinoyl/ 1-Carboxamido/1-Thiocarboxamido-3-(2-hydroxy-5-chlorophenyl)-4-aroyl-3-methyl pyrazoles

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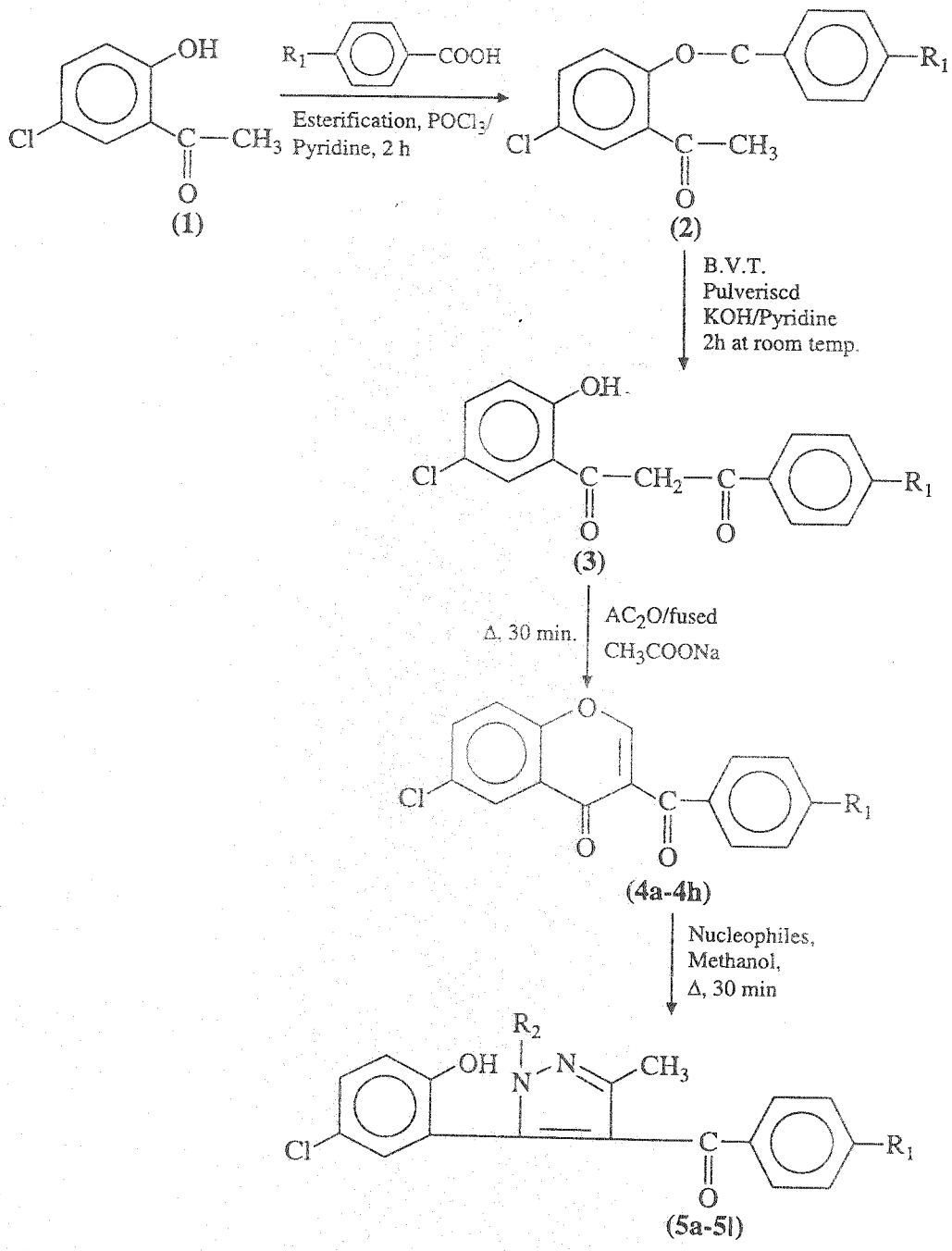
Chromone, the starting material for the preparation of 3-methyl pyrazole, is prepared from 2-hydroxy-5-chloro dibenzoyl methane by the action of acetic anhydride and fused sodium acetate in an oil bath at 160°C for 30 min. 1,4,5-Trisubstituted pyrazoles are obtained by refluxing the mixture of 3-benzoyl-2-methyl-6-chloro-chromone and nucleophiles sch as isonicotinic acid, semicarbazide and thiosemicarbazide in methanol medium. The structures are confirmed by IR and NMR spectral data.

Key Words: Synthesis, Isonicotinoyl, Carboxamido, Thiocarboxamido derivatives.

Pyrazoles are neutral azoles reported as having antifungal[2], insecticidal[3], pesticidal[4], anticancer[5], antidibetics[6] and antipyretic[7] activities. Pyrazoles are ALSO found useful for prevention and treatment of ischemic heart disease, angina, migraine and Parkinson's disease[8]. Many drugs and dyes contain pyrazole nucleus[9]. Pyrazoles are evaluated for inhibitory activity against xanthine oxidase and cyclin dependent kinase (CDK)[10]. 4-Substituted pyrazoles are tested for analgesic and antiinflammatory activities using albino rats[11].

The present work deals with the synthesis of 1-isonicotinoyl/1-carboxamidol/1-thiocarboxamido-(2-hydroxy-5-chlorophenyl)-4-aroyl-3-methyl pyrazoles from 5-chloro-3-aroyl chromones and nucleophiles such as isonicotinic acid, semicarbazide and thiosemicarbazide hydrochloride in methanol medium.

All melting points were taken in paraffin oil bath instrument in open capillary and are uncorrected. Purity of compounds was checked by TLC on silica gel-G and IR spectrum was recorded on Perkin-Elmer spectrophotometer and PMR spectra on Bruker AC-300 F NMR spectrophotometer at 300 MHz.



R_1 = H, NO_2, OCH_3, Cl

R_2 = C_5H_4NCO, $CONH_2$, $CSNH_2$

Scheme-1

2-Hydroxy 5-chloro acetophenone and 2-hydroxy 5-chloro dibenzoyl methane (2) was synthesized according to the procedure described elsewhere[12].

Preparation of 3-aroyl 6-chloro-2-methyl chromones (4a-d)

2-Hydroxy 5-chloro dibenzoyl methane (1 g) was heated with acetic anhydride (5 mL) and fused with sodium acetate (1 g) for 1/2 h at 160°C in an oil bath. The mixture on cooling was diluted with ice-cold water. The solid obtained was filtered, washed with water and then crystalized with ethanol to get a white wooly product. The characterization data are recorded in Table-1.

4a: IR (KBr, cm^{-1}): 3069 ν(C—H *str.*), 1074–634 ν(C—H bend), 2918–2848 ν(CH_3 *str.*), 1669–1637 ν(C=C *str.*), 1312–1249 ν(C—O *str.*), 1277–1074 ν(C—C—O *str.*), 1801 ν(C=O *str.*, benzoyl), 512 ν(C—Cl *str.*), 887–815 ν(C=O *str.*).

^{1}H NMR ($CDCl_3$ + $CHCl_3$) δ ppm: 7.26–8.1 (11H, m aromatic) 2.38 (3H, 9, C—H).

TABLE-1
PHYSICAL CHARACTERIZATION DATA OF
3-AROYL-6-CHLORO-2 METHYL CHROMONES (4a–d)

Compd.	R_1	m.f.	m.p.	Yield	R_f
4a	H	$C_{17}H_{16}O_3Cl$	113	75	0.36
4b	NO_2	$C_{17}H_{10}O_5Cl$	210	70	0.55
4c	OCH_3	$C_{18}H_{13}O_4Cl$	180	70	0.34
4d	Cl	$C_{17}H_{10}O_3Cl$	145	75	0.48

Preparation of 1-isonicotinoyl/1-carboxamido 1-thiocarboxamido 2-hydroxy-5 chlorophenyl 4-aroyl 3-methyl pyrazole (5a-l)

A mixture of 3-aroyl-6-chloro-2 methyl chromone (0.005 mol) and nucleophiles such as isonicotinic acid hydrazide, semicarbazide and thiosemicarbazide hydrochloride (0.025 mol) was suspended in methanol (20 mL) and the reaction mixture was refluxed for 1/2 h on a water bath. The precipitate formed after cooling and addition of water was filtered, washed with water and crystallized from ethanol. The physical characterization data were recorded in Table-2.

5b: IR (KBr, cm^{-1}): 2920 ν(C—OH *str.*), 3068 ν(C—H *str.*), 1278–1209 ν(C—O—C *str.*) 1750–1669 ν(C=O *str.*), 1750 ν(C=O *str.*), 1250 ν(C—N *str.*), 1596–1568 ν(N—H bend), 1467–1433 ν(—N=N— *str.*), 888–584 ν(C—Cl *str.*), 2360 ν(C—H *str.*).

^{1}H NMR ($CDCl_3$ + $CHCl_3$) δ ppm: 7.26 (1–OH aromatic, S), 2.38 (3H, q, C—H), 7.43–7.89 (14H, m aromatic), 8.14 (2H, t, N—H).

TABLE-2
PHYSICAL CHARACTERIZATION DATA OF 1-SUBSTIFUTED-2-HYDROXY-5-CHLOROPHENYL 4-AROYL-3-METHYL PYROZOLES

Compd.	R_1	R_2	m.f.	m.p.	Yield	R_f
5a	H	C_5H_4NCO	$C_{22}H_{17}N_3O_3Cl$	140	65	0.50
5b	H	$CONH_2$	$C_{18}H_{14}N_3O_3Cl$	150	70	0.53
5c	H	$CSNH_2$	$C_{18}H_{13}N_3O_2SCl$	160	65	0.30
5d	NO_2	C_5H_4NCO	$C_{23}H_{17}N_3O_5Cl$	220	65	0.37
5e	NO_2	$CONH_2$	$C_{18}H_{13}N_4O_5Cl$	230	70	0.45
5f	NO_2	$CSNH_2$	$C_{18}H_{13}N_4O_4SCl$	218	65	0.60
5g	OCH_3	C_5H_4NCO	$C_{24}H_{18}N_3O_4Cl$	185	65	0.34
5h	OCH_3	$CONH_2$	$C_{19}H_{16}N_3O_4Cl$	190	70	0.42
5i	OCH_3	$CSNH_2$	$C_{19}H_{16}N_3O_3SCl$	195	60	0.37
5j	Cl	C_5H_4NCO	$C_{24}H_{16}N_3O_3Cl$	230	65	0.48
5k	Cl	$CONH_2$	$C_{18}H_{13}N_3O_3Cl$	220	70	0.82
5l	Cl	$CSNH_2$	$C_{18}H_{13}N_3O_2SCl$	210	65	0.53

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