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Synthesis of 3,5-Diaryl-4-aroyl-1-substituted Pyrazoles

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3,5-Diaryl-4-aroyl-1-substituted pyrazoles have been synthesized by refluxing 2-aryl-3-aroyl-6,8-dichloro flavones with nucleophile such as isonicotinic acid hydrazide/semicarbazide/thiosemicarbazide. The structures of these compounds have been characterized by spectral analysis. Purity of these compounds was checked by TLC.

Key Words: Diketone, 3-Aroyl flavanone, 3-Aroyl flavone, 1,3,5-Tri-substituted-4-aroyl pyrazole.

INTRODUCTION

The azoles containing two nitrogen atoms in the 1,2 position are designated as pyrazoles. Pyrazole is the name given by Knorr[1] to this class of compounds in 1883. Singh *et al.*[2] synthesized 1,3,5-trisubstituted pyrazoles as potential antimicrobial agents. 4-Aroyl-3,5-disubstituted pyrazoles have been synthesized from 3-aroyl flavones by using pyridine/methanol/ethanol/DMSO solvent with phenyl hydrazine[3]. 4-Aroyl-3,5-disubstituted pyrazoles have been synthesized from 3-aroyl flavones by using DMSO with phenyl hydrazine[4]. Various pyrazoles play an important role as antimicrobials[5], anticancer[6], antidibetics[7], fungicides[8], pestisides[9] and insectisides[10].

The present work deals with the synthesis of the titled pyrazoles from 2-aryl-3-aroyl-6,8-dichloro flavones and nucleophiles such as isonicotinic acid hydrazide/semicarbazide/thiosemicarbazide in DMF solvent. The structures of synthesized pyrazoles were confirmed from chemical properties, analytical data and spectral analysis.

EXPERIMENTAL

The melting points were taken in silicon oil bath instrument in open capillary and are uncorrected. The purity of compounds was checked by TLC on silica gel-G plates. IR spectra were recorded on Perkin-Elmer spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ on Bruker AC 300F NMR spectrophotometer at 300 MHz using TMS as internal reference.

Preparation of 2-aroyloxy-3,5-dichloro acetophenones (1a–d)

2-Hydroxy acetophenone derivatives (0.04 mol) and benzoic/anisic/2-chloro benzoic/4-nitrobenzoic acid (0.05 mol) were dissolved in dry pyridine (30 mL) in 250 mL beaker. Phosphorus oxychloride ($POCl_3$) (2.5–3 mL) was added dropwise with constant stirring and external cooling. During addition of $POCl_3$, temperature was maintained below 50°C. After addition it was allowed to stand for about 2 h and then treated with ice-cold dilute HCl (1 : 1) to neutralize pyridine. The product was repeatedly washed with water and with sodium

carbonate solution (10%) to remove any organic acid and then with dilute sodium hydroxide (1%) to remove unreacted phenolic ketone. The product was filtered and crystallized from ethanol to obtain white crystals of 2-aroyloxy-3,5-dichloro acetophenones **(1a–d).** The structures of the compounds have been confirmed on the basis of analytical data and chemical properties (Table-1).

TABLE-1
PHYSICAL DATA OF 2-AROYLOXY-3,5-DICHLORO ACETOPHENONES **(1a–d)**

Compound	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
1a	H	H	70	98	$C_{15}H_{10}O_3Cl_2$
1b	H	OCH_3	85	94	$C_{16}H_{12}O_4Cl_2$
1c	Cl	H	75	106	$C_{15}H_9O_3Cl_3$
1d	H	NO_2	80	140	$C_{15}H_9O_5Cl_2N$

Preparation of 1-(2-hydroxy-3,5-dichlorophenyl)-3-aryl propan-1,3-diones (2a–d)

Acetophenones **(1a–d)**, anhydrous pyridine or dimethyl formamide (0.5 mol) were taken in a dry beaker. The mixture was warmed on low flame. Pulverized KOH (0.02 mol) was added with constant stirring. The mass began to thicken and turned yellow. In case of DMF, the product decomposed with ice-cold HCl (1 : 1) after 2 h. In case of pyridine it decomposed after 6 h (results obtained by both solvents were found identical). The product was filtered, washed with water and crystallized from ethanol to obtain yellowish crystals. The structures of these compounds have been confirmed on the basis of analytical data (Table-2) and spectral analysis.

Spectral data of (2a): IR (ν_{max}, cm^{-1}): 1602 ν(—C=O, str.), 3069.6 ν(—OH, str.), 737.6, 802.4 ν(C—Cl, str.). NMR ($CDCl_3$ + DMSO) (δ ppm): 1.25 (s, 2H, —CH_2), 12.66 (s, 1H, —OH), 6.77–7.96 (m, 7H, Ar-H).

TABLE-2
PHYSICAL DATA OF 1-(2-HYDROXY-3,5-DICHLORO PHENYL)-3-ARYL PROPAN-1,3-DIONES **(2a–d)**

Compound	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
2a	H	H	80	128	$C_{15}H_{10}O_3Cl_2$
2b	H	OCH_3	70	130	$C_{16}H_{12}O_4Cl_2$
2c	Cl	H	75	174	$C_{15}H_9O_3Cl_3$
2d	H	NO_2	70	150	$C_{15}H_9O_5Cl_2N$

Preparation of 2-aryl-3-aroyl-6,8-dichloro flavanones (3a–f)

1-(2-Hydroxy-3,5-dichloro)-3-aryl propan-1,3-diones **(2a–d)** (0.01 mol) and

aromatic aldehydes (0.012 mol) were refluxed in ethanol (25 mL) in presence of a few drops of piperidine for about 1 h. The reaction mixture was cooled and the product thus separated was crystallized from ethanol-acetic acid mixture to get crystals of 2-aryl-3-aroyl-6,8-dichloro flavanones. The structures of these compounds have been confirmed on the basis of analytical data (Table-3) and spectral analysis.

Spectral data of (3a): IR (ν_{max}, cm^{-1}): 1666 ν(C=O, str.), 739, 795.8 ν(C—Cl, str.). NMR ($CDCl_3$ + DMSO) (5 ppm): 3.88 (s, 3Hc), 5.02 (s, 1Ha), 5.99 (s, 1Hb), 6.82–7.95 (m, 11H, Ar-H).

TABLE-3
PHYSICAL DATA OF 2-ARYL-3-AROYL-6,8-DICHLORO FLAVANONES (3a–f)

Compound	R	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
3a	H	OCH_3	H	50	130	$C_{23}H_{16}O_4Cl_2$
3b	OCH_3	OCH_3	H	55	132	$C_{24}H_{18}O_5Cl_2$
3c	H	OH	H	45	138	$C_{22}H_{14}O_4Cl_2$
3d	H	NO_2	H	45	218	$C_{22}H_{13}O_5Cl_2N$
3e	NO_2	NO_2	H	50	210	$C_{22}H_{12}O_7Cl_2N_2$
3f	H	NO_2	Cl	50	130	$C_{22}H_{12}O_5Cl_2N$

Preparation of 2-aryl-3-aroyl-6,8-dichloro flavones (4a–f)

2-Aryl-3-aroyl-6,8-dichloro flavanones (**3a–f**) (0.01 mol) were refluxed for 30 min with the crystals of iodine in DMSO (20 mL). The reaction mixture was diluted with water to obtain the product. The product was washed with sodium thiosulphate and then with water. The product thus separated was crystallized from ethanol-acetic acid mixture. The structures of these compounds have been confirmed on the basis of analytical data (Table-4) and spectral analysis.

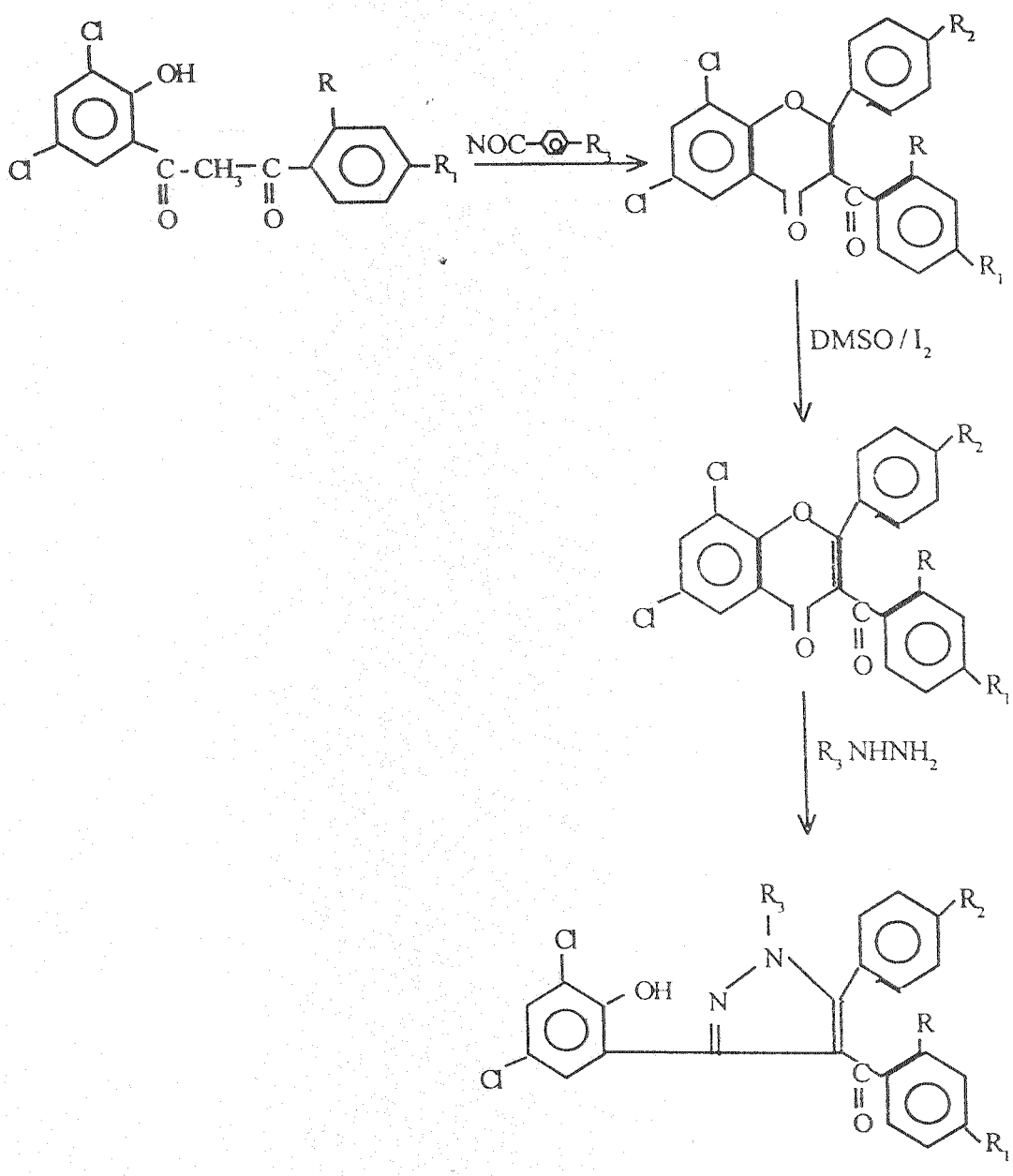
Spectral data of (4a): IR (ν_{max}, cm^{-1}): 1666 ν(C=O, str.), 739, 795.8 ν(C—Cl, str.). NMR ($CDCl_3$ + DMSO) (5 ppm): 3.88 (s, 3H, OCH_3), 5.02 (s, 1Ha), 5.99 (s, 1Hb), 6.82–7.95 (m, 11H, Ar-H).

TABLE-4
PHYSICAL DATA OF 2-ARYL-3-AROYL-6,8-DICHLORO FLAVONES (4a–f)

Compound	R	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
4a	H	OCH_3	H	50	160	$C_{23}H_{14}O_4Cl_2$
4b	OCH_3	OCH_3	H	55	164	$C_{24}H_{16}O_5Cl_2$
4c	H	OH	H	45	152	$C_{22}H_{12}O_4Cl_2$
4d	H	NO_2	H	45	230	$C_{22}H_{11}O_5Cl_2N$
4e	NO_2	NO_2	H	50	238	$C_{22}H_{10}O_7Cl_2N_2$
4f	H	NO_2	Cl	50	150	$C_{22}H_{10}O_5Cl_2N$

Preparation of 3,5-diaryl-4-aroyl-1-substituted pyrazoles [5,6,7(a–f)]

2-Aryl-3-aroyl-6,8-dichloro flavones **(4a–f)** (0.01 mol) and nucleophile such as isonicotinic acid hydrazide/semicarbazide/thiosemicarbazide were refluxed in DMF (20 mL) in presence of piperidine (0.05 mol) for about 1.5 h. After cooling the reaction mixture was acidified with dil. HCl (1 : 1). The product thus separated was crystallized from ethanol-acetic acid mixture to get 3,5-diaryl-4-aroyl-1-substituted pyrazoles **(Scheme-1)**.



The structures of these compounds have been confirmed on the basis of analytical data (Table-5), and spectral analysis.

Spectral Data

(6b): IR (ν_{max}, cm^{-1}): 1647 ν(C=O, str.), 754, 828 ν(C—Cl, str.), 1269 ν(C—N, str.), 1601.7 ν(C=N, str.). NMR ($CDCl_3$ + DMSO) (δ ppm): 3.90 (s, 6H, 2-OCH_3), 8.10 (s, 1H, OH), 7.25 (s, 2H, —NH_2), 6.77–8.09 (m, 10H, Ar-H).

(6c): IR (ν_{max}, cm^{-1}): 753, 827 ν(C—Cl, str.), 1269.8 ν(C—N, str.), 1601.5 ν(C=N, str.). NMR ($CDCl_3$ + DMSO) (δ ppm): 3.90 (s, 6H, 2—OCH_3), 7.25 (s, 1H, OH), 6.77 (s, 2H, NH_2), 7.03–8.09 (m, 10H, Ar-H).

TABLE-5

PHYSICAL DATA OF 3,5-DIARYL-4-AROYL-1-SUBSTITUTED PYRAZOLES [5,6,7(a–f)]

Comp.	R	R_1	R_2	R_3	Yield (%)	m.p. (°C)	R_f	m.f.
5a	H	OCH_3	H	C_5H_4NCO	55	265	0.91	$C_{29}H_{19}O_4Cl_2N_3$
5b	OCH_3	OCH_3	H	C_5H_4NCO	60	280	0.86	$C_{30}H_{22}O_5Cl_2N_3$
5c	H	OH	H	C_5H_4NCO	50	290	0.86	$C_{28}H_{17}O_4Cl_2N_3$
5d	H	NO_2	H	C_5H_4NCO	50	220	0.82	$C_{28}H_{16}O_5Cl_2N_4$
5e	NO_2	NO_2	H	C_5H_4NCO	55	178	0.86	$C_{28}H_{15}O_7Cl_2N_5$
5f	H	NO_2	Cl	C_5H_4NCO	50	210	0.84	$C_{28}H_{15}O_5Cl_3N_4$
6a	H	OCH_3	H	$CONH_2$	55	175	0.67	$C_{24}H_{17}O_4Cl_2N_3$
6b	OCH_3	OCH_3	H	$CONH_2$	50	148	0.60	$C_{25}H_{19}O_5Cl_2N_3$
6c	H	OH	H	$CONH_2$	60	146	0.73	$C_{23}H_{15}O_4Cl_2N_3$
6d	H	NO_2	H	$CONH_2$	60	280	0.40	$C_{23}H_{14}O_5Cl_2N_4$
6e	NO_2	NO_2	H	$CONH_2$	65	270	0.47	$C_{23}H_9O_7Cl_2N_5$
6f	H	NO_2	Cl	$CONH_2$	50	255	0.57	$C_{23}H_{13}O_5Cl_3N_4$
7a	H	OCH_3	H	$CSNH_2$	50	260	0.42	$C_{24}H_{17}O_3Cl_2N_3S$
7b	OCH_3	OCH_3	H	$CSNH_2$	55	190	0.44	$C_{25}H_{19}O_4Cl_2N_3S$
7c	H	OH	H	$CSNH_2$	45	210	0.39	$C_{23}H_{15}O_3Cl_2N_3S$
7d	H	NO_2	H	$CSNH_2$	50	220	0.37	$C_{23}H_{14}O_4Cl_2N_4S$
7e	NO_2	NO_2	H	$CSNH_2$	55	280	0.41	$C_{23}H_9O_7Cl_2N_5S$
7f	H	NO_2	Cl	$CSNH_2$	60	250	0.43	$C_{22}H_{13}O_4Cl_3N_4S$

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