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NOTE

Synthesis and Characterization of 1-Substituted-3,5-Diaryl-4-Bromo Pyrazoles

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1-(2-Hydroxy-3,5-dichloro phenyl)-3-aryl-2-bromo propan-1,3-diones are prepared by the action of bromine on 1-(2-hydroxy-3,5-dichloro phenyl)-3-aryl propan-1,3-diones.. 3,5-Diaryl-1- substituted-4-bromo pyrazoles have been synthesized by refluxing 1-(2-hydroxy-3,5-dichloro phenyl)-3-aryl-2-bromo propan-1,3-diones with nucleophile such as isonicotinic acid hydrazide, semicarbazide, thiosemicarbazide in ethyl alcohol for about 2.5 h in basic medium. The structures of these compounds have been characterized by spectral analysis. Purity of the synthesized heterocycles was checked by TLC.

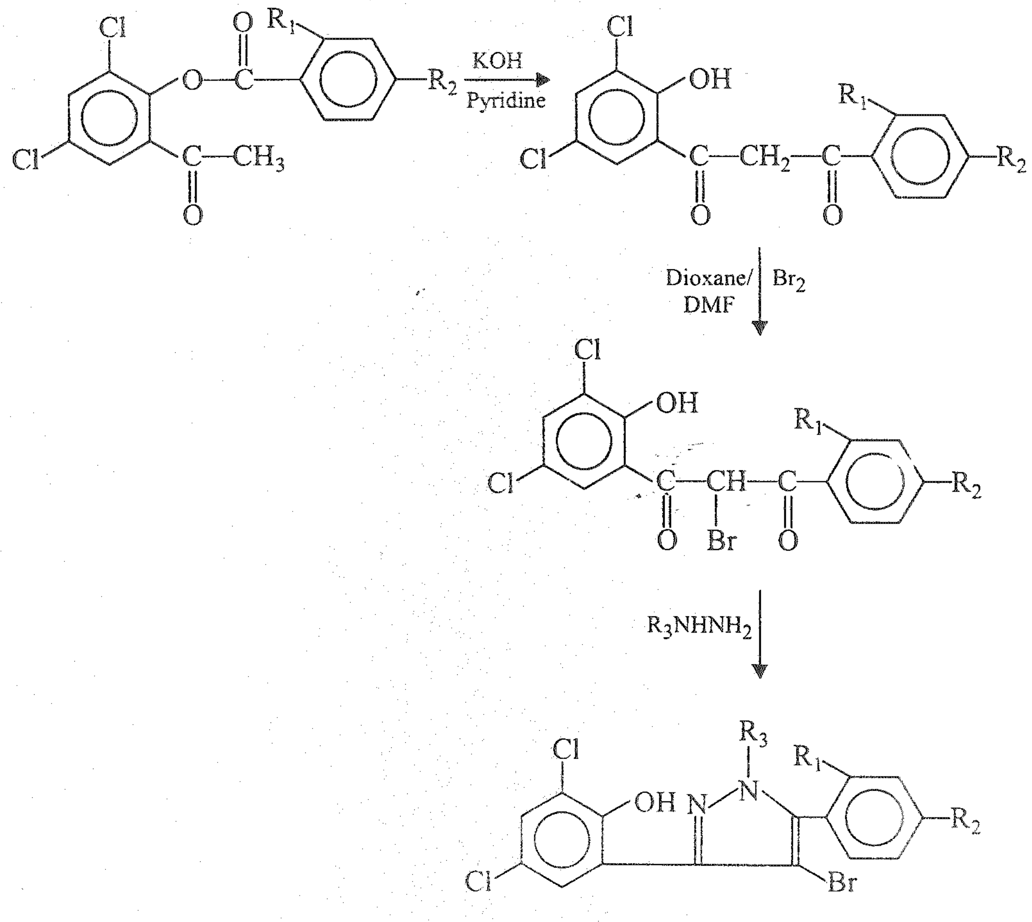
Key Words: Diketone, Bromo diketone, 1,3,5-trisubstituted -4-bromo pyrazole.

Azoles are well known for their enhanced biological activities[1] and have been extensively used as drugs in pharmaceuticals. Various pyrazoles have been found to possess antibacterial[2], antimicrobial[3], physiological[4], anticancer[5], herbicidal[6], antidibetic[7], pesticide[8] and fungicidal activities[9].

The present work deals with the synthesis of 3,5-diaryl-1-substituted-4-bromo pyrazoles from 1-(2-hydroxy-3,5-dichloro phenyl) 3-aryl- 2-bromo propan-1,3-diones and nucleophiles like isonicotinic acid hydrazide, semicarbazide and thiosemicarbazide. The structures of synthesized pyrazoles were confirmed from chemical properties and spectral analysis.

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. ^{1}H NMR spectra were recorded in $CDCl_3$ on Brucker 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 a 250 mL beaker. Phosphorus oxychloride ($POCl_3$) (2.5–3 mL) was added dropwise with constant stirring and external cooling. During addition of $POCl_3$ the temperature was maintained below 50°C. After addition it was allowed to stand for about 2 h



4/5/6(a-d)

and then treated with ice-cold dilute HCl (1 : 1) to neutralize pyridine. The product was repeatedly washed with water and then 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**).

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

Compounds	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
1a	H	H	75	98	$C_{15}H_{10}O_3Cl_2$
1b	H	OCH_3	75	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	$C_{15}H_9NO_5Cl_2$

The structures of the above compounds have been confirmed on the basis of analytical data and chemical properties.

Preparation of 1-(-2-hydroxy-3,5-dichloro phenyl)-3-aryl propan-1,3-diones (2a–d): Acetophenones **(1a–d)**, anhydrous pyridine or dimethyl formamide (0.5 mol) were taken in dry beaker. The mixture was warmed on low flame. Pulverized KOH (0.02 mol) was added with constant stirring. In case of DMF, the product was decomposed with ice-cold HCl (1 : 1) after 2 h. In case of pyridine it was 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 of **(2a–d)**.

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

Compounds	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	$C_{15}H_9NO_5Cl_2$

Spectral interpretation (2a): IR (ν_{max} KBr, 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).

Preparation of 1-(2-hydroxy-3,5-dichloro phenyl)-3-aryl-2-bromo propan-1,3-diones (3a–d): 1-(2-Hydroxy-3,5-dichloro phenyl)-3-aryl-propan-1,3-diones (2a–d) (0.02 mol) was dissolved in a mixture of dioxane and DMF (20 mL). To this liquid bromine (0.5 mL) was added slowly. It was kept for about 1 h and then diluted with water. The product was washed with water several times and crystallized from ethanol to obtain yellowish crystals of **(3a–d)**.

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

Compounds	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
3a	H	H	70	120	$C_{15}H_{10}O_3Cl_2$
3b	H	OCH_3	70	140	$C_{16}H_{12}O_4Cl_2$
3c	Cl	H	75	122	$C_{15}H_9O_3Cl_3$
3d	H	NO_2	70	Semi-solid	$C_{15}H_9O_5Cl_2N$

Spectral interpretation (3a): IR (ν_{max} KBr, cm^{-1}): 1659 ν(—C=O, *str.*), 373.4 ν(—OH, *str.*), 769.2, 812.4 ν(C—Cl, *str.*), 556.7 ν(C—Br, *str.*). NMR ($CDCl_3$ + DMSO) (δ ppm): 13.34 (S, 1H, —CH), 12.66 (S, 1H, —OH), 6.76–8.42 (m, 7H, Ar-H)

Preparation of 3,5-diaryl-1-substituted-4-bromo pyrazoles [4,5,6(a–d)]: 1-(2-Hydroxy-3,5-dichloro phenyl)-3-aryl-2-bromo propan-1,3-dione **(3a–3d)** (0.01 mol) was dissolved in ethanol (20 mL) and nucleophile such as isonicotinic acid hydrazide, semicarbazide, thiosemicarbazide was added to it. The reaction mixture was refluxed for about 2.5 h in basic medium. It was cooled and poured into water. The product was filtered, washed with water and crystallized from ethanol to obtain pale yellowish crystals of **[4,5,6(a–d)]**.

TABLE-4
PHYSICAL DATA OF 3,5-DIARYL-1-SUBSTITUTED-4-BROMO PYRAZOLES **[4,5,6(a–d)]**

Compounds	R_1	R_2	R_3	Yield (%)	m.p. (°C)	R_f	m.f.
4a	H	H	C_5H_4NCO	75	208	0.95	$C_{21}H_{12}O_2Cl_2BrN_3$
4b	H	OCH_3	C_5H_4NCO	70	150	0.80	$C_{22}H_{14}O_3Cl_2BrN_3$
4c	Cl	H	C_5H_4NCO	70	280	0.89	$C_{21}H_{11}O_2Cl_3BrN_3$
4d	H	NO_2	C_5H_4NCO	60	210	0.92	$C_{21}H_{11}O_4Cl_2BrN_4$
5a	H	H	$CONH_2$	65	178	0.92	$C_{16}H_{10}O_2Cl_2BrN_3$
5b	H	OCH_3	$CONH_2$	70	172	0.88	$C_{17}H_{12}O_3Cl_2BrN_3$
5c	Cl	H	$CONH_2$	75	132	0.88	$C_{16}H_{10}O_2Cl_3BrN_3$
5d	H	NO_2	$CONH_2$	70	198	0.88	$C_{16}H_9O_4Cl_2BrN_4$
6a	H	H	$CSNH_2$	70	182	0.88	$C_{16}H_{10}OCl_2BrN_3S$
6b	H	OCH_3	$CSNH_2$	65	160	0.92	$C_{16}H_{10}O_2Cl_2BrN_3S$
6c	Cl	H	$CSNH_2$	70	228	0.86	$C_{16}H_9OCl_3BrN_3S$
6d	H	NO_2	$CSNH_2$	75	125	0.95	$C_{16}H_9O_3Cl_2BrN_4S$

Specral interpretation (4a): IR (KBr, cm^{-1}): 31264.7 ν(—OH, *str.*), 1657.2 ν(C═O, *str.*), 1613.4 ν(C═N, *str.*), 682, 716 ν(C—Cl, *str.*), 543.6 ν(—C—Br, *str.*). NMR ($CDCl_3$ + DMSO) (δ ppm): 1.25 (S, 1H, —OH), 6.87–8.77 (m, 11H, Ar-H)

(5a): IR (ν_{max} KBr, cm^{-1}): 3422.8 ν(—OH, Str.), 1664.5 ν(C═O, *str.*), 594.9 ν(ON, *str.*), 766, 854 (C—Cl, *str.*), 563.4 ν(—C—Br, *str.*), 1292 ν(C—N, *str.*). NMR ($CDCl_3$ + DMSO) (δ ppm): 8.39 (S, 1H, —OH), 8.02 (S, 2H, —NH_2), 6.87–8.00 (m, 7H, Ar-H).

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