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SYNTHESIS OF CHLOROSUBSTITUTED 4–BROMO–3, 5–DIARYL–1–SUBSTITUTED PYRAZOLES

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ABSTRACT

New 1-thiocarboxamido/1-isonicotinoyl/1-carboxamido-4-bromo-3,5-diaryl pyrazoles (**4a-f/5a-f/ 6a-f**) have been synthesized by the action of thiosemicarbazide/isonicotinicacidhydrizide/semicarbazide hydrochloride with α-bromo 1,3-diaryl-propan-1,3-diones (**3a-f**) in ethanol medium. The synthesized compounds have been characterized by IR and NMR spectral analysis.

Key words: Pyrazoles, Synthesis.

INTRODUCTION

Synthesis and characterization of pyrazole derivatives has been a developing field within the realm of heterocyclic chemistry because of their accessibility through synthesis, wide range of chemical reactivity and broad spectrum of biological activity.

Pyrazole nucleus is present in number of drugs and dyes moieties. Hence, this class of compounds has been extensively studied and still attract the attention of synthetic organic chemists. Pyrazoles and their annulated derivatives have been widely investigated for therapeutic uses, especially as antipyretic[1,2] and active CNS regulants[3,4]. They were also reported to have hyptonic[5] and herbicidal[6] activities. Pyrazoles exhibit versatile physiological activity[7]. Pyrazoles were also reported[8] as plant diseases control agents, which were highly effective against fungi and safe for crops.

3,5-Diphenyl pyrazoles have been reported[9] by condensation of 1,3-diketones or flavones with substituted hydrazine in alcohol solvent. The most useful synthesis of pyrazole is by the action of hydrazine on 1,3-diones[10-13].

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The present work deals with the synthesis of chlorosubstituted 4-bromo-3,5-diaryl-1-substituted pyrazoles from α-bromo-1,3-diaryl-propan-1,3 diones on treatment with nucleophiles like thiosemicarbazide, isonicotinicacidhydrizide and semicarbazide hydrochloride in ethanol solvent.

RESULTS AND DISCUSSION

-OH Structures of synthesized compounds have been elucidated by IR and ^{1}HNMR spectroscopic data studies. IR spectra showed absorption bands around 1650-1550 cm^{-1}, which is a characteristic of C=N stretch of Pyrazole. Bands around 1440-1475 cm^{-1} which indicates C=C stretch of pyrazole. In 1,3-diones and α-bromo 1,3 diones, enol form [-C = C] form appear at 15.3-15.6 ppm due to electronegativity of oxygen atom the proton are deshielded hence its peak is shifted to downfield. The protons of aromatic ring and a $-NH_2$ were observed at 6.9-8.1 ppm and 5.6-7.9 ppm. Purity of these heterocycles was checked by TLC. All the compounds gave satisfactory nitrogen analysis.

EXPERIMENTAL

All melting points were taken in silicon oil bath instrument in open capillary and are uncorrected. Purity of the synthesized compounds was checked by TLC on silica Gel-G plates and the spots were visualized by exposure to iodine vapours. IR spectra (ν_{max} in cm^{-1}) were recorded on Perkin-Elmer spectrophotometer and PMR spectra (chemical shifts in δ, ppm) on Brucker AC-300 FT-NMR spectrophotometer (300 MHz) using ($CDCl_3$ + DMSO) as an internal reference.

Preparation of 1,3-diaryl-propan-1,3 diones (2a-f)

2-Benzoyloxy/Anisoyloxy-5-chloro acetophenone (0.05 mole) was dissolved in pyridine (15 mL). The mixture was warmed up to about 60°C. Pulverized KOH (0.15 mole) was added with constant stirring. The reaction mixture began to thicken and turned to yellowish brown mass. It was kept overnight. The reaction mixture was acidified by adding ice cold dil. HCl (1 : 1). The yellowish brown solid product thus separated was filtered, washed with sodium bicarbonate solution (5%) and then with excess of water. The product was crystallized from ethanol to afford yellow coloured product 1,3-diaryl-propan-1,3 dione **(2a-f)**. The identity of the product was confirmed by their IR and NMR spectroscopic data studies.

Similar compounds **(2a-f)** of the series were prepared and their physical data are recorded in Table 1.

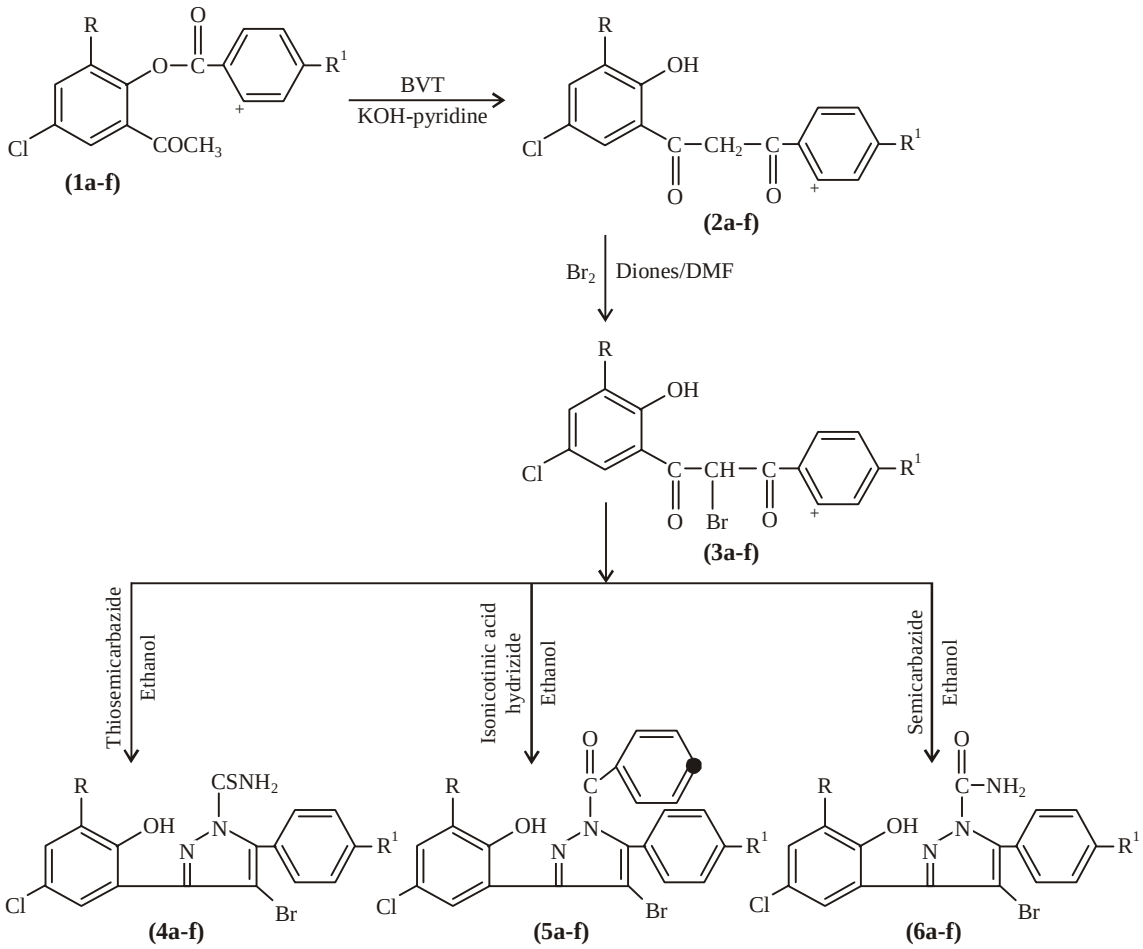

Table 1: Physical data of the diketone

Compound	R	R'	Molecular formula	M.P.	Yield
2a	H	H	$C_{15}H_{11}O_3Cl$	122^0C	70%
2b	Br	H	$C_{15}H_{10}O_3ClBr$	126^0C	75%
2c	NO_2	H	$C_{15}H_{10}O_5ClN$	132^0C	65%
2d	H	$-OCH_3$	$C_{16}H_{13}O_4Cl$	80^0C	70%
2e	Br	$-OCH_3$	$C_{16}H_{12}O_4ClBr$	129^0C	65%
2f	NO_2	$-OCH_3$	$C_{16}H_{12}O_6ClN$	139^0C	60%

Spectral interpretation

(2a) IR (ν_{max}) (cm^{-1}): 3052 (–OH stretch), 1610 (C=O stretch), 774 (C–Cl stretch), 1209 (C–O stretch)

NMR ($CDCl_3$ + DMSO) (δ ppm): 6.5 (s, 2H, $–CH_2–$), 6.9 – 8.2 (m, 8H, Ar–H) 12.1 (s, H, –OH), 15.4 [s, H, –C=C (enol)], -OH

Synthesis of α-bromo-1, 3 diaryl–propan-1,3 diones (3a-f)

1,3–Diaryl–propan–1,3 diones (0.01 mole) was dissolved in dioxane (10 mL) and DMF (10 mL) and treated with bromine (0.5 mL).

The reaction mixture was kept for an hour. It was then diluted with water. A solid separated was filtered, washed with water several times. Then it was crystallized with ethanol to obtain α-bromo-1,3-diaryl-propan-1,3 dione **(3a-f)**.

Similar compounds **(3a-f)** of the series were prepared and their physical data are recorded in Table 2.

Table 2: Physical data of the diketone

Compound	R	R’	Molecular formula	M.P. (^oC)	Yield (%)
3a	H	H	$C_{15}H_{10}O_3ClBr$	80	60
3b	Br	H	$C_{15}H_9O_3ClBr_2$	63	65
3c	NO_2	H	$C_{15}H_9O_5ClNBr$	85	55
3d	H	$–OCH_3$	$C_{16}H_{12}O_4ClBr$	65	60
3e	Br	$–OCH_3$	$C_{16}H_{11}O_4ClBr_2$	60	55
3f	NO_2	$–OCH_3$	$C_{16}H_{11}O_6ClNBr$	71	60

Spectral interpretation

(3a) IR (ν_{max}) (cm^{-1}): 3052 (–OH stretch), 1610 (C=O stretch), 775 (C–Cl stretch), 1186 (C–O stretch).

NMR ($CDCl_3$ + DMSO) (δ ppm) : 6.6 (s, H, –CH), 6.8 – 8 (m, 8H, Ar–H), 12 – 12.1 (s, H, –OH), 15.3 – 15.6 [s, H, –C=C(enol)], OH

Synthesis of pyrazoles

α-Bromo-1,3-diaryl-propan-1,3-dione (0.01 mole) **(3a-f)** was dissolved in ethanol (20 mL) and nucleophile (0.02 mole) like thiosemicarbazide, isonicotinicacidhydrizide and semicarbazide hydrochloride was added to it. The reaction mixture was refluxed for 2.5 h and then it was poured into water. Crude product was filtered and crystallized from ethanol to obtain pyrazoles **(4a-f)**, **(5a-f)** and **(6a-f)**. The identity of the products was confirmed by their IR and ^{1}HNMR spectroscopic data studies.

Similarly compounds **(4a-f)**, **(5a-f)** and **(6a-f)** of the series were prepared and their physical data are recorded in Table 3.

Table 3: Physical data of the pyrazoles

Compd.	R	R'	Molecular formula	R_f	M.P. (^oC)	N (%)		Yield (%)
						Calculated	Found	
4a	H	H	$C_{16}H_{11}N_3OSClBr$	0.66	220	10.63	10.12	60
4b	Br	H	$C_{16}H_{10}N_3OSCl_2$	0.66	175	8.87	8.54	65
4c	NO_2	H	$C_{16}H_{10}N_4O_3SClBr$	0.63	184	12.72	11.96	55
4d	H	$-OCH_3$	$C_{17}H_{13}N_3O_2SClBr$	0.68	242	9.88	9.15	65
4e	Br	$-OCH_3$	$C_{17}H_{12}N_3O_2SClBr_2$	0.63	222	8.03	8.17	70
4f	NO_2	$-OCH_3$	$C_{17}H_{12}N_4O_4SClBr$	0.67	231	11.91	11.23	65
5a	H	H	$C_{21}H_{13}N_3O_2ClBr$	0.81	>270	9.27	8.97	55
5b	Br	H	$C_{21}H_{12}N_3O_2ClBr_2$	0.63	237	7.90	7.15	50
5c	NO_2	H	$C_{21}H_{14}N_4O_4ClBr$	0.78	>270	11.2	10.87	50
5d	H	$-OCH_3$	$C_{21}H_{15}N_3O_3ClBr$	0.53	181	8.91	8.21	65
5e	Br	$-OCH_3$	$C_{21}H_{14}N_3O_4ClBr_2$	0.61	162	7.43	6.96	55
5f	NO_2	$-OCH_3$	$C_{21}H_{14}N_4O_5ClBr$	0.69	168	10.85	10.21	60
6a	H	H	$C_{16}H_{11}N_3O_2ClBr$	0.71	204	10.74	10.38	50
6b	Br	H	$C_{16}H_{10}N_3O_2ClBr_2$	0.63	174	8.95	8.76	45

Cont…

Compd.	R	R'	Molecular formula	R_f	M.P. (^oC)	N (%)		Yield (%)
						Calculated	Found	
6c	NO_2	H	$C_{16}H_{10}N_4O_4ClBr_2$	0.80	180	12.84	11.98	55
6d	H	$–OCH_3$	$C_{17}H_{13}N_3O_3ClBr$	0.68	>270	9.97	9.14	50
6e	Br	$–OCH_3$	$C_{17}H_{12}N_3O_3ClBr_2$	0.63	210	8.41	8.63	55
6f	NO_2	$–OCH_3$	$C_{17}H_{12}N_4O_5ClBr$	0.61	218	12.01	11.86	45

Spectral interpretation

(4a) IR (ν_{max}) (cm^{-1}): 3169 (–OH stretch), 1609 (C=N stretch), 2945 (C–H stretch), 1466 (C=C stretch), 827 (C–Cl stretch)

NMR ($CDCl_3$ + DMSO) (δ ppm) : 5.6 (s, 2H, – NH_2), 6.9-7.8 (m, 8H, Ar–H), 9.2 (s, H, –OH)

(5a) IR (ν_{max}) (cm^{-1}): 3083 (–OH stretch), 1648 (C=O stretch), 1600 (C=N stretch), 1456 (C=C stretch), 771 (C–Cl stretch),

NMR ($CDCl_3$ + DMSO) (δ ppm) : 6.9 (s, H, -OH), 7.5-8.1 (m, 12H, Ar–H)

(6a) IR (ν_{max}) (cm^{-1}): 3081 (–OH stretch), 1650 (C=O stretch), 1599 (C=N stretch), 1447 (C=C stretch), 771 (C–Cl stretch),

NMR ($CDCl_3$ + DMSO) (δ ppm) : 6.8-7.7 (m, 8H, Ar–H), 7.9 (s, 2H, –NH_2), 8.2 (s, H, –OH).

REFERENCES

1. H. Ochi, T. Miyasaka and K. Kanada, Bull. Chem. Soc. Jpn, **49**, 1980 (1976).
2. M. H. Elnagdi, Tetrahedron, **30**, 2791 (1974).
3. T. Nouinson, R. Hanson, M. K. Dimmitt, K. N. Simon, R. K. Robins and D. E. Brien, J. Med. Chem., **17**, 645 (1974).
4. H. A. Dewald, S. Lobbestael and D. E. Bulter, J. Med. Chem., **20**, 1562 (1977).
5. E. Kanz, T. Haffineistered and W. Woltke, Ger. Pat., **2131**, 790 (1971).
6. B. W. Doming, U. S. Pat, 3833582 (1974), Chem. Abstr., **81**, 152270 (1974).

7. E. Herman and J. Gablis, Cancer Chemother. Rept., **14**, 85 (1961).

8. Akiyama, Shigeaki, Niki, Toshis, Otsunosmia, Watanabe, Junichi, Nishioka, Masanari, Suzuki, Hiroyuki, Yahasaka, Fumis, Yamagishi, PCT Int. Apptl. W09912, 910, (Cl CO_7 D231/16), Chem. Abstr., **130**, 237562 a (1999).

9. Takoyoshi, Nagosaka, Hideki, Nishimora, Akis, Chem. Abstr., **77**, 417 (1972).

10. S. S. Joshi and I. R. Gambhir, J. Am. Chem. Soc., **79**, 2222 (1956).

11. H. G. Garg and S. S. Joshi, J. Org. Chem., **26**, 943 (1961).

12. Horst Bohme and Hans Scheidr, Chem. Ber., 91 (1958).

13. B. Estert and R. Wessendarf, Chem. Ber., **94**, 2590 (1961).

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