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Antimicrobial Activity of 3,5-Diaryl-4-bromo-1-substituted Pyrazoles

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1-(2-Hydroxy-3,5-dichlorophenyl)-3-aryl-2-bromo-propan-1,3-diones were prepared by the action of bromine on 1-(2-hydroxy-3,5-dichlorophenyl)-3-aryl-propan-1,3-diones. The 3,5-diaryl-4-bromo-1-substituted pyrazoles have been synthesized by refluxing 1-(2-hydroxy-3,5-dichlorophenyl)-3-aryl-2-bromo-propan-1,3-diones with 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 (NMR and IR). Purity of these heterocycles was checked by TLC. These compounds were testred for antimicrobial activity against pathogenic bacterial and are found to have remarkable activity.

Key Words: Diketone, Bromo diketone, 3,5-Diaryl-4-bromo-1-substituted pyrazoles.

INTRODUCTION

From literature survey it has been established that pyrazoles and/or substituted pyrazoles possess wide range of antimicrobial properties[1,2]. Bromo pyrazoles are more active towards each microorganisms as compared to other pyrazoles. This may be due to presence of bromine atom in structure of pyrazoles. Pyrazoles and their synthetic analogous have been found to exhibit industrial, agricultural and biological applications[3,4]. They are also found to be antibasic[5], pesticides[6], antiinflammatory[7], hypolipodermic agents[8], antiparasitic[9] and effective insectisides[10].

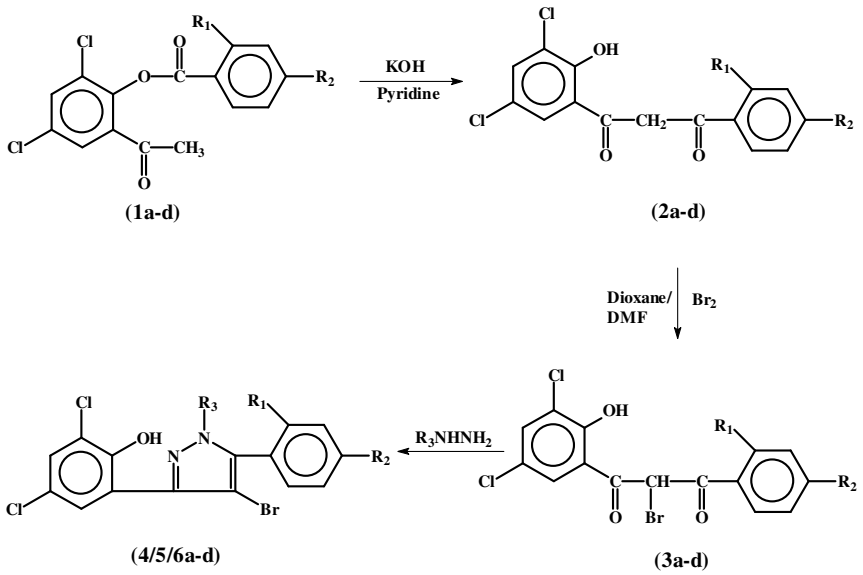
Present work deals with the study of 1-(2-hydroxy-3,5-dichlorophenyl)-3-aryl-propan-1,3-diones, 1-(2-hydroxy-3,5-dichlorophenyl)-3-aryl-2-bromo-propan-1,3-diones and 3,5-diaryl-4-bromo-1-substituted pyrazoles for antimicrobial activity. These compounds were testred against *S. aureus, K. pneumoniae, S. typhi, P. vulgaris, S. flexurei, E. coli* and *P. aerugivosa*. All compounds were found to be active against these organisms.

EXPERIMENTAL

The melting points were determined in open capillary tube and are uncorrected, purity of compounds was checked by TLC on silica gel-G plates. IR spectra was recorded on Pertein Elmer spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ on Bruker AC 300 F NMR spectrophotometer at 300 MHz using TMS as internal reference. Antimicrobial activity of the compounds was tested by cup plate agar diffusion method[11].

RESULTS AND DISCUSSION

The structures of all synthesized compounds (**Scheme-I**) *viz.*, 2-aroyloxy-3,5-dichloro acetophenone (**1a-d**), 1-(2-hydroxy-3,5-dichlorophenyl)-3-aryl-propan-1,3-dione (**2a-d**), 1-(2-hydroxy-3,5-dichlorophenyl)-3-aryl-2-bromo-propan-1,3-diones (**3a-d**) and 3,5-diaryl-1-substituted-4-bromo pyrazoles (**4/5/6a-d**) have been confirmed on by analytical data (Table-1) and chemical properties.



Scheme-I

Spectral data

2a: IR (ν_{max} cm^{-1}): 1602 (–C=O), 3069.6 (–OH), 737.6, 802.4 (C–Cl); NMR ($CDCl_3$ + DMSO) δ: 6.77 (s, 2H, $–CH_2$), 7.25-7.96 (m, 7H, Ar-H), 12.66 (s, 1H, -OH).

3a: IR (ν_{max} cm^{-1}): 1605.7 (–C=O), 3070.8 (–OH), 719, 769.2 (C–Cl), 682 (C–Br); NMR ($CDCl_3$ + DMSO) δ: 12.66 (s, 1H, –CH), 6.76-8.42 (m, 7H, Ar-H), 7.2 (s, 1H, -OH).

TABLE-1
PHYSICAL DATA OF COMPOUNDS **1a-d, 2a-d, 3a-d, 4a-d, 5a-d** AND **6a-d**

Compd.	R_1	R_2	R_3	Yield (%)	m.p. (ºC)	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	$C_{15}H_9NO_5Cl_2$
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	$C_{15}H_9NO_5Cl_2$
3a	H	H	–	70	120	$C_{15}H_9O_3BrCl_2$
3b	H	OCH_3	–	70	140	$C_{16}H_{11}O_4BrCl_2$
3c	Cl	H	–	75	122	$C_{15}H_8O_3BrCl_3$
3d	H	NO_2	–	70	150	$C_{15}H_8NO_5BrCl_2$
4a	H	H	C_5H_4NCO	75	208	$C_{21}H_{12}N_3O_2BrCl_2$
4b	H	OCH_3	C_5H_4NCO	70	150	$C_{22}H_{14}N_3O_3BrCl_2$
4c	Cl	H	C_5H_4NCO	70	280	$C_{21}H_{11}N_3O_2\ BrCl_3$
4d	H	NO_2	C_5H_4NCO	60	210	$C_{21}H_{11}N_4O_4BrCl_2$
5a	H	H	$CONH_2$	65	178	$C_{16}H_{10}N_3O_2BrCl_2$
5b	H	OCH_3	$CONH_2$	70	172	$C_{17}H_{12}N_3O_3BrCl_2$
5c	Cl	H	$CONH_2$	75	132	$C_{16}H_{10}N_4O_2BrCl_2$
5d	H	NO_2	$CONH_2$	70	198	$C_{16}H_9N_4O_4BrCl_2$
6a	H	H	$CSNH_2$	70	182	$C_{16}H_{10}N_3OSBrCl_2$
6b	H	OCH_3	$CSNH_2$	65	160	$C_{16}H_{10}N_3O_2SBrCl_2$
6c	Cl	H	$CSNH_2$	70	228	$C_{16}H_9N_3OSBrCl_3$
6d	H	NO_2	$CSNH_2$	75	125	$C_{16}H_9N_4O_3SBrCl_2$

4a: IR (ν_{max} cm^{-1}): 31264.7 (–OH), 1657.2 (C=O), 1613.4 (C=N), 682, 768 (C–Cl), 587 (C–Br); NMR ($CDCl_3$ + DMSO) δ: 6.87 (s, 1H, –CH), 7.26-8.77 (m, 11H, Ar-H).

5a: IR (ν_{max} cm^{-1}): 3422.8 (–OH), 1664.5 (C=O), 1556 (C=N) 766, 886 (C–Cl), 563.4 (–C–Br), 1312 (C–N); NMR ($CDCl_3$ + DMSO) δ: 7.25 (s, 1H, –OH), 8.39 (s, 2H, -NH_2), 7.52-8.17 (m, 7H, Ar-H).

Antimicrobial activity

The present compounds were tested against pathogenic bacteria for their antibacterial activity by paper disk method[12]. The organisms tested were *S. aureus, K. pneumoniae, S. typhi, P. vulgaris, S. flexurei, E. coli* and

P. aerugivosa. The solution of these compounds was prepared in DMSO as a solvent at a concentration of 50 μ/mL. The culture medium used was nutrient agar. After 24 h of inhibition at 37ºC, the zones of inhibition were measured in mm (Table-2).

TABLE-2
ANTMICROBIAL ACTIVITY OF COMPOUNDS **1a-d, 2a-d, 3a-d, 4a-d, 5a-d** AND **6a-d**

Compd.	Microorganisms						
	S. aureus	*K. pneumoniae*	*S. typhi*	*P. vulgaris*	*S. flexueri*	*E. coli*	*P. aerugivosa*
1a	12	11	–	11	11	13	–
1b	–	–	–	–	11	15	14
1c	12	12	–	12	14	15	–
1d	13	18	11	14	22	17	12
2a	16	16	–	11	11	13	–
2b	12	11	–	11	–	11	–
2c	21	14	17	20	19	14	–
2d	15	21	16	–	20	13	12
3a	14	14	16	16	17	14	–
3b	15	14	12	12	–	13	–
3c	13	16	19	13	22	15	–
3d	–	–	–	–	–	–	–
4a	23	23	14	19	16	21	13
4b	14	12	17	18	17	13	22
4c	22	25	16	17	12	18	20
4d	15	22	24	20	13	15	22
5a	12	21	14	15	12	17	15
5b	24	14	18	23	15	14	24
5c	18	14	20	14	21	21	21
5d	17	23	21	15	12	13	22
6a	20	21	17	16	15	17	24
6b	22	14	18	15	21	16	22
6c	16	22	15	16	13	21	11
6d	18	15	16	19	20	12	13

From the Table-2 it is observed that *S. flexueri* highly active against **1d** and moderately active against rest of compounds. *E. coli* are moderate active against all. The compounds of this series, where as *S. typhi* is inactive against **1a-c**. Rests of the organisms are weakly active against these compounds. *S. aureus* and *P. vulgaris* are highly active against **2c**. *K.*

pneumoniae and *S. flexueri* are highly active against **2d**. *E. coli* are moderately active against all four compounds of **c** this series. Where as *P. aerugivosais* active against **2d**. **3d** is the compound which is inactive against all tested organisms. Only *S. flexueri* is highly active against **3c** and *P. aerugivosa* in active against all compounds of this series. Rest of organisms are moderately active. S. aureus is highly active against **4a**, **4c**, **5b**, **6a** and **6b**. Moderately active against **4d**, **5c-d** and **6c-d** and weakly against **4b** and **5a**. *K. pneumoniae* is highly active against **4a**, **4c-d**, **5a**, **5d**, **6a** and **6c**. Moderately active against **6d** and *S. typhi* is highly active against **4a**, **5c** and **5d**. Moderately active against **4b-c**, **5b**, **6-d** and weakly against **4a** and **5a**. *P. vulgaris* is highly active against **4d** and **5b**. Moderately active against **4a-c**, **5a**, **5d**, **6a-d** and weakly against **5c**. *S. flexueri* is highly active against **5c**, **6b-c**. Moderately active against **4a-b**, **5b**, **6a** and weakly against **4c-d**, **5a**, **5d**, **6c**. *E. coli* is highly active against **4a**, **5c** and **6c**. Moderately active against **4c-d**, **6a-b** and weakly against **4b**, **5b**, **5d** and **6d**. *P. aerugivosa* is highly active against **4b-c**, **5b-d** and **6a-b**. Moderately active against **5a** and weakly against **4a**, **5c** and **6d**.

From all this data it is concluded that *S. aureus, K. pneumoniae* and *P. aerugivosa* are more highly active against many compounds. *S. aureus, S. typhi, P. vulgaris, S. flexueri* and *E. coli* are moderately active against many compounds. Rest are weakly active.

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