STUDIES IN HETEROCYCLIC COMPOUNDS*—PART VII

Synthesis of Some new 3,5-diaryl-4-(substituted sulphonamidobenzeneazo) pyrazoles as potential antibacterials

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Different azo compounds, 1-(*m*-nitrophenyl)-3-(*p*-bromophenyl)- and 1-(*m*-nitrophenyl) 3-(*p*-chlorophenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones on condensation with hydrazine hydrate (100%), phenylhydrazine, *p*-nitrophenylhydrazine and benzoylhydrazine yield the corresponding 1-simple/substituted-3-(*m*-nitrophenyl)-5- (*p*-bromo chlorophenyl)-4-(substituted sulphonamidobenzeneazo) pyrazoles. The homogeneity and purity of these was confirmed by TLC and these on screening *in vitro* against *S. aureus* and *E. coli* were found to exhibit antibacterial activity.

In continuation of our earlier work on the synthesis and antibacterial study of some pyrazole derivatives[1-4] and encouraged by the observations, and also on account of their use as potential explosives[5], it was thought of interest to synthesise other new pyrazoles having *m*-nitrophenyl group at position-3 and halogeno phenyl at position-5 of the azole nucleus. This work would provide an opportunity of studying the comparative effect of the halogens as well as the effect of exchange of the alkyl/alkoxyl group [4,6] by halogens on their antibacterial properties.

The present communication describes the synthesis and antibacterial study of 1-simple/substituted-3-(*m*-nitrophenyl)-5-(*p*-bromo/chlorophenyl)-4-(substituted sulphonamidobenzeneazo) pyrazoles (Fig. 1). These were synthesised by condensing various 1-(*m*-nitrophenyl)-3-(*p*-bromo/chlorophenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones with hydrazinehydrate (100%), phenylhydrazine, *p*-nitrophenylhydrazine, and benzoylhydrazine. These compounds when subjected to TLC using benzene-methanol mixture (45 : 5) as the solvent system gave only one spot thereby proving the homogeneity and purity of the compounds.

EXPERIMENTAL PROCEDURE

Different 1-(*m*-nitrophenyl)-3-(*p*-bromophenyl)-and 1-(*m*-nitrophenyl)-3-(*p*-chlorophenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones required for this work were prepared by the method described earlier[7].

Synthesis of 3-(m-nitrophenyl)-5-(p-chlorophenyl)-4-(substituted sulphonamidobenzeneazo) pyrazoles

A solution of 1-(*m*-nitrophenyl)-3-(*p*-chlorophenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-dione (0·1 g) in glacial acetic acid and hydrazine hydrate (100%; 0·05 g) was refluxed in an oil bath at 160-70° for 6-7 hr and the contents left overnight. The separated solid was filtered, washed with water, dried and crystallised from glacial acetic acid, glacial acetic acid—ethanol mixture or from an ethanol—DMF mixture.

Reactions with phenylhydrazine, *p*-nitrophenylhydrazine and benzoylhydrazine were carried out in glacial acetic acid—ethanol mixture by refluxing in a water bath; however, in the case of benzoylhydrazine and *p*-nitrophenylhydrazine, addition of few drops of concentrated sulphuric acid was found essential.

Pyrazoles from 1-(*m*-nitrophenyl)-3-(*p*-bromophenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones were similarly prepared. All the pyrazoles and the results of their antibacterial tests are entered in Tables[1-8].

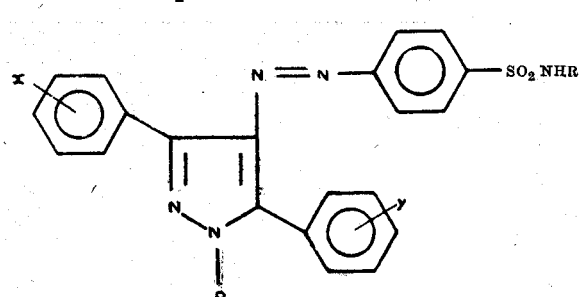

Fig. 1

Antibacterial activity

These pyrazole derivatives have been screened *in vitro* against *S. aureus* and *E. coli* employing the cup-plate agar diffusion method[8].

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The pyrazole derivatives exhibit mixed activity and it was observed that the exchange of chlorine by bromine shows overall increase in the activity; however, the activity tends to show greater increase in the case of *E. coli* as compared to *S. aureus*.

The effect of exchanging the alkyl/alkoxyl groups by halogens cause an overall decrease in the activity.

Another conclusion drawn is that in general the pyrazoles having a heterocyclic ring in the sulphonamide moiety exhibit greater activity as compared to others. The compounds containing 5-methyl-1, 3,4-thiadiazolyl ring are found to be the most active against both organisms.

TABLE 1

3-(*m*-NITROPHENYL)-5-(*p*-CHLOROPHENYL)-4-(SUBSTITUTED SULPHONAMIDOBENZENEAZO) PYRAZOLES

(Fig. 1 x=*m*-NO_2; *y*=*p*-Cl; R_1=H)

R	M.P. (°C)	Colour	Yield (%)	Molecular formula	C (Found) (%)	H (Found) (%)	C (Required) (%)	H (Required) (%)	Antibacterial activity *S. aureus*	Antibacterial activity *E. coli*
H	273	SO	76	$C_{21}H_{15}O_4N_6SCl$	52·0	3·2	52·2	3·1	(++)	(++)
Acetyl	277	ON	74	$C_{23}H_{17}O_5N_6SCl$	52·5	3·3	52·6	3·2	(+)	(—)
Phenyl	222	O	73	$C_{27}H_{19}O_4N_6SCl$	58·0	3·6	58·0	3·4	(+)	(—)
o-Methylphenyl	230	SR	70	$C_{28}H_{21}O_4N_6SCl$	58·5	3·9	58·7	3·7	(+)	(++)
o-Methoxyphenyl	223	BO	76	$C_{28}H_{21}O_5N_6SCl$	57·0	3·5	57·1	3·6	(+)	(—)
p-Methoxyphenyl	235	O	78	$C_{28}H_{21}O_5N_6SCl$	57·3	3·5	57·1	3·6	(—)	(—)
Guanidyl	284	BR	74	$C_{22}H_{17}O_4N_8SCl$	50·1	3·0	50·3	3·2	(—)	(+)
α-Pyridyl	256	OR	75	$C_{28}H_{18}O_4N_7SCl$	55·9	3·5	55·8	3·2	(+)	(++)
Pyrimidyl	305	RN	72	$C_{25}H_{17}O_4N_8SCl$	53·6	3·2	53·5	3·0	(+++)	(+)
4,6-Dimethylpyrimidyl	169	R	73	$C_{27}H_{21}O_4N_8SCl$	55·2	3·6	55·0	3·6	(++)	(—)
2,6-Dimethylpyrimidyl	273	O	74	$C_{27}H_{21}O_4N_8SCl$	55·1	3·8	55·0	3·6	(+)	(+)
2,6-Dimethoxypyrimidyl	274	SO	76	$C_{27}H_{21}O_6N_6SCl$	52·4	3·5	52·2	3·4	(—)	(—)

B=Bright, D=Dark, F=Flakes, N=Needles, O=Orange, R=Red, S=Shining

TABLE 2

1-PHENYL-3-(*m*-NITROPHENYL)-5-(*p*-CHLOROPHENYL)-4-(SUBSTITUTED SULPHONAMIDOBENZENEAZO) PYRAZOLES

(Fig. 1 x=*m*-NO_2; y=*p*-Cl, R_1=C_6H_5)

R	M.P. (°C)	Colour	Yield (%)	Molecular formula	C (Found) %	H (Found) %	C (Required) %	H (Required) %	Antibacterial activity *S. aureus*	Antibacterial activity *E. coli*
H	201	BR	77	$C_{27}H_{19}O_4N_6SCl$	58·2	3·5	58·0	3·4	(+)	(—)
Acetyl	210	OF	72	$C_{29}H_{21}O_5N_6SCl$	58·1	3·6	57·9	3·5	(+)	(—)
Phenyl	241	RN	70	$C_{33}H_{23}O_4N_6SCl$	62·5	3·4	62·4	3·6	(—)	(—)
o-Methylphenyl	201	OR	66	$C_{34}H_{25}O_4N_6SCl$	62·8	3·9	62·9	3·8	(—)	(—)
o-Methoxyphenyl	200	R	65	$C_{34}H_{25}O_5N_6SCl$	61·4	3·7	61·4	3·8	(—)	(—)
p-Methoxyphenyl	261	R	68	$C_{34}H_{25}O_5N_6SCl$	61·5	3·6	61·4	3·8	(+)	(—)
Guanidyl	278	ON	72	$C_{28}H_{21}O_4N_8SCl$	55·7	3·5	55·9	3·5	(++)	(—)
α Phridyl	251	SON	74	$C_{32}H_{22}O_4N_7SCl$	60·3	3·4	60·4	3·5	(+)	(+)
Phrimidyl	240	BO	76	$C_{31}H_{21}O_4N_8SCl$	58·5	3·3	58·4	3·3	(—)	(—)
4 6-Dimethylpyrimidyl	230	O	72	$C_{33}H_{25}O_4N_8SCl$	59·5	3·9	59·6	3·8	(+)	(+)
2,6-Dimethylpyrimidyl	210	O	70	$C_{33}H_{25}O_4N_8SCl$	55·6	3·8	59·6	3·8	(—)	(—)
2,6 Dimethoxypyrimidyl	200	RN	67	$C_{33}H_{25}O_6N_8SCl$	56·7	3·4	56·8	3·6	(++)	(+)

Table 3

1-(*p*-Nitrophenyl)-3-(*m*-nitrophenyl)-5-(*p*-chlorophenyl)-4-(substituted sulphonamidobenzeneazo) pyrazoles

(Fig. 1 x=*m*-NO_2 ; y=*p*-Cl; R_1=*p*-$NO_2 \cdot C_6H_5$)

R	M.P.	Colour	Yield	Molecular formula	C (Found)	H (Found)	C (Required)	H (Required)	Antibacterial activity	
	(°C)		(%)		%	%	%	%	*S. aureus*	*E. coli*
H	308	SR	72	$C_{27}H_{18}O_6N_7SCl$	53·6	3·1	53·7	3·0	(++)	(—)
Acetyl	292	BR	70	$C_{29}H_{20}O_7N_7SCl$	53·8	3·1	53·9	3·1	(+)	(—)
Phenyl	215	R	68	$C_{33}H_{22}O_6N_7SCl$	58·5	3·1	58·3	3·2	(+)	(—)
o-Methylphenyl	240	SR	68	$C_{34}H_{24}O_6N_7SCl$	58·9	3·5	58·8	3·5	(—)	(—)
o-Methoxyphenyl	210	SRN	63	$C_{34}H_{24}O_7N_7SCl$	57·6	3·6	57·5	3·4	(++)	(—)
p-Methoxyphenyl	238	RF	66	$C_{34}H_{24}O_7N_7SCl$	57·6	3·4	57·5	3·4	(+)	(—)
Guanidyl	240	OF	68	$C_{28}H_{20}O_6N_9SCl$	52·0	3·3	52·0	3·1	(++)	(+)
α-Pyridyl	243	DR	70	$C_{32}H_{21}O_6N_8SCl$	56·2	3·2	56·4	3·1	(—)	(+)
Pyrimidyl	252	R	71	$C_{31}H_{20}O_6N_9SCl$	54·5	3·0	54·6	2·9	(+)	(—)
4,6-Dimethylpyrimidyl	175	R	68	$C_{33}H_{24}O_6N_9SCl$	55·7	3·5	55·8	3·4	(+)	(—)
2,6-Dimethylpyrimidyl	198	ON	64	$C_{33}H_{24}O_6N_9SCl$	55·9	3·5	55·8	3·4	(++)	(++)
2,6-Dimethoxypyrimidyl	216	DR	66	$C_{33}H_{24}O_8N_9SCl$	53·3	3·1	53·4	3·2	(++)	(++)

Table 4

1-Benzoyl-3-(*m*-nitrophenyl)-5-(*p*-chlorophenyl)-4-(substituted sulphonamidobenzeneazo) pyrazoles

(Fig. 1 x = *m*-NO_2 ; y = *p*-Cl; R_1 = COC_6H_5)

R	M.P.	Colour	Yield	Molecular formula	C (Found)	H (Found)	C (Required)	H (Required)	Antibacterial activity	
	(°C)		(%)		%	%	%	%	*S. aureus*	*E. coli*
H	280	O	69	$C_{28}H_{19}O_5N_6SCl$	57·5	3·1	57·3	3·2	(+)	(+)
Acetyl	275	SON	70	$C_{30}H_{21}O_6N_6SCl$	57·4	3·4	57·3	3·3	(—)	(++)
Phenyl	220	OF	72	$C_{34}H_{23}O_5N_6SCl$	61·5	3·4	61·6	3·5	(—)	(—)
o-Methylphenyl	235	RN	68	$C_{35}H_{25}O_5N_6SCl$	62·2	3·6	62·1	3·7	(—)	(+)
o-Methoxyphenyl	218	SRN	74	$C_{35}H_{25}O_6N_6SCl$	60·8	3·5	60·6	3·6	(+)	(+)
p-Methoxyphenyl	240	O	75	$C_{35}H_{25}O_6N_6SCl$	60·5	3·6	60·6	3·6	(+)	(+)
Guanidyl	288	SR	72	$C_{29}H_{21}O_5N_8SCl$	55·3	3·1	55·4	3·3	(—)	(+)
α-Pyridyl	245	BO	70	$C_{33}H_{22}O_5N_7SCl$	59·9	3·2	59·7	3·3	(+)	(+)
Pyrimidyl	>300	R	71	$C_{32}H_{21}O_5N_8SCl$	57·9	3·0	57·8	3·2	(++)	(—)
4,6-Dimethylpyrimidyl	281	O	72	$C_{34}H_{25}O_5N_8SCl$	59·0	3·6	58·9	3·6	(+)	(—)
2,6-Dimethylpyrimidyl	>300	RN	73	$C_{34}H_{25}O_5N_8SCl$	58·8	3·7	58·9	3·6	(+)	(++)
2,6-Dimethoxypyrimidyl	165	OF	67	$C_{34}H_{25}O_7N_8SCl$	56·1	3·4	56·3	3·4	(+)	(+)

TABLE 5

3-(*m*-NITROPHENYL)-5-(*p*-BROMOPHENYL)-4-(SUBSTITUTED SULPHONAMIDOBENZENEAZO) PYRAZOLES
(Fig. 1 x=*m*-NO ; y=*p*-Br; R_1 =H)

R	M.P. (°C)	Colour	Yield (%)	Molecular formula	C (Found) %	H (Found) %	C (Required) %	H (Required) %	Antibacterial activity *S. aureus*	Antibacterial activity *E. coli*
H	280	OF	74	$C_{21}H_{15}O_4N_6SBr$	47·9	2·8	47·8	2·8	(+)	(—)
Acetyl	285	RN	76	$C_{23}H_{17}O_5N_6SBr$	48·3	3·1	48·5	3·0	(+)	(—)
Phenyl	226	O	72	$C_{27}H_{19}O_4N_6SBr$	53·8	3·3	53·7	3·1	(+)	(+)
o-Methylphenyl	240	BO	73	$C_{28}H_{21}O_4N_6SBr$	54·5	3·5	54·4	3·4	(—)	(+)
o-Methoxyphenyl	209	RN	70	$C_{28}H_{21}O_5N_6SBr$	53·1	3·4	53·1	3·3	(+)	(+)
p-Methoxyphenyl	214	SO	76	$C_{28}H_{21}O_5N_6SBr$	53·2	3·3	53·1	3·3	(—)	(—)
Guanidyl	282	SR	75	$C_{22}H_{17}O_4N_8SBr$	46·5	3·1	46·4	3·0	(—)	(+)
α-Pyridyl	258	OR	68	$C_{26}H_{18}O_4N_7SBr$	51·4	2·9	51·6	3·0	(+)	(+)
Pyrimidyl	306	R	69	$C_{25}H_{17}O_4N_8SBr$	49·5	2·7	49·6	2·8	(+++)	(+)
4,6-Dimethylpyrimidyl	170	DR	73	$C_{27}H_{21}O_4N_8SBr$	51·4	3·5	51·2	3·3	(++)	(++)
2,6-Dimethylpyrimidyl	272	RN	74	$C_{27}H_{21}O_4N_8SBr$	51·3	3·4	51·2	3·3	(—)	(+)
5-Methyl-1,3,4-thiadiazolyl	244	OF	75	$C_{24}H_{17}O_4N_8S_2Br$	46·2	2·9	46·1	2·7	(+++)	(++)

TABLE 6

1-PHENYL-3-(*m*-NITROPHENYL)-5-(*p*-BROMOPHENYL)-4-(SUBSTITUTED SULPHONAMIDOBENZENEAZO) PYRAZOLES
(Fig. 1 x=*m*-NO_2; y=*p*-Br; R_1=C_6H_5)

R	M.P. (°C)	Colour	Yield (%)	Molecular formula	C (Found) %	H (Found) %	C (Required) %	H (Required) %	Antibacterial activity *S. aureus*	Antibacterial activity *E. coli*
H	246	OF	70	$C_{27}H_{19}O_4N_6SBr$	53·5	3·0	53·7	3·1	(—)	(+)
Acetyl	242	BO	71	$C_{29}H_{21}O_5N_6SBr$	53·8	3·4	53·9	3·2	(—)	(+)
Phenyl	248	RN	70	$C_{33}H_{23}O_4N_6SBr$	58·2	3·5	58·3	3·4	(+)	(—)
o-Methylphenyl	200	SRN	69	$C_{34}H_{25}O_4N_6SBr$	59·0	3·6	58·9	3·6	(—)	(—)
o-Methoxyphenyl	218	SR	72	$C_{34}H_{25}O_5N_6SBr$	57·7	3·4	57·5	3·5	(—)	(+)
p-Methoxyphenyl	252	R	71	$C_{34}H_{25}O_5N_6SBr$	57·8	3·3	57·5	3·5	(—)	(+)
Guanidyl	290	OR	69	$C_{28}H_{21}O_4N_8SBr$	52·0	3·5	52·1	3·3	(+)	(+)
α-Pyridyl	234	R	70	$C_{32}H_{22}O_4N_7SBr$	56·4	3·3	56·5	3·2	(+)	(+)
Pyrimidyl	285	OF	73	$C_{31}H_{21}O_4N_8SBr$	54·5	3·0	54·6	3·1	(+)	(+)
4,6-Dimethylpyrimidyl	227	SO	72	$C_{33}H_{25}O_4N_8SBr$	55·9	3·7	55·8	3·5	(+)	(—)
2,6-Dimethylpyrimidyl	217	BO	74	$C_{33}H_{25}O_4N_8SBr$	55·6	3·6	55·8	3·5	(+)	(—)
5-Methyl-1, 3,4-thiadiazolyl	240	O	75	$C_{30}H_{21}O_4N_8S_2Br$	51·1	3·0	51·3	3·0	(++)	(—)

Table 7

1-(*p*-Nitrophenyl)-3-(*m*-nitrophenyl)-5-(*p*-bromophenyl)-4-(substituted sulphonamidobenzeneazo) pyrazoles

(Fig. 1 x=*m*-NO_2 ; y=*p*-Br; R_1 =*p*-$NO_2C_6H_5$)

R	M.P.	Colour	Yield	Molecular formula	C (Found)	H (Found)	C (Required)	H (Required)	Antibacterial activity	
	(°C)		(%)		%	%	%	%	*S. aureus*	*E. coli*
H	279	R	68	$C_{27}H_{18}O_6N_7SBr$	50·2	2·9	50·0	2·8	(+)	(—)
Acetyl	>300	DR	67	$C_{29}H_{20}O_7N_7SBr$	50·3	3·0	50·4	2·9	(+)	(—)
Phenyl	268	RN	62	$C_{33}H_{22}O_6N_7SBr$	54·5	3·1	54·7	3·0	(+)	(—)
o-Methylphenyl	240	BR	66	$C_{34}H_{24}O_6N_7SBr$	55·5	3·3	55·3	3·2	(—)	(+)
o-Methoxyphenyl	165	R	69	$C_{34}H_{24}O_7N_7SBr$	54·2	3·4	54·1	3·2	(—)	(—)
p-Methoxyphenyl	140	R	68	$C_{34}H_{24}O_7N_7SBr$	54·2	3·2	54·1	3·2	(—)	(—)
Guanidyl	225	O	70	$C_{28}H_{20}O_6N_9SBr$	48·6	2·8	48·7	2·9	(+)	(—)
α-Pyridyl	480	SR	69	$C_{32}H_{21}O_6N_8SBr$	52·7	2·9	52·9	2·9	(—)	(+)
Pyrimidyl	247	SR	70	$C_{31}H_{26}O_6N_9SBr$	51·3	2·5	51·2	2·7	(+)	(—)
4,6-Dimethylpyrimidyl	235	DR	68	$C_{33}H_{24}O_6N_9SBr$	52·6	3·1	52·5	3·2	(+)	(—)
2,6-Dimethylpyrimidyl	252	DR	70	$C_{33}H_{24}O_6N_9SBr$	52·6	3·3	52·5	3·2	(+)	(+)
5-Methyl-1,3,4-thiadiazolyl	182	R	69	$C_{30}H_{20}O_6N_9S_2Br$	48·4	2·7	48·2	2·7	(++)	(—)

Table 8

1-Benzoyl-3-(*m*-nitrophenyl)-5-(*p*-bromophenyl)-4-(substituted sulphonamidobenzeneazo) pyrazoles

(Fig. 1 x=*m*-NO_2 ; y=*p*-Br ; R_1 =COC_6H_5)

R	M.P.	Colour	Yield	Molecular formula	C (Found)	H (Found)	C (Required)	H (Required)	Antibacterial activity	
	(°C)		(%)		%	%	%	%	*S. aureus*	*E. coli*
H	284	R	78	$C_{28}H_{19}O_5N_6SBr$	53·4	3·1	53·2	3·0	(+)	(+)
Acetyl	285	SON	76	$C_{30}H_{21}O_6N_6SBr$	53·4	3·0	53·5	3·1	(—)	(+)
Phenyl	230	SON	76	$C_{34}H_{23}O_5N_6SBr$	57·6	3·3	57·2	3·2	(—)	(—)
o-Methylphenyl	237	SO	75	$C_{35}H_{25}O_5N_6SBr$	58·3	3·6	58·2	3·5	(+)	(+)
o-Methoxyphenyl	214	RN	78	$C_{35}H_{25}O_6N_6SBr$	57·1	3·5	57·0	3·4	(+)	(+)
p-Methoxyphenyl	200	OF	74	$C_{35}H_{25}O_6N_6SBr$	57·2	3·6	57·0	3·4	(—)	(+)
Guanidyl	291	OR	75	$C_{29}H_{21}O_5N_8SBr$	51.9	3.0	51.7	3.1	(+)	(—)
α-Pyridyl	265	BO	76	$C_{33}H_{22}O_5N_7SBr$	56·1	3·1	55·9	3·1	(+)	(+)
Pyrimidyl	>300	ON	74	$C_{32}H_{21}O_5N_8SBr$	54·3	3·1	54·2	3·0	(++)	(—)
4,6-Dimethylpyrimidyl	208	O	72	$C_{34}H_{25}O_5N_8SBr$	55·4	3·5	55·3	3·4	(+)	(+)
2,6-Dimethylpyrimidyl	270	O	75	$C_{34}H_{25}O_5N_8SBr$	55·4	3·3	55·3	3·4	(—)	(—)
5-Methyl-1, 3, 4-thiadiazolyl	250	OR	76	$C_{31}H_{21}O_5N_8S_2Br$	51·2	3·0	51·0	2·9	(+++)	(++)

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