Synthesis of 1, 3-diaryl-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones and evaluation of their antibacterial properties

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Different 1, 3-diarylpropane-1, 3-diones, 1-(*p*-nitrophenyl) 3-phenyl-, *p*-nitrophenyl) -3-(*p*-methylphenyl)-, 1-(*p*-nitrophenyl)-3-(*p*-methoxyphenyl)-, and 1-(*m*-nitrophenyl)-3- (*p*-methylphenyl) propane 1, 3-diones have been synthesised and coupled with a number of diazotised sulphonamide bases to yield the respective 1, 3-diaryl-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones. All these substituted sulphonamidobenzeneazo propane-1, 3- diones have been screened *in vitro* for their antibacterial properties using cup-plate agar diffusion method and some of these have been found active.

Encouraged by the findings on the study of coupling reactions of β-diketones and antibacterial properties of the azo compounds reported earlier[1], some new β-diketones were prepared and coupled with various diazotised sulphonamide bases having aromatic as well as heterocyclic rings attached at N^1-Nitrogen as represented in general formula (A).

This work was taken up with a view to (1) study the effect of the electron attracting and electron repelling groups present in the phenyl rings of the β-diketones on the rate of coupling reaction and make a comparison amongst these and also with the results obtained earlier, and (2) observe the effect of intro ducing the heterocyclic ring in the sulphonamide moiety on the antibacterial properties and (3) cyclise these azo compound to the correspnding pyrazole derivatives as very recently picryl, picrylamino and nitro substituted pyrazoles have been reported as potential high explosives, besides their uses in the field of medicine and dye industry.

The antibacterial properties of all the synthesised compounds were studied *in vitro* against two organisms, *S. aureus* and *E. coli*.

EXPERIMENTAL PROCEDURE

Out of the four, the following three new β-diketones were prepared by us employing the method of Barnes and Dodson[2].

1-(p-Nitrophenyl)-3-(p-methylphenyl) propane-1, 3-dione

p-Nitrobenzaldehyde (0·05 mol) and *p*-methylacetophenone (0·05 mol) on condensation in presence of aqueous sodium hydroxide furnished *p-nitrobenzylidene p-methylacetophenone* (ethanol), m.p.162 °.

(Found : C, 71·7; H, 5·0. $C_{16}H_{13}O_3N$ requires C, 71·9; H, 4·9%).

This on bromination gave the dibromide, m.p. 155°, which on dehydrobromination and subsequent hydrolysis yielded the required β-diketone (ethanol-glacial acetic acid) m.p. 194° in 75% yield.

(Found : C, 67·7; H, 4·9, $C_{16}H_{13}O_4N$ requires C, 67·8; H, 4·6%).

The β-diketone gave an intense violet colouration with aqueous ferric chloride and formed a copper chelate

1-p-Nitrophenyl)-3-(p-methoxyphenyl) propane-1, 3-dione

Equimolecular quantities of *p*-nitrobenzaldehyde and *p*-methoxyacetophenone were condensed in presence of aqueous sodium hydroxide to give *p-nitrobenzylidene p-methoxyacetophenone* crystallised from ethanol as cream coloured solid, m.p. 156°.

(Found : C, 67·6; H, 4. 6. $C_{16}H_{13}O_4N$ requires C, 67·8; H, 4·6%).

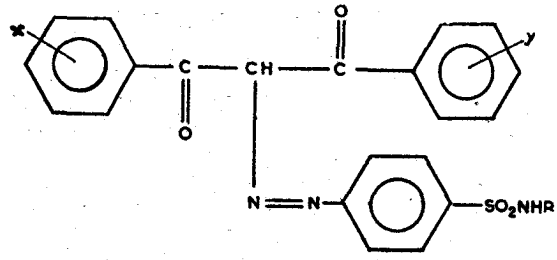
The dibromide of the above styryl ketone, m.p. 130° on dehydrobromination and hydrolysis furnished the β-diketone as a bright-yellow crystalline solid (ethanol-glacial acetic acid), m.p. 182° in 80% yield.

(Found : C, 64·6; H, 4·3. $C_{16}H_{13}O_5N$ requires C, 64·2; H, 4·3%).

It gave a violet colouration with aqueous ferric chloride and formed a copper chelate with aqueous cupric acetate.

1-(m-Nitrophenyl)-3-(p-methylphenyl) propane-1, 3-dione

m-Nitrobenzaldehyde (0·05 mol) and *p*-methylacetophenone (0·05 mol) in presence of aqueous sodium hydroxide furnished *m-nitrobenzylidene p-methylacetophenone* (ethanol), m.p. 131°.



(Found : C, 72·0; H, 4·7. $C_{16}H_{13}O_3N$ requires C, 71·9; H, 4·9%).

Its dibromide, m.p. 170° on dehydrobromination and hydrolysis furnished the β-diketone (ethanol glacial acetic acid) as a pale yellow crystalline solid in 78% yield and had m.p. 157°.

(Found : C, 68·0; H, 4·7. $C_{16}H_{13}O_4N$ requires C, 67·8; H, 4·6%).

The β-diketone gave a violet colouration with aqueous ferric chloride and formed a copper chelate

The fourth β-diketone, 1-(*p*-nitrophenyl)-3-phenylpropane-1, 3-dione[3] and the sulphonamides[4—16] required for the present work were prepared by us by the standard methods.

Synthesis of 1, 3-diaryl-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones.

A diazotised solution of the sulphonamide (0·002 mol) was gradually added to a well-cooled (0-5°) and well-stirred solution of 1, 3-diarylpropane-1, 3-dione (0·002 mol) in acetone containing sufficient quantity of sodium acetate. The contents were further stirred for 10 minutes and excess of ice-cold water added. The yellow solid which separated out was filtered, washed well with water, dried , and pure *1, 3-diaryl-2-(substituted sulphonamidobenzeneazo) propane-1, 3-dione* of the type A was crystallised from glacial acetic acid or D.M.F. or from a mixture of the two solvents.

All the azo compounds synthesised are given in Tables 1 to 4.

During the course of this work it was observed that the rate of coupling reaction was higher when only nitro group was present in any of the phenyl rings of the β-diketone. However, if one of the phenyl rings of the β-diketone contained the nitro group and the other an electron repelling group, such as methyl or methoxyl, the rate of coupling reaction was lower as compared to the β-diketone containing only nitro group but more as compared to the β-diketone containing the electron repelling groups[1]. The yield of the azo compounds ranged between 68-85%.

EVALUATION OF THE ANTIBACTERIAL ACTIVITY

The antibacterial study of the azo compounds was carried out *in vitro* at concentrations of 500 μg/ml and 1,000 μg/ml against two organisms *S. aureus* and *E. coli* and the results with the solutions having concentration of 500 μg/ml are given in Tables 1 to 4. Test solutions were prepared in DMF which also worked as a control. The results have been indicated by (+), (++), and (+++) depending upon the clarity and the diameter of the zones of inhibition; where the zones of inhibition of the test solutions were equal to that of the control it is represented by (—) in the Tables.

The results of the antibacterial tests clearly indicated that the antibacterial properties vary with the nature of the substitutents as well as their positions in the phenyl rings. Thus if a nitro group is present in *para* position in one of the phenyl rings of the β-diketone, the azo compounds syenthesised show feeble activity against *E. coli* and hardly any activity against *S. aureus* except compounds number 11, 12 and

13 (Table 1) which showed activity against *S. aureus* but no activity against *E. coli*. In the case of 1-(*p*-nitrophenyl)-3-(*p*-methylphenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones, most of the compounds showed activity against both *S. aureus* and *E. coli* except compounds 5 and 6 (Table 2) which showed activity only against *S. aureaus*. But if the nitro group is present in *meta*-position instead of *paras* the activity was more or less of the same order with the only difference that some compounds did exhibit good activity as compared to the *para*-analogue.

However, if the methyl group was replaced by methoxyl, as in 1-(*p*-nitrophenyl)-3-(*p*-methoxyphenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-dione, the activity of the compounds against *E. coli* decreased.

Another conclusion drawn from the results has been that the nature of the atom or group attached at N^1-nitrogen atom of the sulphonamide group also affects the antibacterial properties. It is also worthwhile to mention that the azo compounds synthesised by coupling diazotised N^1-5-methyl-1, 3, 4-thiadiazol-2-yl sulphanilamide with all the β-diketones were found to possess a fairly high degree of activity against *S. aureus* and exhibited no activity against *E. coli*.

TABLE 1

1-(*p*-Nitrophenyl)-3-phenyl-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones

(A : X-*p*-Nitro ; Y-H)

S. No.	R	M.P. (°C)	Colour	Yield (%)	Molecular formula	C (Found) (%)	H (Found) (%)	C (Required) (%)	H (Required) (%)	Antibacteria activity *S aureus*	Antibacteria activity *E coli*
1.	H	228	SY	85	$C_{18}H_{16}O_6N_4S$	55·7	3·3	55·7	3·5	—	+
2.	Acetyl	211	YN	82	$C_{23}H_{18}O_7N_4S$	56·0	3·6	55·9	3·6	—	+
3.	Phenyl	216	SYN	83	$C_{27}H_{20}O_6N_4S$	61·5	3·9	61·4	3·8	—	+
4.	*o*-Methylphenyl	206	BYF	80	$C_{28}H_{22}O_6N_4S$	62·2	4·0	62·0	4·0	—	+
5.	*o*-Methoxyphenyl	212	SO	81	$C_{28}H_{22}O_7N_4S$	60·4	4·0	60·2	3·9	—	+
6.	*p*-Methoxyphenyl	235	Y	82	$C_{28}H_{22}O_7N_4S$	60·0	4·0	60·2	3·9	—	+
7.	Gauanidyl	220	Y	72	$C_{22}H_{18}O_6N_6S$	53·4	3·8	53·4	3·6	—	+
8.	α-Pyridyl	232	SY	81	$C_{26}H_{19}O_6N_5S$	59·1	3·6	59·0	3·6	—	—
9.	Pyrimidyl	255	SY	84	$C_{25}H_{18}O_6N_6S$	56·5	3·6	56·6	3·4	—	+
10.	4, 6-Dimethylpyrimidyl	236	Y	80	$C_{27}H_{22}O_6N_6S$	58·0	4·0	58·1	3·9	—	+
11.	2, 6-Dimethylpyrimidyl	231	Y	80	$C_{27}H_{22}O_6N_6S$	58·4	4·0	58·1	3·9	+	—
12.	2, 6-Dimethoxypyrimidyl	217	BY	81	$C_{27}H_{22}O_8N_6S$	55·1	3·7	54·9	3·7	+	—
13.	5-Methyl-1, 3, 4-thiadiazol-2-yl	223	Y	82	$C_{24}H_{28}O_6N_6S_2$	52·7	5·2	52·4	5·1	++	—

B—Bright; Br—Brownish; D—Dark; F—Flakes ; N—Needles; O—Orange; P—Pale; R—Red; S—Shining; Y—Yellow.

TABLE 2

1-(*p*-Nitrophenyl)-3-(*p*-methylphenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones

(A: X-*p*-Nitro; Y-*p*-Methyl)

S. No.	R	M.P. (°C)	Colour	Yield (%)	Molecular formula	C (Found) (%)	H (Found) (%)	C (Requires) (%)	H (Requires) (%)	Antibacterial activity *S. aureus*	Antibacterial activity *E. coli*
1.	H	270	DY	75	$C_{22}H_{18}O_6N_7S$	56·6	4·0	56·6	3·9	+	+
2.	Acetyl	258	SY	73	$C_{24}H_{20}O_7N_4S$	56·8	4·0	56·7	3·9	+	+
3.	Phenyl	225	YF	73	$C_{28}H_{22}O_6N_4S$	61·7	3·9	62·0	4·0	—	—
4.	*o*-Methylphenyl	225	O	70	$C_{29}H_{24}O_6N_4S$	62·4	4·5	62·6	4·3	+	+
5.	*o*-Methoxyphenyl	214	BYN	71	$C_{29}H_{24}O_7N_4S$	61·0	4·1	60·8	4·2	+	—
6.	α-Methoxyphenyl	220	Y	72	$C_{29}H_{24}O_7N_4S$	61·1	4·2	60·8	4·2	+	—
7.	Guanidyl	254	SO	68	$C_{23}H_{20}O_6N_6S$	54·5	3·9	54·3	3·9	—	—
8.	α-Pyridyl	268	SO	75	$C_{27}H_{21}O_6N_5S$	60·0	4·0	59·7	3·9	+	+
9.	Pyrimidyl	253	YON	77	$C_{26}H_{20}O_6N_6S$	57·1	3·8	57·3	3·7	—	—
10.	4, 6-Dimethylpyrimidyl	231	Y	75	$C_{28}H_{24}O_6N_6S$	58·9	4·3	58·7	4·2	+	+
11.	2, 6-Dimethylpyrimidyl	230	Y	74	$C_{28}H_{24}O_6N_6S$	58·5	4·4	58·7	4·2	—	—
12.	2, 6-Dimethoxypyrimidyl	223	BY	75	$C_{28}H_{24}O_8N_6S$	55·9	4·1	55·6	4·0	+	+
13.	5-Methyl-1, 3,4-thiadiazol2-yl	241	Y	73	$C_{25}H_{20}O_6N_6S_2$	53·4	3·6	53·2	3·5	++	+

TABLE 3

1-(*p*-Nitrophenyl)-3-(*p*-methoxyphenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones
(A : X-*p*-Nitro; Y-*p*-Methoxy)

S. No.	R	M.P.	Colour	Yield	Molecular formula	C (Found)	H (Found)	C (Required)	H (Required)	Antibacterial activity	
		(°C)		(%)		(%)	(%)	(%)	(%)	*S. aureus*	*E. coli*
1.	H	238	SY	77	$C_{29}H_{18}O_7N_4S$	54·9	3·5	54·8	3·7	+	—
2.	Acetyl	195	O	74	$C_{24}H_{20}O_8N_4S$	55·1	3·8	54·9	3·8	+	+
3.	Phenyl	237	O	76	$C_{28}H_{22}O_7N_4S$	60·1	4·0	60·2	3·9	+	++
4.	*o*-Methylphenyl	224	SO	74	$C_{29}H_{22}O_7N_4S$	61·0	4·1	60·8	4·2	+	+
5.	*o*-Methoxyphenyl	226	SO	75	$C_{29}H_{24}O_8N_4S$	58·9	4·3	59·1	4·1	+	+
6.	*p*-Methoxyphenyl	220	YO	72	$C_{29}H_{24}O_8N_4S$	59·0	4·1	59·1	4·1	+	+
7.	Guanidyl	281	YBR	70	$C_{23}H_{20}O_7N_6S$	52·8	3·9	52·6	3·8	—	—
8.	α-Pyridyl	254	OR	76	$C_{27}H_{21}O_7N_5S$	58·1	3·5	58·0	3·7	+	+
9.	Pyrimidyl	214	Y	80	$C_{26}H_{20}O_7N_6S$	55·4	3·8	55·7	3·6	—	+
10.	4, 6-Dimethylpyrimidyl	210	Y	76	$C_{28}H_{24}O_7N_6S$	57·0	4·2	57·1	4·1	—	—
11.	2, 6-Dimethylpyrimidyl	231	YBr	74	$C_{28}H_{24}O_7N_6S$	57·3	4·2	57·1	4·1	—	—
12.	2, 6-Dimethoxypyrimidyl	175	Y	75	$C_{28}H_{24}O_9N_6S$	54·0	4·0	54·2	3·9	—	+
13.	5-Methyl-1, 3, 4-thiadiazol-2-yl	254	PY	74	$C_{25}H_{20}O_7N_6S_2$	51·9	3·1	51·7	3·4	++	++

TABLE 4

1-(*m*-Nitrophenyl)-3-(*p*-methylphenyl)-2-(substituted sulphonamidobenzeneazo) propane-1, 3-diones
(A : X-*m*-Nitro; Y-*p*-Methyl)

S. No.	R	M.P.	Colour	Yield	Molecular formula	C (Found)	H (Found)	C (Required)	H (Required)	Antibacterial activity	
		°C		%		(%)	(%)	(%)	(%)	*S. aureus*	*E. coli*
1.	H	235	YO	74	$C_{22}H_{18}O_6N_7S$	56·9	4·0	56·6	3·9	+	+
2.	Acetyl	225	Y	70	$C_{24}H_{20}O_7N_4S$	56·5	4·1	56·7	3·9	++	+
3.	Phenyl	260	SY	71	$C_{28}H_{22}O_6N_4S$	62·2	4·0	62·0	4·0	+	+
4.	*o*-Methylphenyl	206	YN	68	$C_{29}H_{24}O_6N_4S$	62·6	4·1	62·6	4·3	+	+
5.	*o*-Methoxyphenyl	219	BYN	69	$C_{29}H_{24}O_7N_4S$	60·7	4·0	60·8	4·2	—	—
6.	*p*-Methoxyphenyl	224	BrY	68	$C_{29}H_{24}O_7N_4S$	60·8	4·3	60·8	4·2	—	+
7.	Guanidyl	251	PY	65	$C_{23}H_{20}O_6N_6S$	54·5	4·0	54·3	3·9	—	—
8.	α-Pyridyl	250	SBrY	71	$C_{27}H_{21}O_6N_5S$	59·6	3·5	59·7	3·9	+	+
9.	Pyrimidyl	270	SPY	77	$C_{26}H_{20}O_6N_6S$	57·5	3·9	57·3	3·7	+	++
10.	4, 6-Dimethylpyrimidyl	224	BYN	75	$C_{28}H_{24}O_6N_6S$	58·8	4·2	58·7	4·2	++	+
11.	2, 6-Dimethylpyrimidyl	245	PY	75	$C_{28}H_{24}O_6N_6S$	58·7	4·2	58·7	4·2	+	—
12.	2, 6-Dimethoxypyrimidyl	231	Y	76	$C_{28}H_{24}O_8N_6S$	55·4	3·9	55·6	4·0	+	—
13.	5-Methyl-1, 3, 4-thiadiazol-2-yl	249	Y	74	$C_{25}H_{20}O_6N_6S_2$	53·0	3·6	53·2	3·5	++	+

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