STUDIES IN SULPHONAMIDES—PART VI

Synthesis of 1 : 3-disubstituted phenyl-2-(substituted sulphonamidobenzeneazo) propane-1 : 3-diones and evaluation of their antibacterial properties

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Five different 1 : 3-diaryl propane-1 : 3-diones, 1-(m-nitrophenyl)-3-phenyl-, 1-(m-nitrophenyl)-3-(p-methoxyphenyl)-, 1-(p-methoxyphenyl)-3-(p-methylphenyl)-, 1-(p-methoxyphenyl)-3-(p-bromophenyl)-and 1-(p-methoxyphenyl)-3-(p-chlorophenyl) propane-1 : 3-diones have been synthesised and coupled with eight different diazotised sulphonamide bases to give 1 : 3-diaryl-2-(substituted sulphonamidobenzeneazo) propane-1 : 3-diones. The pharmacological properties of all these azo-compounds have been studied *in vitro* by the cup-plate method.

The preparation of some 1 : 3-diaryl propane-1 : 3-diones, their coupling with different diazotised sulphonamide bases and the antibacterial properties of the azo-compounds so obtained have already been described[1]. We have now extended this work to the condensation of some disubstituted β diketones with the object of studying the effect of the various substituents and their position on the rate of coupling as well as the antibacterial properties of the azo-compounds so obtained.

It has been observed that the rate of coupling reaction increases when both the phenyl rings of the 1 : 3-diones possess electron attracting groups thereby giving higher yields of the resulting azo-compounds. However, if one phenyl ring has an electron attracting group and the other an electron releasing, the rate of coupling decreases giving lower yields of the resulting azo-compounds. The yield of the azo-compounds ranged between 58–76%

EXPERIMENTAL PROCEDURE

The 1 : 3-diaryl propane-1 : 3-diones[2-6] and various sulphonamides required for this work were prepared.

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 an ice-cold solution of 1 : 3-dione (0·002 mol) in acetone, containing sodium acetate during stirring and cooling (0—5°) and the contents further stirred for 10 minutes. Excess of ice-cold water was then added and the yellow coloured solid so obtained was filtered, washed well with water, dried and pure 1 : 3-diaryl-2-(substituted sulphonamidobenzeneazo) propane -1 : 3-diones crystallised from ethanol or glacial acetic acid or D.M.F. or from a mixture of any two of the above solvents. In some cases the azo-compound was obtained after adding ice-cold water to the reaction mixture and keeping overnight. The general structure of the azo-compounds is given in Fig. 1.

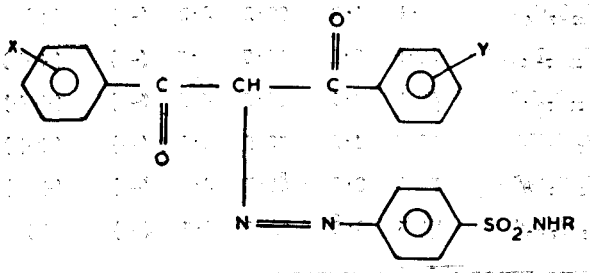

Fig. 1—General structure of azo-compounds.

The antibacterial properties of all these azo-compounds were studied by the usual cup-plate agar diffusion method against *S. aureus* and *E. coli in vitro* at two different concentrations 500 μg/ml and 1000 μg/ml. Results with dilutions of 500 μg/ml have been entered in Tables 1 to 5. The test solutions were prepared in a mixture of D.M.F. and water (3 : 7). The results of the biological assay indicate that azo-compounds of the disubstituted β-diketones showed greater activity against *E. coli* as compared to

monosubstituted analogues and no activity against *S. aureus* except in a few cases like the compound 1 in Table 1, 1 and 2 in Table 2, 2 in Table 3 , and 1 and 2 in both the Tables 4 and 5.

TABLE 1

GENERAL PROPERTIES AND ANTIBACTERIAL PROPERTIES OF 1-PHENYL-3-(m-NITROPHENYL)-2-(SUBSTITUTED SULPHONAMIDOBENZENE AZO) PROPANE-1 : 3-DIONES

(X = m-Nitrophenyl; Y = H)

S. No.	R	M.P. (°C)	Colour	Yield (%)	Mol. formula	Percentage Found C	Found H	Reqd. C	Reqd. H	Antibacterial activity *S. aureus*	*E. coli*
1	H	213	Y	80	$C_{21}H_{16}O_6N_4S$	55·6	3·6	55·7	3·5	(++)	(—)
2	acetyl	210	BYF	78	$C_{23}H_{18}O_7N_4S$	55·8	3·7	55·8	3·6	(+)	(—)
3	phenyl	216	SYF	75	$C_{27}H_{20}O_6N_4S$	61·4	3·6	61·3	3·7	(—)	(++)
4	p-chlorophenyl	238	Y	77	$C_{27}H_{19}O_6N_4SCl$	57·6	3·0	57·5	3·3	(—)	(++)
5	p-methylphenyl	226	PY	73	$C_{28}H_{22}O_6N_4S$	61·8	4·2	61·9	4·0	(—)	(++)
6	p-methoxyphenyl	207	SGY	75	$C_{28}H_{22}O_7N_4S$	60·3	4·0	60·2	3·9	(+)	(++)
7	pyrimidyl	>300	SY	78	$C_{25}H_{18}O_6N_6S$	56·7	3·6	56·6	3·4	(—)	(+++)

TABLE 2

GENERAL PROPERTIES AND ANTIBACTERIAL ACTIVITIES OF 1-(m-NITROPHENYL)-3-(p-METHOXYPHENYL)-2-(SUBSTITUTED SULPHONAMIDOBENZENE AZO) PROPANE-1 : 3-DIONES

(X = m-Nitrophenyl; Y = p-Methoxyphenyl)

S. No.	R	M. P. (°C)	Colour	Yield (%)	Mol. formula	Percentage Found C	Found H	Reqd. C	Reqd. H	Antibacterial activity *S. aureus*	*E. coli*
1	H	191	PY	75	$C_{22}H_{18}O_7N_4S$	54·3	3·6	54·7	3·7	(+)	(+)
2	acetyl	198-9	PY	72	$C_{24}H_{20}O_8N_4S$	55·2	3·7	54·9	3·8	(++)	(+)
3	phenyl	243-4	PY	68	$C_{28}H_{22}O_7N_4S$	60·1	4·0	60·2	3·9	(—)	(+)
4	p-chlorophenyl	231-2	Y	70	$C_{28}H_{21}O_7N_4SCl$	56·9	3·4	56·7	3·5	(—)	(++)
5	p-methylphenyl	245	BY	69	$C_{29}H_{24}O_7N_4S$	60·9	4·1	60·8	4·2	(—)	(++)
6	p-methoxyphenyl	197	BrY	69	$C_{29}H_{24}O_8N_4S$	59·3	4·2	59·2	4·1	(—)	(++)
7	pyrimidyl	212	DY	71	$C_{26}H_{20}O_7N_6S$	55·6	3·6	55·7	3·5	(—)	(++)
8	guanidyl	244	Y	67	$C_{23}H_{20}O_7N_6S$	52·5	3·6	52·6	3·8	(—)	(+)

TABLE 3

GENERAL PROPERTIES AND ANTIBACTERIAL ACTIVITIES OF 1-(p-METHOXYPHENYL)-3-(p-METHYLPHENYL)-2-(SUBSTITUTED SULPHONAMIDOBENZENE AZO) PROPANE-1 : 3-DIONES

(X = p-Methoxyphenyl ; Y = p-Methylphenyl)

S. No.	R	M. P (°C)	Colour	Yield (%)	Mol. formula	Percentage Found C	Found H	Reqd. C	Reqd. H	Antibacterial activities *S. aureus*	*E. coli*
1	H	188	OY	75	$C_{23}H_{21}O_5N_3S$	61·4	4·6	61·2	4·6	(+)	(+++)
2	acetyl	187	OY	71	$C_{25}H_{23}O_6N_3S$	60·7	4·7	60·8	4·6	(+++)	(—)
3	phenyl	165	PY	60	$C_{29}H_{25}O_5N_3S$	66·1	4·8	66·0	4·7	(—)	(++)
4	p-chlorophenyl	187-8	GYF	63	$C_{29}H_{24}O_5N_3SCl$	61·6	4·1	61·9	4·2	(—)	(++)
5	p-methylphenyl	192	PY	58	$C_{30}H_{27}O_5N_3S$	66·8	4·8	66·6	5·0	(—)	(+)
6	p-methoxyphenyl	195	Y	60	$C_{30}H_{27}O_6N_3S$	64·6	4·8	64·6	4·8	(—)	(+++)
7	pyrimidyl	269	YW	70	$C_{27}H_{23}O_5N_5S$	61·3	4·5	61·2	4·3	(—)	(++)
8	guanidyl	264	Y	68	$C_{24}H_{23}O_5N_5S$	58·7	4·5	58·4	4·6	(—)	(+)

TABLE 4

GENERAL PROPERTIES OF ANTIBACTERIAL ACTIVITIES OF 1-(p-METHOXYPHENYL)-3-(p-CHLOROPHENYL)-2-(SUBSTITUTED SULPHONAMIDOBENZENE AZO) PROPANE-1 : 3-DIONES

(X = p-Methoxyphenyl ; Y = p-Chlorophenyl)

S. No.	R	M. P. (°C)	Colour	Yield (%)	Mol. formula	Percentage Found C	Found H	Reqd. C	Reqd. H	Antibacterial activity *S. aureus*	*E. coli*
1	H	192	Y	75	$C_{22}H_{18}O_5N_3SCl$	56·1	3·9	55·9	3·8	(+++)	(—)
2	acetyl	194-5	PY	76	$C_{24}H_{20}O_6N_3SCl$	56·2	3·7	56·1	3·9	(+++)	(+)
3	phenyl	158-9	Y	70	$C_{28}H_{22}O_5N_3SCl$	61·0	4·1	61·3	4·0	(—)	(++)
4	p-chlorophenyl	193-4	Y	70	$C_{28}H_{21}O_5N_3SCl_2$	57·6	3·5	57·7	3·6	(—)	(++)
5	p-methylphenyl	193	GYF	68	$C_{29}H_{24}O_5N_3SCl$	61·7	4·3	61·9	4·3	(—)	(++)
6	p-methoxyphenyl	199	Y	70	$C_{29}H_{24}O_6N_3SCl$	60·3	3·9	60·2	4·1	(—)	(+++)
7	pyrimidyl	269-70	YW	74	$C_{26}H_{20}O_5N_5SCl$	56·6	3·7	56·7	3·6	(—)	(++)
8	guanidyl	285	PY	71	$C_{23}H_{20}O_5N_5SCl$	53·9	4·0	53·7	3·9	(—)	(+)
9	4′:6′-dimethyl pyrimidyl	171-2	Y	75	$C_{28}H_{24}O_5N_5SCl$	57·9	4·2	58·1	4·1	(—)	(+)

TABLE 5

GENERAL PROPERTIES AND ANTIBACTERIAL ACTIVITIES OF 1-(p-METHOXYPHENYL)-3-(p-BROMOPHENYL)-2-(SUBSTITUTED SULPHONAMIDOBENZENE AZO) PROPANE-1 : 3-DIONES

(X = p-Methoxyphenyl ; Y = p-Bromophenyl)

S. No.	R	M. P. (°C)	Colour	Yield (%)	Mol. formula	Percentage Found C	Found H	Reqd. C	Reqd. H	Antibacterial Activity *S. aureus*	*E. coli*
1	H	177	PY	76	$C_{22}H_{18}O_5N_3SBr$	51·0	3·1	51·1	3·5	(+++)	(—)
2	acetyl	177-8	PY	75	$C_{24}H_{20}O_6N_3SBr$	51·7	3·4	51·6	3·5	(+++)	(—)
3	phenyl	163	Y	68	$C_{28}H_{22}O_5N_3SBr$	56·6	3·8	56·7	3·7	(—)	(++)
4	p-chlorophenyl	206	Y	70	$C_{28}H_{21}O_5N_3SBrCl$	53·7	3·4	53·6	3·3	(—)	(++)
5	p-methylphenyl	200	GYF	68	$C_{29}H_{24}O_5N_3SBr$	57·1	3·8	57·4	3·9	(—)	(++)
6	p-methoxyphenyl	205	Y	69	$C_{29}H_{24}O_6N_3SBr$	56·2	3·5	55·9	3·8	(—)	(+)
7	pyrimidyl	260	GYF	75	$C_{26}H_{20}O_5N_5SBr$	52·6	3·5	52·5	3·4	(—)	(++)

B—Bright; Br—Brownish; D—Dark; F—Flakes; G—Golden; O—Orange; P—Pale; Y—Yellow; S—Shining; W—White

REFERENCES

1. SAHARIA, G. S. & SHARMA, H. R., *Def. Sci. J.*, **22** (1972).

2. SHENOI, R. B., SHAH, R. C. & WHEELER, T. S., *J. Chem. Soc.*, (1940), **247**.

3. BARNES, R. P. & BRANDORE, A., *J. Amer. Chem. Soc.*, **65** (1946), 1070.

4. BARNES, R. P. & DODSON, L. B., *ibid.*, **65** (1943), 1585.

5. BARNES, R. P. & SNEAD, J. L., *ibid.*, **67** (1945), 138.

6. BARNES, R. P., GOODWIN, T. C. Jr. & COTTON, T. W. Jr., *ibid.*, **69** (1947), 3135.