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Synthesis of Some New Azosulphonamides Based on Salicylic Acid and Thiosalicylic Acid, and Having Antibacterial and Antifungal Activity

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ABSTRACT

New azo-dyes have been prepared by diazotization of 4-amino benzene 4'-(substituted heterocyclo)sulphonamide derivatives and coupling with salicylic or thiosalicylic acid in acid medium, to afford the corresponding substituted 4-azo-(4'-substituted benzene sulphonamido)-salicylic and thiosalicylic acids as ligands. Interaction of these ligands with metal salts (Fe^{3+}, Cu^{2+} and Hg^{2+}) in solution afforded the corresponding metal chelates.

The compounds were screened in vitro *for antibacterial and antifungal activity.*

1 INTRODUCTION

Initial investigations on the sulphur drugs[1,2] resulted in the discovery of prontosil, a drug of high antibacterial activity.[3–5] The replacement of the carbonyl oxygen atom by sulphur in some heterocyclic compounds enhances the fungicidal activity.[6] Some of the sulphonamides were later found to be biologically versatile compounds, having anticancer,[7] antimalarial[8] and antitubercular[9] properties.

2 RESULTS AND DISCUSSION

Observations on the antibacterial activity of prontosil (2,4-diamino-phenylazo benzenesulphonamide) and a large number of novel[10–16]

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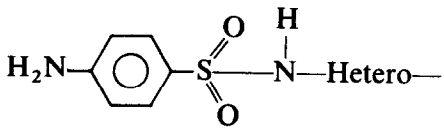

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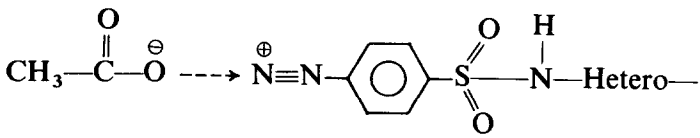

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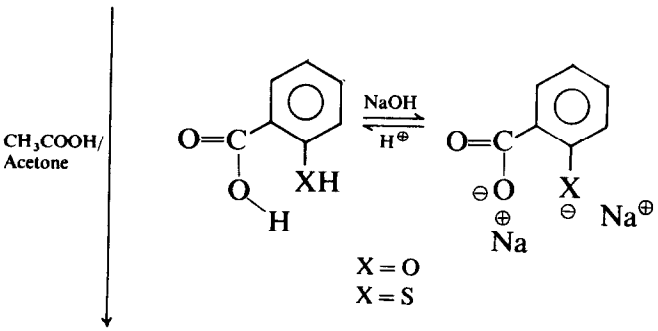

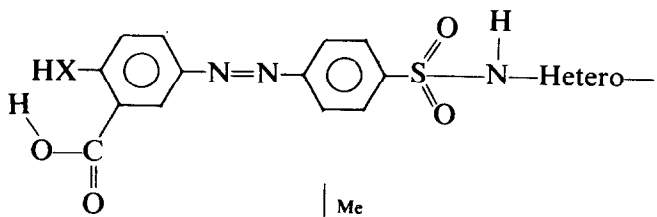

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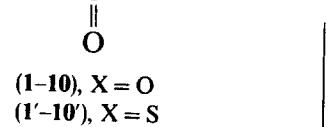
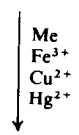
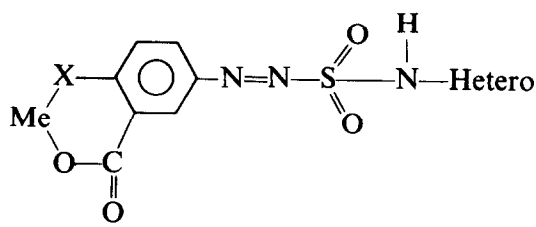
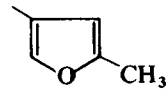
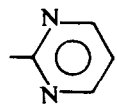
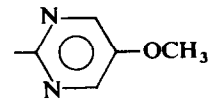
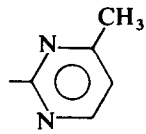
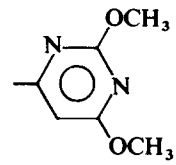
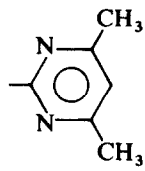
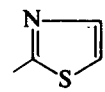
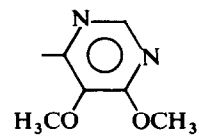






Me
a: Fe^{3+}
b: Cu^{2+}
c: Hg^{2+}

(1a,b,c–10a,b,c), X = O
(1′a,b,c–10′a,b,c), X = S

X = O	X = S	Hetero	X = O	X = S	Hetero
1	**1′**	H			
2	**2′**	CH_3—CO—	**6**	**6′**	
3	**3′**		**7**	**7′**	
4	**4′**		**8**	**8′**	
5	**5′**		**9**	**9′**	
			10	**10′**	

Scheme 1

azosulphonamides prompted us to synthesize some new azo dyes based on salicylic acid and thiosalicylic acid as ligands and their Fe^{3+}, Cu^{2+} and Hg^{2+} chelates and to examine their antibacterial and antifungal activities. We report here the preparation, and the antibacterial and antifungal activity of a range of azosulphonamides and their metal chelates. The substituents in the sulphonamide moiety were chosen so as to ensure a wide variation in their size, electronegativity, chemical reactivity and biological (antibacterial and antifungal) activity. The resulting compounds, on diazotization and coupling with salicylic or thiosalicylic acid afforded the corresponding substituted 4-azo-(4′-substituted benzenesulphonamido)salicylic acids (**1–10**) and/or thiosalicylic acid (**1′–10′**); interaction of these ligands with metal salts of Fe^{3+}, Cu^{2+} and Hg^{2+} in solution afforded the corresponding metal chelates (**1a–c–10a–c**) and (**1′a–c–10′a–c**), respectively. The IR spectra of the compounds confirmed the presence in the azo precursor compounds of the OH and/or SH bands at 3260–3250 cm^{-1} and/or at 2600–2550 cm^{-1}, these absorptions disappearing on chelation. The presence of the sulphonamide group was shown by its characteristic band in the vicinity of 1325 cm^{-1} (Table 1).

^{1}H-NMR spectra showed a singlet signal within the range $\delta =$ 11·50–11·10 ppm, which corresponds to the proton of the OH group for salicylic acid, or within the range $\delta = 4{\cdot}00$–3·74 ppm, which corresponds to

the proton of the SH group for thiosalicylic acid. This signal disappears on deuteration. The position of this down-field signal can be attributed to the OH and/or SH group, being intramolecularly hydrogen bonded with the carboxylic COOH group. The carboxylic protons show a signal in the range $\delta = 10{\cdot}50$–$10{\cdot}15$ ppm. The signals of the aromatic protons appear in two regions, assigned to ring(**a**) $\delta = 7{\cdot}30$–$6{\cdot}85$ ppm (three protons), to ring(**b**) at $\delta = 8{\cdot}25$–$7{\cdot}30$ ppm (four protons) and the protons for the heterocyclic ring (**c**) (Table 2).

TABLE 1
IR Spectra of Some Ligands and Their Iron, Copper and Mercury Chelates (cm^{-1})

Compound no.	ν_{OH}	ν_{SH}	$\nu_{N\ N}$	ν_{SO_2} *(asym.)*	ν_{SO_2} *(sym.)*	ν_{COOH}	ν_{NH}	$\nu_{C\ O}$	ν_{M-O}
3	3 600	—	1 600	1 350	1 160	3 000	3 280	1 760	—
3a	3 450[a]	—	1 580	1 340	1 150	2 700[a]	3 275	1 710	350
3′	—	2 800	1 580	1 345	1 150	2 550	3 270	1 755	—
3′a	—	2 700	1 570	1 340	1 140	2 400[a]	3 275	1 705	340
5	3 550	—	1 590	1 345	1 155	2 900	3 270	1 755	—
5c	3 500[a]	—	1 585	1 340	1 145	2 650[a]	3 285	1 710	345
5′	—	2 850	1 575	1 345	1 150	2 600	3 275	1 765	—
5′c	—	2 700	1 575	1 345	1 145	2 450[a]	3 265	1 715	350
7	3 600	—	1 590	1 355	1 160	2 950	3 280	1 760	—
7b	3 400	—	1 575	1 340	1 155	2 600[a]	3 270	1 710	350
7′	—	2 800	1 585	1 350	1 150	2 600	3 280	1 755	—
7′b	—	2 750	1 575	1 345	1 145	2 400	3 275	1 705	345

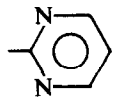
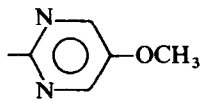
[a] Broad band.

The results obtained from the antibacterial effects indicated that the compounds exhibited variable activities against the bacteria used (inhibition zones ranged from 10–160 mm). It appears that all the thiosalicylic acid derivatives, and their chelates, have more potent activities than the salicylic acid analogues (inhibition zones ranged from 40–160 mm). Furthermore, the mercury chelates (**1c**, **1′c**–**10c**, **10′c**) showed particularly strong effects (inhibition zones 70–160 mm) (Table 3).

The compounds also possessed excellent antifungal activities (inhibition zones 10–120 mm). The thiosalicylic azosulphonamide derivatives, and most of their chelates, were more active than the salicylic azosulphonamide derivatives. All the mercury chelates showed higher activities than the iron and copper chelates (inhibition zones ranged form 50–150 mm) (Table 3).

TABLE 2

^{1}H-NMR Spectra of Some Ligands and Their Copper Mercury Chelates

Compound no.		*δ (ppm)*							
		—OH (*S*)	*—SH* (*S*)	*—NH* (*S*)	*—COOH* (*S*)	*Aromatic protons*			*OCH_3* (*S*)
						Ring (**a**) (*m*)	*Ring* (**b**) (*m*)	*Hetero* (**c**) (*m*)	
Hetero (**c**)	**3**	11·45	—	9·45	10·50	7·30–6·85	8·25–7·30	6·80–6·75	—
	**3b**	—	—	9·40	—	7·20–6·75	8·10–7·25	6·75–6·60	—
	3′	—	4·20	9·42	10·45	7·25–6·80	8·20–7·30	6·78–6·68	—
	3′b	—	—	9·38	—	7·15–6·75	8·18–7·25	6·74–6·58	—
	**7**	11·50	—	9·50	10·52	7·35–6·80	8·25–7·35	6·80–6·65	3·8
	7c	—	—	9·45	—	7·25–6·78	8·22–4·30	6·78–6·60	3·75
	7′	—	4·25	9·55	10·48	7·35–6·80	8·15–7·28	6·75–6·62	3·85
	7′c	—	—	9·48	10·50	7·32–6·85	8·20–7·30	6·78–6·65	3·90

(S) = singlet.
(m) = multisignals.

TABLE 3

Biological Screening of Salicylic (**1–10**) and Thiosalicylic (**1′–10′**) Ligands and Their Iron, Copper and Mercury (**1a–c–10a–c**), (**1′a–c–10′a–c**) Chelates (Inhibition Zones, mm)

Compound no.	*O X = or S*	*Antibacterial activity*				*Antifungal activity*		
		Staphylococcus aureus	Serratia rhodnii	Bacillus cereus	Pseudomans aruginosa	Alternaria alternata	Penicillum chrysogenum	Aspergillus flavus
1	O	20	−ve	40	30	40	−ve	60
1a		30	20	30	40	50	20	70
1b		20	10	30	40	40	20	40
1c		70	30	60	70	80	30	90
1′	S	90	80	−ve	−ve	−ve	40	−ve
1′a		20	70	30	−ve	50	40	30
1′b		20	50	20	10	30	20	−ve
1′c		100	95	60	50	70	60	40
2	O	40	−ve	10	−ve	50	20	−ve
2a		40	30	30	20	20	30	30
2b		30	40	−ve	30	40	50	−ve
2c		80	90	60	70	70	60	50
2′	S	50	20	40	−ve	85	50	−ve
2′a		50	30	40	20	30	40	40
2′b		40	30	20	40	50	40	−ve
2′c		90	105	70	60	95	85	80
3	O	−ve	−ve	30	40	20	30	−ve
3a		−ve	40	−ve	40	40	40	−ve
3b		−ve	20	20	50	30	50	50
3c		80	95	30	60	170	105	70
3′	S	70	50	−ve	10	−ve	−ve	30
3′a		75	20	−ve	20	40	−ve	50
3′b		−ve	20	10	40	20	30	10
3′c		110	120	40	60	160	140	90

4	O	30	90	20	50	50	160	−ve
4a		35	80	−ve	20	10	20	−ve
4b		−ve	−ve	−ve	40	50	30	20
4c		105	110	30	20	180	170	95
4′	S	60	−ve	30	20	70	185	60
4′a		50	10	50	30	−ve	20	−ve
4′b		60	20	50	10	20	50	50
4′c		120	90	−ve	40	120	95	50
5	O	45	50	10	40	20	50	−ve
5a		40	30	60	−ve	20	80	95
5b		135	110	20	−ve	160	140	90
5c		110	60	80	90	60	100	60
5′	S	40	20	20	30	−ve	90	30
5′a		65	−ve	−ve	−ve	90	80	30
5′b		60	30	40	50	10	80	10
5′c		110	110	60	70	50	80	−ve
6	O	50	60	10	−ve	−ve	10	50
6a		80	30	10	−ve	90	20	110
6b		40	−ve	40	10	20	50	100
6c		120	90	20	−ve	180	30	110
6′	S	40	−ve	20	20	−ve	−ve	−ve
6′a		50	30	−ve	−ve	90	80	−ve
6′b		85	90	30	10	100	50	40
6′c		120	50	40	45	45	120	95
7	O	65	30	50	50	10	30	50
7a		40	20	−ve	−ve	30	−ve	−ve
7b		50	20	50	80	50	−ve	100
7c		105	80	20	70	110	150	65
7′	S	50	−ve	−ve	20	10	50	120
7′a		30	40	−ve	20	40	−ve	−ve
7′b		60	30	65	90	70	30	120
7′c		150	90	30	30	160	180	95

(*continued*)

TABLE 3—*contd.*

Compound no.	*O X = or S*	*Antibacterial activity*				*Antifungal activity*		
		Staphylococcus aureus	Serratia rhodnii	Bacillus cereus	Pseudomans aruginosa	Alternaria alternata	Penicillum chrysogenum	Aspergillus flavus
8	O	−ve	−ve	30	−ve	−ve	20	30
8a		30	−ve	35	−ve	20	−ve	20
8b		40	20	30	30	20	30	−ve
8c		80	60	80	75	80	70	30
8′	S	20	−ve	40	30	−ve	30	50
8′a		40	30	50	40	30	20	−ve
8′b		50	40	45	50	40	30	40
8′c		110	80	95	105	90	110	95
9	O	50	100	−ve	20	70	20	−ve
9a		65	40	−ve	30	65	40	30
9b		45	60	10	−ve	50	55	40
9c		95	120	10	10	140	100	105
9′	S	50	40	20	−ve	−ve	−ve	−ve
9′a		75	50	10	−ve	80	50	50
9′b		80	60	−ve	−ve	90	80	50
9′c		120	70	−ve	10	110	120	90
10	O	60	30	20	20	20	−ve	−ve
10a		40	20	30	30	30	20	25
10b		30	−ve	20	20	20	−ve	20
10c		95	80	70	80	60	40	45
10′	S	85	120	50	−ve	30	105	50
10′a		80	110	60	30	40	80	30
10′b		60	70	40	10	30	40	20
10′c		130	150	95	70	105	85	70

−ve: compound not effective.

3 EXPERIMENTAL

3.1 General

All melting points are uncorrected. IR spectra were recorded on Pye-Unicam SP-200G and Perkin-Elmer 599B spectrophotometers. ^{1}H-NMR spectra were recorded on a Varian EM-390 MHz spectrometer in a suitable deuterated solvent using TMS as internal standard. Analytical data were obtained using a Perkin-Elmer 240E microanalyser.

4-Substituted benzenesulphamoyldiazonium acetates were prepared by diazotization of 0·05 mol 4-aminobenzenesulphonyl derivatives I, dissolved in a mixture of either alcohol or acetone and 50% acetic acid, with sodium nitrite at 5°C. The diazonium acetates II were used immediately, without separation, for the synthesis of the corresponding azo compounds III.

3.2 General method for the synthesis of 4-azo′(4-substituted benzenesulphamoyl) salicylic and thiosalicylic acids (1–10, 1′–10′)

To a solution of salicylic or thiosalicylic acid (0·05 mol) in 20% aq. sodium hydroxide (40 ml), the appropriate diazonium salt was added portionwise with stirring. The temperature was maintained at 5°C, and stirring was continued for 1 h. The reaction mixture was kept at ambient temperature for a further 1 h, during which time, the product precipitated. This was filtered, washed with water, dried and recrystallized (Table 4).

3.3 General method for the preparation of iron, copper and mercury chelates (1a–c–10a–c), (1′a–c–10′a–c)

To the hot solution of the appropriate ligand (0·02 mol) in a mixture of ethanol and dilute acetic acid (4:1), an aqueous solution of copper acetate, ferric chloride or mercuric chloride (0·01 mol) was added, with stirring. Stirring was continued for a further 30 min at 60–70°C. The reaction mixture was cooled, and the precipitated product was filtered, washed thoroughly with distilled water, dried and recrystallized (Table 5).

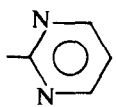
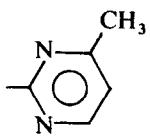
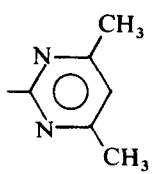
3.4 Biological screening: antibacterial and antifungal activities

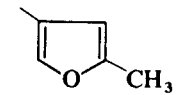
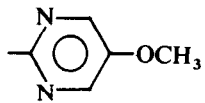
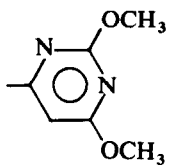
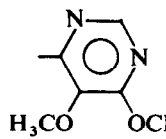
The compounds were screened *in vitro* for their antibacterial activities against: *Staphylococcus aureus*, *Serratia rhodnii*, *Bacillus cereus* and *Pseudomans aruginosa*, and also for their antifungal activities against: *Alternaria alternata*, *Penicillium chrysogenum* and *Aspergillus flovus*.

The biological properties were studied by the cup-plate agar diffusion

TABLE 4

4-Azo-(4′-substituted Benzenesulphonyl) salicylic and/or Thiosalicylic Acid (**1–10**), (**1′–10′**)

Compound no.	*R*	*X* = *O* or *S*	*m.p.* (°C)	*Yield* (%)	*Formula*[a] (*mol. wt*)	*Microanalysis: calc./found* (%)			
						C	*H*	*N*	*S*
1	H	O	165	70	$C_{13}H_{11}N_3O_5S$ (321·23)	48·61 48·57	3·42 3·50	13·08 12·73	9·98 10·00
1′		S	215	69	$C_{13}H_{11}N_3O_5S_2$ (353·29)	44·20 44·13	3·11 3·18	11·89 11·80	18·15 18·28
2	CH_3CO	O	230	63	$C_{15}H_{13}N_3O_6S$ (363·25)	49·59 49·53	3·58 3·67	11·57 11·48	8·83 8·91
2′		S	188	67	$C_{15}H_{13}N_3O_5S_2$ (379·41)	49·49 49·19	3·45 3·39	11·08 11·12	16·90 16·81
3		O	192	75	$C_{17}H_{13}N_5O_5S$ (399·29)	51·14 50·95	3·26 3·30	17·54 17·49	8·03 8·10
3′		S	225	79	$C_{17}H_{13}N_5O_4S_2$ (415·45)	49·15 49·28	3·15 3·09	16·86 16·79	15·44 15·40
4		O	167	73	$C_{18}H_{15}N_5O_5S$ (413·289)	52·31 52·39	3·63 3·59	16·95 16·87	7·76 7·82
4′		S	190	71	$C_{18}H_{15}N_5O_4S_2$ (429·48)	50·34 50·44	3·52 3·50	16·31 16·29	14·93 14·87
5		O	187	79	$C_{19}H_{17}N_5O_5S$ (427·31)	53·41 53·50	3·48 3·56	16·39 16·29	7·58 7·46
5′		S	174	79	$C_{19}H_{17}N_5O_4S_2$ (443·52)	51·45 51·51	3·87 3·80	15·82 15·76	14·45 14·53

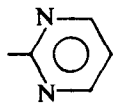
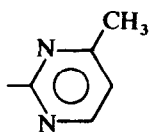
6		O	239	69	$C_{17}H_{14}N_4O_5S$ (402·22)	50·76 50·80	3·48 3·51	13·93 14·00	23·86 23·76
6′		S	158	72	$C_{17}H_{14}N_4O_5S_2$(418·45)	48·80 48·79	3·37 3·45	13·39 13·45	15·32 15·29
7		O	178	66	$C_{18}H_{15}N_5O_6S$ (429·29)	50·36 50·47	3·49 3·56	16·31 16·27	7·47 7·39
7′		S	170	70	$C_{18}H_{15}N_5O_5S_2$ (445·48)	48·53 48·48	3·39 3·46	15·72 15·68	14·40 14·49
8		O	148	58	$C_{19}H_{17}N_5O_7S$ (459·31)	49·59 49·60	3·70 3·77	15·25 15·20	6·98 6·90
8′		S	155	51	$C_{19}H_{17}N_5O_6S_2$ (475·51)	47·99 47·91	3·60 3·68	14·73 14·82	13·49 13·50
9		O	225	73	$C_{16}H_{14}N_4O_5S_2$ (406·34)	47·29 47·36	3·45 3·39	13·79 13·83	15·78 15·69
9′		S	259	69	$C_{16}H_{14}N_4O_4S_3$ (422·52)	54·48 54·50	3·34 3·42	13·26 13·31	22·77 22·63
10		O	184	54	$C_{19}H_{17}N_5O_7S$ (459·00)	49·69 49·61	3·70 3·63	15·25 15·32	6·98 6·90
10′		S	165	50	$C_{19}H_{17}N_5O_6S_2$ (475·00)	47·29 47·31	3·60 3·58	14·73 14·69	13·49 13·52

[a] Compounds **8**, **8′**, **9**, **9′**, **10**, **10′** and **8′** were recrystallized from aqueous acetone, and the others from aqueous ethanol.

TABLE 5

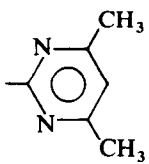
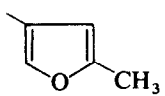
Iron, Copper and Mercury Chelates of Salicylic and Thiosalicylic Acids (**1a–c–10a–c**), (**1′a–c–10′a–c**)

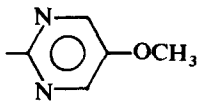
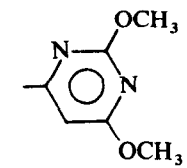
Compound no.	*R*	*X* = *O* or *S*	*m.p.* (°C)	*Yield* (%)	*Formula*[a] (*mol. wt*)	*Microanalysis: calc./found* (%)	
						N	*S*
1a		O	> 300	70	$C_{13}H_9N_3O_5SFe.NO_3$ (437·51)	12·81	7·33
						12·69	7·40
1b			281	82	$C_{13}H_9N_3O_5SCu$ (340·82)	12·41	9·41
						12·50	9·38
1c	H		290	80	$C_{13}H_9N_3O_5SHg$ (477·87)	8·85	6·71
						8·91	6·68
1′a		S	> 300	65	$C_{13}H_9N_3O_4S_2Fe.NO_3$ (453·57)	12·35	14·14
						12·40	14·08
1′b			207	68	$C_{13}H_9N_3O_4S_2Cu$ (356·89)	11·85	17·97
						11·90	18·00
1′c			268	71	$C_{13}H_9N_3O_4S_2H_9$ (493·94)	8·56	12·98
						8·60	13·00
2a		O	276	75	$C_{15}H_{12}N_3O_6SFe.NO_3$ (424·71)	13·19	7·55
						13·21	7·49
2b			270	80	$C_{15}H_{12}N_3O_6SCu$ (328·02)	12·89	9·78
						12·91	9·81
2c	CH_3CO		300	86	$C_{15}H_{12}N_3O_6SHg$ (465·07)	9·09	6·89
						9·12	6·80
2′a		S	> 266	63	$C_{15}H_{12}N_3O_5S_2Fe.NO_3$ (440·77)	12·71	14·55
						12·66	14·61
2′b			285	60	$C_{15}H_{12}N_3O_5S_2Cu$ (344·09)	13·04	18·64
						13·10	18·60
2′c			275	72	$C_{15}H_{12}N_3O_5S_2Hg$ (481·13)	8·79	13·33
						8·82	13·40

3a		O	>320	78	$C_{17}H_{12}N_5O_5SFe.NO_3$ (516·77)	16·26 16·40	6·20 6·19
3b			>300	72	$C_{17}H_{12}N_5O_5SCu$ (420·08)	16·78 16·69	7·64 7·56
3c			290	85	$C_{17}H_{12}N_5O_5SHg$ (557·13)	12·65 12·70	5·76 5·70
3'a		S	>300	80	$C_{17}H_{12}N_5O_4S_2Fe.NO_3$ (532·82)	15·77 15·69	12·04 12·00
3'b			>330	71	$C_{17}H_{12}N_5O_4S_2Cu$ (436·14)	16·16 16·09	14·70 14·74
3'c			288	80	$C_{17}H_{12}N_5O_4S_2Hg$ (543·19)	12·30 12·28	11·19 11·09
4a		O	263	68	$C_{18}H_{14}N_5O_5SFe.NO_3$ (530·79)	15·83 15·69	6·04 6·00
4b			274	65	$C_{18}H_{14}N_5O_5SCu$ (435·10)	16·21 16·19	7·37 7·40
4c			283	75	$C_{18}H_{14}N_5O_5SHg$ (572·15)	12·32 12·29	5·61 5·59
4'a		S	>300	70	$C_{18}H_{14}N_5O_4S_2Fe.NO_3$ (546·85)	15·37 15·29	11·73 11·69
4'b			>300	65	$C_{18}H_{14}N_5O_4S_2Cu$ (451·16)	15·62 15·58	14·21 14·25
4'c			292	68	$C_{18}H_{14}N_5O_4S_2Hg$ (588·21)	11·98 12·00	10·90 11·00

(*continued*)

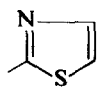
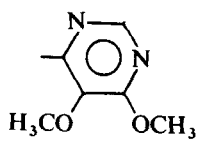
TABLE 5—*contd.*

Compound no.	*R*	*X* = *O or S*	*m.p.* (°C)	*Yield* (%)	*Formula*[a] (*mol. wt*)	*Microanalysis: calc./found* (%)	
						N	*S*
5a		O	218	60	$C_{19}H_{18}N_9O_5SFe.NO_3$ (546·84)	15·37 15·40	5·86 5·80
5b			240	62	$C_{19}H_{18}N_5O_5SCu$ (450·15)	15·66 15·60	7·12 7·09
5c			253	70	$C_{19}H_{18}N_5O_5SHg$ (587·20)	12·00 11·89	5·46 5·50
5'a		S	293	59	$C_{19}H_{18}N_5O_4S_2Fe.NO_3$ (562·91)	14·93 15·00	11·39 11·40
5'b			281	61	$C_{19}H_{13}N_5O_5S_2Cu$ (466·21)	15·12 15·08	13·76 13·80
5'c			228	63	$C_{19}H_{18}N_5O_4S_2Hg$ (603·27)	11·68 11·70	10·63 10·59
6a		O	290	71	$C_{17}H_{12}N_4O_6SFe.NO_3$ (518·67)	13·50 13·52	6·18 6·12
6b			298	65	$C_{17}H_{12}N_4O_6SCu$ (421·98)	13·36 13·29	7·61 7·68
6c			>300	75	$C_{17}H_{12}N_4O_6SHg$ (559·03)	10·09 10·12	5·74 5·68
6'a		S	>300	68	$C_{17}H_{12}N_4O_5S_2Fe.NO_3$ (534·73)	13·10 13·00	11·99 12·00
6'b			282	71	$C_{17}H_{12}N_4O_5S_2Cu$ (438·04)	12·87 12·79	14·64 14·70
6'c			291	69	$C_{17}H_{12}N_4O_5S_2Hg$ (575·09)	9·81 9·79	11·15 11·09

7a		O	>300	80	$C_{18}H_{13}N_5O_6SFe.NO_3$ (545·78)	15·40 15·37	5·88 5·90
7b			>300	75	$C_{18}H_{13}N_5O_6SCu$ (449·09)	15·69 15·73	7·14 7·09
7c			295	70	$C_{18}H_{13}N_5O_6SHg$ (586·14)	12·03 12·10	5·47 5·50
7′a		S	>320	71	$C_{18}H_{13}N_5O_5S_2Fe.NO_3$ (561·85)	14·96 15·00	10·41 10·39
7′b			>300	65	$C_{18}H_{13}N_5O_5S_2Cu$ (465·16)	15·15 15·09	13·79 13·85
7′c			280	68	$C_{18}H_{13}N_5O_5S_2Hg$ (602·20)	11·70 11·68	10·65 10·70
8a		O	>300	69	$C_{19}H_{15}N_5O_7SFe.NO_3$ (575·69)	14·60 14·58	5·57 5·62
8b			290	71	$C_{19}H_{15}N_5O_7SCu$ (478·99)	14·72 14·80	6·70 6·69
8c			298	78	$C_{19}H_{15}N_5O_7SHg$ (616·05)	11·44 11·39	5·21 5·19
8′a		S	>310	68	$C_{19}H_{15}N_5O_6S_2Fe.NO_3$ (591·76)	14·20 14·18	10·82 10·90
8′b			>300	61	$C_{19}H_{15}N_5O_6S_2Cu$ (495·06)	14·24 14·10	12·95 12·99
8′c			285	64	$C_{19}H_{15}N_5O_6S_2Hg$ (632·11)	11·15 11·22	10·15 10·12

(*continued*)

TABLE 5—*contd.*

Compound no.	*R*	*X* = *O or S*	*m.p.* (°C)	*Yield* (%)	*Formula*[a] (*mol. wt*)	*Microanalysis: calc./found* (%)	
						N	*S*
9a		O	252	68	$C_{16}H_{10}N_4O_5S_2Fe.NO_3$ (505·71)	13·85	6·34
						13·91	6·29
9b			265	71	$C_{16}H_{10}N_4O_5S_2Cu$ (409·02)	13·79	15·68
						13·83	15·61
9c			287	66	$C_{16}H_{16}N_4O_5S_2Hg$ (578·15)	9·75	10·92
						9·82	10·97
9′a		S	258	65	$C_{16}H_{10}N_4O_4S_3Fe.NO_3$ (521·78)	13·42	18·44
						13·39	18·49
9′b			241	70	$C_{16}H_{10}N_4O_4S_3Cu$ (425·09)	13·31	22·69
						13·26	22·63
9′c			248	75	$C_{16}H_{10}N_4S_3Hg$ (594·21)	9·47	16·19
						9·53	16·21
10a		O	268	70	$C_{19}H_{15}N_5O_7SFe.NO_3$ (575·69)	14·60	5·57
						14·55	5·83
10b			274	65	$C_{19}H_{15}N_5O_7SCu$ (478·99)	14·72	6·70
						14·80	6·68
10c			241	81	$C_{19}H_{15}N_5O_7SHg$ (616·05)	11·44	5·21
						11·50	5·19
10′a		S	>300	75	$C_{19}H_{15}N_5O_6S_2Fe.NO_3$ (591·88)	14·20	10·83
						14·17	10·89
10′b			235	69	$C_{19}H_{15}N_5O_6S_2Cu$ (495·06)	14·24	12·95
						14·30	12·90
10′c			275	76	$C_{19}H_{15}N_5O_6S_2Hg$ (632·11)	11·15	10·15
						11·20	10·19

[a] Iron and copper chelates **5a–c**, **5′a–c**, **8a–c**, **8′a–c** and **10a–c**, **10′a–c** were recrystallized from aqueous DMSO, and the other compounds from aqueous DMF.

technique; [17–19] 0·5% (w/v) solutions of the compounds in dimethylformamide were prepared. The dishes were allowed to stand in a refrigerator at 4–8°C for 0·5 h to allow diffusion of the solutions, and were then incubated at 37±1°C (18 h) for antibacterial activity and at 28°C (36 h) for antifungal activity. The inhibition zones were measured with callipers.

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