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Azo-Dyes Related to 5-Sulphonylpiperidino- and/or Morpholino-8-Quinolinol

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ABSTRACT

Some new azo-dye sulphonamides based on 5-sulphonylpiperidino and/or (morpholino)-8-hydroxyquinoline (1,1') have been synthesized by diazotization of 4-aminobenzene 4'-(substituted heterocyclo-)-sulphonamide derivatives and coupling with 5-sulphonylpiperidino-(morpholino)-8-hydroxyquinoline in acid medium, affording the corresponding substituted 7-[4-azo-4'-substituted benzene sulphonamido]-5-sulphonyl piperidino-(morpholino)-8-hydroxyquinoline (2_{a-h}, $2'_{a-h}$) as ligands. Interaction of these ligands with metal salts Hg^{2+}, Cu^{2+} and Fe^{3+} in solution afforded the corresponding metal chelates (3_{a-c}–10_{a-c}). All the synthesized compounds have been screened in vitro *for their antibacterial activities. The synthesized compounds were investigated on the basis of microanalytical data, IR, UV and [1H]-NMR spectroscopy.*

1 INTRODUCTION

Sulphonamide derivatives are biologically important compounds[1–6] and some 8-hydroxyquinoline derivatives and their complexes with transition metals have been reported to be active against bacteria.[7] In view of the biological significance of these compounds and the versatile chemistry[8–11] of the metal oxinates, we report here an investigation concerning the synthesis and characterization of seven substituted 5-sulphonyl

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Table 1
Physical and Analytical Data of Compounds (2_{a-h}, $2'_{a-h}$)

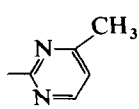
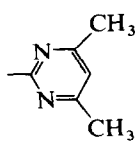
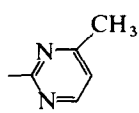
Compound no.	*R*	*X*	*m.p. (°C)*	*Yield (%)*	*Molecular formula (MW)*	*Microanalysis calculated/found*			
						%C	*%H*	*%N*	*%S*
2_a	H	CH_2	290	75	$C_{20}H_{21}O_5N_5S_2$ (475·55)	50 52 50·91	4·45 4·51	14·73 14·83	13·49 13·43
$2'_a$	H	O	265	77	$C_{19}H_{19}O_6N_5S_2$ (477·52)	47·79 47 72	4·01 4·07	14·67 14 59	13 43 13 51
2_b	$-CCH_3$ (O)	CH_2	188	79	$C_{22}H_{23}O_6N_5S_2$ (517·59)	51·05 51·16	4 48 4·53	13·53 13·47	12·39 12·43
$2'_b$	$-CCH_3$ (O)	O	195	80	$C_{21}H_{21}O_7N_5S_2$ (519·56)	48·55 48·64	4 07 4 14	13·48 13·53	12·34 12·28
2_c	$-CNH_2$ (NH)	CH_2	150	74	$C_{21}H_{23}O_5N_7S_2$ (517 59)	48·73 48·83	4·48 4·52	18·94 18·88	12 39 12·46
$2'_c$	$-CNH_2$ (NH)	O	240	77	$C_{20}H_{21}O_6N_7S_2$ (477·52)	46·24 46·32	4·07 4·12	18·87 18·92	12·34 12·28
2_d		CH_2	>300	78	$C_{25}H_{24}O_5N_6S_2$ (552 64)	54·34 54·43	4·38 4·41	15·21 15·14	11·60 11·52
$2'_d$		O	>300		$C_{24}H_{22}O_6N_6S_2$ (554·61)	51·98 52·05	4·00 3 94	15·15 15 08	11·26 11·62
2_e		CH_2	292	82	$C_{24}H_{23}O_5N_7S_2$ (553·62)	52·07 52·16	4·19 4·22	17·17 17·66	11·58 11·67
$2'_e$		O	>300	85	$C_{23}H_{21}O_6N_7S_2$ (555·60)	49·72 49 83	3·81 3·78	17·65 17·71	11·54 11·46
2_f		CH_2	285	85	$C_{25}H_{25}O_5N_7S_2$ (567·65)	52·90 52 80	4·44 4·38	17·27 17·35	11·30 11 21
$2'_f$		O	290	82	$C_{24}H_{23}O_6N_7S_2$ (569·62)	50 61 50·70	4·07 4·12	17·21 17·17	11·26 11·32
2_g		CH_2	>300	84	$C_{26}H_{27}O_5N_7S_2$ (581·68)	53·69 53·76	4·68 4·72	16·86 16·92	11·02 11·11
$2'_g$		O	205	88	$C_{25}H_{25}O_6N_7S_2$ (583·65)	51·45 51·53	4 32 4·28	16·80 16·72	10·99 11·05
2_h		CH_2	>300	86	$C_{23}H_{22}O_5N_6S_3$ (558·66)	49·45 49·55	3·97 4·02	15·04 15·11	17·21 17·15
$2'_h$		O	>300	88	$C_{22}H_{20}O_6N_6S_3$ (560·63)	47·13 47·22	3·60 3·54	14·99 14·91	17 16 17·11

TABLE 2
Physical Data of Azo Sulpha Drugs—Mercury, Copper and Iron Chelates

Compound no.	*R*	*X*	*m.p. (°C)*	*Yield (%)*	*Molecular formula (MW)*	*Microanalysis calculated/found*	
						S	*Cl*
3_a			220	60	$C_{20}H_{20}O_5N_5S_2$. HgCl	9·02	4·99
					(710·59)	9·06	4·92
3_b		$\backslash CH_2$ /	235	58	$C_{20}H_{20}O_5N_5S_2$. CuCl	11·18	6·18
					(573·54)	11·24	6·22
3_c			250	56	$C_{20}H_{20}O_5N_5S_2$. $FeCl_2$	10·66	11·79
					(601·30)	10·73	11·85
	H						
$3'_a$			248–50	61	$C_{19}H_{18}O_6N_5S_2$. HgCl	8·99	4·97
					(712·56)	9 08	5·03
$3'_b$		$\backslash O$ /	253	63	$C_{19}H_{18}O_6N_5S_2$. CuCl	11·14	6·16
					(575·51)	11·20	6·00
$3'_c$			280	65	$C_{19}H_{18}O_6N_5S_2$. $FeCl_2$	10·63	11·75
					(603·27)	10·54	11·68
4_a			200	56	$C_{22}H_{22}O_6N_5S_2$. HgCl	8·52	4·71
					(752·63)	8·60	4·63
4_b		$\backslash CH_2$ /	235	60	$C_{22}H_{22}O_6N_5S_2$. CuCl	10·42	5·76
					(615·58)	10·33	5·81
4_c	O ‖ —CCH₃		270	58	$C_{22}H_{22}O_6N_5S_2$. $FeCl_2$	9·97	11·02
					(643·34)	10·03	10·94
$4'_a$			225	61	$C_{21}H_{20}O_7N_5S_2$. HgCl	9·00	4·70
					(754·50)	8·54	4·75
$4'_b$		$\backslash O$ /	240	60	$C_{21}H_{20}O_7N_5S_2$. CuCl	10·38	5·74
					(617·55)	10·46	5·81
$4'_c$			256	63	$C_{21}H_{20}O_7N_5S_2$. $FeCl_2$	9·94	10·98
					(645·31)	9·99	11·03
5_a			210	64	$C_{21}H_{22}O_5N_7S_2$. HgCl	8·52	4·71
					(752·63)	8·45	4·63
5_b		$\backslash CH_2$ /	233	61	$C_{21}H_{22}O_5N_7S_2$. CuCl	10·42	5·76
					(615·58)	10·34	5·82
5_c			>300	68	$C_{21}H_{22}O_5N_7S_2$. $FeCl_2$	9·97	11·02
	NH ‖ —C—NH₂				(643·34)	9·88	10·92
$5'_a$			255	73	$C_{20}H_{20}O_6N_7S_2$. HgCl	8·50	4·70
					(754·60)	8·40	4 73
$5'_b$		$\backslash O$ /	270	71	$C_{20}H_{20}O_6N_7S_2$. CuCl	10·38	5·74
					(617·55)	10·44	5·68
$5'_c$			>300	69	$C_{20}H_{20}O_6N_7S_2$. $FeCl_2$	9·94	10·99
					(645·31)	9·84	10·88

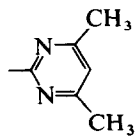
Continued

TABLE 2—*contd.*

Compound no.	*R*	*X*	*m.p. (°C)*	*Yield (%)*	*Molecular formula (MW)*	*Microanalysis calculated/found*	
						S	*Cl*
6_a			212	69	$C_{25}H_{23}O_5N_6S_2$. HgCl	8·14	4·50
					(787·68)	8·22	4·56
6_b		$\backslash CH_2 /$	228	71	$C_{25}H_{23}O_5N_6S_2$. CuCl	9·86	5·45
					(650·63)	9·91	5·52
6_c			>300	66	$C_{25}H_{23}O_5N_6S_2$. $FeCl_2$	9·45	10·45
					(678·39)	9·39	10·51
$6'_a$			235	73	$C_{24}H_{21}O_6N_6S_2$. HgCl	8·12	4·49
					(789·65)	9·00	4·56
$6'_b$		$\backslash O /$	240	65	$C_{24}H_{21}O_6N_6S_2$. CuCl	9·83	5·43
					(652·60)	9·75	5·35
$6'_c$			260	71	$C_{24}H_{21}O_6N_6S_2$. $FeCl_2$	9·43	10·42
					(680·37)	9·33	10·50
7_a			185	71	$C_{24}H_{22}O_5N_7S_2$. HgCl	8·13	4·49
					(788·66)	8·19	4·54
7_b		$\backslash CH_2 /$	200	80	$C_{24}H_{22}O_5N_7S_2$. CuCl	9·84	5·44
					(651·61)	9·77	5·39
7_c			>300	80	$C_{24}H_{22}O_5N_7S_2$. $FeCl_2$	9·44	10·44
					(679·38)	9·52	10·37
$7'_a$			240	78	$C_{23}H_{20}O_6N_7S_2$. HgCl	8·11	4·48
					(790·64)	8·03	4·52
$7'_b$		$\backslash O /$	270	72	$C_{23}H_{20}O_6N_7S_2$. CuCl	9·81	5·42
					(653·59)	9·73	5·37
$7'_c$			>300	83	$C_{23}H_{20}O_6N_7S_2$. $FeCl_2$	9·41	10·41
					(681 36)	9 31	10·44
8_a			220	68	$C_{25}H_{24}O_5N_7S_2$. HgCl	7·99	4·42
					(802·69)	8·04	4·35
8_b		$\backslash CH_2 /$	230	65	$C_{25}H_{24}O_5N_7S_2$. CuCl	9·63	5·33
					(665·64)	9·54	5·40
8_c			241	70	$C_{25}H_{24}O_5N_7S_2$. $FeCl_2$	9·25	10·23
					(693·41)	9·21	10·18
$8'_a$			210	75	$C_{24}H_{22}O_6N_7S_2$. HgCl	7·97	4·41
					(804·66)	7·88	4·34
$8'_b$		$\backslash O /$	230	65	$C_{24}H_{22}O_6N_7S_2$. CuCl	9·61	5·31
					(667·61)	9·64	5·21
$8'_c$			250	68	$C_{24}H_{22}O_6N_7S_2$. $FeCl_2$	9·22	10·20
					(695·38)	9·17	10·24

Continued

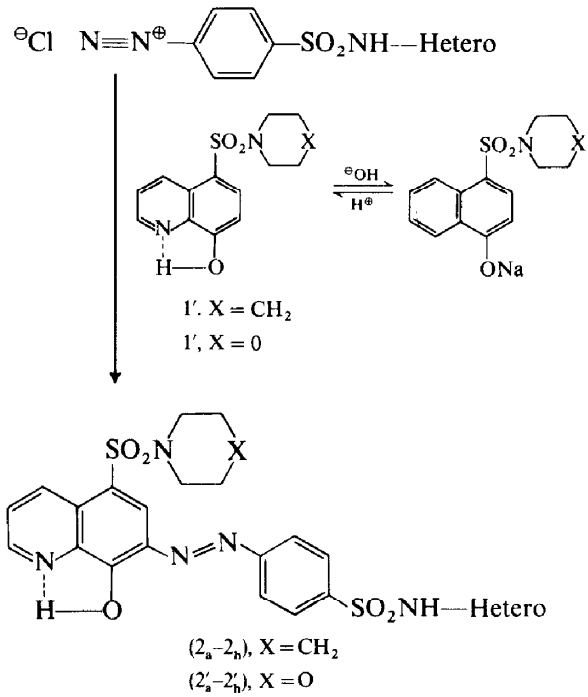
TABLE 2—*contd.*

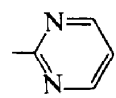
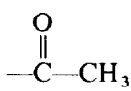
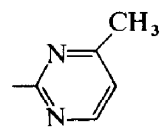
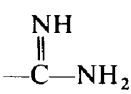
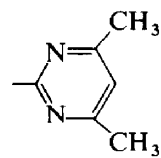
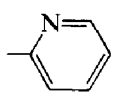
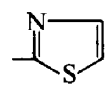
Compound no.	*R*	*X*	*m.p. (°C)*	*Yield (%)*	*Molecular formula (MW)*	*Microanalysis calculated/found*	
						S	*Cl*
9_a		$\backslash CH_2 /$	185	63	$C_{26}H_{26}O_5N_7S_2$. HgCl (816·72)	7·85 7·78	4·34 4·41
9_b			200	60	$C_{26}H_{26}O_5N_7S_2$. CuCl (679·67)	9·44 9·35	5·21 5·18
9_c			300	57	$C_{26}H_{26}O_5N_7S_2$. $FeCl_2$ (707·44)	9·06 9·13	10·02 10·10
$9'_a$		$\backslash O /$	240	70	$C_{25}H_{24}O_6N_7S_2$. HgCl (818·69)	7·83 7·91	4·33 4·26
$9'_b$			270	62	$C_{25}H_{24}O_6N_7S_2$. CuCl (681·64)	9·41 9·45	5·20 5·24
$9'_c$			>300	60	$C_{25}H_{24}O_6N_7S_2$. $FeCl_2$ (709·41)	9·04 9·11	9·99 9·89
10_a		$\backslash CH_2 /$	218	75	$C_{23}H_{21}O_5N_6S_3$. HgCl (793·70)	12·12 12·16	4·47 4·51
10_b			242	70	$C_{23}H_{21}O_5N_6S_3$. CuCl (656·65)	14·65 14·58	5·40 5·46
10_c			291	65	$C_{23}H_{21}O_5N_6S_3$. $FeCl_2$ (684·42)	14·05 14·10	10·36 10·42
$10'_a$		$\backslash O /$	222	67	$C_{22}H_{19}O_6N_6S_3$. HgCl (795·67)	12·09 12·14	4·46 4·50
$10'_b$			243	71	$C_{22}H_{19}O_6N_6S_3$. CuCl (658·62)	14·61 14·63	5·38 5·44
$10'_c$			>300	66	$C_{22}H_{19}O_6N_6S_3$. $FeCl_2$ (686·39)	14·01 13·91	10·33 10·28

piperidino(morpholino)-7-azobenzenesulphamido)-8-hydroxyquinoline (2_{a-h}, $2'_{a-h}$) and their complexes with some transition metal ions and on the changes in antimicrobial activity of these ligands on chelation.

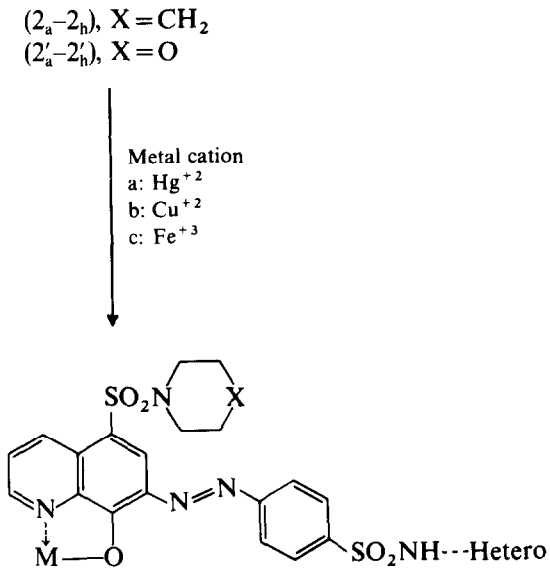
2 RESULTS AND DISCUSSION

In continuation of earlier work[12–18] on azosulphonamides, the synthesis of some new azo-dyes based on 5-sulphonylpiperidino- and/or (morpholino)-8-hydroxyquinoline as ligands, and of their Hg^{2+}, Cu^{2+}, Fe^{3+} chelates (3_{a-c}–10_{a-c}) and an evaluation of their biological activities was effected.

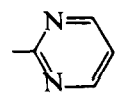
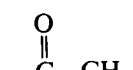
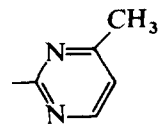
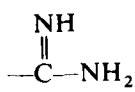
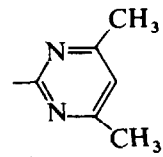
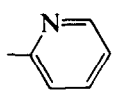
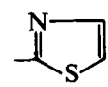


Compd	*Hetero-*	*Compd*	*Hetero-*
(2_a, $2'_a$)	H	(2_c, $2'_c$)	
(2_b, $2'_b$)		(2_f, $2'_f$)	
(2_c, $2'_c$)		(2_g, $2'_g$)	
(2_d, $2'_d$)		(2_h, $2'_h$)	

Scheme 1



$(3_{a\text{-}c}–10_{a\text{-}c})$, X = CH_2
$(3'_{a\text{-}c}–10'_{a\text{-}c})$, X = O

Compd	*Hetero-*	*Compd*	*Hetero-*
$(3_{a\text{-}c}, 3'_{a\text{-}c})$	H	$(7_{a\text{-}c}, 7'_{a\text{-}c})$	
$(4_{a\text{-}c}, 4'_{a\text{-}c})$		$(8_{a\text{-}c}, 8'_{a\text{-}c})$	
$(5_{a\text{-}c}, 5'_{a\text{-}c})$		$(9_{a\text{-}c}, 9'_{a\text{-}c})$	
$(6_{a\text{-}c}, 6'_{a\text{-}c})$		$(10_{a\text{-}c}, 10'_{a\text{-}c})$	

Scheme 2

TABLE 3
UV and IR Spectra of Some Ligands and Their Copper and Iron Chelates

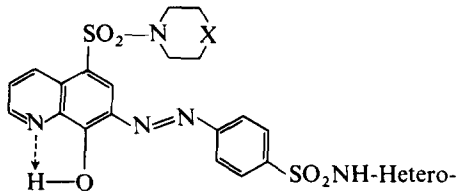
Compound No.	*UV: λ_{max} (nm)*	*IR: cm^{-1}*				
		νOH	*νN=N*	*νC=N*	*νSO_2 Asym.*	*νSO_2 Sym.*
2_b		3450	1600	1640	1340	1160
4_b		—	1595	1610	1330	1140
4_c		—	1595	1565	1330	1150
2_e	520, 460, 440, 340					
7_b	495, 460, 440					
7_c	510, 450					
2_h	520, 415	3320	1590	1630	1330	1150
10_b	480, 435	—	1580	1610	1320	1140
10_c	510, 450, 330	—	1585	1620	1330	1150

The substituents in the sulphonamide moiety were selected so as to ensure a wide variation in their size, electronegativity, chemical reactivity and biological activity. The resulting compounds on diazotization and coupling with 5-sulphonylpiperidino- and/or (morpholino)-8-hydroxyquinoline afforded the corresponding substituted 5-sulphonylpiperidino- and/or (morpholino)-7-azobenzenesulphonamido-8-hydroxyquinoline (2_a, $2'_a$–2_h, $2'_h$). Interaction of these ligands with Hg^{2+}, Cu^{2+}, Fe^{3+} salts in solution afforded the corresponding metal chelates (3_{a-c}, $3'_{a-c}$–10_{a-c}, $10'_{a-c}$) through the formation of a heterocyclic five-membered ring between the metal ion and the quinoline moiety (molar ratio 1:1, metal to ligand). The ligands (2_a, $2'_a$–2_h, $2'_h$) and their chelates (3_{a-c}, $3'_{a-c}$–10_{a-c}, $10'_{a-c}$) were characterized by UV, IR and NMR spectrometry, and by microanalysis. The azo compounds displayed a prominent maximum at 520 nm, in addition to other maxima at different wavelengths, depending on the nature of the substituents. These UV characteristics of the ligands were in good agreement with recently reported data concerning the utility of 8-hydroxyquinoline for the colorimetric microdetermination of some sulpha drugs.[19] However, this absorption maximum is shifted to slightly lower wavelength (480–510 nm) for the copper and iron chelates (Table 3), this shift being attributed to the contribution of the n-electrons of the auxochrome (OH) group in the chelated formation.

IR spectra (Table 3) indicate that attachment of the ligands to the Cu^{2+} or Fe^{3+} ions occurs through the OH group, since the *ν*OH band in the 3450–3320 cm^{-1} region is absent.The band observed in the 1640–1590 cm^{-1} range is assigned to the *ν*C=N stretching frequency, a slight shift of this band to lower frequency being generally observed on

TABLE 4

[^{1}H]-NMR Spectra of Some Representative Compounds (Chemical Shifts in δ ppm; DMSO)



X = CH_2, O

Compound No.	*CH3 (s)*	*NH (s)*	*OH (s)*	*Aromatic protons (m)*	—N X
2_e		9·30	8·75	7·56–8·25 (11 H)	2·60 (m, 3H, γ-protons, piperidine), 3·00 (m, 4H, β-protons, pip.), 3·60 (t, 4H, *a*-protons, pip.).
$2'_e$		9·25	8·80	7·58–8·25 (11 H)	3·50 (t, 4H, α-protons of morph.), 3·00 (t, 4H, β-protons of morph.).
8_b	2·20	9·30		7·62–8·15 (10 H)	2·65 (m, 2H, γ-protons, pip.), 2·90 (m, 4H, β-protons, pip.), 3 55 (t, 4H, α-protons, pip.).
$9'_c$	2·25	9·35		7·60–8·20 (9 H)	3·40 (t, 4H, α-protons, morph.), 3·15 (t, 4H, β-protons, morph.).

coordination. The asymmetric (1340–1320 cm^{-1}) and the symmetric (1150–1140 cm^{-1}) of the νSO_2 band for the chelates appear at almost the same frequencies as in the ligands (Table 3).

The antibacterial results showed that the ligands and their metal Hg^{2+}, Cu^{2+}, Fe^{3+} chelates exhibited pronounced activities against at least four out of the test bacteria (inhibition zones ranged from 20 to 110 mm). It is of interest to note that the majority of the mercury chelates (3_c–10_c, $3'_c$–$10'_c$) were more active than the iron and copper chelates (cf. Table 5).

3 EXPERIMENTAL

3.1 General

Melting points are uncorrected. IR spectra were recorded on Pye-Unicam SP-200G and Perkin-Elmer 599B spectrophotometers and [1H] NMR spectra on a Varian EM-390 MHz spectrometer in an appropriate

TABLE 5

Antibacterial Activity of Ligands (2_{a-h}, $2'_{a-h}$) and Their Iron, Copper and Mercury (3_{a-c}–10_{a-c}, $3'_{a-c}$–$10'_{a-c}$) Chelates (Inhibition Zones in mm)

Compound No.	Serratia marescens *sp. DSM 1608*	Bacillus cereus *DSM 345*	Pseudomonas aeruginosa *DSM 1299*	Micrococcus luteus *DSM 348*	Klebsiella pneumonia	Staphylococcus aureus *DSM 346*
2_a	20	30	15	25	20	30
$2'_a$	30	30	20	40	10	10
2_b	30	20	−ve	10	10	−ve
$2'_b$	40	50	30	20	40	−ve
2_c	10	10	30	−ve	20	20
$2'_c$	−ve	30	20	10	40	20
2_d	40	−ve	25	15	20	10
$2'_d$	40	60	60	50	70	80
2_e	10	20	−ve	40	15	−ve
$2'_e$	30	70	70	30	40	70
2_f	25	−ve	20	20	−ve	20
$2'_f$	20	20	80	20	10	30
2_g	10	10	−ve	30	20	−ve
$2'_g$	−ve	20	90	−ve	−ve	10
2_h	40	30	10	−ve	25	20
$2'_h$	50	30	−ve	20	30	40
3_a	−ve	−ve	−ve	−ve	30	−ve
3_b	10	−ve	−ve	40	−ve	30
3_c	40	30	70	40	20	90
$3'_a$	30	40	10	50	20	20
$3'_b$	20	20	10	40	30	10
$3'_c$	70	50	30	60	30	20
4_a	30	10	30	10	40	20
4_b	−ve	30	10	20	30	10
4_c	60	80	90	50	50	40
$4'_a$	30	30	30	20	30	10
$4'_b$	20	40	20	10	20	10
$4'_c$	80	60	40	30	50	20
5_a	10	−ve	20	20	−ve	−ve
5_b	20	10	10	40	20	−ve
5_c	50	30	60	10	10	30
$5'_a$	10	−ve	20	−ve	20	−ve
$5'_b$	10	30	−ve	10	30	10
$5'_c$	40	60	40	30	60	50
6_a	20	−ve	10	10	10	−ve
6_b	−ve	20	−ve	−ve	10	10
6_c	50	30	50	30	40	30
$6'_a$	30	20	30	20	30	20
$6'_b$	40	30	15	40	10	30
$6'_c$	90	80	65	60	70	90

TABLE 5—*contd.*

Compound No.	Serratia marescens *sp.*	Bacillus cereus *DSM 345*	Pseudomonas aeruginosa *DSM 1299*	Micrococcus luteus *DSM 348*	Klebsiella pneumonia	Staphylococcus aureus *DSM 346*
7_a	−ve	10	20	10	15	−ve
7_b	20	20	−ve	25	20	10
7_c	30	30	20	60	20	30
$7'_a$	20	60	70	30	40	50
$7'_b$	30	60	50	20	30	60
$7'_c$	60	90	80	40	50	80
8_a	20	−ve	−ve	30	10	20
8_b	10	−ve	20	10	−ve	−ve
8_c	40	20	30	40	40	60
$8'_a$	20	30	60	20	30	10
$8'_b$	40	20	50	30	20	20
$8'_c$	40	40	90	40	30	50
9_a	−ve	−ve	10	40	30	−ve
9_b	10	10	−ve	−ve	20	10
9_c	30	30	20	50	30	20
$9'_a$	10	30	80	10	−ve	20
$9'_b$	10	20	60	10	10	10
$9'_c$	30	50	116	30	40	60
10_a	30	20	15	10	30	30
10_b	10	40	20	30	10	30
10_c	60	40	20	20	40	50
$10'_a$	60	20	10	20	30	20
$10'_b$	40	30	20	30	20	30
$10'_c$	80	50	30	40	60	80

−ve = Not active compounds.

deuterated solvent using TMS as internal standard. Analytical data were obtained using a Perkin-Elmer 240E Microanalyzer.

4-Substituted benzenesulphamoyl diazonium chlorides were prepared by diazotization with sodium nitrite at 5°C of the 4-aminobenzenesulphonyl derivatives (0·05 mole) in dil. alcohol and 50% hydrochloric acid. The diazonium chlorides were used directly for the synthesis of the corresponding azo-dye compounds.

3.2 General method for synthesis of '5-sulphonylpiperidino- and/or (morpholino)-7-(4-azo-4'-substituted benzenesulphonamoyl)-8-hydroxyquinoline

The appropriate diazonium salt was added portion-wise with stirring to a solution of 5-sulphonylpiperidino- and/or (morpholino)-8-hydroxyquinoline

(0·05 mol) in 20% sodium hydroxide (40 ml). The temperature was maintained at 5°C, and stirring was continued for 1 h. The reaction mixture was then kept at ambient temperature for 1 h, when the product precipitated. It was filtered, washed with water and recrystallized from methanol.

3.3 General method for preparation of mercury, copper and iron chelates

To a hot solution of the appropriate ligands (0·01 mol) in aqueous ethanol ferric chloride, copper chloride or mercuric chloride (0·01 mol) was added with stirring and stirring was continued for a further 30 min at 60–70°C. The reaction mixture was then cooled and the precipitated product filtered, washed with water, dried and recrystallized from ethanol.

3.4 Biological screening

The disc-diffusion method was used to measure the antimicrobial activity.[20,21] The test compounds were dissolved in sterile dimethyl formamide and added at a concentration of 0·5 mg/disc (Whatman No. 3 filter paper, 0·5 cm diameter). The antibacterial spectra of the different compounds were tested with six strains of bacteria, i.e. *Serratia marcescens*, *Bacillus cereus*, *Pseudomonas aeruginosa*, *Micrococcus luteus*, *Klebsiella pneumonia* and *Staphylococcus aureus*. Incubation was carried out at 37(±1)°C for 36 h and zones of inhibition were measured in mm.

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