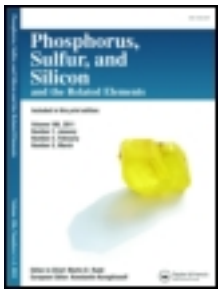

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SYNTHESIS AND CHEMISTRY OF SOME NEW 2-MERCAPTOIMIDAZOLE DERIVATIVES OF POSSIBLE ANTIMICROBIAL ACTIVITY

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SYNTHESIS AND CHEMISTRY OF SOME NEW 2-MERCAPTOIMIDAZOLE DERIVATIVES OF POSSIBLE ANTIMICROBIAL ACTIVITY

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*4,5-Diaryl-2,3-dihydro-2-mercaptoimidazoles (**2a–e**) were synthesized. They reacted with chloroacetic acid in gl. acetic acid/Ac_2O in presence of anhyd. sodium acetate afforded 5,6-diaryl-2,3-dihydroimidazo[2,1-*b*]thiazol-3-ones (**3a–d**). Also these compounds were prepared by the action of chloroacetyl chloride on compounds (**2**) in pyridine. Compounds (**3a–d**) on condensation with aromatic aldehydes yield 2-arylmethylene-5,6-diaryl-2,3-dihydroimidazo[2,1-b]-thiazol-3-ones (**4a–q**). The latter compounds were prepared directly by the reaction of (**2**) with chloroacetic acid and the aromatic aldehydes. Compounds (**3a–d**) coupled with aryldiazonium salts in pyridine to give 2-arylhydrazono-5,6-diaryl-2,3-dihydroimidazo-[2,1-b]thiazol-3-ones (**5a–r**). Also compounds (**2**) when reacted with 2 or 3-bromopropionic acid afford 2,3-di-hydro-5,6-diaryl-2-methylimidazo[2,1-b]thiazol-3-ones (**6a–d**) and 2,3-di-hydro-6,7-diaryl imidazo-[2,1-b]-1,3-thiazin-4-ones (**7a–d**), respectively. Compounds (**3**, **6**, and **7**) have been cleaved by aromatic amines to give the corresponding 2-(4′,5′-diaryl-2′,3′-dihydroimidazol-2′-yl)thioacetanilide (**8a–f**), 2-(2′,3′-dihydro-4′,5′-diaryl imidazol-2′-yl)thiopropionamide (**9a–c**), and 3-(2′,3′-dihydro-4′,5′-diaryl-imidazol-2′-yl)thiopropionamide (**10a–d**) respectively. All the prepared compounds show considerable antimicrobial activity against bacteria, yeast, and fungi.*

Keywords: 4,5-Diaryl-2-mercaptoimidazole derivatives

The chemistry of imidazole derivatives has received considerable attention due to their biological activities.[1–7] Accordingly, we have undertaken the preparation of some new related derivatives for biological evaluation.

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RESULTS AND DISCUSSION

Synthesis of new compounds were achieved by fusion of diaryl benzoin[8,9] with thiourea at 200°C to give 2,3-dihydro-4,5-diaryl-2-mercaptoimidazoles (**2**). The IR spectra of compounds (**2**) showed absorption bands arounds 3470-3080 cm^{-1}. (cf. Table II). The ^1H NMR spectrum of (**2a**) [DMSO-d_6] led to the following assignments: the 2NH protons as two broad singlets at $\delta = 9.36$ and 9.26 (br., 2H, 2NH) and the aromatic protons as a multiplet (m, 8H, ArH's) (cf. Table II).

Compounds (**2**) were reacted with chlororacetic acid in acetic acid/acetic anhydride in the presence of anhydrous sodium acetate to produce 5,6-diaryl-2,3-dihydroimidazo[2,1-*b*]thiazol-3-ones (**3**); also compounds (**3**) were prepared by the action of chloroacetyl chloride on compounds (**2**) in presence of pyridine. The IR spectra of compounds (**3**) showed the carbonyl absorption bands around 1700 cm^{-1}. The ^1H-NMR spectrum of compound (**3a**) [in DMSO-d_6] showed a methylene group as a singlet, (2H) at 3.25 ppm and the aromatic protons as a multiplet centred in the $\delta = 7.40$-8.60 (m, 8H, ArH's) (cf. Table II).

The formulation of the cyclised products as (**3**) is favored over the isomeric structures (**3**).[10]

Compounds (**3**) were condensed with aromatic aldehydes in acetic acid/acetic anhydride mixture in the presence of anhydrous sodium acetate to produce 2-arylmethylene-5,6-diaryl-2,3-dihydroimidazo[2,1-*b*]-thiazol-3-ones (**4a-q**). The latter compounds were prepared directly from (**2**) by the action of chloroacetic acid, aromatic aldehyde and sodium acetate in acetic acid/acetic anhydride mixture. The reaction product was found to be identical in all aspects (m.p., mixed m.p., and IR) with (**4**). The IR spectra of compounds (**4**) showed carbonyl absorption around 1685–1700 cm^{-1}. This shift to lower frequency is due to the conjugation with the exocyclic double bond. The ^1H-NMR spectrum of (**4a**) [DMSO-d_6] revealed the disappearance of the singlet at $\delta = 3.25$ (compared with that of **3a**) belonging to the activated methylene group, besides the appearance of the expected signals at $\delta = 7.0$–8.60 ppm region (13H) for the aromatic protons and the benzylic proton (cf. Table II).

Compounds (**3**) coupled with aryldiazonium salts in the presence of pyridine to give 2-arylhydrazono-5,6-diaryl-2,3-dihydroimidazo[2,1-*b*]-thiazol-3-ones (**5**). The presence of a peak at 2.70 and 3.70 pp in ^1H-NMR spectra, and the absence of NH-groups in compounds (**5n)** and (**5o**) indicate that their coupling products exist in solution in the azo-form[11] (cf. Table II).

TABLE I Physical Data of Compounds **2–10**

Comp.	Ar/Ar$_1$	Yield (%)	Mol. form. (mol. wt.)	m.p. °C Solvent	% Analysis (calcd./found) C	H	N	S
2a	*o*-C_5H_4N/ *o*-C_5H_4N	95	$C_{13}H_{10}N_4S$ (254)	149 AcOH	64.41 61.82	3.93 3.90	22.04 22.00	12.59 12.35
2b	*p*-C_5H_4N/ *p*-C_5H_4N	98	$C_{13}H_{10}N_4S$ (254)	215 DMF	61.41 62.50	3.93 3.97	21.04 21.90	12.59 12.72
2c	*p*-C_6H_4F/ *p*-C_6H_4F	98	$C_{13}H_{10}F_2N_2S$ (288)	150 AcOH	62.50 62.30	3.47 3.43	9.72 9.70	11.11 11.00
2d	*o*-C_6H_4F/ C_6H_5	96	$C_{13}H_{11}FN_2S$ (270)	200 AcOH	66.66 66.16	4.07 4.00	10.37 10.00	11.85 12.02
2e	*o*-C_4H_3S/ *o*-C_4H_3S	97	$C_{11}H_8N_2S_3$ (264)	95 AcOH	50.00 49.83	3.03 3.00	10.60 10.60	36.36 36.24
3a	*o*-C_5H_4N/ *o*-C_5H_4N	87	$C_{15}H_{10}N_4OS$ (294)	143 AcOH	61.22 60.95	3.40 3.42	19.04 19.00	10.88 10.41
3b	*p*-C_6H_4F/ *p*-C_6H_4F	87	$C_{17}H_{10}F_2N_2OS$ (328)	108 EtOH/AcOH	62.19 62.19	3.04 3.04	8.53 8.52	9.75 9.75
3c	*o*-C_6H_4F/ C_6H_5	85	$C_{17}H_{11}FN_2OS$ (310)	90 EtOH	65.80 65.55	3.54 3.24	9.03 9.03	10.32 10.36
3d	*o*-C_4H_3S/ *o*-C_4H_3S	81	$C_{13}H_8N_2OS_3$ (304)	240 AcOH	51.31 51.20	2.63 2.43	9.21 9.21	31.57 31.57
4a	*o*-C_5H_4N/ *o*-C_5H_4N, X = 4-Cl	73	$C_{22}H_{13}ClN_4OS$ (416.5)	160 AcOH	63.38 63.05	3.12 3.12	13.44 13.43	7.68 7.65
4b	*o*-C_5H_4N/ *o*-C_5H_4N, X = 4-OMe	69	$C_{23}H_{16}N_4O_2S$ (412)	280 AcOH	66.99 67.24	3.88 3.90	13.59 13.59	7.76 7.54
4c	*o*-C_5H_4N/ *o*-C_5H_4N, X = 2-NO_2	56	$C_{22}H_{13}N_5O_3S$ (427)	192 Benzene/pet. ether 40–60°C	61.82 61.69	3.04 2.98	16.39 16.21	7.49 7.49
4d	*o*-C_5H_4N/ *o*-C_5H_4N, X = 4-NO_2	75	$C_{22}H_{13}N_5O_3S$ (427)	172 $CHCl_3$/pet. ether 40–60°C	61.82 61.69	3.04 2.98	16.39 16.21	7.49 7.49
4e	*p*-C_6H_4F/ *p*-C_6H_4F, X = 4-Cl	85	$C_{24}H_{13}ClF_2N_2OS$ (450.5)	170 AcOH	63.92 63.70	2.88 2.80	6.21 6.20	7.10 7.10
4f	*p*-C_6H_4F/ *p*-C_6H_4F, X = 4-OMe	76	$C_{25}H_{16}F_2N_2O_2S$ (446)	150 EtOH	76.26 76.00	3.58 3.50	6.27 6.27	7.17 7.15
4g	*p*-C_6H_4F/ *p*-C_6H_4F, X = 2-NO_2	71	$C_{24}H_{13}F_2N_3O_3S$ (461)	110 $CHCl_3$/pet. ether 40–60°C	62.47 62.47	2.81 2.97	9.11 9.11	6.94 6.82
4h	*p*-C_6H_4F/ *p*-C_6H_4F, X = 4-NO_2	87	$C_{24}H_{13}F_2N_3O_3S$ (461)	235 $CHCl_3$/pet. ether 40–60°C	62.47 62.47	2.81 2.60	9.11 9.00	6.94 6.72
4i	*p*-C_6H_4F/ *p*-C_6H_4F, X = 4-Br	80	$C_{24}H_{13}BrF_2N_2OS$ (494.9)	158 $CHCl_3$/pet. ether 40–60°C	58.19 57.87	2.62 2.42	5.65 5.65	6.46 6.73
4j	C_6H_5/ *o*-C_6H_4F, X = 4-Cl	87	$C_{24}H_{14}ClFN_2OS$ (432.5)	160 AcOH	66.58 66.92	3.23 3.43	6.47 6.47	7.39 7.35
4k	C_6H_5/ *o*-C_6H_4F, X = 4-OMe	75	$C_{25}H_{17}FN_2O_2S$ (428)	140 EtOH	70.09 70.00	3.97 3.90	6.54 6.54	7.47 7.32

(Continued on next page)

TABLE I Physical Data of Compounds **2–10** *(Continued)*

Comp.	Ar/Ar$_1$	Yield (%)	Mol. form. (mol. wt.)	m.p. °C Solvent	% Analysis (calcd./found) C	H	N	S
4l	C_6H_5/ *o*-C_6H_4F, X = 2-NO_2	78	$C_{24}H_{14}FN_3O_3S$ (443)	120 MeOH	65.01 64.98	3.16 3.03	9.48 9.24	7.22 7.22
4m	C_6H_5/ *o*-C_6H_4F, X = 4-NO_2	81	$C_{24}H_{14}FN_3O_3S$ (443)	132 MeOH	65.01 65.01	3.16 2.98	9.48 9.41	7.22 7.00
4n	*o*-C_4H_3S/ *o*-C_4H_3S X = 4-Cl	73	$C_{20}H_{11}ClN_2OS_3$ (426.5)	190 DMF	56.27 56.22	2.57 2.32	6.56 6.56	22.50 22.00
4o	*o*-C_4H_3S/ *o*-C_4H_3S, X = 4-OMe	77	$C_{21}H_{14}N_2O_2S_3$ (422)	245 DMF	59.71 59.21	3.31 2.28	6.63 6.92	22.74 22.93
4p	*o*-C_4H_3S/ *o*-C_4H_3S, X = 2-NO_2	79	$C_{20}H_{11}N_3O_3S_3$ (437)	212 $CHCl_3$/pet. ether 40–60°C	54.91 54.82	2.51 2.32	9.61 9.64	21.96 22.34
4q	*o*-C_4H_3S/ *o*-C_4H_3S, X = 4-NO_2	82	$C_{20}H_{11}N_3O_3S_3$ (437)	182 $CHCl_3$/pet. ether 40–60°C	54.91 54.91	2.51 2.45	9.61 9.48	21.96 22.73
5a	*o*-C_5H_4N/ *o*-C_5H_4N, X = H	63	$C_{21}H_{14}ClN_6O_3S$ (398)	230 AcOH	63.31 63.00	3.51 3.50	21.10 21.00	8.04 8.31
5b	*o*-C_5H_4N/ *o*-C_5H_4N, X = 4-NO_2	87	$C_{21}H_{13}N_7O_3S$ (443)	118 AcOH	56.88 56.42	2.93 2.81	22.12 22.44	7.22 7.57
5c	*o*-C_5H_4N/ *o*-C_5H_4N, X = 2-NO_2	79	$C_{21}H_{13}N_7O_3S$ (443)	110 $CHCl_3$/pet. ether 40–60°C	56.88 56.71	2.93 2.92	22.12 22.19	7.22 7.24
5d	*o*-C_5H_4N/ *o*-C_5H_4N, X = 4-Br	85	$C_{21}H_{13}BrN_6OS$ (476.9)	117 AcOH	52.84 52.95	2.72 2.77	17.61 17.94	6.71 6.79
5e	*o*-C_5H_4N/ *o*-C_5H_4N, X = 4-Cl	75	$C_{21}H_{13}ClN_6OS$ (432.5)	276 AcOH	58.26 58.62	3.00 3.10	19.42 19.71	7.39 7.75
5f	*o*-C_5H_4F/ *o*-C_5H_4F, X = H	76	$C_{23}H_{14}F_2N_4OS$ (432)	108 $CHCl_3$/pet. ether 40–60°C	63.88 63.95	3.24 3.31	12.96 13.24	7.40 7.76
5g	*o*-C_5H_4F/ *o*-C_5H_4F, X = 4-NO_2	89	$C_{23}H_{13}F_2N_5OS$ (477)	98 MeOH	57.86 57.79	2.72 2.72	14.67 14.61	6.70 6.92
5h	*o*-C_5H_4F/ *o*-C_5H_4F, X = 2-NO_2	81	$C_{23}H_{13}F_2N_5OS$ (477)	110 MeOH	57.86 57.52	2.72 2.70	14.67 14.65	6.70 6.96
5i	*o*-C_5H_4F/ *o*-C_5H_4F, X = 4-Br	93	$C_{23}H_{13}F_2BrN_4OS$ (510.9)	128 MeOH	54.02 53.87	2.54 2.78	10.96 10.89	6.26 6.54
5j	*o*-C_5H_4F/ *o*-C_5H_5, X = H	79	$C_{23}H_{15}FN_4OS$ (414)	112 AcOH	66.66 66.61	3.62 3.62	13.52 13.27	7.72 7.62
5k	*o*-C_5H_4F/ C_5H_5, X = 4-NO_2	86	$C_{23}H_{14}FN_5O_3S$ (459)	190 Benzene/pet. ether 40–60°C	60.13 59.86	3.05 3.00	15.25 15.25	6.97 6.81

(Continued on next page)

TABLE I Physical Data of Compounds **2–10** *(Continued)*

Comp.	Ar/Ar$_1$	Yield (%)	Mol. form. (mol. wt.)	m.p. °C Solvent	% Analysis (calcd./found) C	H	N	S
5l	*o*-C_5H_4F/ C_5H_5, X = 2-NO_2	83	$C_{23}H_{14}FN_5O_3S$ (459)	190 Benzene/pet. ether 40–60°C	60.13 60.34	3.05 3.22	15.25 15.18	6.97 6.99
5m	*o*-C_5H_4F/ *o*-C_5H_5, X = 4-Br	90	$C_{23}H_{14}BrFN_4O_3S$ (492.9)	147 MeOH	55.99 56.17	2.84 2.89	11.36 11.36	6.49 6.75
5n	*o*-C_4H_3S/ *o*-C_4H_3S, X = H	65	$C_{19}H_{12}N_4OS_3$ (408)	156 Benzene/pet. ether 40–60°C	55.88 55.62	2.94 2.92	13.72 13.72	23.52 23.20
5o	*o*-C_4H_3S/ *o*-C_4H_3S, X = 4-NO_2	73	$C_{19}H_{11}N_5O_3S_3$ (453)	163 $CHCl_3$/pet. ether 40–60°C	50.33 50.31	2.42 2.42	15.54 15.43	21.19 21.25
5p	*o*-C_4H_3S/ *o*-C_4H_3S, X = 2-NO_2	77	$C_{19}H_{11}N_5O_3S_3$ (453)	108 $CHCl_3$/pet. ether 40–60°C	50.33 50.48	2.42 2.51	15.54 15.45	21.19 21.23
5q	*o*-C_4H_3S/ *o*-C_4H_3S, X = 4-Br	81	$C_{19}H_{11}BrN_4OS_3$ (486.9)	175 Benzene/pet. ether 40–60°C	46.82 46.75	2.25 2.25	11.50 11.35	19.71 19.50
5r	*o*-C_4H_3S/ *o*-C_4H_3S, X = 4-Cl	67	$C_{19}H_{11}ClN_4OS_3$ (442.5)	128 $CHCl_3$/pet. ether 40–60°C	51.52 51.80	2.48 2.34	12.65 12.63	21.69 21.87
6a	*o*-C_5H_4N/ *o*-C_5H_4N	65	$C_{16}H_{12}N_4OS$ (308)	132 Pyridine	62.33 62.17	3.89 3.85	18.18 18.16	10.38 10.71
6b	*p*-C_6H_4F/ *p*-C_6H_4F	91	$C_{18}H_{12}F_2N_2OS$ (342)	140 AcOH	63.15 63.11	3.50 3.51	8.18 8.24	9.35 9.30
6c	*p*-C_6H_4F/ C_6H_5	89	$C_{18}H_{13}FN_2OS$ (324)	83 EtOH	66.66 66.94	4.01 3.97	8.64 8.51	9.87 10.13
6d	*o*-C_4H_3S/ *o*-C_4H_3S	76	$C_{14}H_{10}N_2OS_3$ (318)	145 $CHCl_3$	52.83 52.94	3.14 3.21	8.80 8.78	30.18 30.00
7a	*o*-C_5H_4N/ *o*-C_5H_4N	57	$C_{16}H_{12}N_4OS$ (308)	118 Pyridine	62.33 62.00	3.89 3.71	18.18 18.20	10.38 10.87
7b	*p*-C_6H_4F/ *p*-C_6H_4F	82	$C_{18}H_{12}F_2N_2OS$ (342)	95 AcOH	63.15 63.00	3.50 3.71	8.18 8.42	9.35 9.31
7c	*p*-C_6H_4F/ C_6H_5	74	$C_{18}H_{13}FN_2OS$ (324)	97 EtOH	66.66 66.96	4.01 3.89	8.64 8.51	9.87 9.91
7d	*o*-C_4H_3S/ *o*-C_4H_3S	69	$C_{14}H_{10}N_2OS_3$ (318)	152 $CHCl_3$/pet. ether 40–60°C	52.83 52.71	3.14 3.31	8.80 8.71	30.18 30.43
8a	*o*-C_5H_4N/ *o*-C_5H_4N	89	$C_{21}H_{17}N_5OS$ (387)	128 EtOH	65.11 64.86	4.39 4.31	18.08 18.00	8.26 8.45
8b	*p*-C_6H_4F/ *p*-C_6H_4F	98	$C_{23}H_{17}F_2N_3OS$ (421)	95 AcOH	65.55 65.50	4.03 3.85	9.97 9.72	7.60 7.51
8c	*p*-C_6H_4F/ *p*-C_6H_4F, 4-NO_2	92	$C_{23}H_{16}F_2N_4O_3S$ (466)	172 MeOH	59.22 59.00	3.43 3.41	12.01 12.37	6.86 6.89
8d	*p*-C_6H_4F/ C_6H_5	93	$C_{23}H_{18}FN_3OS$ (403)	105 EtOH	68.48 68.91	4.46 4.53	10.42 10.41	7.94 8.12
8e	*p*-C_6H_4F/ C_6H_5, 4-NO_2	88	$C_{23}H_{17}FN_4O_3S$ (448)	178 AcOH	61.60 61.42	3.79 3.71	12.50 12.30	7.14 7.14

(Continued on next page)

TABLE I Physical Data of Compounds **2–10** *(Continued)*

Comp.	Ar/Ar$_1$	Yield (%)	Mol. form. (mol. wt.)	m.p. °C Solvent	% Analysis (calcd./found) C	H	N	S
8f	*o*-C_4H_3S/ *o*-C_4H_3S	91	$C_{19}H_{15}N_3OS_3$ (397)	135 $CHCl_3$/pet. ether 40–60°C	57.43 57.00	3.77 3.72	10.57 10.23	24.18 24.58
9a	*o*-C_5H_4N/ *o*-C_5H_4N	92	$C_{22}H_{19}N_5OS$ (401)	122 $CHCl_3$/pet. ether 40–60°C	65.83 65.55	4.73 4.71	17.45 17.09	7.98 7.67
9b	*p*-C_6H_4F/ *p*-C_6H_4F	98	$C_{24}H_{19}F_2N_3OS$ (435)	98 AcOH	66.20 66.00	4.36 4.32	9.65 9.63	7.35 7.35
9c	*o*-C_6H_4F/ C_6H_5	97	$C_{24}H_{20}FN_3OS$ (417)	92 Benzene/pet. ether 40–60°C	69.06 69.04	4.79 4.78	10.07 10.00	7.67 7.83
10a	*o*-C_5H_4N/ *o*-C_5H_4N	89	$C_{22}H_{19}N_5OS$ (401)	210 $CHCl_3$/pet. ether 40–60°C	65.83 65.92	4.73 4.71	17.45 17.61	7.98 7.92
10b	*p*-C_6H_4F/ *p*-C_6H_4F	97	$C_{24}H_{19}F_2N_3OS$ (435)	110 AcOH	66.20 66.08	4.36 4.31	9.65 9.25	7.35 7.11
10c	*o*-C_6H_4F/ C_6H_5	93	$C_{24}H_{20}FN_3OS$ (417)	148 Benzene/pet. ether 40–60°C	69.06 69.00	4.79 4.45	10.07 9.73	7.67 7.15
10d	*o*-C_4H_3S/ *o*-C_4H_3S	95	$C_{20}H_{17}N_3OS_3$ (411)	135 $CHCl_3$/pet. ether 40–60°C	58.39 58.80	4.13 4.13	10.21 10.25	23.35 22.87

Compounds (**2**) was reacted with 2- or 3-bromopropanoic acid in refluxing acetic acid/acetic anhydride mixture to produce 5,6-diaryl-2,3-dihydro-2-methylimidazo[2,1-*b*]thiazol-3-ones (**6**) and 6,7-diaryl-2,3-dihydroimidazo[2,1-*b*]-1,3-thiazin-4-ones (**7**) respectively. The IR spectra of compounds (**6**) showed absorption around 1710–1750 cm^{-1} (C=O) and the ^{1}H-NMR spectrum of compound (**6a**) [DMSO-d_6] showed the following peaks in δ ppm: a doublet at δ 1.8 (3H) for the methyl group, quartet at δ 2.3 (1H) for (CH) of the thiazole ring and a multiplet at δ 7.30–8.70 region (8H) for the aromatic protons (cf. Table II).

The IR spectra of compounds (**7**) showed absorption band at 1700 cm^{-1} (C=O) and the ^{1}H-NMR spectrum of compound (**7a**) [DMSO-d_6 + $CDCl_3$] showed the following assignments in δ ppm, a multiplet centered at δ = 2.60–3.40 (4H, thiazin protons) and at δ 7.30–8.70 (m, 8H, Ar's) (cf. Table II).

Compounds (**3**, **6**, and **7**) have been cleaved by aniline to give the corresponding 2-(4′,5′-diaryl-2′,3′-dihydroimidazol-2′-yl)thioacetanilide (**8**), 2-(4′,5′-diaryl-2′,3′-dihydroimidazol-2′-yl)thiopropionamide (**9**), and 3-(4′,5′-diaryl-2′,3′-dihydroimidazol-2′-yl)thiopropionamide derivatives (**10**) respectively. Compounds (**8**, **9**, and **10**) showed correct values in elemental analyses as well as the expect IR peaks. ^{1}H-NMR [DMSO-d_6]

TABLE II IR and ^{1}H-NMR Spectral Data of Compounds **3–10**

Comp. No.	IR ν [cm^{-1}]	^{1}H-NMR Solvent	^{1}H-NMR [δ ppm]
2a	3160, 3470 (br., NH), 1260 (C=S)	A[a]	9.36–9.56 (br., 2H, 2NH); 7.2–9.0 (m, 8H, ArH's)
2b	3150 (br., NH), 1220 (C=S)	A	3.3 (br., 1H, NH), 5.6 (br., 1H, NH); 7.0–8.6 (m, 8H, ArH's)
2c	3080, 3120 (br., NH), 1260 (C=S)	A	4.2 (s, 1H, NH), 5.9 (s, 1H, NH); 6.65–8.20 (m, 8H, ArH's)
2d	3100 (br., NH), 1220 (C=S)	A	43.10 (br., 1H, NH), 6.8–8.4 (m, 9H, ArH's); 12.4 (br., 1H, NH)
2e	3080 (br., NH), 1220 (C=S)	A	3.3 (br., 2H, 2NH); 6.60–8.00 (m, 6H, Ar'H)
3a	1710 (C=O), 2925 (CH_2)	A	3.25 (s, 2H, CH_2); 7.4–8.6 (m, 8H, ArH's)
3b	1700 (C=O), 2920 (CH_2)	A	3.75 (s, 2H, CH_2); 7.0–7.75 (m, 8H, ArH's)
3c	1700 (C=O), 2930 (CH_2)	A	3.50 (s, 2H, CH_2); 7.1–8.3 (m, 9H, ArH's)
3d	1700 (C=O), 2920 (CH_2)	A	3.5 (s, 2H, CH_2); 6.9–8.3 (m, 6H, thiophene protons)
4a	1700 (C=O)	A	7.0–8.6 (m, 13H, Ar's and benzilic proton)
4b	1675 (C=O), 2910 (CH_3)	A	3.8 (s, 3H, OCH_3); 7.06–9.1 (m, 13H, ArH's and benzilic proton)
4c	1690 (C=O)	A	7.4–8.6 (m, 13H, ArH's and and benzilic proton)
4d	1685 (C=O)	A	7.8–8.7 (m, 13H, ArH's and benzilic proton)
4e	1700 (C=O)	B[b]	6.8–8.0 (m, 13H, ArH's and benzilic proton)
4f	1700 (C=O), 2920 (CH_3)	A	3.3 (s, 3H, OCH_3); 7.1–7.9 (m, 13H, ArH's and benzilic proton)
4g	1740 (C=O)	A	6.9–8.2 (m, 13H, ArH's and benzilic proton)
4h	1740 (C=O)	B	7.0–8.4 (m, 13H, ArH's and benzilic proton)
4i	1680 (C=O)	B	7.1–8.0 (m, 13H, ArH's and benzilic proton)
4j	1730 (C=O)	A	6.9–8.2 (m, 13H, ArH's and benzilic proton)
4k	1700 (C=O), 2940 (CH_3)	A	3.8 (s, 3H, OCH_3); 7.00–8.0 (m, 14H, ArH's and benzilic proton)
4l	1740 (C=O)	A	7.2–8.4 (m, 14H, ArH's and benzilic proton)
4m	1730 (C=O)	A	6.09–8.0 (m, 14H, ArH's and benzilic proton)
4n	1690 (C=O)	B	6.9–8.0 (m, 11H, ArH's, thiophene protons and benzilic proton)
4o	1690 (C=O), 2920 (OCH_3)	A	3.9 (s, 3H, OCH_3); 7.00–7.9 (m, 11H, ArH's, thiophene protns and benzilic proton)
4p	1685 (C=O)	A	7.1–8.2 (m, 11H, ArH's, thiophene protns and benzilic proton)
4q	1690 (C=O)	B	6.8–7.9 (m, 11H, ArH's, thiophene protns and benzilic proton)
5a	1690 (C=O), 3100 (br., NH)	A	7.0–8.5 (m, 13H, ArH's); 9.4 (s, 1H, NH)

(Continued on next page)

TABLE II IR and ^{1}H-NMR Spectral Data of Compounds **3–10** *(Continued)*

Comp. No.	IR ν [cm^{-1}]	^{1}H-NMR Solvent	^{1}H-NMR [δ ppm]
5b	1680 (C=O), 3250 (br., NH)	A	6.6–9.0 (m, 12H, ArH's); 10.04 (s, 1H, NH)
5c	1680 (C=O), 3150 (br., NH)	A	6.6–9.4 (m, 12H, ArH's); 11.8 (s, 1H, NH)
5d	1680 (C=O), 3280 (br., NH)	A	3.31 (s, 1H, NH); 6.6–8.7 (m, 12H, ArH's)
5e	1685 (C=O), 3230 (br., NH)	A	6.8–8.2 (m, 12H, ArH's); 10.4 (s, 1H, NH)
5f	1680 (br., C=O), 3050 (br., NH)	A	3.39 (br., 1H, NH); 6.6–7.8 (m, 13H, ArH's)
5g	1700 (br., C=O), 3050 (br., NH)	A	3.2 (br., 1H, NH); 6.8–8.7 (m, 12H, ArH's)
5h	1710 (br., C=O), 3060 (br., NH)	A	3.3 (br., 1H, NH); 6.6–8.0 (m, 12H, ArH's)
5i	1680 (br., C=O), 3050 (br., NH)	A	3.2 (br., 1H, NH); 6.9–7.8 (m, 12H, ArH's); 9.4 (s, 1H, NH)
5j	1700 (br., C=O), 3050 (br., NH)	A	2.3 (br., 1H, NH); 6.8–7.8 (m, 14H, ArH's)
5k	1700 (br., C=O), 3100 (br., NH)	B	2.3 (br., 1H, NH); 6.6–7.8 (m, 13H, ArH's)
5l	1700 (br., C=O), 3080 (br., NH)	B	2.3 (br., 1H, NH); 6.5–8.0 (m, 13H, ArH's)
5m	1680 (br., C=O), 3050 (br., NH)	A	3.5 (br., 1H, NH); 6.6–7.8 (m, 13H, ArH's)
5n	1700 (br., C=O)	A	2.7 (s, 1H, CH); 6.2–8.0 (m, 11H, ArH's and thiophene protons)
5o	1700 (br., C=O)	A	3.4 (s, 1H, CH); 6.8–8.5 (m, 10H, ArH's and thiophene protons)
5p	1700 (br., C=O), 3090 (br., NH)	B	3.85 (br., 1H, NH); 6.8–8.5 (m, 10H, ArH's and thiophene protons)
5q	1650 (br., C=O), 3100 (br., NH)	B	6.7–8.0 (m, 10H, ArH's and thio-phene protons); 8.7 (br., 1H, NH)
5r	1685 (C=O), 3150 (br., NH).	A	3.5 (br., 1H, NH); 6.7–8.9 (m, 10H, ArH's and thiophene protons)
6a	1710 (C=O), 2910 (CH_3)	B	1.8 (d, 3H, CH_3); 2.3 (q, 1H, CH); 7.3–8.7 (m, 8H, ArH's)
6b	1750 (C=O), 2930 (CH_3)	A	1.5 (d, 3H, CH_3); 2.3 (q, 1H, CH); 6.6–8.4 (m, 8H, ArH's)
6c	1710 (C=O), 2920 (CH_3)	A	1.7 (d, 3H, CH_3); 2.3 (q, 1H, CH); 6.6–8.2 (m, 9H, ArH's)
6d	1710 (C=O), 2920 (CH_3)	A	1.7 (d, 3H, CH_3); 2.4 (q, 1H, CH); 6.8–8.2 (m, 6H, thiophene protones)
7a	1700 (C=O)	A+B	2.6–3.4 (m, 4H, thiazine protons); 7.3–8.7 (m, 8H, ArH's)
7b	1700 (C=O)	B	3.9–4.5 (m, 4H, thiazine protons); 6.9–7.3 (m, 8H, ArH's)

(Continued on next page)

TABLE II IR and ^{1}H-NMR Spectral Data of Compounds **3–10** *(Continued)*

Comp. No.	IR ν [cm^{-1}]	^{1}H-NMR Solvent	^{1}H-NMR [δ ppm]
7c	1700 (C=O)	B	1.8–3.3 (m, 4H, thiazine protons); 6.6–8.1 (m, 9H, ArH's)
7d	1700 (C=O)	B	2.75 (m, 2H, thiazine protons); 6.5–8.0 (m, 6H, ArH's)
8a	1700 (C=O), 3040 (NH), 3400 (NH), 2920 (CH_2)	A	1.8 (s, 1H, NH); 3.2 (s, 2H, CH_2); 6.4–8.8 (m, 13H, ArH's); 10.6 (s, 1H, NH)
8b	1680 (C=O), 3090 (br., NH), 2916 (CH_2)	B	3.6 (s, 1H, NH); 3.8 (s, 2H, CH_2); 6.7–8.4 (m, 13H, ArH's); 10.7 (s, 1H, NH)
8c	1680 (C=O), 3280 (NH), 2920 (CH_2)	A	3.4 (s, 1H, NH); 3.9 (s, 2H, CH_2); 6.9–8.2 (m, 12H, ArH's); 10.5 (s, 1H, NH)
8d	1680 (C=O), 3060 (NH), 3390 (br., NH), 2915 (CH_2)	B	3.5 (s, 1H, NH); 4.0 (s, 2H, CH_2); 6.8–8.0 (m, 14H, ArH's); 10.2 (s, 1H, NH)
8e	1680 (C=O), 3100 (NH), 3280 (NH), 2920 (CH_2)	A	2.5 (s, 1H, NH); 3.35 (s, 2H, CH_2); 7.2–8.2 (m, 13H, ArH's); 10.5 (s, 1H, NH)
8f	1670 (C=O), 3080 (NH), 3350 (NH), 2915 (CH_2)	B	1.4 (s, 1H, NH); 1.9 (s, 1H, NH); 4.3 (s, 2H, CH_2); 5.0–8.0 (m, 11H, ArH's and thiophene protons)
9a	1630 (C=O), 3060 (br., NH), 3400 (br., OH)	A	1.2 (d, 3H, CH_3); 2.9 (s, 1H, NH); 3.5 (q, 1H, CH); 7.0–8.2 (m, 13H, ArH's); 8.7 (s, 1H, NH)
9b	1740 (C=O), 3050 (br., NH)	B	1.6 (d, 3H, CH_3); 2.6 (s, 1H, NH); 4.2 (q, 1H, CH); 6.8–7.5 (m, 13H, ArH's); 8.1 (s, 1H, NH)
9c	1740 (C=O), 3060 (br., OH)	B	1.5 (d, 3H, CH_3); 2.15 (s, 1H, NH); 4.25 (q, 1H, CH); 6.7–7.8 (m, 14H, ArH's); 8.2 (s, 1H, NH)
10a	1690 (C=O), 3060 (br., NH), 3400 (br., OH)	A	1.3 (s, 1H, NH); 2.5–3.6 (m, 4H, $2CH_2$); 6.5–7.8 (m, 13H, ArH's); 8.7 (s, 1H, NH)
10b	1700 (C=O), 3040 (br., NH), 3400 (br., OH)	B	1.25 (s, 1H, NH); 2.1–3.0 (m, 4H, $2CH_2$); 6.7–8.0 (m, 13H, ArH's); 8.4 (s, 1H, NH)
10c	1715 (C=O), 3060 (br., NH), 3400 (br., OH)	B	1.4 (s, 1H, NH); 3.2–3.9 (m, 4H, $2CH_2$); 6.7–7.8 (m, 14H, ArH's); 9.0 (s, 1H, NH)
10d	1680 (C=O), 3040 (br., NH), 3400 (br., OH)	A	1.4 (s, 1H, NH); 3.0–3.7 (m, 4H, $2CH_2$); 6.8–7.8 (m, 11H, ArH's); 8.0 (s, 1H, NH)

[a] A = DMSO-d_6.
[b] B = $CDCl_3$.

of compound (**8a**) as an example, showed signals at δ 1.80 ppm (s, 1H, NH), δ 3.20 ppm (s, 2H, CH_2), δ 6.40-8.80 ppm (m, 13H, ArH's), and δ 10.60 ppm (s, 1H, NH) (cf. Table II).

The structures of the new compounds were established by chemical analysis, mass spectra, ^{1}H-NMR and IR spectra. Physical data of compounds (**2–20**) are given in (Table I and II).

Antimicrobial Activity

The antimicrobial activity of the compounds considered was tested on *Bacillus subtilis*, *Staphylocoucus aureus*, *Escherichia Coli*, *Proteus mirabilis*, *Candida albicans*, and *Aspergillus niger*. The biological activity was determined according to the cup plate method.[12] The sensitivity of microorganisms to the compound is identified in the following manner:

(++++) = highly sensitive (inhibition zone > 15 mm);
(+++) = fairly sensitive (inhibition zone > 12 mm);
(++) = slightly sensitive (inhibition zone > 9 mm);
(+) = very slightly sensitive (inhibition zone > 6 mm).

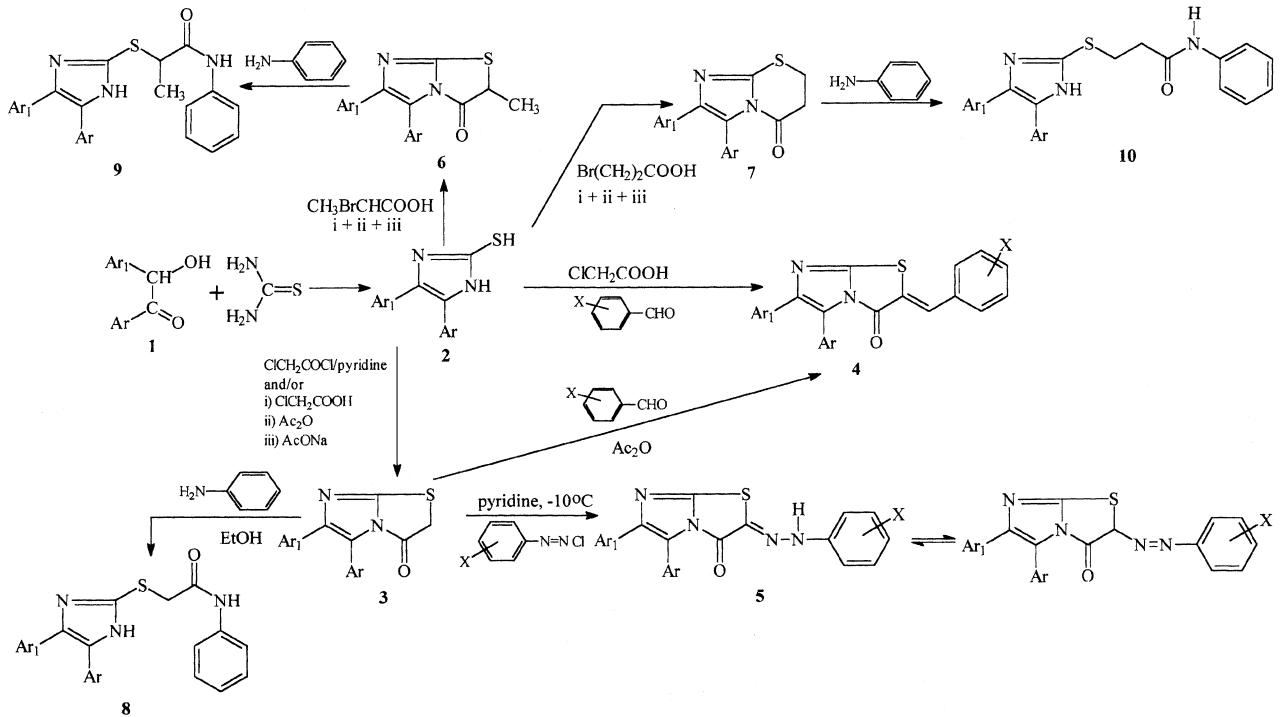
It could be mentioned that, the most determined effect is brought about by compounds **4i**, **4o**, **4f**, **4r**, **5d**, **5i**, **5j**, **5k**, **5o**, **5p**, **5r**, **7d**, **9a**, and **10d** (Table III).

EXPERIMENTAL

All melting points uncorrected. The ^{1}H-NMR spectra were recorded on a Varian 1H, Gemini 200 Spectrometer (National Research Centre, Egypt) and chemical shifts were expressed as δ-value against TMS as internal standard. The IR spectra (KBr) were recorded on a Perkin-Elmer 1430 Spectrometer (Cairo Univesity). The mass spectra were recorded on Finnigan SSQ 7000 Spectrometer. Microanalytical data performed by the Microanalytical Center at the Faculty of Science, Cairo University.

4,5-Diaryl-2,3-dihydro-2-mercaptoimidazoles 2a–e

Compounds **2** were prepared from disubstituted benzoin[13–15] derivatives, by fusion with thiourea at 200°C.[10] Physical data, IR, and ^{1}H-NMR spectra (Tables I and II).



Ar, **a**, *o*-C_5H_4N; **b**, *p*-C_5H_4N; **c**, *p*-C_6H_4F; **d**, *o*-C_6H_4F; **e**, *o*-C_4H_3S Ar_1, **a**, *o*-C_5H_4N; **b**, *p*-C_5H_4N; **c**, *p*-C_6H_4F; **d**, *o*-C_6H_4F; **e**, *o*-C_4H_3S

X = H; 4-Br; 4-Cl; 4-OCH_3; 2-NO_2; 4-NO_2

5,6-Diaryl-2,3-dihydro-2-mercaptoimidazo[2,1-*b*]thiazol-3-ones 3a–d

Method A

A mixture of compounds **2** (0.01 mmol) and chloroacetic acid (0.01 mmol) and 2 g of fused anhyd. Sodium acetate in 15 mL of acetic acid and 7 mL of acetic anhydride was refluxed for 3 h and left to cool. The reaction mixture was poured onto water. The solid obtained was filtered off and crystallized from the proper solvent (Tables I and II).

Method B

Chloroacetyl chloride (0.01 mmol), was added gradually while stirring to a cooled solution of compound **2** (0.01 mmol) in 30 mL pyridine. The reaction mixture was left while cooling for 1 h, then poured into cold water, filtered and crystallised from the proper solvent (Tables I and II).

2-Arylmethylene-5,6-diaryl-2,3-dihydroimidazo[2,1-*b*]-thiazol-3-ones 4a–q

Method A

A mixture of compound **3** (0.01 mmol), aromatic aldehyde (0.01 mmol) in a mixture of glacial acetic acid (20 mL) and acetic anhydride (10 mL) in the presence of anhydrous sodium acetate was refluxed for 2 h. After cooling, water was added and the precipitate was filered off and crystallized from the proper solvent (Tables I and II).

Method B

A mixture of compounds **2** (0.01 mmol), chloroacetic acid (0.01 mmol), aromatic aldehyde and 2 g of anhydrous sodium acetate in a mixture of 20 mL acetic acid/10 mL acetic anhydride was refluxed for 1 h. It was cooled and then poured onto water. The solid obtained was filtered off and crystallized from the proper solvent (Tables I and II).

2-Arylhydrazono-5,6-diaryl-2,3-dihydroimidazo[2,1-*b*]-thiazol-3-ones 5a–r

The aromatic amine (0.01 mmol) was dissolved in 3 mL of conc. HCl acid and 2 mL of water, cooled to –10°C and treated with 0.07 g of sodium nitrile in 3 mL of water. The diazotized amine was added gradually while stirring to cold solution of compound **3** (0.01 mmol) in 15 mL of pyridine. The reaction mixture was cooled for 30 min. The product was filtered off and crystallized from the proper solvent (Tables I and II).

TABLE III Antimicrobial Screening for the Selected Compounds Against Bacteria, Yeast and Fungi

Comp.	*B. subtilis*	*S. aureus*	*E. coli*	*P. mirabilis*	*C. allbicans*	*A. niger*
Control[a]	++++	+++++	+++	+++	++	++
1c	+	+	−	−	+	+
2d	+	+	−	−	+	+
3a	++	++	+	+	++	++
3b	+	+	−	−	+	+
3c	+	+	−	−	+	+
4a	++	++	++	++	++	++
4d	++	++	++	++	++	++
4e	++	++	+	+	++	++
4f	+	+	+	+	++	++
4g	++	++	+	+	+	+
4h	++	++	+	+	++	++
4i	++	++	+	+	+	+
4j	+++	+++	+	+	++	++
4k	++	++	+	+	++	++
4o	+++	+++	+	+	+	+
4p	++	++	+	+	+	+
4q	+	+	+	+	+++	+++
4r	+	+	+	+	+++	+++
5d	++	++	++	++	+++	+++
5f	++	++	+	+	++	++
5g	++	++	+	+	++	++
5h	++	++	+	+	+	+
5i	+++	+++	+	+	+++	+++
5j	++	++	+	+	+++	+++
5k	++	++	++	+++	+++	+++
5l	++	++	+	+	++	++
5n	++	++	+	+	+	+
5o	++	++	++	++	+++	+++
5p	+	+	+	+	+++	+++
5q	+	+	+	+	+++	+++
5r	+++	+++	++	++	+++	+++
6a	++	++	++	++	++	++
6b	+	+	−	−	+	+
6c	++	++	+	+	+	+
7a	++	++	++	++	++	++
7b	+	+	−	−	+	+
7c	+	+	−	−	+	+
7d	++	++	+	+	+++	+++
8b	++	++	++	++	++	++
8c	+	+	−	−	+	+
8d	+	+	−	−	+	+
8e	+	+	−	−	+	+
8f	+	+	+	+	+	+
9a	+++	+++	++	++	+++	+++
9b	+	+	−	−	+	+
10a	+	+	−	−	+	+
10d	++	++	+	+	+++	+++

[a]Control Ampicillin.

5,6-Diaryl-2,3-dihydro-2-methylimidazo[2,1-*b*]-thiazol-3-ones 6a–d

Compounds **6** were prepared by the same method used for compounds **3**, but by using 2-bromopropionic acid instead of chloroacetic acid (Tables I and II).

6,7-Diaryl-1,3-thiazino[3,2-*a*]imidazol-4-ones 7a–d

Compounds **7** were prepared by the same method use for compounds **3** but by using 3-bromopropionic acid instead of chloroacetic acid (Tables I and II).

2(4′,5′-diaryl-2′,3′-dihydroimidazo-2′-yl thio)acetanilide Derivatives 8a–f

Compounds **3** (0.005 mmol) and (0.006 mmol) of the aromatic amine were refluxed in 15 mL of ethanol for 2 h. The reaction mixture was allowed to cool then poured into water. The solid product formed was collected, washed with little ethanol and crystallized from the proper solvent (Tables I and II).

2-(4′,5′-Diaryl-2′,3′-dihydroimidazol-2′-yl)-thiopropionamide Derivatives 9a–c

Compounds **9** were prepared by the same method used for compounds **8** (Tables I and II).

3-(4′,5′-Diaryl-2′,3′-dihydroimidazol-2′-yl)-thiopropionamide 10a–d

Compounds **10** were prepared by the same method used for compounds **8** (Table I and II).

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