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Research Article

Preparation and Biological Activities of Some Heterocyclic Compounds Derivatives from 2-Aminothiazoles

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Abstract

In the current investigation, two series of 2-amino thiazole derivatives were prepared. The first series involved synthesis of (Z)-3-(thiazol-2-ylimino)indolin-2-one (A1) as Schiff base derivatives of 2-amino thiazole and isatin, then synthesis of compounds A5, A6 and A7 as five membered rings (imidazolidins) by using different amino acids, and synthesis of compounds A3 and A4 as seven membered rings (1,3-oxazepine-di-one) by using maleic and phthalic anhydrides respectively. In the second series, 2-amino thiazole was treated with acetyl acetone to form (2E,4E)-N2,N4-di(thiazol-2-yl) pentane-2,4-diimine (A2) as di-Schiff base derivatives, and finally the preparation of imidazolidin (A8) by using 2 mol of tyrosine and preparation of tetrazole derivative (A9) by using 2 mol of sodium azide. The biological study for the above two series indicated that both gram-negative and gram-positive activities were noticed.

Keywords: 2-aminothiazoles; Tetrazole; Imidazolodine; Benzoxazepine; Oxazepin; Isatin; Schiff base

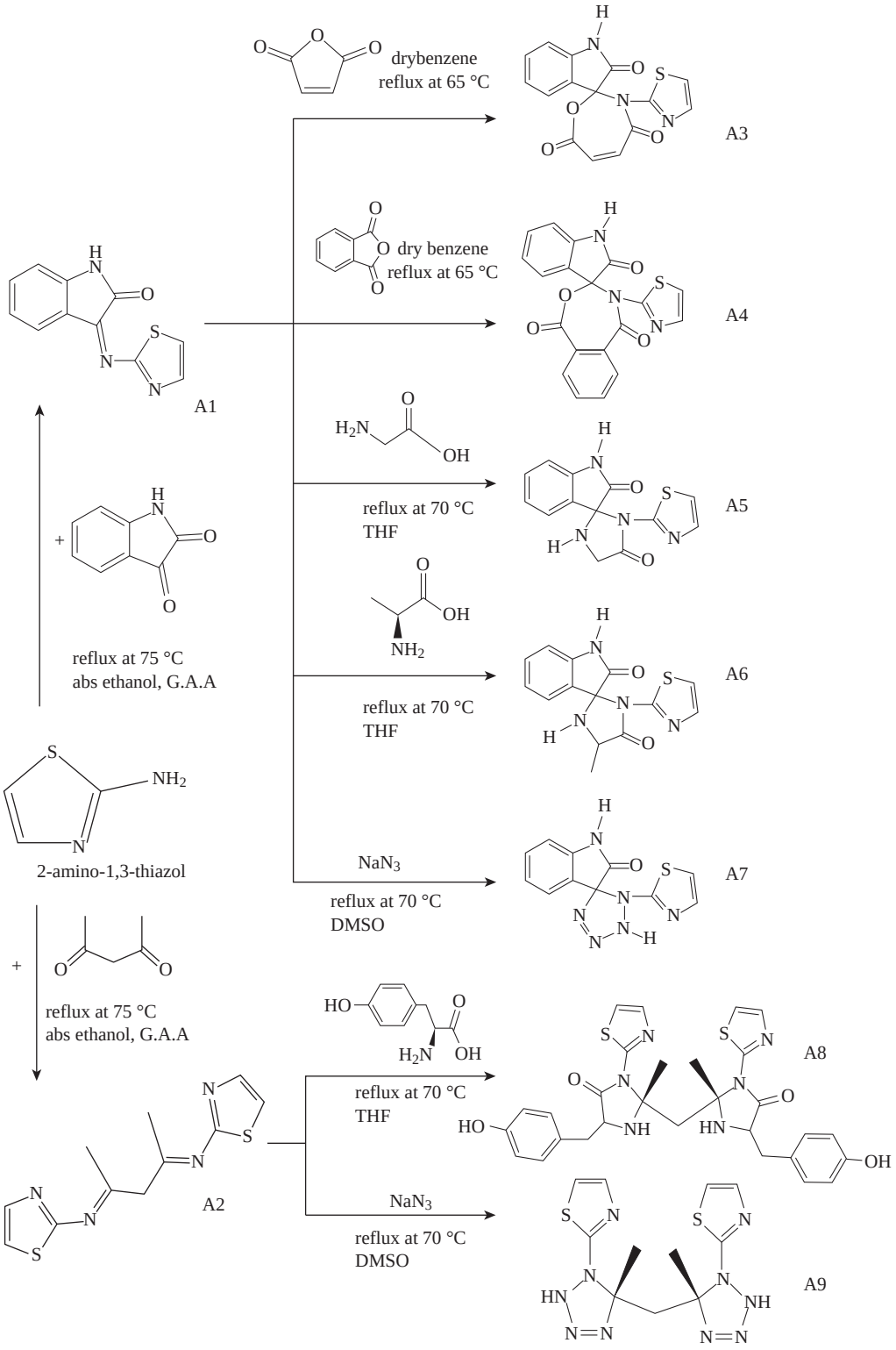
Introduction

Thiazoles are five-membered heterocyclic aromatic compound which was first prepared by A. Hantzsch [1] in 1888. The ability of aminothiazoles to form proton-transfer complexes was developed in order to gain structural information enabling a study of the effect of amino group on 2-aminohistamine derivatives [2, 3]. The synthesis of 2-aminothiazoles derivatives has several problems including low yield, harsh reactions, difficult isolation procedures, use of expensive catalysts [4-6] and so on. Thiazole derivatives are significantly important heterocyclic compounds which exhibit a wide range of biological activities such as fungicidal [7], bactericidal [8], cardiovascular [9], antitumor [10], anti-allergic [11], central nervous system stimulate [12, 13] and antipyretic [14]. Due to the broad range of their applications, 2-aminothiazoles have been used in the synthesis of polymers [15, 16]. In this study, some of the heterocyclic compound derivatives from 2-aminothiazoles were prepared and investigated.

Scheme 1 summarized pathway of the preparation of compounds A1-A9.

Experimental

Physical properties of compounds A1-A9 are listed



Scheme 1 Synthetic pathway of the preparation of compounds A1-A9.

in Table 1.

Synthesis of (Z)-3-(thiazol-2-ylimino)indolin-2-one (A1)

Isatin (6 mmol, 0.6 g) was dissolved in (30 mL) absolute ethanol (abs. EtOH) in a 100 mL round bottom flask; two drops of glacial acetic acid (GAA) were added and stirred; 0.883 g of 6 mmol 2-aminothiazole was added. The reaction mixture was refluxed for 7 h at 70-75 °C. Progress of the reaction was monitored by thin layer chromatography (TLC); the resulting product was washed, dried and recrystallized from ethanol.

Fourier-transform infrared spectroscopy (FTIR/

Table 1 Physical properties for product compounds

Compounds	Molecular formula	Molecular weight (gm/mol)	m.p. (°C)	Colors	Ylide (%)	R_f Methanol: Benzene = 1:4
A1	$C_{11}H_7N_3OS$	239	195	Red	78	0.62
A2	$C_{11}H_{12}N_4S_2$	264	107-108	Dark Brawn	67	0.76
A3	$C_{15}H_9N_3O_4S$	327	175	Red Brown	83	0.42
A4	$C_{19}H_{11}N_3O_4S$	377	165	black Brown	80	0.41
A5	$C_{13}H_{10}N_4O_2S$	166	177-179	Deep Brown	74	0.53
A6	$C_{14}H_{12}N_4O_2S$	300	144	Dark Red	79	0.43
A7	$C_{11}H_8N_6OS$	277	180-181	Brown	77	0.52
A8	$C_{29}H_{30}O_4N_6S_2$	590	165	Brown	79	0.58
A9	$C_{11}H_{14}N_{10}S_2$	350.43	174	Dark Brawn	65	0.44

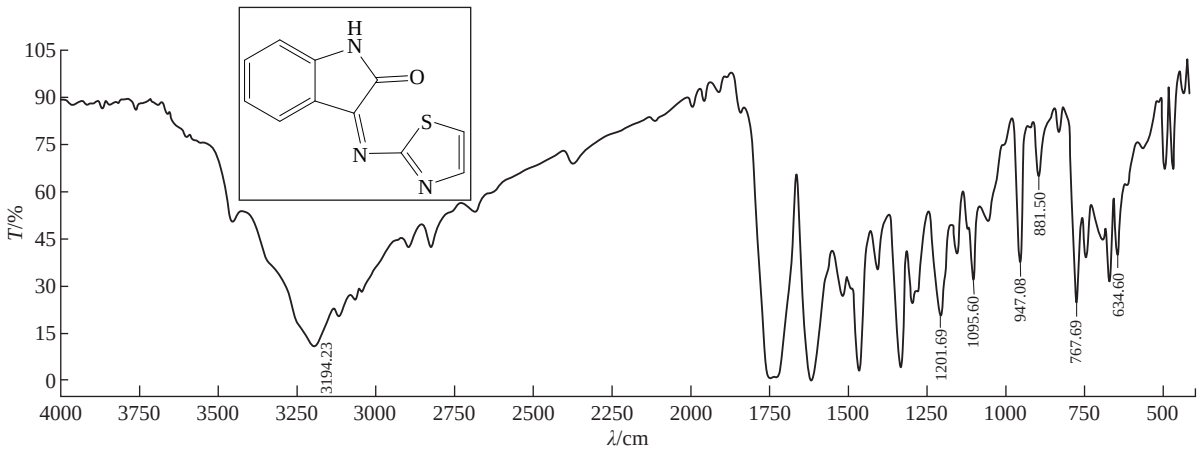


Fig. 1 FTIR spectrum of compound A1.

cm: 1637 (**υ**C=N, imine); 1750 (**υ**C=O, carbonyl of indolone); 1450 and 1500 (**υ**C=C, aromatic and vinyl and **υ**C=N, thiazole, vib. coupling); 3450 (N-H, of indolone); 3135 (C-H, aromatic); and 767 (δo.o.p. C-H, benzene) (Fig. 1; Table 2).

Proton nuclear magnetic resonance (^{1}H-NMR): ɗ/ppm: 7.32-7.951 (s, 4H, phenyl); 7.271 (2H, olifinic of thiazole); and 8,049 (s, H, N-H, indolone) (Fig. 2; Table 3).

Elemental analysis calculated for A1 ($C_{11}H_7N_3OS$): C, 61; H, 3.16; N, 19.5; S, 14.6; Found C, 61.47; H, 3.28; N, 19.7; and S, 15 (Table 4).

Synthesis of (N,N'E,N,N'E)-N,N'-(pentane-2,4-diylidene) bis (thiazol-2-amine) (A2)

0.3 g of 3 mmol acetyl acetone was dissolved in 30 mL abs. EtOH in a 100 mL round bottom flask; three drops of GAA were added and stirred; 0.6 g of 6 mmol 2-aminothiazole was added. The reaction mixture was refluxed for 8 h at 70 °C. Progress of the reaction was monitored by TLC. The resulting product was washed, dried and recrystllizaed from ethanol.

FTIR/cm: 1608 (**υ**C=N, imine); 1589 and 1500 (**υ**C=C, vinyl and **υ**C=N, thiazole, vib. coupling); 3450 (N-H, of indolone); 3182 (C-H, aromatic); 2972 (C-H, methyl); 1442 (C-N, thiazole); and 1041.6 (C-S, thiazole) (Fig. 3; Table 2).

H^1-NMR: ɗ/ppm: 1.408 (s, 6H, methyl); 6,917-7.271 (2H, olifinic of thiazole); and 2.419 (s, CH_2) (Fig. 4; Table 3).

Elemental analysis for A1 ($C_{11}H_7N_3OS$): C, 61; H, 3.16; N, 19.5; S, 14.6; Found C, 61.47; H, 3.28; N, 19.7; and S, 15 (Table 4).

Table 2 FTIR for product compounds A1-A9

Compounds	FTIR / cm						
	Amide υ(C=O)		Imine υ(C=N)	Aromatic υ(C=C)	Aromatic υ(C-H)	Aliphatic υ(C-H)	
A1	1750		1637	1450.09	3135	2900	
	Imine υ(C=N)	Thiazole υ(C=N)	Aliphatic υ(C-H)	Aromatic υ(C-H)	Thiazole υ(C-N)	Thiazole υ(C-S)	
A2	1608.96	1589	2972	3182	1442	1041	
	Ester υ(C=O)	Amide υ(C=O)	Alkene υ(C=C)	Aromatic υ(C-H)	Aliphatic υ(C-H)	Amine υ(NH)	
A3	1735	1680	1618, 1462	3194	2985	3400	
A4	1724	1651	1618	3194	2995	3381	
	Ketone υ(C=O)	Amine υ(NH)	Alkene υ(C=C)	Aliphatic υ(C-H)	Aromatic υ(C-H)	Thiazole υ(C=N)	Hydroxyl υ(OH)
A5	1738, 1653	3194, 3292	1620	2956	3052	1506	--
A6	1725	3194, 3300	1620	2928	3050	1512	--
A8	1735.93	3300	1627	2962	3120.82	1525	3415
	Keton υ(C=O)	Azo υ(N=N)	Imine υ(C=N)	Amine υ(NH)		Aliphatic υ(C-H)	
A7	1745	1508.38	1629	3250, 3487		2856	
A9	--	1560	1592	3363		2956	

Table 3 H^1-NMR for product compounds A1, A2, A3 and A8

Compounds	Molecular formula.	OH hydroxyl	CH aromatic	CH olivine of oxazepine	CH olivine of thiazole	NH indolone	CH_3 methyl	CH_2^+ CH_2-phenyl
A1	$C_{11}H_7N_3OS$	--	7.32-7.951	--	7.271	8.049	--	--
A2	$C_{11}H_{12}N_4S_2$	--	--	--	6,917-7.271	--	1.408	2.419
A3	$C_{15}H_9N_3O_4S$	--	7.584-7.484	7.009-6.577	6.390-6.244	8.094	--	--
A8	$C_{29}H_{30}O_4N_6S_2$	9.014	7.772-7.416	--	7.929	7.947-7.839	2.503	3.329-7.016

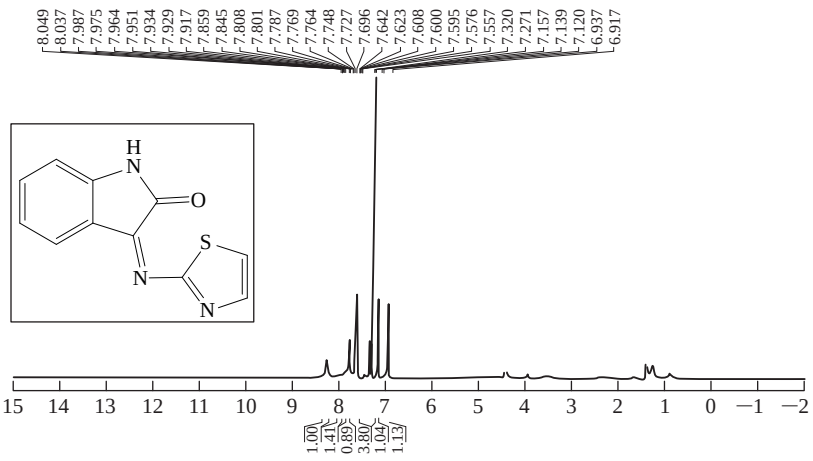


Fig. 2 ^{1}H-NMR spectrum of compound A1.

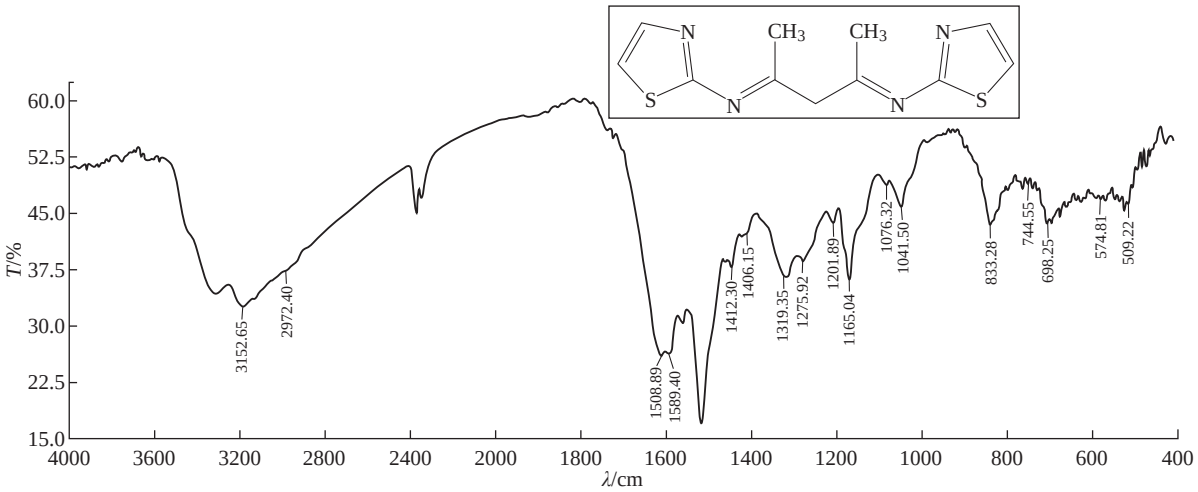


Fig. 3 FTIR spectrum of compound A2.

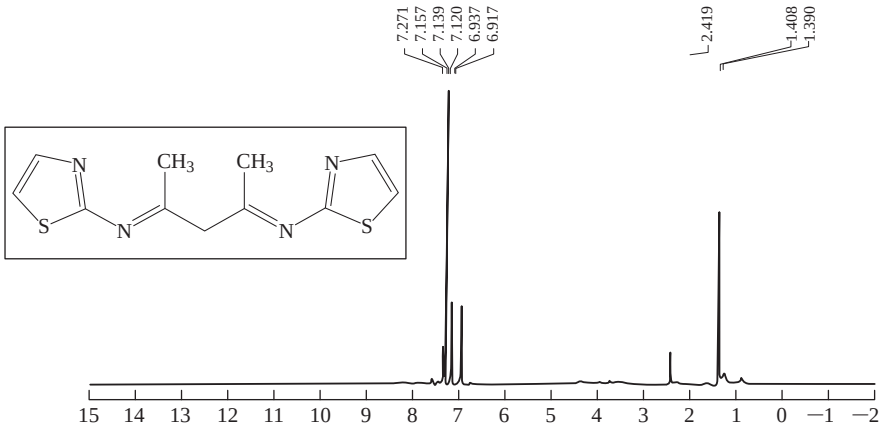


Fig. 4 ^{1}H-NMR spectrum of compound A2.

Table 4 Elemental analysis for product compounds A1, A3, A4, A6 and A8

Compounds	Molecular formula	Calculated/Observed	C%	H%	N%	S%	O%
A1	$C_{11}H_7N_3OS$	Cal.	58.22	3.16	19.00	14.40	6.99
		Obs.	57.47	3.28	18.57	14.00	--
A3	$C_{15}H_9N_3O_4S$	Cal.	54.53	2.50	12.24	9.20	19.55
		Obs.	55.02	2.72	12.80	9.71	--
A4	$C_{19}H_{11}N_3O_4S$	Cal.	60.00	2.86	10.98	8.35	16.96
		Obs.	60.47	2.91	11.14	8.48	--
A6	$C_{14}H_{12}N_4O_2S$	Calc.	55.89	3.40	18.21	10.18	10.66
		Obs.	56.10	3.67	18.65	10.7	--
A8	$C_{29}H_{30}O_4N_6S_2$	Cal.	61.09	4.91	14.84	11.33	10.83
		Obs.	61.45	5.03	15.17	11.52	--

Synthesis of 3'-(thiazol-2-yl)-3'H-spiro[indoline-3,2'-[1,3]oxazepine]-2,4',7'-trione (A3)

A mixture (6 mmol, 0.128 g) of compound A1 and 0.059 g of 6 mmol maleic anhydride were refluxed in 30 mL benzene, at 60 °C for about 20 h, and then recrystllizaed from ethanol.

FTIR/cm: 1680 (υC=O, amide); 1735 (υC=O, carbonyl of indolone and ester); 1618 and 1462 (υC=C, aromatic and vinyl, vib. coupling); 3400 (N-H, of indolone); 3192 (C-H, aromatic); and 750 (δo.o.p. C-H, benzene) (Fig. 5; Table 2).

H^{1}-NMR: ɗ/ppm: 7.584-7.484 (s, 4H, phenyl); 7.009-6.577 (2H, olivinic of oxazepine); 6.390 (2H,

olivinic of thiazole); and 8,094 (s, H, N–H, indolone) (Fig. 6; Table 3).

Elemental analysis for A3 ($C_{15}H_9N_3O_4S$): C, 54.5; H, 2.5; N, 12.24; S, 14.6; Found C, 55.02; H, 2.72; N, 12.80; and S, 9.71 (Table 4).

Synthesis of 4-(thiazol-2-yl)-1H-spiro[benzo[e][1,3]oxazepine-3,3'-indoline]-1,2',5(4H)-trione (A4)

A mixture (6 mmol, 0.128 g) of compound A1 and 0.089 g of 6 mmol phthalic anhydride were refluxed in 30 mL benzene, at 75 for about 24 h, and then recrystllizaed from ethanol.

FTIR/cm: 1727 (υC=O, amide); 1651 (υC=O, carbonyl of indolone and ester); 1618 .8 (υC=C, aromatic and vinyl, vib. coupling); 3381 (N-H, of indolone); 3194 (C-H, aromatic); and 669 (δo.o.p. C-H, benzene) (Fig. 7; Table 2).

Elemental analysis for A4 ($C_{19}H_{11}N_3O_4S$): C, 60.00; H, 2.86; N, 10.98; S, 8.35; Found C, 60.47; H, 2.91; N, 11.14; and S, 8.48 (Table 4).

Synthesis of 1-(thiazol-2-yl)spiro[imidazolidine-2,3'-indoline]-2',5-dione (A5)

A mixture (0.47 mmol , 0.085 g) of compound A1 and 0.03 g of 0.47 mmol glycine (an amino acid) were refluxed in 30 mL tetrahydrofuran (THF), at 70 °C for about 24 h, and then recrystallized from ethanol.

FTIR/cm: 1738 (υC=O, amide); 1506 (υC=N, carbonyl); 1620 (υC=C, aromatic and vinyl, vib. coupling); 3292 and 3194 (2N-H, of indolone and imidazolodine); 3052 (C-H, aromatic); 2956 (C-H, aliphatic); and 656 (δo.o.p. C-H, benzene) (Fig. 8; Table 2).

Synthesis of 4-methyl-1-(thiazol-2-yl)spiro[imidazolidine-2,3'-indoline]-2',5-dione (A6)

A mixture (6 mmol, 0.128 g) of compound A1 and 0.089 g of 6 mmol alanine (an amino acid) were refluxed in 30 mL THF, at 70 °C for about 24 h, and

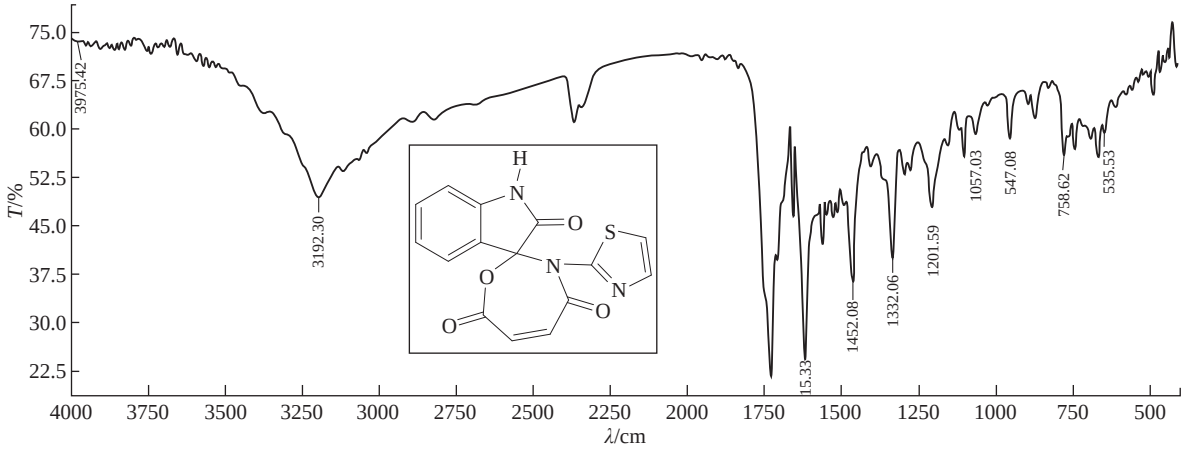


Fig. 5 FTIR spectrum of compound A3.

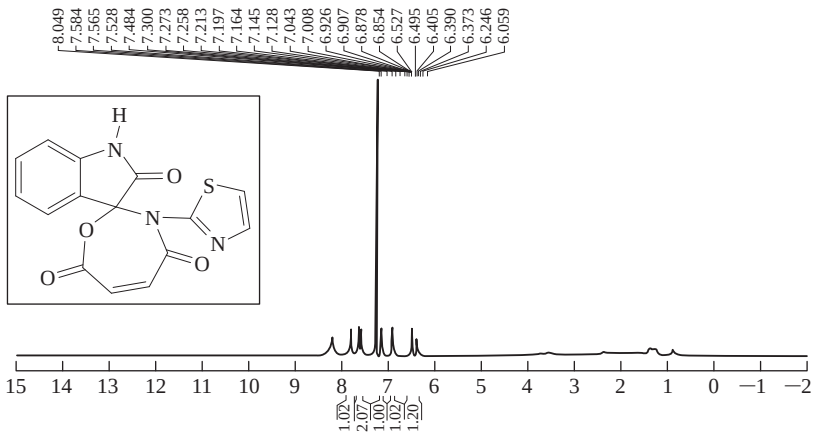


Fig. 6 ^{1}H-NMR spectrum of compound A3.

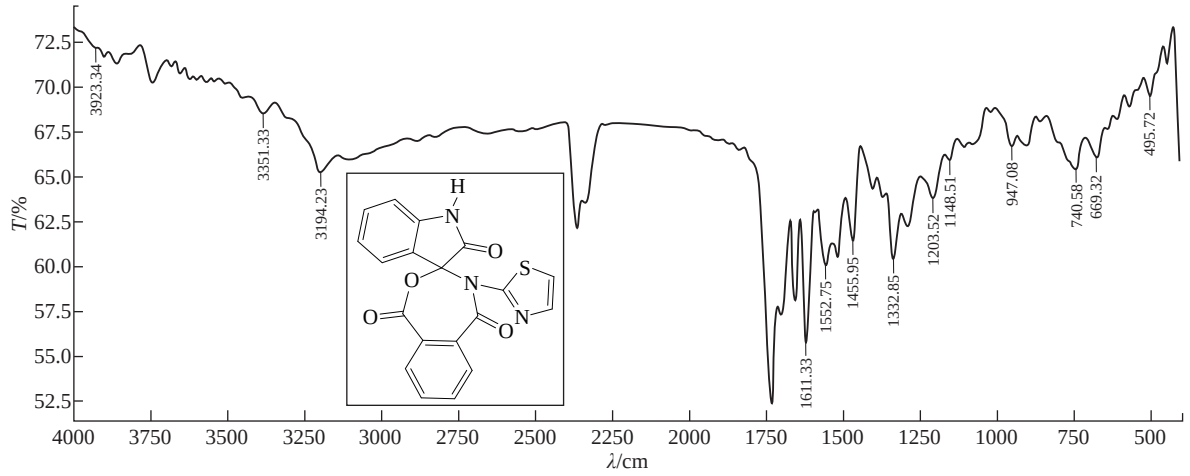


Fig. 7 FTIR Spectrum of compound A4.

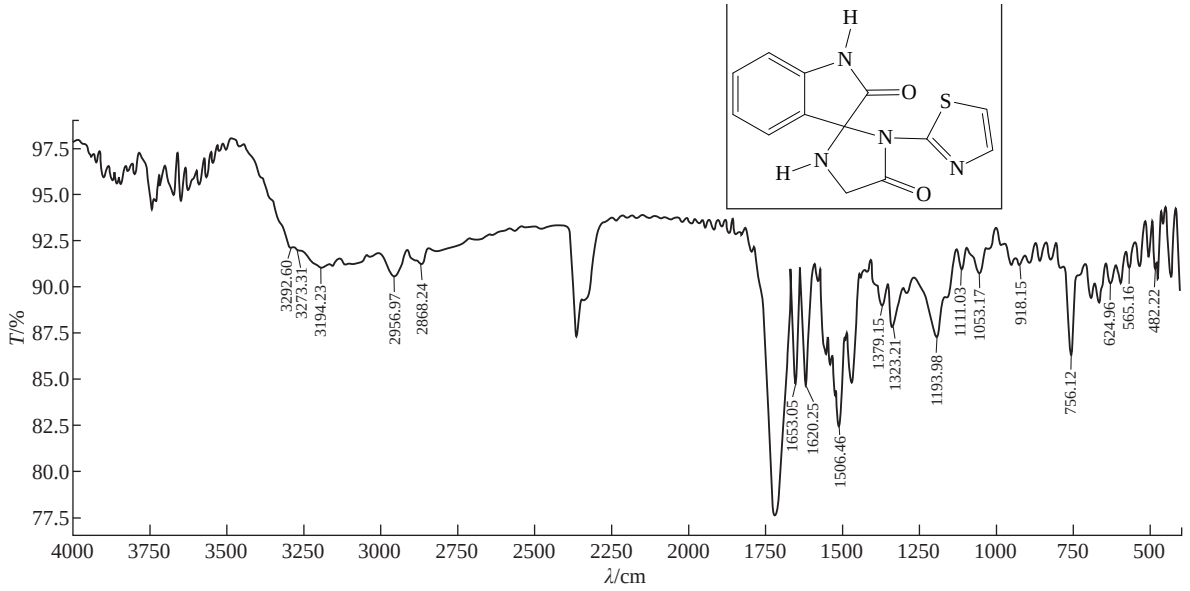


Fig. 8 FTIR spectrum of compound A5.

then recrystallized from ethanol.

FTIR/cm: 1725 (**υ**C=O); 1651 (**υ**C=O, carbonyl of amide); 1620 (**υ**C=C, aromatic and vinyl); 3300 and 3194 (2N-H, of indolone and imidazolodine); 1512 (νC = N, of thiazole); 3050 (C-H, aromatic); 2928 (C-H, alphatic); and 677 (δo.o.p. C-H, benzene) (Fig. 9; Table 2).

Elemental analysis for A6 ($C_{14}H_{12}N_4O_2S$): C, 60.00; H, 2.86; N, 10.98; S, 8.35; Found C, 60.47; H, 2.91; N, 11.14; and S, 8.48.

Synthesis of 1'-(thiazol-2-yl)-1',2'-dihydrospiro [indoline-3,5'-tetrazol]-2-one (A7)

A mixture (4.7 mmol, 0.1 g) of compound A1 and 0.031 g of 4.7 mmol sodium azide were refluxed in 20 mL THF, at 70 °C for about 12 h, and then recrystallized from ethanol.

FTIR/cm: 3487 and 3250 (2N-H, of tetrazole); 2856 (C-H, aliphatic); 1622 (**υ**C=C, of vinyl in thiazole); 1629 (**υ**C=N, of thiazole); 1508 (**υ**N=N, of tetrazole); and 667 (δo.o.p. C-H, benzene) (Fig. 10; Table 2).

Synthesis of (2S,2'R)-2,2'-methylenebis(5-(4-hydroxybenzyl)-2-methyl-3-(thiazol-2-yl) imidazolidin-4-one) (A8)

A mixture (1.5 mmol, 0.396 g) of compound A2 and 0.543 g of 3 mmol tyrosine (an amino acid) were refluxed in 30 mL THF, at 70 °C for about 24 h, and then recrystallized from ethanol.

FTIR/cm: 1608 (**υ**C=N, imine); 1589 and 1500 (**υ**C=C, vinyl and **υ**C=N, thiazole, vib. coupling); 3450 (N-H, indolone); 3182 (C-H, aromatic); 2972 (C-H, methyl); 1442 (C-N thiazole); and 1041.6 (C-S thiazole) (Fig. 11; Table 2).

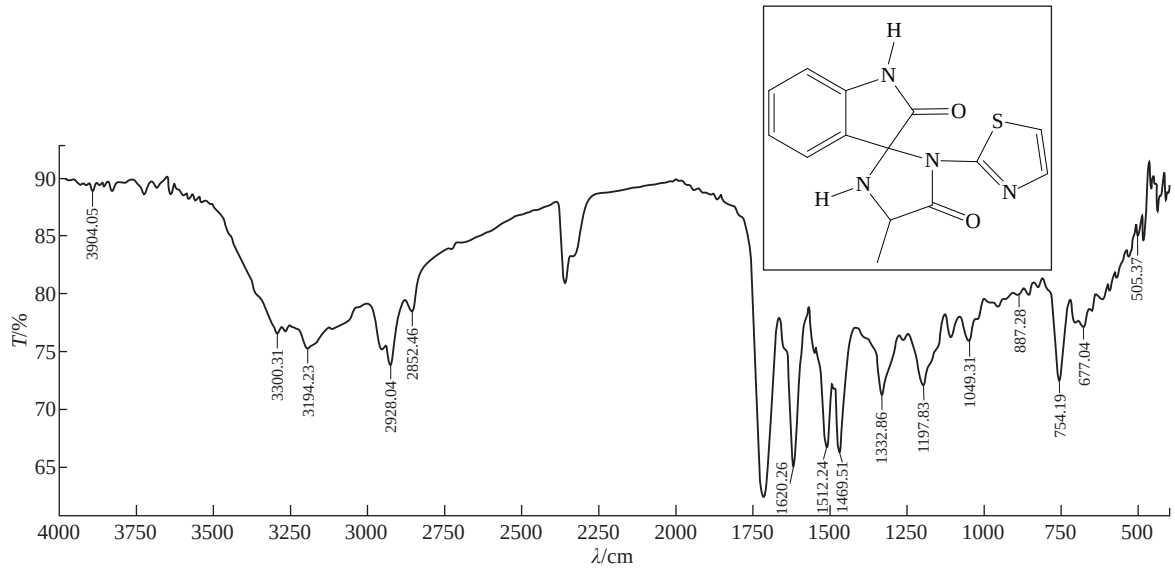


Fig. 9 FTIR spectrum of compound A6.

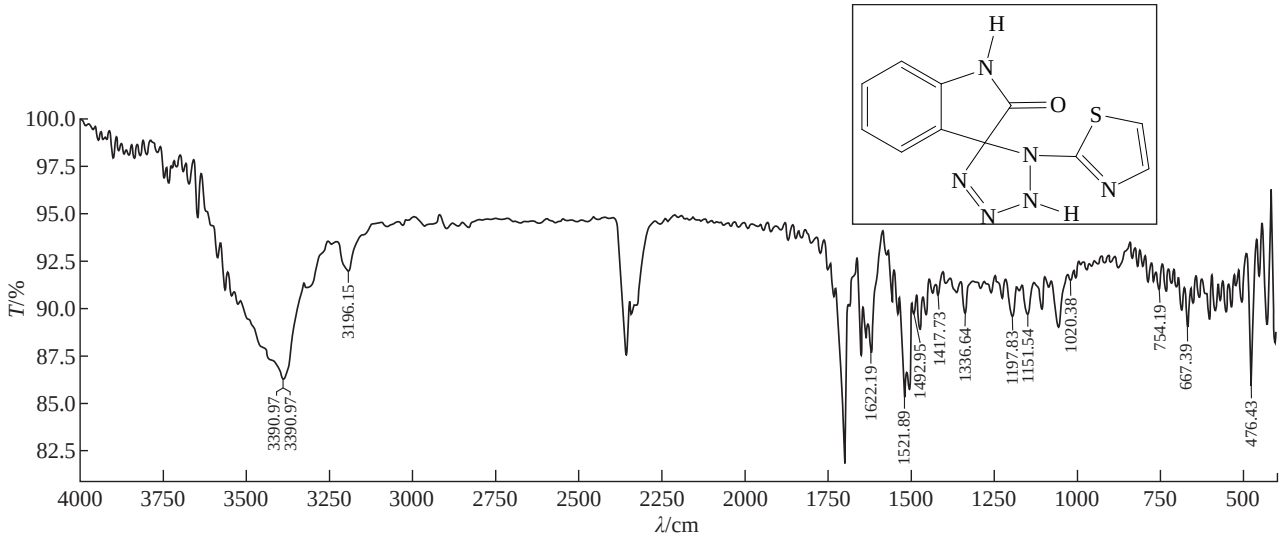


Fig. 10 FTIR spectrum of compound A7.

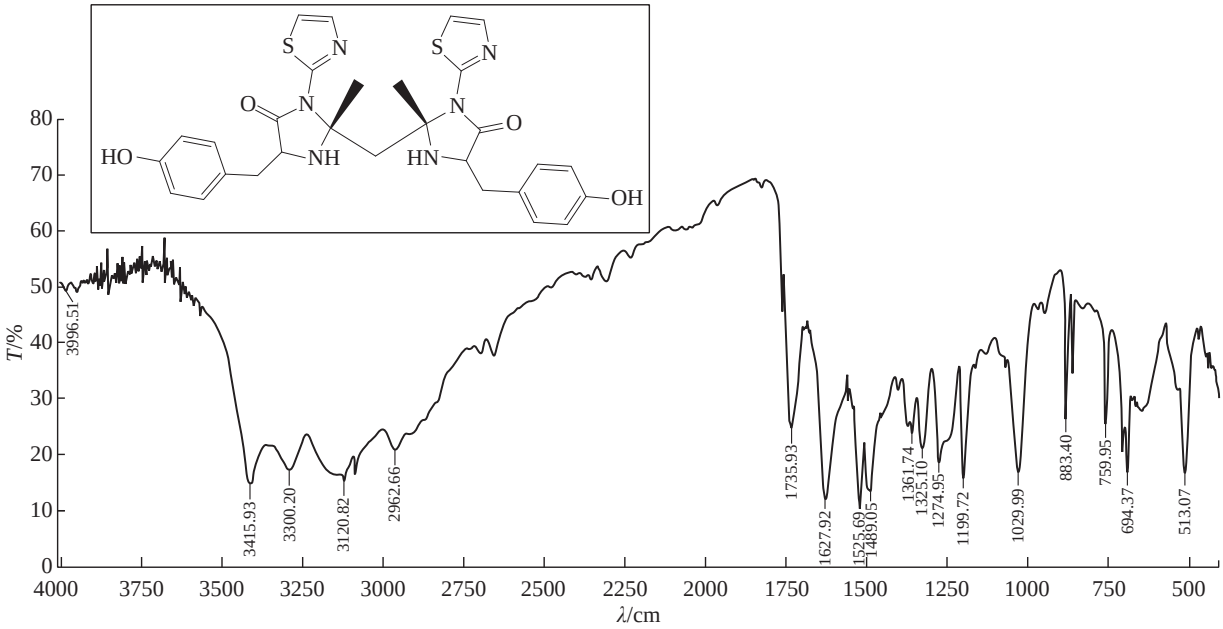


Fig. 11 FTIR spectrum of compound A8.

H^1-NMR: ḍ/ppm): 1.408 (s, 6H, methyl); 6,917-7.271 (2H, olifinic of thiazole); and 2.419 (s, CH_2) (Fig. 12; Table 3).

Elemental analysis for A8 ($C_{29}H_{30}O_4N_6S_2$): C, 61.09; H, 4.91; N, 14.84; S, 11.33; Found C, 61.45; H, 5.03; N, 15.17; and S, 11.52 (Table 4).

Synthesis of ((R)-5-methyl-1-(thiazol-2-yl)-2,5-dihydro-1H-tetrazol-5-yl)((S)-5-methyl-1-(thiazol-2-yl)-2,5-dihydro-1H-tetrazol-5-yl) methane (A9)

A mixture (1.0 mmol , 0.264 g) of compound A2 and 0.13 g of 2.0 mmol sodium azide were refluxed in 30 mL dimethyl sulfoxide (DMSO), at 70 °C for about 14 h, and then recrystallized from ethanol.

FTIR/cm: 3400 and 3363 (N-H, of tetrazole); 2856 (C-H, aliphatic); 1629 (υC=N, of thiazole); and 1592 (υC=N, thiazole) (Fig. 13; Table 2).

Results and Discussion

Biological activity

According to the World Health Organization (WHO), microorganisms are still the main obstacle to the treatment of infectious diseases, and the preparation of therapeutic agents as a highly selective antimicrobials within the limits of specific concentrations [17, 18]. Five types of pathogenic bacteria were used in the current study, two of them were gram-negative and the other three were gram-positive. The sensitivity was calculated using 1000 ppm degree drilling method, and the employed solvent was DMF [19, 20]. The composition of bacterial cell walls in the gram-negative bacteria presented lower thickness and higher lipophilicity as compared with those of the gram-positive bacteria, thus facilitating the passage of compounds which could be dissolved into the fatty compounds and transferred into the cell. These

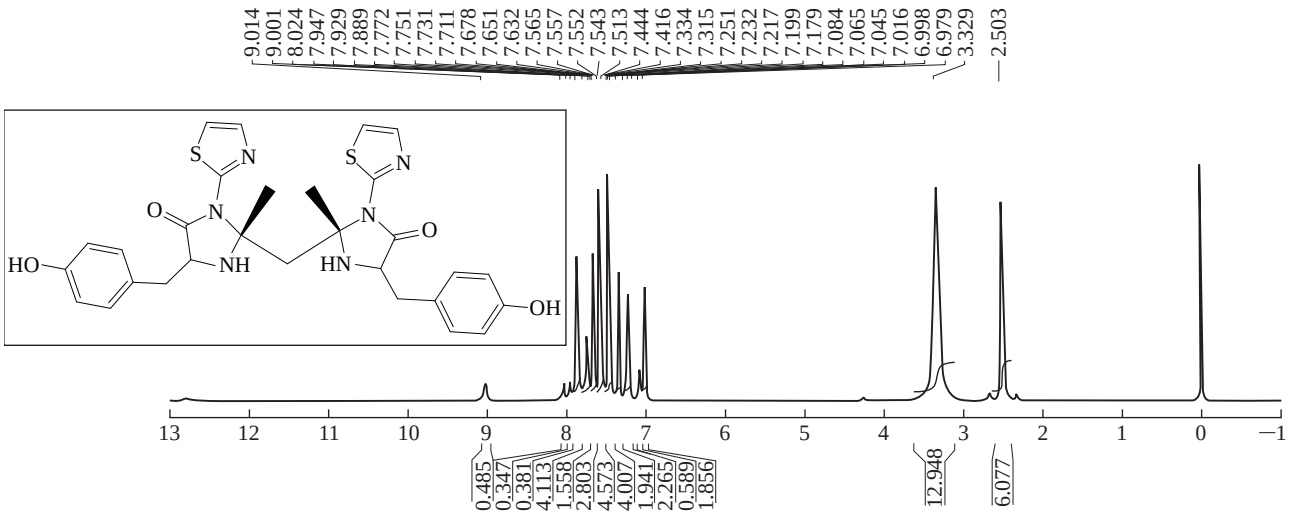


Fig. 12 ^{1}H-NMR spectrum of compound A8.

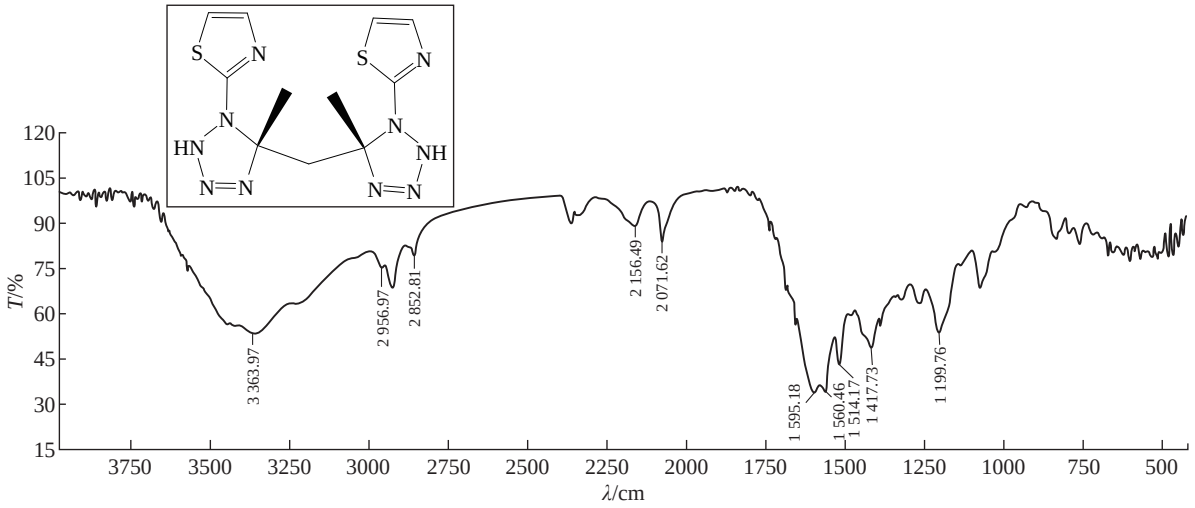


Fig. 13 FTIR spectrum of compound A9.

compounds inhibited the capture. The bacterial growth through the hardiness of the active sites depended on the Overton concept, the phenomenon of plasmolysis, i.e. a retraction of the protoplasm from the cellulose wall of plant cells exposed to impermeable external solutes. (Overton's system explored the relationship between the chemical constitution of solutes, mainly organic, and their plasmolytic effects, with reference to the properties of the putative osmotic barrier) [21-24]. These sites for respiration and protein synthesis inhibit the formation of hydrogen bonds of some interface-active center. Certain cell components or enzymes cause them to stop and change the natural states of cell, leading ultimately to cell death [25]. Table 4 shows the results of biological activity data and the inhibition range in millimeters. Fig. 14 illustrates bacteria wall

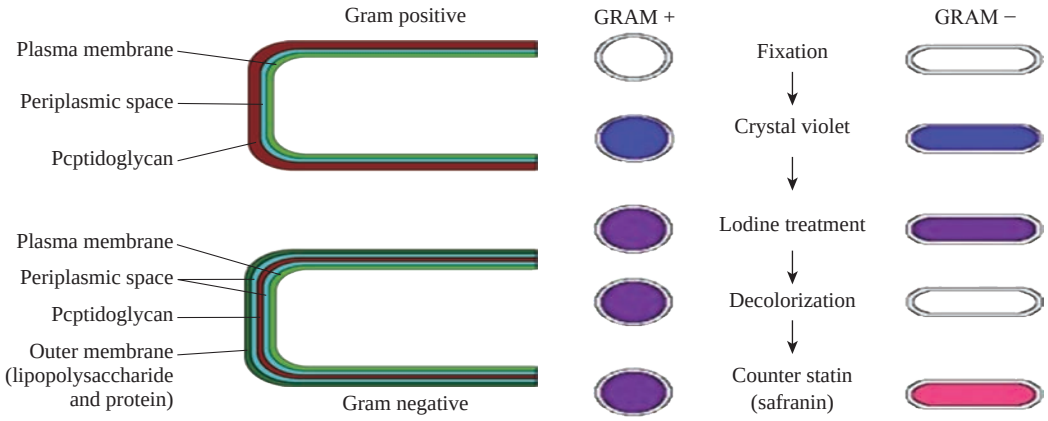


Fig. 14 Bacteria wall and the method of using a gram dyes to differentiate between gram-positive and gram-negative bacteria.

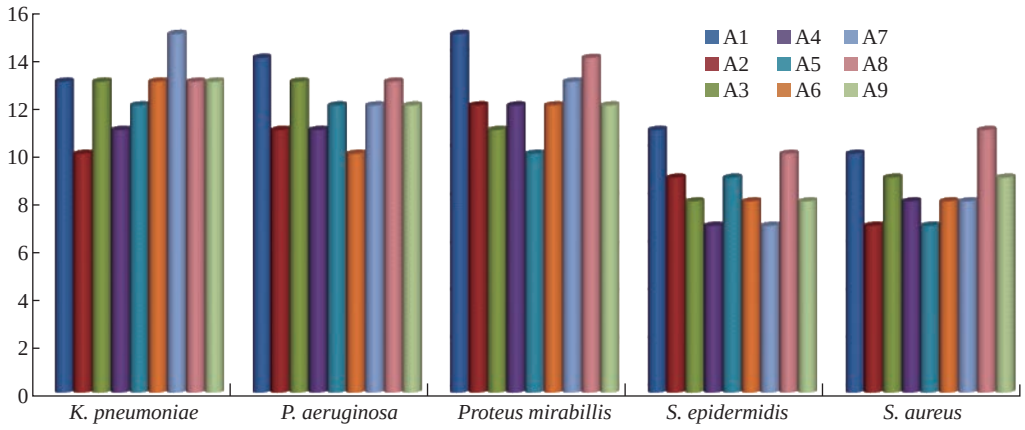


Fig. 15 Statistical representation for antibacterial activity of compounds A1-A9.

Table 5 Biological activity data (zone of inhibition in mm) of the compounds A1-A9

Compounds	Bacteria				
	Gram-negative			Gram-positive	
	K. pneumoniae	*P. aeruginosa*	*P. mirabill*is	*S. epidermidis*	*S. aureus*
A1	13	14	15	11	10
A2	10	11	12	9	7
A3	13	13	11	8	9
A4	11	11	12	7	8
A5	12	12	10	9	7
A6	13	10	12	8	8
A7	15	12	13	7	8
A8	13	13	14	10	11
A9	13	12	12	8	9

and the method of using a gram dye to differentiate between gram-positive and gram-negative bacteria. Statistical representation for antibacterial activity of compounds A1-A9 is shown in Fig. 15 and Table 5.

Conclusions

Two series of 2-amino thiazole derivatives were prepared and characterized in this study. FTIR spectroscopy and NMR technique confirmed the formation of these derivatives. Five types of pathogenic bacteria were used, two of them were gram-negative and the other three were gram-positive. A significant biological activity was observed for the above compounds.

Conflict of Interests

The authors declare that no competing interest exists.

References

[1] M. Sheikhi, New derivatives of (E,E)-azomethines: Design, quantum chemical modeling, spectroscopic (FT-IR, UV/Vis, polarization) studies, synthesis and their applications: Experimental and theoretical investigations. *Journal of Molecular Structure*, 2018, 1152: 368-385.

[2] H. Chen, Degradation of azo dye Orange II under dark ambient conditions by calcium strontium copper perovskite. *Applied Catalysis B: Environmental*, 2018, 221: 691-700.

[3] G. Agnieszka, Synthesis, structure, DNA binding and anticancer activity of mixed ligand ruthenium (II) complex. *Journal of Molecular Structure*, 2018, 1155: 288-296.

[4] S. Shubha, S. Biju, and V. Sadasivan, Synthesis, structure characterization and biological studies on a new aromatic hydrazone, 5-(2-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) hydrazono)-2,2-dimethyl-1,3-dioxane-4,6-dione, and its transition metal complexes. *Journal of Molecular Structure*, 2018, 1156: 201-209.

[5] T. Heraert, Metabolic studies on histidine, histamine, and related imidazoles. *Pharmacological reviews*, 1954, 6: 299-343.

[6] R. Kenchappa, Y. Bodke, Antifungal and anthelmintic activity of novel benzofuran derivatives containing thiazolo benzimidazole nucleus: an in vitro evaluation. *Journal of Chemical Biology*, 2017, 10(1): 11-23.

[7] M.V. Papadopoulou, W.D. Bloomer, and H.S. Rosenzweig, The antitubercular activity of various nitro (triazole/imidazole)-based compounds. *Bioorganic & Medicinal Chemistry*, 2017, 25(21): 6039-6048.

[8] R.T. Iminov, TA.V. verdokhlebov, A.A. Tolmachev, et al., Simple and convenient synthesis of 2, 3, 4, 5-tetrahydro-1, 5-dioxopyrrolo [1, 2-a] quinazoline-3a (1H)-carboxylic acids in multi-gram scale. *Heterocycles*, 2008, 75(7): 1673-1680.

[9] N. Liu, D. Ding, L. Wang, et al., Two novel Mg (II)-based and Zn (II)-based complexes: inhibiting growth of human liver cancer cells. *Brazilian Journal of Medical and Biological Research*, 2018, 51(2): 12-19.

[10] K. Karrouchi, S. Radi, Y. Ramli, et al., Y., Synthesis and Pharmacological Activities of Pyrazole Derivatives: A Review. *Molecules*, 2018, 23(1): 134-142.

[11] P. Palanisamy, S.J. Jenniefer, and P.T. Muthiah, Synthesis, characterization, antimicrobial, anticancer, and antituberculosis activity of some new pyrazole, isoxazole, pyrimidine and benzodiazepine derivatives containing thiochromeno and benzothiepino moieties. *RSC Advances*, 2013, 3(42): 19300-19310.

[12] M.A. Metwally, Y.A. Suleiman, M.A. Gouda, et al., Synthesis, antitumor and antioxidant evaluation of some new antipyrine based azo dyes incorporating pyrazolone moiety. *Int. J. Mod. Org. Chem.*, 2012, 1(3): 213-225.

[13] R.E. Hoover, R.A. Day, Preparation of some imidazole derivatives of 1, 4-naphthoquinone. *Journal of the American Chemical Society*, 1954, 76(16): 4148-4152.

[14] S. Shozo, F. Masamichi, and N. Ryozo, Syntheses of azo dyes containing 4,5-diphenylimidazole and their evaluation as analytical reagents. *Analytica Chimica Acta*, 1976, 81: 131-141.

[15] H. Huheey, E.A. Keiter, and R.L. Keiter, *Inorganic chemistry: principles of structure and reactivity*, 4th ed. Harper Collin College Publishers, 1993: 122-124.

[16] N. Raman, J.D. Raja, Synthesis, structural, characterization and antibacterial studies of some bio sensitive mixed ligand copper (II) complexes. *Indian J. Chem.*, 2007, 46A: 1611-1614.

[17] A.S. Al-Rammahi, A.H. Al-khafagy, Synthesis and characterization of oxazepen and imidazolin derivatives from 2-amino-5-mercapto 1,3,4-thiadiazol and studing of their biological activity. *Word J. pharm. Res.*, 2015, 4(2): 1668-1680.

[18] A.H. Al-Khafagy, Synthesis, characterization and biological study of some new metal-azo chelate complexes. *J. Chem. Pharm. Res.*, 2016, 8(8): 296-302.

[19] A.A. Saeyda, Synthesis and characterization of some metal complexes derived from azo compound of 4, 4′-methylenedianiline and antipyrine: Evaluation of their biological activity on some land snail species. *Journal of Molecular Structure*, 2015, 1099: 567-578.

[20] S. Suhad, Synthesis and spectral studies of heterocyclic azo dye complexes with Y (III) and La (III) ions. *Al-Qadisiyah Journal of Pure Science*, 2017, 19(1): 67-77.

[21] T. Giuseppe, Ligating properties of thionitrosoamines: I. Neutral mononuclear N-thionitrosodimethylamine-palladium (II) and-platinum (II) complexes. *Journal of Organometallic Chemistry*, 1983, 252(3): 381-387.

[22] B. Anupamp, C. Kumari Gyana, Cobalt (II) complexes of ONO donor Schiff bases and N,N donor ligands: Synthesis, characterization, antimicrobial and DNA binding study. *International Journal of Research in Chemistry and Environment*, 2013, 3(2): 172-180.

[23] P.A.L. Sanjib, Synthesis, spectral and electrochemical properties of 1-alkyl-2-(naphthyl-β-azo) imidazole complexes of platinum (II) and the reaction with pyridine bases. Single-crystal X-ray structure of dichloro-[1-ethyl-

2-(naphthyl-β-azo) imidazole] platinum (II). *Polyhedron*, 2000, 19(10): 1263-1270.

[24] M. Kurtoğlu, M. Baydemir, and S. Ayşe, Studies on mononuclear transition metal chelates derived from a novel (E, E)-dioxime: Synthesis, characterization and biological activity. *Journal of Coordination Chemistry*, 2007, 60(6): 655-665.

[25] K. Nakamoto, *Infrared and Raman spectra of inorganic and coordination compounds*, 6th ed. John Wiley & Sons, Inc., 2009: 131-142.