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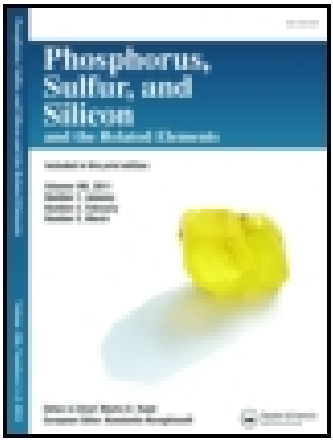

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Synthesis, Characterization, and Biological Activity of Some New Benzoic Acid and Thiazoloacridine Derivatives

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Synthesis, Characterization, and Biological Activity of Some New Benzoic Acid and Thiazoloacridine Derivatives

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*A series of acridine derivatives **5** have been synthesized by cylization of benzoic acid derivatives **4** using $POCl_3$. Compounds **4** were synthesized by Ullamnn Condensation of bromo derivatives **2** and substituted anthranilic acid, respectively, which in turn have been prepared from the Schiff bases of 4-aryl-2-amino thiazole **1** and substituted aldehydes. Biological activities of all the compounds have been studied using gram positive and gram negative bacteria and their anti-fungal activity using fungal species Aspergillus Parasiticus and Sclerotium Rolfsii. All structures of the newly synthesized heterocyclic compounds were established based on elemental analyses, IR, ^1H NMR, ^{13}C NMR, and mass spectra.*

Keywords Arylaminothiazole; biological activity; thiazoloacridine; thiazoloamino benzoic acid

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INTRODUCTION

Thiazoles are familiar group of heterocyclic compounds possessing a wide variety of biological activities and their utility as medicaments is very much established.[1–4] Thiazole nucleus is also integral part of all the available penicillin's, which have revolutionized the therapy of bacterial diseases.[5–10] A detailed literature survey[11,12] reveal that a large number of thiazole derivatives containing other heterocyclic system have been designed synthesized and evaluated for their antimicrobial activity involving several strains of bacteria, fungi and viruses.[13–16] Schiff bases play an important role in many biological processes. Their ready synthesis and numerous biological activities [17–21] contributed greatly to their popularity. Acridine and its derivatives,

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well known as DNA intercalates, have been widely studied from a variety of viewpoints, such as synthesis,[22] physicochemical properties,[23] structural requirement,[24] biological activities,[25] anticancer activity,[26] antimalarial,[27] and anti-inflammatory[28] activities. The above shortcomings have motivated our research, and we considered it worthwhile to synthesize variety of thiazoloacridine derivatives and to study their biological activity.

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RESULTS AND DISCUSSION

4-aryl-2-aminothiazole **1** was prepared by the solid phase reaction of thiourea, 4-bromo acetophenone and iodine. The 4-aryl-2-aminothiazole **1** was reacted with substituted aldehydes to obtain Schiff base derivatives containing thiazole moiety **2**. The compounds **2** were reacted with substituted anthranilic acids **3** to give benzoic acid derivatives **4**. These benzoic acid derivatives **4** were cyclized in the presence of $POCl_3$ to obtain acridine derivatives **5** (Scheme 1). All synthesized compounds were well characterized by their elemental analysis, IR, ^{1}H NMR, ^{13}C NMR spectral studies and continues monitoring of TLC during the reaction.

The IR spectra of compounds 4a–l showed absorption band in the region of 1700–1730 cm^{-1} (>C=O str.). The ^{1}H NMR (DMSO-d_6) spectra of compounds 4a-l exhibited the signal around 8.0–9.0 δ value of (—NH), 11.5–12.0 δ of (—COOH) and the ^{13}C NMR spectra of compounds 4a-l exhibited the peak around δ 160–170 value confirms the assumed structure of benzoic acid derivatives. The IR spectra of compounds 5a–l showed the disappearance of (>C=O str. and —NH str.) band. ^{1}H NMR (DMSO-d_6) of 5a–l exhibited the disappearance of the sharp singlet (around 8.0–9.0 δ value of (—NH) and 11.5–12.0 δ value of (—COOH)) and in ^{13}C NMR disappearance of the signal around δ 160–170 confirms the cyclization of benzoic acid derivatives to acridine derivatives.

BIOLOGICAL ACTIVITY

Antibacterial Activity

Anti-bacterial activities of synthesized compounds were examined *in vitro* by known agar diffusion cup method.[29–32] All the compounds were tested for activity against gram-positive bacteria like *Bacillus cereus,* and *Bacillus subtilis* and gram-negative bacteria *Escherichia coli*. The culture medium was nutrient agar. All compounds were dissolved in N,N'-dimethylformamide (DMF). DMF was used as control. Antibacterial activity was determined by measuring the diameter of the inhibition zone. All the compounds were screened with reference

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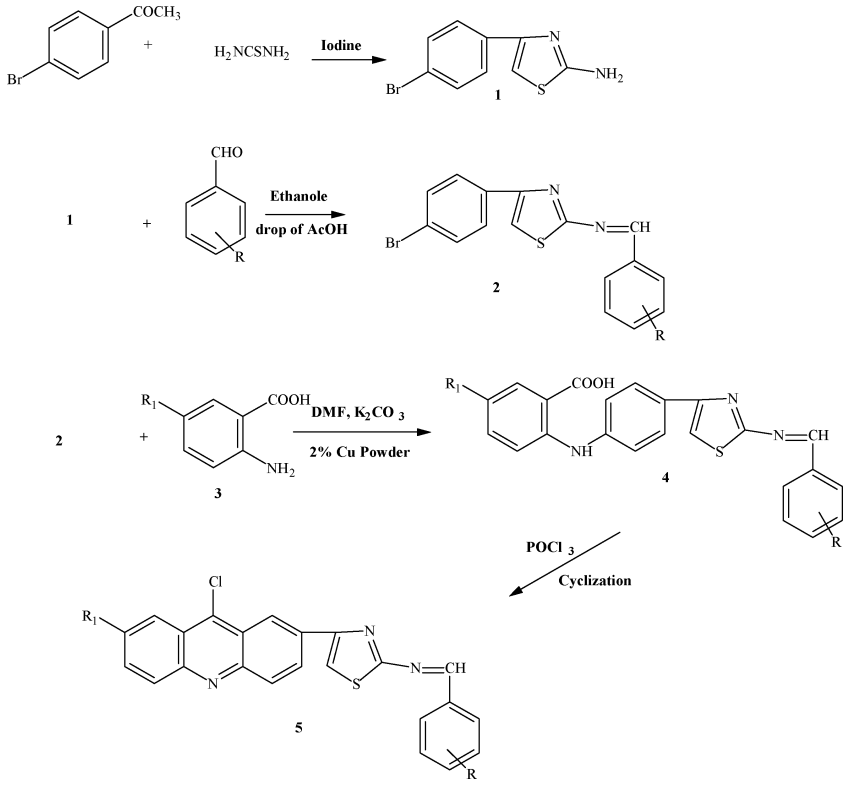

Compd.	R	R_1	Compd.	R	R_1
4a	4-H	H	5a	4-H	H
4b	4-OH	H	5b	4-OH	H
4c	4-OCH_3	H	5c	4-OCH_3	H
4d	3-NO_2	H	5d	3-NO_2	H
4e	4-H	Br	5e	4-H	Br
4f	4-OH	Br	5f	4-OH	Br
4g	4-OCH_3	Br	5g	4-OCH_3	Br
4h	3-NO_2	Br	5h	3-NO_2	Br
4i	4-H	NO_2	5i	4-H	NO_2
4j	4-OH	NO_2	5j	4-OH	NO_2
4k	4-OCH_3	NO_2	5k	4-OCH_3	NO_2
4l	3-NO_2	NO_2	5l	3-NO_2	NO_2

SCHEME 1

TABLE I Antibacterial Screening Results of the Compounds 4a-l and 5a-l

	Inhibition zone (mm)				Inhibition zone (mm)		
Compd.	*B.subtilis*	*B.cereus*	*E.coli*	Compd.	*B.subtilis*	*B.cereus*	*E.coli*
4a	7	7	14	**5a**	9	10	14
4b	10	10	14	**5b**	7	6	11
4c	7	6	14	**5c**	7	7	10
4d	8	9	12	**5d**	6	8	12
4e	7	8	12	**5e**	5	6	11
4f	7	9	11	**5f**	6	7	10
4g	7	8	12	**5g**	7	7	10
4h	6	6	12	**5h**	6	7	10
4i	6	7	11	**5i**	6	6	13
4j	8	14	11	**5j**	7	6	12
4k	7	6	12	**5k**	8	7	12
4l	7	6	13	**5l**	7	8	13
Ampicillin	17	14	15	Ampicillin	17	14	15
Ciprofloxacin	35	29	40	Ciprofloxacin	35	29	40

to standard drugs Ciprofloxacin and Ampicillin. The results are summarized in Table I. It is observed that the compounds having hydroxyl group in 4b and 4j show good activity against gram positive bacteria *B.Subtilus* and *B.Cereus,* as well as gram negative bacteria *Escherichia coli* compared to standard drug Ampicillin, while moderately active against Ciprofloxacin. Compounds 5a, 5d, 5i, and 5j are moderately active against gram-negative bacteria *Escherichia coli* compared to standard drug Ampicillin.

Antifungal Activity

The control DMF, commercial fungicides, and newly synthesized compounds have been tested for their effect on the growth of fungal cultures (*Aspergillus parasiticus* and *Sclerotium rolfsii)* using plate poison technique.[33,34] The results are summarized in Table II. It is observed that the compounds containing dibromo group in 4e, 4f, and 4g show good activity and 5e, 5f, and 5g are moderately active against *Aspergillus parasiticus* and *Sclerotium rolfsii* compared to std. drug Griseofulvin.

EXPERIMENTAL

All melting points were taken in open capillaries and are uncorrected. IR spectra were recorded in KBr on a Nicolet 400D spectrophotometer and only characteristic peaks are reported. ^{1}H NMR and ^{13}C NMR were

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TABLE II Antifungal Screening Results of the Compounds 4a-l and 5a-l

	Inhibition (%)			Inhibition (%)	
Compd.	Aspergillus parasiticus	*Sclerotium rolfsii*	Compd.	*Aspergillus parasiticus*	*Sclerotium rolfsii*
4a	69.94	65.45	**5a**	68.51	63.72
4b	78.20	74.60	**5b**	71.08	66.56
4c	80.62	77.60	**5c**	69.51	64.51
4d	82.76	78.86	**5d**	66.95	63.56
4e	80.91	80.91	**5e**	71.08	67.82
4f	85.47	82.49	**5f**	72.36	71.45
4g	85.61	81.86	**5g**	73.64	69.24
4h	76.78	76.18	**5h**	71.36	66.71
4i	80.91	78.07	**5i**	68.09	63.88
4j	79.34	77.60	**5j**	66.95	64.66
4k	82.47	79.33	**5k**	69.94	66.40
4l	77.92	75.70	**5l**	68.09	66.08
Griseofulvin	100	100	Griseofulvin	100	100

recorded in DMSO-d_6 on a Bruker AC 300F (300 MHz) using TMS as an internal standard. Chemical shifts are reported in parts per million (ppm). Thin layer chromatography (TLC) was performed on silica gel G for TLC (Merck) and spots were visualized by iodine vapors or by irradiation with ultraviolet light.

General Procedure

2-((4-[2-((1E)-1-aza-2-phenylvinyl) 1,3-thiazol-4-yl] phenyl) amino) Benzoic Acid (4a)

A mixture of substituted anthranilic acid (1.37 g, 0.01 mol) in dimethyl formamide (5 ml) and (3.43 g, 0.01 mo)l of compound **2** were refluxed for 12–15 h in the presence of K_2CO_3(1.08 g, 0.01 mole) and 2% cu-powder. The resulting clear solution was cooled, poured onto 100 g of crushed ice, and HCl (25 ml) was added to it, while stirring. The solid product, thus obtained was filtered and washed thoroughly with water, dried, and crystallized from chloroform to give compound **4a**. All the other compounds (4b-l) have been synthesized following the same method.

2-[(1E)-1-aza-2-(phenyl)vinyl]-4-(9-chloroacridin-2-yl)-1, 3-thiazole (5a)

Compound **4a** (3.99 g, 0.01 mol) and $POCl_3$ (30 ml) were taken in flask and the reaction mixture was refluxed for 14–15 h. The excess solvent

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was distilled out, and the resulting clear solution was cooled, poured onto crushed ice, and the solid thus separated was filtered, washed thoroughly with water, dried, and crystallized from dimethyl formamide to give compound **5a**. All the other compounds (5b-l) have been synthesized using the same method.

2-((4-[2-((1E)-1-aza-2-phenylvinyl) 1,3-thiazol-4-yl]phenyl) amino) Benzoic Acid (4a)

M.p. 140–141°C, Yield 59%, anal. calcd. for $C_{23}H_{17}N_3O_2S$: C 69.15, H 4.28, N 10.51; found C 69.01, H 4.13, N 10.40. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.82–7.71 (14H, m, Ar-H), 6.01 (1H,s, N=CH), 12.0 (1H, s, –COOH), 8.01 (1H,s, –NH). IR: ν_{max} (KBr, cm^{-1}) 1720 (C=O stret.) 2800 (O–H stret. in –COOH), 3330 (NH stret.) 1340 (C–N stret.). ^{13}C NMR δ_c (DMSO-d_6) 114.0, 124.4, 125.6, 126.4, 128.1, 129.0, 129.4, 129.6, 130.4, 131.8, 133.8, 134.2, 135.6, 137.4, 138.0, 138.8, 145.6, 146.8, 152.1, 152.7, 166.8.

2-((4-[2-((1E)-1-aza-2-(4-hydroxyphenyl)vinyl]-1,3-thiazol-4-yl) phenyl) amino) Benzoic Acid (4b)

M.p. 159–160°C, Yield 55%, anal. calcd. for $C_{23}H_{17}N_3O_3S$: C 66.49, H 4.12, N 10.11; found C 66.31, H 4.03, N 10.25. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.81–7.72 (13H,m, Ar-H), 6.03 (1H,s, N=CH), 12.01 (1H,s, –COOH), 8.02 (1H,s, –NH) 4.6 (1H, s, –OH). IR: ν_{max} (KBr, cm^{-1}) 1725 (C=O stret.) 2809 (O–H stret. in –COOH), 3331 (NH stret.) 1341 (C–N stret.) 3127 (O–H stret.). ^{13}C NMR δ_c (DMSO-d_6) 114.1, 124.2, 125.5, 126.3, 128.0, 129.2, 129.6, 129.8, 130.5, 131.6, 133.7, 134.1, 135.5, 137.3, 138.2, 138.5, 145.6, 146.4, 152.2, 152.6, 166.6.

2-((4-[2-((1E)-1-aza-2-(4-methoxyphenyl) vinyl]-1,3-thiazol-4-yl) phenyl) amino) Benzoic Acid (4c)

M.p. 147–148°C, Yield 53%, anal. calcd. for $C_{24}H_{19}N_3O_3S$: C 67.11, H 4.45, N 9.78; found C 67.01, H 4.33, N 9.90. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.80–7.73 (13H,m, Ar-H), 6.04 (1H,s, N=CH), 12.03 (1H,s, –COOH), 8.04 (1H,s, –NH) 3.75 (3H, s, –OCH_3). IR: ν_{max} (KBr, cm^{-1}) 1721 (C=O stret.) 2804 (O–H stret. in –COOH), 3334 (NH stret.) 1345 (C–N stret.). ^{13}C NMR δ_c (DMSO-d_6) 56.8, 114.2, 124.3, 125.5, 126.1, 128.3, 129.6, 129.8, 129.9, 130.5, 131.6, 133.6, 134.4, 135.8, 137.3, 138.2, 138.9, 145.5, 146.2, 152.3, 152.4, 166.6.

2-((4-[2-((1E)-1-aza-2-(3-nitrophenyl)vinyl]-1,3-thiazol-4-yl) phenyl) amino) Benzoic Acid (4d)

M.p. 151–52°C, Yield 47%, anal. calcd. for $C_{23}H_{16}N_4O_4S$: C 62.15, H 3.62, N 12.60; found C 62.01, H 3.53, N 12.46. ^{1}H NMR δ_H (DMSO-d_6,

300 MHz) 6.72–7.75 (13H,m, Ar-H), 6.05 (1H,s, N=CH), 11.90 (1H,s, –COOH), 7.91 (1H,s, –NH). IR: ν_{max} (KBr, cm^{-1}) 1723 (C=O stret.) 2809 (O–H stret. in –COOH), 3338 (NH stret.) 1354 and 1536 (NO_2 stret.), 1346 (C–N stret.). ^{13}C NMRδ_c(DMSOd_6)114.8, 124.1, 125.9, 126.8, 128.4, 128.6, 129.5, 129.8, 129.9, 130.2, 131.5, 132.4, 133.3, 134.4, 135.3, 137.2, 138.4, 138.3, 145.1, 146.4, 152.7, 152.5, 166.3.

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2-((4-[2-((1E)-1-aza-2-phenylvinyl) 1,3-thiazol-4-yl]phenyl) amino)-5-bromo Benzoic Acid (4e)

M.p. 145–146°C, Yield 49%, anal. calcd. for $C_{23}H_{16}BrN_3O_3S$: C 57.74, H 3.37, N 8.78; found C 57.61, H 3.23, N 8.65 ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.85–7.79 (13H,m, Ar–H), 6.03 (1H,s, N=CH), 12.06 (1H,s, –COOH), 8.05 (1H,s, –NH). IR: ν_{max} (KBr, cm^{-1}) 1720 (C=O stret.) 2800 (O–H stret. in –COOH), 559 (C–Br stret.) 3330 (NH stret.) 1340 (C–N stret.). ^{13}C NMR δ_c (DMSOd_6)114.5, 124.6, 125.7, 126.2, 128.2, 129.6, 129.1, 129.4, 130.3, 131.4, 133.5, 134.1, 135.5, 137.5, 138.3, 138.7, 145.3, 146.2, 152.4, 152.3, 166.4.

2-((4-[2-((1E)-1-aza-2-(4-hydroxyphenyl)vinyl]-1,3-thiazol-4-yl) phenyl)amino)-5-bromo Benzoic Acid (4f)

M.p. 168–169°C, Yield 56%, anal. calcd. for $C_{23}H_{16}BrN_3O_3S$: C 55.88, H 3.26, N 8.50; found C 55.76, H 3.16, N 8.45. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.82–7.71 (12H,m, Ar–H), 6.05 (1H,s, N=CH), 12.06 (1H,s, –COOH), 8.04 (1H,s, –NH) 4.5 (1H, s, –OH). IR: ν_{max} (KBr, cm^{-1}) 1729 (C=O stret.) 2811 (O–H stret. in –COOH), 3336 (NH stret.) 552 (C–Br stret.) 1349 (C–N stret.) 3126(OHstret.). ^{13}C NMRδ_c(DMSOd_6)114.2, 124.3, 125.6, 126.4, 128.1, 129.3, 129.5, 129.9, 130.6, 131.2, 133.6, 134.2, 135.4, 137.6, 138.5, 138.1, 145.5, 146.7, 152.4, 152.5, 166.7.

2-((4-[2-((1E)-1-aza-2-(4-methoxyphenyl)vinyl]-1, 3-thiazol-4-yl)phenyl)amino)-5-bromo Benzoic Acid (4g)

M.p. 157–158°C, Yield 53%, anal. Calcd. for $C_{24}H_{18}BrN_3O_3S$: C 56.70, H 3.56, N 8.26; found C 56.61, H 3.43, N 8.35. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.88–7.79 (12H,m, Ar–H), 6.02 (1H,s, N=CH), 12.05 (1H,s, –COOH), 8.06 (1H,s, –NH) 3.72 (3H, s, –OCH_3). IR: ν_{max} (KBr, cm^{-1}) 1720 (C=O stret.) 2806 (O–H stret. In –COOH), 3333 (NH stret.), 554 (C–Br stret.), 1349 (C–N stret.). ^{13}C NMRδ_c(DMSOd_6)56.4, 114.1, 124.5, 125.4, 126.0, 128.3, 129.4, 129.6, 130.2, 131.3, 133.4, 134.6, 135.4, 137.7, 138.6, 138.4, 145.6, 146.3, 152.4, 152.6, 166.5.

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2-((4-[2-((1E)-1-aza-2-(3-nitrophenyl)vinyl]-1,3-thiazol-4-yl) phenyl)amino)-5-bormo Benzoic Acid (4h)

M.p. 171–172°C, Yield 45%, anal. calcd. for $C_{23}H_{15}BrN_4O_4S$: C 52.78, H 2.88, N 10.70; found C 52.85, H 2.99, N 10.82. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.71–7.78 (12H,m, Ar-H), 6.02 (1H,s, N=CH), 11.80 (1H,s, –COOH), 7.90 (1H,s, –NH). IR: ν_{max} (KBr, cm^{-1}) 1724 (C=O stret.) 2806 (O–H stret. in –COOH), 3335 (NH stret.), 555 (C–Br stret.), 1355 and 1532 (NO_2 stret.), 1347 (C–N stret.). ^{13}C NMR δ_c (DMSO-d_6) 114.2,124.0,125.6, 126.2, 128.2, 128.5, 129.3, 129.5, 129.7, 130.9, 131.8, 132.6, 133.5, 134.2, 135.4, 137.5, 138.3, 138.7, 145.5, 146.6, 152.2, 152.6, 166.4.

2-((4-[2-((1E)-1-aza-2-(phenyl)vinyl)1,3-thiazol-4-yl] phenyl) amino)-5-nitrobenzoic Acid (4i)

M.p. 138–139°C, Yield 47%, anal. calcd. for $C_{23}H_{16}N_4O_4S$: C 62.15, H 3.62, N 12.60; found C 62.01, H 3.53, N 12.44. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.86–7.74 (12H,m, Ar-H), 6.07 (1H,s, N=CH), 12.03 (1H,s, –COOH), 8.04 (1H,s, –NH). IR: ν_{max} (KBr, cm^{-1}) 1721 (C=O stret.) 2802 (O–H stret. in –COOH), 3339 (NH stret.), 1351 and 1532 (NO_2 stret.), 1339 (C–N stret.). ^{13}C NMR δ_c (DMSO-d_6) 114.9, 124.1, 125.5, 126.1, 128.6, 129.1, 129.5, 129.7, 130.3, 131.9, 133.7, 134.1, 135.5, 137.3, 138.2, 138.4, 145.3, 146.4, 152.5, 152.4, 166.1.

2-((4-[2-((1E)-1-aza-2-(4-hydroxyphenyl)vinyl]-1,3-thiazol-4-yl) phenyl) amino)-5-nitrobenzoic Acid (4j)

M.p. 155–156°C, Yield 51%, anal. calcd. for $C_{23}H_{16}N_4O_5S$: C 59.99, H 3.50, N 12.16; found C 59.86, H 3.62, N 12.25. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.88–7.77 (12H,m, Ar–H), 6.07 (1H,s, N=CH), 12.09 (1H,s, –COOH), 8.05 (1H,s, –NH) 4.7 (1H, s, –OH). IR: ν_{max} (KBr, cm^{-1}) 1729 (C=O stret.) 2802 (O–H stret. in –COOH), 1352 and 1533 (NO_2 stret.), 3339 (NH stret.) 1344 (C–N stret.), 3126 (O–H stret.). ^{13}C NMR δ_c (DMSO-d_6) 114.5, 124.5, 125.4, 126.6, 128.1, 129.1, 129.5, 129.7, 130.4, 131.5, 133.6, 134.0, 135.6, 137.4, 138.1, 138.4, 145.5, 146.3, 152.1, 152.4, 166.1.

2-((4-[2-((1E)-1-aza-2-(4-methoxyphenyl)vinyl]-1,3-thiazol-4-yl) phenyl) amino)-5-nitrobenzoic acid (4k)

M.p. 162–163°C, Yield 55%, anal. calcd. for $C_{24}H_{18}N_4O_5S$: C 60.75, H 3.82, N11.80; found C 60.86, H 3.73, N 11.91. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.85–7.72 (12H,m, Ar–H), 6.02 (1H,s, N=CH), 12.01 (1H,s, –COOH), 8.03 (1H,s, –NH) 3.79 (3H, s, –OCH_3). IR: ν_{max} (KBr, cm^{-1}) 1722 (C=O stret.) 2804 (O–H stret. in –COOH), 1357 and 1538 (NO_2

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stret.), 3336 (NH stret.) 1349 (C—N stret.). ^{13}C NMR δ_c (DMSO-d_6) 56.5, 114.1, 124.2, 125.6, 126.2, 128.7, 129.8, 129.9, 130.4, 130.6, 131.7, 133.4, 134.6, 135.9, 137.7, 138.5, 138.4, 145.6, 146.4, 152.6, 152.7, 166.3.

2-((4-[2-((1E)-1-aza-2-(3-nitrophenyl)vinyl]-1,3-thiazol-4-yl) phenyl) amino)-5-nitrobenzoic Acid (4l)

M.p. 157–158°C, Yield 47%, anal. calcd. for $C_{23}H_{15}N_5O_6S$: C 56.44, H 3.08, N 14.30; found C 56.33, H 3.03, N 14.46. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.70–7.71 (12H,m, Ar—H), 6.07 (1H,s, N=CH), 11.80 (1H,s, —COOH), 7.95 (1H,s, —NH). IR: ν_{max} (KBr, cm^{-1}) 1730 (C=O stret.) 2811 (O—H stret. in —COOH), 3340 (NH stret.) 1359 and 1540 (NO_2 stret.), 1344 (C—N stret.). ^{13}C NMR δ_c (DMSO-d_6) 114.2, 124.2, 125.1, 126.2, 128.5, 128.2, 129.1, 129.3, 129.4, 130.4, 131.1, 132.6, 133.1, 134.6, 135.4, 137.6, 138.3, 138.1, 145.2, 146.5, 152.8, 152.6, 166.4.

2-[(1E)-1-aza-2-(phenyl)vinyl]-4-(9-chloroacridin-2-yl)-1, 3-thiazole (5a)

M.p. 181–182°C, Yield 43%, anal. calcd. for $C_{23}H_{14}ClN_3S$: C 69.05, H 3.52, N 10.50; found C 69.16, H 3.63, N 10.40. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.82–7.65 (12H,m, Ar—H), 6.0 (1H,s, N=CH), IR: ν_{max} (KBr, cm^{-1}) 1535 and 1609 (C=C stret.) 1340 (C—N stret.), 790 (C—Cl stret.) 710 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 123.6, 124.0, 124.6, 125.0, 125.6, 126.3, 127.6, 128.7, 129.3, 130.0, 130.8, 131.2, 132.7, 133.8, 134.9, 138.0, 138.7, 139.3, 139.9, 140.6, 141.2.

2-[(1E)-1-aza-2-(4-hydroxyphenyl)vinyl]-4-(9-chloroacridin-2-yl)-1,3-thiazole (5b)

M.p. 193–194°C, Yield 39%, anal. calcd. for $C_{23}H_{14}ClN_3OS$: C 66.42, H 3.39, N 10.10; found C 66.31, H 3.33, N 10.15. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.81–7.73 (12H,m, Ar—H), 6.02 (1H,s, N=CH), 4.72 (1H, s, —OH). IR: ν_{max} (KBr, cm^{-1}) 1533 and 1612 (C=C stret.) 1341 (C—N stret.) 3127 (O—H stret.) 795 (C—Cl stret.) 712 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 123.5, 124.1, 124.5, 125.1, 125.4, 126.2, 127.7, 128.8, 129.4, 130.2, 130.9, 131.3, 132.8, 133.9, 134.5, 138.2, 138.4, 139.2, 139.4, 140.4, 141.3.

2-[(1E)-1-aza-2-(4-methoxyphenyl)vinyl]-4-(9-chloroacridin-2-yl)-1,3-thiazole (5c)

M.p. 179–180°C, Yield 41%, anal. calcd. for $C_{24}H_{16}ClN_3OS$: C 67.05, H 3.75, N 9.77; found C 67.11, H 3.83, N 9.90. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.81–7.77 (12H,m, Ar—H), 6.05 (1H,s, stret.), 3128 (O—H stret.), 791 (C—Cl stret.), 716 (C—S stret.), 559 (C-Br stret.). ^{13}C NMR δ_c

56.3, 123.6,124.2, 124.6, 125.3, 125.6, 126.1, 127.5, 128.7, 129.3, 130.1, 130.4, 131.5, 132.7, 133.6, 134.2, 138.4, 138.6, 139.4, 139.3, 140.1, 141.2.

2-[(1E)-1-aza-2-(3-nitrophenyl)vinyl]-4-(9-chloroacridin-2-yl)-1, 3-thiazole (5d)

M.p. 205–206°C, Yield 37%, anal. calcd. for $C_{23}H_{13}ClN_4O_2S$: C 62.09, H 2.94, N 12.59; found C 62.01, H 2.43, N 12.46. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.70–7.70 (12H, m, Ar—H), 6.06 (1H,s, N=CH). IR: ν_{max} (KBr, cm^{-1}) 1539 and 1616 (C=C stret.), 1354 and 1536 (NO_2 stret.), 1346 (C—N stret.) 793 (C—Cl stret.) 706 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 123.2, 124.3, 124.4, 125.7, 125.8, 126.2, 127.4, 128.2, 129.7, 130.3, 130.1, 131.8, 132.4, 133.3, 134.1, 138.4, 138.5, 139.7, 139.2, 140.6, 141.1.

2-[(1E)-1-aza-2-(phenyl)vinyl]-4-(7-bromo-9-chloroacridin-2-yl)-1,3-thiazole (5e)

M.p. 214–215°C, Yield 44%, anal. calcd. for $C_{23}H_{13}BrClN_3S$: C 57.69, H 2.73, N 8.77; found C 57.56, H 2.63, N 8.60. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.83–7.69 (11H, m, Ar—H), 6.07 (1H,s, N=CH), IR: ν_{max} (KBr, cm^{-1}) 1530 and 1611 (C=C stret.) 1341 (C—N stret.), 796 (C—Cl stret.), 555 (C—Br stret.), 712 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 123.2, 124.2, 124.5, 125.6, 125.8, 126.4, 127.4, 128.9, 129.6, 130.4, 130.1, 131.3, 132.4, 133.7, 134.5, 138.6, 138.1, 139.4, 139.6, 140.4, 141.1.

2-[(1E)-1-aza-2-(4-hydroxyphenyl)vinyl]-4-(7-bromo-9-chloroacridin-2-yl)-1, 3-thiazole (5f)

M.p. 187–188°C, Yield 41%, anal. calcd. for $C_{23}H_{13}BrClN_3OS$: C 55.83, H 2.64, N 8.49; found C 55.71, H 2.53, N 8.35. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.85–7.79 (11H,m, Ar—H), 6.07 (1H,s, N=CH), 4.78 (1H, s, —OH). IR: ν_{max} (KBr, cm^{-1}) 1534 and 1611 (C=C stret.), 1344 (C—N stret.), 3128 (O—H stret.), 791 (C—Cl stret.), 716 (C—S stret.), 559 (C—Br stret.). ^{13}C NMR δ_c (DMSO-d_6) 123.1, 124.2, 124.3, 125.7, 125.8, 126.9, 127.4, 128.5, 129.6, 130.8, 130.2, 131.4, 132.6, 133.2, 134.2, 138.1, 138.4, 139.7, 139.9, 140.8, 141.8.

2-[(1E)-1-aza-2-(4-methoxyphenyl)vinyl]-4-(7-bromo-9-chloroacridin-2-yl)-1, 3-thiazole (5g)

M.p. 197–198°C, Yield 43%, anal. calcd. for $C_{24}H_{15}BrClN_3OS$: C 56.55, H 2.97, N 8.25; found C 56.41, H 3.13, N 8.10. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.80–7.70 (11H,m, Ar—H), 6.02 (1H,s, N=CH), 3.78 (3H, s, —OCH_3). IR: ν_{max} (KBr, cm^{-1}) 1534 and 1619 (C=C stret.), 1355 (C—N stret.) 785 (C—Cl stret.), 562 (C—Br stret.), 715 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 56.4, 123.4, 124.1, 124.7, 125.2, 125.4, 126.6, 127.1, 128.7,

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129.2, 130.3, 130.5, 131.4, 132.6, 133.2, 134.6, 138.5, 138.4, 139.2, 139.4, 140.2, 141.3.

2-[(1E)-1-aza-2-(3-nitrophenyl)vinyl]-4-(7-bromo-9-chloroacridin-2-yl)-1,3-thiazole (5h)

M.p. 208–209°C, Yield 39%, anal. calcd. for $C_{23}H_{12}BrClN_4O_2S$: C 52.74, H 2.30, N 10.69; found C 52.61, H 2.43, N 10.56. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.74–7.71 (11H,m, Ar—H), 6.04 (1H,s, N=CH). IR: ν_{max} (KBr, cm^{-1}) 1540 and 1610 (C=C stret.), 1355 and 1535 (NO_2 stret.), 1345 (C—N stret.), 566 (C—Br stret.), 794 (C—Cl stret.) 710 (C—S stret.). ^{13}C NMR δ_c (DMSOd_6)123.0, 124.4, 125.5, 125.6, 126.1, 127.3, 128.5, 129.1, 130.4, 130.7, 131.9, 132.2, 133.1, 134.6, 138.5, 138.1, 139.2, 139.3, 140.1, 141.4.

2-[(1E)-1-aza-2-(phenyl)vinyl]-4-(7-nitro-9-chloroacridin-2-yl)-1,3-thiazole (5i)

M.p. 202–203°C, Yield 40%, anal. calcd. for $C_{23}H_{13}ClN_4O_2S$: C 62.09, H 2.94, N 12.59; found C 62.16, H 2.83, N 12.47. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.85–7.60 (11H,m, Ar—H), 6.02 (1H,s, N=CH), IR: ν_{max} (KBr, cm^{-1}) 1534 and 1618 (C=C stret.), 1348 (C—N stret.), 798 (C—Cl stret.) 714 (C—S stret.), 1525 and 1330 (NO_2stret.). ^{13}C NMR δ_c (DMSOd_6)123.2,124.1, 124.3, 125.8, 125.7, 126.9, 127.5, 128.6, 129.4, 130.2, 130.3, 131.4, 132.4, 133.3, 134.8, 138.2, 138.4, 139.6, 139.7, 140.4, 141.1.

2-[(1E)-1-aza-2-(4-hydroxyphenyl)vinyl]-4-(7-nitro-9-chloroacridin-2-yl)-1,3-thiazole (5j)

M.p. 193–194°C, Yield 41%, anal. calcd. for $C_{23}H_{13}ClN_4O_3S$: C 59.93, H 2.84, N 12.15; found C 59.81, H 2.73, N 12.27. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.82–7.78 (11H,m, Ar—H), 6.06 (1H,s, N=CH), 4.77 (1H, s, —OH). IR: ν_{max} (KBr, cm^{-1}) 1534 and 1611 (C=C stret.), 1340 (C—N stret.), 3130 (O—H stret.), 785 (C—Cl stret.), 1524 and 1326 (NO_2 stret.), 722 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 123.2, 124.6, 124.2, 125.6, 125.5, 126.2, 127.1, 128.4, 129.5, 130.6, 130.9, 131.5, 132.5, 133.3, 134.8, 138.1, 138.6, 139.4, 139.3, 140.5, 141.1.

2-[(1E)-1-aza-2-(4-methoxyphenyl)vinyl]-4-(7-nitro-9-chloroacridin-2-yl)-1,3-thiazole (5k)

M.p. 189–190°C, Yield 39%, anal. calcd. For $C_{24}H_{15}ClN_4O_3S$: C 60.69, H 3.18, N 11.79; found C 60.55, H 3.06, N 11.69. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.80–7.77 (11H, m, Ar—H), 6.05 (1H, s, N=CH), 3.70 (3H, s, —OCH_3). IR: ν_{max} (KBr, cm^{-1}) 1536 and 1611 (C=C stret.), 1344 (C—N stret.) 794 (C—Cl stret.) 703 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 56.2,

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123.5, 124.3, 124.5, 125.7,125.9, 126.4, 127.2, 128.3, 129.4, 130.4, 130.5, 131.6, 132.4, 133.6, 134.6, 138.2, 138.5, 139.1, 139.6, 140.2, 141.3.

2-[(1E)-1-aza-2-(3-nitrophenyl)vinyl]-4-(7-nitro-9-chloroacridin-2-yl)-1,3-thiazole (5l)

M.p. 216–217°C, Yield 37%, anal. calcd. for $C_{23}H_{12}ClN_5O_4S$: C 56.39, H 2.46, N 14.29; found C 56.31, H 2.33, N 12.36. ^{1}H NMR δ_H (DMSO-d_6, 300 MHz) 6.78–7.82 (11H,m, Ar—H), 6.04 (1H,s, N=CH). IR: ν_{max} (KBr, cm^{-1}) 1532 and 1615 (C=C stret.), 1352 and 1534 (NO_2 stret.), 1342 (C—N stret.) 791 (C—Cl stret.) 704 (C—S stret.). ^{13}C NMR δ_c (DMSO-d_6) 123.1, 124.2, 124.4, 125.7, 125.4, 126.2, 127.1, 128.7, 129.8, 130.4, 130.2, 131.4, 132.1, 133.7, 134.2, 138.5, 138.6, 139.2, 139.8, 140.5, 141.6.

CONCLUSION

Some new 2-((4-[2-((1E)-1-aza-2- (substituted phenyl) vinyl) 1, 3-thiazol-4-yl] phenyl) amino)-5-substituted benzoic acid derivatives (**4a-l**), 2-[(1E)-1-aza-2- (substituted phenyl) vinyl]-4-(7-substituted-9-chloroacridin-2-yl)-1,3-thiazole(**5a-l**) were synthesized and screened for their antibacterial and antifungal activity. The antimicrobial study revealed that compounds 4a, 4b, 4c, 4j, 5a, 5i, and 5l show excellent antibacterial activity against the tested organism *E coli*. Further, all the synthesized compounds show significant activity against the tested fungus species.

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