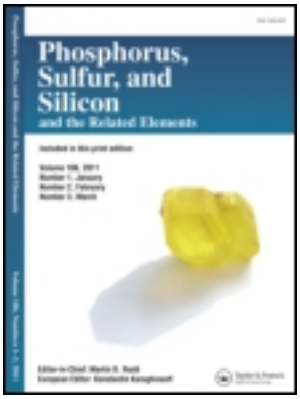


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Studies of Thiazolopyridines, Part 6: Synthesis and Antimicrobial Evaluation of Some Novel Thiazolo[3,2-a] Pyridine and Thiazolo[2′,3′:6,1]-pyrido[2,3-d]pyrimidine Derivatives

G. A. M. El-Hag Ali [a] , A. K. Khalil [b] , R. Q. Lamphon [c] & A. A. El-Maghraby [a]

[a] Department of Chemistry, Al-Azhar University, Nasr City, Cairo, Egypt

[b] Department of Chemistry, Ain Shams University Cairo, Egypt

[c] Department of Chemistry, King Abdel-Aziz University, Madine Munawarah, Saudia

Published online: 18 Aug 2006.

To cite this article: G. A. M. El-Hag Ali , A. K. Khalil , R. Q. Lamphon & A. A. El-Maghraby (2005): Studies of Thiazolopyridines, Part 6: Synthesis and Antimicrobial Evaluation of Some Novel Thiazolo[3,2-a] Pyridine and Thiazolo[2′,3′:6,1]-pyrido[2,3-d]pyrimidine Derivatives, Phosphorus, Sulfur, and Silicon and the Related Elements, 180:8, 1909-1919

To link to this article: http://dx.doi.org/10.1080/104265090889620

Phosphorus, Sulfur, and Silicon, 180:1909–1919, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090889620

Taylor & Francis
Taylor & Francis Group

Studies of Thiazolopyridines, Part 6: Synthesis and Antimicrobial Evaluation of Some Novel Thiazolo[3,2-a] Pyridine and Thiazolo[2′,3′:6,1]-pyrido[2,3-d]pyrimidine Derivatives

G. A. M. El-Hag Ali
Department of Chemistry, Al-Azhar University, Nasr City, Cairo, Egypt

A. K. Khalil
Department of Chemistry, Ain Shams University Cairo, Egypt

R. Q. Lamphon
Department of Chemistry, King Abdel-Aziz University, Madine Munawarah, Saudia

A. A. El-Maghraby
Department of Chemistry, Al-Azhar University, Nasr City, Cairo, Egypt

*Condensation of thiazolinone **1** with aromatic aldehydes yielded the corresponding methylidene derivatives **2a–f**. Cyclization of compounds **2a–f** with arylidenemalononitrile **3** (1:1 molar ratio) in ethanol in the presence of piperidine furnished the novel thiazolo[3,2-a]pyridines **5a–v**, via Michael adduct **4**. Compounds **5p**,**r** were cyclized with malononitrile in the presence of piperidine to yield thiazolo[3,2-a][1,8]naphthryidines **7a**,**b**. Thiazolo-[2′,3′:1,6]pyrido[2,3-d]pyrimidine **9a–c** were obtained by cyclization of compounds **5c**,**p**,**r** with formic acid. The structure of the synthesized compounds was established by analytical and spectral data. Also, some of the synthesized compounds were screened for antimicrobial activity in vitro.*

Keywords Naphthryidine; thiazoline; thiazolo[3,2-a]pyridine;

Thiazolo[3,2-a]pyridines were reported to furnish various biological and pharmacological activities such as antimicrobial,[1] bactericide,[2] coronary dilator, antihypertensive, and muscle relaxant[3] activities. In continuation with our work on the synthesis of thiazolo[3,2-a]pyridines, from readily available starting materials,[4–7] we report here on the synthesis of thiazolo[3,2-a] pyridine, thiazolo[3,2-a][1,8]naphthyridine and

Received June 6, 2004; accepted September 7, 2004.
Address correspondence to A. A. El-Maghraby, Department of Chemistry, Al-Azhar University, Nasr City, Cairo, Egypt. E-mail: m_elgaby@hotmail.com

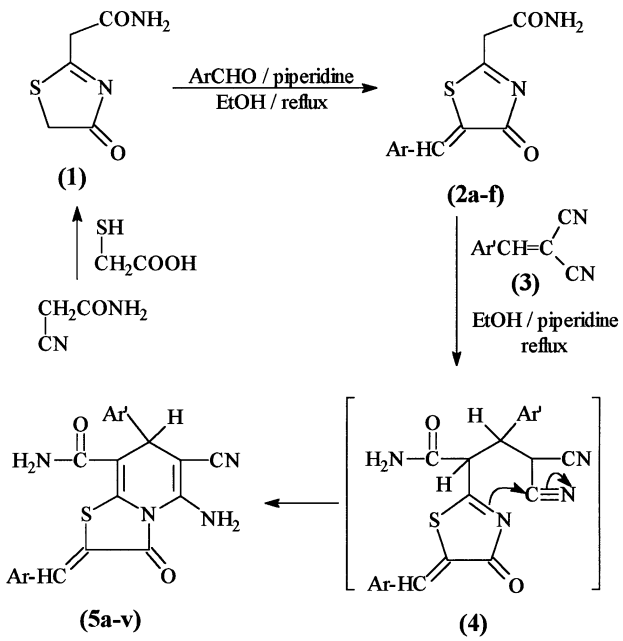
thiazolo[2′,3′:1,6]pyrido-[2,3-d]pyrimidine derivatives in order to investigate the antimicrobial activity of them.

RESULTS AND DISCUSSION

The starting material **1** was synthesized by cyclocondensation of cyanoacetamide with thioglycolic acid.[8] Thiazoline **1** was condensed with various aromatic aldehydes in ethanol in the presence of piperidine under reflux to furnish 2-acetamido-5-arylmethylidene-4,5-dihydro-4-thiazolinones **2a–f** (Scheme 1). Cyclocondensation of compounds **2a–f** with benzylidenemalononitriles **3** (1:1 molar ratio) in ethanol at reflux temperature in the presence of piperidine yielded the novel thiazolo[3,2-a]-pyridines **5a–v** in high yields (Scheme 1). The structures of all the compounds **5a–c** were established using microanalysis and spectroscopy. The infrared spectra of thiazolopyridines **5a–v** exhibited the presence of amino, cyano, and carbonyl (thiazolinone and carbamoyl) function groups. Also, the ^{1}H-NMR spectra revealed a signal characteristic for the 4H-pyridine. The formation of thiazolopyridine **5** is assumed to proceed via Michael addition of methylene function group in compound **2** to the benzylidene moiety **3** to yield Michael adduct **4** followed by intramolecular cyclization[7] at the cyano group to form thiazolopyridine **5** (Scheme 1). Also, the structure of thiazolopyridine **5** was established by another synthetic route by ternary condensation of compound **2**, aromatic aldehyde, and malononitrile (1:1:1 molar ratio) in ethanol in the presence of piperidine under reflux.

The reactivity of thiazolopyridine **5** towards malononitrile was studied. Thus, when compound **5p**,**r** were allowed to react with malononitrile in ethanol containing piperidine under reflux, the condensed pyridine derivatives **7a**,**b** were obtained. On the basis of analytical and spectral data, the other possible structure **6** was ruled out. The infrared spectrum of compound **7a** showed $\nu_{C=O}$ at 1698 cm^{-1} characteristic for thiazolinone and $\nu_{C=O}$ at 1674 cm^{-1} ($CONH_2$). Formation of **7** is assumed to proceed through the addition of an amino group in **3** to the cyano group of malononitrile followed by intramolecular cyclization to furnish **7** (Scheme 2).

Cyclization of compounds **5c**,**p**,**r** with formic acid furnished the novel thiazolo[2′,3′:6,1]pyrido[2,3-d]pyrimidines **9a–c**, via intermediate amide formation[9] **8** followed by intramolecular cyclization with formic acid. Also, cyclocondensation of compound **5c** with acetic anhydride under reflux yielded the corresponding thiazolopyridopyrimidine derivative **10** (Scheme 3). Compound **10** was characterized through the absence of cyano functional group in its infrared spectrum.



2a; Ar= C_6H_4Cl-4 **2b**; Ar= $C_6H_4CH_3$-4

2c; Ar= C_6H_4Cl-2 **2d**; Ar= C_6H_4OH-4

2e; Ar= $C_6H_4OCH_3$-4 **2f**; Ar= $C_6H_3(OCH_3)(OH)$-3,4

5a; Ar= C_6H_4Cl-4 , Ar'= $C_6H_3(OCH_3)(OH)$-3,4 **5b**; Ar= C_6H_4Cl-4 , Ar'= C_6H_4Cl-2

5c; Ar= C_6H_4Cl-4 , Ar'= C_6H_4OH-4 **5d**; Ar= $C_6H_4CH_3$-4 , Ar'= C_6H_4OH-4

5e; Ar= $C_6H_4CH_3$-4 , Ar'= C_6H_4Cl-2 **5f**; Ar= $C_6H_4CH_3$-4 , Ar'= C_6H_4Cl-4

5g; Ar= C_6H_4Cl-2 , Ar'= C_6H_4OH-4 **5h**; Ar= C_6H_4Cl-2 , Ar'= $C_6H_3(OCH_3)(OH)$-3,4

5i; Ar= C_6H_4Cl-2 , Ar'= C_6H_4Cl-4 **5j**; Ar= C_6H_4OH-4 , Ar'= $C_6H_4CH_3$-4

5k; Ar= C_6H_4OH-4 , Ar'= C_6H_4Cl-2 **5l**; Ar= C_6H_4OH-4 , Ar'= C_6H_4Cl-4

5m; Ar= C_6H_4OH-4 , Ar'= $C_6H_4OCH_3$-4 **5n**;Ar= C_6H_4OH-4, Ar'= $C_6H_3(OCH_3)(OH)$-3,4

5o; Ar= $C_6H_4OCH_3$-4, Ar'= $C_6H_3(OCH_3)(OH)$-3,4 **5p**; Ar= $C_6H_4OCH_3$-4 , Ar'= C_6H_4Cl-2

5q; Ar= $C_6H_4OCH_3$-4 , Ar'= C_6H_4Cl-4 **5r**; Ar= $C_6H_4OCH_3$-4 , Ar'= $C_6H_4CH_3$-4

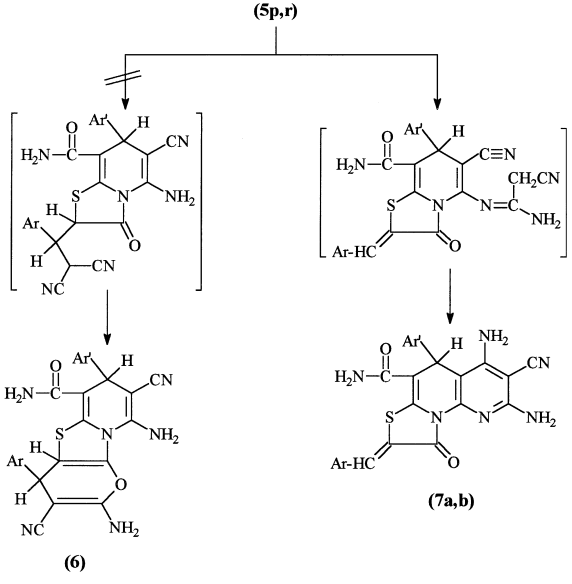
5s; Ar= $C_6H_4OCH_3$-4 , Ar'= C_6H_4OH-4 **5t**; Ar= $C_6H_3(OCH_3)(OH)$-3,4, Ar'= C_6H_4OH-4

5u; Ar= $C_6H_3(OCH_3)(OH)$-3,4 , Ar'= $C_6H_4CH_3$-4 **5v**; Ar= $C_6H_3(OCH_3)(OH)$-3,4 , Ar'= C_6H_4Cl-2

SCHEME 1

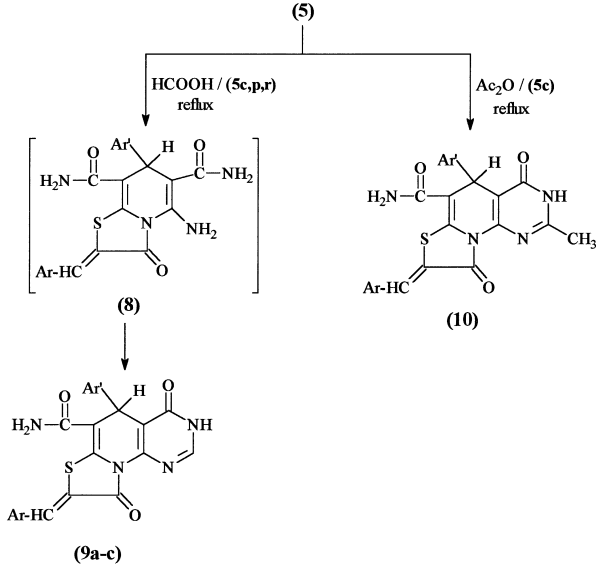
ANTIMICROBAL ACTIVITY

Some of the synthesized compounds were screened *in vitro* for their antimicrobal activities against three strains: *Staphylococcus aureus*



7a; Ar= $C_6H_4OCH_3$-4 , Ar'= C_6H_4Cl-2 **7b**; Ar= $C_6H_4OCH_3$-4, Ar'= $C_6H_4CH_3$-4

SCHEME 2



9a; Ar= C_6H_4Cl-4 , Ar'= C_6H_4OH-4
9b; Ar= $C_6H_4OCH_3$-4 , Ar'= C_6H_4Cl-2
9c; Ar= $C_6H_4OCH_3$-4 , Ar'= $C_6H_4CH_3$-4
10; Ar= C_6H_4Cl-4 , Ar'= C_6H_4OH-4

SCHEME 3

TABLE I Antimicrobial Activity of the Synthesized Compounds and Inhibition Zones (mm). Standard: for Gram Positive and Gram Negative Bacteria, Ampicillin 25 μg mL^{-1}; for fungi: Mycostatine 30 μg mL^{-1}

Compound no.	*Staphylococcus aureus* (NCTC-7447)	*Saracia maxima* (ATCC-33910)	*Aspergillus funigatus*
5b	16	19	14
5d	12	12	18
5f	12	19	18
5h	14	17	14
5k	17	12	16
5p	19	18	15
5q	15	18	17
5r	18	14	12
5s	20	20	25
5t	12	13	13
5v	13	18	12
7a	20	21	20
9b	21	20	22

(NCTC-7447), *Saracia maxima* (ATCC-33910), and *Aspergillus funigatus* by the agar diffusion techniques.[10] The tested compounds were dissolved in *N*,*N*-dimethylformamide (DMF) to get a solution of 1000 μg mL^{-1} concentration. The bacteria and fungi cultures were maintained on nutrient agar and Czapek's-Dox agar media, respectively. DMF showed no inhibition zones. The agar media were incubated with different microorganisms culture tested. After 24 h of incubation at 30°C for bacteria and 48 h of incubation at 28°C for fungi, the diameter of inhibition zone (mm) was measured (Table I). Ampicillin in a concentration 25 μg mL^{-1} and mycostatine in a concentration 30 μg mL^{-1} were used as references for antibacterial and antifungal activities, respectively. The results are illustrated in Table I. None of the tested compounds showed a superior activity than the reference.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded (KBr) on a Perkin Elmer 1650 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Gemini spectrometer 200 (200 MHz), using DMSO-d_6 as a solvent and TMS as an internal standard. Chemical shifts are expressed as δ ppm units. Microanalytical data were obtained from the Microanalytical Data Unit at Cairo University. Physical data for the synthesized compounds are given in Table II. Also, the spectral data are collected in Table III.

TABLE II Characteristics Data for the Prepared Compounds

Compound no.	Yield (%)	Solvent cryst.	M.p. (°C)	Molecular formula (Mol. Wt.)	Elemental analysis Calcd./Found % C	H	N
2a	62	Benzene/ ethanol	240–2	$C_{12}H_9ClN_2O_2S$ (280)	51.42 51.40	3.21 3.00	10.00 10.10
2b	57	Ethanol	197–8	$C_{13}H_{12}N_2O_2S$ (260)	60.10 60.05	4.61 4.60	10.76 10.70
2c	71	Benzene	241–3	$C_{12}H_9ClN_2O_2S$ (280)	51.42 51.30	3.21 3.20	10.00 10.10
2d	83	Benzene/ ethanol	190–2	$C_{12}H_{10}N_2O_3S$ (262)	54.96 54.80	3.81 3.90	10.68 10.70
2e	62	Benzene	230–2	$C_{13}H_{12}N_2O_3S$ (276)	56.52 56.50	4.34 4.30	10.14 10.10
2f	56	Benzene	220–2	$C_{13}H_{13}N_2O_4S$ (293)	55.42 55.40	4.43 4.40	9.55 10.00
5a	63	Dioxane	256–8	$C_{23}H_{17}ClN_4O_4S$ (480.5)	57.44 57.40	3.52 3.50	11.65 11.60
5b	77	Benzene	258–9	$C_{22}H_{14}Cl_2N_4O_2S$ (469)	56.28 56.30	2.98 3.00	11.94 11.90
5c	81	Benzene	286–8	$C_{22}H_{15}ClN_4O_3S$ (450.5)	58.60 58.60	3.32 3.30	12.43 12.40
5d	69	Benzene	>300	$C_{23}H_{18}N_4O_3S$ (430)	64.18 64.20	4.18 4.20	13.02 13.10
5e	88	Benzene	220–2	$C_{23}H_{17}ClN_4O_2S$ (448.5)	61.53 61.50	3.79 3.80	12.48 12.50
5f	79	Benzene	226–8	$C_{23}H_{17}ClN_4O_2S$ (448.5)	61.53 61.50	3.79 3.80	12.48 12.40
5g	74	Benzene	271–3	$C_{22}H_{15}ClN_4O_3S$ (450.5)	58.60 58.60	3.32 3.30	12.43 12.40
5h	64	Dioxane	262–4	$C_{23}H_{17}ClN_4O_4S$ (480.5)	57.44 57.40	3.52 3.50	11.65 11.60
5i	66	Benzene	253–5	$C_{22}H_{14}Cl_2N_4O_2S$ (469)	56.28 56.30	2.98 2.90	11.94 11.90
5j	75	Benzene	>300	$C_{23}H_{18}N_4O_3S$ (430)	64.18 64.20	4.18 4.20	13.02 13.10
5k	80	Benzene/ ethanol	270–2	$C_{22}H_{15}ClN_4O_3S$ (450.5)	58.60 58.60	3.32 3.30	12.43 12.40
5l	90	Dioxane	260–2	$C_{22}H_{15}ClN_4O_3S$ (450.5)	58.60 58.60	3.32 3.30	12.43 12.40
5m	72	Benzene	282–4	$C_{23}H_{18}N_4O_4S$ (446)	61.88 61.70	4.03 4.000	12.55 12.50
5n	82	Benzene	254–6	$C_{23}H_{18}N_4O_5S$ (462)	59.74 59.70	3.89 3.90	12.12 12.10
5o	59	Benzene	262–4	$C_{24}H_{20}N_4O_5S$ (476)	60.50 60.40	4.20 4.20	11.76 11.80
5p	77	Dioxane	190–2	$C_{23}H_{17}ClN_4O_3S$ (464.5)	59.41 59.40	3.65 3.50	12.05 12.10

(Continued on next page)

TABLE II Characteristics Data for the Prepared Compounds *(Continued)*

Compound no.	Yield (%)	Solvent cryst.	M.p. (°C)	Molecular formula (Mol. Wt.)	Elemental analysis Calcd./Found % C	H	N
5q	67	Ethanol	160–2	$C_{23}H_{17}ClN_4O_3S$ (464.5)	59.41 59.40	3.65 3.40	12.05 12.00
5r	87	Dioxane	258–9	$C_{24}H_{20}N_4O_3S$ (444)	64.86 64.80	4.50 4.40	12.61 12.60
5s	67	Benzene	240–2	$C_{23}H_{18}N_4O_4S$ (446)	61.88 61.70	4.03 4.10	12.55 12.50
5t	72	Dioxane	>300	$C_{23}H_{18}N_4O_5S$ (462)	59.74 59.70	3.89 3.90	12.12 12.10
5u	68	Benzene/ ethanol	238–9	$C_{24}H_{20}N_4O_4S$ (460)	62.60 62.60	4.34 4.30	12.17 12.20
5v	85	Dioxane	270–2	$C_{23}H_{17}ClN_4O_4S$ (480.5)	57.44 57.40	3.53 3.50	11.65 11.60
7a	69	Benzene/ ethanol	288–9	$C_{26}H_{19}ClN_6O_3S$ (530.5)	58.81 58.80	3.58 3.60	15.83 15.80
7b	59	Benzene/ ethanol	218–9	$C_{27}H_{22}N_6O_3S$ (510)	63.52 63.50	4.31 4.20	16.74 16.70
9a	70	Dioxane	290	$C_{23}H_{15}ClN_4O_4S$ (478.5)	57.68 57.70	2.92 2.90	11.70 11.70
9b	81	Benzene	210–2	$C_{24}H_{17}ClN_4O_3S$ (492.5)	58.47 58.50	3.45 3.40	11.37 11.40
9c	63	Dioxane	>300	$C_{25}H_{20}N_4O_4S$ (472)	63.55 63.50	4.233 4.20	11.86 11.50
10	71	Dioxane	>300	$C_{24}H_{17}ClN_4O_4S$ (492.5)	58.48 58.50	3.45 3.60	11.37 11.30

2-(Acetamido-2-yl)-5-arylmethylidene-4,5-dihydro-4-thiazolinones (2a–f)

A mixture of compound **1** (0.01 mole), aromatic aldehyde (0.01 mole), and piperidine (0.5 mL) in ethanol (40 mL) was heated under reflux for 3 h. The product obtained was recrystallized from suitable solvent to give **2a–f**.

5-Amino–7-aryl-8-carbamoyl-3-oxo-2-arylmethylidene-2,3-dihydro-*H*-thiazolo[3,2-a]pyridine-6-carbonitriles (5a–v)

Method (A):

A mixture of compound **2** (0.01 mole), benzylidene-malononitrile **3** (0.01 mole), and piperidine (0.5 mL) in ethanol (30 mL) was heated

TABLE III Spectral Data of the Synthesized Compounds

Compound no.	IR/.ν_{max} (cm^{-1})	^{1}H NMR(δ/ppm)(DMSO-d_6)
2a	3379, 3147 (NH_2), 2977 (CH-aliph), 1720 (C═O; thiazolinone), 1666 (C═O, amide).	3.15 (s, 3H, CH_2), 5.40 (s, 2H, NH_2), 6.40–7.62 (m, 5H, Ar-H and methine-H).
2b	3334, 3127 (NH_2), 2977 (CH-alph), 1710 (C═O; thiazolinone), 1658 (C═O; amide).	2.20 (s, 3H, CH_3), 3.10 (s, 2H, CH_2), 5.20 (s, 2H, NH_2), 6.30–7.70 (m, 5H, Ar-H and methine-H).
2e	3300, 3180 (NH_2), 2980 (CH-aliph), 1712 (C═O; thiazolinone), 1660 (C═O; amide).	3.20 (s, 2H, CH_2), 3.60 (s, 3H, OCH_3), 5.30 (s, 2H, NH_2), 6.25–7.82 (m, 5H, Ar-H and methine-H).
2f	3379, 3147 (NH_2), 2930 (CH-aliph), 1720 (C═O; thiazolinone), 1666 (C═O; amide).	3.21 (s, 2H, CH_2), 3.85 (s, 3H, OCH_3), 5.76 (s, 2H, NH_2), 6.90–7.46 (m, 4H, Ar-H and methine-H), 10.80 (s, 1H, OH).
5a	3471, 3433 (NH_2), 2180 (C≡N), 1710 (C═O; thiazolinone), 1651 (C═O; amide).	3.81 (s, 3H, OCH_3), 3.99 (s, 1H, pyridine-H), 5.65 (s, 2H, NH_2), 6.66–7.25 (m, 8H, Ar-H and methine-H), 7.39 (s, 3H, NH_2), 10.10 (br, 1H, OH).
5b	3386, 3170 (NH_2); 2183 (C≡N), 1697 (C═O; thiazolinone), 1651 (C═O; amide).	3.99 (s, 1H, pyridine-H), 5.76 (s, 2H, NH_2), 6.73–7.50 (m, 9H, Ar-H and methine-H), 7.54 (s, 2H, NH_2).
5c	3433, 3332 (NH_2); 2183 (C≡N); 1700 (C═O; thiazolinone), 1658 (C═O; amide).	4.08 (s, 1H, pyridine-H), 5.73 (s, 2H, NH_2), 6.74–7.43 (m, 9H, Ar-H and methine-H), 7.47 (s, 1H, NH_2), 10.90 (br, 1H, OH).
5d	3433, 3147 (NH_2), 2109 (C≡N); 1720 (C═O; thiazolinone), 1666 (C═O; amide).	2.19 (s, 3H, CH_3), 4.15 (s, 1H, pyridine-H), 5.46 (s, 2H, NH_2), 5.87–6.40 (m, 9H, Ar-H and methine-H), 6.42 (s, 2H, NH_2), 10.30 (br, 1H, OH).
5e	3359, 3225 (NH_2), 2191 (C≡N), 1681 (C═O; thiazolinone), 1651 (C═O; amide).	2.20 (s, 3H, CH_3), 4.00 (s, 1H, pyridine-H), 5.10 (s, 2H, NH_2), 6.74–7.51 (m, 9H, Ar-H and methine-H), 7.54 (s, 2H, NH_2).
5g	3433, 3320 (NH_2), 2214 (C≡N), 1720 (C═O; thiazoline), 1666 (C═O; amide).	4.09 (s, 1H, pyridine-H), 5.73 (s, 2H, NH_2), 6.74–7.42 (m, 9H, Ar-H and methine-H), 7.54 (s, 2H, NH_2), 10.90 (br, 1H, OH).
5h	3440, 3350 (NH_2), 2191 (C≡N), 1681 (C═O; thiazolinone), 1651 (C═O; amide).	3.90 (s, 3H, OCH_3), 4.08 (s, 1H, pyridine-H), 5.70 (s, 2H, NH_2), 6.75–7.48 (m, 8H, Ar-H and methine-H), 8.04 (s, 2H, NH_2), 10.90 (br, 1H, OH).

(Continued on next page)

TABLE III Spectral Data of the Synthesized Compounds *(Continued)*

Compound no.	IR/.ν_{max} (cm^{-1})	^{1}H NMR(δ/ppm)(DMSO-d_6)
5i	3379, 3309 (NH_2), 2190 (C≡N), 1720 (C=O; thiazolinone), 1666 (C=O; amide).	4.08 (s, 1H, pyridine-H), 5.70 (s, 2H, NH_2), 6.82–7.33 (m, 9H, Ar-H and methine-H), 7.52 (s, 2H, NH_2).
5k	3425, 3340 (NH_2), 2180 (C≡N), 1700 (C=O; thiazolinone), 1666 (C=O; amide).	4.09 (s, 1H, pyridine-H), 5.73 (s, 2H, NH_2), 6.79–7.52 (m, 9H, Ar-H and methine-H), 7.62 (s, 2H, NH_2), 10.72 (br, 1H, OH).
5l	3386, 3170 (NH_2), 2183 (C≡N); 1690 (C=O; thiazolinone), 1658 (C=O; amide).	4.24 (s, 1H, pyridine-H), 5.70 (s, 2H, NH_2), 6.74–7.58 (m, 9H, Ar-H and methine-H), 7.62 (s, 2H, NH_2), 10.00 (br, 1H, OH).
5n	3433, 3355 (NH_2), 2191 (C≡N), 1700 (C=O; thiazolinone), 1658 (C=O; amide).	3.74 (s, 3H, OCH_3), 4.32 (s, 1H, pyridine-H), 5.71 (s, 2H, NH_2), 6.73–7.46 (m, 8H, Ar-H and methine-H), 10.0 (br, 2H, 2OH).
5o	3433, 3355 (NH_2), 2214 (C≡N), 1700 (C=O; thiazolinone), 1651 (C=O; amide).	3.76, 3.89 (2s, 6H, $2OCH_3$), 4.07 (s, 1H, pyridine-H), 5.50 (s, 2H, NH_2), 6.45–7.59 (m, 8H, Ar-H and methine-H), 8.03 (s, 2H, NH_2), 11.20 (br, 1H, OH).
5p	3440, 3209 (NH_2), 2214 (C≡N), 1700 (C=O; thiazolinone), 1651 (C=O; amide).	3.70 (s, 3H, OCH_3), 4.12 (s, 1H, pyridine-H), 5.71 (s, 2H, NH_2), 6.48–7.45 (m, 9H, Ar-H and methine-H), 7.51 (s, 2H, NH_2).
5q	3355, 3232 (NH_2), 2214 (C≡N), 1720 (C=O; thiazolinone), 1657 (C=O; amide).	3.74 (s, 3H, OCH_3), 3.99 (s, 1H, pyridine-H), 5.47 (s, 2H, NH_2), 6.03–7.42 (m, 9H, Ar-H and methine-H), 11.70 (s, 2H, NH_2).
5r	3463, 3348 (NH_2), 2214 (C≡N), 1689 (C=O; thiazolinone), 1651 (C=O; amide).	2.2 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.99 (s, 1H, pyridine-H), 5.67 (s, 2H, NH_2), 6.68–7.42 (m, 9H, Ar-H and methine-H), 7.78 (s, 2H, NH_2).
5s	3379, 3147 (NH_2), 2191 (C≡N), 1720 (C=O; thiazolinone), 1666 (C=O; amide).	3.80 (s, 3H, OCH_3), 4.11 (s, 1H, pyridine-H), 5.70 (s, 2H, NH_2), 6.85–7.42 (m, 9H, Ar-H and methine-H), 7.41 (s, 2H, NH_2), 10.56 (s, 1H, OH).
5t	3379, 3147 (NH_2), 2221 (C≡N), 1720 (C=O; thiazolinone), 1658 (C=O; amide).	3.78 (s, 3H, OCH_3), 4.09 (s, 1H, pyridine-H), 5.55 (s, 2H, NH_2), 6.75–7.90 (m, 8H, Ar-H and methine-H), 7.90 (s, 2H, NH_2), 9.01, 13.00 (2br, 2H, 2OH).

(Continued on next page)

TABLE III Spectral Data of the Synthesized Compounds *(Continued)*

Compound no.	IR/.ν_{max} (cm^{-1})	^{1}H NMR(δ/ppm)(DMSO-d_6)
5v	3463, 3348 (NH_2), 2214 (C≡N), 1689 (C=O; thiazolinone), 1651 (C=O; amide).	3.76 (s, 3H, OCH_3), 4.09 (s, 1H, pyridine-H), 5.55 (s, 2H, NH_2), 6.47–7.35 (m, 9H, Ar-H and methine-H), 7.90 (s, 2H, NH_2), 11.30 (br, 1H, OH).
7a	3376, 3318 (NH_2), 2190 (C≡N), 1698 (C=O; thiazolinone), 1674 (C=O; amide).	3.60 (s, 3H, OCH_3), 4.10 (s, 1H, pyridine-H), 5.62 (s, 2H, NH_2), 6.48–7.45 (m, 9H, Ar-H and methine-H), 7.53, 8.62 (s, 2H, NH_2).
7b	3318, 3200 (NH_2), 2188 (C≡N), 1700 (C=O; thiazolinone), 1676 (C=O; amide).	
9c	3358, 3176 (NH_2), 1702 (C=O; thiazolinone), 1656 (C=O; amide).	2.30 (s, 3H, CH_3), 3.69 (s, 3H, OCH_3), 4.21 (s, 1H, pyridine-H), 5.67 (s, 2H, NH_2), 6.75–7.50 (m, 9H, Ar-H and methine-H), 7.78 (s, 1H, NH), 8.90 (s, 1H, pyrimidine-H).
10	3318, 3200 (NH_2), 1700 (C=O; thiazolinone), 1676 (C=O; amide).	3.10 (s, 3H, CH_3), 4.32 (s, 1H, pyridine-H), 5.55 (s, 2H, NH_2), 6.74–7.43 (m, 9H, Ar-H and methine-H), 8.54 (s, 1H, NH), 10.72 (br, 1H, OH).

under reflux for 6 h; the solid product which produced on heating was collected to give **5**.

Method (B):

A mixture of compound **2** (0.01 mole), aromatic aldehyde (0.01 mole), and malononitrile (0.01 mole) in ethanol (40 mL) was heated under reflux for 6 h; the solid product which produced on heating was collected to give **5**.

5-Aryl-8-arylmethylidene-6-carbamoyl-2,4-diamino-8,9-dihydro-*H*-thiazolo[3,2-a][1,8]naphthyridine-3-carbonitriles (7a,b)

General Procedure

A mixture of compound **5** (0.01 mole), malononitrile (0.01 mole) in ethanol (30 mL) was heated under reflux for 3 h. The solid product which precipitated upon heating was collected by filtration and recrystallized to give **7**.

5-Aryl-8-arylmethylidene-4-oxo-3,4,8,9-tetrahydro-5*H*-thiazolo-[2′,3′:1,6]pyrido[2,3-d]pyrimidine-6-carbamoyl (9a–c)

General Procedure

A mixture of compound **5** (0.01 mole) and formic acid (10 mL) was heated under reflux for 24 h. The reaction mixture was concentrated in vacuo and the precipitate was collected by filtration, washed with water, and recrystallized from a proper solvent to give **9**.

Formation of thiazolo[2′,3′:1,6]pyrido[2,3-d]pyrimidine derivative (10)

A solution of compound **5c** (0.01 mole) in acetic anhydride (5 mL) was refluxed for 24 h. The solid product, thus formed after cooling, was collected and recrystallized to give **10**.

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