STUDIES ON THIAZOLOPYRIDINES. PART 2. SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NOVEL THIAZOLO[3,2–*a*] PYRIDINE AND THIAZOLO[3,2 – *a*] [1,8] NAPHTHYRIDINE DERIVATIVES HAVING TWO DIFFERENT ARYL MOIETIES

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Received 24-10-2001

Abstract

Condensation of thiazolinone **1** with aromatic aldehydes in ethanol / piperidine solution furnished the novel thiazolidinone derivatives **2a-e.** Ternary condensation of **2**, malononitrile and aromatic aldehydes (1: 1: 1 molar ratio) in absolute ethanol containing a catalytic amount of piperidine yielded the thiazolo[3,2–*a*]pyridines **3a-h** in good yields. Thiazolo[3,2 – a][1,8]naphthyridines **6a-c** were obtained by treatment of **3a, d,h** with malononitrile in ethanol in the presence of piperidine as a basic catalyst. Refluxing of compounds **3b, g, h** in formic acid furnished the novel thiazolo[2`,3`:1,6] pyrido[2,3–*d*]pyrimidines **8a–c.** Interaction of **8c** with malononitrile in ethanol / piperidine solution produced the pyrano[2`,3`:4,5]thiazolo[3`,2:1,6]pyrido[2,3-*d*]pyrimidine **9.** Structures of the synthesized compounds have been established by elemental analyses and spectral data. Compounds **3a-h**, **6a-c** and **8a-c** have been screened for antimicrobial activity.

Introduction

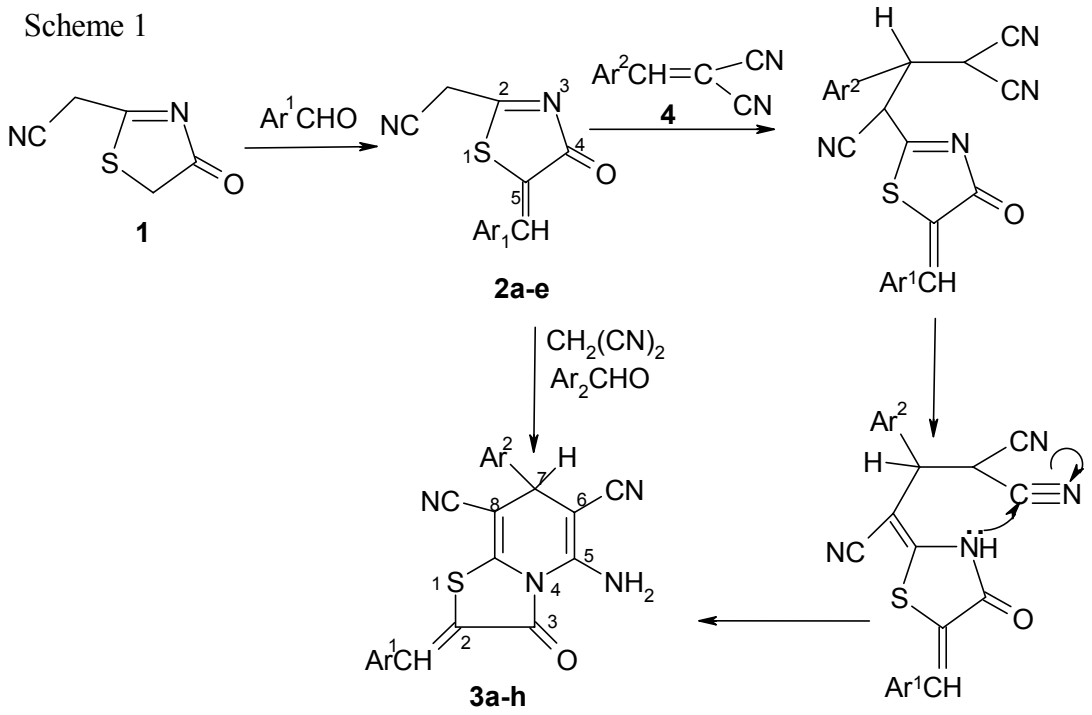
Our search of the literature revealed that, some thiazolo[3,2–*a*]pyridine derivatives have been reported to possess antibacterial,[1] bactericide,[2] coronary dilator, antihypertensive and muscle relaxant[3] activities. Also, it is observed from the literature[4-7] that,7*H*-thiazolo[3,2-*a*] pyridines were synthesized from 2-alkoxycarbonyl - methylidene-5-(arylmethylidene)-1,3-thiazolidin-4-one and arylmethylidenemalono-nitriles . In view of the above and in continuation of our research programme[8-12] on the synthesis of heterocyclic compounds for antimicrobial activity, we reported here the synthesis and antimicrobial activity of some novel thiazolo[3,2 –*a*]pyridine, thiazolo[3,2 –*a*][1,8]naphthyridine and thiazolo[2`,3` :1,6]pyrido[2,3 – *d*]pyrimidine derivatives.

Results and discussion

Thiazolidinones **2a-e** were obtained by refluxing of 2-cyanomethyl-4- thiazolinone **1** with aromatic aldehydes in ethanol / piperidine mixture. Ternary condensation of **2**, malononitrile and aromatic aldehydes (1:1:1 molar ratio) in absolute ethanol containing

a catalytic amount of piperidine furnished the novel 5-amino–2–arylmethylidene-7–aryl–6,8-dicyano-3-oxo-2,3–dihydro–7H–thiazolo[3,2–a]pyridines **3a-h** in good yields. The structures of the synthesized compounds **3a-h** are in agreement with analytical and spectroscopic data (IR, ^{1}H NMR and MS). The IR spectra of compounds **3a-h** exhibited characteristic absorption bands for NH_2, C≡N and C=O (thiazolidinone) groups. ^{1}H-NMR spectrum of **3b** recorded in deuterated dimethylsulfoxide revealed a signal in the region δ 4.67 ppm, attributed to the pyridine –H. The molecular ion of thiazolopyridine **3b** was observed at m/z = 479 (5; 7%) corresponding to the molecular formula $C_{22}H_{12}BrFN_4OS$, (Chart 1). Also, a further conformation of the prepared compounds **3a–h** was obtained by an independent synthetic route by treatment of compounds **2** with arylidene malononitriles **4** in refluxing ethanol and triethylamine (Scheme 1).

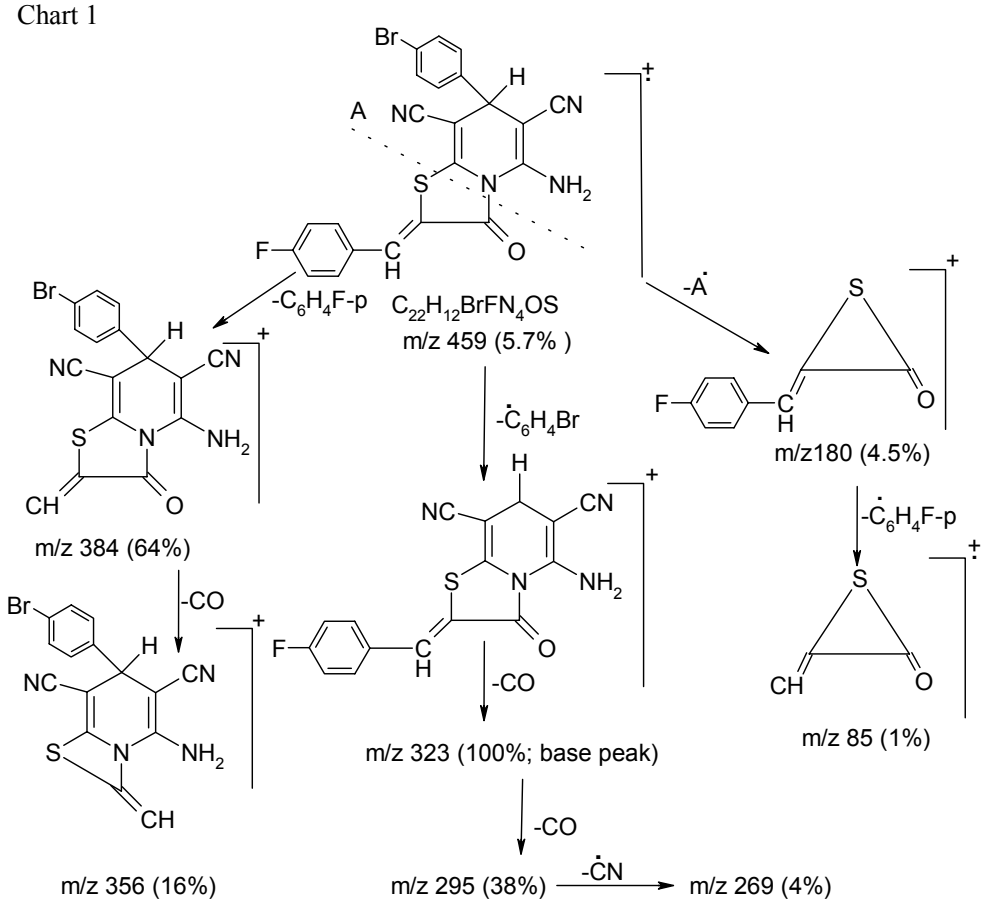
Scheme 1



2a; $Ar_1 = C_6H_4$ Br-p
2b; $Ar_1 = C_6H_4$ F-p
2c; $Ar_1 = C_6H_3(OCH_3)(OH)$-3,4
2d; $Ar_1 = C_6H_4$ Cl-p
2e; $Ar_1 = C_6H_4CH_3$ -p

3a; $Ar_1 = C_6H_4$ Br-p, $Ar_2 = C_6H_4$ F-p
3b; $Ar_1 = C_6H_4$ F-p, $Ar_2 = C_6H_4$ Br-p
3c; $Ar_1 = C_6H_3(OCH_3)(OH)$-3,4, $Ar_2 = C_6H_4$ F-p
3d; $Ar_1 = C_6H_4$Cl-p, $Ar_2 = C_6H_4$ F-p
3e; $Ar_1 = C_6H_4CH_3$ –p, $Ar_2 = C_6H_4$ F-p
3f; $Ar_1 = C_6H_4$ F-p, $Ar_2 = C_6H_3(OCH_3)(OH)$ –3,4
3g; $Ar_1 = C_6H_4$ F-,p, $Ar_2 = C_6H_4$ Cl-p
3h; $Ar_1 = C_6H_4$ F-p, $Ar_2 = C_6H_4CH_3$ - p

Chart 1

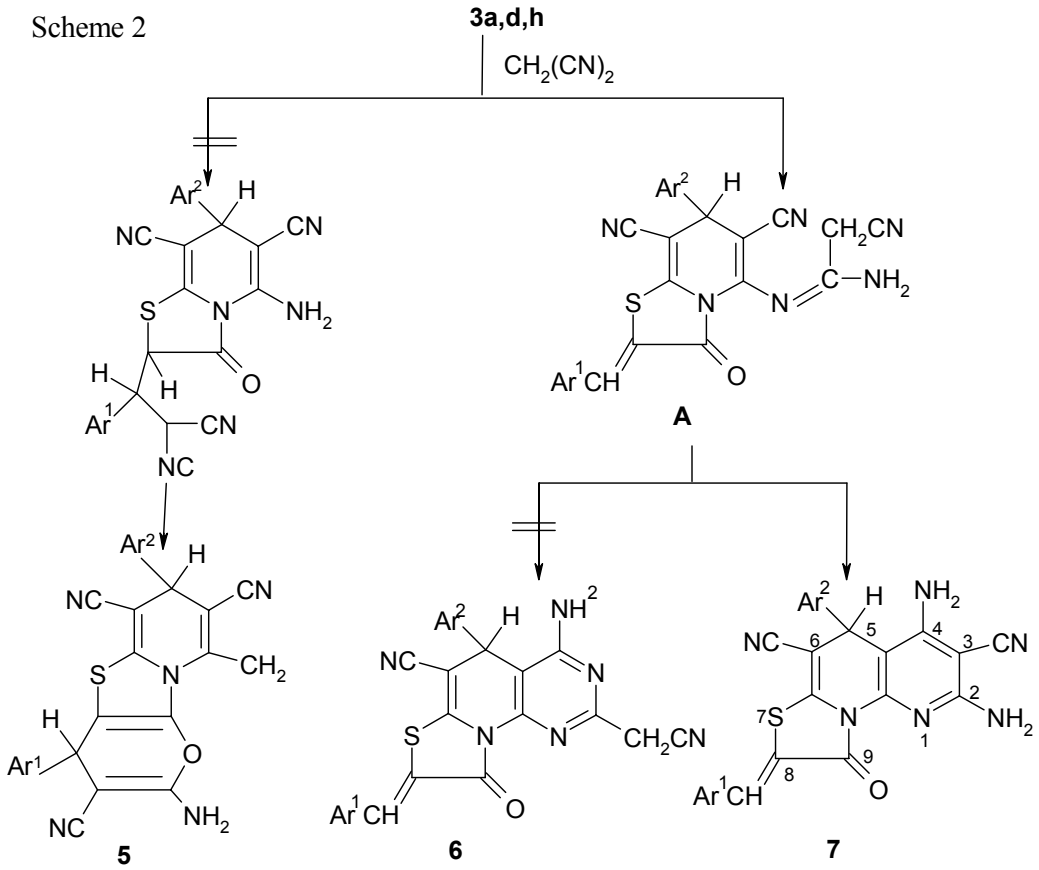


Fragmentation pattern of compound 3b

The reactivity of thiazolopyrimidines **3**, which contains chalcone and *o*-aminonitrile moieties, towards malononitrile was investigated. When compounds **3a,d,h** were allowed to react with malononitrile in ethanol/piperidine solution under reflux, for which three possible structures **5**, **6** and **7** can be formulated, Scheme 2. The structure of **7** was established and the other possible structures were easily discarded on the basis of spectral data. The IR spectrum of compound **7a** showed a cyano stretch at 2214 cm^{-1}, C=O (thiazolidinone) at 1720 cm^{-1} and a primary amino bands at 3479 and 3363 cm^{-1}. 1HNMR spectrum of 7c in DMSO–d6 displayed a singlet at δ 4.12 ppm, attributed to 5H and a broad singlet at δ 3.36 ppm due to the amino group, in addition to a multiplet in the region δ 7.23–7.56 ppm, which was assigned to the aromatic protons, methine proton and amino group. The formation of **7** is assumed to proceed via the addition of

amino group in **3** to the cyano group of malononitrile to give the intermediate **A**, which cyclized to yield **7** (Scheme 2).

Scheme 2

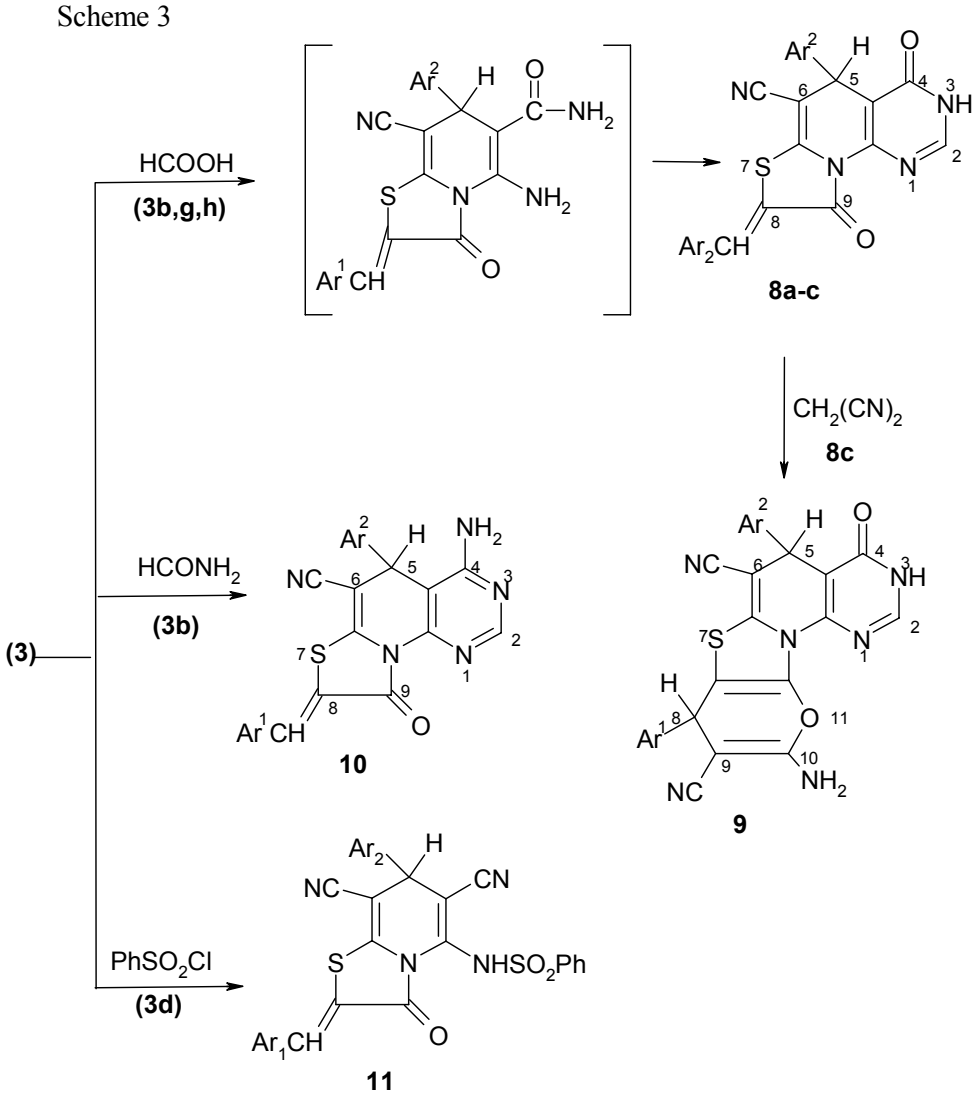


	Ar^1	Ar^2
7a;	C_6H_4 Br-p	C_6H_4 F-p
7b;	C_6H_4 Cl-p	C_6H_4 F-P
7c;	C_6H_4 F-p	$C_6H_4CH_3$-p

Heterocyolic *o*-aminonitriles are well established as versatile starting materials for the synthesis of a wide variety of fused heterocyclic compounds.[13] Thus, refluxing of *o*-aminonitriles **3b,g,h** in formic acid yielded the corresponding thiazolo [2`,3` : 6,1]pyrido[2,3-d]pyrimidines **8a-c,** (Scheme 3). The formation of **8** is supposed to proceed *via* intermediate amide formation, resulted from the partial hydrolysis of cyano functionality present at the position 6 of **3**, followed by intramolecular cyclization with formic acid.[14] The IR spectrum of **8a** exhibited stretching vibrations in the region 3193 cm^{-1} (NH), 2198 cm^{-1} (C≡N) together with characteristic bands for C=O (thiazolidinone)

at 1700 cm^{-1} and C = O (pyrimidinone) at 1680 cm^{-1} . When the α,β-unsaturated ketone **8c** was treated with malononitrile in ethanol containing a catalytic amount of piperidine, the pyrano [2`,3` : 4,5]thiazolo[3`,2` :6,1] pyrido[2,3-d] pyrimidine **9** was obtained. The IR spectrum of **9** exhibited stretching vibrations near 3320 and 3201 cm^{-1} (NH_2), 2214 cm^{-1} (C≡N) and 1666 cm^{-1} (C=O). The ^{1}HNMR spectrum of **9** in DMSO-d_6 displayed a singlet at δ 4.59 (pyran-H) .The formation of **9** *via* initial Michael addition[15] to the α,β-

Scheme 3



8a; Ar_1 = C_6H_4 F-p Ar_2 = C_6H_4Br-p
b; Ar_1 = C_6H_4 F-p Ar_2 = C_6H_4Cl-p
c; Ar_1 = C_6H_4 F-p Ar_2 = $C_6H_4CH_3$-p
9a; Ar_1 = C_6H_4 F-p Ar_2 = $C_6H_4CH_3$
10 and 11 Ar_1 = C_6H_4 F-p Ar_2 = C6H_4Br-p

unsaturated system followed by nucleophilic attack of hydroxyl group of the heterocyclic ring to one of the cyano groups of malononitrile to yield the pyran derivative **9.** Thiazolo[2`,3`:6,1] pyrido [2,3-d]pyrimidine **10** was obtained by cyclocondensation of **3b** with formamide under reflux conditions. Finally, treatment of **3b** with benzene sulfonyl chloride in benzene furnished the novel sulfonamide derivative **11**, (Scheme 3).

Antimicrobial Activity

Fourteen compounds were screened *in vitro* for their antimicrobial activities against four strains of bacteria *Staphylococcus aureus* (NCTC-7447), *Bacillus cereus* (ATCC-14579), *Serratia marcesens* (IMRU-70), *Proteus mirabilis* (NCTC-289) and two strains of fungi *Aspergillus ochraceus Wilhelm* (AUCC-230) and *Pencillium chrysoegenum Thom (AUCC-530)* by the agar diffusion technique.[16] A 1 mg/mL solution in dimethylformamide was used. The bacteria and fungi were maintained on nutrient agar and Czapek's-Dox agar media, respectively. DMF showed no inhibition zones. The agar media were inoculated with different microorganisms culture tested. After 24h of incubation at 30 ºC for bacteria and 48 h of incubation at 28 ºC for fungi, the diameter of inhibition zone (mm) was measured (Table 1). Ampicillin in a concentration 25 μg mL^{-1} and Mycostatine (30 μg mL^{-1}) used as a references for antibacterial and antifungal activities, respectively. The minimal inhibitory concentration (MIC) of some of the tested compounds was measured by a twofold serial dilution method.[17] Most of the synthesized compounds exhibited antimicrobial activity towards all the microorganisms used.

Experimental

All melting points are uncorrected (Stuart Scientific Co., UK). IR spectra were measured as KBr pellets on Shimadzu IR 200 spectrophotometer. ^{1}H-NMR spectra were recorded in deutrated DMSO-d_6 at 200 MHz on a Varian Gemini NMR spectrometer using tetramethylsilane as an internal reference. Elemental analyses were carried out at the Microanalytical Center of Cairo University. The characteristic data for prepared compounds are given in Table 2. The spectral data are collected in Table 3. Compound **1** was prepared according to reported method.[18]

TABLE (1): Antimicrobial activity of some synthesized compounds and inhibition zones

Compd. No.	Gram positive bacteria		Gram negative bacteria		Fungi	
	Staphyloccus aureus (NCTC 7447)	*Bacillus cereus* (NCTC-14579)	*Serratia marcesens* (IMRU-70)	*Proteus mirabilis* (NCTC-289)	*Aspergillus ochraceus Wilhelm* (AUCC-230)	*Penicillium chrysogenum Thom* (AUCC-530)
3a	+++	+	++	+	+	++
3b	++	++	+	++	+	+
3c	+++	+	+++	+	++	+
3d	+	++	++	+	+	+
3e	+	+	+	+	+	+
3f	+	+	+	+	+	+
3g	++	++	++	++	++	+
3h	++	+	+++	+	+	++
6a	++	+	+	++	+	+
6b	++	++	++	+	++	++
6c	+++	++	+	+	++	+
8a	+++	+	+	+	++	+
8b	++	+	+	++	+	++
8c	+	++	+	+	++	+
Standard	++++	++++	+++ +	+++ +	++++	++++

\+ : Less active (0.2-0.5 cm)
++ : Moderately active (0.6-1.4 cm)
+++ : Highly active (1.5-3.0 cm)
++++ : Very highly activity (over 3.0 cm)

Standard: For Gram positive and Gram negative bacteria: Ampicillin 25 μg mL^{-1}; for fungi: Mycostatine 30 μg mL^{-1}.

Experimental

All melting points are uncorrected (Stuart Scientific Co., UK). IR spectra were measured as KBr pellets on Shimadzu IR 200 spectrophotometer. ^{1}H-NMR spectra were recorded in deutrated DMSO-d_6 at 200 MHz on a Varian Gemini NMR spectrometer using tetramethylsilane as an internal reference. Elemental analyses were carried out at the Microanalytical Center of Cairo University. The characteristic data for prepared compounds are given in Table 2. The spectral data are collected in Table 3. Compound **1** was prepared according to reported method.[18]

5-Arylmethylidene–2–cyanomethyl–4,5-dihydro-4-thiazolinones (2a-e). A mixture of **1** (0.01 mole), aromatic aldehyde (0.01 mole) and piperidine (0.5 mL) in anhydrous ethanol (30 mL) was heated under reflux at 120 ^{o}C for 3h, and then allowed to cool to room temperature. The precipitate was collected by filtration and recrystallized from ethanol / benzene to give **2a-e**.

5-Amino–2-arylmethylidene–7-aryl-2,3-dihydro-*7H*-3-oxothiazolo[3,2-*a*]pyridin – 6,8- dicarbonitriles (3a-h). ***Method (A)***: A mixture of **2** (0.01 mole), malononitrile (0.01 mole), aromatic aldehyde (0.01 mole) and piperidine (0.5 mL) in anhydrous ethanol (30 mL) was heated under reflux for 4h, the solid product which precipitated upon heating was collected by filtration and recrystallized from dioxane to give **2a-h**
Method B: A mixture of **2** (0.01 mole), arylidenemalononitrile **4** (0.01 mole) and piperidine (0.5mL) in absolute ethanol (30 ml) was heated under reflux for 2 h. The precipitate was collected by filtration and recrystallized to give **3**.

5–Aryl-8-arylmethylidene–2,4-diamino-8,9-dihydro-*5H*-thiazolo[3,2-*a*][1,8] naphthryidine-3,6-dicarbonitriles (6a-c). A mixture of **3** (0.01 mole), malononitrile (0.01 mole) and piperidine (0.5 mL) in absolute ethanol (30 mL) was heated under reflux for 0.5 h. The solid product which precipitated upon on heating was collected by filtration and recrystallized from dioxane to give **6a-c**.

5-Aryl-8-Arylmethylidene-4-oxo–3,4,8,9-tetrahydro-*5H*-thiazolo[2`,3`:1,6][2,3–*d*] pyrimidine–6–carbonitriles (8a-c). A mixture of **3** (0.01 mole) and formic acid (15 mL) was heated under reflux for 8h. The reaction mixture was concentrated in vacuo and the precipitate was collected by filtration, washed with water and recrystallized from dioxane to give **8a-c**.

10- Amino –5,8-diaryl 3,4-dihydro–4-oxo–*5H,8H*- pyrano [2`,3`:5,4]thiazolo[3`,2`: 1,6]pyrido[2,3-*d*]pyrimidine–6,9-dicarbonitrile (9). A mixture of **8c** (4.42 g; 0.01 mole), malononitrile (0.66 gm; 0.01 mole) and piperidine (0.5 mL) in anhydrous ethanol (30 mL) was heated under reflux for 3h, then allowed to cool poured into cold water

(100 mL), and acidified with HCl (3 mL; 36%). The solid product was collected by filtration and recrystallized from ethanol to give **9** .

4-Amino–5-aryl-8-arylmethylidene-8,9-dihydro-*5H*-thiazolo[2`,3`:1,6]pyrido[2,3-*d*]pyrimidine-6-carbonitrile (10). A mixture of **3b** (4.79 g; 0.01 mole) and formamide (10 mL) was refluxed for 4h. The precipitate was collected by filtration and recrystallized from ethanol to give **10** .

5-Benzenesulfonylamino–2-(4-fluorphenylmethylidene)-7-(4-bromophenyl)-2,3-dihydro-3-oxo-*7H*-thiazolo[3,2-*a*]pyridin–6,8-dicarbonitrile (11). A mixture of **3b** (4.79 g; 0.01 mole) and benzene sulfonyl chloride (1.77 g; 0.01 mole) in anhydrous benzene (30 mL) was heated under reflux for 1 h. The precipitate was collected by filtration and recrystallized from benzene to give **11**.

Table 2: Physical and analytical data for compounds **2, 3, 6, 8, 9, 10** and **11.**

Compd. No	Yield (%)	Solvent cryst.	mp (°C)	Mol. Formula (M. Wt)	Calculated / found (%)		
					C	H	N
2a	82	B/H	176-8	$C_{12}H_7BrN_2OS$ (307.17)	46.92 46.80	2.30 2.10	9.12 9.30
2b	76	B/E	169-71	$C_{12}H_7FN_2OS$ (246.26)	58.53 58.40	2.87 2.80	11.38 11.40
2c	80	B/E	166-8	$C_{13}H_{10}N_2O_3S$ (274.30)	56.92 56.70	3.67 4.10	10.21 10.20
2d	74	B/H	162-4	$C_{12}H_7ClN_2OS$ (262.72)	54.86 54.70	2.69 2.70	10.66 10.50
2e	67	B/E	183-5	$C_{13}H_{10}N_2OS$ (242.30)	64.44 64.40	4.16 4.10	11.56 11.50
3a	87	D	258-60	$C_{22}H_{12}BrFN_4OS$ (479.99)	55.13 55.20	2.52 2.50	11.67 13.70
3b	84	D	260-2	$C_{22}H_{12}BrFN_4OS$ (479.99)	55.13 55.10	2.52 2.60	11.67 13.80
3c	82	DMF/E	233-5	$C_{23}H_{15}FN_4O_3S$ (446.45)	61.88 61.70	3.39 3.40	12.55 12.60
3d	77	D	248-50	$C_{22}H_{12}ClFN_4OS$ (434.87)	60.76 60.60	2.78 2.70	12.88 12.80
3e	72	DMF/H_2O	246-8	$C_{23}H_{15}FN_4OS$ (414.46)	66.65 66.70	3.65 3.60	13.52 13.50
3f	75	DMF/H_2O	250-2	$C_{23}H_{15}FN_4O_3S$ (446.45)	61.88 61.70	3.39 3.40	12.55 12.60

Table 2 Continued.

Compd. No	Yield (%)	Solvent cryst.	mp (°C)	Mol. Formula (M. Wt)	Calculated / found (%)		
					C	H	N
3g	64	DMF/H_2O	255-6	$C_{22}H_{12}$ C/F N_4 OS	60.76	2.78	12.88
				(434.87)	60.70	2.70	12.90
3h	68	DMF/H_2O	240-2	$C_{23}H_{15}$ F N_4 OS	66.65	3.65	13.52
				(41446)	66.70	3.70	13.60
6a	76	D	200-1	$C_{25}H_{14}$ Br F N_6 OS	55.06	2.59	15.41
				(545.39)	55.10	2.10	15.30
6b	72	D	205-7	$C_{25}H_{14}$ Cl F N_6 OS	59.94	2.82	16.78
				(500.94)	59.90	2.80	16.70
6c	70	DMF	> 300	$C_{26}H_{17}$ F N_6 OS	64.99	3.57	17.49
				(480.52)	65.10	3.40	17.60
8a	90	DMF	> 300	$C_{23}H_{12}$ Br F N_4 O_2S	54.45	2.42	11.04
				(507.34)	54.40	2.30	11.10
8b	67	D	232-4	$C_{23}H_{12}$ Cl F N_4 O_2S	59.68	2.61	12.10
				(462.88)	59.60	2.50	12.20
8c	82	DMF	> 300	$C_{24}H_{15}$ F N_4 O_2S	65.15	3.42	12.66
				(442.47)	65.10	3.40	12.70
9	64	E	132-4	$C_{27}H_{17}$ F N_6 O_2S	63.77	3.37	16.53
				(508.53)	63.80	3.30	16.40
10	84	DMF	> 300	$C_{23}H_{13}$ Br FN_5 OS	54.56	2.59	13.83
				(506.35)	54.50	2.56	13.80
11	72	B	130	$C_{28}H_{16}$ Br F $N_4O_3S_2$	54.29	2.60	9.04
				(619.49)	54.10	2.50	9.10

B = benzene , H = *n*-hexane, E = ethanol , DMF = dimethylformamide , D = dioxane

Table (3): Spectral data for compounds **2, 3, 7, 8, 9, 10,**and **11**

Cmp. No	IR (cm^{-1}) (KBr disc)	^{1}HNMR (DMSO-d_6) δ (ppm)
2a	2950 (CH-aliph.), 2199 (C≡N),1715 (C=O; thiazolidinone).	4.04 (s, 2H, CH_2CN), 7.12-7.85 (m, 5H, 4H-Ar and methine-H).
2b	2900 (CH-aliph.), 2200 (C≡N), 1719 (C=O; thiazolidinone).	
2c	3483–2958 (broad; OH), 2200 (C≡N), 1707 (C=O; thiazolidinone)	3.84 (s, 3H, OCH_3),4.76(s, 2H, CH_2CN), 6.67-7.89 (m, 4H, 3H-Ar and methine–H), 10.00 (s, 1H, OH; exchangeable).
2d	293 4 (CH-aliph.), 2200 (C≡N), 1718 (C=O; thiazolidinone).	
2e	2924 (CH-aliph.), 2200 (C≡N), 1711 (C=O; thiazolidinone)	2.35 (s, 3H, CH_3), 4.02 (s, 2H, CH_2CN), 7.06 – 7.87 (m, 5H ,4H-Ar and methine-H,)
3a	3400, 3290 (NH_2), 2200 (C≡N), 1712 (C=O; thiazolidinone)	4.64(s,1H,pyridine –H), 7.20-7.82 (m, 9H, 8H – Ar and methine –H), 7.87 (s, 2H, NH_2 exchangeable)
3b	3410, 3350 (NH_2), 2200 (C≡N), 1708 (C=O; thiazolidinone)	4.67 (s, 1H, pyridine-H), 7.22 – 7.85 (m, 9H, 8H Ar and methine-H), 7.89 (s, 2H, NH_2; exchangeable).
3c	3400 - 2400 (NH_2 + OH), 2200 (C≡N), 1705 (C=O; thiazolidinone)	3.83 (s, 3H, OCH_3), 4.46 (s, 1H, pyridine-H), 6.80 (s, 1H, OH; exchangeable), 6.93-7.85 (m, 8H, 7H- Ar-and methine-H), 7.87 (s, 2H, NH_2; exchangeable).

Table (3) Continued.

Cmp. No.	IR (cm^{-1}) (KBr disc)	^{1}HNMR (DMSO-d_6) δ (ppm)
3f	3500, 2450 (NH_2 + OH), 2200 (C≡N), 1700 (C=O; thiazolidinone).	
3d	3430, 3300 (NH_2), 2200 (C≡N), 1710 (C=O; thiazolidinone)	4.67 (s, 1H, pyridine-H), 7.23 – 7.68 (m, 9H, 8H-Ar- and methine-H), 7.88 (s,2H, NH_2; exchangeable).
3g	3390, 3300 (NH_2), 2200 (C≡N), 1710 (C=O ; thiazolidinone).	
3e	3400, 3200 (NH_2), 2200 (C≡N), 1705 (C=O; thiazolidinone).	
3h	3400, 3300 (NH_2), 2200 (C≡N), 1710 (C=O; thiazolidinone)	2.34 (s, 3H, CH_3), 4.67 (s, 1H, pyridine–H), 7.22-7.71 (m, 9H, 8H-Ar, and methine–H), 7.90 (s, 2H, NH_2; exchangeable).
7a	3479, 3363 (NH_2), 2985 (CH-aliph.) 2214 (C≡N), 1720 (C=O; thiazolidinone)	4.00 – 4.51 (broad, 3H, pyridine – H+ NH_2), 7.42 – 8.03 (m,11H, 8H-Ar, and methine – H and NH_2)
7b	3409, 3332 (NH_2), 2923 (CH-aliph.) 2214 (C≡N), 1720 (C=O; thiazolidinone).	4.08 (s, 1H, pyridine-H), 4.19 (s,2H, NH_2; exchangeable) 7.23-7.66 (m, 9H, 8H-Ar and methine–H) 7.96 (s, 2H, NH_2; exchangeable).
7c	3479, 3170 (NH_2), 2923 (CH-aliph.), 2214 (C≡N), 1720 (C=O; thiazolidinone)	2.39 (s, 3H, CH_3), 3.36 (b, 2H, NH_2), 4.12 (s, 1H, pyridine–H), 7.23–7.56 (m, 11H, Ar-H+ methine-H+NH_2)
8a	3193, (NH), 2198 (C≡N), 1700 (C=O; thiazolidinone), 1680 (C=O; pyrimidinone)	
8b	3186, (NH), 2206 (C≡N), 1705 (C=O); thiazolidinone), 1658 (C=O; pyrimidinone)	4.91(s, 1H, pyridine–H), 7.18-7.79 (m, 9H, 8H- Ar and methine–H) , 8.19 (s, 1H, pyrimidine–H), 11.50 (s, 1H NH ; exchangeable)
8c	3200, (NH), 2206 (C≡N), 1710 (C=O; thiazolidinone), 1666 (C=O; pyrimidinone).	2.37 (s, 3H, CH_3), 4.67 (s, 1H, pyridine –H), 7.19 – 7.75 (m, 9H, 8H-Ar, and methine–H), 8.15 (s, 1H, pyrimidine-H), 11.66 (broad, 1H, NH, exchangeable).
9	3320, 3201 (NH_2), 2931(CH-aliph.) 2214 (C≡N), 1666 (C=O; pyrimidinone).	2.32 (s, 3H, CH_3), 4.59 (s, 1H, pyran–H), 4.67 (s, 1H, pyridine –H), 5.81 (s, 2H, NH_2), 7.15 – 7.72 (m, 8H, 8H, Ar), 10.85 (s, 1H, pyrimidine –H), 11.60 (s, 1H, NH; exchangeable)
10	3270, 3200 (NH_2), 2200 (C≡N), 1704 (C=O; thiazolidinone) .	4.80 (s, 1H, pyridine–H), 6.21(s, 2H, NH_2; exchangeable), 7.04-7.54 (m, 9H ,8H–Ar and methine-H), 8.00 (s, 1H, pyrimidine – H) .
11	3350, (NH), 2923 (CH-aliph.), 2214 (C≡N), 1705 (C=O; thiazolidinone) .	4.80 (s, 1H pyridine –H), 7.28- 7.67 (m, 9H, 8H–Ar and methine–H), 8.00 (s, 1H, NH; exchangeable).

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Povzetek

S kondenzacijo tiazolina **1** z aromatskimi aldehidi in sledečo ternerno kondenzacijo z malononitrilom in aromatskimi aldehidi smo pripravili tiazolo[3,2–*a*]piridine **3a-h** z dobrimi izkoristki. Le-te smo z nadaljnimi reakcijami pretvorili v tiazolo[2`,3`:1,6] pirido[2,3–*d*]pirimidine **8a–c**. Slednji je z malononitrilom v zmesi etanol-piperidin dal pirano[2`,3`:4,5]tiazolo[3`,2:1,6]pirido[2,3-*d*]pirimidin **9**. Spojine **3a-h**, **6a-c** in **8a-c** smo testirali na antimikrobno učinkovanje.