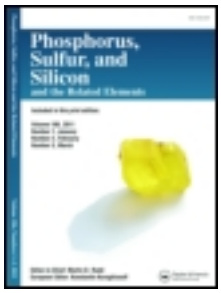

Phosphorus, Sulfur, and Silicon and the Related Elements

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STUDIES ON THIAZOLOPYRIDINES. PART 5: SYNTHESIS OF HITHERTO UNKNOWN THIAZOLINONE AND THIAZOLO[3,2-a]PYRIDINE DERIVATIVES HAVING IN THEIR STRUCTURE THE MORPHOLIN-4-YL MOIETY

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STUDIES ON THIAZOLOPYRIDINES. PART 5: SYNTHESIS OF HITHERTO UNKNOWN THIAZOLINONE AND THIAZOLO[3,2-a]PYRIDINE DERIVATIVES HAVING IN THEIR STRUCTURE THE MORPHOLIN-4-YL MOIETY

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*Condensation of thiazolinone **1** with benzaldehydes **2a**,**b** in ethanolic piperidine afforded the methylidene derivatives **3a**,**b**. Cyclocondensation of compound **3b** with malononitrile furnished the novel thiazolo[3,2-a]-pyridine **5**. Also, compound **3b** was condensed with dimethylformamide-dimethylacetal (DMF-DMA) and triethylorthoformate to yield* N,N-*dimethylamino **6** and ethoxymethylene **7** derivatives respectively. The novel thiazolo[3,2-a]pyridines **10a**,**b** were obtained by cyclocondensation of compounds **3a**,**b** with benzylidenemalononitriles **8a**,**b**. Similarly, cyclocondensation of compound **3b** with benzylidenemalononitrile **11** afforded the thiazolopyridines **12a–c**. Ternary condensation of compound (**12**), 4-morpholinobenzaldehyde **2b** and malononitrile (1:1:1 molar ratio) produced the thiazolopyridines **14a–c**. When compound **10b** was subjected to react with malononitrile in dioxane/piperidine under reflux the novel condensed heterocyclic system **18** was obtained. Treatment of ortho-aminocarbonitrile **10b** with formic acid, aromatic aldehyde and triethylorthoformate furnished the thiazolo[2′,3′:1,6] pyrido[2,3-d] pyrimidine **20**, azomethine **21a**,**b** and ethoxymethylene **22** derivatives respectively. The structure of the synthesized compounds was established by analytical and spectral data.*

Keywords: Condensed thiazole derivatives; morpholine; thiazoline; thiazolo[3,2-a]pyridine

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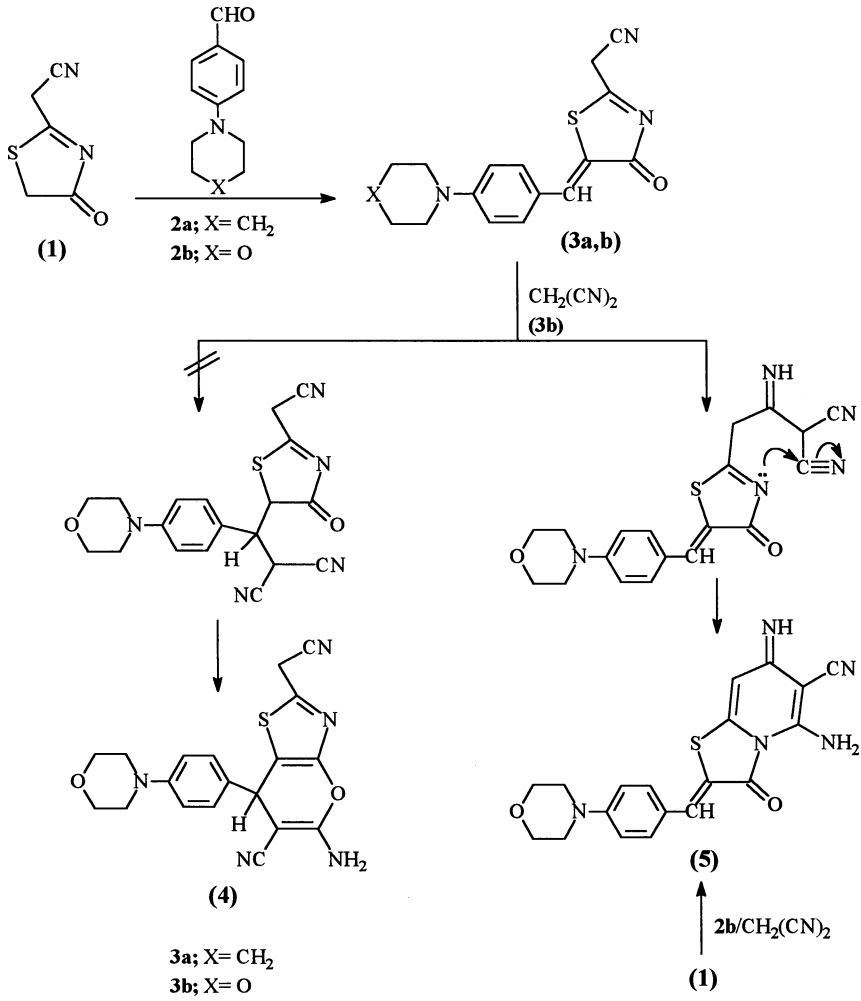
Morpholine derivatives have been reported to possess antimicrobial,[1] hypoglycemic,[2] antagonists of leukocyte,[3] tyrosine kinase inhibitory,[4] potent and selective M_2 muscarinic receptor antagonist,[5] hypolipidemic,[6] and inhibition of collagen-induced blood aggregation[7] activities. Also, morpholine derivatives have medical bactericide, fungicide, virucide, and anthelmintic[8] activities. In addition morpholines are commerically important as basic dyes for acrylic fibers,[9] hair dyes,[10] sensitizers of photopolymerizable compounds[11] and inflammation inhibitors.[12] Thiazolo[3,2-a]pyridine derivatives were reported to furnish various biological and pharmacological activities such as antimicrobial,[13] bactericide,[14] coronary dilator, antihypertensive, and muscle relaxant[15] activities. In continuation with our work on the synthesis of heterocyclic compounds from readily available starting materials,[16–20] we report here on the synthesis of some novel thiazolinone and thiazolo[3,2-a]pyridine derivatives having in their structure the morpholin-4-yl moiety in order to investigate the antimicrobial activity.

RESULTS AND DISCUSSION

Condensation of thiazolinone **1** with 4-piperidinobenzaldehyde **2a** and 4-morpholinobenzaldehyde **2b** in ethanol and piperidine afforded the methylidene derivatives **3a** and **3b** respectively. In the mass spectrum of compound **3b**, the molecular ion peak was observed at m/z 313 (78%) and the base peak was found in the spectrum at m/z 314 (M + 1; 100%). Cyclocondensation of compound **3b** with malononitrile in ethanol in the presence of triethylamine under reflux furnished the novel thiazolo[3,2-a]-pyridine derivative **5**, Scheme (1). Analytical and spectral data are consistent with the structure of thiazolopyridine **5** and excluded the other possible structure **4**. The infrared spectrum revealed the presence of carbonyl function group at 1701 cm^{-1}, as well as amino, and carbonitrile function groups. Also, the ^1H NMR spectrum of the reaction product recorded in DMSO-d_6 displayed a signal at δ 4.44 for an pyridine-H in addition to $N(CH_2)_2$, $O(CH_2)_2$, aromatic, methylidene, amino, and imino protons. The molecular ion peak of compound **5** was observed at m/z 379 (25%) corresponding to the molecular formula $C_{19}H_{17}N_5O_2S$ and the base peak at m/z 378 (M-1). The formation of thiazolopyridine **5** is assumed to proceed via the addition of the active methylene in malononitrile to the cyano function group in **3b** followed by intramolecular cyclization at the cyano group and tautomerization to furnish **5**, Scheme (1). Also, compound **5** was obtained by another synthetic route via the ternary condensation of compound **1**,

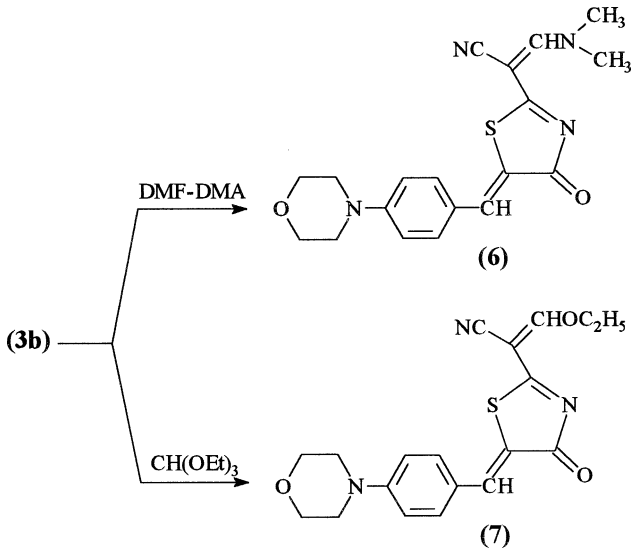
4-morpholinobenzaldehyde **2b** and malononitrile (1:1:1 molar ratio) under reflux in ethanol in the presence of triethylamine.



SCHEME 1

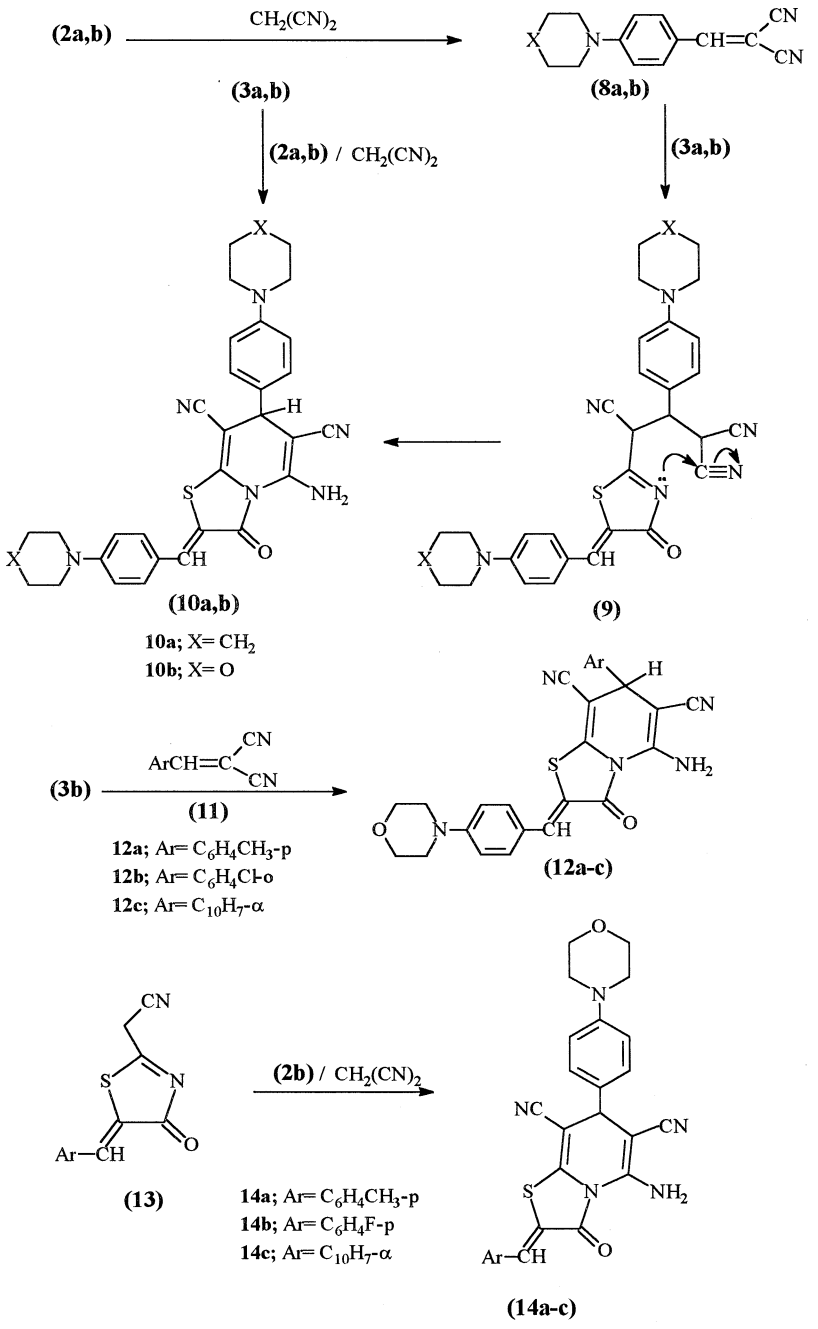
The reactivity of compound **3b** towards some electrophilic reagents was studied. Condensation of compound **3b** with dimethylformamide-dimethylacetal (DMF-DMA) in refluxing *m*-xylene produced the *N*,*N*-dimethylamino derivative **6**. The ^{1}H NMR spectrum of compound **6** indicated the presence of *N*,*N*-dimethyl protons and the absence of methylene protons which present in the parent compound. In a

similar manner, compound **3b** reacted with triethyl orthoformate to yield ethoxymethylene derivative **7** (Scheme 2).



SCHEME 2

Cyclocondensation of compounds **3a**,**b** with benzylidenemalononitriles **8a**,**b** (1:1 molar ratio) in ethanolic piperidine at reflux temperature yielded the novel thiazolo[3,2-a]pyridines **10a**,**b** in good yields (Scheme 3). Structural elucidation of compounds **10a**,**b** was accomplished from their analytical and spectral data. The infrared spectra indicated the presence of amino, cyano and carbonyl function groups. Also, the ^{1}H NMR spectrum of compound **10a** recorded in DMSO-d_6 displayed a signal at δ 4.43, attributed to the pyridin-H. In the mass spectrum of compound **10b** a molecular ion peak was observed at m/z 525 (0.2%; M^+-HCN). The formation of **10** is assumed to proceed via Michael addition of methylene function group in **3** to the benzylidene **8** to yield Michael adduct **9** followed by intramolecular cyclization[21,22] at the cyano group to form thiazolopyridine **10** (Scheme 3). Also, thiazolopyridines **10** were synthesized by another synthetic route through ternary condensation of compound **3**, benzaldehyde **2** and malononitrile (1:1:1 molar ratio) in ethanolic piperidine under reflux. Similarly, cyclocondensation of compound **3b** with benzylidenemalononitriles **11** in refluxing ethanol containing piperidine afforded the novel thiazolopyridines **12a–c**. The mass spectrum of compound **12a** exhibited a molecular ion peak at m/z 481 (15%) and base peak at m/z 279. Also,



SCHEME 3

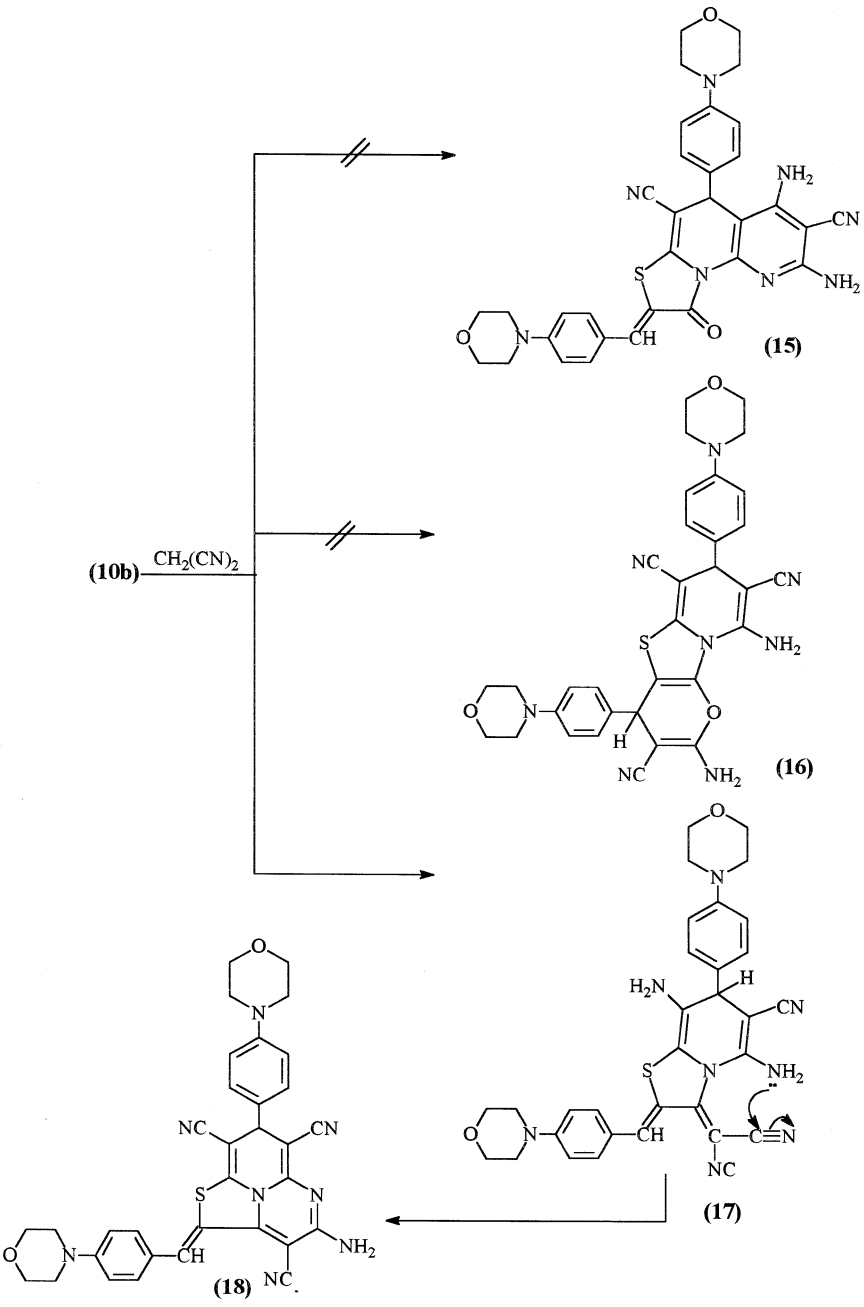
ternary condensation of thiazolidine **13**, 4-morpholinobenzaldehyde **2b** and malononitrile (1:1:1 molar ratio) under reflux in ethanolic piperidine afforded the thiazolopyridines **14a–c** (Scheme 3).

Our investigation was extended to study the reactivity of thiazolopyridine **10b**, which contain chalcone and *ortho*-amino carbonitrile moieties, towards malononitrile. Thus, three possible structures **15**, **16** and **18** can be formulated when compound **10b** was subjected to react with malononitrile in dioxane in the presence of piperidine under reflux (Scheme 4). The structure of the novel condensed system **18** was established and the other possible structures **15** and **16** were easily eliminated on the basis of analytical and spectral data. The infrared spectrum indicated the lack of a ring carbonyl function group and the presence of amino and cyano function groups. Also, the ^{1}H NMR spectrum of compound **18** recorded in DMSO-d_6 revealed the presence of a singlet at δ 4.19 attributed to pyridine-H in addition to morpholinyl, amino, methylidene, and aromatic protons. The formation of **18** is assumed to proceed through initial condensation of malononitrile with carbonyl function group in **10b** to form intermediate **17** followed by intramolecular cyclization to one of the cyano group and tautomerization to furnish **18** (Scheme 4).

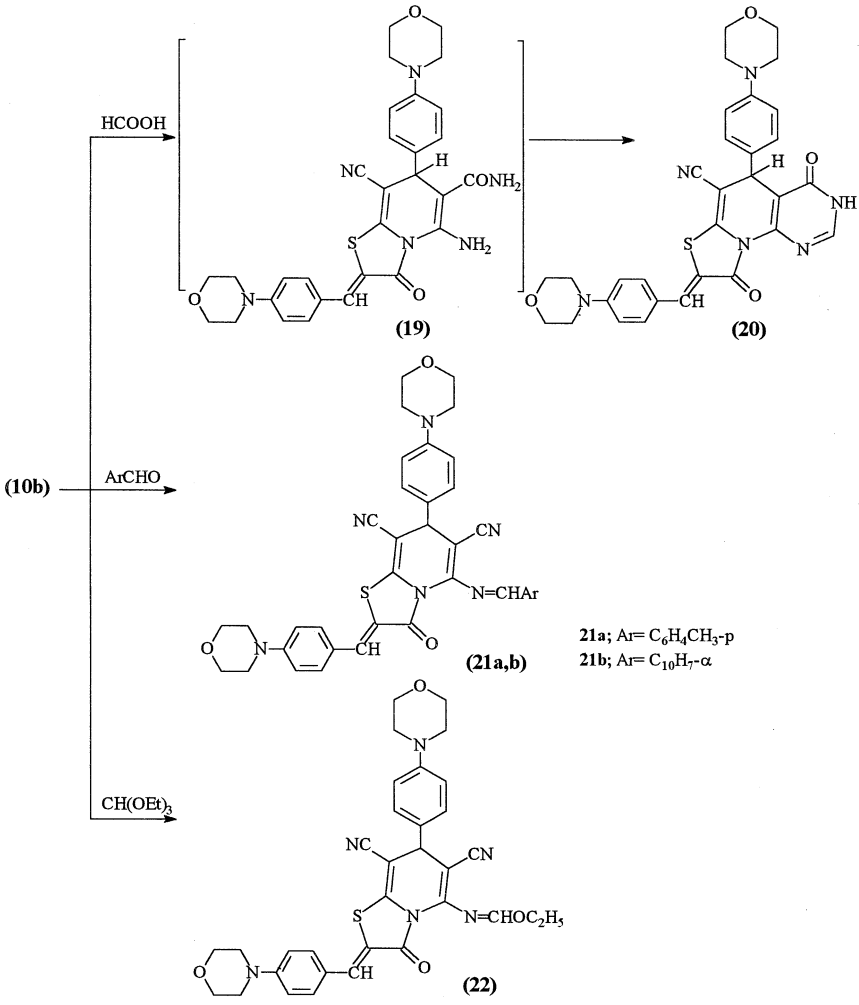
Refluxing of *ortho*-aminocarbonitrile **10b** with formic acid furnished the corresponding thiazolo[2′,3′:1,6]pyrido[2,3-d]pyrimidine derivative **20**. The formation of **20** is supposed to proceed through intermediate amide formation[23] **19**, resulting from the partial hydrolysis of cyano functionality present at position six of **10b**, followed by intramolecular cyclization with formic acid to give **20** (Scheme 5). Condensation of compound **10b** with aromatic aldehyde in dioxane containing a catalytic amount of triethylamine yielded the novel azomethine derivatives **21a**,**b**. Also, fusion of compound **10b** with triethyl orthoformate afforded the ethoxymethylene derivative **22** (Scheme 5).

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded (KBr) on a Perkin Elmer 1650 spectrophotometer. ^{1}H NMR spectra were recorded on Varian Gemini spectrometer 200 (200 MHz), using DMSO-d_6 as a solvent and TMS as internal standard. Chemical shifts are expressed as δ ppm units. Mass spectra were recorded on a gas chromatographic GC-MS qp 1000 Ex Shimadzu instrument at 70 eV. Microanalytical data were obtained from the Microanalytical Data Unit at Cairo University. Physical data for the synthesized compounds are given in Table I. Also, the spectral data are collected in Table II.



SCHEME 4



SCHEME 5

2-Cyanomethyl-5-[4-(piperidin-1-yl) or 4-(Morpholin-4-yl)benzylidenyl]-4,5-dihydro-4-thiazolinones (3a,b)

A mixture of compound **1**[24] (0.01 mmol) and benzaldehyde **2a**[25] or **2b**[25] (0.01 mmol) and piperidine (0.5 mL) in absolute ethanol (40 mL) was heated under reflux for 1 h, the solid product which produced on heating was collected to give **3a** and **3b** respectively.

MS (**3b**): 313 (M^+; 78%), 314 (M + 1; base peak), 315 (M + 2; 18.8%), 255 (87.6%), 219 (12.5%), 161 (82.2%), 86 (2.8%) and 80 (27%).

TABLE I Physical Data for the Synthesized Compounds

Compd. no.	m.p. (°C)	Yield (%)	Solvent cryst.	Molecular formula (mol. wt.)	Elemental analyses calcd./found %		
					C	H	N
3a	235-7	67	Dioxane	$C_{17}H_{17}N_3OS$	65.57	5.50	13.49
				(311.41)	65.40	5.50	13.50
3b	210-1	74	Dioxane	$C_{16}H_{15}N_3O_2S$	61.32	4.82	13.41
				(313.38)	61.30	4.70	13.40
5	260-2	82	Dioxane	$C_{19}H_{17}N_5O_2S$	60.14	4.52	18.46
				(379.44)	60.20	4.50	18.30
6	190-2	71	Dioxane	$C_{19}H_{20}N_4O_2S$	61.94	5.47	15.21
				(368.46)	61.80	5.40	15.10
7	250-2	74	Dioxane	$C_{19}H_{19}N_3O_3S$	61.77	5.18	11.37
				(369.45)	61.80	5.00	11.40
10a	262-4	65	Dioxane	$C_{32}H_{32}N_6OS$	70.05	5.88	15.32
				(548.72)	70.10	5.80	15.40
10b	>300	76	Dioxane	$C_{30}H_{28}N_6O_3S$	65.20	5.11	15.21
				(552.66)	65.20	5.10	15.30
12a	290-1	84	Dioxane	$C_{27}H_{23}N_5O_2S$	67.34	4.81	14.54
				(481.58)	67.30	4.80	14.60
12b	230-2	64	Dioxane	$C_{26}H_{20}ClN_5O_2S$	62.21	4.02	7.06
				(502.00)	62.20	4.10	7.20
12c	234-6	56	Dioxane	$C_{30}H_{23}N_5O_2S$	69.61	4.48	13.53
				(517.61)	69.70	4.40	13.40
14a	276-8	79	Dioxane	$C_{27}H_{23}N_5O_2S$	67.34	4.81	14.54
				(481.58)	67.40	4.80	14.60
14b	240-2	83	Dioxane	$C_{26}H_{20}FN_5O_2S$	64.32	4.15	14.42
				(485.54)	64.30	4.00	14.60
14c	238-9	80	Dioxane	$C_{30}H_{23}N_5O_2S$	69.61	4.48	13.53
				(517.61)	69.70	4.50	13.40
18	150-2	87	Dioxane	$C_{33}H_{28}N_8O_2S$	65.98	4.70	18.65
				(600.71)	65.80	4.70	18.70
20	152-4	67	Dioxane	$C_{31}H_{28}N_6O_4S$	64.12	4.86	14.47
				(580.67)	64.00	4.70	14.30
21a	260-2	62	Ethanol	$C_{38}H_{34}N_6O_3S$	69.70	5.23	12.83
				(654.80)	69.60	5.00	12.90
21b	243-4	69	Ethanol	$C_{41}H_{34}N_6O_3S$	71.28	4.96	12.17
				(690.83)	71.20	4.90	12.20
22	170-2	57	Dioxane	$C_{33}H_{32}N_6O_4S$	65.11	5.30	13.81
				(608.72)	65.10	5.20	13.60

5-Amino-7-imino-2-[4-(morpholin-4-yl)benzylidenyl]-3-oxo-2,3-dihydro-thiazolo[3,2-a]pyridin-6-carbonitrile (5)

Method A: A mixture of compound **3b** (0.01 mmol), malononitrile (0.01 mmol), and triethylamine (0.5 mL) in absolute ethanol (30 mL)

TABLE II Spectral Data of the Synthesized Compounds

Compd. no.	IR /ν_{max} (cm^{-1})	^1H NMR (δ/ppm) (DMSO-d_6)
3a	2929, 2851 (CH-aliph), 2201 (C≡N), 1702 (C═O).	1.59 (s, 6H, $3CH_2$), 3.34 (s, 4H, $N(CH_2)_2$), 4.04 (s, 2H, CH_2), 7.02–7.51 (m, 5H, 4H-Ar and methine proton).
3b	2958, 2851 (CH-aliph), 2198 (C≡N), 1709 (C═O).	
5	3392, 3319, 3284 (NH, NH_2), 2961, 2846 (CH─ aliph), 2184 (C≡N), 1701 (C═O), 1649 (C═N).	3.31 (s, 4H, $N(CH_2)_2$), 3.75 (s, 4H, $O(CH_2)_2$), 4.44 (d, 1H, pyridine-H), 6.93, 7.21 (2d, 4H, Ar-H), 7.12 (s, 1H, methine proton), 7.52 (s, 2H, NH_2), 7.72 (s, 1H, NH).
6	2923, 2854 (CH-aliph), 2183 (C≡N), 1681 (C═O).	3.10 (s, 6H, $N(CH_3)_2$), 3.38 (s, 4H, $N(CH_2)_2$), 3.75 (s, 4H, $O(CH_2)_2$), 6.91–7.60 (m, 5H, 4H-Ar and methine proton), 7.99 (s, 1H, methine-H).
7	2962, 2846 (CH-aliph), 2198 (C≡N), 1705 (C═O).	1.11 (t, 3H, CH_3), 3.30 (s, 4H, $N(CH_2)_2$), 3.74 (s, 4H, $O(CH_2)_2$), 4.05 (q, 2H, OCH_2), 6.97–8.15 (m, 6H, 4H-Ar and two methine protons).
10a	3421, 3327 (NH_2), 2929, 2851 (CH-aliph), 2202 (C≡N), 1696 (C═O).	1.61 (s, 12H, $6CH_2$), 3.36 (s, 8H, two $N(CH_2)_2$), 4.43 (s, 1H, pyridine-H), 6.91–7.53 (m, 10H, 8H-Ar and NH_2), 7.71 (s, 1H, methine-H).
10b	3394, 3322 (NH_2), 2961, 2848 (CH-aliph), 2184 (C≡N), 1702 (C═O).	3.38 (s, 8H, two $N(CH_2)_2$), 3.76 (s, 8H, two 3.38 $(O(CH_2)_2$), 4.47 (s, 1H, pyridine-H), 6.99–7.85 (m, 11H, 8H-Ar, NH_2 and methine-H).
12a	3398, 3323 (NH_2), 2961, 2847 (CH-aliph), 2185 (C≡N), 1702 (C═O).	
12b	3387, 3330 (NH_2), 2959, 2852 (CH-aliph), 2194 (C≡N), 1713 (C═O).	3.39 (s, 4H, $N(CH_2)_2$), 3.75 (s, 4H, $O(CH_2)_2$), 4.45 (s, 1H, pyridine-H), 6.90–7.80 (m, 10H, 8H-Ar and NH_2), 8.00 (s, 1H, methine-H).
12c	3396, 3324 (NH_2), 2958, 2850 (CH-aliph), 2191 (C≡N), 1687 (C═O).	3.25 (s, 4H, $N(CH_2)_2$), 3.73 (s, 4H, $O(CH_2)_2$, 4.42 (s, 1H, pyridine-H), 6.92–8.10 (m, 14H, 11H-Ar, NH_2 and methine-H).
14a	3415, 3327 (NH_2), 2959, 2851 (CH-aliph), 2193 (C≡N), 1701 (C═O).	2.33 (s, 3H, CH_3), 3.34 (s, 4H, $N(CH_2)_2$), 3.75 (s, 4H, $O(CH_2)_2$), 4.46 (s, 1H, pyridine -H), 6.93–7.53 (m, 10H, 8H-Ar and NH_2), 7.75 (s, 1H, methine-H).
14b	3413, 3320 (NH_2), 2959, 2853 (CH-aliph), 2194 (C≡N), 1692 (C═O).	3.25 (s, 4H, $N(CH_2)_2$), 3.75 (s, 4H, $O(CH_2)_2$), 4.44 (s, 1H, pyridine-H), 6.92 (m, 10H, 8H-Ar and NH_2), 7.78 (s, 1H, methine-H).
14c	3400, 3331 (NH_2), 2959, 2852 (CH-aliph), 2210 (C≡N), 1695 (C═O).	
18	3330, 3209 (NH_2), 2957, 2855 (CH-aliph), 2214 (C≡N).	3.35 (s, 8H, two $N(CH_2)_2$), 3.76 (s, 8H, two $O(CH_2)_2$), 4.19 (s, 1H, pyridine-H), 7.07, 7.90 (2d, 8H, Ar-H), 7.42 (s, 1H, methine-H), 8.13 (s, 2H, NH_2).

(Continued on next page)

TABLE II Spectral Data of the Synthesized Compounds

Compd. no.	IR /ν_{max} (cm^{-1})	^1H NMR (δ/ppm) (DMSO-d_6)
20	3165 (NH), 2957, 2852 (CH-aliph), 2214 (C≡N), 1678 (C═O, broad).	3.34 (s, 8H, two $N(CH_2)_2$), 3.74 (s, 8H, two $O(CH_2)_2$), 4.10 (s, 1H, pyridine-H), 6.92–7.90 (m, 9H, 8H-Ar and methine-H), 8.01 (s, 1H, NH), 8.14 (s, 1H, CH-pyrimidine).
21a	2960, 2853 (CH-aliph), 2214 (C≡N), 1704 (C═O).	2.21 (s, 3H, CH_3), 3.28 (m, 8H, two $N(CH_2)_2$), 3.74 (s, 8H, two $O(CH_2)_2$), 4.15 (s, 1H, pyridine-H), 6.90–7.80 (m, 9H, 8H-Ar and methine-H), 8.20 (s, 1H, CH═N).
21b	2957, 2852 (CH-aliph), 2203 (C≡N), 1703 (C═O).	
22	2962, 2854 (CH-aliph), 2214 (C≡N), 1712 (C═O).	1.22 (t, 3H, CH_3), 3.38 (s, 8H, two $N(CH_2)_2$, 3.73 (s, 8H, two $O(CH_2)_2$), 4.10 (q, 2H, OCH_2), 4.67 (s, 1H, pyridine-H), 6.97–7.89 (m, 9H, 8H-Ar and methine-H), 8.13 (s, 1H, CH═N).

was heated under reflux for 10 min, the solid product which produced on heating was collected to give **5**.

MS (**5**): 379 (M^+; 25%), 378 (M-1; base peak), 216 (75%), 147 (34%), 131 (28%) and 77 (30%).

Method B: A mixture of compound **1** (0.01 mmol), benzaldehyde **2b** (0.01 mmol), malononitrile (0.01 mmol), and triethylamine (0.5 mL) in absolute ethanol (30 mL) was heated under reflux for 10 min and the solid product was collected to give **5**.

3-Dimethylamino-2-[5-(4-(morpholin-4-yl)benzylidenyl)-4-oxo-4,5-dihydro-thiazol-2-yl]acrylonitrile (6)

A mixture of compound **3b** (0.01 mmol) and dimethylformamide-dimethylacetal (0.01 mmol) in dry *m*-xylene (30 mL) was refluxed for 3 h, then cooled and the precipitated product was filtered off, washed with ether to give **6**.

3-Ethoxy-2-[5-(4-(morpholin-4-yl)benzylidenyl)-4-oxo-4,5-dihydro-thiaol-2-yl]acrylonitrile (7)

A mixture of compound **3b** (0.01 mmol) and triethyl orthoformate (5 mL) was heated under reflux for 3 h, then allowed to cool and poured into pet. ether 40/60 and the solid product was collected to give **7**.

5-Amino-3-oxo-2-[4-(piperidin-1-yl)benzylidenyl]-7-[4-(piperidin-1-yl)phenyl]-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6,8-dicarbonitrile (10a) and 5-Amino-3-oxo-2-[4-(morpholin-4-yl)benzylidenyl]-7-[4-(morpholin-4-yl)phenyl]-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6,8-dicarbonitrile (10b)

Method A: General Procedure: A mixture of compound **3** (0.01 mmol), benzylidenemalononitrile **8** (0.01 mmol), and piperidine (0.01 mmol) in absolute ethanol (30 mL) was heated under reflux for 2 h, the solid product which produced on heating was collected to give **10**.

MS (**10b**): 525 (M-HCN; 0.2%), 313 (31%), 255 (28%), 176 (44%), 162 (40%) and (86; base peak).

Method B: A mixture of compound **3** (0.01 mmol), malononitrile (0.01 mmol), benzaldehyde **2** (0.01 mmol), and piperidine (0.01 mmol) in absolute ethanol was heated under reflux for 2 h, the solid product which produced on heating was collected to give **10**.

5-Amino-3-oxo-2-[4-(morpholin-4-yl)benzylidenyl]-7-aryl-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6,8-dicarbonitriles (12a–c): General Procedure

A mixture of compound **3b** (0.01 mmol), benzylidenemalononitrile **11** (0.01 mmol), and piperidine (0.01 mmol) in absolute ethanol (30 mL) was heated under reflux for 3 h. The solid product which produced on heating was collected to give **12**.

MS (**12a**): 481 (M^+; 15%), 417 (94%), 337 (78%), 279 (base peak), 170 (80%), 149 (57%) and 104 (27%).

5-Amino-2-arylmethylidene-7-[4-(morpholin-4-yl)phenyl]-3-oxo-2,3-dihydro-7H-thiazolo[3,2-a]pyridin-6,8-dicarbonitriles (14a–c): General procedure

A mixture of compound **3**[22] (0.01 mmol), benzaldehyde **2b** (0.01 mmol), malononitrile (0.01 mmol), and piperidine (0.01 mmol) in absolute ethanol (30 mL) was heated under reflux for 30 min and the precipitate was collected by filtration to give **14a–c**.

4-Amino-2-[4-(morpholin-4-yl)benzylidenyl]-7-[4-(morpholin-4-yl)-phenyl]-2,7-dihydro-1-thia-5,8b-diaza-acenaphthylene-3,6,8-tricarbonitrile (18)

A mixture of compound **10b** (0.01 mmol), malononitrile (0.01 mmol), and piperidine (0.01 mmol) in dioxane (20 mL) was heated under reflux

for 3 h, then allowed to cool. The solid product was collected to give **18**.

8-[4-(Morpholin-4-yl)benzylidenyl]-5-[4-(morpholin-4-yl)phenyl]-3,4,8,9-tetrahydro-5H-4-oxo-thiazolo[2′,3′:1,6]pyrido[2,3-d]-pyrimidin-6-carbonitrile (20)

A mixture of compound **10b** (0.01 mmol) in formic acid (10 mL) was heated under reflux for 12 h. The reaction mixture was concentrated in vacuo and the solid product was collected, washed with water to give **20**.

2-[4-(Morpholin-4-yl)benzylidenyl]-5-arylideneamino-7-[4-(morpholin-4-yl)phenyl]-3-oxo-2,3-dihydro-7H-thiazolo[3,2-a]-pyridin-6,8-dicarbonitriles (21a,b)

A mixture of compound **10b** (0.01 mmol) and aromatic aldehydes (0.01 mmol) in dioxane (20 mL) and a few drops of piperidine was refluxed for 3 h, then allowed to cool and poured into cold water (60 mL) and the solid product was collected to give **21a**,**b**.

5-Ethoxmethyleneamino-2-[4-(morpholin-4-yl)benzylidenyl]-7-[4-(morpholin-4-yl)phenyl]-3-oxo-2,3-dihydro-7H-thiazolo[3,2-a]-pyridin-6,8-dicarbonitrile (22)

A mixture of compound **10b** (0.01 mmol) and triethyl orthoformate (3 mL) was heated under reflux for 1 h. The solid product was collected to give **22**.

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