ELSEVIER

www.elsevier.nl/locate/farmac

Il Farmaco 55 (2000) 109–118

IL FARMACO

Synthesis of some new thiazolo[3,2-*a*]pyridines and related heterocyclic systems

Marzoog S. Al-Thebeiti *

Department of Chemistry, Faculty of Applied Sciences, Umm Al-Qura University, Makkah Almukkarramah, PO Box 6876, Saudi Arabia

Received 15 July 1999; accepted 8 November 1999

Abstract

New 2,7-disubstituted 5-amino-6,8-dicyano-2,3-dihydro-3-oxo thiazolo[3,2-*a*]pyridines have been prepared. Their cyclization with formamide, nitrous acid and triethylorthoformate afforded a series of polycyclic heterocycles containing condensed pyrimidine and triazine rings. Antifungal tests were also performed.

Keywords: Thiazolopyridines; Thiazolopyridopyrimidines; Thiazolopyridotriazines

1. Introduction

Several annulated pyridines isolated from natural sources possess a broad spectrum of therapeutic activity. Members of this class were found to be protectors against gastric erosion [1] and coronary vasodilator and blood-pressure-heightening agents [2]. They also proved to be tuberculostatic, antiviral, fungicidal, insecticidal and pesticidal [3,4]. In addition to the previously mentioned properties, many thiazolopyridines, thiazolopyrimidines and thiazolotriazines are used as therapeutic tools [5–7]. The quinoline derivatives were reported to be antibacterial and antifungal agents [8–13]. As a continuation of our previous work [14–23] and considering the particular interest inherent in the above-mentioned properties, we aimed to synthesize the title compounds in the hope that members of them would find interesting biological applications.

2. Chemistry

5-Amino-2,3-dihydro-7*H*-7-(8′-hydroxyquinolin-5′-yl)-2-(8″-hydroxyquinolin-5″-yl methylidene)-3-oxothiazolo[3,2-*a*]pyridin-6,8-dicarbonitrile (**3**) was prepared by the reaction of the aldehyde **1** with malononitrile and thioglycolic acid (2:2:1 molar ratio) in ethanol with a catalytic amount of piperidine (Method A). The treatment of **2** with thioglycolic acid in a molar ratio of 2:1 in the presence of a catalytic amount of piperidine afforded the structural evidence of **3** (Method B) (Scheme 1).

Fused heterocyclic-like thiazolopyridopyrimidine **4** and thiazolopyrido-1,2,3-triazines **5** were produced by the reaction of thiazolo[3,2-*a*]pyridine (**3**) with formamide and nitrous acid, respectively (Scheme 1).

Afterwards, our attempts were directed towards the synthesis of polyfunctional 7-arylsubstituted 2,3-dihydro-7*H*-2[8′-hydroxyquinolin-5′-yl methylidene]thiazolo[3,2-*a*]pyridines by reaction of **6** with arylidenemalonodinitriles or by using equimolar amounts of **1** and arylaldehyde instead of 2 mol of **1** as previously described (Scheme 2).

The thiazolopyridine derivatives **7a**–**g** proved to be a useful key intermediate in the synthesis of fused heterocyclic derivatives. Thus, when **7a**–**g** were reacted with triethylorthoformate they gave the corresponding ethyoxymethylene derivatives **8a**–**g**, which by treatment with aniline compounds underwent aminolysis and cyclization to give in a 'one step reaction' fused **9a**–**g**. Furthermore, **7a**–**g** gave the corresponding thiazolopyridopyrimidine derivatives **10a**–**g** by treatment with formamide and the thiazolopyridotriazine derivatives **11a**–**g** by means of diazotization with sodium nitrite in a mixture of hydrochloric and acetic acid (Scheme 3).

* Tel.: +966-2-559 4010; fax: +966-2-558 5830.
E-mail address: althebeiti@yahoo.com (M.S. Al-Thebeiti)

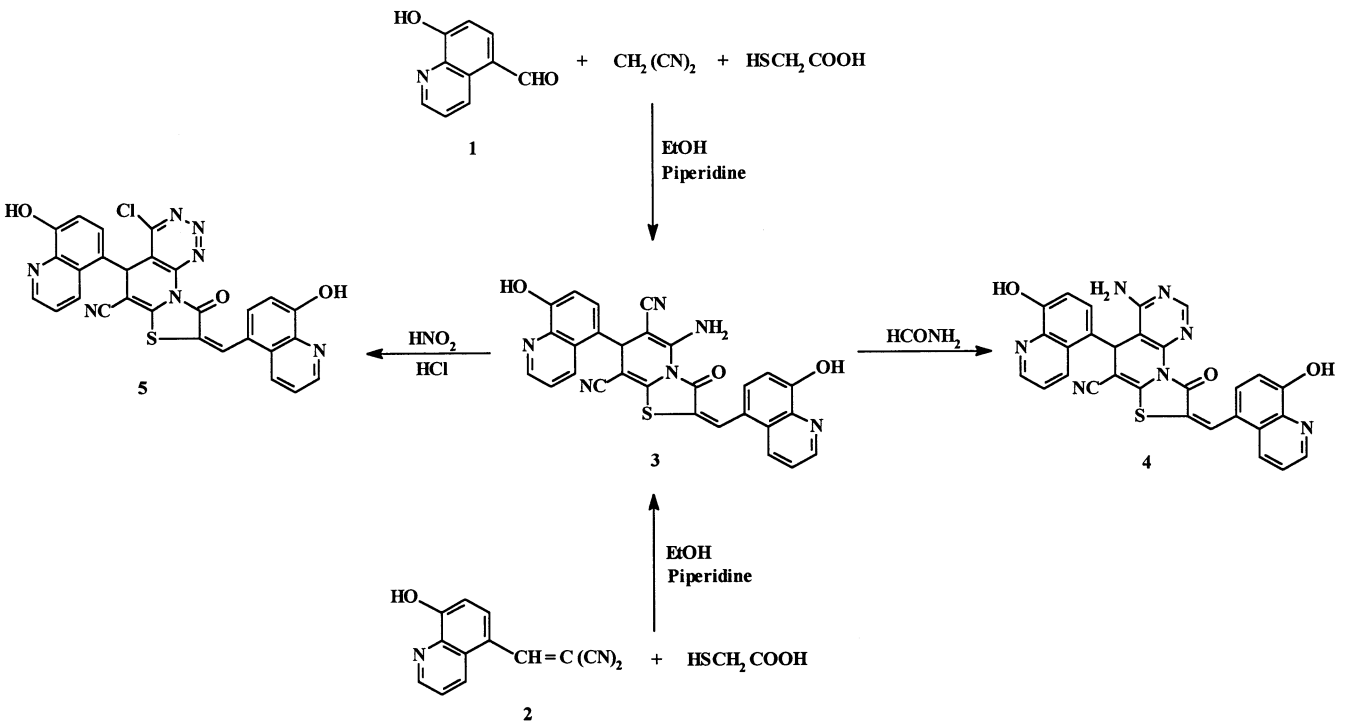
0014-827X/00/$ - see front matter
PII: S0014-827X(99)00130-5

The chlorine atom reactivity of **11c** was highlighted by its easy displacement with nucleophilic reagents such as hydrazine hydrate to give the hydrazino derivative **12** which, in turn, proved to be a useful intermediate.

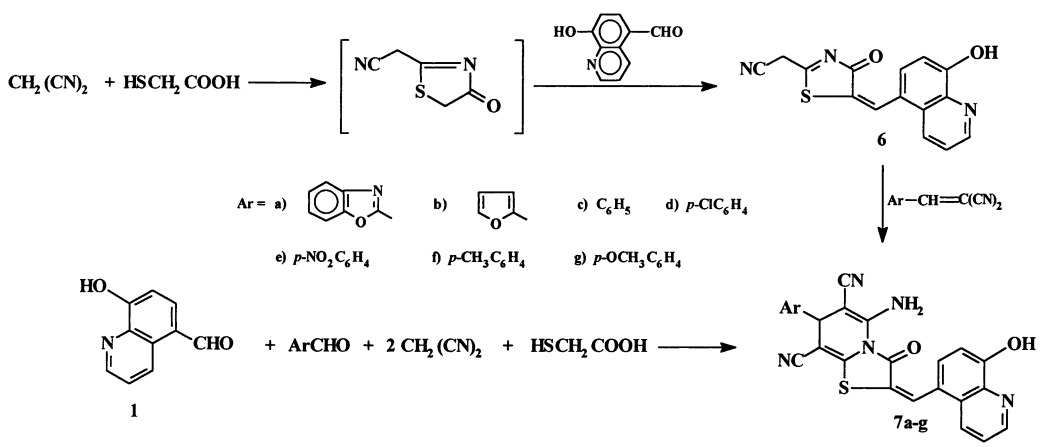
In fact, the triazolo derivatives **13** and **14** were produced from the reaction of **12** with formic acid and carbon disulfide, respectively. In addition, treatment of **12** in acetic acid and an aqueous solution of sodium nitrite, at room temperature, gave the azido derivative **15**, the structure of which was assigned on the basis of its IR spectral data (N_3 stretching at 2140 cm^{-1}), thus ruling out the alternative tetrazolo structure **15c**. Finally, the key intermediate **7c** when reacted with ethyl cyanoacetate afforded 8-amino-3,6-dioxo-2-(8′-hydroxyquinolin-5′-yl methylidene)-9-phenyl-2,3,5,9-tetrahydrothiazolo[3,2-*a*] [1,8]naphthyridin-7,10-dicarbo-nitrile (**16**).

3. Experimental

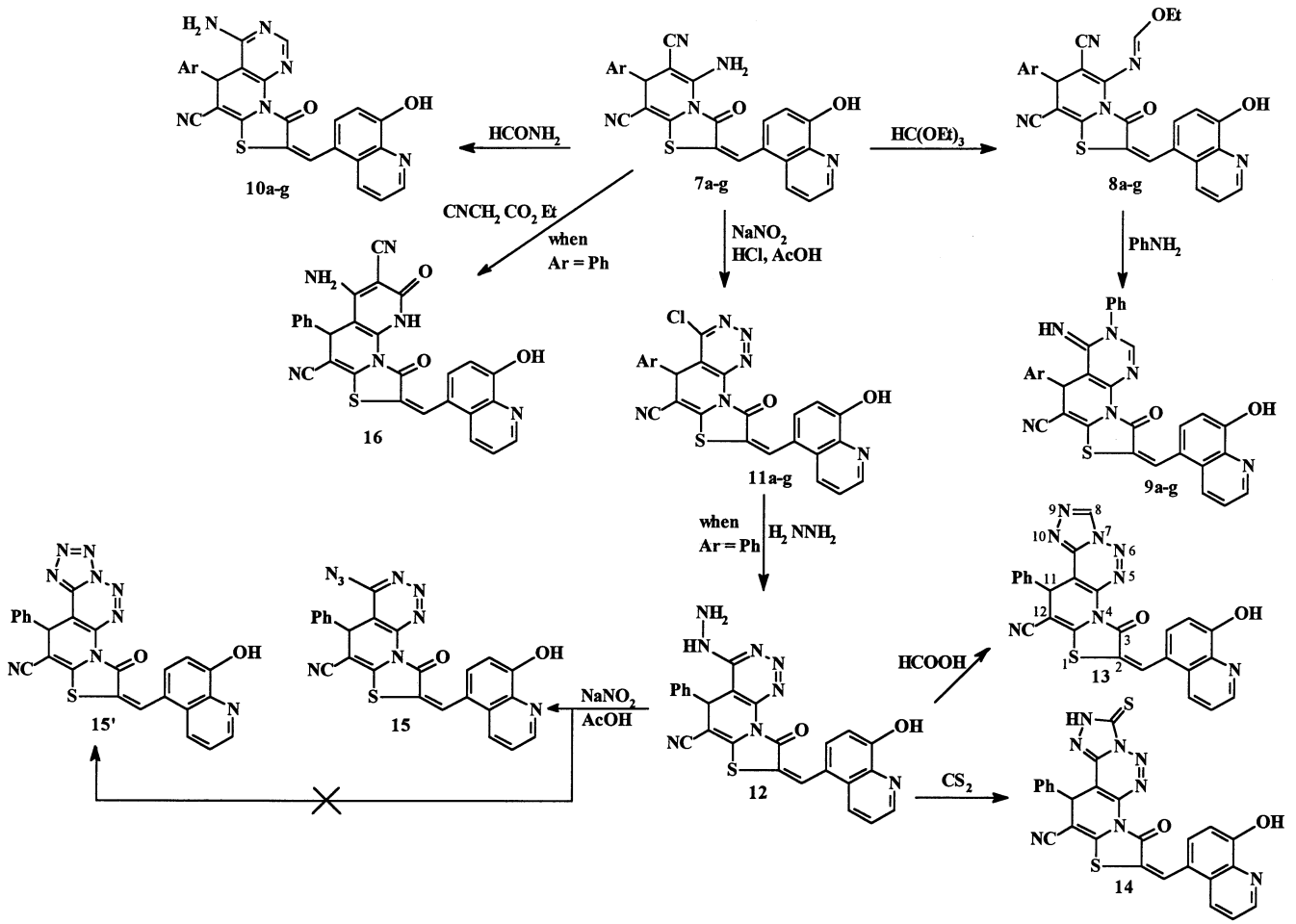
All melting points are uncorrected. IR (cm^{-1}) spectra were recorded on a Pye–Unicam SP3-100 spectrophotometer. ^1H NMR spectra were recorded on a 90 MHz Varian EM-390 NMR spectrometer in suitable deuterated solvents using TMS as an internal standard. Mass spectra were recorded on a Jeol JMS 600 instrument. Elemental analyses were determined on a



Scheme 1.



Scheme 2.



Scheme 3.

Perkin–Elmer 240 C. Analyses indicated by the symbols were within ±0.4% of the theoretical values.

3.1. 5-Amino-2,3-dihydro-7H-7-(8′-hydroxyquinolin-5′-yl)-2-(8″-hydroxyquinolin-5″-yl methylidene)-3-oxothiazolo[3,2-a]pyridin-6,8-dicarbonitrile ***(3)***

3.1.1. General procedure

3.1.1.1. Method A. A solution of **1** (0.02 mol), malononitrile (0.02 mol) and thioglycolic acid (0.01 mol) in ethanol (50 ml) and a catalytic amount of piperidine was heated under reflux for 5 h. The reaction mixture was cooled at room temperature (r.t.) and the solution was concentrated by evaporation under reduced pressure and then the product was collected and recrystallized from ethanol as pale brown crystals, m.p. 230–232°C (58% yield). *Anal.* $C_{28}H_{16}N_6O_3S$ (C, H, N, S).

3.1.1.2. Method B. A solution of **2** (0.02 mol) and thioglycolic acid (0.01 mol) in ethanol (50 ml) and a catalytic amount of piperidine was refluxed for 5 h. The solvent was evaporated and the solid product was collected by filtration and recrystallized from ethanol as pale brown crystals, m.p. 230–232°C (58% yield). IR (ν cm^{-1}, KBr): 3250–3350 (NH_2), 2200 (CN), 1700 (C=O). ^1H NMR (δ ppm, DMSO-d_6): 6.00 (s, 2H, NH_2), 6.60–8.70 (m, 14H, arom.). MS, m/e 516. *Anal.* $C_{28}H_{16}N_6O_3S$ (C, H, N, S).

3.2. 8-Amino-2,3-dihydro-9H-9-(8′-hydroxyquinolin-5′-yl)-2-(8″-hydroxyquinolin-5″-yl methylidene)-3-oxo thiazolo[2′,3′:1,6]pyrido[2,3-d]pyrimidin-10-carbonitrile ***(4)***

A mixture of **3** (0.01 mol) and formamide (15 ml) was refluxed for 2 h. The solid product thus formed, after cooling, was filtered off and recrystallized from dioxane as yellowish–brown crystals, m.p. 296–298°C (dec.) (51% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3200–3300 (NH_2), 2200 (CN), 1710 (C=O). ^1H NMR (δ ppm, CF_3COOD): 7.20 (s, 1H, pyrimidine ring), 7.25 (s, 1H, pyridine ring), 7.40 (s, 1H, methylidene), 7.50–8.30 (m, 12H, arom.). MS, m/e 543. *Anal.* $C_{29}H_{17}N_7O_3S$ (C, H, N, S).

3.3. 8-Chloro-2,3-dihydro-9H-9-(8′-hydroxyquinolin-5′-yl)-2-(8″-hydroxyquinolin-5″-yl methylidene)-3-oxothiazolo[2′,3′:1,6]pyrido[2,3-d][1,2,3]-triazin-10-carbonitrile (**5**)

To a cold stirred solution of **3** (0.01 mol) in a mixture of acetic acid (20 ml) and hydrochloric acid (10 ml) sodium nitrite (0.01 mol in 10 ml H_2O) was added for 30 min and the stirring was continued for 3 h in an ice bath. The product was collected and recrystallized from acetic acid as brown crystals, m.p. > 310°C (42% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 2210 (CN), 1700 (C=O). ^1H NMR (δ ppm, $CDCl_3$): 6.90–8.10 (m, 14H, arom.). MS, *m*/*e* 563/565. *Anal.* $C_{28}H_{14}ClN_7O_3S$ (C, H, Cl, N, S).

Table 1
Antifungal activity of thiazolopyridopyrimidines and thiazolopyridotriazines [a]

Comp.	*P. chrysogenum*	*F. moniliforme*	*R. stalonifer*	*A. terreus*
3	9	7		
4		5	10	8
5	15	9	12	16
6	5		8	
7a	11	5		
7b		9	5	
7c			8	11
7d	12		10	8
7e		7		10
7f			11	6
7g	8	5		
8a		10	8	
8b	10			9
8c	11		8	
8d	11	6		
8e				
8f	13	9		11
8g		11	7	
9a		8		8
9b				
9c	11	10		
9d			6	12
9e		8	9	
9f	9			
9g	7			
10a	12	6		9
10b			5	
10c		8	11	
10d		7	9	
10e	11			6
10f				12
10g	9	10	11	
11a	22	12	16	19
11b	17	10	13	17
11c	19	11	15	20
11d	25	14	17	21
11e	18	12	14	19
11f	17	10	15	18
11g	17	11	13	18
12	7	11	10	13
13	12	9	14	17
14	16	14	12	19
15	8	10	9	11
16		9	4	6

[a] The activity is expressed as the diameter of the inhibitor zone (mm) and only the active compounds are indicated.

3.4. 2,3-Dihydro-4-oxo-5-(8′-hydroxyquinolin-5′-yl-methylidene)thiazolo-2-carbonitrile (**6**)

A mixture of malononitrile (0.01 mol) and thioglycolic acid (0.01 mol) was heated under reflux at 120°C for 30 min, then absolute ethanol (50 ml) and 8-hydroxyquinoline-5-carboxyaldehyde were added and the mixture was refluxed for 6 h. The solvent was evaporated and the solid product was collected and recrystallized from dioxane as pale brown crystals, m.p. 211–213°C (dec.) (39% yield). IR (ν cm^{-1}, KBr): 3490 (OH), 2200 (CN), 2890 (CH aliph.), 1710 (C=O). ^1H NMR (δ ppm, $CDCl_3$): 4.50 (s, 2H, CH_2), 6.80–7.90 (m, 7H, arom.). MS, *m*/*e* 295. *Anal.* $C_{15}H_9N_3O_2S$ (C, H, N, S).

3.5. 7-Arylsubstituted 5-amino-2,3-dihydro-7H-2-(8′-hydroxyquinolin-5′-yl-methylidene)-3-oxothiazolo-[3,2-a]pyridin-6,8-dicarbonitrile (**7a–g**)

3.5.1. General procedure

These compounds were prepared as previously described in method A by using **1** (0.01 mol) and the selected aldehydes (0.01 mol) instead of **1** (0.02 mol) or by the interaction of **6** (0.01 mol) and arylidenemalononitrile (0.01 mol) in ethanol (50 ml) on heating under reflux for 7 h. The reaction mixture was cooled and the product was collected by filtration and recrystallized from the proper solvent.

7a: Yellowish–brown crystals from dioxane, m.p. 248–250°C (51% yield). IR (ν cm^{-1}, KBr): 3080–3180 (NH_2), 2200 (CN), 1690 (C=O). ^1H NMR (δ ppm, DMSO-d_6): 5.20 (s, 2H, NH_2), 6.5–7.7 (m, 12H, arom.). MS, *m*/*e* 490. *Anal.* $C_{26}H_{14}N_6O_3S$ (C, H, N, S).

7b: Brown crystals from ethanol, m.p. 296–298°C (61% yield). IR (ν cm^{-1}, KBr): 3130–3230 (NH_2), 2200 (CN), 1700 (C=O). ^1H NMR (δ ppm, DMSO-d_6): 5.20 (s, 2H, NH_2), 6.50–7.90 (m, 11H, arom.). MS, *m*/*e* 439. *Anal.* $C_{23}H_{13}N_5O_3S$ (C, H, N, S).

7c: Brown crystals from diluted ethanol, m.p. 162–164°C (dec.) (53% yield). IR (ν cm^{-1}, KBr): 3200–3300 (NH_2), 2200 (CN), 1700 (C=O). ^1H NMR (δ ppm, CF_3COOD): 6.90–8.20 (m, 13H, arom.). *Anal.* $C_{25}H_{15}N_5O_2S$ (C, H, N, S).

7d: Yellowish–brown crystals from dioxane, m.p. 205–207°C (dec.) (56% yield). IR (ν cm^{-1}, KBr): 3230–3350 (NH_2), 2200 (CN), 1700 (C=O). ^1H NMR (δ ppm, CF_3COOD): 7.30–9.10 (m, 12H, arom.). *Anal.* $C_{25}H_{14}ClN_5O_2S$ (C, H, Cl, N, S).

Table 2
Analysis data of synthesized compounds

Comp.	Formula (mol. wt.)	Analysis (calc./found)				
		C	H	Cl	N	S
3	$C_{28}H_{16}N_6O_3S$	65.11	3.12		16.27	6.21
	(516.53)	65.22	3.21		16.16	6.11
4	$C_{29}H_{17}N_7O_3S$	64.08	3.15		18.04	5.90
	(543.56)	64.19	3.08		18.13	5.83
5	$C_{28}H_{14}ClN_7O_3S$	59.63	2.50	6.29	17.38	5.69
	(563.98)	59.55	2.61	6.32	17.48	5.74
6	$C_{15}H_9N_3O_2S$	61.01	3.07		14.23	10.86
	(295.32)	61.11	2.96		14.21	10.76
7a	$C_{26}H_{14}N_6O_3S$	63.67	2.88		17.13	6.54
	(490.50)	63.77	2.82		17.21	6.46
7b	$C_{23}H_{13}N_5O_3S$	62.86	2.98		15.94	7.30
	(439.45)	62.78	3.04		15.87	7.39
7c	$C_{25}H_{15}N_5O_2S$	66.80	3.36		15.58	7.13
	(449.49)	66.71	3.44		15.67	7.22
7d	$C_{25}H_{14}ClN_5O_2S$	62.05	2.92	7.33	14.47	6.62
	(483.93)	62.11	2.86	7.28	14.54	6.56
7e	$C_{25}H_{14}N_6O_4S$	60.72	2.85		17.00	6.48
	(494.48)	60.83	2.76		16.91	6.58
7f	$C_{26}H_{17}N_5O_2S$	67.37	3.70		15.11	6.92
	(463.51)	67.48	3.80		15.16	7.02
7g	$C_{26}H_{17}N_5O_3S$	65.13	3.57		14.61	6.69
	(479.51)	65.23	3.49		14.55	6.80
8a	$C_{29}H_{18}N_6O_4S$	63.73	3.32		15.38	5.87
	(546.56)	63.83	3.41		15.42	5.97
8b	$C_{26}H_{17}N_5O_4S$	63.02	3.46		14.13	6.47
	(495.51)	63.12	3.52		14.27	6.42
8c	$C_{28}H_{19}N_5O_3S$	66.52	3.79		13.85	6.34
	(505.55)	66.43	3.72		13.92	6.41
8d	$C_{28}H_{18}ClN_5O_3S$	62.28	3.36	6.57	12.97	5.94
	(540.00)	62.39	3.41	6.66	12.89	5.87
8e	$C_{28}H_{18}N_6O_5S$	61.09	3.30			
	(550.55)	61.20	3.36		15.26	5.82
8f	$C_{29}H_{21}N_5O_3S$	67.04	4.07		13.48	6.17
	(519.58)	67.14	4.12		13.56	6.22
8g	$C_{29}H_{21}N_5O_4S$	65.04	3.95		13.08	5.99
	(535.58)	65.12	3.86		13.14	5.91
9a	$C_{33}H_{19}N_7O_3S$	66.77	3.23		16.52	5.40
	(593.62)	66.88	3.29		16.61	5.34
9b	$C_{30}H_{18}N_6O_3S$	66.41	3.34		15.49	5.91
	(542.57)	66.32	3.30		15.41	5.99
9c	$C_{32}H_{20}N_6O_2S$	69.55	3.65		15.21	5.80
	(552.61)	69.66	3.71		15.31	5.90
9d	$C_{32}H_{19}ClN_6O_2S$	65.47	3.26	6.04	14.32	5.46
	(587.05)	65.57	3.31	6.11	14.25	5.42
9e	$C_{32}H_{19}N_7O_4S$	64.32	3.20		16.41	5.36
	(597.61)	64.20	3.12		16.49	5.42
9f	$C_{33}H_{22}N_6O_2S$	69.95	3.91		14.83	5.66
	(566.64)	70.05	4.01		14.91	5.72

Table 2 (Continued)

Comp.	Formula (mol. wt.)	Analysis (calc./found)				
		C	H	Cl	N	S
9g	$C_{33}H_{22}N_6O_3S$ (582.64)	68.03 68.18	3.81 3.92		14.42 14.51	5.50 5.44
10a	$C_{27}H_{15}N_7O_3S$ (517.52)	62.66 62.76	2.92 3.01		18.95 19.02	6.19 6.27
10b	$C_{24}H_{14}N_6O_3S$ (466.47)	61.80 61.91	3.03 3.12		18.02 18.16	6.87 6.96
10c	$C_{26}H_{16}N_6O_2S$ (476.51)	65.54 65.65	3.38 3.44		17.64 17.71	6.73 6.69
10d	$C_{26}H_{15}ClN_6O_2S$ (510.96)	61.12 61.23	2.96 3.03	6.94 7.03	16.45 16.56	6.27 6.33
10e	$C_{26}H_{15}N_7O_4S$ (521.51)	59.88 59.75	2.90 3.01		18.80 18.71	6.15 6.22
10f	$C_{27}H_{18}N_6O_2S$ (490.54)	66.11 66.12	3.70 3.62		17.13 17.07	6.54 6.61
10g	$C_{27}H_{18}N_6O_3S$ (506.54)	64.02 64.12	3.58 3.62		16.59 16.67	6.33 6.21
11a	$C_{26}H_{12}ClN_7O_3S$ (537.94)	58.05 58.17	2.25 2.34	6.59 6.54	18.23 18.17	5.96 6.06
11b	$C_{23}H_{11}ClN_6O_3S$ (486.89)	56.74 56.88	2.28 2.36	7.28 7.33	17.26 17.34	6.58 6.62
11c	$C_{25}H_{13}ClN_6O_2S$ (496.93)	60.43 60.53	2.64 2.71	7.13 7.23	16.91 16.94	6.45 6.39
11d	$C_{25}H_{12}Cl_2N_6O_2S$ (531.38)	56.51 56.60	2.28 2.27	13.34 13.42	15.82 15.90	6.03 6.19
11e	$C_{25}H_{12}ClN_7O_4S$ (541.93)	55.41 55.31	2.23 2.26	6.54 6.49	18.09 18.13	5.92 5.81
11f	$C_{26}H_{15}ClN_6O_2S$ (510.96)	61.12 61.22	2.96 3.01	6.94 6.89	16.45 16.51	6.27 6.22
11g	$C_{26}H_{15}ClN_6O_3S$ (526.96)	59.26 59.36	2.87 2.82	6.73 6.86	15.95 15.88	6.08 6.12
12	$C_{25}H_{16}N_8O_2S$ (492.51)	60.97 60.90	3.27 3.31		22.75 22.81	6.51 6.49
13	$C_{26}H_{14}N_8O_2S$ (502.51)	62.15 62.20	2.81 2.78		22.30 22.34	6.38 6.42
14	$C_{26}H_{14}N_8O_2S_2$ (534.57)	58.42 58.34	2.64 2.66		20.96 20.91	11.99 12.07
15	$C_{25}H_{13}N_9O_2S$ (503.50)	59.64 59.58	2.60 2.57		25.04 25.10	6.37 6.42
16	$C_{28}H_{16}N_6O_3S$ (516.53)	65.11 65.16	3.12 3.15		16.27 16.22	6.21 6.25

7e: Brown crystals from ethanol, m.p. 215–217°C (dec.) (44% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3150–3250 (NH_2), 2220 (CN), 1720 (C=O). ^1H NMR (δ ppm, $CDCl_3$): 5.50 (s, 2H, NH_2), 6.80–8.10 (m, 12H, arom.). MS, m/e 494. *Anal.* $C_{25}H_{14}N_6O_4S$ (C, H, N, S).

7f: Yellowish–brown crystals from ethanol, m.p. 290–292°C. (42% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3200–3300 (NH_2), 2210 (CN), 1720 (C=O). ^1H NMR (δ ppm, CF_3COOD): 2.30 (s, 3H, CH_3), 7.50–9.00 (m, 12H, arom.). *Anal.* $C_{26}H_{17}N_5O_2S$ (C, H, N, S).

7g: Pale brown crystals, m.p. 275–277°C. (47% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3230–3350 (NH_2), 2200 (CN), 1700 (C=O). ^1H NMR (δ ppm, CF_3COOD): 2.10 (s, 3H, CH_3), 7.80–8.90 (m, 12H, arom.). *Anal.* $C_{26}H_{17}N_5O_3S$ (C, H, N, S).

3.6. 7-Arylsubstituted 2,3-dihydro-5-ethoxy-methyleneamino-7H-2-(8′-hydroxyquinolin-5′-yl methylidene)-3-oxothiazolo[3,2-a]pyridin-6,8-dicarbonitrile (**8a–g**)

3.6.1. General procedure

A mixture of **7a–g** (0.01 mol) and triethylorthoformate (3 ml) in acetic acid (20 ml) was refluxed for 6 h. The reaction mixture was cooled, diluted with cold water and the solid product was collected and recrystallized from ethanol as pale brown crystals.

8a: m.p. 274–276°C (dec.) (60% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 2200 (CN), 1700 (C=O), 1610 (C=N). ^{1}H NMR (δ ppm, $CDCl_3$): 2.10 (t, 3H, CH_3, $J = 7.10$ Hz), 4.15 (q, 2H, CH_2, $J = 7.10$ Hz), 7.20–8.00 (m, 13H, arom. + N=CH). *Anal.* $C_{29}H_{18}N_6O_4S$ (C, H, N, S).

8b: m.p. 265–267°C (65% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 2200 (CN), 1690 (C=O), 1610 (C=N). ^{1}H NMR (δ ppm, $CDCl_3$): 2.10 (t, 3H, CH_3, $J = 7.10$ Hz), 4.15 (q, 2H, CH_2, $J = 7.10$ Hz), 7.30–8.25 (m, 12H, arom. + N=CH). MS, m/e 495. *Anal.* $C_{26}H_{17}N_5O_4S$ (C, H, N, S).

8c: m.p. 203–205°C (dec.) (56% yield). IR (ν cm^{-1}, KBr): 3490 (OH), 2200 (CN), 1710 (C=O), 1600 (C=N). ^{1}H NMR (δ ppm, $CDCl_3$): 2.10 (t, 3H, CH_3, $J = 7.10$ Hz), 4.15 (q, 2H, CH_2, $J = 7.10$ Hz), 7.20–8.00 (m, 14H, arom. + N=CH). *Anal.* $C_{28}H_{19}N_5O_3S$ (C, H, N, S).

8d: m.p. 230–232°C (51% yield). IR (ν cm^{-1}, KBr): 3490 (OH), 2200 (CN), 1700 (C=O), 1600 (C=N). ^{1}H NMR (δ ppm, $CDCl_3$): 1.95 (t, 3H, CH_3, $J = 6.95$ Hz), 4.15 (q, 2H, CH_2, $J = 6.95$ Hz), 7.30–8.20 (m, 13H, arom. + N=CH). *Anal.* $C_{28}H_{18}ClN_5O_3S$ (C, H, Cl, N, S).

8e: m.p. 250–252°C (55% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 2200 (CN), 1690 (C=O), 1590 (C=N). ^{1}H NMR (δ ppm, $CDCl_3$): 2.10 (t, 3H, CH_3, $J = 7.10$ Hz), 4.20 (q, 2H, CH_2, $J = 7.10$ Hz), 7.30–8.35 (m, 13H, arom.). MS, m/e 550. *Anal.* $C_{28}H_{18}N_6O_5S$ (C, H, N, S).

8f: m.p. 278–280°C (48% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 2200 (CN), 1690 (C=O), 1600 (C=N). ^{1}H NMR (δ ppm, $CDCl_3$): 2.10 (s, 3H, CH_3), 2.30 (t, 3H, CH_3, $J = 7.30$ Hz), 4.30 (q, 2H, CH_2, $J = 7.30$ Hz), 7.10–7.90 (m, 13H, arom. + N=CH). *Anal.* $C_{29}H_{21}N_5O_3S$ (C, H, N, S).

8g: m.p. 291–293°C (dec.) (49% yield). IR (ν cm^{-1}, KBr): 3480 (OH), 2200 (CN), 1710 (C=O), 1590 (C=N). ^{1}H NMR (δ ppm, $CDCl_3$): 1.90 (s, 3H, OCH_3), 2.40 (t, 3H, CH_3, $J = 7.25$ Hz), 4.15 (q, 2H, CH_2, $J = 7.25$ Hz), 7.30–8.10 (m, 13H, arom. + N=CH). *Anal.* $C_{29}H_{21}N_5O_4S$ (C, H, N, S).

3.7. 9-Arylsubstituted 2,3-dihydro-9H-2-(8′-hydroxy-quinolin-5′-yl methylidene)-8-imino-3-oxo-7-phenylthiazolo [2′,3′:1,6]pyrido[2,3-d]pyrimidin-10-carbonitrile (**9a–g**)

3.7.1. General procedure

A mixture of **8a–g** (0.01 mol) and aniline (2 ml) in ethanol (50 ml) was heated under reflux for 4 h. The reaction mixture was concentrated and allowed to stand overnight. The solid product was filtered off and recrystallized from the proper solvent.

9a: Yellow crystals from ethanol, m.p. 318–320°C (dec.) (61% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3355 (NH), 2230 (CN), 1715 (C=O). ^{1}H NMR (δ ppm, DMSO-d_6): 7.30–8.50 (m, 18H, arom.), 9.70 (s, 1H, NH). MS, m/e 593. *Anal.* $C_{33}H_{19}N_7O_3S$ (C, H, N, S).

9b: Yellowish–brown crystals from ethanol, m.p. 295–297°C (68% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3350 (NH), 2200 (CN), 1720 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 7.10–8.30 (m, 17H, arom.), 10.10 (s, 1H, NH). MS, m/e 542. *Anal.* $C_{30}H_{18}N_6O_3S$ (C, H, N, S).

9c: Pale brown crystals from dioxane, m.p. 230–233°C (dec.) (60% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3350 (NH), 2200 (CN), 1720 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 7.20–8.10 (m, 19H, arom.), 9.80 (s, 1H, NH). *Anal.* $C_{32}H_{20}N_6O_2S$ (C, H, N, S).

9d: Brown crystals from ethanol, m.p. 268–270°C (55% yield). IR (ν cm^{-1}, KBr): 3490 (OH), 3350 (NH), 2200 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 7.10–8.30 (m, 18H, arom.), 10.10 (s, 1H, NH). *Anal.* $C_{32}H_{19}ClN_6O_2S$ (C, H, Cl, N, S).

9e: Brown crystals from ethanol, m.p. 286–288°C (51% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3320 (NH), 2200 (CN), 1690 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 7.25–8.40 (m, 18H, arom.), 9.80 (s, 1H, NH). MS, m/e 597. *Anal.* $C_{32}H_{19}N_7O_4S$ (C, H, N, S).

9f: Brown crystals from ethanol, m.p. 305–307°C (dec.) (56% yield). IR (ν cm^{-1}, KBr): 3480 (OH), 3320 (NH), 2200 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 2.10 (s, 3H, CH_3) 7.30–8.10 (m, 18H, arom.). *Anal.* $C_{33}H_{22}N_6O_2S$ (C, H, N, S).

9g: Pale brown crystals from dioxane, m.p. > 310°C (45% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3330 (NH), 2220 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 1.95 (s, 3H, CH_3), 7.20–8.10 (m, 18H, arom.). MS, m/e 582. *Anal.* $C_{33}H_{22}N_6O_3S$ (C, H, N, S).

3.8. 9-Arylsubstituted 8-amino-2,3-dihydro-9H-2-(8′-hydroxyquinolin-5′-yl methylidene)-3-oxo thiazolo-[2′,3′:1,6]pyrido[2,3-d]pyrimidin-10-carbonitrile (**10a–g**)

3.8.1. General procedure

A mixture of **7a–g** (0.01 mol) and formamide (15 ml) was refluxed for 2 h. The solid product thus formed after cooling was filtered off and recrystallized from the proper solvent.

10a: Brown crystals from dioxane, m.p. 288–290°C. (53% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3200–3300 (NH_2), 2220 (CN), 1730 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 7.10 (s, 1H, pyrimidine ring), 7.25 (s, 1H, pyridine ring), 7.50 (s, 1H, methylidene), 7.55–7.80 (m, 10H, arom.). MS, *m/e* 517. *Anal.* $C_{27}H_{15}N_7O_3S$ (C, H, N, S).

10b: Brown crystals from dioxane, m.p. > 310°C (48% yield). IR (ν cm^{-1}, KBr): 3480 (OH), 3200–3300 (NH_2), 2220 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 6.90 (s, 1H, pyrimidine ring), 7.00 (s, 1H, pyridine ring), 7.25 (s, 1H, methylidene), 7.30–7.75 (m, 9H, arom.). MS, *m/e* 466. *Anal.* $C_{24}H_{14}N_6O_3S$ (C, H, N, S).

10c: Pale brown crystals from ethanol, m.p. 215–217°C (dec.) (43% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3200–3300 (NH_2), 2220 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 7.10 (s, 1H, pyrimidine ring), 7.25 (s, 1H, pyridine ring), 7.30 (s, 1H, methylidene), 7.45–8.00 (m, 11H, arom.). MS, *m/e* 476. *Anal.* $C_{26}H_{16}N_6O_2S$ (C, H, N, S).

10d: Pale brown crystals from diluted acetic acid, m.p. 265–267°C (dec.) (51% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3200–3300 (NH_2), 2200 (CN), 1720 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 7.00 (s, 1H, pyrimidine ring), 7.25 (s, 1H, pyridine ring), 7.35 (s, 1H, methylidene), 7.50–8.10 (m, 10H, arom.). *Anal.* $C_{26}H_{15}ClN_6O_2S$ (C, H, Cl, N, S).

10e: Brown crystals from ethanol, m.p. 287–289°C (dec.) (46% yield). MS, *m/e* 521. IR (ν cm^{-1}, KBr): 3500 (OH), 3230–3340 (NH_2), 2230 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 7.00 (s, 1H, pyrimidine ring), 7.15 (s, 1H, pyridine ring), 7.35 (s, 1H, methylidene), 7.50–8.10 (m, 10H, arom.). *Anal.* $C_{26}H_{15}N_7O_4S$ (C, H, N, S).

10f: Brown crystals from ethanol, m.p. > 310°C (40% yield). IR (ν cm^{-1}, KBr): 3480 (OH), 3200–3300 (NH_2), 2200 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 2.30 (s, 3H, CH_3), 7.20 (s, 1H, pyrimidine ring), 7.35 (s, 1H, pyridine ring), 7.50 (s, 1H, methylidene), 7.55–8.15 (m, 10H, arom.). *Anal.* $C_{27}H_{18}N_6O_2S$ (C, H, N, S).

10g: Pale brown crystals from dioxane, m.p. > 310°C (45% yield). IR (ν cm^{-1}, KBr): 3520 (OH), 3200–3300 (NH_2), 2200 (CN), 1720 (C=O). ^{1}H NMR (δ ppm, CF_3COOD): 2.25 (s, 3H, CH_3), 6.90 (s, 1H, pyrimidine ring), 7.10 (s, 1H, pyridine ring), 7.25 (s, 1H, methylidene), 7.40–8.00 (m, 10H, arom.). *Anal.* $C_{27}H_{18}N_6O_3S$ (C, H, N, S).

*3.9. 9-Arylsubstituted 8-chloro-2,3-dihydro-2-(8′-hydroxyquinolin-5′-yl methylidene)-3-oxo-thiazolo[2′,3′:1,6]pyrido[2,3-d][1,2,3]-triazin-10-carbonitrile (**11a–g**)*

3.9.1. General procedure

To an ice-cold solution of **7a–g** (0.01 mol) in a mixture of acetic acid (20 ml) and hydrochloric acid (10 ml), sodium nitrite (0.01 mol in 10 ml H_2O) was added with stirring for 30 min and the stirring was continued for 3 h. The product was collected and recrystallized from diluted acetic acid.

11a: Pale brown crystals, m.p. 277–279°C (dec.) (46% yield). MS, *m/e* 538. IR (ν cm^{-1}, KBr): 3520 (OH), 2200 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 7.00 (s, 1H, pyridine ring), 7.25 (s, 1H, methylidene), 7.40–8.10 (m, 10H, arom.). *Anal.* $C_{26}H_{12}ClN_7O_3S$ (C, H, Cl, N, S).

11b: Pale brown crystals, m.p. > 310°C. (41% yield). IR (ν cm^{-1}, KBr): 3510 (OH), 2220 (CN), 1720 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 7.10 (s, 1H, pyridine ring), 7.30 (s, 1H, methylidene), 7.50–8.30 (m, 9H, arom.). MS, *m/e* 487/489. *Anal.* $C_{23}H_{11}ClN_6O_3S$ (C, H, Cl, N, S).

11c: Yellowish–brown crystals from ethanol, m.p. 266–268°C (dec.) (46% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 2200 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 6.90 (s, 1H, pyridine ring), 7.15 (s, 1H, methylidene), 7.35–7.80 (m, 11H, arom.). *Anal.* $C_{25}H_{13}ClN_6O_2S$ (C, H, Cl, N, S).

11d: Brown crystals from ethanol, m.p. 295–297°C (dec.) (38% yield). IR (ν cm^{-1}, KBr): 3510 (OH), 2200 (CN), 1710 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 6.90 (s, 1H, pyridine ring), 7.10 (s, 1H, methylidene), 7.25–8.00 (m, 10H, arom.). *Anal.* $C_{25}H_{12}Cl_2N_6O_2S$ (C, H, Cl, N, S).

11e: Dark brown crystals from diluted acetic acid, m.p. 267–269°C (dec.) (44% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 2210 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 6.90 (s, 1H, pyridine ring), 7.10 (s, 1H, methylidene), 7.25–8.10 (m, 10H, arom.). *Anal.* $C_{25}H_{12}ClN_7O_4S$ (C, H, Cl, N, S).

11f: Brown crystals from diluted acetic acid, m.p. > 310°C (40% yield). IR (ν cm^{-1}, KBr): 3500 (OH), 3230–3340 (NH_2), 2200 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 1.95 (s, 3H, CH_3), 7.30 (s, 1H, pyridine ring), 7.45 (s, 1H, methylidene), 7.50–8.20 (m, 10H, arom.). *Anal.* $C_{26}H_{15}ClN_6O_2S$ (C, H, Cl, N, S).

11g: Brown crystals from dioxane, m.p. > 310°C (42% yield). IR (ν cm^{-1}, KBr): 3480 (OH), 2220 (CN), 1700 (C=O). ^{1}H NMR (δ ppm, $CDCl_3$): 2.40 (s, 3H, OCH_3), 7.50 (s, 1H, pyridine ring), 7.70 (s, 1H, methylidene), 7.90–9.00 (m, 10H, arom.). *Anal.* $C_{26}H_{15}ClN_6O_3S$ (C, H, Cl, N, S).

*3.10. 2,3-Dihydro-8-hydrazino-2-(8′-hydroxyquinolin-5′-yl methylidene)-3-oxo-9-phenyl thiazolo-[2′,3′:1,6]pyrido[2,3-d][1,2,3]triazin-10-carbonitrile (**12**)*

A mixture of **11c** (0.002 mol) and hydrazine hydrate (2 ml, 98%) in ethanol (30 ml) was heated under reflux for 5 h. The product obtained after cooling was filtered off, washed with water and recrystallized from ethanol as brown crystals, m.p. 288–290°C (81% yield). IR (ν

cm^{-1}, KBr): 3530 (OH), 3280–3380 (NH_2), 3180 (NH), 2220 (CN), 1690 (C=O). ^1H NMR (δ ppm, CF_3COOD): 7.10 (s, 1H, pyridine ring), 7.20 (s, 1H, methylidene), 7.25–7.70 (m, 11H, arom.). *Anal.* $C_{25}H_{16}N_8O_2S$ (C, H, N, S).

*3.11. 2,3-Dihydro-11H-2-(8′-hydroxyquinolin-5′-yl methylidene)-3-oxo-11-phenyl thiazolo-[2′,3′:1,6]pyrido[2,3-d][1,2,4]triazolo[3″,4″-f][1,2,3]-triazin-12-carbonitrile (**13**)*

A mixture of **12** (0.001 mol) in formic acid (20 ml) was heated under reflux for 6 h. The reaction mixture was concentrated in vacuo and the solid product was collected, washed with water and recrystallized from ethanol to give brown crystals, m.p. 310–312 (dec.) (78% yield). IR (ν cm^{-1}, KBr): 3520 (OH), 2210 (CN), 1700 (C=O). ^1H NMR (δ ppm, $CDCl_3$): 6.80 (s, 1 H, CH–triazole ring), 7.20–7.65 (m, 13H, arom.). *Anal.* $C_{26}H_{14}N_8O_2S$ (C, H, N, S).

*3.12. 2-(8′-Hydroxyquinolin-5′-yl methylidene)-3-oxo-11-phenyl-2,3,9,11-tetrahydro-8-thioxo-thiazolo[2′,3′:1,6]pyrido[2,3-d][1,2,4]triazolo[3″,4″-f]-[1,2,3]triazin-12-carbonitrile (**14**)*

A mixture of **12** (0.0012 mol), carbon disulfide (5 ml) in ethanol (50 ml) and two pellets of potassium hydroxide was heated under reflux on a water bath for 5 h. The solid product obtained was dissolved in water and then acidified with acetic acid. Recrystallization from acetic acid gave dark yellow crystals, m.p. > 340°C (62% yield). IR (ν cm^{-1}, KBr): 3515 (OH), 3180 (NH), 2200 (CN), 1700 (C=O), 1190 (CS). ^1H NMR (δ ppm, $CDCl_3$): 7.20 (s, 1H, pyridine ring), 7.25 (s, 1H, methylidene), 7.35–7.90 (m, 11H, arom.). *Anal.* $C_{26}H_{14}N_8O_2S_2$ (C, H, N, S).

*3.13. 8-Azido-2,3-dihydro-9H-2-(8′-hydroxy-quinolin-5′-yl methylidene)-3-oxo-9-phenyl thiazolo[2′,3′:1,6]pyrido[2,3-d][1,2,3]-triazin-10-carbonitrile (**15**)*

To a well-stirred solution of **12** (0.002 mol) in glacial acetic acid (50 ml) a solution of sodium nitrite (1 g in 10 ml of water) was added at r.t. and stirring was continued for 1 h. The solid obtained was filtered off, washed with water and recrystallized from acetic acid to give brown crystals m.p. 215–217 (60% yield). IR (ν cm^{-1}, KBr): 3520 (OH), 2220 (CN), 2130 (N_3), 1700 (C=O). ^1H NMR (δ ppm, CF_3COOD): 7.10 (s, 1H, pyridine ring), 7.25 (s, 1H, methylidene), 7.30–7.70 (m, 11H, arom.). *Anal.* $C_{25}H_{13}N_9O_2S$ (C, H, N, S).

*3.14. 8-Amino-3,6-dioxo-2-(8′-hydroxyquinolin-5′-yl methylidene)-9-phenyl-2,3,5,9-tetrahydro thiazolo[3,2-a][1,8]naphthyridin-7,10-dicarbonitrile (**16**)*

A mixture of **7c** (0.002 mol) and ethyl cyanoacetate (0.002 mol) was fused at 180–200°C for 2 h. The reaction mixture was allowed to cool and the solid product was collected and recrystallized from acetic acid as pale brown crystals, m.p. > 340°C (62 yield). IR (ν cm^{-1}, KBr): 3520 (OH), 3280–3380 (NH_2), 3180 (NH), 1700, 1720 (C=O). ^1H NMR (δ ppm, CF_3COOD): 7.20 (s, 1H, pyridine ring), 7.25 (s, 1H, methylidene), 7.40–7.85 (m, 11H, arom.), 8.60 (s, 1H, NH), 9.10 (s, 2H, NH_2). *Anal.* $C_{28}H_{16}N_6O_3S$ (C, H, N, S).

4. Antifungal activity

The newly synthesized compounds were screened for their antifungal activity against four species of fungi, namely, *Penicillium chrysogenum*, *Fusarium moniliforme*, *Rhizopus stalonifer* and *Aspergillus terreus*, using the disk diffusion method [12,13].

The tested compounds were dissolved in *N*,*N*-dimethylformamide (DMF) to get a solution of 1% concentration. Filter paper discs (Whatman, 5 mm diameter) were saturated with this former solution. The saturated filter paper discs were placed on the surface of solidified Czapek's Dox agar dishes seeded by the test fungi. The inhibition zones were measured in mm at the end of an incubation period of 48 h at 28°C. As appears in Table 1, only compounds **5** and **11a–g** exhibited moderate activity. Analysis data of the synthesized compounds are given in Table 2.

References

[1] D.E. Beattie, R. Crossley, A.C.W. Curran, G.T. Dixon, D.G. Hill, A.E. Lawrence, R.G. Sheperd, 5,6,7,8-Tetrahydroquinolines. 4. Antiulcer and antisecretory activity of 5,6,7,8-tetrahydroquinolinenitriles and -thioamides, J. Med. Chem. 20 (1977) 714–718.

[2] S. Masahiko, K. Eiji, K. Mitsutaka, 5-Substituted aminoethylidene-1-azadibenzo[*a*,*d*]-cycloheptadienes, Japan Patent No. 7200,811 (Cl. C07D, A61k) (15 Mar. 1969); Chem. Abstr., 76, 140574 j (1972).

[3] A. Studeneer, G. Salbeck, L. Emmel, W. Knauf, *N*,*N*,-Dialkylaminocarbamic acid ester of substituted hydroxypyridine derivatives, Ger. Offen. 2,361,438 (Cl. C07D) (26 Jun. 1975); Chem. Abstr., 83, 114227 y (1975).

[4] A. Studeneer, G. Salbeck, L. Emmel, W. Knauf, Dimethylaminocarbonyloxypyridine 1-oxide and quinoline oxide insecticides, Ger. Offen. 2,432,635 (Cl. C07D) (22 Jan. 1976); Chem. Abstr., 84, 150525 y (1976).

[5] R.C. Tweit, R.D. Muir, S. Mizuba, Antimicrobial activity of a series of aminoalkyl esters of benzyldithiocarbamic acids, J. Med. Chem. 12 (1969) 343–346.

[6] M. Di Braccio, G. Roma, M. Mazzei, A. Balbi, R. Testa, 1,2-Condensed pyrimidines derivatives. Note II. Synthesis and pharmacological studies on *N*,*N*-disubstituted 5-amino-7*H*-thiazolo[3,2-*a*]pyrimidin-7-ones, Farmaco 41 (1986) 183–195.
[7] F. Arndt, W. Franke, W. Klose, J. Lorenz, K. Schwarz, Syntheses of thiazolo- and [1,3]thiazino[1,2,4]triazinones, Justus Liebigs Ann. Chem. 7 (1984) 1302–1307.
[8] A.A. Abdel Hafez, Nitriles in heterocyclic synthesis. Part II. Synthesis and application of pyrano[3,2-*h*]quinoline sulfonamide derivatives, J. Chem. Technol. Biotechnol. 55 (1992) 95–101.
[9] A.A. Abdel Hafez, I.M.A. Awad, Azo-dyes related to 5-sulphonyl piperido and/or morpholino-8-quinolinol, Dyes Pigm. 20 (1992) 197–209.
[10] Z.H. Khalil, A.A. Abdel Hafez, A.A. Geies, A.M. Kamal El-Dean, Nitriles in heterocyclic synthesis. Synthesis and reactions of pyrano[3,2-*h*]quinoline derivatives, Bull. Chem. Soc. Jpn. 64 (1991) 668–670.
[11] A.A. Abdel Hafez, A.M. Kama El-Deanl, A.A. Hassan, H.S. El-Kashef, S. Rault, M. Robba, Synthesis of some pyrimido[4′,5′:4,5]thieno[2,3-*b*]quinolines and related heterocycles, J. Heterocycl. Chem. 33 (1996) 431–438.
[12] L.P. Carrod, P.D. Grady, Antibiotic and Chemotherapy, third ed., Churchill Livingstone, Edinburgh, 1972, p. 477.
[13] A. Cremer, Antibiotic Sensitivity and Assay Tests, fourth ed., Butterworth, London, 1980, p. 521.
[14] M.S. Al-Thebeiti, M.F. El-Zohry, Synthesis of some new spiroheterocycles related to spiro[indoline-3,2′-[1,3]oxathiane-2,5′-dione, Phosphorus, Sulfur, Silicon 88 (1994) 251–256.
[15] M.S. Al-Thebeiti, Synthesis of some new spiro[indoline-3-heterocycle]-2-one derivatives, Heteroatom Chem. 5 (1994) 571–577.
[16] M.S. Al-Thebeiti, M.F. El-Zohry, Synthesis of some new spiroindoline derivatives incorporated with pyrazoloheterocycles, Heteroatom Chem. 6 (1995) 567–573.
[17] M.S. Al-Thebeiti, M.F. El-Zohry, A facile route for the synthesis of some new spiro[indoline-3,3′-indan]-2,1′-dione derivatives, Heterocycles 41 (1995) 2475–2480.
[18] M.S. Al-Thebeiti, Synthesis of some new spiro[indoline-3,2′-(1′,2′,3′,4′-tetrahydro-quinoline)]-2,4′-dione derivatives, Heterocycles 48 (1998) 145–150.
[19] M.S. Al-Thebeiti, M.F. El-Zohry, Synthesis of some new spirothiazolidinone and spiroazetidinone derivatives incorporated with quinazoline, Indian J. Chem. 37B (1998) 804–809.
[20] M.S. Al-Thebeiti et al, Synthesis of some new spiroquinazoline-4-heterocyclic derivatives, Bull. Pol. Acad. Sci. Chem. 46 (1998) 351–360.
[21] M.S. Al-Thebeiti, Synthesis of some new spiro[indoline-3,2′-(thiochroman)]-2,4′-dione derivatives, Phosphorus, Sulfur, Silicon 141 (1998) 89–95.
[22] M.S. Al-Thebeiti, Synthesis of some new pyranoquinoline and related heterocyclic systems, Heterocycles 51 (1999) 1311–1319.
[23] M.S. Al-Thebeiti, Regiocontrolled incorporation and annulation of glucose into spirothiazole and spirothiazoloxazole derivatives, J. Carbohydr. Chem. 18 (1999) 667–674.