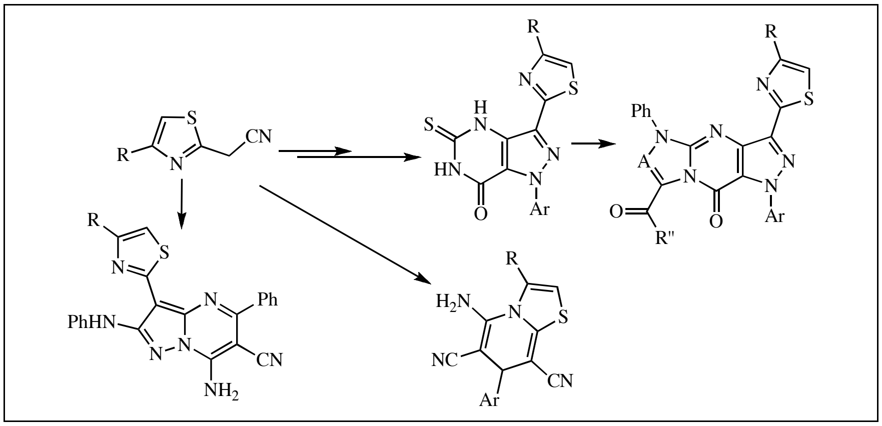
Utility of 2-[4-(3-Oxobenzo[*f*]-2*H*-chromen-2-yl)-1,3-thiazol-2-yl]ethanenitrile in Heterocyclic Synthesis

Abdou O. Abdelhamid and Hassan M. Abdelaziz[a]

Department of Chemistry, Faculty of Science, Cairo University, Giza 12613, Egypt
[a]Department of Chemistry, Faculty of Science, Beni-Suef University, Beni-Suef, Egypt
Abdelhamid45@gmail.com

Received March 22, 2007



Pyrazolo[4,3-*d*]pyrimidines, pyrazolo[4,3-*d*]triazolino[4,3-*a*]pyrimidines, 3-(2-thiazolyl)thiophenes, thiazolo[3,2-*a*]pyridine and pyrazolo[1,5-*a*]pyrimidines were synthesized from 2-[4-(3-oxobenzo[*f*]-2H-chromen-2-yl)-1,3-thiazol-2-yl]ethanenitrile. The newly synthesized compounds were elucidated by elemental analysis, spectral data, chemical transformation and alternative synthesis route whenever possible.

J. Heterocyclic Chem., **45**, 1719 (2008).

INTRODUCTION

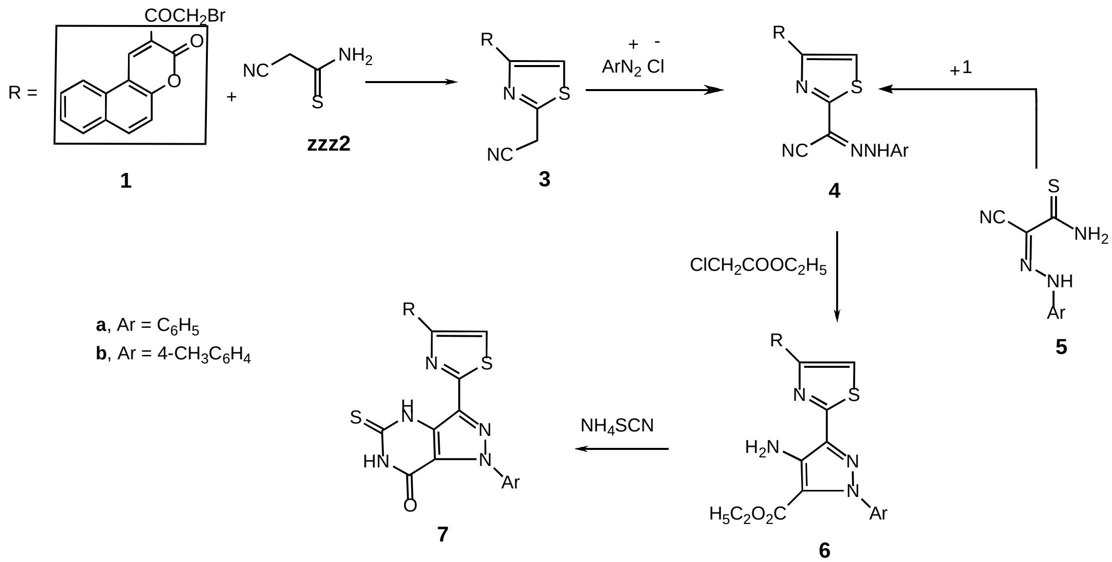
Coumarin derivatives constitute an important class of heterocyclic compounds with anticoagulant [1,2], anticoagulant rodenticide [3], insecticide [4] and antibacterial [5,6] pharmacolgical properties. On the other hand, 1,3,4-thiadiazole derivatives have become very useful compounds in medicine, agriculture and in many other fields of technology [7]. We report here the synthesis of some new pyrazolo[4,3-*d*]pyrimidines, pyrazolo[4,3-*d*]triazolino[4,3-*a*]pyrimidines, 3-(2-thiazol-yl)thiophenes, thiazolo[3,2-*a*]pyridine and pyrazolo[1,5-*a*]pyrimidines.

RESULTS AND DISCUSSION

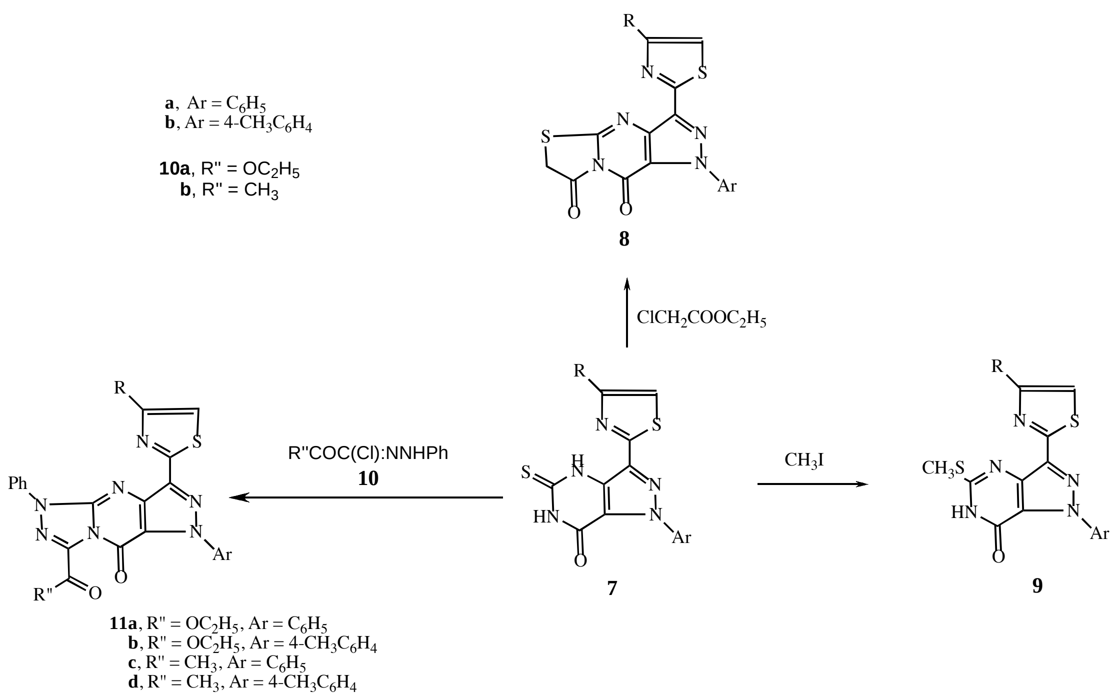
3-(2-Bromoacetyl)benzo[*f*]chromen-2-one [8] (**1**) was heated with cyanothioacetamide (**2**) in ethanol under reflux to give 2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)-1,3-thiazol-2-yl]ethanenitrile (**3**). Compound **3** was reacted with arendiazonium chloride in ethanolic sodium acetate solution at 0°C to afford 3-azo-2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)-1,3-thiazol-2-yl]-3-(aryl-amino)prop-2-ene-nitrile **4a,b** (Scheme 1). Compound **4** was elucidated by elemental analysis, spectral data, alternative synthesis route and chemical transformation. Compound **4a** was also obtained by heating 2-aminothioxomethyl-3-aza-3-(phenylamino)-prop-2-enenitriles [9] (**5a**) with **1** in boiling ethanol. Compounds **4a,b** were reacted with ethyl chloroacetate in boiling *N,N*-dimethylformamide solution containing potassium carbonate and triethylamine to afford the ethyl 4-amino-3-[4-oxobenzo[*f*]chromen-2-yl]-1,3-thiazol-2-yl-1-arylpyrazole-5-carboxylates **6a,b**. Treatment of **6a,b** with ammonium thiocyanate in acetic acid under reflux afforded 2-[2-oxo-1-aryl-5-thioxo-4,6-dihydropyrazolo[4,3-*d*]pyrimidin-3-yl-1,3-thiazol-4-yl]-benzo[*f*]chromen-3-one **7a,b**. Compound **7** was elucidated on the basis of elemental analysis, spectral data and chemical transformation. Thus, treatment of **7a,b** with each of ethyl chloroacetate and iodomethane afforded 1-aryl-3-[4-(3-oxobenzo[*f*]-2*H*-chromen-2yl)-1,3-thiazol-2-yl]-7a-hydro-6*H*-pyrazolo-[4,3-*d*]-1,3-thiazolidino[3,2-*a*]pyrimidine-4,8-dione **8a,b** and 1-aryl-2-[5-methylthio-7-oxo-6-hyd-ropyrazolo-[4,5-*d*]pyrimidin-3-yl]-1,3-thiazol-4-yl)benzo[*f*]chromen-3-one **9a,b** (Scheme 2)

Treatment of **7a** with the appropriate hydrazonyl chlorides **10a**,**b** in boiling chloroform containing triethyl-amine gave ethyl 8-oxo-3-[4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]-1,5-diphenyl-7a-hydro-pyrazolo[4,3-*d*]triazolino[4,3-*a*]pyrimidine-7-carboxylate **11a** and 2-[2-(7-acetyl-8-oxo-1,5-diphenyl-7a-hydro-

Scheme 1



Scheme 2

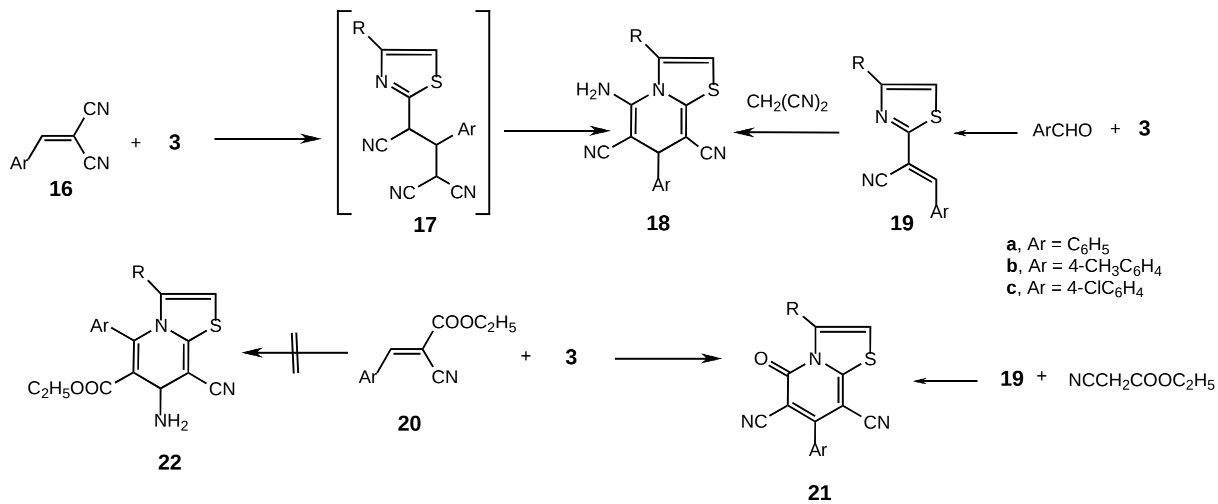


pyrazolo[4,3-*d*]-1,2,4-triazolino[4,3-*a*]pyrimidin-3-yl)-1,3-thiazol-4-yl]benzo-[*f*]-2H-chromen-3-one (**11b**), respectively.

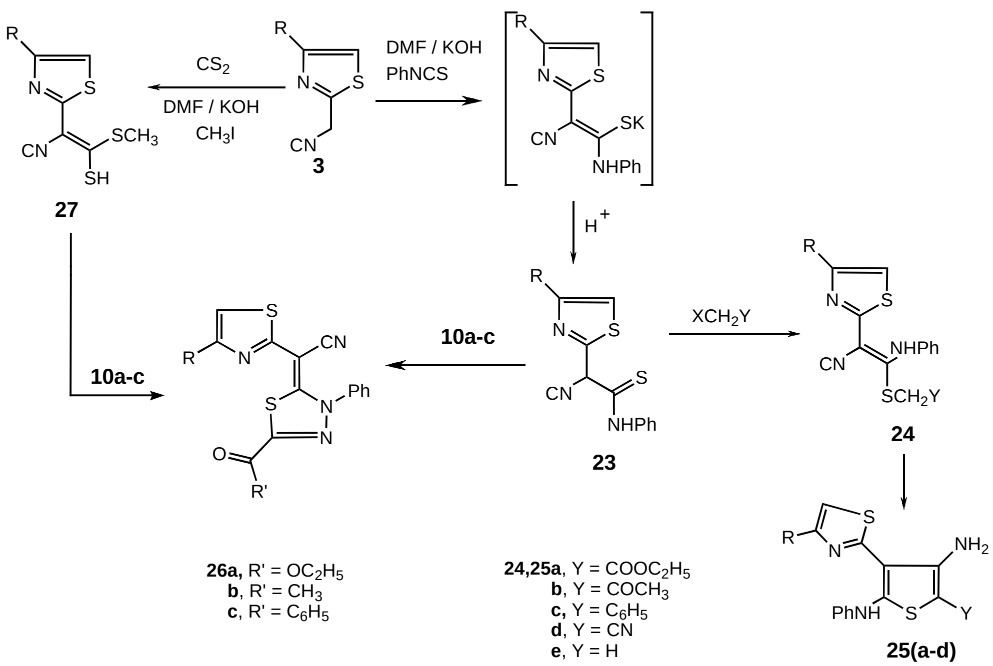
Formation of **11** can be explained *via* reaction of nitrile imide **12**, which formed *in situ* from hydrazonoyl chlorides and triethylamine, with thiol isomer of **7** *via* 1,3-addition to afford the thiohydrazonate ester **13**, which undergoes nucleophilic cyclization to yield **11**. Alternatively, 1,3-cyloaddition of nitrilimine to C=S double bond to give spiro intermediate **14**, which was afforded **11** directly *via* intermediate **15** by loss hydrogen sulfide (Chart 1).

Treatment of **3** with the appropriate 2-aryl-1-cyanoacrylonitrile **16a-c** in boiling ethanol under reflux containing catalytic amount of piperidine gave one isolable product by evidence of which could be formulated as 4-amino-6-aryl-3-(3-oxobenzo[*f*]chromen-2-yl)-6,3a-dihydro-1,3-thiazolino[3,2-*a*]pyridine-5,7-

Scheme 3



Scheme 4



dicarbonitrile **18a-c**. Structure **18** was elucidated on the basis of elemental analysis, spectral data and alternative synthesis. The reaction seemed to proceed through Michael addition reaction between **3** and **16** to give intermediate **17**, which underwent cyclization *via* addition of NH hydrogen to nitrile function to give the final product **18** (Scheme 3).

More evidence for structure **18** came from its independent synthesis route by treatment of the appropriate 3-aryl-2-[4-(3-oxobeno[*f*]-2*H*-chromen-2-yl)-(1,3-thiazol-2-yl)]-3-prop-2-enenitrile **19a-c**, which was prepared *via* reaction of **3** with benzaldehyde (or reaction of **1** with arylidenecyanothioacetamide [10]), with malononitrile in boiling ethanol containing catalytic amount of piperidine gave a product identical in all respects (mp. mixed mp. and spectra) with **18a**.

Also, **3** was reacted with the appropriate 2-aryl-1-cyanoacrylates **20a-c** in boiling ethanol and piperidine to afford **21a-c** and not **22a-c** on the base of spectral data and analytical analyses. Thus, the ^{1}HNMR spectrum of **21b** showed signals at δ = 2.32 (s, 3H, CH_3) and 7.26 – 9.21 (m, 13H, ArH's) and no signals for ethoxy group. Its

IR spectrum revealed bands at 2210 (CN), 1720, 1693 (CO's) and 1604 (C=C).

Furthermore, **3** was reacted with phenyl isothiocyanate in *N,N*-dimethylformamide to afford a product which was converted by hydrochloric acid to thioamide **23** (Scheme 4). Structure **23** was confirmed by elemental analysis, spectral data and chemical transformation. Thus, treatment of **23** with the appropriate ethyl chloroacetate, chloroacetone, ω-bromoacetophenone, chloroacetonitrile and iodomethane to afford ethyl {2-cyano-2-[4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)](phenylamino)-vinylthio}-acetate (**24a**), 2-[4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)-3-(2-oxopropylthio)-3-(phenylamino)prop-2-enenitrile (**24b**), 2-[4-(3-oxobenzo-[*f*]-2H-chromen-2-yl)(1,3-thiazol-2-yl)-3-(2-oxophenyl-ethylthio)-3-(phenylamino)prop-2-enenitrile (**24c**), 3-(cyanoethylthio)2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)-(1,3-thiazol-2-yl)-3-phenylamino)prop-2-enenitrile (**24d**) and 3-methylthio-2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)-(1,3-thiazol-2-yl)-3-(phenylamino)prop-2-enenitrile (**24e**) respectively (Scheme 4).

Compound **24a** was converted to ethyl 3-amino-4-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]-5-phenylamino)-thiophene-2-carboxylate (**25a**) by boiling in ethanol containing a catalytic amount of piperidine. All the appropriate compounds **24b-d** were boiled in ethanol containing catalytically amount of piperidene to give the corresponding thiophene derivatives **25b-d**, respectively.

Also, treatment of **23** with the appropriate hydrazonyl halides **10a-c** in the presence of triethylamine afforded 2,3-dihydro-1,3,4-thiadiazoles **26a-c**, respectively (Scheme 4). Structure **26** was elucidated by elemental analysis, spectral data and alternative synthesis. Thus, methylcarbodithioate **27**, which was prepared *via* reaction of **3** with carbon disulfide in the presence of potassium hydroxide followed by iodomethane, reacted with the appropriate hydrazonoyl halides **10a-c** to give products identical in all respects (mp. mixed mp. and spectra) with **26a-c**.

Next, treatment of **24e** with hydrazine hydrate in boiling ethanol under reflux afforded 2-{2-[5-amino-3-(phenylamino)pyrazol-4-yl]-1,3-thiazol-4-yl}benzo[*f*]-

Scheme 5

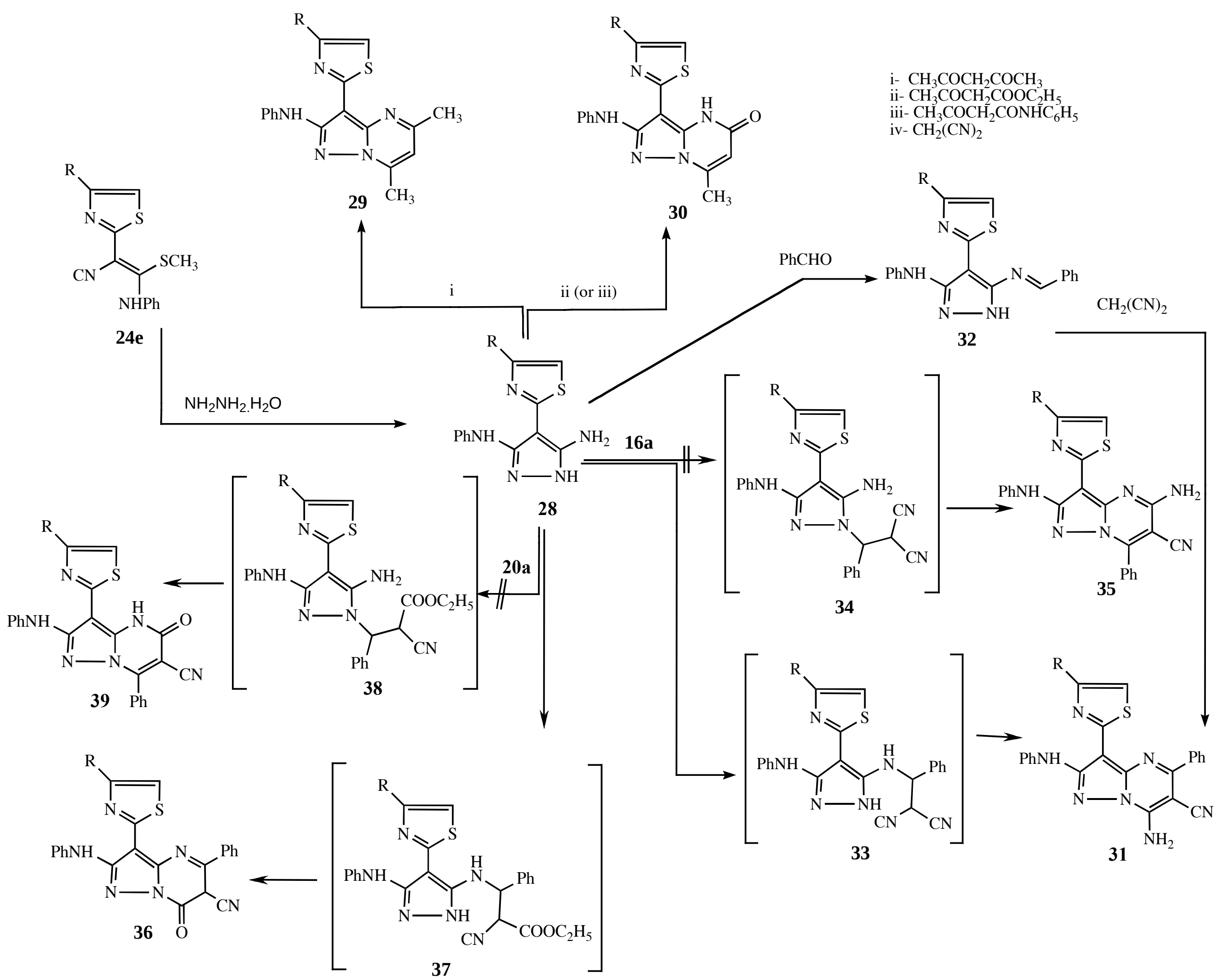


Table 1

Characterization data of the newly synthesized compounds.

Compound	Mp	Yield %	Molecular Formula	Analysis % Calcd./Found C	H	N	S
3	200-205	Brown	$C_{18}H_{10}N_2O_2S$	67.91	3.17	8.80	10.07
	Dioxan	80	318.36	67.85	3.09	8.73	9.99
4a	290-92	Green	$C_{24}H_{14}N_4O_2S$	68.23	3.34	13.26	7.59
	DMF	78	442.47	68.16	3.26	13.19	7.48
4b	285-86	Yellow	$C_{25}H_{16}N_4O_2S$	68.79	3.69	12.84	7.35
	DMF	80	436.50	68.67	3.62	12.73	7.29
6a	170-72	Brown	$C_{28}H_{20}N_4O_4S$	66.13	3.96	11.02	6.30
	Dioxan	68	508.56	66.07	3.88	10.96	6.27
6b	258-60	Brown	$C_{29}H_{22}N_4O_4S$	66.65	4.24	10.72	6.14
	Dioxan	72	522.59	66.59	4.16	10.58	6.03
7a	243-45	Brown	$C_{27}H_{15}N_5O_3S_2$	62.18	2.90	13.43	12.29
	Dioxan	68	521.58	62.12	2.78	13.29	12.26
7b	250-52	Brown	$C_{28}H_{17}N_5O_3S_2$	62.79	3.20	13.08	11.97
	DMF	68	535.61	62.68	3.12	13.00	11.78
8a	233-35	Brown	$C_{29}H_{15}N_5O_4S_2$	62.02	2.69	12.47	11.42
	Dioxan	68	561	61.97	2.49	12.38	11.37
8b	242-45	Brown	$C_{30}H_{17}N_5O_4S_2$	62.60	2.98	12.17	11.14
	Dioxan	65	575.63	62.48	2.86	12.06	11.07
9a	198-200	Brown	$C_{28}H_{17}N_5O_3S_2$	62.79	3.20	13.08	11.97
	Dioxan-EtOH	72	535.61	62.68	3.11	12.99	11.88
9b	223-25	Brown	$C_{29}H_{19}N_5O_3S_2$	63.37	3.48	12.74	11.67
	Dioxan-EtOH	65	549.63	63.24	3.37	12.65	11.62
11a	185-87	Brown	$C_{37}H_{23}N_7O_5S$	65.58	3.42	14.47	4.73
	Dioxan	69	677.70	65.42	3.36	14.29	7.64
11b	223-25	Brown	$C_{38}H_{25}N_7O_5S$	65.98	3.64	14.17	4.64
	Dioxan	75	691.73	65.87	3.54	14.06	4.57
11c	200-202	Brown	$C_{36}H_{21}N_7O_4S$	66.76	3.27	15.14	4.95
	DMF	68	647.68	66.59	3.09	15.03	4.88
11d	>300	Brown	$C_{37}H_{23}N_7O_4S$	67.16	3.50	14.82	4.85
	DMF	65	661.70	67.05	3.37	14.89	4.76
18a	218-20	Gray	$C_{28}H_{16}N_4O_2S$	71.17	3.41	11.91	6.79
	Dioxan	75	472.53	71.35	3.20	11.74	6.78
18b	260-62	Yellow	$C_{29}H_{18}N_4O_2S$	71.69	3.73	11.51	6.59
	Dioxan	80	486.58	71.77	3.57	11.63	6.57
18c	265-56	Gray	$C_{28}H_{15}ClN_4O_2S$	66.34	2.98	11.05	6.32
	Dioxan	78	506.97	66.52	3.86	11.04	6.28
19a	220-22	Brown	$C_{25}H_{14}N_2O_2S$	73.88	3.47	6.89	7.89
	Dioxan-EtOH	80	406.47	73.79	3.43	6.75	7.77
19b	255-57	Yellow	$C_{26}H_{16}N_2O_2S$	74.28	3.84	6.66	7.63
	Dioxan	82	420.49	74.16	3.75	6.57	7.57
19c	235-37	Yellow	$C_{25}H_{13}ClN_2O_2S$	68.10	2.97	6.35	7.27
	Dioxan	85	440.91	68.02	2.88	6.30	7.16
21a	224-42	Brown	$C_{28}H_{13}N_3O_3S$	71.33	2.78	8.91	6.80
	Dioxan	75	471.33	71.28	2.67	8.85	6.72
21b	245-46	Brown	$C_{29}H_{15}N_3O_3S$	71.74	3.11	8.65	6.60
	Dioxan	80	485.53	71.68	3.08	8.59	6.45
21c	230-32	Brown	$C_{28}H_{12}ClN_3O_3S$	66.47	2.39	8.31	6.34
	Dioxan	78	505.94	66.38	2.27	8.27	6.27
23	185-86	Brown	$C_{25}H_{15}N_3O_2S_2$	66.21	3.33	9.26	14.14
	EtOH	68	453.55	66.17	3.29	9.19	14.06
24a	230-31	Brown	$C_{29}H_{21}N_3O_4S_2$	64.55	3.92	7.79	11.88
	DMF-EtOH	75	539.64	64.48	3.87	7.68	11.75
24b	260-62	Brown	$C_{28}H_{19}N_3O_3S_2$	65.99	3.76	8.25	12.58
	EtOH	65	509.61	65.92	3.64	8.19	12.45
24c	>300-301	Brown	$C_{33}H_{21}N_3O_3S_2$	69.33	3.70	7.35	11.22
	Dioxan	69	571.68	69.28	3.59	7.24	11.17

Table 1: Continued

Compound	Mp	Yield %	Molecular Formula	Analysis % Calcd./Found C	H	N	S
24d	185-87	Brown	$C_{27}H_{16}N_4O_2S_2$	65.84	3.27	11.37	13.02
	DMF	60	492.58	65.75	3.19	11.32	12.96
24e	250-52	Brown	$C_{26}H_{17}N_3O_2S_2$	66.79	3.66	8.99	13.72
	DMF-EtOH	75	467.57	66.69	3.59	8.77	13.63
25a	260-61	Brown	$C_{29}H_{21}N_3O_4S_2$	64.55	3.92	7.79	11.88
	DMF	68	539.64	64.47	3.87	7.62	11.76
25b	280-81	Brown	$C_{28}H_{19}N_3O_3S_2$	65.99	3.76	8.25	12.58
	EtOH	65	509.68	65.86	3.74	8.18	12.39
25c	>300	Brown	$C_{33}H_{21}N_3O_3S_2$	69.33	3.70	7.35	11.22
	Dioxan	68	571.56	69.26	3.61	7.30	11.17
25d	230-32	Brown	$C_{27}H_{16}N_4O_2S_2$	65.84	3.27	11.37	13.02
	DMF	60	492	65.79	3.15	11.35	12.98
26a	235-36	Brown	$C_{29}H_{18}N_4O_4S_2$	63.26	3.30	10.18	11.65
	DMF-EtOH	95	550.62	63.18	3.25	10.06	11.58
26b	235-37	Brown	$C_{28}H_{16}N_4O_3S_2$	64.60	3.10	10.76	12.32
	DMF-EtOH	95	520.50	64.48	3.25	10.56	12.48
26c	>300	Brown	$C_{33}H_{18}N_4O_3S_2$	68.03	3.11	9.62	11.01
	Dioxan	69	582.66	67.98	3.08	9.58	10.96
27	257-260	Brown	$C_{20}H_{12}N_2O_2S_2$	58.80	2.96	6.86	23.55
	DMF	79	408.52	58.73	2.88	6.75	23.41
28	>300	Brown	$C_{25}H_{17}N_5O_2S$	66.50	3.80	15.51	7.10
	Dioxan	70	451.51	66.45	3.74	15.47	6.98
29	>300	Brown	$C_{30}H_{21}N_5O_2S$	69.89	4.11	13.58	6.22
	DMF-EtOH	65	515.60	69.85	4.07	13.42	6.17
30	>300	Red	$C_{29}H_{19}N_5O_3S$	67.30	3.70	13.53	6.20
	AcOH	68	517.57	67.21	3.58	13.49	6.18
31	>300	Brown	$C_{35}H_{21}N_7O_2S$	69.64	3.51	16.24	5.31
	DMF	72	603.62	69.59	3.43	16.13	5.19
32	245-46	Black	$C_{32}H_{21}N_5O_2S$	71.23	3.92	12.98	5.94
	Dioxan	68	539.62	71.16	3.85	12.77	5.79
36	>300	Brown	$C_{35}H_{20}N_6O_3S$	69.52	3.33	13.90	5.30
	DMF	68	604.65	69.47	3.26	13.86	5.23

Table 2

Spectroscopic data of the newly synthesized compounds

Compound	Spectral data
3	IR: 3058, 2977 (CH), 2198 (CN), 1712 (CO) and 1596 (C=C)
	^{1}H NMR: 4.68 (s, 2H, CH_2), 7.57-8.33 (m, 6H, ArH's), 8.44 (s, 1H, ArH) and 9.35 (s, 1H, ArH). .
4a	IR: 3159 (NH), 2213 (CN), 1716, 1686 (CO) and 1596 (C=C)
	^{1}HNMR: 7.40-8.64 (m, 12H), 9.36 (s, 1H) and 11.35 (s, 1H).
4b	IR: 3132 (NH); 2218 (CN); 1720, 1639 (CO); 1616 (C=C).
	^{1}HNMR: 2.29 (s, 3H, CH_3); 7.19- 9.36 (m, 11H, ArH's); 9.63 (s, 1H); 11.35 (s, 1H, NH).
6a	IR: 3359, 3288 (NH_2), 3136 (CH), 1720 (CO) and 1596 (C=C).
	^{1}HNMR: 1.16 (t, 3H, J = 7Hz, CH_3**CH_2**), 4.19 (q, 2H, J = 7Hz, **CH_3**CH_2), 6.04 (s, br, 2H, NH_2), 7.27-8.67 (m, 12H, ArH's) and 9.49 (s, 1H, ArH).
6b	IR: 3483, 3413 (NH_2); 3136 (CH aromatic); 2974 (CH aliphatic); 1720, 1639 (CO's); 1616 (C=C).
	^{1}HNMR: 1.25 (t, 3H, CH_3**CH_2**), 2.47 (s, 3H, CH_3), 4.31(q, 2H, **CH_3**CH_2), 6.13 (s, br, 2H, NH_2); 7.35- 9.60 (m, 12H, ArH's).
7a	^{1}HNMR: 7.40-8.64 (m, 12H, ArH's), 9.54 (s, 1H, ArH), 12.00 (s, 1H), and 13.95 (s, 1H).
7b	IR: 3278 (NH); 1720(CO); 1620 (C=N).
	^{1}HNMR: 2.27 (s, 3H, CH_3); 7.19- 9.56 (m, 12H, ArH's); 11.91 (s, 1H, NH); 13.95 (s, 1H, NH).
8a	IR: 3136, 2981 (CH), 1725, 1674 (CO's) and 1596 (C=C).
	^{1}HNMR: 4.30 (s, 2H, CH_2) and 7.38 - 9.48 (m, 12H, ArH's).
8b	IR: 3136 (CH aromatic); 2923 (CH aliphtic); 1720, 1639 (CO's); 1616 (C=C).
	^{1}HNMR: 2.39 (s, 3H, CH_3); 4.29 (s, 2H, CH_2); 7.28- 9.54 (m,12H, ArH's)
9a	IR: 3402 (NH); 3058 (CH aromatic); 1724, 1674 (CO's); 1596C=C).
	^{1}HNMR: 2.73 (s, 3H, SCH_3); 7.40- 9.55 (m, 13H, ArH`s);12.01 (s, 1H, NH)
9b	IR: 3413 (NH); 1720, 1639 (CO's); 1616 (C=C).
	^{1}HNMR: 2.36 (s, 3H, CH_3); 2.66 (s, 3H, SCH_3); 7.19- 9.36 (m, 12H, ArH's); 11.92 (s, 1H, NH).

Table 2 (continued)

11a	IR: 3132, (CH aromatic); 2927 (CH aliphatic); 1720 (CO), 1624 (C=N); 1596 (C=C).
	^{1}HNMR: 1.25 (t, 3H, $CH_3\mathbf{CH_2}$), 4.31(q, 2H, $\mathbf{CH_3}CH_2$), 7.30- 9.55 (m, 13H, ArH`s and thiazole H-5).
11b	IR: 3.056 (CH aromatic); 2993, 2974 (CH aliphatic); 1716, 1639 (C=O); 1616 (C=C).
	^{1}HNMR: 1.25 (t, 3H, $CH_3\mathbf{CH_2}$), 2.35 (s, 3H, CH_3), 4.31(q, 2H, $\mathbf{CH_3}CH_2$), 7.19-9.48 (m, 17H, ArH`s)
11c	IR: 3136, (CH aromatic); 2974, (CH aliphatic); 1720, 1639 (CO's).1616 (C=N).
	^{1}HNMR: 2.35 (s, 3H, CH_3), 7.15- 9.36 (m, 18H, ArH`s).
11d	IR: 1716, 1639 (CO's); 1616 (C=C).
	^{1}HNMR: 2.32 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.15- 9.36 (m, 17H, ArH`s).
18a	IR: 3220, 3157 (NH_2), 2194 (CN); 1716, (CO); 1594 (C=C).
	^{1}HNMR: 4.29 (s, 2H, NH_2); 4.89 (s, 1H), 7.28-9.54 (m, 13H, ArH's)
18b	IR: 3425 (NH), 2218 (CN), 1720, 1639 (CO's) and 1616 (C=N).
	^{1}HNMR: 2.39 (s, 3H, CH_3), 4.29 (s, 2H, NH_2), 4.82 (s, 1H) and 7.37 – 9.47 (m, 12H, ArH's).
18c	IR: 3220, 3157 (NH_2), 3036 (CH aromatic), 1720, 1639 (CO's), 1616 (C=C).
	^{1}HNMR: 4.29 (s, 2H, NH_2), 4.89 (s, 1H), 7.28 - 9.54 (m, 12H, ArH's)
19a	IR: 3136 (CH aromatic); 2198 (CN); 1716, (CO); 1593 C=C).
	^{1}HNMR: 7.35- 9.49 (m, ArH's)
19b	IR: 3058 (CH aromatic); 2171 (CN); 1720 (CO); 1585 (C=C).
	^{1}HNMR: 2.37 (s, 3H, CH_3); 7.34-9.41 (m, 13H, ArH's)
21a	IR: 2194 (CN); 1716, 1684 (CO's); 1594 (C=C).
	^{1}HNMR: 7.28-9.54 (m, ArH's).
21c	IR (KBr): 3136 (CH aromatic); 2923 (CH aliphtic); 1720, 1682 (CO's); 1616 (C=N).
	^{1}HNMR: 7.28 - 9.54 (m, ArH's).
23	IR: 3232 (NH), 2195 (CN), 1725 (C=O) and 1611 (C=C).
	^{1}HNMR: 7.21-9.54 (m, 13H, ArH's), 11.85 (s, 1H, NH) and 12.10 (s, 1H, SH).
24a	^{1}HNMR: 1.15 (t, 3H, $\underline{CH_3}CH_2$), 3.60 (s, 2H, CH_2), 4.08 (q, 2H, $CH_3\underline{CH_2}$), 7.32 – 9.15 (m, 13H, ArH's) and 11.86 (s, br, 1H, NH).
24b	IR: 3136 (CH aromatic); 2923 (CH aliphtic); 1720, 1716 (CO's); 1616 (C=N).
	^{1}HNMR = 2.28 (s, 3H, CH_3), 5.69 (s, 2H, CH_2), 7.51-9.29 (m, 12H, ArH`s) and 11.98 (s, 1H, NH).
24c	IR: 3417 (NH aromatic); 2175 (CN); 1716; 1665 (CO's); 1616 (C=N).
	^{1}HNMR = 4.12 (s, 2H, CH_2), 7.32- 9.12 (m, 18H, ArH's) and 11.87 (s, 1H, NH).
24d	IR: 3425 (NH); 2923 (CH aliphatic); 2187 (CN); 1716 (CO); 1593 (C=C).
	^{1}HNMR: 4.70 (s, 2H, CH_2); 7.46- 9.29 (m, 13H, ArH's); 12.03 (s, 1H, NH).
24e	IR: 3402 (NH); 2912 (CH aliphatic); 2202 (CN); 1716, (CO).
	^{1}HNMR: 2.28 (s, 3H, SCH_3); 7.51-9.30 (m, 13H, ArH`s); 11.98 (s, 1H, NH).
25a	IR: 3420, 3321 (NH, NH_2), 1716, 16243 (CO's), 1581 (C=C).
	^{1}HNMR:1.15 (t, 3H, $\mathbf{CH_3}CH_2$), 4.08 (q, 2H, $CH_3\mathbf{CH_2}$), 6.12 (s, br, 2H, NH_2), 7.32 – 9.16 (m, 13H, ArH's) and 11.84 (s, br, 1H, NH).
25b	IR: 3425, 3420 (NH_2); 1716 (CO); 1593 (C=C).
	^{1}HNMR: 2.40 (s, 3H, CH_3); 6.05 (s, br, 2H, NH_2), 7.27- 9.49 (m, 13H, ArH's), 11.98 (s, 1H, NH).
25c	IR: 3406, 3317 (NH_2); 1716, 1727 (CO's); 1600 (C=C).
	^{1}HNMR: 6.05 (s, br, 2H, NH_2), 7.27- 9.49 (m, 18H, ArH`s), 12.53 (s, 1H, NH).
25d	IR: 2198 (CN); 1724, 1674 (CO's).
	^{1}HNMR: 6.11 (s, br, 2H, NH_2), 7.32- 9.16 (m, 13H, ArH`s),11.83 (s, 1H, NH).
26a	IR: 2198 (CN), 1743, 1716 (CO's), 1594 (C=C).
	^{1}HNMR: 1.15 (t, 3H, $CH_2\mathbf{CH_3}$), 4.08 (q, 2H, $\mathbf{CH_2}CH_3$), 7.14–9.63 (m, 13H, ArH's).
26b	IR: 2923 (CH aliphtic); 2198 (CN); 1743, 1765 (CO's); 1593 (C=C).
	^{1}HNMR: 3.60 (s, 3H, CH_3); 7.32- 9.16 (m, 13H, ArH`s).
26c	IR: 2923 (CH aliphtic); 2198 (CN); 1743, 1700 (CO's); 1593(C=C).
	^{1}HNMR: 7.32- 9.16 (m, ArH`s).
27	IR: 2923 (CH aliphtic); 2198 (CN); 1743 (CO); 1593 (C=C).
	^{1}HNMR: 3.60 (s, 3H, CH_3); 7.32- 9.16 (m, 8H, ArH`s); 11.87 (s, 1H, SH).
28	IR: 3506, 3317, 3285 (NH, NH_2) 1716 (CO); 1594 (C=C).
	^{1}HNMR: 6.12 (s, br, 2H, NH_2); 7.19- 9.3 (m, 13H, ArH`s); 11.87 (s, 1H, NH), 13.82 (s, 1H, NH).
29	IR: 3290 (NH), 1716, 1624 (CO's) and 1596 (C=C).
	^{1}HNMR: 2.35 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 7.57 – 9.35 (m, 14H, ArH's) and 11.98 (s, br, 1H, NH).
30	IR: 1716, 1664 (CO's); 1594 (C=C).
	^{1}HNMR: 2.39 (s, 3H, CH_3), 3.98 (s, 2H, CH_2), 7.27- 9.49 (m, 13H, ArH`s), 11.98 (s, 1H, NH)
31	IR: 2214 (CN), 1716, 1624 (CO's) and 1594 (C=C).
	^{1}HNMR: 6.12 (s, 2H, NH_2), 7.32 - 9.16 (m, 18H, ArH's), 11.87 (s, br, 1H, NH).
32	IR: 1716, (CO); 1624 (C=N); 1593 (C=C).
	^{1}HNMR: 7.32- 9.16 (m, 19H, ArH`s), 11.86 (s, 1H, NH), 13.95 (s, 1H, NH).
36	IR: 2198 (CN); 1716 (CO); 1624 (C=N); 1593 (C=C).
	^{1}HNMR: 5.64 (s, 1H, pyrimidi9ne H-5), 7.27- 9.49 (m, 18H, ArH`s), 11.86 (s, 1H, NH).

2*H*-chromen-3-one (**28**). Structure **28** was confirmed on the basis of elemental analysis, spectral data and chemical transformation. Thus, compound **28** was reacted with 2,4-pentanedione in boiling acetic acid under reflux to afford 2-{2-[5,7-dimethyl-2-(phenylamino)-7a-hydropyrazolo-[1,5-*a*]pyrimidin-3-yl]-1,3-thiazol-4-yl}benzo[*f*]-chromen-3-one (**29)**.

Analogously, 2-{2-[5-amino-3-(phenylamino)pyrazol-4-yl]-1,3-thiazol-4-yl}-benzo[*f*]-2*H*-chromen-3-one (**28**) was reacted with ethyl 2-oxobutanoate in boiling acetic acid to give one isolable product was formulated as: 2-{2-[7-methyl-5-oxo-2-(phenylamino)-4,7a-hydropyrazolo-[1,5-*a*]pyrimidin-3-yl]-1,3-thiazol-4-yl}benzo[*f*]chromen-3-one (**30)**. Structure **30** was elucidated by elemental analysis, spectral data and alternative synthesis route. Thus, treatment of **28** with acetoacenalide in boiling acetic acid gave product identical in all respects (mp. mixed mp. and spectra) with **30**. Treatment of **28** with α-cyanocinnamonitrile **16a** in boiling ethanol containing catalytic amounts of piperidine under reflux gave isolable product evidence by mechanism which could be formulated 7-amino-3-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]-2-phenyl-amino-5-phenyl-7a-hydro-pyrazolo[1,5-*a*]pyrimidine-6-carbonitrile **(31)** (Scheme 5). The reaction seemed to proceed through Michael addition reaction between **28** and **16a** to give intermediate **33** or **34**, which underwent cyclization *via* addition of the NH hydrogen to the nitrile functional group followed by autoxidation to give the final product **31** (Scheme 5). More evidence for structure **31** came from its independent synthesis, treatment of 2-{2-[5-(1-aza-2-phenylvinyl)-3-phenylaminopyrazol-4-yl]-1,3-thiazo-4-yl}benzo[*f*]-2*H*-chromen-3-one **(32)**, which was prepared *via* reaction of **28** with benzaldehyde and malononitrile in boiling ethanol containing catalytic amount of piperidine gave product identical in all respects (mp. mixed mp. and spectra) with **31** (Scheme 5).

Finally, ethyl α-cyanocinnamate was reacted with **20a** and **28** in boiling ethanol containing catalytic amount of piperidine under reflux gave isolable product which could be formulated 7-oxo-3-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]-2-phenyl-amino-5-phenyl-6,7a-dihydro-pyrazolo[1,5-*a*]pyrimidine-6-carbonitrile **(36)** (Scheme 5). Also, treatment of **32**, with ethyl cyanoacetate in boiling ethanol containing catalytic amount of piperidine under reflux to give product identical in all respects (mp. mixed mp. and spectra) with **36** (Scheme 5). The reaction seemed to proceed through Michael addition of the hydrogen from exocyclic amine to **28** to give adduct intermediate **37** which underwent cyclization to **38** *via* elimination of ethanol followed by outoxidation to give the final product **36** *via* elimination of ethanol.

EXPERIMENTAL

All melting points were determined on an Electrothermal apparatus and are uncorrected. The IR spectra are expressed in cm^{-1} and recorded in KBr pellets on a Pa-9721 IR spectrometer. ^{1}H NMR spectra were obtained on a Varian EM-390 (90) MHz spectrometer in DMSO-d_6 as solvent and TMS as internal reference. Chemical shifts (δ) are expressed in ppm. Mass spectra were recorded on Kratos (75eV) MS equipment. Elemental analysis was carried out at the Microanalytical Data Unit at the National Research Center, Giza, Egypt. Hydrazonoyl halides were prepared as previously methods [11-13].

2-[4-(3-Oxo-3*H*-benzo[*f*]chromen-2-yl)thiazol-2-yl)-1,3-thiazol-2-yl]ethanenitrile (**3**). A mixture of **1** (3.17 g, 0.01mol) and cyanothioacetamide (1 g, 0.01 mol) in ethanol (20 mL) was refluxed for 3 hrs. The resulting solid was collected and washed with boiling water containing sodium acetate then recrystallized from dioxan-ethanol mixture to give **3** (tables 1and 2).

2-(2-Arylhydrazono)-2-(4-oxo-3*H*-benzo[*f*]chromen-2-yl)thi-azol-2-yl)ethanenitrile 4a,b. Method (A). A mixture of **1** (3.17 g, 0.01mol) and the appropriate of arylazocyanothio-acetamide (1.0 g, 0.01 mol) in ethanol (20 mL) was heated under reflux for 2 hrs. The resulting solid was collected, washed with boiling water containing sodium acetate recrystallized from *N,N*-dimethylformamide to give **4a** and **4b**, respectively (Tables 1 and 2).

Method (B). A solution of the appropriate aryldiazonium chlorides (0.01 mol) was added to a solution of **3** (3.18 g, 0.01 mol) and sodium acetate (1.3 g, 0.01 mol) in ethanol (30 mL) at 0-5°C while stirring. The reaction mixture was stirred for 6 hrs at 0°C; the resulting solid was collected and recrystallized from *N,N*-dimethylformamide to give **4a** and **4b**, respectively (Tables 1 and 2)

Ethyl 4-amino-1-aryl-3-[4-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)-1,3-thiazol-2-yl]-1*H*-pyrazole-5-carboxylate 6a,b. A mixture of the appropriate **4a, b** (0.01 mol) and ethyl chloroacetate (0.01 mol) in DMF (20 mL) containing anhydrous potassium carbonate (0.01 mol) was refluxed in an oil bath at 130°C for 3 hrs. The mixture was cooled and triethylamine (1 mL) was added then the reaction mixture was refluxed for 1 h at 90°C. The reaction mixture was then poured over 100 mL of an ice-water mixture. The resulting solid was collected and recrystallized from dioxan to give **6a** and **6b**, respectively (Tables 1 and 2).

1-Aryl-3-[4-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)-1,3-thiazol-2-yl]-5-thioxo-1,4,5,6-tetrahydro-7*H*-pyrazolo[4,3-*d*]pyrimid-in-7-one 7a,b. A mixture of the appropriate **6a, b** (0.01 mol) and ammonium thiocyanate (0.76 g, 10 mmol) in acetic acid (20 mL) containing hydrochloric acid (1 mL, 12 *M*) was heated under reflux for 3 hrs. The reaction mixture was poured over ice (100 g). The resulting solid was collected and recrystallized from the proper solvent to give 7a and 7b, respectively (Tables 1 and 2).

1-Aryl-3-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]-7a-hydro-6*H*-pyrazolo[4,3-*d*]-1,3-thiazolino[3,2-*a*]-pyrimidin-7,8-dione 8a,b and 1-aryl-2-[5-methylthio-7-oxo-6-hydropyrazolo[4,5-*d*]pyrimidin-3-yl]-1,3-thiazol-4-yl)benzo-[*f*]chromen-3-one 9a,b. A mixture of the appropriate **7a, b** (0.01 mol), potassium hydroxide (0.56 g, 0.01 mol) in *N,N*-dimethylformamide (25 mL) was stirred for 4 hrs. The appropriate ethyl chloroacetate (1.22 g, 0.01 mol) or iodomethane (1.42 g, 0.01 mol) was added dropwise while stirring to the above mixture and stirring was continued for 30 min. The resulting solid was collected, washed with water and recrystallized from dioxan to give **8a**, **8b** and **9a**, **9b**, respectively (tables 1 and 2).

Ethyl 2-aryl-3-oxo-3[4-(3-oxobenzo[*f*]-2H-chormen-2-yl)-(1,3-thiazol-2-yl)-1-phenyl-7a-hydropyrazolo[4,5-*d*]1,2,4-triazolino[4,3-*a*]pyrimidine-7-carboxylate 11a,b. and 2-[2-(7-Acetyl-2-aryl-3-oxo-5-phenyl-7a-hydropyrazolo[4,5-*d*]triazolino[4,3-*a*]-pyrimidin-3-yl)-1,3-thiazol-4-yl]benzo[*f*]-2*H*-chromen-3-one 11c, d. Equimolar amounts of each **7a** and **7b**, the appropriate of hydrazonyl halides **10a,b** and triethylamine (0.01mol of each) in chloroform (20 mL) was refluxed for 10 hrs. The reaction mixture was evaporated under vacuum. The resulting solid was collected and recrystallized from *N,N*-dimethylformamide to give **11a-d** respectively (Tables 1 and 2).

5-Amino-7-aryl-3-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)-6,3a-dihydro-1,3-thiazolino[3,2-*a*]pyridine-5,7-dicarbonitrile 18a-c and 4-oxo-3-(3-oxobenzo[*f*]-2H-chromen-2-yl)-6-aryl-3a-hydro-1,3-thiazolino[3,2-*a*]pyridine-5,7-dicarbonitrile 21a-c. Method A. A mixture of **3** (3.18 g, 0.01 mol) and the appropriate of 2-aryl-1-cyanoacrylonitrile derivatives **16a-c** or 2-arylacrylate derivatives **20a-c** (0.01 mol) in ethanol (20 mL) containing a catalytic amount of piperidine was refluxed for 4 hrs. The resulting solid was collected and recrystallized from dioxan to give **18a-c** and **21a-c**, respectively (Tables 1 and 2).

Method B. A mixture of the appropriate of **19a-c** (0.01 mol) and malononitrile (or ethyl cyanoacetate) (0.01 mol) in ethanol (20 mL) containing a catalytic amount of piperidine was refluxed for 4 hrs. The resulting solid was collected and recrystallized from dioxan to give **18a-c** and **21a-c**, respectively.

3-Aryl-2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]prop-2-enenitrile 19a-c. Method (A). A mixture of **1** (0.01 mol, 3.17 g) and the appropriate of α-arylidenecyanothioamide derivatives (0.01 mol) in ethanol (20 mL) was refluxed for 2 hrs. The resulting solid was washed with boiling water containing sodium acetate and recrystallized from dioxan to give **19a-c**, respectively (Tables 1 and 2).

Method (B). A mixture of **20** (3.18 g, 0.01 mol) and the appropriate of aromatic aldehyde (0.01 mol) in ethanol (20 mL) containing a catalytic amount of piperidine was refluxed for 4 hrs. The resulting solid was collected and recrystallized from dioxan to give **19a-c**, respectively.

3-Methylthio-2-[4-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]-3-thioxopropanenitrile 27. A mixture of **3** (3.18 g, 0.01 mol), potassium hydroxide (0.56 g, 0.01 mol) and carbon disulfide (0.76 g, 0.01 mol) in *N,N*-dimethylformamide (15 mL) was stirred for 4 hrs. Iodomethane (1.52 g, 0.01 mol) was added drop wise while stirring to the above mixture and stirring was continued for 30 min. The resulting solid was collected, and crystallized from *N,N*-dimethylformamide to give **27** (Tables 1 and 2).

Ethyl {2-cyano-2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)](phenylamino)vinylthio}-acetate (24a), 2-[4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)-3-(2-oxopropylthio)-3-(phenylamino)prop-2-enenitrile (24b), 2-[4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)-3-(2-oxophenylethylthio)-3-(phenylamino)prop-2-enenitrile (24c), 3-(cyanoethylthio)2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)-3-phenylamino)prop-2-enenitrile (24d) and 3-methylthio-2-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)-3-(phenylamino)-prop-2-enenitrile (24e). A mixture of **3** (3.18 g, 0.01 mol), potassium hydroxide (0.56 g, 0.01 mol) and phenyl isothiocyanate (1.35 g, 0.01 mol) in *N,N*-dimethylformamide (25 mL) was stirred for 4 hrs. The appropriate of ethyl chloroacetate, chloroacetone, phenacyl bromide, chloroacetonitrile and iodomethane (0.01 mol) was added dropwise while stirring to the above mixture and stirring was continued for 30 min. The resulting solid was collected, and recrystallized from proper solvent to give **24a-e**, respectively (Tables 1 and 2).

3-Amino-4-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)]-5-phenylamino)-2-substituted thiophenes 25a-d. A solution of the appropriate **24a-d** (1 g) in ethanol (20 mL) containing a catalytic amount of piperidine (3 drops) was heated for 1 hour. The resulting solid was collected and recrystallized from proper solvent to give **25a-d,** respectively (Tables 1 and 2).

2-(3-Oxobenzo[*f*]-2*H*-chromen-2-yl)-3-(phenylamino)-3-sulfanylprop-2-enenitrile (23). A mixture of **3** (3.18 g, 0.01 mol), potasium hydroxide (0.56 g, 0.01 mol) and phenyl isothiocyanate (1.35 g, 0.01 mol) in *N,N*-dimethylformamide (25 mL) was stirred for 4 hrs. Iodomethane (1.42 g, 0.01 mol) was added dropwise while stirring to the above mixture and stirring was continued for 30 min. The resulting solid was acidified with hydrochloric acid (3 *M*). The resulting solid was collected and recrystallized from ethanol **23** (Tables 1 and 2).

2-(5-Acetyl-3-phenyl(1,3,4-thiadiazol-2-ylidene)-2-(4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazo-2-yl)ethanenitrile (26a), ethyl 2-{cyano[(4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazo-2-yl)methylene)-3-phenyl-1,3,4-thiadiazole-2-carboxylate (26b) and 2-(5-benzoyl-3-phenyl(1,3,4-thiadiazol-2-ylidene)-2-(4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazo-2-yl ethanenitrile (26c). Method (A). Triethylamine (0.75 ml, 0.005 mol) was added to a mixture of **27** (0.005 mol) and the appropriate hydrazonoyl halides**10a-c** (0.005 mol) in ethanol (15 mL) at room temperature. The reaction mixture was stirred for 2 hrs. The resulting solid was collected and recrystallized from proper solvent to give **26a-c**, respectively (tables 1 and 2).

Method (B). A mixture of **3** (3.18 g, 0.01 mol), potassium hydroxide (0.56 g, 0.01 mol) and phenyl isothiocyanate (1.35 g, 0.01 mol) in *N,N*-dimethylformamide (15 mL) was stirred for 4 hrs. The appropriate of hydrazonoyl halides **10a-c** (10 mmol) was added portion-wise while stirring to the above mixture and stirring was continued for 30 min. The resulting solid was collected and recrystallized from proper solvent to give **26a-c**, respectively.

2-{2-[5-Amino-3-(phenylamino)pyrazol-4-yl]-1,3-thiazol-4-yl}benzo[*f*]-2*H*-chromen-3-one (28). A mixture of **24e** (4.67 g, 0.01 mol) and hydrazine hydrate (1 mL, 99%) in ethanol (20 mL) was refluxed for 18 hrs, the solid product formed was collected and recrystallized from *N,N*-dimethylformamide to give **28** (tables 1 and 2).

3-{2-[5,7-Dimethyl-2-(phenylamino)-7a-hydropyrazolo-[1,5-*a*]pyrimidin-3-yl]-1,3-thiazol-4-yl}benzo[*f*]-2*H*-chromen-3-one (29) and 3-{2-[7-methyl-5-oxo-2-phenylamino]-4,7a-dihydropyrazolo[1,5-*a*]pyrimidin-3-yl]-1,3-thiazol-4-yl}benzo-[*f*]-2*H*-chromen-3-one (30). A mixture of **28** (4.51 g, 0.01 mol) and the appropriate 2,4-pentanedione or ethyl 3-oxobutanoate (or acetoacetanilide) (0.01 mol) in acetic acid (20 mL) was boiled under refluxed for 3 hrs. The resulting solid was collected and recrystallized from *N,N*-dimethylformamide to give **29** and **31**, respectively (Tables 1 and 2).

7-Amino-3-[4-(3-oxo-benzo[*f*]-2*H*-chromen-2-yl)(1,3-thiazol-2-yl)-5-phenyl-2-(phenylamino)-7a-hydropyrazolo[1,5-*a*]-pyrimidine-6-carbonitrile (31) and 7-oxo-3-[4-(3-oxobenzo[*f*]-2*H*-chromen-2-yl)(-1,3-thiazol-2-yl)-5-phenyl-2-(phenylamino-6,7a-dihydropyrazolo[1,5-*a*]pyrimidine-6-carbonitrile (36).

Method (A). Equimolar amounts of **28** and the appropriate of 2-phenyl-1-cyanoacrylonitrile derivatives **16a** or ethyl 2-phenyl acrylate (0.01 mol) in ethanol (20 mL) containing a catalytic amount of piperidine was refluxed for 4 hrs. The resulting solid was collected and recrystallized from DMF to give **31** and **36**, respectively (Tables 1 and 2).

Method (B). Equimolar amounts of **32** and malononitrile (or ethyl cyanoacetate) (0.01 mol) in ethanol (20 mL) containing a catalytic amount of piperidine was refluxed for 4 hrs. The resulting solid was collected and recrystallized from *N,N*-dimethylformamide to give **31** and **36**, respectively.

3-{2-[5-(1-Aza-2-phenylvinyl)-3-(phenylamino)pyrazol-4-yl)-1,3-thiazol-4-yl]-2*H*-benzo[*f*]chromen-3-one (32). Equimolar amounts of **28** and benzaldehyde (0.01 mol) in ethanol (20 mL) containing a catalytic amount of piperidene was refluxed for 3 hrs. The solid product formed was collected and recrystallized from dioxan to give **32** (tables 1 and 2).

REFERENCES

[1] Anderson, D.M.; Shelley, S.; Crick, N.; Buraglio, M. *J. Clin. Pharmacol,* **2002**, *42*, 1358.

[2] Tassies, D.; Freire, C. J. Monteagudo; Ordinas, A.; Reverter, J.C. *Haematolgica*, **1992**, *87*, 1185

[3] Stone, W.B.; Okoniewski, J.C.; Stedelin, J.R. *J. Wildlife Dis*. **1999**, *35*, 187.

[4] Weick, J.; Thorn, R.S. *J. Econ. Entomol*, **2002**, *95*, 227.

[5] Mitscher, L.A. "Principles of Medicinal Chemistry" W. O. Foye, T. L.Lemke and D. A. Williams, pp. 819-864, 5th ed. Williams and Wikins, Baltimore, 2002.

[6] Lafitte,D.; V. Lamour, V.; Tsvetkov, P. O.; Makarov, A.A.; Klich, M.; Deprez, P.; Moras, D.; Briand, C.; Gilli, R. *Biochemistry* **2002**, *41*, 7217.

[7] Kornis, D.I. Comperhensive Heterocyclic Chemistry, edited by A. R. Katritzky, C. W. Ress and E. F. V. Scriven (Pergamon, Oxford, **1996**), Vol. 4.

[8] Moustapha, C.; Abdel-Riheem, N.A.; Abdelhamid, A.O. *Synthetic Communication* **2005**, *35*, 249.

[9] Brunskill, J.S.A; De, A.; Ewing, O.F., *J. Chem. Soc, Perkin Trans I*, **1978**, 629.

[10] Broggiui, G.; Garanti, L.; Molteui, G.; Zecch, G., *Tetrahedron* **1988**, *54*, 2843.

[11] Fravel, G.; Bull. *Soc. Chim. Fr*. **1904**, *31*, 150.

[12] Eweiss, N.E.; Osman, A. *Tetrahedron Lett*. **1979**, 1169.

[13] Shawali, A.S.; Abdelhamid, A.O. *Bull. Chem. Soc. Jpn*., **1976**, *49*, 321.