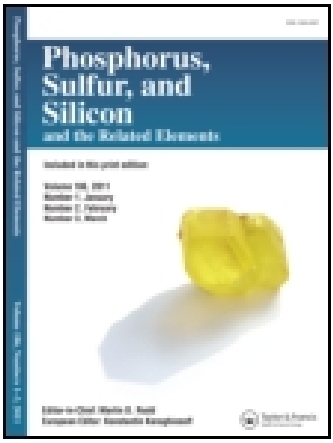

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Reactions of Hydrazonoyl Halides 41: Synthesis of 1,2,4-Triazoles, 2,3-Dihydro-1,3,4-thiadiazoles, and Triazolo[4, 3-a]pyrimidines

Abdou O. Abdelhamid [a] , Ahmed H. Elghandour [b] , Ahmed M. Hussein [b] & Yasser H. Zaki [b]

[a] Department of Chemistry , Faculty of Science, Cairo University (Beni-Suef Branch) , Beni-Suef, Egypt

[b] Department of Chemistry , Faculty of Science, Cairo University , Giza, Egypt

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Reactions of Hydrazonoyl Halides 41:[1] Synthesis of 1,2,4-Triazoles, 2,3-Dihydro-1,3,4-thiadiazoles, and Triazolo[4,3-*a*]pyrimidines

Abdou O. Abdelhamid
Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt

Ahmed H. Elghandour
Ahmed M. Hussein
Yasser H. Zaki
Department of Chemistry, Faculty of Science, Cairo University (Beni-Suef Branch), Beni-Suef, Egypt

*Triazoles, thiadiazoles, and triazolo[4,3-*a*]pyrimidines were synthesized via reaction of hydrazonoyl halides with each of 3-methyl-4-(methylthiothioxomethyl)-2-pyrazolin-5-one, 3-methyl-4-[methylthio(phenylamino)methyl]-2-pyrazolin-5-one, and pyrimidine-2-thiones. Structures of the newly synthesized compounds were elucidated on the basis of elemental analysis, spectral data, and alternative-methods synthesis whenever possible.*

Keywords 1,2,4-Triazoles; 2,3-dihydro1,3,4-thiadiazolines; hydrazonoyl halides; triazolino[4,3-*a*]pyrimidines

INTRODUCTION

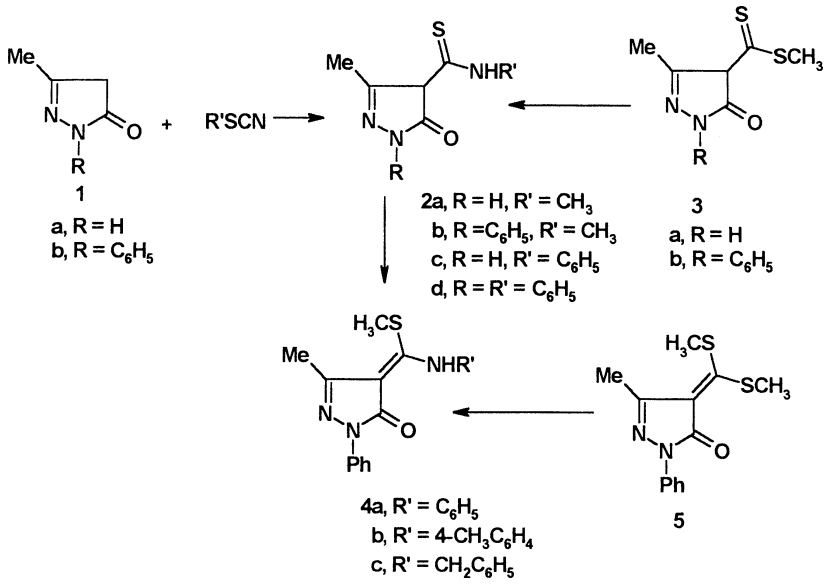
1,2,4-Triazoles display biological activity such as inhibition of cholinesterase, interference with mitosis, and reversible denaturation of serum proteins.[2] 1,3,4-thiadiazole and its derivatives have become very useful compound in medicine, agriculture, and in many fields of technology.[3] As an extension of our study[4–9] and as a part of our program aiming at the synthesis of different 1,2,4-triazoles and 2,3-dihydro-1,3,4-thiadiazoles for medicine, we report here the reactivity of hydrazonoyl halides toward some alkyl carbodithioates, thioanilides, and dihydropyrmidine-2-thiones derivatives.

Received July 24, 2004; accepted October 25, 2004.
Address correspondence to Abdou O. Abdelhamid, Cairo University, Department of Chemistry, Faculty of Science, Giza 12613, Egypt. E-mail: abdou_abdelhamid@yahoo.com

RESULTS AND DISCUSSION

Treatment of methyl isothiocyanate with each of 3-methyl-2-pyrazolin-5-one (**1a**) or 3-methyl-1-phenyl-2-pyrazolin-5-one (**1b**) in N,N-dimethylformamide containing potassium hydroxide afforded 3-methyl-4-(methylthiothioxomethyl)-2-pyrazolin-5-one (**2a**) and 3-methyl-4-(methylthiothioxomethyl)-1-phenyl-2-pyrazolin-5-one (**2b**), respectively. Structure **2** was elucidated by elemental analysis, spectral data, and chemical transformation. ^{1}H NMR spectrum of **2a** showed signals at $\delta = 2.25$ (s, 3H), 3.22 (s, 3H), 5.26 (s, 1H), 9.88 (s, br., 1H), 11.10 (s, br., 1H), and ^{1}H NMR spectrum of **2b** showed signals at $\delta = 2.17$ (s, 3H), 3.32 (s, 3H|), 5.26 (s, 1H), 7.26–7.42 (m, 3H), 7.77–7.81 (d, 2H) and 10.85 (s, br., 1H). The appropriate **1a** or **1b** reacted with phenyl isothiocyanate to give **2c**[10,11] and **2d**,[10,11] respectively. Also, each **3a**[10,13] and **3b** that reacted with aniline in boiling ethanol have products identical in all respects (mp., mixed mp., and spectra) with **2c** and **2d**, respectively.

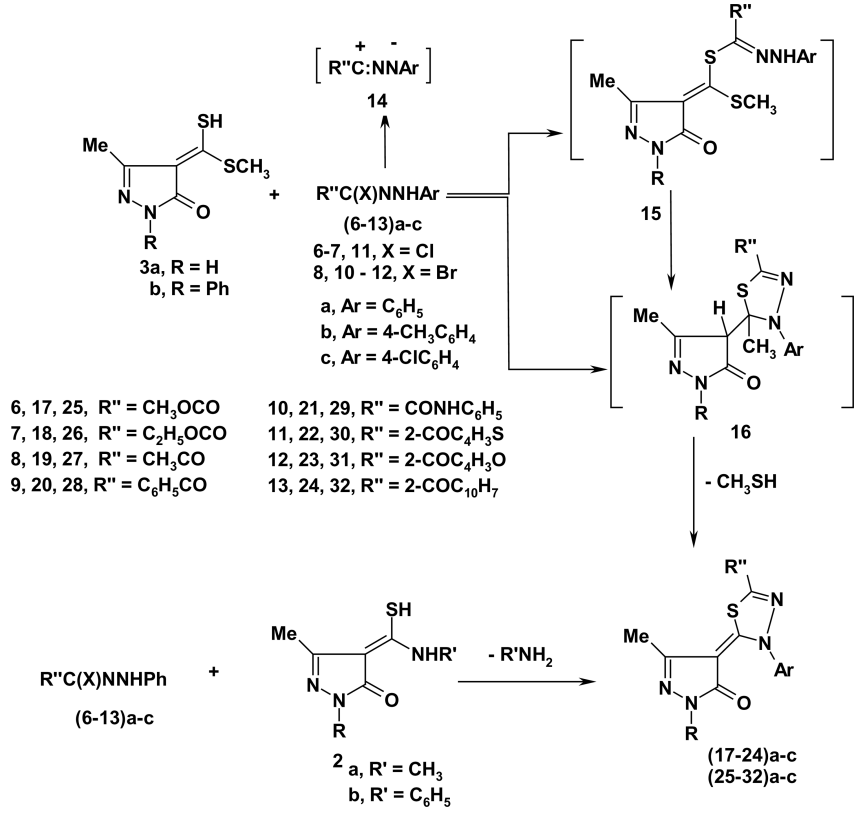
Compound **4a**[10] was obtained via methylation of **2d** or by the reaction of 4-(dimethylthiomethylene)-3-methyl-1-phenyl-2-pyrazolin-5-one (**5**)[12] with aniline. By a similar route, compound **5** reacted with the appropriate *p*-toluidene and benzylamine to give **4b** and **4c**, respectively (Scheme 1). Structures **4b** and **4c** were elucidated by elemental analysis and spectral and chemical transformation.



SCHEME 1

Treatment of the appropriate *C*-methoxycarbonyl-*N*-phenylhydrazonoyl chloride **6a** with **2a** in ethanolic triethylamine at room temperature afforded one isolable product **17a**. ^{1}H NMR spectrum of the product showed signals 1.04 (s, 3H), 3.95 (s, 3H), 7.46–7.80 (m, 5H, ArH's), and 11.26 (s, 1H, NH). Compound **6a** reacted with each of **2c** or **3a** in ethanolic triethylamine to afford a product identical in all respects (mp., mixed mp., and spectra) with **17a**.

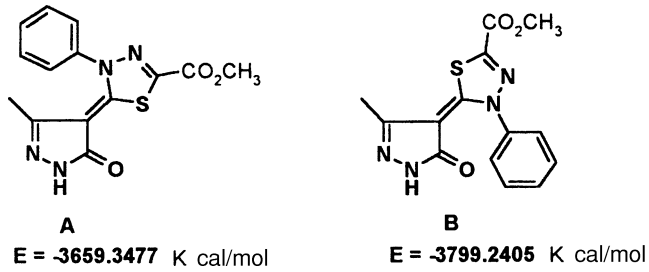
Also, treatment the appropriate of **2a** (**3a**) and **2b** (or **2c–d**, **3b**) with the appropriate hydrazonoyl halides **6–13(a–c)** in ethanolic triethylamine afforded 2,3-dihydro-1,3,4-thiadiazoles **17–24(a–c)** and **25–32(a–c)**, respectively (Scheme 2). Structures **17–24** and **25–32** were confirmed on the basis of elemental analysis and spectral data. Thus, ^{1}H NMR spectrum of **25a** showed signals at $\delta = 1.29$ (s, 3H), 4.04 (s, 3H), 7.26–7.30 (m, 3H), 7.60 (s, 5H), and 7.88–8.03 (d, 2H).



SCHEME 2

Two possible pathways can account for the formation of **17a** (1) 1,3-addition of the thiol isomer **3a** to the hydrazonoyl chloride **6a** (or nitrilium imide **14a**, which is prepared in situ from **6a** and triethylamine) can give the thiohydrazonate ester **15**, which undergoes nucleophilic cyclization to yield **16,** which then affords **17a** by loss of CH_3SH and (2) alternatively, 1,3-cycloaddition of the nitrilum imide **14a** to the C=S of **3a** can give **16a**, which converted to **17a** via elimination of CH_3SH (Scheme 2).

Sterochemically, the isolated products can have either the configuration A or B. According to M. O. Calculation, using the Hyper Chem. AM1 semiemperical method, the total energy proved that the most stable isomer formulated as B as shown (Scheme 3):

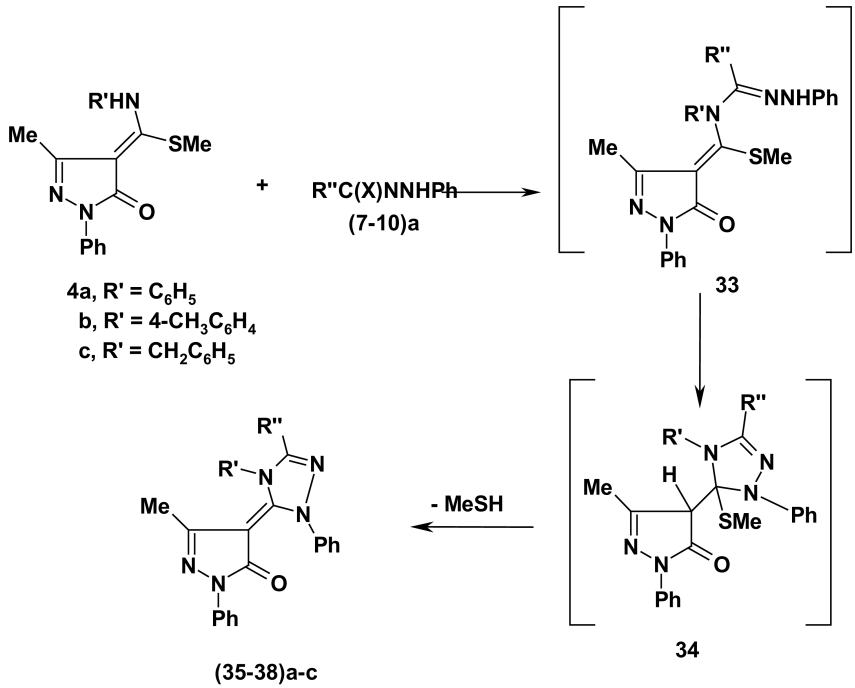


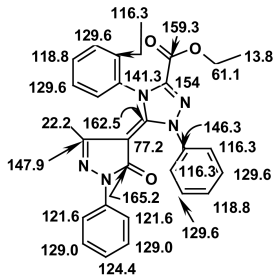
SCHEME 3

Treatment of **4a** with *C*-ethoxycarbonyl-*N*-phenylhydrazonoyl chloride (**7a**) in boiling ethanolic triethylamine under reflux gave ethyl 5-(3-methyl-5-oxo-1-phenyl(2-pyrazolin-4-ylidene))-1,4-diphenyl-1,2,4-triazoline-3-carboxylate (**35a**) in good yield. Structure **35** was confirmed on the basis of elemental analysis and spectral data (Scheme 4). Thus, ^{1}H NMR spectrum of **35a** showed signals at $\delta = 1.28$ (s, 3H), 1.31 (t, 3H), 4.12 (q, 2H) and 7.21–7.89 (m, 15H). ^{13}C NMR spectrum of **35a** is shown in Scheme 4.

Treatment of the appropriate hydrazonoyl halides **7a–10a** with each of **4a–c** under the same condition afforded 1,2,4-triazolin-5-ylidene-2-pyrazolin-5-one derivatives **35–38(a–c)**, respectively. Mass spectrum of **38a** revealed peaks at m/z (%) = 512 (12), 328 (33), 206 (46.9), 200 (42.5), 181 (19.8), 180 (32.3), 119 (31), 108 (11), 104 (56), and 77 (100).

Treatment of the appropriate hydrazonoyl halides **7a–10a** with each of ethyl 4-methyl-5-substituted-2-thioxo-1,3,6-trihydropyridine-5-carboxylates **39a** and **39b** in boiling chloroform containing trietyhlamine under reflux, which afforded ethyl 6-methyl-1-phenyl-3,4-disubstituted-4,3a-dihydro-1,2,4-triazolino[4,3-a]pyrimidine-5-carboxylates **(43–46)a**,**b**, respectively (Scheme 5).



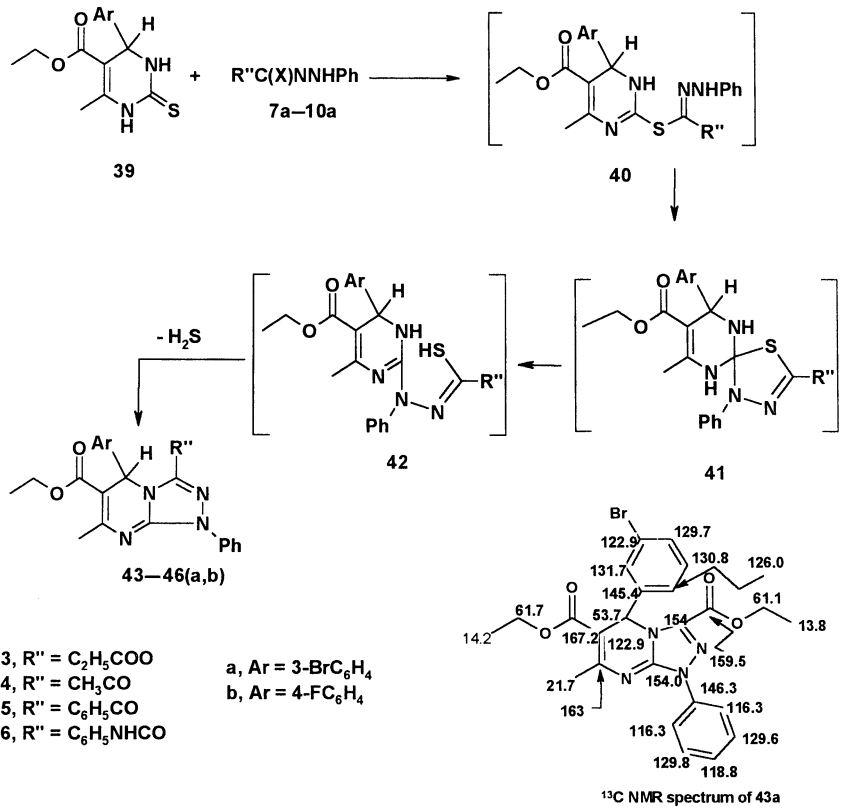


^{13}C NMR spectrum of 35a

SCHEME 4

Structures of **43–46** were elucidated on the basis of elemental analysis and spectral data. Thus, the ^{1}H NMR spectrum of **43a** showed signals at $\delta = 1.20$ (t, 3H), 1.35 (t, 3H), 2.53 (s, 3H), 4.09 (q, 2H), 4.41 (q, 2H), 6.83 (s, 1H), 7.12–7.55 (m, 7H), 8.17–8.21 (d, 2H), and its ^{13}C NMR spectrum shown in Scheme 5.

In the light of the foregoing results, the mechanism outlined in Scheme 5 seems to be the most plausible pathway for the formation



SCHEME 5

of **43–46**(**a**,**b**) from the reaction of the appropriate **7a–10a** with the appropriate **39a**,**b**. The reaction involves initial formation of thiohydrazonates (**40**), which undergoes intermolecular cyclization as soon as it is formed to give the spiro intermediate (**41**). Ring chain tautomerism of spiro intermediate (**41**) leads to the end products **43–46** via the elimination of hydrogen sulfide.

EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300 MHz spectrometer and chemical shifts are expressed in δ units using TMS as an internal reference. Mass spectra were recorded on a GC-MS

QP1000 EX Shimadzu. Elemental analyses were carried out at the Microanalytical Center of the Cairo University, Egypt. Compounds **2c**,[10,11] **3a**,**b**,[13,14] **4a**,[12] and (**6–13**)**a–c**[15–22] were prepared as previously reported.

3-Methyl-1-substituted 4-[(Substituted Amino)thioxomethyl]-2-pyrazolin-5-ones 2a–d

Method A

An equimolar amount of the appropriate **1a** and **1b**, the appropriate methyl isothiocyanate, and phenyl isothiocyanate and potassium hydroxide (5 mmol each) in dry dimethylformamide (15 mL) were stirred for 6 h at room temperature. The reaction mixture was diluted with water (50 mL) and then acidified with dilute hydrochloric acid. The resulting solid was collected and crystallized to give **2a–d**, respectively, as yellow crystals (Tables I and II).

Method B

A mixture of the appropriate **3a**, **3b** and aniline (5 mmol each) in ethanol (20 mL) was boiled under reflux for 3 h. The resulting solid was collected and crystallized from ethanol to give identical products with the corresponding **2a** and **2b**.

3-Methyl-4-[methylthio(arylamino)methyl-1-phenyl-2-pyrazolin-5-ones 4a–c

Method A

A mixture of 4-(dimethylthiomethylene)-3-methyl-1-phenyl-2-pyrazolin-5-one (**5**) (2.78 g, 5 mmol) and the appropriate amine (aniline, p-topluidine, or benzylamine) (5 mmol) in ethanol (20 mL) was refluxed for 3 h. The resulting solid was collected and crystallized from ethanol to give **4a–c**, respectively (Tables I and II).

Method B

A mixture of equimolar amounts of **2b** and potassium hydroxide (5 mmol each) in N,N-dimethylformamide (15 mL) was stirred for 2 h. Iodomethane (0.71 g (0.32 mL), 5 mmol) was added to the above reaction mixture with stirring for 2 h and then diluted with water (50 mL). The resulting solid was collected and crystallized to afford a product identical in all respects (mp., mixed mp., and spectra) with **4a**.

TABLE I Characterization Data of the Newly Synthesized Compounds

Comp. no.	Mp. °C solvent	Color yield %	Mol. formula (Mol. Wt.)	Calcd./Found % C	H	N	S
2a	215–7	Yellow	$C_6H_9N_3O\,S$	42.09	5.30	24.54	18.73
	EtOH	65	171.22	42.20	5.10	24.30	18.50
2b	203–205	Yellow	$C_{12}H_{13}N_3O\,S$	58.28	5.30	16.99	12.97
	EtOH	70	247.31	58.40	5.50	17.20	13.10
2c	223–5	Yellow	$C_{11}H_{11}N_3O\,S$	56.63	4.75	18.01	13.75
	EtOH	65	233.29	56.80	4.50	17.90	13.90
4b	152–4	Yellow	$C_{19}H_{19}N_3O\,S$	67.63	5.68	12.45	9.50
	EtOH	82	337.44	67.50	5.80	12.50	9.40
4c	99–101	Yellow	$C_{19}H_{19}N_3O\,S$	67.63	5.68	12.45	9.50
	EtOH	85	337.44	67.80	5.80	12.60	9.30
17a	252–5	Yellow	$C_{14}H_{12}N_4O_3S$	53.16	3.82	17.71	10.14
	AcOH	88	316.33	53.00	3.90	17.90	10.30
17b	231–4	Yellow	$C_{15}H_{14}N_4O_3S$	54.53	4.27	16.96	9.71
	AcOH	90	330.36	54.70	4.30	16.80	9.80
17c	284–7	Yellow	$C_{14}H_{11}Cl\,N_4O_3S$	47.94	3.16	15.97	9.14
	AcOH	90	350.78	47.70	2.90	15.70	9.30
18a	249–1	Yellow	$C_{15}H_{14}N_4O_3S$	54.53	4.27	16.96	9.71
	AcOH	85	330.36	54.70	4.30	17.10	9.60
18b	237–9	Yellow	$C_{16}H_{16}N_4O_3S$	55.80	4.68	16.27	9.31
	AcOH	89	344.38	55.90	4.60	16.40	9.50
18c	247–50	Yellow	$C_{15}H_{13}Cl\,N_4O_3S$	49.39	3.59	15.36	8.79
	AcOH	87	364.80	49.50	3.70	15.60	8.90
19a	281–3	Yellow	$C_{14}H_{12}N_4O_2S$	55.99	4.03	18.65	10.68
	AcOH	90	300.33	56.10	4.00	18.50	10.80
19b	257–60	Yellow	$C_{15}H_{14}N_4O_2S$	57.31	4.49	17.82	10.20
	AcOH	85	314.36	57.10	4.60	17.90	10.00
19c	289–91	Yellow	$C_{14}H_{11}Cl\,N_4O_2S$	50.23	3.31	16.74	9.58
	AcOH	85	334.78	50.10	3.30	16.60	9.70
20a	259–62	Yellow	$C_{19}H_{14}N_4O_2S$	62.97	3.89	15.46	8.85
	AcOH	85	362.40	62.80	3.80	15.20	8.60
20b	270–72	Yellow	$C_{20}H_{16}N_4O_2S$	63.81	4.28	14.88	8.52
	AcOH	90	376.43	63.90	4.00	14.90	8.70
20c	280–3	Yellow	$C_{19}H_{13}Cl\,N_4O_2S$	57.50	3.30	14.12	8.08
	AcOH	90	396.85	57.30	3.10	14.10	8.00
21a	280–2	Yellow	$C_{19}H_{15}N_5O_2S$	60.46	4.01	18.56	8.50
	AcOH	85	377.42	60.30	3.90	18.70	8.30
21c	172–175	Yellow	$C_{19}H_{14}Cl\,N_5O_2S$	55.41	3.43	17.00	7.79
	AcOH	90	411.86	55.30	3.30	17.20	7.90
22a	>300	Pale red	$C_{17}H_{12}N_4O_2S_2$	55.42	3.28	15.21	17.41
	AcOH	89	368.43	55.20	3.10	15.30	17.60
22b	188–191	Pale red	$C_{18}H_{14}N_4O_2S_2$	56.53	3.69	14.65	16.77
	AcOH	85	382.46	56.30	3.80	14.60	16.50
22c	245–247	Pale red	$C_{17}H_{11}Cl\,N_4O_2S_2$	50.68	2.75	13.91	15.92
	AcOH	90	402.88	50.80	2.90	14.10	15.70

(Continued)

TABLE I Characterization Data of the Newly Synthesized Compounds *(Continued)*

Comp. no.	Mp. °C solvent	Color yield %	Mol. formula (Mol. Wt.)	Calcd./Found % C	H	N	S
23a	245–248	Pale red	$C_{17}H_{12}N_4O_3S$	57.95	3.43	15.90	9.10
	AcOH	90	352.36	58.10	3.30	16.10	8.90
23b	235–238	Pale red	$C_{18}H_{14}N_4O_3S$	59.01	3.85	15.29	8.75
	AcOH	87	366.39	59.00	3.70	15.10	8.50
23c	231–234	Pale red	$C_{17}H_{11}Cl\ N_4O_3S$	52.79	2.87	14.48	8.29
	AcOH	80	386.81	52.90	2.70	14.60	8.40
24a	213–215	Pale red	$C_{23}H_{16}N_4O_2S$	66.97	3.91	13.58	7.77
	AcOH	85	412.46	66.80	4.10	13.70	7.90
24b	225–227	Pale red	$C_{24}H_{18}N_4O_2S$	67.59	4.25	13.14	7.52
	AcOH	88	426.49	67.60	4.40	13.00	7.70
24c	233–235	Pale red	$C_{23}H_{15}Cl\ N_4O_2S$	61.81	3.38	12.54	7.18
	AcOH	90	446.91	61.90	3.40	12.70	7.00
25a	265–67	Yellow	$C_{20}H_{16}N_4O_3S$	61.21	4.11	14.28	8.17
	AcOH	90	392.43	61.10	4.00	14.30	8.00
25b	250–52	Yellow	$C_{21}H_{18}N_4O_3S$	62.05	4.46	13.78	7.98
	AcOH	88	406.45	62.10	4.60	13.80	7.90
25c	254–56	Yellow	$C_{20}H_{15}ClN_4O_3S$	56.27	3.54	13.12	7.51
	AcOH	85	426.87	56.40	3.40	13.20	7.70
26a	266–68[11]	Yellow	$C_{21}H_{18}N_4O_3S$	62.05	4.46	13.87	7.89
	AcOH	90	406.45	62.20	4.60	13.80	7.90
26b	242–44	Yellow	$C_{22}H_{20}N_4O_3S$	62.84	4.79	13.32	7.63
	AcOH	89	420.48	62.60	4.90	13.20	6.36
26c	250–52	Yellow	$C_{21}H_{17}ClN_4O_3S$	57.21	3.89	12.71	7.27
	AcOH	87	440.90	57.10	4.00	12.60	7.30
27a	280–82[11]	Yellow	$C_{20}H_{16}N_4O_2S$	63.81	4.28	14.88	8.52
	AcOH	88	376.43	63.90	4.40	14.70	8.60
27b	200–203	Yellow	$C_{21}H_{18}N_4O_2S$	64.60	4.65	14.35	8.21
	AcOH	90	390.45	64.40	4.50	14.20	8.10
27c	255–57	Yellow	$C_{20}H_{15}ClN_4O_2S$	58.46	3.68	13.46	7.80
	AcOH	85	410.87	58.60	3.80	13.40	7.90
28a	>300[11]	Yellow	$C_{25}H_{18}N_4O_2S$	68.48	4.14	12.78	7.31
	AcOH	85	438.50	68.60	4.00	12.90	7.10
28b	290–91	Yellow	$C_{26}H_{20}N_4O_2S$	69.01	4.415	12.38	7.09
	AcOH	87	452.52	69.20	4.40	12.40	6.90
28c	280–82	Yellow	$C_{25}H_{17}ClN_4O_2S$	63.49	3.62	11.85	6.78
	AcOH	88	472.94	63.60	3.80	11.90	6.90
29a	>300[11]	Yellow	$C_{25}H_{19}N_5O_2S$	66.21	4.22	15.44	7.07
	AcOH	85	453.51	66.00	4.10	14.30	6.90
29b	260–62	Yellow	$C_{25}H_{21}N_5O_2S$	66.79	4.53	14.98	6.89
	AcOH	90	467.54	66.90	4.40	15.10	7.00
29c	290–3	Yellow	$C_{25}H_{18}Cl\ N_5O_2S$	61.54	3.72	14.35	6.57
	AcOH	90	487.96	61.70	3.60	14.50	6.60
30a	>300	Pale red	$C_{23}H_{16}N_4O_2S_2$	62.14	3.63	12.60	14.43
	AcOH	85	444.53	62.10	3.50	12.50	14.60

(Continued on next page)

TABLE I Characterization Data of the Newly Synthesized Compounds *(Continued)*

Comp. no.	Mp. °C solvent	Color yield %	Mol. formula (Mol. Wt.)	Calcd./Found % C	H	N	S
30b	>300	Pale red	$C_{24}H_{18}N_4O_2S_2$	62.86	3.96	12.22	13.99
	AcOH	80	458.55	62.60	4.10	12.10	14.10
30c	270–2	Pale red	$C_{23}H_{15}Cl\ N_4O_2S_2$	57.67	3.16	11.70	13.39
	AcOH	80	478.97	57.80	3.00	11.90	13.50
31a	>300	Pale red	$C_{23}H_{16}N_4O_3S$	64.47	3.76	13.08	7.48
	AcOH	85	428.46	64.60	3.50	12.80	7.50
31b	>300	Pale red	$C_{24}H_{18}N_4O_3S$	65.14	4.10	12.66	7.25
	AcOH	87	442.49	65.00	3.90	12.80	7.40
31c	>300	Pale red	$C_{23}H_{15}Cl\ N_4O_3S$	59.68	3.27	12.10	6.93
	AcOH	80	462.90	59.80	3.30	12.20	7.10
32a	240–3	Pale red	$C_{29}H_{20}N_4O_2S$	71.29	4.13	11.47	6.56
	AcOH	85	488.56	71.40	4.12	11.60	6.70
32b	230–32	Pale red	$C_{30}H_{22}N_4O_2S$	71.69	4.41	11.15	6.38
	AcOH	85	502.58	71.50	4.20	11.00	6.50
32c	272–75	Pale red	$C_{29}H_{19}Cl\ N_4O_2S$	66.60	3.66	10.71	6.13
	AcOH	88	523.00	66.50	3.50	10.80	6.30
35a	217–219	Yellow	$C_{27}H_{23}N_5O_3$	69.66	4.98	15.04	
	EtOH	70	465.50	70.10	5.00	14.80	
35b	225–227	Yellow	$C_{28}H_{25}N_5O_3$	70.13	5.25	14.60	
	EtOH	65	479.53	70.00	5.40	14.40	
35c	247–249	Yellow	$C_{28}H_{25}N_5O_3$	70.13	5.25	14.60	
	EtOH	70	479.53	70.20	5.10	14.50	
36a	160–163	Yellow	$C_{26}H_{21}N_5O_2$	71.71	4.86	16.08	
	EtOH	68	435.47	71.90	4.60	15.90	
36b	185–187	Yellow	$C_{27}H_{23}N_5O_2$	72.14	5.16	15.58	
	EtOH	65	449.50	72.20	5.30	15.70	8.00
36c	243–245	Yellow	$C_{27}H_{23}N_5O_2$	72.14	5.16	15.58	
	EtOH	70	449.50	72.00	5.30	15.70	
37a	147–149	Yellow	$C_{31}H_{23}N_5O_2$	74.83	4.66	14.08	
	EtOH	65	497.54	74.80	4.50	13.80	
37b	185–187	Yellow	$C_{32}H_{25}N_5O_2$	75.13	4.93	13.69	
	EtOH	65	511.57	75.30	5.10	13.90	
37c	190–193	Yellow	$C_{32}H_{25}N_5O_2$	75.13	4.93	13.69	
	EtOH	70	511.57	75.00	5.10	13.60	
38a	203–205	Yellow	$C_{31}H_{24}N_6O_2$	72.64	4.72	16.40	
	EtOH	65	512.56	72.60	4.50	16.20	
38b	254–256	Yellow	$C_{32}H_{26}N_6O_2$	72.99	4.98	15.96	
	EtOH	70	526.58	73.10	4.70	15.80	
38c	277–279	Yellow	$C_{32}H_{26}N_6O_2$	72.99	4.98	15.96	
	EtOH	70	526.58	72.80	5.20	16.10	
39a	193–95	Yellow	$C_{14}H_{15}Br\ N_2O_2S$	47.33	4.26	7.89	9.03
	EtOH	85	355.25	47.30	4.10	7.90	9.20
39b	151–53	White	$C_{14}H_{15}F\ N_2O_2S$	57.13	5.14	9.52	10.89
	EtOH	80	294.34	57.00	4.20	9.70	10.90

(Continued)

TABLE I Characterization Data of the Newly Synthesized Compounds *(Continued)*

Comp. no.	Mp. °C solvent	Color yield %	Mol. formula (Mol. Wt.)	Calcd./Found % C	H	N	S
43a	163–65 EtOH	Yellow 85	$C_{24}H_{23}F\ N_4O_4$ 511.36	56.37 56.10	4.53 4.70	10.95 11.20	
43b	190–192 EtOH	Yellow 89	$C_{24}H_{23}F\ N_4O_4$ 511.36	56.37 56.10	4.53 4.70	10.95 11.20	
44a	212–214 EtOH	Yellow 88	$C_{23}H_{21}Br\ N_4O_3$ 481.34	57.39 57.40	4.40 4.10	11.64 11.80	
44b	220–222 EtOH	Yellow 81	$C_{23}H_{21}F\ N_4O_3$ 420.43	65.70 65.60	5.03 5.10	13.33 13.50	
45a	143–145 EtOH	Yellow 89	$C_{28}H_{23}Br\ N_4O_3$ 543.41	61.89 61.80	4.27 4.00	10.31 10.60	
45b	163–165 EtOH	Yellow 90	$C_{28}H_{23}F\ N_4O_3$ 482.50	69.70 69.60	4.80 4.70	11.61 11.50	
46a	177–178 EtOH	Yellow 87	$C_{28}H_{24}Br\ N_5O_3$ 558.42	60.22 60.10	4.33 4.10	12.54 12.40	
46b	113–115 EtOH	Yellow 85	$C_{28}H_{24}F\ N_5O_3$ 497.52	67.60 67.70	4.86 4.60	14.08 13.90	

2,3-Dihydro-1,3,4-thiadiazoles (17–24)a–c, (25–32)a–c, 5-(3-Methyl-5-oxo-1-phenyl(2-pyrazolin-4-ylidene))-1,4-disubstituted-1,2,4-triazolines (35–38)a–c

General method. Equimolar ammount of the appropriate hydrazonoyl halides (**6–13)a–c**, the appropriate pyrazoline-5-ones (**2**, **3)a,b** or **4a–c**, and triethylamine (5 mmol) in ethanol (20 mL) was stirred at room temperature (or boiled under reflux) for 2 h. The resulting solid was collected and crystallized to give 2,3-dihydro-1,3,4-thiadiazoles**(17–24)a–c, (25–32)a–c** and 5-(3-methyl-5-oxo-1-phenyl(2-pyrazolin-4-ylidene))-1,4-disubstituted-1,2,4-triazolines (**35–38**)**a–c**, respectively (Tables I and II).

Ethyl 4-Methyl-5-substituted-2-thioxo-1,3,6-trihydropyridine-5-carboxylates 39a and 39b

A mixture of ethyl acetoacetate (0.1 mol, 13 g), thiourea (0.12 mol, 8.2 g) and the appropriate aromatic aldehydes (3-bromobenzaldehyde or 4-florobenzaldehyde) (0.1 mol) in ethanol (30 mL) containing a catalytic amount of concentrated hydrochloric acid (10 drops) was refluxed for 3 h. The reaction mixture was then allowed to stand at room temperature overnight. The solid precipitate that formed was collected by filtration, washed with ethanol, and crystallized from ethanol to give **39a** and **39b**, respectively (Table I).

TABLE II ^{1}H NMR Spectra of Some Selected Synthesized Compounds

Comp. no.	^{1}H NMR (δ)
4c	2.16 (s, 3H), 2.21 (s, 3H), 4.54 (s, 2H), 7.23–7.39 (m, 8H), 7.95–7.99 (d, 2H), 12.92 (s, br., 1H)
17c	1.14 (s, 3H), 3.97 (s, 3H), 7.73–7.87 (m, 4H), 11.29 (s, br., 1H)
18a	1.04 (s, 3H), 1.34 (t, 3H), 4.41 (q, 2H), 7.64–7.80 (m, 5H), 11.26 (s, br., 1H)
18b	0.82 (s, 3H), 1.08 (t, 3H), 2.25 (s, 3H), 4.15 (q, 2H), 7.18–7.23 (d, 2H), 7.36–7.40 (d, 2H), 10.97 (s, br., 1H)
19a	1.21 (s, 3H), 2.54 (s, 3H), 7.08–7.81 (m, 5H), 11.56 (s, br., 1H)
21b	2.35 (s, 3H), 2.55 (s, 3H), 7.11–7.65 (m, 9H), 11.94 (s, br., 1H), 14.75 (s, br., 1H)
22a	1.07 (s, 3H), 7.35–7.37 (m, 1H), 7.68–7.90 (m, 5H), 8.24–8.38 (d, 2H), 11.28 (s, br., 1H)
25b	1.38 (s, 3H), 2.50 (s, 3H), 4.03 (s, 3H), 7.11–7.42 (m, 3H), 7.56 (s, 4H), 7.92–8.02 (d, 2H)
25c	1.39 (s, 3H), 4.01 (s, 3H), 7.15–7.42 (m, 3H), 7.56 (s, 4H), 7.97–8.20 (d, 2H)
26a	1.28 (s, 3H), 1.42 (t, 3H), 4.45 (q, 2H), 7.09–7.42 (m, 4H), 7.59 (s, 4H), 7.99–8.03 (d, 2H)
26c	1.28 (s, 3H), 1.33 (t, 3H), 4.44 (q, 2H), 7.12–7.99 (m, 9H)
27a	1.37 (s, 3H), 2.56 (s, 3H), 7.07–8.02 (m, 10H)
29b	1.31 (s, 3H), 2.50 (s, 3H), 7.12–7.61 (m, 12H), 7.98–8.03 (d, 2H), 8.44 (sb, br., 1H)
30a	1.30 (s, 3H), 6.63 (m, 1H), 7.25–7.44 (m, 5H), 7.66–7.70 (m, 5H), 7.81–7.86 (d, 2H)
36a	2.18 (s, 3H), 2.33 (s, 3H), 7.14–8.03 (m, 15H)
36c	2.13 (s, 6H), 4.62 (s, 2H), 7.22–8.43 (m, 15H)
38b	1.84 (s, 3H), 2.51 (s, 3H), 6.24–8.70 (m, 19H), 11.25 (s, br., 1H)
43b	1.22 (t, 3H), 1.37 (t, 3H), 2.52 (s, 3H), 4.04 (q, 2H), 4.39 (q, 2H), 6.85–6.97 (m, 3H), 7.31–7.47 (m, 5H), 8.17–8.21 (d, 2H)
44a	1.23 (t, 3H), 2.52 (s, 3H), 2.54 (s, 3H), 4.04 (q, 2H), 6.84 (s, 1H), 7.26–7.55 (m, 7H), 8.20 (d, 2H)
44b	1.21 (t, 3H), 2.52 (s, 6H), 4.07 (q, 2H), 6.85–6.96 (m, 3H), 7.34–7.54 (m, 5H), 8.24–8.25 (d, 2H)
45a	1.21 (t, 3H), 2.57 (s, 3H), 4.08 (q, 2H), 6.85–7.01 (m, 3H), 7.34–7.51 (m, 8H), 8.06–8.11 (d, 2H), 8.21–8.26 (d, 2H)
45b	1.24 (t, 3H), 2.57 (s, 3H), 4.07 (q, 2H), 6.99 (s, 1H), 7.06–7.55 (m, 10H), 8.09–8.14 (d, 2H), 8.21–8.25 (d, 2H)
46a	1.23 (t, 3H), 2.55 (s, 3H), 4.07 (q, 2H), 7.01 (s, 1H), 7.11–7.34 (m, 2H), 7.38–7.69 (m, 10H), 8.16–8.53 (d, 2H), 8.45 (s, br., 1H)
46b	1.22 (t, 3H), 2.53 (s, 3H), 4.07 (q, 2H), 6.91–7.34 (m, 3H), 7.42–7.60 (m, 10H), 8.16–8.20 (d, 2H), 8.47 (s, br., 1H)

Ethyl 6-Methyl-1-phenyl-3,4-disubstituted-4,3a-dihydro-1,2,4-triazolino[4,3-a]pyrimidine-5-carboxylates (43–46)a,b

An equimolar amount of each of the appropriate hydrazonoyl halides (**7–10**)**a** and the appropriate pyrimidine-2-thione derivatives **39a,b** and triethylamie (5 mmol) in chloroform (20 mL) was boiled under

reflux for 10 h. Chloroform was evaporated under reduced pressure and the residue solid was crystallized from ethanol to give triazlino[4,3-*a*]pyrimidines **(43–46)a**,**b** (Tables I and II).

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