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Reactions with Hydrazonoyl Halides 63: Synthesis and Anticancer Activity of Some New 1,3,4-Thiadiazoles, 1,3,4-Selenadiazoles, and 1,2,4-Triazolo[4,3-a]pyrimidines

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REACTIONS WITH HYDRAZONOYL HALIDES 63: SYNTHESIS AND ANTICANCER ACTIVITY OF SOME NEW 1,3,4-THIADIAZOLES, 1,3,4-SELENADIAZOLES, AND 1,2,4-TRIAZOLO[4,3-*a*]PYRIMIDINES

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*2,3-Dihydro-1,3,4-thiadiazoles, 2,3-dihydro-1,3,4-selenadiazoles, and triazolino[4,3-*a*]pyrimidines containing benzoxazole or benzothiazole moieties were prepared from the reaction of each of ethyl 3-aza-3-(benzoxazol-2-ylamino)-2-chloroprop-2-enoate and ethyl 3-aza-3-(benzothiazolo-2-ylamino)-2-chloroprop-2-enoate with each of potassium thiocyanate, potassium selenocyanate, alkyl carbodithioate, and pyrimidine-2-thione derivatives. All the newly synthesized compounds were confirmed by elemental analysis, spectral data, and alternative route synthesis whenever possible. Some of the newly synthesized compounds were screened toward certain cancer tumors.*

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Keywords Anticancer activity; hydrazonoyl bromide; 1,3,4-selenadiazoles; 1,3,4-thiadiazoles; triazolo[4,3-*a*]pyrimidines

INTRODUCTION

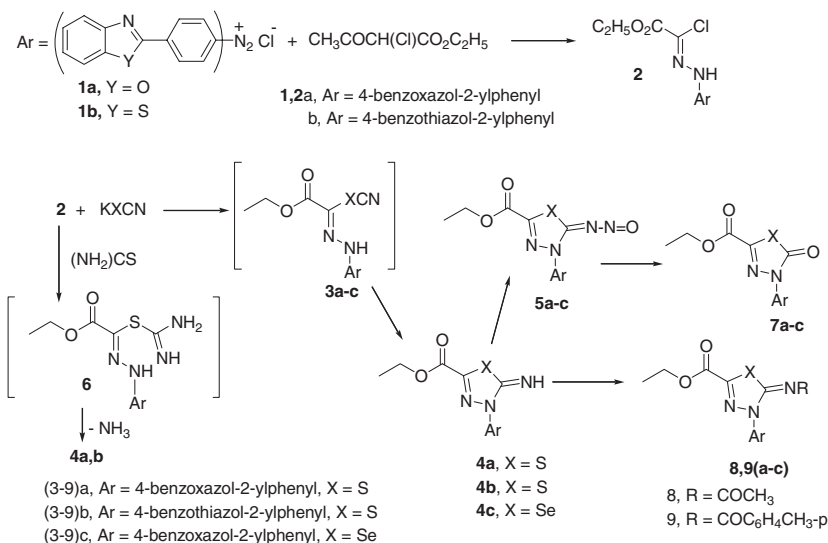
Hydrazonoyl halides have been widely employed for the synthesis of heterocyclic compounds.^{1–4} 1,3,4-Thiadiazole derivatives have become useful in medicine, agriculture, and in many fields of technology.⁵ In addition, 2-(4-aminophenyl)benzothiazole and oxazole and their analogues are a novel class of potent and selective antitumor agents.^{6–10} As an extension of our study^{11–16} and of our synthesis of 1,3,4-thiadiazoles, we report here the synthesis of hydrazonoyl halides containing 4-phenylbenzothiazole and 4-phenylbenzoxazole moieties and their reactions toward some potassium thiocyanate, potassium selenocyanate, alkyl carbodithioate, and pyrimidine-2-thione derivatives.

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RESULTS AND DISCUSSION

Treatment of the appropriate diazotized [4-(1,3-benzoxazol-2-yl)phenyl]amine⁶ (**1a**) and diazotized [4-(1,3-benzothiazol-2-yl)phenyl]amine¹⁰ (**1b**) with ethyl 2-chloro-3-oxobutanoate in ethanolic sodium acetate gave ethyl 3-aza-3-[(benzoxazol-2-ylphenyl)amino]-2-chloroprop-2-enoate (**2a**) and ethyl 3-aza-3-(benzothiazolo-2-ylphenylamino)-2-chloroprop-2-enoate (**2b**), respectively. Structure **2** was elucidated by elemental analysis and spectral data. The ¹H NMR spectrum of **2a** showed signals at δ = 1.37 (t, 3H, J = 7.5 Hz, CH₂CH₃), 4.35 (q, 2H, J = 7.5 Hz, CH₂CH₃), 7.40 (d, 2H, J = 8Hz, ArH's), 7.50 (d, 2H, J = 8Hz, ArH's), 8.00 (d, 2H, J = 8Hz, ArH's), 8.07 (d, 2H, J = 8Hz, ArH's), and 10.89 (s, br., 1H, NH). Treatment of the appropriate **2a** with each of potassium thiocyanate and potassium selenocyanate gave ethyl 3-(4-(benzoxazol-2-ylphenyl)-2-imino-1,3,4-thiadiazoline-5-carboxylate (**4a**) and ethyl 3-(4-(benzoxazol-2-ylphenyl)-2-imino-1,3,4-selenadiazoline-5-carboxylate (**4c**), respectively (Scheme 1). The structure of **4** was elucidated on the basis of elemental analyses, spectral data, alternative synthetic route, and its nitrosation and acylation reactions.



Scheme 1

In addition, treatment of the appropriate **2a** with thiourea in boiling ethanol gave a product identical in all respects (mp, mixed mp, and spectra) with **4a**. These results indicate that hydrazone **3a** and amidiazone **6a** are not the final products, and that **3a** and **6a** readily gave **4a** either by cyclization or by elimination of one molecule of ammonia (Scheme 1). Acylation of **4a** with acetic anhydride or with 4-methylbenzoyl chloride in pyridine afforded ethyl 2-(1-aza-2-oxopropylidene)-3-(4-benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (**8a**) and ethyl 2-[1-aza-2-(4-methylphenyl)-2-oxoethylidene]-3-(4-benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (**9a**), respectively. Spectral data and elemental analyses confirmed their structures. ¹H NMR spectrum of **8a** showed

signals at $\delta = 1.45$ (t, 3H, $J = 7.5$ Hz, CH_2CH_3), 2.41 (s, 3H, $\text{CH}_3\text{CON}=\text{O}$), 4.47 (q, 2H, $J = 7.5$ Hz, CH_2CH_3), 7.40 (d, 2H, $J = 8$ Hz, ArH's), 7.50 (d, 2H, $J = 8$ Hz, ArH's), and 8.44 (d, 2H, $J = 8$ Hz, ArH's).

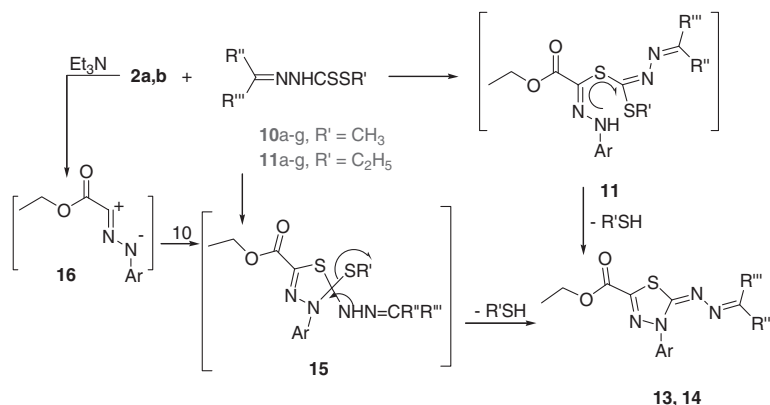
Analogously, acylation of each of **4b** and **4c** gave **8b,c** and **9b,c**, respectively. Nitrosation of each **4a** and **4c** with saturated sodium nitrite in acetic acid at $0-5^\circ\text{C}$ gave ethyl 2-(azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (**5a**) and ethyl 2-(azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-selenadiazoline-5-carboxylate (**5c**), respectively. Ethyl 3-(4-benzoxazol-2-ylphenyl)-2-oxo-1,3,4-thia/selenadiazoline-5-carboxylate **7a,c** and 3-(4-benzothiazol-2-ylphenyl)-2-oxo-1,3,4-thiadiazoline-5-carboxylate **7b** were prepared by thermolysis of **5a,c** and **5b** in boiling xylene. The IR spectrum of **7** revealed a band near $\nu = 1685\text{ cm}^{-1}$ (CO).

Compound **2a** reacted with the methyl carbodithioates^{18,19} **10a** to give the 1,3,4-thiadiazoline derivative **13a**. The structure of **13a** was confirmed by elemental analysis, spectral data, and alternative synthetic route. ^1H NMR of **13a** showed signals at $\delta = 1.36$ (t, 3H, CH_3CH_2), 4.39 (q, 2H, CH_2CH_3), 7.54–8.33 (m, 13H, ArH's), and 8.57 CH (vinyl). Also, treatment of **2a** with ethyl carbodithioates **11a** in ethanolic triethylamine gave a product identical in all respects (mp, mixed mp, and spectra) with **13a**. Product **13a** was assumed to be formed via elimination of alkanethiol (R^1SH) from the corresponding cycloadduct **15**, which formed from 1,3-dipolar cycloaddition (or 1,3-addition) of nitrile imide **16** (generated in situ from hydrazonoyl chlorides **2** and triethylamine) to $\text{C}=\text{S}$ **14** (Scheme 2). Analogously, treatment of the appropriate **2a,b** with the appropriate **10a–g** (or **11a–g**) in ethanolic triethylamine gave the thiadiazolines **13a–g** and **14 a–g**, respectively (Scheme 2).

Next, treatment of ethyl 4-methyl-6-phenyl-2-thioxo-1,3,6-trihydro-pyrimidine-5-carboxylate (**17a**) with **2a** in chloroform and triethylamine gave the 1,2,4-triazolo[4,3-*a*]pyrimidine-5-carboxylates **20a**. The structure of **20a** was elucidated by elemental analysis, spectra, and alternative synthesis. The ^1H NMR spectrum of **20a** showed signals at $\delta = 1.23$ (t, 3H, CH_3CH_2), 1.12 (t, 3H, CH_3CH_2), 2.88 (s, 3H, CH_3), 4.02 (q, 2H, CH_2CH_3), 4.11 (q, 2H, CH_2CH_3), 6.67 (s, 1H, CH), and 6.8–8.43 (m, 13H, ArH). Its IR spectrum revealed bands at $\nu = 1735\text{ cm}^{-1}$ (CO). Ethyl 6-methyl-4-[4-phenyl-2-methylthio-3,4-dihydropyrimidine-5-carboxylate (**22a**) reacted with **2a** in boiling ethanolic sodium ethoxide solution gave products identical in all aspects (mp, mixed mp, and spectra) with the corresponding **20a**. Analogously, treatment of each **2a** with the appropriate **17b,c** and **2b** with the appropriate **17a–c** gave triazolo[4,3-*a*]pyrimidines **20b,c** and **21a–c**, respectively (Scheme 3).

The formation of **20** can be explained via 1,3-dipolar cycloaddition or 1,3-addition of nitrile imide **16** (prepared in situ from hydrazonoyl chlorides **2** with triethylamine or sodium ethoxide) to $\text{C}=\text{S}$ of **16** (or NH of **22**) to give intermediate **18** (or **23**), with ring opening and ring closure to afford the final products **20** by elimination of hydrogen sulfide from **19** (or methyl mercaptan from **23**) (Scheme 3).

Treatment of **2a** with methyl benzoylhydrazinecarbodithioate (**24**) in ethanolic triethylamine gave 2,3-dihydro-1,3,4-thiadiazole **26** (Scheme 4). Its structure was elucidated by elemental analysis, spectral data, and alternative synthetic route. The ^1H NMR spectrum showed signals at $\delta = 1.39$ (t, 3H, CH_3CH_2), 4.42 (q, 2H, CH_2CH_3), 7.42–8.35 (m, 13H, ArH), and 11.42 (s, br, 1H, NH). Thus, treatment of **2a** with 5-phenyl-1,3,4-oxadiazole-2-thiol (**27**) gave products identical in all respects (mp, mixed mp, and spectra) with **26a** (Scheme 4). Similarly, treatment of the appropriate **2a,b** with **28** gave thiadiazolines **29a** and **29b**, respectively.



- 10a, R'' = H, R''' = C₆H₅, R' = CH₃
 b, R'' = H, R''' = 2,3-(OCH₂O)C₆H₃, R' = CH₃
 c, R'' = H, R''' = 4-(CH₃)₂CHC₆H₄, R' = CH₃
 d, R'' = CH₃, R''' = C₆H₅, R' = CH₃
 e, R'' = CH₃, R''' = 2-C₄H₃O, R' = CH₃
 f, R''-R''' = 1,2-C₆H₄(NHCOC=), R' = CH₃
 g, R''-R''' = 1,2-C₆H₄(COC=CO), R' = CH₃
- 11a, R'' = H, R''' = C₆H₅, R' = C₂H₅
 b, R'' = H, R''' = 2,3-(OCH₂O)C₆H₃, R' = C₂H₅
 c, R'' = H, R''' = 4-(CH₃)₂CHC₆H₄, R' = C₂H₅
 d, R'' = CH₃, R''' = C₆H₅, R' = C₂H₅
 e, R'' = CH₃, R''' = 2-C₄H₃O, R' = C₂H₅
 f, R''-R''' = 1,2-C₆H₄(NHCOC=), R' = C₂H₅
 g, R''-R''' = 1,2-C₆H₄(COC=CO), R' = C₂H₅
- 13a, R'' = H, R''' = C₆H₅, Ar = 4-benzoxazol-2-ylphenyl
 b, R'' = H, R''' = 2,3-(OCH₂O)C₆H₃, Ar = 4-benzoxazol-2-ylphenyl
 c, R'' = H, R''' = 4-(CH₃)₂CHC₆H₄, Ar = 4-benzoxazol-2-ylphenyl
 d, R'' = CH₃, R''' = C₆H₅, Ar = 4-benzoxazol-2-ylphenyl
 e, R'' = CH₃, R''' = 2-C₄H₃O, Ar = 4-benzoxazol-2-ylphenyl
 f, R''-R''' = 1,2-C₆H₄(NHCOC=), Ar = 4-benzoxazol-2-ylphenyl
 g, R''-R''' = 1,2-C₆H₄(COC=CO), Ar = 4-benzoxazol-2-ylphenyl
- 14a, R'' = H, R''' = C₆H₅, Ar = 4-benzothiazol-2-ylphenyl
 b, R'' = H, R''' = 2,3-(OCH₂O)C₆H₃, Ar = 4-benzothiazol-2-ylphenyl
 c, R'' = H, R''' = 4-(CH₃)₂CHC₆H₄, Ar = 4-benzothiazol-2-ylphenyl
 d, R'' = CH₃, R''' = C₆H₅, Ar = 4-benzothiazol-2-ylphenyl
 e, R'' = CH₃, R''' = 2-C₄H₃O, Ar = 4-benzothiazol-2-ylphenyl
 f, R''-R''' = 1,2-C₆H₄(NHCOC=), Ar = 4-benzothiazol-2-ylphenyl
 g, R''-R''' = 1,2-C₆H₄(COC=CO), Ar = 4-benzothiazol-2-ylphenyl

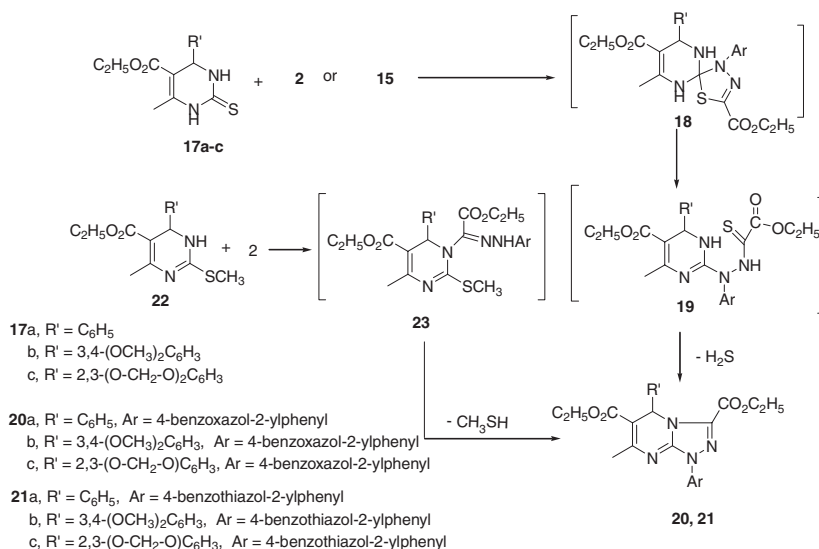
Scheme 2

ANTICANCER AND CYTOTOXIC ACTIVITY

Twelve of the synthesized compounds were subjected to anticancer screening, and some of these compounds showed a cytotoxic effect. Female Swiss albino mice from the Animal House of the Egyptian Cancer Institute were maintained on standard pellet diet and water, and in vitro test for cytotoxic effect was operated using Ehrlich ascites carcinoma (EAC)¹⁷ induced through interperitoneal transplantation in female Swiss albino mice. (See the Supplemental Materials, available online, for full details.)

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. ¹H NMR spectra were recorded in CDCl₃ and (CD₃)₂SO solutions on a Varian

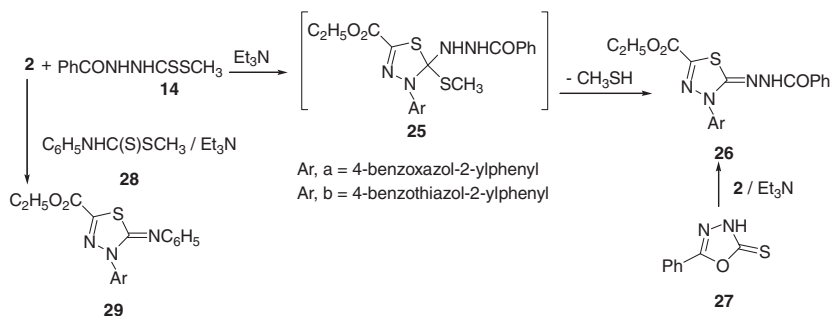


Scheme 3

Gemini 300 MHz spectrometer, and chemical shifts were expressed in δ units using TMS as internal reference. Elemental analyses were carried out at the Microanalytical Center of the Cairo University. Alkyl carbodithioates^{18,19} were prepared as previously reported.

Synthesis of Ethyl 3-Aza-3-(benzoxazol-2-ylamino)-2-chloroprop-2-enoate (2a) and Ethyl 3-Aza-3-(benzothiazolo-2-ylamino)-2-chloroprop-2-enoate (2b)

The appropriate amount of diazotized [4-(1,3-benzoxazol-2-yl)phenyl]amine (**1a**) and diazotized [4-(1,3-benzothiazol-2-yl)phenyl]amine (**1b**) (0.005 mol) were added dropwise to cold solution (0°C) of ethyl 2-chlorobutanoate (1.65 g, 0.005 mol) and sodium acetate trihydrate (0.65 g, 0.005 mol) while stirring. The yellow precipitate was collected and recrystallized from ethanol to give **2a** and **2b**, respectively (Tables I and II).



Scheme 4

Table I Characterization data of the newly synthesized compounds

% Analyses, Calcd./Found				Mol. Formula Mol. Wt.	Yield ^a % Color	Mp, °C Solvent	Compound no.
S	N	H	C				
—	12.22	4.10	59.40	C ₁₇ H ₁₄ ClN ₃ O ₃	82	199–201	2a
	12.02	3.99	59.23	343.76	Yellow	EtOH	
8.91	11.68	3.92	56.74	C ₁₇ H ₁₄ ClN ₃ O ₂ S	80	172–174	2b
9.01	11.79	3.99	56.59	359.83	Orange	EtOH	
8.75	15.29	3.85	59.01	C ₁₈ H ₁₄ N ₄ O ₃ S	60	170–174	4a
8.59	15.32	3.77	59.12	366.39	Brown	EtOH	
16.77	14.65	3.69	56.53	C ₁₈ H ₁₄ N ₄ O ₂ S ₂	60	165–168	4b
16.70	14.65	3.80	56.66	382.46	Brown	EtOH	
—	13.56	3.41	52.31	C ₁₈ H ₁₄ N ₄ O ₃ Se	65	169–170	4c
	13.50	3.32	52.32	413.29	Brown	EtOH	
8.11	17.71	3.31	54.68	C ₁₈ H ₁₃ N ₅ O ₄ S	85	134–137	5a
8.01	17.65	3.22	54.60	395.39	Red	Acetone	
15.59	17.02	3.18	52.54	C ₁₈ H ₁₃ N ₅ O ₃ S ₂	80	128–131	5b
15.48	16.99	3.10	52.44	411.46	Pale rose	Acetone	
—	15.83	2.96	48.88	C ₁₈ H ₁₃ N ₅ O ₄ Se	80	134–137	5c
	15.75	3.01	48.75	442.29	Pale rose	Acetone	
8.73	11.44	3.57	58.85	C ₁₈ H ₁₃ N ₃ O ₄ S	60	155–157	7a
8.70	11.41	3.77	58.77	367.38	Shiny yellow	EtOH	
16.72	10.96	3.42	56.38	C ₁₈ H ₁₃ N ₃ O ₃ S ₂	65	151–155	7b
16.66	11.01	3.32	56.30	383.44	Shiny yellow	EtOH	
—	10.14	3.16	52.19	C ₁₈ H ₁₃ N ₃ O ₄ Se	60	124–125	7c
	9.86	3.11	52.09	414.27	Shiny yellow	DMF/EtOH	
7.85	13.72	3.95	58.81	C ₂₀ H ₁₆ N ₄ O ₄ S	85	164–166	8a
7.69	13.69	3.79	58.79	408.43	Buff	EtOH	
15.11	13.20	3.80	56.59	C ₂₀ H ₁₆ N ₄ O ₃ S ₂	80	155–156	8b
1501	13.30	3.87	56.55	424.5	Buff	DMF/EtOH	
—	12.30	3.54	52.76	C ₂₀ H ₁₆ N ₄ O ₄ Se	80	152–154	8c
	12.36	3.44	52.59	455.33	Buff	Aq. EtOH	
6.62	11.56	4.16	64.45	C ₂₆ H ₂₀ N ₄ O ₄ S	90	202–204	9a
6.55	11.39	4.17	64.39	484.53	Buff	DMF/EtOH	
12.81	11.19	4.03	62.38	C ₂₆ H ₂₀ N ₄ O ₃ S ₂	85	207–209	9b
12.69	11.22	4.11	62.40	500.59	Buff	DMF/EtOH	
—	10.54	3.79	58.76	C ₂₆ H ₂₀ N ₄ O ₄ Se	85	175–177	9c
	10.39	3.63	58.59	531.42	Buff	DMF/EtOH	
6.83	14.92	4.08	63.95	C ₂₅ H ₁₉ N ₅ O ₃ S	75	213–214	13a
6.72	14.79	4.01	63.75	469.52	Yellow	DMF/EtOH	
6.24	13.64	3.73	60.81	C ₂₆ H ₁₉ N ₅ O ₅ S	76	236–238	13b
6.20	13.59	3.66	60.77	513.52	Yellow	DMSO	
6.27	13.69	4.93	65.74	C ₂₈ H ₂₅ N ₅ O ₃ S	75	187–189	13c
6.20	13.66	4.90	65.59	511.59	Yellow	DMF	
6.63	14.48	4.38	64.58	C ₂₆ H ₂₁ N ₅ O ₃ S	65	170–173	13d
6.55	14.45	4.33	64.52	483.54	Yellow	DMF/EtOH	
6.77	14.79	4.04	60.88	C ₂₄ H ₁₉ N ₅ O ₄ S	70	220–222	13e
6.71	14.66	4.00	60.95	473.5	Yellow	DMF	
6.28	16.46	3.55	61.17	C ₂₆ H ₁₈ N ₆ O ₄ S	72	289–290	13f
6.21	16.33	3.49	61.09	510.52	Orange	DMF/EtOH	
6.12	13.38	3.27	61.94	C ₂₇ H ₁₇ N ₅ O ₅ S	78	234–236	13g
6.00	13.31	3.11	61.70	523.52	Red	DMF/EtOH	
13.21	14.42	3.94	61.84	C ₂₅ H ₁₉ N ₅ O ₂ S ₂	72	245–247	14a
13.09	14.31	3.79	61.77	485.58	Orange	DMF/EtOH	

(Continued on next page)

Table I Characterization data of the newly synthesized compounds (*Continued*)

% Analyses, Calcd./Found				Mol. Formula Mol. Wt.	Yield ^a % Color	Mp, °C Solvent	Compound no.
S	N	H	C				
12.11	13.22	3.62	58.97	C ₂₆ H ₁₉ N ₅ O ₄ S ₂	70	247–249	14b
12.00	13.09	3.69	58.89	529.59	Pale orange	DMF	
12.15	13.27	4.78	63.73	C ₂₈ H ₂₅ N ₅ O ₂ S ₂	70	181–184	14c
12.01	13.09	4.71	63.66	527.66	Pale orange	DMF	
12.84	14.02	4.24	62.50	C ₂₆ H ₂₁ N ₅ O ₂ S ₂	74	267–269	14d
12.90	14.21	4.05	62.41	499.61	Orange	DMF	
13.10	14.31	3.91	58.88	C ₂₄ H ₁₉ N ₅ O ₃ S ₂	76	251–253	14e
13.01	14.19	3.82	58.69	489.57	Yellow	DMF	
12.18	15.96	3.45	59.30	C ₂₆ H ₁₈ N ₆ O ₃ S ₂	78	> 300	14f
12.09	16.02	3.33	59.49	526.59	Pale orange	DMF/EtOH	
11.89	12.98	3.18	60.10	C ₂₇ H ₁₇ N ₅ O ₄ S ₂	80	241–243	14g
11.79	12.78	3.01	60.00	539.58	Red	DMF/EtOH	
—	12.74	4.95	67.75	C ₃₁ H ₂₇ N ₅ O ₅	66	267–269	20a
	12.69	4.79	67.69	549.58	Yellow	CHCl ₃ /MeOH	
—	11.49	5.13	65.02	C ₃₃ H ₃₁ N ₅ O ₇	64	244–246	20b
	11.33	5.23	64.92	609.63	Orange	CHCl ₃ /MeOH	
—	11.80	4.58	64.75	C ₃₂ H ₂₇ N ₅ O ₇	60	252–254	20c
	11.77	4.66	64.96	593.59	Orange	CHCl ₃ /MeOH	
5.67	12.38	4.81	65.82	C ₃₁ H ₂₇ N ₅ O ₄ S	61	260–263	21a
5.61	12.49	4.78	65.69	565.64	Orange	CHCl ₃ /MeOH	
5.12	11.19	4.99	63.35	C ₃₃ H ₃₁ N ₅ O ₆ S	62	181–182	21b
5.00	11.30	4.89	63.46	625.69	Orange	CHCl ₃ /MeOH	
5.26	11.49	4.46	63.04	C ₃₂ H ₂₇ N ₅ O ₆ S	66	267–269	21c
5.16	11.36	4.33	63.22	609.65	Orange	CHCl ₃ /MeOH	
6.60	14.42	3.94	61.85	C ₂₅ H ₁₉ N ₅ O ₄ S	78	251–253	26a
6.67	14.53	3.81	61.79	485.51	Yellow	EtOH	
7.25	12.66	4.10	65.14	C ₂₄ H ₁₈ N ₄ O ₃ S	68	228–231	29a
7.16	12.73	4.00	65.01	442.49	Yellow	Acetic acid	
13.99	12.22	3.96	62.86	C ₂₄ H ₁₈ N ₄ O ₂ S ₂	65	221–223	29b
13.82	12.00	3.82	62.89	458.56	Yellow	Acetic acid	

Synthesis of Ethyl 3-(4-(Benzoxazol-2-ylphenyl)-2-imino-1,3,4-thiadiazoline-5-carboxylate (4a), Ethyl 3-(4-(Benzothiazol-2-ylphenyl)-2-imino-1,3,4-thiadiazoline-5-carboxylate (4b), and Ethyl 3-(4-(Benzoxazol-2-ylphenyl)-2-imino-1,3,4-selenadiazoline-5-carboxylate (4c)

Method A. A mixture of the appropriate **2a,b** (0.005 mol) and the appropriate amount of potassium thiocyanate (or potassium selenocyanate) (0.006 mol) in ethanol (25 mL) was stirred at room temperature for 24 h. The resulting solid was collected, washed with water, and crystallized from ethanol to give **4a,b** and **4c**, respectively (Tables I and II).

Method B. A mixture of the appropriate **2a,b** (0.005 mol) and thiourea (0.38 g, 0.005 mol) in ethanol (25 mL) was refluxed for 3 h. The solid product that formed after cooling was collected and crystallized from ethanol to give products identical in all respects (mp, mixed mp, and spectra) with **4a** and **4b**, respectively.

Table II ^1H NMR spectroscopic data of some synthesized compounds

Spectral data	Compound
IR: 3258 (NH), 3055 (CH, aromatic), 2981 (CH, aliphatic), 1747 (CO), 1605 (C=C), 1476 (CH ₂), 1363 (CH ₃) ^1H NMR: δ = 1.37 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.35 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.40 (d, 2H, J = 8Hz, ArH's), 7.50 (d, 2H, J = 8Hz, ArH's), 8.00 (d, 2H, J = 8Hz, ArH's), 8.07 (d, 2H, J = 8Hz, ArH's) and 10.89 (s, br., 1H, NH).	2a
IR: 3132 (NH), 3055 (CH, aromatic), 2926 (CH, aliphatic), 1743 (CO), 1605 (C=C), 1476 (CH ₂), 1355 (CH ₃) ^1H NMR: δ = 1.37 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.35 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.40 (d, 2H, J = 8Hz, ArH's), 7.50 (d, 2H, J = 8Hz, ArH's), 8.00 (d, 2H, J = 8Hz, ArH's), 8.07 (d, 2H, J = 8Hz, ArH's) and 10.89 (s, br., 1H, NH).	2b
IR: 3462 (NH), 3057 (CH, aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.41 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.35 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.36–8.36 (m, 9H, ArH's and NH protons)	4a
IR: 3460 (NH), 30.55 (CH, aromatic), 2981 (CH, aliphatic), 1729 (CO, ester), 1636 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.41 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.34 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.36–8.36 (m, 9H, ArH's and NH protons)	4b
IR: 3463 (NH), 30.55 (CH, aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1636 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.26 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.31 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.38–8.28 (m, 8H, ArH's), 9.85 (s, br., 1H, NH, exchangeable)	4c
IR: 3055 (CH, aromatic), 2984 (CH, aliphatic), 1720 (CO, ester), 1636 (C=N), 1550 (NO), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.41 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.35 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.36–8.36 (m, 8H, ArH's)	5a
IR: 3055 (CH, aromatic), 2980 (CH, aliphatic), 1722 (CO, ester), 1636 (C=N), 1603 (C=C), 1535 (NO), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.41 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.35 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.36–8.36 (m, 8H, ArH's)	5b
IR: 3057 (CH, aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1628 (C=N), 1603 (C=C), 1537 (NO), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.35 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.38 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.39–8.36 (m, 8H, ArH's)	5c
IR: 3055 (CH, aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1685 (CO), 1660 (CO, conjugated), 1636 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.44 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.47 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.27–8.36 (m, 8H, ArH's)	7a
IR: 3055 (CH, aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1683 (CO), 1636 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.44 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.47 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.27–8.38 (m, 8H, ArH's)	7b
IR: 3057 (CH, aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1685 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.44 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.47 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.27–8.36 (m, 8H, ArH's)	7c
IR: 3057 (CH, aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1685 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.45 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.41 (s, 3H, CH ₃ CO=N), 4.47 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.27–8.44 (m, 8H, ArH's)	8a
IR: 3055 (CH, aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1683 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃) ^1H NMR: δ = 1.45 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.41 (s, 3H, CH ₃ CO=N), 4.47 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.27–8.44 (m, 8H, ArH's)	8b

(Continued on next page)

Table II ^1H NMR spectroscopic data of some synthesized compounds (*Continued*)

Spectral data	Compound
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1683 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.45 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.32 (s, 3H, CH ₃ CO=N), 4.41 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.44–8.42 (m, 8H, ArH's)	8c
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1675 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.46 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.43 (s, 3H, 4-CH ₃ C ₆ H ₄), 4.53 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.26–8.50 (m, 12H, ArH's)	9a
IR: 3050 (CH,aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1678 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.46 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.43 (s, 3H, 4-CH ₃ C ₆ H ₄), 4.53 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.26–8.50 (m, 12H, ArH's)	9b
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1674 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.34 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.36 (s, 3H, 4-CH ₃ C ₆ H ₄), 4.41 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.32–8.48 (m, 12H, ArH's)	9c
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.36 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.39 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.48–8.33 (m, 13H, ArH's), 8.57 (s, 1H, CH=)	13a
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1466 (CH ₂), 1653 (CH ₃). ^1H NMR: δ = 1.37 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.41 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 6.10 (s, 2H, OCH ₂ O), 7.01–8.30 (m, 11H, ArH's), 8.44 (s, 1H, CH=)	13b
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.28 (d, 6H, (CH ₃) ₂ CH), 1.36 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.99 (sex, 1H, (CH ₃) ₂ CH), 4.39 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.23–8.35 (m, 12H, ArH's), 8.46 (s, 1H, CH=)	13c
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.28 (d, 6H, (CH ₃) ₂ CH), 1.36 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.99 (sex, 1H, (CH ₃) ₂ CH), 4.39 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.23–8.35 (m, 12H, ArH's), 8.46 (s, 1H, CH=)	13d
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: insoluble	13e
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.37 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.35 (s, 3H, CH ₃), 4.35 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 6.35 (s, 1H, furan H-4), 7.48–8.38 (m, 10H, ArH's)	13f
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1680 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.36 (t, 3H, CH ₂ CH ₃), 4.42 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 6.85–8.38 (m, 12H, ArH's), 8.46 (s, br., 1H, NH)	13g
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1695 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.35 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.38 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.42–8.51 (m, 12H, ArH's)	14a
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.36 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.39 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.48–8.33 (m, 13H, ArH's), 8.57 (s, 1H, CH=)	14b
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.35 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 4.41 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 6.10 (s, 2H, OCH ₂ O), 6.98–8.23 (m, 11H, ArH's), 8.42 (s, 1H, CH=)	14c
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.28 (d, 6H, (CH ₃) ₂ CH), 1.36 (t, 3H, J = 7.5 Hz, CH ₂ CH ₃), 2.99 (sex, 1H, (CH ₃) ₂ CH), 4.39 (q, 2H, J = 7.5 Hz, CH ₂ CH ₃), 7.23–8.35 (m, 12H, ArH's), 8.46 (s, 1H, CH=)	

Table II ^1H NMR spectroscopic data of some synthesized compounds (*Continued*)

Spectral data	Compound
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: insoluble	14d
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.37 (t, 3H, J = 7.5 Hz, (CH₃CH₂)), 2.35 (s, 3H, CH ₃), 4.35 (q, 2H, J = 7.5 Hz, CH₂CH₃), 6.35 (s, 1H, furan H-4), 7.48–8.38 (m, 10H, ArH's)	14e
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1682 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.36 (t, 3H, J = 7.5 Hz, CH₃CH₂), 4.42 (q, 2H, J = 7.5 Hz, CH₂CH₃), 6.85–8.38 (m, 12H, ArH's), 8.46 (s, br., 1H, NH)	14f
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1690 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.30 (t, 3H, J = 7.5 Hz, CH₃CH₂), 4.29 (q, 2H, J = 7.5 Hz, CH₂CH₃), 7.48–8.48 (m, 12H, ArH's)	14g
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.23 (t, 3H, J = 7.5 Hz, CH₃CH₂), 1.42 (t, 3H, J = 7.5 Hz, CH₃CH₂), 2.88 (s, 3H, CH ₃), 4.11 (q, 2H, J = 7.5 Hz, CH₂CH₃), 4.45 (q, 2H, J = 7.5 Hz, CH₂CH₃), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 13H, ArH's)	20a
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.23 (t, 3H, J = 7.5 Hz, CH₃CH₂), 1.42 (t, 3H, J = 7.5 Hz, CH₃CH₂), 2.88 (s, 3H, CH ₃), 3.47 (s, 3H, OCH ₃), 3.72 (s, 3H, OCH ₃), 4.11 (q, 2H, J = 7.5 Hz, CH₂CH₃), 4.45 (q, 2H, J = 7.5 Hz, CH₂CH₃), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	20b
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.23 (t, 3H, J = 7.5 Hz, CH₃CH₂), 1.42 (t, 3H, J = 7.5 Hz, CH₃CH₂), 2.88 (s, 3H, CH ₃), 4.11 (q, 2H, J = 7.5 Hz, CH₂CH₃), 4.45 (q, 2H, J = 7.5 Hz, CH₂CH₃), 5.91 (s, 2H, OCH ₂ O), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	20c
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.23 (t, 3H, J = 7.5 Hz, CH₃CH₂), 1.42 (t, 3H, J = 7.5 Hz, CH₃CH₂), 2.88 (s, 3H, CH ₃), 4.11 (q, 2H, J = 7.5 Hz, CH₂CH₃), 4.45 (q, 2H, J = 7.5 Hz, CH₂CH₃), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 13H, ArH's)	21a
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.23 (t, 3H, J = 7.5 Hz, CH₃CH₂), 1.42 (t, 3H, J = 7.5 Hz, CH₃CH₂), 2.88 (s, 3H, CH ₃), 3.47 (s, 3H, OCH ₃), 3.72 (s, 3H, OCH ₃), 4.11 (q, 2H, J = 7.5 Hz, CH₂CH₃), 4.45 (q, 2H, J = 7.5 Hz, CH₂CH₃), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	21b
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.23 (t, 3H, J = 7.5 Hz, CH₃CH₂), 1.42 (t, 3H, J = 7.5 Hz, CH₃CH₂), 2.88 (s, 3H, CH ₃), 4.11 (q, 2H, J = 7.5 Hz, CH₂CH₃), 4.45 (q, 2H, J = 7.5 Hz, CH₂CH₃), 5.91 (s, 2H, OCH ₂ O), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	21c
IR: 3382 (NH), 3050 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1682 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.39 (t, 3H, J = 7.5 Hz, CH₃CH₂), 4.42 (q, 2H, J = 7.5 Hz, CH₂CH₃), 7.42–8.35 (m, 13H, ArH's), 11.42 (s, br., 1H, NH)	26
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.39 (t, 3H, J = 7.5 Hz, CH₃CH₂), 4.42 (q, 2H, J = 7.5 Hz, CH₂CH₃), 7.06–8.38 (m, 13H, ArH's)	29a
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH ₂), 1663 (CH ₃). ^1H NMR: δ = 1.39 (t, 3H, J = 7.5 Hz, CH₃CH₂), 4.44 (q, 2H, J = 7.5 Hz, CH₂CH₃), 7.08–8.23 (m, 13H, ArH's)	29b

Synthesis of Ethyl 2-(Azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (5a), Ethyl 2-(Azanitrosomethylene)-3-(benzothiazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (5b), and Ethyl 2-(Azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-selenadiazoline-5-carboxylate (5c)

A cold saturated solution of sodium nitrite (10 mL) was added dropwise to a solution of the appropriate **4a–c** (1 g) in acetic acid (20 mL) in an ice bath while stirring. The reaction mixture was stirred for 30 min. The resulting solid was collected, washed with water, and crystallized from acetone to give **5a–c**, respectively (Tables I and II).

Synthesis of Ethyl 3-(4-Benzoxazol-2-ylphenyl)-2-oxo-1,3,4-thiadiazoline-5-carboxylate (7a,) 3-(4-Benzothiazol-2-ylphenyl)-2-oxo-1,3,4-thiadiazoline-5-carboxylate (7b), and Ethyl 3-(4-Benzoxazol-2-ylphenyl)-2-oxo-1,3,4-selenadiazoline-5-carboxylate (7c)

A solution of the appropriate **5a–c** (0.5 g) in xylene (20 mL) was refluxed for 15 min. Then the solvent was evaporated under reduced pressure. The residue oil was triturated with petroleum ether (40–60°C), and the solid formed was collected and crystallized from the proper solvent to give 1,3,4-thiadiazolinone **7a,b** and 1,3,4-selenadiazolinone **7c**, respectively (Tables I and II).

Acylation of 4a–c

Acetylation. A mixture of the appropriate **4a–c** (1 g) in acetic acid (10 mL) and acetic anhydride (5 mL) was warmed for 5 min at 70°C. The reaction mixture was poured onto ice water (40 mL). The solid was collected and crystallized to give the *N*-acetyl derivatives **8a–c**, respectively (Tables I and II).

Benzoylation. 4-Methylbenzoyl chloride (1 mL) was added to a solution of the appropriate **4a–c** (0.5 g) in pyridine (15 mL), and the mixture was refluxed for 10 min, then poured onto ice water (50 mL) and acidified with hydrochloric acid. The resulting product was collected and washed several times with boiling water. The solid was recrystallized from *N,N*-dimethylformamide to give the *N*-4-methylbenzoyl derivatives **9a–c**, respectively (Tables I and II).

Synthesis of Thiadiazolines 13a–g and 14a–g

Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of the appropriate alkyl carbodithioates **10a–g(a,b)** or **101a–g(a,b)** (0.005 mol) and compound **2** (1.8 g, 0.005 mol) in ethanol (20 mL). The resulting solid, which formed after 30 min, was collected and recrystallized from the proper solvent and gave the corresponding thiadiazolines **13a–g** and **14a–g**, respectively, in a good yield (Tables I and II).

Synthesis of 1,2,4-Triazolo[4,3-a]pyrimidines 20a–c and 21a–c

Method A. A mixture of the appropriate hydrazonoyl chlorides **2a,b** (0.005 mol) and the appropriate **17a–c** (1.9 g, 0.005 mol) in chloroform (20 mL) containing triethylamine (0.75 mL, 0.005 mol) was refluxed for 10 h. Chloroform was evaporated under reduced

pressure, and the residue solid was recrystallized from chloroform/methanol mixture to give **20a–c** and **21a–c**, respectively (Tables I and II).

Method B. Equimolar amounts of the appropriate hydrazoneyl chlorides **2a,b**, **22a–c**, and sodium ethoxide (0.005 mol each) in ethanol (20 mL) were refluxed for 3 h. The reaction mixture was cooled, and the resulting solid was collected and recrystallized from the proper solvent to give products identical in all respects (mp, mixed mp, and spectra) with corresponding products obtained by method A.

Synthesis of Ethyl 4-(4-(Benzo[d]oxazol-2-yl)phenyl)-5-(benzoylimino)-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (26)

Method A. Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of methyl benzoylcarbodithioate (**24**) (0.005 mol) and compound **2a** (1.8 g, 0.005 mol) in ethanol (20 mL). The resulting solid, which formed after 30 min, was collected and recrystallized from ethanol to give **26** (Tables I and II).

Method B. Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of 5-phenyl-1,3,4-oxadiazole-2-thiol (**27**) (0.005 mol) and compound **2a** (1.8 g, 0.005 mol) in ethanol (20 mL). The resulting solid, which formed after 30 min, was collected and recrystallized from ethanol to give **26** (Tables I and II).

Synthesis of Ethyl 4-(4-(Benzo[d]oxazol-2-yl)phenyl)-4,5-dihydro-5-(phenylimino)-1,3,4-thiadiazole-2-carboxylate (29a) and Ethyl 4-(4-(Benzo[d]thiazol-2-yl)phenyl)-4,5-dihydro-5-(phenylimino)-1,3,4-thiadiazole-2-carboxylate (29b)

Method A. Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of methyl phenylcarbomodithioate (**28**) (0.005 mol) and the appropriate amount of hydrazoneyl chlorides **2a** and **2b** (1.8 g, 0.005 mol) in ethanol (20 mL) for 30 min. The resulting solid was collected and recrystallized from acetic acid to give **29a** and **29b**, respectively (Tables I and II).

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