Heteroatom Chemistry
Volume 14, Number 5, 2003

1,3,4-Thia- and -Selenadiazole and 1,2,4-Triazolo[4,3-*a*]pyrimidine Derivatives from Hydrazonoyl Halides

Nadia A. Abdel-Riheem, Nora M. Rateb, Ali A. Al-Atoom, and Abdou O. Abdelhamid

Department of Chemistry, Faculty of Science, Cairo University, Giza 12316, Egypt

Received 14 October 2002; revised 3 January 2003

ABSTRACT: *1,2,4-Triazolo[4,3-a]pyrimidines, thiadiazolines, selenadiazolines, and unsymmetrical azines were synthesized via reactions of a 4-isopropylbenzoyl bromide 4-nitrophenylhydrazone with each of potassium thiocyanate, potassium selenocyanate, ethyl 6-methyl-4-[4-(methylethyl)phenyl]-2-methylthio-3,4-dihydropyrimidine-5-carboxylate, and alkyl carbodithioate.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:421–426, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10156

INTRODUCTION

Hydrazonoyl halides have been widely employed for the synthesis of heterocyclic compounds [2–4]. 1,3,4-Thiadiazole derivatives have become useful in medicine, agriculture, and in many fields of technology [5]. As an extension of our study [6–10] and of our syntheses of 1,3,4-thiadiazoles, we report here the reactivity of hydrazonoyl halides toward some alkyl carbodithioates, potassium thiocyanate, potassium selenocyanate, and pyrimidine thione.

RESULTS AND DISCUSSION

Treatment of 4-isopropylbenzoyl bromide 4-nitrophenylhydrazone (**1**) [11] with methyl carbodithioate **2aA** [12] in ethanolic triethylamine at room temperature gave benzaldehyde 3-(4-nitrophenyl)-5-(4-isopropylphenyl)-1,3,4-thiadiazol-2(3*H*)-ylidenehydrazone (**4a**) (Scheme 1).

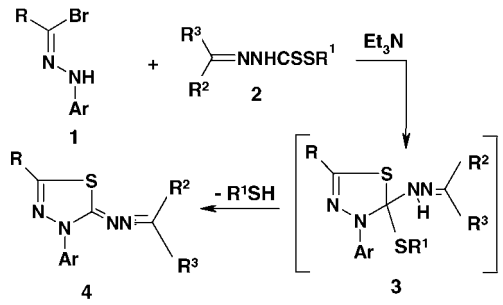
The structure of **4a** was confirmed by elemental analysis, spectral data, and alternative synthesis. ^{1}H NMR of **4a** showed signals at $\delta = 1.26$ (d, 6H, $(CH_3)_2CH$—), 2.95 (sept, 1H, $(CH_3)_2CH$—), and 6.97–8.53 (m, 14H, ArH and CH (vinyl)). Also, treatment of **1** with each of **2aB** [13] and **2aC** [13] in ethanolic triethylamine gave a product identical in all respects (mp, mixed mp, and spectra) with **4a**.

Similarly, compound **1** reacted with other alkyl carbodithioates **2b–q**(**A–C**) [12,13] to give the 1,3,4-thiadiazole derivatives **4b–q**, respectively. Products **4a–q** are assumed to be formed via elimination of alkanethiol (R^1SH) from the corresponding cycloadduct **3**, which formed from 1,3-dipolar cycloaddition (or 1,3-addition) of nitrile imide (generated in situ from **1** and triethylamine) to C=S **2** (Scheme 1).

Moreover, treatment of **1** with each of potassium thiocyanate and potassium selenocyanate gave 5-[4-(methylethyl)phenyl]-3-(4-nitrophenyl)-1,3,4-thiadiazol-2(3*H*)imine (**6a**) and 5-[4-methylethyl)-phenyl]-3-(4-nitrophenyl)-1,3,4-selenadiazol-2(3*H*)-imine (**6b**), respectively. The structures of **6a** and **6b** were elucidated on the basis of elemental analyses, spectral data, an alternative synthesis, and

Reactions of Hydrazonoyl Halides, Part 36 [1].

Correspondence to: Abdou O. Abdelhamid; e-mail: abdou@main-scc.cairo.eun.eg.



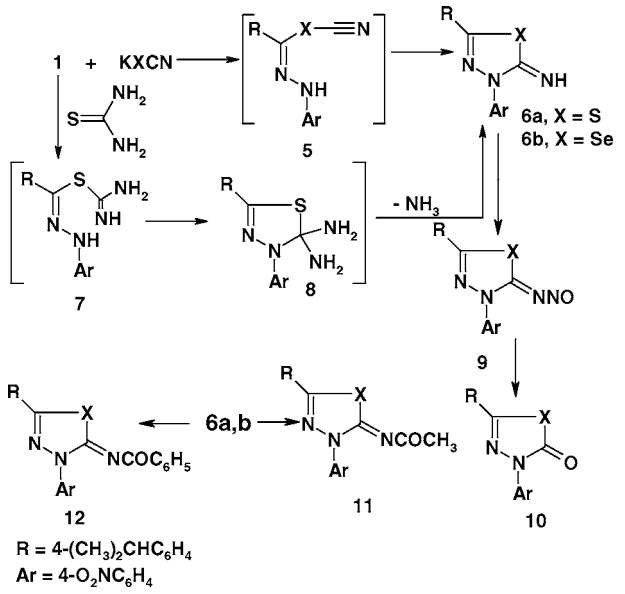
R = 4-$(CH_3)_2CHC_6H_4$
Ar = 4-$O_2NC_6H_4$

2A, $R^1 = CH_3$
B, $R^1 = C_2H_5$
C, $R^1 = CH_2C_6H_5$

a, R^2 = H, $R^3 = C_6H_5$
b, R^2 = H, R^3 = 4-$CH_3C_6H_4$
c, R^2 = H, R^3 = 4-$CH_3OC_6H_4$
d, R^2 = H, R^3 = 2-C_4H_3S
e, R^2 = H, R^3 = 2-C_4H_3O
f, R^2 = H, R^3 = 2-C_5H_4N
g, R^2 = H, $R^3 = C_6H_5CH{=}CH$
h, R^2 = H, $R^3 = (CH_3)_2CHC_6H_4$
i, R^2 = H, R^3 = 5-$CH_2O_2C_6H_3$

j, $R^2 = CH_3$, $R^3 = C_6H_5$
k, $R^2 = CH_3$, R^3= 2-C_4H_3O
l, $R^2 = CH_3$, R^3= 2-C_4H_3S
m, $R^2 = CH_3$, R^3= 2-C_5H_4N
n, R^2 - $R^3 = C_4H_8$
o, R^2- $R^3 = C_5H_{10}$
p, R^2- $R^3 = C_6H_{12}$
q, R^2- $R^3 = C_9H_{10}$

SCHEME 1



R = 4-$(CH_3)_2CHC_6H_4$
Ar = 4-$O_2NC_6H_4$

SCHEME 2

its nitrosation and acylation reactions. The ^{1}H NMR spectrum of **6a** showed signals at $\delta = 1.29$ (d, 6H, $(CH_3)_2CH$—), 2.97 (sept, 1H, $(CH_3)_2CH$—), and 7.25–8.42 (m, 9H, ArH and NH). The IR of **6a** and **6b** each revealed a band at $\nu = 3380$ cm^{-1} (NH) and no absorption bands in $\nu = 2000$–2200 cm^{-1} due to free SCN or SeCN. Also, treatment of **1** with thiourea in boiling ethanol gave a product identical in all respects (mp, mixed mp, and spectra) with **6a**. These results indicate that hydrazone **5**, amidiazone **7**, or 2,2-diaminothiadiazoline **8** are not the final products, and that **5** and **8** readily gave **6a** either by cyclization or by elimination of one molecule of ammonia (Scheme 2).

Acylation of each **6a** and **6b** with acetic anhydride or with benzoyl chloride in pyridine afforded 5-[4-(methylethyl)phenyl]-3-(4-nitrophenyl)-(1,3,4-thia/selenadiazolin-2-ylidene)amide (**11a,b**), and benzamide (**12a,b**), respectively. Spectral data and elemental analyses confirmed their structures. ^{1}H NMR spectrum of **11a** showed signals at $\delta = 1.30$ (d, 6H, $(CH_3)_2CH$—), 2.40 (s, 3H, $CH_3CON{=}$), 3.00 (sept, 1H, $(CH_3)_2CH$—), and 7.25–8.48 (m, 8H, ArH). Its IR revealed a band at $\nu = 1640$ cm^{-1} ($CH_3CON{=}$).

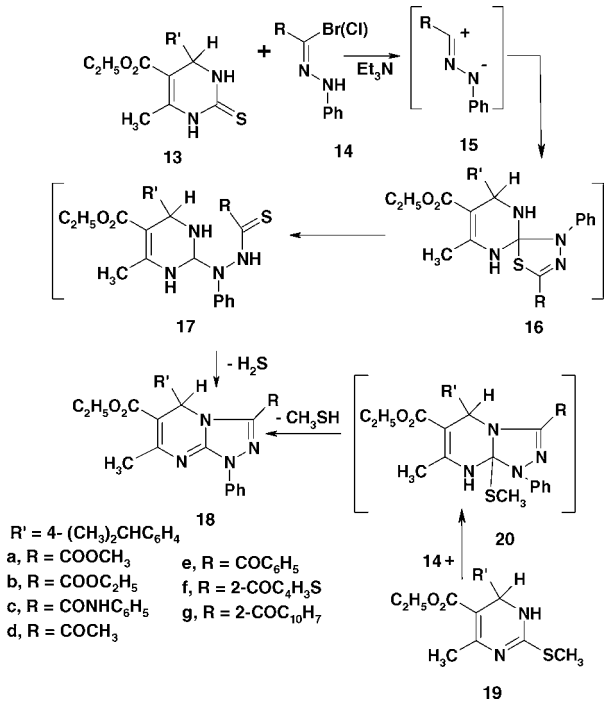
Nitrosation of each **6a** and **6b** with saturated sodium nitrite in acetic acid at 0–5°C gave *N*-nitroso-5-[4-(methylethyl)phenyl]-3-(4-nitrophenyl)-1,3,4-thia/selenadiazol-2(3*H*)imine (**9a,b**), respectively.

5-[4-(Methylethyl)phenyl]-3-(4-nitrophenyl)-1,3,4-thia/selenadiazolin-2-one (**10a,b**) were prepared by thermolysis of **9a** and **9b** in boiling xylene. IR spectra of **10a,b** revealed a band near $\nu = 1685$ cm^{-1} (CO).

Next, treatment of ethyl 4-methyl-6-[4-(methylethyl)phenyl]-2-thioxo-1,3,6-trihydropyrimidine-5-carboxylate (**13**) with the hydrazonoyl halides **14a–g** in chloroform and triethylamine gave the 1,2,4-triazolo[4,3-*a*]pyrimidine-5-carboxylates **18a–g**, respectively. The structure of **18** was elucidated on the base of elemental analysis, spectra, and alternative synthesis. ^{1}H NMR spectrum of **18a** showed signals at $\delta = 1.18$ (d, 6H, $(CH_3)_2CH$)), 1.25 (t, 3H, CH_2CH_3), 2.52 (s, 3H, CH_3), 2.83 (sept, 1H, $(CH_3)_2CH$—)), 3.94 (s,3H,OCH_3), 4.12 (q, 2H, CH_2CH_3), 6.83 (s, 1H, CH), and 7.07–8.21 (m, 9H, ArH). Its IR spectrum revealed bands at $\nu = 1735$ and 1689 cm^{-1} (CO). Ethyl 6-methyl-4-[4-(methylethyl)phenyl]-2-methylthio-3,4-dihydropyrimidine-5-carboxylate (**19**) reacted with the appropriate hydrazonoyl halides **14a–g** in boiling ethanolic sodium ethoxide solution gave products identical in all respects (mp, mixed mp, and spectra) with the corresponding **18a–g**.

The formation of **18** can be explained via 1,3-dipolar cycloaddition or 1,3-addition of nitrile imides **15** (prepared in situ from hydrazonoyl halides **14** with triethylamine or sodium ethoxide) to C=S of **13** (or C=N of **19)** to give intermediate **16** (or **20**), with ring opening and ring closure to afford the final products **18** by elimination of hydrogen sulfide (or methyl mercaptan from **20**) (Scheme 3).

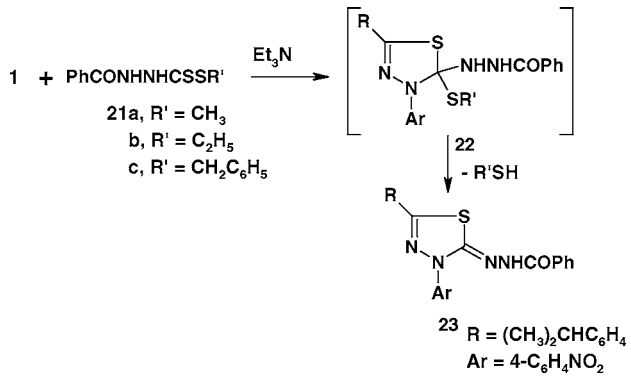
Treatment of **1** with methyl benzoylhydrazinecarbodithioate (**21a**) in ethanolic triethylamine gave



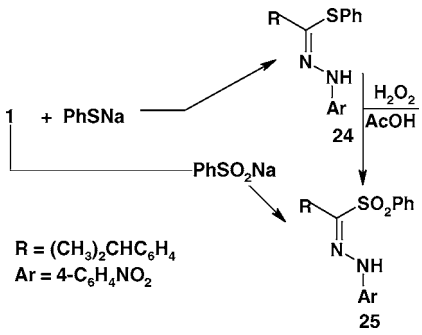
SCHEME 3

2,3-dihydro-1,3,4-thiadiazole **23** (Scheme 4). Its structure was elucidated on the basis of elemental analysis, spectral data, and alternative synthesis. ^{1}H NMR spectrum showed signals at $\delta = 1.20$ (d, 6H, $(CH_3)_2CH$—), 2.96 (sept, 1H, $(CH_3)_2CH$—), 7.20–8.35 (m, 13H, ArH), and 8.42 (s, br, 1H, NH). Treatment of **1** with each of **21b** and **21c** gave products identical in all respects (mp, mixed mp, and spectra) with **23**.

Finally, treatment of **1** with each of sodium benzenethiolate and sodium benzenesulfinate in ethanol afforded the hydrazones **24** and **25**, respectively (Scheme 5). Compound **24** was easily oxidized by



SCHEME 4



SCHEME 5

hydrogen peroxide in acetic acid to give a product identical in all respects (mp, mixed mp, and spectra) with compound **25**.

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 were expressed in δ units using TMS as internal reference. Elemental analyses were carried out at the Microanalytical Center of the Cairo University. Hydrazonoyl halides [14–21] and alkyl carbodithioates [12,13] were prepared as previously reported.

Synthesis of Thiadiazolines **4a–q** *and* **23**

Triethylamine (0.75 ml, 0.005 mol) was added dropwise with stirring to a mixture of the appropriate alkyl carbodithioates **2a–q**(**A–C**) or **21a–c** (0.005 mol) and compound **1** (1.8 g, 0.005 mol) in ethanol (20 ml). The resulting solid, which formed after 30 min, was collected and crystallized from acetic acid and gave the corresponding thiadiazolines **4a–q** and **23**, respectively, in a good yield (Tables 1 and 2).

Synthesis of 1,3,4-Thiadiazoline **6a** *and 1,3,4-Selenadiazoline* **6b**

Method A. A mixture of **1** (1.8 g, 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 3 h. The resulting solid was collected, washed with water, and crystallized from ethanol to give **6a** and **6b**, respectively (Tables 1 and 2).

TABLE 1 Characterization Data of the Newly Synthesized Compounds

	m.p. (°C)	Yield (%)	Mol. Formula (Mol. Wt)	Analyses: Calcd, Found			
				C	H	N	S
4a	200–202 (yellow)	89	$C_{24}H_{21}N_5O_2S$ (443.53)	64.99, 65.10	4.77, 4.90	15.79, 15.60	7.23, 7.40
4b	178–180 (yellow)	85	$C_{25}H_{23}N_5O_2S$ (457.54)	65.63, 65.80	5.07, 4.99	15.31, 15.30	7.00, 7.20
4c	157–158 (yellow)	80	$C_{25}H_{23}N_5O_3S$ (473.54)	63.41, 63.50	4.49, 4.60	14.79, 14.80	6.77, 6.50
4d	162–164 (yellow)	82	$C_{22}H_{19}N_5O_2S_2$ (449.52)	58.78, 58.60	4.26, 4.40	15.58, 15.80	14.26, 14.20
4e	164–165 (yellow)	84	$C_{22}H_{19}N_5O_3S$ (433.48)	60.10, 60.20	4.42, 4.30	16.16, 16.20	7.39, 7.10
4f	238–240 (yellow)	75	$C_{23}H_{20}N_6O_2S$ (444.50)	62.12, 62.00	4.54, 4.60	18.91, 19.10	7.21, 7.30
4g	205–207 (yellow)	78	$C_{26}H_{23}N_5O_2S$ (469.55)	66.51, 66.40	4.94, 5.10	14.92, 15.00	6.82, 6.70
4h	153–155 (yellow)	88	$C_{27}H_{27}N_5O_2S$ (485.59)	66.78, 66.80	5.60, 5.50	14.42, 14.30	6.60, 6.70
4i	226–228 (yellow)	89	$C_{25}H_{21}N_5O_4S$ (487.52)	61.59, 61.60	4.34, 4.50	14.37, 14.40	6.57, 6.30
4j	166–168 (yellow)	90	$C_{25}H_{23}N_5O_2S$ (457.54)	65.63, 65.40	5.07, 4.80	15.31, 15.10	7.00, 7.20
4k	221–223 (yellow)	86	$C_{23}H_{21}N_5O_3S$ (447.50)	61.73, 61.70	4.73, 4.80	15.65, 15.50	7.16, 7.10
4l	213–215 (yellow)	78	$C_{23}H_{21}N_5O_2S_2$ (463.55)	59.60, 59.50	4.57, 4.70	15.12, 15.10	13.83, 14.00
4m	188–191 (yellow)	88	$C_{24}H_{22}N_6O_2S$ (458.53)	62.87, 62.70	4.84, 4.50	18.33, 18.20	6.99, 7.10
4n	220–222 (yellow)	89	$C_{23}H_{23}N_5O_2S$ (433.52)	63.72, 63.70	5.35, 5.50	16.15, 16.00	7.39, 7.50
4o	170–172 (yellow)	69	$C_{24}H_{25}N_5O_2S$ (447.55)	64.41, 64.20	5.63, 5.30	15.65, 15.50	7.16, 6.90
4p	150–152 (yellow)	75	$C_{25}H_{27}N_5O_2S$ (461.57)	65.06, 65.10	5.90, 6.00	15.17, 15.00	6.94, 6.80
4q	250–252 (yellow)	74	$C_{28}H_{25}N_5O_2S$ (495.59)	67.86, 67.60	5.08, 4.90	14.13, 14.00	6.47, 6.50
6a	168–170 (yellow)	73	$C_{17}H_{16}N_4O_2S$ (340.39)	59.99, 60.10	4.74, 4.70	16.46, 16.60	9.41, 9.30
6b	114–115 (yellow)	78	$C_{17}H_{16}N_4O_2Se$ (387.30)	52.72, 52.80	4.16, 4.00	14.47, 14.60	
9a	145 (pale yellow)	72	$C_{17}H_{15}N_5O_3S$ (369.39)	55.28, 55.30	4.09, 4.10	18.96, 19.00	8.68, 8.80
9b	150 (pale yellow)	70	$C_{17}H_{15}N_5O_3Se$ (416.29)	49.05, 48.90	3.63, 3.70	16.82, 16.90	
10a	154–155 (red)	78	$C_{17}H_{15}N_3O_3S$ (341.37)	59.81, 59.60	4.42, 4.40	12.31, 12.10	9.39, 9.40
10b	155–157 (red)	77	$C_{17}H_{15}N_3O_3Se$ (388.29)	52.58, 52.60	3.89, 3.90	10.82, 10.90	
11a	186–188 (pale yellow)	76	$C_{19}H_{18}N_4O_3S$ (382.43)	59.67, 60.00	4.74, 4.80	14.65, 14.60	8.38, 8.40
11b	210–212 (pale yellow)	79	$C_{19}H_{18}N_4O_3Se$ (429.34)	53.15, 53.20	4.23, 4.30	13.05, 13.10	
12a	172–173 (pale yellow)	82	$C_{24}H_{20}N_4O_3S$ (444.50)	64.85, 65.00	4.54, 4.60	12.60, 12.70	7.21, 7.10
12b	165–167 (pale yellow)	77	$C_{24}H_{20}N_4O_3Se$ (491.41)	58.66, 58.70	4.00, 3.90	11.40, 11.30	
13	178–180 (yellow)	68	$C_{17}H_{22}N_2O_2S$ (318.42)	64.13, 64.10	6.96, 7.00	8.80, 8.60	10.06, 9.20
18a	119–120 (yellow)	75	$C_{26}H_{28}N_4O_4$ (460.54)	67.81, 67.70	6.09, 6.10	12.17, 12.00	
18b	109–110 (yellow)	77	$C_{27}H_{30}N_4O_4$ (474.57)	68.33, 68.10	6.37, 6.30	11.81, 11.70	
18c	149–151 (yellow)	76	$C_{31}H_{31}N_5O_3$ (521.63)	71.38, 71.10	5.99, 6.10	13.43, 13.20	
18d	128–129 (yellow)	79	$C_{26}H_{28}N_4O_3$ (444.54)	70.25, 70.30	6.35, 6.40	12.60, 12.50	
18e	120–122 (orange)	72	$C_{31}H_{30}N_4O_3$ (506.61)	73.50, 73.40	6.00, 6.20	11.06, 10.90	
18f	187–188 (orange)	70	$C_{29}H_{28}N_4O_3S$ (512.62)	67.95, 67.10	5.51, 5.30	10.93, 10.70	6.26, 6.40
18g	113–115 (brown)	77	$C_{35}H_{32}N_4O_3$ (556.65)	75.52, 75.30	5.80, 5.60	10.07, 9.80	
19	69–70 (colorless)	85	$C_{18}H_{24}N_2O_2S$ (332.45)	65.03, 65.10	7.28, 7.40	8.43, 8.30	9.64, 9.50
23	190–192 (yellow)	85	$C_{24}H_{21}N_5O_3S$ (459.51)	62.73, 62.90	4.61, 4.50	15.24, 15.30	6.97, 7.10
24	220–222 (yellow)	88	$C_{22}H_{21}N_3O_2S$ (391.48)	67.50, 67.30	5.41, 5.60	10.73, 10.80	8.19, 8.30
25	120 (yellow)	77	$C_{22}H_{21}N_3O_4S$ (423.48)	62.40, 62.20	5.00, 5.10	9.92, 10.00	7.57, 7.80

Method B. A mixture of **1** (1.8 g, 0.005 mol) and thiourea (0.38 g, 0.005 mol) in ethanol (25 ml) was refluxed for 30 min. The solid product that formed after cooling was collected and crystallized from ethanol. It was identical in all respects (mp, mixed mp, and spectra) with **6a**.

Nitrosation of **6a** *and* **6b**

A cold saturated solution of sodium nitrite (10 ml) was added dropwise to a solution of **6a** or **6b** (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 **9a** and **9b**, respectively (Tables 1 and 2).

Thermolysis of **9a** *and* **9b**

A solution of **9a, 9b** (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 acetic acid to give 1,3,4-thiadiazolinone **10a** and 1,3,4-selenadiazolinone **10b**, respectively (Tables 1 and 2).

Acylation of **6a** *and* **6b**

Acetylation. A mixture of **6a** or **6b** (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

TABLE 2 ^{1}H NMR Spectroscopic Data of Some Synthesized Compounds

4b	1.26 (d, 6H, $(CH_3)_2CH$), 2.37 (s, 3H, 4-$CH_3C_6H_4$), 2.97 (sept, 1H, $(CH_3)_2CH$), 6.97–8.50 (m, 13H, ArH and CH=N).
4c	1.26 (d, 6H, $(CH_3)_2CH$), 2.98 (sept, 1H, $(CH_3)_2CH$), 3.84 (s, 3H, 4-CH3OC_6H_4), 6.97–8.53 (m, 13H, ArH and CH=N).
4d	1.28 (d, 6H, $(CH_3)_2CH$), 2.98 (sept, 1H, $(CH_3)_2CH$), 7.07–8.61 (m, 12H, ArH and CH=N).
4e	1.28 (d, 6H, $(CH_3)_2CH$), 2.98 (sept, 1H, $(CH_3)_2CH$), 6.53–8.52 (m, 12H, ArH's and CH=N).
4f	1.28 (d, 6H, $(CH_3)_2CH$), 2.98 (sept 1H, $(CH_3)_2CH$), 7.25–8.68 (m, 13H, ArH and CH=N).
4j	1.15 (d, 6H, $(CH_3)_2CH$), 2.40 (s, 3H, CH_3), 2.85 (sept, 1H, $(CH_3)_2CH$), 7.12–8.41 (m, 13H, ArH).
4k	1.18 (d, 6H, $(CH_3)_2CH$), 2.40 (s, 3H, CH_3), 2.86 (sept, 1H, $(CH_3)_2CH$), 6.95–8.41 (m, 11H, ArH).
4l	1.16 (d, 6H, $(CH_3)_2CH$), 2.32 (s, 3H, CH_3), 2.90 (sept, 1H, $(CH_3)_2CH$), 6.39–8.42 (m, 11H, ArH's).
4m	1.28 (d, 6H, $(CH_3)_2CH$), 2.50 (s, 3H, CH_3), 2.97 (sept, 1H, $(CH_3)_2CH$), 7.26–8.51 (m, 12H, ArH).
6b	1.28 (d, 6H, $(CH_3)_2CH$), 2.96 (sept, 1H, $(CH_3)_2CH$), 7.25–8.34 (m, 9H, ArH and NH).
9a	1.28 (d, 6H, $(CH_3)_2CH$), 2.95 (sept, 1H, $(CH_3)_2CH$), 7.25–8.21 (m, 8H, ArH).
9b	1.27 (d, 6H, $(CH_3)_2CH$), 2.92 (sept, 1H, $(CH_3)_2CH$), 7.25–8.25 (m, 8H, ArH).
10a	1.28 (d, 6H, $(CH_3)_2CH$), 2.92 (sept,1H, $(CH_3)_2CH$), 7.20–8.15 (m, 8H, ArH).
10b	1.28 (d, 6H, $(CH_3)_2CH$), 2.90 (sept, 1H, $(CH_3)_2CH$), 7.20–8.24 (m, 8H, ArH).
11b	1.28 (d, 6H, $(CH_3)_2CH$), 2.40 (s, 3H, CH_3CON=), 2.98 (sept, 1H, $(CH_3)_2CH$), 7.25–8.48 (m, 8H, ArH).
12a	1.29 (d, 6H, $(CH_3)_2CH$), 2.92 (sept, 1H, $(CH_3)_2CH$), 7.35–8.52 (m, 13H, ArH).
12b	1.20 (d, 6H, $(CH_3)_2CH$), 2.90 (sept, 1H, $(CH_3)_2CH$), 7.16–8.40 (m, 13H, ArH).
13	1.15 (t, 3H, CH_2CH_3), 1.26 (d, 6H, $(CH_3)_2CH$), 2.53 (s, 3H, CH_3), 2.82 (sept, 1H, $(CH_3)_2CH$), 4.08 (q, 2H, CH_2CH_3), 6.76 (s, 1H, CH), 7.21–8.35 (m, 4H, ArH), 9.61 (s, 1H, NH), 10.53 (s, 1H, NH).
18b	1.19 (t, 3H, CH_3CH_2), 1.25 (d, 6H, $(CH_3)_2CH$), 1.34 (t, 3H, CH_3CH_2), 2.51 (s, 3H, CH_3), 2.82 (sept, 1H, $(CH_3)_2CH$), 4.11 (q, 2H, CH_2CH_3), 4.42 (q, 2H, CH_2CH_3), 6.83 (s, 1H, CH), 7.06–8.21 (m, 9H, ArH).
18c	1.15 (t, 3H, CH_3CH_2), 1.22 (d, 6H, $(CH_3)_2CH$), 2.54 (s, 3H, CH_3), 2.83 (sept, 1H, $(CH_3)_2CH$), 4.07 (q, 2H, CH_2CH_3), 7.03–8.20 (m, 15H, ArH and CH), 8.37 (s, br, 1H, NH).
18d	1.13 (t, 3H, CH_3CH_2), 1.21 (d, 6H, $(CH_3)_2CH$), 2.51 (s, 3H, CH_3), 2.53 (s, 3H, CH_3), 2.81 (sept, 1H, $(CH_3)_2CH$), 4.08 (q, 2H, CH_2CH_3), 6.85 (s, 1H, CH), 7.05–8.23 (m, 9H, ArH).
18e	1.12 (t, 3H, CH_3CH_2), 1.23 (d, 6H, $(CH_3)_2CH$), 2.56 (s, 3H, CH_3), 2.75 (sept, 1H, $(CH_3)_2CH$), 4.13 (q, 2H, CH_2CH_3), 6.96 (s, 1H, CH), 7.01–8.24 (m, 14H, ArH).
18f	1.12 (d, 6H, $(CH_3)_2CH$), 1.24 (t, 3H, CH_3CH_2), 2.55 (s, 3H, CH_3), 2.80 (sept, 1H, $(CH_3)_2CH$), 4.08 (q, 2H, CH_2CH_3), 7.00–8.29 (m, 13H, ArH and CH).

crystallized to give the *N*-acetyl derivatives **11a** and **11b**, respectively (Tables 1 and 2).

Benzoylation. **6a** or **6b** (0.5 g) and benzoyl chloride (3 ml) in pyridine (15 ml) were refluxed for 10 min, 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 crystallized from acetic acid or *N,N*-dimethylformamide to give the *N*-benzoyl derivatives **12a** and **12b**, respectively (Tables 1 and 2).

*Synthesis of Ethyl 4-Methyl-6-[4-(methylethyl)-phenyl]-2-thioxo-1,3,6-trihydropyrimidine-5-carboxylate (***13***)*

A mixture of ethyl acetoacetate (0.1 mol, 13 g), thiourea (0.012 mol, 8.2 g), and 4-(methylethyl)-benzaldehyde (14.9 g, 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 formed was collected by filtration, washed with ethanol, and crystallized from ethanol to give **13** (Tables 1 and 2).

*Synthesis of Ethyl 6-Methyl-4-[4-(methylethyl)-phenyl]-2-methylthio-3,4-dihydropyrimidine-5-carboxylate (***19***)*

Iodomethane (0.006 mol) was added portionwise with stirring to a warm ethanolic sodium ethoxide solution [prepared by dissolving sodium metal (0.005 mol) in ethanol 15 ml] and compound **13** (0.005 mol). The reaction mixture was left overnight at room temperature; the solid precipitate was collected and crystallized from ethanol to give **19** (Table 1).

*Synthesis of 1,2,4-Triazolo[4,3-*a*]pyrimidines* **18a–g**

Method A. A mixture of the appropriate hydrazonoyl halides **14a–g** (0.005 mol) and compound **13** (1.9 g, 0.005 mol) in chloroform containing triethylamine (0.75 ml, 0.005 mol) was refluxed for 10 h. Chloroform was evaporated under reduced pressure and the residue solid was crystallized from ethanol to give **18a–g**, respectively (Tables 1 and 2).

Method B. Equimolar amounts of the hydrazonoyl halides **14a–g, 19**, 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 crystallized from ethanol to give products identical in all respects (mp, mixed mp, and spectra) with corresponding products obtained by method A.

Synthesis of Hydrazones **24** *and* **25**

A mixture of equimolar amounts of hydrazonoyl bromide **1** and the appropriate sodium benzenethiolate or sodium benzene sulfinate (0.005 mol each) in ethanol (20 ml) was stirred for 4 h and left at room temperature overnight. The resulting solid was collected, washed with water, and crystallized from ethanol to give hydrazones **24** and **25**, respectively (Table 1).

Alternative synthesis of **25** hydrogen peroxide (5 ml, 30%) was added with stirring to a solution of hydrazone **24** (0.5 g) in acetic acid (20 ml). The reaction mixture was left at room temperature for 48 h and poured onto ice-cold water (50 ml). The resulting solid was collected and crystallized from ethanol to give a product identical in all respects (mp, mixed mp, and spectra) with **25**.

REFERENCES

[1] Part 35: Rateb, N. M.; Abdel-Riheem, N. A.; Al-Atoom, A. A.; Abdelhamid, A. O. Phosphorus, Sulfur Silicon Relat Elem (in press).
[2] Padwa, A. Angew Chem, Int Ed Engl 1976, 15, 123.
[3] Huisgen, R.; Sustmann, R.; Wallbillich, G. Chem Ber 1976, 100, 1786.
[4] Abdelhamid, A. O.; Attaby, F. A. J Heterocycl Chem 1991, 28, 41.
[5] Kornis, D. I. In Comprehensive Heterocyclic Chemistry; Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V. (Eds.); Pergamon: Oxford, 1996; Vol. 4.
[6] Abdelhamid, A. O.; Sallam, M. M. M.; Amer, S. A. Heteroat Chem 2001, 12, 468.
[7] Abdelhamid, A. O.; Zohdi, H. F.; Ali, N. A. Molecules 2001, 5, 961.
[8] Abdelhamid, A. O.; Rateb, N. M.; Dawood, K. M. Phosphorus Sulfur 2000, 167, 251.
[9] Zohdi, H. F.; Rateb, M. M.; Sallam, M. M. M.; Abdelhamid, A. O. J Chem Res (S) 1998, 742; J Chem Res (M) 3329.
[10] Abdelhamid, A. O.; Abdelgawad, S. M.; El-Sharnoby, S. F. Phosphorus Sulfur Silicon Relat Elem 2002, 177, 2699.
[11] Scott, F. L.; Aylward, J. B. Tetrahedron Lett 1965, 841.
[12] Korosi, J. Ger Offen 1,934,899,29 Jan. 1970; Chem Abstr 1970, 72, 100334s.
[13] Klayman, D. L.; Bartosevich, J. F.; Griffin, T. S.; Mason, C. J.; Scovill, J. P. J Med Chem 1979, 22, 855.
[14] Fravel, G. Bull Soc Chim Fr 1904, 31, 150.
[15] Eweiss, N. F.; Osman, A. Tetrahedron Lett 1979, 1169.
[16] Wolkoff, P. Can J Chem 1975, 53, 1333.
[17] Shawali, A. S.; Osman, A. Tetrahedron 1971, 27, 2571.
[18] Shawali, A. S.; Abdelhamid, A. O. Bull Chem Soc Jpn 1976, 49, 321.
[19] Abdelhamid, A. O.; El-Shiatey, F. H. H. Phosphorus Sulfur Silicon Relat Elem 1988, 39, 45.
[20] Abdelhamid, A. O.; Attaby, F. A.; Khalifa, F. A.; Ghabrial, S. S. Arch Pharm Res 1992, 15, 14.
[21] Hassaneen, H. M.; Shawali, A. S.; Elwan, N. M.; Abounada, N. M. Sulfur Lett 1992, 14, 41.