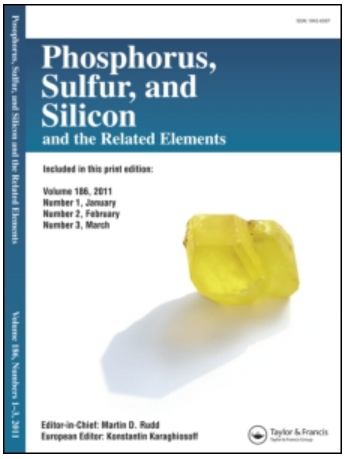


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Reactions with Hydrazonoyl Halides 61[1]: Synthesis of 2,3-Dihydro-1,3,4-Thiadiazoles

Abdou O. Abdelhamid[a]; Mamdouh A. M. Afifi[a]
[a] Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt

To cite this Article Abdelhamid, Abdou O. and Afifi, Mamdouh A. M.(2008) 'Reactions with Hydrazonoyl Halides 61[1]: Synthesis of 2,3-Dihydro-1,3,4-Thiadiazoles', Phosphorus, Sulfur, and Silicon and the Related Elements, 183: 11, 2703 — 2713

To link to this Article: DOI: 10.1080/10426500801968185

URL: http://dx.doi.org/10.1080/10426500801968185

Phosphorus, Sulfur, and Silicon, 183:2703–2713, 2008

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500801968185

Taylor & Francis
Taylor & Francis Group

Reactions with Hydrazonoyl Halides 61[1]: Synthesis of 2,3-Dihydro-1,3,4-Thiadiazoles

Abdou O. Abdelhamid and Mamdouh A. M. Afifi
Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt

2-[1,2-Diaza-3-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))prop-2-enylidene]-3-phenyl-5- substituted 1,3,4-thiadiazolines and 2-{[4-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))(1,3-thiazol-2-yl)]cyanomethylene}-3-phenyl-5-substituted 1,3,4-thiadiazolines were synthesized from hydrazonoyl halides and 4-{-2-aza-2-[(methylthiothioxomethyl)amino]vinyl}-2,3-dimethyl-1-phenyl-3-pyrazoin-5-one and 2-[4-(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)-1,3-thiazol-2-yl]ethanenitrile, respectively. All synthesize compounds were elucidated by elemental analysis, spectra, and alternative synthesis routes, whenever possible.

Keywords 2,3-Dihydro-1,3,4-thiadiazoles; alkyl carbodithiates; antipyrine; hydrazonoyl halides; thioamides

INTRODUCTION

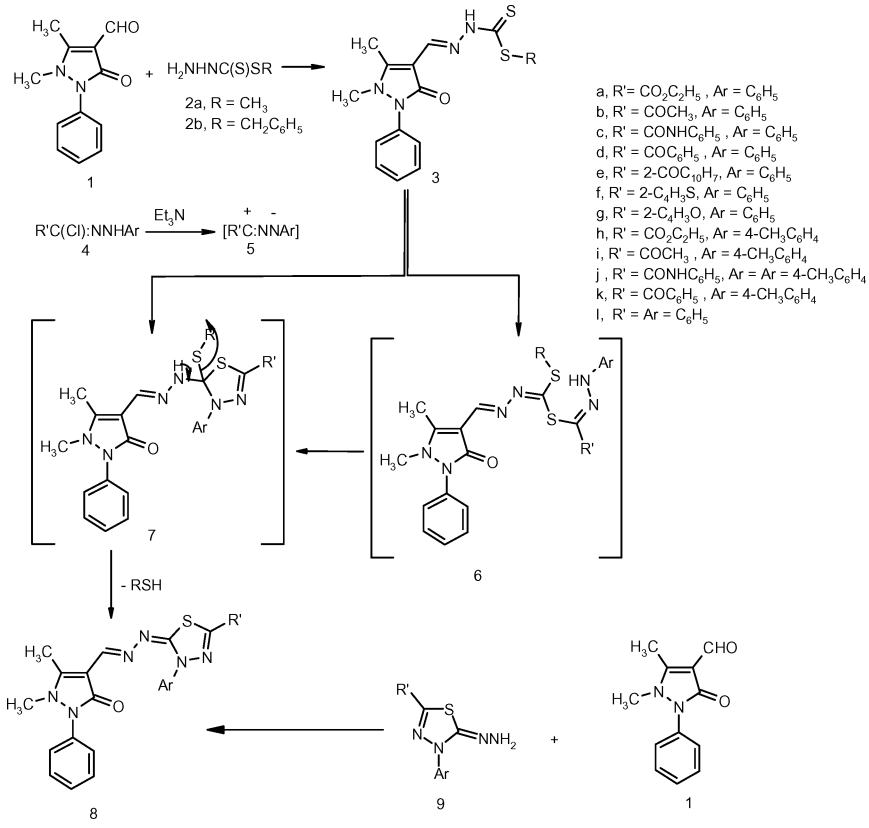
Hydrazonoyl halides have been widely used for the synthesis of heterocyclic compounds.[1–9] Also, 1,3,4-thiadiazoles are active in many biological systems such as antitumor,[10] hypoglycemic properties,[11] antihistamine,[12] and anticholinergic.[13] We report herein the reactivity of hydrazonoyl halides towards 4-{-2-aza-2-[(methylthiothioxomethyl)amino]vinyl}-2,3-dimethyl-1-phenyl-3-pyrazoin-5-one and 2-[4-(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)-1,3-thiazol-2-yl]ethanenitrile.

RESULTS AND DISCUSSION

Treatment of the appropriate alkyl hydrazinecarbodithioate[14] (**2a,b**) with 2,3-dimethyl-5-oxo-1-phenyl-3-pyrazoline-4-carbaldehyde[15] (**1**)

Received 2 December 2007; accepted 4 February 2008.
Address correspondence to Abdou O. Abdelhamid, Department of Chemistry, Faculty of Science, Cairo University, Giza 12613, Egypt. E-mail: abdelhamid45@gmail.com

in 2-propanol afforded 4-{-2-aza-2-[(methylthiothioxomethyl)amino] vinyl}-2,3-dimethyl-1-phenyl-3-pyrazoin-5-one (**3a**) and 4-{-2-aza-2-[(phenylmethylthio)thioxomethyl]amino}vinyl}-2,3-dimethyl-1-phenyl -3-pyrazoin-5-one (**3b**). The ^{1}H NMR spectrum of **3a** showed signals at $\delta = 2.44$ (s, 3H, CH_3), 2.55 (s, 3H), 2.62 (s, 3H), 7.56–8.38 (m, 7H) and 12.52 (s, br., 1H). Compound **3a** reacted with the appropriate hydrazonoyl halides **4a** in ethanolic triethylamine at room temperature to give ethyl 2-[1,2-diaza-3-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))prop-2-enylidene]-3-phenyl-1,3,4-thiadiazoline-5-carboxylate **8a** (Scheme 1). Structure **8** was confirmed by elemental analysis, spectral data and an alternate synthetic route. Thus, ^{1}H NMR spectrum of **8a** showed signals at $\delta = 1.42$ (t, 3H, CH_2 CH_3), 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3) 4.44 (q, 2H, CH_2CH_3), 7.23–7.47 (m, 8H, ArH's),



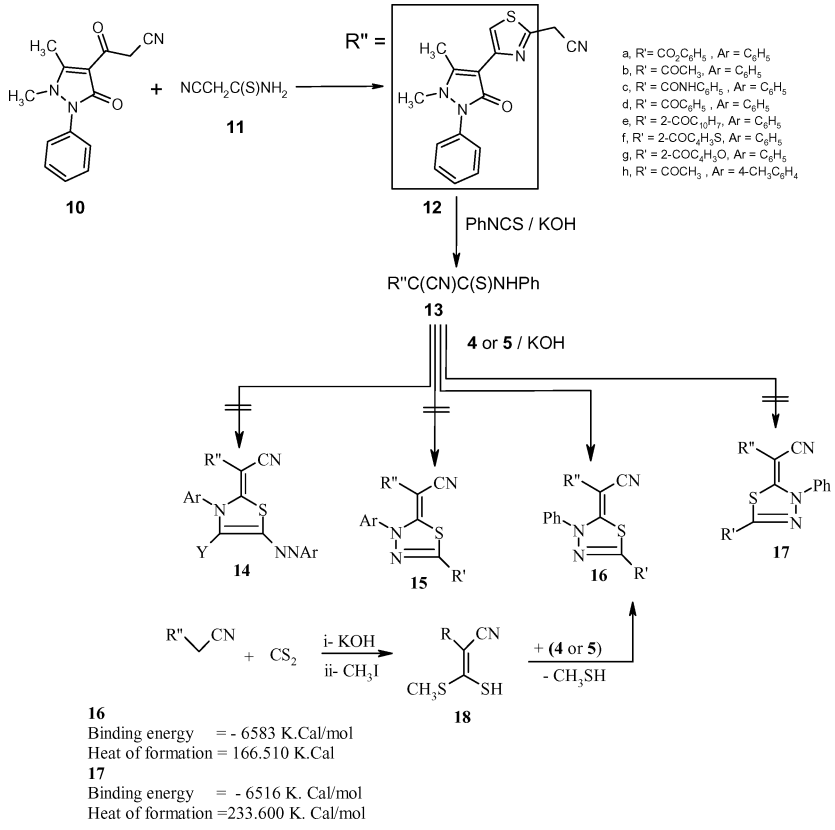
SCHEME 1

7.85 (d, 2H, J = 5 Hz, and 8.43 (s, 1H, vinyl CH=N). Its IR revealed bands at 1708, 1668 (CO's), and 1506 (C=C). Also, treatment of ethyl 2-hydrazino-3-phenyl-2,3-dihydro-1,3,4-thiadiazole-5-carboxylate[16] (**9**) with **1** in 2-propanol afforded a product identical to **8a**. In the light of the forgoing results, the mechanism outlined in Scheme 1 seems to be the most plausible pathway for the formation of **8** from the reaction between **3** and **4**. The reaction involves initial formation of thiohydrazonate **6**, which undergoes intramolecular cyclization as soon as it is formed to yield the intermediate **7** or via 1,3-dipolar cycloaddition of nitrilimine **5**, which prepared in situ from **4** with triethylamine, to C=S double bond of **3** to give the intermediate **7**. Intermediate **7** is converted to the final product **8** via elimination of methyl mercaptan.

Analogously, treatment of the appropriate **4b**–**l** with each of methyl hydrazinecarbodithioate **3a** or benzyl hydrazinecarbodithioate **3b** in ethanolic triethylamine at room temperature, afforded the corresponding 2,3-dihydro-1,3,4-thiadiazoles **8b**–**l**, respectively.

Treatment of 4-(2-chloroacetyl)-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one (**10**) with cyanothioacetamide (**11**) in ethanol afforded 2-[4-(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)-1,3-thiazol-2-yl]ethanenitrile (**12**). The structure of the product was supported by its elemental analysis and spectral data. Compound **12** was reacted with phenyl isothiocyanate in *N*, *N*-dimethylformamide containing potassium hydroxide to give 2-[4-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))(1,3-thiazol-2-yl)]-3-(phenylamino)-3-thioxopropanenitrile (**13**) (Scheme 2). Thus, the reaction of **13** with *C*-ethoxycarbonyl-*N*-phenylhydrazonoyl chloride **4a** in ethanolic triethylamine gave the ethyl 2-[4-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))(1,3-thiazol-2-yl)]cyanomethylene-3-phenyl-1,3,4-thiadiazoline-5-carboxylate (**16a**), as evidenced from its elemental analysis and spectral data, in good yield (Scheme 2).

Structure **16** was confirmed by elemental analysis, spectral data, and an alternate synthetic route. Thus, ^{1}H NMR spectrum of **16a** showed signals at δ = 1.46 (t, 3H, CH_3CH_2), 2.90 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 4.48 (q, 2H, CH_2CH_3), 7.25-7.58 (m, 10H, ArH's) and 8.06 (s, 1H, thiazole H-5). Its IR revealed bands at 2191 (CN), 1705, 1691 (CO's), and 1595 (C=C). Meanwhile, the product seemed to be one of two isomeric structures **16** and **17**. By M.O. calculation using Hyper-Chem and MBI_3 method[15] showed for structure **16** the binding energy = −6583 K.Cal / mol and heat of formation = 166.51 K.Cal/mol, whereas the structure **17** the binding energy = -6516 K.Cal / mol and heat of formation = 233.60 K.Cal /mol. From these results, the isomeric **16** more stable than isomeric **17**.

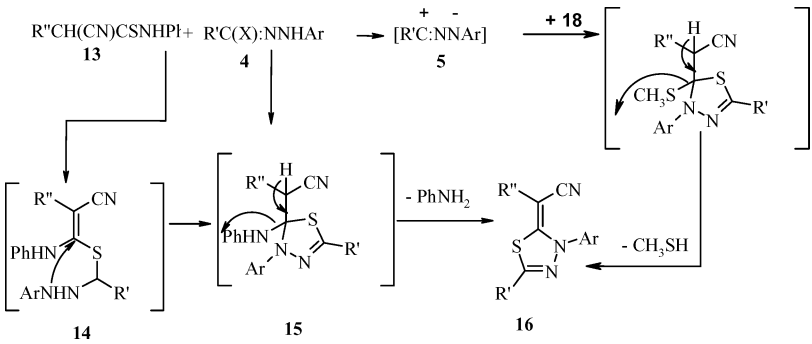


16
Binding energy = - 6583 K.Cal/mol
Heat of formation = 166.510 K.Cal
17
Binding energy = - 6516 K. Cal/mol
Heat of formation =233.600 K. Cal/mol

SCHEME 2

The formation of product **16** can be explained via elimination of aniline from the cycloadduct of nitrile imide **5** (which was generated in situ by treatment of hydrazonoyl chloride **4** with base) to CS double bond of thioanilide **13** or by stepwise path involving substitution to give a cyclic hydrazone **14**, which easy converted into cyclic intermediate **15**. The latter gave**16** via the elimination of aniline (Scheme 3).

An unequivocal support for structure **16a**, came from the reaction of the appropriate *C*-ethoxycarbonyl-*N*-phenylhydrazonoyl chloride **4a** with 2-[4—(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))(1,3-thiazol-2-yl)]-3-methylthio-3-sulfanylprop-2-enenitrile (**18**), which was prepared from **12** with carbon disulfide in *N*, *N*-dimethylformamide containing potassium hydroxide followed by addition of iodomethane, in presence of triethylamine gave product identical in all aspects (m.p.,



SCHEME 3

mixed m.p. and spectra) with **16a** via elimination of methyl mercaptan (Scheme 3).

EXPERIMENTAL

All melting points were determined on an electrothermal melting point Gallen-Kamp apparatus and are uncorrected. IR (cm^{-1}) spectra were recorded on KBr disk on a FTIR-8201 PC Shimadzu spectrophotometer. ^{1}HNMR spectra were recorded in $CDCl_3$ or $(CD_3)_2SO$ on Gemini 200 MHz and Varian 300 MHz spectrometers, using TMS as internal reference. and chemical shifts are express as δ ppm unit. Elemental analysis was performed at the Microanalytical Center in Cairo University. Hydrazonoyl halides **4a**–**l** were prepared as previously reported in literature.[17–21]

Synthesis of 4-{-2-Aza-2-[(methylthiothioxomethyl)amino] vinyl}-2,3-dimethyl-1-phenyl-3-pyrazoin-5-one (3a) and 4-{-2-Aza-2-[(phenylmethylthio)thioxomethyl]amino}vinyl}-2,3-dimethyl-1-phenyl-3-pyrazoin-5-one (3b)— General Procedure

A mixture of the appropriate alkyl hydrazinecarbodithioate[14] (**2a,b**) with 2,3-dimethyl-5-oxo-1-phenyl-3-pyrazoline-4-carbaldehyde (**1**) (10 mmoles) in 1-propanol (20 mL) was stirred at room temperature for 2 h. The solid, so formed, was collected and recrystallized from ethanol to give **3a** and **3b**, respectively (Tables I and II).

TABLE I Characterization Data of the Newly Synthesized Compounds

Compd. no.	M.p.,°C solvent	Yield[a] % Color	Mol. formula m.wt.	% Analyses, calcd./found C	H	N	S
3a	240–242	80	$C_{14}H_{16}N_4OS_2$	52.48	5.03	17.48	20.01
	DMF	Yellow	320.44	52.53	4.92	17.56	19.95
3b	228–232	85	$C_{20}H_{20}N_4OS_2$	60.58	5.08	14.13	16.17
	AcOH	Yellow	396.54	60.37	4.89	14.28	16.00
8a	244–246	68	$C_{23}H_{22}N_6O_3S$	59.73	4.79	18.17	6.93
	EtOH	Yellow	462.58	59.62	4.58	18.27	7.11
8b	288–290	69	$C_{22}H_{20}N_6O_2S$	61.10	4.66	19.43	7.41
	EtOH	Orange	432.51	61.20	4.85	19.34	7.28
8c	332–335	64	$C_{27}H_{23}N_7O_2S$	63.64	4.55	19.24	6.29
	AcOH	Yellow	509.59	63.54	4.65	19.15	6.34
8d	272–274	68	$C_{27}H_{22}N_6O_2S$	65.57	4.48	16.99	6.48
	AcOH	Yellow	494.58	65.75	4.68	17.22	6.45
8e	218–220	65	$C_{31}H_{24}N_6O_2S$	68.37	4.44	15.43	5.89
	EtOH	Yellow	544.64	68.45	4.24	15.33	5.98
8f	240–242	66	$C_{25}H_{20}N_6O_2S_2$	59.98	4.03	16.79	12.81
	AcOH	Yellow	500.61	59.85	3.92	16.97	12.68
8g	235–237	67	$C_{25}H_{20}N_6O_3S$	61.97	4.16	17.34	6.62
	AcOH	Yellow	484.54	61.88	4.15	17.43	6.58
8h	215–217	69	$C_{24}H_{24}N_6O_3S$	60.49	5.08	17.63	6.73
	EtOH	Yellow	476.56	60.57	5.11	17.68	6.58
8i	248–252	65	$C_{23}H_{22}N_6O_2S$	61.87	4.97	18.82	7.18
	EtOH	Orange	446.53	61.74	4.79	18.78	7.00
8j	288–290	63	$C_{28}H_{25}N_7O_2S$	64.23	4.81	18.72	6.12
	DMF	Yellow	523.62	64.33	4.92	18.67	6.34
8k	280–282	69	$C_{28}H_{24}N_6O_2S$	66.12	4.76	16.52	6.30
	AcOH	Yellow	508.61	66.00	4.67	16.45	6.15
8l	262–264	62	$C_{26}H_{22}N_6OS$	66.93	4.75	18.01	6.87
	AcOH	Yellow	466.57	66.88	4.65	17.89	6.78
12	180–182	78	$C_{16}H_{14}N_4OS$	61.92	4.55	18.05	10.33
	EtOH	Buff	310.38	61.82	4.62	17.89	10.24
13	247–249	70	$C_{23}H_{19}N_5OS_2$	62.00	4.30	15.72	14.39
	DMF	Buff	445.57	62.12	4.21	15.60	14.21
16a	318–321	60	$C_{27}H_{22}N_6O_3S_2$	59.76	4.09	15.49	11.82
	AcOH	Yellow	542.64	59.67	3.89	15.35	11.72
16b	326–329	61	$C_{26}H_{20}N_6O_2S_2$	60.92	3.93	16.39	12.51
	AcOH	Orange	512.62	60.85	3.75	16.54	12.65
16c	351–354	59	$C_{31}H_{23}N_7O_2S_2$	63.14	3.93	16.63	10.87
	AcOH	Orange	589.70	63.00	3.85	16.57	10.78
16d	301–303	58	$C_{31}H_{22}N_6O_2S_2$	64.79	3.86	14.62	11.06
	AcOH	Orange	574.69	64.97	3.68	14.57	11.00
16e	319–321	56	$C_{35}H_{24}N_6O_2S_2$	67.29	3.87	13.45	10.26
	AcOH	Orange	624.75	67.35	3.78	13.54	10.32
16f	324–326	53	$C_{29}H_{20}N_6O_2S_3$	59.98	3.47	14.47	16.56
	AcOH	Orange	580.71	59.89	3.64	14.52	16.40

(Continued on next page)

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

Compd. no.	M.p.,°C solvent	Yield[a] % Color	Mol. formula m.wt.	% Analyses, calcd./found C	H	N	S
16g	332–334	55	$C_{29}H_{20}N_6O_3S_2$	61.69	3.57	14.88	11.36
	AcOH	Orange	564.65	61.54	3.75	14.77	11.21
16h	288–289	60	$C_{27}H_{22}N_6O_2S_2$	61.58	4.21	15.96	12.18
	AcOH	Orange	526.64	61.85	4.32	15.72	12.00
18	345–347	62	$C_{18}H_{16}N_4OS_3$	53.98	4.03	13.99	24.02
	DMF	Orange	400.55	53.78	4.10	14.12	23.82

Synthesis of 2-[1,2-Diaza-3-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))prop-2-enylidene]-3-phenyl-5-substituted 1,3,4-thiadiazoline 8a-l

Method A

Triethylamine (1.5 ml, 10 mmol) was added to a stirred solution of the appropriate of alkyl carbodithioates **3a** or **3b** (10 mmol) and the appropriate hydrazonyl halides **4a**–**l** (10 mmol) in ethanol (20 ml) at room temperature. The reaction mixture was stirred for 2 h, the resulting solid was collected and recrystallized from ethanol to give 2-[1,2-diaza-3-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))prop-2-enylidene]-3-phenyl–5-substituted 1,3,4-thiadiazolines **8a**–**l** (Tables I and II).

Method B

Triethylamine (1.5 ml, 10 mmol) was added to a stirred solution of ethyl 2-hydrazino-3-phenyl-2,3-dihydro-1,3,4-thiadiazole-5-carboxylate (2.63 g, 10 mmol) and the 4-formylantipyrine (**1**) (2.16 g, 10 mmol) in ethanol (20 ml) at room temperature. The reaction mixture was stirred for 2 h; the resulting solid was collected and recrystallized from ethanol to give the products identical in all aspects (m.p., mixed m.p., and spectra) with obtained from Method A.

Synthesis of 2-[4-(2,3-Dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)-1,3-thiazol-2-yl]ethanenitrile (12)

A mixture of **10** (2.64 g, 10 mmol) and cyanothioacetamide **11** (1g, 10 mmol) was heated under reflux in ethanol (20 mL methanol) for 2 h. The reaction mixture was cooled and stirred at room temperature over 1 h and a few drops of ammonium hydroxide were added. The precipitate

TABLE II Spectral Data of Some Newly Synthesized Compounds

Compound No.	Spectral data
3b	^{1}H NMR: 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 4.14 (s, 2H, SCH_2), 7.23–7.85 (m, 10 H, ArH's), 8.43 (s, 1H, vinyl CH=N), and 11.62 (s, 1H, NH).
8b	^{1}H NMR: 2.21 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.47 (m, 8H, ArH's), 7.85 (d, 2H, J = 5 Hz), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
8c	^{1}H NMR: 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.47 (m, 13H, ArH's), 7.85 (d, 2H, J = 5 Hz), 8.43 (s, 1H, vinyl CH=N), and 8.68 (s, br., 1H, NH). IR: 1668 (CO's) and 1506 (C=C).
8d	^{1}H NMR: 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.47 (m, 13H, ArH's), 7.85 (d, 2H, J = 5 Hz), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
8e	^{1}H NMR: 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.87 (m, 17H, ArH's), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
8f	^{1}H NMR: 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.67 (m, 13H, ArH's), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
8g	^{1}H NMR: 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 6.68–7.57 (m, 13H, ArH's), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
8h	^{1}H NMR: 1.42 (t, 3H, CH_2 CH_3), 2.42 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 4.44 (q, 2H, $\underline{CH_2}CH_3$), 7.23–7.58 (m, 9H, ArH's), and 8.43 (s, 1H, vinyl CH=N). IR: 1708, 1668 (CO's) and 1506 (C=C).
8i	^{1}H NMR: 2.21 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.67 (m, 9H, ArH's), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
8j	^{1}H NMR: 2.40 (s 3H, CH_3), 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.87 (m, 14H, ArH's), 8.43 (s, 1H, vinyl CH=N), and 8.68 (s, br., 1H, NH). IR: 1668 (CO's) and 1506 (C=C).
8k	^{1}H NMR: 2.41 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.67 (m, 14H, ArH's), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
8l	^{1}H NMR: 2.67 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 7.23–7.47 (m, 15H, ArH's), and 8.43 (s, 1H, vinyl CH=N). IR: 1668 (CO's) and 1506 (C=C).
12	^{1}H NMR: 2.76 (s, 3H, CH_3), 3.20 (s, 3H, CH_3), 4.14 (s, 2H, CH_2), 7.26–7.52 (m, 5H, ArH's), and 8.16 (s, 1H, thiazole H-5). IR: 3095 (CH), 2191 (CN), 1643 (CO0, 1614 (C=N).
13	^{1}H NMR: 2.76 (s, 3H, CH_3), 3.20 (s, 3H, CH_3), 7.26–7.52 (m, 10H, ArH's), 8.16 (s, 1H, thiazole H-5), 9.12 (s, br., 1H, NH), and 12.13 (s, 1H, SH).

(Continued on next page)

TABLE II Spectral Data of Some Newly Synthesized Compounds *(Continued)*

Compound No.	Spectral data
16a	^{1}H NMR: 1.46 (t, 3H, CH_3CH_2), 2.90 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 4.48 (q, 2H, CH_2CH_3), 7.25–7.58 (m, 10H, ArH's), and 8.06 (s, 1H, thiazole H-5).
	IR: 2191 (CN), 1705, 1691 (CO), and 1595 (C═C)
16b	^{1}H NMR: 2.67 (s, 3H, CH_3), 2.94 (s, 3H, CH_3), 3.27 (s, 3H, CH_3), 7.29–7.68 (m, 10H, ArH's), and 8.09 (s, 1H, thiazole H-5).
	IR : 2191 (CN), 1690, 1680 (CO), and 1589 (C═C)
16c	^{1}H NMR: 2.94 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 7.19—7.65 (m, 15H, ArH's), 8.04 (s, 1H, thiazole H-5), and 8.48 (s, 1H, NH).
	IR: 3354 (NH), 2190 (CN), 1667, (CO), 1643, 1616 (C═N), and 1600 (C═C).
16d	^{1}H NMR: 2.98 (s, 3H, CH_3), 3.27 (s, 3H, CH_3), 7.25–7.64 (m, 13H, ArH's), 8.09 (s, 1H, thiazole H-5), and 8.31 (d, J = 8Hz, 2H, ArH's).
	IR: 2189 (CN), 1670, (CO), 1633, 1622 (C═N), and 1593 (C═C).
16e	^{1}H NMR: 2.88 (s, 3H, CH_3), 3.28 (s, 3H, CH_3), 7.25–7.98 (m, 16H, ArH's), 8.01 (s, 1H, thiazole H-5), and 9.00 (s, 1H, ArH's).
	IR: 2189 (CN), 11743, 1651 (CO), 1620, 1622 (C═N), and 1593 (C═C).
16f	^{1}H NMR: 2.96 (s, 3H, CH_3), 3.26 (s, 3H, CH_3), 7.17–7.81 (m, 12H, ArH's), 8.09 (s, 1H, thiazole H-5), and 8.39 (s, 1H, ArH).
	IR: 2191 (CN), 1705, 1658, (CO), 1604 (C═N).
16g	^{1}H NMR: 2.94 (s, 3H, CH_3), 3.25 (s, 3H, CH_3), 6.59 (m, 1H), 7.25–7.84 (m, 12H, ArH's), and 8.09 (s, 1H, thiazole H-5).
	IR: 2191 (CN), 1743, 1651 (CO).
16h	^{1}H NMR: 2.49 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 2.90 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 7.25–7.48 (m, 9H, ArH's), and 8.05 (s, 1H, thiazole H-5).
	IR: 2185 (CN), 1691, 1660 (CO).
18	^{1}H NMR: 2.49 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 7.25–7.45 (m, 5H, ArH's), and 8.05 (s, 1H, thiazole H-5), 12.42 (s, 1H, SH).

was filtered, washed with water, and recrystallized from methanol to give **12** (Tables I and II).

Synthesis of 2-[4-(2,3-Dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))(1,3-thiazol-2-yl)]-3-(phenylamino)-3-thioxopropanenitrile (13)

An equimolar amounts of 2-[4-(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)-1,3-thiazol-2-yl]ethanenitrile (**12**) and phenyl isothiocyanate, potassium hydroxide (10 mmol) in *N*, *N*-dimethylformamide (25 mL) was stirred at room temperature for 6 h. Hydrochloric acid (2 mL, 3 M) was added; then the resulting solid was collected and recrystallized from ethanol to give (**13**) (Tables I and II).

Synthesis of 2-{[4-(2,3-Dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))(1,3-thiazol-2-yl)]cyanomethylene}-3-phenyl-5-substituted 1,3,4-thiadiazoline 16a-h

Method A

A mixture of 2-[4-(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)-1,3-thiazol-2-yl]ethanenitrile (**12**) (3.10 g, 10 mmol), potassium hydroxide (0.56 g, 10 mmol) and phenyl isothiocyanate (1.35 g, 10 mmol) in dry *N*, *N*-dimethylformamide (10 ml) was stirred for 6 h; then the appropriate hydrazonoyl halides **4a-e** (10 mmol) were added and stirring was continued for 2 h. The reaction mixture was left overnight and diluted with water (10 mL). The solid was collected by filtration, washed with water, dried, and crystallized from acetic acid to give **16a**–**h.**

Method B

A mixture of **12** (3.10 g, 10 mmol), carbon disulfide (0.7 g, 10 mmol) and potassium hydroxide (0.56 g, 10 mmol) in *N*, *N*-dimethylformamide (15 mL) was stirred at room temperature for 1 h. Iodomethane (1.4 g, 0.62 mL, 10 mmol) was added to the mixture. The reaction mixture was stirred for 2 h. The appropriate of hydrazonyl halides **4a**–**e** (10 mmol) and triethylamine (1.5 mL, 10 mmol) were added to the above mixture, and then the reaction mixture was stirred for 2 h. The resulting solid was collected and crystallized to give products that were identical in all respects that (m.p., mixed m.p. and spectra) with **16a**–**e** that were obtained from Method A.

Synthesis of 2-[4—(2,3-Dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))(1,3-thiazol-2-yl)]-3-methylthio-3-sulfanylprop-2-enenitrile (18).

An equimolar amounts of 2-[4-(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)-1,3-thiazol-2-yl]ethanenitrile (**12**) (3.10 g, 10 mmol), carbon disulfide (0.7 g, 10 mmol) and potassium hydroxide (0.65 g, 10 mmol) in *N*, *N*-dimethylformamide (25 mL) was stirred at room temperature for 6 h. Iodomethane (0.6 mL (10 mmol) was added then the resulting solid was collected and recrystallized from ethanol to give (**18**) (Tables I and II).

REFERENCES

[1] Part 60: A. O. Abdelhamid, Z. M. Ismail, and A. Abdel-Aziem, *J. Chem. Res.*, **10,** 609 (2007).

[2] A. Padwa, *Angew. Chem. Int. Ed. Engl.*, **15,** 123 (1976).

[3] R. Huisgen, R. Sustmann, and G. Wallbillich, *Chem. Ber*., **100,** 1786 (1976).
[4] A. O. Abdelhamid and F. A. Attaby, *J. Heterocyclic Chem*., **28,** 41 (1991).
[5] A. O. Abdelhamid, M. M. M. Sallam, and S. A. Amer, *Heteroatom Chem*, **12,** 468 (2001).
[6] A. O. Abdelhamid, H. F. Zohdi, and N. A. Ali, *Molecules*, **5,** 961 (2001).
[7] A. O. Abdelhamid, N. M. Rateb, and K. M. Dawood, *Phosphorus, Sulfur, Silicon, and Relat. Elem.*, **167,** 251 (2000).
[8] H. F. Zohdi, N. M. Rateb, M. M. M. Sallam, and A. O. Abdelhamid, *J. Chem. Res. (S),* 742; *J. Chem. Res. (M),* 3329 (1998).
[9] A. O. Abdelhamid, S. M. Abdelgawad, and S. F. El-Shrarnoby, *Phosphorus, Sulfur, Silicon, and Relat. Elem.,* **177,** 2699 (2002).
[10] D. I. Kornis, In *Comprehensive Heterocyclic Chemistry*, A. R. Katritzky, C. W. Rees, and E. F. V. Scriven, Eds. (Oxford: Pergamon, 1996), Vol. 4.
[11] W. E. Kirkpatrick, T. Okabe, J. W. Hillyard, R. K. Robins, A. I. Dren, and T. Kovenison, *J. Med. Chem*., **20,** 386 (1977).
[12] A. J. Ryan, P. G. Welling, and S. E. Wright, *Food Cosmet Toxicol.*, **7**, 287 (1970).
[13] A. Ebnother, E. Jucker, and A. Lindeman, *Helv. Chim. Acta*, **42**, 1201 (1959).
[14] C. S. Pak, I. K. Youn, and Y. S. Lee, *Synthesis*, 969 (1982).
[15] C. F. Boehringer and G. M. B. H. Soehne. German Patent 900,577, (1953); *Chem. Abstr*., **52,** 12927^{c} (1953).
[16] H. F. Zohdi, N. M. Rateb, M. M. M. Sallam, and A. O. Abdelhamid, *J. Chem. Res. S* (742), M(3329), 1998.
[17] G. Fravel, *Bull. Soc. Chim. Fr*., **31,** 150 (1904).
[18] N. E. Eweiss and A. Osman, *Tetrahedron Lett*., 1169 (1979).
[19] A. S. Shawali, A. O. Abdelhamid, *Bull. Chem. Soc. Jpn*., **49,** 321 (1976).
[20] A. S. Shawali and A. Osman, *Tetrahedron*. **27,** 2517 (1971).
[21] A. O. Abdelhamid and F. H. H. El-Shiaty, *Phosphorus, Sulfur, Silicon, and Related Elem.*, **39,** 35 (1988).