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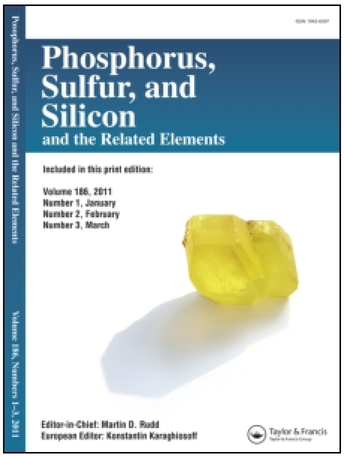

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Synthesis and Antimicrobial Activity of Some New 5-Arylazothiazole, Pyrazolo[1,5-*a*] Pyrimidine, [1,2,4]Triazolo[4,3-*a*]Pyrimidine, and Pyrimido[1,2-*a*]Benzimidazole Derivatives Containing the Thiazole Moiety

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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW 5-ARYLAZOTHIAZOLE, PYRAZOLO[1,5-*a*] PYRIMIDINE, [1,2,4]TRIAZOLO[4,3-*a*]PYRIMIDINE, AND PYRIMIDO[1,2-*a*]BENZIMIDAZOLE DERIVATIVES CONTAINING THE THIAZOLE MOIETY

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Nadia A. Abdel-Riheem,[1] and Sayed A. Ahmed[3]
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1-(2-(4,5-Dihydro-3-(4-methyl-2-phenylthiazol-5-yl)-5-phenylpyrazol-1-yl)-4-substituted thiazol-5-yl)-2-phenyldiazene were synthesized from hydrazonoyl halides and 3-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-5-phenyl-4,5-dihydro-1**H*****-pyrazole-1-carbothioamide in ethanolic triethylamine. Also, pyrazolo[5,1-a]pyrimidines, 2,3,6-trisubstituted pyridines, and pyrazolo[3,4-d]pyridazines were obtained from sodium salt of 3-hydroxy-1-(4-methyl-2-phenylthiazol-5-yl)prop-2-en-1-one and different heterocyclic amines. All structures of the newly synthesized compounds were elucidated by elemental analysis, spectral data, and alternative synthetic route whenever possible. The newly synthesized compounds were tested towards different microorganisms.***

Supplemental materials are available for this article. Go to the publisher's online edition of **Phosphorus, Sulfur, and Silicon and the Related Elements** ***to view the free supplemental file.***

Keywords Hydrazonoyl halides; 5-phenylazothiazoles; pyrazolines; pyrazolo[1,5-*a*]pyrimidines; 2,3,6-trisubstituted pyridines

INTRODUCTION

Differently substituted pyrazolines and their derivatives are important biological agents, and a significant amount of research activity has been directed towards this class. In particular, they are used as antitumor,[1] antibacterial, antifungal, antiviral, antiparasitic, antitubercular, and insecticidal agents.[2–8] Some of these compounds also have anti-inflammatory, antidiabetic, anaesthetic, and analgesic properties.[9,10] In addition, pyrazolopyrimidine systems are reported as inhibitors for the synthesis of DNA and RNA in

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the cells of some types of cancer[11] and viruses.[12] We report in this article the synthesis and antimicrobial studies of some new 5-arylazothiazole, pyrazolo[1,5-*a*]pyrimidine, [1,2,4]triazolo[4,3-*a*]pyrimidine, and pyrimido[1,2-*a*]benzimidazole derivatives.

RESULTS AND DISCUSSION

Treatment of 1-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-3-phenylprop-2-en-1-one[13] (**2**) with thiosemicarbazide in ethanol under reflux gave 3-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-5-phenyl-4,5-dihydro-1*H*-pyrazole-1-carbothioamide (**3**). Structure **3** was elucidated by elemental analysis, spectral data, and chemical transformation. The ^{1}H NMR spectrum of **3** showed signals at $\delta = 2.66$ (s, 3H, CH_3), 3.14–3.16 (d, 1H, $J = 6$ Hz, pyrazoline) 3.32–3.35 (d, 1H, $J = 6$ Hz, pyrazoline), 6.00–6.02, 6.05–6.07 (q, 1H, $J = 6$ Hz, pyrazoline), 6.15 (s, br., 2H, NH_2), 6.95–7.95 (m, 10H, ArH's). The mass spectrum showed peaks *m/e* at 380 (M^{+2}, 2.24%), 379 (M^{+1}, 21.3%), 378 (M, 100%). Thus, compound **3** reacted with *C*-benzoyl-*N*-phenylhydrazonoyl bromide in ethanolic triethylamine to afford 1-(2-(4,5-dihydro-3-(4-methyl-2-phenylthiazol-5-yl)-5-phenylpyrazol-1-yl)-4-phenylthiazol-5-yl)-2-phenyldiazene (**4a**) (Scheme 1). Structure **4a** was confirmed by elemental analysis, spectral data, and an alternate synthetic route. The ^{1}H NMR spectrum of **4a** showed signals at $\delta = 2.76$ (2, 3H, CH_3), 3.32 (dd, 1H, $J = 6$ Hz, pyrazoline), 3.90 (dd, 1H, $J = 12$ Hz, pyrazoline), 5.76 (dd, 1H, $J = 6$ Hz, pyrazoline), and 7.26–8.15 (m, 20H, ArH's). The ^{13}C NMR spectrum showed peaks at $\delta = 18.13$ (CH_3), 45.91 (CH_2), 63.74 (CH), 119.78, 119.78, 122.35, 123.54, 126.33, 127.61, 128.11, 128.95, 129.02, 129.24, 130.30, 130.65, 132.89, 134.11, 140.74, 142.87, 148.34, 152.61, 154.89,

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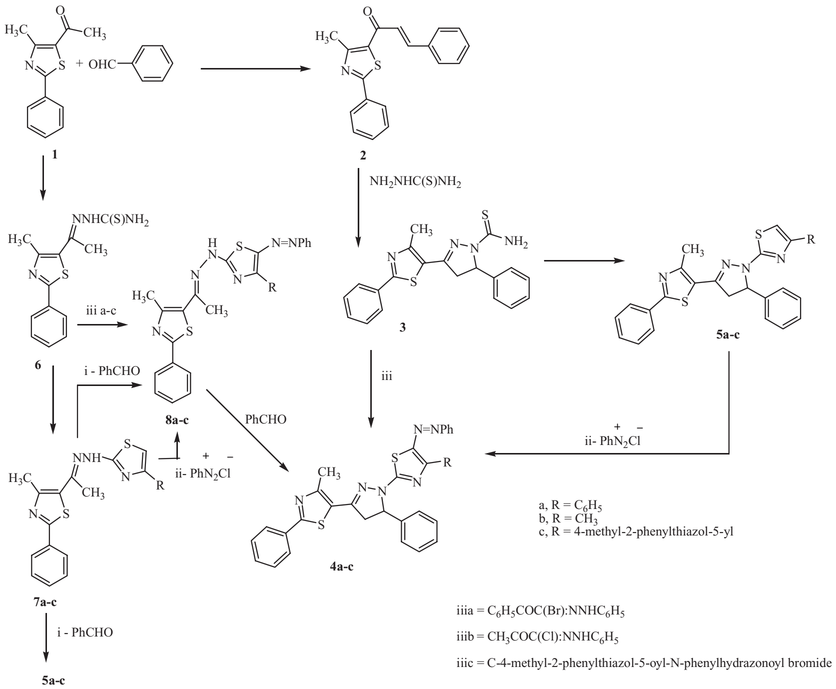

a, R = C_6H_5
b, R = CH_3
c, R = 4-methyl-2-phenylthiazol-5-yl

iiia = $C_6H_5COC(Br){:}NNHC_6H_5$
iiib = $CH_3COC(Cl){:}NNHC_6H_5$
iiic = C-4-methyl-2-phenylthiazol-5-oyl-N-phenylhydrazonoyl bromide

Scheme 1

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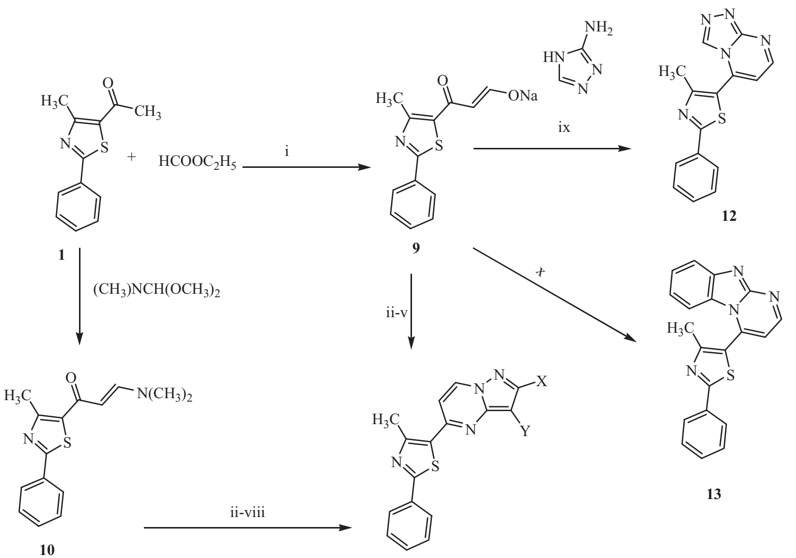
163.69, 167.34. The mass spectrum of **4a** showed *m/e* = 582 (M^+). Compound **3** reacted with ω-bromoacetophenone in ethanol to give 4,5-dihydro-3-(4-methyl-2-phenylthiazol-5-yl)-5-phenyl-1-(4-phenylthiazol-2-yl)-1*H*-pyrazole (**5a**). The latter was coupled with benzenediazonium chloride in alcoholic sodium acetate to afford a product identical in all respects (mp, mixed mp, and spectra) to **4a**. An unequivocal support for structure **4a** came from the reaction of each of the compounds **7a**, which was prepared via **6**[14] with ω-bromoacetophenone, with benzaldehyde in ethanolic sodium hydroxide followed by benzenediazonium chloride in alcoholic sodium acetate or by reaction with compound **8a**, which was prepared via reaction of **6** with *C*-benzoyl-*N*-phenyl hydrazonoyl bromide, with benzaldehyde in ethanolic sodium hydroxide, and gave a product identical in all respects (mp, mixed mp, and spectra) with **4a**.

On the other hand, 1-(4-methyl-2-phenyl-1,3-thiazol-5-yl)ethanone (**1**) reacted with ethyl formate in dried ether containing sodium methoxide to afford a sodium salt of 3-hydroxy-1-(4-methyl-2-phenylthiazol-5-yl)prop-2-en-1-one (**9**). Structure **9** was confirmed by its reactions. Thus, treatment of 3-amino-4-phenyl-1*H*-pyrazole in acetic acid containing piperidine acetate afforded a product, namely 5-(4-methyl-2-phenylthiazol-5-yl)-3-phenylpyrazolo[1,5-*a*]pyrimidine (**11a**) (Scheme 2). Structure **11a** was elucidated by elemental analysis, spectral data and an alternate synthetic route. The ^{1}H NMR spectrum of **11a** showed signals at $\delta = 2.53$ (s, 3H, CH_3) and 7.44–7.82 (m, 13H, ArH's, pyrazole H-5, pyrimidine H4 & H5). Thus, treatment of 3-(dimethylamino)-1-(4-methyl-2-phenylthiazol-5-yl)prop-2-en-1-one (**10**)[15] with 3-amino-4-phenylpyrazole in acetic acid and ammonium



i - CH_3ONa
ii- 3-amino-4-phenylpyrazole
iii- 3-amino-5-phenylpyrazole
iv = 3-amino-4-phenylamino-5-phenylcarbamoylpyrazole
v = 3-amino-4-phenylamino-5-(4-chlorophenyl)carbamoylpyrazole
vi = 3-amino-4-phenylamino-5-(4-bromophenyl)carbamoylpyrazole
vii- 3-amino-4-cyanopyrazole
viii- 3-amino-4-methyl-5-phenylpyrazole
ix-3-amino-1,2,4-triazole
x- 2-aminobenzimidazole

a, X = phenyl, Y = H
b, X = H, Y = phenyl
c, X = phenylamino, Y = phenylcarbamoyl
d, X = phenylamino, Y = (4-chlorophenyl)carbamoyl
e, X = phenylamino, Y = (4-bromophenyl)carbamoyl
f, X = cyano, Y = H
g, X = 4-methyl, Y = phenyl

Scheme 2

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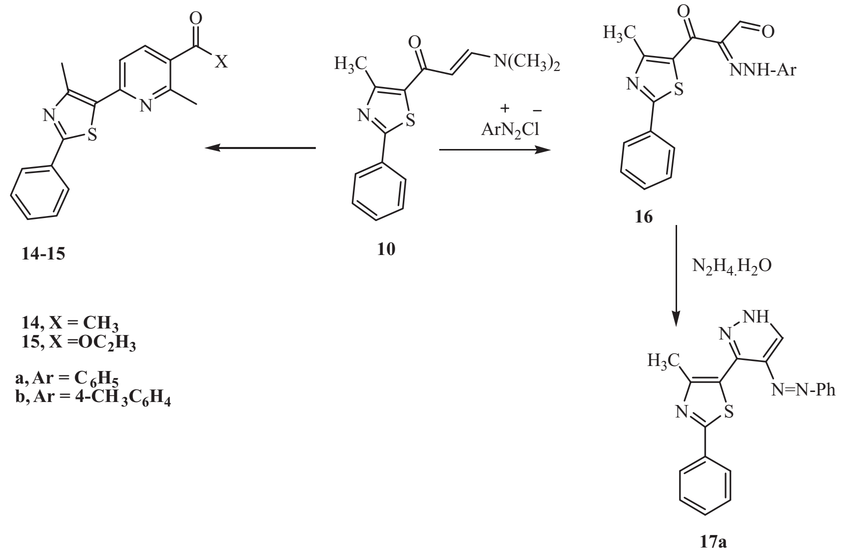
acetate by heating under reflux gave a product identical in all respects (mp, mixed mp, spectra) with **11a**.

Analogously, either compound **9** or **10** reacted with the appropriate 3-aminopyrazoles, 3-amino-1,2,4-triazole, or 2-aminobenzimidazole gave pyrazolo[1,5-*a*]pyrimidines **11b–g**, 5-(4-methyl-2-phenylthiazol-5-yl)-[1,2,4]triazolo[4,3-*a*]pyrimidine (**12**), and 4-(4-methyl-2-phenyl-4,5-dihydro-1,3-thiazol-5-yl)pyrimido[1,2-*a*]benzimidazole (**13**), respectively.

Treatment of 3-(dimethylamino)-1-(4-methyl-2-phenylthiazol-5-yl)prop-2-en-1-one (**10**) with 2,4-pentanedione or ethyl 3-oxobutanoate in boiling acetic acid and ammonium acetate under reflux gave 3-acetyl-2-methyl-6-(4-methyl-2-pheny)lthiazol-2-ylpyridine (**14**) and ethyl 2-methyl-6-(4-methyl-2-phenyl)thiazol-2-ylpyridine-3-carboxylate (**15**), respectively (Scheme 3).



Scheme 3

Finally, treatment of the appropriate of **9** or **10** with the arenediazonium chloride in ethanol containing sodium acetate as a buffer solution yielded 2-(2-phenylhydrazono)-3-(4-methyl-2-phenylthiazol-5-yl)-3-oxopropanal (**16a**) and 2-(2-(4-tolyl)hydrazono)-3-(4-methyl-2-phenylthiazol-5-yl)-3-oxopropanal (**16b**), respectively. Structure **16** was confirmed by elemental analysis, spectral data, and chemical transformation. The ^{1}H NMR spectrum of **16a** showed signals at $\delta = 2.46$ (s, 3H, CH$_3$), 6.67–8.05 (m, 10H, ArH's), 9.98 (s, 1H, -CHO), and 14.39 (s, br., 1H, NH). Thus, **16a** was reacted with hydrazine hydrate in boiling ethanol under reflux and gave 1-(3-(4-methyl-2-phenylthiazol-5-yl)-4H-pyrazol-4-ylidene)-2-phenylhydrazine (**17a**) (Scheme 3).

PHARMACOLOGY: ANTIMICROBIAL SCREENING

Sixteen compounds were screened by the Agar dilution technique[16] for their antimicrobial activity (see Supplemental Materials, Table S1, available online).

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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 and ^{13}C NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300 MHz spectrometer, and chemical shifts are expressed as δ using TMS as an internal reference. Mass spectra were recorded on a GC-MS QP1000. Elemental analyses were carried out at the Microanalytical Center of Cairo University. The hydrazonoyl halides were prepared as previously described.[17–19]

3-(4-Methyl-2-phenyl-1,3-thiazol-5-yl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carbothioamide 3

To a mixture of 1-(4-methyl-2-phenyl-1,3-thiazol-5-yl)-3-phenylprop-2-en-1-one (**2**) (1.55 g, 5 mmol) and thiosemicarbazide (0.46 g, 5 mmol) in ethanol (20 mL), a catalytic amount of triethylamine was added, then heated under reflux for 6 h. The resulting solid was collected and recrystallized from ethanol to give **3** (Tables I and II).

4,5-Dihydro-3-(4-methyl-2-phenylthiazol-5-yl)-1-(4-substituted thiazol-2-yl)-5-phenyl-1H-pyrazole 5a–c

A mixture of compound **3** (1.8 g, 5 mmol) and the appropriate of ω-bromoacetophenone, chloroacetone, or 5-bromoacetyl-4-methyl-2-phenylthiazole (5 mmol) in ethanol (20 mL) was heated under reflux for 2 h. The resulting solid was neutralized with sodium bicarbonate (10%), collected, and recrystallized from ethanol to give compounds **5a–c** (Tables I and II).

1-(2-(4,5-Dihydro-3-(4-methyl-2-phenylthiazol-5-yl)-5-phenylpyrazol-1-yl)-4-substituted thiazol-5-yl)-2-phenyldiazene 4a–c

Method A. A mixture of the appropriate hydrazonoyl halides (5 mmol), **3** (1.8 g, 5 mmol), and triethylamine (0.5 g, 0.75 mL, 5 mmol) in ethanol (20 mL) was boiled under reflux for 2 h. The resulting solid was collected and recrystallized from DMF-EtOH mixture to give **4a–c** (Tables I and II).

Method B. An equimolar amount of the appropriate **8a–c** (5mmol) and benzaldehyde (0.53g, 5 mmol) in ethanol (20 mL) was cooled at 5°C, then sodium hydroxide solution (10 mL, 4N) was added portionwise while stirring. The resulting solid was collected and recrystallized from DMF/ethanol to give identical product in all aspects (mp, mixed mp, and spectra) with corresponding **4a–c** (Tables I and II).

Method C. A solution of benzenediazonium chloride (10 mmol) was added dropwise to a stirred solution of the appropriate **5a–c** in ethanol (50 mL) containing sodium acetate trihydrate (1.3g, 10 mmol) at 0–5°C. The reaction mixture was stirred for 3 h at 0–5°C. The resulting solid was collected and crystallized from DMF/ethanol to give **4a–c** identical in all aspects (mp, mixed mp, and spectra) with those above.

Synthesis of N-[1-(4-Methyl-2-substituted thiazol-5-yl)-ethylidene]-N′-(4-phenyl-thiazol-2-yl)-hydrazine 7a–c

A mixture of **6** (1.45 g, 5 mmol) and the appropriate of ω-bromoacetophenone, chlroacetone, or 5-bromoacetyl-4-methyl-2-phenylthiazole (5 mmol) in ethanol (20 mL)

Table I Characterization data of the newly synthesized compounds

% Analyses, Calcd./ Found				Mol. Formula/ Mol. Wt.	Color/ Yield%	Mp, °C/ Solvent	Compd. No.
S	N	H	C				
16.94	14.80	4.79	63.47	$C_{20}H_{18}N_4S_2$	Yellow	210–213	**3**
16.78	14.61	4.82	63.33	378.5	80	EtOH	
11.00	14.42	4.40	70.08	$C_{34}H_{26}N_6S_2$	Violet	254–256	**4a**
10.82	14.72	4.35	69.85	582.74	86	DMF/EtOH	
12.32	16.14	4.65	66.90	$C_{29}H_{24}N_6S_2$	Violet	248–250	**4b**
12.22	16.01	4.60	66.81	520.67	82	DMF/EtOH	
14.15	14.42	4.30	67.13	$C_{38}H_{29}N_7S_3$	Violet	262–263	**4c**
14.01	14.30	4.14	67.30	679.87	80	DMF/EtOH	
15.39	13.45	4.84	66.32	$C_{23}H_{20}N_5$	Brown	192–195	**5a**
15.17	13.21	4.62	66.45	416.56	66	EtOH	
13.40	11.70	4.63	70.26	$C_{28}H_{22}N_4S_2$	Orange	202–204	**5b**
13.21	11.50	4.55	70.10	478.63	69	EtOH	
16.70	12.16	4.38	66.75	$C_{32}H_{25}N_5S_3$	Orange	195–197	**5c**
16.58	12.21	4.50	66.58	575.76	62	EtOH	
16.42	14.35	4.65	64.59	$C_{21}H_{18}N_4S_2$	Brown	145–147	**7a**
16.23	14.20	4.60	64.42	390.52	80	EtOH	
19.52	17.06	4.91	58.51	$C_{16}H_{16}N_4S_2$	Green	151–153	**7b**
19.30	17.09	5.72	58.20	494.63	90	EtOH	
19.72	14.36	4.34	61.57	$C_{25}H_{21}N_5S_3$	Brown	161–163	**7c**
19.63	14.21	4.49	61.33	487.66	69	EtOH	
12.96	16.99	4.48	65.56	$C_{27}H_{22}N_6S_2$	Red	164–166	**8a**
12.91	16.67	4.56	65.55	494.63	80	EtOH	
14.82	19.43	4.66	61.09	$C_{22}H_{20}N_6S_2$	Red	119–121	**8b**
14.69	19.43	4.50	61.00	432.56	82	EtOH	
16.25	16.57	4.26	62.92	$C_{31}H_{25}N_7S_3$	Red	143–145	**8c**
16.19	16.52	4.22	62.78	591.77	69	EtOH	
8.70	15.21	4.38	71.72	$C_{22}H_{16}N_4S$	Yellow	149–150	**11a**
8.57	15.10	4.22	71.60	368.4	75	EtOH	
8.70	15.21	4.38	71.72	$C_{22}H_{16}N_4S$	Orange	238–240	**11b**
8.50	15.00	4.28	71.55	368.4	89	DMF	
6.38	16.72	4.41	69.31	$C_{29}H_{22}N_6OS$	Yellow	260–261	**11c**
6.54	16.85	4.32	69.51	502.58	66	EtOH	
5.97	15.65	3.94	64.86	$C_{29}H_{21}ClN_6OS$	Yellow	245–247	**11d**
6.12	15.56	4.12	64.74	537.05	66	DMF/EtOH	
5.51	14.45	3.64	59.90	$C_{29}H_{21}BrN_6OS$	Orange	263–265	**11e**
5.25	14.65	3.75	60.12	581.50	70	DMF/EtOH	
10.10	22.07	3.49	64.34	$C_{17}H_{11}N_5S$	Pale yellow	252–255	**11f**
9.90	21.85	3.56	64.34	317.35	85	AcOH	
8.38	14.65	4.74	72.23	$C_{23}H_{18}N_4S$	Yellow	154–157	**11g**
8.42	14.56	4.85	72.13	382.49	78	Benzene	
10.93	23.87	3.78	61.42	$C_{15}H_{11}N_5S$	Colorless	190–192	**12**
11.12	23.95	3.87	61.66	293.35	82	AcOH	
9.35	16.36	4.12	70.15	$C_{20}H_{14}N_4S$	Yellow	160–163	**13**
9.53	16.46	3.90	70.00	342.43	78	AcOH	
10.40	9.08	5.23	70.10	$C_{18}H_{16}N_2OS$	Colorless	138–140	**14**
10.25	9.12	5.32	70.20	308.41	77	EtOH	
9.47	8.28	5.36	67.43	$C_{19}H_{18}N_2O_2S$	Colorless	80–81	**15**
9.57	8.42	5.52	67.34	338.43	67	EtOH	
9.18	12.03	4.33	65.31	$C_{19}H_{15}N_3O_2S$	Orange	222–224	**16a**
9.00	11.85	4.35	65.23	349.41	78	EtOH	
4.71	11.56	4.71	66.10	$C_{20}H_{17}N_3O_2S$	Orange	232–235	**16b**
4.60	11.45	4.65	66.20	363.44	75	EtOH	
9.28	20.27	4.38	66.07	$C_{19}H_{15}N_5S$	Pale yellow	254–257	**17a**
9.34	20.05	4.52	66.12	345.43	68	EtOH	

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Table II Spectral data of some newly synthesized compounds

Spectral data	Compound No.
IR: 3380, 2160 (NH$_2$), 3056, 2980 (CH, aromatic and aliphatic), 1623 (C=N), 1370 (CH$_3$), 1430 (CH$_2$). ^{1}H NMR: $\delta = 2.66$ (s, 3H, CH$_3$), 3.14–3.16 (d, 1H, $J = 6$ Hz, pyrazoline) 3.32–3.35 (d, 1H, $J = 6$ Hz, pyrazoline), 6.00–6.02, 6.05–6.07 (q, 1H, $J = 6$ Hz, pyrazoline), 6.15 (s, br., 2H, NH$_2$), 6.95–7.95 (m, 10H, ArH's). Ms: m/e = 380 (M^{+2}, 2.24%), 379 (M^{+1}, 21.3%), 378 (M, 100%).	**3**
IR: 3051, 2994 (CH, aromatic and aliphatic), 1623 (C=N), 1370 (CH$_3$), 1433 (CH$_2$). ^{1}H NMR: $\delta = 2.76$ (2, 3H, CH$_3$), 3.32 (dd, 1H, $J = 6$ Hz, pyrazoline), 3.90 (dd, 1H, $J = 12$ Hz, pyrazoline), 5.76 (dd, 1H, $J = 6$ Hz, pyrazoline) and 7.26–8.15 (m, 20 H, ArH's). ^{13}C NMR: $\delta = 18.13$ (CH$_3$), 45.91 (CH$_2$), 63.74 (CH), 119.78, 119.78, 122.35, 123.54, 126.33, 127.61, 128.11, 128.95, 129.02, 129.24, 130.30, 130.65, 132.89, 134.11, 140.74, 142.87, 148.34, 152.61, 154.89, 163.69, 167.34. Ms: m/e = 582 (M).	**4a**
IR: 3050, 2990 (CH, aromatic and aliphatic), 1623 (C=N), 1365 (CH$_3$), 1435 (CH$_2$). ^{1}H NMR: $\delta = 2.42$ (s, 3H, CH$_3$CO), 2.76 (2, 3H, CH$_3$), 3.32 (dd, 1H, $J = 6$ Hz, pyrazoline), 3.90 (dd, 1H, $J = 12$ Hz, pyrazoline), 5.76 (dd, 1H, $J = 6$ Hz, pyrazoline) and 7.26–8.15 (m, 15 H, ArH's).	**4b**
^{1}H NMR: $\delta = 2.76$ (s, 6H, 2-CH$_3$), 3.32 (dd, 1H, $J = 6$ Hz, pyrazoline), 3.90 (dd, 1H, $J = 12$ Hz, pyrazoline), 5.76 (dd, 1H, $J = 6$ Hz, pyrazoline) and 7.26—8.15 (m, 20 H, ArH's).	**4c**
IR: 3056, 2992 (CH, aromatic and aliphatic), 1623 (C=N), 1345 (CH$_3$), 1437 (CH$_2$). ^{1}H NMR: $\delta = 2.42$ (s, 3H, CH$_3$CO), 2.76 (2, 3H, CH$_3$), 3.32 (dd, 1H, $J = 6$ Hz, pyrazoline), 3.90 (dd, 1H, $J = 12$ Hz, pyrazoline), 5.76 (dd, 1H, $J = 6$ Hz, pyrazoline) and 7.26–8.15 (m, 17 H, ArH's).	**5a**
IR: 3058, 2985 (CH, aromatic and aliphatic), 1623 (C=N), 1370 (CH$_3$), 1440 (CH$_2$). ^{1}H NMR: $\delta = 2.76$ (2, 3H, CH$_3$), 3.32 (dd, 1H, $J = 6$ Hz, pyrazoline), 3.90 (dd, 1H, $J = 12$ Hz, pyrazoline), 5.76 (dd, 1H, $J = 6$ Hz, pyrazoline) and 7.26–8.15 (m, 16 H, ArH's).	**5b**
IR: 3056, 2980 (CH, aromatic and aliphatic), 1623 (C=N), 1370 (CH$_3$), 1440 (CH$_2$). ^{1}H NMR: $\delta = 2.76$ (s, 6H, 2-CH$_3$), 3.32 (dd, 1H, $J = 6$ Hz, pyrazoline), 3.90 (dd, 1H, $J = 12$ Hz, pyrazoline), 5.76 (dd, 1H, $J = 6$ Hz, pyrazoline) and 7.26–8.15 (m, 16 H, ArH's).	**5c**
IR: 3350 (NH), 3056, 2988 (CH, aromatic and aliphatic), 1623 (C=N), 1350 (CH$_3$). ^{1}H NMR: $\delta = 2.29$ (s, 3H, CH$_3$), 2.59 (s, 3H, CH$_3$), 7.16 (s, 1H, thiazole H-5), 7.27–7.89 (m, 10 H, ArH's) and 8.99 (s, br., 1H, NH).	**7a**
IR: 3350 (NH), 3056, 2993 (CH, aromatic and aliphatic), 1623 (C=N), 1356 (CH$_3$). ^{1}H NMR: $\delta = 2.19$ (s, 3H, CH$_3$), 2.29 (s, 3H, CH$_3$), 2.59 (s, 3H, CH$_3$), 7.16 (s, 1H, thiazole H-5), 7.67–7.89 (m, 5 H, ArH's) and 8.62 (s, br., 1H, NH).	**7b**
IR: 3350 (NH), 3050, 2987 (CH, aromatic and aliphatic), 1623 (C=N), 1360 (CH$_3$). ^{1}H NMR: $\delta = 2.29$ (s, 3H, CH$_3$), 2.46 (s, 3H, CH$_3$), 2.59 (s, 3H, CH$_3$), 6.96 (s, 1H, thiazole H-5), 7.66–7.88 (m, 10 H, ArH's) and 8.99 (s, br., 1H, NH).	**7c**
IR: 3350 (NH), 3056, 2988 (CH, aromatic and aliphatic), 1623 (C=N), 1340 (CH$_3$). ^{1}H NMR: $\delta = 2.29$ (s, 3H, CH$_3$), 2.59 (s, 3H, CH$_3$), 7.37–8.00 (m, 15 H, ArH's) and 9.74 (s, br., 1H, NH).	**8a**
IR: 3350 (NH), 3062, 2980 (CH, aromatic and aliphatic), 1623 (C=N), 1350 (CH$_3$). ^{1}H NMR: $\delta = 2.29$ (s, 3H, CH$_3$), 2.54 (s, 3H, CH$_3$), 2.59 (s, 3H, CH$_3$), 7.50–8.07 (m, 10 H, ArH's) and 8.89 (s, br., 1H, NH).	**8b**
IR: 3350 (NH) 3050, 2985 (CH, aromatic and aliphatic), 1623 (C=N), 1347 (CH$_3$). ^{1}H NMR: $\delta = 2.29$ (s, 3H, CH$_3$), 2.46 (s, 3H, CH$_3$), 2.59 (s, 3H, CH$_3$), 7.50–7.08 (m, 15 H, ArH's) and 9.47 (s, br., 1H, NH).	**8c**
IR: 3310 (NH) 3066, 2992 (CH, aromatic and aliphatic), 1623 (C=N), 1340 (CH$_3$). ^{1}H NMR: $\delta = 2.46$ (s, 3H, CH$_3$), 6.53 (s, 1H, pyrazole H-4), 7.13 (d, 1H, J = 4Hz, pyrimidine H-5), 7.46–7.82 (m, 10H, ArH's) and 8.74 (d, 1H, 8Hz, pyrimidine H-6).	**11a**

(Continued on next page)

Table II Spectral data of some newly synthesized compounds *(Continued)*

Spectral data	Compound No.
IR: 3320 (NH), 3050, 2990 (CH, aromatic and aliphatic), 1623 ($C{=}N$), 1340 (CH_3). ^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 6.90 (d, 2H, J = 8H, ArH's), 7.14 (d, 1H, J = 4Hz, pyrimidine H-5), 7.56–7.78 (m, 8H, ArH's), 8.74 (d, 1H, 8Hz, pyrimidine H-6 and 9.05 (s, 1H, pyrazole H-3).	**11b**
IR: 3299 (NH), 3065, 2994 (CH, aromatic and aliphatic), 1662 (CO), 1623 ($C{=}N$), 1340 (CH_3). ^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 6.98 (d, 2H, J = 8H, pyrimidine H-5), 7.07–8.00 (m, 15H, ArH's), 8.49 (d, 1H, 8Hz, pyrimidine H-6) and 11.34 (s, br., 1H, 2NH).	**11c**
IR: 3299 (NH), 3056, 2980 (CH, aromatic and aliphatic), 1662 (CO), 1623 ($C{=}N$), 1340 (CH_3). ^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 6.98 (d, 2H, J = 8H, pyrimidine H-5), 7.07–8.00 (m, 14H, ArH's), 8.49 (d, 1H, 8Hz, pyrimidine H-6) and 11.34 (s, br., 1H, 2NH).	**11d**
IR: 3299 (NH), 3056, 2990 (CH, aromatic and aliphatic), 1665 (CO), 1620 ($C{=}N$), 1340 (CH_3). ^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 6.98 (d, 2H, J = 8H, pyrimidine H-5), 7.07–8.00 (m, 14H, ArH's), 8.49 (d, 1H, 8Hz, pyrimidine H-6) and 11.34 (s, br., 1H, 2NH).	**11e**
IR: 3056, 2996 (CH, aromatic and aliphatic), 2160 (CN), 1623 ($C{=}N$), 1340 (CH_3). ^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 7.35 (d, 2H, J = 8H, pyrimidine H-5), 7.62–7.79 (m, 5H. ArH's), 9.23 (s, 1H, pyrazole H-5), and 9.50 (d, 1H, 8Hz, pyrimidine H-6).	**11f**
^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 7.11 (d, 2H, J = 8H, pyrimidine H-5), 7.23–7.85 (m, 10H, ArH's) and 8.60 (d, 1H, 8Hz, pyrimidine H-6).	**11g**
^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 6.99 (d, 2H, J = 4H, pyrimidine H-5), 7.62–7.79 (m, 5H, ArH's), 9.01 (d, 4H, 8Hz, pyrimidine H-6) and 9.57 (s, 1H, triazole H-5).	**12**
^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 7.26 (d, 2H, J = 8H, pyrimidine H-5), 7.32–7.94 (m, 9H, ArH's) and 8.88 (d, 4H, 8Hz, pyrimidine H-6)	**13**
IR: 3056, 2980 (CH, aromatic and aliphatic), 1675 (CO), 1623 ($C{=}N$), 1340 (CH_3). ^{1}H NMR: $\delta = 2.49$ (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 7.62–7.76 (m, 5H, ArH's), 7.86 (d, 1H, 4Hz, pyridine H-5) and 7.06 (d, 1H, 4Hz, pyridine H-6).	**14**
IR: 3056, 2980 (CH, aromatic and aliphatic), 1713 (CO), 1623 ($C{=}N$), 1340 (CH_3). ^{1}H NMR: $\delta = 1.34$ (t, J = 7Hz, $CH_2\mathbf{CH_3}$), 2.73 (s, 3H, CH_3), 2.75 (s, 3H, CH_3), 4.31 (q, J = 7H, $\mathbf{CH_2}CH_3$), 7.62–7.92 (m, 5H, ArH's), 8.98(d, 1H, 4Hz, pyridine H-5) and 8.29 (d, 1H, 4Hz, pyridine H-6).	**15**
IR: 32280 (NH), 3056, 2980 (CH, aromatic and aliphatic), 2870, 2780 (CH), 1690 (CO), 1340 (CH_3). ^{1}H NMR: $\delta = 2.46$ (s, 3H, CH_3), 7.28–8.05 (m, 10H, ArH's), 9.75 (s, 1H, C**H**O) and 15.09 (s, 1H, br., NH).	**16a**
IR: 32280 (NH), 3056, 2980 (CH, aromatic and aliphatic), 2870, 2780 (CH), 1690 (CO), 1340 (CH_3). ^{1}H NMR: $\delta = 2.33$ (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 7.44–8.05 (m, 9H, ArH's), 9.75 (s, 1H, C**H**O) and 15.09 (s, 1H, br., NH).	**16b**
IR: 32280 (NH), 3056, 2980 (CH, aromatic and aliphatic), 1340 (CH_3). ^{1}H NMR: $\delta = 2.60$ (s, 3H, CH_3), 6.85–8.12 (m, 11H, ArH's and pyrazole H-5), and 11.40 (s, 1H, br., NH).	**17a**

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was heated under reflux for 2 h. The resulting solid was collected and recrystallized from the proper solvent to give compounds **7a–c** (Tables I and II).

Sodium Salt of 3-Hydroxy-1-(4-methyl-2-phenylthiazol-5-yl)prop-2-en-1-one 9

A mixture of 1-(4-methyl-2-phenyl-thiazol-5-yl)ethanone (2.17 g, 10 mmol) and ethyl formate (0.74 g, 10 mmol) in dry ether (20 mL) was added portionwise while stirring to solution sodium methoxide (0.54 g, 10 mmol) in dry ether (10 mL) at 0–5°C. The resulting solid was collected, dried, and was used without purification.

N-[1-(4-Methyl-2-substituted thiazol-5-yl)-ethylidene]-N′-(4-phenyl-5-phenylazo-thiazol-2-yl)-hydrazine 8a–c

A mixture of **6** (1.45 g, 5 mmol), the appropriate hydrazonoyl halides **iiia–c**, and triethylamine (0.75 mL, 5 mmol) in ethanol (20 mL) was heated under reflux for 2 h. The resulting solid was collected and recrystallized from the proper solvent to give **8a–c** (Tables I and II).

Pyrazolo[5,1-a]pyrimidines 11a–g, [1,2,4]Triazolo[4,3-a]pyrimidine 12, Pyrimido[1,2-a]benzimidazole 13, and Pyridines 14, 15

Method A. A mixture of the sodium salt **9** (1.2g, 5 mmol) and the appropriate amount of 3-amino-4-phenylpyrazole, 3-amino-5-phenylpyrazole, 3-amino-4-phenylcarbamoyl-5-phenylaminopyrazole, 3-amino-4-(4-chlorophenyl)carbamoyl-5-phenylaminopyrazole, 3-amino-4-(4-bromophenyl)carbamoyl-5-phenylaminopyrazole, 3-amino-4-cyanopyrazole, 3-amino-4-methyl-5-phenylpyrazole, 3-amino-1,2,4-triazole, 2-aminobenzimidazole, acetylacetone, or ethyl acetoacetate (5 mmol) in a solution of piperidine acetate [piperidine (2.5 mL)], water (5 mL), and acetic acid (2.5 mL) was heated under reflux for about 10 min. Then acetic acid (1.5 mL) was added while boiling, and the resulting solid was collected and recrystallized from the appropriate solvents (Tables I and II).

Method B. An equimolar amount of **10** (1.02 g, 5 mmol), the appropriate amount of 3-amino-4-phenylpyrazole, 3-amino-5-phenylpyrazole, 3-amino-4-phenylcarbamoyl-5-phenylaminopyrazole, 3-amino-4-(4-chlorophenyl)carbamoyl-5-phenylaminopyrazole, 3-amino-4-(4-bromophenyl)carbamoyl-5-phenylaminopyrazole, 3-amino-4-cyanopyrazole, 3-amino-4-methyl-5-phenylpyrazole, 3-amino-1,2,4-triazole, 2-aminobenzimidazole, acetylacetone, or ethyl acetoacetate (5 mmol) and ammonium acetate (5 mmole) in acetic acid (10 mL) was heated under reflux for 4 h. The resulting solid was collected and recrystallized from the proper solvent to give products (Tables I and II).

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2-(2-Arylhydrazono)-3-(4-methyl-2-phenylthiazol-5-yl)-3-oxopropanal 16a,b

Arenediazonium chloride (5 mmol) was added to the appropriate cold solution of **9** or **10** (5 mmol) and sodium acetate (0.65 g, 5 mmol) in ethanol (50 mL) while stirring. The crude solid was collected and recrystallized from ethanol to give **16** (Tables I and II).

(1-(3-(4-Methyl-2-phenylthiazol-5-yl)-4H-pyrazol-4-ylidene)-2-phenylhydrazine 17a

An equimolar amount of **16a** and hydrazine hydrate (5 mmole) in ethanol (20 mL) was boiled under refluxed for 15 min. The resulting solid was collected and recrystallized from the proper solvent to give the pyrazole **17a** (Tables I and II).

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