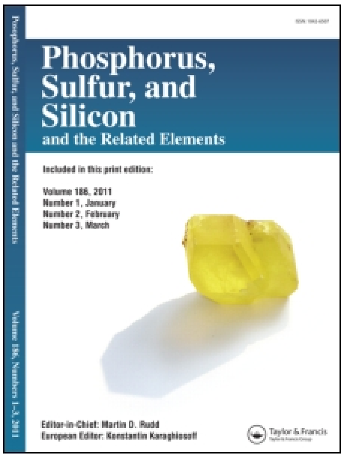

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REACTIONS WITH HYDRAZONOYL HALIDES XXII[1]: SYNTHESIS OF PYRROLO[3,4-C]PYRZOLINE, PYRAZOLINE, PYRAZOLE, AND 2,3-DIHYDRO- 1,3,4-THIADIAZOLE DERIVATIVES

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5-Bromoacetyl-4-methyl-2-phenylthiazole reacted with dimethylsulfide, potassium thiocyanate, sodium benzenesulfinate and thiourea to afford products **2–5**, respectively. Hydrazonoyl bromides **7a-c** obtained via reaction N-nitrosoarylacetamides with sulfonium bromide **2**. Hydrazonoyl bromides were used in synthesis of pyrrolidinopyrazolione, pyrazole, triazoline, thiadiazoline and 5-arylazothiazole derivatives. The structure of the newly synthesized compounds were confirmed on the basis of spectral, analytical analyses and alternative route whenever possible.

Keywords: Thiazoles; Hydrazonoyl Halides; Pyrazoles; pyrazolo[3,4-d]pyrimidines; Pyrazolo[3,4-d]pyridazines

INTRODUCTION

Hydrazonoyl halides have emerged as an important class of intermediates, particularly for the synthesis of heterocyclic compounds[2–6]. The interesting pharmacological properties of thiazole derivatives[7–9] in relation to the various changes in the structure of these compounds are worth studying in

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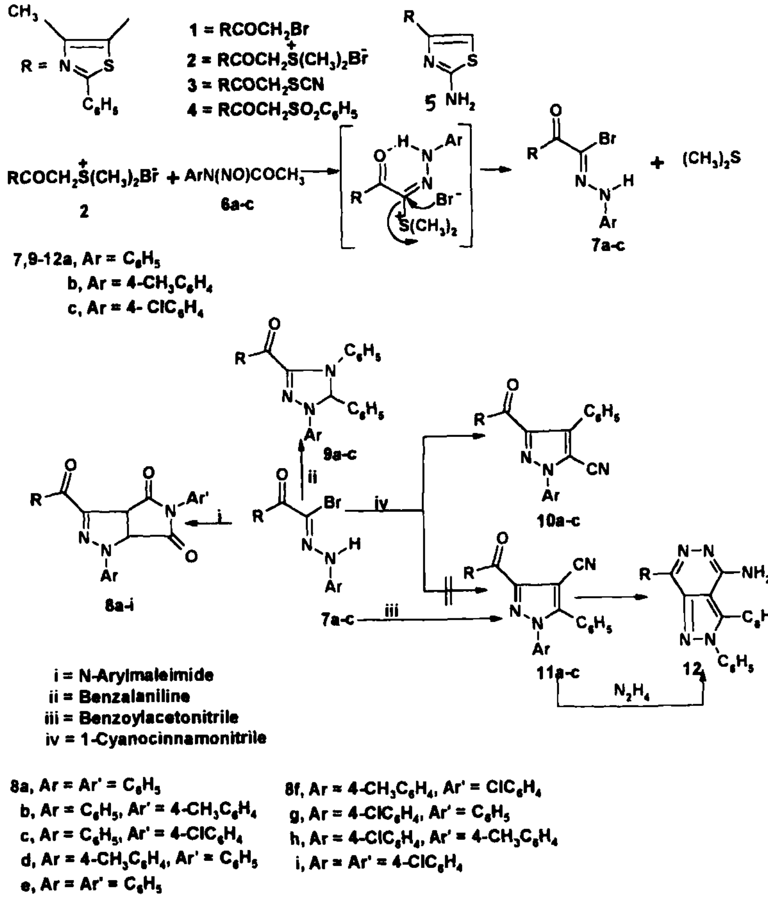
order to synthesize less toxic and more potent drugs. However, the hydrazonoyl halides with C-thiazole moiety have not yet been reported. The results of synthesis and utilization of hydrazonoyl bromide **7** in heterocyclic synthesis is reported here.

RESULTS AND DISCUSSION

Treatment of N-nitrosoarylacetamides[10] with [2-(4-methyl-2-phenylthiazol-5-yl)-2-oxoethyl]sulfonium bromide **(2)** in ethanol gave 1-bromo-2-(4-methyl-2-phenyl-5-thiazolyl)ethanedione-1-arylhydrazones **(7a-c)**. Spectral data, microanalysis, and reactions with different reagents confirmed the structure of **7**. Compounds **7a-c** reacted with N-arylmaleimide to give products **8a-c** respectively, which were assigned the structure 3a, 6a dihydro-1H-pyrrolidino[3,4-c]pyrazol-2,6-diones based on the elemental analyses an spectral data. IR spectra revealed absorption bands at 1770–1720 and 1710–1690 attributed to -CO-NR-CO- group[11] and 1670(CO). ^{1}H NMR spectrum of **8b** showed signals at 2.46(s, 3H, 4-$CH_3C_6H_4$), 2.90(s, 3H, CH_3 (thiazole C-4)), 5.20(d, 1H, J=10 Hz, pyrazoline H-4), 5.54(d, 1H, J=10 Hz, pyrazoline H-5) and 7.26–8.06(m, 14H, ArH's)

Also, compounds **8a-c** on treatment with benzalaniline in the presence of triethylamine afforded a single product (tlc) The product formulated as 1-aryl-3-(4′-methyl-2′-phenyl)thiazol-5′-oyl)-4,5-diphenyltriazolines **(9a-c)** on the basis of elemental analysis and spectral data. For example, ^{1}H NMR spectrum of **9a** showed signals at 2.75(s, 3H, CH_3 (thiazole C-4), 3.70(s, 1H, triazoline H-5) and 7.20–8.02(m, 20H, ArH's). IR spectra of **9a-c** revealed bands at 1660(CO), 1600(C=C) and 1100–1040(triazole ring).

Similarly, compounds **7a-c** reacted with 1-cyanocinamonitrile in benzene in the presence of triethylamine to give a single product (tlc). The structure seemed to be **10** or **11** (cf Scheme 1). The structure **11** was ruled out and the product was formulated as 1-aryl-5-cyano-4-phenyl-3-[(4-methyl-2-phenyl)thiazol-5-oyl]pyrazole **(10)** based on the following data: a) the spectral data (cf. Expermintal). b) the reaction of hydrazonoyl bromide **7a** with benzoylacetonitrile in sodium ethoxide solution to afford corresponding pyrazole **11a**, which had different melting point and easy converted to pyrazolo[3,4-d]pyridazine **12**.

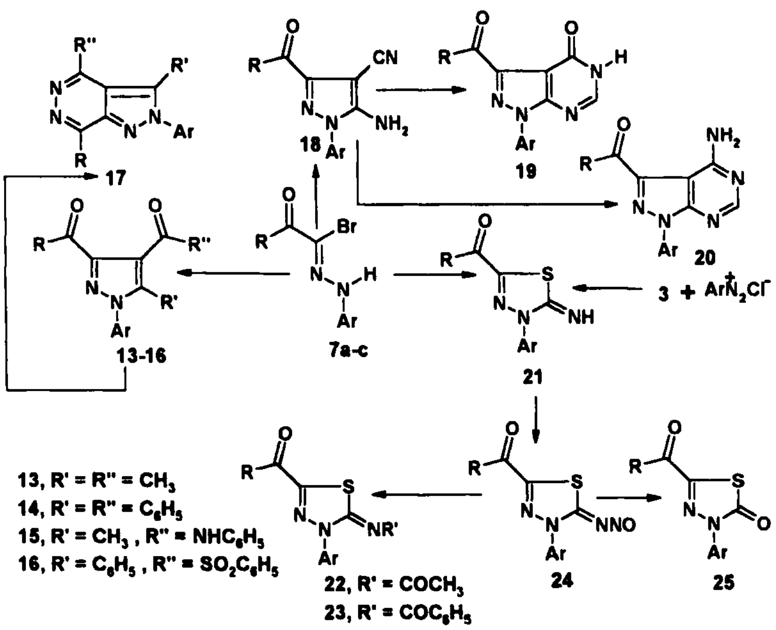


SCHEME 1

Treatment of the hydrazonoyl bromides **7a-c** with sodium enolate of pentane-2,4-dione, 1,3-diphenyloropane-1,3-dione acetoacetanilide and 5-benzenesulfonylacetyl-4-methyl-2-phenylthiazole (**4**) in ethanol afforded pyrazoles **13–16**. The structure of pyrazoles was confirmed on the basis of spectral and elemental analyses. For example, IR spectra of **13–16** revealed bands near to 1685, 1660(CO's) and 162(C=N). ^1H NMR spectrum of **13a** showed signals at 2.50(s, 3H CH_3CO); 2.55(s, 3H, CH_3(pyrazole C-5)), 2.85(s, 3H, CH_3(thiazole C-4) and 7.44–8.03(m, 10H, ArH's). Pyrazoles **13a-c** were converted to pyrazolo[3,4-d]pyrazines

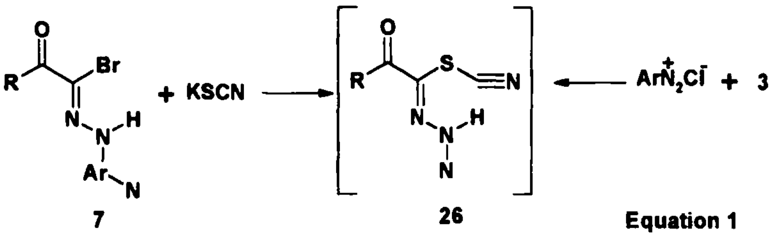
17 by boiling with hydrazine hydrate in ethanol (cf. Scheme 2). The structure **17** was confirmed on the basis of elemental analyses and spectral data (cf. Experimental).

Hydrazonoyl bromides **7a-c** reacted with malononitrile in ethanolic sodium ethoxide (or ethanolic sodium hydroxide) at room temperature afforded 5-amino-4-cyano-3-thiazoloyl derivatives **18a-c**. The structure **18** was elucidated on the basis of elemental analyses, spectral data and it's converted to pyrazolo[3,4-d]pyrimidine **19** and **20** via its reaction with formic acid and formamide, respectively. For example, IR spectra of **18a-c** revealed bands near 3320,3270(NH_2), 2220(CN), 1670(CO) and 1620(C=N). ^1H NMR spectrum of **18a** showed signals at 2.92(s, 3H, CH_3(thiazole C-4)), 4.77(s, br., 2H, NH_2) and 7.26–8.02(m, 10H, ArH's).



SCHEME 2

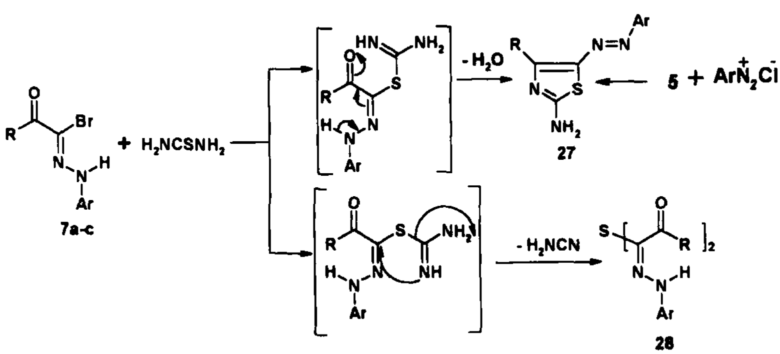
Treatment of hydrazonoyl bromides **7a-c** with potassium thiocyanate in ethanol at room temperature afforded products which gave analytical and spectral data in accord with their formulation as 3-aryl-2-imino-5-(4′-methyl-2′-phenylthiazol-5′-oyl-2,3-dihydro-1,3,4-thiadiazoles **21a-c**, respectively. The IR spectra revealed the absence bands at 2156(ν_{SCN}) and showed bands at 3330 (NH), 1660 (conjugated CO) and 1610 (C=N). The ^{1}H NMR spectrum of **21a** showed signal at 2.77(s, 3H, CH_3(thiazole C-4)), 7.39–8.05(m, 10H, ArH's) and 9.64(s, br., 1H, NH). Upon shaking with D_2O a new singlet appeared at 4.55 assignable to DOH proton and the singlet signal at 9.64 disappeared. The results indicate that the azo coupling of **21** proceeded through the intermediacy of **26** which cyclized readily to give **21** (cf. equation 1). Compounds **21a-c** were authentically sample by the reaction of thiocyanate **3** with arenediazonium chlorides in ethanolic sodium acetate solution.



Equation 1

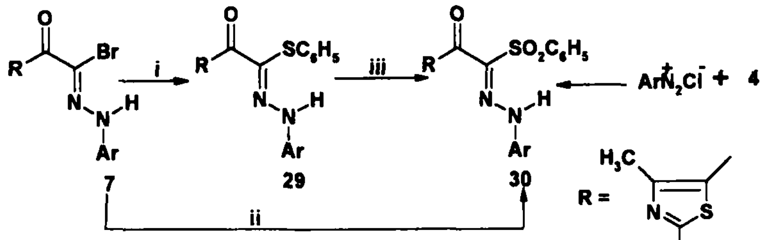
Acylation of **21** with acetic anhydride and with benzyl chloride in pyridine yielded the corresponding N-acyl derivatives **22** and **23**, respectively. Both elemental and spectral data were consistent with the assigned structures **22** and **23**. The ^{1}H NMR spectrum of **22a** revealed the presence of two singlets at 2.36(3H, CH_3CON) and 2.92(3H, CH_3(thiazole C-4)) and a multiplet at 6.26–8.00(10H, ArH's). The IR spectra of compounds **22** and **23** contain two carbonyl bands at 1650 and 1630 cm^{-1}. Nitrosation of **21** gave the N-nitroso derivatives **24**. The electronic absorption of **24** in ethanol showed two common maxima in the 510–470(log $\varepsilon < 2$) and 340–365(log $\varepsilon < 4$)nm region. These are assigned to the n-π^* and π-π^* transitions of the nitrosoimino group[12]. The IR spectra of 20 showed no NH band, but contained a common bands at 1660(CO) and 1490(NO). All compounds **24** decomposed to the corresponding of thiadiazolones **25** upon boiling in a xylene solution. The IR spectra of **25** revealed in each case two absorption bands near 1705 and 1650.

Treatment of hydrazonoyl bromide **7a-c** with thiourea in boiling ethanol gave two isolated products, in each case, according to tlc. Both elemental and spectral data of the products were consistent with the assigned structures **27** and **28**, respectively. ^{1}H NMR spectrum of **27a** showed 2.89(s, 3H, CH_3(thiazole C-4)), 5.48(s, br., 2H, NH_2) and 7.26–8.04(m, 10H, ArH's). Its IR spectrum revealed bands at 3350, 3280(NH_2), 1620(C=N) and no bands in the range 1650–1800 due to the absence of carbonyl group[13]. ^{1}H NMR spectrum of **28a** showed signals at 2.88(s, 6H, 2(CH3) thiazole), 7.12–7.98(m, 20H, ArH's) and 9.35(s, 2H, 2NH). Its IR spectrum revealed bands at 3450(NH) and 1685(CO). The structure **27** was further confirmed by its alternative synthesis. Thus, treatment of arenediazonium chloride with 2-amino-4-(4′-methyl-2′-phenylthiazol-5′-yl)thiazole **5** in ethanolic sodium acetate solution (cf. Scheme 3). The formation of the products **27** and **28** takes place via elimination of H_2O or NH_2CN from intermediate, respectively according to previously reported[14].



SCHEME 3

Treatment of hydrazonoyl bromide **7a-c** with sodium benzenesulfinate in boiling ethanol yielded corresponding hydrazone **30a-c**. Both elemental and spectral data were consistent with the assigned structure **30**. The structure **30** was further confirmed by its alternative synthesis. Thus, treatment of arenediazonium chloride with ω-(4-methyl-2-phenylthiazol-5-yl)acetophenone **4** in ethsodium acetate solution or by oxidation of compound **29a** (prepared by the reaction of hydrazonoyl bromide **7a** with thiophenol and sodium ethoxide in ethanol) with hydrogen peroxide in acetic acid (cf. Scheme 4).



SCHEME 4

EXPERIMENTAL

All melting points were determined on an electrothermal melting point apparatus and are uncorrected. IR (cm^{-1}) spectra were recorded on KBr discs on a FT IR-8201 PC Shimadzu spectrophotometer. ^1H NMR spectra were recorded in $CDCl_3$ on Gemini 200 MHz spectrometer using TMS as an internal reference and chemical shifts are expresses as δ unit. Electronic absorption were recorded on a Perkin-Elimer Lamda 4 spectrophotometer. Elemental analyses were performed at the Microanalytical center, Cairo University. 5-bromoacetyl-4-methyl-2-phenylthiazole was prepared as previous reported[15].

Synthesis of [2-(4-methyl-2-phenylthiazol-5-yl)-2-oxoethyl]sulfonium bromide (2)

A mixture of **1** (29.6g, 0. 1 mol) and dimethyl sulfide (6.8g, 0.11 mol) in ethanol (75 ml) was refluxed for 30 min. The reaction mixture was cooled and the solid was collected by filtration from ethanol to give the sulfonium bromide (**2**). Colorless crystals, 25.5 g, 70%, had mp. 148°C (ethanol); Found: C, 47.00; H, 4.40; N, 4.10; S, 17.70. $C_{14}H_{16}BrNOS_2$ (358.28), requires C, 46.93; H, 4.50; N, 3.90; S, 17.88.

1-Bromo-2-(4-methyl-2-phenylthiazol-5-yl)ethanedione 1-arylhydrazones 7a-c

A mixture of **2** (35.8g, 0.1 mol) and the appropriate N-nitrosoacetarylanilides (0.11mol) was stirred in ethanol (100 ml) for 1h at room temperature. The yellow solid was collected and crystallized to give **7a-c**, respectively (cf. Tables I and II).

TABLE I characterization data of the newly synthesized compound

Compound No.	*Mp., °C*	*Yiled %*	*Mol. Formula (M.Wt.)*	*% Analysis Calcd /Found*			
				C	*H*	*N*	*S*
3	131	70	$C_{13}H_{10}N_2OS_2$	56.91	3.67	10.21	23.37
			(274.37)	56.90	3.70	10.20	23.40
4	160	85	$C_{18}H_{15}NO_3S_2$	60.48	4.23	3.92	17.94
			(357.45)	60.50	4.201	3.80	17.90
5	189	78	$C_{13}H_{11}N_3S_2$	57.12	4.06	15.37	23.46
			(273.38)	57.00	4.10	15.50	23.40
7a	169	70	$C_{18}H_{14}BrN_3OS$	54.01	3.53	10.50	8.01
			(400.30)	54.10	3.50	10.60	8.10
7b	197	65	$C_{19}H_{16}B_3OS$	55.08	3.98	10.14	7.74
			(414.35)	55.00	3.90	10.10	7.70
7c	200	70	$C_{18}H_{13}BrCl_3OS$	49.72	3.01	9.67	7.38
			(434.74)	49.80	3.00	9.60	7.30
8a	290	70	$C_{28}H_{20}N_4O_3S$	68.27	4.10	11.38	6.51
			(492.58)	68.20	4.00	11.30	6.40
8b	266	65	$C_{29}H_{22}N_4O_3S$	68.75	4.39	11.06	6.33
			(506.61)	68.70	4.40	10.90	6.20
8c	285	70	$C_{28}H_{19}ClN_4O_3S$	63.81	3.6	10.63	6.08
			(527.20)	.90	3.6	10.80	5.90
8d	275	70	$C_{29}H_{22}N_4O_3S$	68.75	4.39	11.06	6.33
			(506.61)	68.50	4.30	11.00	6.40
8e	282	65	$C_{30}H_{24}N_4O_3S$	69.20	4. 66	10.67	6.16
			(520.64)	69.10	4.70	10.80	6.00

Compound No.	*Mp., °C*	*Yiled %*	*Mol. Formula (M.Wt.)*	*% Analysis Calcd /Found*			
				C	*H*	*N*	*S*
8f	279	70	$C_{29}H_{21}ClN_4O_3S$	64.37	3.92	10.36	5.93
			(541.05)	64.50	3.80	10.20	5.80
8g	281	70	$C_{28}H_{19}ClN_4O_3S$	63.81	3.64	10.64	6.08
			(527.02)	63.10	3.50	10.70	5.90
8h	274	65	$C_{29}H_{21}ClN_4O_3S$	64.37	3.92	10.36	5.93
			(541.05)	64.50	3.90	10.60	5.80
8i	293	68	$C_{28}H_{18}Cl_2N_4O_3S$	59.89	3.24	9.98	5.71
			(561.46)	60.10	3.40	9.80	5.90
9a	296	65	$C_{31}H_{24}N_4OS$	74.37	4.84	11.19	6.40
			(500.65)	74.60	4.70	11.30	6.20
9b	273	60	$C_{32}H_{26}N_4OS$	74.68	5.10	10.89	6.23
			(514.68)	74.50	5.30	10.70	6.30
9c	308	60	$C_{31}H_{23}ClN_4OS$	69.58	4.34	10.47	5.99
			(535.09)	69.80	4.40	10.70	6.10
10a	269	60	$C_{27}H_{18}N_4OS$	72.62	4.07	12.55	7.18
			(446.58)	72.40	4.00	12.70	7.30
10b	260	60	$C_{28}H_{20}N_4OS$	73.01	4.39	12.17	6.96
			(460.58)	73.20	4.30	12.30	7.00
10c	265	60	$C_{27}H_{14}C_{12}N_4OS$	67.42	3.57	11.65	6.67
			(480.99)	67.60	3.40	11.50	6.80
11a	237	70	$C_{27}H_{18}N_4OS$	72.62	4.07	12.55	7.18
			(446.55)	72.50	3.90	12.60	7.30
11b	227	75	$C_{28}H_{20}N_4OS$	73.01	4.39	12.17	6.96
			(460.58)	73.00	4.50	12.30	7.10
11c	236	75	$C_{27}H_{17}ClN_4OS$	67.42	3.57	11.65	6.67
			(480.99)	67.50	3.60	11.40	6.80
12	>300	65	$C_{27}H_{20}N_6O$	70.41	4.38	18.25	6.96
			(460.56)	70.60	4.20	18.00	7.20
13a	156	73	$C_{23}H_{19}N_3O_2S$	68.80	4.78	10.47	7.99

Compound No.	*Mp., °C*	*Yiled %*	*Mol. Formula (M.Wt.)*	*% Analysis Calcd /Found*			
				C	*H*	*N*	*S*
			(401.51)	68.90	4.70	10.30	8.10
13b	170	71	$C_{24}H_{21}N_3O_2S$	69.37	5.10	10.12	7.70
			(415.54)	69.40	5.00	10.20	7.90
13c	215	75	$C_{23}H_{18}ClN_3O_2S$	63.36	4.17	9.64	7.35
			(435.95)	63.40	4.00	9.80	7.50
14a	293	77	$C_{33}H_{23}N_3O_2S$	75.40	4.42	8.00	6.10
			(525.65)	75.60	4.30	8.90	5.90
15a	244	68	$C_{28}H_{22}N_4O_2S$	70.26	4.64	11.71	6.70
			(478.60)	70.30	4.65	11.60	6.60
15b	234	70	$C_{29}H_{24}N_4O_2S$	70.70	4.92	11.38	6.51
			(492.63)	70.50	4.80	11.30	6.60
15c	282	70	$C_{28}H_{21}ClN_4O_2S$	65.55	4.13	10.92	6.25
			(513.04)	65.40	4.00	10.80	6.40
16a	122	60	$C_{36}H_{26}N_4O_3S_3$	65.62	3.99	8.5 1	14.60
			(658.84)	65.50	4.10	8.40	14.60
16b	126	69	$C_{37}H_{28}N_4O_3S_3$	66.04	4.20	8.33	14.29
			(672.87)	66.00	4.30	8.40	14.40
16c	216	60	$C_{36}H_{25}ClN_4O_3S_3$	62.36	3.64	8.08	13.87
			(693 28)	62.40	3.50	8.20	13.90
17a	267	70	$C_{23}H_{19}N_5S$	69.49	4.83	17.62	8.06
			(397.53)	69.40	4.70	17.50	7.90
17b	250	70	$C_{24}H_{21}N_5S$	70.04	5.15	17.02	7.79
			(411.56)	69.90	5.20	17.20	7.90
17c	259	75	$C_{23}H_{18}ClN_5S$	63.95	9.21	16.22	7.42
			(431.97)	63.80	9.10	10.10	7.30
18a	260	77	$C_{21}H_{15}N_5OS$	65.43	3.93	18.17	8.32
			(385.47)	65.20	4.00	18.20	8.20
18b	264	70	$C_{22}H_{17}N_5OS$	66.14	4.30	17.53	8.03
			(399.50)	66.10	4.10	17.50	7.90

Compound No.	*Mp., °C*	*Yiled %*	*Mol. Formula (M.Wt.)*	*% Analysis Calcd /Found*			
				C	*H*	*N*	*S*
18c	300	75	$C_{21}H_{14}ClN_5OS$	60.06	3.37	16.68	7.64
			(419.91)	59.90	3.40	16.70	7.40
19a	305	80	$C_{22}H_{15}N_5OS$	63.91	3.66	16.94	7.75
			(413.48)	63.90	3.80	16.80	7.90
19b	314	75	$C_{23}H_{17}N_5O_2S$	64.62	4.02	16.39	7.50
			(427.51)	64.40	3.90	16.20	7.70
19c	322	80	$C_{22}H_{14}ClN_5O_2S$	58.99	3.16	15.64	7.16
			(447.92)	59.10	3.30	15.80	7.30
20a	280	80	$C_{22}H_{16}N_6OS$	64.04	3.92	20.38	7.77
			(412.50)	64.20	3.80	20.50	7.60
20b	317	75	$C_{23}H_{18}N_6OS$	64.76	4.26	19.71	7.52
			(426.53)	64.90	4.40	19.80	7.90
20c	270	77	$C_{22}H_{15}ClN_6OS$	59.12	3.39	18.81	7.17
			(446.94)	59.00	3.40	18.70	6.90
21a	178	85	$C_{19}H_{14}N_4OS_2$	60.30	3.73	14.80	16.94
			(378.49)	60.10	3.90	14.70	17.109
21b	172	82	$C_{20}H_{16}N_4OS_2$	61.20	4.11	14.27	16.34
			(392.58)	61.40	4.00	14.40	16.50
21c	180	84	$C_{19}H_{13}ClN_4OS_2$	55.27	3.17	13.57	15.53
			(412.92)	55.00	3.30	13.60	15.40
22a	228	75	$C_{21}H_{16}N_4O_2S_2$	59.98	3.84	13.32	15.25
			(420.52)	59.80	3.60	13.10	15.40
22b	195	72	$C_{22}H_{18}N_4O_2S_2$	60.81	4.18	12.98	14.76
			(434.54)	60.60	4.30	12.70	14.90
22c	204	74	$C_{21}H_{15}ClN_4O_2S_2$	55.43	3.32	12.3 1	14.10
			(454.97)	55.50	3.10	12.10	13.90
23a	269	75	$C_{26}H_{18}N_4O_2S_2$	64.71	3.76	11.61	13.29
			(482.59)	64.90	3.90	11.80	13.50
23b	212	77	$C_{27}H_{20}N_4O_2S_2$	65.30	4.08	11.28	12.91

Compound No.	*Mp., °C*	*Yiled %*	*Mol. Formula (M.Wt.)*	*% Analysis Calcd /Found*			
				C	*H*	*N*	*S*
			(496.61)	65.10	4.00	11.40	13.10
23c	230	75	$C_{26}H_{17}ClN_4O_2S_2$	60.40	3.3 1	10.84	12.40
			(517.03)	60.20	3.10	10.60	12.50
24a	140	65	$C_{19}H_{13}N_5O_2S_2$	56.01	3 22	17.19	15.74
			(407.49)	55.90	3.40	17.30	15.60
24b	150	62	C20H15N5O2S2	56.99	3.59	16.62	15.21
			(421.50)	56.80	3.70	16.50	15.20
24c	205	75	$C_{19}H_{12}ClN_5O_2S_2$	51.64	2.74	15.85	14.51
			(441.93)	51.50	2.3.4	16.00	14.50
25a	160	60	$C_{19}H_{13}N_3O_2S_2$	60.14	3.46	11.07	16.90
			(379.47)	60.30	3.40	11.20	17.10
25b	186	62	$C_{20}H_{15}N_3O_2S_2$	61.05	3.84	10.68	16.30
			(393.49)	61.20	3.70	10.50	16.20
25c	229	65	$C_{19}H_{12}ClN_3O_2S_2$	55.14	2.92	10.15	15.49
			(423.91)	55.00	2.80	10.30	15.30
27a	212	66	$C_{19}H_{15}N_5S_2$	60.45	4.01	18.56	16.99
			(377.49)	60.60	4.00	18.70	17.10
27b	220	58	$C_{20}H_{15}N_5S_2$	61.36	4.39	17.89	16.38
			(391.52)	60.90	4.50	17.80	16.50
27c	229	67	$C_{19}H_{14}ClN_5S_2$	55.40	3.43	17.00	15.56
			(411.95)	55.30	3.40	17.20	15.70
30a	200	90	$C_{24}H_{19}N_3O_3S_2$	62.45	4.15	9.10	13.89
			(461.57)	62.60	4.30	9.20	13.70
30b	202	85	$C_{25}H_{21}N_3O_3S_2$	63.14	4.45	6.84	13.48
			(475.59)	63.00	4.60	8.60	13.60
30c	230	90	$C_{24}H_{18}ClN_3S_2O_3$	58.12	3.66	8.47	12.93
			(496.01)	58.00	3.70	8.50	13.20

TABLE II IR and 1H NMR Spectra of Selected New Compounds

No.	R (cm^{-1})	^{1}H NMR (δ)
	2320(SCN) AND 1670(CO).	2.82(s, 3H, CH3, thiazole C-4); 4.45(s, 2H, CH_2) and 6.90–7.40(m, 1oH, ArH'
	1670(CO); 1600(C=C) and 1350,1150(SO_2).	2.80(s, 3H, CH_3, thiazole C-4); 4.45(s, 2H, CH2) and 6.90–7.40(m, 10H, ArH'
	3350(NH) and 1670(CO).	2.87(s, 3H, CH_3, thiazole C-4); 7.24- 8.06(m, 10H, ArH's) and 8.61(s, br., 1H,
	3350(NH) and 1670(CO).	2.38(s, 3H, 4-$CH_3C_6H_5$); 2.87(s, 3H, CH_3, thiazole C-4); 7.24–8.06(m, 9H, Ar and 8.60(s, 1H, NH).
	1770–1720 and 1710–1690- CO-NR-CO and 1670(CO).	2.46(s, 3H, 4-$CH_3C_6H_4$), 2.90(s, 3H, CH_3, thiazole C-4), 5.20(d, 1H, J=10 Hz, zoline H-4), 5.54(d, 1H, J=10 Hz, pyrazoline H-5) and 7.26–8.06(m, 14H, ArH
	1770–1720 and 1710–1690- CO-NR-CO and 1670(CO).	2.46(s, 6H, 2(4-$CH_3C_6H_4$)), 2.90(s, 3H, CH3, thiazole C-4), 5.20(d, 1H J=10 H pyrazoline H-4), 5.54(d, 1H, J=10 Hz, pyrazoline H-5) and 7.26–8.06(m, 18H, ArH's).
	1660(CO); 1600(C=C) and 1100–1040 (triazole ring).	2.75(s, 3H, CH_3, thiazole C-4), 3.70(s, 1H, CH) and 7.20–8.02(m, 20H, ArH,s
	2220(CN); 1660(CO) and 1620(C=N).	2.41(s, 3H, $CH_3C_6H_4$); 2.94(s, 3H, CH_3, thiazole C-4) and 7.26–8.28(m, 14H,
	2220(CN); 1670(CO) and 1620(C=N).	2.42(s, 3H, $CH_3C_6H_4$); 2.97(s, 3H, CH_3, thiazole C-4) and 7.24–8.06(m, 14H,
	1680,1660(2 CO) and 1620 (C=N).	2.38(s, CH_3, 4-$CH_3C_6H_4$); 2.50(s, 3H, CH_3CO); 2.55(s, 3H, CH_3, pyrazole C- 2.85(s, 3H, CH_3, thiazole C-4) and 7.44 8.03(m, 9H, ArH's).
	1685, 1660(2CO) and 1620 (C=N).	2.88(s, 3H, CH_3, thiazole C-4) and 7.99 8.05(m, 20H, ArH's).
	3350(NH); 1670,1650(2 CO) and 1620(C=N).	2.73(s, 3H, CH_3, pyrazole C-5); 2.95(s, 3H, CH_3, thiazole C-4); 7.26–8.03(m, ArH's) and 11.97(s, br., 1H, NH).

No.	R (cm^{-1})	^1H NMR (δ)
	1670(CO); 1620(C=N); 1600 (C=C) and 1350,1150(SO_2).	2.77(s, 3H, CH_3, thiazole C-4); 2.81(s, 3H, CH_3, thiazole C-4) and 7.13–8.28(r ArH's).
	1620(C=N) and 1600(C=C).	2.48(s, 3H, CH_3); 2.58(s, 3H, CH_3); 2.92(s, 3H, CH_3, thiazole C-4) and 7.36–8 10H, ArH's).
	3320,3270(NH_2); 2220(SCN) and 1670(CO).	2.47(s, 3H, $CH_3C_6H_4$); 2.92(s, 3H, CH_3, thiazole C-4); 4.77(s, br., 2|H, NH_2) a 7.26–8.52(m, 9H, ArH's).
	3350(nh); 1680, 1660(2 CO) and 1620(C=NH).	2.76(s, 3H, CH_3, thiazole C-4) and 7.25- 8.26(m, 12H, ArH's and pyrimidine I
	3250,3180(NH_2); 1660(CO) and 1620(C=N).	2.77(s, 3H, CH_3, thiazole C-4); 5.82(s, br., 2H, NH_2) and 7.42–8.26(m, 11H, A and pyrimidine H-2).
	3330(NH); 1660(CO) and 1610(C=N).	2.37(s, 3H, 4-$CH_3C_6H_4$); 2.77(s, 3H, CH_3, thiazole C-4); 7.39–8.05(m, 9H, Ar and 9.64(s, br., 1H, NH).
	1650,1630(2CO) and 1620 (C=N).	2.36(s, 3H, CH_3CON), 2.48(s, 3H, CH_3, thiazole C-4) and 7.26–8.00(m, 9H, A
	1660,1650(2CO) and 1620 (C=N).	2.95(s, 3H, CH_3, thiazole C-4) and 7.26- 8.03(m, 14H, ArH's).
	1660(CO); 1600(C=C) and 1490(NO).	2.77(s, 3H, CH_3, thiazole) and 7.39- 8.05(m, 10H, ArH's).
	1705,1650(CO).	2.36(s, 3H, CH_3, 4-$CH_3C_6H_5$); 2.78(s, 3H, CH_3, thiazole C-4) and 7.39–8.00(n ArH's).
	3350,3280(NH_2); 1620(C=N).	2.90(s, 3H, CH_3, thiazole C-4); 5.49(s, br., 2H, NH_2) and 7.26–8.05(m, 9H, Ar
	3360(NH); 1680(CO); 1600 (C=C) and 1314.1140(SO_2).	2.72(s, 3H, CH_3, thiazole C-4) and 7.23- 8.18(m, 16H, ArH's and NH).

Pyrrolidino[3,4-c]pyrazolines 8a-i, triazolines 9a-c and pyrazoles 10a-c, General procedure

Equimolar amount of the appropriate hydrazonoyl bromide **7a-c**, the appropriate N-arylmaleimide or benzalaniline or α-cyanocinamonitrile and triethylamine (0.005 mol) in dry benzene were refluxed for 2hs, then filter while hot. The filtrate was evaporate near dryness and triturated with pet-ether (40–60°C), the resulting solid was collected and crystallized from ethanol (or acetic acid) to give **8, 9, 10**, respectively (cf. Tables I and II).

Synthesis of thiocyante 3, ketosulfone 4, and thiazole 5

A mixture of **1** (14.8g, 0.05 mol) and potassium thiocyanate or sodium benzenesulfinate or thiourea (0.06 mol) in ethanol (50 ml) was refluxed for 1h. The reaction mixture was cooled and then diluted to complete precipitation. The crude solid was crystallized from ethanol to afford compounds **3–5**, respectively.

Reaction of 7 with Nuclophiles, General method

Equimolecular quantities of the appropriate **7a-c** and the appropriate reagents (PhSNa or $PhSO_2Na$ or KSCN) (0.005 mol) were stirred for 3hs. at room temperature. The resulting solid was collect and crystallized from ethanol to afford **21, 29** and **30**, respectively (cf Tables I and II).

Reaction of 7 with thiourea

A mixture of the appropriate **7a-c** (0.005 mol), thiourea (0.75g, 0.01 mol) and triethylamine (0.7 ml, 0.05 mol) in ethanol (20 ml) was stirred at room temperature for 30 min. The solid was collected and crystallized from ethanol to give **28a-c**. The filtration was continued stirring for 4 h. The new resulting solid was collected and crystallized from ethanol to give the corresponding 2-amino-4-[4-methyl-2-phenylthiazol-5-yl)-5-arylazothiazoles **27a-c** (cf. Tables I and II).

Reaction of arenediazonium chloride with compounds 3, 4 and 5

A solution of the appropriate arenediazonium chloride (0.01 mol) was added dropwise to a stirred solution of the appropriate reactant (**3, 4** and **5**) in ethanol (50 ml) containing sodium acetate trihydrate (1.3g, 0.01 mol) at 0–5°C. The reaction mixture was stirred for 3h at 0°C, the resulting solid was collected and crystallized from ethanol to give **21a-c, 27a-c** and **30a-c**, respectively. The products obtained were identical in all respects (mp., mixed mp., and spectra) with those above.

Nitrosation of 3-aryl-2-imino-5-(4′-methyl-2′-phenylthiazol-5′-oyl-2,3-dihydro-1,3,4-thiadiazoles 21a-c

A saturated solution of $NaNO_2$ (10 ml) was added dropwise to a solution of the appropriate 2,3-dihydrothiadiazole **21a-c** (1g) in acetic acid (20 ml) while stirring at 0–5°C. The rosy precipitated was collected, washed with water and crystallized from ethanol, to give 2-nitroso **(24a-c)**, respectively (cf. Tables I and II).

Decomposition of 3-aryl-2-iminonitroso-5-(4′-methyl-2′-phenylthiazol-5′-oyl-2,3-dihydro-1,3,4-thiadiazoles 24a-c

The appropriate of N-nitroso derivative (1g) in xylene (10 ml) was boiled for 10 min., then evaporated under reduced pressure. The residue was triturated with light petroleum ether, the resulting solid was collected and crystallized from ethanol to give the 2,3-dihydrothiadiazolinones **25** (cf. Tables I and II).

Acylation of 3-aryl-2-imino-5-(4′-methyl-2′-phenylthiazol-5′-oyl-2,3-dihydro-1,3,4-thiadiazoles 21a-c

The appropriate of **21a-c** (1g) was warmed and stirred in acetic anhydride (20 ml) for 10 min and poured onto crushed ice (30 g). The crude precipitated was collected, washed with water and crystallized from ethanol to give N-acetyl derivatives **22a-c** (cf Tables I and II). Stirring equimolecular amount of the appropriate **20a-c** and benzoyl chloride in pyridine effected Benzoylation. The reaction mixture was refluxed for 5 min., then cold, poured onto ice and crystallized from acetic acid to afford N-benzyl derivatives **23a-c** (cf. Tables I and II).

Pyrazoles 11, 13–16 and 18

A solution of the appropriate **7a-c** (0.005 mol) was added to solution of benzoylacetonitrile or pentane-2,4-dione, or 1,3-diphenyloropane-1,3-dione or acetoacetanilide or 5-benzenesulfonylacetyl-4-methyl-2-phenylthiazole or malononitrile (0.005 mol) in ethanol (20 ml) containing sodium metal 0.11g-atom while stirring at room temperature. The reaction mixture was continued stirred for 4hs. the resulting solid was collected and crystallized from ethanol to gives pyrazoles **11, 13–16** and **18**, respectively (cf. Table I and II).

Pyrazolo[3,4-d]pyridazines 12a-c and 17a-c

A mixture of the appropriate of pyrazoles **11a** or **13a-c** (0.005 mol) and hydrazine hydrate (1 ml) in ethanol (20) was refluxed for 2h. Then cooled. The resulting solid was collected, washed and crystallized in ethanol to give pyrazolo[3,4-d]pyridazines **12** and **17a-c**, respectively (cf. Tables I and II).

Pyrazolo[3,4-d]pyrimidines 19 and 20

A mixture of the appropriate of pyrazoles **17a-c** (1g) and formic acid (or formamide) (5 ml) in dimethylformamide (5 ml) was rfluxed for 4h, then poured onto ice (30g). The precipitated formed was collected and crystallized from dimethylformamide to give **19** (or **20**) in good yields (cf. Table I and II).

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