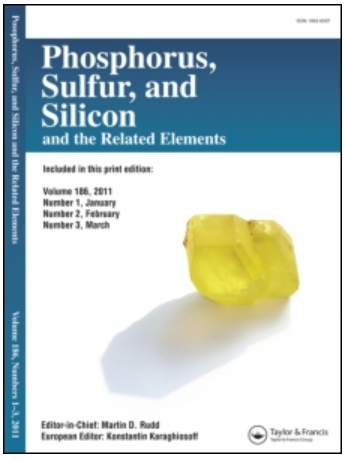

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

REACTIONS WITH HYDRAZIDOYL HALIDES VII[1]: SYNTHESIS OF SEVERAL NEW ANNELATED PYRAZOLE, QUINAZOLINE AND THIAZOLE DERIVATIVES

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To cite this Article Abdelhamid, Abdou O. , Khalifa, Fathy A. , Attaby, Fawzy A. and El-shiaty, Fathia H.(1992) 'REACTIONS WITH HYDRAZIDOYL HALIDES VII[1]: SYNTHESIS OF SEVERAL NEW ANNELATED PYRAZOLE, QUINAZOLINE AND THIAZOLE DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 72: 1, 135 — 144
To link to this Article: DOI: 10.1080/10426509208031547
URL: http://dx.doi.org/10.1080/10426509208031547

Phosphorus, Sulfur, and Silicon, 1992, Vol. 72, pp. 135–144
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REACTIONS WITH HYDRAZIDOYL HALIDES VII[1]: SYNTHESIS OF SEVERAL NEW ANNELATED PYRAZOLE, QUINAZOLINE AND THIAZOLE DERIVATIVES

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(Received May 28, 1992; in final form July 16, 1992)

Several new annelated pyrazole, 3H-quinazolinone and thiazole derivatives are synthesized via the reaction of 2-bromothienylglyoxal-2-arylhydrazones with different reagents. The structures of the newly synthesized compounds were established on the basis of elemental analyses and spectral data studies.

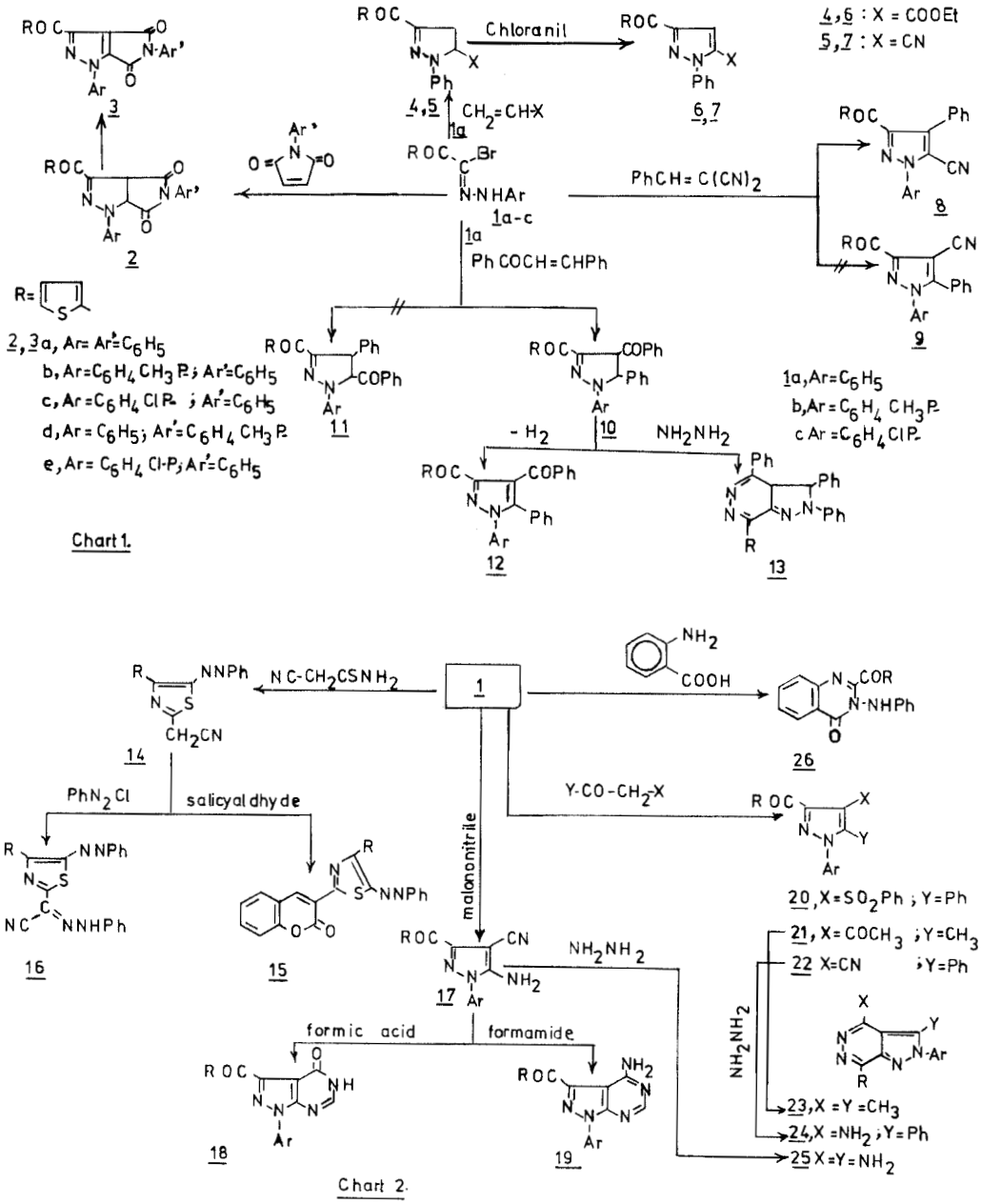
Key words: Pyrrolo[3,4-*c*]pyrazoles; pyrazolo[3,4-*d*]pyrimidines; Coumarines; 3H-quinazolinones; pyrazoles; thiazoles.

INTRODUCTION

1,3-Dipolar compounds are reported to be useful reagents for the preparation of various heterocyclic compounds.[3–7] As a part of our interest in the study of the reactivity of hydrazidoyl halides towards unsaturated systems and nucleophilic reagents, we now reported on the preparation of several pyrrolo[3,4-*c*]pyrazole, pyrazolo[3,4-*d*]pyrimidine, pyrazolo[3,4-*d*]pyridazine, 3H-quinazolinone, thiazole derivatives (cf. Charts 1 and 2). The above systems are also reported to be biologically active[8–15] and could be used as antipyretic, bactericidal, bacteriostatic and fungicidal agents. The newly synthesised derivatives of these ring systems are required for medicinal chemistry as well as for chemical transformation.

RESULTS AND DISCUSSION

Treatment of 2-bromothienylglyoxal-2-arylhydrazones (**1a–c**) with *N*-arylmaleimides and triethylamine in toluene gave, in each case, unique products which are identified as 3-thienoyl-1,5-diarylpyrrolidino[3,4-*c*]-Δ^2-pyrazolin-4,6-diones (**2**). The structures of **2** were assigned on the basis of the elemental and spectral data. The ^{1}H-NMR spectrum of each compound in the series of **2** showed two characteristic doublets due to the proton at C—4 and C—5 of the pyrazoline ring at δ 5.2 and



5.4 ppm. IR spectra of **2** revealed absorption bands at 1790–1720 and 1710–1690 cm^{-1} attributed to the presence of the (—CO—NR—CO—) grouping and 1650 cm^{-1} for (CO) group. Pyrazolines **2** can be easily aromatized by refluxing their xylene solutions with chloranil[3,16] to give **3**. The structures of **3** were established using elemental analyses and spectral data ^{1}H-NMR spectra of **3** showed no signale at 5.2 and 5.4 due to the pyrazoline ring. **1a** reacted with ethylacrylate and acryl-

onitrile to give the pyrazolines **4** and **5**, respectively. The structures of **4** and **5** were confirmed on the basis of elemental analyses and spectral data. ^{1}H-NMR (δ ppm.) of **4** revealed signals at 1.3 (t, 3H, $CH_2\underline{CH_3}$), 3.6 (*d*, 2H, 4—$\underline{CH_2}$), 4.2 (q, 2H, $\underline{CH_2}CH_3$), 4.9 (t, 1H, 5—$\underline{CH}$) and 6.9–7.5 (*m*, 8H, ArH's and thiophene). Compound 5 revealed signals at 4.8 (*d*, 2H, 4—$\underline{CH_2}$), 5.1 (t, 1H, 5—$\underline{CH}$) and 7.0–7.6 (*m*, 8H, ArH's and thiophene). Compounds **4** and **5** were converted by refluxing their xylene solution containing chloranil into corresponding pyrazoles **6** and **7** respectively. The ^{1}H-NMR spectra of **6** and **7** showed a singlet signal at δ 6.5 ppm. in addition to the signals at δ 6.9–7.5 due to the ArH's and thiophene protons together with the characteristic signals attributed to the ethoxy protons in case of compounds **6**. IR spectra of **4** and **5** showed absorption bands at 1650 cm^{-1} (CO) and 1710 cm^{-1} (CO ester). IR spectra of **5** and **7** showed absorption bands at 1690 cm^{-1} (CO) and 2220 cm^{-1} due to cyano group. **1a** reacted with benzalmalononitrile and benzalacetophenone in toluene containing triethylamine as the acceptor of hydrogen bromide to give the pyrazole **8** and pyrazoline **10**, respectively. The structures of **8** and **10** were confirmed on the basis of elemental analysis and spectral data. The ^{1}H-NMR spectrum of **8a** revealed only one signal at δ 6.9–7.8 ppm. (*m*, ArH's and thiophene). Its IR (cm^{-1}) spectrum showed absorption at 2225 (C≡N), 1660 (CO) and 1620 (C=N). The isomeric structure **9** was readily ruled out by comparison with the product obtained from the reaction of **1a** with benzoylacetonitrile.[6] The ^{1}H-NMR spectrum of **10** revealed signals at δ 4.6 (*d*, 1H, CHph), 5.6 (*d*, 1H, CHCOph) and 6.8–7.8 (*m*, 8H, ArH's and thiophene). IR spectrum showed absorption bands due to two carbonyl at 1660 and 1690 cm^{-1}. The isomeric structure of **11** was excluded on these basis: a) compound **10** reacted with hydrazine hydrate in refluxing ethanol to give, 3-thienyl-1,6,7-triphenyldihydropyrazolo[3,4-*d*]pyridazine (**13**). b) Compound **10** can be easily aromatized by refluxing with chloranil in xylene to give 4-benzoyl-3-thienoyl-1,5-diphenylpyrazole (**12**). The structure of **12** was elucidated on the basis of elemental analysis, spectral data and authentic sample.[6] **1a** reacted with cyanothioacetamide in ethanolic solution containing triethylamine to affored 2-(2′-thiazolyl-4′-thienyl-5-phenylazo)acetonitrile (**14**). The structure of **14** was confirmed on the basis of elemental analysis, spectral data and chemical reactions. The ^{1}H-NMR of **14** revealed signals at (δ ppm.) 3.6 (*s*, 2H, CH_2CN) and 6.9–8.0 (*m*, 8H, ArH's and thiophene). Its IR spectrum showed absorption bands at 2220 cm^{-1} due to the cyano group. Compound **14** reacted with salicyaldhyde in ethanolic sodium ethoxide solution to yield 3-(2′-thiazolyl-4′-arylazo)coumarine (**15**). Compound **14** reacted also with benzenedizonium chloride in pyridine to give 1-cyano-1-(2′-thiazolyl-4′-thienyl-5′-phenylazo)formylhydrazone (**16**), (cf. Tables I and II).

Treatment of **1** with malononitrile, ω-benzenesulfonylacetophenone, acetylacetone and benzoylacatonitrile in ethanolic sodium ethoxide solution gave, in each case, one product according to TLC, which were formulated as pyrazole derivatives **17** and **20–22**, respectively. The structures of **17** and **20–22** were established on the basis of elemental analyses, spectral data and chemical reactions (cf. Tables I and II). The ^{1}H-NMR spectrum of **17b** revealed signals at (δ ppm.) 2.3 (*s*, 3H, CH_3Ar-p), 5.6 (*s*, br., 2H, NH_2) and 6.9–7.8 (*m*, 7H, ArH's and thiophene). Upon shaking with D_2O, the signal at 5.6 ppm disappeared and a new signal at 4.7 ppm due to H_2O appeared. Its IR (cm^{-1}) spectrum showed absorption at 1650 (CO),

TABLE I

Characterization data of the newly synthesised compounds

Compd. No.	Color	M.P. °C	Molecular Formula	% Analyses C	H	N	S	Calcd / Found
2a	Pale yellow	270	$C_{22}H_{15}N_3SO_3$	65.83	3.74	10.47	7.98	Calcd
				65.90	3.90	10.60	8.10	Found
2b	Pale yellow	240	$C_{23}H_{17}N_3SO_3$	66.51	4.10	10.12	7.71	Calcd
				66.30	4.20	10.00	7.80	Found
2c	Pale yellow	331	$C_{22}H_{14}ClN_3SO_3$	60.62	3.21	9.64	7.35	Calcd
				60.40	3.20	9.60	7.30	Found
2d	Yellow	243	$C_{23}H_{17}N_3SO_3$	66.51	4.10	10.12	7.71	Calcd
				66.40	3.90	10.00	7.80	Found
2e	Yellow	255	$C_{22}H_{14}ClN_3SO_3$	60.62	3.24	9.64	7.35	Calcd
				60.70	3.30	9.80	7.50	Found
3a	Yellow	272	$C_{22}H_{13}N_3SO_3$	66.16	3.25	10.52	8.02	Calcd
				66.30	3.40	10.60	7.90	Found
3d	Yellow	247	$C_{23}H_{15}N_3SO_3$	66.83	3.63	10.16	7.75	Calcd
				66.90	3.70	10.20	7.60	Found
3e	Pale yellow	259	$C_{22}H_{12}ClN_3SO_3$	60.90	2.76	9.68	7.38	Calcd
				60.50	2.50	9.80	7.40	Found
4	Yellowish-green	104	$C_{17}H_{16}N_2SO_3$	62.20	4.88	8.54	9.76	Calcd
				62.40	5.00	8.60	9.90	Found
5	Greenish-yellow	164	$C_{15}H_{11}N_3SO$	64.06	3.91	14.94	11.93	Calcd
				64.30	4.10	5.10	11.60	Found
6	Pale yellow	115	$C_{17}H_{14}N_2SO_3$	62.58	4.29	8.59	9.81	Calcd
				62.70	4.30	8.40	9.80	Found
7	Colourless	175	$C_{15}H_9N_3SO$	64.52	3.23	15.05	11.47	Calcd
				64.60	3.40	15.20	11.60	Found
8a	Colourless	160	$C_{21}H_{13}N_3SO$	70.98	3.66	11.83	9.01	Calcd
				71.00	3.80	11.90	9.10	Found
8b	Colourless	179-180	$C_{22}H_{15}N_3SO$	71.54	4.06	11.38	8.67	Calcd
				71.40	4.10	11.50	8.70	Found
10	Yellow	218	$C_{27}H_{20}N_2SO_2$	74.31	4.58	6.42	7.33	Calcd
				74.50	4.40	6.60	7.50	Found
13	Yellow	254	$C_{27}H_{20}N_4S$	75.00	4.63	12.96	7.41	Calcd
				75.20	4.70	12.00	7.50	Found
14	Brown	220	$C_{15}H_{10}N_4S_2$	58.06	3.23	18.06	20.65	Calcd
				58.20	3.40	18.20	20.80	Found
15	Black	285	$C_{22}H_{14}N_3S_2O_2$	63.46	3.36	10.09	15.38	Calcd
				63.40	3.40	10.00	15.30	Found

TABLE I (*Continued*)

Compd. No.	Color	M.P. °C	Molecular Formula	% Analyses C	H	N	S	Calcd / Found
16	Redish-brown	231	$C_{21}H_{14}N_6S_2$	61.01 61.00	3.14 3.50	20.34 20.40	15.49 15.60	
17a	Pale yellow	197	$C_{15}H_{10}N_4SO$	61.22 61.40	3.40 3.50	19.04 18.80	10.88 10.60	
17b	Pale yellow	260	$C_{16}H_{12}N_4SO$	62.33 62.40	3.90 4.80	18.18 18.30	10.39 10.30	
17c	Pale Yellow	270	$C_{15}H_9ClN_4SO$	54.79 54.90	2.74 2.80	17.04 17.20	9.74 9.80	
18a	Colourless	304	$C_{16}H_{10}N_4SO_2$	59.62 59.60	3.10 3.20	17.39 17.40	9.94 10.10	
18b	Colourless	314	$C_{17}H_{12}N_4SO_2$	60.71 60.60	3.60 3.50	16.66 16.70	9.52 9.60	
18c	Colourless	358	$C_{16}H_9ClN_4SO_2$	53.86 54.00	2.52 2.50	15.70 15.60	8.98 9.00	
19a	Colourless	230	$C_{16}H_{11}N_5SO$	59.81 59.70	3.43 3.50	21.80 21.90	9.97 10.00	
19b	Colourless	220	$C_{17}H_{13}N_5SO$	60.89 60.80	3.88 4.00	20.89 20.80	9.55 9.70	
19c	Colourless	196	$C_{16}H_{10}ClN_5SO$	54.01 53.90	2.81 2.90	19.68 19.80	9.00 8.80	
20b	Pale Yellow	169	$C_{27}H_{20}N_2S_2O_3$	66.94 66.90	4.13 4.30	5.78 5.80	13.22 13.30	
20c	Pale Yellow	178	$C_{26}H_{17}ClN_2S_2O_3$	61.84 62.00	3.36 3.40	5.55 5.66	12.69 12.80	
21a	Colourless	180	$C_{17}H_{14}N_2SO_2$	65.81 65.90	4.51 4.40	9.03 8.90	10.32 10.10	
21b	Colourless	105	$C_{18}H_{16}N_2SO_2$	66.66 66.70	4.94 5.00	8.64 8.60	9.88 9.90	
21c	Colourless	151	$C_{17}H_{13}ClN_2SO_2$	59.21 59.10	3.77 3.80	8.13 8.10	9.29 9.40	
22b	Pale yellow	177	$C_{22}H_{15}N_3SO$	71.54 71.70	4.06 4.10	11.38 11.40	8.67 8.70	
22c	Pale yellow	184	$C_{21}H_{12}ClN_3SO$	64.69 64.80	3.08 3.00	10.78 10.80	8.22 8.30	
23a	Colourless	266	$C_{17}H_{14}N_4S$	66.66 66.80	4.57 4.50	18.30 18.10	10.46 10.40	

TABLE I (*Continued*)

Compd. No.	Color	M.P. °C	Molecular Formula	% Analyses C	H	N	Calcd S Found
23b	Colourless	293	$C_{18}H_{16}N_4S$	67.50	5.03	17.50	10.00
				67.60	5.00	17.60	10.20
23c	Colourless	318	$C_{17}H_{13}ClN_4S$	59.91	3.84	16.44	9.40
				60.00	3.96	16.30	9.50
24b	Pale yellow	180	$C_{22}H_{17}N_5S$	68.93	4.44	18.28	8.36
				69.00	4.50	18.40	8.20
24c	Pale Yellow	186	$C_{21}H_{14}ClN_5S$	62.45	3.47	17.34	7.93
				62.60	3.60	17.30	8.10
25a	Colourless	189	$C_{15}H_{12}N_6S$	58.44	3.89	27.27	10.39
				58.50	4.10	27.40	10.50
25b	Colourless	241	$C_{16}H_{14}N_6S$	59.63	4.38	26.09	9.94
				59.70	4.40	26.20	10.10
25c	Pale yellow	274	$C_{15}H_{11}ClN_6S$	52.55	3.21	24.52	9.35
				52.70	3.30	24.60	9.50
26	Yellow	190	$C_{19}H_{13}N_3SO_2$	65.71	3.74	12.10	9.22
				65.80	3.60	11.90	9.40

2220 (C═N), and 3150,3200 (NH_2). Compound **17** reacted with formic acid, and also reacted with formic acid, formamide in presence of dimethylformamide to afford products which could be formulated as 1-aryl-3-thienoylpyrazolo[3,4-*d*]pyrimidin-4-one (**18**) and 4-amino-1-aryl-3-thienoyl[3,4-*d*]pyrimidine (**19**) respectively. The structures of **18** and **19** were elucidated based on elemental analyses and spectral data (cf. Tables I and II). On the other hand, **17** reacted with hydrazine hydrate in refluxing ethanol to give the 1-aryl-6,7-diamino-3-thienylpyrazolo[3,4-*d*]pyridazine (**25**) (cf. Tables I and II). The structures of the pyrazoles **20–22** were established on the basis of spectral data and elemental analyses. For example, the ^{1}H-NMR (δ ppm) spectra of **21** revealed signals at 2.2 (*s*, 3H, CH_3 pyrazole C—5), 2.3 (*s*, 3H, CH_3CO pyrazole C—4) and 6.9–7.8 (*m*, ArH's and thiophene). Its IR (cm^{-1}) spectra showed absorption bands at 1650 (CO) and 1670 (CH_3CO). Compound **21** and **22** reacted with hydrazine hydrate in ethanol to afford the pyrazolo[3,4-*d*]pyridazines **23** and **24**, respectively (cf. Tables I and II).

Reactions of **1a** with anthranilic acid in ethanol in the presence of triethylamine gave a product which was identified as 3-anilino-2-thienoyl-4(3H)quinazolinone (**26**). The structure of **26** is supported by spectral data and elemental analysis. The ^{1}H-NMR spectrum of **26** revealed at δ 6.9–7.8 (*m*, 12H, ArH's and thiophene) and 9.4(*s*, br., 1H, NH) while its IR spectrum showed two carbonyl bands at 1650 and 1690 cm^{-1}.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a Pye-Unicam SP 1100 spectrophotometer. ^{1}H-NMR spectra were measured in $CDCl_3$ and $(CD_3)_2SO$ on a Varian EM-390-90 MHz

TABLE II

Characterization data of the newly synthesised compounds

Compd.	IR (cm^{-1})	^{1}H-NMR (δ ppm)
2b	1790-1720 and 1710-1690 (-CO-NAr-CO) group and 1670 (CO).	1.9(s,3H,$C_6H_4CH_3$-p), 5.1(d,1H, C-4 pyrazoline), 5.3 (d, 1H, C-5 pyrazoline) and 6.9-7.8(m, 12H, ArH's and thiophene)
2d	1790-1720 and 1710-1690 (-CO-NAr-CO-) group and 1670 (CO).	2.1(s,3H,$C_6H_4CH_3$-p),5.2(d,1H, C-pyrazoline) ,5.4 (d,1H,C-5 pyrazoline) and 6.9-7.8(m.12H, thiophene).
15	1690(CO) and 1620 (C=N)	6.9-7.8(m,ArH's ,thiophene and coumarine).
16	3300 (NH),2227(C=N) and 1630 (C=N)	6.9-7.8(m,13H,ArH's and thiophene) and 9.5(s,br.,1H,NH).
18a	3200(NH),1670, 1650 (two CO) and 1630 (C=N).	6.9-7.8 (m,8H,ArH's and thiophene) and 9.2(s,1H,C-2 pyrimidine) and 10.8(s,br.,1H,NH).
18b	3200(NH),1670, 1650 (two CO) and 1630 (C=N).	2.1 (s,3H,$C_6H_4CH_3$-p),6.9-7.8 (m,7H,ArH's and thiophene) , 9.4(s,1H,C-2 pyrimidine) and 10.8(s,br.,1H,NH).
18c	3200(NH),1670,1650 (two CO) and 1620 (C=N).	6.7-7.7(m,7H,ArH's and thiophene),9.6(s,1H,C-2pyrimidine) and 10.9(s,br.,1H,NH).
19a	3400,3350(NH_2),1660(CO) and 1620(C=N).	5.6(s,br.,2H,NH_2), 6.9-7.8 (m,8H,ArH's and thiophene) and 9.5(s,1H,C-2 pyrimidine).
19b	3400,3360 (NH_2),1655 (CO) and 11620 (C=N).	2.2(s,3H,$C_6H_4CH_3$-p), 5.7(s,br. 2H, NH_2), 6.9-7.8(m,7H,ArH's and thiophene) and 9.4(s,1H, C-2 pyrimidine).
19c	3390,3350 (NH_2), 1650 (CO) and 1620 (C=N).	5.6(s,br.,2H,NH_2), 6.9-7.8(m, 7H,ArH's and thiophene) and 9.3(s, 1H, C-2 pyrimidine).
20b	1650 (CO),1620 (C=N) and 1520,1350 (SO_2).	2.3(s,3H,$C_6H_4CH_3$ p) and 6.9-8.0(m,17H,ArH's and thiophene)
20c	1650(CO), 1620(C=N) and 1520,1350 (SO_2).	6.9-7.9(m,ArH's and thiophene)

TABLE II (*Continued*)

Compd.	IR (cm-1)	^{1}H-NMR (δ ppm)
22b	2225(C≡N),1650 (CO) and 1620(C=N).	2.1(s,3H,$C_6H_4CH_3$-p),6.8-8.0 (m,12H,ArH's and thiophene).
22c	2225(C≡N),1650(CO) and 1620(C=N).	6.9-8.0(m,ArH's and thiophene)
23a	1660(CO) and1620 (C=N).	2.2(s,3H,CH_3pyrazole C-4), 2.4(s,3H,CH_3pyrazole C-5) and 6.9-7.8 (m,8H,ArH's and thiophene).
23b	1650(CO) and 1620 (C=N).	2.1(s,3H,$C_6H_4CH_3$-p),2.3(s,3H, CH_3pyrazole C-4), 2.5(s,3H, CH_3pyrazole C-5) and 6.9-7.9 (m,7H,ArH's and thiophene).
23c	1660(CO) and 1620 (C=N).	2.2(s,3H,CH_3-pyrazole C-4), 2.4(s,3H,CH_3-pyrazole C-5) and 6.8-8.0 (m,7H,ArH's and thiophene).
24b	1650 (CO) and 1620 (C=N).	2.2(s,3H,$C_6H_4CH_3$-p), 5.6 (s, br.,2H,NH_2) and 6.9-8.0(m,12H, ArH's and thiophene).
24c	1660 (CO)and 1620 (C=N).	5.6(s,br.,2H,NH_2) and 6.9-8.0 (m,12H,ArH's and thiophene).
25a	3400.3350(NH_2) and 1620(C=N).	6.2(s,br.,4H,2 NH_2) and 6.9-7.8(m,8H,ArH's and thiophene).
25b	3400,3350(NH_2) and 1620 (C=N)	2.2(s,3H,$C_6H_4CH_3$-p),6.2(s,br., 4H,2 NH_2) and 6.9-7.9 (m, 7H, ArH's and thiophene).
25c	3400,3360(NH_2) and 1620(C=N).	6.1(s,br.,4H,2 NH_2) and 6.9-8.0(m,7H,ArH's and thiophene).

spectrometer using TMS as internal indicator and chemical shifts are expressed as δ ppm. Elemental analyses were carried out in microanalytical centre at Cairo University. Hydrazidoyl bromide **1** was prepared according to literature procedure.[6]

Synthesis of **2**, **4**, **5**, **8** *and* **10**: A mixture of equimolecular quantities (5 mmol) of the appropriate **1a–c** and N-arylmaleimide (or ethylacrylate, acrylonitrile, benzalmalononitrile, ω-benzalacetophenone)

in toluene (50 ml) were treated dropwise with triethylamine (0.5 ml) in toluene (10 ml) at room temperature. The mixture was refluxed for 2h and filtered while hot. The solvent was evaporated under vacuum, the oily residue was solidified by trituration with petroleum ether (60/80°C). The solid was collected and crystallized from ethanol to give **2**, **4**, **5**, **8** and **10**, respectively (cf. Tables I and II).

Synthesis of **3**, **6**, **7** *and* **12**: A mixture of chloranil (0.006 mol) and the appropriate **2**, **4**, **5** and **10** (0.005 mol) in xylene (40 ml) was refluxed for 48 h. The reaction mixture was cooled, washed with sodium hydroxide solution (0.1N, 3 × 50 ml) dried and evaporated under reduced pressure. The solid was collected and crystallized from dimethylformamide or ethanol to give **3**, **6**, **7** and **12**, respectively (cf. Tables I and II).

Synthesis of pyrazoles **12**, **17** *and* **20–22**: Dibenzoylmethane (or malononitrile, ω-benzenesulfonylacetophenone, acetylacetone, benzoylacetonitrile) (0.005 mol) was added to an ethanolic sodium ethoxide solution obtained by dissolving sodium metal (0.1 g, 0.005 g atom) in ethanol (20 ml) while stirring. The appropriate hydrazidoyl bromide **1a–c** (0.005 mol) was added to the resulting solution and stirring was continued for 3 h at room temperature. The solid which precipitated was collected by filtration and crystallized from ethanol or acetic acid to give the pyrazoles **12**, **17** and **20–22** in 85–90% yield, respectively (cf. Tables I and II).

Synthesis of **2**-*(2'-thiazolyl-4'-thienyl-5'-phenylazo)acetonitrile* (**14**): A solution of (0.005 mol triethylamine was added dropwise to a stirred solution of **1a** (1.5 g, 0.005 mol) and cyanothioacetamide (0.5 g, 0.005 mol) in ethanol (25 ml) at room temperature. The reaction mixture was stirred for 30 min. The separated product was filtered off and crystallized from acetic acid (cf. Tables I and II).

Synthesis of **15**: Equimolecular amounts of **14** and salicylaldehyde in ethanolic solution containing sodium ethoxide was refluxed for 3 h. The reaction mixture was diluted with water (100 ml) and acidified with hydrochloric acid. The solid so formed was collected, washed with water and crystallized from acetic acid to give **15** in 72% yield (cf. Tables I and II).

Synthesis of **16**: An aqueous solution of benzenediazonium chloride (0.01 mol) was added dropwise to a stirred solution of **14** in pyridine (50 ml) at 0 C. The reaction mixture was stirred for 3 h. The solid was collected, washed with water and crystallized from dioxan to give **16** (cf. Tables I and II).

Synthesis of pyrazolo[3,4-d]pyrimidinones **18**: A solution of **17** (2 g) in formic acid (20 ml, 85%) was refluxed for 7 h. The reaction mixture was cooled and diluted with water. The precipitate was collected and crystallized from ethanol to give **18** (cf. Tables I and II).

Synthesis of pyrazolo[3,4-d]pyrimidines **19**: A solution of **17** (2 g) in formic acid 99%, formamide and dimethylformamide (5 ml each) was refluxed for 9 h. The reaction mixture was cooled and diluted with water. The crude product was isolated by filtration and crystallized from ethanol to give **19** (cf. Tables I and II).

Synthesis of the pyrazolo[3,4-d]pyridazines **13** *and* **23–25**: A solution of the appropriate **10** or **17** or **20–22** (1 g) and hydrazine hydrate (5 ml) in ethanol (20 ml) was refluxed for 2 h. The solid was collected and crystallized from dimethylformamide to give compounds **13** and **23–25**, respectively (cf. Tables I and II).

Synthesis of **26**: Anthranilic acid (1.37 g, 0.01 mol) was dissolved in ethanol (50 ml) together with **1a** (3.0 g, 0.01 mol) and triethylamine (1 ml, 0.01 mol) was then added. The reaction mixture was refluxed for 4 h and cooled. The solid so formed was collected and crystallized from ethanol to give 3-anilino-2-thienoyl 4(3H)quinazolinone(**26**) in 80% yield (cf. Tables I and II).

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