Reactions of Hydrazonoyl Halides 43 [1]: Synthesis of Some New 2,3-Dihydro-1,3,4-thiadiazoles, Pyrazoles, Pyrazolo[3,4-*d*]-pyridazines, Thieno[2,3-*b*]pyridines, Pyrimidino[4',5':4,5]thieno[2,3-*b*]-pyridines and Pyrrolo[3,4-*d*]pyrazoles

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2,3-Dihydro-1,3,4-thiadiazoles, pyrazoles, pyrazolo[3,4-*d*]pyridazines, thieno[2,3-*b*]pyridines, pyrimidino[4',5':4,5]thieno[2,3-*b*]pyridines and pyrrolo[3,4-*d*]pyrazoles were obtained in a good yields by treatment of hydrazonoyl halides with each of alkyl carbodithioates, 3-(dimethylamino)-1-naphtho[1,2-*d*]furan-2-ylprop-2-en-1-one and *N*-arylmalemides.

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1,3,4-Thiadiazoles are active in many biological systems such as: antitumor [2], hypoglycemic properties [3], antihistamine [4] and anticholinergic [5]. Pyrazoles and annelated pyrazoles have long been known to exhibit diverse biological activities. Among these activities include their use as antipyretic [6], analgesic drugs [7-9], antitumor [10], hypnotic [11], fungicides [12] and herbicidal [13] agents. Moreover thienopyridines are of special importance due to reported biological activities [14]. Also hydrazonoyl halides have been widely used for the synthesis of heterocyclic compounds [15-19]. We report here the synthesis of some new 2,3-dihydro-1,3,4-thiadiazoles, pyrazoles, pyrazolo[4,3-*d*]pyridazines, thieno[2,3-*b*]-pyridines, pyrimidino[4',5':4,5]thieno[2,3-*b*]pyridines and pyrrolo[4,3-*d*]pyrazoles.

Results and Discussion.

Treatment of methyl hydrazinecarbodithioate (**2**) [20] with 1-naphtho[1,2-*d*]furan-2-ylethan-1-one (**1**) in 2-propanol afforded methyl *N*'-(naphtha[1,2-*d*]furan-2-ylethylidine)hydrazinecarbodithioate (**3**). The ^{1}H NMR spectrum of **3** showed signals at δ = 2.55 (s, 3H), 2.62 (s, 3H), 7.56-8.38 (m, 7H) and 12.52 (s, br., 1H). Compound **3** reacted with the appropriate hydrazonoyl halides **4a-h** in ethanolic triethylamine at room temperature to give 5-substituted 2-naphtho[1,2-*d*]furan-2-ylethylidene-3-phenyl-1,3,4-thiadiazoline **7a-h**, respectively (Scheme 1). Structure **7** was confirmed by elemental analysis, spectral data and alternative synthesis route. Thus, ^{1}H NMR spectrum of **7b** showed signals at δ = 1.42 (t, 3H), 1.93 (s, 3H), 4.46 (q, 2H) and 7.26-8.16 (m, 12H). Also, treatment of ethyl 2-hydrazino-3-phenyl-2,3-dihydro-1,3,4-thiadiazole-5-carboxylate (**9**) [21] with **1** in 2-propanol afforded product identical with **7b**.

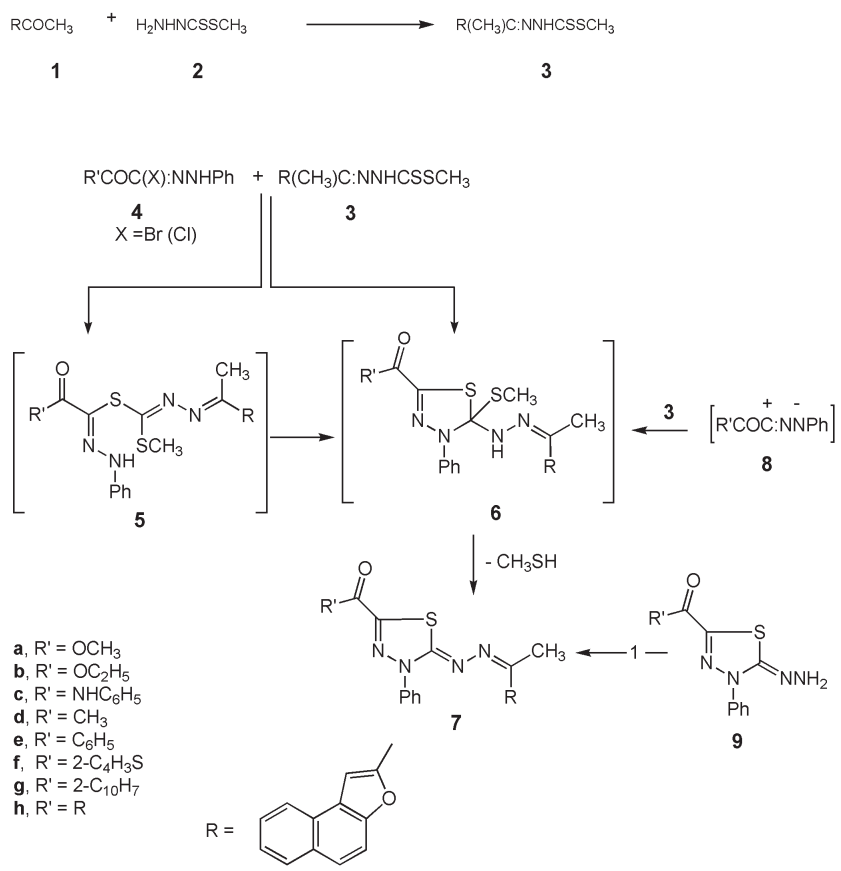
In the light of the foregoing results, the mechanism outlined in Scheme 1 seems to be the most plausible pathway for the formation of **7** from the reaction between **3** and **4**. The reaction involves initial formation of thiohydrazonate **5**, which undergoes intramolecular cyclization as soon as it is formed to yield the intermediate **6** or *via* 1,3-dipolar cycloaddition of nitrilimine **8**, which prepared *in situ* from **4** with triethylamine, to C=S double bond of **3** to give the intermediate **6**. Intermediate **6** is converted to the final product **7** *via* elimination of methyl mercaptane.

Similarly, 2-hydroxynaphthaline-1-carboxyaldehyde reacted with methyl- or benzyl hydrazinecarbodithioate (**10a,b**) to give alkyl *N*'-(2-hydroxynaphthalin-1-ylmethylene)hydrazinecarbodithioates **11a** and **11b**, respectively. ^{1}H NMR spectrum of **11a** showed signals at δ = 2.61 (s, 3H), 7.12 (d, 1H), 7.40-7.95 (m, 4H), 8.74 (d, 1H), 9.12 (s, 1H), 11.08 (s, 1H) and 13.40 (s, 1H). Treatment of each of **11a** or **11b** with the appropriate hydrazonoyl halides **4b-h** in ethanol containing triethylamine afforded the 5-substituted 3-aryl-2-(hydroxynaphthaline-1-ylmethylenehydrazino)-2,3-dihydro-1,3,4-thiadiazoles **12b-h**, respectively (Scheme 2).

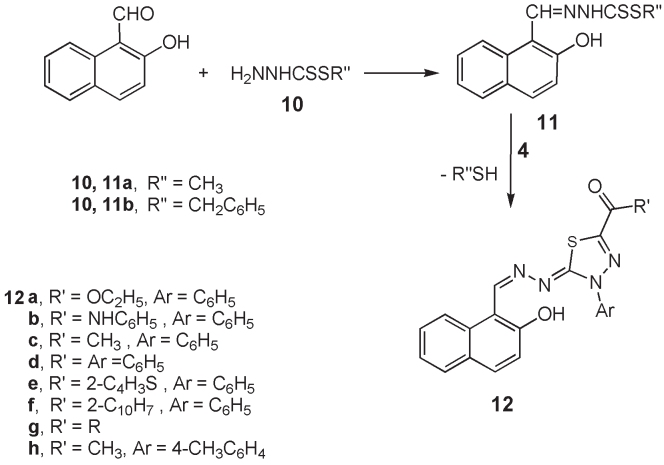
On the other hand, **1** reacted with DMF-DMA **13** under reflux to give 3-(dimethylamino)-1-naphtho[1,2-*d*]furan-2-ylprop-2-en-1-one (**14**). ^{1}H NMR spectrum of **14** showed signals at δ = 2.97 (s, 3H), 3.15 (s, 3H), 5.89 (d, 1H), 7.50-7.96 (m, 7H) and 8.16 (d, 1H). Thus, *C*-methoxycarbonyl-*N*-phenylhydrazonoyl chloride **4a** and **14** was refluxed in toluene containing triethylamine afforded, one isolable product according to tlc, methyl 4-(naphtho[1,2-*d*]furan-2-ylcarbonyl)-4-phenylpyrazole-3-carboxylate (**17a**) (Scheme 3). The ^{1}H NMR spectrum of **17a** showed signals at δ = 3.81 (s, 3H, OCH_3), 7.27-8.21 (m, 12H, ArH's) and 8.55 (s, 1H, pyrazole C-5). Compound **17a** was converted to 4-naphtho[1,2-*d*]furan-2-yl-2-phenyl-6-hydropyrazolo[3,4-*d*]pyridazin-7-one (**19a**) by refluxing with hydrazine hydrate in ethanol. The ^{1}H NMR spectrum of **19a** showed signals at δ = 7.33-7.62 (m, 12 H, ArH's), 8.23 (s, 1H, pyrazole C-5) and 11.12 (s, br., 1H, NH).

Also, 1**7b** and **17c** were refluxed with hydrazine hydrate in ethanol to give product identical with **19a**. Formation of

Scheme 1



Scheme 2

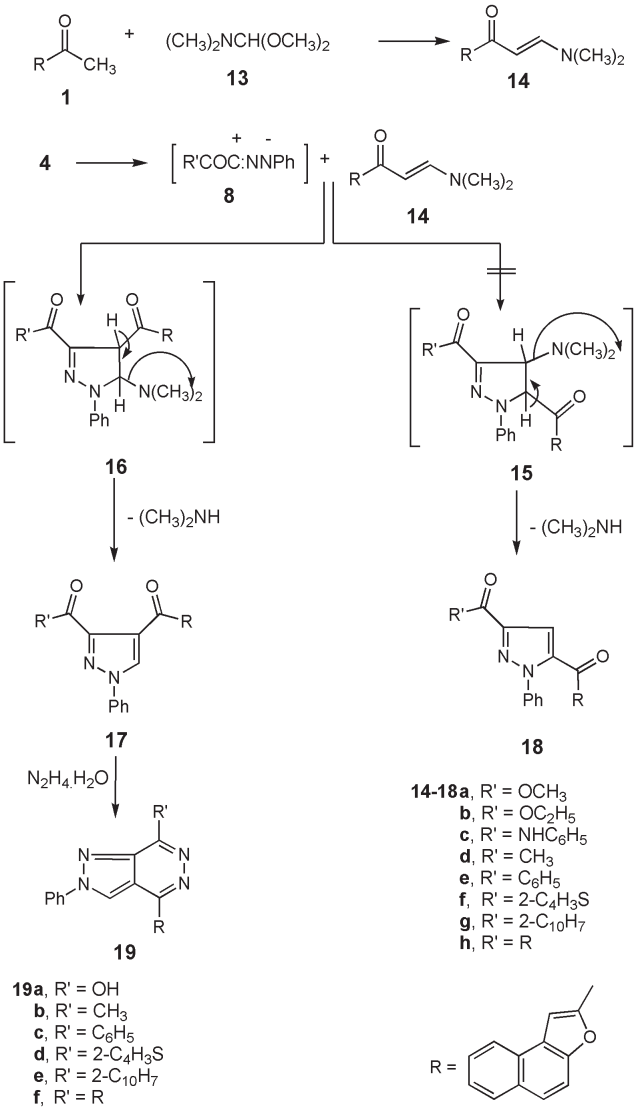


17 can be explained *via* reaction of nitrileimine **8** with **14** to afford cyclo adduct intermediate **15** or **16**, and then elimination of diethylamine to give pyazole as final product **17** or pyrazole **18**. The latter was ruled out on the basis of the foregoing data.

Compound **14** was refluxed with cyanothioacetamide in pyridine (or in ethanol containing catalytic amount of piperdine) gave 6-naphtho[1,2-*d*]furan-2-yl-2-sulfanylpyridine-3-carbonitrile (**20**). Compound **20** reacted with iodomethane in presence of potassium hydroxide to afford 2-methylthio-6-naphtho[1,2-*d*]furan-2-ylpyridine-3-carbonitrile (**21**). IR spectrum of **21** revealed a band at 2219 (CN) and its ^{1}H NMR spectrum showed signals at δ =2.75 (s, 3H), 7.53-8.23 (m, 9H) ppm.

Treatment of **20** with ethyl chloroacetate in *N*,*N*-dimethylformamide containing potassium hydroxide to afford ethyl 2-(3-cyano-6-naphtho[2,1-*d*]furan-2-yl-2-pyridylthio) acetate (**22a**) *via* addition and dehydrochlorination reactions. The IR spectrum of this product showed bands at 2214 (CN) and 1735 (CO) groups. Its ^{1}H NMR spectrum revealed signals at δ = 1.28 (t, 3H, CH_2CH_3), 4.07 (s, 2H, SCH_2), 4.28 (q, 2H, CH_3CH_2) and 7.54-8.25 (m, 9H, ArH's). Further confirmation of the structure of **22a** arose from their cyclization in boiling ethanol containing catalytic amount of piperidine to give the corresponding thieno[2,3-*b*]pyridine **23a** (Scheme 4). The IR spectrum of **23a** showed no bands of the CN function while the bands at 3294, 3201 the new NH_2 group. On the other hand, the ^{1}H NMR spectrum of **23a** revealed absence of

Scheme 3



signal of the -SCH_2- group and the presence of signals at δ = 1.34 (t, 3H), 4.24 (q, 2H), 6.63 (s, br., 2H) and 7.57-8.69 (m, 9H). The above findings proved that the CN and the –SCH_2- groups were both involved in the cyclization step leading to **23a**.

Similarly, compound **20** reacted also with chloroacetone to afford 6-naptho[1,2-*d*]furan-2yl-2-(2-oxopropylthio)-pyridine-3-carbonitrile **22b**. The reaction seemed to proceed through dehydrochlorination to give **22b**, which underwent cyclization *via* addition of the SCH_2- hydrogens to the nitrile function to give **23b**. IR, ^{1}H NMR, and elemental analyses were the basis on which the structure of **23b** was established (Tables 1 and 2).

Similarly, compound **20** reacted with chloroacetonitrile to give 2-(cyanomethylthio)-6-naphtho[1,2-*d*]furn-2-oylpyridine-3-carbonitrile (**22c**). Compounds **22c** was converted to 3-amino–6-naphtho[1,2-*d*]furan-2-ylthieno[2,3-*b*]pyridine-2-carbonitrile (**23c**) by boiling in ethanol containing catalytical amount of piperidine (Tables 1 and 2). Compound **23c** reacted with each of formic acid and formamide to give the corresponding 7-naphtho[1,2-*d*]furan-2-yl-3-pyrimidino[4',5':4,5]thieno-[2,3-*b*]pyridine-4-one (**24a**) and 7-naphtho[1,2-*d*]furan-2-yl-3-pyrimidino[4',5':4,5]thieno[2,3-*b*]pyridine-4-ylamine (**24b**), respectively (Scheme 4). IR spectrum of **24a** revealed band at 1674(CO) and IR spectrum of **24b** revealed bands at 3340, 3232 (NH_2).

Hydrazonoyl bromide **4h** with the appropriate *N*-arylmaleimide [21] **25a-d** was refluxed in toluene containing triethylamine yielded 5-aryl-3-naphtho[1,2-*d*]furan-2-ylcarbonyl)-1-phenyl-3a,6a-dihydro-1*H*-pyrrolidino[3,4-*d*]pyrazole-4,6-diones **26a-d**, respectively (Scheme 5). IR spectra of **26a-d** revealed bands at 1790-1716 cm^{-1} and 1710-1690 cm^{-1} due to (-CO-NR-CO) [22]. ^{1}H NMR spectrum of **26a** showed

Scheme 4

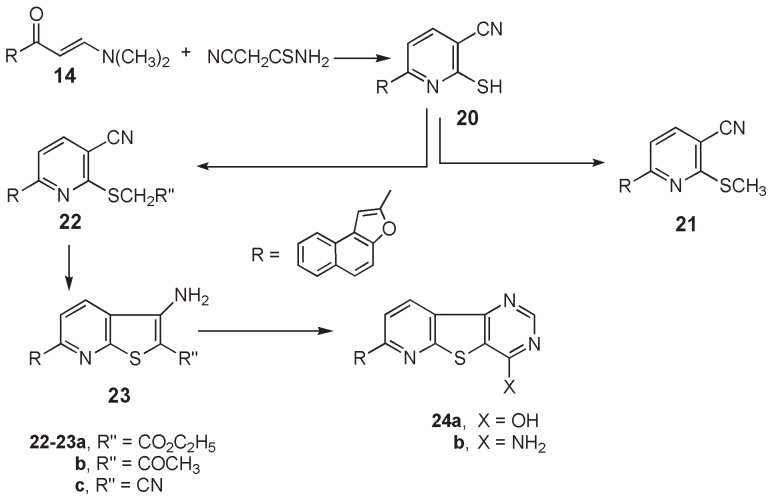


Table 1

Characterization Data of the Newly Synthesized Compounds

Comp. No.	Mp.,°C Solvent	Color Yield %	Mol. Formula Mol.Wt.	Calcd./Found % C	H	N	S
3	180-82	Yellowish brown	$C_{16}H_{14}N_2OS_2$	61.11	4.48	8.90	20.39
	AcOH	78	314.43	61.23	4.35	9.12	20.27
7a	116-17	Yellow	$C_{24}H_{18}N_4O_3S$	65.14	4.10	12.66	7.24
	EtOH	74	442.50	65.07	4.00	12.47	7.42
7b	145-47	Yellow	$C_{25}H_{20}N_4O_3S$	65.77	4.42	12.27	7.02
	AcOH	79	456.52	65.65	4.40	12.35	6.90
7c	190-92	Yellow	$C_{29}H_{21}N_5O_2S$	69.17	4.20	13.91	6.37
	AcOH	70	503.58	69.00	4.35	14.10	6.45
7d	204-206	Yellow	$C_{24}H_{18}N_4O_2S$	67.59	4.25	13.14	7.52
	AcOH	74	426.50	67.72	4.13	12.95	7.61
7e	172-74	Orange	$C_{29}H_{20}N_4O_2S$	71.29	4.13	11.47	6.56
	AcOH	78	488.57	71.30	4.25	11.62	6.67
7f	226-28	Pale brown	$C_{27}H_{18}N_4O_2S_2$	65.57	3.67	11.33	12.97
	AcOH	75	494.59	65.70	3.74	11.28	13.14
7g	261-63	Reddish brown	$C_{33}H_{22}N_4O_2S$	73.59	4.12	10.40	5.95
	DMF	73	538.63	73.82	3.95	10.57	6.22
7h	>300	Reddish brown	$C_{35}H_{22}N_4O_3S$	72.65	3.83	9.68	5.54
	DMF	71	578.65	72.50	3.70	9.82	5.40
11a	215-17	Yellow	$C_{13}H_{14}N_2OS_2$	56.49	4.37	10.13	23.20
	Dioxan	78	276.38	56.60	4.30	9.85	21.92
11b	222-24	Yellow	$C_{19}H_{16}N_2OS_2$	64.74	4.57	7.94	18.19
	Dioxan	73	352.47	64.50	4.32	7.78	17.93
12a	214-15	Yellow	$C_{22}H_{18}N_4O_3S$	63.14	4.34	13.39	7.66
	AcOH	76	418.48	63.00	4.43	13.57	7.82
12b	254-56	Yellow	$C_{26}H_{19}N_5O_2S$	67.08	4.11	15.04	6.89
	AcOH	72	465.54	67.60	4.23	14.82	6.92
12c	212-15	Yellow	$C_{21}H_{18}N_4O_2S$	65.65	4.50	13.92	7.95
	AcOH	75	402.47	65.56	4.27	14.12	8.15
12d	214-15	Yellow	$C_{26}H_{16}N_4O_2S$	64.93	4.15	14.42	8.25
	AcOH	74	388.45	64.70	3.90	14.21	8.10
12e	262-65	Yellow	$C_{24}H_{16}N_4O_2S_2$	63.14	3.53	12.27	14.05
	AcOH	69	456.55	63.10	3.30	12.40	13.92
12f	220-23	Brown	$C_{30}H_{20}N_4O_2S$	71.98	4.03	11.19	6.41
	AcOH	74	500.58	72.10	3.90	11.00	6.55
12g	212-14	Brown	$C_{32}H_{20}N_4O_3S$	71.10	3.73	10.36	5.93
	AcOH	78	540.61	71.20	3.82	10.50	5.80
12h	222-25	Orange	$C_{22}H_{18}N_4O_2S$	65.65	4.51	13.92	7.97
	AcOH	71	402.48	65.40	4.70	13.82	8.10
14	207-208	Yellow	$C_{17}H_{15}NO_2$	76.96	5.69	5.27	
	AcOH	74	265.31	76.85	5.72	5.41	
17a	190-92	Pale yellow	$C_{24}H_{16}N_2O_4$	72.71	4.06	7.06	
	EtOH	68	396.40	72.65	3.90	7.12	
17b	135-36	Pale yellow	$C_{25}H_{18}N_2O_4$	73.16	4.42	6.82	
	EtOH	70	410.43	73.06	4.23	6.90	
17c	217-18	Pale yellow	$C_{29}H_{19}N_3O_3$	76.13	4.18	9.18	
	EtOH	67	457.49	76.34	4.22	9.21	
17d	188-90	Pale yellow	$C_{24}H_{16}N_2O_3$	75.77	4.23	7.36	
	EtOH	61	380.40	75.87	4.15	7.24	
17e	174-76	Pale yellow	$C_{29}H_{18}N_2O_3$	78.72	4.10	6.33	
	EtOH	70	442.47	78.62	3.95	6.15	
17f	205-207	Pale brown	$C_{27}H_{16}N_2O_3S$	72.31	3.59	6.24	7.14
	EtOH	59	448.50	72.43	3.69	6.40	7.10
17g	192-94	Yellowish brown	$C_{33}H_{20}N_2O_3$	80.47	4.09	5.68	
	AcOH	70	492.53	80.52	4.10	5.80	
17h	240-42	Brown	$C_{35}H_{20}N_2O_4$	78.93	3.78	5.26	
	AcOH	61	532.55	79.05	3.87	5.30	
19a	>300	Pale yellow	$C_{23}H_{14}N_4O_2$	73.00	3.72	14.80	
	AcOH	57	378.39	73.28	3.95	14.50	
19b	218-20	Yellow	$C_{24}H_{16}N_4O$	76.58	4.28	14.88	
	AcOH	63	376.42	76.72	4.17	14.71	
19c	250-52	Yellow	$C_{29}H_{18}N_4O$	79.43	4.13	12.77	
	AcOH	68	438.49	79.20	3.90	12.57	

Table 1 (Continued)

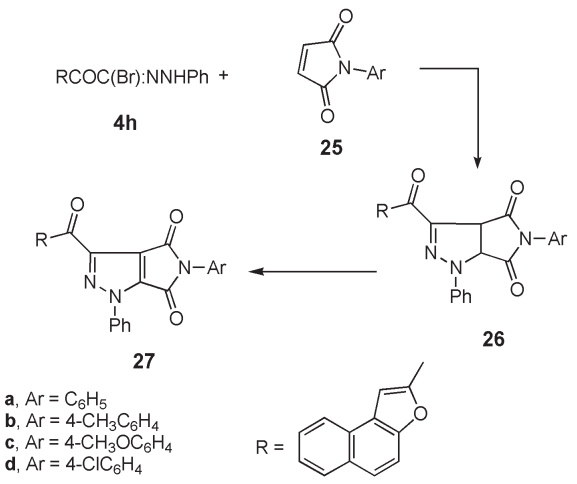
Comp. No.	Mp.,°C Solvent	Color Yield %	Mol. Formula Mol.Wt.	Calcd./Found % C	H	N	S
19d	244-46	Orange	$C_{27}H_{16}N_4O$	72.95	3.62	12.60	7.21
	AcOH	70	444.51	73.10	3.43	12.58	7.35
19e	250-52	Orange	$C_{33}H_{20}N_4O$	81.13	4.12	11.46	
	AcOH	62	488.55	81.00	4.23	11.58	
19f	>300	Reddish Orange	$C_{35}H_{20}N_4O_2$	79.53	3.18	10.59	
	DMF	59	528.57	79.35	3.08	10.45	
20	242-5	Brown	$C_{18}H_{10}N_2OS$	71.51	3.33	9.27	10.60
	EtOH	61	302.36	71.43	3.12	9.10	10.42
21	220-22	Brown	$C_{19}H_{12}N_2OS$	72.13	3.82	8.85	10.13
	AcOH	58	316.38	72.00	4.05	8.75	10.25
22a	188-90	Brown	$C_{22}H_{16}N_2O_3S$	68.03	4.15	7.21	8.25
	AcOH	50	388.45	67.91	4.20	7.40	8.12
22b	204-206	Brown	$C_{21}H_{14}N_2O_2S$	70.37	3.93	7.82	8.95
	AcOH	51	358.42	70.10	4.10	7.90	9.20
22c	245-47	Brown	$C_{20}H_{11}N_3OS$	70.37	3.25	12.31	9.39
	AcOH	40	341.39	70.45	3.40	12.10	9.31
23a	281-83	Brown	$C_{22}H_{16}N_2O_3S$	68.03	4.15	7.21	8.25
	AcOH	51	388.45	68.11	4.00	7.30	8.10
23b	291-93	Brown	$C_{21}H_{14}N_2O_2S$	70.37	3.93	7.82	8.95
	AcOH	49	358.42	70.40	4.20	8.00	9.20
23c	> 300	Brown	$C_{20}H_{11}N_3OS$	70.37	3.25	12.31	9.39
	DMF	41	341.39	70.25	3.10	12.40	9.50
24a	> 300	Pale brown	$C_{21}H_{11}N_3O_2S$	68.28	3.00	11.38	8.68
	DMF	47	369.40	68.40	2.89	11.10	8.80
24b	> 300	Pale brown	$C_{21}H_{12}N_4OS$	68.46	3.28	15.21	8.70
	DMF	44	368.42	68.60	3.14	14.94	8.92
26a	288-90	Yellow	$C_{30}H_{19}N_3O_4$	74.22	3.94	8.66	
	AcOH	64	485.50	74.10	4.20	8.75	
26b	284-86	Yellow	$C_{31}H_{21}N_3O_4$	74.54	4.24	8.41	
	AcOH	61	499.53	74.52	4.10	8.34	
26c	280-81	Yellow	$C_{31}H_{21}N_3O_5$	72.22	4.11	8.15	
	AcOH	58	515.53	72.10	4.10	8.20	
26d	302-304	Yellow	$C_{30}H_{18}Cl\,N_3O_4$	69.30	3.49	8.08	
	AcOH	49	519.94	69.45	3.20	8.12	
27a	266-68	Yellow	$C_{30}H_{17}N_3O_4$	74.53	3.54	8.69	
	DMF	61	483.48	74.50	3.45	8.57	
27b	282-84	Yellow	$C_{31}H_{19}N_3O_4$	74.84	3.85	8.45	
	DMF	57	497.51	74.92	3.90	8.52	
27c	282-84	Yellow	$C_{31}H_{19}N_3O_5$	72.51	3.73	8.18	
	DMF	54	513.51	72.43	3.90	8.10	
27d	>300	Yellow	$C_{30}H_{16}Cl\,N_3O_4$	69.57	3.11	8.11	
	DMF	46	517.93	69.75	3.00	8.20	

Table 2

^{1}H NMR Spectra of some Newly Synthesized Compounds

Compound No.	^{1}H NMR (δ ppm)
7a	2.54 (s, 3H), 3.78 (s, 3H), 7.26-8.16 (m, 12H).
7c	2.54 (s, 3H), 7.26-8.16 (m, 17H), 8.45 (s, br., 1H).
7d	2.54(s, 3H), 2.65 (s, 3H), 7.26-8.20 (m, 12H).
12a	1.40 (t, 3H), 4.45 (q, 2H), 7.26-7.97 (m, 11H), 9.42 (s, 1H), 12.25 (s, br., 1H)
12c	2.58 (s, 3H), 7.19-8.10 (m, 11H), 9.41 (s, 1H), 12.21 (s, 1H).
12g	7.18-9.22 (m, 18H), 11.04 (s, 1H), 13.35 (s, 1H).
17b	1.13 (t, 3H), 4.23 (q, 2H), 7.45-8.21 (m, 12H), 8.57 (s, 1H).
17d	2.75 (s, 3H), 7.41-8.15 (m, 12H), 8.45 (s, 1H).
19b	2.99 (s, 3H), 7.50-8.27 (m, 12H), 9.01 (s, 1H).
19c	7.09-8.22 (m, 16H), 8.28 (s, 1H), 9.03 (s, 1H).
22b	2.42 (s, 3H), 4.04 (s, 2H), 7.45-8.28 (m, 9H), 9.13 (s, 1H).
23b	2.49 (s, 3H), 6.65 (s, br., 2H), 7.45-8.28 (m, 9H).
26b	2.39 (s, 3H), 5.36 (d, 1H), 5.56 (d, 1H), 6.91-7.99 (m, 14H), 8.19 (d, 1H), 8.520 (d, 1H).
26c	3.79 (s, 3H), 5.34 (d, 1H), 5.50 (d, 1H), 7.17-7.98 (m, 14H), 8.24 (d, 1H), 8.52 (d, 1H),
26d	5.24 (d, 1H), 5.82 (d, 1H), 7.39-8.08 (m, 14H), 8.52 (d, 1H), 8.76 (s, 1H).
27a	7.11-7.98 (m, 14H), 8.26 (d, 1H), 8.84 (d, 2H).

Scheme 5



signals at δ = 5.36 (d, 1H), 5.53 (d, 1H) and 7.04-8.25 (m, 17H, ArH).

Compound **26a-d** were oxidized in a reaction with *p*-chloranil in boiling xylene to give 5-aryl-3-(naphtha[1,2-*d*]furan-2-ylcarbonyl)-1-phenylpyrrolo[3,4-*d*]pyrazole-4,6-diones **27a-d**, respectively (Scheme 5). Structure of **27** was elucidated by elemental analysis and spectral data. Thus, IR spectrum of **27c** revealed bands at 1789, 1718, 1668 (CO's) and 1621 (C=N). Its ^{1}H NMR spectrum showed signals at 3.75 (s, 3H), 6.98 (d, 2H), 7.52-8.17 (m, 11H), 8.58 (d, 1H), 8.90, (s, 1H), and 9.25 (s, 1H). MS spectrum of **27d** showed m/z = 471 (20%), 366 (25%), 365 (100%), 195 (29.8%), 139 (74.2%), 77 (33.9%). MS spectrum of **27d** showed m/z = 519 (20%), 517 (47.3%), 278 (41%), 280 (13.8%), 195 (70%), 169 (22%), 139 (100%), 77 (79%).

EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300 MHz spectrometer and chemical shifts are expressed in δ units using TMS as an internal reference. Elemental analyses were carried out at the Microanalytical Center of the Cairo University. Hydrazonoyl halides were obtained as previously reported [23-29].

Synthesis of Methyl *N*'-(Naphtho[1,2-*d*]furan-2-ylethylidine)-hydrazine-carbodithioate (**3**) and Alkyl *N*'-(2-Hydroxy-naphthalin-1-ylmethylene)-hydrazinecarbodithioates **11a,b**.

General Method.

Equimolar a mounts of each 1-naphtho[1,2-*d*]furan-2-ylethan-1-one (**1**) or 2-hydroxynaphthalene-1-carboxyaldehyde and the appropriate alkyl hydrazinocarbodithioate (5 mmoles) in 2-propanol (20 ml) was stirred at room temperature for 2 h. The resulting solid was collected and crystallized to give **3, 11a** and **11b**, respectively (Tables 1 and 2).

Synthesis of 5-Substituted 2-Naphtho[1,2-*d*]furan-2-ylethylidene-3-phenyl-1,3,4-thiadiazoles **7a-h** and 5-Substituted 3-Aryl-2-(hydroxynaphthaline-1-ylmethylenehydrazino)-2,3-dihydro-1,3,4-thiadiazoles **12a-h**.

General Method.

Triethylamine (0.5 g (0.75 mL), 5 mmole) was added dropwise with stirring to a mixture of the appropriate methyl carbodithioate **3, 11a** and **11b** and the appropriate hydrazonoyl halides **4b-i** (5 mmoles) in ethanol (20 ml). The resulting solid, which formed after 30 min, was collected and crystallized from acetic acid to give 2,3-dihydrothiadiazoles **7a-h** and **12a-h** in a good yield (Tables 1and 2).

Synthesis of 3-(Dimethylamino)-1-naphtho[1,2-*d*]furan-2-ylprop-2-en-1-one (**14**).

Equimolar a mounts of 1-naphtho[1,2-*d*]furan-2-ylethan-1-one (**1**) and dimethylformamide-dimethylacetal (50 mmoles, each) were refluxed in dry xylene (40 ml) for 4 h. The half of solution was evaporated and then cooled. The resulting solid was collected and crystallized to give **14** (Tables 1 and 2).

Synthesis of 3-Substituted 4-(Naphtho[1,2-*d*]furan-2-ylcarbonyl)-4-phenyl-pyrazoles **17a-h**.

General Method.

Equimolar a mounts of each **14** and the appropriate hydrazonoyl halides **4a-h** (5 mmoles) were refluxed in dry toluene (20 ml) containing triethylamine (0.5 g (0.75 ml), 5 mmoles) for 3 h. The hot solution was filtered and the filtrate was evaporated and triturated with petroleum ether (40-60 °C). The resulting solid was collected and crystallized to give **17a-h**, respectively (Tables 1 and 2).

Synthesis of 7-Substituted 4-Naphtho[1,2-*d*]furan-2-yl-2-phenyl-6-hydropyrazolo[3,4-*d*]pyridazines **19a-f**.

General Method.

An equimolar amount of each of the appropriate pyrazoles **17a-h** (5 mmoles) and hydrazine hydrate (1 ml, 99%) in ethanol (20 ml) was boiled under reflux for 2 h. The resulting solid was collected and crystallized to give pyrazolo[3,4-*d*]pyridazines **19a-f**, respectively (Tables 1 and 2).

Synthesis of 6-Naphtho[1,2-*d*]furan-2-yl-2-sulfanylpyridine-3-carbonitrile (**20**).

Method A.

A mixture of compound **14** (2.65 g, 10 mmoles) and cyanothioacetamide (1 g, 10 mmoles) was refluxed in pyridine (25 ml) for 5 hs, then poured onto ice-cold water and neutralized with 10% hydrochloric acid. The resulting solid was collected and crystallized from ethanol to give **20** (Tables 1 and 2).

Method B.

A mixture of compound **14** (2.65 g, 10 mmole), cyanothioacetamide (1 g, 10 mmoles) and piperidine (0.5 ml) was refluxed in ethanol (20 ml) for 3 h, then poured onto ice-cold water and neutralized with hydrochloric acid (3 drops). The resulting solid was collected and crystallized from ethanol to product identical in all respects (mp., mixed mp. and spectra) with sample obtained in method A.

Synthesis of 2-Methylthio-6-naphtho[1,2-*d*]furan-2-ylpyridine-3-carbonitrile (**21**).

A mixture of 20 (1.5 g, 5 mmoles) and potassium hydroxide (0.28 g, 5 mmoles) in *N*,*N*-dimethylformamide (15 ml) was stirred at room temperature for 6 h. Iodomethane (0.71 g, 5 mmoles) was added to the above solution while stirring. The resulting solid was collected and crystallized to afford **21** (Tables 1 and 2).

Synthesis of Thieno[2,3-*b*]pyridines **23a-c**.

A mixture of **20** (1.5 g, 5 mmoles) and potassium hydroxide (0.28 g, 5 mmoles) in *N*,*N*-dimethylformamide (15 ml) was stirred at room temperature for 6 h. An appropriate quantity of ethyl chloroacetate, chloroacetone, or chloroacetonitrile, (5 mmoles) was added to above solution while stirring. The reaction mixture was stirred for 3 h; the resulting solid was collected and crystallized to afford **22a-c**, respectively (Tables 1 and 2). An appropriate quantity of **22a-c** (0.5 g) was refluxed in ethanol (15 ml) containing piperidine (3 drops) under reflux for 2 h. The solid formed while boiling was collected and crystallized to give **23a-c**, respectively (Tables 1 and 2).

Synthesis of 7-Naphtho[1,2-*d*]furan-2-yl-3-hydropyrimidino-[4',5':4,5]thieno[2,3-*b*]pyridine-4-one (**24a**) and 7-Naphtho[1,2-*d*]-furan-2-yl-3-hydropyrimidino-[4',5':4,5]thieno[2,3-*b*]pyridine-4-ylamine (**24b**).

A mixture of **23c** (1.7 g, 5 mmoles) and formic acid (99%) or formamide (5 ml) in *N*,*N*-dimethylformamide (10 ml) was refluxed for 5 h. The reaction mixture was poured onto crushed ice (20 g). The resulting solid was collected and crystallized to give **24a** and **24b** (Tables 1 and 2).

Synthesis of 5-Aryl-3-naphtho[1,2-*d*]furan-2-ylcarbonyl)-1-phenyl-3a,6a-dihydro-1*H*-pyrrolidino[4,3-*d*]pyrazole-4,6-diones **26a-d**.

General Method.

Equimolar amounts of hydrazonoyl bromide **4h** and appropriate *N*-arylmalemide **25a-d** (5 mmoles) were refluxed in dry toluene (25 ml) containing triethylamine for 3 h. The hot solution was filtered and the filtrate was evaporated and triturated with petroleum ether (40-60 °C). The resulting solid was collected and crystallized from acetic acid to give **26a-d**, respectively (Tables 1 and 2).

Synthesis of 5-Aryl-3-(naphtha[1,2-*d*]furan-2-ylcarbonyl)-1-phenylpyrrolo[4,3-*d*]pyrazole-4,6-diones **27a-d**.

General Method.

Equimolar amounts of the appropriate **26a-d** and *p*-chloranil (5 mmoles each) in xylene (25 ml) was refluxed for 48 h. The reaction mixture was cooled, washed with sodium hydroxide (0.1 *N*, 50 ml x 3) and then with water. The solution was evaporated and triturated with petroleum ether (40-60 °C). The resulting solid was collected and crystallized from acetic acid to give **27a-d**, respectively (Tables 1 and 2).

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