A New Approach for the Synthesis of Some Pyrazolo [5,1-*c*]triazines and Pyrazolo[1,5-*a*]pyrimidines Containing Naphtofuran Moiety

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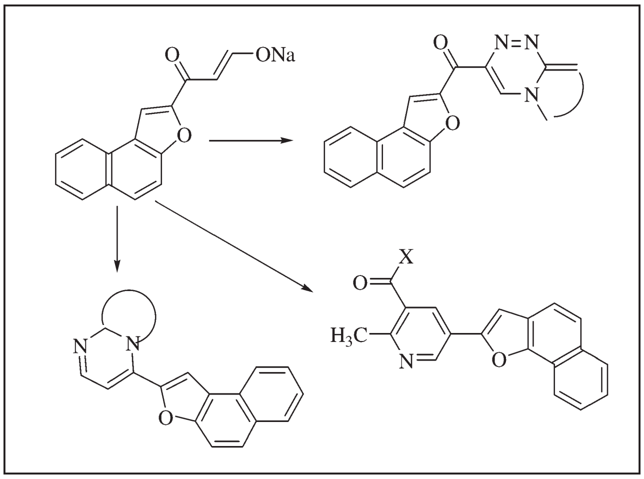

Naphtho[2,1-*b*]furan-2-yl)(8-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)methanone, ([1,2,4]triazolo[3, 4-*c*][1,2,4]triazin-6-yl)(naphtho[2,1-*b*]furan-2-yl)methanone, benzo[4,5]imidazo[2,1-*c*][1,2,4]triazin-3-yl-naphtho[2,1-*b*]furan-2-yl-methanone, 5-(naphtho[2,1-*b*]furan-2-yl)pyrazolo[1,5-*a*]pyrimidine, 7-(naphtho[2,1-b]furan-2-yl)-[1,2,4]triazolo[4,3-a]pyrimidine, 2-naphtho[2,1-*b*]furan-2-yl-benzo[4,5]imidazo[1, 2-*a*]pyrimidine, pyridine, and pyrazole derivatives are synthesized from sodium salt of 5-hydroxy-1-naphtho[2,1-*b*]furan-2-ylpropenone and various reagents. The newly synthesized compounds were elucidated by elemental analysis, spectral data, chemical transformation, and alternative synthetic route whenever possible.

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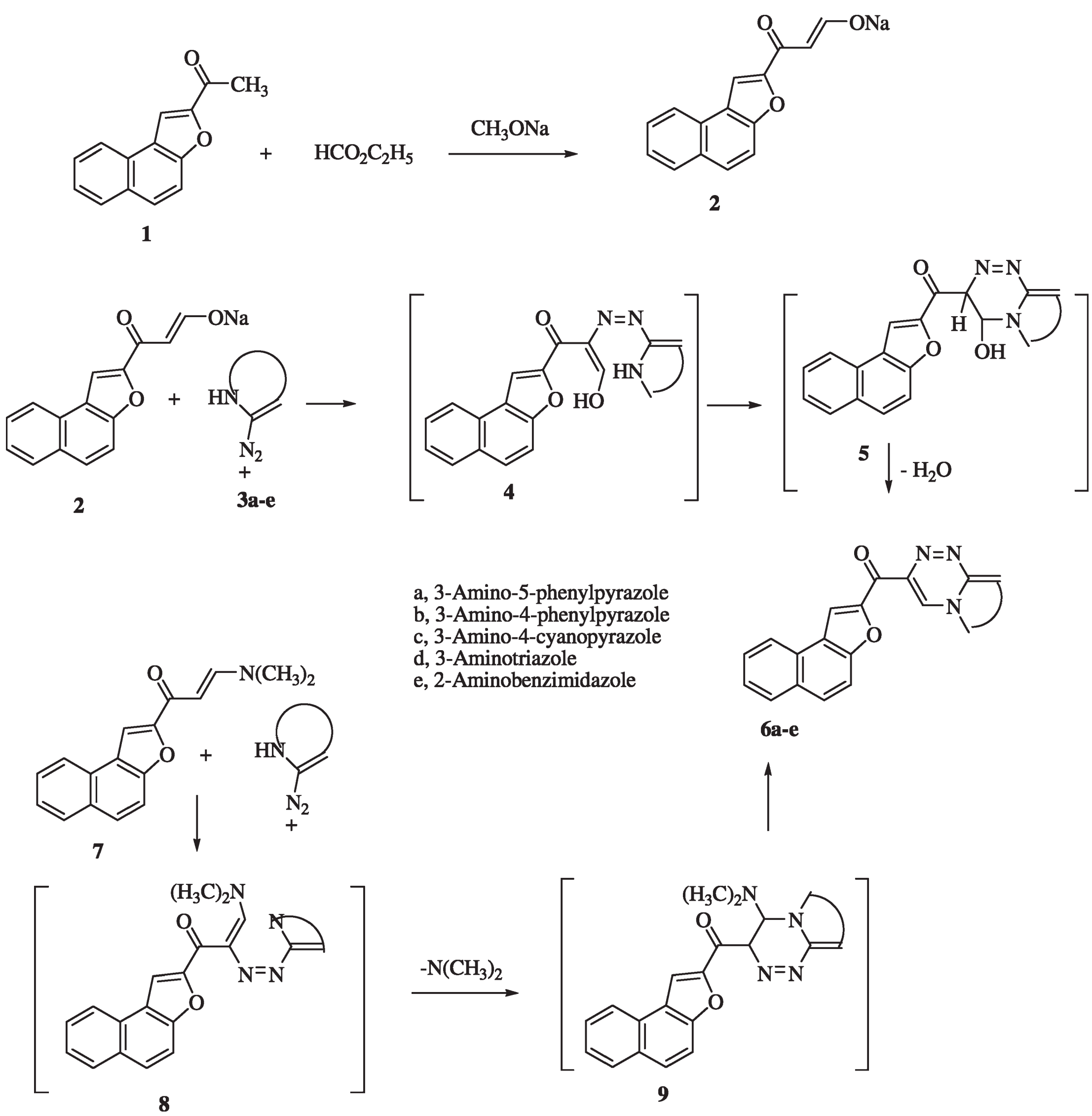
INTRODUCTION

The considerable biological and medicinal activities of pyrazolotriazines and triazolotriazines, as adenine analogues, antagonists, antischistosomal, and antitumor agents [1–3] have stimulated recent interest in the synthesis of these ring systems. Pyrazolo[1,5-*a*] pyrimidines are purine analogues and as such have useful properties as antimetabolites in purine biochemical reactions. Compounds of this class have attracted wide pharmaceutical interest because their antitrypanisommal activity, [4] antischistosomal activity [5], activity as HMG-CoA reductase inhibitors [6], COX-2 selective inhibitors [7], AMP phosphodiesterase inhibtors [8], KDR kinas inhibitors [9], selective peripheral benzodiazepine receptor ligands [10], and as antianxiety agents [11]. Recently other pharmaceutical activity has been reported, for example, as an agent for the treatment of sleep disorders [12] and as an oncological agent [8,13]. The show examples highlight the high level of interest in variously substituted pyrazolo[1,5-*a*]pyrimidines and their modified analogues there is a wide range of methods available for the synthesis of pyrazolo[1,5-*a*]pyrimidines [14]. In continuation of our interest in the synthesis of heterocycles [15–19], we report herein, a convenient method for the synthesis of pyrazolo[5,1-*c*]triazines, pyrazolo[1,5-*a*]pyrimidines, and pyridine containing naphthofuran moiety as antimicrobial agents.

RESULTS AND DISCUSSION

Treatment of the diazotized 3-amino-5-phenylpyrazole (**3a**) with sodium salt of 5-hydroxy-1-naphtho[2,1-*b*]furan-2-ylpropenone (**2**), which prepared from 1-naphtho[2,1-*b*]furan-2-ylethanone and ethyl formate in

Scheme 1

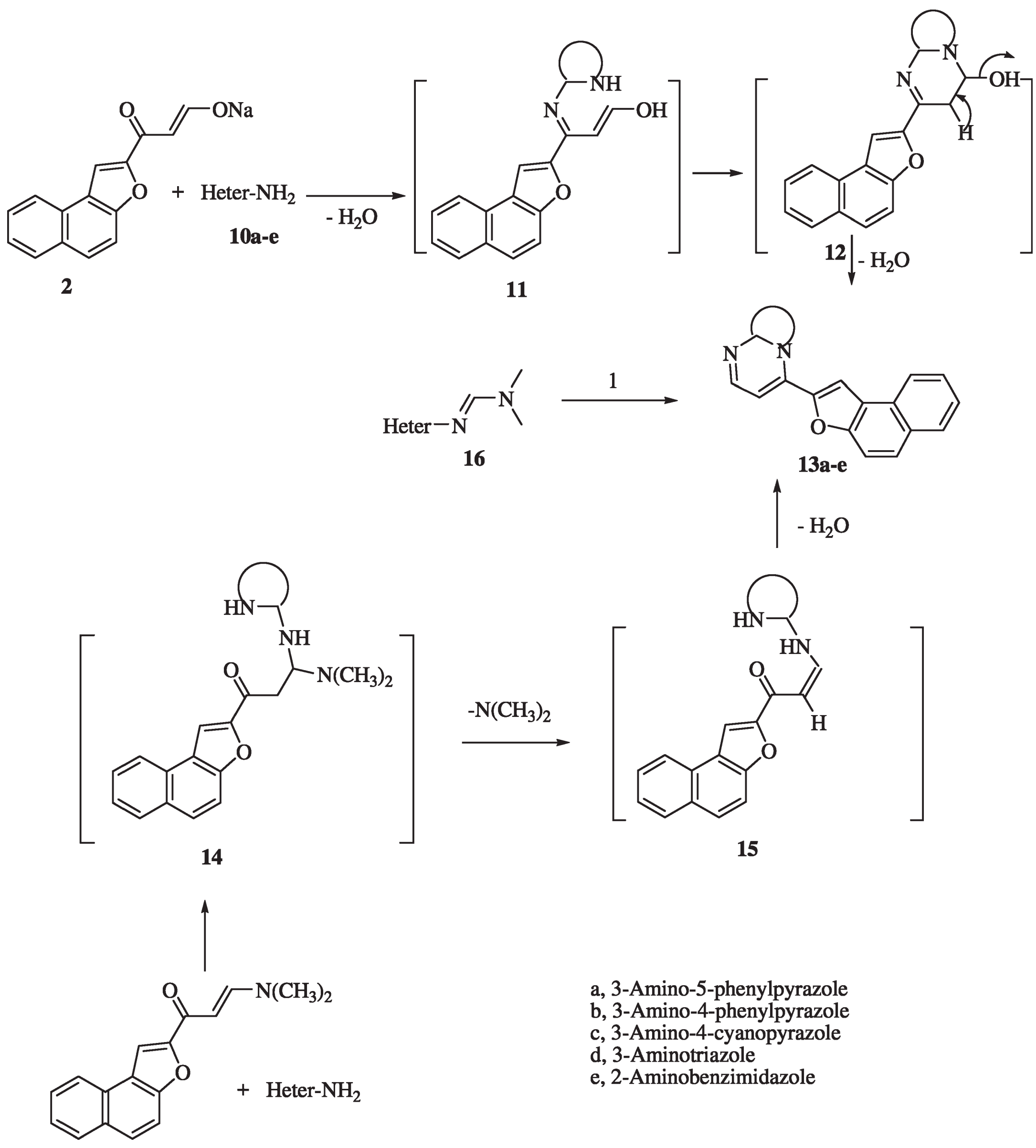


presence of sodium methoxide, in ethanolic sodium acetate solution gave (naphtho[2,1-*b*]furan-2-yl)(7-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)methanone (**6a**) in good yield (Scheme 1). Structure **6a** was elucidated by elemental analysis, spectral data and alternative synthetic route. The formation of **6a** accorded via coupling diazonium chloride **3a** to **2** to form the intermediate **4** which converted to **5**. The later afforded the final product **6** through elimination of one molecule of water. Meanwhile, treatment of 3-dimethylamino-1-naphtho[2,1-*b*]furan-2-ylpropenone [20] (**7**) with **3a** in ethanolic sodium acetate as buffer solution gave product identical in all respects mp., mixed mp., and spectra with **6a** (Scheme 1). Analogously, treatment of the appropriate diazonium salt **3b-e** with **2** in ethanolic sodium acetate afforded (naphtho[2,1-*b*]furan-2-yl)(8-phenylpyrazolo[5,1-*c*][1,2,4]triazin-3-yl)methanone (**6b**), 3-(naphtho[2,1-*b*]furan-2-carbonyl)-pyrazolo[5,1-*c*][1,2,4] triazine-8-carbonitrile (**6c**), ([1,2,4]triazolo[3,4-*c*][1,2,4] triazin-6-yl)(naphtho[2,1-*b*]furan-2-yl)methanone (**6d**), and benzo[4,5]imidazo[2,1-*c*][1,2,4]triazin-3-yl-naphtho [2,1-*b*]furan-2-yl-methanone (**6e**), respectively.

On the other hand, treatment of **2** with 3-amino-5-phenylpyrazole (**10a**) in piperidenium acetate yielded 7-naphtho[2,1-*b*]furan-2-yl-2-phenylpyrazolo[1,5-*a*]pyrimidine (**13a**). The structure **13a** was established by elemental analysis, spectral data, and alternative synthetic route. Thus, treatment of **7** with **3a** in boiling acetic acid containing ammonium acetate gave product identical in all aspects (mp., mixed mp., and spectra) with **13a** (Scheme 2).

^{1}H NMR spectrum of **13a** revealed multiple band at δ = 7.35–8.55 (m, aromatic protons). The formation of

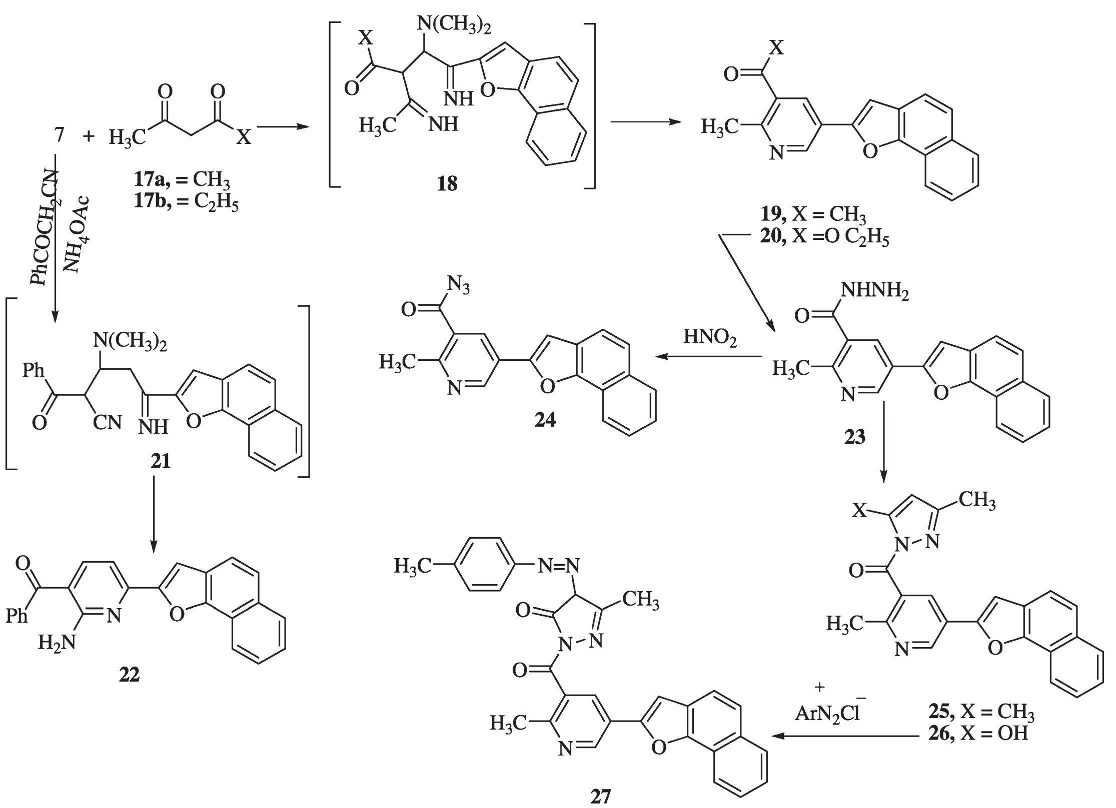
Scheme 2



compounds **13** assumed to take place via an initial Michael addition of the exocyclic amino group in compound **7** (or **2**) to the activated double bond in **7** to give the acyclic non-isolable intermediate **14**, which undergo cyclization and aromatization via loss of both dimethylamine and water molecules producing the final isolable products **13a-e**. Although the endocyclic imino group in compounds **10a–e** is the most nucleophilic center, nevertheless, it is the most sterically hindered site [21] as shown in Scheme 2. Structure **13a** was further confirmed *via* an independent synthesis by reacting equimolar amounts of **16** [22] with **1** in ethanol under reflux to provide a product identical in all respects (m.p., thin-layer chromatography, and spectra) with those of the proposed structure **13a**. Analogously, compound **2** was reacted with the appropriate of 3-amino-4-phenylpyrazole (**10b**), 3-amino-4-cyanopyrazole (**10c**), 3-aminotriazole or 2-aminbenzimidazole (**10d**) to give 7-naphtho[2,1-*b*]furan-2-yl-2-phenylpyrazolo[1,5-*a*]pyrimidine (**13b**), 7-naphtho[2,1-*b*]furan-2-yl-pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**13c**), 7-naphtho[2,1-*b*]furan-2-yl-[1,2,4]triazolo[4,3-*a*]pyrimidine (**13d**), and 4-naphtho[2,1-*b*]furan-2-yl-benzo[4,5]imidazo[1,2-*a*]pyrimidine (**13e**), respectively (Scheme 2).

Next, treatment of 3-dimethylamino-1-naphtho[2,1-*b*]furan-2-ylpropenone (**7**) with each of acetylacetone,

Scheme 3



ethyl acetoactate, or benzoylacetonitrile in boiling acetic acid containing ammonium acetate under reflux gave 1-(2-methyl-6-(naphtho[1,2-*b*]furan-2-yl)pyridin-3-yl)ethanone (**19**), ethyl 2-methyl-6-(naphtho[1,2-*b*]furan-2-yl) pyridine-3-carboxylate (**20**), and (2-amino-6-(naphtho [1,2-b]furan-2-yl)pyridin-3-yl)(phenyl)methanone (**22**), respectively (Scheme 3). Compound **20** was reacted with hydrazine hydrate to afford 2-methyl-6-(naphtho[1,2-*b*]furan-2-yl)pyridine-3-carbohydrazide (**23**). The structure of **23** was elucidated by elemental analysis, spectra and chemical transformations. Thus, compound **23** was reacted with each of nitrous acid, acetylacetone, and ethyl acetoacetate to give azido(2-methyl-6-(naphtho[2,1-b]furan-2-yl)pyridin-3-yl)methanone (**24**), (3,5-dimethyl-1*H*-pyrazol-1-yl)(2-methyl-6-(naphtho[2,1-*b*] furan-2-yl)pyridin-3-yl)methanone (**25**) and (5-methyl-2-(2-methyl-6-naphtho[2,1-*b*]furan-2-yl-pyridine-3-carbonyl)-2,4-dihydro-pyrazol-3-one (**26**), respectively. Treatment the compound **26** with 4-methylbenzenediazonium chloride gave the corresponding **27**.

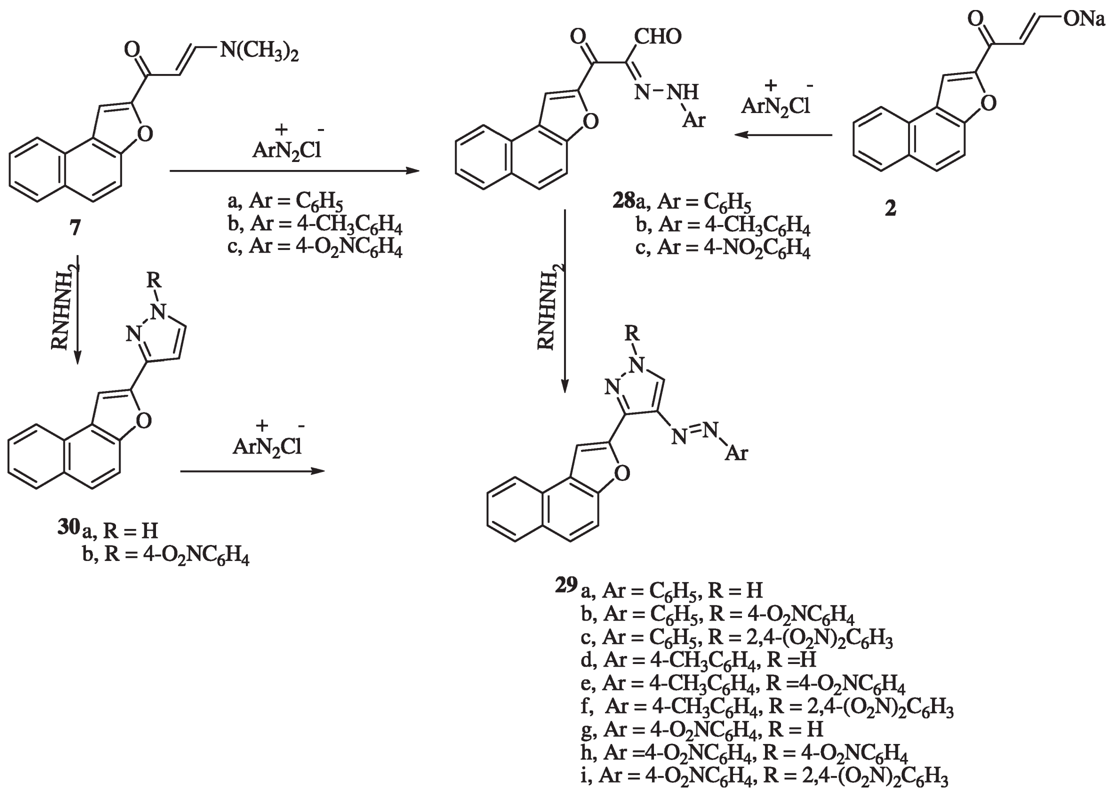
Finally, treatment of **2** or **7** with the benzenediazonium chloride in ethanol containing sodium acetate as a buffer solution yielded 2-(2-phenylhydrazono)-3-(naphtho[2,1-*b*]furan-2-yl)-3-oxopropanal (**28a**). Structure **28**a was confirmed by elemental analysis, spectral data, and chemical transformation. ^{1}H NMR spectrum of **28a** showed signal at $\delta = 7.26$–7.93 (m, 7 H, ArH's), 9.98 (s, 1H, —CHO) and 14.39 (s, br., 1H, NH). Thus, **28a** was reacted with hydrazine hydrate in boiling ethanol under reflux to give 1-(3-(naphtho[2,1-*b*]furan-2-yl)-1*H*-pyrazol-4-yl)-2-phenyldiazene (**29a**) (Scheme 4). Also, **7** reacted with hydrazine hydrate to give 3-(naphtho[2,1-*b*]furan-2-yl)-1*H*-pyrazole (**30a**). Compound **30a** was reacted with benzenediazonium chloride in ethanolic sodium acetate solution to afford product identical in all respect mp., mixed mp., and spectra with **29a**.

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 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 tetramethylsilane as an internal reference. Mass spectra were recorded on a GC-MS QP1000 EX Shimadzu. Elemental analyses were carried out at the Microanalytical Center of the Cairo University.

Sodium salt of 5-hydroxy-1-naphtho[2,1-*b*]furan-2-ylpropenone (2). In three-necked flask (250 mL) take of sodium methoxide (0.054 g, 10 mmoles) and ether (20 mL) and pour over it through separating funnel the 1-(naphtho[2,1-*b*]furan-2-yl)ethanone (**1**) (2.1g, 10 mmoles) with ethyl formate (0.74 g, 10 mmoles) with efficient stirring. The solid product was collected and used directly in the reactions.

Scheme 4



(Naphtho[2,1-b]furan-2-yl)(7-phenylpyrazolo[5,1-c][1,2,4] triazin-3-yl)methanone (6a), (naphtho[2,1-b]furan-2-yl)(8-phenylpyrazolo[5,1-c][1,2,4]triazin-3-yl)methanone (6b), 3-(naphtho[2,1-b]furan-2-carbonyl)-pyrazolo[5,1-c][1,2,4]triazine-8-carbonitrile (6c), ([1,2,4]triazolo[3,4-c][1,2,4]triazin-6-yl)(naphtho[2,1-b]furan-2-yl)methanone (6d), and benzo[4,5]imidazo[2,1-c][1,2,4]triazin-3-yl-naphtho[2,1-b]furan-2-yl-methanone (6e). *Method A*. A solution of the appropriate diazonium salt of heterocyclic amines (3-amino-5-phenylpyrazole (**3a**), 3-amino-4-phenylpyrazole (**3b**), 3-amino-4-cyanopyrazole (**3c**), 3-amino-1,2,4-triazole (**3d**), 2-amino-benzimidazole (**3e**) (5 mmole) was added to a mixture of sodium salt of 5-hydroxy-1-naphtho[2,1-*b*]furan-2-ylpropenone (**2**) (5 mmole), sodium acetate (0.65 g, 5 mmole) in ethanol (30 mL) at 0–5°C while stirring. The resulting solid which formed after 3 h was collected, washed with water, and recrystallized to give **6a-d**.

Method B. A solution of the appropriate diazonium salt of heterocyclic amines (3-amino-5-phenylpyrazole (**3a**), 3-amino-4-phenylpyrazole (**3b**), 3-amino-4-cyanopyrazole (**3c**), 3-amino-1,2,4-triazole (**3d**), 2-amino-benzimidazole (**3e**) **3a–e** (5 mmole) was added to a mixture of 3-dimethylamino-1-naphtho[2,1-*b*]furan-2-ylpropenone (**7**) (1.32 g, 5 mmole), sodium acetate (0.65 g, 5 mmole) in ethanol (30 mL) at 0–5°C while stirring. The resulting solid which formed after 3 h was collected, washed with water, and recrystallized from acetic acid to give products identical in all aspects mp., mixed mp., and spectra with the corresponding obtained in method A.

(Naphtho[2,1-b]furan-2-yl)(7-phenylpyrazolo[5,1-c][1,2,4]triazin-3-yl)methanone (6a). Yellow crystals from AcOH, yield (68%), mp: 272–74°C; IR (KBr): 3059 (CH, aromatic), 1638 (C=O conjugated), 1618 (C=N), and 1586 (C=C); ^{1}H NMR ($CDCl_3$): δ = 7.53–8.35 (m, 12H, ArH's), 9.0 (d, 1H, ArH) and 9.43 (s, 1H, ArH); MS: m/z = 390 (M+, 77.1%), 206 (36.2%), 139 (100%), 77 (77.1%); *Anal*. Calcd. for C24H14N4O_2 (390.11) C, 73.84; H, 3.61; N, 14.35. Found: C, 73.67; H, 3.81; N, 14.51%.

(Naphtho[2,1-b]furan-2-yl)(8-phenylpyrazolo[5,1-c][1,2,4]triazin-3-yl)methanone (6b). Yellow crystals from AcOH, yield (76%), mp: 280–82°C; IR (KBr): 3031 (CH, aromatic), 1638 (C=O conjugated), and 1580 (C=C); ^{1}H NMR ($CDCl_3$): δ = 7.44–8.28 (m, 12H, ArH's), 8.74 (s, 1H, ArH) and 9.40 (s, 1H, ArH); MS: m/z = 390 (M^+, 43%), 195 (20%), 139 (100%), and 115 (27%); Anal. Calcd. for $C_{24}H_{14}N_4O_2$ (390.11) C, 73.84; H, 3.61; N, 14.35. Found: C, 73.62; H, 3.37; N, 14.28%.

3-(Naphtho[2,1-b]furan-2-carbonyl)-pyrazolo[5,1-c][1,2,4]triazine-8-carbonitrile (6c). Yellow crystals from AcOH, yield (68%), mp: 224–62°C; IR (KBr): 3089 (CH, aromatic), 2228 (C≡N) and 1636 (C=O conjugated); ^{1}H NMR ($CDCl_3$): δ = 7.54–8.44 (m, 7H, ArH's), 8.59 (s, 1H, pyrazole H-3) and 8.72 (s, H, ArH); MS: m/z = 315 (M^+, 91%), 205 (56%), 139 (100%) and 63 (28%); Anal. Calcd. for $C_{19}H_9N_5O_2$ (399.31); C, 67.26; H, 2.67; N, 20.64. Found: C, 64.82; H, 2.49; N, 20.48%.

([1,2,4]Triazolo[3,4-c][1,2,4]triazin-6-yl)(naphtho[2,1-b]furan-2-yl)methanone (6d). Buff crystals from EtOH, yield (74%), mp: 219–21°C; IR (KBr): 3055 (CH, aromatic) and 1639 (C=O conjugated); ^{1}H NMR ($CDCl_3$): δ = 6.85 (s, 1H, furan H-3), 7.55–8.05 (m, 6H, ArH's), 8.19 (s, 1H, ArH) and 8.55 (s,1H, 1,2,4-triazine); MS: m/z = 315 (M+, 91.7%), 205

(56%), 139 (100%), 63 (28.2%); *Anal*. Calcd. for $C_{17}H_9N_5O_2$ (315.29), C, 64.76; H, 2.88; N, 22.21. Found: C, 64.82; H, 3.00; N, 22.12.

Benzo[4,5]imidazo[2,1-c][1,2,4]triazin-3-yl-naphtho[2,1-b] furan-2-yl-methanone (6e). Brown crystals from AcOH, yield (68%), mp: 254–56°C; IR (KBr): 3128 (CH, aromatic), 1662 (C═O), 1633 (C═N) and 1585 (C═C); MS: m/z = 363 (M+1, 35%), 328 (23%), 195 (58%), 139 (100%) and 92 (29%); Anal. Calcd. for $C_{22}H_{12}N_4O_2$ (364.36) C, 72.52; H, 3.32; N, 15.38. Found: C, 72.33; H, 3.25; N, 15.53%.

7-(Naphtho[1,2-b]furan-2-yl)-2-phenylpyrazolo[1,5-a]pyrimidine (13a), 7-(naphtho[1,2-b]furan-2-yl)-3-phenylpyrazolo [1,5-a]pyrimidine (13b), 7-(naphtho[1,2-b]furan-2-yl)pyrazolo [1,5-a]pyrimidine-3-carbonitrile (13c), 5-(naphtho[1,2-b]furan-2-yl)-[1,2,4]triazolo[4,3-a]pyrimidine (13d), Naphtho[1,2-b]furan-2-yl-benzo[4,5]imidazo[1,2-a]pyrimidine (13e). *Method A*. A solution of (0.01 mol) sodium salt of 5-hydroxy-1-naphtho[2, 1-*b*]furan-2-ylpropenone (2) (1.3 g, 0.01 mol), the appropriate of amino pyrazoles, aminotriazole or 2-aminobenzimidazole (0.01 mol), and piperidine acetate (1 mL) in H_2O (3 mL) was refluxed for 15 min. Acetic acid (1.5 mL) was added to the hot solution. The solid product was filtered off and recrystallized from the proper solvent.

Method B. A mixture of the appropriate **10a–e** (5 mmole), 3-dimethylamino-1-naphtho[2,1-*b*]furan-2-ylpropenone (**7**) (1.32 g, 5 mmole), ammonium acetate (0.37 g, 5 mmole) in acetic acid (30 mL) was reflux for 4 h. The resulting solid which formed was collected and recrystallized from acetic acid to give products identical in all aspects mp., mixed mp. And spectra with the corresponding obtained in method A.

7-(Naphtho[2,1-b]furan-2-yl)-2-phenylpyrazolo[1,5-a]pyrimidine (13a). Yellow crystals from AcOH, yield (78%), mp: 252–53°C; IR (KBr): 3043 (CH, aromatic), 1613 (C═N) and 1586 (C═C); ^{1}H NMR ($CDCl_3$): δ = 7.09–8.52 (m, 14H, ArH's) and 9.11 (s, 1H, ArH); MS: m/z = 361 (M^+, 84%), 181 (10%), 163 (14%), 77 (100%) and 51 (81%); Anal. Calcd. for $C_{24}H_{15}N_3O$ (361.4) C, 79.76; H, 4.18; N, 11.63. Found: C, 79.72; H, 4.22; N, 11.65%.

7-(Naphtho[2,1-b]furan-2-yl)-3-phenylpyrazolo[1,5-a]pyrimidine (13b). Orange crystals from Dioxan, yield (66%), mp: 252–54°C; IR (KBr): 3055 (CH, aromatic), 1614 (C═N) and 1585 (C═C); ^{1}H NMR (dimethyl sulfoxide [DMSO]-d_6): δ = 7.50–8.27 (m, 14H, ArH's) and 9.17 (s, 1H, ArH); MS: m/z = 361 (M^+, 84.5%), 332 (5.2%), 181 (10.2%), 163 (14.5%), 77 (100%), 51 (81.4.2%); Anal. Calcd. for $C_{24}H_{15}N_3O$ (361.4) C, 79.76; H, 4.18; N, 11.63. Found: C, 79.61; H, 4.11; N, 11.39%.

7-(Naphtho[2,1-b]furan-2-yl)pyrazolo[1,5-a]pyrimidine-3-car bonitrile (13c). Orange crystals from Dioxan, yield (54%), mp: 264–66°C; IR (KBr): 3049 (CH, aromatic), 2233 (CN), 1612 (C═N); ^{1}H NMR ($CDCl_3$): δ = 6.95 (s, 1H, Pyrazole H-5), 7.35 (s, 1H, furan H-3), 7.58–8.05 (m, 7H, ArH's, pyrimidine H-5), 9.48 (d, 1H, *J* = 8 Hz, pyrimidine H-4), 9.04 (s, 1H, pyrazole H-5); MS: m/z = 310 (M+, 100.5%), 155 (37.5%), 141 (56.3%), 74 (50%), 63 (62.5%); *Anal*. Calcd. for $C_{19}H_{10}N_4O$ (310.31) C, 73.54; H, 3.25; N, 18.06. Found: C, 73.27; H, 3.34; N, 18.24%.

7-(Naphtho[2,l-b]furan-2-yl)-[l,2,4]triazolo[4,3-a]pyrimidine (13d). Yellow crystals from AcOH, yield (75%), mp: 255–57°C; IR (KBr): 055 (CH, aromatic), 1614 (C═N), and 1584 (C═C); ^{1}H NMR ($CDCl_3$): δ = 7.56–8.27 (m, 7H, ArH's), 8.67 (s, 1H, triazole H-2), 8.58 (d, 1H, pyrimidine H-4) and 9.00 (d, 1H, pyrimidine H-5); MS: m/z = 286 (M^+, 100%), 163 (25%), 129 (26%), 88 (36%) and 53 (67%); Anal. Calcd. for $C_{17}H_{10}N_4O$ (286.29) C, 71.32; H, 3.52; N, 19.75. Found: C, 70.90; H, 3.71; N, 19.92%.

4-Naphtho[2,1-b]furan-2-yl-benzo[4,5]imidazo[1,2-a]pyrimidine (13e). Yellow crystals from dioxan, yield (79%), mp: 239–41°C; IR (KBr): 3051 (CH, aromatic), 1634 (C═N), and 1586 (C═C); ^{1}H NMR ($CDCl_3$): δ = 7.52–8.58 (m, 12H, ArH's) and 951 (d, 1H, pyrimidine H-4); Anal. Calcd. for $C_{22}H_{13}N_3O$ (335.36) C, 78;79 H, 3.91; N, 12.53. Found: C, 78.59; H, 4.20; N, 12.34%.

1-(2-Methyl-6-(naphtho[2,1-b]furan-2-yl)pyridin-3-yl)ethanone (19), ethyl 2-methyl-6-(naphtho[2,1-b]furan-2-yl)pyridine-3-carboxylate (20) and 6-(2-amino-6-(naphtho[1, 2-b]furan-2-yl)pyridin-3-yl)(phenyl)methanone (22). A mixture of the appropriate of acetylacetone, ethyl acetoacetate, or benzoylacetonitrile (5 mmole), 3-dimethylamino-1-naphtho[2,1-*b*]furan-2-ylpropenone (7) (1.32 g, 5 mmole), ammonium acetate (0.37 g, 5 mmole) in acetic acid (30 mL) was reflux for 4 h. The resulting solid which formed was collected and recrystallized from ethanol to give **19**, **20**, and **22**.

1-(2-Methyl-6-(naphtho[2,1-b]furan-2-yl)pyridin-3-yl)ethanone (19). Brown crystals from diluted AcOH, yield (54%), mp: 177–78°C; IR (KBr): 3051 (CH, aromatic), 1682 (C═O conjugated), 1636 (C═N), and 1594 (C═C); ^{1}H NMR ($CDCl_3$): δ = 2.64 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), and 7.27–8.26 (m, 9H, ArH's); MS: m/z = 301 (M^+, 100%), 286 (53%), 258 (16%), 240 (19%), 202 (22%), 163 (16%); Anal. Calcd. for $C_{20}H_{15}NO_2$ (301.34) C, 79.72; H, 5.02; N, 4.65. Found: C, 79.63; H, 4.91; N, 4.41%.

Ethyl 2-methyl-5-(naphtho[1,2-b]furan-2-yl)pyridine-3-carboxylate (20). Brown crystals from diluted AcOH, yield (68%), mp: 141–42°C; IR (KBr): 3051 (CH, aromatic), 1716 (C═O), 1640 (C═N) and 1580 (C═C); ^{1}H NMR ($CDCl_3$): δ = 1.42 (t, 3H, $-CH_2CH_3$), 2.97 (s, 3H, pyridine CH_3), 4.39 (q, 2H, $-CH_2CH_3$) and 7.27–8.34 (m, 9H, ArH's); MS: m/z = 331 (M^+, 100%), 303 (68%), 139 (20%), 88 (22%) and 63 (20%); Anal. Calcd. for $C_{21}H_{17}NO_3$ (331.36) C, 76.12; H, 5.17; N, 4.23. Found: C, 76.27; H, 5.24; N, 4.18%.

(2-Amino-6-(naphtho[1,2-b]furan-2-yl)pyridin-3-yl)(phenyl) methanone (22). Yellow crystals (diluted acetic acid), mp: 234–36°C; ^{1}H NMR ($CDCl_3$): δ = 7.29–8.25 (m, 15H, ArH's) and 9.49 (s, 1H, pyridine H-6); IR (KBr), (cm^{-1}) = 3483 and 3342 (NH_2), 3051 (CH, aromatic), 1664 (C═O amide), and 1585 (C═C); MS, *m/z* (%) = 364 (M^+, 57%), 205 (16%), 139 (13%), and 77 (100%); Anal. Calcd. For $C_{24}H_{16}N_2O_2$ requires (364.4): C, 79.11; H, 4.43; N, 7.69. Found: C, 79.33; H, 4.21; N, 7.75%.

2-Methyl-6-(naphtho[2,1-b]furan-2-yl)pyridine-3-carbohydrazide (23). Equimolar amounts of ethyl 2-methyl-6-naphtho[1,2-*b*]furan-2-ylpyridine-3-carboxylate (**20**) and hydrazine hydrate (5 mmol for each) in ethanol (10 mL) were refluxed for 5 h. The resulting solid, was cooled and recrystallized to give **23**, as pale yellow crystals (diluted acetic acid), mp: 258–60°C; IR (KBr), (cm^{-1}) = 3289 and 3215 (NH_2 amide), 1679 (C═O amide), 1637 (C═N), and 1596 (C═C); MS, *m/z* (%) = 317 (M^+, 36%), 286 (100%), 258 (14.6%), 101 (5.8%); Anal. Calcd. For $C_{19}H_{15}N_3O_2$ requires (317.34): C, 71.91; H, 4.76; N, 13.24. Found: C, 72.07; H, 4.80; N, 13.83%.

Azido(2-methyl-6-(naphtho[2,1-b]furan-2-yl)pyridin-3-yl)methanone (24). To a stirred solution of 2-methyl-5-(naphtho[l, 2-*b*]furan-2-yl)pyridine-3-carbohydrazide (**21**)(5 mmole) in acetic acid (15 mL) at 0–5°C, sodium nitrite was added portion-wise tell effervescence ended. The reaction mixture stirred for 1 h. The resulting solid, was collected, filtered, washed with water, and recrystallized from acetic acid to give the corresponding **22**, as buff crystals, mp: 137–38 °C; ^{1}H NMR ($CDCl_3$): δ = 2.97 (s, 3H, pyridine CH_3) and 7.56–8.26 (m, 9H, ArH's); IR (KBr), (cm^{-1}) = 2136 (azide), 1689 (C=O), 1636 (C=N), and 1595 (C=C); MS, *m/z* (%) = 314 (0.1%), 300 (100%), 150 (12.5%), and 88 (16.7%); Anal. Calcd. For $C_{19}H_{12}N_4O_2$ requires (328.32): C, 69.51; H, 3.68; N, 17.06. Found: C, 69.57; H, 3.96; N, 17.22%.

(3,5-Dimethyl-1*H*-pyrazol-1-yl)(2-methyl-6-(naphtho[2,1-b] furan-2-yl)pyridin-3-yl)methanone (25) and (3-methyl-l*H*-pyrazol-5-one-1-yl)(2-methyl-5-(naphtho[1,2-*b*]furan-2-yl)pyridin-3-yl)methanone (26). ***General procedure.*** Equimolar amounts of 2-methyl-5-(naphtho[l,2-*b*]furan-2-yl)pyridine-3-carbohydrazide (**23**) and acetyl acetone or ethyl acetoacetate (4 mmol for each) in ethanol (10 mL) with two drops of acetic acid were refluxed for 4 h. The resulting solid, so formed, was cooled and recrystallized from diluted acetic acid to give the corresponding **25** and **26**, respectively.

(3,5-Dimethyl-1H-pyrazol-l-yl)(2-methyl-5-(naphtho[l,2-b] furan-2-yl)pyridin-3-yl)methanone (25). This compound was obtained as pale yellow crystals (diluted acetic acid), mp: 213–15 °C; ^{1}H NMR ($CDCl_3$): δ = 0.88 (s, 3H, pyrazole CH_3), 1.83 (s, 3H, pyrazole CH_3), 2.29 (s, 3H, pyridine CH_3), 5.71 (s,1H, pyrazole H-4), 6.88 (s, 1H, furan H-3), and 7.40–8.17 (m, 8H, ArH's); IR (KBr), (cm^{-1}) = 3051 (CH, aromatic), 1698 (C=O), 1630 (C=N), and 1595 (C=C); MS, *m/z* (%) = 381 (M^+, 73%), 286 (100%), 258 (17%), and 139 (7%); Anal. Calcd. For $C_{24}H_{19}N_3O_2$ requires (381,43): C, 75.57; H, 5.02; N, 11.02. Found: C, 75.60; H, 5.15; N, 10.96%.

(3-Methyl-lH-pyrazol-5-one-1-yl)(2-methyl-5-(naphtho[1,2-b] furan-2-yl)pyridin-3-yl)methanone (26). This compound was obtained as yellow crystals (diluted acetic acid), mp: 143–45 °C; ^{1}H NMR ($CDCl_3$): δ = 0.90 (s, 3H, pyrazolin Me), 1.68 (s, 2H, methylene), 2.31 (s, 3H, pyridine Me), 6.89 (s, 1H, furan H-3), and 7.42–8.54 (m, 8H, ArH's); IR (KBr), (cm^{-1}) = 3054 (CH, aromatic), 1722 (C=O), 1663 (CO, pyrazol-3-one), and 1581 (C=C); Anal. Calcd. For $C_{23}H_{17}N_3O_3$ requires (383.4): C, 72.05; H, 4.47; N, 10.96. Found: C, 71.96; H, 4.31; N, 11.17%.

3-Methyl-1-[(2-methyl-6-naphtho[1,2-d]furan-2-yl(3-pyridyl)) carbonyl]-4-{[(4-methylphenyl)amino]azamethylene}-1,2-diazolin-5-one (27). *Method A.* *p*-tolyldiazonium chloride (5 mmole), which is prepared via reaction of p-toluidine (0.5 gm, 5 mmole), hydrochloric acid (3 mL, 6 M), and sodium nitrite (0.37 gm, 5 mmole) at 0–5°C, was added to a mixture of **25** (2.51 gm, 5 mmole) and sodium acetate (0.41 gm, 5 mmole) in ethanol (30 mL) at 0–5°C, while stirring. The reaction mixture was stirred for 3 h. The resulting solid, was collected, washed with water and recrystallized from acetic acid to give **27**.

Method B. A mixture of 23 and ethyl 2-*p*-tolylazo-3-oxo-4-butanoate (5 mmol for each) in ethanol (20 mL) and catalytic amount of acetic acid (2 drops) was refluxed for 3 h. The resulting solid, so formed, was collected and recrystallized from acetic acid to give product identical in all aspects with 27.

This compound was obtained as brown crystals (acetic acid), mp: 134–36°C; ^{1}H NMR ($CDCl_3$): δ = 0.88 (s, 3H, pyrazoline CH_3), 1.99 (s, 3H, *p*-CH_3), 2.37 (s, 3H, pyridine Me), 6.87 (s, 1H, furan H-3), 7.15–7.86 (m, 12H, ArH's) and 12.89 (s, 1H, NH); IR (KBr): 3039 (CH, aromatic), 1729 (C=O), 1663 (C=O), 1635 (C=N) and 1581 (C=C); MS, *m/z* (%) = 501 (M^+, 25.5%), 286 (100%), 258 (11.8%), and 106 (6%); Anal. Calcd. For $C_{30}H_{23}N_5O_3$ requires (501.54): C, 71.84; H, 4.62; N, 13.96. Found: C, 71.43; H, 4.43; N, 13.46%.

2-(2-Phenylhydrazono)-3-(naphtho[l,2-*b*]furan-2-yl)-3-oxopropanal (28a), 3-(naphtho[2,1-*b*]furan-2-yl)-3-oxo-2-(2-p-tolylhydrazono)propanal (28b) and 3-(naphtho[2,1-*b*]furan-2-yl)-2-(2-(4-nitrophenyl)hydrazono)-3-oxopropanal (28c). A solution of the appropriate arendiazonium chloride (5 mmole) was added to a mixture of 3-dimethylamino-1-naphtho[2,1-*b*]furan-2-ylpropenone (**7**) (1.32 g, 5 mmole), sodium acetate (0.65 g, 5 mmole) in ethanol (30 mL) at 0–5°C while stirring. The resulting solid which formed after 3 h was collected, washed with water and recrystallized to give **28a-c**.

3-(Naphtho[2,1-b]furan-2-yl)-3-oxo-2-(2-phenylhydrazono)-propanal (28a). This compound was obtained as brown crystals (acetic acid), yield (81%), mp: 134–36°C; IR (KBr): 3089 (CH, aromatic), 1645 (C=O conjugated), 1622 (C=N), and 1583 (C=C); ^{1}H NMR ($CDCl_3$): δ = 7.28–7.93 (m, 12H, ArH's), 9.98 (s, 1H, —CHO) and 14.39 (s, br., 1H, NH); MS, *m/z* (%) = 342 (M^+, 16%), 258 (35%), 222 (80%), 139 (100%), and 77 (55%); Anal. Calcd. For $C_{21}H_{14}N_2O_3$ requires (342.35): C, 73.68; H, 4.12; N, 8.18. Found: C, 73.49; H, 3.99; N, 7.92%.

3-(Naphtho[2,1-b]furan-2-yl)-3-oxo-2-(2-p-tolylhydrazono)-propanal (28b). This compound was obtained as yellow crystals (ethanol), yield (83%), mp: 190–91°C; IR (KBr): 3056 (CH, aromatic), 1640 (C=O conjugated), 1616 (C=N), and 1586 (C=C); ^{1}H NMR ($CDCl_3$): δ = 2.42 (s, 3H, CH_3), 7.28–7.89 (m, 11H, ArH's), 8.29 (s, 1H, —CHO) and 10.19 (s, 1H, NH); MS, *m/z* (%) = 356 (M^+,15%), 272 (19%), 222 (50%), 139 (100%), and 77 (56%); Anal. Calcd. For $C_{22}H_{16}N_2O_3$ requires (356.37): C, 74.15; H, 4.53; N, 7.86. Found C, 74.53; H, 4.85; N, 7.79%.

3-(Naphtho[2,1-b]furan-2-yl)-2-(2-(4-nitrophenyl)hydrazono)-3-oxopropanal (28c). This compound was obtained as red crystals (acetic acid), yield (78%), mp: 250–52°C; IR (KBr): 3113 (CH, aromatic), 1650 (C=O conjugated), 1618 (C=N), and 1596 (C=C); ^{1}H NMR (DMSO-d_6): δ = 7.67–8.75 (m, 11H, ArH's), 9.77 (s, 1H, —CHO), and 10.07 (s, 1H, NH); MS, *m/z* (%) = 387 (M^+, 10%), 303 (21%), 222 (90%), 139 (100%), and 107 (16%) Anal. Calcd. For $C_{21}H_{13}N_3O_5$ requires (387.35): C, 65.12; H, 3.38; N, 10.85. Found C, 64.81; H, 3.11; N, 11.12%.

1-(3-(Naphtho[2,1-b]furan-2-yl)-1H-pyrazol-4-yl)-2-phenyldiazene 29a–i. A mixture of the appropriate **28a–c** (5 mmole) and the appropriate the appropriate of hydrazine, *p*-nitrophenylhydrazine or 2,4-dinitrophenylhydrazine (5 mmole) (5 mmole) in ethanol (15 mL) was refluxed for 2 h. The resulting solid was collected and recrystallized to give **29a–i**.

Alternative method. A solution of the appropriate arendiazonium chloride (5 mmole) was added to a mixture of the appropriate **30a,b** (5 mmole), sodium acetate (0.65 g, 5 mmole) in ethanol (30 mL) at 0–5°C while stirring. The resulting solid which formed after 3 h was collected, washed with water and recrystallized from acetic acid to give identical in all aspects mp: mixed mp., and spectra with the corresponding obtained **29a–i**.

3-(Naphtho[2,1-b]furan-2-yl)-4-phenyazo-1H-pyrazole (29a). This compound was obtained as brown crystals (acetic acid), yield (76%), mp: 309–10°C; IR (KBr): 3210 (NH), 3045 (CH, aromatic), 1613 (C=N), and 1594 (C=C); ^{1}H NMR $CDCl_3$): δ = 7.41–8.43 (m, 13H, ArH's) and 13.44 (s, 1H, NH); IR (KBr), (cm^{-1}) = 3210 (NH); MS: m/z = 338 (M+, 10.5%), 206 (23.7%), 139 (0.9%), 77 (100%); Anal. Calcd. for $C_{21}H_{14}N_4O$ (338.36) C, 74.54; H, 4.17; N, 16.56. Found: C, 74.42; H, 4.21; N, 16.42.

3-(Naphtho[2,1-b]furan-2-yl)-1-(4-nitrophenyl)-4-(phenyldiazenyl)-1H-pyrazole (29b). This compound was obtained as red crystals (acetic acid) mp: 246–48°C; yield (93%), ^{1}H NMR (DMSO-d_6): δ = 7.32–9.05 (m, 17H, ArH's); IR (KBr): 3085 (CH, aromatic), 1614 (C=N), 1589 (C=C) and 1538 & 1319 (NO_2); Anal. Calcd. For $C_{27}H_{17}N_5O_3$ requires (459.46): C, 70.58; H, 3.73; N, 15.24. Found: C, 70.78; H, 3.58; N, 15.40%.

1-(2,4-Dinitrophenyl)-3-(naphtho[2,1-b]furan-2-yl)-4-(phenyldiazenyl)-1H-pyrazole (29c). This compound was obtained as red crystals (acetic acid), yield (75%), mp: 246–47°C; IR (KBr): 3092 (CH, aromatic), 1625 (C=N), 1602 (C=C), and 1545 & 1322 (NO_2); MS, *m/z* (%) = 506 (M+2, 3.7%), 339 (53.5%), 195 (51.5%), 139 (99.5%) and 77 (100%); Anal. Calcd. For $C_{27}H_{16}N_6O_5$ requires (504.45): C, 64.29; H, 3.20; N, 16.66. Found: C, 64.00; H, 3.30; N, 16.42%.

3-(Naphtho[2,1-b]furan-2-yl)-4-(4-methylphenyl)azo-1H-pyrazole (29d). Red crystals from AcOH, yield (75%), mp: 246–48°C; IR (KBr): 3045 (CH, aromatic), 1627 (C=N), 1514, 1319 (NO_2); ^{1}H NMR $CDCl_3$): δ = 6.98 (s, 1H, furan H-3), 7.39–8.06 (m, 13H, ArH's, and pyrazole H-5), 8.89 (d, 2H, *J* = 12Hz, ArH's); MS: m/z = 459 (M+, 10.5%), 206 (23.7%), 139 (0.9%), 77 (100%); *Anal*. Calcd. for $C_{27}H_{16}NO$ (352.39) C, 74.98; H, 4.58; N, 15.90. Found: C, 75.12; H, 4.71; N, 15.84.

3-(Naphtho[2,1-b]furan-2-yl)-1-(4-nitrophenyl)-4-(p-tolyldiazenyl)-1H-pyrazole (29e). This compound was obtained as red crystals (acetic acid), yield (75%), mp: 212–14°C; IR (KBr): 3089 (CH, aromatic), 1614 (C=N), 1596 (C=C), and 1537 & 1332 (NO_2); MS, *m/z* (%) = 473 (M^+, 0.7%), 353 (62.8%), 195 (72.5%), 139 (100%), and 91 (90.8%); Anal. Calcd. For $C_{28}H_{19}N_5O_3$ requires (473.48): C, 71.03; H, 4.04; N, 14.79. Found: C, 70.81; H, 4.01; N, 14.63%.

1-(2,4-Dinitrophenyl)-3-(naphtho[2,1-b]furan-2-yl)-4-(p-tolyldiazenyl)-1H-pyrazole (29f). This compound was obtained as red crystals (acetic acid), yield (75%), mp: 298–301°C; IR (KBr): 3103 (CH, aromatic), 1617 (C=N), 1594 (C=C) and 1540, 1321 (NO_2); MS, *m/z* (%) = 550 (M+1, 5.6%), 384 (68.9%), 303(13.3%), 195 (45.9%), 139 (100%), 107 (28.6%), and 63 (87.2%); Anal. Calcd. For $C_{28}H_{18}N_6O_5$ requires (518.48): C, 64.86; H, 3.50; N, 16.21. Found: C, 64.93; H, 3.70; N, 16.44%.

1-(3-(Naphtho[2,1-b]furan-2-yl)-1H-pyrazol-4-yl)-2-(4-nitrophenyl)diazene (29g). This compound was obtained as red crystals (acetic acid), yield (75%), mp: 352–55°C; IR (KBr): 3087 (CH, aromatic), 1628 (C=N) and 1599 (C=C); ^{1}H NMR (DMSO-d_6): δ = 7.46–8.53 (m, 12H, ArH's) and 13.85 (s, 1H, NH); MS, *m/z* (%) = 383 (M^+, 73.6%), 261 (22.9%), 206 (100%), 139 (34.7%) and 88 (22.6%); Anal. Calcd. For $C_{27}H_{13}N_3O_3$ requires (383.36): C, 70.98; H, 3.69; N, 11.83. Found: C, 71.22; H, 3.32; N, 11.79%.

3-(Naphtho[2,1-b]furan-2-yl)-4-(2-(4-nitrophenyl)hydrazono)-4H-pyrazole (29h). This compound was obtained as red crystals (acetic acid), yield (75%), mp: 274–76°C; IR (KBr): 3087 (CH, aromatic), 1618 (C=N), 1595 (C=C), and 1541, 1339 (NO_2); ^{1}H NMR (DMSO-d_6): δ = 7.60–8.98 (m, ArH's); Anal. Calcd. For $C_{27}H_{16}N_6O_5$ requires (504.45): C, 64.29; H, 3.20; N, 16.66. Found: C, 63.97; H, 3.35; N, 16.99%.

1-(2,4-Dinitrophenyl)-3-(naphtho[2,1-b]furan-2-yl)-4-((4-nitrophenyl)diazenyl)-1H-pyrazole (29i). This compound was obtained as red crystals (acetic acid), yield (75%), mp: 298–301°C; IR (KBr): 3098 (CH, aromatic), 1617 (C=N), 1594 (C=C), and 1540, 1321 (NO_2); MS, *m/z* (%) = 550 (M^{+1}, 5.6%), 384 (68.9%), 303(13.3%), 195 (45.9%), 139 (100%), 107 (28.6%), and 63 (87.2%); Anal. Calcd. For $C_{27}H_{15}N_7O_7$ requires (549.45): C, 59.02; H, 2.75; N, 17.84. Found: C, 58.93; H, 2.70; N, 17.64%.

3-(Naphtho[l,2-b]furan-2-yl)-1H-pyrazole (30a) and 3-(naphtho[2,1-b]furan-2-yl)-1-(4-nitrophenyl)-1H-pyrazole (30b). A mixture of 3-dimethylamino-1-naphtho[2,1-*b*]furan-2-ylpropenone (**7**) (1.32 g, 5 mmole) and the appropriate of hydrazine or p-nitrophenylhydrazine (5 mmole) in ethanol (15 mL) was refluxed for 2 h. The resulting solid was collected and recrystallized from ethanol to give **30a,b**.

3-(Naphtho[l,2-b]furan-2-yl)-1H-pyrazole (30a). This compound was obtained as buff crystals (ethanol) mp: 183–84°C; yield (81%), IR (KBr): 3123 (NH), 3050 (CH, aromatic), 1627 (C=N) and 1583 (C=C); ^{1}H NMR ($CDCl_3$): δ = 6.81 (d, 1H, pyrazole H-4), 7.46–8.17 (m, 8H, ArH's), and 10.38 (s, 1H, NH); Anal. Calcd. For $C_{15}H_{10}N_2O$ requires (234,25): C, 76.91; H, 4.30; N, 11.96. Found: C, 77.15; H, 4.47; N, 11.68%.

3-(Naphtho[2,1-b]furan-2-yl)-1-(4-nitrophenyl)-1H-pyrazole (30b). This compound was obtained as yellow crystals (ethanol), yield (76%), mp:190–91°C; IR (KBr): 3089 (CH, aromatic), 1615 (C=N), 1587 (C=C), and 1539 & 1332 (NO_2); ^{1}H NMR ($CDCl_3$): δ = 5.95 (d, 1H, pyrazole H-4) and 7.48–8.19 (m, 12H, ArH's, furan H-3 and pyrazole H-5); Anal. Calcd. For $C_{21}H_{13}N_3O_3$ requires (355.35): C, 70.98; H, 3.69; N, 11.83. Found: C, 70.63; H, 3.85; N, 11.79%.

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