Synthesis and Reactions of Naphtho[1′,2′:4,5]furo[3,2-b]pyridine and Naphtho[1′,2′:4,5]furo[3,2-d]pyrimidine Derivatives

M. Z. A. Badr, A. M. Kamal El-Dean,* O. S. Moustafa and R. M. Zaki
Chemistry Department, Faculty of Science, Assiut University, Assiut 71516, Egypt

2-Acyl-3-aminonaphtho[2,1-b]furan (**1**) reacts with activated methylene such as malono nitrile or ethyl cyanoacetate to afford naphtho[1′,2′:4,5]furo[3,2-b]pyridine **2a,b**. Chloroacylation of the amino group in compound (**1**) gave compound **3** which reacts with different amines to produce compound **4**.

Keywords: Synthesis; Reactions; Naphthofuran; Naphthofuropyridines; Naphthofuropyrimidines.

INTRODUCTION

Benzo[b]furan moiety constitutes a major group of natural biologically active heterocycle compounds,[1–5] which have attracted much attention owing to their wide range of biological activities, such as acting as antioxidants, antifungal agents, modulators of estrogen receptors, 5-lipoxygenase inhibitors, cyclooxygenase-2 inhibitors, and Na^+, K^+-ATPase inhibitors.[6–11]

RESULTS AND DISCUSSION

When 2-acetyl-3-aminonaphtho[2,1-b]furan (**1a**) refluxed with malononitrile in ethanol in the presence of catalytic drops of piperidine, 2-amino-4-methylnaphtho-[1′,2′:4,5]furo[3,2-b]pyridine-3-carbonitrile **2a** was produced. The reaction proceeded through Knovenagel condensation followed by addition of amino group to cyano group to give compound **2a**. The same compound was prepared under another condition by using ammonium acetate/acetic acid mixture. The confirmation of the produced compound was performed using IR spectra which showed a band at 3390, 3290 cm^{-1} characteristic for (NH_2), and at 2220 cm^{-1} (CN) and also revealed the disappearance of the band characteristic for –C=O in the starting material.

While when compound (**1a**) was refluxed with ethyl cyanoacetate in ammonium acetate in acetic acid as a solvent, condensation of the carbonyl group with active methylene followed by elimination of ethanol to give 3-cyano-4-methyl-naphtho[1′,2′:4,5]furo[3,2-b]pyridin-2(1H)-one **2b**. The structure of compound **2b** was elucidated using IR spectra; it gave a characteristic band for NH at 3490 and at 2220 cm^{-1} for CN group and at 1640 cm^{-1} for –C=O. ^1H NMR (DMSO-d_6) gave a signals at 2.55 as a singlet for CH_3, 7.7-9.0 for aromatic protons and at 9.25 for –NH group.

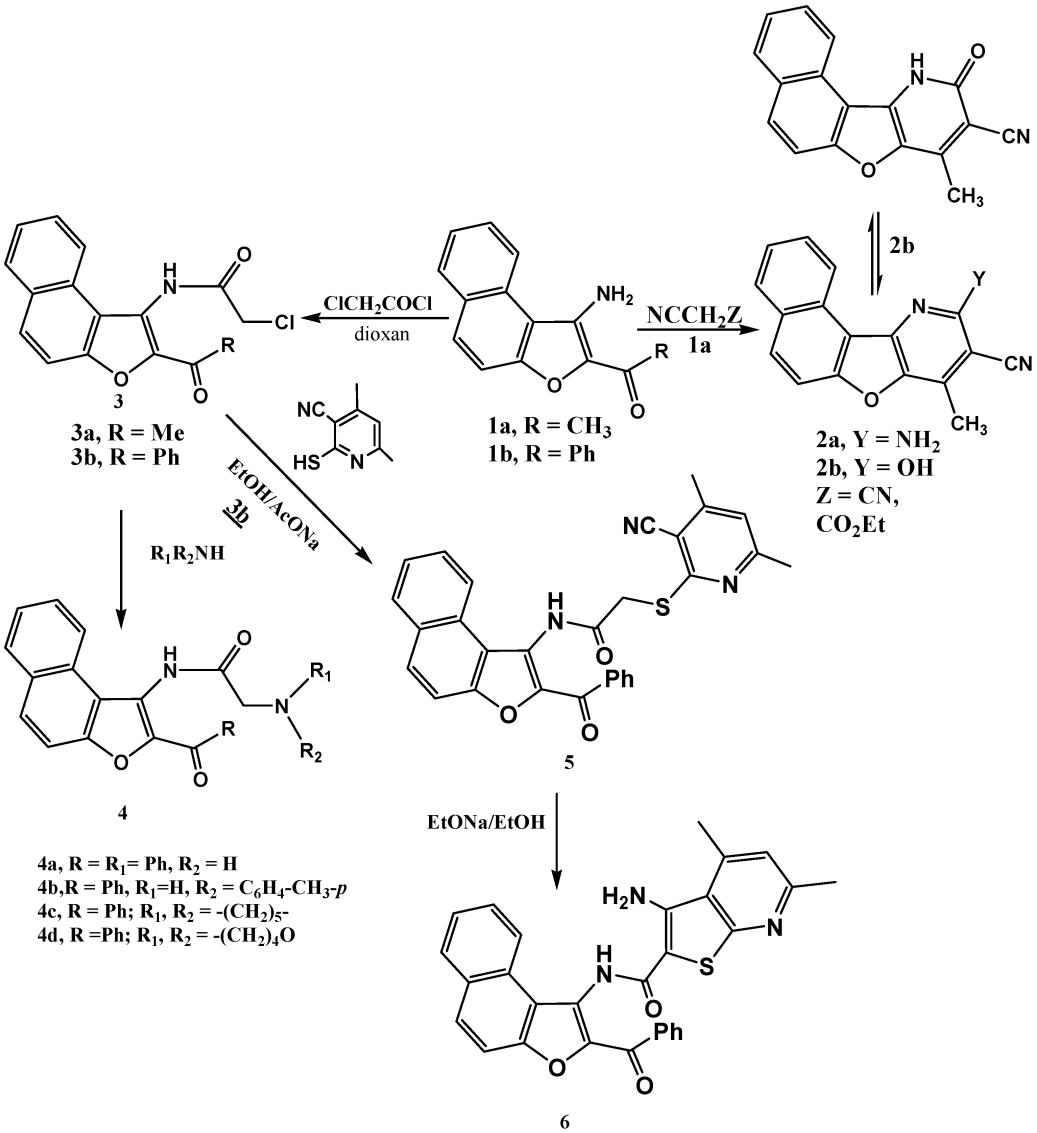
Chloroacylation of (**1**) using chloroacetyl chloride in dioxan followed by treating with sodium carbonate solution afforded 2-acetyl-3-chloroacetylaminonaphtho[2,1-b]furan (**3**). The structure of the produced compound was elucidated on the basis of NMR spectra, which revealed the disappearance of signals at 6.55 characteristic for $–NH_2$- and appearance of signals at δ 4.5 characteristic for $–CH_2$- and at 11.9 for –NH-.

Chloroacetyl derivative **3** underwent nucleophilic substitution reaction with various primary and secondary amines in refluxed ethanol to afford N-[2-acetylnaphtho-[2,1-b]furan-3-yl]-2-alkyaminoacetamide **4**. Also when the chlorine atom in compound **3** was substituted with another nucleophilic reagent, it reacted with mercaptopyridine derivative to give sulfide derivative **5**. The latter compound was cyclized in ethanol in the presence of sodium ethoxide to afford 3-amino-4,6-dimethyl-2-(N-naphtho-[2,1-b]furan-2-yl)-thieno[2,3-b]pyridincarboxamide **6** (Scheme I).

3-Aminonaphtho[2,1-b]furan-2-carbohydrazide (**8**), prepared by refluxing of 3-ethyl 3-aminonaphtho[2,1-b]-furan-2-carboxylate (**7**) with hydrazine hydrate in ethanol, was used as versatile starting material for the synthesis of other heterocyclic compounds containing naphthofuran moiety.

* Corresponding author. E-mail: a.eldean@acc.aun.edu.eg

Scheme I



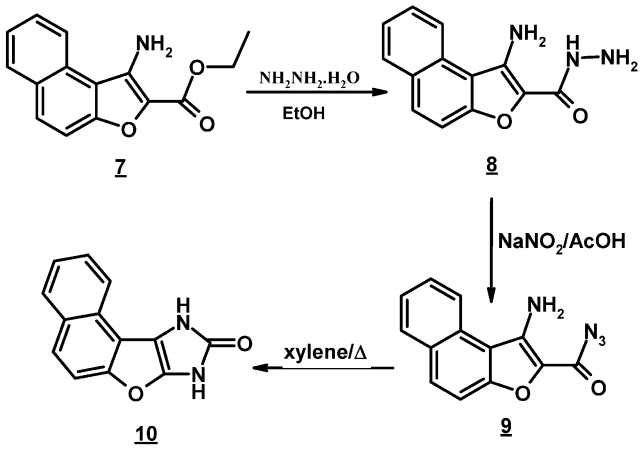
Treatment of carbohydrazide **8** with sodium nitrite in acetic acid produced 3-aminonaphtho[2,1-b]furan-2-carboazide **9**. Upon heating, the produced carboazide derivative **9** in xylene underwent Curtius rearrangement to give naphthofuroimidazole derivative **10** (Scheme II).

The carbohydrazide **8** underwent condensation reaction with acetyl acetone in ethanol to afford naphtho[2,1-b]furan-2-yl-pyrazol-1-yl-ketone **11**. Also it was condensed with aromatic aldehydes in ethanol in the presence of a catalytic amount of acetic acid to give the corresponding carbohydrazones **12**. The produced carbohydrazone **12** was reacted with triethyl orthoformate which cyclized to 3-aryl hydrazononaphtho[1′,2′:4,5]furo[3,2-d]pyrimidin-4-one **13**. While when allowed to react with CS_2 in pyridine, 2-(naphtho[2,1-b]furan-2-yl)-5-mercaptooxadiazole **14** was produced.

Other naphthofuropyrimidines (**15-17**) were synthesized from carbohydrazide **8**. 3-Formylaminonaphtho-[1′,2′:4,5]furo[3,2-d]pyrimidin-4-one **15** was prepared by refluxing carbohydrazide **8** with formic acid, while 3-ethoxymethyleneaminonaphtho[1′,2′:4,5]furo[3,2-d]pyrimidin-4-one **16** was prepared by refluxing carbohydrazide **8** with triethyl orthoformate in the presence of a catalytic amount of acetic acid.

Also 3-diacetylaminonaphtho[1′,2′:4,5]furo[3,2-d]-pyrimidin-4-one **17** was prepared by refluxing carbohydra-

Scheme II

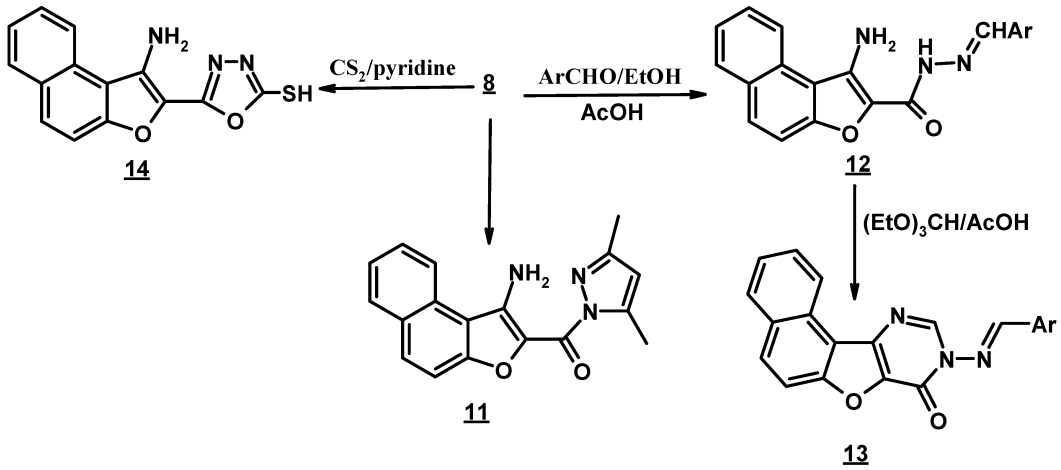


zide **8** with acetic anhydride.

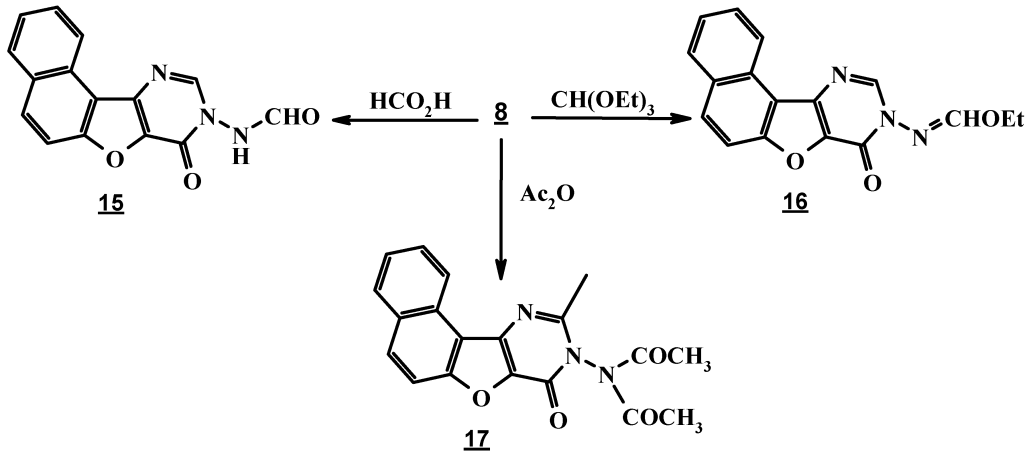
EXPERIMENTAL

Melting points were uncorrected and determined using a Kofler melting point apparatus. IR spectra were recorded on a Pye Unicam SP 3-100 spectrometer using the KBr Wafer technique. ^{1}H NMR spectra were recorded on a Varian EM-390 90 MHz and Joel 400 MHz spectrometers in a suitable deuteriated solvent using TMS as internal standard. Mass spectra were recorded on a Joel MS600 mass spectrometer. 2-Hydroxynapthonitrile was prepared according to a literature procedure.[12]

Scheme III



Scheme IV



2-Amino-4-methyl-naphtho[1′,2′:4,5]furo[3,2-b]pyridine-3-carbonitrile 2a

A mixture of compound **1a** (2.25 g, 0.01 mol), (0.66 g, 0.01 mol) malononitrile, and few drops of piperidine in ethanol (30 mL) was heated under reflux for 3 h, then allowed to cool. The solid product was collected and recrystallized from DMF as yellow crystals 1.8 g, 66% yield, m.p. > 300 °C.

Anal. Calc. for $C_{17}H_{11}N_3O$ (273.29): C, 74.71; H, 4.06; N, 15.38%.

Found: C, 74.94; H, 3.88; N, 15.25%.

IR: ν = 3390, 3290 cm^{-1} (NH_2), and 2220 cm^{-1} (CN).

^{1}H NMR (DMSO-d_6): δ = 2.65 (s, 3H, CH_3), 6.5 (s, 2H, NH_2), and at 7.6-8.5 (m, 6H, Ar-H).

^{13}C NMR of **2a** 15 signals at 116-155 for aromatic rings carbons, at 15.6, 25.5 2 signals for C-(CH_3) carbons and at 115.3 s for –CN carbons.

3-Cyano-4-methyl-naphtho[1′,2′:4,5]furo[3,2-b]pyridine-2(1H)-one 2b

A mixture of 2-acetyl-3-aminonaphthofuran **1a** (1.12 g, 0.005 mol), ethyl cyanoacetate (1.13 g, 0.01 mol) and ammonium acetate (3.35 g, 0.05 mol) was fused on a heater for one hour, then acetic acid (15 mL) was added and the mixture was refluxed for 2 h. The solid product was collected and recrystallized from DMF as yellow crystals (0.85 g, 62% yield), m.p. > 300 °C.

Anal. Calc. for $C_{17}H_{10}N_2O_2$ (274.28): C, 74.45; H, 3.67; N, 10.21%.

Found: C, 74.22; H, 3.48; N, 10.00%.

IR: ν = 3490 cm^{-1} (NH), 2220 cm^{-1} (CN) and at 1640 cm^{-1} (–C=O).

^{1}H NMR (DMSO-d_6): δ = 2.55 (s, 3H, CH_3), 7.7-9.0 (m, 6H, Ar-H) and at 9.25 (s, 1H, NH).

Chloroacetylation of 2-acetyl(benzoyl)-3-aminonaphtho[3,2-b]furan (General procedure)

To a solution of compound **1a** (2.25 g, 0.01 mol) or **1b** (2.87 g, 0.01 mol) in dioxian (20 mL), chloroacetyl chloride (1.12 g, 0.01 mol) was added. The mixture was heated on a steam bath at 70 °C for 3 h, allowed to cool and poured into cold water (100 mL), then the mixture was neutralized with sodium carbonate solution (10%) until reach to just alkaline. The solid product was collected and recrystallized from ethanol.

N-(2-Acetylnaphtho[2,1-b]furan-1-yl)-2-chloroacetamide (3a)

Produced as yellow crystals 2.72 g; 90% yield; m.p. 188-90 °C.

Anal. Calc. for $C_{16}H_{12}ClNO_3$ (301.73): C, 63.69; H, 4.01; Cl, 11.75; N, 4.64%.

Found: C, 63.54; H, 3.81; Cl, 11.97; N, 4.80%.

IR: ν = 3260 cm^{-1} (NH), 1700, 1680 cm^{-1} (2C=O).

^{1}H NMR (DMSO-d_6): δ = 2.35 (s, 3H, CH_3), 4.2 (s, 2H, CH_2), 7.7-8.0 (m, 6H, Ar-H) and at 9.25 (s, 1H, NH).

2-Benzoyl-3-chloroacetylaminonaphtho[2,1-b]furan (3b)

Produced as yellow crystals 3.45 g; 95% yield, m.p. 200 °C.

Anal. Calc. for $C_{16}H_{12}ClNO_3$ (363.80): C, 69.33; H, 3.88; Cl, 9.75; N, 3.85%.

Found: C, 69.09; H, 4.11; Cl, 9.98; N, 4.07%.

IR: ν = 3250 cm^{-1} (NH), 1700, 1670 cm^{-1} (2C=O).

^{1}H NMR (DMSO-d_6): δ = 4.3 (s, 2H, CH_2), 7.2-8.0 (m, 11H, Ar-H) and at 10.5 (s, 1H, NH).

N-[2-Acetyl(bezoyl)-naphtho[2,1-b]furan-3-yl]-2-aryl (alkyl)aminoacetamide (4a-d)

A mixture of compound **3a** (3.017 g, 0.01 mol), primary or secondary amine (0.01 mol) and potassium carbonate (2.76 gm, 0.02 mol) in ethanol (30 mL) was refluxed for 5 hrs, then allowed to cool and poured into water (100 mL). The solid precipitate was filtered off, dried and recrystallized from ethanol.

N-(2-Benzoyl-naphtho[2,1-b]furan-3-yl)-2-phenylaminoacetamide (4a)

Obtained from **3b** and aniline as green crystals 3.38 g, 80.5% yield; m.p. 110-112 °C.

Anal. Calcd. for $C_{27}H_{20}N_2O_3$ (420.47): C, 77.13; H, 4.79; N, 6.66%.

Found: C, 76.89; H, 5.00; N, 6.52%.

IR: ν = 3350, 3200 cm^{-1} (2NH), 1690, 1670 cm^{-1} (2C=O).

^{1}H NMR (DMSO-d_6): δ = 4.0 (s, 2H, CH_2), 7.0-8.2 (m, 16H, Ar-H) and at 8.5, 10.5 (2s, 2H, 2NH).

N-(2-Benzoyl-naphtho[2,1-b]furan-3-yl)-2-*p*-tolylaminoacetamide (4b)

Obtained from **3b** and *p*-toluidine as green crystals

3.61 g, 83% yield; m.p. 140 °C.

Anal. Calcd. for $C_{28}H_{22}N_2O_3$ (434.50): C, 77.40; H, 5.10; N, 6.45%.

Found: C, 77.59; H, 4.91; N, 6.57%.

IR: ν = 3340, 3250 cm^{-1} (2NH), 1690, 1670 cm^{-1} (2C=O).

^1H NMR (DMSO-d_6): δ = 2.3 (s, 3H, CH_3), 4.0 (s, 2H, CH_2), 7.0-8.2 (m, 15H, Ar-H) and at 8.5, 10.5 (2s, 2H, 2NH).

N-(2-Benzoyl-naphtho[2,1-b]furan-3-yl)-2-(N-pipredinyl)-acetamide (4c)

Obtained from **3b** and piperidine as pale yellow crystals, m.p. 130 °C in Yield 78%.

Anal. Calcd. for $C_{26}H_{24}N_2O_3$ (412.49): C, 75.71; H, 5.86; N, 6.79%.

Found: C, 75.48; H, 6.20; N, 7.01%.

IR: ν = 3050 cm^{-1} (CH aromatic), 2950 cm^{-1} (CH aliphatic), 1690 cm^{-1} (CO) and at 3350 cm^{-1} (NH).

^1H NMR ($CDCl_3$): δ = 1.3-1.5 (m, 6H, $3CH_2$), 2.3 (m, 4H, $2CH_2$), 2.4 (s, 2H, CH_2), 7.3-8.4 (m, 11H, Ar-H) and at 10.5 (s, H, NH).

N-(2-Benzoyl-naphtho[2,1-b]furan-3-yl)-2-(N-morpholinyl)-acetamide (4d)

Obtained from **3b** and morpholine as pale yellow crystals in 63% yield, m.p. 82 °C.

Anal. Calcd. for $C_{25}H_{22}N_2O_4$ (414.47): C, 72.45; H, 5.35; N, 6.76%.

Found: C, 72.38; H, 5.52; N, 7.00%.

IR: ν = 3050 cm^{-1} (CH aromatic), 2950 cm^{-1} (CH aliphatic), 1690 cm^{-1} (CO) and at 3350 cm^{-1} (NH).

^1H NMR ($CDCl_3$): δ = 2.3-2.5 (m, 4H, $3CH_2$), 3.3-3.5 (m, 4H, $2CH_2$), 3.9 (s, 2H, CH_2), 7.3-8.4 (m, 11H, Ar-H) and at 11.5 (s, H, NH).

[N-(2-Benzoyl-naphtho[2,1-b]furan-1-yl)-aminomethyl]-[3-cyano-4,6-dimethylpyridin-2-yl]-sulfide 5

A mixture of N-(2-acetyl-naphtho[2,1-b]furan-1-yl)-2-chloro-acetamide (**3b**) (0.75 g, 0.0025 mol), anhydrous sodium acetate (0.41 g, 0.005 mol) and 4,6-dimethyl-2-mercaptopyridin-3-carbonitrile (0.41 g, 0.0025 mol) in ethanol (30 mL) was heated under reflux for 3 h, then allowed to cool. The solid precipitate was filtered off, washed with water several times, dried and recrystallized from ethanol, in 85% yield, m.p. 190-192 °C.

Anal. Calcd. for $C_{29}H_{21}N_3O_3S$ (491.57): C, 70.86; H, 4.31; N, 8.55; S, 6.52%.

Found: C, 71.05; H, 4.22; N, 8.73; S, 6.31%.

IR: ν = 3350 cm^{-1} (NH), 3050 cm^{-1} (CH aromatic), 2220 cm^{-1} (CN), and at 1690 cm^{-1} (CO).

^1H NMR (DMSO-d_6): δ = 2.3 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 4.0 (s, 2H, CH_2), 7.0 (s, 1H, CH-pyridine), 7.3-8.4 (m, 11H, Ar-H) and at 10.9 (s, H, NH).

3-Amino-4,6-dimethyl-2-N-(2-benzoyl-naphtho[2,1-b]-furan-1-yl)thieno[2,3-b]pyridine carboxamide 6

To a solution of (**5**) (245 mg, 0.0005 mol) in ethanol (20 mL), a few drops of sodium ethoxide solution were added. The mixture was refluxed for 1 hr and left to cool. The solid product obtained on dilution with water was filtered off, dried and recrystallized from ethanol as orange crystals in 79% yield; m.p. 274-276 °C.

Anal. Calcd. for $C_{29}H_{21}N_3O_3S$ (491.57): C, 70.86; H, 4.31; N, 8.55; S, 6.52%.

Found: C, 7.73; H, 4.55; N, 8.23; S, 6.71%.

IR: ν = 3450, 3310 cm^{-1} (NH_2), 3050 cm^{-1} (CH aromatic), and at 1680 cm^{-1} (CO).

^1H NMR (DMSO-d_6): δ = 2.3 (s, 3H, CH_3), 2.7 (s, 3H, CH_3), 6.0 (s, 2H, NH_2), 7.0 (s, 1H, CH-pyridine), 7.3-8.4 (m, 11H, Ar-H) and at 10.9 (s, H, NH).

Ethyl 3-Amino-naphtho[2,1-b]furan-2-carboxylate (7)

Was prepared according to the procedure reported in a previous work.[13]

3-Aminonaphtho[2,1-b]furan-2-carboxylic hydrazide (8)

Ethyl 3-amino-naphtho[2,1-b]furan-2-carboxylate (**7**) (5 gm, 0.02 mol) and hydrazine hydrate (2 mL, 0.04 mol) in ethanol (20 mL) was refluxed for 3 hrs., then allowed to cool. The solid precipitate was collected and recrystallized as yellow crystals in 71% yield; m.p. 158-160 °C.

Anal. Calcd. for $C_{13}H_{11}N_3O_2$ (241.25): C, 64.72; H, 4.60; N, 17.42%.

Found: C, 64.49; H, 4.82; N, 17.21%.

IR: ν = 3450, 3350, 3200 cm^{-1} ($NHNH_2$, NH) and 1670 cm^{-1} (C=O).

^1H NMR (DMSO-d_6): δ = 3.8 (s, 2H, hydrazide NH_2), 5.9 (s, 2H, NH_2), 7.2-7.9 (m, 6H, Ar-H) and at 9.5 (s, 1H, NH).

3-Aminonaphtho[2,1-b]furan-2-carboxylic azide (9)

Sodium nitrite solution (5.5 mL 5%, 0.04 mol) was added to a solution of 3-aminonaphtho[2,1-b]furan-2-carbohydrazide (**8**) (2.41 gm, 0.01 mol) in acetic acid (10 mL) at room temperature over 5 minutes with stirring. The solid product was filtered off, dried, and collected as buff crystals; in 60% yield, m.p. 140 °C and used without further purification.

Anal. Calcd. for $C_{13}H_8N_4O_2$ (252.23): C, 61.90; H, 3.20; N, 22.21%.

Found: C, 64.49; H, 4.82; N, 17.21%.

IR: ν = 3350, 3250 cm^{-1} (NH_2), 2200 cm^{-1} (N_3) and 1710 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$): δ = 5.9 (s, 2H, NH_2) and 7.2-7.9 (m, 6H, Ar-H).

1,3-Dihydro-naphtho[2′,1′:2,1]imidazol-2-one (10)

3-Aminonaphtho[2,1-b]furan-2-carbonylazide (**9**) (0.5 gm) in xylene (20 mL) was heated under reflux for 1 hr. The solid product was filtered off and washed several times with xylene. Dried and recrystallized from xylene as brown crystals (0.4 gm) in 90% yield, m.p. > 360 °C.

Anal. Calcd. for $C_{13}H_8N_2O_2$ (224.22): C, 69.64; H, 3.60; N, 12.49%.

Found: C, 69.40; H, 3.38; N, 12.73%.

IR: ν = 3310, 32300 cm^{-1} (2NH), and 1670 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$): δ = 7.2-7.9 (m, 6H, Ar-H) and 9.9 (s, 2H, 2NH).

[3-Amino-naphtha[2,3-b]furan-2-yl]-[3,5-dimethylpyrazol-1-yl]ketone 11

A mixture of carbohydrazide (**8)** (0.5 gm, 0.002 mol) and acetylacetone (0.4 mL, 0.004 mol) was refluxed in ethanol for 4 hrs. On cooling the preciptated solid which formed was filtered off and recrystallized from ethanol as pale yellow needles, m.p. 215-217 °C; yield 94%.

Anal. Calcd. for $C_{18}H_{15}N_3O_2$ (305.34): C, 70.81; H, 4.95; N, 13.76%.

Found: C, 71.00; H, 5.18; N, 13.92%.

IR: ν = 3350, 3250 cm^{-1} (NH_2), and 1690 cm^{-1} (C=O).

^{1}H NMR ($CDCl_3$): δ = 2.9 (s, 6H, $2CH_3$), 5.5 (s, 1H, CH-pyrazole), 6.0 (s, 2H, NH_2), 7.2-7.9 (m, 6H, Ar-H).

Arylidene 3-aminonaphtho[2,1-b]furan-2-carbohydrazone (12a-c) General procedure

To a mixture of carbohydrazide **8** (1.2 g, 0.005 mol) and an appropriate aromatic aldehyde (0.005 mol) in ethanol (20 mL), a few drops of acetic acid was added. The mixture was heated under reflux for 3 h, then allowed to cool. The solid product was collected and recrystallized from dioxan.

Benzyledine 3-aminonaphtho[2,1-b]furan-2-carbohydrazone (12a)

Produced in 91% yield; m.p. 240-242 °C.

Anal. Calcd. for $C_{20}H_{15}N_3O_2$ (329.36): C, 72.94; H, 4.59; N, 12.76%.

Found: C, 73.18; H, 4.71; N, 12.92%.

IR: ν = 3450, 3310, 3270 cm^{-1} (NH, NH_2), and 1690 cm^{-1} (C=O).

^{1}H NMR (DMSO-d_6): δ = 6.0 (s, 2H, NH_2), 7.2-8.4 (m, 11H, Ar-H), 8.8 (s, 1H, CH=N-), and 11.05 (s, 1H, NH).

4-Methoxy-benzyledine 3-aminonaphtho[2,1-b]furan-2-carbohydrazone (12b)

Obtained from carbohydrazide **8** and 4-methoxybenzaldehyde in 89% yield; m.p. 234-236 °C.

Anal. Calcd. for $C_{21}H_{17}N_3O_3$ (359.39): C, 70.18; H, 4.77; N, 11.69%.

Found: C, 69.99; H, 5.02; N, 11.47%.

IR: ν = 3440, 3320, 3250 cm^{-1} (NH, NH_2), and 1690 cm^{-1} (C=O).

^{1}H NMR (DMSO-d_6): δ = 3.9 (s, 3H, CH_3), 5.8 (s, 2H, NH_2), 7.0-8.5 (m, 10H, Ar-H), 8.6 (s, 1H, CH=N-), and 11.5 (s, 1H, NH).

4-Chloro-benzyledine 3-aminonaphtho[2,1-b]furan-2-carbohydrazone (12c)

Obtained from carbohydrazide **8** with 4-chlorobenzaldehyde in 84% yield; m.p. 248-250 °C.

Anal. Calcd. for $C_{20}H_{14}ClN_3O_2$ (363.81): C, 66.03; H, 3.88; Cl, 9.75; N, 11.55%.

Found: C, 65.89; H, 4.05; Cl, 9.94; N, 11.72%.

IR: ν = 3390, 3290, 3250 cm^{-1} (NH, NH_2), and 1750 cm^{-1} (C=O).

^{1}H NMR (DMSO-d_6): δ = 5.9 (s, 2H, NH_2), 7.3-8.4 (m, 10H, Ar-H), 8.7 (s, 1H, CH=N-), and 10.9 (s, 1H, NH).

3-Aryledineaminonaphtho[3′,2′:4,5]furo[3,2-d]pyrimidine-4(3H)-one (13a-c) General procedure

A mixture of (**12a-c**) (0.002 mol) and triethyl orthoformate (5 mL) was heated under reflux for 10 minutes in the presence of a few drops of acetic acid (2-3 mL). The

solid product which formed on hot was collected and recrystallized from dioxan as white crysals of (**13a-c**).

3-Benzyledineaminonaphtho[3′,2′:4,5]furo[3,2-d]pyrimidine-4(3H)-one (13a)

Obtained from (**12a**) in 92% yield; m.p. 225-227 °C.

Anal. Calcd for $C_{21}H_{13}N_3O_2$ (339.36): C, 74.33; H, 3.86; N, 12.38%.

Found: C, 74.18; H, 4.04; N, 12.49%.

IR: ν = 3050 cm^{-1} (CH, aromatic), and 1685 cm^{-1} (C=O).

^{1}H NMR (DMSO-d_6): δ = 7.2-8.4 (m, 11H, Ar-H), 8.9, 9.1 (2s, 1H, CH=N- and CH pyrimidine).

3-(*p*-Methoxybenzylideneamino)-naphtho[3′,2′:4,5]furo-[3,2-d]pyrimidine-4(3H)-one (13a)

Obtained from (**12b**) in 95% yield; m.p. 248-250 °C.

Anal. Calcd for $C_{22}H_{15}N_3O_3$ (369.38): C, 71.54; H, 4.09; N, 11.38%.

Found: C, 71.31; H, 3.88; N, 11.51%.

IR: ν = 3050 cm^{-1} (CH, aromatic), and 1680 cm^{-1} (C=O).

^{1}H NMR (DMSO-d_6): δ = 3.5 (s, 3H, CH_3), 7.0-8.2 (m, 10H, Ar-H), 9.2, 9.5 (2s, 1H, CH=N- and CH pyrimidine).

3-(*p*-Chloro)-benzyledineaminonaphtho[3′,2′:4,5]furo-[3,2-d]pyrimidine-4(3H)-one (13c)

Obtained from **12c** in 93% yield; m.p. 289-290 °C.

Anal. Calcd. for $C_{21}H_{12}ClN_3O_2$ (373.80): C, 67.48; H, 3.24; Cl, 9.48; N, 11.24%.

Found: C, 67.29; H, 3.01; Cl, 9.71; N, 11.46%.

IR: ν = 3050 cm^{-1} (CH, aromatic), and 1690 cm^{-1} (C=O).

^{1}H NMR (DMSO-d_6): δ = 7.2-8.3 (m, 10H, Ar-H), 8.9, 9.3 (2s, 1H, CH=N- and CH pyrimidine).

2-(Naphtha[2,3-b]furan-2-yl)-5-mercaptooxadiazole 14

A mixture of 3-aminonaphtho[2,1-b]furan-2-carbohydrazide (**8**) (1 gm) and carbondisulphide (2 mL) was refluxed in pyridine (4 mL) on a water bath for 12 hrs. A solid precipitate formed on hot was filtered off and recrystallized from ethanol as buff crystals, in 69% yield, m.p. > 360 °C.

Anal. Calcd. for $C_{14}H_9N_3O_2S$ (283.31): C, 59.35; H, 3.20; N, 14.83; S, 11.32%.

Found: C, 59.14; H, 3.38; N, 15.05; S, 11.51%.

IR: ν = 3340, 3240 cm^{-1} (NH_2), 3050 cm^{-1} (CH, aromatic), and 1220 cm^{-1} (S-H).

^{1}H NMR (DMSO-d_6): δ = 3.5 (s, 1H, SH), 5.95 (s, 2H, NH_2), 7.0-8.1 (m, 6H, Ar-H).

3-Formylaminonaphtho[3′,2′:4,5]furo[3,2-d]pyrimidine-4(3H)-one (15)

3-Aminonaphtho[2,1-b]furan-2-carbohydrazide (0.5 gm) in formic acid (10 mL) was refluxed for 4 hrs. On cooling the precipitated solid was filtered off and recrystallized from ethanol as white needles in 60% yield; m.p. 290-292 °C.

Anal. Calcd for $C_{15}H_9N_3O_3$ (279.26): C, 64.52; H, 3.25; N, 15.05%.

Found: C, 64.69; H, 3.44; N, 14.83%.

IR: ν = 3400 cm^{-1} (NH), 3050 cm^{-1} (CH, aromatic), and 1710, 1690 cm^{-1} (2C=O).

^{1}H NMR (DMSO-d_6): δ = 7.2-8.4 (m, 8H, Ar-H, 1H, CH=N- and CH pyrimidine), 8.9 (s, 1H, CH formyl) and 9.9 (s, 1H, NH).

3-Ethoxymethyleneaminonaphtho[2′,1′,4,5]furo[3,2-d]-pyrimidine-4(3H)-one (16)

A mixture of carbohydrazide (**8**) (0.3 gm, 0.001 mol) and triethylorthoformate (3 mL) was refluxed for 15 minutes in the presence of a few drops of glacial acetic acid (2-3 drops). The solid that formed on hot was collected and recrystallized from DMF as clear white crystals in 76% yield; m.p. 170-171 °C.

Anal. Calcd. for $C_{17}H_{13}N_3O_3$ (307.31): C, 66.44; H, 4.26; N, 13.67%.

Found: C, 66.61; H, 4.50; N, 13.44%.

IR: ν = 3050 cm^{-1} (CH, aromatic), 2950 cm^{-1} (CH, aliphatic), and 1690 cm^{-1} (C=O).

^{1}H NMR (DMSO-d_6): δ = 1.15 (t, 3H, CH_3), 3.6 (q, 2H, CH_2), 7.2-8.4 (m, 8H, Ar-H, 1H, CH=N- and CH pyrimidine).

Diacetylaminonaphtho[3′,2′:4,5]furo[3,2-d]pyrimidine-4(3H)-one (17)

3-Aminonaphtho[2,1-b]furan-2-carbohydrazide (0.5 gm) was refluxed in acetic anhydride (20 mL) for 3 hrs. The solid precipitated on cooling was recrystallized from ethanol as white needles in 60% yield; m.p. 240-242 °C.

Anal. Calcd. for $C_{19}H_{15}N_3O_4$ (349.35): C, 65.32; H, 4.33; N, 12.03%.

Found: C, 65.09; H, 4.42; N, 11.88%.

IR: $\nu = 3050\ cm^{-1}$ (CH, aromatic), $2950\ cm^{-1}$ (CH, aliphatic), and $1690\ cm^{-1}$ (C=O).

^1H NMR (DMSO-d_6): $\delta = 2.1$ (s, 3H, CH_3), 2.4 (s, 6H, $2CH_3$), 7.2-8.4 (m, 6H, Ar-H).

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