Synthesis of novel 2-aryl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*] pyridin-4(1*H*)-ones of biological importance

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Abstract
2-Aryl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(*1H*)-ones **5a-f** were synthesized from 2-hydroxy-1-naphthonitrile **2** and characterized on the basis of chemical, analytical and spectral data. The compounds were screened for antibacterial and antifungal activity.

Keywords: 2-Hydroxy-1-naphthonitrile, thrope-ziegler cyclisation, naphtho[2,1-*b*]furan, microwave, antimicrobial

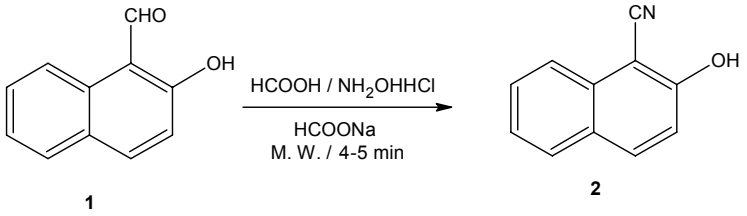
Introduction

Naphthofuran nuclei are key structural moieties found in a large number of biologically important natural products, mainly belonging to the sesquiterpene and arylquinone classes.[1] Most of the natural naphthofurans such as (±)-laevigatin,[2] (+)-heritol [3] and balsaminone [4] possess interesting pharmacological and cytotoxic properties. Several synthetic compounds bearing this ring skeleton are associated with diverse biological activities such as antifungal,[5] antibacterial,[6] antiviral,[7] β-adrenolytic,[8] antitumour,[9] and anthelmintic.[10] The wide pharmacological potential of these bioactive moieties has attracted many organic and medicinal chemists to develop efficient routes for their synthesis. Moreover, there has been considerable research work in the synthesis of angularly fused tetracyclic compounds owing to their close relationship with anticancer agents.[11] At the same time, organic reactions using conventional organic solvents especially chlorinated hydrocarbons have posed a serious threat to the environment due to their toxicity and volatile nature.[12-14] The conventional procedures are not fully satisfactory with regard to

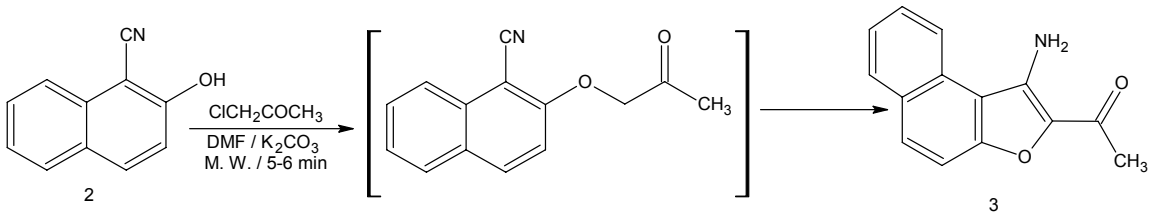
operational simplicity, cost of the reagent and isolated yield. In recent years, microwave irradiation has been demonstrated not only to dramatically accelerate many organic reactions, but also to improve yields and selectivity.[15-18] Thus; the drive continues to find a better and improved methodology. In recent communications [19-22] we have demonstrated a very simple procedure for the synthesis of fused heterocyclic compounds proving the synthetic utility of MORE chemistry in routine organic synthesis. In view of the above reports and in continuation of research in the synthesis of pharmacologically potent naphtho[2,1-*b*]furan derivatives, we report in this paper the synthesis of 2-aryl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(*1H*)-ones and their microbial activities.

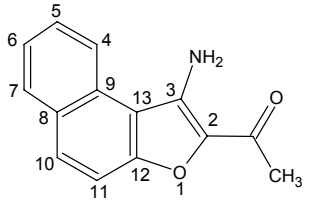
Caption For Figures (Schemes)

Schemes: General synthetic Procedure of 2-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*] pyridin-4 (*1H*)-ones 5a-f

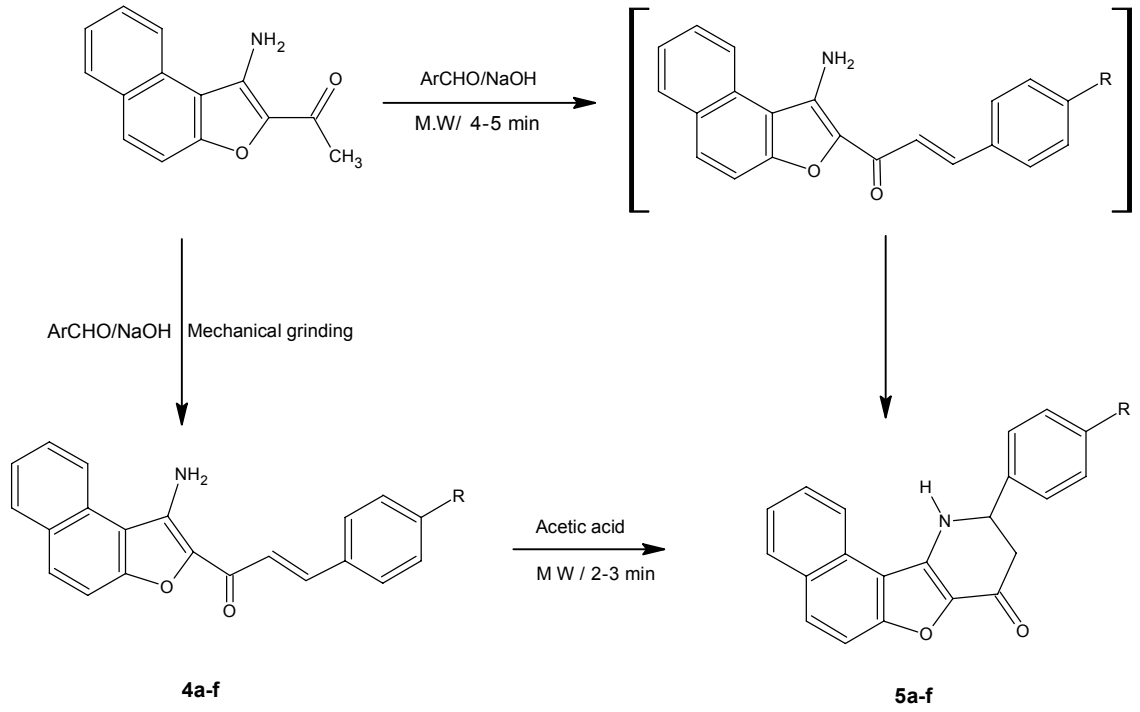


Scheme 1





Scheme 2



Scheme 3. R=H, Cl, Br, CH_3, OCH_3, NO_2.

Results and Discussion

The key intermediate 2-hydroxy-1-naphthonitrile **2,** was synthesized from 2-hydroxy-1-naphthaldehyde. The compound **2** was prepared from an equimolar mixture of 2-hydroxy-1-naphthaldehyde and hydroxylamine hydrochloride in formic acid and sodium formate. The reaction mixture was irradiated to microwave. The structure of **2** was confirmed by its IR spectrum, which exhibited strong absorption band at 2233 cm^{-1} due to the CN group and a broad absorption band at 3300 cm^{-1} due to the OH group. The ^1H NMR data revealed consistent with the structure. This is a novel method for the conversion of 2-hydroxy-1-naphthaldehyde into 2-hydroxy-1-naphthonitrile with 75% yield (Scheme 1).

The nitrile compound **2** on reaction with chloroacetone in presence of potassium carbonate and dimethylformamide underwent Thrope-Ziegler cyclisation to produce compound **3** in moderate yield. In order to improve the yield, the same reaction between **2** and chloroacetone was carried out in microwave oven for 4-5 min, which resulted in considerable increase in yield to the extent of 85% (Scheme 2).

The structure of **3** was confirmed by its spectral data. The IR spectrum of **3** showed the absence of nitrile group, instead it exhibited two absorption bands due to symmetric and asymmetric stretching frequencies of primary amine at 3373 cm^{-1} and 3485 cm^{-1} and another band at 1630 cm^{-1} due to carbonyl group, which is intermolecular hydrogen bonded with

adjacent NH_2 group. ^1H NMR spectrum of **3** showed a broad singlet integrating for 2 protons at δ 5.95 ppm, due to the NH_2 group (D_2O exchangeable) and a singlet integrating for 3 protons at δ 2.55 ppm due to the CH_3 group. Other signals appeared in the aromatic region corresponding to 6 protons as multiplet at δ 7.58-8.63 ppm, in particular C_5 & C_6 resonate as triplets δ 7.60 ppm (J=7 Hz) and δ 7.70 ppm (J=7 Hz) respectively. C_{10} and C_{11} resonate as doublet at δ 7.90 ppm (J=9 Hz), & δ 8.45 ppm (J=8 Hz), and C_4 & C_7 at δ 8.05-8.15 ppm as a double doublet (J=8 Hz) of naphthofuran confirmed the structure. In order to further ascertain the structure, the mass & ^{13}C were also recorded. The ^{13}C NMR spectrum of this compound was in good agreement with the structure assigned. In the broad band decoupled ^{13}C spectrum of **3**, a small peak at δ 189.17 was assigned to carbonyl carbon atom. The remaining small peaks appearing at 153.04, 141.09, 136.27, 130.32, 128.83 and 114.14 were attributed to C_2, C_9, C_8, C_{12}, C_{13} and C_3 carbon atoms respectively which are quaternary carbon atoms. The large peak at 131.28, 129.61, 127.71, 124.89 and 122.07 were assigned to C_{10}, C_7, C_4, C_6 and C_5 carbon atoms of naphthalene ring respectively. As expected C_{11} of naphthalene nucleus exhibited a large peak at 113.27. Methyl carbon atom exhibited a medium peak at δ 25.86 ppm. Finally mass spectrum of **3** also confirmed the structure. It exhibited a molecular ion peak at m/z 225 corresponding to its molecular weight. Other peaks appearing at m/z 210, 182, 154, 127 and 77 were in accordance with the fragmentation pattern of an assigned structure.

As a set target to synthesize the title compounds, **3** was made to undergo Claisen-Schmidt condensation followed by intramolecular Michael addition with aromatic aldehyde in presence of ethanolic sodium hydroxide solution. The mixture was taken in a mortar and ground well for 10 min to get uniform mass. Then the reaction mixture was subjected to microwave irradiation in ethanol at low power-2 for 4 to 5 min exposure to give 2-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(1*H*)-ones **5** in 73% yield. We also noticed that, when the mixture was pounded to get uniform mass before exposure to microwave, the compound **3** underwent Claisen-Schmidt condensation to produce an intermediate i.e. 1-aminonaphtho[2,1-*b*]furan-2-yl-3-phenylprop-2-en-1-one **4a-f** in 68-75% yield. This underwent intra molecular Michael types of addition in acetic acid media under microwave irradiation to give the title compounds **5a-f** hitherto unknown in literature. The structures of **5a-f** obtained by two pathways were confirmed by superimposing their ^1H NMR and mass spectral data. The sequence of reaction is cited in Scheme-3 and the products are tabulated in experimental section.

The IR spectrum of **4a** showed two absorption bands at 3200 and 3350 cm^{-1} due to symmetric and asymmetric stretching frequencies of NH_2 group and another band at 1622 cm^{-1} due to carbonyl group. The ^1H NMR spectrum of **4a** shows broad singlet at δ 6.2 due to NH_2 group (D_2O exchangeable) was found to be little higher δ value than before (δ 5.85). Further, a singlet at δ 2.55 attributed to the $COCH_3$ group of compound **3** was found to be absent, instead two doublets appeared between δ 7.75 (J=8 Hz) and 7.90 (J=9 Hz) was due to the protons of the CO-CH=CH-R group (merged with aromatic protons). The spectrum of **5a** was in well agreement to the assigned structure, showing absence of two sharp bands in the region of 3300-3400 due to the NH_2 group and appearance of bands in the region between 3300-3400 cm^{-1},

3100-3400 cm^{-1}, 1629 cm^{-1} characteristic of tetrahydroquinoline, assignable to –NH and –C=O frequencies in the IR spectrum. In the ^1H NMR spectrum of **5a** signals due to COCH=CHR and -NH_2 protons were not observed and instead a new peaks at δ 4.92-5.1 and at δ 2.64-3.1 as doublet of a doublet and two quartets respectively were observed due to -CH and -CH_2 protons of the nitrogen heterocycles. Similar observations were made in the case of tetrahydropyridine derivatives.[23]

Since the reactions took place well in microwave method, we would also like to disclose reaction features under conventional method. The results obtained pertaining to time & yields of both the methods are felt appropriate to discuss. So the results are given in the Table 1. In conclusion, the present protocol describes a simple and efficient method for the synthesis of angularly fused tetracyclic condensed heterocycles.

Table 1. Relative percentage of products formed under two methods (Column purified yields are reported)

Compounds	Conventional method		Microwave method	
	Time (hrs)	Yield (%)	Time (min)	Yield (%)
4a	4	55	4	72
4b	5	53	5	68
4c	4	61	4	70
4d	6	62	6	75
4e	7	58	5	70
4f	5	53	4	68
5a	6	55	6	68
5b	8	57	7	70
5c	5	60	8	67
5d	6	52	6	65
5e	8	55	5	68
5f	7	53	7	68

Experimental Section

General Procedures. Melting points were determined on a glass disk with an electrical bath and are uncorrected. ^1H NMR (400 MHz) spectra were run in $CDCl_3$ solutions. Chemical shifts are expressed in δ ppm. IR spectra were taken as neat for liquid compounds and as KBr pellet for solids. Elemental analysis was done by a Perkin-Elmer auto analyzer at IISc Bangalore. Column chromatography was performed on silica gel (60-120 mesh, SRL, India). Chloroacetone and dimethylformamide were distilled before use. The microwave-assisted procedures were carried out in a domestic Whirlpool Microwave oven operating at 1000 W.

Antimicrobial Screening. The *in vitro* antimicrobial activity was carried out against 24 hrs old cultures of two bacteria and two fungi by cup-plate method.[24] Compounds **4a-f** and **5a-f** has been tested for their antibacterial activity against *Pseudomonas aerugenosa* and *Staphylococcus aureus* and antifungal activity against *Aspergillus niger* and *Candida albicans.* Nutrient agar and potato dextrose agars were used to culture the bacteria and fungus respectively. The compounds were tested at varied concentration. The minimum inhibition concentration was found to be of 0.005 mol / ml in DMF against all organisms. The solution of chloramphenicol (2 mg/ ml) and fluconazole (2 mg/ ml) were prepared in sterilized water and used as standards for comparison of antibacterial and antifungal activities respectively. The compounds were tested at varied concentration. The minimum inhibition concentration was found to be 0.001mol/ ml in DMF against all organisms. Inhibition was recorded by measuring the diameter of the inhibition zone at the end of 24 hrs for bacteria at 28 ^{o}C and 48 h for fungus at 35 ^{o}C. Each experiment was repeated thrice and the average of the three independent determinations were recorded. The protocols were summarized in (Table 2). The compounds **5d**, **4d** and **5f** showed promising activity against *P. aerugenosa* and the **5b**, **5c** and **5e** against *S. aureus*. The compounds **5e**, **5d** and **5f** against *A. niger* and **5d**, **5f** and **5b** against *C. albicans* exhibited significant activity.

Table 2. Antimicrobial activities of **4a-f** and **5a-f**

	Antibacterial activity Zone of inhibition in mm		Antifungal activity Zone of inhibition in mm	
Compd.	P. aerugenosa	S. aureus	A. niger	C. albicans
4a	14	14	13	14
4b	15	14	15	15
4c	15	-	15	16
4d	17	15	16	15
4e	15	16	17	16
4f	-	16	15	-
5a	15	16	-	16
5b	16	18	17	18
5c	15	17	15	17
5d	19	16	18	20
5e	-	17	19	17
5f	17	-	18	20
Standard	26	24	25	26
DMF	+ ve	+ve	+ve	+ve

Chloramphenicol and fluconazole were used as standards for antibacterial and antifungal Activity, respectively:
Control (DMF) (-) - No activity.

Highly active (inhibition zone > 12 mm);
Moderately active (inhibition zone 9-12 mm);
Slightly active (inhibition zone 6-9 mm);
Inactive - inhibition zone < 6 mm).

2-Hydroxy-1-naphthonitrile (2). A mixture of 2-hydroxy-1-naphthaldehyde (1.72g, 0.01 mol) and hydroxylamine hydrochloride (0.68g, 0.01 mol) was taken in formic acid (0.46g, 0.01 mol) and sodium formate (0.68g, 0.01 mol). The reaction mixture was irradiated to microwave in domestic microwave oven (Whirlpool Microwave oven) at 500 W (50% of total power) for 4-5 min (with an short interruptions of 30 sec to 1 min in between) as required to complete the reaction (TLC). The resulting mixture was then poured into ice cold water. The solid separated was collected by filtration and recrystallized from methanol to obtain 1.47g, 85% yield. mp 71-72 ^{o}C.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl) ethanone (3). To a solution of 2-hydroxy-1-naphthonitrile **2** (1.69g, 0.01 mol) in dimethylformamide (10 ml) was added aq. KOH (10% 10 ml) and chloroacetone (0.92g, 0.01 mol). The reaction mixture was irradiated by microwave for 5-6 min to complete the reaction (TLC). To the reaction mixture an additional amount of KOH (10 %, 15 ml) was added with stirring, the deep orange precipitate of **3** that separated was collected by filtration and recrystallized from aq. dimethylformamide as yellow crystals to give 1.25g, 73% yield. mp 128-130^{o}C.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)-3-phenylprop-2-en-1-ones (4a-f). General procedure
1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)ethanone **3** (2.25g, 0.01mol) and benzaldehyde (1.06g, 0.01 mol) in sodium hydroxide were taken in a mortar; the whole mixture was minced well for 10 min to get uniform mass. The solid mass thus obtained was poured into water. The yellow solid obtained was recrystallized from ethyl acetate, purified by column chromatography using silica gel (60-120 mesh) and eluted with ethyl acetate pet-ether (25:75) to obtain 1.61g, 72% yield.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)-3-phenylprop-2-en-1-one (4a). Brown solid, (72%), mp 156-158^{o}C, MS: (M^{+}) 313; Anal.Calcd for $C_{21}H_{15}NO_2$: C 80.49, H 4.82, N 4.47, Found: C 80.23, H 4.52, N 4.27. IR (KBr, cm^{-1}): 1622 (C=O), 3424 (N-H); ^{1}H NMR (δ, DMSO): 6.23 (s, 2H, NH_2), 7.75 (d, 1H, -CO-CH=), 7.90 (d, 1H, C=CH), 7.34-7.55 (m, 5H, H_{arom}), 7.57 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.71 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.82 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.96 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.11 (d, 1H, $H_{arom,}$ J=8.1 Hz), 8.34 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 113.27, 114.14, 122.07, 124.89, 127.71, 128.62, 128.83, 129.69, 130.32, 131.28, 136.27, 137.53, 141.09, 144.82, 153.04. 196.93.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)-3-(4-chlorophenyl) prop-2-en-1-one (4b). Brown solid, (68%), mp 132-135^{o}C, MS: (M^{+}) 347; Anal.Calcd for $C_{21}H_{14}ClNO_2$: C 72.52, H 4.06, N 4.03, Found: C 71.85, H 4.13, N 4.06. IR (KBr, cm^{-1}): 1628 (C=O), 3425 (N-H); ^{1}H NMR (δ, DMSO-D_6): 6.21 (s, 2H, NH_2), 7.73 (d, 1H, -CO-CH=), 7.92 (d, 1H, C=CH), 7.32-7.57 (m, 4H, H_{arom}), 7.57 (t, 1H, $H_{arom,}$ J=7.2 Hz), 7.71 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.81 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.95 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.11 (d, 1H, $H_{arom,}$ J=8.2 Hz), 8.34 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C

NMR (DMSO-D_6) δ: 113.24, 114.13, 122.07, 124.87, 127.73, 128.63, 128.82, 129.60, 130.32, 131.28, 134.92, 136.26, 137.52, 141.12, 144.81, 153.06.196.95.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)-3-(4-bromophenyl) prop-2-en-1-one (4c). Brown solid, (70%), mp 135-136°C, MS: (M^+) 392; Anal.Calcd for $C_{21}H_{14}BrNO_2$: C 64.30, H 3.60, N 3.57, Found: C 64.15, H 3.55, N 3.59. IR (KBr, cm^{-1}): 1626 (C=O), 3424 (N-H); ^{1}H NMR (δ, DMSO): 6.22 (s, 2H, NH_2), 7.71 (d, 1H, -CO-CH=), 7.93 (d, 1H, C=CH), 7.33-7.54 (m, 4H, H_{arom}), 7.55 (t, 1H, $H_{arom,}$ J=7.2 Hz), 7.72 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.83 (d, 1H, $H_{arom,}$ J=9.2 Hz), 7.96 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.10 (d, 1H, $H_{arom,}$ J=8.3 Hz), 8.35 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 113.26, 114.15, 122.09, 123.12, 124.85, 127.71, 128.64, 128.84, 129.63, 130.31, 131.25, 136.28, 137.53, 141.09, 144.83, 153.06, 196.93.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)-3-(4-methylphenyl) prop-2-en-1-one (4d). Brown solid, (75%), mp 145-148°C, MS: (M^+) 327; Anal.Calcd for $C_{22}H_{17}NO_2$: C 80.71, H 5.23, N 4.28, Found: C 80.53, H 5.52, N 4.27. IR (KBr, cm^{-1}): 1622 (C=O), 3426 (N-H); ^{1}H NMR (δ, DMSO): 3.23 (s, 3H, CH_3), 6.23 (s, 2H, NH_2), 7.75 (d, 1H, -CO-CH=), 7.95 (d, 1H, C=CH), 7.35-7.55 (m, 4H, H_{arom}), 7.58 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.70 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.83 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.97 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.10 (d, 1H, $H_{arom,}$ J=8.1 Hz), 8.35 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 36.23, 113.26, 114.12, 122.10, 124.84, 127.72, 128.63, 128.83, 129.63, 130.33, 131.25, 136.26, 137.54, 137.83, 141.09, 144.82, 153.05, 196.96.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)-3-(4-methoxyphenyl) prop-2-en-1-one (4e). Brown solid, (70%), mp 140-141°C, MS: (M^+) 343; Anal.Calcd for $C_{22}H_{17}NO_3$: C 76.95, H 4.99, N 4.08, Found: C 76.55, H 4.98, N 4.05. IR (KBr, cm^{-1}): 1626 (C=O), 3424 (N-H); ^{1}H NMR (δ, DMSO): 3.93 (s, 3H, OCH_3), 6.21 (s, 2H, NH_2), 7.73 (d, 1H, -CO-CH=), 7.92 (d, 1H, C=CH), 7.33-7.54 (m, 4H, H_{arom}), 7.55 (t, 1H, $H_{arom,}$ J=7.2 Hz), 7.72 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.83 (d, 1H, $H_{arom,}$ J=9.2 Hz), 7.96 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.10 (d, 1H, $H_{arom,}$ J=8.3 Hz), 8.35 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 56.28, 113.27, 114.14, 122.07, 124.89, 127.71, 128.62, 128.83, 129.61, 130.32, 131.28, 136.27, 137.57, 141.09, 144.83, 153.04, 196.93.

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)-3-(4-nitrophenyl) prop-2-en-1-one (4f). Brown solid, (68%), mp 112-115°C, MS: (M^+) 358; Anal.Calcd for $C_{21}H_{14}N_2O_4$: C 70.39, H 3.94, N 7.82, Found: C 70.55, H 3.96, N 7.88. IR (KBr, cm^{-1}): 1628 (C=O), 3425 (N-H); ^{1}H NMR (δ, DMSO): 6.23 (s, 2H, NH_2), 7.75 (d, 1H, -CO-CH=), 7.90 (d, 1H, C=CH), 7.34-7.55 (m, 4H, H_{arom}), 7.57 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.71 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.82 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.96 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.11 (d, 1H, $H_{arom,}$ J=8.1 Hz), 8.34 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 113.26, 114.15, 122.09, 124.85, 127.71, 128.64, 128.84, 129.63, 130.31, 131.25, 136.28, 137.55, 141.09, 144.83, 148.15, 153.06, 196.95.

2-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4 (*1H*)-ones (5a-f). General procedure

1-(1-Aminonaphtho[2,1-*b*]furan-2-yl)ethanone **3** (2.25g, 0.01mol) was dissolved in ethanol (50 ml) containing NaOH (1g) and benzaldehyde (1.06g, 0.01 mol) was added to the above solution with stirring. The reaction mixture was irradiated by microwave at 500 W (50% of total power) for 4-5 min as required to complete the reaction. The reaction mixture was poured onto ice-cold

water to get solid which was filtered, washed with water, dried and recrystallized from dimethylformamide. The recrystallized crude product was purified by column chromatography on silica gel {eluent: ethyl acetate: petroleum-ether (1:9) to give 1.53g, 68% yield.

2-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(*1H*)-one (5a). Brown solid, (68%), mp 130-132^{o}C, MS: (M^{+}) 313; Anal.Calcd for $C_{21}H_{15}NO_2$: C 80.51, H 4.47, N 4.47, Found: C 80.53, H 4.45, N 4.37. IR (KBr, cm^{-1}): 1629 (C=O), 3426 (N-H); ^{1}H NMR (δ, DMSO): 4.92-5.12 (dd, 1H, -CH-), 2.64-3.13 (q, 2H, -CH_2 -), 5.25 (s, 1H, N-H), 7.35-7.55 (m, 5H, H_{arom}), 7.58 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.70 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.83 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.97 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.10 (d, 1H, $H_{arom,}$ J=8.1 Hz), 8.35 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 41.85, 47.94, 113.24, 114.13, 122.07, 124.87, 127.73, 128.82, 129.60, 130.32, 131.28, 136.26, 141.12, 153.06, 209.73.

2-(4-Chloro)-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(*1H*)-one (5b). Brown solid, (70%), mp 152-153^{o}C, MS: (M^{+}) 347; Anal.Calcd for $C_{21}H_{14}ClNO_2$: C 72.62, H 4.03, N 4.03, Found: C 72.65, H 4.09, N 4.02. IR (KBr, cm^{-1}): 1626 (C=O), 3424 (N-H); ^{1}H NMR (δ, DMSO): 4.93-5.14 (dd, 1H, -CH-), 2.64-3.12 (q, 2H, -CH_2-), 5.25 (s, 1H, N-H), 7.34-7.55 (m, 4H, H_{arom}), 7.57 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.71 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.82 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.96 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.11 (d, 1H, $H_{arom,}$ J=8.1 Hz), 8.34 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 41.84, 47.91, 113.26, 114.12, 122.10, 124.84, 127.72, 128.83, 129.63, 130.33, 131.25, 134.94, 136.26, 141.09, 153.05, 209.75.

2-(4-Bromo)-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(*1H*)-one (5c). Brown solid, (67%), mp 164-167^{o}C, MS: (M^{+}) 392; Anal.Calcd for $C_{21}H_{14}BrNO_2$: C 64.28, H 3.57, N 3.57, Found: C 64.23, H 3.71, N 3.63. IR (KBr, cm^{-1}): 1624 (C=O), 3426 (N-H); ^{1}H NMR (δ, DMSO): 4.91-5.13 (dd, 1H, -CH-), 2.63-3.12 (q, 2H, -CH_2-), 5.23 (s, 1H, N-H), 7.33-7.54 (m, 4H, H_{arom}), 7.55 (t, 1H, $H_{arom,}$ J=7.2 Hz), 7.72 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.83 (d, 1H, $H_{arom,}$ J=9.2 Hz), 7.96 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.10 (d, 1H, $H_{arom,}$ J=8.3 Hz), 8.35 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 41.85, 47.93, 113.26, 114.15, 122.09, 123.13, 124.85, 127.71, 128.84, 129.63, 130.31, 131.25, 136.28, 141.09, 153.06, 209.74.

2-(4-Methyl)-Phenyl-2,3-dihydronaphtho[2,1-*b*] furo[3,2-*b*]pyridin-4(*1H*)-one (5d). Brown solid, (65%), mp 195-197^{o}C, MS: (M^{+}) 327; Anal.Calcd for $C_{22}H_{17}NO_2$: C 80.73, H 5.19, N 4.28, Found: C 80.56, H 5.15, N 4.29. IR (KBr, cm^{-1}): 1626 (C=O), 3424 (N-H); ^{1}H NMR (δ, DMSO): 3.23 (s, 3H, CH_3), 4.93-5.13 (dd, 1H, -CH-), 2.64-3.13 (q, 2H, -CH_2-), 5.25 (s, 1H, N-H), 7.32-7.57 (m, 4H, H_{arom}), 7.57 (t, 1H, $H_{arom,}$ J=7.2 Hz), 7.71 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.81 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.95 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.11 (d, 1H, $H_{arom,}$ J=8.2 Hz), 8.34 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 36.25, 41.81, 47.86, 113.26, 114.12, 122.10, 124.84, 127.72, 128.83, 129.63, 130.33, 131.25, 136.26, 137.83, 141.09, 153.05, 209.75.

2-(4-Methoxy)-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(*1H*)-one (5e). Brown solid, (68%), mp 145-146°C, MS: (M^+) 343; Anal.Calcd for $C_{22}H_{17}NO_3$: C 76.95, H 4.95, N 4.08, Found: C 76.55, H 4.98, N 4.05. IR (KBr, cm^{-1}): 1630 (C=O), 3424 (N-H); ^{1}H NMR (δ, DMSO): 3.93 (s, 3H, OCH_3), 4.93-5.13 (dd, 1H, -CH-), 2.64-3.14 (q, 2H, $-CH_2-$), 5.26 (s, 1H, N-H), 7.35-7.55 (m, 4H, H_{arom}), 7.58 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.70 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.83 (d, 1H, $H_{arom,}$ J=9.1 Hz), 7.97 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.10 (d, 1H, $H_{arom,}$ J=8.1 Hz), 8.35 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 41.87, 47.96, 56.26, 113.27, 114.14, 122.07, 124.89, 127.71, 128.83, 129.61, 130.32, 131.28, 136.27, 141.09, 153.04, 209.76.

2-(4-Nitro)-Phenyl-2,3-dihydronaphtho[2,1-*b*]furo[3,2-*b*]pyridin-4(*1H*)-one (5f). Brown solid, (70%), mp 175-177°C, MS: (M^+) 358; Anal.Calcd for $C_{21}H_{14}N_2O_4$: C 70.39, H 43.91, N 7.82, Found: C 70.65, H 43.93, N 7.85. IR (KBr, cm^{-1}): 1632 (C=O), 3424 (N-H); ^{1}H NMR (δ, DMSO): 4.93-5.14 (dd, 1H, -CH-), 2.64-3.12 (q, 2H, $-CH_2-$), 5.25 (s, 1H, N-H), 7.33-7.54 (m, 4H, H_{arom}), 7.55 (t, 1H, $H_{arom,}$ J=7.2 Hz), 7.72 (t, 1H, $H_{arom,}$ J=7.3 Hz), 7.83 (d, 1H, $H_{arom,}$ J=9.2 Hz), 7.96 (d, 1H, $H_{arom,}$ J=9.3 Hz), 8.10 (d, 1H, $H_{arom,}$ J=8.3 Hz), 8.35 (d, 1H, $H_{arom,}$ J=7.8 Hz). ^{13}C NMR (DMSO-D_6) δ: 41.86, 47.96, 113.26, 114.15, 122.09, 124.85, 127.71, 128.84, 129.63, 130.31, 131.25, 136.28, 141.09, 148.16, 153.06, 209.74.

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