Chapter VI

A novel approach for the synthesis of 2-aryl-2,3-dihydronaphtho[2,1-b]furo[3,2-b]pyridin-4(1H)-ones
Introduction

Pyridine ring fused with furan ring system in linear fashion is found in natural products as well as in the synthetic compounds of biological interest. Quinoline condensed with furan in linear fashion is present in the alkaloids isolated from Rutaceae. Dictamnine 1, skimmianine 2 and γ-fagarine 3 are the most important among them.\(^1\) Synthesis of thienoquinolines 4 and tetrahydrothieno quinolines 5 have also been reported in the literature and are found to display antibacterial and antimicrobial activity.\(^2,3\) Recently Katsumi et al., have reported that thienoquinolones 6 exhibit antitumor activity in mice inoculated with p388 cells in addition to antibacterial activity.

A tetra fused condensed heterocyclic ring system play significant role for the development of anticancer therapeutic agents. Recently, Xia et al., reported the synthesis of series of 2-phenyl-1,2,3,4-tetrahydroquinolin-4-ones as a new class of antimitotic,
antitumour agents. Most of the compounds showed promising cytotoxicity in human tumour cell line assay\textsuperscript{4-10}.

Prompted by these findings, Ambekar\textsuperscript{11,12} et al., synthesized pyrimido[4,5:4,5]thieno[2,3-b]quinolin-4(3H)-ones 7 and 4-aminopyrimido[4,5:4,5]thieno[2,3-b]quinolines 8 and 2-aryl-1,2,3,4-tetrahydropyrido[2,3,:4,5]thieno[2,3-b]quinolin-4-ones 9. These compounds exhibited significant blood platelet disaggregating property induced by ADP and collagen.

Taking a cue from these findings, a project on the synthesis of linearly fused tetracyclic heterocycles was under taken in this laboratory. Vaidya\textsuperscript{13,16} et al., under took the synthesis of naphtho[2,1-b]furopyrimidines and naphtho[2,1-b] azepines and tested them for their biological activities. Encouraged by these findings, synthesis of another new tetracyclic heterocycles system namely 2-aryl-2, 3-dihyronaphtho[2,1-b]furo[3,2-b]pyridin-4(1H)-ones was taken up and the same is described in this chapter.
Present work

The strategy adopted for the synthesis of this new heterocyclic system involves successive building up of furan and pyridone ring on naphthalene (Scheme 2 and 4). The method adopted for the building up of furan ring on naphthalene nucleus is essentially the one earlier reported by Vaidya from this laboratory. Since, we are interested in the fusion of pyridone ring system in a linear fashion, a new method for the synthesis of such a system was thought. Previous report on the synthesis of flavanones from corresponding chalcones came handy for this purpose. There is similarity between 2-aryl-1,2,3,4-tetrahydroquinolin-4-one 10 and flavanones 11.

![Diagram](image1)

Flavanones are usually obtained by the acid catalyzed cyclization of 2-hydroxy chalcones ie 1-[2-hydroxy-phenyl]-3-phenyl-2-propen-1-one (Scheme-1).

![Diagram](image2)

On the same line one can expect the acid catalyzed cyclization of 1-aminonaphtho[2,1-b]furan-2-yl-3-phenylprop-2-en-one which may be considered as analogue of 2-hydroxy chalcones and which would yield the desired target compounds. Therefore, for the building up of pyridone nucleus on to the naphthofuran ring, it must
**Furo[3, 2-b]pyridin-4(1H)-ones**

have acetyl and amino groups at 2 and 3 positions respectively. The naphthofurans with such substituents would be the best obtained by Thorpe-Ziegler type cyclization of 2-hydroxy-1-naphthonitrile with chloroacetone. The key intermediate is therefore 2-hydroxy-1-naphthonitrile.

The various steps involved in this synthetic strategy are as follows:


1. **Synthesis of 2-hydroxy-1-naphthonitrile 16**

The key intermediate 2-hydroxy-1-naphthonitrile 16 was synthesized from 2-hydroxy-1-naphthaldehyde. The compound 16 was prepared from equimolar mixture of 2-hydroxy-1-naphthaldehyde, hydroxylamine hydrochloride in formic acid and sodium formate. The microwave irradiation was done at power-40 (half of the power) in the unmodified domestic microwave oven. This was done for 4-5 minute until the completion of the reaction, which was monitored by TLC. The required 2-hydroxy-1-naphthaldehyde was prepared from 2-naphthol by Reimer-Tiemann reaction by following the literature procedure. The sequence of reaction is as follows (Scheme-2).
Mechanism

The structure of 2-hydroxy-1-naphthonitrile was confirmed by its IR spectrum, which exhibited strong absorption band at 2223 cm\(^{-1}\) due to \(-\text{CN}\) group and a broad absorption band at 3300 cm\(^{-1}\) due to \(-\text{OH}\) group [Fig: 6.1]. \(^{13}\)C NMR data is also consistent with the structure [Fig: 6.2]. This is a novel method for the conversion of 2-hydroxy-1-naphthaldehyde into 2-hydroxy-1-naphthonitrile. The overall yield is 90% and the product is obtained in high purity.

2. Condensation of 2-hydroxy-1-naphthonitrile with chloroacetone, followed by Thorpe-Ziegler cyclisation into 2-acetyl-3-aminonaphtho[2,1-b]furan

2-Hydroxy-1-naphthonitrile 16 on reaction with chloroacetone in presence of anhydrous potassium carbonate and dry acetone at reflux temperature underwent
condensation and Thorpe-Ziegler cyclization to produce 2-acetyl-3-aminonaphtho [2,1-b]furan 17 in moderate yield. Better yield (85%) of the product was obtained when this reaction was carried out in potassium hydroxide and dimethylformamide by irradiation under microwave for 5-6 minutes (Scheme-3).

Mechanism

Scheme-3

The structure of 17 was confirmed by elemental analysis and spectral data. The IR spectrum of 17 exhibited two absorption bands due to symmetric and asymmetric
stretching frequencies of primary amine at 3375 and 3489 cm\(^{-1}\) and another absorption band at 1630 cm\(^{-1}\) due to intramolecularly hydrogen-bonded carbonyl group [Fig: 6.3] (2-amino ketone). The \(^1\)H NMR spectrum of 17 showed a broad singlet (exchangeable with D\(_2\)O) integrating for two protons at \(\delta\) 5.95 ppm due to –NH\(_2\) group, a singlet integrating for three protons at \(\delta\) 2.55 ppm due to –CH\(_3\) group and a multiplet at \(\delta\) 7.26-8.3 ppm integrating for six aromatic protons [Fig: 6.4].

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 17, a small peak at \(\delta\) 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 \(\delta\) 25.86 ppm [Fig: 6.5].

Finally, mass spectrum of 17 also confirmed the structure. It exhibited a molecular ion peak at m/z 225 corresponding to its molecular weight [Fig: 6.6]. Other peaks appearing at m/z 210, 182, 154, 127 and 77 were in accordance with the fragmentation pattern as shown in the (Scheme-4).
3. Conversion of 2-acetyl-3-aminonaphtho[2,1-b]furan into naphthofuran analogues of 2-amino chalcones (18a-f)

As the systems containing o-hydroxy acetyl functionalities are easily accessible, 2-hydroxy chalcones can be readily prepared. Several heterocyclic analogues of 2-hydroxy chalcones have been prepared for further structural modifications. 2-Hydroxy chalcones are also an important class of organic molecules, due to their association with useful biological activities and their synthetic potentiality.

2-Amino chalcones are also of great interest for the same reasons. However, owing to the difficulties encountered in the synthesis of systems containing 2-amino acetyl functions, there are only a few scattered reports on the synthetic investigations of these compounds. Hence, it was contemplated to convert 2-acetyl-3-amino naphtho[2,1-b]furan into 2-amino chalcones analogues i.e., 1-(1-aminonaphtho
The desired conversion was accomplished by the reaction of 17 with different aromatic aldehyde in presence of strong base. The following aldehydes were selected for this investigation, in order to study structure activity relationship.

1. Benzaldehyde
2. 4-Chlorobenzaldehyde
3. 4-Bromobenzaldehyde
4. 4-Methylbenzaldehyde
5. 4-Methoxybenzaldehyde
6. 4-Nitrobenzaldehyde

The 3-amino-2-acetylnaphtho[2,1-b]furan 17 was then subjected to Claisen-Schmidt condensation with benzaldehyde in presence of sodium hydroxide was subjected to microwave at low power-2 for 4-5 minute exposure to obtain 2-phenyl-2,3-dihydronaphtho[2,1-b]furo[3,2-6]pyridine-4(1H)-ones 19a. However, the pinch of mass taken out was worked up to gave 1-aminonaphtho[2,1-b]furan-2-yl-3-phenylprop-2-en-1-one 18a. It was observed that, the compound 17 underwent Claisen-Smith condensation followed by simultaneous Michael addition under basic condition to gave 2-phenyl-2,3-dihydronaphtho [2,1-b]furo[3,2-6]pyridine-4(1H)-ones in single step.

The free amino group in the condensation product 18a was indicated by colour reaction with neutral ferric chloride and spectroscopic data. The direct condensation of 3-amino-2-acetylnaphtho[2,1-b]furan 17 with benzaldehyde gave a product identical with 2-phenyl-2,3-dihydronaphtho[2,1-b]furo[3,2-6]pyridine-4(1H)-ones 19a in good yield. The identity of product 19a obtained by both the methods was established by mixed m.p.
Furo[3,2-b]pyridin-4(1H)-ones and superimposable IR spectra. The remaining compounds 18b-f were prepared similarly from 3-amino-2-acetylnaphto[2,1-b]furan 17 by condensation with appropriate aldehydes under microwave to get the compound with high yield in the single step (Scheme-5).

The IR spectrum of 18a showed two absorption bands at 3200 and 3433 cm⁻¹ which were attributed to symmetric and asymmetric stretching frequencies of −NH₂ group and another band at 1622 cm⁻¹ due to α, β-unsaturated carbonyl group [Fig: 6.7].

\[18a-f\]

\[ArCHO / NaOH\]

\[M W / 4-5 \text{ min}\]

\[17\]

\[ArCHO / NaOH\]

\[Mechanical \text{ grinding}\]

\[18a-f\]

\[Acetic \text{ acid}\]

\[M W / 2-3 \text{ min}\]

\[19a-f\]

\[R = \text{ a H, b. 4-Cl, 4-Br, 4-CH₃, 4-OCH₃, 4-NO₂}\]

Scheme-5

Appearance of a broad singlet at δ 6.23 (D₂O exchangeable) due to two −NH₂ protons in ¹H NMR spectrum of 18a confirmed non-involvement of amino group in the reaction with aldehydes. Further, a singlet at δ 2.55 ppm attributed to -CO-CH₃ group of compound 17 was found to be conspicuously absent in the ¹H NMR spectrum of 18a,
instead a doublet of doublet appeared between $\delta$ 7.75 and 7.90 ppm which was attributed to the protons of $-\text{CO-CH=CH-R}$ group (merged with aromatic protons) [Fig: 6.8]. The multiplet at $\delta$ 7.21-8.32 ppm integrating for 11 aromatic protons confirms the assigned structure to the molecule.


Analogous to the preparation of flavones from 2-hydroxyl chalcones, it was contemplated to synthesize 2-phenyl-$2,3$-dihydronaphtho[$2,1-b$]$furo[3,2-6]$pyridin-$4(1H)$-ones 19a-f from 3-amino-2-acetyl naphtho[$2,1-b$]$furan$ 17 in single step. The intermediate chalcone 1-(1-aminonaphtho[$2,1-6$]$furan-2-yl)$-3$-phenylprop-2-en-1-one 18a were also converted into 19a on refluxing with phosphoric acid in acetic acid media under conventional method for about 8-10 hrs. The authenticity of the compounds obtained by either method has been ascertained by overlapping their IR and $^1$H NMR spectral data.

The IR spectrum of 19a exhibited single absorption band at 3450 cm$^{-1}$ due to $-\text{NH}$ group and sharp absorption band at 1629 cm$^{-1}$ due to $-\text{C=O}$ group are the characteristic frequencies of tetrahydropyridone [Fig: 6.9]. The $^1$H NMR spectrum of 19a revealed the
absence of signals due to \(-\text{CO-CH}=\text{CH-}\) and \(-\text{NH}_2\) protons. Where as new peaks at \(\delta\) 4.92-5.12 and at \(\delta\) 2.64-3.13 as doublet of a doublet and two quartets respectively were observed due to \(-\text{CH-}\) and \(-\text{CH}_2-\) protons of newly formed tetrahydropyridone ring system. As expected 11 aromatic protons appeared as multiplet at \(\delta\) 7.2 and 7.7 and broad singlet at 7.85 appeared (D\(_2\)O exchangeable) due to \(-\text{NH}\) proton [Fig: 6.10].

The mass spectrum of 19a was recorded as additional evidence for the proposed structure. It exhibited molecular ion peak at m/z 313 corresponding to its molecular weight [Fig: 6.11]. The other predominant peaks which appeared at m/z 295, 236, 210, 170, 144, 115, 91 and 77 were in consistent with expected fragmentation pattern as shown in the (Scheme-6).
Mass fragmentation pattern of compound 19a

Scheme-6
Fig: 6.3; IR Spectra of 17

![Chemical Structure of 17]

- Wavenumbers: 3440.93, 1630.93, 1541.72, 1519.66, 1292.21, 1176.87, 963.52, 869.30, 750.17, 574.41
Fig: 6.4; 'H NMR Spectra of 17

NAME: J-1  
EXPNO: 1  
PROCNO: 1

F2 - Acquisition Parameters

Time 4.16  
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PROBNO 5 mm DUL 13C-1  
PULPROG zg30  
TD 32768  
SOLVENT CDC13  
NS 32  
DS 0  
SNH 5995.204 Hz  
FIDRES 0.182599 Hz  
AQ 2.7352011 sec  
RG 203.2  
DW 83.400 usec  
DE 0.00 usec  
TE 300.0 K  
DI 2.00000000 usec  

********** CHANNEL f2 **********

NUC1 1H  
F1 8.00 usec  
P1 -1.00 db  
SFO1 300.1327012 MHz

F2 - Processing parameters

SI 16384  
SF 300.1239999 MHz  
NOW EM  
SSB 0  
LB 1.00 Hz  
GB 0  
PC 7.00

ID NMR plot parameters

CX 20.00 cm  
CY 30.00 cm  
F1P 19.988 ppm  
F1 5698.87 Hz  
F2P -0.987 ppm  
F2 -296.34 Hz  
PWCHM 0.99877 ppm/cm  
HZCM 299.76019 Hz/cm
Fig: 6.5, $^{13}$C NMR Spectra of 17
Fig: 6.6; Mass Spectrum of 17

![Mass Spectrum of 17](image)

Scan #: 746
Mass Peak #: 339 Ret. Time : 15.417
Base Peak : 44.05 (45427)

**** Peak Report ****

PKNO R.Time I.Time - E.Time Area Height A/H(sec) MK % Total Name
1 15.409 15.300 - 15.833 1908415 166903 11.434 V 100.00

Total 1908415 100.00
Fig: 6.8; $^1$H NMR Spectra of 18a

Current Data Parameters

**F2 - Acquisition Parameters**
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PULPROG: zg
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SOLVENT: CDC13
NS: 64
DS: 0
SWH: 5102.041 H
FIDRES: 0.155702 H
AQ: 3.211140 s
RG: 256
DW: 98.000 u
DE: 122.50 u
TE: 300.0 K
HL1: 1 d
DI: 1.00000000 s
PL: 12.25 u
SFO1: 400.1363420 M
NUCLEUS: 1H

**F2 - Processing parameter**
SI: 32768
SF: 400.1343949 M
WDW: EM
SSB: 0
LB: 0.30 H
GB: 0
PC: 2.00
Fig: 6.9; IR Spectra of 19a
Fig: 6.10; $^1$H NMR Spectra of 19a
Fig: 6.11; Mass Spectrum of 19a
Experimental

2-Hydroxy-1-naphthonitrile 16

A mixture of 2-hydroxy-1-naphthaldehyde 15 (3.44 gm, 20 mmol) and hydroxylamine hydrochloride (1.36 g, 20 mmol) were taken in formic acid (0.92 g, 20 mmol) and sodium formate (1.36 g, 20 mmol). The reaction mixture was irradiated to microwave in domestic microwave oven (Whirlpool Microwave oven) at 500 W (50% of the total power) for 4-5 minutes (with short exposure of 30 Sec at each shot) as required to complete the reaction (TLC). The resulting mixture was poured into ice cooled water. The solid separated was collected by filtration and recrystallized from methanol. (5.45 g, 98%), mp 72°C

1-(1-Aminonaphtho[2,1-b]furan-yl) ethanone 17

To a solution of 2-hydroxy-1-naphthonitrile 16 (1.69 g, 10 mmol) in DMF (10 mL) was added aqueous KOH (10%, 10 mL) and chloroacetone (0.92 g, 10 mmol). The reaction mixture was irradiated by microwave for 5-6 minutes to complete the reaction (TLC). To reaction mixture an additional amount of KOH (10 %, 15 mL) was added with stirring, the deep orange precipitate of 16 that separated was collected by filtration and recrystallized from aq, dimethylformamide as yellow crystals (1.12 g, 70%) m.p. 130°C.

1-(1-Aminonaphtho[2,1-b]furan-2-yl)-3-phenylprop-2-en-1-one 18a-f

1-(1-Aminonaphtho[2,1-b]furan-yl) ethanone 17 (2.25 g, 10 mmol) and benzaldehyde (1.06 g, 10 mmol) in sodium hydroxide were taken in mortar, the whole mixture was ground well for 10 min to get uniform mass. The solid mass 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). (2.0 g, 90 %), m p 156° C.

**2-Pheny1-2,3-dihydronaphtho[2,1-6]furo[3,2-b]pyridin-4(1H)-ones 19a-f**

1-(1-Aminonaphtho[2,1-b]furan-yl)ethanone 17 (2.25 g, 10 mmol) was dissolved in ethanol ( 50 mL) containing NaOH ( 1g) and benzaldehyde (1.06 g, 10 mmol) was added to the above solution with stirring. The reaction mixture was irradiated by microwave at 500 W (50 % of the total power) for 4-5 minute as required to complete the reaction. The reaction mixture was poured onto ice-cold water to get solid which was filtered, washed with ethanol, dried and recrystallized from DMF. The recrystallized crude product was purified by column chromatography on silica gel {eluent: ethyl acetate: Petroleum-ether (1:9).}

**1-(1-Aminonaphtho[2,1-b]furan-2-yl)-3-phenylprop-2-en-1-one (18a)**

Brown solid, (72%), mp 156-158°C, MS m/z: (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) \( \gamma_{\text{max/cm}^{-1}} \): 1622 (C=O), 3433 (N-H); \(^1\)H NMR (δ, DMSO): 6.23 (s, 2H, NH\(_2\)), 7.10-7.70 (m, 11H, Ar-H), 7.75 (d, 1H, -CO-CH=), 7.90 (d, 1H, C=CH); \(^{13}\)C NMR (DMSO) δ: 174.13 (C=O), [113.26 (C-9), 114.12 (C-3), 124.87 (C-5), 127.73 (C-4), 131.27 (C-8), 136.15 (C-11), naphthofuran carbons].
1-(1-Aminonaphtho[2,1-b]furan-2-yl)-3-(4-chlorophenyl) prop-2-en-1-one (18b)

Brown solid, (68%), mp 132-135°C, MS m/z: (M⁺) 347; Anal.Calcd for C₂₁H₁₄ClNO₂: C 72.52, H 4.06, N 4.03, Found: C 71.85, H 4.13, N 4.06; IR (KBr) \( \gamma_{\text{max}}/\text{cm}^{-1} \): 1624 (C=O), 3434 (N-H); ¹H NMR (δ, DMSO): 6.21 (s, 2H, NH₂), 7.15-7.60 (m, 10H, Ar-H), 7.73 (d, 1H, -CO-CH=), 7.92 (d, 1H, C=CH); ¹³C NMR (DMSO) δ: 134.52 (C-Cl), 174.15 (C=O), [113.23 (C-9), 114.12 (C-3), 124.88 (C-5), 127.71 (C-4), 131.27 (C-8), 136.16 (C-11), naphthofuran carbons].

1-(1-Aminonaphtho[2,1-b]furan-2-yl)-3-(4-bromophenyl) prop-2-en-1-one (18c)

Brown solid, (70%), mp 135-136°C, MS m/z: (M⁺) 392; Anal.Calcd for C₂₁H₁₄BrNO₂: C 64.30, H 3.60, N 3.57, Found: C 64.15, H 3.55, N 3.59; IR (KBr) \( \gamma_{\text{max}}/\text{cm}^{-1} \): 1626 (C=O), 3432 (N-H); ¹H NMR (δ, DMSO): 6.22 (s, 2H, NH₂), 7.00-7.60 (m, 10H, Ar-H), 7.71 (d, 1H, -CO-CH=), 7.93 (d, 1H, C=CH); ¹³C NMR (DMSO) δ: 125.60 (C-Br), 174.15 (C=O), [113.25 (C-9), 114.14 (C-3), 124.87 (C-5), 127.71 (C-4), 131.25 (C-8), 136.17 (C-11), naphthofuran carbons].

1-(1-Aminonaphtho[2,1-b]furan-2-yl)-3-(4-methylphenyl) prop-2-en-1-one (18d)

Brown solid, (75%), mp 145-148°C, MS m/z: (M⁺) 327; Anal.Calcd for C₂₂H₁₇NO₂: C 80.71, H 5.23, N 4.28, Found: C 80.53, H 5.52, N 4.27; IR (KBr) \( \gamma_{\text{max}}/\text{cm}^{-1} \): 1622 (C=O), 3436 (N-H); ¹H NMR (δ, DMSO): 1.23 (s, 3H, CH₃), 6.23 (s, 2H, NH₂), 7.15-7.63 (m, 10H, Ar-H), 7.75 (d, 1H, -CO-CH=), 7.95 (d, 1H, C=CH); ¹³C NMR (DMSO) δ: 36.16 (CH₃), 143.13 (C-CH₃), 174.17 (C=O), [113.26 (C-9), 114.12 (C-3), 124.87 (C-5), 127.73 (C-4), 131.27 (C-8), 136.15 (C-11), naphthofuran carbons].
1-(1-Aminonaphtho[2,1-b]furan-2-yl)-3-(4-methoxyphenyl) prop-2- en-1-one (18e)

Brown solid, (70%), mp 140-141°C, MS m/z: (M⁺) 343; Anal.Calcd for C₂₂H₁₇NO₃: C 76.95, H 4.99, N 4.08, Found: C 76.55, H 4.98, N 4.05; IR (KBr) \( \gamma_{\text{max}} / \text{cm}^{-1} \): 1626 (C=O), 3435 (N-H); \(^1\)H NMR (δ, DMSO): 3.93 (s, 3H, OCH₃), 6.21 (s, 2H, NH₂), 7.05-7.60 (m, 10H, Ar-H), 7.73 (d, 1H, -CO-CH=), 7.92 (d, 1H, C=CH), \(^{13}\)C NMR (DMSO) δ: 56.16 (OCH₃), 159.93 (C-OCH₃), 174.17 (C=O), [113.25 (C-9), 114.14 (C-3), 124.87 (C-5), 127.71 (C-4), 131.25 (C-8), 136.17 (C-11), naphthofuran carbons].

1-(1-Aminonaphtho[2,1-b]furan-2-yl)-3-(4-nitrophenyl) prop-2-en-1-one (18f)

Brown solid, (68%), mp 112-115°C, MS m/z: (M⁺) 358; Anal.Calcd for C₂₁H₁₄N₂O₄: C 70.39, H 3.94, N 7.82, Found: C 70.55, H 3.96, N 7.88; IR (KBr) \( \gamma_{\text{max}} / \text{cm}^{-1} \): 1628 (C=O), 3434 (N-H); \(^1\)H NMR (δ, DMSO): 6.23 (s, 2H, NH₂), 7.10-7.60 (m, 10H, Ar-H), 7.75 (d, 1H, -CO-CH=), 7.90 (d, 1H, C=CH), \(^{13}\)C NMR (DMSO) δ: 144.14 (C-NO₂), 174.16 (C=O), [113.26 (C-9), 114.12 (C-3), 124.87 (C-5), 127.73 (C-4), 131.27 (C-8), 136.15 (C-11), naphthofuran carbons].

2-Phenyl-2,3-dihydronaphtho[2,1-b]furo[3,2-b]pyridin-4 (1H)-one (19a)

Brown solid, (68%), mp 130-132°C, MS m/z: (M⁺) 313; Anal.Calcd for C₂₁H₁₃NO₂: C 80.49, H 4.82, N 4.47, Found: C 80.50, H 4.85, N 4.45; IR (KBr) \( \gamma_{\text{max}} / \text{cm}^{-1} \): 1629 (C=O), 3453 (N-H); \(^1\)H NMR (δ, DMSO): 4.99-
5.02 (dd, 1H, -CH-), 2.64-2.91 (q, 2H, -CH₂-), 7.30-7.80 (m, 11H, Ar-H), 7.85 (s, 1H, N-H); \(^{13}\)C NMR (DMSO) δ: 185.61 (C=O), [113.23 (C-9), 114.14 (C-3), 124.85 (C-5), 127.72 (C-4), 131.28 (C-8), 136.18 (C-11), naphthofuran carbons].

2-(4-Chloro)-phenyl-2,3-dihydronaphtho[2,1-\(b\)]furo[3,2-\(b\)]pyridin-4 (1H)-one (19b)

Brown solid, (70%), mp 152-153°C, MS m/z: (M^+) 347;
Anal. Calcd for C\(_{21}\)H\(_{14}\)ClNO\(_2\): C 72.65, H 4.06, N 4.03, Found: C 72.65, H 4.09, N 4.02; IR (KBr) \(\gamma_{\text{max}}/\text{cm}^{-1}\): 1626 (C=O), 3452 (N-H); \(^1\)H NMR (δ, DMSO): 4.98-5.05 (dd, 1H, -CH-), 2.64-2.92 (q, 2H, -CH₂-), 7.35-7.85 (m, 10H, Ar-H), 7.83 (s, 1H, N-H); \(^{13}\)C NMR (DMSO) δ: 134.52 (C-Cl), 185.63 (C=O), [113.26 (C-9), 114.17 (C-3), 124.85 (C-5), 127.70 (C-4), 131.25 (C-8), 136.18 (C-11), naphthofuran carbons].

2-(4-Bromo)-phenyl-2,3-dihydronaphtho[2,1-\(b\)]furo[3,2-\(b\)]pyridin-4 (1H)-one (19c)

Brown solid, (67%), mp 164-167°C, MS m/z: (M^+) 392; Anal. Calcd for C\(_{21}\)H\(_{14}\)BrNO\(_2\): C 64.30, H 3.60, N 3.57, Found: C 64.33, H 3.61, N 3.59; IR (KBr) \(\gamma_{\text{max}}/\text{cm}^{-1}\): 1624 (C=O), 3453 (N-H); \(^1\)H NMR (δ, DMSO): 4.97-5.05 (dd, 1H, -CH-), 2.63-2.91 (q, 2H, -CH₂-), 7.32-7.88 (m, 10H, Ar-H), 7.86 (s, 1H, N-H); \(^{13}\)C NMR (DMSO) δ: 125.51 (C-Br), 185.62 (C=O), [113.23 (C-9), 114.15 (C-3), 124.85 (C-5), 127.77 (C-4), 131.25 (C-8), 136.16 (C-11), naphthofuran carbons].
2-(4-Methyl)-phenyl-2,3-dihydropyrido[2,1-b]furo[3,2-b]pyridin-4(1H)-one (19d)

Brown solid, (65%), mp 195-197°C, MS m/z: (M⁺) 327; Anal.Calcd for C₂₂H₁₇NO₂: C 80.71, H 5.23, N 4.28, Found: C 80.73, H 5.25, N 4.29; IR (KBr) νmax/cm⁻¹: 1626 (C=O), 3452 (N-H); ¹H NMR (δ, DMSO): 1.23 (s, 3H, CH₃), 4.99-5.03 (dd, 1H, -CH-), 2.64-3.29 (q, 2H, -CH₂-), 7.31-7.85 (m, 10H, Ar-H), 7.83 (s, 1H, N-H); ¹³C NMR (DMSO) δ: 36.14 (CH₃), 143.14 (C-CH₃), 185.65 (C=O), [113.26 (C-9), 114.14 (C-3), 124.86 (C-5), 127.79 (C-4), 131.26 (C-8), 136.15 (C-11), naphthofuran carbons].

2-(4-Methoxy)-phenyl-2,3-dihydropyrido[2,1-b]furo[3,2-b]pyridin-4(1H)-one (19e)

Brown solid, (68%), mp 145-146°C, MS m/z: (M⁺) 343; Anal.Calcd for C₂₂H₁₇NO₃: C 76.95, H 4.99, N 4.08, Found: C 76.95, H 4.98, N 4.05; IR (KBr) νmax/cm⁻¹: 1630 (C=O), 3453 (N-H); ¹H NMR (δ, DMSO): 3.93 (s, 3H, OCH₃), 4.97-5.01 (dd, 1H, -CH-), 2.69-2.93 (q, 2H, -CH₂-), 7.35-7.84 (m, 10H, Ar-H), 7.86 (s, 1H, N-H); ¹³C NMR (DMSO) δ: 56.26 (OCH₃), 159.92 (C-OCH₃), 185.65 (C=O), [113.22 (C-9), 114.16 (C-3), 124.87 (C-5), 127.78 (C-4), 131.25 (C-8), 136.14 (C-11), naphthofuran carbons].
2-(4-Nitro)-phenyl-2,3-dihydronaphtho[2,1-b]furo[3,2-b]pyridin-4 (1H)-one (19f)

Brown solid, (70%), mp 175-177°C, MS m/z: (M⁺) 358; Anal. Calcd for C₂₁H₁₄N₂O₄: C 70.39, H 3.94, N 7.82, Found: C 70.35, H 3.93, N 7.85; IR (KBr) νmax/cm⁻¹: 1632 (C=O), 3453 (N-H); ¹H NMR (δ, DMSO): 4.98-5.01 (dd, 1H, -CH-), 2.70-2.95 (q, 2H, -CH₂-), 7.36-7.84 (m, 10H, Ar-H), 7.82 (s, 1H, N-H), ¹³C NMR (DMSO) δ: 144.14 (C-NO₂), [113.26 (C-9), 114.12 (C-3), 124.87 (C-5), 127.73 (C-4), 131.27 (C-8), 136.15 (C-11), naphthofuran carbons].
Furo[3, 2-b]pyridin-4(1H)-ones

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