CHAPTER-3

Introduction

In view of the close association of pyrimidines with important biodynamic agents, numerous compounds containing such a ring system have been extensively investigated. Pyrimidine nucleus occurs in biologically important products such as nucleic acids, vitamins, coenzymes and pharmacologically useful natural products of plant origin. This fact led to the wide exploration of several condensed pyrimidines containing various heterocycles like furan\(^1\), thiophene\(^2\), pyrrole\(^3\), pyrazole\(^4-5\), thiazole\(^6\), imidazole\(^7-8\), pyridine\(^9-10\), pyrazine\(^11\), indole\(^12\) etc. Such fusion, resulted in the compounds possessing one or the other biological or pharmacological activities\(^13-17\). The detailed discussion regarding these investigations is not within the limits of this thesis. However, a few important compounds enclosing pyrimidine moiety are described in the following pages.

Pyrimidine ring when fused with thiophene or furan nucleus exhibits marked gastric antisecretory activity\(^18\). Cytotoxic property was observed when pyrimidine moiety is fused with triazole moiety\(^19\). Agarwal \textit{et al.}, synthesized the tri substituted pyrimidine derivatives I-II, and found them to exhibit the antimalarial activity\(^20-21\).
The compounds encompassing pyrimidine nucleus are known to possess various biological\textsuperscript{22}, antioxidant\textsuperscript{23} and antitumour\textsuperscript{24} activities, and also act as analogues to ATP\textsuperscript{25}. They find application as probes of base reactivity in DNA\textsuperscript{26}. Yamashita et al., synthesized pyrimidine nucleoside III very efficiently\textsuperscript{27} and such compounds exhibited potent anti HIV activity, when tested in vitro\textsuperscript{28}. Bruno et al., synthesized the pyrimidine derivatives fused with benzopyran nucleus IV, and these compounds act as antiplatelet and analgesic agent\textsuperscript{29-30}.

\begin{center}
\begin{tikzpicture}
\node (a) {\includegraphics[width=0.3\textwidth]{pyrimidine.png}};
\node (b) at (0.2,-0.5) {III};
\node (c) at (0.8,-0.5) {IV};
\end{tikzpicture}
\end{center}

The major interest in fused pyrimidine systems is mainly due to purine based components of nucleic acids. The two purine bases adenine and guanine V-VI which are the imidazolopyrimidine derivatives are most important components of DNA, RNA and ultimately the genetic materials.

\begin{center}
\begin{tikzpicture}
\node (d) {\includegraphics[width=0.3\textwidth]{purine.png}};
\node (e) at (0.2,-0.5) {V};
\node (f) at (0.8,-0.5) {VI};
\end{tikzpicture}
\end{center}
Several synthetic analogues of the natural nucleosides, adenosine and guanosine, are prepared by modifying the base component for different purposes, such as exploration of antiviral and anticancer agents.

Although, voluminous synthetic work involving fusion of pyrimidine ring with various heterocyclic systems has been carried out, similar work involving fusion of pyrimidine ring system with oxygen heterocycle is considerably very less.

There are few reports in which pyrimidine ring is fused with substituted furans VII-X, which exhibit various biological and physiological activities\textsuperscript{31-42}. Tanaka \textit{et al.}, synthesized the various benzoylpyrimidine derivatives and studied the pre and post emergence herbicidal activity at low rates, these compounds exhibited good activity\textsuperscript{43}.

\begin{equation}
\text{VII}
\end{equation}

\begin{equation}
\text{VIII}
\end{equation}

\begin{equation}
\text{IX}
\end{equation}

\begin{equation}
\text{X}
\end{equation}
There are few reports available for the synthesis of pyrimidine derivatives in which pyrimidine ring fused with benzofurans, which exhibit various biological activities. This fact revealed the wide scope for systematic investigation in this area of heterocyclic chemistry. This led Agasimundin et al., to initiate an exhaustive research programme devoted to the synthesis and biological evaluation of benzofuro[3,2-d]pyrimidines XI. The results of such an investigation are published in a series of research papers.

As a logical extension of this work, it was thought of, to construct biologically potent pyrimidine nucleus on naphthofuran. Hence, extensive work in this direction was taken up in our laboratory, which led to the publication of few research papers.

In continuation of earlier work from this laboratory it was contemplated to explore few more such condensed heterocycles for important pharmacological activities.

Yoshiyuki et al., synthesized the mercapto substituted furopyrimidines and they studied the antiulcer activity of the compounds with rats. These compounds exhibited very good antiulcer activity. Sondhi et al., synthesized the mercapto substituted pyrimidine derivatives which showed very good analgesic and cyclin-dependent kinase (CDK-1) and glycogen synthase kinase (GSK-3) inhibitory activity. Acetic acid and mercapto substituted pyrimidine derivatives exhibit anti-inflammatory activity. Hence, it was envisaged to synthesis new mercapto

Present work

The present investigation involves the synthesis of substituted naphtho[2,1-b]furo[3,2-d]pyrimidine derivatives. O-Aminoacyl system was thought of as one of the suitable functionality for further modification into pyrimidine ring system. The most convenient approach for the synthesis of these compounds, involves building up of pyrimidine ring on appropriately functionalized naphtho[2,1-b]furan. Such a key intermediate, 2-acetyl-3-aminonaphtho[2,1-b]furan 2a was prepared from 2-hydroxy-1-naphthonitrile and then successfully converted into the desired compounds. The various steps involved in this synthetic strategy are as follows

2. Reaction of 2-hydroxy-1-naphthonitrile with haloketone to obtain 2-acyl-3-aminonaphtho[2,1-b]furans 2a-d.
1. **Synthesis of 2-hydroxy-1-naphthonitrile.**

The required starting material 2-hydroxy-1-naphthonitrile 1 was synthesized by well established method in our laboratory, by Reimerr-Tiemann reaction using 2-naphthol. The sequence of reaction is as follows. (Scheme-1)

The structure of 2-hydroxy-1-naphthonitrile 1 was confirmed by its IR spectrum, which exhibited strong absorption band at 2233 cm\(^{-1}\) due to \(-\text{CN}\) group and a broad absorption band at 3300 cm\(^{-1}\) due to \(-\text{OH}\) group. \(^1\text{H}\) NMR data is also consistent with the structure. Both IR and \(^1\text{H}\) NMR spectra were superimposable with the spectra of authentic sample, mixed melting point did not show any depression. The overall yield is \(\approx 90\%\) and the product is obtained in high purity.
2. Reaction of 2-hydroxy-1-naphthonitrile with haloketone to obtain 2-acyl-3-aminonaphtho[2,1-b]furans. 2a-d

Conversion of 2-hydroxy-1-naphthonitrile 1 into 2-acetyl-3-aminonaphtho[2,1-b]furan 2a was accomplished by a known procedure\(^{53}\). It involved the reaction of 2-hydroxy-1-naphthonitrile 1 with chloroacetone in presence of base. Condensation and Thorpe-Ziegler cyclisation occurred in single step to yield 2-acetyl-3-aminonaphtho[2,1-b]furan 2a. (Scheme-2)

Scheme-2
Initially the reaction was carried out using potassium hydroxide as a base and N,N-dimethylformamide as solvent, which gave 60% yield. However, when the same reaction was carried out using potassium carbonate as base and acetone as solvent, better yield, to the extent of 85% was obtained.

The structure of 2a was confirmed by comparing the IR and $^1$H NMR spectra with the known sample. No depression in the melting point was observed when mixed melting point was determined. As an additional support to the assigned structure to 2a, its $^{13}$C NMR spectrum was 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 2a, 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$_2^\prime$, C$_8^\prime$, C$_4^\prime$, C$_2$, C$_1$ and C$_3^\prime$ carbon atoms respectively which are quaternary carbon atoms. The large peaks at 131.28, 129.61, 127.71, 124.89 and 122.07 were assigned to C$_4$, C$_5$, C$_8$, C$_6$ and C$_7$ carbon atoms of naphthalene ring respectively. As expected C$_3$ of naphthalene nucleus exhibited a large peak at 113.27. Methyl carbon atom exhibited a medium peak at $\delta$ 25.86 ppm.

Finally mass spectrum of 2a 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 as shown in the Scheme-3.
$^1$H NMR Spectrum of 2a
$^{13}$C NMR spectrum of 2a
*** CLASS-5000 *** Report No. = 4 Data: KUM14121.D02 101/12/1 416:27:1

Sample : khm
Sample Amount: 1
Operator : Shivaswamy
Method File Name: KUM3.MET

MASS Spectrum of 2a

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

**Peak Report**

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<th>Area</th>
<th>Height</th>
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<td>1908415</td>
<td>166903</td>
<td>11.434</td>
<td>V 100.00</td>
<td></td>
</tr>
</tbody>
</table>

Total 1908415 100.00
It was thought of to synthesise 2-benzoyl-3-aminonaphtho[2,1-\textit{b}]furan \textit{2b} and 2-(4-chlorobenzoyl)-3-aminonaphtho[2,1-\textit{b}]furan \textit{2c} by adopting the similar procedure. The main aim for the synthesis of these compounds is to assess the effect of substituent on biological and pharmacological activities. The synthesis of 2-acyl-3-aminonaphthofurans \textit{2b-c} was achieved by the reaction of 2-hydroxy-1-naphthonitrile with phenacyl bromide and 4-chlorophenacyl bromide in presence of anhydrous potassium carbonate in refluxing dry acetone. 2-(4-Hydroxybenzoyl)-3-aminonaphtho[2,1-\textit{b}]furan \textit{2d}, was also synthesized similarly by using 4-hydroxyphenacyl bromide for the first time in our laboratory. As observed earlier both condensation and cyclisation occurred in a single step producing 2-benzoyl-3-aminonaphthofuran \textit{2b} and 2-(4-chlorobenzoyl)-3-aminonaphtho[2,1-\textit{b}]furan \textit{2c} and 2-(4-hydroxybenzoyl)-3-aminonaphtho[2,1-\textit{b}]furan \textit{2d} respectively.
The structures of 2b-c were evident by superimposable IR and $^1$H NMR data with authentic samples. The IR spectrum of 2b contained characteristic absorption bands at 3086 cm$^{-1}$ due to -NH$_2$ group and at 1632 cm$^{-1}$ due to carbonyl group. $^1$H NMR of 2b revealed a broad, D$_2$O exchangeable singlet at $\delta$ 5.7 due to -NH$_2$ protons and a multiplet at $\delta$ 7.3-8.6 due to eleven aromatic protons. The $^{13}$C NMR exhibited peak at $\delta$ 182.88, which is attributed to carbonyl carbon atom. The peaks at $\delta$ 116.36, 118.49, 122.71, 123.70, 124.01, 125.68, 126.40, 126.64, 127.51, 127.91, 128.75, 128.82, 128.95, 129.21, 129.31, 130.23, 132.90, 133.75, 134.14 and 134.55 are due to other twenty four carbon atoms. The spectral data of 2d confirmed its structure.


The reaction of 2-acyl-3-aminonaphtho[2,1-b]furan 3a-d with ammonium thiocyanate and benzoyl chloride in dry acetone gave the respective N-benzoyl-N$^1$-(2-acyl-naphtho[2,1-b]furan)-thioureas. 3a-d
The structures of 3a-d were confirmed by spectroscopic data. The IR spectrum of 3b exhibited the absorption band at 1676 cm⁻¹ (Ketone C=O), 1637 cm⁻¹ (amide C=O). ¹H NMR spectrum (CDCl₃) showed a broad singlet integrating for one proton at δ 6.1 due SH proton and a multiplet integrating for sixteen aromatic protons at δ 7.2-8.4. Two singlets integrating for one proton each at δ 9.4 and δ 12.7 are attributed to NHCS and NHCO protons. The ¹³C NMR spectrum of 3b contained peaks at δ 180.7 and δ 183.8 due to two carbonyl carbon atoms COPh and NHCOPh respectively. Peak at δ 166.75 was assigned to C=S carbon atom, and peaks at δ 112.90, 119.30, 124.64, 125.84, 127.48, 127.84, 128.44, 128.65, 128.94, 129.24, 129.82, 130.99, 131.57, 132.04, 132.92, 133.87 and 137.00 were attributed to twenty four aromatic ring carbon atoms.

Thus, based on this spectroscopic data the structures of compounds 3a-d were confirmed. The IR and ¹H NMR spectral data of the compounds 3a-d is summarized in Table-3.1.
$^1$H NMR Spectrum of 3b

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EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
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Time_ 14:50
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PROBHDL 10 mm QNP 1H
PULPROG zg
TD_ 16384
SOLVENT cdc13
NS_ 32
DS_ 0
SWE 6410.253 Hz
FIDRES 0.391251 Hz
AQ_ 1.2790020 sec
RG_ 1024
DW_ 78.000 usec
DE_ 97.50 usec
TE_ 300.0 K
HL1_ 1 db
D1_ 1.00000000 sec
F1_ 11.50 usec
SF01_ 400.1397291 MHz
NUCLEUS 1H

F2 - Processing parameters
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SF_ 400.1343945 MHz
WDW_ EM
SSB_ 0
LB_ 0.30 Hz
GB_ 0
PC_ 2.00
Table 3.1: IR and $^1$H NMR Spectral data of N-Benzoyl-N$^1$- (2-acyl-naphtho[2,1-b]furan)-thioureas. 3a-d

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>IR (KBr) cm$^{-1}$</th>
<th>$^1$H NMR in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(C=O) amide</td>
<td>(C=O) ketone</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>CH$_3$</td>
<td>1645 1660</td>
<td>δ 2.55 (s, 3H, CH$_3$), δ 7.5-8.25 (m, 11H, ArH), δ 9.2 (1H, NHCS), δ 12.5 (1H, NHCO)</td>
</tr>
<tr>
<td>3b</td>
<td>C$_6$H$_5$</td>
<td>1637 1676</td>
<td>δ 7.2-8.4 (m, 16H, ArH), δ 9.4 (1H, NHCS), δ 12.7 (1H, NHCO).</td>
</tr>
<tr>
<td>3c</td>
<td>4-Cl-C$_6$H$_4$</td>
<td>1640 1655</td>
<td>δ 7.2-8.4 (m, 15H, ArH), δ 9.3 (1H, NHCS), δ 12.6 (1H, NHCO).</td>
</tr>
<tr>
<td>3d</td>
<td>4-OH-C$_6$H$_4$</td>
<td>1665 1672</td>
<td>δ 4.7 (s, 1H, OH), δ 7.2-8.4 (m, 15H, ArH ), δ 9.2 (1H, NHCS), δ 12.9 (1H, NHCO).</td>
</tr>
</tbody>
</table>

The reaction of various N-benzoyl-N¹-(2-acylnaphtho[2,1-b]furan)-thioureas 3a-d with NaOH in aqueous ethanol at reflux temperature gave the respective 2-mercapto-4-alkyl/aryl-naphtho[2,1-b]furo[3,2-d]pyrimidines 4a-d.

\[
\begin{align*}
\text{R} &= \text{CH}_3, \text{C}_6\text{H}_5, 4-\text{Cl-C}_6\text{H}_4, 4-\text{OH-C}_6\text{H}_4
\end{align*}
\]

The reaction proceeds, probably by initial hydrolysis of benzoyl group followed by the cyclisation to give pyrimidine ring. The plausible mechanism for the reaction is as follows. (Scheme-4)
The main diagnostic feature for the ring closure of 3a-d into 4a-d was the absence of absorption due to carbonyl group as indicated by the IR spectra of 4a-d. The IR spectrum of 4a showed a sharp absorption band at 1599 cm\(^{-1}\) due to C=N. The further evidence in favour of ring closure was provided by \(^1\)H NMR. The \(^1\)H NMR spectrum of 4b revealed the absence of two singlets at \(\delta\) 9.4 (1H, NHCS), \(\delta\) 12.7 (1H, NHCO) and presence broad singlet at \(\delta\) 5.0 due to SH proton and a multiplet integrating for eleven protons at \(\delta\) 7.3-9.2 due to aromatic protons.

\(^{13}\)C NMR spectrum of 4b showed peaks at \(\delta\) 157.47 due to C=N carbon atom of pyrimidine ring and \(\delta\) 163.62 due to C=N (C, NCS). The peaks at \(\delta\) 112.60, 114.56, 124.95, 125.86, 127.45, 127.81, 128.47, 128.64, 128.84, 129.33, 129.85, 130.49, 131.36, 133.49, 133.63, 133.88, 143.02 and 147.27 were attributed to eighteen aromatic carbon atoms. Finally the structure of 4b was confirmed by the mass spectral analysis. The mass spectral data showed molecular ion peak at m/z 328 (M\(^+\)) corresponding to its molecular weight and other peaks appearing at m/z 327, 269, 154, 127, 105, 77 were in accordance with the fragmentation pattern as shown in the scheme-5.

The IR and \(^1\)H NMR spectral data of the compounds 4a-d is summarized in Table-3.2.
$^{1}H$ NMR Spectrum of 4b

Current Data Parameters
NAME 0923-kumar-1h
EXPN 5
PROCNO 1

F2 - Acquisition Parameters
Date 20040923
Time 15.03
INSTRUM amx400
PROBHD 10 mm QNP 1H
PULPROG 2G
TD 16384
SOLVENT cdc13
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DS 0
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PDR 0.391251 Hz
AQ 1.2780020 sec
RG 1024
DW 78.000 usec
DE 97.50 usec
time 300.0 K
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P1 11.50 usec
SP01 400.1367291 MHz
NUCLEUS 1H

F2 - Processing parameters
SI 32768
SP 400.1343945 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 2.00
$^{13}$C NMR Spectrum of 4b
Scheme-5

Mass fragmentation pattern of compound 4b

- HCN
- C-C₆H₅

m/z 328

m/z 327

m/z 269

m/z 127

m/z 155

m/z 77

m/z 105
Table 3.2: IR and $^1$H NMR Spectral data of

2-mercapto-4-alkyl/aryl-naphtho [2,1-b]furo[3,2-d]pyrimidines. 4a-d

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>IR (KBr) cm$^{-1}$ C=N</th>
<th>$^1$H NMR in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>CH$_3$</td>
<td>1609</td>
<td>δ 2.6 (s, 3H, CH$_3$), δ 4.9 (1H, SH), δ 7.2-7.6 (m, 6H, ArH).</td>
</tr>
<tr>
<td>4b</td>
<td>C$_6$H$_5$</td>
<td>1599</td>
<td>δ 5.0 (1H, SH), δ 7.3-9.2 (m, 11H, ArH)</td>
</tr>
<tr>
<td>4c</td>
<td>4-Cl-C$_6$H$_4$</td>
<td>1604</td>
<td>δ 5.1 (1H, SH), δ 7.3-9.2 (m, 10H, ArH)</td>
</tr>
<tr>
<td>4d</td>
<td>4-OH-C$_6$H$_4$</td>
<td>1692</td>
<td>δ 4.7 (s, 1H, OH), δ 5.0 (1H, SH), δ 7.2-8.4 (m, 10H, ArH)</td>
</tr>
</tbody>
</table>

mercapto acetic acids. 5a-d

It is known that thiols on treatment with α-halo acids in presence of weak base produces mercapto acid derivatives$^{59}$. As already mentioned such mercapto, acetic acid derivatives are well known for their anti-inflammatory activity$^{58}$. Thus the compounds 4a-d on treatment with chloroacetic acid in presence of base, furnished S-(4-alkyl/aryl)naphtho[2,1-b]furo[3,2-d]pyrimidine)-mercapto acetic acids. 5a-d
The structures of 5a-d were confirmed by spectroscopic data. The IR spectrum of 5b revealed the presence of a broad absorption band at 3368 cm\(^{-1}\) due to OH group of COOH, and a sharp absorption band at 1710 cm\(^{-1}\) due to carbonyl group. The \(^1\)H NMR spectrum of 5b also revealed the absence of SH proton and presence of singlet integrating for two protons at \(\delta\) 4.0 due to S-CH\(_2\) protons and a multiplet integrating for twelve aromatic protons at \(\delta\) 7.3-9.2 due to aromatic protons. A singlet integrating for one proton at \(\delta\) 12.7 was attributed due to –COOH proton.

\(^{13}\)C NMR spectrum of 5b showed peaks at \(\delta\) 163.73 due to carbonyl carbon atom of acid group (COOH) and peaks at \(\delta\) 153.49 and \(\delta\) 157.50 and due to C=N carbon atoms of pyrimidine ring. Peaks at \(\delta\) 112.57, 114.76, 124.37, 124.93, 125.85, 127.45, 127.83, 128.47, 128.63, 128.83, 129.34, 129.85, 130.39, 131.36, 133.36, 133.50, 133.86 and 143.51 attributed to eighteen carbon atoms. Peak at \(\delta\) 34.7 was due to CH\(_2\) (-S-CH\(_2\)) carbon atom. Finally the structure of 5b was confirmed by the mass spectral analysis. In the mass spectrum of 5b molecular ion peak was not observed, which may be due to less stability of molecular ion and peaks at m/z 342,
$^{13}$C NMR Spectrum of 5b
327, 154, 127, 105 and 77 were in consistent with the fragmentation pattern shown in scheme-4. Analytical data of the compounds supports for the proposed structures.

Thus, based on this spectroscopic data and earlier observations the structures of compounds 5a, 5c-d were confirmed and summarized in Table-3.3

**Scheme-4**

**Mass fragmentation pattern of compound 5b**
Table-3.3: IR and $^1$H NMR Spectral data of S-(4-alkyl/aryl)-naptho[2,1-b]furo[3,2-d]-pyrimidine)-mercapto acetic acids.

5a-d

![Structure](image)

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>IR (KBr) cm$^{-1}$ C=O</th>
<th>$^1$H NMR $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>CH$_3$</td>
<td>1660</td>
<td>$\delta$ 2.6 (s, 3H, CH$_3$), $\delta$ 3.9 (s, 2H, S-CH$_2$), 7.0-7.6 (m, 6H, ArH), $\delta$ 12.5 (s, 1H, COOH)</td>
</tr>
<tr>
<td>5b</td>
<td>C$_6$H$_5$</td>
<td>1625</td>
<td>$\delta$ 4.0 (s, 2H, S-CH$_2$), $\delta$ 7.3-9.2 (m, 11H, ArH), $\delta$ 12.7 (s, 1H, COOH)</td>
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<tr>
<td>5c</td>
<td>4-Cl-C$_6$H$_4$</td>
<td>1685</td>
<td>$\delta$ 4.1(s, 2H, S-CH$_2$), $\delta$ 7.2-9.0 (m, 10H, ArH), $\delta$ 12.6 (s, 1H, COOH)</td>
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<tr>
<td>5d</td>
<td>4-OH-C$_6$H$_4$</td>
<td>1670</td>
<td>$\delta$ 3.8 (s, 2H, S-CH$_2$), $\delta$ 4.7 (b, 1H, OH), $\delta$ 7.1-8.9 (m, 10H, ArH), $\delta$ 12.9 (s, 1H, COOH)</td>
</tr>
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</table>

All these newly synthesized compounds 4a-d, 5a-d were screened for antibacterial, antifungal, diuretic and anti-inflammatory activity. The method of screening, results and discussion are described in detail in chapter-7.
Experimental

Synthesis of 2-acyl-3-aminonaphtho[2,1-b]fuans 2a-d

To a solution of 2-hydroxy-1-naphthonitrile 1 (3.26 g, 0.02 mol) in dry acetone (100 mL), phenacyl bromide (3.98 g, 0.02 mol) and anhydrous potassium carbonate (27.6 g, 0.2 mol) were added and the reaction mixture was refluxed on water bath for 8 hrs. The potassium salt was filtered off and washed thoroughly with acetone. Removal of solvent from the filtrate and subsequent trituation with ethanol gave 2-benzoyl-3-aminonaphtho[2,1-b]furan 2b.

The compounds 2a, 2c-d were synthesised using chloroacetone, 4-chloro-phenacyl bromide, 4-hydroxy-phenacyl bromide in place of phenacyl bromide by the same method described above.

Synthesis of N-benzoyl-N'-(2-benzoyl-naphtho[2,1-b]furan)-thiourea. 3b

To a solution of ammonium thiocyanate (0.82 g, 0.011 mol) in dry acetone (25 mL), benzoyl chloride (1.4 g, 0.01 mol) was added slowly while stirring. The reaction mixture was heated at reflux for 15 minutes. The heating bath was removed and a solution of 2-benzoyl-3-aminonaphtho[2,1-b]furan (2.87 g, 0.01 mol) in dry acetone (50 mL) was added to maintain reflux. After the addition was complete the mixture was stirred for 90 minutes at room temperature. On pouring into ice cold water, white solid separated which was filtered, washed with water and ethanol and recrystallised from ethanol.

The compounds 3a, 3c-d were synthesised from 2-acetyl-3-aminonaphtho[2,1-b]furan 2a, 2-(4-chloro-benzoyl)-3-aminonaphtho[2,1-b]furan 2c, 2-(4-hydroxybenzoyl)-3-aminonaphtho-[2,1-b]furan 2d respectively, following the same procedure described above.

A mixture of 3b (3.06 g, 0.06 mol), sodium hydroxide (3 g) and water (50 mL) was heated under reflux for 15 minutes, cooled, diluted with water and acidified with dilute hydrochloric acid. The precipitate was filtered, washed with water, dried and recrystallised from aqueous DMF to obtain 2-mercapto-4-phenyl-naphtho[2,1-b]furo[3,2-d]pyrimidine 4b. The compounds 4a, 4c-d were synthesised from 3a, 3c-d respectively by the same method.

Synthesis of S-(4-phenyl-naphtho[2,1-b]furo[3,2-d]pyrimidine)-mercapto acetic acid. 5b

A solution of chloroacetic acid (0.47g, 0.005 mol) and sodium carbonate (0.25 g, 0.00275 mol) in water (10 mL) was added slowly while stirring, for 30 minutes to a solution of 4b (1.56 g, 0.0055 mol) and sodium hydroxide (0.6 g, 0.015 mol) in water (10 mL) and the reaction mixture was stirred overnight at room temperature acidified with dilute hydrochloric acid and extracted with chloroform. The organic layer was dried over sodium sulphate, filtered evaporated and recrystalized from ethanol the compound 5a, 5c-d were prepared similarly by using 4a and 4c-d. Physical data of newly synthesized compounds is reported in Table-3.4.
Table-3.4: Physical data of various compounds synthesized.

<table>
<thead>
<tr>
<th>Comp.</th>
<th>R</th>
<th>M.P. °C</th>
<th>Yield %</th>
<th>Mol. formula</th>
<th>Found (Calcd.) %</th>
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References:


42. S. Naya, Y. Yamaguchi and M. Nitta, Tetrahedron, 2005, 61, 7384.


