Chapter-C: A new approach for the one-pot synthesis of dibenzo[a,i]phenanthridines, dibenzo[b,d]pyridines(phenanthridines) and dicyclopenta[b,d]pyridines

Chapter-C

C.1 Introduction

C.1.1 Significance of phenanthridines

Phenanthridines are an important class of nitrogen containing tricyclic compounds formed by replacing a carbon atom by a nitrogen atom in the central ring of phenanthrene as is represented in Scheme-1. These are infact nitrogenous hydrocarbon bases akin to phenanthrenes, benzo[c]quinolines and benzo[c]isoquinolines and are present in a large number of naturally occurring alkaloids.1

![Scheme-1]

The history of phenanthridines dates back to 1891 when these were first discovered by A. Pictet and H. J. Ankersmit by the pyrolysis of the condensation product of benzaldehyde and aniline.2 However, the method was modified by Morgan and Walls by using phosphorus oxychloride instead of the zinc metal and adopting nitrobenzene as a reaction solvent.3 Phenanthridines have enormous synthetic and medicinal utility.4 Their wide spread spectrum covers activities such as antifungal, antibacterial, antiprotozoal, antitumour and anticancer activities.5 A wide variety of

natural products contain the phenanthridine core and the examples of this category include trispheridine 1 and bicolorine 2. They are readily used in the treatment of biological disorders such as trypsominiasis. In addition to this, various drugs such as isometadium, dimidium and holium contain phenanthidine as their pharmacophore. Dibenzophenanthridines possess topoisormerase-I targetting activity.

Besides their use as potential therapeutic agents, the chemistry and biomedical applications of these have been widely explored. Ethidium bromide 3, an efficient DNA intercalator and stain belongs to this class of compounds. Its analogue propidium bromide is used as probe for detecting the presence of duplex nucleic acids.

Some derivatives of phenanthridines have been found to possess potent antifungal activity against both plant and animal pathogens, for example, chelerythrine 4. N-Methyl substituted phenanthidine derivatives such as

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Sanguinarine 5 exhibit profuse antibacterial activity.\textsuperscript{11} Benzo[c]phenanthridines are distributed profusely in nature and nitidine 6 and fagaronine 7 have proven to be potential antitumour agents in last twenty years.\textsuperscript{12} Apart from their antitumour properties, earlier studies have disclosed that these phenanthridines also act as the nematocidal agents.\textsuperscript{13}

Phenantridione core is present in phenantriplatin\textsuperscript{14} 8 which is an improved anticancer compound. The mode of action of this drug involves the formation of monofunctional adducts with guanosine residues in the DNA. Recent studies have proved that benzophenantridines also possess cytotoxic activity.\textsuperscript{15} Besides the cytotoxic activity, certain phenantridium compounds have potent trypanocidal activity. This action of the nucleus is strongly related to the substitution pattern, as quaternary salts (containing a primary amino group at position-7 and phenyl group at position-9 have exceptionally high activity). Additional amino group in the ring further enhances the biological activity of the molecule. Thus, 2,7-diamino-9-phenyl-

\textsuperscript{11} A. Seaman, M. Woodbine, Brit. J. Pharma Col., 1954, 9, 265- 270.
\textsuperscript{13} B. D. Crane, M. O. Fagbule, M. J. Shamma, Nat. Prod., 1984, 47, 1- 43.
\textsuperscript{15} L. P Sandjo1, V. Kuete, R. S. Tchangna, T. Efferth, B. T. Nagadjui, Chem. Cenral J., 2014, 8, 1-5.
10-methyl phenanthridinium bromide 9 (dimidium bromide) is particularly active against various *trypanosomal* species.\textsuperscript{16}

![Chemical structure of 9](image1)

The benzo[c]phenanthridine analogues like decarine 10 (rutaceae family) can significantly retard the fMLP-induced (formyl-L-methionyl-L-leucyl-L-phenylalanine) $O_2$ generation and elastase release of the neutrophils and hence represent their use as potential agents for the prevention of various inflammatory responses in near future.\textsuperscript{17}

![Chemical structure of 10](image2)

Lycobetaine 11 which is extracted from lycorine (amaryllidaceae family) exhibits strong antitumour effects against the several animal tumours. The structure activity relationship indicates that it acts as selective topoisomerase-II poison and strongly inhibits the human tumour cells.\textsuperscript{18} Chelidonine 12 has been found to exhibit strong antimitotic activity.\textsuperscript{19}

\begin{itemize}
  \item \textsuperscript{16} B. A. Newton, *J. Gen. Microbial*, 1957, 17, 718-730.
  \item \textsuperscript{19} J. Wolff, L. Knipling, *Bio Chem.*, 1993, 32, 13334-13339.
\end{itemize}
Apart from these, their uses in the physical domain include photoconducting and photovoltaic activities.\textsuperscript{20} Their utility lies in the generation of optical materials such as in holography, lithographic plates for printing and electric equipments.\textsuperscript{21} The latest available literature reports phenanthridine derivatives to be molecular scale devices which undergo reversible ring opening and ring closure under carefully monitored pH conditions.\textsuperscript{22}

In addition to these, substituted phenanthridines constitute an important class of heterocycles that act as important synthons for the generation of various compounds of synthetic value. Phenanthridine core based linkers \textbf{13}, \textbf{14} and \textbf{15} are renowned for solid phase synthesis of acid containing compounds due to their tolerance to acidic, basic and reductive reaction conditions.\textsuperscript{23} These linkers can also be utilized for making the N- or O- alkylated compounds.

\textsuperscript{23} W. Li, Y. S. Lin, N. M. Hsu, \textit{J. Comb. Chem.}, \textbf{2001}, 3, 634- 643.
C.1.2 Reported routes for the synthesis of phenanthridines

A mild and efficient method for the synthesis of substituted phenanthridines was reported by M. Tobisu et al.\textsuperscript{24} by one-pot annulations of 2-isocyanobiaryls with organoboronic acids under heating conditions. In this particular reaction sequence, the isocyanogroup was used as an radical acceptor, which followed by radical cyclisation gave phenanthridines (\textbf{Scheme-2}).

\begin{equation}
\text{NC} + \text{R-B(OH)}_2 \xrightarrow{[\text{Mn(acac)}_3](3eq.)} \text{PhMe, 80 °C, 1-24 hr} \rightarrow \text{16}
\end{equation}

\textbf{Scheme-2}

Substituted phenanthridines were obtained by microwave assisted [2+2+2] cyclotrimerisation reaction of alkynes as reported by L. Sripada et al.\textsuperscript{25} (\textbf{Scheme-3}).

\begin{equation}
\text{R}_1 \text{R}_2 + \text{NPG} \xrightarrow{\text{Microwave}} \text{17}
\end{equation}

\textbf{Scheme-3}

A new method using microwave has been adopted for the synthesis of phenanthridines using \textit{o}-furyl allyl amines. The intermediate gets oxidised using benzoquinone (\textbf{Scheme-4}).\textsuperscript{26}

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Q. Wang et al.27 have reported the synthesis of 6-(trifluromethyl)phenanthridines through oxidative cyclisation of 2-isocyanobiphenyls using benzoquinone (BQ) as promoter. The reaction allows the direct formation of C-CF₃ bonds and a very rapid access to phenanthidine ring system under one catalytic cycle (Scheme-5).

Another method involves the photochemical conversion of halogenated N-benzylanilines by subjecting to photolysis in presence of the UV radiation reported by A. M. Leisenmeier et al.28 (Scheme-6).

A novel method for the synthesis of phenanthridines was achieved by C. W. Muth et al.\textsuperscript{29} using methyl 2-(2-nitrophenyl)phenylacetate. The parent compound on treatment with methanolic sodium hydroxide gave an acid that on reductive decarboxylation gave phenanthidine nucleus (Scheme-7).

![Scheme-7](image)

Synthesis of substituted pyrido[1,2-f]phenanthridines have been achieved using phenanthridine, activated acetylenes and arylidenemalononitriles in dichloromethane at room temperature refluxing (Scheme-8).\textsuperscript{30}

![Scheme-8](image)

R. Pearson et al.\textsuperscript{31} has proposed the synthesis of phenanthridines using the palladium catalysed picolinamide directed sequential C-H functionalisation (Scheme-9).

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![Chemical Structures](image)

**Scheme-9**

J. Liu et al.\(^{32}\) have reported the synthesis of benzimidazo[1,2-f]phenanthridines from readily available benzimidazoles and 1,2-dibromobenzenes (Scheme-10).

![Chemical Structures](image)

**Scheme-10**

Y. T. Hsu et al.\(^{33}\) have reported the synthesis of phenanthridines by flash pump pyrolysis by direct introduction of a solution of \(N\)-benzylidene-4-methoxyaniline in benzene as sprayed aerosol into a hot quartz tube and subsequent conversion into \(N\)-benzilidene-4-hydroxyaniline and 2-phenylphenanthridine (Scheme-11).

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In an alternative procedure, 6-substituted phenanthridines have been synthesised on the principles of green chemistry by T. Xiao et al. 34 The method involves the irradiation of azido compounds in presence of multiple kinds of organic free radicals which irradiate to give 6-substituted phenanthridines (Scheme-12).

6-Benzoylphenanthridines can be prepared by a one-pot reaction of 2-isocyanobiphenyl and potassium oxophenylacetate using silver carbonate as catalyst (Scheme-13). 35

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Subjecting the hydrazines to visible light in presence of organic dyes such as eosin-B generates free radicals which react with isocyanobiaryls to produce the substituted phenanthridines (Scheme-14).\(^{36}\)

![Scheme-14](image)

Ligand free domino Suzuki reaction using K\(_3\)PO\(_4\) catalyst has been utilised for the synthesis of substituted phenanthridines by M. Ghosh et al\(^{37}\) (Scheme-15).

![Scheme-15](image)

T. Gerfaud et al.\(^{38}\) reported the synthesis of phenanthridines using N-acyloximes and arynes (Scheme-16).

![Scheme-16](image)

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6-Substituted phenanthridines have been prepared by T. Xiao \textit{et al.} \cite{36} by the metal free ion visible light induced aerobic oxidative cyclisation of 2-isocyanobiaryl (Scheme-17).

![Scheme-17](image)

A series of phenanthridinequinone derivatives have been prepared by reductive cyclisation using hydroquinones by J. A. Valderrama \textit{et al.} \cite{39} (Scheme-18).

![Scheme-18](image)

M. Lia \textit{et al.} \cite{40} reported phenanthridine synthesis by novel 1,4-Dipolar cycloaddition under argon atmosphere (Scheme-19).

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6-Substituted phenanthridine derivatives were synthesised by Z. Xia et al.  using benzoyl peroxide (BPO) and $N,N'$- Dimethyl ethylenediamine (DMEDA) in sodium acetate (Scheme-20).

Scheme-20

However, the above reported methods remain associated with certain disadvantages such as stringent conditions, use of uneconomical metal catalysts and poor diversity. Therefore, the search of more efficient, ecofriendly and versatile synthesis method for phenanthridine ring system with diverse physical and chemical properties remains target of continuous investigations in the present study. Initially, we targeted the generation of dibenzo[\textit{a,}\textit{i}]phenanthridine nucleus and later extended it in the generation of dicyclopenta[\textit{b},\textit{d}]pyridines and highly bridged dibenzo[\textit{b},\textit{d}]pyridines (basically a phenanthridine nucleus).

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C.1.3 Significance of pyridines

The history of pyridine dates back to 1849 when it was discovered by Thomas Anderson as one of the constituents of the bone oil.\textsuperscript{42} It is colourless, highly flammable, weakly alkaline, water soluble liquid with a distinctive unpleasant fish like odour. It serves as the parent compound of majority of biologically important molecules and natural products.\textsuperscript{43} The parent compound, pyridine, itself is represented by 36. Substituents are indicated either by the numbering shown, 1 to 6, or by the Greek letters, $\alpha$, $\beta$ or $\gamma$. The Greek symbols refer to the position of the substituent relative to the ring nitrogen atom, and are usually used for naming monosubstituted pyridines. The ortho, meta and para nomenclature commonly used for disubstituted benzenes is not used in naming pyridine compounds. The various important alkyl pyridines are $\alpha$-picoline, $\beta$-picoline, $\gamma$-picoline; the six dimethylpyridines are called lutidines and ten trimethyl pyridines are called collidines.

Interestingly there is large range and sweep of the biological importance of pyridines. This nucleus is associated with a large number of pharmacological activities including antimicrobial,\textsuperscript{44} anticonvulsant,\textsuperscript{45} antiviral,\textsuperscript{46} anti-HIV,\textsuperscript{47} antifungal\textsuperscript{48} and

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{pyridine.png}
\caption{Structure of pyridine.}
\end{figure}
antimycobacterial activities.\textsuperscript{49} It is the prosthetic pyridine nucleotide NADP that is involved in the various oxidation-reduction processes particularly in enzymology during various metabolic pathways.\textsuperscript{50} This ring system is profusely distributed in nature, especially in the plant kingdom and it is the core structure found in various alkaloids e.g. atropine extracted from \textit{Atropa belladona} contains saturated pyridine nucleus and is associated with mydriatic properties. Moreover, many compounds of biological importance e.g. water soluble vitamins\textsuperscript{51} like niacin (B\textsubscript{3}) and pyridoxine (B\textsubscript{6})\textsuperscript{37} contain pyridine as their main core. In the pharmaceutical industry it forms the key nucleus of over more than 7000 existing drugs.\textsuperscript{52} A large number of commercially available drugs are derived from pyridines. Many important anti-TB drugs\textsuperscript{53} such as isoniazide \textsuperscript{38} contain pyridine moiety. Thienopyridine derivatives such as \textsuperscript{39} display strong antiviral activity against Herpes simplex virus (HSV) type-1.\textsuperscript{54} In addition to it imidazopyridine derivatives \textsuperscript{40} show strong inhibitory action against \textit{Candida} species.\textsuperscript{55}

\begin{thebibliography}{99}
\bibitem{52} D. G. Henry, \textit{Tetrahedron}, 2004, 60, 6043- 6060.
\end{thebibliography}
The highly substituted pyridine derivatives such as the 2-amino-4-aryl pyridines act as potent agonists for human adenosine receptors and act as widely acknowledged therapeutic agents for the treatment of Jacobs disease, Parkinson’s disease, hypoxia, asthma and kidney disease.

3,5,6-Trichloropyridine derivatives\textsuperscript{57} \textsuperscript{41} show potent herbicidal properties. The pyridine nucleus has also been investigated for their antimycobacterial and antidiabetic activity. Bahekar et al.\textsuperscript{58} synthesised two series of antidiabetic 2,5-disubstituted-3-imidazol-2-yl-pyrollopyridines \textsuperscript{42}. The mono and quaternary ammonium salts of the pyridine nucleus \textsuperscript{43} have been found to act as powerful antidotes against nerve agent poisoning.\textsuperscript{59} The nicotinic acid\textsuperscript{60} \textsuperscript{44} based complexes


Pyridines also form useful substructures in supramolecular chemistry. Many pyridines have immense use because of commercial interest as these have bioactive properties. Pyridine nucleus is used in the synthesis of sulphapyridine, antihistaminic drugs tripeleneamine and mepyramine as well as water repellants, bactericides and herbicides. Pyridine is the key nucleus to organic chemists for drug discovery and drug synthesis. Aminopyridines serve as valuable synthons for the manufacture of pharmaceutical and agricultural products. Sulphasalazine, a veterinary antibiotic is synthesised in good amounts from 2-aminopyridine. 2-Ethylpyridine part acts as precursor to psychotropic agent thioridazine. 2, 3, 5-Collidine finds its extensive application in the manufacture of antiulcer agent omeprazole.

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Picolinic acid (2-carboxypyridine) acts as an intermediate for local anaesthetic mepivacaine. Potent tranquiliser amphenidone and cardiotonic amrinone are derived from 2-pyridone. In addition to it 2-pyridylcarbinol is used in the synthesis of anti-inflammatory drug ibuprophenicol. Substituted 6-sulphanylpyridines act as potassium channel openers and hence are beneficial in the treatment of urinary incontinence.

The fused pyridine based heterocycles other than phenanthridines are also biologically potent compounds. Many fused pyridine based heterocycles possess tyrosinase inhibiting activities, other acknowledged properties are the antiviral, antileishmanial and antmicrobial activities. Besides these, fused pyridine systems exhibit remarkable pharmacological efficiency as antihypertensive and calcium antagonists. In view of these important observations and many others, it was
thought worthwhile to synthesise some condensed heterocyclic systems that contain the pyridine moiety.

### C.1.4 Reported routes for the synthesis of pyridines

Pyridines have been synthesised in the classical format by the reaction of 1,2-diketones with aldehyde in presence of ammonia (Hantzsch dihydropyridine synthesis) (Scheme-21).

![Scheme-21](image)

**Scheme-21**

X. Xiong *et al.* have reported the preparation of polysubstituted pyridines by one-pot reaction of alkynone, 1,3-dicarbonyl compound and ammonium acetate in alcoholic solvents (Scheme-22).

![Scheme-22](image)

**Scheme-22**

A one-pot synthesis of polysubstituted pyridines has been achieved by X. Xin *et al.* from 3-aza-1,5-enzyme frameworks (Scheme-23).

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![Chemical Structure]

Three component one-pot synthesis of highly substituted pyridines has been achieved by M. L. Kantam et al.\(^76\) using nanocrystalline magnesium oxide in ethanol (Scheme-24).

![Scheme-23]

M. C. Bagley et al.\(^77\) has reported the synthesis of pyridines in a flow microwave reactor (Scheme-25).

![Scheme-24]

In an alternative method, the synthesis of pyridine derivatives was achieved by using ionic liquids in a presence of silver carbonate (Scheme-26).\(^78\)

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A heavy metal based synthesis of poly substituted pyridines based on Lewis acid based multicomponent reactions has been developed by V. P. A. Raja et al.\textsuperscript{79} (Scheme-27).

\begin{equation}
\begin{align*}
\text{OR}_3 & \quad \text{OR}_4, \\
\text{R}_2 & \quad \text{R}_5, \\
\text{NH}_2 & \quad \text{NH}_2 \\
\text{R}_1 & \quad \text{R}_3, \\
\text{R}_4 & \quad \text{R}_5, \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\end{equation}

\textbf{Scheme-27}

F. Minisci et al.\textsuperscript{80} reported the synthesis of phenyl substituted pyridines using benzoyl peroxide and acetic acid (Scheme-28).

\begin{equation}
\begin{align*}
\text{2} & \quad \text{Bz}_2\text{O}_2, \\
\text{AcOH},118 \text{ °C} & \quad \text{Ph} \\

\text{60} & \quad \text{Ph} \\
\text{61} & \quad \text{Ph}
\end{align*}
\end{equation}

\textbf{Scheme-28}

An environment friendly protocol was adopted for the synthesis of thieno[2,3-b]pyridines using a 1:1 mixture of acetic acid in water (Scheme-29).\textsuperscript{81}

\begin{equation}
\begin{align*}
\text{Bz}_2\text{O}_2 & \quad \text{AcOH},118 \text{ °C} \\

\text{60} & \quad \text{Ph} \\
\text{61} & \quad \text{Ph}
\end{align*}
\end{equation}

\textbf{Scheme-29}

\textsuperscript{80} F. Minisci, O. Porta, F. Fontana, \textit{Heterocycles}, 1989, 28, 489.
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\[
\text{R}^\text{N}\text{H}_2 \quad \text{CHO} + \text{CH}_3\text{O} \quad \text{CN} \quad \text{O} \quad \text{NaOH or NaOMe} \quad \text{Methanol water(2:1) reflux} \\
\text{N} \quad \text{CN} \quad \text{NH}_2 \quad \text{R}_1 \quad \text{R}_2 \quad \text{R}_3 \\
\text{Scheme-31}
\]

The synthesis of 2-(1H-Indol-3-yl)-6-methoxy-4-aryl pyridine-3,5-dicarbonitrile derivatives was achieved by three component reaction of arylaldehyde, 3-(3-indolyl)-3-ketopropanenitrile and malononitrile under refluxing conditions (Scheme-30).82

\[
\text{R} \quad \text{S}^\text{N} \quad \text{NH}_2 \quad \text{R} \quad \text{CHO} \quad \text{AcOH,Water (1:1v/v)} \quad \text{uv} \\
\text{R}^\text{N} \quad \text{N} \quad \text{S} \quad \text{O} \quad \text{H} \quad \text{N} \quad \text{S} \quad \text{R} \quad \text{R}' \quad \text{AcOH,Water (1:1v/v)} \quad \text{uv} \\
\text{R} \quad \text{NH}_2 \\
\text{Scheme-29}
\]

One-pot reaction of tetrazolo[1,5-a]quinoline-4-carbaldehyde, malononitrile, heterocyclic methyl ketone in ammonium acetate yielded 2-amino-3-cyano-4-tetrazoloquinolinylpyridine derivatives (Scheme-31).83

\[
\text{R}_1 \quad \text{N} = \text{N} \quad \text{CHO} + \text{CN} \quad \text{O} \quad \text{NH}_2\text{OAc} \quad \text{Ethanol, reflux} \\
\text{R}_2 \quad \text{R}_3 \\
\text{Scheme-31}
\]

Synthesis of pyridines has also been achieved by reaction of acylazides with alkanoyne diesters using potassium carbonate as base (Scheme-32).  

\[
\text{ArN}_3 + \text{MeOOC} = \text{COOMe} \xrightarrow{\text{K}_2\text{CO}_3, \text{CH}_3\text{CN, 55 °C}} \text{Ar-}\text{COOMe} \\
\]

\[\text{Scheme-32}\]

Greener methodology using sodium dodecyl sulphate (SDS) was adopted for the synthesis of pyrazolo[3,4-b]pyridines (Scheme-33).

\[
\text{H}_3\text{C} - \text{N} - \text{NH}_2 + \text{Ar-}\text{CH} = \text{C-CN} \xrightarrow{\text{H}_2\text{O, SDS, 90 °C}} \text{H}_3\text{C} - \text{N} - \text{NH}_2 \\
\]

\[\text{Scheme-33}\]

C.1.5 Role of ammonium acetate in organic synthesis

Ammonium acetate (\(\text{NH}_4\text{OAc}\)), is an easily available versatile and biodegradable chemical which is used in a wide variety of organic transformations. It is extensively utilised in the synthesis of various \(N\)-heterocyclic compounds such as pyridines, pyrimidopyridines, aziridines, imidazoles and benzoxazoles etc.

Ammonium acetate acts as a dual activation agent and catalyses the formation of the manich products as well as the cross-aldol products. The ammonium acetate has sufficient basicity to catalyse the cross aldol reaction of aromatic as well as heteroaromatic aldehydes with selective ketones, thereby replacing sodium hydroxide. Moreover, it is an easily available, cheap and safe reagent and hence used in the present reaction protocol.

The role of ammonium acetate is highlighted in the following reactions.

2-Amino-3-cyano-2H-pyran derivatives have been obtained in good yields by using silica supported ammonium acetate (Scheme-34).  

![Scheme-34](image)

$\beta$-Nitrostyrenes are prepared in good yield by employing ammonium acetate in acetic acid (Scheme-35).

![Scheme-35](image)

Ammonium acetate supported on silica has also been used in the synthesis of substituted alkenes (Scheme-36).

![Scheme-36](image)

Trans-cinnamic acids can be synthesised in good amounts like in knoevenagel condensation from aldehydes and malonic acid using ammonium acetate under solvent free conditions (Scheme-37).

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\[
\text{Ar-CHO} + H_2C\text{COOH} \xrightarrow{NH_4OAc, UV} \text{Ar-} \underset{\text{COOH}}{\text{C}}
\]

Scheme-37

It is involved in the synthesis of pyran derivatives from silica supported ammonium acetate (Scheme-38).\(^{91}\)

\[
\begin{array}{c}
\text{\includegraphics[width=0.8\textwidth]{Scheme-38.png}} \\
\text{Scheme-38}
\end{array}
\]

C.2 Synthesis of phenanthridines catalysed by ammonium acetate

C.2.1 Genesis

Phenanthridines and their derivatives have a lot of biological activities associated with them. The most commonly employed reaction for their synthesis, is the Bischler Napieralski cyclisation,\(^{92}\) which involves the use of \(\text{P}_4\text{O}_{10}, \text{POCl}_3\) or \(\text{PCl}_5\) at elevated temperature and hence only a few functional groups can be tolerated. Moreover, despite their potential utility, the routine methods involved possess lengthy syntheses, metal catalysts, low yields, strict anhydrous conditions, lack of generality and often structurally complicated precursors. Thus, only a limited number of strategies and routes are available which as such or in some modified form have been successfully applied in the generation of heteropolycyclic scaffolds.\(^{93}\) The development of new, rapid and clean synthetic routes, trends and techniques towards focussed library of such compounds is, therefore, of great importance to both organic

and synthetic chemists. So, owing to the mild and non-toxic nature of ammonium acetate, it was envisaged to use it for the synthesis of phenanthridines.

C.2.2 Results and discussion

Initially, we started with the generation of dibenzophenanthridines and encouraged with the obtention of these partially reduced dibenzo[a,i]phenanthridines 69 from α-tetralone and aryl/hetaryl aldehydes in very good yields using this one step synthesis, this method was extended for the generation of partially reduced dicyclopenta[b,d]pyridines starting from cyclopentanone and different aryl/hetaryl aldehydes and later for the generation of highly bridged dibenzo[b,d]pyridines.

In our initial attempt, a mixture of α-tetralone 67 (2 mmol), benzaldehyde 68a (1 mmol) and ammonium acetate (1.5 mmol) was refluxed in ethanol (Scheme-39).

![Scheme-39](image)

After about one hour, the formation of product was noticed as indicated on TLC, which showed a distinct spot when eluted with 30% petroleum ether and ethyl acetate. After completion of the reaction, the product was isolated and purified by column chromatography. The structure of the isolated product was arrived at by spectral means viz. $^1$H NMR, $^{13}$C NMR, IR and EIMS. In $^1$H NMR spectrum of 69a, the most diagnostic signal appeared at δ 2.8-3.2 as multiplet attributing to eight benzylic protons on saturated carbon atoms. Further, a multiplet in the range of δ 7.1-7.5 integrating to thirteen protons indicated the presence of three benzene rings. All these features of $^1$H NMR coupled with the appearance of a peak at 1353 cm$^{-1}$ in IR spectrum for ring nitrogen were in favour of formation of the expected product. The

assigned structure also finds support from the EIMS data [360(M+H)+] and CHNS analysis and comparison with the spectral data of the known compound.

To demonstrate the generality of the method we next investigated the scope of the reaction under optimised conditions. Further with α-tetralone under similar conditions, all aryl and heterarylaldehydes including ortho and para substituted arylaldehydes in presence of ammonium acetate under anhydrous methanol media give entirely the dibenzophenanthridine 69 products as shown in Scheme-39a. No azabicyclo[3.3.1]nonane analogues were obtained as the alternative products even with the ortho substituted benzaldehydes unlike in some of such reactions reported in literature. However, when reaction was tried with liquid ammonia in presence of fused sodium acetate in ethanol replacing the ammonium acetate under ethanol /methanol, azabicyclononane[3.3.1] analogues were also obtained as the bi-products though in less than 5% proportion with the main dibenzophenanthridine product. Hence, we have discovered a one-step reaction with all the aryl and heterarylaldehydes substituted variedly in ortho and para positions with ammonium acetate and α-tetralone generating 5-aryl/heteryl-7,8,13,14-tetrahydrodibenzo[a,i]phenanthridines 69.

![Scheme-39a](image)

As summarised in the Table-1, the reaction proceeds smoothly with good yields and tolerates several kinds of electron releasing aryl and heteryl aldehydes.

The formation of phenanthridines can be explained by the possible mechanism as shown in the following scheme (Scheme-40).
Chapter-C: A new approach for the one-pot synthesis of dibenzo[\textit{a,i}]phenanthridines, dibenzo[\textit{b,d}]pyridines (phenanthridines) and dicyclopenta[\textit{b,d}]pyridines

**Step-1:** Aldol condensation of \(\alpha\)-tetralone

\[
\begin{align*}
\text{O} & \quad \text{OH} \\
\text{H} & \quad \text{C} \quad \text{O} \\
\text{H} & \quad \text{H} \quad \text{C} \quad \text{H} \\
\text{N} & \quad \text{H} \quad \text{C} \quad \text{N} \\
\text{H} & \quad \text{H} \\
\text{N} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\]

**Step-2:** Generation of Aldimine ion

**Step-3:** Condensation of binaphthalenone and aldimine (formation of phenanthridine nucleus).

\[
\begin{align*}
\text{HN} & \quad \text{H} \\
\text{H} & \quad \text{C} \quad \text{OH} \\
\text{H} & \quad \text{H} \quad \text{C} \quad \text{N} \\
\text{H} & \quad \text{H} \\
\text{N} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\]

Scheme-40

**Scheme-40**
Table-1: Data for compounds 69(a-h).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ketone (67)</th>
<th>Aldehyde (68a-h)</th>
<th>Product (69a-h)</th>
<th>Reaction Time (hr)</th>
<th>Yield(^a) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>![Image]</td>
<td>![Image]</td>
<td>![Image]</td>
<td>1</td>
<td>75</td>
</tr>
<tr>
<td>b</td>
<td>![Image]</td>
<td>![Image]</td>
<td>![Image]</td>
<td>1.6</td>
<td>85</td>
</tr>
<tr>
<td>c</td>
<td>![Image]</td>
<td>![Image]</td>
<td>![Image]</td>
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<tr>
<td>d</td>
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</tr>
<tr>
<td>e</td>
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<td>![Image]</td>
<td>![Image]</td>
<td>1.7</td>
<td>78</td>
</tr>
<tr>
<td>f</td>
<td>![Image]</td>
<td>![Image]</td>
<td>![Image]</td>
<td>1.6</td>
<td>72</td>
</tr>
<tr>
<td>g</td>
<td>![Image]</td>
<td>![Image]</td>
<td>![Image]</td>
<td>2.7</td>
<td>60</td>
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<tr>
<td>h</td>
<td>![Image]</td>
<td>![Image]</td>
<td>![Image]</td>
<td>2.5</td>
<td>65</td>
</tr>
</tbody>
</table>

\(^a\) Isolated yields
C.2.3 Experimental:

C.2.3.1 General Considerations:

All experiments were performed in oven dried glass apparatus. The melting points were determined in open capillary tubes on Perfit melting point apparatus and are uncorrected. The progress of the reaction was monitored by thin layer chromatography (TLC) using silica gel pre-coated aluminium sheets (60 F254, Merck). Visualisation of spots was effected by exposure to ultraviolet radiation (UV), iodine vapours and Draggendroff reagent. Column chromatography was performed on silica gel (60-120 and 100-200 mesh) and compounds were eluted with graded solvent systems of petroleum ether and ethyl acetate. The IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer using KBr discs ($\nu_{\text{max}}$ in cm$^{-1}$). $^1$H and $^{13}$C NMR spectra were recorded on Bruker Ac-400 (400& 100 MHz respectively). The abbreviations s, d, t, q, m in spectra refer to singlet, doublet, triplet, quartet and multiplet respectively. EIMS were recorded on Bruker Micro mass VG-7070 mass spectrometer. Elemental analysis was performed on Leco CHNS 932 analyser. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as internal standard and expressed in $\delta$ scale, $J$ is expressed in Hertz. Commercial grade solvents were purified and dried as per established procedure before use.

C.2.3.2 General experimental procedure for the synthesis of 5-aryl/heteryl tetrahydrodibenzo[a,i]phenanthridines 69:

In a round bottom flask a mixture of $\alpha$-tetralone (2 mmol), and respective aldehyde (1mmol) was taken and treated with 1.5 mmol of ammonium acetate in 25 ml of anhydrous ethanol. The mixture was refluxed on oil bath at 80 °C when the colour changed to yellow. The reaction mixture was kept overnight at room temperature. The progress of reaction was monitored by TLC. The solid thus, settled was separated and the crude product was purified by column chromatography using petroleum ether and ethyl acetate as eluent. The structures of the products 69(a-h) were established by spectroscopy.
C.2.4 Spectroscopic details:

5-Phenyl-7,8,13,14-tetrahydrodibenzo[a,i]phenanthidine (69a):

Physical state: Black solid, M.pt. 172 °C.

IR (KBr, νmax cm⁻¹): 1235, 1353, 1382, 1418, 1599, 2834, 3035.

¹H NMR (CDCl₃, 400 MHz): δ 2.8-3.2 (m, 8H, 4×CH₂), 7.1-7.5 (m, 13H, ArH’s).

¹³C NMR (CDCl₃, 100 MHz): δ 24.3, 27.4, 29.5, 31.3, 124.5, 125.8, 126.2, 127.1, 127.2, 128.3, 128.6, 129.3, 129.8, 130.6, 132.7, 132.9, 136.8, 138.5, 139.2, 139.6, 140.2, 142.5, 145.6, 153.4, 157.6.


EIMS (m/z) = 360 (M+H)+.

5-(4-Chlorophenyl)-7,8,13,14-tetrahydrodibenzo[a,i]phenanthidine (69b):

Physical state: Light grey solid, M.pt.178 °C.

IR (KBr, νmax cm⁻¹): 752, 1235, 1351, 1427, 1532, 1605, 2829, 3029.

¹H NMR (CDCl₃+DMSO, 400 MHz): δ 2.8-3.2 (m, 8H, 4×CH₂), 6.79-6.94 (m, 4H, ArH’s), 7.1-7.4 (m, 8H, ArH’s).

¹³C NMR (CDCl₃+DMSO-d₆, 100 MHz): δ 23.9, 27.7, 29.4, 31.3, 124.6, 125.5, 126.1, 126.5, 127.3, 127.4, 128.3, 128.5, 128.7, 129.1, 129.2, 129.3, 129.4, 129.5, 132.3, 132.5, 132.7, 134.5, 136.5, 136.8, 148.5, 151.4, 156.5.

Anal. Calcd. for C₂₇H₂₀ClN: C, 82.33; H, 5.12; N, 3.56. Found: C, 82.18; H, 4.82; N, 3.44. EIMS (m/z) = 394, 396 (M+H)+.

5-(4-Methoxyphenyl)-7,8,13,14-tetrahydrodibenzo[a,i]phenanthidine (69c):

Physical state: Orange solid, M.pt. 175 °C.

IR (KBr, νmax cm⁻¹): 1223, 1354, 1423, 1564, 1603, 2829, 3032.

¹H NMR (CDCl₃, 400 MHz): δ 2.8-3.2 (m, 6H, 3×CH₂), 3.2-3.5 (t, 2H, CH₂), 3.73 (s, 3H, OCH₃), 6.7-6.9 (m, 4H, ArH’s), 7.3-7.5 (m, 8H, ArH’s).
A new approach for the one-pot synthesis of dibenzo[a,i]phenanthridines, dibenzo[b,d]pyridines(phenanthridines) and dicyclopenta[b,d]pyridines

$^{13}$C NMR (CDCl$_3$, 100 MHz): \( \delta \) 23.9, 27.2, 29.6, 30.2, 55.8, 114.5, 114.6, 126.4, 126.5, 127.3, 127.6, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 128.9, 132.3, 132.4, 136.5, 142.3, 148.5, 151.2, 156.4, 159.8.

**Anal. Calcd.** for C$_{28}$H$_{23}$NO: C, 86.34; H, 5.95; N, 3.60. Found: C, 86.19, 5.43, 3.32.

**EIMS (m/z) = 390 (M+H)$^+$**.

5-(3,4-Dimethoxyphenyl)-7,8,13,14-tetrahydrodibenzo[a,i]phenanthridine (69d):

| Physical state: Brown solid, M.pt. 190 °C. |
| IR (KBr, \( \nu_{\text{max}} \) cm$^{-1}$): 1236, 1469, 1579, 1648, 3014. |

$^1$H NMR (DMSO-$d_6$, 400 MHz): \( \delta \) 2.9-3.2 (m, 8H, 4×CH$_2$), 3.75 (s, 3H, OCH$_3$), 3.81 (s, 3H, OCH$_3$), 6.7 (d, 1H, ArH), 7.1-7.6 (m, 10H, ArH’s).

$^{13}$C NMR (DMSO-$d_6$, 100 MHz): \( \delta \) 25.6, 25.8, 26.7, 27.4, 56.1, 56.3, 112.7, 115.7, 120.8, 126.5, 127.4, 128.3, 128.4, 128.7, 129.1, 132.3, 135.7, 142.4, 147.9, 150.8, 155.3, 158.9.

**Anal. Calcd.** for C$_{29}$H$_{25}$NO$_2$: C, 83.03; H, 6.01; N, 3.34. Found: C, 83.18; H, 5.94; N, 3.21. **EIMS (m/z) = 420 (M+H)$^+$**.

5-(3,4-Methylenedioxyphenyl)-7,8,13,14-tetrahydrodibenzo[a,i]phenanthridine (69e):

| Physical State: Dark brown solid, M.pt. 185 °C. |
| IR (KBr, \( \nu_{\text{max}} \) cm$^{-1}$): 1123, 1247, 1589, 1642, 1745, 3128. |

$^1$H NMR (DMSO-$d_6$, 400 MHz): \( \delta \) 2.79 (m, 6H, 3×CH$_2$), 3.32 (t, 2H, CH$_2$), 5.8 (s, 2H, CH$_2$, -O-CH$_2$-O-), 7.1-7.6 (m, 11H, ArH’s).

$^{13}$C NMR (DMSO-$d_6$, 100 MHz): \( \delta \) 24.4, 24.9, 29.8, 30.7, 105.2, 107.1, 112.4, 115.7, 120.9, 126.5, 128.3, 127.4, 134.3, 135.6, 142.8, 151.4, 155.3, 157.6, 164.3.

**Anal. Calcd.** for C$_{29}$H$_{21}$NO$_2$: C, 83.35; H, 5.25; N, 3.47. Found: C, 83.21; H, 5.15; N, 3.31. **EIMS (m/z) = 404 (M+H)$^+$**.
5-(2-Methoxyphenyl)-7,8,13,14-tetrahydrodibenzo[a,i]phenanthidine (69f):

Physical State: Light brown solid, M.pt. 180 °C.

IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)): 1218, 1347, 1421, 1565, 3035.

\(^1\)H NMR (DMSO-\(d_6\), 400 MHz): \( \delta \) 2.7-3.1 (m, 8H, 4xCH\(_2\)), 3.73 (s, 3H, OCH\(_3\)), 6.7-6.9 (m, 3H, ArH’s), 7.3-7.7 (m, 9H, ArH’ s).

\(^{13}\)C NMR (DMSO-\(d_6\), 100 MHz): \( \delta \) 23.8, 27.8, 29.6, 30.1, 56.4, 114.7, 122.1, 121.4, 126.5, 127.1, 127.2, 127.3, 128.3, 128.4, 128.5, 128.6, 128.7, 132.2, 132.3, 136.4, 142.2, 148.4, 151.4, 156.7, 157.5, 159.1.

Anal. Calcd. for C\(_{28}\)H\(_{33}\)NO: C, 86.34; H, 5.95; N, 3.60. Found: C, 83.21; H, 4.92; N, 3.42. EIMS (m/z) = 390 (M+H\(^+\)).

5-(2-Furyl)-7,8,13,14- tetrahydrodibenzo[a,i]phenanthidine (69g):

Physical State: Brown solid, M.pt. 167 °C.

IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)): 1143, 1256, 1435, 1645, 2893, 3238.

\(^1\)H NMR (DMSO-\(d_6\), 400 MHz): \( \delta \) 2.7-3.1 (m, 8H, 4xCH\(_2\)), 6.7-6.9 (m, 2H, ArH’s), 7.5 (d, 1H, ArH), 7.6-7.9 (m, 8H, ArH’ s).

\(^{13}\)C NMR (DMSO-\(d_6\), 100 MHz): \( \delta \) 24.4, 27.8, 29.5, 30.5, 105.2, 107.1, 126.5, 127.4, 128.3, 128.7, 132.5, 128.5, 134.3, 135.6, 142.1, 142.8, 151.4, 155.3, 158.6.

Anal. Calcd. for C\(_{25}\)H\(_{19}\)NO: C, 85.93; H, 5.48; N, 4.01. Found: C, 85.12; H, 5.24; 3.73. EIMS (m/z) = 350 (M+H\(^+\)).

5-(3-Indolyl)-7,8,13,14-tetrahydrodibenzo[a,i]phenanthidine (69h):

Physical state: Grey Black solid, M.pt. 169 °C.

IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)): 1348, 1434, 1572, 1674, 3049, 3241.

\(^1\)H NMR (DMSO-\(d_6\), 400 MHz): \( \delta \) 2.8-3.2 (m, 8H, 4xCH\(_2\)), 7.14-7.17 (m, 9H, ArH’s), 7.43 (d, 4H, ArH’ s), 10.23 (br s, 1H, NH).

\(^{13}\)C NMR (DMSO-\(d_6\), 100 MHz): \( \delta \) 24.4, 27.8, 30.3, 30.5, 111.7, 114.9, 119.4, 120.4, 122.4, 126.5, 127.4, 128.3, 128.4, 128.6, 132.2, 135.7, 142.4, 148.6, 156.7.
Analytical Calculated for $C_{29}H_{22}N_2$: C, 87.41; H, 5.56; N, 7.03. Found: C, 87.20; H, 5.43; N, 6.67. EIMS ($m/z$) = 399 (M+H)$^+$.  

C.2.5 Pharmacological report of the synthesised compounds

Antibacterial and antifungal activities of the synthesised compounds were performed using the microdilution method against two gram positive strains *Staphylococcus aureus* ATCC 29213, Methicillin Resistant *Staphylococcus aureus* 15187), two gram negative strains (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC-9027), two yeast strains (*Candida albicans* ATCC 22019, *Candida albicans* V-01-27853) and two filamentous fungi (*Asperigillus fumigates* LSI-II, *Asperigillus niger* ATCC 16404). Antibacterial testing was performed in Muller Hinton Broth (Becton- Dickenson, Cockeysville, MD, USA) where as for antifungal testing RPMI 1640 with L- glutamine (Sigma-Aldrich, St. Louis, MO, USA) buffered to pH 7.0 supplemented with 0.165 M 3-(N-morphilino)propanesulphonic acid(MOPS) [Sigma-Aldrich] was used. The stock solution of the compounds was prepared was prepared in DMSO. The MIC (Minimum Inhibitory Concentration of the compounds was determined by a serial two fold diluting the solution in the above mentioned media in 100µL volume in 96 well U bottom micro litre plate. The final concentrations of compounds ranged from 128 to 0.25 µg/ml. Amphotericin B and Ciprofloxacin [16 to 0.03 µg/ml](both from Sigma-Aldrich) were used as standard antifungal and antibacterial agents respectively. The bacterial and fungal suspension of the overnight grown bacterial and fungal cultures was prepared in sterile normal saline and the density was adjusted to 0.5 McFarland. The bacterial cultures were


further diluted and added in 100µl volume at final inoculums of $1 \times 10^5$ CFU/ml. For fungal cultures $1 \times 10^3$ CFU/ml was used. The plates were incubated at 37°C for 24 hr for bacteria and at 26°C 48 hr for fungal cultures. The plates were read visually and the minimum concentration of the compound showing no turbidity was recorded as MIC.

C.2.5.1 Activity results:

Table-2: MIC determination of the compounds for antibacterial activity

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compounds</th>
<th>MIC(µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>S. aureus ATCC-29213</td>
</tr>
<tr>
<td>1</td>
<td>69a</td>
<td>&gt;125</td>
</tr>
<tr>
<td>2</td>
<td>69b</td>
<td>&gt;125</td>
</tr>
<tr>
<td>3</td>
<td>69c</td>
<td>&gt;125</td>
</tr>
<tr>
<td>4</td>
<td>69d</td>
<td>&gt;125</td>
</tr>
<tr>
<td>5</td>
<td>69e</td>
<td>&gt;125</td>
</tr>
<tr>
<td>6</td>
<td>69f</td>
<td>&gt;125</td>
</tr>
<tr>
<td>7</td>
<td>69g</td>
<td>&gt;125</td>
</tr>
<tr>
<td>8</td>
<td>69h</td>
<td>&gt;125</td>
</tr>
<tr>
<td>9</td>
<td>Ciprofloxacin</td>
<td>0.25</td>
</tr>
</tbody>
</table>
Table-3: MIC determination of the compounds for antifungal activity

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compounds</th>
<th>C. albicans ATCC 90028</th>
<th>C. albicans V-01-191</th>
<th>A. Fumigates LS-I</th>
<th>A. Niger ATCC 16404</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>69a</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
</tr>
<tr>
<td>2</td>
<td>69b</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
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<tr>
<td>3</td>
<td>69c</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
</tr>
<tr>
<td>4</td>
<td>69d</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
</tr>
<tr>
<td>5</td>
<td>69e</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
</tr>
<tr>
<td>6</td>
<td>69f</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
</tr>
<tr>
<td>7</td>
<td>69g</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
</tr>
<tr>
<td>8</td>
<td>69h</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
<td>&gt;125</td>
</tr>
<tr>
<td>9</td>
<td>Amphotericin B</td>
<td>0.5</td>
<td>0.5</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Most of the synthesised dibenzo[a,i]phenanthridine derivatives were screened for their antibacterial activity against two gram positive strains (*Staphylococcus aureus* ATCC 29213, Methicillin resistant *staphylococcus aureus* 15187) and two gram negative strains (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC-9027). Regarding the antifungal activity, the compounds were screened against the two yeast strains (*Candida albicans* ATCC 22019, *Candida albicans* V-01-27853) and two filamentous fungi strains (*Aspergillus fumigates* LSI-II, *Asperigillus niger* ATCC 16404). The preliminary screening was carried out by measuring MIC values in µg/ml. The screening results are summarised in Table-2 and Table-3 and it was noticed that the compounds screened did not display any significant antibacterial and antifungal activity. Ciprofloxacin and Amphotericin-B were used as standard antibiotics in the present study.
C.3 Synthesis of cyclopenta[b,d]pyridines catalysed by ammonium acetate

C.3.1 Genesis

Various pharmacological properties are associated with fused pyridines but the methods of preparation generally involve the stringent reaction conditions, low yielding steps, cumbersome procedures, use of expensive metal catalysts and generally strong reagents like POCl₃. In view of the advantages associated with ammonium acetate, it was thought to employ it for the synthesis of dicyclopenta[b,d]pyridines and highly bridged dibenzo[b,d]pyridines. In continuation to work on α-tetralone, hence, this one-step reaction was extended to other cyclic ketones like cyclopentanone and camphor.

C.3.2 Results and Discussion

In our initial attempt, a mixture of cyclopentanone 70 (2 mmol), aldehyde 68 (1 mmol) and ammonium acetate (1.5 mmol) was refluxed in anhydrous methanol (25 mL) in a round bottom flask. The formation of a new compound 71 was noticed on TLC (Scheme-41). Visualization of spots was effected by exposure to iodine vapours and DNP reagent.

![Figure]

Scheme-41

![Figure]

Scheme-42
Chapter-C: A new approach for the one-pot synthesis of
dibenzo[a,i]phenanthridines, dibenzo[b,d]pyridines(phenanthridines) and
dicyclopenta[b,d]pyridines

Scheme-43

With cyclopentanone using ammonium acetate in methanol, the para
substituted and ortho substituted aldehydes gave different products. With
parasubstituted and unsubstituted aryl/heterylaldehydes, the products obtained were
characterised as 5-phenyl-1,2,3,6,7,8-hexahydrodicyclopenta[b,d]pyridines as
exhibited by Scheme-41. However, the yield could not be obtained above 50% in all
the cases. With ortho-substituted aromatic aldehydes using ammonium acetate in
methanol, a new product was generated which was characterised as 3-
azabicyclo[3.2.1]octan-8-one 72 (Scheme-42). The two reactions were not competing
with each other and the product formation was exclusive but the yield was poorer in
case of azabicyclo compounds. The same conditions when extended on camphor, it
behaved like α-tetralone producing entirely a single product 6-aryl/heteryl-4,10-
dimethyl-1,4,7,10-bisdimethylmethano-1,2,3,4,7,8,9,10-octahydrophenanthridine{a
bridged partially reduced dibenzo[b,d]pyridine} 74 (Scheme-43) with ammonium
acetate in methanol.

It is concluded logically that cyclic ketones like α-tetralone and camphor
which have only one methylene group adjoining the carbonyl functionality produce
entirely single product using ammonium acetate in methanol whereas cyclic ketones
like cyclopentanone in which the carbonyl functionality is flanked by methylene
moieties on either side produce two different products with differently substituted
(ortho or para) aryl aldehydes. The structures of the compounds were arrived at by
spectral means viz. ¹H NMR, ¹³C NMR, IR and EIMS. It was found that the most
diagnostic signals in ¹H NMR appeared at δ value 1.8-2.1 and 2.4-2.8 as multiplets
corresponding to twelve protons of saturated carbon atoms in compound 71. Further a
multiplet at δ value 7-7.8 for 5 protons indicated the presence of a phenyl ring in 71a.
The structure was further strengthened by peak [at 236(M+H)+] in EIMS and CHNS analysis data. The reaction proceeds with both aryl and heteryl aldehydes and the results are summarised in Table-2.

The formation of 1,2,3,6,7,8-hexahydrodicyclopenta[b,d]pyridine 71a can be explained by the following mechanism. (Scheme-44)

**Step-1: Aldol condensation of cyclopentanone**

![Aldol condensation of cyclopentanone](image)

**Step-2: Generation of Aldimine ion**

![Generation of Aldimine ion](image)

**Step-3: Condensation of aldol product and aldimine**

![Condensation of aldol product and aldimine](image)

Scheme-44
Chapter-C: A new approach for the one-pot synthesis of dibenzo[\textit{a,i}]phenanthridines, dibenzo[\textit{b,d}]pyridines(phenanthridines) and dicyclopenta[\textit{b,d}]pyridines

Table-4: Data for the compounds 71(a-g), 72(a-b)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ketone (70)</th>
<th>Aldehyde (68a-h)</th>
<th>Product (71, 72)</th>
<th>Time (hr)</th>
<th>Yield(^\circ) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>O</td>
<td>CHO</td>
<td><img src="71a" alt="Image" /></td>
<td>1.5</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>O</td>
<td>CHO</td>
<td><img src="71b" alt="Image" /></td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>O</td>
<td>CHO</td>
<td><img src="71c" alt="Image" /></td>
<td>2.5</td>
<td>42</td>
</tr>
<tr>
<td>4</td>
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Chapter-C: A new approach for the one-pot synthesis of dibenzo[a,i]phenanthridines, dibenzo[b,d]pyridines(phenanthridines) and dicyclopenta[b,d]pyridines

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*Isolated yields.

C.3.3 Experimental

C.3.3.1 General Considerations

All experiments were performed in oven dried glass apparatus. The melting points were determined in open capillary tubes on Perfit melting point apparatus and are uncorrected. The progress of the reaction was monitored by thin layer chromatography (TLC) using silica gel pre-coated aluminium sheets (60 F254, Merck). Visualisation of spots was effected by exposure to iodine vapours and Draggendorff reagent. Column chromatography was performed on silica gel (60-120 and 100-200 mesh) and compounds were eluted with graded solvent systems of petroleum ether and ethyl acetate. The IR spectra were recorded on Perkin-Elmer.
FTIR spectrophotometer ($\nu_{\text{max}}$ in cm$^{-1}$). $^1$H and $^{13}$C NMR spectra were recorded on Bruker Ac-400 (400 & 100 MHz respectively). The abbreviations s, d, t, q, m in spectra refer to singlet, doublet, triplet, quartet and multiplet respectively. EIMS were recorded on Bruker Micro mass VG-7070 mass spectrometer. Elemental analysis was performed on Leco CHNS 932 analyser. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as internal standard and expressed in $\delta$ scale, $J$ is expressed in Hertz. Commercial grade solvents were purified and dried as per established procedure before use.

C.3.3.2 General Experimental procedure for the synthesis of cyclopenta[b,d]pyridines (71):

Cyclopentanone (2 mmol) 70 was taken in a round bottom flask and was treated with 1mmol of the concerned aryl/hetarylaldehyde (68 a-e, 68g-h) and 1.5 mmol of ammonium acetate in 25 ml in anhydrous methanol. The mixture was refluxed on water bath for 1.5-3 hours when colour changed to yellow. Reaction mixture was kept overnight at room temperature. The progress of reaction was monitored by TLC. The solid, thus settled was separated and the crude product 71 a-g was purified by running it over silica gel column using petroleum ether and ethyl acetate as eluent (9:1). When reaction was carried using ortho substituted aldehydes 68f, 68i under similar conditions of catalyst and solvent, the product obtained was entirely different and were characterised as azabicyclo compounds 72. The structures of the product were confirmed by spectroscopy.

C.3.3.3 General procedure for the synthesis of 6-Aryl/hetryl-4,10-dimethyl-1,4;7,10-bisdimethylmethano-1,2,3,4,7,8,9,10-octahydrophenanthridines (74):

In a round bottom flask camphor (2 mmol) and aryl/hetarylaldehyde (1mmol) were taken and reacted with 1.5 mmol of ammonium acetate and the reaction was refluxed in ethanol. The reaction was monitored using the TLC. The reaction mixture was refluxed till the colour changed to yellow. The crude product was purified by column chromatography using petroleum ether and ethyl acetate as eluent.
C.3.4 Spectroscopic details:

5-Phenyl-1,2,3,6,7,8-hexahydropyridino[2,4,5-\mathbf{d}]pyridine (71a):

Physical state: Green solid, M.pt. 135 °C.

IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)): 1297, 1448, 1589, 2992, 3052.

\(^1^H\) NMR (CDCl\(_3\), 400 MHz): \( \delta \) 1.8-2.1 (m, 4H, 2\( \times \)CH\(_2\)), 2.4-2.8 (t, 8H, 4\( \times \)CH\(_2\)), 7.1-7.8 (m, 5H, ArH’s).

\(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 24.8, 25.3, 25.7, 26.7, 26.8, 35.4, 126.8, 127.1, 127.8, 128.8, 129.5, 132.7, 135.1, 135.9, 151.6, 157.3, 165.2.

Anal. Calcd. for C\(_{17}\)H\(_{17}\)N: C, 86.77; H, 7.28; N, 5.95. Found: C, 85.12; H, 6.09; N, 5.14. EIMS (m/z) = 236 (M+H)^+.

5-(4-Chlorophenyl)-1,2,3,6,7,8-hexahydropyridino[2,4,5-\mathbf{d}]pyridine (71b):

Physical state: Yellow grey solid, M.pt. 154 °C.

IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)): 700, 1242, 1278, 3018, 3043.

\(^1^H\) NMR (CDCl\(_3\), 400 MHz): \( \delta \) 1.9-2.2 (m, 4H, 2\( \times \)CH\(_2\)), 2.6-2.8 (t, 8H, 4\( \times \)CH\(_2\)), 7.3-7.8 (m, 4H, ArH’s).

\(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 24.8, 25.3, 25.7, 26.7, 27.1, 27.8, 35.4, 128.5, 128.8, 129.1, 129.4, 132.2, 134.4, 134.5, 136.1, 152.5, 156.1, 164.3.

Anal. Calcd. for C\(_{17}\)H\(_{16}\)ClN: C, 75.69; H, 5.98; N, 5.19. Found: C, 74.42; H, 5.21; N, 4.63. EIMS (m/z) = 270, 272 (M+H)^+.

5-(4-Methoxyphenyl)-1,2,3,6,7,8-hexahydropyridino[2,4,5-\mathbf{d}]pyridine (71c):

Physical state: Light yellow, M.pt. 142 °C.

IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)): 1228, 1417, 1568, 2994, 3037.
Chapter-C: A new approach for the one-pot synthesis of dibenzo[a,i]phenanthridines, dibenzo[b,d]pyridines(phenanthridines) and dicyclopenta[b,d]pyridines

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.9-2.1 (m, 4H, 2×CH$_2$), 2.8-3.2 (t, 8H, 4×CH$_2$), 3.71 (s, 3H, OCH$_3$), 7.4-7.8 (m, 4H, ArH’s).

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 25.3, 25.7, 26.3, 27.1, 27.4, 35.6, 55.2, 114.5, 114.7, 128.3, 128.5, 128.9, 134.1, 134.8, 150.2, 155.2, 159.4, 164.3.

Anal. Calcd. for C$_{15}$H$_{19}$NO: C, 81.47; H, 7.22; N, 5.28. Found: C, 80.38; H, 7.05; N, 4.61. EIMS ($m/z$) = 266 (M+ H)$^+$. 

5-(3,4-Dimethoxyphenyl)-1,2,3,6,7,8-hexahydricyclopenta[b,d]pyridine (71d):

Physical State: Bright orange solid, M.pt. 155 °C.

IR (KBr, $\nu$$_{\text{max}}$ cm$^{-1}$): 1272, 1422, 1563, 2839, 3033.

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.8-2.4 (m, 4H, 2×CH$_2$), 2.7-2.9 (t, 8H, 4×CH$_2$), 3.65 (s, 3H, OCH$_3$), 3.7 (s, 3H, OCH$_3$), 7.1-7.7 (m, 3H, ArH’s).

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 25.3, 26.3, 26.8, 27.5, 35.1, 56.2, 56.7, 112.3, 115.3, 120.5, 129.1, 134.1, 135.8, 148.2, 150.1, 150.3, 155.4, 155.8, 163.8.

Anal. Calcd. for C$_{19}$H$_{21}$NO$_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 76.14; H, 5.14; N, 3.76. EIMS ($m/z$) = 296 (M+ H)$^+$. 

5-(3,4-Methylenedioxyphenyl)-1,2,3,6,7,8-hexahydricyclopenta[b,d]pyridine (71e):

Physical State: Yellow solid, M.pt. 158 °C.

IR (KBr, $\nu$$_{\text{max}}$ cm$^{-1}$): 1135, 1156, 1289, 1581, 2956, 3049.

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 1.87-2.23 (m, 4H, 2×CH$_2$), 2.7-2.81 (t, 8H, 4×CH$_2$), 5.93 (s, 2H, CH$_2$, -O-CH$_2$-O-), 6.7 (d, 1H, ArH), 7.2-7.4 (m, 2H, ArH’s).

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 25.6, 25.7, 26.4, 27.1, 27.4, 35.3, 101.5, 111.2, 115.4, 120.6, 129.7, 134.2, 135.7, 147.3, 149.2, 151.2, 153.2, 164.2.

Anal. Calcd. for C$_{18}$H$_{17}$NO$_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 76.28; H, 4.53; N, 4.47. EIMS ($m/z$) = 280 (M+ H)$^+$. 

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5-(2-Furyl)-1,2,3,6,7,8-hexahydridicyclopenta[b,d]pyridine (71f):

**Physical State:** Oily liquid.

**IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)):** 1170, 1277, 1574, 2992, 3045.

**¹H NMR (CDCl₃, 400 MHz):** \( \delta \) 1.9-2.3 (m, 4H, 2×CH₂), 2.4-2.9 (t, 8H, 4×CH₂), 6.23 (d, 2H, ArH’s), 7.34 (d, 1H, ArH).

**¹³C NMR (CDCl₃, 100 MHz):** \( \delta \) 24.2, 25.1, 26.3, 26.9, 27.8, 34.5, 104.9, 107.6, 134.8, 135.7, 142.4, 151.2, 155.9, 157.2, 164.5.

**Anal. Calcd. for C₁₅H₁₅NO:** C, 79.97; H, 6.71; N, 6.22. Found: C, 78.62; H, 6.58; N, 5.98. **EIMS (m/z) = 226 (M+H)⁺.**

5-(3-Indolyl)-1,2,3,6,7,8-hexahydridicyclopenta[b,d]pyridine (71g):

**Physical State:** Black solid, M.pt. 161 °C.

**IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)):** 871, 1242, 1578, 2917, 3043, 3257.

**¹H NMR (CDCl₃, 400 MHz):** \( \delta \) 1.8-2.2 (m, 4H, 2×CH₂), 2.8-3.1 (t, 8H, 4×CH₂), 7.3-7.8 (m, 5H, ArH’s), 10.1 (br s, 1H, NH).

**¹³C NMR (CDCl₃, 100 MHz):** \( \delta \) 25.3, 25.8, 26.2, 27.3, 27.8, 35.7, 111.4, 111.6, 118.7, 120.4, 122.6, 128.5, 131.5, 134.2, 135.4, 135.9, 151.2, 154.3, 163.6.

**Anal. Calcd. for C₁₉H₁₈N₂:** C, 83.18; H, 6.61; N, 10.21. Found: C, 83.13; H, 6.41; N, 10.14. **EIMS (m/z) = 275 (M+H)⁺.**

2,4-Di(o-methoxyphenyl)- 3-azabicyclo[3.2.1]octan-8-one (72a):

**Physical State:** Yellowish solid, M. pt. 208 °C.

**IR (KBr, \( \nu_{\text{max}} \text{ cm}^{-1} \)):** 1142, 1245, 1492, 1732, 3072.

**¹H NMR (DMSO-d₆, 400 MHz):** \( \delta \) 1.8-2.1 (m, 4H, 2×CH₂), 2.8-3.3 (m, 2H, CH), 3.76 (s, 6H, 2×OCH₃), 4.2 (br s, 1H, NH), 4.3-4.8 (d, 2H, CH), 7.1-7.4 (m, 8H, ArH’s).
Chapter-C: A new approach for the one-pot synthesis of dibenzo[\textit{a,i}]phenanthridines, dibenzo[\textit{b,d}]pyridines (phenanthridines) and dicyclopenta[\textit{b,d}]pyridines

\textbf{13}^C \text{NMR (DMSO-d}_6, 100 MHz): \delta 12.7, 56.1, 57.1, 64.3, 114.2, 120.9, 126.4, 127.1, 129.2, 157.8. \textit{EIMS (m/z)} = 338 (M+H)^+.

\textbf{Anal. Calcd. for} \text{C}_{21}\text{H}_{23}\text{NO}_3: \text{C, 77.45; H, 6.87; N, 4.15. Found: C, 77.42, 6.82, N, 4.13.}

\textbf{2,4-Di(o-chlorophenyl)-3-azabicyclo[3.2.1]octan-8-one (72b):}

\begin{center}
\includegraphics[width=0.5\textwidth]{schematic.png}
\end{center}

\textbf{Physical state:} Dark grey solid, M.pt. 220 °C.

\textbf{IR (KBr, \nu_{\text{max}} \text{ cm}^{-1}):} 765, 1142, 1783, 2852, 3016, 3028.

\textbf{1H NMR (DMSO-d}_6, 400 MHz): \delta 1.8-2.2 (m, 4H, 2\times\text{CH}_2), 2.7-2.9 (m, 2H, CH), 3.1 (br s, 1H, NH), 4.1-4.7 (d, 2H, CH), 6.8-7.3 (m, 8H, ArH’s).

\textbf{13}^C \text{NMR (DMSO-d}_6, 100 MHz): \delta 12.8, 57.1, 64.3, 114.3, 120.5, 126.3, 127.2, 128.6, 129.4, 157.3, 215.5.

\textbf{Anal. Calcd. for} \text{C}_{19}\text{H}_{17}\text{Cl}_2\text{NO}: \text{C, 65.91; H, 4.95; N, 4.05, Found: C, 65.87; H, 4.92; N, 3.87. \textit{EIMS (m/z)} = 347, 349, 351 (M+H)^+.}

\textbf{6-Phenyl-4,10-dimethyl-1,4;7,10-bisdimethylmethano-1,2,3,4,7,8,9,10-octahydrophenanthidine (74a):}

\begin{center}
\includegraphics[width=0.5\textwidth]{schematic.png}
\end{center}

\textbf{Physical state:} Yellow solid, M.pt. 280 °C.

\textbf{IR (KBr, \nu_{\text{max}} \text{ cm}^{-1}):} 1265, 1280, 1427, 1634, 2967.

\textbf{1H NMR (CDCl}_3, 400 MHz): \delta 1.2 (s, 12H, 4\times\text{CH}_3), 1.4 (s, 6H, 2\times\text{CH}_3), 2.1-2.5 (m, 8H, 4\times\text{CH}_2), 3.7 (s, 2H, CH), 7.2-7.7 (m, 5H, ArH’s).

\textbf{13}^C \text{NMR (CDCl}_3, 100 MHz): \delta 24.1, 28.1, 29.4, 34.1, 38.6, 126.7, 127.4, 130.6, 132.3, 132.4, 155.7, 161.6, 163.3.

\textbf{Anal. Calcd. for} \text{C}_{25}\text{H}_{33}\text{N}: \text{C, 86.40; H, 9.57; N, 4.03. Found: C, 86.36; H, 9.52, N, 3.87, \textit{EIMS (m/z)} = 348 (M+H)^+.}
6-(4-Chlorophenyl)-4,10-dimethyl-1,4;7,10-bisdimethylmethano-1,2,3,4,7,8,9,10-octahydrophenanthridine (74b):

**Physical State:** Pale Yellow solid, M.pt. 295 °C.

**IR (KBr, $v_{\text{max}}$ cm$^{-1}$):** 1258, 1296, 1643, 1670, 2971, 3012.

**$^1$H NMR (CDCl$_3$, 400 MHz):** $\delta$ 1.3 (s, 12H, 4×CH$_3$), 1.4 (s, 6H, 2×CH$_3$), 1.9-2.4 (m, 8H, 4×CH$_2$), 3.6 (s, 2H, CH), 7.2-7.6 (m, 4H, ArH’s).

**$^{13}$C NMR (CDCl$_3$, 100 MHz):** $\delta$ 24.3, 28.9, 29.2, 34.1, 38.6, 38.7, 38.9, 127.4, 127.8, 130.7, 155.7, 161.7, 163.4.

**Anal. Calcd. for C$_{25}$H$_{32}$ClN:** C, 78.61; H, 8.44; N, 3.67; Found: C, 78.5; H, 8.23; N, 3.5; EIMS ($m/z$) = 383, 385 (M+H)$^+$. 

6-(4-Methoxyphenyl)-4,10-dimethyl-1,4;7,10-bisdimethylmethano-1,2,3,4,7,8,9,10-octahydrophenanthridine (74c):

**Physical State:** Dark Yellow, M.pt. 305 °C.

**IR (KBr, $v_{\text{max}}$ cm$^{-1}$):** 1235, 1300, 1428, 2965, 3062.

**$^1$H NMR (CDCl$_3$, 400 MHz):** $\delta$ 1.2 (s, 12H, 4×CH$_3$), 1.4 (s, 6H, 2×CH$_3$), 2.3-2.9 (m, 8H, 4×CH$_2$), 3.61 (s, 2H, CH), 3.73 (s, 3H, OCH$_3$), 6.7-7.2 (d, 2H, ArH’s), 7.88 (d, 2H, ArH’s).

**$^{13}$C NMR (CDCl$_3$, 100 MHz):** $\delta$ 24.8, 28.7, 29.2, 29.8, 33.2, 34.8, 126.5, 127.3, 129.3, 129.5, 130.7, 136.3, 155.7, 161.6, 163.3.

**Anal. Calcd. for C$_{26}$H$_{35}$NO:** C, 82.71; H, 9.34; N, 3.71; Found: C, 82.31; H, 9.32; N, 3.69; EIMS ($m/z$) = 378 (M+H)$^+$. 

6-(2-Methoxyphenyl)-4,10-dimethyl-1,4;7,10-bisdimethylmethano-1,2,3,4,7,8,9,10-octahydrophenanthridine (74d):

**Physical State:** Orange solid, M.pt. 308 °C.

**IR (KBr, $v_{\text{max}}$ cm$^{-1}$):** 1235, 1352, 1432, 3014.

**$^1$H NMR (CDCl$_3$, 400 MHz):** $\delta$ 1.3 (s, 12H, 4×CH$_3$), 1.4 (s, 6H, 2×CH$_3$), 2.4-2.8 (m, 8H, 4×CH$_2$), 3.2 (s, 2H, CH), 3.7 (s, 3H, OCH$_3$), 6.7-7.5 (m, 4H, ArH’s).
Chapter-C: A new approach for the one-pot synthesis of dibenzo[a,i]phenanthridines, dibenzo[b,d]pyridines(phenanthridines) and dicyclopenta[b,d]pyridines

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 24.5, 28.5, 33.4, 38.7, 55.7, 111.3, 112.7, 119.7, 130.2, 132.3, 137.3, 155.4, 155.7, 161.5, 163.4.

Anal. Calcd. for C$_{26}$H$_{35}$NO: C, 82.71; H, 9.34; N, 3.71; Found: C, 82.38; H, 9.16; N, 3.41. EIMS (m/z) = 378 (M+H)$^+$. 

C.3.5 Pharmacological report of the synthesised compounds

Antibacterial and antifungal activities of the synthesised compounds were performed using the microdilution method $^{98, 99, 100}$ against two gram positive strains Staphylococcus aureus ATCC 29213, Methicillin Resistant Staphylococcus aureus 15187), two gram negative strains (Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC-9027), two yeast strains (Candida albicans ATCC 22019, Candida albicans V-01-27853) and two filamentous fungi (Asperigillus fumigates LSI-II, Asperigillus niger ATCC 16404). Antibacterial testing was performed in Muller Hinton Broth (Becton- Dickinson, Cockeysville, MD, USA) where as for antifungal testing RPMI 1640 with L-glutamine (Sigma-Aldrich, St. Louis, MO, USA) buffered to pH 7.0 supplemented with 0.165 M 3-(N-morphilino)propanesulphonic acid (MOPS) [Sigma-Aldrich] was used. The stock solution of the compounds was prepared was prepared in DMSO. The MIC (Minimum Inhibitory Concentration of the compounds was determined by a serial two fold diluting the solution in the above mentioned media in 100µL volume in 96 well U bottom micro litre plate. The final concentrations of compounds ranged from 128 to 0.25 µg/ml. Amphotericin B and Ciprofloxacin [16 to 0.03 µg/ml] (both from Sigma -Aldrich) were used as standard.


antifungal and antibacterial agents respectively. The bacterial and fungal suspension of the overnight grown bacterial and fungal cultures was prepared in sterile normal saline and the density was adjusted to 0.5 McFarland. The bacterial cultures were further diluted and added in 100µl volume at final inoculums of $1 \times 10^5$ CFU/ml. For fungal cultures $1 \times 10^3$ CFU/ml was used. The plates were incubated at 37°C for 24 hr for bacteria and at 26°C for 48 hr for fungal cultures. The plates were read visually and the minimum concentration of the compound showing no turbidity was recorded as MIC.

C.3.5.1 Activity results:

Table-5: MIC determination of the compounds for antibacterial activity

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Chapter-C: A new approach for the one-pot synthesis of dibenzo[\(a,i\)]phenanthridines, dibenzo[\(b,d\)]pyridines(phenanthridines) and dicyclopenta[\(b,d\)]pyridines

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Table-6: MIC determination of the compounds for antifungal activity
Most of the synthesised cyclopenta\([b,d]\)pyridine derivatives were screened for their antibacterial activity against two gram positive strains (\textit{Staphylococcus aureus} ATCC 29213, Methicillin Resistant \textit{Staphylococcus aureus} 15187) and two gram negative strains (\textit{Escherichia coli} ATCC 25922, \textit{Pseudomonas aeruginosa} ATCC-9027). Regarding the antifungal activity, the compounds were screened against the two yeast strains (\textit{Candida albicans} ATCC 22019, \textit{Candida albicans} V-01-27853) and two filamentous fungi strains (\textit{Asperigillus fumigates} LSI-II, \textit{Asperigillus niger} ATCC 16404). The preliminary screening was carried out by measuring MIC values in \(\mu\text{g/ml}\). The screening results are summarised in Table-5 and Table-6 and it was noticed that none of the compounds display any significant antibacterial and antifungal activity. Ciprofloxacin and Amphotericin-B were used as standard antibiotics in the present study.