I.1 Introduction

The pyridine skeleton is of great importance to chemists as well as to biologists as it is found in a large variety of naturally occurring compounds and also in clinically useful molecules having diverse biological activities. The pyridine ring systems have emerged as integral backbones of over 7000 existing drugs.\(^1\),\(^2\) The pyridine ring is also an integral part of anticancer and anti-inflammatory agents.\(^3\)

In association with those, Pyridone and their derivatives play an essential role in several biological processes and have considerable chemical and pharmacological importance.\(^4\)\(^-\)\(^6\) 2-Pyridones represent a unique class of pharmacophore, which are observed in various therapeutic agents\(^7\) and antibiotics\(^8\). These heterocycles attracted attention because of their applications as bioactive compounds for example as a promising class of HIV-1 non-nucleoside reverse transcriptase inhibitors (NNRTIs)\(^9\), as antibacterial\(^10\), antifungal\(^11\), sedative\(^12\) and cardiotonic agents\(^13\). Moreover, such derivatives have recently become important due to their structural similarity to nucleosides.\(^14\) Also, 2-pyridones were used as ligands for the late 3d-metals.\(^15\)

They are also versatile precursors for the construction of complex natural products\(^16\), pyridines\(^17\) and larger pyridone systems such as those found in the nitroguanidine insecticide Imidacloprid\(^18\) and subtype selective GABAA receptor agonists\(^19\). Consequently, methodologies for the preparation of pyridones have attracted much attention from both industry and academia. 3-Cyano-2-Pyridones are much interest in the anticancer activity of these compounds owing to different types of biological targets they might interfere with for this effect to occur e.g. PDE3, PIM1 Kinase, and Survivin protein.

The 3-cyanopyridin-2-one nucleus is the structural basis of the alkaloid ricinine, the first known alkaloid containing a cyano-group Figure 1.
Figure 1

Milrinone (Figure 1) is a 3-cyano-2-oxopyridine derivative that has been introduced to the clinic for the treatment of congestive heart failure. Its mechanism of action involves PDE3 inhibition, leading to high levels of cAMP and consequent inotropic effect. Recent studies showed that PDE3, PDE4 and PDE5 are over expressed in cancerous cells compared with normal cells. In addition, cross inhibition of PDE3 together with other PDEs may lead to inhibition of tumor cell growth and angiogenesis. The inhibition of PDE3 was able to inhibit the growth and proliferation of the squamous cell carcinoma cell line HeLa, and in HSG cells and further studies revealed that the pyridone derivative, cilostamide- a selective PDE3 inhibitor- has synergism action to the anti-apoptotic action of PDE4 inhibitors in leukemia cells.

Cheney et al. reported 4,6-diaryl-2-oxo-1,2-dihydropyridine-3-carbonitriles (1), as inhibitors of the oncogenic serine/threonine kinase PIM-1, which plays a role in cancer cell survival, differentiation and proliferation. PIM-1 kinase has been shown to be over expressed in a variety of cancer cell lines (Figure 2).

Wendt et al. showed that several compounds with the same general formula as above but with higher lipophilic properties (2) can inhibit survivin which is a member of the inhibitor of apoptosis family (IAP). The level of expression of surviving in tumor cells is often associated with poor prognosis and shorter patient survival rates. Survivin is highly expressed in most human tumors and fetal tissue but undetectable in most terminally differentiated adult tissues. This fact therefore makes survivin an ideal target for cancer therapy.
I.2 Synthesis of Various Cyanopyridone Derivatives

I.2.1. One-pot multi-component synthesis of 3-cyano-2-pyridinones

Beheshtia et al., developing new selective and environmental friendly methodologies for the preparation of fine chemicals, they performed the synthesis of 4-alkyl(aryl)-6-aryl-3-cyano-2(1H)-pyridinones and their 2-imino isosteres\(^{30,31}\) through one-pot multi-component reaction of 3,4-dimethoxyacetophenone, malonitrile or ethyl cyanoacetate, an aldehyde and ammonium acetate in the presence of \(K_2CO_3\). This reaction was carried out in various solvents such as water, DMF, chloroform, ethanol, \(CH_2Cl_2\) and toluene. The best results in terms of yield and time were obtained in ethanol. By carrying out reactions with different amounts of ammonium acetate, it has been found that 8 mmol of the ammonium acetate furnished the maximum yield for 1 mmol of the reactants. When ethyl cyanoacetate was used instead of malononitrile, the corresponding 2-pyridone was obtained in good yield Figure 3.
PART I  Section 1

1.2.2 From α,β-unsaturated reagents

Condensation of ethyl cyanoacetate with α,β-unsaturated ketones in presence of excess ammonium acetate afforded 3-cyanopyridin-2-ones \(^{32-35}\) (Figure 4). Also, a green chemistry approach describing reaction of α,β-unsaturated ketones with ethyl cyanoacetate using samarium iodide as catalyst has been reported recently\(^ {34}\).

![Figure 4](image)

Barat et al., have reported first that condensation of cyanoacetamide with α,β-unsaturated ketones also affords 3-cyanopyridin-2-ones. Number of reports following this approach has been reported till date\(^ {36-38}\) (Figure 5).

![Figure 5](image)

Chase \textit{et al.} have synthesized 6-amino-5-phenyl-3-cyanopyridin-2-one by the reaction of 3-isobutoxy-2-phenylacrylonitrile with cyanoacetamide\(^ {39}\) (Figure 6).

![Figure 6](image)

Reaction of ethyl-(2,3,4-trimethoxybenzoyl)-pyruvate with cyanoacetamide in ethanol in presence of piperidine gave 4-carbehtoxy-6-(2,3,4-trimethoxybenzyl)-3-cyanopyridin-2-one\(^ {40}\) (Figure 7).
Alnajjar et al.\textsuperscript{41} reported the conversions of 2-cyano-5-(dimethylamino)-5-phenylpenta-2,4-dienamides into nicotinic acid derivatives by boiling in EtOH/HCl. But, when 2-cyano-5-(dimethylamino)-5-phenylpenta-2,4-dienamides are heated under reflux in AcOH, nicotinic nitrile derivatives are obtained (Figure 8).

The condensation of an enone or enal with cyanoacetamide derivatives and $t$-BuOK furnishes either 3-cyano-2-pyridones or 3-unsubstituted-2-pyridones (Figure 9), depending on whether the reaction is carried out in the presence or in the absence of O2. In the first case, \textit{in situ} oxidation of Michael-type intermediates takes place; in the second case, a "decyanidative aromatization" of such intermediates occurs\textsuperscript{42,43}. 
The synthesis of 2,6-piperidindione derivatives (Figure 10) was achieved by the Michael addition of dialkylmalonates to benzylidene cyanoacetamide derivative. Here benzylidene cyanoacetamide derivative were obtained by reaction of cyanoacetamide with certain aromatic aldehydes according to the reported procedure \(^4^4\).

Enaminonitrile reacted with an equimolar amount of \(\alpha\)-cinnamonitriles to provide pyridine and pyridinone derivatives\(^4^5\), respectively. Formation of pyridine and pyridinone derivatives is assumed to proceed via an acyclic intermediate form followed by intramolecular cyclization and spontaneous autooxidation under the reaction conditions in the case of pyridine derivatives and elimination of ethanol in the case of pyridone derivatives (Figure 11). Here, the enaminonitrile can be readily prepared by reaction of acetonitrile with 4-cyanopyridine in the presence of potassium-\(t\)-butoxide\(^4^6\).
Mathews et al. attempted the reaction of 2-aroyl-3,3-bis(alkylsulfanyl) acrylaldehydes with cyanoacetamide in the presence of ammonium acetate/acetic acid at 80 °C, it afforded only the Knoevenagel condensation adduct, 4-aroyl-2-cyano-5,5- bis-(methylsulfanyl)-2,4-pentadien-amides and no 2-pyridone was formed. As the condensation product has the scope for cyclization to produce 2-pyridones by the elimination of an alkylsulfanyl group, they tried the thermal cyclization of the condensation products by heating in xylene at 130 °C (Figure 12).

Condensation of ketone with dimethylformamide, dimethylacetal afforded vinylogous amide, which in turn reacted with cyanoacetamide under basic conditions to generate the 5,6-diaryl-3-cyano-2-pyridones (Figure 13).
The reaction of \((E)-1-(\beta-D-glucopyranosyl)-4-(aryl)but-3-en-2-ones\) and cyanoacetamide was carried out (Figure 14) with \(t\)-BuOK in DMSO under N\(_2\) atmosphere at ambient temperature to give the respective 3-cyano-4-phenyl-6-[(\(\beta-D\)-glucopyranosyl)methyl]pyridones\(^{49}\). The reaction mixture was brought under the influence of an O\(_2\) atmosphere to carry out oxidative aromatization. Here, the starting butenonyl C-glycosides were prepared from commercially available D-glucose following earlier reported protocols\(^{50-53}\).

![Figure 14](image1)

2-alkoxy-3-cyanopyridines is achieved by the reaction of chalcones with malononitrile in corresponding sodium alkoxide\(^{54-57}\) (Figure 15).

![Figure 15](image2)

Another frequently used approach for the synthesis of 2-alkoxy-3-cyanopyridines is the \(O\)-alkylation of 3-cyanopyridin-2-ones by the reaction with appropriate alkyl/aryl halide\(^{58}\) (Figure 16).

![Figure 16](image3)
A series of novel 2-amino-3-cyanopyridines supported with some functional groups was synthesized and tested as potential inhibition effects against both cytosolic human CA I and II isoenzymes (hCA I and II) using by Sepharose-4B-L-tyrosine-sulfanilamide affinity chromatography. The structural elucidations of novel 2-amino-3-cyanopyridines were achieved by NMR, IR, and elemental analyses. $K_i$ values of the novel synthesized compounds were found in range of 2.84–112.44 $\mu$M against hCA I and 2.56–31.17 $\mu$M against hCA II isoenzyme. While compound 7d showed the best inhibition activity against hCA I ($K_i : 2.84 \mu M$), the compound 7b demonstrated the best inhibition profile against hCA II isoenzyme ($K_i: 2.56 \mu M$) (Figure 17). The conversion of carbon dioxide (CO2) and bicarbonate (HCO$_3^-$) to each other is very important for living metabolism. Carbonic anhydrase (CA, E.C.4.2.1.1), a metallo enzyme family, catalyzes the interconversion of these ions (CO2 and HCO$_3^-$) and are very common in living organisms.\(^{59}\)

![Figure 17](image)

About ten substituted cyanopyridine compounds have been synthesized and the purities of these pyridines were examined with their physical constants, analytical and spectroscopic data provided in the literature. They have characterized infrared stretches and NMR chemical shifts and these data were correlated with Hammett substituent constants using single and multi-linear regression analysis. From the results, the effect of substituents on the spectral data of cyanopyridine has been discussed (Figure 18).\(^{60}\)

![Figure 18](image)
A series of 2-pyridone derivatives have been synthesized via a formal [3+3] annulation strategy starting from readily available α-EWG-α-formyl ketene-S,S-acetal 1 and α-carbamoyl ketene-S,S-acetals 2 in the presence of CH₃COOH at 80°C in excellent yields (91-98%). A mechanism involving sequential Baylis–Hillman reaction, intramolecular cycloaddition, Michael addition and alkylthiol elimination processes for this novel reaction was described. In addition, substituted 1-aryl pyridine-2(1H)-ones have also been prepared in high yields via a Cu(OAc)₂-mediated three-component reaction of 1, 2, and aryl boronic acid (Figure 19).

![Figure 19]

A highly efficient procedure has been reported for the synthesis of 3-Cyano-2(1H)-pyridones and their 2-imino isosteres via a one-pot multicomponent reaction of 3,4-dimethoxyacetophenone, malonitrile or ethyl cyanoacetate, an aldehyde, ammonium acetate in the presence of nano-TiO₂ with good yields (Figure 20).

![Figure 20]

Cyanopyridines play a vital role owing to their range of biological and physiological activities. In the light of these biological activities and variety of industrial applications, some new of 6-Aryl-4-[4’-(p-chlorobenzyloxy)-3’-methoxyphenyl]-2-methoxy-3-cyanopyridines (1a-l) & 6-Aryl-4-[4’-(p-chlorobenzyloxy)-3’-methoxyphenyl]-2-ethoxy-3-cyanopyridine (2a-l) have been prepared, by the cyclocondensation of 1-Aryl-3-[4’-(p-chlorobenzyloxy)-3’-methoxyphenyl]-propenones type (I) with malononitrile in presence of Sodiummethoxide & Sodiumethoxide. All the prepared compounds were characterized by their spectral (I.R., N.M.R.,Mass) data and screened for their antimicrobial activities Figure 21.
A simple and efficient method for the selective synthesis of 2-pyridones from 4H-pyrans using iodine as catalyst and ethanol as solvent was developed. The method was equally effective for both aromatic and hetero aromatic ring containing 4H-pyrans. The compatibility with various functional groups, mild reaction conditions, high yields and application of inexpensive, readily and easily available iodine as catalyst and formation of 2-pyridones as major products were the advantages of the present procedure. In vitro antiproliferative activity of the final synthesized compounds was evaluated with four different Human cancer cell lines (Lung adenocarcinoma-A549, Hepatocarcinoma-HepG2, Breast carcinoma-MCF-7 and Ovarian carcinoma-SKOV3) and Normal human lung fibroblast cell line (MRC-5). Among them, one compound showed better inhibition against MCF-7, HepG2 and A549 cell lines (IC50 8.00±0.11, 11.93±0.01 and 15.85±0.04 μM respectively) as compared with doxorubicin and also other showed moderate inhibition against MCF-7, HepG2 (IC50 9.32±0.21 and 20.22±0.01 μM respectively cell lines respectively) as compared with doxorubicin. As many clinically used antiproliferative agents induce apoptosis in cancer cells hence, the 2-pyridone analogues were also tested for their ability to induce apoptosis in MCF-7 cells using the caspases-3 and -9 assays Figure 22.

A series of variously substituted 5-carboxy-6-methyl-3,4-dihydro-2(1H)-pyridone derivatives (Figure 23) were synthesized and their oxidation potentials determined by cyclic voltammetry. The resulting 2-pyridone structure and a tricyclic heterocycle which was
formed during an attempted synthesis of 4-(2-hydroxyphenyl) substituted 3,4-dihydro-2(1H)-pyridone were confirmed by single crystal X-ray crystallography.\textsuperscript{65}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image1.png}
\caption{Figure 23}
\end{figure}

Author have synthesized new cyanopyridine based conjugated polymer P1 and P2 along with the synthesis of its monomers (Figure 24). The synthesized polymers can be used for electro luminescence and photovoltaic (PV) application. The physical data of the polymers were provided in this data file along with the morphological data of the polymer thin films. The data provided there were in association with the research article entitled ‘Cyanopyridine based conjugated polymer-synthesis and characterization’\textsuperscript{66}.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image2.png}
\caption{Figure 24}
\end{figure}
An efficient and convenient method was developed for synthesis of 2-amino-3-cyanopyridine derivatives via the four-component coupling reaction between ketone, aldehyde, malononitrile, and ammonium acetate in the presence of 2 mol% copper nanoparticles on charcoal (Cu/C) catalyst. A variety of ketones and aldehydes were used to afford the corresponding products in good to excellent yields. The method was applicable to large-scale operation without any problem. The catalyst could be quantitatively recovered from the reaction mixture by simple filtration and reused at least eight times with almost consistent activity (Figure 25).

A series of 2-amino-3-cyanopyridines were obtained from aryl aldehydes, substituted acetophenones, malononitrile and ammonium acetate in good to excellent yields by proceeding through a simple, mild and efficient procedure utilizing \(N,N,N^0,N^0\)-tetra-bromobenzene-1,3-disulfonamide [TBBDA] and poly(\(N\)-bromo-\(N\)-ethylbenzene-1,3-disulfonamide) [PBBS] as catalysts (Figure 26).

A series of 2-amino-3-cyanopyridine derivatives have been prepared by one-pot condensation of malononitrile, aromatic aldehyde, methyl ketone and ammonium acetate under microwave irradiation without solvent. This method had the advantage of short routine, high yields and being environmentally-friendly (Figure 27).
**Figure 27**

*N*-substituted 4,6-dimethyl-3-cyano-2-pyridones have been prepared from acetylacetone, *N*-substituted cyanoacetamide, and pyperidine as catalyst under microwave irradiation without solvent. The rapid and simple method produced pure products in high yields (Figure 28).70

**Figure 28**

I.3 **Biological Activity of Some Cyanopyridone Derivatives.**

The continued emergence of bacteria resistant to current standard of care antibiotics presents a rapidly growing threat to public health. New chemical entities (NCEs) to treat these serious infections are desperately needed. The discovery, synthesis, SAR and in vivo efficacy of a novel series of 4-hydroxy-2-pyridones (Figure 29) exhibiting activity against Gram-negative pathogens have been reported. Compound 1c, derived from the *N*-debenzylation of 1b, preferentially inhibits bacterial DNA synthesis as determined by standard macromolecular synthesis assays. The structural features of the 4-hydroxy-2-pyridone scaffold required for antibacterial activity were explored and compound 6q, identified through further optimization of the series, had an MIC$_{90}$ value of 8 lg/mL against a panel of highly resistant strains of E. coli. In a murine septicemia model, compound 6q exhibited a PD$_{50}$ of 8 mg/kg in mice infected with a lethal dose of E. coli. This novel series of 4-hydroxy-2-pyridones serves as an excellent starting point for the identification of NCEs treating Gram-negative infections.71
The discovery of potent non-nucleoside hepatitis B virus (HBV) inhibitors with novel structures, have been employed bioisosterism and hybrid pharmacophore-based strategy to explore the chemically diverse space of bioactive compounds. Cytotoxicity, anti-HBV antigen secretion activities and anti-HBV DNA replication activity were assayed with cell counting kit-8 (CCK-8), enzyme linked immunosorbent assay (ELISA) and a real-time PCR, respectively. Some of the new compounds were able to inhibit the replication of HBV DNA activity in the low micromolar range. In particular, compound 8u displayed the most potent activity against the replication of HBV DNA with IC\textsubscript{50} value of 3.4 mM. The preliminary structure-activity relationship (SAR) of these new compounds was investigated, which may help designing more potent molecules (Figure 30).64

Pyridone shown in figure 31 was identified from a high-throughput cell-based phenotypic screen against \textit{Mycobacterium tuberculosis} (Mtb) including multi-drug resistant tuberculosis (MDRTB) as a novel anti-TB agent and subsequently optimized series using cell-based Mtb assay. Preliminary structure activity relationship on the isobutyl group with higher cycloalkyl groups at 6-position of pyridone ring has enabled significant improvement of potency against Mtb. The lead compound, dimethylcyclohexyl group on the 6-position of the pyridone, displayed desirable in vitro potency against both drug sensitive and multi-drug resistant TB clinical isolates. In addition, it displayed favorable oral pharmacokinetic
properties and demonstrated *in vivo* efficacy in mouse model. These results emphasize the importance of 4-hydroxy-2-pyridones as a new chemotype and further optimization of properties to treat MDR-TB.\(^{72}\)

![Figure 31](image)

**Figure 31**

Survivin is overexpressed in most of the cancerous tissues but not in terminally differentiated normal tissues, making it an attractive target for diagnosis and therapy of various types of cancers. To develop 4,6-diaryl-3-cyano-2-pyridinone (DCP) derivatives, as novel cancer imaging probes that target survivin. Chloro and iodo analogs of DCP (CDCP and IDCP, respectively) were successfully synthesized by using a previously unreported carbon monoxide-free procedure. IDCP exhibited a slightly higher binding affinity for recombinant human survivin (K\(_d\) = 34 nM) than that of CDCP (K\(_d\) = 44 nM). Fluorescence staining indicated that both CDCP and IDCP showed high signals in MDA-MB-231 cells with high levels of survivin expression. Significantly low fluorescent signals were observed in MCF-10A cells, which showed low levels of survivin expression. \(^{[125]}\)IDCP was synthesized for the application of IDCP to single photon emission computed tomography (SPECT) imaging. Quantitative *in vitro* binding of \(^{[125]}\)IDCP in cell cultures showed results consistent to those observed after fluorescent staining. *In vivo* biodistribution studies in tumor-bearing mice demonstrated that the tumor uptake of \(^{[125]}\)IDCP increased gradually with time and was 0.65% injected dose per gram (% ID/g) at 180 min. The maximum tumor/blood and tumor/muscle ratio at 60 min were 0.87 and 2.27, respectively, indicating inadequate \(^{[125]}\)IDCP accumulation in tumors necessary for *in vivo* imaging. Although further structural modifications are necessary to improve pharmacokinetic properties of IDCP, this study demonstrates the feasibility of using the DCP backbone as a scaffold for the development of survivin-targeting tumor imaging probes (Figure 32).\(^{73}\)
Naturally occurring pyridone alkaloids as well as synthetic derivatives were previously shown to induce neurite outgrowth. However, the molecular basis for this biological effect remains poorly understood. New pyridones have been prepared and tested the effect of thirteen 4-hydroxy-2-pyridone derivatives on the components of the endocannabinoid system. Investigation of binding affinities towards CB1 and CB2 receptors led to the identification of a compound binding selectively to CB1 (12). Compound shown in figure 33, inhibited anandamide (AEA) hydrolysis by fatty acid amide hydrolase. Interestingly, none of the compounds tested showed any effect on 2-AG hydrolysis by monoacylglycerol lipase at 10 nM. Assessment of AEA uptake did, however, lead to the identification of four inhibitors with IC50 values in the submicromolar range and high selectivity over the other components of the endocannabinoid system.

Synthesis of new heterocyclic compounds incorporating sulfamoyl moiety suitable for use as antimicrobial agents via a versatile, readily accessible \( N-[4-(aminosulfonyl)phenyl]-2-cyanoacetamide (3) \) has been described. The 2-pyridone derivatives were obtained via reaction of cyanoacetamide with acetylacetone or arylidenes malononitrile. Cycloaddition reaction of cyanoacetamide with salicyaldehyde furnished chromene derivatives. Also, the reactivity of the hydrazone towards hydrazine hydrate to give Pyrazole derivatives was studied. In addition, treatment of 3 with elemental sulfur and phenyl isothiocyanate or malononitrile furnished thiazole and thiophene derivatives respectively. Reaction of 3 with
phenyl isothiocyanate and KOH in DMF afforded the intermediate salt 17 which reacted in situ with 3-(2-bromoacetyl)-2H-chromen-2-one and methyl iodide afforded the thiazole and ketene N,S-acetal derivatives respectively. Finally, reaction of 3 with carbon disulfide and 1,3-dibromopropane afforded the N-[4-(aminosulfonyl) phenyl]-2-cyano-2-(1,3-dithian-2-ylidene)acetamide product (Figure 34). All newly synthesized compounds were elucidated by considering the data of both elemental and spectral analysis. The compounds were evaluated for both their in vitro antibacterial and antifungal activities and showed promising results.75

![Figure 34](image)

A series of benzimidazole bearing 2-pyridones were synthesized and assessed in vitro for their activity as antimicrobial agents using the conventional broth dilution method. The results of the antimicrobial study revealed that 4 compounds exhibited substantial antibacterial activity while one compound shown in figure 35, has more potent antifungal agent compared to the standard drugs chloramphenicol and ketoconazole, respectively. It was observed that the presence of inductively electron withdrawing groups remarkably enhance the antibacterial activity of the newly synthesized compounds. Cytotoxicity studies suggested that none of the tested compounds exhibited any significant cytotoxic effects.76

![Figure 35](image)

Syntheses of some new heterocyclic compounds containing pyridone, thioxopyridine, halogenated-pyridinecarbonitriles, pyrazolopyridine, and pyridine derivatives were achieved. Besides, a modified synthetic method for the synthesis of 2-chloro-4,6-dimethyl-nicotinonitrile (3) through the reaction of acetylacetonate and
malononitrile as starting materials was implemented. The reaction of 2-chloronicotinonitrile with substituted amines to 2-aminonicotinonitrile were also investigated. Fused or binary pyridines were tested for cytotoxicity against well-known established model Ehrlich ascites cells in vitro. Compound shown in figure 36 exhibited a high antitumor activity compared with 5-fluorouracil.77

![Figure 36](image)

A variety of novel bis-heterocyclic derivatives were synthesized via the reaction of bis-cyanoacetanilide derivative with various aromatic aldehydes (1:2 molar ratio), to give the corresponding bis-arylidene derivatives. On the other hand, reacting compound with substituted 2-hydroxybenzaldehydes afforded 2-iminochromene-3-carboxamides in good yields. Followed by reaction with malononitrile afforded the novel bis-pyridones. Some of the newly synthesized compounds show moderate to high antimicrobial activity (Figure 36).78

![Figure 36](image)

A general and easy method for the synthesis of 4,6-disubstituted-3-cyano-2(1H)-iminopyridine or 3-amino-6-chloro-1-aryl-1H-benzo[h]chromen-2-yl cyanide derivatives in the presence of high surface area MgO as a highly effective heterogeneous base catalyst is described. These compounds were synthesized using one-pot multicomponent reactions of the properly substituted acetophenone, appropriate aldehyde, ammonium acetate and malononitrile or three component reactions of 4-chloro-2-naphthol, aldehydes and malononitrile, respectively, in DMF. The compound shown in figure 37 has potent anxiolytic activity.79
A novel series of sulfonamide derivatives have been synthesized starting from the strategic starting material (E)-4-Chloro-N-(4-(1-(2-(2-cyanoacetyl)hydrazono)ethyl)phenyl)benzenesulfonamide. Two series of hydrazone, and pyridone derivatives bearing a sulfonamide moiety were obtained. All the newly synthesized compounds were evaluated for their in vitro cytotoxic activity against human liver cancer cell line (HepG2). Among them, ten compounds have showed higher activity compared to doxorubicin as a positive control. The radio sensitizing ability of the most promising three compounds was studied which showed an increase in the cell killing effect of γ-radiation after combination with these derivatives. The molecular design was performed to predict the binding mode of the most promising compounds with the active site of hCA IX, that showed appropriate fitting with the relevant amino acids in the binding pocket on the basis of standard bond lengths, angles, S score and E conformation data (Figure 38).$^{80}$
1.1 Current Research Work

Our group is involved in the development of various synthetic methodologies for the synthesis of functionalized azines for last few years. Substitution of carboxamide and cyano functionality in the pyridine moiety may alter their biological action. Reports reveal that cyano functionalized dihydropyridines which might have potential biological activities were less studied. Very promising results may obtain with these modifications to DHP skeleton. This concept prompted us to introduce Cyano group at C5 position in pyridone skeleton. For this modification acetoacetanilide was required as a precursor, which was synthesized by the reported procedure in literature.\(^{81}\)

During the course of our ongoing interest on the development of useful synthetic methodologies by utilizing various catalysts\(^{93}\), we were observed that piperidine is an efficient catalyst for the synthesis of pyridines via Hantzsch synthesis. A series of carboxamide at C3 and cyano at C5 functionalized pyridone derivatives \textbf{AYC01-17} have been synthesized via one pot synthesis of various aldehydes \textbf{1a-q}, acetoacetanilides \textbf{2} and cyanoacetamide \textbf{3}. The reaction was simple in ethanol and piperidine as base, and afforded pyridone derivatives in good yield 89 to 93\%. Moreover, the synthesized compounds were screened against Gram positive and Gram negative bacteria and fungi for their activity. Among them, compound \textbf{AYC-03} shows highest inhibition at 4.25 mm against \textit{S. aureus} and 3.75 mm against \textit{E. Coli} Gram-positive and Gram-negative bacteria, respectively. The newly synthesized compounds were characterized by IR, Mass, \(^1\)H NMR, \(^{13}\)C NMR spectroscopy and elemental analysis.
1.2 Results and Discussion

The tremendous biological potential of pyridone derivatives bearing carboxamide and cyano groups motivated us to synthesis some novel pyridones. Thus we have selected acetoacetaldehyde as a precursor for carboxamide group and cyanoacetamide for cyano group. Initially, the reaction of benzaldehyde 1a, acetoacetanilides 2 and cyanoacetamide 3 was examined using various solvent and base. We found that good yield of compound AYC-01 was obtained using ethanol as solvent and piperidine as base at reflux temperature Table I.1.

Scheme-I.1: Synthesis of carboxamide and cyano bearing pyridone derivatives AYC01-17.

Using the above standard process we have synthesized all pyridone derivatives in good to excellent yields. The data are depicted in Table I.2.
Table I.1: Optimization of the reaction condition for the synthesis of AYC-01.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Solvent</th>
<th>Base</th>
<th>Yield in %</th>
<th>Time in hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeOH</td>
<td>K₂CO₃</td>
<td>75</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>EtOH</td>
<td>K₂CO₃</td>
<td>78</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>THF</td>
<td>K₂CO₃</td>
<td>70</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>MeOH</td>
<td>Morpholine</td>
<td>83</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>EtOH</td>
<td>Morpholine</td>
<td>85</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>Morpholine</td>
<td>87</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>MeOH</td>
<td>Piperidine</td>
<td>89</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>EtOH</td>
<td>Piperidine</td>
<td>93</td>
<td>8</td>
</tr>
<tr>
<td>9</td>
<td>THF</td>
<td>Piperidine</td>
<td>87</td>
<td>9</td>
</tr>
</tbody>
</table>

The structures of compounds were established on the basis of spectral studies. The \(^1\)H NMR of compound **AYC-01 (R=H)** showed a singlet of \(NH\) proton of pyridine ring at 12.93 δ ppm due to deshielding effect of adjacent groups. The proton of amide group was appeared at 10.22 δ ppm. The -CH₃ protons were appeared as singlet at 2.37 δ ppm. Aromatic protons showed at 7.0 to 7.48 δ ppm. The IR signal appeared at 2220 cm\(^{-1}\) and at 1658 at 1629 cm\(^{-1}\) due to presence of cyano and keto group, respectively. The data suggests the formation of pyridone ring system. The present methods may give library of pyridone derivatives with high diversity. The physical properties of newly synthesized compounds are given in **Table I.2**.
Table I.2: Physical properties of pyridones AYC01-17.

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>R</th>
<th>Yield in %</th>
<th>Time in hr</th>
<th>Melting range</th>
</tr>
</thead>
<tbody>
<tr>
<td>AYC-01</td>
<td>H</td>
<td>93</td>
<td>8</td>
<td>170-172</td>
</tr>
<tr>
<td>AYC-02</td>
<td>2-F</td>
<td>92</td>
<td>7</td>
<td>225-227</td>
</tr>
<tr>
<td>AYC-03</td>
<td>2-Br</td>
<td>93</td>
<td>8</td>
<td>211-213</td>
</tr>
<tr>
<td>AYC-04</td>
<td>4-OCH₃</td>
<td>92</td>
<td>8</td>
<td>121-123</td>
</tr>
<tr>
<td>AYC-05</td>
<td>4-N(CH₃)₂</td>
<td>91</td>
<td>7</td>
<td>172-174</td>
</tr>
<tr>
<td>AYC-06</td>
<td>2-OH</td>
<td>92</td>
<td>7</td>
<td>198-200</td>
</tr>
<tr>
<td>AYC-07</td>
<td>2-Cl</td>
<td>93</td>
<td>7</td>
<td>208-210</td>
</tr>
<tr>
<td>AYC-08</td>
<td>4-Cl</td>
<td>91</td>
<td>8</td>
<td>200-202</td>
</tr>
<tr>
<td>AYC-09</td>
<td>4-Br</td>
<td>93</td>
<td>7</td>
<td>228-230</td>
</tr>
<tr>
<td>AYC-10</td>
<td>4-F</td>
<td>89</td>
<td>8</td>
<td>231-233</td>
</tr>
<tr>
<td>AYC-11</td>
<td>3-NO₂</td>
<td>91</td>
<td>8</td>
<td>236-238</td>
</tr>
<tr>
<td>AYC-12</td>
<td>4-OH</td>
<td>92</td>
<td>8</td>
<td>162-164</td>
</tr>
<tr>
<td>AYC-13</td>
<td>4-OH-3-OCH₃</td>
<td>92</td>
<td>7</td>
<td>222-224</td>
</tr>
<tr>
<td>AYC-14</td>
<td>2-NO₂</td>
<td>91</td>
<td>8</td>
<td>200-202</td>
</tr>
<tr>
<td>AYC-15</td>
<td>3-Cl</td>
<td>90</td>
<td>7</td>
<td>198-200</td>
</tr>
<tr>
<td>AYC-16</td>
<td>4-CH₃</td>
<td>93</td>
<td>7</td>
<td>182-184</td>
</tr>
<tr>
<td>AYC-17</td>
<td>Furfural</td>
<td>91</td>
<td>8</td>
<td>225-227</td>
</tr>
</tbody>
</table>
1.3 Antimicrobial Activity

Table I.3. Antimicrobial activity of selected compounds (Zone of inhibition in mm)

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>R</th>
<th>Gram-positive</th>
<th>Gram-negative</th>
<th>Fungi</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>B. subtilis</td>
<td>S. aureus</td>
<td>E. coli</td>
</tr>
<tr>
<td>AYC-01</td>
<td>H</td>
<td>3.00</td>
<td>-</td>
<td>4.00</td>
</tr>
<tr>
<td>AYC-02</td>
<td>2-F</td>
<td>3.25</td>
<td>-</td>
<td>3.00</td>
</tr>
<tr>
<td>AYC-03</td>
<td>2-Br</td>
<td>3.50</td>
<td>4.25</td>
<td>3.75</td>
</tr>
<tr>
<td>AYC-04</td>
<td>4-OCH₃</td>
<td>3.50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>AYC-05</td>
<td>4-N(CH₃)₂</td>
<td>3.25</td>
<td>-</td>
<td>3.50</td>
</tr>
<tr>
<td>AYC-17</td>
<td>2-Cl</td>
<td>-</td>
<td>3.50</td>
<td>3.25</td>
</tr>
</tbody>
</table>

*Concentration 1000 microgram per ml, - = No inhibition
Among the tested compounds, **AYC-03** exhibited potent inhibition against both Gram positive and Gram negative bacteria as well as fungi. However, compounds **AYC-01**, **AYC-02** and **AYC-17** showed moderate inhibition. While few compounds were inactive and did not showed inhibition against microorganisms.
1.4 Conclusion

In summary, we have developed an efficient and simple method for the synthesis of cyano and carboxamide bearing pyridone derivatives using one pot system. The yields were good to excellent of all compounds. Among the synthesized compounds selected compounds were screened against gram positive and gram negative bacteria and fungi and examined zone of inhibition. Out of six compounds AYC-03 has shown inhibition against Gram-positive and Gram-negative bacteria. However, all compounds have shown inhibition at 3 to 3.75 mm against fungi *A. niger*.
1.5 Experimental Section

Melting points were measured in open capillaries and are uncorrected. $^1$HNMR (400 MHz) and $^{13}$CNMR (100 MHz) spectra were recorded in DMSO, and TMS was used as an internal reference on a Bruker AVANCE II spectrometer. Mass spectra were determined using direct inlet probe on a GCMS-Agilent mass spectrometer. IR spectra were recorded on KBr discs, using FTIR-8400 Schimadzu spectrophotometer. Laboratory grade chemicals were purchased from Loba, SRL, Molychem and Himedia are used without purification.

➤ General synthesis of 5-cyano-2-methyl-6-oxo-N-phenyl-4-aryl-1,6-dihydropyridine-3-carboxamide AYC01-17.

To a solution of various aldehydes (5.6 mmol) (1a-q) in ethanol (10 ml) piperidine was added in catalytical amount and stirred for 5 min. at room temperature. Then cyanoacetamide (5.6 mmol) and acetoacetanilide (5.6 mmol) was added and refluxed on boiling water bath at 78°C for appropriate time. The reaction was being monitored by TLC using Hexane: EtOAc (8:2). After completion of the reaction, the reaction was cooled in refrigerator for overnight. Filter the separated product and air dried to obtain the desired products AYC01-17 in high yields.

➤ Spectral data of the synthesized compounds AYC01-17.

5-cyano-2-methyl-6-oxo-N,4-diphenyl-1,6-dihydropyridine-3-carboxamide AYC-01. Cream color solid. Rf: 0.24; IR (KBr): 3331, 3205, 3016, 2220, 2206, 1658, 1629, 1518, 1460, 1437, 1234, 802, 765 cm$^{-1}$; $^1$H NMR (400 MHz; DMSO-d$_6$): δ 2.37 (s, 3H), 7.00 to 7.48 (m, 10H), 10.22 (s, 1H), 12.93 (s, 1H); $^{13}$C NMR (100 MHz; DMSO-d$_6$): 17, 99, 110, 115, 117, 119, 123, 126, 127, 128, 129, 134, 136, 138, 141, 150, 159, 160, 162, 166, 169. ms: m/z 329. Anal. Calcd. for C$_{20}$H$_{15}$N$_3$O$_2$: C, 72.94; H, 4.59; N, 12.76. Found: C, 72.90; H, 4.60; N, 12.69.

5-cyano-4-(2-fluorophenyl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-02. Cream color solid. Rf: 0.23; IR (KBr): 3444, 3304, 3200, 3043, 2224, 1660, 1629, 1579, 1527, 1494, 1465, 1437, 1230, 1163, 898, 633 cm$^{-1}$; $^1$H NMR (400 MHz; DMSO-d$_6$): δ 2.36 (s, 3H), 7.12 to 7.62 (m, 9H), 10.31 (s, 1H), 12.89 (s, 1H); ms: m/z 348.
Anal. Calcd. for C_{20}H_{14}FN_{3}O_{2}: C, 69.16; H, 4.06; N, 12.10. Found: C, 69.11; H, 4.02; N, 12.09.

4-(2-bromophenyl)-5-cyano-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-03. Cream color solid. R_f: 0.23; IR (KBr): 3310, 3205, 3023, 2220, 1668, 1622, 1579, 1525, 1485, 1455, 1417, 1220, 1163, 858, 635 cm\(^{-1}\); \(^1\)H NMR (400 MHz; DMSO-d\(_6\)): \(\delta\) 2.50 (d, 3H, \(J = 1.6\)), 7.00 to 7.61 (m, 9H), 9.86 (s, 1H), 12.85 (s, 1H); ms: m/z 409. Anal. Calcd. for C_{20}H_{14}BrN_{3}O_{2}: C, 58.84; H, 3.46; N, 10.29. Found: C, 58.81; H, 3.42; N, 10.29.

5-cyano-4-(4-methoxyphenyl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-04. Yellow color solid. R_f: 0.24; IR (KBr): 3350, 3210, 3041, 2225, 1662, 1620, 1568, 1527, 1485, 1455, 1427, 1250, 1157, 850, 755 cm\(^{-1}\); \(^1\)H NMR (400 MHz; DMSO-d\(_6\)): \(\delta\) 2.35 (s, 3H), 3.74 (s, 3H), 6.97 to 7.44 (m, 9H), 10.34 (s, 1H), 12.87 (s, 1H); ms: m/z 359. Anal. Calcd. for C_{21}H_{17}N_{3}O_{3}: C, 70.18; H, 4.77; N, 11.69. Found: C, 70.15; H, 4.75; N, 11.69.

5-cyano-4-(4-(dimethylamino)phenyl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-05. Reddish brown color solid. R_f: 0.21; IR (KBr): 3485, 3321, 3248, 3097, 2216, 1672, 1610, 1577, 1531, 1488, 1445, 1396, 1224, 1151, 839, 621 cm\(^{-1}\); \(^1\)H NMR (400 MHz; DMSO-d\(_6\)): \(\delta\) 2.51 (s, 3H), 3.05 (s, 6H), 6.80 to 8.01 (m, 9H), 10.32 (s, 1H), 13.23 (s, 1H); \(^13\)C NMR (100 MHz; DMSO-d\(_6\)): 20, 97, 108, 111(d), 113, 118 (d), 119, 128, 129, 132, 142, 150 (d), 152, 160, 163. ms: m/z 372. Anal. Calcd. for C_{22}H_{20}N_{4}O_{2}: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.92; H, 5.42; N, 15.01.

5-cyano-4-(2-hydroxyphenyl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-06. Yellow color solid. R_f: 0.24; IR (KBr): 3296, 3190, 3122, 2218, 1664, 1647, 1552, 1533, 1475, 1458, 1346, 1290, 1149, 852, 761 cm\(^{-1}\); \(^1\)H NMR (400 MHz; DMSO-d\(_6\)): \(\delta\) 2.36 (s, 3H), 6.74 to 7.81 (m, 9H), 10.22 (s, 1H), 10.36 (s, 1H), 13.21 (s, 1H). ms: m/z 345. Anal. Calcd. for C_{20}H_{15}N_{3}O_{3}: C, 69.56; H, 4.38; N, 12.17. Found: C, 69.52; H, 4.36; N, 12.15.

4-(2-chlorophenyl)-5-cyano-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-07. Yellow color solid. R_f: 0.23; IR (KBr): 3396, 3290, 3022, 2223, 1675, 1651, 1542, 1531, 1465, 1455, 1341, 1280, 1150, 851, 765 cm\(^{-1}\); \(^1\)H NMR (400 MHz;
DMSO-d$_6$): \( \delta 2.35 \) (s, 3H), 7.01 to 7.86 (m, 9H), 10.31 (s, 1H), 12.82 (s, 1H). ms: m/z 369. Anal. Calcd. for C$_{20}$H$_{14}$ClN$_3$O$_2$: C, 66.03; H, 3.88; N, 11.55. Found: C, 66.05; H, 3.86; N, 11.52.

4-(4-chlorophenyl)-5-cyano-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-08. Cream color solid. R$_f$: 0.23; IR (KBr): 3396, 3290, 3222, 2220, 1674, 1652, 1541, 1530, 1465, 1455, 1341, 1285, 1149, 852, cm$^{-1}$; $^1$H NMR (400 MHz; DMSO-d$_6$): \( \delta 2.34 \) (s, 3H), 7.00 to 7.86 (m, 9H), 10.33 (s, 1H), 12.85 (s, 1H). ms: m/z 369. Anal. Calcd. for C$_{20}$H$_{14}$ClN$_3$O$_2$: C, 66.03; H, 3.88; N, 11.55. Found: C, 66.05; H, 3.86; N, 11.52.

4-(4-bromophenyl)-5-cyano-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-09. Cream color solid. R$_f$: 0.24; IR (KBr): 3315, 3204, 3021, 2221, 1675, 1625, 1580, 1521, 1484, 1451, 1415, 1222, 1161, 859, 735 cm$^{-1}$; $^1$H NMR (400 MHz; DMSO-d$_6$): \( \delta 2.36 \) (d, 3H), 7.02 to 7.67 (m, 9H), 9.92 (s, 1H), 12.89 (s, 1H); ms: m/z 409. Anal. Calcd. for C$_{20}$H$_{14}$BrN$_3$O$_2$: C, 58.84; H, 3.46; N, 10.29. Found: C, 58.82; H, 3.43; N, 10.27.

5-cyano-4-(4-fluorophenyl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-10. Orange color solid. R$_f$: 0.23; IR (KBr): 3445, 3314, 3201, 3041, 2220, 1671, 1619, 1575, 1517, 1495, 1461, 1417, 1231, 1165, 878, 653 cm$^{-1}$; $^1$H NMR (400 MHz; DMSO-d$_6$): \( \delta 2.38 \) (s, 3H), 7.11 to 7.62 (m, 9H), 10.32 (s, 1H), 12.85 (s, 1H); ms: m/z 348. Anal. Calcd. for C$_{20}$H$_{14}$FN$_3$O$_2$: C, 69.16; H, 4.06; N, 12.10. Found: C, 69.15; H, 4.04; N, 12.08.

5-cyano-2-methyl-4-(3-nitrophenyl)-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-11. Yellow color solid. R$_f$: 0.21; IR (KBr): 3444, 3210, 3044, 2218, 1675, 1575, 1521, 1484, 1427, 1250, 1165, 878, 633 cm$^{-1}$; $^1$H NMR (400 MHz; DMSO-d$_6$): \( \delta 2.36 \) (s, 3H), 7.12 to 8.02 (m, 9H), 10.36 (s, 1H), 13.12 (s, 1H); ms: m/z 374. Anal. Calcd. for C$_{20}$H$_{14}$N$_4$O$_4$: C, 64.17; H, 3.77; N, 14.97. Found: C, 64.15; H, 3.75; N, 14.98.

5-cyano-4-(4-hydroxyphenyl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-12. Reddish color solid. R$_f$: 0.24; IR (KBr): 3454, 3310, 3244, 3014, 2215, 1678, 1550, 1511, 1450, 1417, 1210, 1145, 875 cm$^{-1}$; $^1$H NMR (400 MHz; DMSO-d$_6$): \( \delta 2.35 \) (s, 3H), 6.65 to 7.61 (m, 9H), 10.23 (s, 1H), 10.35 (S, 1H), 12.89 (s, 1H). ms: m/z 345.
5-cyano-4-(4-hydroxy-3-methoxyphenyl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-13. Yellow color solid. Rf; IR (KBr): 3450, 3350, 3204, 3016, 2225, 1658, 1551, 1510, 1451, 1210, 1155, 865 cm⁻¹; 0.22. ¹H NMR (400 MHz; DMSO-d₆): δ 2.34 (s, 3H), 3.81 (s, 3H), 6.71 to 7.75 (m, 8H), 9.81 (s, 1H), 10.32 (s, 1H), 12.87 (s, 1H). ms: m/z 376. Anal. Calcd. for C₂₁H₁₇N₃O₄: C, 67.19; H, 4.56; N, 11.19. Found: C, 67.15; H, 4.55; N, 11.17.

5-cyano-2-methyl-4-(2-nitrophenyl)-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-14. Reddish color solid. Rf: 0.21; IR (KBr): 3345, 3212, 3042, 2219, 1678, 1585, 1520, 1485, 1430, 1255, 1161, 898, 733 cm⁻¹; ¹H NMR (400 MHz; DMSO-d₆): δ 2.33 (s, 3H), 7.11 to 8.02 (m, 9H), 10.35 (s, 1H), 13.11 (s, 1H); ms: m/z 374. Anal. Calcd. for C₂₀H₁₄N₄O₄: C, 64.17; H, 3.77; N, 14.97. Found: C, 64.14; H, 3.77; N, 14.96.

4-(3-chlorophenyl)-5-cyano-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-15. Cream color solid. Rf: 0.24; IR (KBr): 3380, 3280, 3021, 2221, 1665, 1650, 1541, 1531, 1464, 1451, 1345, 1278, 1150, 850, 768 cm⁻¹; ¹H NMR (400 MHz; DMSO-d₆): δ 2.34 (s, 3H), 7.01 to 7.82 (m, 9H), 10.32 (s, 1H), 12.89 (s, 1H). ms: m/z 369. Anal. Calcd. for C₂₀H₁₄ClN₃O₂: C, 66.03; H, 3.88; N, 11.55. Found: C, 66.01; H, 3.85; N, 11.53.

5-cyano-2-methyl-6-oxo-N-phenyl-4-(p-tolyl)-1,6-dihydropyridine-3-carboxamide AYC-16. Cream color solid. Rf: 0.26; IR (KBr): 3326, 3280, 3022, 2984, 2221, 1675, 1651, 1540, 1535, 1460, 1455, 1341, 1288, 1167, 855, 768 cm⁻¹; ¹H NMR (400 MHz; DMSO-d₆): δ 2.34 (s, 3H), 2.32 (s, 3H), 7.02 to 7.72 (m, 9H), 10.23 (s, 1H), 12.85 (s, 1H). ms: m/z 343. Anal. Calcd. for C₂₁H₁₇N₃O₂: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.44; H, 4.95; N, 12.23.

5-cyano-4-(furan-2-yl)-2-methyl-6-oxo-N-phenyl-1,6-dihydropyridine-3-carboxamide AYC-17. Reddish brown color solid. Rf: 0.24; IR (KBr): 3346, 3210, 2221, 1675, 1650, 1542, 1521, 1465, 1551, 1341, 1280, 1250, 851, 765 cm⁻¹; ¹H NMR (400 MHz; DMSO-d₆): δ 2.35 (s, 3H), 6.91 to 8.12 (m, 8H), 10.32 (s, 1H), 12.91 (s, 1H). ms: m/z 319. Anal. Calcd. for C₁₈H₁₃N₃O₃: C, 67.71; H, 4.10; N, 13.16. Found: C, 67.70; H, 4.05; N, 13.13.
\(^1\)H NMR spectrum of compound AYC-01

Expanded \(^1\)H NMR spectrum of compound AYC-01
\[ \text{\textsuperscript{13}C NMR spectrum of compound AYC-01} \]

\[ \text{\textsuperscript{1}H NMR spectrum of compound AYC-05} \]
Expanded $^1$H NMR spectrum of compound AYC-05

$^{13}$C NMR spectrum of compound AYC-05
**1H NMR spectrum of compound AYC-04**

![1H NMR spectrum of compound AYC-04](image-url)
Expanded $^1$H NMR spectrum of compound AYC-04
According to the provided images, the document contains sections on NMR spectroscopy of compound AYC-03. The images depict two spectra: the standard and an expanded view of the proton nuclear magnetic resonance (1H NMR) spectrum of compound AYC-03. The expanded view highlights specific regions of the spectrum, providing a detailed analysis of the chemical shifts and peak assignments. The compound's molecular structure is also shown, aiding in the interpretation of the NMR data.
Mass spectrum of compound AYC-01

Mass spectrum of compound AYC-02
Mass spectrum of compound AYC-03

Mass spectrum of compound AYC-04
IR spectrum of compound AYC-01

IR spectrum of compound AYC-02
IR spectrum of compound AYC-05

IR spectrum of compound AYC-06
1.6 References


91. Kumar, H.; Parmar, A. Ultrasonics Sonochem., 2007, 15, 129.