Chapter - II

Synthesis & Characterization of synthesized molecules
Part - I

Synthesis of
Organic Molecules
Studies on (t)α-Amino Nitrile Derivatives
2.1.1a Introduction:

Nearly a century followed, before the volume of research in nitrile chemistry reached sizable proportions. It is true that many significant contributions to this field were made during this interval, but investigators were probably understandably reluctant to devote major efforts to such researches because of the hazards of toxicity, unavailability, and high price of inorganic cyanides. The problem was solved in the first half of the century. Of the score or more that have become commercially available in the last few years, one might cite acrylonitrile (plastic, synthetic rubber, synthetic fiber), phthalonitrile (dyestuffs), adiponitrile (synthetic fiber), acetone cyanohydrine (plastics), or trichloroacetonitrile (fumigant) as examples of compounds. They have found numerous applications in the fields of synthetic resins, war gases, and insecticides, specialty solvents and especially as intermediates for chemicals synthesis of pharmaceuticals, dyestuffs, vitamins and plastics.

Nitriles do not occur in high concentration in nature but their presence has been detected in minor amounts in a large numbers of plants. They are most commonly present as various glycosides and mandelonitriles. Amygdalin, which is hydrolyzed to gentiobiose and mandelonitrile, is probably best known example of this type. Rosenthaler states that lesser amounts are found in stem, roots, flowers, leaves, fruits and seeds of forty one cyanogenetic plant families. The biochemical formation of cyanophoric glycosides may be partially explained by Parrod's demonstration that certain reducing sugars like d-fructose, d-glucose, d-mannose, d-arabinose, etc, and their several proximate derivatives (e.g. glyoxilic, tartronic, mesoxalic, etc,) can be oxidised in the presence of Cu salts and ammonia at atmospheric temperature to urea and hydrogen cyanide.

Phenyl acetonitrile and β-phenylpropionitrile have been isolated from essential oils. While, acetonitrile has been isolated from coal tar and gas tar. Propionitrile, butyronitrile, valeronitrile and some higher homologs have been identified as components of bone oil.
Because of the low concentration involved, the extraction of nitriles from natural sources does not constitute a convenient method of preparation. On the other hand, nitriles liberate amino acids on hydrolysis and hence are more important synthetically. 9

2.1.1b Synthetic aspects:

Different methods for the preparation of nitriles are as follows:

1. By action of hydrocyanic acid on aldehyde and ammonia.
2. By condensation of cyanohydrine and amine.
3. By addition of hydrocyanic acid on aldemines and ketemines.

The first synthesis of nitriles was reported by Wolher and Leibig, 10 who prepared benzyl cyanide and benzonitrile in 1832 and by Peloue 11 who obtained propionitrile in 1834.

\[
\text{H}_3\text{C} = \text{CHO} + \text{NH}_3 \rightarrow \text{H}_3\text{C} - \text{CH}_2\text{NH}_2 \rightarrow \text{H}_3\text{C} - \text{CH}_2\text{CN} \]

In 1875, Erlenmeyer 12 showed the intermediate compound in Strecker synthesis of alanine to be (±)-α-amino nitrile. It was further demonstrated that iminodinitrile is formed by loss of ammonia from two molecules of (±)-α-amino nitriles. 13

Zelinski and Stadnikov 14 used alkali cyanide and ammonium chloride for the preparation of (±)-α-amino nitriles. Tiemann 15 reversed Stacker's order of addition of reagents and obtained better yields. He extended reaction to ketones and primary and secondary amines.
Knoevenagel and Mechlin \(^{16}\) prepared (±)-α-amino nitriles from (±)-mandelonitrile and aromatic as well as primary and secondary aliphatic amines. They modified the method of synthesis, which involved the addition of KCN and amine on bisulphite compound of aldehyde or ketone. Bucherer \(^{17}\) also proposed the same method.

Several advantages have been proposed for this method. Hazardous HCN fumes are avoided. The reaction medium is always alkaline and benzoin formation in case of aldehyde is minimized. The reaction cannot be applied to ketones which do not give bisulphite addition product. It has been demonstrated that aldemines and ketemines will add HCN to give (±)-α-amino nitriles.\(^{18-19}\)

The (±)-α-amino nitriles have been formed by the following reaction sequence, though with admittedly ambiguous evidences by Sannie. \(^{20}\)

Lapworth \(^{21}\) studied the reaction mechanism of cyanohydrine formation in 1907. He showed the nucleophilic cyanide ion attacked the point of lowest electron density, which was carbonyl carbon atom wherein the intermediate
so formed, absorbed the proton from the solution. It was shown that the rate of reaction was proportional to the concentration of cyanide ion and alkali cyanides and the ammonium cyanides are active catalysts. The original views of Erlenmeyer that aldehyde ammonia are the active intermediates have been supported by Cocker et al. The synthesis of (±)-α-amino nitriles by Sandhu from schiffs base also supports these views. The aldehyde ammonia has a labile -OH group, which is replaced by cyanide ion.

Stewart and Li studied kinetics and mechanism of (±)-α-amino nitrile formation and observation that when a cyanohydrine is placed in an alkaline medium, such as a solution of an amine, the rapid appearance of cyanide ion demonstrates an apparent high activity of carbon-cyanide bond in the cyanohydrine. They suggested that carbonyl compound thus formed reacts with either hydrogen cyanide or a molecule of cyanohydrine as shown below:

\[
\begin{align*}
    \text{R}_2\text{OH} & \quad \text{R}_1\text{NH}_2, \\
    \text{CN} & \quad \text{CN} \\
    \text{OH} & \quad \text{CN} \\
    \text{NR}_2 & \quad \text{CN} \\
\end{align*}
\]

Sch-VI

Albers et al. have studied the same reaction. The mechanism of formation of (±)-α-amino nitriles prepared from bisulphite compound was put forward by Stewart and Li which is as under:

\[
\begin{align*}
    \text{R}_2\text{O} & \quad \text{H}_2\text{SO}_3 \\
    \text{CN} & \quad \text{CN} \\
\end{align*}
\]

Sch-VII
It is proved that the reaction of the formation of cyanohydrine is catalyzed by alkali. It is also claimed that cyano compound formation of aryl-amino type also has a marked increase in the yield in basic or slightly basic pH.


2.1.1c Biological aspects:

This method is usually helpful for the ketones, which do not give cyanohydrine or do not react with KCN, amine and glacial acetic acid. $(\pm)$-$\alpha$-Amino nitrile of benzophenone has been obtained by this method.

Various solvents have been suggested in the preparation of $(\pm)$-$\alpha$-amino nitriles. Knoevenagel used ethanol as solvent. Glacial acetic acid and methanol have been also used as solvent. Over and above these applications, organic $(\pm)$-$\alpha$-amino nitriles have been found to be useful drug potentials.

Klosa synthesized some compounds of the general formula (I) and found those as central nervous system stimulants.

He further described that these compounds had low toxicity and long lasting stimulant activity especially when compared with amphetamine.
lorio et al. \(^{28}\) prepared more than twenty compounds and tested their pharmacological properties. Some of the compounds showed moderate hypotensive action and some showed hypertensive effect, while some of them possessed an acetylcholine-like, nicotine-like curare-like action. Lands et al. \(^{29}\) found basic nitrile of the type \(R-CH-(Ph)-Ph-CN\) \((\text{where } R=CH_3-N-CH-, \text{Et-N-CH-CH etc})\) and their hydrochlorides \((\text{where } R=\text{different alkyl or heterocyclic group})\) to have weak antispasmodic activity and were not very toxic. While some of the corresponding methiodides showed significant anticholinergic activity and had a strong antispasmodic action on intestine stimulant with acetylcholine or barium chloride. Finally he came to conclusion that the nitrile group appears to be important for anticholinergic action. Nitriles have also been used in cancer therapy. \((\pm)-\alpha\)-Amino nitriles have been found to be very active glycine inhibitor in Ehrlich ascite tumor cells. \(^{30}\) Bockmuhl and Ehrhart \(^{31}\) have reported \((\pm)-\alpha\)-amino nitriles with analgesic and antipyretic action. They also pointed out that optical resolution gave a further increase in activity.

Some other workers have also prepared \((\pm)-\alpha\)-amino nitriles and resolved but they have not reported any activity. Undavia et al. \(^{32}\) used acetophenone, KCN and different aryl amines to get \((\pm)-\alpha\)-amino nitriles and resolved them having a p-carboxy group through brucine salts. Thaker et al. \(^{33}\) prepared and resolved \((\pm)-\alpha\)-amino nitriles from different aldehydes, KCN and glacial acetic acid. They also prepared and resolved N-aryl-D-glucoheptose amino nitriles using glucose as aldehyde component and different amines. \(^{34}\)

\((\pm)-\alpha\)-Amino nitriles are widely used as insecticides. \(^{35}\) Highly stable noncorrosive herbicidal composition contains active ingredient malanonirile and its derivatives. Nitriles of \(\alpha,\alpha\)-dialkyl aliphatic acids are used as agriculture insecticides and are effective in combination with other fungicides and insecticides \(^{36}\) (thyroid gland has detoxication effect for acetonitriles but it seems that it is not a properly, peculiar to that tissue or its secretion). \(^{37}\) Barnsley and Yates \(^{38}\) proposed nitriles as herbicides wherein alkyl nitriles containing 10–15 carbon atoms, which are found to promote the growth of stem sections from red light exposed seedling of dwarf peas at very low concentration. \(^{39}\)
Chapter II Synthesis and Characterization of Synthesized Molecules: Studies on (±)-α-amino nitrile derivatives

Dave and Thaker have prepared several 1-(aryloxyacetyl)-2-(α cyanobenzyl) hydrazide and screened for antibacterial activity. Cowper and Thaker prepared α-hydrazononitriles from isonicotinic acid hydrazide and different aldehydes. Antibacterial testing of these compounds showed good activity.

In 1850 Streker treated aldehyde ammonia and hydrogen cyanide, hydrolyzed the product to obtain alanine. This has proved to be extremely useful to synthetic organic chemists.

Tiemann was first to demonstrate that the hydrogen cyanide adds to the carbon-nitrogen bond of aldemines or ketemines, although under aqueous alcoholic conditions, it was questionable whether the aldemines or aldehyde ammonia was the actual reagent. Subsequently, the reaction was carried out under anhydrous conditions, which precluded intermediates of the latter type.

A number of ketemines have been shown to behave similarly.

Similar addition has been effected with other derivatives of aldehydes and ketones such as hydrazones, semicarbazones and schiff’s bases.

Methylene amino acetonitriles have been quantitatively converted into amino diacetonitriles, if a catalytic amount of hydrogen chloride is present.

\[(\text{CH}_2\text{N}=\text{CH}_2\text{CN}) + \text{HCN} \rightarrow \text{NH}-(\text{CH}_2\text{CN})_2\]

In the earlier method imines when allowed to react with HCN produced in situ by equimolar amount of KCN and concentrated HCl, are converted into nitriles via cyanohydrine. However, according to Sandhu et al. use of HCl produced large amount of green resinous material and this could be avoided if glacial acetic acid is used in place of hydrochloric acid.

The cyanide group is always directed to the carbon atom of carbon nitrogen double bond because of the strongly nucleophilic character of the nitrogen atom. This is explained as under:
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Adickes 47 reported that use of aqueous hydrocyanic acid and trace of pyridine produces slightly better results.

During last forty years, the fact has somewhat surprisingly emerged that certain nitrile substances, previously known as carcinogens, are inhibitors of tumor growth 48. However, this has so far not demonstrated any simple and well-defined chain between the existence of such compounds and the incidence of cancer as a human disease. Carcinogenic activity has been observed in azobenzene, and butter yellow (4-4'-dimethyl azobenzene, one time used as a food color) was one of the earliest known carcinogens to be observed. 49

Fieser 50 showed that numerous condensed aromatic hydrocarbons and some of their simple derivatives are found to be carcinogenic. Moreover, Valdecasas et al. 51 have tested some aliphatic cyano compounds and found that the compounds having structure (NC-CH2-CO-NH-NH2) are highly effective against experimental and clinical tuberculosis.

A large number of aliphatic, aromatic and heterocyclic hydrazides, their derivatives and related compounds have been tested for various pharmacological activities like antitubercular, antibacterial, antiseptic, etc.

The introduction of hydroxyl group in aromatic ring causes a great increase in the toxicity together with strong antiseptic property for which phenol is a well-known compound, possessing a high phenolic co-efficient and favorable therapeutic index. On the other hand, depending upon the electrochemical nature, halogen exerts a pronounced influence on the
biological behavior of organic compounds. Halogen usually increases both useful and toxic properties of the parent active compound. The increase in toxicity is often negligible. 52

In case of benzoic acid, the introduction of hydroxyl group is again accompanied by an increase in physiological activity. Salicylic acid has marked antiseptic properties with specific action in rheumatism. 52 3,5–Dibromo salicylic acid hydrazide possesses tubercular activity. 53 Methyl salicylate and its derivatives possess antitubercular, hypoglycemic, antihistaminic like pharmacological activities. 54 Amide derivatives 55 of salicylic acid i.e. 2-hydroxybenzamide is used as an analgesic and antipyretic. One of the well known commercially used drugs aspirin 56 (salicylic acid acetate) possesses analgesic activity. 2,5-Dichloro -4-nitro salicylanilide known as "Niclosamide" is currently used as an anthelmintic. 57

The nitriles are the derivatives of hydrocyanic acid, in which substituting group is attached to the carbon and have the general formula R–C≡N. They can be hydrolyzed to carboxylic acid. The simple members are named not as derivatives of hydrocyanic acid but as derivatives (nitriles) of the acids, which they yield on hydrolysis. Accordingly, CH3CN for example, can be called methyl cyanide but is more frequently called acetonitrile. The prefix cyano is used in naming polyfunctional compounds.

Polochi 58 in 1880 showed that hydrocyanic acid can be added to =C=N– bond of benzylidine aniline and benzylideneidineine. Delepine 59 carried out addition reaction of hydrocyanic acid with numerous alkylidine amines. He observed that methyleneamino acetonitrile (I) did not undergo the addition reaction. Bailey and Synder 60 prepared iminoacetonitrile (II) from (I) using hydrogen cyanide. Later Bailey and Lochte 61 found that reaction could take place only in the presence of hydrochloric acid in quantitative yield.

No addition reaction  \[ \text{CH}_2=\text{N}-\text{CH}_2\text{CN} \quad \rightarrow \quad \text{NH}-(\text{CH}_2\text{CN})_2 \]

Klages 62 had described the preparation of cyanohydrine and its conversion into amino nitriles in 1902. Mange 63 found it unsatisfactory and put forward a new technique of preparation of (±)-α-amino nitriles. He found that Ultee's method 64 of preparation of cyanohydrine gave excellent
results. The product is stabilized by acidification. Low temperature favours high conversion. The cyanohydrines are converted into corresponding amino nitriles using liquid ammonia in place of alcoholic or aqueous ammonia. After a long period and number of experiments, it was found that formation of nitrile takes place after cyanohydrine formation, though cyanohydrine had not been isolated.

Various cyano compounds have been prepared of biological interest. A series of 2-cyano-acetanilides are active against experimental tuberculosis infection in mice. The two most potent compounds are about 8 times as active as p-aminosalicylic acid and about half as active as streptomycin. It is also proved that cyano group is essential for activity. Moreover, some (±)-α-amino nitriles possess herbicidal activity as well as bactericidal activity.

Ueno, Kasunori et al. prepared (±)-α-aminonitriles with a view to get better pharmaceutical activity.

The compound (II) has been tested for both gram positive and gram negative bacteria.

\[
\text{(II)}
\]

Yarovenko et al. have given new synthesis of nitriles enriched with \(^{15}\)N isotope in 1994.

Xiang et al. studied exploratory experiment on thermal reaction of (±)-α-amino nitriles.

O'Callaghan, Conor N. et al. synthesized α-imino-4-methyl-2H-1-benzopyran-3-carbonitriles of the following type.

\[
\text{(III)} \quad \text{(IV)} \quad \text{(V)}
\]
All compounds were tested for both gram positive and gram negative bacteria.

Nekvasov et al. 72 have done reaction of 5-aryl-2,3-furan diones with some N and C substituted aminonitriles with a view to get better results.

Khalafallah et al. 73 synthesized some cyano compounds having antibacterial activity.

\[
\text{(VII)}
\]

Higashiji et al. 74 have given the process of producing 2-cyano-4-oxo 4(H) benzopyran compounds (VII). Compounds also show promising activity against both gram positive and gram negative bacteria.

\[
\text{(VII)}
\]

Evan Phillip et al. 75 synthesized N-aryl-2-cyano-3-hydroxy propenamide derivatives (VIII). The compounds have been found to be useful as antiinflammatory and antidiabetic agents. The compounds also demonstrated 13% inhibition of carrageenan induced rat-paw edema at 50 mg/Kg.
Taking into consideration biological importance of (±)-α-amino nitriles and proven utility of m-phenoxy benzaldehyde we have undertaken the present synthetic work having this moieties. m-Phenoxy benzaldehyde, KCN and amines to get corresponding (±)-α-amino nitriles. The present work is aimed at the biological evaluation among newly synthesized (±)-α-amino nitriles.

2.1.1d Present work:

The literature survey amply exhibits usefulness of (±)-α-amino nitriles with different structural features. To explore new therapeutic agents we have reported here preparation and activity of some newly synthesized (±)-α-amino nitriles.

m-Phenoxy benzaldehyde was converted into hydroxy-(3-phenoxy-phenyl)-acetonitrile. This acetonitrile was condensed with different aromatic amines leading to formation of (±)-α-amino nitriles. IR & NMR spectra and elemental analysis supported the constitution of the product. The products were tested for antibacterial, antifungal and insecticidal activity.
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2.1.1e Experimental:

Preparation of (3-phenoxy-phenyl)-phenylamino-acetonitrile.

Potassium cyanide (1.30 gm, 0.02 mole) was dissolved in water (4ml) and cooled below 5°C. To this was added freshly distilled m-phenoxy-benzaldehyde (3.96gm, 0.02 mole) in ethanol (25ml, 95 %). The mixture was stirred maintaining temperature below 5°C. To this was added glacial acetic acid (1.20 gm, 0.02mole) with constant stirring below 5°C to obtained hydroxy-(3-phenoxy-phenyl)-acetonitrile (II) in situ.

Freshly distilled aniline (0.02 moles 1.86 gm) in 10ml 95% alcohol and 5 ml of acetic acid cooled below 5°C was added with continuos stirring in well ventilated hood to above hydroxy- (3-phenoxy-phenyl)-acetonitrile. Temperature was maintained 15°C during addition. The reaction mixture was stirred for further 2 hours, and was kept at room temperature (25°C) for 24 hrs, to obtain (3-phenoxy-phenyl)-phenylamino-acetonitrile (III)

Long needles were made cyanide and amine free by washing with sufficient diluted hydrochloric acid (0.2M). The compounds are recrystallised with 95% alcohol.

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<tr>
<td>Melting Point</td>
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All the other (±)-α-amino nitriles were prepared by the same procedure and listed in table no. 2.2.1-A
Studies on (±)-α-amino nitrile derivatives

Reaction:

3-phenoxybenzaldehyde

\[ \text{CH}_3\text{COOH} \xrightarrow{\text{KCN}} \]

below 5 °C

3-phenoxyphenyl)acetonitrile

Aromatic Amine in Alcohol & Acid

Stir at 15° C for 2 Hrs & at RT for 24 hrs.

Aryl anilino(3-phenoxyphenyl)acetonitrile

Where Ar = phenyl, o/m/p-chloro phenyl, o/m/p-tolyl, p-fluoro phenyl, p-bromo phenyl, p-isopropyl phenyl, p-carboxy phenyl, p-carbethoxy phenyl, o-methoxy phenyl, p-ethoxy phenyl, 3-chloro-4-fluoro phenyl
Chapter II Synthesis and Characterization of Synthesized Molecules:

Studies on (±)-α-amino nitrile derivatives

Reference:

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68 Ueno Kasunori, JPN. Kokai Tokkyo Koho JP. 07, 126, 249, ; Chem. abstr. 123, 19986146, (1995)
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"A Study of Synthesis & Antimicrobial Study of Some Organic Molecules"

Studies on $(\beta)$ α-Amino Amide Derivatives
2.1.2 Studies on (+)-α-amino amide derivatives:

2.1.2a Introduction:

The structure of amides, acid chlorides, anhydrides, esters are closely related to the carboxylic acid and to each other and are a number of chemical families known as functional derivatives of carboxylic acid. They all contain the acyl group.

Amides are the compounds in which the -OH of the carboxylic acid has been replaced by -NH₂. These are sometimes prepared by heating with the ammonium salts of carboxylic acids, water being driven off by distillation.

\[
R\text{-COOH} + NH_3 \rightarrow RCOO\text{-NH}_4^+ \xrightarrow{\Delta} RCONH_2 + H_2O
\]

In the laboratory amides are more likely to be prepared by reaction of ammonia with acid chlorides.²

\[
R\text{-COOH} \rightarrow RCOCl \rightarrow RCONH_2
\]

The presence of the C=O group makes the acid derivatives polar compounds. Generally amides show quite high boiling points because they are capable of strong intermolecular hydrogen bonding.³

Moreover amides can also be prepared by partial mild hydrolysis of nitriles⁴ to produce amides. Further hydrolysis produces carboxylic acid.
Amides and nitriles, since they are less reactive than the other acid derivatives, require more vigorous conditions for basic hydrolysis. These derivatives are boiled for prolonged periods in order to effect complete hydrolysis to the salt and ammonia or to the amines. Acid conditions are more often used to hydrolyze the nitriles or acid derivatives.

M.A. Metwally, E.M. Keshak, et al.\(^5\) had synthesized various 2-cyano-2-(5-oxo-3-phenyl-thiazolidin-2-yldene)-acetamides.

2.1.2b Synthetic aspects:

There are various methods\(^5-17\) and reagents are available for synthesis of amides from nitriles but among them sulphuric acid is the suitable reagent for partial oxidation of nitriles. Other methods are as follows:

Nitrile is heated at 100°C for long period in dioxin with N,N-di methyl hydroxyl amine to get amide.

Nitriles is kept in microwave oven or at room temperature to 50°C with sodium hydroxide and PEG 400 in water to get convert nitrile into amide.
Nitrile 12 is stirred at room temperature or high temperature with 2N KOH in methanol or ethanol or t-BuOH to get amide.

When Nitrile 6 hydrogen peroxide and potassium hydroxide warmed to 45°C with stirring, source of heat is removed as the reaction is exothermic and evolution of oxygen is found, soon amide begins to separate out after completion of reaction temperature will fall. Mixture is cooled at 3 to 5°C for 2–3 hours crystals are filtered and recrystallized form 95% alcohol.

Amides 7 can also be obtained from nitrile by heating it with methanolic HCl, HBr or HNO₃ with formic acid.

Liang Xu, Mark L. Trudell 14 had synthesized labelled N-(4-hydroxy-[14C (U)] phenyl)-2-[2,3-dihydro-3-oxo-1,2-benzisothiazol-2-yl]-1,1-dioxide] acetamide derivatives.

2.1.2c Biological aspects:

It was noticed that many of antimicrobial agents are having structural features of amide or amide like chemicals groups like 18 amidines (R–CONR₂) e.g. acetophenetidine, hydantoins, benzchloropropamide etc., amines and imides (ArCONH(CH₂)ₙNR₂) e.g. procainamide etc. (ArNHCO(CH₂)ₙNR₂) e.g. lidocain etc. heterocyclic–CONR₂ e.g. nikethamide, lysergic acid diethylamide, purines, sulfonamides, ureides, semicarbazides, cyclic peptides (ACTH, Insuline, oxytocin), cyclic imides (polymyxin, barbiturates, milontin), polyfunctional amides (chloramphenicol, tetracycline, colchicine).

Germicidal properties of the substituted salicyanilides have been studied widely halogenated salicyanilides, substituted on both sides show maximum activity. Compounds are active against gram positive bacteria. They were used for household detergent, toilet soap, laundry softeners and cosmetic salicyanilide, the parent compound, is used in the treatment of tinea capitis.
Chapter II Synthesis and Characterization of Synthesized Molecules:

Studies on (+)-α-amino amide derivatives

Pyrazinamid and nocratimide \(^{20}\) were highly active against *M. lapraemurium* in the mouse even when treatment was delayed, however, pyrazinamide \(^{21}\) was inactive at 0.5% in the diet against *M. leprae* in mice. Its N-morpholinomethyl derivative was somewhat active in a small human trial. Although thalidomide \(^{22}\) had no antimycobacterial action in vitro, it exerted an immunosuppressive effect on experimental tuberculosis in guinea pigs in the treatment of human *Lepromatous leprosy*, thalidomide was rapidly effective in suppressing severe lepra reactions.

![Thalidomide structure](image)

Shiraishi Tadayoshi et al. \(^{23}\) had carried out antibacterial activity of cyano acrylamide of m-phenoxy benzaldehyde derivative (V) against *Bacillus subtilis* at 10\(\mu\)m. Compound also shows 65% inhibition of tyrosine kinase at 100\(\mu\)m.

![Cyano acrylamide structure](image)

Hankovsky Olga H et al. \(^{24}\) had synthesized amide base new antiarrhythmic agent. The compounds show better chemotherapeutic index than quinidine.
Shida Takafumi et al. \(^{25}\) had prepared 1,2,4 triazole-3-carboxamide derivatives (VIII). The derivatives are useful as herbicides. The compounds show 91 to 100% killing capacity of *Ameranthus retroflexus, Brassica juncea, chicken weed* etc., without harming to wheat or corn at 500gm/acre as an aq.spray.

\[
\text{2-[5-(3-phenoxyphenyl)-1-phenyl-1H,2,4-triazol-3-yl]acetamide} \quad (\text{VIII})
\]

Sieverding Ewald et al. \(^{26}\) had synthesized N-(1-cyano 1,2 di methyl propyl-)2-(-2,4-dichloro-phenoxy)-propionamide (IX) and related phenoxy amide derivatives as melanin bio synthesis inhibitor (MBI) and especially useful for controlling pyricularia oryzae in rice the causal agent of the rice blast disease. Effective amounts of compound show fungicidal activity synergistically.

\[
\text{N-(1-Cyano 1,2 di methyl propyl)-2-(2,4 dichloro-phenoxy) propionamide} \quad (\text{IX})
\]
Shida, Takafumi et al. synthesized new amides and tested as herbicides against *Ameranthus retroflexus*, *Brassica juncea*, *Chickweed* etc. with no harm to Wheat or Corn at 500gm/10 acre as an aq. spray.

\[
\text{N-hydroxy-N-[1-methyl-3-(3-phenoxyphenyl)prop-2-yn-1-yl]acetamide}
\]

(\( \text{X} \))

Ziegler Hugo et al. had synthesized the compound (IX) which was used as agrochemical fungicide.

\[
\text{4-[5-(3,4-Dimethoxy-phenyl)-3-(4-trifluoromethyl-phenyl)-penta-2,4-dienyloxy]-morpholine}
\]

(\( \text{XI} \))

Andokazuo et al. had synthesized N-hydroxy-N-(4-aryl-3-butyn-2-yl) acetamide (XII) and analogs as 5-lopoxxygenase inhibitor properties. The compounds were tested for inhibitor of the lipoxygenase-mediated archidonic acid metabolic pathway is indicated esp. spasmogenaric, allergic, inflammatory condition, tumor formation and condition involving blood platelet aggregation.

\[
\text{N-hydroxy-N-[1-methyl-3-(3-phenoxyphenyl)prop-2-yn-1-yl]acetamide}
\]

(\( \text{XII} \))
Kawai Akiyoshi et al. 30 had synthesized dextro rotatory N-[\((\text{phenoxo phenyl})-\text{cyclopentyl}\)]-N-hydroxyurea. The compound is tested for anti-inflammatory, 5-lipoxygenase inhibitor & antiallergenic disease. The compound \((\text{R1=F} \& \text{R2=H})\) 

\[
\text{N}-\{3-[3-(3\text{-fluorophenoxy})\text{phenyl}]\text{cyclopent-2-en-1-yl}\}-1\text{-hydroxy urea}
\]

was demonstrated a LC\(_{50}\) against 5-lipoxygenase of approx 0.5 \(\mu\)m.

\[
\text{R1 = H, Cl, F} \\
\text{R2 = H, CH3}
\]

G. Gupta & S.B. Wagh 31 had synthesized various N-(alkyl/aryl)-2-(3-oxo-1,4-benzothiazine -2-yl)acetamide derivatives and tested against various fungus.

2.1.2d Present work:

The literature survey amply exhibits usefulness of (±)-\(\alpha\)-amino amides with different structural features. To explore new therapeutic agents we have reported here preparation and activity of some newly synthesized (±)-\(\alpha\)-amino amides synthesized from (±)-\(\alpha\)-amino nitriles.

\(m\)-Phenoxy benzaldehyde was converted into (±)-\(\alpha\)-amino nitrile. This (±)-\(\alpha\)-amino nitrile was hydrolyzed under mild conditions with sulphuric acid leading to formation of (±)-\(\alpha\)-amino amides. IR & NMR spectra and elemental analysis supported the constitution of the product. The products were tested for antibacterial, antifungal and insecticidal activity.
2.1.2e Experimental:

Preparation of 2-(3-phenoxy-phenyl)-2-phenylamino-acetamide:

To 20ml solution of 70% sulphuric acid (previously cooled below 10°C), a solution of (3-phenoxy-phenyl)-phenylamino-acetonitrile (0.02 mole, 6.0gm) in minimum amount of alcohol (95%) cooled below 10°C, was added slowly. The resulting solution was kept for 48 hrs., at room temperature. The reaction mixture was poured over crushed ice with vigorous stirring. The solid separated was filtered off & the filtrate was neutralized with ammonia solution. The amide was separated out as oily droplets, upon cooling droplets was solidified slowly. The solid product was recrystallized from alcohol (95% ethanol).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Theoretical</th>
<th>Obtained</th>
</tr>
</thead>
<tbody>
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<td>Weight:</td>
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<td>3.8 gm</td>
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<tr>
<td>Yield</td>
<td>100%</td>
<td>60%</td>
</tr>
<tr>
<td>Elements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>75.45 %</td>
<td>75.30%</td>
</tr>
<tr>
<td>H</td>
<td>5.70 %</td>
<td>5.77%</td>
</tr>
<tr>
<td>N</td>
<td>8.80 %</td>
<td>8.91%</td>
</tr>
<tr>
<td>Melting Point</td>
<td>------</td>
<td>196°C</td>
</tr>
</tbody>
</table>

All the other (+)-α-amino amides were prepared by the same procedure and listed in table no. 2.2.1-B.
Chapter II Synthesis and Characterization of Synthesized Molecules: Studies on (+)-\(\alpha\)-amino amide derivatives

**Reaction:**

\[
\text{Mild hydrolysis} \quad 70\% \text{ Conc H}_2\text{SO}_4 \quad \text{keep for 48 hrs. at RT}
\]

\[
\begin{align*}
\text{(I)} & \quad \text{Aryl amino(3-phenoxyphenyl)acetonitrile} \\
\text{(II)} & \quad \text{2-Aryl amino-2-(3-phenoxyphenyl)acetamide}
\end{align*}
\]

Where \(\text{Ar} = \text{phenyl, o/m/p-chloro phenyl, o/m/p-tolyl, p-fluoro phenyl, p-bromo phenyl, p-isopropyl phenyl, p-carboxy phenyl, p-carbethoxy phenyl, o-methoxy phenyl, p-ethoxyl phenyl, 3-chloro-4-fluoro phenyl}\)
Chapter II Synthesis and Characterization of Synthesized Molecules:

Studies on (+)-α-amino amide derivatives

Reference:

Chapter II Synthesis and Characterization of Synthesized Molecules: Studies on (+)-α-amino amide derivatives


26 Sieverding Ewald., US Patent 6268371

27 Shida Takafumi ; Jp. Patent 68290687


Studies on
Sydnonimine Hydrochloride
Derivatives
2.1.3 **Studies on sydnonimine hydrochloride derivatives:**

2.1.3a **Introduction:**

The sydnonimine are mesoionic substance. The meaning of the term mesoionic was applied primarily to compound which cannot be represented even approximately by any one covalent formula or as a hybrid of a number of covalent formula, but which can be depicted as a hybrid of a number of ionic (dipolar, tetrapolar etc.,) forms. The revised definition of the word mesoionic & the use of accepted, instead of a special symbolism, were advanced by the reviewer in 1955 who realized the advantage of discussing these compounds in term of molecular orbital theory. Almost exactly similar proposals were put forward a few week later and independently by Bieber, the difference being a very minor one of symbolism which is mentioned below. These new proposals emphasize the essentially aromatic character of the sydnone and related compounds, which was explicitly recognized in 1946.

The situation very similar to occurring in tropone which has been represented both by covalent structure (I) and by polar structure (II) with its sextet of electrons in association with positive charge. The large incircle circle is representing the sextet. The symbolism, which is now widely accepted was first used by Doering & Knox, formula (I)& (II) are both acceptable and for this reason tropones & its derivatives are regarded as meso ionic & definition given later does not imply that a complete negative charge is rendent upon the exocyclic oxygen atom.

It is now suggested that a compound may be approximately be called meso ionic if it is a five member or possibly six member heterocyclic compound.
which cannot be represented satisfactorily by any one covalent or polar structure and possesses a sextet of electrons in association with all the atoms comparing the ring. The ring bears a fractional positive charge balanced by a corresponding negative charge located on a covalently attached atoms or group of atoms. The inevitable ambiguity here is the word satisfactorily and chemists are not likely always to agree in what may or may not be satisfactory constitutional formula for a given compound. Indeed different formula may rightly be used on different occasion for the same compound according to the structural feature which is desired to emphasize, e.g., the two representation of tropone (I) & (II) were already been mentioned. As a corollary to the definition it follows that in any particular polar structure which may be written for a meso ionic compound, the charge cannot wholly neutralize one another to give covalent structure.

Different types of meso-ionic substances reported in the literature are of following types of substances:

\[ \text{Meso ionic sydnonimine} \quad \text{Thiadiazoles endothiadihydro} \]

\[ \text{Endo thiatriazolines} \]

\[ \text{Sch-1} \]
Sydnonimine hydrochloride is a new class of compound containing two adjacent nitrogen atoms.

These compounds are of interest because of their electronic structure & also because of the varied types of biological activity displayed by some of them.

The sign $(\pm)$ is used with single bond in the heterocyclic rings and can be conveniently applied to such compound as antipyrine $^5$ which if it is wished to emphasize its meso ionic character may be written as follows:
Chapter II Synthesis and Characterization of Synthesized Molecules: Studies on sydnonimine hydrochloride derivatives

Their molecular structure is still in doubt and they are therefore referred as sydnones. \(^6\) Bochvar & Bagatur's Yants \(^7\) suggest that \(\pi\) electrons shell of 4 sydnonimines was calculated by the simple LCAO (MO) method by using the parameter given by Pullman & Pullman. The parameter \(\beta\) (=N=O) was accepted as equal to \(\beta\). The inter atom distance calculated by this methods were in closer agreement with available and experimental data than those calculated by Longuet-Higgins & by Oryl et al. \(^8\)

These compounds are of interest because of the problem of their electronic structure and also because of the varied types of biological activity displayed by some of them.

Two points must be especially emphasized. First that no covalent structure for the sydnones can be written corresponding to the covalent structure (I) for tropones and secondary that the use sydnone sand structure (II) for the tropones. Sydnone sand structure (III) or (IV) does not imply that unit -ve and +ve charge are associated with the ring structure and exo-cyclic oxygen atoms respectively.
Polarographically for a series of 3 & 3,4 substituted sydnonimine hydrochloride stability of these heterocyclic compounds increase with decrease in electronegativity and with increase in substituent size at 3 & 4 position. Steric effect was explained by the widening of substituent at the N-3 & N-4 atoms correlation of equal, constant for 3 substituted was accomplished simultaneously by means of Taft's induction and steric constant. The estimated magnitude of non-polar conjugation energy with 4-phenyl nucleus was about 2 Kcal.

II electron structure of substituted sydnonimine studied by Huckel method with parameters obtained by Pariser-Para-Pole method. Schmidt studies the electronic structure of sydnone by CNDO (complete neglect of differential overlaps) method. Sydnonimine hydrochlorides possess good biological activities like antituberculostatic, antiallergic, antipyretic, antiinflammatory, analgesic, anticancer, antihypertensive and hypnotic activity. Nitrogen mustard derivatives possess good therapeutic activity.

2.1.3b Synthetic aspects:

Bhatt and coworker prepared sydnonimine dihydrochloride by the action of nitrous acid and methanolic hydrochloric acid on α-aryl amino [N,N-bis-(2-chloroethyl)-amino] phenyl acetonitrile. The nitriles were obtained by condensing 4-[N, N - bis - ( 2' - Chloro ethyl ) - amino ] - benzaldehyde cyanohydrine with different amines.

With a view to synthesize better therapeutic agents we had synthesized sydnonimine hydrochlorides by the action of nitrous acid & methanolic hydrochloric acid on condensing different benzaldehyde cyanohydrines with different amines.

Yashunki & Khodidor, prepared 4,4'-dimethylene bis sydnonimines & polymethylene bis (3- sydnonimines), CIBA limited has investigated xylene bis - sydnonimine dihydrochloride.
Chapter II Synthesis and Characterization of Synthesized Molecules: Studies on sydnonimine hydrochloride derivatives

![Diagram](XII)

<table>
<thead>
<tr>
<th>R</th>
<th>R'</th>
<th>Mp</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>(CH₂)₂</td>
<td>197-198</td>
<td>22</td>
</tr>
<tr>
<td>H</td>
<td>(CH₂)₄</td>
<td>183</td>
<td>23</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>145-148</td>
<td>1</td>
</tr>
<tr>
<td>H</td>
<td>P-C₆H₄</td>
<td>80</td>
<td>25</td>
</tr>
<tr>
<td>H</td>
<td>(CH₂)₆</td>
<td>194-195</td>
<td>22</td>
</tr>
</tbody>
</table>

2.1.3c Biological aspects:

Parikh and co workers\(^2^6\) prepared some sydnonimine hydrochlorides by taking diamino diphenyl sulphone and p-amino acetophenone as a starting material and tested for antibacterial activity.

G.C. Kamdar and Parikh\(^2^7\) prepared 3-carbethoxy phenyl-4-aryl sydnonimine hydrochloride, 4-aryl-3-(phenazole-4'-yl) sydnonimine hydrochloride and 4-aryl-3-(pyridyl carbamyl) sydnonimine hydrochloride and tested for antimicrobial activity against \(S.\) \(aureus\) and \(E.\) \(coli\). 4-hydroxy-3-methoxy-phenyl and cinnamyl derivatives show good activity against \(S.\) \(aureus\). While phenyl-3-bromo-2-hydroxy phenyl, 4-hydroxy-3-methoxy phenyl and isobuteryl derivatives show good activity against \(E.\) \(coli\).

The oxadiazolyl sulphanilamides, which have even lower \(pK_a\)'s (4.1-4.4) than the thiadiazoles, have in \(vitro\) and in \(vivo\) activities 1/10-1/30 of sulphadiazine. \(^2^8\) 2-Sulpha-5-methyl-1,3,4-oxadiazole, 3-Sulpha-5-methyl-1,2,4-oxadiazole, and 3-Sulpha-4-methyl-1,2,5-oxadiazole have been investigated. The first is rapidly converted in \(vivo\) to an inactive arylamine.\(^2^9\) The meso ionic 1,2,3-oxadiazoles with phenyl or \(C_1-8\), alkyl as \(R_3\), and with H, CH₃, or Br as \(R_4\), have weak activity in vivo.\(^3^0\)
As few compounds have been prepared in this series, we have selected m-phenoxymethoxy benzaldehyde as starting material, which is widely used, in insecticidal preparation.

2.1.3d Present work:

The literature 31-43 survey shows usefulness of sydnonimine hydrochloride with different structural features. To explore new therapeutic agents we have reported here preparation and biological activity of some newly synthesized sydnonimine hydrochloride.

m-Phenoxy benzaldehyde cyanohydrine was condensed with different amines leading to formation of (±)-α-amino nitrile. The product was treated with nitrous acid and ethanolic hydrochloric acid to get cyclic sydnonimine hydrochloride. IR & NMR spectra and elemental analysis supported the constitution of the product. The products were tested for antibacterial, antifungal and insecticidal activity.

We have undertaken the preparation of different types of sydnonimine hydrochlorides as under:
2.1.3e Experimental:

Preparation of [(4-chloro-phenyl)-5-imino-4-(3-phenoxy-phenyl)-4,5-dihydro-[1,2,3]oxadiazol-3-ium hydrochloride

OR

(3-(4-chloro-phenyl)-4-(3-Phenoxy Phenyl) sydnonimine hydrochloride:

To a solution of [(4-chloro-phenyl) amino](phenoxy-phenyl) acetonitrile (I) (0.02 mole, 6.70gm) (previously prepared in 2.1.1) in ethanolic hydrochloride solution (25ml), a solution of saturated sodium nitrite (4 gm in 10 ml water) was added by maintaining temperature at 0°C. The content was kept at 0-5°C with constant stirring for an hour to form [(4-chloro-phenyl)-(nitroso)-amino](3-phenoxy-phenyl) acetonitrile (II). Compound (II) was extracted in chilled chloroform. 20ml ethanolic hydrochloride solution was added to chloroform extract, dry hydrogen chloride gas was passed for an hour through it, by maintaining temperature below 5°C. the reaction mass was kept at 0-5°C for 24 hrs. to obtain crude sydnonimine hydrochloride(III).

The product was recrystallized from methyl ethyl ketone.

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<td>Yield:</td>
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</tr>
<tr>
<td>Elements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>59.86 %</td>
<td>59.75 %</td>
</tr>
<tr>
<td>H</td>
<td>4.02 %</td>
<td>3.98 %</td>
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<tr>
<td>N</td>
<td>10.47 %</td>
<td>10.56 %</td>
</tr>
<tr>
<td>Cl</td>
<td>17.67 %</td>
<td>17.85</td>
</tr>
<tr>
<td>Melting Point</td>
<td>--</td>
<td>&gt;360°C</td>
</tr>
</tbody>
</table>

All the other sydnonimine hydrochloride were prepared by the same procedure and listed in table no. 2.2.1-C.
Chapter II Synthesis and Characterization of Synthesized Molecules: Studies on sydnonimine hydrochloride derivatives

Reaction:

\[
\begin{array}{c}
\text{Aryl anilino(3-phenoxyphe}n\text{l)acetonitrile} \\
\text{(I)} \\
\text{[nitroso(arylyl)amino](3-phenoxyphe}n\text{l)acetonitrile hydrochloride} \\
\text{(II)} \\
\text{Compound synthesized in Section I of Chapter 2} \\
\text{(III)} \\
5\text{-imin\text{o}-4-(3-phenoxyphe}n\text{n)}-3\text{-aryl-4,5-dihydro-3H-1,2,3-oxadiazol-1-ium hydrochloride} \\
\text{Where } \text{Ar} = \text{phenyl, o/m/p-chloro phenyl, o/m/p-tolyl, p-fluoro phenyl, p-bromo phenyl, p-isopropyl phenyl, p-carboxy phenyl, p-carbethoxy phenyl, o-methoxy phenyl, p-ethoxy phenyl, 3-chloro-4-fluoro phenyl, benzyl amine}
\end{array}
\]
Chapter II Synthesis and Characterization of Synthesized Molecules:
Studies on sydnonimine hydrochloride derivatives

Reference:
2. Bieber, ibid, 1055,
8. Longuet G., Higgins F., & Oryl, ; Federation Proc. 6, 65, (1944)
Chapter II Synthesis and Characterization of Synthesized Molecules:
Studies on sydnonimine hydrochloride derivatives

26 Parikh A.R., Jotani K.P.,
31 Bockmuhl, Med. U. Chem. 1, 169, (1933)
38 Putzer B. and Schonhofer F. (to I.G. Farbenindustrie A.G.); German Patent 550327, Chem. abstr. 26, 4062, (1932)
39 Yamaguchi Hisashi, Nakai Toshio; J. Pharm. Sci., 603(2), 254, (1971)
43 Clayton G.C., Ber, 28, 1665, (1895).
Studies on 5-Oxo-Imidazoline Derivatives
Chapter II Synthesis and Characterization of Synthesized Molecules:

Studies on 5-oxo-imidazoline derivatives:

2.1.4a Introduction:

The discovery of the 2-substituted 2-imidazolines or "anhydro bases of the aliphatic series" dates back to the year 1888 when Hofmann prepared 2-methyl-2-imidazoline (lysidine) by heating N,N'-diacetyl-ethylenediamine in a stream of dry hydrogen chloride. Ladenburg prepared the same compound by fusing two equivalents of sodium acetate with one equivalent of ethylenediamine dihydrochloride. A number of other simple 2-substituted 2-imidazolinone have been prepared by this same procedure.

The oxo-imidazolines are associated with many biological activities. 2-Methyl / Phenyl oxazolines-5-ones and imidazoline derivatives are associated with medicinal chemistry. They proved their worth as chemotherapeutic agents. The activity of oxazoles as anti microbial agent is widely reported in the literature. It has been noted that an unsubstituted nucleus is seldom active but introduction of lipophilic substitutents either alkyl or aryl or heteroaryl very often induces activity.

2.1.4b Synthetic aspects:

5-Oxo-2-imidazoline is a five-member ring having two nitrogen atoms in the 1 and 3 positions and a carbonyl group at 5-position (I). According to IUPAC, 5-oxo-2-imidazoline is 1,3-diazaacyclpentene-5-ones.

![Chemical Structure](I)

Azalctone reacts with variety of compounds such as water, alcohol, amines and hydrogen halides. Amides of α-acyl amino acrylic acids obtained from the condensation of azalactone and primary amine can be converted into imidazolinones as shown in reaction.
The ring closure can be affected under a variety of conditions, substituted anilides have been converted into imidazolinones by the action of phosphorous oxychloride. In order to get variety of useful compounds, reaction of azalactone have been extensively investigated with different types of compounds such as alcohol 5, thiophenol 6, hydrazine hydrate 7, aromatic amino acids, phenyl hydrazine 8, and ammonia 9.

Different methods have been documented for the synthesis of imidazolinones by several investigators in literature. 10-18, 112-113 As one of the preparations describes the aminations of azalactone it becomes necessary to discuss azlactone chemistry.

Plochi 19 prepared the first unsaturated azlactone (oxazolone) by the condensation of benzaldehyde with hippuric acid in the presence of acetic anhydride.

Erlenmeyer 20 then determined the structure of the product and also extended the reaction to other aldehyde in order to establish the usefulness of unsaturated azalactone as intermediate in the synthesis of α-keto and α-amino acids.
Rebuffat \(^{21}\) proposed three members ring skeleton (II) for azalactone. Later, however, Erlenmeyer abandoned this formula in favor of five member ring (III)

\[
\begin{align*}
\text{(II)} & \quad \text{R} \quad \text{O} \\
\text{(III)} & \quad \text{R} \quad \text{C} \quad \text{O} \\
\end{align*}
\]

P. Shanthanrao and R.V. Venkataratnam \(^{22}\) have reported an improved procedure for the synthesis of arylidine oxazolones from hippuric acid and aromatic aldehydes in presence of acetic anhydride and anhydrous zinc chloride in 62–76 % yields

**MECHANISM:**

(I) \[ \text{CH}_3\text{COONa} \rightarrow \text{CH}_3\text{COO}^- + \text{Na}^+ \]

(II) \[ \text{HN} \quad \text{CO} \quad \text{OH} \rightarrow \text{H}_2\text{O} + \text{N} \quad \text{O} \]

(III) \[ \text{N} \quad \text{O} \quad \text{+ CH}_3\text{COO}^- \rightarrow \text{N} \quad \text{O} \quad \text{CH}_3\text{COOH} \]

(IV) \[ \text{N} \quad \text{O} \quad \text{+ R} \quad \text{C} \quad \text{H} \rightarrow \text{N} \quad \text{O} \quad \text{H} \]
Erlenmeyer 23 believed this synthesis to be a special type of Perkin condensation in which reaction between aldehyde and acyl glycine proceeds first followed by ring closure.

However, convincing evidence now indicates that aldehydes condense under the influence of base with the reactive methylene group in the azlactone which is formed by the dehydration of benzoyl / acetyl glycine, when the later is heated with acetic anhydride in the presence of sodium acetate.

2.1.4c Biological aspects:

Therapeutic importance:

Literature survey revealed that various imidazolinones have resulted in many potential drugs and are known to possess a broad biological spectrum such as:

- Anticonvulsant 24-33
- Potent CNS depressant 34-38
Chapter II Synthesis and Characterization of Synthesized Molecules:
Studies on 5-oxo-imidazoline derivatives:

- Sedative and hypnotic
- Monoamino Oxidase (MAO) inhibitory
- Antihypertensive
- Insecticidal
- Fungicidal
- Antiperkinsonian
- Local anaesthetic
- Antiallergenic
- Antihistamine
- Antineoplastic
- Antipyretic and analgesic
- Antibacterial
- Anti-inflammatory
- Herbicidal
- Anthelmintic
- Antifilarial

Bohmann, C. et al. had studied imidazoline derivatives which are effective in inhibiting coradrenaline release in rat isolated kidney. Locombe and Villar have studied the properties of imidazoline to stimulate insulin release by hamster pancreatic islets.

Dhandeshwar et al. had synthesized some Mannich bases of 2-methyl & 2-phenyl-4-(2-hydroxy-benzylidine)-oxazoline-5-ones and antimicrobial activity of the synthesized compounds was evaluated against E.coli, S. aureus and C. albicans. Neomycin and Nystatin were used as standard antibacterial and antifungal agents. Two compounds have shown significant activity against the three-test organism.

Kanellakopulos et al. had prepared the imidazolidinone derivatives (IV and V). The compounds were tested for their fungicidal activity and gave complete control of Podosphaera leucotricha on apple seedling when sprayed at 25 ppm.
Bascou et al. \textsuperscript{91} prepared optically active 2-imidazolin-5-ones and thiones as agro-chemicals fungicide. The compound (VI) had LC\textsubscript{50} of 37 ppm against \textit{Puccinia recondita}.

Mita Takeshi \textsuperscript{92} has prepared new imidazolinone derivatives (VII) as pesticides which killed 100\% brown rice plant hopper and 28 spotted lady beetles at 1000 ppm.

Kalman Thomas \textsuperscript{93} has prepared imidazolinone derivatives of the type 1-(2-deoxy-\textbeta-D-ribofuranosyl)-4-acety imidazoline-2-one. The synthesized compound inhibited HIV-1 with EC\textsubscript{50} = 8.1 \mu M in MT-4 cells.
Kohle et al. 94 have synthesized some new 1-substituted phenyl -2-(2'-chloro-5'-nitro phenyl)-4-(p-N,N-bis-cyano ethyl amino benzylidene)-5-imidazolinones (VIII) and tested for their anticancer, anti HIV, fungicidal and antibacterial activities.

Where R = Substituted Phenyl

Jolly and Pathak 95 have synthesized some new 1-substituted 2-aryloxy methyl-4-( p-bis-3-cyanoethyl amino benzylidine)-5-imidazolinones. The compounds were tested in vitro against infected treated cultures and uninfected treated culture of the human immuno deficiency virus (HIV). They also tested compounds for their antibacterial and antifungal but results were not promising.

Emeric, Gilbert et al. 96 prepared imidazoline derivative (IX) and tested for their fungicidal activity. Most of the compounds were found to be excellent fungicides.

Where R₁ = H, vinyl, allyl, halo alkyl etc.  
R₂ = hetero aryl, 
R₃ = H, (n=0), halo alkyl, cyclopropyl  
R₄ = hetero aryl 
R₅ = H, alkyl, acyl, etc.  
W = O, S, SO  
Z = O or S  
n = 0 or 1
Sun King has synthesized new imidazolinones (X) and tested for their agrochemical fungicides for the treatment of crop plants. Out of the synthesized compounds $A = O$, $B = Me$, $R_1 = CH_3$, $R_2 = R_3 = Ph$, $R_4 = H$, (M.P =132-134°) demonstrated complete control of wheat powdery mildew on wheat seeding at 100 ppm.

\[
\begin{array}{c}
\text{N} \\
\text{B} \\
\text{R}_1 \\
\text{R}_2 \\
\text{A} \\
\text{R}_3 \\
\text{R}_4 \\
\end{array}
\]

(B) - 0, (B) - Me, (R) - CH$_3$, (R) - Ph, (R) - H, (M.P =132-134°)

Bascou, Jean-Philippe et al. have prepared imidazolinone derivatives (XI) and tested for their agrochemical fungicidal activity. Some of the synthesized compounds show more than 75 % control of $P$. recondita on wheat when sprayed at 1gm / lit.

\[
\begin{array}{c}
\text{S} \\
\text{CH}_3 \\
\text{N} \\
\text{N} \\
\text{A} \\
\text{R}_1 \\
\text{R}_2 \\
\text{R}_3 \\
\text{R}_4 \\
\end{array}
\]

(XI)

Arakawa, Eitaro et al. have prepared some new imidazole derivatives as antiulcer drugs. The compound (XII) showed inhibitory effect on induced gastric ulcer of 71.9% at 30mg/Kg in male rats.

\[
\begin{array}{c}
\text{O} \\
\text{R}_1 \\
\text{R}_2 \\
\text{A} \\
\text{R}_3 \\
\end{array}
\]

(XII)

Where $R_1 = R_2 = R_3 = H$ and $A = 2$-pyridylmethyl thio
G.V.S. Ram Sharma and V. Malla Reddy had synthesized 1,2 disubstituted-4-[(benzoxazole-2-yl) methylene] imidazoline-5 (4H)-ones (XIII) all these compounds were evaluated for antihistaminic, antibacterial and antifungal activities. An antihistaminic study indicates that most of the compounds were active with a degree of variation. Among them the most effective one was \( R = \text{phenyl}, \ R_1 = \text{benzyl} \), antibacterial and antifungal potency of the test compounds was not comparable with that of standards benzyl penicillin, streptomycin and clotrimazole.

\[
\begin{align*}
\text{N} &= \text{O} \quad \text{R} \\
\text{R}_1
\end{align*}
\]

Where \( R = \text{CH}_3, \ C_6H_5 \)

\( R_1 = \text{2} - \text{Cl}-C_6H_5, \text{2} - \text{CH}_3-C_6H_5, \text{2} - \text{OCH}_3-C_6H_5 \) etc.

Shah N.S. et al. had synthesized 2-(4"-arylidine-2"-phenyl-5" oxo-imidazoline -1- yl ) - 4 - (6"- methoxy - β - naphthyl) - thiazoles (XIV). The synthesized compounds were screened for antimicrobial activity. All the compounds showed moderate activity against specified microbes.

\[
\begin{align*}
\text{O} &= \text{N} \\
\text{R}
\end{align*}
\]

Where \( R = C_6H_5, \text{2-Furyl, C}_6\text{H}_5-\text{CH=CH}, \text{2-(OCH}_3)-C_6\text{H}_4 \) etc.

Undavia and Jadeja had synthesized 1-(benzylidine acetyl amino)-4-arylidine-2-phenyl-5-oxo-imidazoles (XV). The synthesized compounds were tested for their antibacterial, anti HIV, anti cancer activities. Most of the compounds showed marked activity against \text{E.coli and S. aureus}., however, the highest activity was shown by this compound having.
Studies on 5-oxo-imidazoline derivatives:

Undavia and Zala \(^{103}\) have synthesized 1-\((\alpha\text{-methyl}\text{-}(4\text{-}(2\text{-methyl propyl})\text{-}phenyl)acetyl amino)\text{-}4\text{-}aryl methine-2\text{-}methyl-5\text{-}oxoimidazoles (XVI). They had tested compounds for anticancer, anti-HIV, anti-inflammatory and analgesic activities. They had also found structural activity relationship.

Several substituted oxazolones (Sch-III) were synthesized by condensation of benzoylglycine with different aldehydes, \(^{104}\) to form oxazolones. Substituted imidazolinones were synthesized by condensation with ethylenediamine, urea and 4-N,N-dimethylaminoaniline. All these synthesized compounds produced significant antibacterial activities. Furthermore, compounds containing -CH(2)CH(2)NH(2), -CONH(2) and -C(6)H(4)-N(CH(3))(2) groups as substitutents on the imidazolinones were found to be potent antibacterial agents.
Chapter II Synthesis and Characterization of Synthesized Molecules:
Studies on 5-oxo-imidazoline derivatives:

Thus, among the twelve compounds, 1-(2-aminoethyl)-2-phenyl-4-(4-(dimethyl amino) benzylidene) imidazole-5-(4H)-one, 1-carboxamido-2-phenyl-4-(4-(dimethyl amino) benzylidene) imidazole-5-(4H)-one and 1-(4-(N,N-dimethyl amino)-phenyl)-2-phenyl-4-(4-(dimethyl amino) benzylidene) imidazole-5-(4H)-one were found to have a significant higher antibacterial activity than the other substituted imidazolines.

Vinay kumar et. al 105 had synthesized 5-oxo-imidazoline derivatives and tested for antimicrobial activity.

Upadhyay, Pandya et al. 106 had synthesized 5-oxo imidazoline from oxazolones and isoniazid and screened for antibacterial activity. They had synthesized 5-oxo imidazoline by condensation of isoniazide and oxazolone at 140°C the mass was treated with methanol to obtained 5-oxo-imidazoline.
Studies on 5-oxo-imidazoline derivatives:

Where $R = \text{CH}_3$ or $\text{C}_6\text{H}_5$

$R' = \text{H, 2,3,4 tri methoxy, 2-hydroxy, 4-chloro etc.}$

S. Singh, Dave U.S. et al.\textsuperscript{107} had synthesized 6-(4'-substituted benzylidene-2' methyl/phenyl-5'-imidazolinon-1'yl)-2-methyl 4-(3H)-quinazolinone and tested for antimicrobial activity. They had tested against gram positive and gram negative bacteria, they also carried antifungal activity \textit{Aspergillus niger}.

Where $R = \text{CH}_3$ or $\text{C}_6\text{H}_5$

$R' = \text{H, 2,3,4 tri methoxy, 2-hydroxy, 4-chloro etc.}$

\textbf{2.1.4d Present work:}

The literature survey amply exhibits usefulness of 5-oxo-imidazolines with different structural features. To explore new therapeutic agents we have reported here preparation and biological activity of some newly synthesized 5-oxo-imidazolines.

m-Phenoxy benzaldehyde was converted into m-phenoxy benzohydrazide. This hydrazide was condensed with different oxazolones leading to formation of 5-oxo-imidazoline. IR & NMR spectra and elemental analysis supported the constitution of the product. The products were tested for antibacterial, antifungal and insecticidal activity.
2.1.4e Experimental:

Preparation of \( N-[(4Z)-4\text{-benzylidene}-2\text{-methyl}-5\text{-oxo}-4,5\text{-dihydro}-1H\text{-}
\text{imidazol-1-yl}]-3\text{-phenoxybenzamide} \):
Preparation of 5-oxo-imidazolone was carried out in three stages:
• Preparation of 3-phenoxybenzohydrazide from 3-phenoxy benzoaldehyde
• Preparation of 5-oxozolone derivatives
• Preparation of \( N-[(4Z)-4\text{-benzylidene}-2\text{-methyl}-5\text{-oxo}-4,5\text{-dihydro}\
1H\text{-imidazol-1-yl}]-3\text{-phenoxybenzamide} \):

(1) 3-Phenoxybenzohydrazide
3-phenoxy benzohydrazide was made in three stages:
(a) Preparation of 3-phenoxy benzoic acid (Cannizaro reaction)
(b) Preparation of 3-phenoxy methyl benzoate (esterification)
(c) Preparation of 3-phenoxy benzohydrazide
(a) Preparation of 3-phenoxy benzoic acid:
Potassium hydroxide (50%, 50ml) was added slowly to freshly distilled m-
phenoxy benzaldehyde (0.05 mole, 11.26gm) at room temperature with
constant stirring for 3 to 4 hours. Thick mass was diluted with 100ml water
and slurry was stirred for further half an hour. The benzyl alcohol (organic
layer) formed during the Cannizaro reaction was complete extracted by
means of isopropyl ether (30ml, 3 wash). The aqueous layer was acidify
with glacial acetic acid to precipitate out 3-phenoxy benzoic acid. The
product was filtered and washed with water, recrystallized it from alcohol
and checked for TLC. Melting point 148°-149°C against reported 149°-
150°C.
(b) Preparation of 3-phenoxy methyl benzoate.
3-phenoxy benzoic acid prepared as earlier (0.03 mole, 6.4gm) was reflux
with 50 ml methanol and 3ml conc. \( \text{H}_2\text{SO}_4 \) in water bath for 6 hours. Excess
of methanol was distilled off. The ester produced was washed with water
(30ml, 3 wash). The ester was purified by fractional distillation. TLC was
carried out using silica gel–G. Boiling point of compound was showed
162°C
c(c) Preparation of 3-phenoxy benzohydrazide.
Mixture of 3-phenoxy methyl benzoate (0.03 mole, 6.84gm) in 25ml 95%
ethanol, hydrazine hydrate (8 ml, 80 %) was refluxed for 10 to 12 hrs.
Chapter II Synthesis and Characterization of Synthesized Molecules:

Studies on 5-oxo-imidazoline derivatives:

Excess of solvent and hydrazine hydrate was distilled off and the resulting liquid mass was cooled at 4-5°C. Separated product was filtered off & washed with cold water. The product was dried, recrystallized. Melting point of compound was showed 83°C.

(II) Preparation of 5-oxozolone derivatives

To a mixture of freshly distilled benzaldehyde (or aromatic aldehyde) (2.12 gm, 0.02mole) and acetyl glycine (0.02mole, 2.34 gm) or hippuric acid (0.02 mole, 3.59 gm), acetic anhydride (6.12 gm, 0.06mole) and freshly fused sodium acetate (1.64gm, 0.02 mole) were added. The mixture was stirred on hot plate. After the liquidification of mixture it was heated on water bath for 3 to 4 hours. Then 100ml of absolute alcohol was added to the content of the flask and left overnight at room temperature. The product was filtered off and washed with abs. alcohol & then with boiling water. Recrystallized the 4(Z)-benzylidine-2-methyl-1,3-oxazol-5(4H)-one with benzene. The oxazolones were checked for TLC.

(III) Preparation of N-[(4Z)-4-benzylidene-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]-3-phenoxybenzamide:

To a mixture of 4(Z)-benzylidine-2-methyl-1,3-oxazol-5(4H)-one (0.02mole, 3.74gm ) and 3-phenoxy benzohydrazide (0.01mole, 4.56gm) 10 ml pyridine (freshly distilled) was added and refluxed for 6 hrs., after cooling reaction mass poured over ice and acidified with HCl to remove excess of pyridine, solid mass washed with cold water & dried, recrystallized the product from ethanol.

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<th>Theoretical</th>
<th>Obtained</th>
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<td>Elements</td>
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<tr>
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<td>72.48 %</td>
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<tr>
<td>H</td>
<td>4.82 %</td>
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<td>N</td>
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<tr>
<td>Melting Point</td>
<td>----</td>
<td>100°C</td>
</tr>
</tbody>
</table>

All the other 2-phenyl/methyl 5-oxo-imidazolones were prepared by the same procedure and listed in table no. 2.2.1-E & 2.2.1 F resp.
Chapter II Synthesis and Characterization of Synthesized Molecules: Studies on 5-oxo-imidazoline derivatives:

Reaction:

(I) Preparation of 3-phenoxy benzohydrazide.

\[
3\text{-phenoxybenzaldehyde} + \text{50\% KOH} \xrightleftharpoons{\text{Stirring for 4 Hrs}} \xrightarrow{\text{Conc. H}_2\text{SO}_4} \text{3-phenoxybenzoic acid} + \text{(3-phenoxyphenyl) methanol} + \text{3-phenoxybenzohydrazide}
\]

(II) Preparation of 5-oxazolone.

\[
\text{(4E)}-\text{4-arylidene-2-methyl/Phenyl-1,3-oxazol-5(4H)-one}
\]

Where \( R \) is CH₃ or C₆H₅

Where \( \text{Ar} = \text{Phenyl, cinnamyl, furyl, o/p-chloro phenyl, p/m/o-nitro phenyl, p/m/o-hydroxy phenyl, p-methoxy phenyl, 3,4-dimethoxy phenyl, 2,3,4-trimethoxy phenyl, m-phenoxy phenyl, 2-hydroxy naphthyl} \)

(III) Preparation of 2-methyl/phenyl 5-oxo-imidazoline.

\[
\text{(4E)}-\text{4-arylidene-2-methyl/Phenyl-1,3-oxazol-5(4H)-one}
\]

Where \( R = \text{CH₃ or C₆H₅} \)

Where \( \text{Ar} = \text{Phenyl, cinnamyl, furyl, o/p-chloro phenyl, p/m/o-nitro phenyl, p/m/o-hydroxy phenyl, p-methoxy phenyl, 3,4-dimethoxy phenyl, 2,3,4-trimethoxy phenyl, m-phenoxy phenyl, 2-hydroxy naphthyl} \)
Reference:

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(1992)
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<td>69</td>
<td>G. V. S. Ram Sharma; B. Suresh; V. Malla Reddy; Indian Drugs; 34, 17-20, (1997).</td>
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<td>74</td>
<td>V. P. Arya; Drugs of the future; 13, 411, (1988).</td>
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Studies on 5-oxo-imidazoline derivatives:

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Part - II

Elemental Analysis & Spectral Characterization
Elemental Analysis &
Spectral (IR, NMR) data of
\((\pm) = \alpha\)-Amino Nitrite
Derivatives
Chapter II Synthesis and Characterization of Synthesized Molecules:
Part -II Characterization (Elemental Analysis) of (t)-α-amino nitrile derivatives

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<th>% C Theo.</th>
<th>% H Theo.</th>
<th>% N Theo.</th>
<th>% O Theo.</th>
<th>% Cl Theo.</th>
<th>% F Theo.</th>
<th>% Br Theo.</th>
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Table No. 2.2.1-A
Chapter II Synthesis and Characterization of Synthesized Molecules:
Part -II  Characterization (IR Spectra) of (z)-α-amino nitrile derivatives

Sample Name: (3-Phenoxy phenyl)-m-tolylamino-acetonitrile
Data File: Infrared Spectra And Jivani
Date & Time: 16/12/2005 10.45.00

Spectra 2.2.1a
Chapter II Synthesis and Characterization of Synthesized Molecules 

Part II Characterization of 1H-CMR spectra of (E)-4-aminomethyl derviatives
(3-Phenoxy-phenyl)-m-tolylamino-acetonitrile

Spectra 2.2.1c
Elemental Analysis & Spectral (IR, NMR) data of $^{(1)}\alpha$-Amino amide (Acetamide deri.) Derivatives
Chapter II Synthesis and Characterization of Synthesized Molecules:
Part -II  Characterization (Elemental Analysis)of (±)-α-amino amide derivatives

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<td>8.53</td>
<td>9.51</td>
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<td>72.91</td>
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<td>64.88</td>
<td>4.35</td>
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Table No. 2.2.1-B
Chapter II Synthesis and Characterization of Synthesized Molecules:

Part -II  Characterization (IR Spectra) of (±)-α-amino amide derivatives

Sample Name: 2-(5-phenoxy-phenyl)-2-phenyl-amino-acetamide
Data File: Infrared Spectra And Jivani
Date & Time: 18/12/2005 12:48:46

![Infrared Spectra](image_url)
Chapter II: Synthesis and Characterization of Synthesized Molecules

Part II: Characterization (13C NMR Spectra) of 2-phenoxynaphthyl-2-phenylamino acetamide

Spectra 2.26
Chapter II Synthesis and Characterization of Synthesized Molecules

Part II Characterization (1 H NMR Spectra) of (2)-(6-Amino-amide derivatives)
Elemental Analysis & Spectral (IR, NMR) data of Sydnonimine Hydrochloride Derivatives
**Chapter II Synthesis and Characterization of Synthesized Molecules:**

**Part -II  Characterization (Elemental Analysis) of sydnonimine hydrochloride derivatives**

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<td>&gt;360°C</td>
<td>65.49</td>
<td>4.67</td>
<td>11.46</td>
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<td>&gt;360°C</td>
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<td>4.02</td>
<td>10.47</td>
<td>7.97</td>
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<td>m-chloro phenyl</td>
<td>401.27</td>
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<td>4.02</td>
<td>10.47</td>
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<td>4.02</td>
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<td>7.97</td>
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<td>5.03</td>
<td>11.03</td>
<td>8.40</td>
<td>9.31</td>
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<td>&gt;360°C</td>
<td>66.23</td>
<td>5.03</td>
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<td>66.23</td>
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<td>p-fluro phenyl</td>
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<td>&gt;360°C</td>
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<td>4.83</td>
<td>10.59</td>
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Table No. 2.2.1-C
Chapter II Synthesis and Characterization of Synthesized Molecules:

Part II Characterization (IR Spectra) of Sydnonimine Hydrochloride Derivatives

Sample Name: 3-(3-Chloro-4-fluoro-phenyl)-4-(3-phenoxypy-phenyl)-4H-[1,2,3]oxadiazol-5-ylideneamine hydrochloride

Data File: Infrared Spectra Anil Sivani

Date & Time: 16/12/2005 15:15:35

Spectra 2.2.3a
Chapter II Syntheses and Characterization of Synthesized Molecules

Part II Characterization of 
^13C NMR Spectra of Synthonimine Hydrochloride Derivatives

1,2,3-trioxadiazole-5-imino-Acridine

3-(3-Chloro-4-(fluoro-phenyl)-5-imino-4-(3-phenox-phenyl)-4,5-dihydro-Acridine
Chapter II Synthesis and Characterization of Synthesized Molecules:

Part II Characterization (\(^1\)HNMR Spectra) of sydnonimine hydrochloride derivatives

3-(3-Chloro-4-fluoro-phenyl)-5-imino-4-(3-phenoxy-phenyl)-4,5-dihydro-[1,2,3]oxadiazole-3-iumhydrochloride

![HNMR spectra and structure diagram]
Elemental Analysis & Spectral (IR, NMR) data of 2-Phenyl-5-Oxo-Imidazoline Derivatives
Chapter II Synthesis and Characterization of Synthesized Molecules:
Part -II Characterization (elemental analysis) of synthesized molecules 2-phenyl-5-oxo-imidazoline derivatives

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<td>101°C</td>
<td>75.80</td>
<td>4.61</td>
<td>9.14</td>
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<td>IV(f)</td>
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<td>IV(g)</td>
<td>m-Nitro phenyl</td>
<td>504.49</td>
<td>C&lt;sub&gt;29&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;N&lt;sub&gt;4&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
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<td>73.25</td>
<td>4.45</td>
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<td>13.46</td>
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<td>84°C</td>
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Table No. 2.2.1-D
Chapter II Synthesis and Characterization of Synthesized Molecules:

Part -II Characterization (IR Spectra) of synthesized Molecules. 2-phenyl-5-oxo-imidazoline derivatives

Sample Name: \(N\)-(5-Oxo-2-phenyl-4-(3-phenyl-allylidene)-4,5-dihydr o-imidazol-1-yl)-3-phenoxy-benzoamide

Infrared Spectra Anil Jinani

Date & Time: 11/12/2005 09:56:12

Spectra 2.2.4a
Chapter II Synthesis and Characterization of Synthesized Molecules:
Part -II  Characterization (¹³C NMR Spectra) of synthesized Molecules. 2-phenyl-5-oxo-imidazoline derivatives

N-[(5-Oxo-2-phenyl-4-(3-phenyl-allylidene)-4,5-dihydro-imidazol-1-yl)-3-phenoxy-benzamide

Spectra 2.2.4b
Elemental Analysis & Spectral (IR, NMR) data of 2-Methyl-5-Oxo-Imidazoline Derivatives
### Chapter II Synthesis and Characterization of Synthesized Molecules:

#### Part -II Characterization (elemental analysis) of synthesized molecules: 2-methyl-5-oxo-imidazoline derivatives

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<tr>
<td>V(a)</td>
<td>Phenyl</td>
<td>397.42</td>
<td>C_{24}H_{19}N_{3}O_{3}</td>
<td>100° C</td>
<td>72.53</td>
<td>4.82</td>
<td>10.57</td>
<td>12.08</td>
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<tr>
<td>V(b)</td>
<td>Cinnamyl</td>
<td>423.46</td>
<td>C_{26}H_{20}N_{3}O_{3}</td>
<td>110° C</td>
<td>73.74</td>
<td>5.00</td>
<td>9.92</td>
<td>11.33</td>
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<td>V(c)</td>
<td>Furyl</td>
<td>387.38</td>
<td>C_{24}H_{17}N_{3}O_{3}</td>
<td>105° C</td>
<td>68.21</td>
<td>4.42</td>
<td>10.85</td>
<td>16.52</td>
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<td>V(d)</td>
<td>o-Chloro phenyl</td>
<td>431.87</td>
<td>C_{24}H_{14}ClN_{3}O_{3}</td>
<td>80° C</td>
<td>66.75</td>
<td>4.20</td>
<td>9.73</td>
<td>11.11</td>
<td>8.21</td>
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<td>V(e)</td>
<td>p-Chloro phenyl</td>
<td>431.87</td>
<td>C_{24}H_{14}ClN_{3}O_{3}</td>
<td>90° C</td>
<td>66.75</td>
<td>4.35</td>
<td>9.60</td>
<td>10.74</td>
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<td>V(f)</td>
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<td>442.42</td>
<td>C_{24}H_{14}N_{4}O_{3}</td>
<td>120° C</td>
<td>65.15</td>
<td>4.40</td>
<td>12.66</td>
<td>18.08</td>
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<td>V(g)</td>
<td>m-Nitro phenyl</td>
<td>442.42</td>
<td>C_{24}H_{14}N_{4}O_{3}</td>
<td>110° C</td>
<td>65.15</td>
<td>3.96</td>
<td>12.88</td>
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<td>V(h)</td>
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<td>442.42</td>
<td>C_{24}H_{14}N_{4}O_{3}</td>
<td>95° C</td>
<td>65.15</td>
<td>4.10</td>
<td>12.66</td>
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<td>V(i)</td>
<td>p-Hydroxy phenyl</td>
<td>413.42</td>
<td>C_{24}H_{14}N_{4}O_{3}</td>
<td>120° C</td>
<td>69.72</td>
<td>4.63</td>
<td>10.16</td>
<td>15.48</td>
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<td>V(j)</td>
<td>m-Hydroxy phenyl</td>
<td>413.42</td>
<td>C_{24}H_{14}N_{4}O_{3}</td>
<td>80° C</td>
<td>69.72</td>
<td>4.63</td>
<td>10.16</td>
<td>15.48</td>
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<td>V(k)</td>
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<td>413.42</td>
<td>C_{24}H_{14}N_{4}O_{3}</td>
<td>70° C</td>
<td>69.72</td>
<td>4.63</td>
<td>10.16</td>
<td>15.48</td>
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<td>p-Methoxy phenyl</td>
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<td>105° C</td>
<td>68.26</td>
<td>5.07</td>
<td>9.19</td>
<td>17.49</td>
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<td>V(n)</td>
<td>2,3,4 Tri Hydroxy phenyl</td>
<td>487.50</td>
<td>C_{25}H_{19}N_{3}O_{3}</td>
<td>100° C</td>
<td>66.52</td>
<td>5.17</td>
<td>8.62</td>
<td>19.69</td>
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<td>V(o)</td>
<td>m-Phenoxy phenyl</td>
<td>489.52</td>
<td>C_{25}H_{20}N_{3}O_{3}</td>
<td>120° C</td>
<td>73.61</td>
<td>4.74</td>
<td>8.58</td>
<td>13.07</td>
<td>0</td>
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<td>V(p)</td>
<td>2-Hydroxy Naphthyl</td>
<td>463.48</td>
<td>C_{24}H_{19}N_{3}O_{4}</td>
<td>80° C</td>
<td>72.56</td>
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<td>9.07</td>
<td>13.81</td>
<td>0</td>
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Table No. 2.2.1-E
Chapter II Synthesis and Characterization of Synthesized Molecules:
Part -II Characterization (IR Spectra) of synthesized Molecules 2-methyl-5-oxo-imidazoline derivatives

Sample Name: N-(2-Methyl-5-oxo-4-(3-phenoxyl-benzylidene)-4,5-dihydro-imidazol-1-yl)-3-phenoxyl-benzamide

Data File: Infrared Spectra Aniljivani

Date & Time : 18/12/2005 18:48:39

[Graph showing infrared spectra of synthesized molecules]

Spectra 2.2.5a
Chapter II Syntheses and Characterization of Synthesized Molecules.

Part II Characterization of $^1$H NMR Spectra of Synthesized Molecules, 2-Methyl-5-oxo-imidazolione Derivatives.

N-[2-(Methyl-5-oxo-1-(3-phenoxypyridine)-4,5-dihydro-imidazole-1-yl]-3-phenoxypyrazamide

Speerta 2:05 C

BRUKER