SYNTHESIS, STRUCTURE AND PROPERTIES OF SOME HETEROCYCLIC COMPOUNDS

Thesis

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in partial fulfilment of the requirements for the degree of

DOCTOR OF PHILOSOPHY IN CHEMISTRY

By

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CERTIFICATE

This is to certify that the thesis entitled **Synthesis, structure and properties of some heterocyclic compounds** is an authentic record of the research work carried out by **P. Jyothi**, in the Department of Chemistry, under my supervision in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry under the Faculty of Science of the University of Calicut and that no part thereof has been presented earlier for any other degree.

C.U Campus,
28.11.2009.

Dr. P. Mohamed Shafi
(*Supervising Teacher)*

DECLARATION

I, P. Jyothi, hereby declare that this thesis is an authentic record of original research work carried out by me under the supervision of Dr. P. Mohamed Shafi, Professor, Department of Chemistry, University of Calicut. No part of this thesis has previously formed the basis for the award of any other degree.

C.U. Campus,
28.11.2009. **P. Jyothi**

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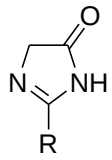
PREFACE

The structural diversity and biological importance of nitrogen containing heterocycles have made them attractive targets for synthesis over many years. They are found in various natural products and have been identified as products of chemical and biological importance.[1] Nitrogen heterocycles have been widely studied and used in the synthesis of numerous alkaloids. Their importance as precursors to many biologically active compounds have focussed a tremendous amount of attention on developing methods to functionalise these systems. The synthesis of nitrogen heterocycles and their derivatives occupy an important place in the realm of natural and synthetic organic chemistry due to their therapeutic and pharmacological properties. They have emerged as integral backbones of over seven thousand existing drugs.[2-4] In addition to these important biological applications nitrogen heterocycles are ideal scaffolds for making libraries of drug like compounds and to generate libraries of inhibitors of HIV-1 protease.[5-7]

Heterocyclic compounds are very widely distributed in nature and are essential to life. They play a vital role in the metabolism of all living cells. The pyrimidine and purine bases of DNA, essential amino acids, proline, histidine, tryptophan, the vitamin and co-enzyme precursors thyamine,

riboflavin, pyridoxin, folic acids, the B_{12} and E families of vitamin, the photosynthesizing pigment chlorophyll, the oxygen transporting pigment, haemoglobin and its breakdown products, the bile pigments are heterocyclic compounds. Majority of synthetic heterocycles have found widespread, use as anticancer agents, analgesics, hypnotics, pesticides, weedicides and rodenticides. There are also a large number of synthetic heterocycles with other practical applications as dyestuffs, co-polymers, solvents, photographic sensitisers, developers, antioxidants, and vulcanisation accelerators in rubber industry.

Debus prepared the parent compound imidazole from glyoxal and ammonia and to indicate its source proposed the name 'glyoxaline'. The name imidazoles is due to Hantzsch. The first chemical study of imdiazole was carried out by Wyss who substantiated the work of Debus. The heterocyclic compounds studied and presented in this thesis belong to imidazolinones **(I)**.



I

This compound can be prepared by the reaction between glycine ethyl ester and imidic acid ester. During this reaction condensation of aldehydes and ketones with **I** gives the corresponding 4-Arylidene, or Alkylidene-2-imidazolin-5-ones.

These compounds can also be prepared from the corresponding azlactones by reaction with ammonia or amines followed by cyclisation. The active methylene group of **(I)** can undergo double Michael addition with divinyl ketones giving the corresponding spiro compounds. Imdiazolinone **I** can further react with another molecule of imidic acid ester to give amino imidazolinones.

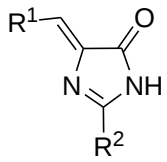
In the present work 2,4-disubstituted imidazolinones with pyridyl group at position 2 were synthesised and is discussed in Chapter I. Spiro imidazolinones containing pyridyl group were also synthesised and is given in chapter II. Synthesis of amino imidazolinones and their properties are discussed in chapter III. Chapter IV deals with the corrosion inhibiting property of the amino imidazolinones and the antimicrobial properties of the imidazolinones synthesised are discussed in chapter V.

REVIEW

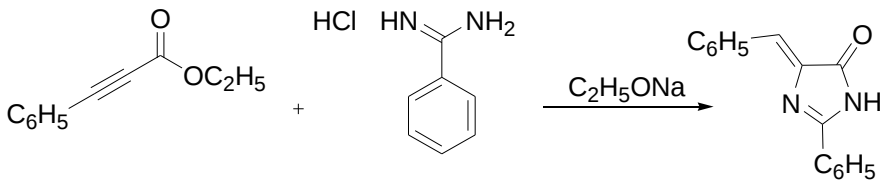
The work presented in this thesis deals with the synthesis and properties of 2-imidazolin-5-ones. As a background to these investigations a critical survey of the literature on the synthesis of 2-imidazolin-5-ones is quite appropriate. The following review so prepared deals with synthesis of 2,4-disubstituted imidazolin-5-ones.

Synthesis of Unsaturated 2-Imidazolin-5-ones

Imdiazolinones with an exocyclic double bond at the 4th position is usually called unsaturated 2,4-disubtituted 2-imidazolin-5-ones. They are also known as unsaturated 2,4-disubstituted 5(4H)-imidazolones and unsaturated 2,4-disubstituted 5-ketodihydro glyoxalines. They are usually called unsaturated 2-imidazolin-5-ones for convenience.



The synthesis of unsaturated 2-imidazolin-5-one was first reported in 1899 by Ruheman and Cunnington.[8,9] They synthesised 2-phenyl-4-benzylidene-2-imidazolin-5-one by condensing phenylpropiolic ester with benzamidine hydrochloride in presence of sodium ethoxide. But no other unsaturated 2-imidazolin-5-one have been prepared by this method.

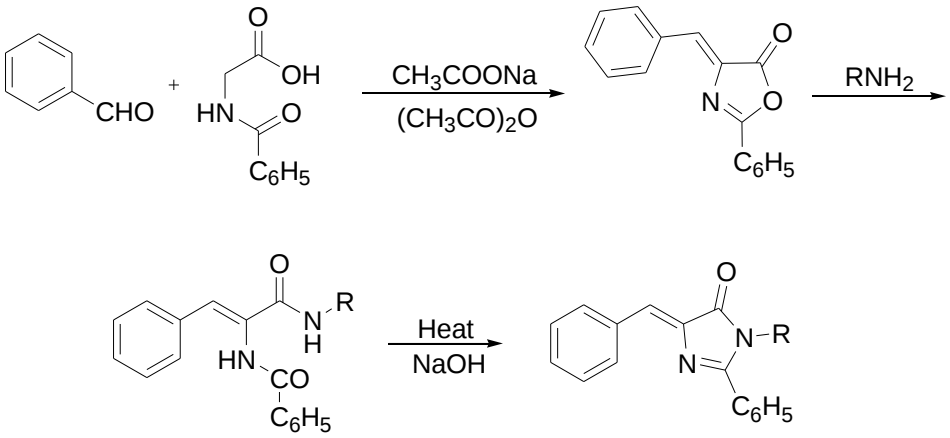


At present there are four general methods for the synthesis of unsaturated 2-imidazolin-5-ones namely azlactone, imidine-glyoxal, imidic acid ester-glycine ester and amidine-haloacetic ester method.

Azlactone method

Azlactones may be considered as anhydrides of alpha-acylamino acids. Erlenmeyer[10-18] prepared 2-phenyl-4-arylidene-2-imidazolin-5-ones starting from azlactone. On heating a mixture of benzaldehyde and hippuric acid in presence of fused sodium acetate and acetic anhydride, the azlactone of alpha benzoylaminocinnamic acid is formed. This azlactone readily affords alpha benzoylaminocinnamic acid amide on heating with conc.ammonia in presence of alcohol. The amide then cyclises to give 2-phenyl-4-benzylidine-2-imidazolin-5-ones, under the influence of hot dilute sodium hydroxide solution.

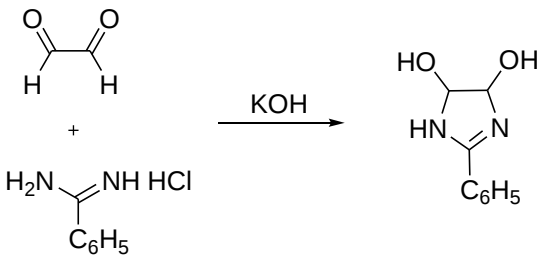
The method was further extended by various workers[19-30] to synthesise 1,2,4-trisubstituted-2-imidazolin-5-ones.



(R= H, alkyl, aryl, etc.)

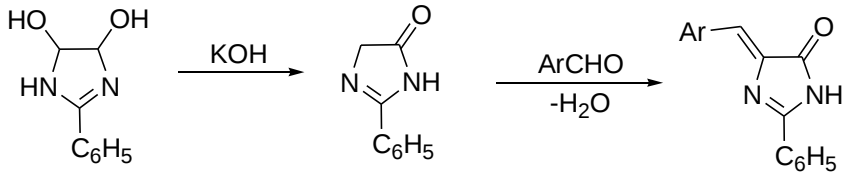
Amidine-Glyoxal method

In 1935 Ekeley and Ronzio[31] developed a method for the synthesis of 2-aryl-4-arylidene-2-imidazolin-5-one by condensing aromatic aldehydes with aromatic amidine-glyoxal addition products. Actually they thought that the condensation products obtained were either diarylpyrimidones or 2-aryl-4-aroylglyoxalones. For example on treating a mixture of glyoxal and benzamidine hydrochloride with potassium hydroxide, a labile basic substance is formed. It may be represented either as an open chain compound or preferably as a 2-phenyl-4,5-dihydroxy-2-imidazoline.



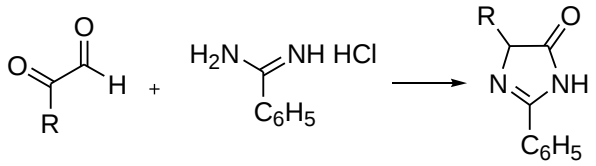
On condensing aromatic aldehydes with this substance in the presence of NaOH or KOH good yields of 2-phenyl-4-arylidene-2-imidazolin-5-ones are obtained. The reaction may be formulated in the manner illustrated below using the more possible 4,5-dihydroxy-2-imidazoline structure for the benzamidine-glyoxal complex. It is assumed that the dihydroxyimidazoline loses one molecule of water under the influence of the base to form 2-phenyl-2-imidazolin-5-one containing a highly active methylene group.

The 2-phenyl-2-imidazolin-5-one thus formed readily undergoes condensation with the aldehyde to give the final product.



Ekeley and co-workers[31,32] prepared numerous 2-aryl-4-arylidene-2-imidazolin-5-ones by this method using addition product of glyoxal with different aromatic amidines like benzamidine, p-toluamidine, m-toluamidine, etc.

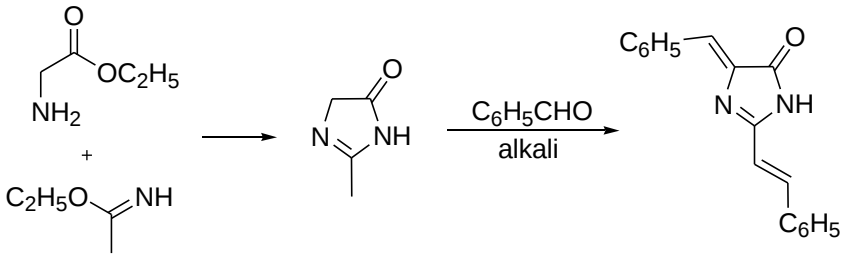
In 1948 Cornforth[33,34] prepared 5-imidazolones by the reaction between benzamidine hydrochloride and monosubstituted glyoxals.



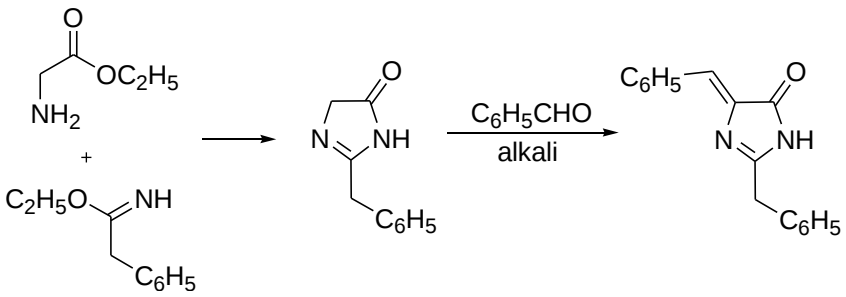
The 4(5)-imidazolones which have a methylene group adjacent to the carbonyl group form benzylidene derivatives and also couple with diazonium salts.

Imidic acid ester – Glycine ester method

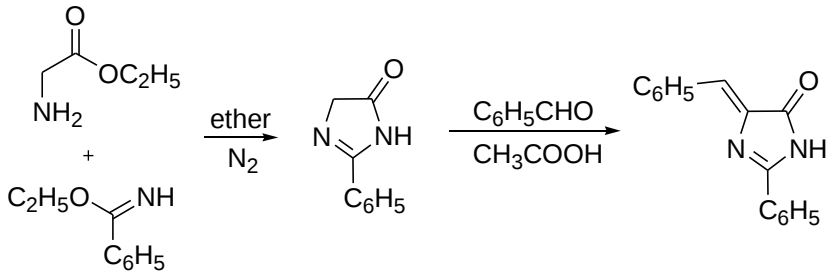
In 1907 Finger[35] obtained 2-methyl-2-imidazolin-5-one by condensing glycine ester with acetimidic acid ester at room temperature. The 2-methyl-2-imidazolin-5-one condensed with two molecules of benzaldehyde to form 2-benzylidene-methyl-4-benzylidene-2-imidazolin-5-one.



Finger and Zeh[36] prepared 2-benzyl-2-imidazolin-5-one by condensing phenylacetimidic ester and glycine ester. This imidazolone condenses with benzaldehyde in presence of alkali to give 2-benzyl-4-benzylidene-2-imidazoline-5-ones.

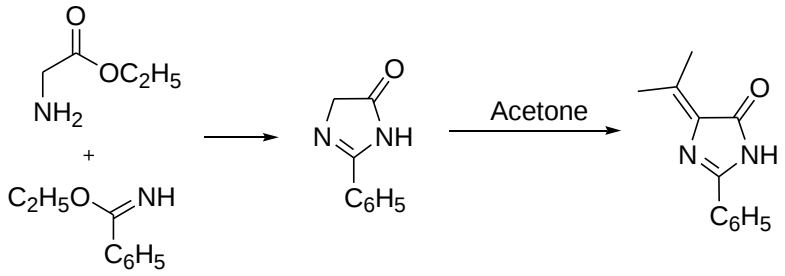


In 1953 Kjaer[37] prepared 2-phenyl-2-imidazolin-5-ones in 18.8% yield by condensing benzimidic acid ester with glycine ester in presence of anhydrous ether in nitrogen atmosphere. The product was recrystallised from benzene in an oxygen free atmosphere followed by sublimation. He obtained 2-phenyl-4-benzylidene-2-imidazolin-5-one by condensing benzaldehyde with 2-phenyl-2-imidazolin-5-one.



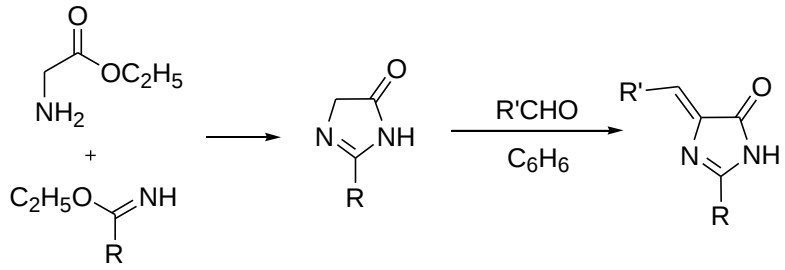
1-Naphthaldehyde, furfuraldehyde, isatin and pyruvic acid were also condensed with 2-phenyl-2-imidazolin-5-one and obtained the corresponding unsaturated 2-imidazolin-5-ons.

In 1953 Lehr and coworkers[38] obtained 2-substituted 4-isopropylidene-2-imdiazolin-5-ones instead of the expected 2-substituted 2-imidazolin-5-ones when imidic acid esters were condensed with glycine ester using acetone as solvent. Glycine ester and imidic acid ester first condense to form 2-substituted 2-imidazolin-5-one which in turn reacts with acetone to form 2-substituted-4-isopropylidene-2-imidazolin-5-one.

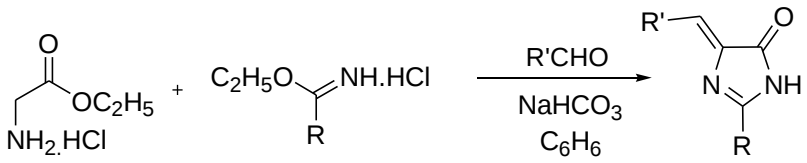


Lehr and coworkers[38] prepared a large number of unsaturated 2-imidazolin-5-ones by refluxing aliphatic and aromatic ketones, acetoacetic ester, levulinic ester and acetophenone with a mixture of imidic acid ester and glycine ester. Benzene was used as solvent in the case of high boiling ketones while in the case of low boiling ketones excess of ketones themselves were the solvents. The structure of these compounds were confirmed by synthesising one of them namely 2-benzyl-4-cyclohexylidene-2-imidazolin-5-one by the simultaneous reaction of phenylacetimidic acid ester, glycine ester and cyclohexanone and also by the condensation of the preformed 2-benzyl-2-imidazolin-5-one with cyclohexanone.

In 1962 Kidwai and Devasia[39] prepared a number of unsaturated 2-imdiazolin-5-ones by condensing aldehydes (aromatic aldehydes and isobutyraldehyde) with a mixture of an imidic acid ester and glycine ester in the presence of benzene at room temperature. When benzimidic acid ester was used they obtained very high yields of 2-phenyl-4-arylidene-2-imidazolin-5-ones. Phenylacetimidic acid ester and acetimidic acid ester are other imidic acid esters used by them.

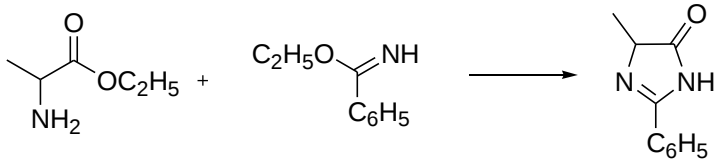


They further improved this method by condensing aromatic aldehydes directly with a mixture of the hydrochlorides of an imidic acid ester and glycine ester in presence of sodium bicarbonate in benzene at 72°C. Thus they prepared a few 2-phenyl-4-arylidene-2-imidazolin-5-ones in very high yields.



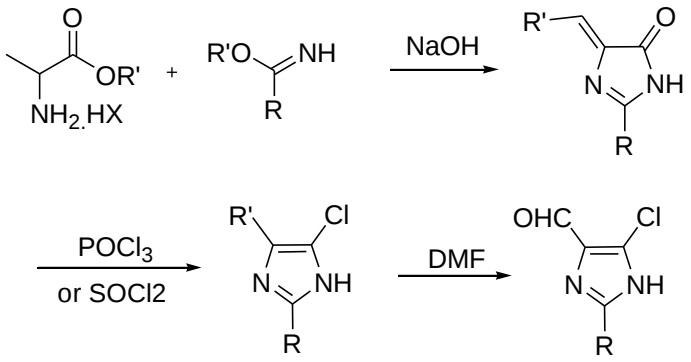
In 1975 Devasia and Pillai[40] prepared a few 2-phenyl-4-arylidene-2-imidazolin-5-ones employing the above methods of Kidwai and Devasia.

It is relevant to mention here that saturated 2,4-disubstituted-2-imidazolin-5-ones were prepared by condensing benzimidic acid ester with amino acid esters.[41]



Imidazolinones having hypotensive activity were synthesised[42] by cyclocondensation of various imidic acid esters with glycine ethyl ester.

In 1994 Griffiths and coworkers[43] prepared imidazolones by the cyclocondensation of glycine ester hydrochloride (eg., glycine methyl ester hydrochloride) with imidic ester (e.g., pentanimidic acid methyl ester) in presence of base (e.g., sodium hydroxide). These imdiazolones were chlorinated with phosphorus oxychloride or through chloride to get their chloroderivatives which on treatment with DMF and $POCl_3$ yielded their formyl derivatives.

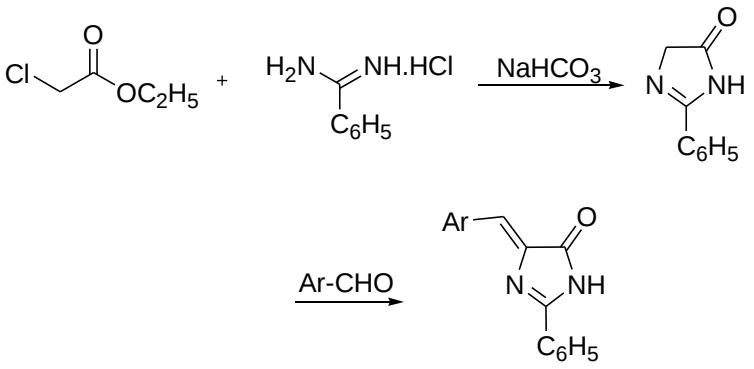


These compounds are useful as pharmaceuticals and agrochemicals.

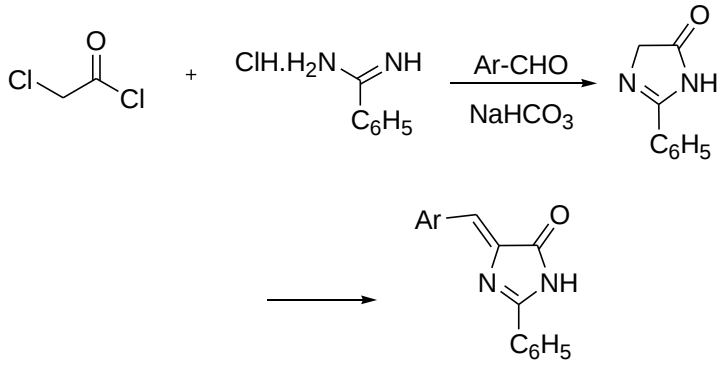
Amidine-Haloacetic Ester method

In 1976 Devasia[44] developed the amidine-chloroacetic ester method for the synthesis of unsaturated 2-imidazolin-5-ones. He obtained moderately good yields of 2-phenyl-4-arylidene-2-imidazolin-5-ones by condensing aromatic aldehydes with a mixture of benzamidine hydrochloride and ethyl

chloroacetate in the presence of sodium bicarbonate in n-propanol at reflux temperature. As in the cases of amidine-glycerol and imidic acid ester-glycine ester methods, 2-phenyl-2-imidazolin-5-one with a highly active methylene group may be formed as intermediate and the aldehyde condense with it to form the final product.

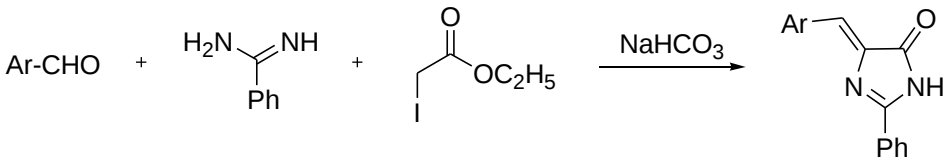


Devasia and Shafi[45] synthesised 4-arylidene-2-phenyl-2-imidazolin-5-ones by condensing aroamtic aldehydes with a mixture of chloroacetyl chloride and benzamidine in presence of sodium bicarbonate.



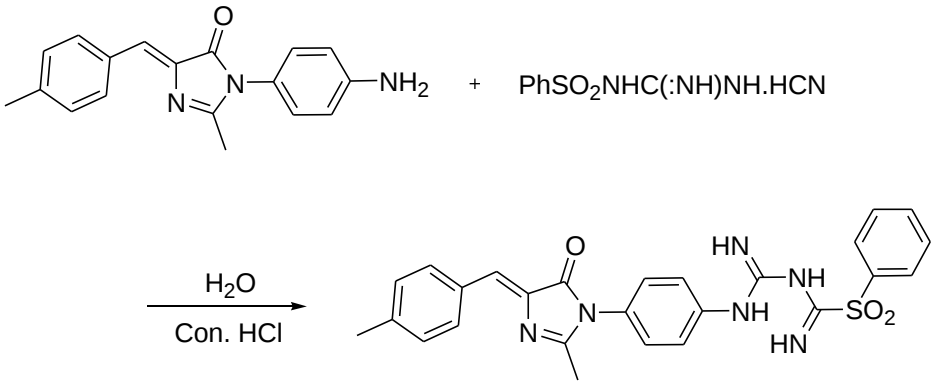
Devasia and Shafi[46] prepared a large number of unsaturated 2,4-disubstituted 2-imidazolin-5-ones employing the known amidine-haloacetic ester method.

In 1985 Shafi[47] prepared 2-aryl-4-arylidene-2-imidazolin-5-ones in quantitative yield by condensing aromatic aldehydes with benzamidine and ethyl iodoacetate in presence of sodium bicarbonate.

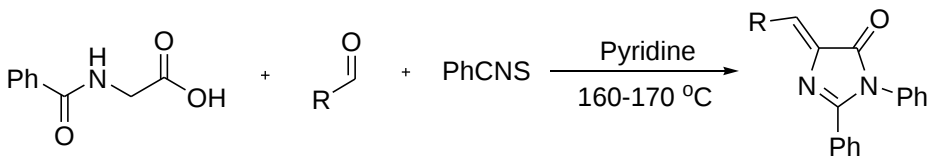


Other Methods

Husain and coworkers[48] synthesised new imidazolinones by heating amine with $PhSO_2NHC(:NH)NHHCN$, water and concentrated hydrochloric acid at 130-140°C.

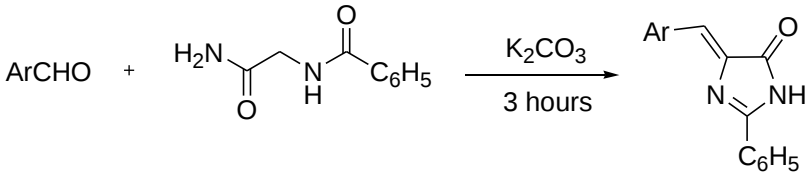


In 1985 Ashare and coworkers[49] synthesised 4-(arylmethylene)-1,2-diphenyl-2-imidazolin-5-ones by the reaction between hippuric acid, phenyl isothiocyanate and aromatic aldehydes.



In 1991 Saxena and coworkers[50] prepared novel imidazole congeners as antiinflammatory agents. A number of furylmethylene imidazolone derivatives were prepared from furfuraldehyde and aroyl glycine via Mannich or cyclisation reactions of intermediate imidazolones and tested their anti-inflammatory activity. It was found that they were strongly active.

In 1999 Sobha and Shafi[51] synthesised 2-imidazolin-5-ones by heating benzoylglycine amide and aromatic aldehyde with saturated aqueous potassium carbonate solution for 3 hrs. They got 2-imidazolin-5-ones in 44-60% yields.



Shafi and Basheer[52] synthesised novel spiro imidazolinones from divinyl ketone, glycine ethyl from ester and benzimidic acid methyl ester. The reaction is carried out in presence of pyridine.

CHAPTER 1

SYNTHESIS OF 4-ARYLIDENE(ALKYLIDENE)-2-PYRIDYL-2-IMIDAZOLIN-5-ONES

Introduction

Imidazolinones are found to have several pharmacological activities.[53-56] The benzylidene imidazolinone chemistry with its diverse biological properties like central nervous system depressant,[57] anticonvulsant[58] and monoamine oxidase inhibitor[54] has received importance in recent years. In this chapter the synthesis of some new imidazolinones with a pyridyl moiety at position 2 is presented. Due to the introduction of a pyridyl group in the compound, better biological activity is expected.

Results and Discussion

In the present work 0.02 mol of cyanopyridines (2-cyanopyridine, 3-cyanopyridine and 4-cyanopyridine) were converted into the corresponding imidic ester in presence of methanol and sodium methoxide. The imidic ester formed were then refluxed with glycine ethylester hydrochloride (0.02 mol) sodium bicarbonate and aromatic aldehyde (ketone) (0.0198 mol) for half an hour.

If the ketone was not a low boiling one, then 10 ml benzene was also added to the reaction mixture to act as a solvent. If the ketone was low boiling, excess ketone itself acts as the solvent. Six aldehydes and two ketones were thus condensed with the imidic esters of all the three cyanopyridines to get a total number of twenty four 4-arylidene-2-pyridyl-2-imidazolin-5-ones in 70-85% yields (Table 1).

All the compounds given in Table 1 are reported for the first time.

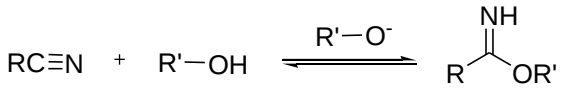
TABLE 1

4-(Arylidine, alkylidene, cycloalkylidene)-2-pyridyl-2-imidazolin-5-ones

	Name	M.P. ^{o}C	Yield (%)	ν_{CO} (cm^{-1})	λ_{max} (nm)
1	4-Benzylidene-2-(2-pyridyl)-2-imidazolin-5-one	182	72	1706	378
2	4-Benzylidene-2-(3-pyridyl)-2-imidazolin-5-one	220	78	1705	377.8
3	4-Benzylidene-2-(4-pyridyl)-2-imidazolin-5-one	244	82	1704	378.2
4	4-(p-methoxybenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one	210	72	1720	401
5	4-(p-methoxybenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one	229	83	1715	401
6	4-(p-methoxybenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one	259	85	1719	409
7	4-(p-methylbenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one	217	76	1709	386.8
8	4-(p-methylbenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one	271	78	1703	384.8
9	4-(p-methylbenzylidene)-2-(4-	261	70	1697	389.6

	Name	M.P. °C	Yield (%)	ν_{CO} (cm^{-1})	λ_{max} (nm)
	pyridyl)-2-imidazolin-5-one				
10	4-(p-chlorobenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one	240	75	1708	383.4
11	4-(p-chlorobenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one	276	80	1704	384.4
12	4-(p-chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one	269	75	1709	387.2
13	4-(o-chlorobenzylidene-2-(2-pyridyl)-2-imidazolin-5-one	242	70	1714	386.4
14	4-(o-chlorbenzlidene)-2-(3-pyridyl)-2-imidazolin-5-one	235	75	1718	383.6
15	4-(o-chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one	266	79	1711	387.2
16	4-(o-hydroxybenzylidene)-2-(2-pyridyl)-2-imidazlin-5-one	249	77	1698	412.6
17	4-(o-hydroxybenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one	270	73	1702	413.6
18	4-(o-hydroxybenzylidene-2-(4-pyridyl)-2-imidazolin-5-one	258	71	1701	421
19	4-(isopropylidene)-2-(2-pyridyl)-2-imidazolin-5-one	172	76	1719	327.2
20	4-(isopropylidene)-2-(3-pyridyl)-2-imidazolin-5-one	196	81	1717	328
21	4-(isopropylidene)-2-(4-pyridyl)-2-imidazolin-5-one	200	86	1713	3368
22	4-(cyclohexylidene)-2-(2-pyridyl)-2-imidazolin-5-one	158	80	1716	332
23	4-(cyclohexylidene)-2-(3-pyridyl)-2-imidazolin-5-one	175	74	1710	329.6
24	4-(cyclohexylidene)-2-(4-pyridyl)-2-imidazolin-5-one	212	80	1704	336.8

We tried to prepare imidic acid ester hydrochlorides of cyanopyridines according to the method suggested by Pinner[59] and improved by others.[60-62] But this method was a failure in the case of cyanopyridines because the cyanopyridines got precipitated as cyanopyridine hydrochlorides on passage of HCl gas. Therefore the preparation of imidic acid ester was carried out following the method suggested by Fred and Grace.[63] They suggested a synthetic method which is useful for a wide variety of electronegatively substituted aliphatic and aromatic nitriles for the preparation of imidic ester. In this method imidic ester is formed by the base catalysed addition of alcohols to nitriles.



The identity of the compounds prepared were confirmed by spectral and elemental analysis. The mass spectrum and H' NMR spectrum of one of the compounds 4-benzylidene-2-(2-pyridyl)-2-imidazolin-5-one was recorded. The structure was arrived at as follows:

The mass spectrum has M^+ peak at 249 corresponding to the proposed structure. The odd mass justified the presence of three nitrogen atoms. Other important peaks in the mass spectrum were at m/z = 117, 105, 89 and 78 which further supported the proposed structure.

The ^1H NMR spectrum also supported this structure. It showed

absorptions due to nine aromatic protons (protons of phenyl ring and pyridyl ring) and the methine proton in the region δ 7.1 to 8.7. The –NH proton of the imidazolinone ring at δ 12.09.

The uv-visible spectra of these compounds showed an absorption maximum in the range 327-421 nm. This is attributed to the n → π* transitions of the carbonyl group perturbed by intramolecular charge-transfer from arylidene residue to the polarised carbonyl group.[64] All the substituents in the arylidene ring was found to produce a red shift.

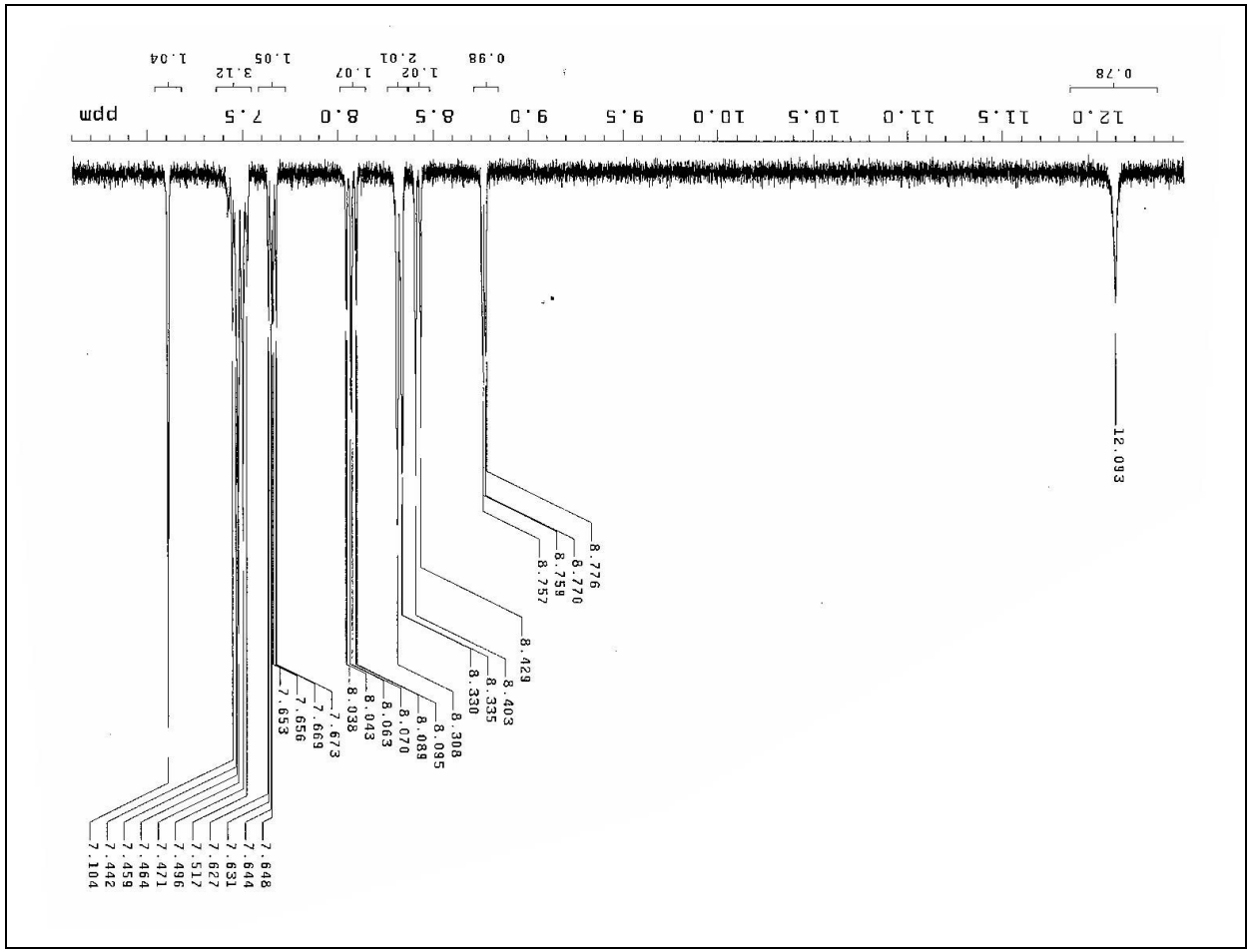
The important bands observed in the infrared spectra of 4-arylidene-2-pyridyl-2-imidazolin-5-ones are due to the C=O, C=N, C=C and N–H vibrations. The imidazolinones are similar to cyclic five membered lactams. The carbonyl group is in conjugation with the exocyclic double bond extends the conjugation to the aromatic ring of the arylidene group. The carbonyl absorption frequencies of the 24 compounds synthesised fall in the range 1697 to 1720 cm^{-1}. These compounds are comparable to five membered cyclic lactams which have a carbonyl absorption frequency 1700-1750 cm^{-1}.[65]

The C=N stretching absorption frequency ranged between 1633 to 1648 cm^{-1}. It is known that C=N absorption frequency is 1640 cm^{-1} in compounds where this bond is conjugated with C=C bond.[66]

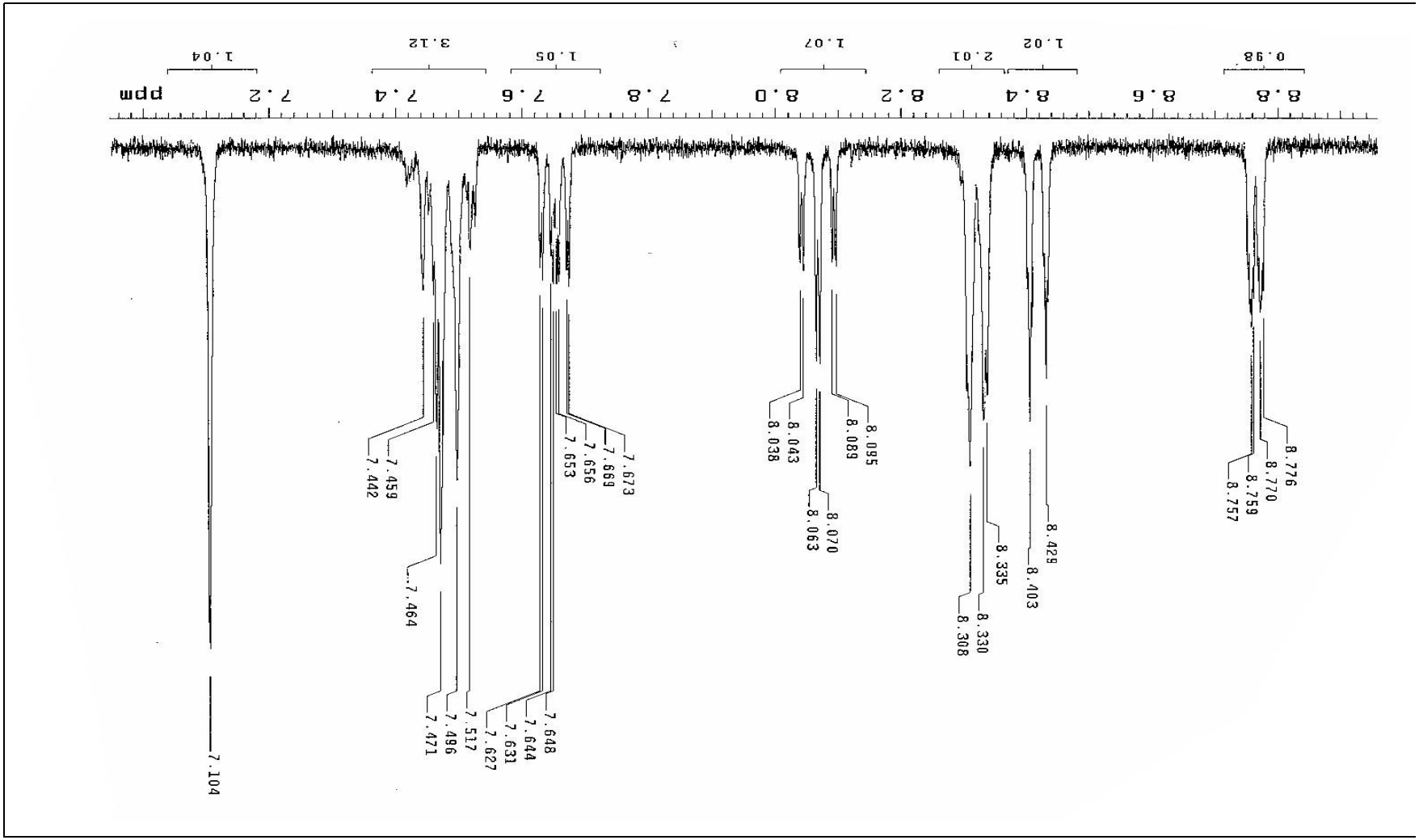
The N–H stretching absorption is appearing at a group of slightly broad, medium intensity peaks in the regions 3049-3157 cm^{-1}.

Mass spectrum of 4-Benzylidene-2-(2-pyridyl)-2-imidazolin-5-one

^{1}H NMR spectrum of 4-Benzylidene-2-(2-pyridyl)-2-imidazolin-5-one

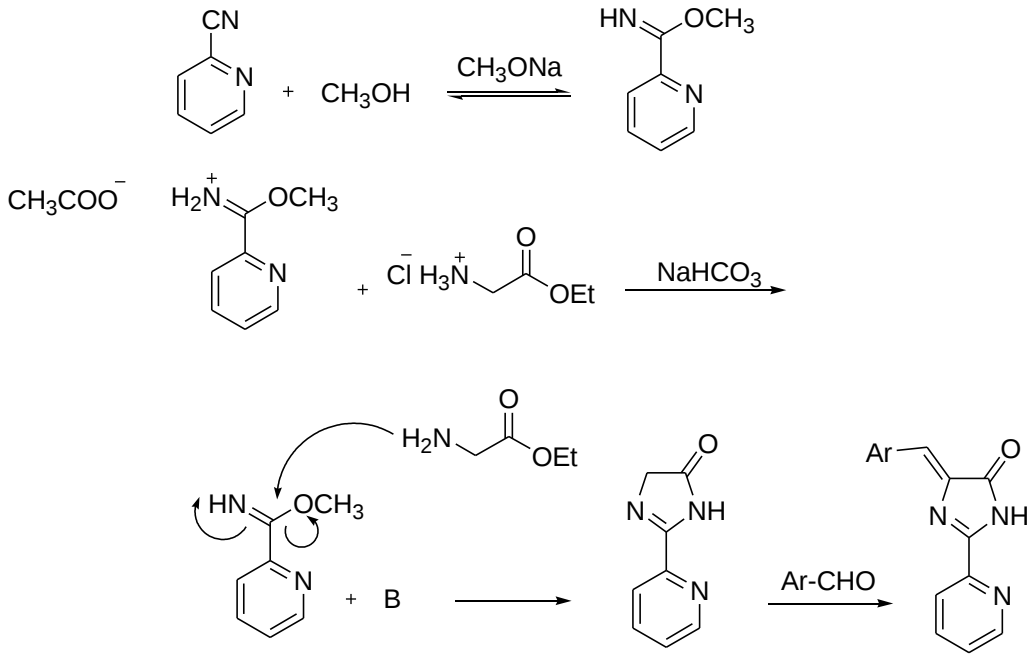


^{1}H NMR spectrum of 4-Benzylidene-2-(2-pyridyl)-2-imidazolin-5-one (expanded)



Once the structure of the compound was established the following mechanism could be proposed for its formation.

Mechanism



This type of compounds with phenyl/substituted phenyl/alkyl groups at 2nd position gave acylamino acids on reduction and hydrolysis.[67-69] We expected a similar reaction in our compounds. But we didn't get the acylamino acids. This may be due to the presence of pyridyl group which make the carbonyl carbon more electronegative leading to further hydrolysis to give amino acids instead of acyl amino acids.

Experimental

Melting points recorded on Toshniwal capillary melting point apparatus are uncorrected. Uv-vis spectra were recorded in ethanol on a

Shimadzu 1601 UV-visible spectrometer. IR spectra were recorded as KBr pellets using Shimadzu 8101A FTIR equipment. The mass spectrum was recorded on Finnigan MAT 8200 spectrometer. The ^{1}H NMR spectrum were recorded on unity plus 300 varian spectrometer using TMS as internal standard.

Synthesis of starting materials

Glycine ethyl ester hydrochloride

Glycine ethyl ester hydrochloride was prepared according to the method developed by Curtius and Geoble[70] and improved by others.[39,71,72]

In a 2 litre round bottomed flask with ground glass joint was placed a mixture of glycine (75 g, 1 mol) and absolute ethanol (750 ml) and the flask was filled with a rubber cork carrying an inlet tube and a calcium chloride guard tube. HCl dried by bubbling through concentrated sulphuric acid was passed into the mixture till 100 g (2.7 mol) of the gas was absorbed. The flask was fitted with a reflux condenser carrying a calcium chloride guard tube and the mixture was heated under reflux. The glycine completely went into solution within about 30 minutes.

After a total refluxing of two hours the flask was allowed to cool and the solution was transferred into a 1000 ml conical flask for the sake of convenience. The solution was seeded to induce crystallisation. When a lot

of glycine ethyl ester hydrochloride crystals separated. The flask was tightly stoppered and placed in the refrigerator overnight to effect complete crystallisation of the product. The crystals were quickly filtered on a large Buchner funnel, washed with two 50 ml portions of ice cold absolute ethanol and dried in the oven at 80°C for one hour. The colourless glycine ethyl ester hydrochloride weighed 118 g (84%) and melted at 144-146°C. Kidwai and Devasia reported m.p. 144-145°C for this compound.[39]

Synthesis of imidazolinones

4-Benzylidene-2-(2-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyidine (2.3 ml, 0.02 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Benzaldehyde (2 ml, 0.0196 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-benzylidene-2-(2-pyridyl)-2-imidazolin-5-one formed was filtered, washed twice with water and then with 10 ml of ethanol and dried. The yellow product weighed 3.5 g (72%) and melted at 179°C. The 4-benzylidene-2-(2-pyridyl)-2-imidazolin-5-

one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 182°C.

Analysis

	N%	C%	H%
Found	16.68	71.74	4.47
Calculated	16.86	72.28	4.41

$C_{15}H_{11}N_3O$

IR ν (cm^{-1}) = 3172, 1706, 1641, 1567, 1534, 1517

Uv-vis λ_{max} = 378 nm

4-Benzylidene-2-(3-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 3-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.021 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Benzaldehyde (2 ml, 0.0196 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-benzylidene-2-(3-pyridyl)-2-imidazolin-5-one formed was filtered. Washed twice with water

and then with 10 ml of ethanol and dried. The yellow product weighed 3.8 g (78%) and melted at 218°C.

4-Benzylidene-2-(3-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 220°C.

Analysis

	N%	C%	H%
Found	16.58	72.43	4.36
Calculated	16.86	72.28	4.41

$C_{15}H_{11}N_3O$

IR ν (cm^{-1}) = 3061, 1705, 1643, 1592, 1536

Uv-vis λ_{max} = 377.8 nm

4-Benzylidene-2-(4-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 4-Cyanopyridine 2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Benzaldehyde (2 ml, 0.0196 mol) and benzene (5 ml) were also added to the round bottomed flask

and refluxed for half an hour. Yellow crystals of 4-benzylidene-2-(4-pyridyl)-2-imidazolin-5-one formed was filtered. Washed twice with water and then with 10 ml of ethanol and dried. The yellow product weighed 4 g (82%) and melted at 242ºC.

4-Benzylidene-2-(4-pyridyl)-2-imidazolin-5-one (0.5g) was recrystallised from ethanol (50 ml). The crysgtallised product melted at 244ºC.

Analysis

	N%	C%	H%
Found	16.88	71.86	4.39
Calculated	16.86	72.28	4.41

$C_{15}H_{11}N_3O$

IR ν (cm^{-1}) = 3138, 1704, 1645, 1588, 1537

Uv-vis λ_{max} = 378.2 nm

4-(p-methoxybenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (2.3 ml, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask.

p-Methoxybenzaldehyde (2.7 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-methoxybenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one formed was filtered and washed twice with water and then with 10 ml of ethanol and dried. The yellow product weighed 4 g (72%) and melted at 208°C.

The 4-(p-methoxybenzylidene)-2-2-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 210°C.

Analysis

	N%	C%	H%
Found	15.02	68.83	4.69
Calculated	15.05	68.81	4.66

$C_{16}H_{13}N_3O_2$

IR ν (cm^{-1}) = 3188, 1720, 1643, 1600, 1566, 1536, 1512

Uv-vis λ_{max} = 401 nm

4-(p-methoxybenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 3-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl

alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Methoxybenzaldehyde (2.7 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-methoxybenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one formed was filtered. Washed twice with water and then with 10 ml of ethanol and dried. The yellow product weighed 4.6 g (85%) and melted at 228°C.

The 4-(p-methoxybenzalidene)-2-(3-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 229°C.

Analysis

	N%	C%	H%
Found	15.08	68.32	4.72
Calculated	15.05	68.81	4.66

$C_{16}H_{13}N_3O_2$

IR ν (cm^{-1}) = 3134, 1715, 1638, 1602, 1512

Uv-vis λ_{max} = 401 nm

4-(p-methoxybenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one

One gram sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 4-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml)

was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Methoxybenzaldehyde (2.7 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-methoxybenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one formed were filtered and washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 4.7 g (85%) and melted at 256°C. The 4-(p-methoxybenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 259°C.

Analysis

	N%	C%	H%
Found	15.1	68.96	4.92
Calculated	15.05	68.81	4.66

$C_{16}H_{13}N_3O_2$

IR ν (cm^{-1}) = 3154, 1719, 1694, 1633, 1650, 1593, 1540, 1509

Uv-vis λ_{max} = 409 nm

4-(p-Methylbenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one

One gram sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (2.3 ml, 0.021 mol) was

added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Methyl benzaldehyde (2.35 g, 0.0196 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-methoxybenzylidene)-2-(2-pyridyl)-2-imidazlin-5-one were filtered, washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 3.9 g (76%) and melted at 215°C. 4-(p-Methylbenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 217°C.

Analysis

	N%	C%	H%
Found	15.38	72.54	5.49
Calculated	15.86	73.00	5.32

$C_{16}H_{13}N_3O$

IR ν (cm^{-1}) = 3176, 1709, 1643, 1603, 1566, 1537

Uv-vis λ_{max} = 386.8 nm

4-(p-Methylbenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one

One gram sodium metal was dissolved in 15 ml absolute methanol in a

100 ml round bottomed flask. 3-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydochloide (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Methyl benzladehyde (2.35 g, 0.0196 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-methylbenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one were filtered, washed twice with water and then with 10 methanol and dried. The yellow product weighed 4 g (78%) and melted at 270°C.

4-(p-Methylbenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 271°C.

Analysis

	N%	C%	H%
Found	15.48	72.73	5.59
Calculated	15.86	73.00	5.86

$C_{16}H_{13}N_3O$

IR ν (cm^{-1}) = 3160, 1703, 1638, 1603, 1589, 1533

Uv-vis λ_{max} = 384.8 nm

4-(p-Methylbenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 4-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Methylbenzoaldehyde (2.35 g, 0.0196 mol) and benzene (5 ml) were also added to the round bottomed flaks and refluxed for half an hour. Yellow crystals of 4-(p-methylbenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 3.6 g (70%) and melted at 258°C.

The 4-(p-methylbenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 261°C.

Analysis

	N%	C%	H%
Found	15.73	73.11	5.59
Calculated	15.86	73.00	5.86

$C_{16}H_{13}N_3O$

IR ν (cm^{-1}) = 3157, 1697, 1644, 1594, 1568

Uv-vis λ_{max} = 389.6 nm

4-(p-Chlorobenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (2.3 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Chlorobenzaldehyde (2.8 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-chlorobenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 4.2 g (75%) and melted at 238°C.

The 4-(p-chlorobenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 240°C.

Analysis

	N%	C%	H%
Found	14.29	63.28	3.46
Calculated	14.81	63.49	3.52

$C_{15}H_{10}N_3OCl$

IR ν (cm^{-1}) = 3187, 1708, 1643, 1586

Uv-vis λ_{max} = 383.4 nm

4-(p-Chlorobenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 3-Cyanopyridine (2.3 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Chlorobenzaldehyde (2.8 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-chlorobenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one (0.5 g) formed was filtered. Washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 4.5 g (80%) and melted at 275°C.

The 4-(p-chlorobenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 276°C.

Analysis

	N%	C%	H%
Found	14.74	63.20	3.48
Calculated	14.81	63.49	3.52

$C_{15}H_{10}N_3ClO$

IR ν (cm^{-1}) = 3112, 1704, 1640, 1597

Uv-vis λ_{max} = 384.4 nm

4-(p-Chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 4-Cyanopyridine (2.3 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. p-Chlorobenzaldehyde (2.8 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(p-chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 4.2 g (75%) and melted at 267°C.

The 4-(p-chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 269°C.

Analysis

	N%	C%	H%
Found	14.67	63.78	3.68
Calculated	14.81	63.49	3.52

$C_{15}H_{10}N_3OCl$

IR ν (cm^{-1}) = 3137, 1709, 1644, 1585

Uv-vis λ_{max} = 387.2 nm

4-(o-Chlorobenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (2.3 ml, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added to the round bottomed flask and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. o-Chlorobenzaldehyde (2.8 g, 0.198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(o-chlorobenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one formed were filtered, washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 3.9 g (70%) and melted at 241°C.

The 4-(o-chlorobenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 242°C.

Analysis

	N%	C%	H%
Found	14.63	63.87	3.67
Calculated	14.81	63.49	3.52

$C_{15}H_{10}N_3OCl$

IR ν (cm^{-1}) = 3144, 1714, 1638, 1592, 1570

Uv-vis λ_{max} = 386.6 nm

4-(o-Chlorobenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 3-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added to the round bottomed flask and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. o-Chlorobenzaldehyde (2.8 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(o-chlorobenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one formed were filtered, washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 4.2 g (75%) and melted at 233 ^{o}C.

The 4-(o-chlorobenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 235 ^{o}C.

Analysis

	N%	C%	H%
Found	14.96	63.66	3.78
Calculated	14.81	63.49	3.52

$C_{15}H_{10}N_3OCl$

IR ν (cm^{-1}) = 3105, 1718, 1636, 1588, 1535

Uv-vis λ_{max} = 383.6 nm

4-(o-Chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 4-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added to the round bottomed flask and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. o-Chlorobenzaldehyde (2.8 g, 0.0198 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Yellow crystals of 4-(o-chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one formed were filtered, washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 4.4 g (79%) and melted at 265°C.

The 4-(o-chlorobenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml). The recrystallised product melted at 266°C.

Analysis

	N%	C%	H%
Found	14.56	63.84	3.39
Calculated	14.81	63.49	3.52

$C_{15}H_{10}N_3OCl$

IR ν (cm^{-1}) = 3092, 1711, 1636, 1600, 1532

Uv-vis λ_{max} = 387.2 nm

4-(o-Hydroxybenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one

One gram sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (2.3 ml, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. o-Hydroxybenzaldehyde (2.4 g, 0.0197 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. The yellow crystals of 4-(o-hydroxybenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 4 g (77%) and melted at 247ºC.

The 4-(o-hydroxybenzylidene)-2-(2-pyridyl)-2-imidazolin-5-one (0.5g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 249ºC.

Analysis

	N%	C%	H%
Found	15.63	67.93	4.26
Calculated	15.84	67.92	4.18

$C_{15}H_{11}N_3O_2$

IR ν (cm^{-1}) = 3136, 1698, 1636, 1611, 1586, 1576

Uv-vis λ_{max} = 412.6 nm

4-(o-Hydroxybenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 3-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added to the round bottomed flask and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the round bottomed flask. o-Hydroxybenzaldehyde (2.4 g, 0.0197 mol) and benzene (5 ml) were also added and refluxed for half an hour. The yellow crystals of 4-(o-hydroxybenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one formed were filtered, washed twice with water and then with 10 ml ethanol and dried. The yellow product weighed 3.5 g (73%) and melted at 267°C.

The 4-(o-hydroxybenzylidene)-2-(3-pyridyl)-2-imidazolin-5-one (0.5g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 270°C.

Analysis

	N%	C%	H%
Found	15.92	67.72	4.03
Calculated	15.84	67.92	4.18

$C_{15}H_{11}N_3O_2$

IR ν (cm^{-1}) = 3107, 3050, 1702, 1638, 1611, 1580

Uv-vis λ_{max} = 413.6 nm

4-(o-Hydroxybenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one

One gram sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 4-cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added to the round bottomed flask and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3. 5 g) were ground together and added to the imidate formed in the round bottomed flask. o-Hydroxy benzaldehyde (2.4 g, 0.0197 mol) and benzene (5 ml) were also added and refluxed for half an hour. The yellow crystals of 4-(o-hydroxybenzyloidene)-2-(4-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml methanol and dried. The yellow product weighed 3.7 g (71%) and melted at 256°C.

The 4-(o-hydroxybenzylidene)-2-(4-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 258°C.

Analysis

	N%	C%	H%
Found	15.58	67.73	4.24
Calculated	15.84	67.92	4.18

$C_{15}H_{11}N_3O_2$

IR ν (cm^{-1}) = 3049, 1701, 1642, 1602, 1542

Uv-vis λ_{max} = 421 nm

4-(isopropylidene)-2-(2-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml of absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (2.3 ml, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added to the round bottomed flask and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Acetone (1.14 g, 0.0196 mol) was also added to the round bottomed flask and refluxed for half an hour. The pale yellow crystals of 4-(isopropylidene)-2-(2-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The pale yellow product weighed 3g (76%) and melted at 170°C.

The 4-(isopropylidene)-2-(2-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 172°C.

Analysis

	N%	C%	H%
Found	20.68	65.48	5.62
Calculated	20.88	65.66	5.5

$C_{11}H_{11}N_3O$

IR ν (cm^{-1}) = 3150, 1719, 1653, 1597, 1517

Uv-vis λ_{max} = 327.2 nm

4-(Isopropylidene)-2-(3-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml of absolute methanol in a 100 ml round btotomed flask. 3-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Acetone (1.14 g, 0.0196 mol) was also added to the round bottomed flask and refluxed for half an hour. The pale yellow crystals of 4-(isopropylidene)-2-(3-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The pale yellow product weighed 3.2 g (81%) and melted at 195°C.

The 4-(isopropylidene)-2-(3-pyridyl)-2-imidazlin-5-one (0.5 g) was recrystallised from ethanol and the recrystallised product melted at 196°C.

Analysis

	N%	C%	H%
Found	20.81	65.81	5.59
Calculated	20.88	65.66	5.5

$C_{11}H_{11}N_3O$

IR ν (cm^{-1}) = 3142, 1717, 1639, 1576

Uv-vis λ_{max} = 328 nm

4-(Isopropylidene)-2-(4-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml of absolute methanol in a 100 ml round bottomed flask. 4-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added to the round bottomed flask and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imdiate formed in the round bottomed flask. Acetone (1.14 g, 0.0196 mol) was also added and refluxed for half an hour. The pale yellow crystals of 4-(isopropylidene)-2-(4-pyridyl)-2-imdiazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The pale yellow product weighed 3.4 g (86%) and melted at 198^{o}C.

The 4-(isopropylidene)-2-(4-pyridyl)-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 200^{o}C.

Analysis

	N%	C%	H%
Found	20.74	65.62	5.38
Calculated	20.88	65.66	5.5

$C_{11}H_{11}N_3O$

IR ν (cm^{-1}) = 3142, 1713, 1648, 1605, 1536

Uv-vis λ_{max} = 336.8 nm

4-(Cyclohexylidene)-2-(2-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml of absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (2.3 ml, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Cyclohexanone (1.92 g, 0.0196 mol) and benzene (5 ml) were also added to the round bottomed flask and refluxed for half an hour. Pale yellow crystals of 4-(cyclohexylidene)-2-(2-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The pale yellow product weighed 3.8 g (80%) and melted at 158°C.

The 4-(cyclohexylidene)-2-(2-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 160°C.

Analysis

	N%	C%	H%
Found	17.38	69.71	6.25
Calculated	17.41	69.69	6.27

$C_{14}H_{15}N_3O$

IR ν (cm^{-1}) = 3137, 1716, 1648, 1588, 1566

Uv-vis λ_{max} = 332 nm

4-(Cyclohexylidene)-2-(3-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml absolute methanol in a 100 ml round bottomed flask. 3-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Cyclohexanone (1.92 g, 0.0196 mol) and benzene (5 ml) were also added and refluxed for half an hour. Pale yellow crystals of 4-(cyclohexylidene)-2-(3-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The pale yellow product weighed 3.5 g (74%) and melted at 174°C.

The 4-(cyclohexylidene)-2-(3-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 175°C.

Analysis

	N%	C%	H%
Found	17.18	69.64	6.31
Calculated	17.41	69.69	6.27

$C_{14}H_{15}N_3O$

IR ν (cm^{-1}) = 3048, 1710, 1672, 1645, 1595

Uv-vis λ_{max} = 329.6 nm

4-(Cyclohexylidene)-2-(4-pyridyl)-2-imidazolin-5-one

One gram of sodium metal was dissolved in 15 ml of absolute methanol in a 100 ml round bottomed flask. 4-Cyanopyridine (2.2 g, 0.021 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Cyclohexanone (1.92 g, 0.0196 mol) and benzene (5 ml) were also added and refluxed for half an hour. Pale yellow crystals of 4-cyclohexylidene-2-(4-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with 10 ml ethanol and dried. The pale yellow product weighed 8.8 g (80%) and melted at 209°C.

The 4-cyclohexylidene-2-(4-pyridyl)-2-imidazolin-5-one (0.5 g) was recrystallised from ethanol (50 ml) and the recrystallised product melted at 212°C.

Analysis

	N%	C%	H%
Found	17.52	69.71	6.18
Calculated	17.41	69.69	6.27

$C_{14}H_{15}N_3O$

IR ν (cm^{-1}) = 3088, 1704, 1688, 1596

Uv-vis λ_{max} = 336.8 nm

CHAPTER 2

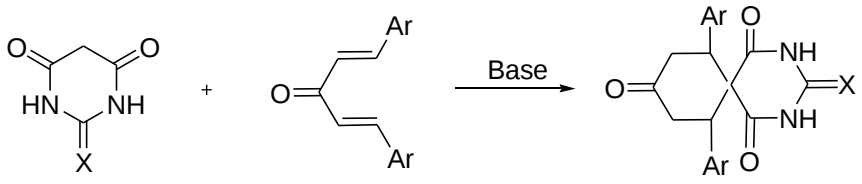
SYNTHESIS OF SPIRO IMIDAZOLINONES

Introduction

Spiro compounds are polycyclic compounds in which one carbon is a common member of two different rings. The spiro compounds containing imidazolinone rings are not many and has generated considerable interest in recent years due to their pharmacological activities. In the present work a new class of spiro compounds, spiro imidazolinones containing pyridyl group are prepared.

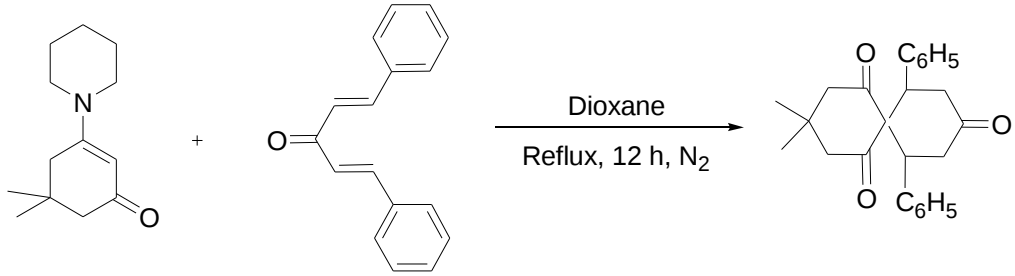
Spiro compounds can be prepared by various methods.[73-81] But the reaction of dibenzalacetone with a compound having active methylene group yielding double michael adduct would be an interesting subject of investigation.

Kandeel[82] and coworkers prepared spiro compounds by the Michael reaction of divinyl ketones with barbituric acid or thiobarbituric acids in ethanol-dioxane mixture in presence of triethylamine. These spiro compounds showed anticonvulsant activity in frogs against pentylene tetrazol induced convulsions in comparison to phenobarbitone as reference drug.

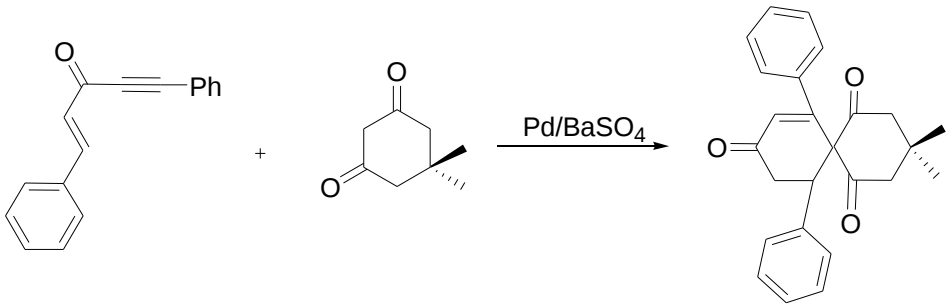


(X= O or S)

Trivedi[83] and co-workers prepared spiro compounds by refluxing bis-benzalacetone with different functionalised enaminones in dioxane for 12 hours under nitrogen atmosphere.



Spiro annulated cyclohexanone derivatives are prepared[84] by the double Michael addition of cross conjugated enyone with dimendone in presence of $Pd/BaSO_4$ in methylene chloride.



Many spiro comounds have been found to show anticancer,[85] narcotic,[86,87] anti-inflammatory[88] and analgesic[89] properties. Some new spiro heterocycles are found to have herbicidal activity and pesticidal activity.[90]

Imidazoliones have been found to be associated with several pharmacological properties[91-94] and cyclohexanone derivatives possess analgesic properties. Spiro compounds containing nitrogen were also synthesised and their properties have been studied.[95] In view of the above data the present investigation was undertaken in which new spiro compounds containing pyridyl group have been synthesised.

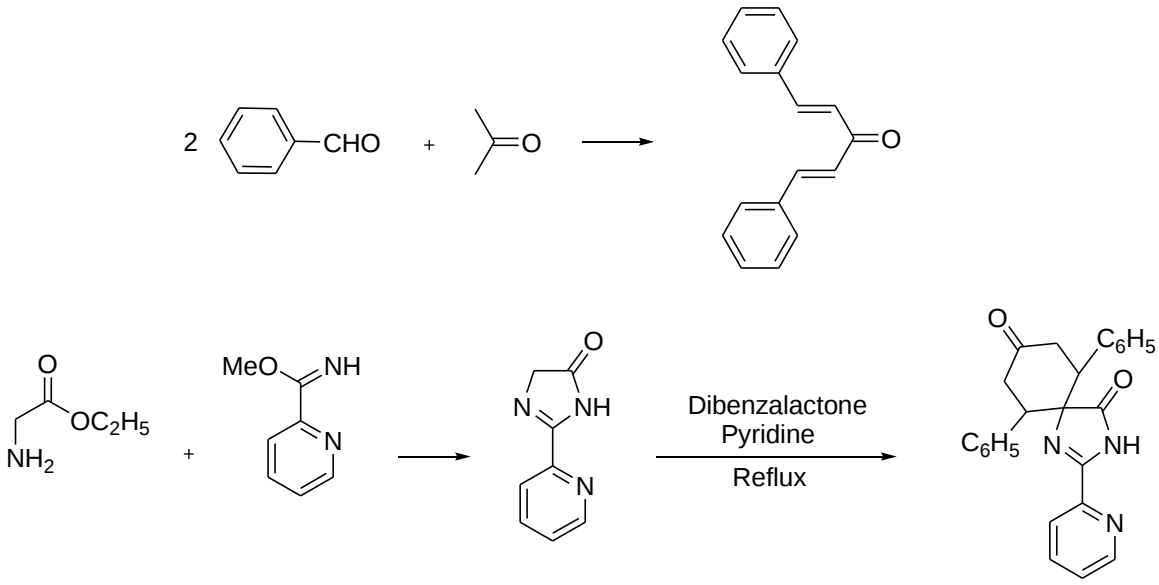
Present work

The Michael reaction of 1,5-diaryl-1,4-pentadien-3-ones with active methylene compounds has long been employed to prepare substituted cyclohexanones.[96-99] The product of these reactions are of interest in terms of their stereochemistry and as starting materials for the synthesis of compounds with possible biological activity.[84,100] The reaction of a cross conjugated olefin, dibenzalacetone and a compound having an active methylene group resulted in the formation of some novel spiro imidazoliones containing cyclohexanone moiety.[52] In the present work spiro compounds containing pyridyl group were synthesised expecting better biological activity.

Results and Discussion

The base catalysed condensation of acetone was carried out with aromatic aldehydes to get the corresponding divinyl ketones.[101-104] This divinyl ketones on Michael addition with 2-pyridyl-2-imidazolin-5-ones, which in turn is formed by the reaction between glycine ethyl ester

hydrochloride, sodium bicarbonate and imidic acid methyl ester formed from cyano pyridine, in presence of pyridine, yielded spiro imidazolinones.

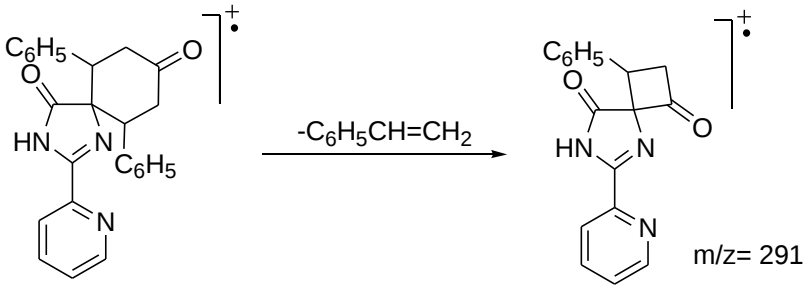


The active methylene group of 2-pyridyl-2-imidazolin-5-one condenses with carbonyl compounds to give 4-Arylidene/alkylidene-2-pyridyl-2-imidazolin-5-one. But dibenzalacetones did not undergo this type of condensation. This observation is not at all unusual as the carbonyl group of dibenzalacetone is conjugated to double bonds and benzene rings on both sides rendering it highly unreactive. However the spiro imidazolinone underwent condensation with the active methylene group of 2-phenyl-2-imidazolin-5-ones.[52]

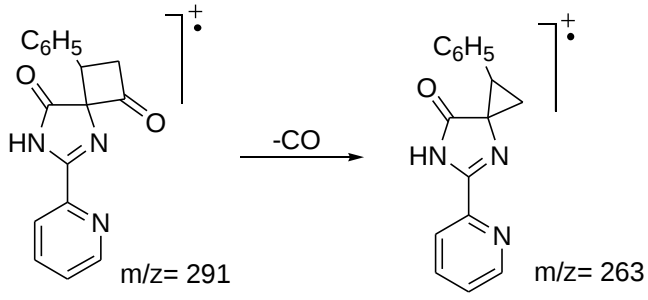
The structure was arrived at as follows. The mass spectrum of 3-(2-pyridyl)-6,10-diphenyl-2,4-diazospiro[4.5]deca-2-en-5,8-dione had a peak at 395 corresponding to the proposed structure. The odd mass justified the presence of odd number of nitrogen atoms. Other important peaks in the mass

spectrum were at m/z = 291, 263, 249, 233, 105, 78 which further supported the proposed structure.

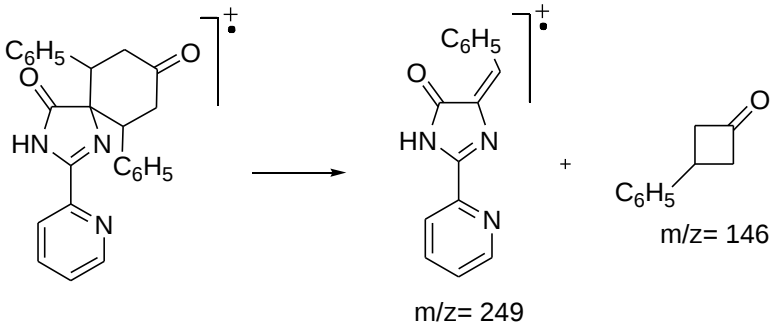
The mass spectral fragmentations of spiro ketones was found to differ from those of the corresponding cycloalkanes or cycloalkanones.[105] The fragment at m/z 291 is formed by the elimination of a styrene molecule with m/z 104 from the molecular ion.



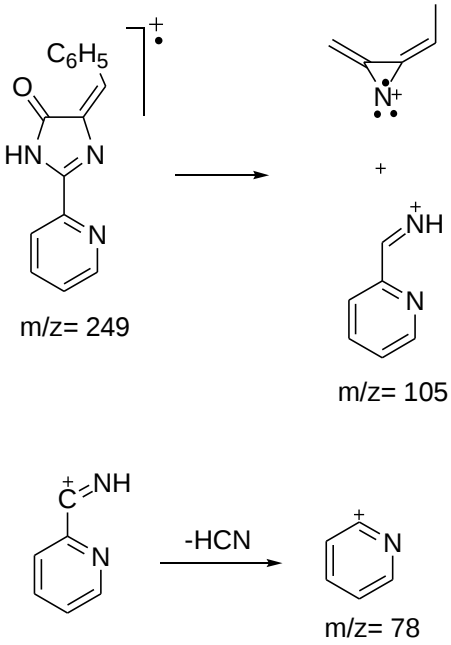
The mass peak at 263 unit corresponds to the radical ion formed by the elimination of neutral molecule of CO from the above ion.



An alternate path way gave rise to the peak of m/z = 249. It is due to the removal of one molecule of 3-phenylcyclobutanone[105] with m/z 164.



The peaks at m/z 105 and 78 are due to the fragmentations given below.



The ^{1}H NMR spectrum of the spiro imidazolinone showed absorption corresponding to the 14 aromatic protons (protons of phenyl and pyridyl) in

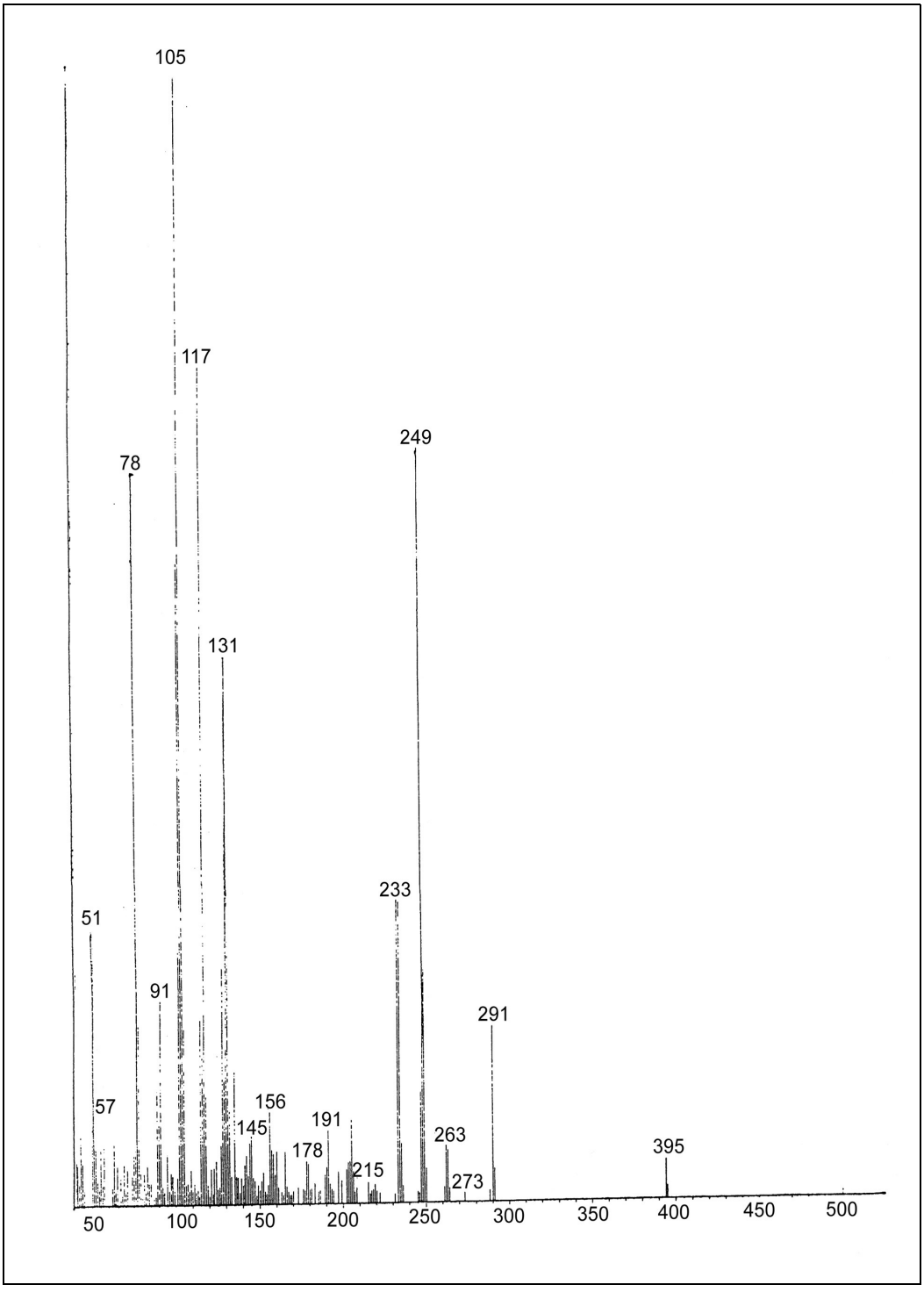
the range of δ 7-7.6. The NH proton was at δ 9.3. The two methine protons and the four methylene protons of the cyclohexanone appeared as six doublet of doublets in the region δ 2.9-3.8. They form the ABX systems and are marked as AA', BB' and XX'. Out of these six protons A, A', B and B' have a coupling constant of 16.8 Hz. This can be due to the geminal HH coupling. Geminal HH coupling depends characteristically on the polarity and hybridisation of the carbon atom on the coupling path and also on the substituents and on the HCH bond angle. In cycloalkanes the geminal coupling constant is around 12.5 Hz. The high coupling constant observed in the ^{1}H nmr spectrum for this methylene protons can be attributed to the presence of carbonyl group, as the neighbouring π-electron generally contribute to the coupling constants. This effect is especially large when the line joining the two coupled protons is parallel to the neighbouring π orbital.[106] This will be the case in the slightly flattened cyclohexanone ring. Hence these four protons should be those of the two methylene groups. At the same time X and X' showed coupling constants of 13 Hz and 9.4 Hz respectively. The bulky phenyl groups occupying the equitorial positions, these two hydrogens should be axial. A coupling constant of 13 Hz is typical of axial protons (X). But X' has a lower coupling constant of 9.4 Hz which can be due to some twist in the conformation that makes it not exactly axial

(i.e., dihedral angle less than 180^{o} with the axial hydrogen of the neighbouring methylene group).

As B and B' also exhibit coupling constants of 13 Hz and 9.4 Hz respectively proves that B and X are coupled to each other while B' and X' are also coupled to each other. Hence both B and B' should be axial hydrogens since equitorial-equitorial and equitorial-axial coupling constants are much lower. It is also known that in similar compounds the axial protons absorbed at downfield region compared to equitorial methylene protons due to the deshielding effect of the carbonyl group of the cyclohexanone moiety.[107]

The appearance of sharp peaks for all the six protons of the cyclohexanone ring proved its fairly rigid conformation.

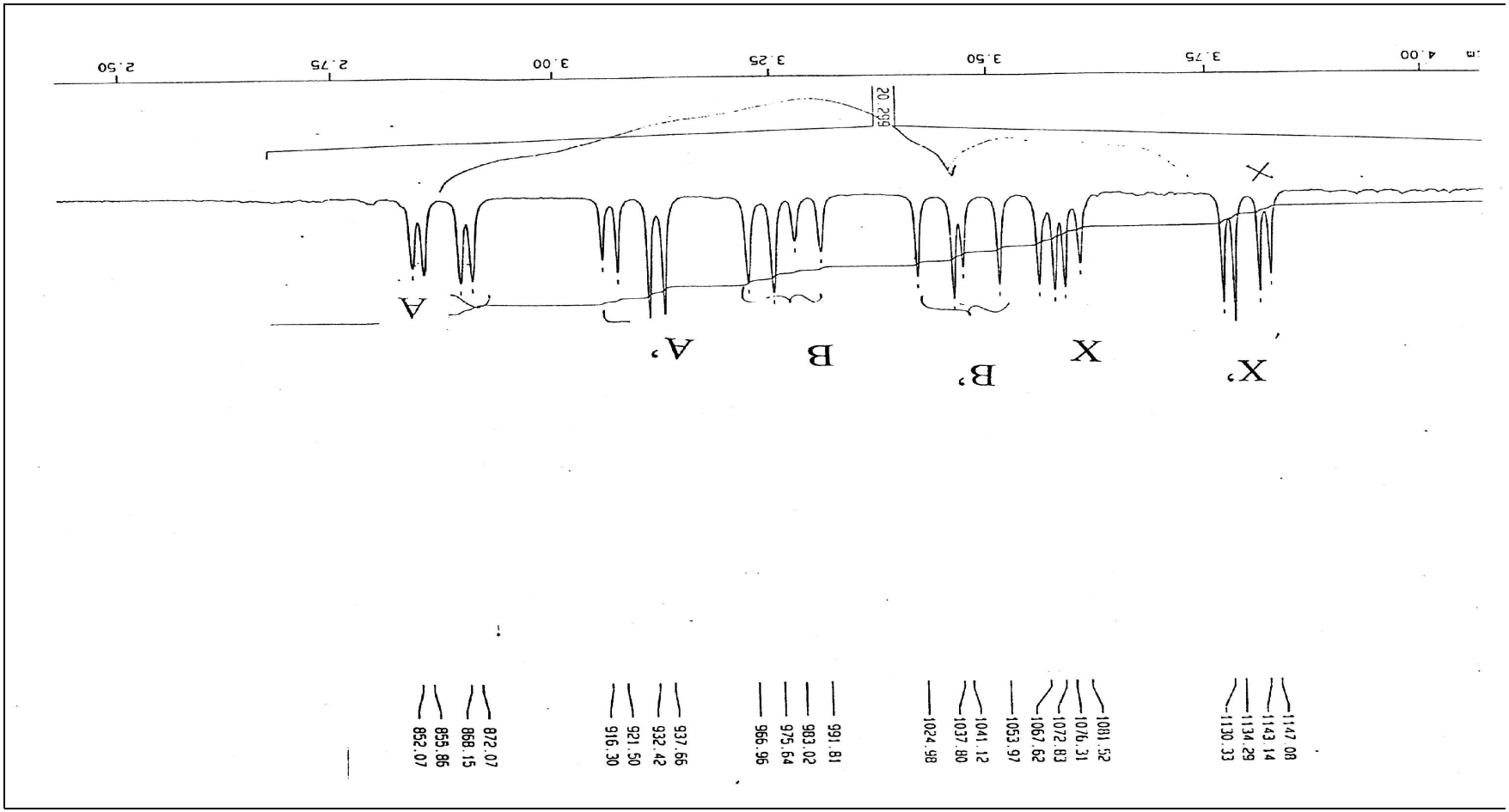
All the nine compounds synthesised are new. This multicomponent reaction could be utilised for their synthesis in good yield.



Mass spectrum of 3-(2-pyridyl)-6,10-diphenyl-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

^{1}H NMR spectrum of 3-(2-pyridyl)-6,10-diphenyl-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

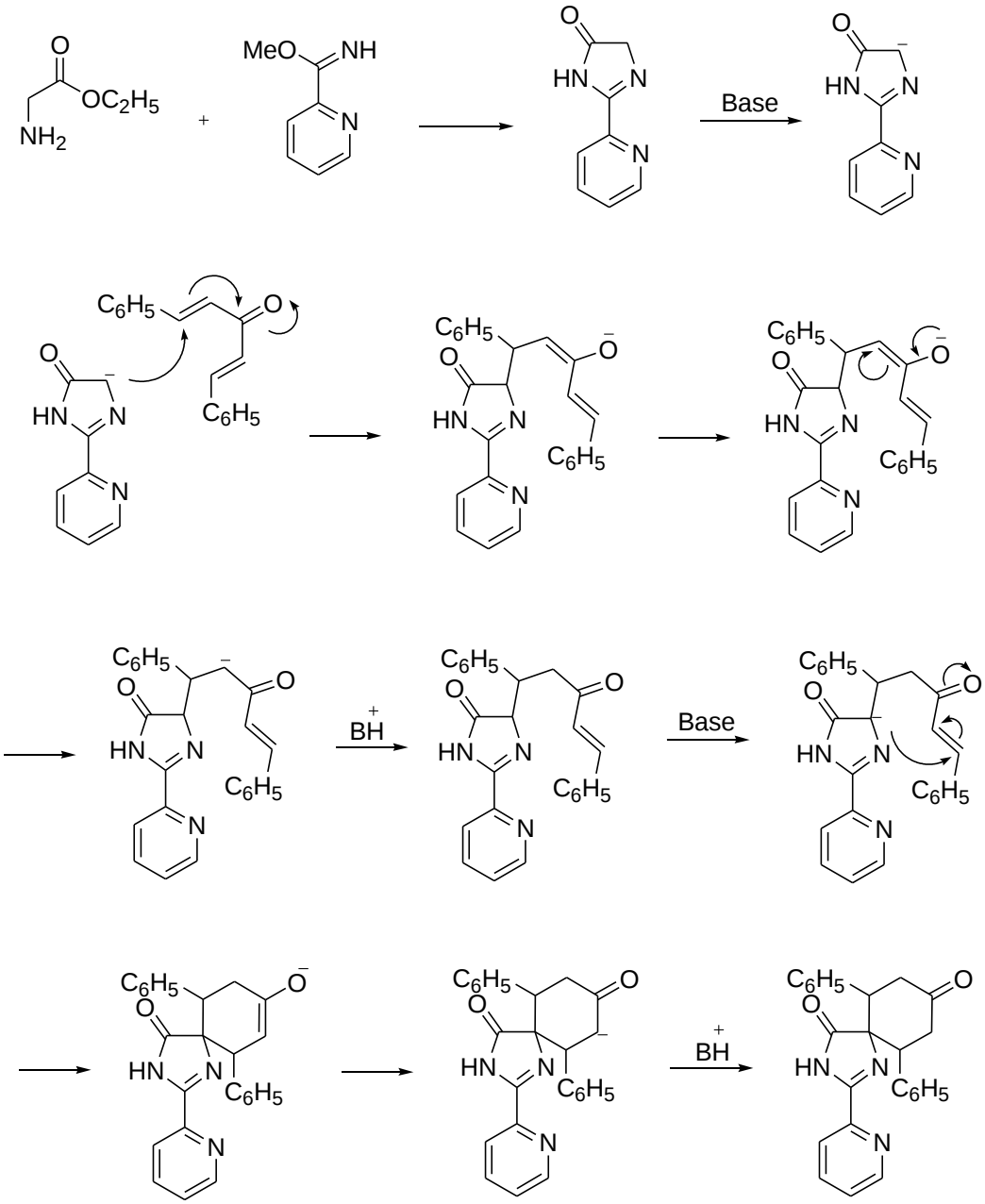
^{1}H NMR spectrum of 3-(2-pyridyl)-6,10-diphenyl-2,4-diazaspiro[4.5]deca-2-en-5,8-dione (expanded)



The IR spectrum is in consistence with the above observations. The IR spectrum of the compound showed two carbonyl absorption frequencies. The absorption frequency of 1722 cm^{-1} is due to the carbonyl group of imidazolinone ring and the other at 1716 cm^{-1} is due to a cyclohexanone ring. If the carbonyl group of dibenzalacetone condense with active methylene group of 2-pyridyl-2-imidazolin-5-one, the product should contain only one carbonyl group. This shows that dibenzalacetone underwent a double Michael addition with 2-pyridyl-2-imidazolin-5-one yielding a spiro imidazolinone containing cyclohexanone moiety. This fact is further supported by other spectral studies.

The UV absorption maximum of these compounds were in the range 320-345 nm. This absorption can be attributed to the $n \rightarrow \pi^*$ transitions in the chromophores including the imidazolinone carbonyl and the adjacent nitrogen that can contribute its lone pair electron for conjugation with the carbonyl group.

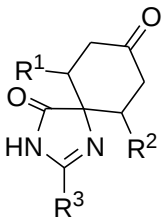
The following mechanism can be suggested for the formation of the spiro imidazolinones.



In the synthesis of spiro imidazolinones pyridine acts as a base. In order to increase the yields of the products, the modified procedure[52] is adopted.

Imidic acid ester, glycine ethyl ester hydrochloride, sodium bicarbonate, and the 1,5-diaryl-1,4-pentadien-3-ones were taken in equimolar

ratio and heated under reflux in pyridine. After three hours the mixture was added to cold water and acidified with dil. HCl to increase the dissolution of pyridine in water. The solid imidazolinone was then filtered, washed and dried. It was then recrystallised from a mixture of benzene and petroleum ether.



(R^1=R^2)

Table II(1)

No.	$R_1 = R_2$	R_3	Yield (%)	M.P. (^oC)	λ_{max} (nm)
1	Phenyl	2-Pyridyl	80	148	325
2	p-Chlorophenyl	2-Pyridyl	79	176	342
3	o-Chlorophenyl	2-Pyridyl	85	162	320
4	Phenyl	3-Pyridyl	85	151	326
5	p-Chlorophenyl	3-Pyridyl	75	181	337
6	o-Chlorophenyl	3-Pyridyl	81	171	323
7	Phenyl	4-Pyridyl	78	145	331
8	p-Chlorophenyl	4-Pyridyl	87	174	345
9	o-Chlorophenyl	4-Pyridyl	77	168	328

Experimental

Melting points are recorded on a Toshniwal capillary melting point apparatus and are uncorrected.. The mass spectra were recorded on Finnigan MAT8200 spectrometer. ^{1}H NMR spectrum was recorded on a Brucker AM 360 spectrometer using TMS as internal standard. IR spectrum was recorded as KBr pellets using Shimadzu 8101 FTIR equipment. UV-vis spectra were recorded in ethanol on a Shimadzu 1601 UV-Vis spectrometer.

Synthesis of starting materials

Glycine ethyl ester hydrochloride was prepared as described in Chapter I.

1,5-Diphenylpenta-1,4-dien-3-one (Dibenzylidene acetone)

Dibenzylidene acetone was prepared by known method.[101-104, 108]

In a 500 ml RB flask placed cold solution of 25 g of sodium hydroxide in 250 ml water and 200 ml ethanol. Equipped the flask with a mechanical stirrer and surrounded with bath of water. The temperature of the solution was maintained at 20-25^{o}C. Stirred vigorously and added one half of the previously prepared mixture of 26.5 g (0.25 mol) of pure benzaldehyde and 7.3 g (0.125 mol) acetone. A flocculent precipitate was formed in two to three minutes. After 15 minutes added the remaining mixture of benzaldehyde and acetone and stirred for 30 minutes. The pale yellow solid

formed is filtered, washed with cold water and dried at room temperature. The product weighed 27 g (93%) melting at 105-107^{o}C.

The crude sample was recrystallised from ethyl acetate and melted at 112^{o}C.

di(p-chlorobenzal)acetone and di(o-chlorobenzal)acetone also were prepared by the same method described above.

SYNTHESIS OF SPIRO IMIDAZOLINONES

1. 3-(2-pyridyl)-6,10-diphenyl-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Sodium metal (0.5 g) was dissolved in 8 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (1.1 g, 0.01 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (0.5 ml) was then added to it and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Dibenzalacetone (2.34 g, 0.01 mol) and pyridine (10 ml) were also added to the round bottomed flask and refluxed for 3 hours. The yellow colour of the solution gradually turned to brown. After refluxing for 3 hours, the reaction mixture was cooled, and added to ice cold water and acidified using dil. HCl. The yellow coloured product formed was filtered, washed with cold water and dried in the oven at

80 °C for one hour. The dull yellow spiro imidazolinone weighed 3.2 g (80%) and melted at 146 °C.

The spiro imidazolinone was recrystallised from benzene-petroleum ether mixture and melted at 148 °C.

Analysis

	N%	C%	H%
Found	10.5	76.2	5.2
Calculated	10.63	76	5.3
UV-Vis	λ_{max} = 325 nm		
Molecular formula	$C_{25}H_{21}N_3O_2$		

2. 3-(2-pyridyl)-6,10-di(p-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Sodium metal (0.5 g) was dissolved in 8 ml of absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (1.1 g, 0.01 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (0.5 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Di(p-chlorobenzal)acetone (2.67 g, 0.01 mol) and pyridine (10 ml) were also added and refluxed for 3 hours. The yellow colour of the solution gradually turned brown. It was cooled and

added to ice cold water and acidified with dil. HCl. The dull yellow product formed was filtered, washed with cold water and dried at 80 ^{o}C for one hour. The spiro imidazolinone weighed 3.7 g (79%) and melted at 173 ^{o}C.

Recrystallisation of the spiro midazolinone was done from benzene-petroleum ether mixture and melted at 176 ^{o}C.

Analysis

	N%	C%	H%
Found	9.3	64.2	3.9
Calculated	9.1	64.6	4.1
UV-Vis	λ_{max} = 342 nm		
Molecular formula	$C_{25}H_{19}N_3O_2Cl_2$		

3. 3-(2-pyridyl)-6,10-di(o-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Sodium metal (0.5 g) was dissolved in 8 ml absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (1.1 g, 0.01 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (0.5 ml) was then added to it and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Di(o-chlorobenzal) acetone (2.67 g, 0.01 mol) and pyridine (10 ml) were also added and refluxed for 3

hours. The yellow colour of the solution gradually turned brown. It was cooled and added to ice cold water and acidified with dil. HCl. The dull yellow product formed was filtered, washed with cold water and dried at 80 °C for one hour. The spiro imidazolinone weighed 4 g (85%) and melted at 160 °C.

The spiroimidazolinone was recrystallised from benzene petroleum ether mixture and melted at 162 °C.

Analysis

	N%	C%	H%
Found	9.4	64.4	3.8
Calculated	9.1	64.6	4.1
UV-Vis	λ_{max} = 320 nm		
Molecular formula	$C_{25}H_{19}N_3O_2Cl_2$		

4. 3-(3-pyridyl)-6,10-diphenyl-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Sodium metal (0.5 g) was dissolved in 8 ml absolute methanol in a 100 ml round bottomed flask. 3-Cyanopyridine (1.1 g, 0.01 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (0.5 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Dibenzalacetone (2.34 g, 0.01

mol) and pyridine (10 ml) were also added and refluxed for 3 hours. The yellow colour of the solution gradually turned brown. The reaction mixture was cooled and added to ice cold water and acidified using dil. HCl. The dull yellow coloured spiro imidazolinone formed was filtered, washed with cold water and dried in the oven at 80 ^{o}C for one hour. The dull yellow spiro imidazolinone weighed 3.4 g (85%) and melted at 147 ^{o}C.

The spiro imidazolinone was recrystallised from benzene-petroleum ether mixture and melted at 151 ^{o}C.

Analysis

	N%	C%	H%
Found	10.7	76.4	5.4
Calculated	10.63	76	5.3
UV-Vis	λ_{max} = 326 nm		
Molecular formula	$C_{25}H_{21}N_3O_2$		

5. 3-(3-pyridyl)-6,10-di(p-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Sodium metal (0.5 g) was dissolved in 8 ml absolute methanol in 100 ml round bottomed flask. 3-Cyanopyridine (1.1 g, 0.01 mol) was added to it and allowed to stand over night at room temperature. Acetic acid (0.5 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol)

and sodium bicarbonate (1.785 g) were ground together and added to the imidate formed in the round bottomed flask. Di(p-chlorobenzal)acetone (2.67 g, 0.01 mol) and pyridine (10 ml) were also added and refluxed for 3 hours. The yellow colour of the solution gradually turned brown. After refluxing it was cooled and added to the ice cold water. It was then acidified with dil. HCl. The dull yellow product formed was filtered, washed with cold water and dried at 80 °C for one hour in the oven. The spiro imidazolinone weighed 3.5 g (75%) and melted at 176 °C.

Recrystallisation of the spiro imidazolinone was done from benzene-petroleum ether mixture and melted at 181 °C.

Analysis

	N%	C%	H%
Found	8.9	64.7	4.3
Calculated	9.1	64.6	4.1
UV-Vis	λ_{max} = 337 nm		
Molecular formula	$C_{25}H_{19}N_3O_2Cl_2$		

6. 3-(3-pyridyl)-6,10-di(o-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Sodium metal (0.5 g) was dissolved in 8 ml absolute methanol in 100 ml round bottomed flask. 3-Cyanopyridine (1.1 g, 0.01 mol) was added to it and allowed to stand over night at room temperature. Acetic acid (0.5 ml) was

then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Di(o-chlorobenzal)acetone (2.67 g, 0.01 mol) and pyridine (10 ml) were also added and refluxed for 3 hours. The yellow colour of the solution gradually turned brown. After refluxing it was cooled and added to the ice cold water. It was then acidified with dil. HCl. The dull yellow product formed was filtered, washed with cold water and dried at 80 ^{o}C for one hour in the oven. The spiro imidazolinone weighed 3.8 g (81%) and melted at 167 ^{o}C.

Recrystallisation of the spiro imidazolinone was done from benzene petroleum ether mixture and melted at 171 ^{o}C.

Analysis

	N%	C%	H%
Found	9.2	64.5	4.2
Calculated	9.1	64.6	4.1
UV-Vis	λ_{max} = 323 nm		
Molecular formula	$C_{25}H_{19}N_3O_2Cl_2$		

7. 3-(4-pyridyl)-6,10-diphenyl-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Metallic sodium (0.5 g) was dissolved in 8 ml absolute methanol in 100 ml round bottomed flask. 4-Cyanopyridine (1.1 g, 0.01 mol) was added

to it and allowed to stand over night at room temperature. Acetic acid (0.5 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Dibenzalacetone (2.34 g, 0.01 mol) and pyridine (10 ml) were also added and refluxed for 3 hours. The yellow colour of the solution gradually turned brown. After refluxing it was cooled and added to the ice cold water. It was then acidified with dil. HCl. The dull yellow product formed was filtered, washed with cold water and dried at 80 ^{o}C for one hour in the oven. The spiro imidazolinone weighed 3.1 g (78%) and melted at 143 ^{o}C.

Recrystallisation of the spiro imidazolinone was done from benzene-petroleum ether mixture and melted at 145 ^{o}C.

Analysis

	N%	C%	H%
Found	10.8	75.8	5.5
Calculated	10.63	76	5.3
UV-Vis	λ_{max} = 331 nm		
Molecular formula	$C_{25}H_{21}N_3O_2$		

8. 3-(4-pyridyl)-6,10-di(p-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Metallic sodium (0.5 g) was dissolved in 8 ml of absolute methanol in 100 ml round bottomed flask. 4-Cyanopyridino (1.1 g, 0.01 mol) was added to it and allowed to stand over night at room temperature. Acetic acid (0.5 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Di(p-chlorobenzal)acetone (2.67 g, 0.01 mol) and pyridine (10 ml) were also added and refluxed for 3 hrs. The yellow colour of the solution turned brown. After refluxing it was cooled and added to the ice cold water. It was then acidified with dil. HCl. the dull yellow product formed was filtered, washed with cold water and dried at 80 ^{o}C for one hour in the oven. The spiro imidazolione weighed 4.1 g (875) and melted at 171 ^{o}C. Recrystallisation of the product was done from benzene-petroleum ether mixture and melted at 174 ^{o}C.

Analysis

	N%	C%	H%
Found	9.5	64.8	4.3
Calculated	9.1	64.6	4.1
UV-Vis	λ_{max} = 345		
Molecular formula	$C_{25}H_{19}N_3O_2Cl_2$		

9. 3-(4-pyridyl)-6,10-di(o-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione

Metallic sodium (0.5 g) was dissolved in 8 ml absolute methanol in 100 ml round bottomed flask. 4-Cyanopyridine (1.1 g, 0.01 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (0.5 ml) was then added and boiled on a water bath to remove the excess methanol present in the reaction mixture. Glycine ethyl ester hydrochloride (1.4 g, 0.01 mol) and sodium bicarbonate (1.75 g) were ground together and added to the imidate formed in the round bottomed flask. Di(o-chlorobenzal(acetone (2.67 g, 0.01 mol) and pyridine (10 ml) were also added and refluxed for 3 hours. The yellow colour of the solution turned brown. After refluxing it was cooled and added to the ice cold water. It was then acidified with dil. HCl. The dull yellow product formed was filtered, washed with cold water and dried at 80 ^{o}C for one hour in the oven. The spiro imidazolinone weighed 3.6 g (77%) and melted at 165 ^{o}C. Recrystallisation of the spiroimidazolinone was done from benzene-petroleum ether mixture and melted at 168 ^{o}C.

Analysis

	N%	C%	H%
Found	9.2	64.2	3.9
Calculated	9.1	64.6	4.1
UV-Vis	λ_{max} = 328 nm		
Molecular formula	$C_{25}H_{19}N_3O_2Cl_2$		

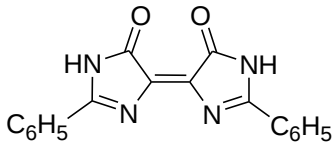
CHAPTER 3

SYNTHESIS OF 4-[AMINO,PYRIDYL METHYLENE]-2-PYRIDYL-2-IMIDAZOLIN-5-ONES

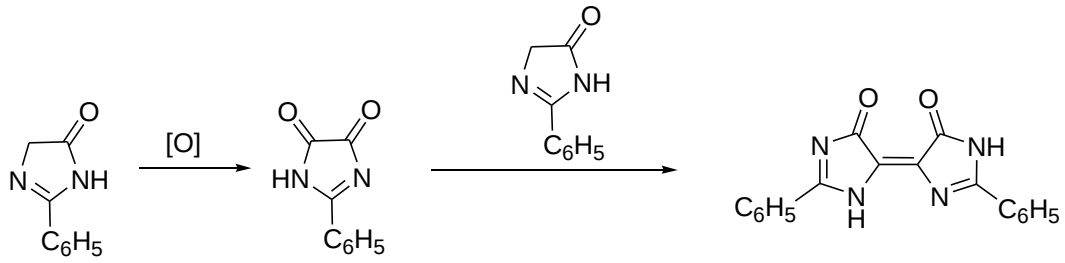
Introduction

The reaction between benzimidic acid ester and glycine ester yielding red coloured products have been thoroughly investigated.[35,37] Wieland and Biener[109] studied the pigment formed by the reaction between benzimidic acid ester and glycine ester and they observed a whole series of red pigments by this study.

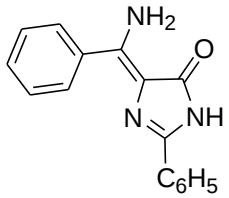
Ekeley and Ronzio[110,111] suggested that the red colour is due to the formation of glyoxaline red with the following structure.



This dye may be formed by the atmospheric oxidation of one molecule of 2-substituted-2-imidazolin-5-one to form a carbonyl compound followed by the condensation with another molecule of 2-substituted-2-imidazolin-5-one. This is just like the formation of indigo from indoxyl by atmospheric oxidation.



A further investigation of the reaction between benzimidic acid ester and glycine ester by Shafi and Sobha[112] resulted in the isolation and structural elucidation of 4-(amino, arylmethylene)-2-aryl-2-imidazolin-5-one and they prepared the acetylated products of the amino imidazolinones.[112] In their method imidic acid ester and glycine ester were taken in the molar ratio 2:1 and heated under reflux in toluene in presence of anhydrous sodium acetate as the base. After refluxing for 5 hours the product was filtered, washed with water, ether and dried. From spectral analysis they assigned the structure as



Present work

III.1. Synthesis of amino imidazolinones

Shafi and Basheer have reported the antibacterial activity of amino imidazolinones with phenyl groups.[113] Amino imidazolinones with pyridyl group in place of phenyl group was expected to result in more active derivatives. With this view it was proposed to synthesise this

class of compounds. Two aminoimidazolinones containing pyridyl ring namely 4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one and 4-[amino,(4-pyridyl) methylene]-2-(4-pyridyl)-2-imidazolin-5-one were synthesised and their structures elucidated by elemental analysis and spectral studies.

Results and discussion

Cyanopyridines (0.04 mol) were converted into the corresponding imidic acid ester in presence of methanol and sodium methoxide as already explained in chapter I. The imidic acid esters formed were then refluxed with glycine ethyl ester hydrochloride (0.02 mol), sodium bicarbonate and toluene for three hours. Then the reaction mixture was cooled and the product formed was filtered. The amino imidazolinones formed were washed with water and then with alcohol and dried.

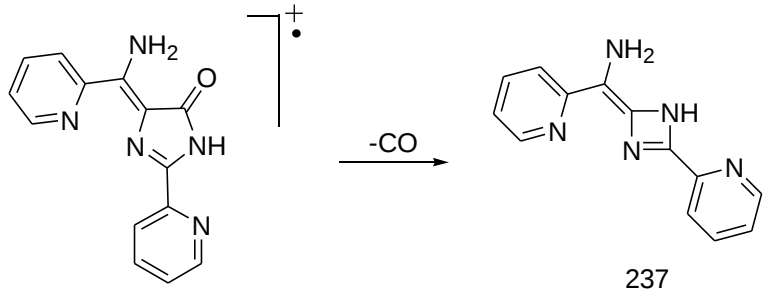
We tried to prepare aminoimidazolinones from 2-cyanopyridine, 3-cyanopyridine and 4-cyanopyridine. 3-Cyanopyridine did not give the expected product even after trying several different conditions. The amino imidazolinones formed from 2-cyanopyridine and 4-cyanopyridine were obtained in good yield (81% and 75%). The compounds synthesised are given in Table III.1. These compounds are reported for the first time.

TABLE III.1

4-[amino, pyridyl methylene]-2-pyridyl-2-imidazolin-5-one

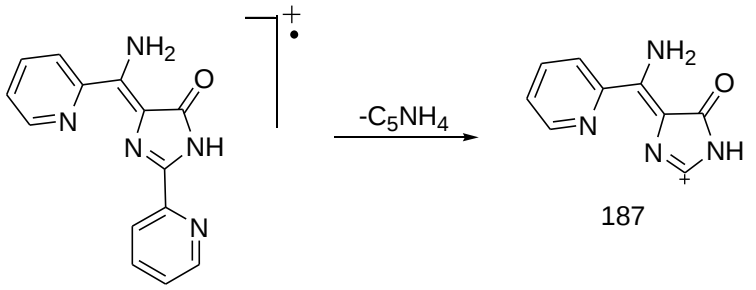
No.	Name of the compound	Yield %	M.P. °C	λ_{max} nm
1	4-[amino, (2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one	81	200	411
2	4-[amino, (4-pyridyl) methylene]-2-(4-pyridyl)-2-imidazolin-5-one	75	330	381

The structures of the compounds were elucidated by spectral and elemental analysis. The structure was arrived at as follows. The mass spectrum of 4-[amino, (2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one had a peak at 265, which is the molecular ion peak corresponding to the proposed structure. The odd mass justified the presence of odd number of nitrogen atoms per molecule. Other important peaks in the mass spectrum were at m/z = 237, 133, 105, 78, which further supported the proposed structure. The mass peak at 237 units corresponds to the radical ion formed by the elimination of a neutral CO molecule from the molecular ion.



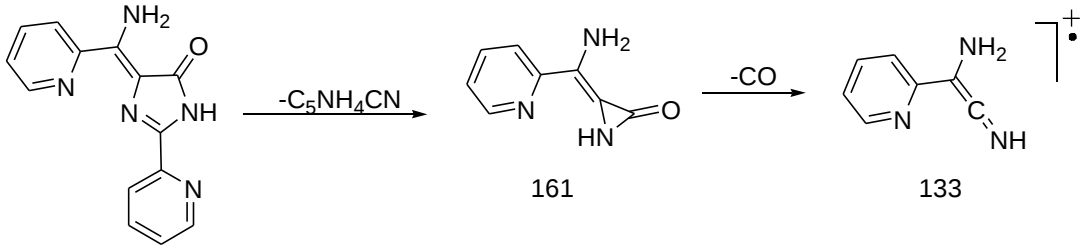
265 237

An alternate fragmentation pathway gives rise to the peak at m/z = 187. It is due to the removal of pyridyl radical in the imidazole ring of the molecular ion.



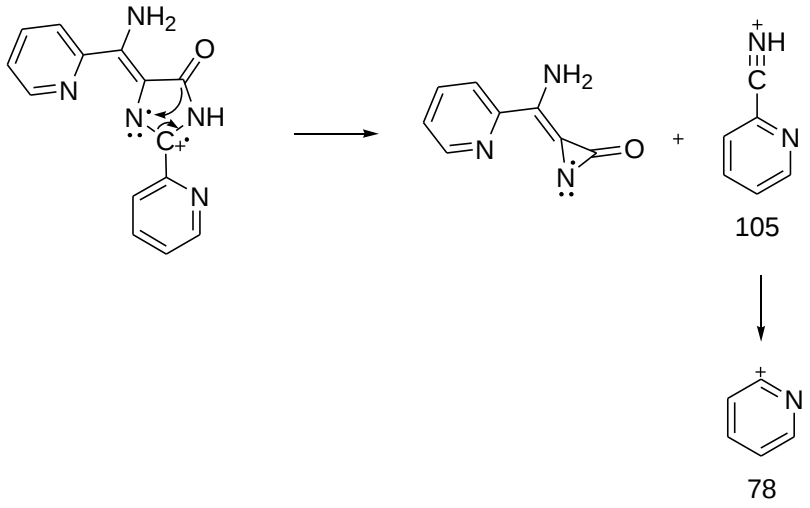
187

Removal of a neutral cyanopyridine molecule from the molecular ion results in the peak at 161 which eliminates a neutral molecule of CO giving the fragment ion at m/z = 133.

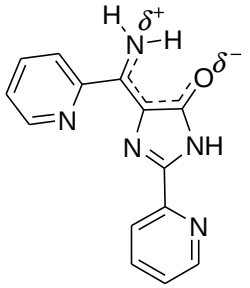


161 133

Intense peaks at m/z = 105 and 78 are due to the fragmentations given below.



The ^{1}H NMR spectrum also supported this structure. The NH proton in the imidazolinone ring absorbed at δ 11.75.[112] It also showed absorptions due to eight aromatic protons in the region δ 7.35 to 9.35. The two hydrogen atoms of the amino group are chemically non equivalent. This happens due to the possible partial double bond character of the C–NH_2 bond as shown below.



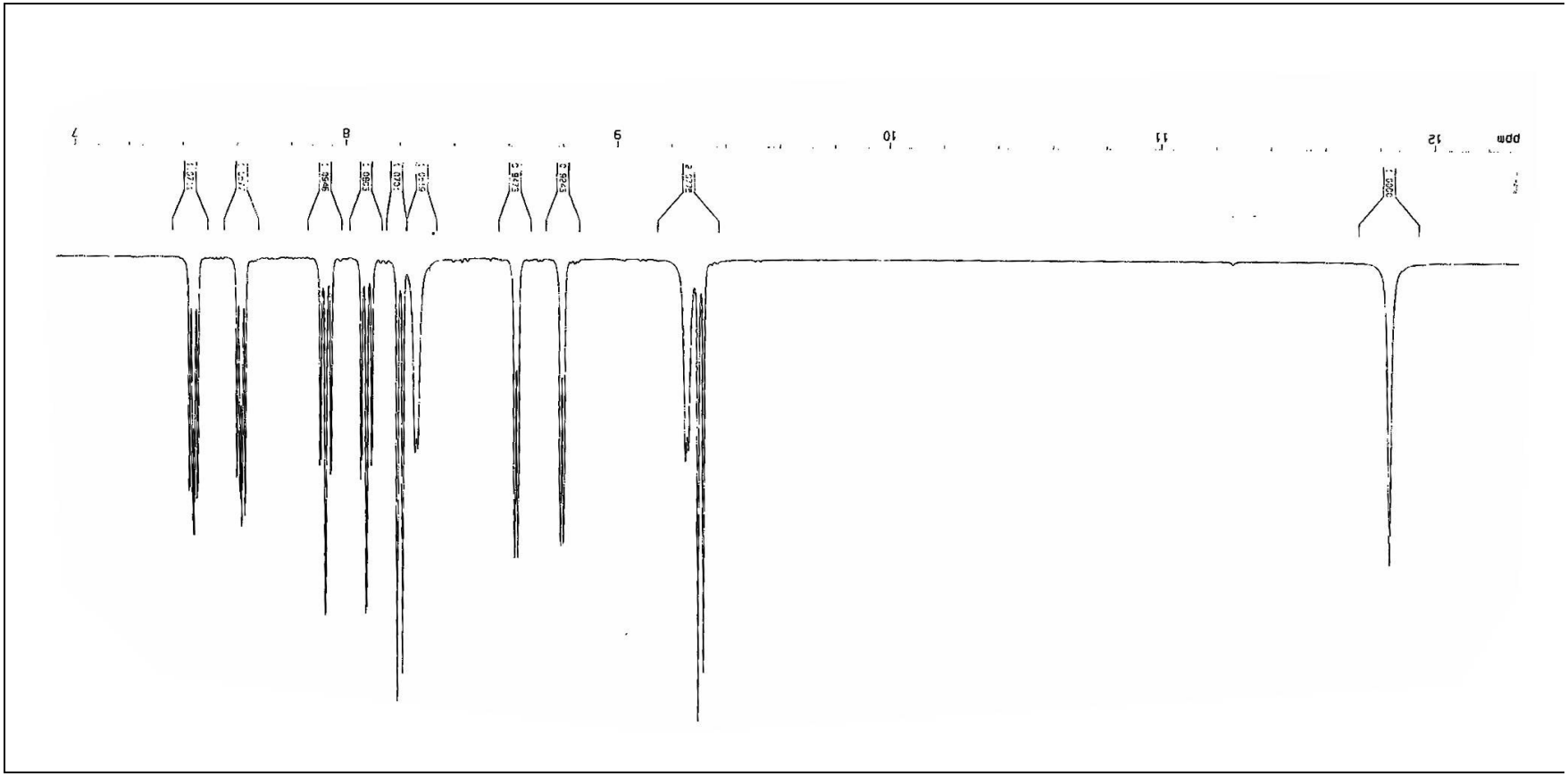
In this structure one of the hydrogen atoms of the amino group falls in the deshielding region of the carbonyl group and hence has a higher chemical shift than the other (δ 9.25 and 8.2). The proton absorption integrating to one proton at δ 9.35 is due to the absorption of the proton adjacent to the nitrogen of the pyridyl group at position 2 of the imidazolinone ring. This high chemical shift is observed for this type of hydrogen when the pyridyl group is bonded to electron withdrawing group.[114]

The ^{13}C nmr spectrum has 14 peaks in the region δ 117.2 to 170.2. The carbonyl carbon of imidazolinone ring absorbs at δ 170.2. All other carbons absorb between δ 117.2 to 149.7.

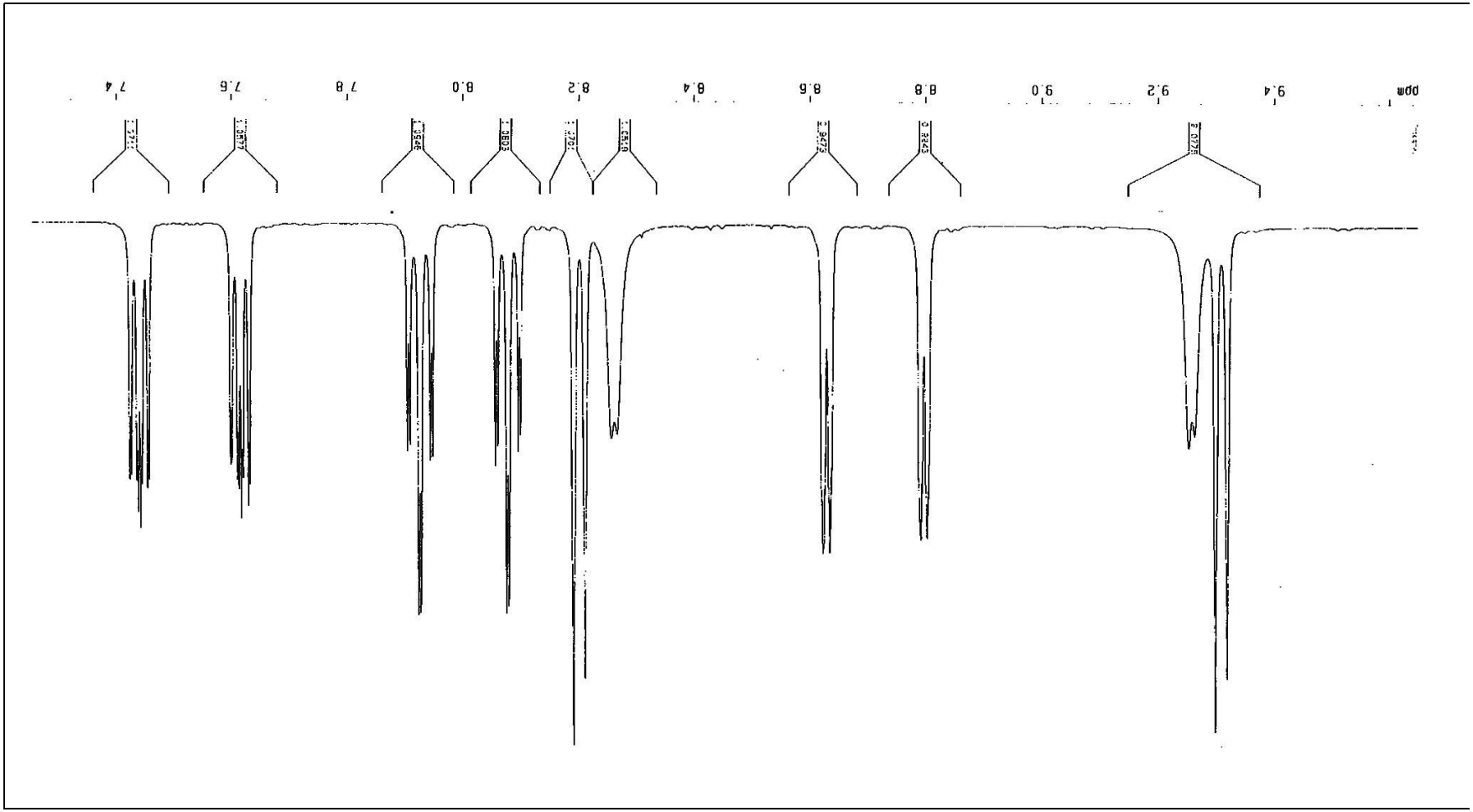
IR spectrum also is in consistence with the above observations. Three medium intensity peaks are found in the region 3160 to 3250 which are due to symmetric and antisymmetric vibrations of NH_2 and the vibration corresponding to NH of the imidazolinone ring. Non hydrogen bonded NH_2 group absorbs at 3336 cm^{-1}.[115] The carbonyl absorption is at 1670 cm^{-1}.

Mass spectrum of 4-[amino, (2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one

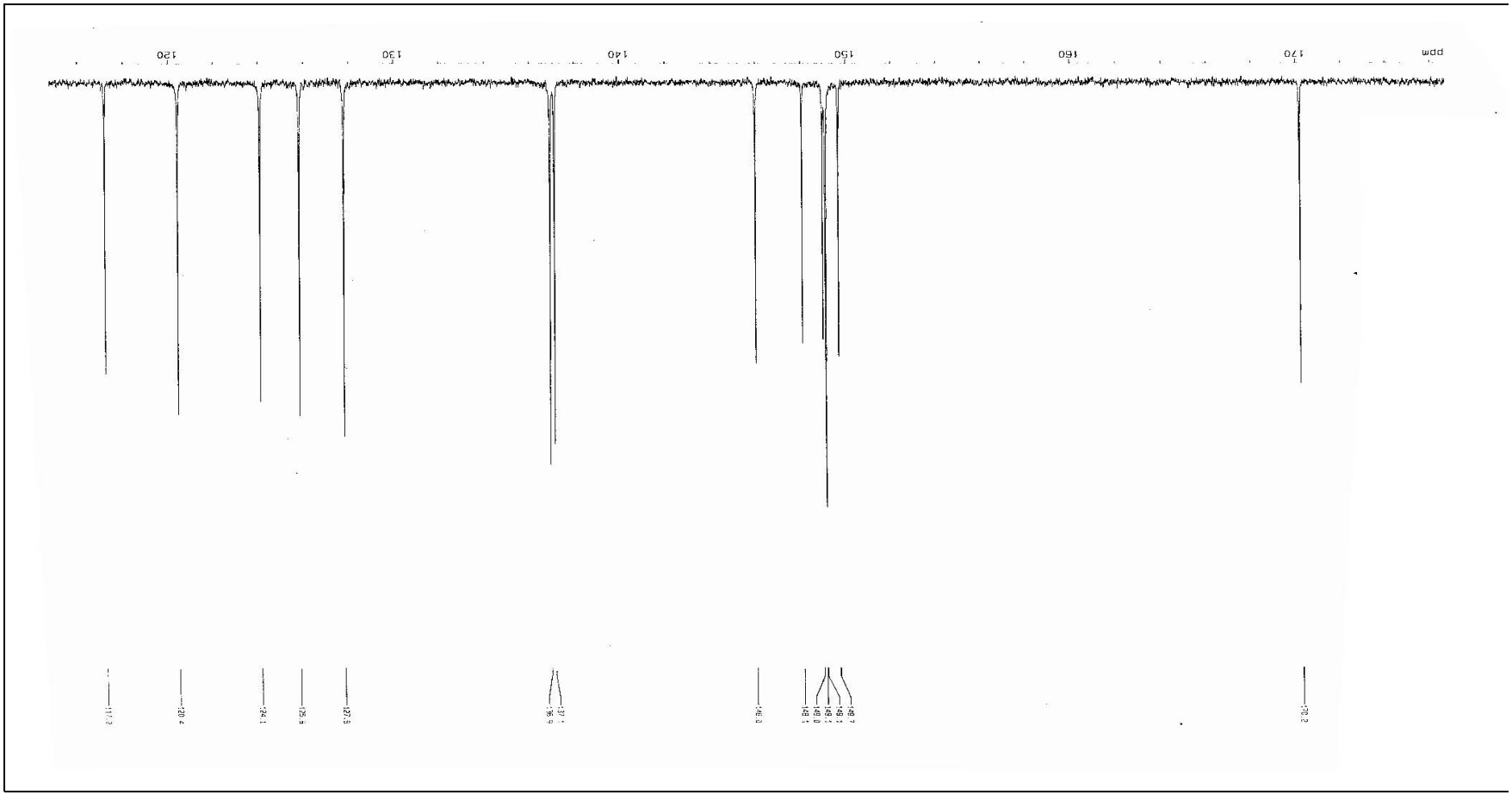
^{1}H NMR spectrum of 4-[amino, (2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one



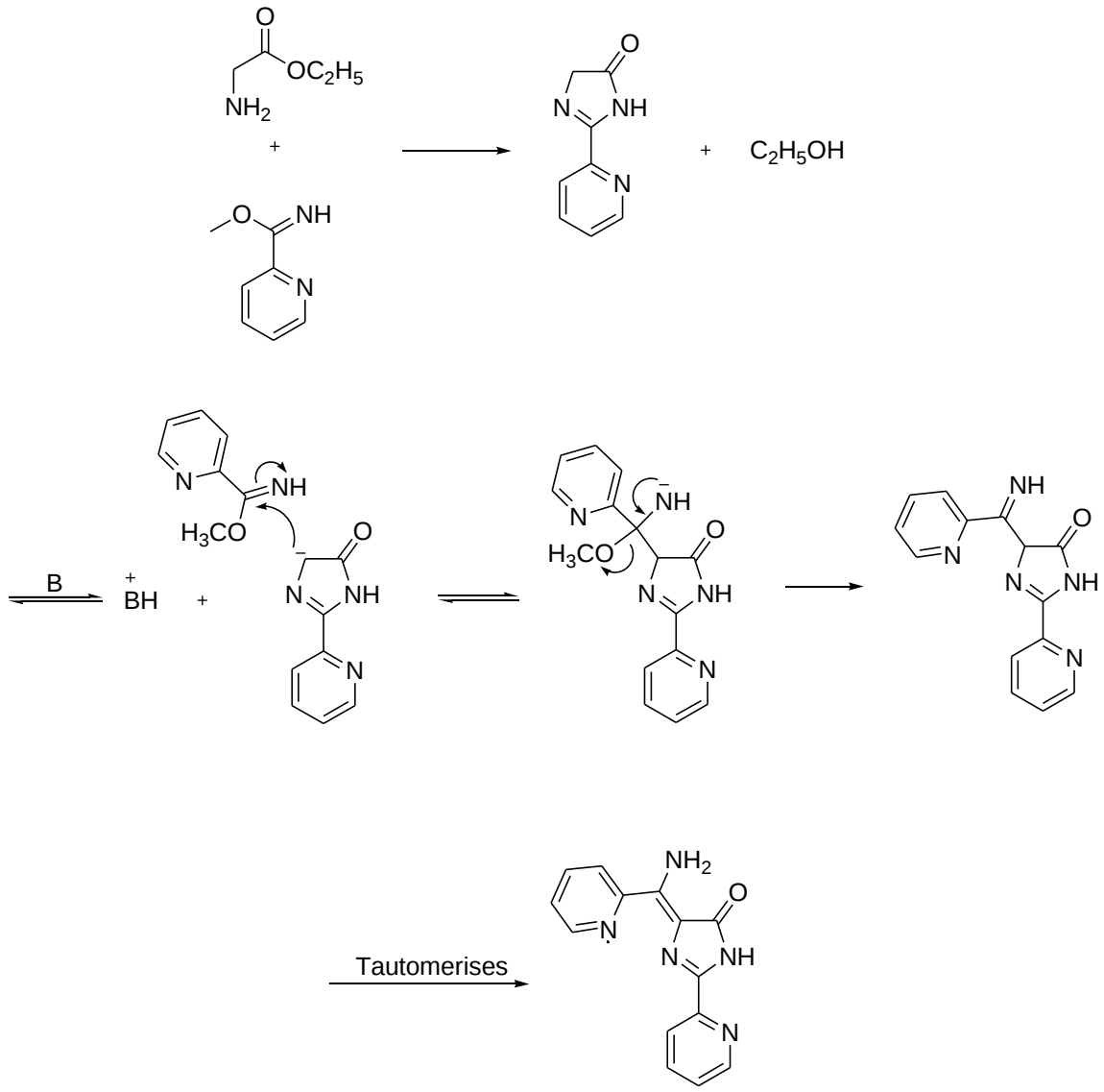
^{1}H NMR spectrum of 4-[amino, (2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one (expanded)



^{13}C NMR spectrum of 4-[amino, (2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one

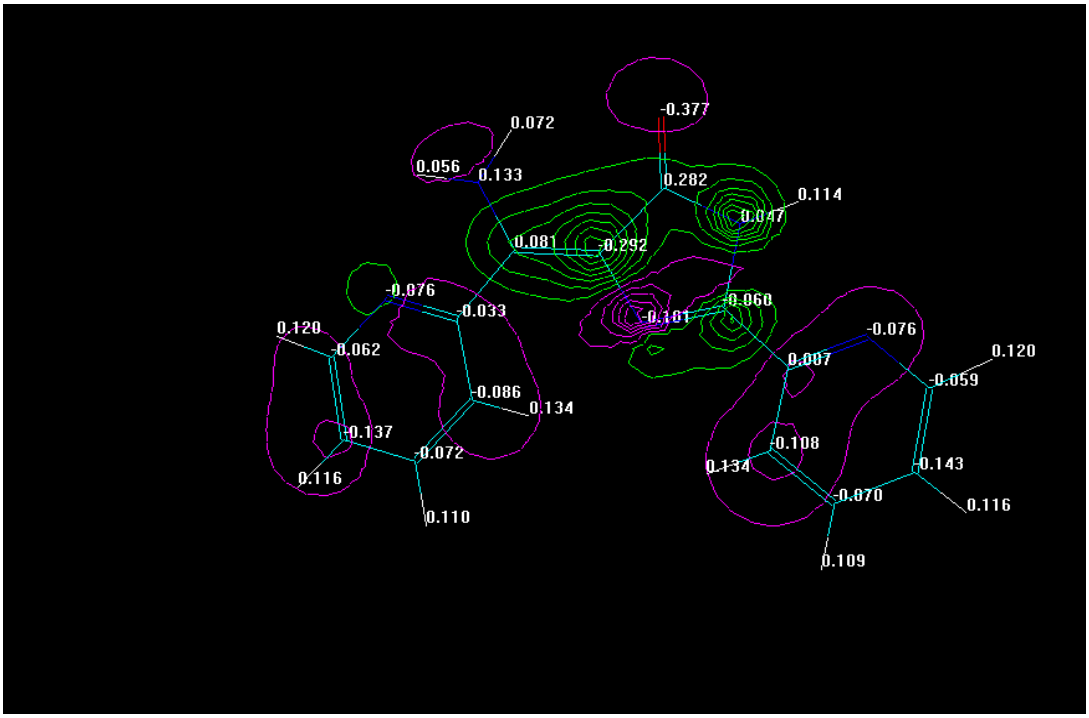


Once the structure of the compound was established, the following mechanism could be proposed for its formation.

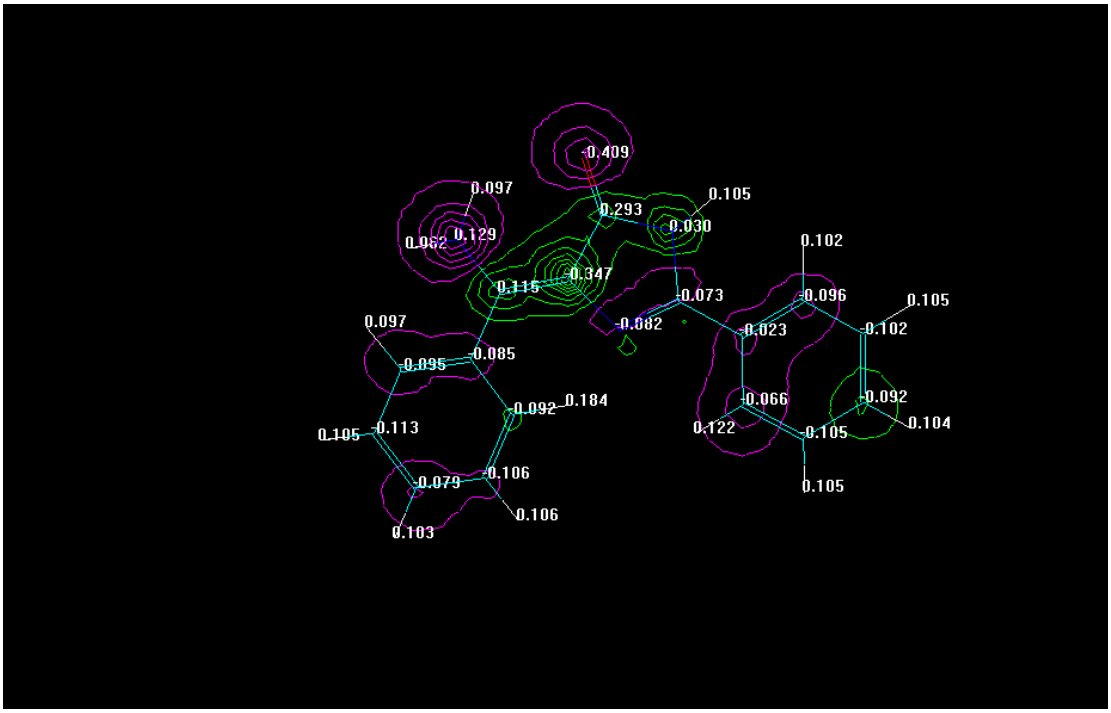


This type of compounds with phenyl rings at the positions of pyridyl rings in these compounds undergo acetylation and benzoylation very easily giving acetylated and benzoylated products.[112] Therefore we attempted the acetylation and benzoylation but failed.

In order to understand the reason for the failure of these reactions, we calculated the electron density at the N of NH_2 group of this compound and the similar compound prepared by Shafi and Sobha with phenyl groups in place of pyridyl group. It was found that the electron density at the nitrogen atom of the amino group in these compounds is very low when compared with the electron density at the nitrogen atom of the amino group in the compounds reported.[112] The contour diagrams of the electron density at various atoms of the two compounds which were compared are given below.



Contour diagram of the electron density at various atoms of 4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one



Contour diagram of the electron density at varoius atoms of 4-[amino, phenyl methylene]-2-phenyl-2-imidazolin-5-one

The low electron density at the nitrogen atom of the amino group justifies the resistance of these compounds towards acetylation and benzoylation.

III.2. Preparation of metal complexes using aminoimidazolinone as ligand

The structure of these compounds have the amino and carbonyl groups so placed that metal ions can form complexes with these compounds.

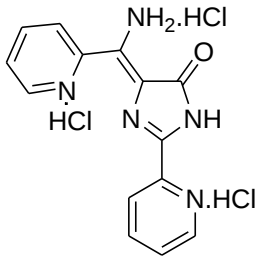
We prepared complexes of copper, cobalt and zinc using the compound 4-[amino,(2-pyridyl) methylene]-2(2-pyridyl)-2-imidazolin-5-one as ligand.

Results and discussions

The metal salts (copper acetate, cobalt acetate and zinc acetate) were dissolved in methanol and the amino imidazolinone was dissolved in ethanol. The amino imidazolinone was taken in excess expecting that we can remove the remaining compound after complexation by washing with alcohol. The ligand solution was added to the metal salt solution while the colour of the salt solution was changed immediately and the complex got precipitated. The complexes of Cu, Co and Zn were dark brown, dark purple and yellow in colour respectively.

The complexes of copper and cobalt were highly water soluble and the zinc complex was practically insoluble in water. Because of the high solubility of the complexes of copper and cobalt, we thought of exploiting this property for the colourimetric estimation of these metals. This amino imidazolinone was made soluble in water by converting it into hydrochloride. This was effected by adding concentrated HCl to the imidazolinone and the hydrochloride formed was reprecipitated by adding ethanol drop by drop. The hydrochloride formed was then filtered and washed with ethanol and dried. From the elemental analysis it was clear that the hydrochloride formed was a trihydrochloride. The trihydrochloride was formed by the addition of three molecules of HCl per molecule of the aminoimidazolinone. These HCl molecules might be attached to the nitrogen atoms of the two pyridyl ring and

to the NH_2 group in the molecule. These three nitrogen atoms are more electron rich when compared with the other two nitrogens of the imidazolinone ring. So the structure of the trihydrochloride can be given as follows:



It was readily soluble in water and its solutions of different concentrations can easily be prepared by just adding the required quantity of the compound to water and making up the solution to definite volume.

We were not able to arrive at the structure of the complex formed from the metal and the amino imidazolinone. Therefore, we could not proceed with the quantitative estimation of the metals using this complexation. Once we get the structure of the complex, the colourimetric estimation can also be easily carried out.

Experimental

Melting points recorded are uncorrected and carried out on a Toshniwal capillary melting point apparatus. The mass spectrum was recorded on Finnigan MAT 8200 spectrometer. All the ^1H nmr spectra were

recorded on a Brucker AM 360 spectrometer using TMS as reference standard. ^{13}C nmr spectra were recorded on Brucker AC 250 spectroscope at 90.5 MHz. IR spectra were recorded as KBr pellets using Shimadzu 8101A FTIR equipment. UV-Vis spectra were recorded in ethanol on a Shimadzu 1601 UV-Vis spectrometer.

Synthesis of the starting materials

Glycine ethyl ester hydrochloride was prepared as described in chapter I. Imidic acid methyl esters were prepared from cyanopyridines (2-cyanopyridine and 4-cyanopyridine) by Fred and Grace method during the synthesis of each amino imidazolinone.

Synthesis of aminoimidazolinones

4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one

Sodium metal (2 g) was dissolved in 20 ml of absolute methanol in a 100 ml round bottomed flask. 2-Cyanopyridine (4.6 ml, 0.04 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Toluene (10 ml) was also added to the round bottomed flask and refluxed for three hours. Yellow

crystals of 4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with ethanol and dried. The yellow product weighed 4.3 g (81%) and melted at 197 ^{o}C.

The amino imidazolinone (0.5 g) was recrystallised from ethanol (50 ml) and melted at 200 ^{o}C.

Analysis

	N%	C%	H%
Found	26.48	63.28	4.12
Calculated	26.41	63.59	4.15
	$C_{14}H_{11}N_5O$		
IR (cm^{-1})	3336, 3194, 1670, 1627, 1592		
Uv-vis	λ_{max} = 411		

4-[amino,(4-pyridyl) methylene]-2-(4-pyridyl)-2-imidazolin-5-one

Sodium metal (2 g) was dissolved in 20 ml of absolute methanol in a 100 ml round bottomed flask. 4-cyanopyridine (4.4 g, 0.04 mol) was added to it and allowed to stand overnight at room temperature. Acetic acid (1 ml) was then added and boiled on a water bath to remove the excess methyl alcohol present in the reaction mixture. Glycine ethyl ester hydrochloride (2.78 g, 0.02 mol) and sodium bicarbonate (3.5 g) were ground together and added to the imidate formed in the round bottomed flask. Toluene (10 ml) was also added to the round bottomed flask and refluxed for three hours. Yellow

crystals of 4-[amino,(4-pyridyl) methylene]-2-(4-pyridyl)-2-imidazolin-5-one formed were filtered. Washed twice with water and then with ethanol and dried. The yellow product weighed 4 g (75%) and melted at 327 ºC.

The amino imidazolinone (0.5 g) was recrystallised from ethanol (50 ml) and melted at 330 ºC.

Analysis

	N%	C%	H%
Found	26.37	63.23	4.13
Calculated	26.41	63.39	4.15
	$C_{14}H_{11}N_5O$		
IR (cm^{-1})	3340, 3198, 1652, 1617, 1586		
Uv-vis	λ_{max} = 381		

Preparation of the metal complexes

Complexes of Co(II), Cu(II) and Zn(II) were prepared by mixing methanolic solutions of the metal acetate (0.005 mol) and ethanolic solutions of the metal acetate (0.005 mol) and ethanolic solution of the amino imidazolinone (0.01 mol) in the presence of sodium acetate. (In the preparation of Cu(II) complex, sodium acetate was not added). On mixing these two solutions, the colour of the solutions changed immediately and the complexes started to precipitate. In order to make the complexation complete, the resulting solution was refluxed for 2 hours, concentrated and

kept overnight in an icebath. The complex formed was filtered using a vacuum pump and washed with ethanol and ether, dried in a desiccator over anhydrous calcium chloride.

Preparation of trihydrochloride

The amino imidazolinone (2 g) was taken in a 50 ml beaker. Con. HCl was added to it slowly. On addition of con. HCl the compound got dissolved by the formation of trihydrochloride and a clear solution was resulted. To this solution lime distilled ethanol was added drop by drop to precipitate the trihydrochloride formed. The precipitate was filtered and washed thrice with lime distilled ethanol and dried in a desiccator over anhydrous NaOH pellets.

Elemental Analysis

	N%	C%	H%
Found	18.52	44.7	4.2
Calculated	18.7	44.9	4
	$C_{14}H_{14}N_5OCl_3$		

CHAPTER 4
AMINOIMIDAZOLINONES AS CORROSION INHIBITORS FOR MILD STEEL

Introduction

Corrosion is the destruction or deterioration of a material because of reaction with its environment. It is an important problem which results in a serious waste of both resources and money during the application of metallic materials. Corrosion control is important in extending the life of equipment. It also limits the dissolution of environmentally toxic metals from the components. Acid solutions are generally used for the removal of undesirable scale and rust in several industrial processes. Hydrochloric acid has been extensively used for drilling operations, pickling baths and in descaling operations.[116] Mild steel (MS) is used to fabricate various reaction vessels, pipes, tanks, etc. in most of the chemical industries due to its easy availability and low cost. But MS suffers severe corrosion in aggressive media.

A corrosion inhibitor is a substance which when added in small quantities to a corroding medium brings about an appreciable reduction of corrosive action. Corrosion inhibitors are commonly added in small amounts to acids, cooling water, steam and other environments, either continuously or intermittently to prevent serious corrosion. The selection of a suitable

inhibitor depends on the type of acid, its concentration, temperature, flow velocity, the presence of dissolved inorganic and organic substances and type of metallic materials exposed to the acid solution.

Corrosion is an electrochemical phenomenon and inhibitors decrease the velocity of electrochemical electrode reactions.[117,118] Depending upon the mechanism of their action, corrosion inhibitors are classified as anodic inhibitors, cathodic inhibitors and organic or mixed type inhibitors. Anodic inhibitors are substances, which reduce anode area by acting on anodic sites and polarize the anodic reaction and displace the corrosion potential in the positive direction. Chromates, nitrates, tungstates and molybdates are some examples of anodic inhibitors.

Cathodic inhibitors reduce the cathode area by acting on the cathodic sites and polarize the cathode reaction and displace the corrosion potential in the negative direction. They reduce corrosion current and thereby retard the cathodic reaction and suppress corrosion rate. Examples for cathodic inhibitors are phosphates, silicates and borates.

Substances, which affect both cathodic and anodic recations, are called mixed inhibitors. In general they are organic compounds, which are also known as organic or adsorption inhibitors, which adsorb on the metal surface and suppress the metal dissolution and reduce the reaction. Organic inhibitors affect the entire surface of the corroding metal when present in sufficient

concentration. Both the anodic and cathodic areas are probably inhibited but to varying degrees, depending on the potential of the metal, chemical structures of the inhibitor molecule and size of the moelcule.

Most of the well known acid inhibitors are organic compounds containing nitrogen, sulphur or oxygen atoms. It has been reported that many heterocyclic compounds containing heteroatoms like nitrogen, sulphur and oxygen have been proved to be effective inhibitors for the corrosion of steel in acid media.[119-129] The inhibition property of these compounds is attributed to their molecular structure. The planarity and the lone electron pairs in the heteroatoms are important features that determine the adsorption of these molecules on the metallic surface. They can adsorb on the metal surface, block the active sites on the surface and thereby reduce the corrosion rate. The mild steel corrosion involves hydrogen formation, which is dissolved by the metal in an atomic form leading to the decrease in the ductility of metal known as pickling brittleness. Inhibitors are added to the acid to overcome these disadvantages associated with metal corrosion pickling.

The use of natural products as corrosion inhibitors is well documented[130] and have successfully identified corrosion inhibitors for mild steel in acid medium from various plant extracts like *Andrographis paniculoata*,[131] *Datura metel*,[132] *D. stramonium*[133] and black pepper[134] extract. The anticorrosion activity of atropine sulfate[135] is also reported.

Present Work

In the present work the inhibitory effect of 4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one (C_1) and 4-[amino,(4-pyridyl) methylene]-2-(4-pyridyl)-2-imidazolin-5-one (C_2) in 1 molar HCl medium on mild steel has been investigated at room temperature. Corrosion inhibition has been determined using weight loss and electrochemical methods.

Results and Discussion

Weight loss experiments and electrochemical analysis were carried out to find out the corrosion inhibition efficiency of two amino imidazolinones on mild steel. The results showed that these two compounds are very effective in inhibiting corrosion of mild steel in HCl.

Weight loss method

Weight loss occurred for MS coupon immersed in 250 ml of 1 M HCl and the weight loss occurred for MS coupons which were immersed in 1 M HCl containing 50 ppm, 100 ppm, 200 ppm and 300 ppm of the amino imidazolinones were measured. The measurements were done after immersing the coupons for 24 hours, 48 hours and 72 hours in 1 M HCl (blank) and also in 1 M HCl containing various quantities of the corrosion inhibitors. The results revealed the fact that the weight loss was maximum for blank and weight loss values decreases with increase in inhibitor

concentration. The coupons immersed in the inhibitor solutions were less corroded while coupons immersed in the blank solution were severely corroded. Weight loss increased with time and it decreased as the concentration of the inhibitor increased.

The weight loss values for C_1 and C_2 are given in Table 1 and Table 2 respectively. Plots of weight loss against concentration of inhibitor for various time intervals for C_1 and C_2 are also obtained (Graph 1 and Graph 2).

Table 1

Weight loss in grams occurred for MS in 1 M HCl containing various quantities of C_1

Inhibitor concentration (ppm)	Wt. loss of coupons after exposure		
	24 hr	48 hr	72 hr
0	1.037	1.4307	1.4857
50	0.2030	0.2830	0.3563
100	0.0952	0.1618	0.2125
200	0.0672	0.1117	0.1458
300	0.0512	0.0981	0.1158

Graph I

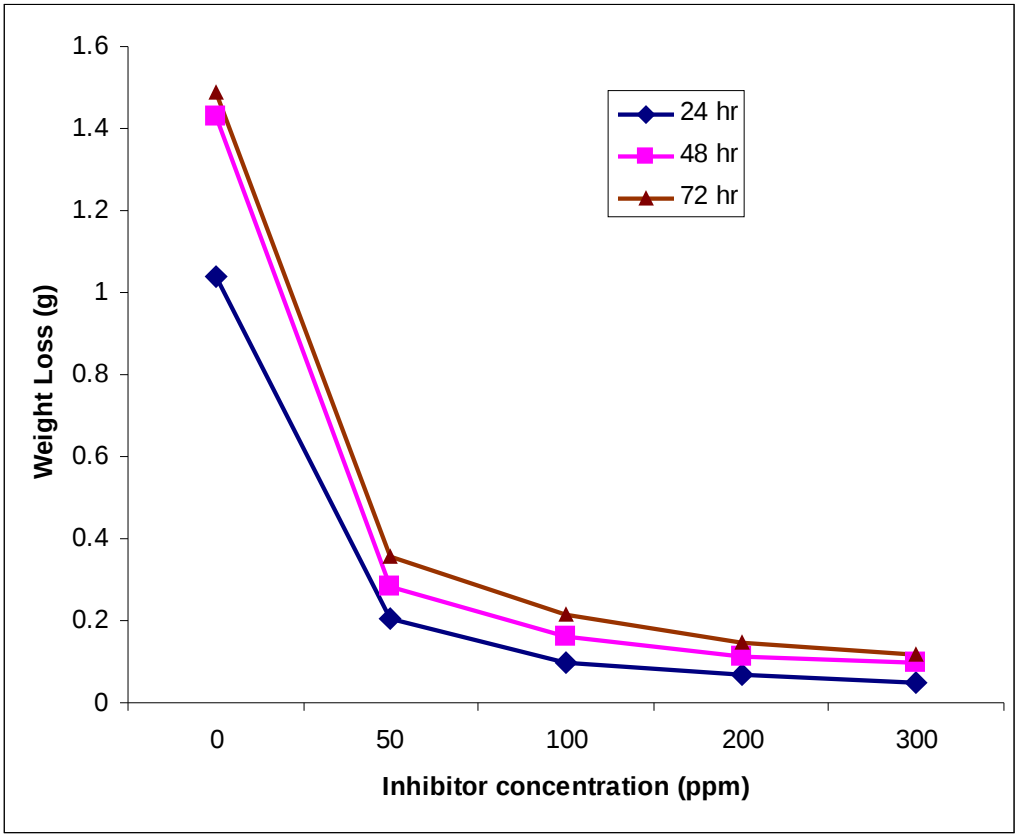
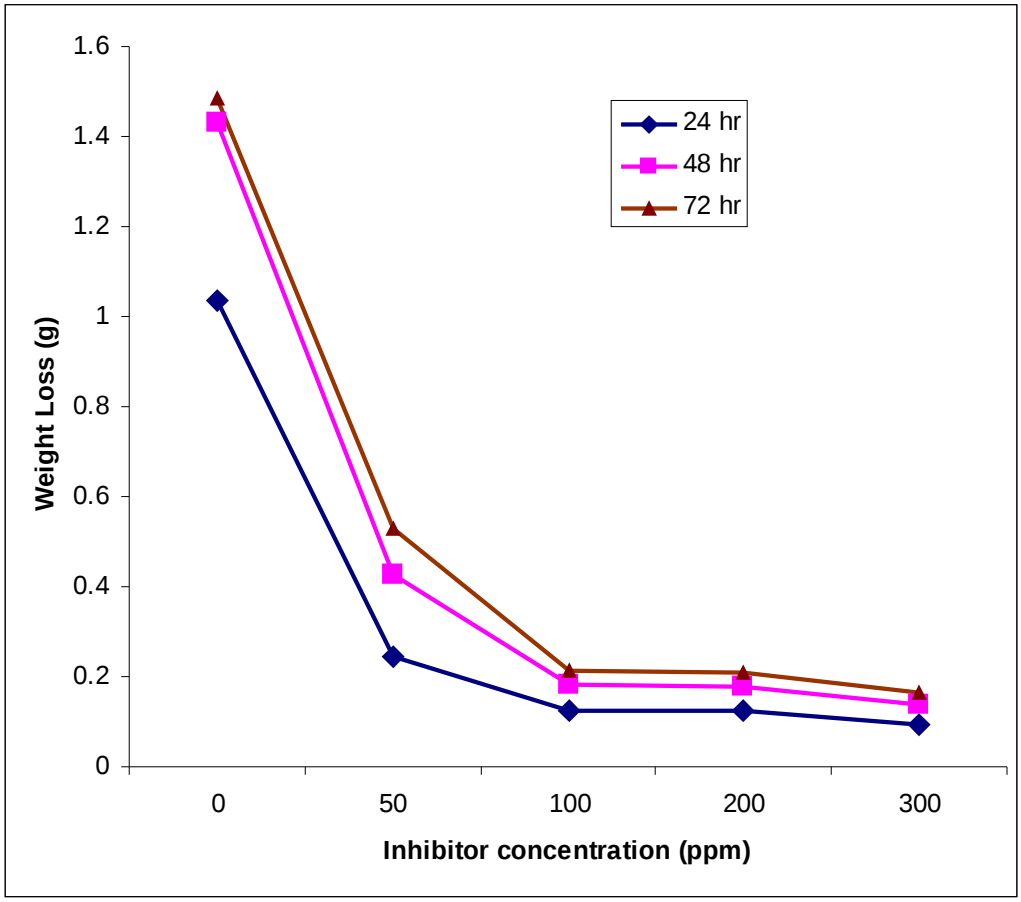


Table 2

Weight loss in grams occurred for MS in 1 M HCl containing various quantities of C_2

Inhibitor concentration (ppm)	Wt. loss of coupons after exposure		
	24 hr	48 hr	72 hr
0	1.037	1.4307	1.4857
50	0.2425	0.4272	0.5295
100	0.1251	0.1804	0.2114
200	0.1242	0.1785	0.2089
300	0.0933	0.1358	0.1649

Graph II



Corrosion rates and percentage inhibition efficiencies

The corrosion rates expressed in mils/year of the MS coupons in 1 M HCl (Blank) and 1 M HCl containing different quantities of the corrosion inhibitors were calculated from the weight loss values. Corrosion rate was decreasing with increasing concentration of the inhibitor. Corrosion rate values for different concentration of C_1 and C_2 at various time intervals are given in Table 3 and Table 4 respectively.

Table 3

Corrosion rates in mils/year observed for different concentrations of C_1 at various time intervals

Inhibitor concentration (ppm)	Corrosion rates		
	24 hr	48 hr	72 hr
0	2169	1496	1036
50	425	296	248
100	199	169	148
200	141	117	102
300	107	103	81

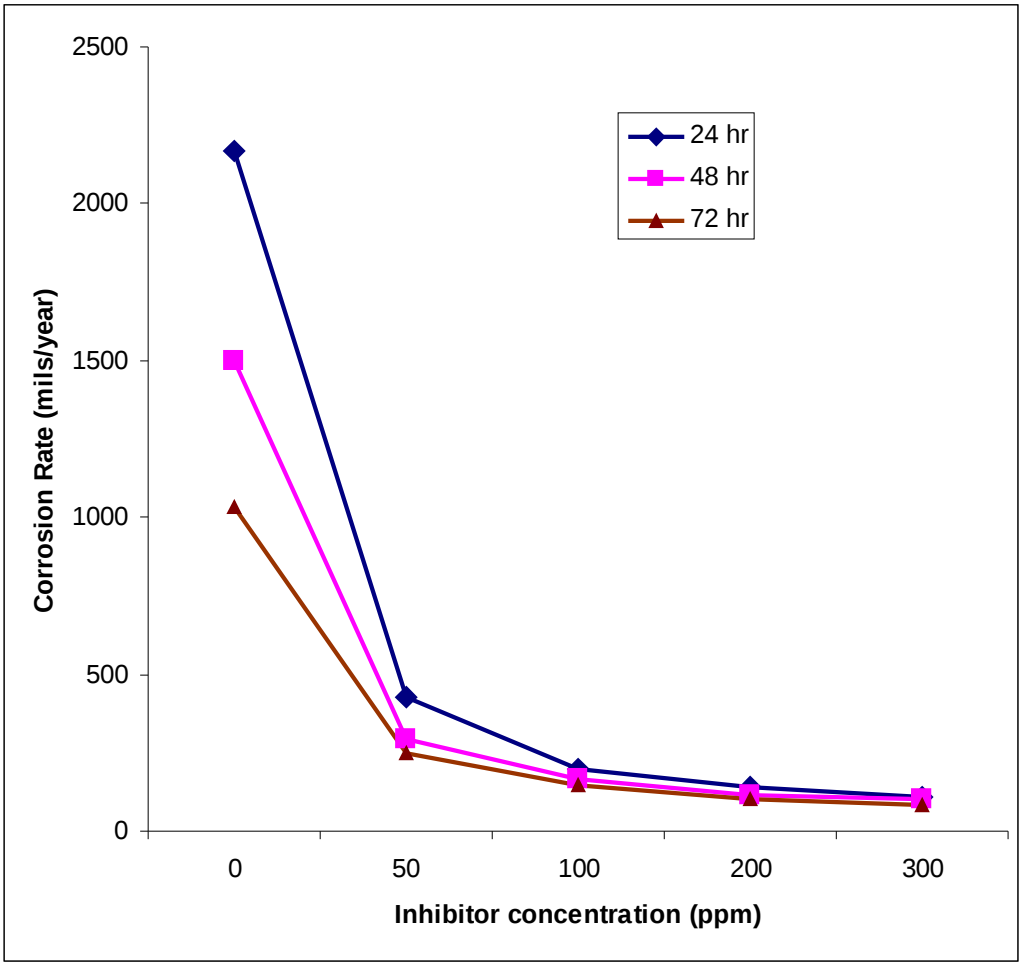
Table 4

Corrosion rates in mils/year observed for different concentrations of C_2 at various time intervals

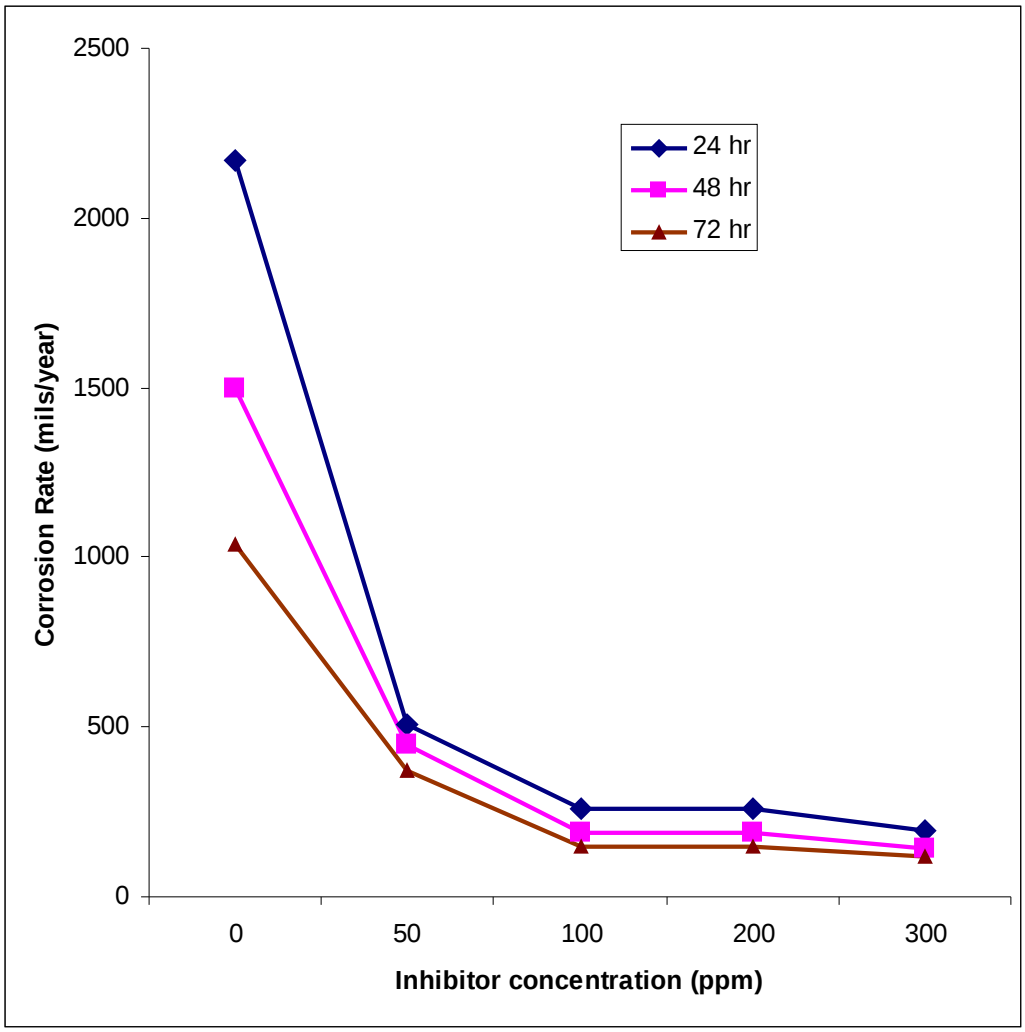
Inhibitor concentration (ppm)	Corrosion rates		
	24 hr	48 hr	72 hr
0	2169	1496	1036
50	507	447	369
100	262	189	147
200	260	186	145
300	195	142	115

Plots of corrosion rate against concentration of C_1 and C_2 for various time intervals are given below (Graph 3 and Graph 4).

Graph 3



Graph 4



The percentage inhibition efficiency of C_1 and C_2 on MS in HCl were calculated from the corrosion rates and are tabulated in Table 5 and Table 6 respectively.

Table 5

Percentage inhibition efficiency of C_1 for different concentrations at various time intervals

Inhibitor concentration (ppm)	Percentage Inhibition Efficiency		
	24 hr	48 hr	72 hr
50	80	79	76
100	91	88	85
200	94	92	90
300	95	93	92

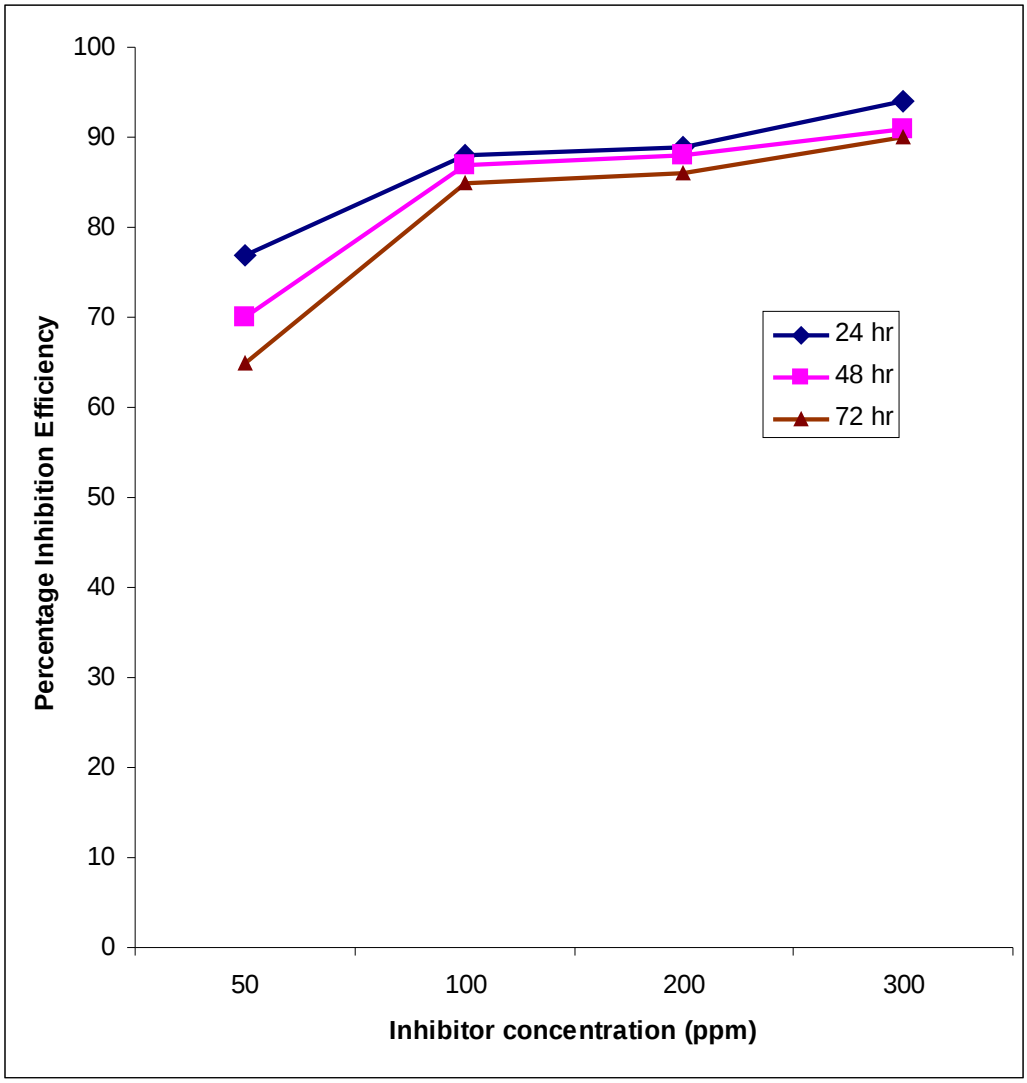
Table 6

Percentage inhibition efficiency of C_2 for different concentrations at various time intervals

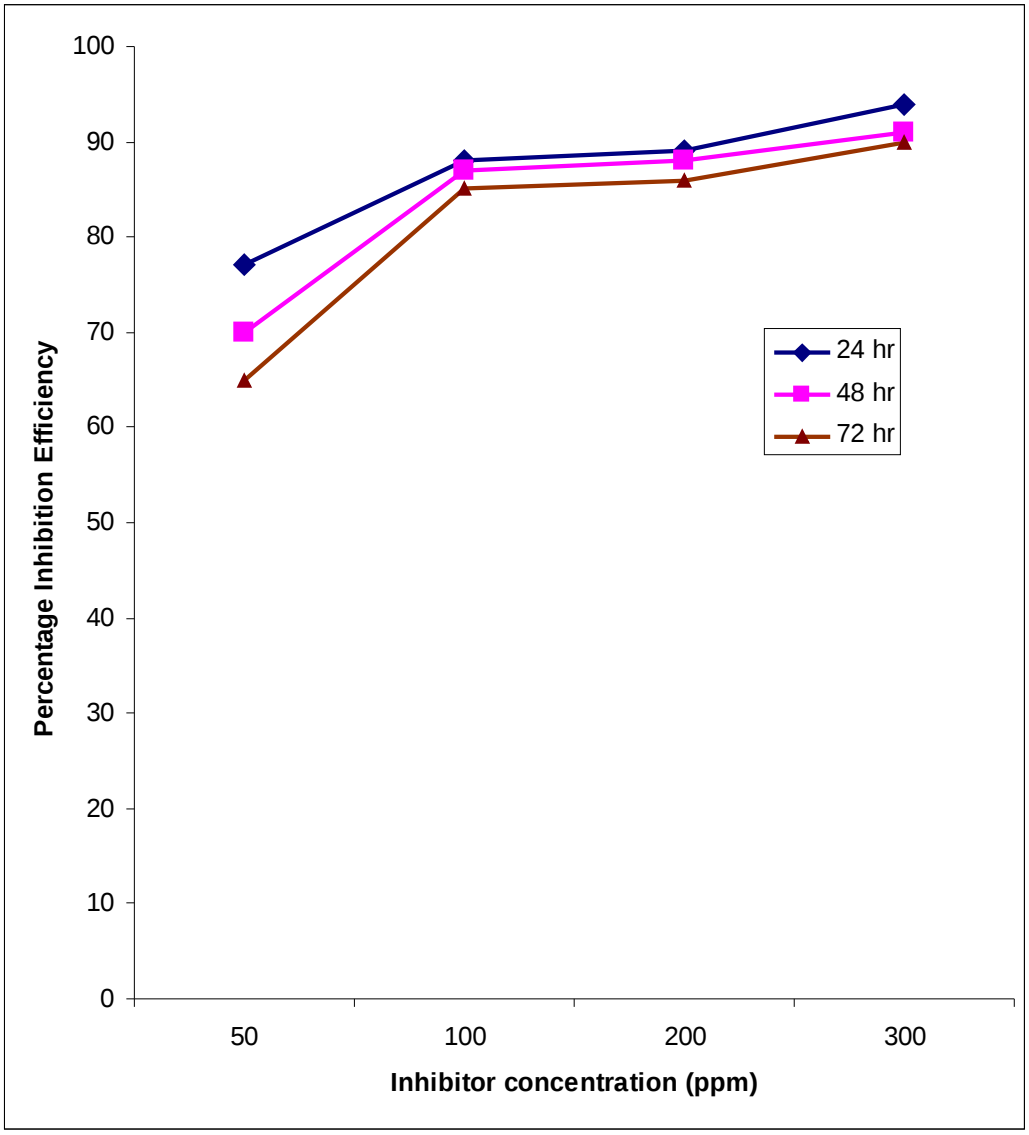
Inhibitor concentration (ppm)	Percentage Inhibition Efficiency		
	24 hr	48 hr	72 hr
50	77	70	65
100	88	87	85
200	89	88	86
300	94	91	90

Percentage inhibition efficiency increased with increase in the inhibitor concentration. To compare the efficiencies of C_1 and C_2 as inhibitors, plots of inhibition efficiency against inhibitor concentration at various time intervals were obtained for C_1 and C_2 (Graph 5 and Graph 6).

Graph 5



Graph 6

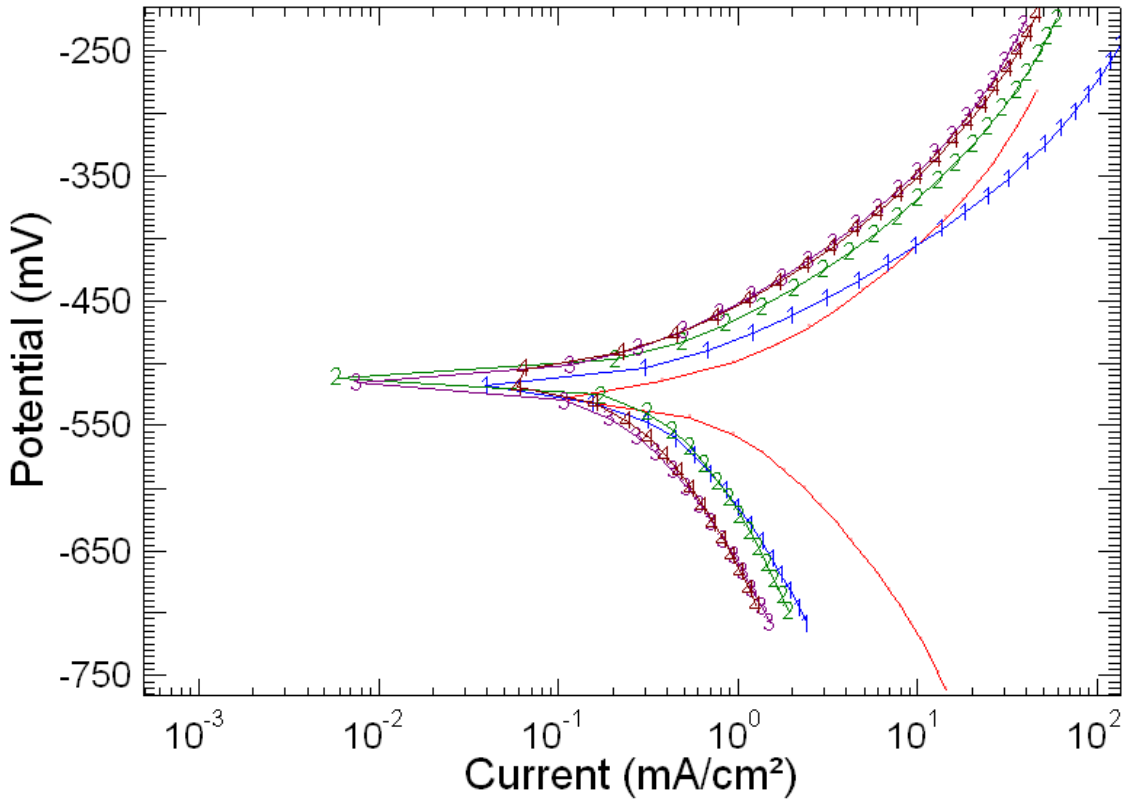


The above results show that compounds C_1 and C_2 are efficient corrosion inhibitors for mild steel in 1 M HCl. From the results obtained it is evident that compound C_1 is a more effective inhibitor than compound C_2. The values of corrosion rate is decreasing more as the concentration of C_1 is increasing when compared with the values of corrosion rate for C_2. Percentage inhibition efficiency and weight loss values also show the same trend.

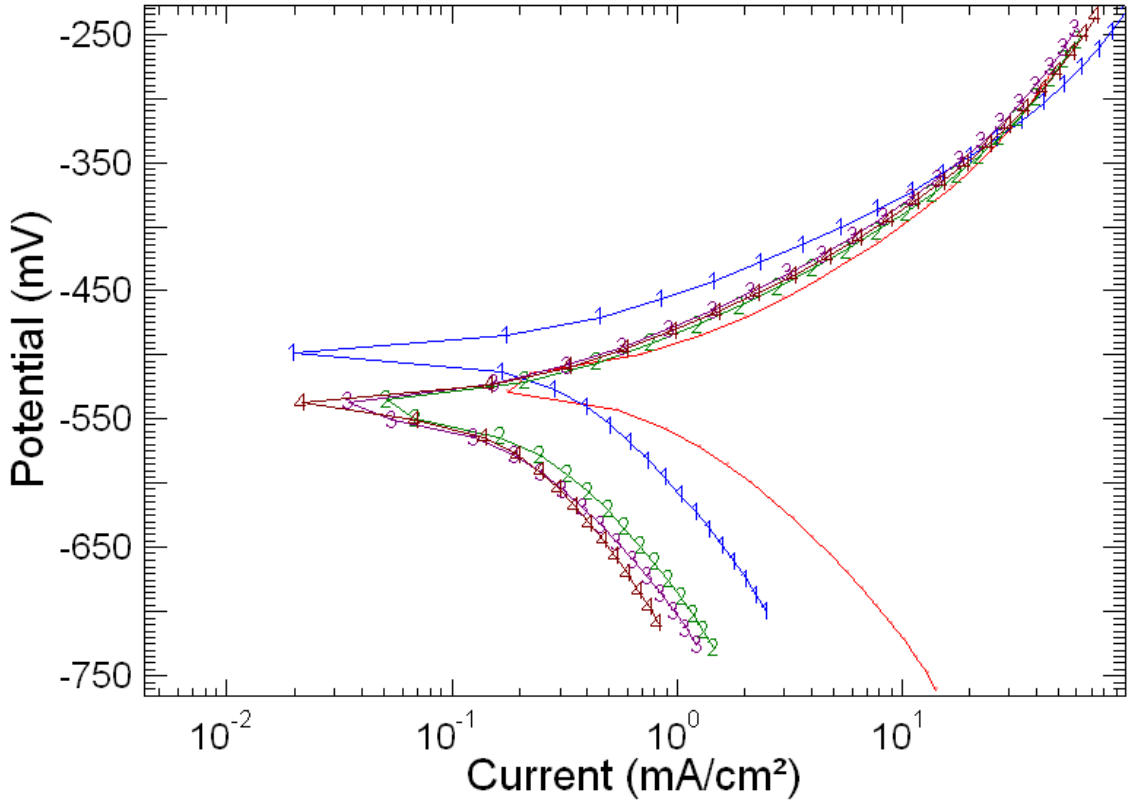
Potentiodynamic polarisation studies

Tafel polarisation curves obtained for MS in 1 M HCl without the presence of the inhibitor and with the presence of the inhibitor in different concentrations for compounds C_1 and C_2 are shown in Graph 7 and Graph 8.

Graph 7



Graph 8



Various corrosion parameters such as corrosion potential (E_{corr}), corrosion current density (i_{corr}), corrosion rate (CR), cathodic and anodic Tafel slopes β_c and β_a are given in table 7 and table 8 for compounds C_1 and C_2 respectively.

Table 7

Electrochemical parameters for compound C_1 obtained from polarisation curves

Inhibitor concentration (ppm)	E_{corr} mV	β_a	β_c	I_{corr} $\mu A\ cm^2$	C.R. mils/year	η %
0	482	140	227	4.475	714	0
50	460	78	127	1.84	682	59
100	455	70	141	1.56	668	65
200	447	59	92	0.92	402	79
300	458	65	119	0.78	360	83

Table 8

Electrochemical parameters for compound C_2 obtained from polarisation curves

Inhibitor concentration (ppm)	E_{corr} mV	β_a	β_c	I_{corr} $\mu A\ cm^2$	C.R. mils/year	η %
0	482	140	227	4.475	714	0
50	469	60	124	2.00	648	55
100	505	69	156	1.37	628	69
200	480	60	112	1.28	585	71
300	457	84	91	1.2	568	73

It is observed that the presence of the compounds C_1 and C_2 lowers i_{corr} value. As the concentration of the inhibitor (C_1 & C_2) is increased i_{corr} values are decreased. Percentage inhibition efficiency increases with increase in the

inhibitor concentration. Here also it is observed that compound C_1 is more efficient than C_2 in inhibiting corrosion.

In compound C_1 the nitrogen atoms are closer than in the compound C_2 and due to this structure the compound can cover the metal surface more effectively than compound C_2. This can be the reason for the better inhibiting efficiency of C_1.

Experimental

The corrosion inhibition efficiency of the aminoimidazolinones were determined using weight loss measurements and electrochemical method like potentiodynamic polarisation. The method of determining the weight loss of metal plates exposed to the corrosive environment using laboratory immersion corrosion testing method is the traditional and most widely used method for in situ corrosion monitoring.[136] As a classical corrosion test method, the weight loss method has provided a great deal of useful informations.

Preparation of Inhibitors

4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one and 4-[amino,(4-pyridyl) methylene]-2-(4-pyridyl)-2-imidazolin-5-one were synthesised as described in chapter III. Their chemical structures are also discussed in chapter III.

Attack solution

One molar HCl solution was prepared from AR, HCl and triply distilled water. All tests have been carried out at room temperature.

Specimen preparation

Mild steel specimen containing C = 0.2%, Mn = 1.0%, P = 0.03%, S = 0.02% and Fe = 98.75% were used for the study. MS pieces of size 0.72 x 1.88 $inch^2$ were used for weight loss study and specimens with exposed area of 1 cm^2 was used for electrochemical study. The surface preparation of the mechanically polished specimens was carried out using different grades of emery papers to mirror polished, then degreased with acetone and weighed using electronic balance having 0.0001 g accuracy. The exposed area of MS coupons was found out using vernier calipers.

Weight loss method

In laboratory immersion corrosion testing method, the metal coupons are exposed to the corrosive environment like acid solutions and weight loss of metal coupons are measured at regular time intervals and corrosion rate is calculated from the weight loss measurements. The inhibition capacity of the inhibitor is calculated from corrosion rates. In the present investigation, American Society for Testing and Materials (ASTM) G-31-72 standard procedure for laboratory immersion corrosion testing published in the year

1990 was adopted for the determination of weight loss and corrosion rate of MS coupons in HCl.[137,138]

The polished MS coupons were immersed in hanging position in 250 ml of testing solutions, 1 M HCl (blank) and 1 M HCl containing 50 ppm, 100 ppm, 200 ppm and 300 ppm of the inhibitors and covered the specimen at room temperature. The specimens were taken out at 24 hours interval, cleaned with acetone and water, dried and weighed. The weight loss of these coupons immersed in 1 M HCl (blank) and 1 M HCl containing inhibitors were recorded at 24 hrs, 48 hrs and 72 hrs period. Corrosion rate (CR), expressed in mils/year is calculated using the equation

$$\text{(Wt. loss in mg x 534) / (area x time x metal density)} = \text{mils/year}$$

where, weight loss is in milligram, area is in square inches of metal surface exposed, time in hour exposed, and density in grams per cubic centimetre. The density of the coupons is substituted with density value of iron, i.e. 7.86 g/cm^3.

The percentage inhibition efficiency of a corrosion inhibitor is calculated from the weight loss values using the equation

$$\eta_w = (w - w') / w \times 100$$

where w and w' are the weight loss of MS coupons in the absence and presence of inhibitor respectively.

Or

$$\eta_{CR} = \frac{(u_0 - u_i)}{u_0} \times 100$$

where u_0 and u_i are the corrosion rates in the absence and presence of inhibitor.

Electrochemical methods for Corrosion Rate Measurements

Most corrosion phenomena are of electrochemical in nature and consist of reactions on the surface of the corroding metal. Therefore, electrochemical methods can be used to characterise corrosion mechanism and predict corrosion rates. Electrochemical methods are used routinely for the evaluation of the efficiency of corrosion inhibitors.[139,140]

The advantages of electrochemical methods are short measurement time and mechanistic information that they provide which help not only in the design of corrosion protection strategies but also in the design of new inhibitors.

When a metal is immersed in a given solution, electrochemical reaction characteristic of the metal-solution interface occur at the surface of the metal to corrode. These reactions create an electrochemical potential called corrosion potential, E_{corr} or open circuit potential at the metal-solution interface. At the E_{corr} the rate of oxidation process is equal to the rate of

reduction. At the E_{corr} system is electronically neutral and said to be at equilibrium. The values of either the anodic or the cathodic current at E_{corr} is called corrosion current, i_{corr}.

Calculation of corrosion rates requires determination of corrosion currents. The current produced in the oxidation and reduction reactions determines the corrosion rate. The amount of current is controlled by the kinetics of reactions and the diffusion of reactants both towards and away from the electrodes. The measurement of corrosion rate is actually equivalent to the determination of kinetics of the corrosion electrochemical process. The common electrochemical techniques used for determination of corrosion rates and characterisations of corrosion systems are potentiodynamic polarization and electrochemical impedance spectroscopy.

Potentiodynamic Polarization Method

The theoretical model used for the corrosion process assumes that the electrochemical corrosion is an activation controlled process. In activation controlled process, an activation controlled reaction is involved for which the rate of reaction is controlled solely by the rate of the electrochemical charge transfer process at the metal surface.

The Tafel Equation and Tafel Plots

The Tafel equation was first found empirically by Tafel in 1951.[116]

This can be deduced from the equation

$$i = i_{corr} [\exp (\alpha n F\eta/RT) - \exp (-\beta n' F\eta / RT)] \quad \ldots (1)$$

where η is the over potential defined as the difference between applied potential E and corrosion potential E_{corr}, $\eta = E - E_{corr}$, i is the measured current density, i_{corr} is the corrosion current density, F is the Faraday's constant, R is the universal gas constant, T is the absolute temperature, n and n' are the number of electrons transferred in anodic and cathodic reactions, and α, β are coefficients related to the potential drop through the electrochemical double layer.[141]

For sufficiently high values of applied potential, as over potentials, either positive or negative, become larger than about 5×10^{-2}V, the second or first term of above equation, Bulter-Volmer equation becomes negligible respectively.

For anodic polarisation when $\eta >> RT/\beta n'F$, the following equations is obtained.

$$i = i_{corr} (\exp (\alpha nF\eta / RT)]$$

i.e., $$\eta = -2.303 RT / \alpha F \log i_{corr} + 2.303 RT / \alpha F \log i \quad \ldots (2)$$

Or

for Cathodic polarization, when $-\eta >> RT / \alpha nF$

$$i = i_{corr} [\exp (-\beta n'F\eta / RT)]$$

i.e., $$-\eta = 2.303 RT / \beta F \log i_{corr} + 2.303 RT / \beta F \log i \quad \ldots (3)$$

Equations (2) and (3) have the form of Tafel equation as shown in the equation below:

$$| \eta | = a + b \log i$$

where a and b are constants, $a = -2.303 RT / \alpha F \log i_{corr}$

and $b = 2.303 RT / \alpha F$

For anodic polarization

Or

$a = -2.303 RT / \beta F \log i_{corr}$ and

$b = 2.303 RT / \beta F$ for cathodic polarization.

Hence, simple exponential relationship between current density and over potential can be considered as logarithmically depended on the current density.

A plot of cathodic potential versus the logarithm of current density is called the "Tafel plot" and the resulting straight line is the 'Tafel line'. The

slope of a Tafel plot, "b" provides information about the mechanism of the reaction. The intercept "a" at $\eta = 0$ gives the exchange current density i_o and provide information about the rate constant of the reaction. This type of analysis is referred to as Tafel slope analysis. The percentage inhibition efficiency is calculated using the corrosion current densities using the relation

$$\eta\% = \frac{i_{corr} - i'_{corr}}{i_{corr}} \times 100$$

where i_{corr} and i'_{corr} are uninhibited and inhibited corrosion current densities respectively.[142,143]

The electrochemical experiment was carried out using a computer controlled Electrochemical work station ACM, UK (Model No.1475). A three-electrode cell consisting of a working electrode, a saturated calomel electrode as reference electrode and a platinum electrode served as auxiliary electrode.

The MS coupon with an exposed area 1 cm^2 was used as the working electrode. One molar HCl was taken as electrolyte. The working electrode was immersed in the test solution for two hours prior to the measurements to establish a steady state open circuit potential. Before that working electrode was polished with 1/0, 2/0, 3/0 and 4/0 grade emery papers and washed with distilled water.

The potentiodynamic polarization curves were obtained with a scan rate of 5 mV/sec in potential range from -250 MV to +250 MV relative to the open circuit potential. The linear Tafel segments of the anodic and cathodic curves were extrapolated to the corrosion potential to obtain the corrosion current densities. Percentage inhibition efficiency values were calculated from the i_{corr} values using the relation

$$\eta\% = \frac{i_{corr} - i'_{corr}}{i_{corr}} \times 100$$

CHAPTER 5
ANTIMICROBIAL PROPERTIES OF AMINOIMIDAZOLINONES

Introduction

Microorganisms are universally associated with the lives of humans, other animals and plants. Some of them are beneficial and others are detrimental. Microorganisms play an important role in the food and pharmaceutical industry. They are involved in the making of yogurt, cheese, wine, buttermilk and in the production of antibiotics. Besides their role as a beneficiary, microorganisms can cause diseases, spoil food and deteriorate materials like iron pipes, glass lenses and wood pilings. There is no field of human endeavour, whether it be in industry or agriculture or in the preparation of food and the combating of diseases, where the microbes do not play an important and often dominant role.

Each kind of microorganism has specific growth requirements. Many of them can be grown in the laboratory culture medium containing necessary nutrients for their growth and multiplication. Some of them require a supply of inorganic salts, particularly the anions, phosphate and sulphate and the cations sodium, potassium, iron, etc. whereas others can grow in a medium containing organic compounds (amino acids, vitamins or coenzymes) in

minute quantities. Some other require complex natural substances (peptone, blood, serum, etc.) and microorganisms like rickettsias cannot be grown in an artificial laboratory medium. On solid culture media microbial cells can grow and form visible masses called colonies.

Bacteria

The bacterium is a single celled organism that does not have intra cellular membrane bound organelles such as nucleus, golgi bodies, endoplasmic reticulum or mitochondria. Therefore, the bacterium's essential metabolic and biosynthetic activities must be carried out within the cytoplasm and the cell envelope. Bacteria lack a true nucleus and are classified as prokaryotes. One of the most important cytological features of bacteria is their reaction to a simple staining procedure, called the Gram-stain. The procedure involves staining the cells with crystal violet and a mordant known as Lugol's solution (3% I_2/KI) is added to set the stain. The bacteria are next decolourised with alcohol. Finally the bacteria are counterstained with Safranin. Gram-positive bacteria retain the crystal violet, whereas Gram-negative bacteria, which lose the crystal violet on counter staining by Safranin, appear red colour.[144] The most possible explanation for this difference in behaviour lies in the relative differences between the cell walls of the above two types of bacteria.

Bacterial cell wall is made up of peptidoglycan, an insoluble, porous, heteropolymer of alternating N-acetylglucosamine and N-acetylmuramic acid units. The cell wall in Gram-positive bacteria has a relatively thick layer of peptidoglycan 20 to 80 mm across. The peptidoglycan layer is closely attached to outer surface of the cell membrane. Chemical analysis shows that 60 to 90 percent of the cell wall of a Gram-positive bacterium is peptidoglycan. The thick cell walls of Gram-positive bacteria retain such stains as crystal violet-iodine dye in the cytoplasm.

The cell wall of a Gram-negative bacterium is thinner but more complex than that of a Gram-positive bacterium. Only 10 to 20 percent of the cell wall is peptidoglycan, the remainder consists of various polysaccharides, proteins and lipids. Gram-negative bacteria fail to retain the crystal violet-iodine dye during the decolourising procedure partly because of their thin cell walls and partly because of the relatively large quantities of lipoproteins and lipopolysaccharides in the wall.[145]

Fungi

Unlike bacteria, which are prokaryotes, fungi are eukaryotes. Each fungus has a golgi apparatus, mitochondria, nucleus, ribosomes, endoplasmic reticulum and a cell membrane, making it difficult to develop antibiotics that are selectively toxic for fungi. A large number of fungi are parasites of

terrestrial plants. Fungi cause the majority of economically significant diseases of crop plants.

Fungal cell walls resemble plant cell walls architecturally, but not chemically. Although cellulose is present in the walls of certain fungi, many fungi have non cellulosic walls.

The cell wall is composed of cross linked polysaccharides, proteins and glycoproteins and it provides the fungus with osmotic stability and acid rigidity. In nature fungi are important decomposers. Trees and leaves that fall in the forest are decomposed in large part by fungi. Many fungi produce enzymes that attack plant polymers such as cellulose and lignin. They also can grow in relatively dry locations. This enables them to decompose complex materials that are difficult for bacteria to attack.

Viruses which traditionally are considered as microorganisms, lack the fundamental structure of living organism. No functioning cytoplasmic membrane separates the virus from its surroundings and viruses have no means of independent life support activities. They have a genetic molecule which may be DNA or RNA and a protein coat.

Modes of Action of Antimicrobial Agents

Micro organisms can be inhibited or killed by various physical and chemical agents. The agents that kill or destroy the organisms are referred to

as 'cidal', whereas the one that merely halts the growth of the micro organism is called 'static'. If a static agent is removed from a culture, the organism will resume growth but the effects of cidal agents are irreversible. The manner in which antimicorbial agents inhibit or kill can be attributed to the following kinds of actions.[146]

Several types of chemical agents damage the cell wall by blocking its synthesis. Some of them will disrupt the cell membrane, so that the cell loses its selective permeability and can neither prevent the loss of vital molecules nor bar the entry of damaging chemicals. Some others will inhibit the enzyme action and will damage the microbial life. Chemicals such as strong solvents (alcohols, acid and phenolics) coagulate bacterial proteins; some agents disrupt or denature protein. Such losses in normal protein function can arrest bacterial metabolism, thereby inhibit the growth or kill them.

Antibiotics

These are chemical substances produced by certain microorganisms that inhibit or kill other microorganisms. An antibiotic that acts on both Gram-positive and Gram-negative bacteria is called a broad-spectrum antibiotic, whereas narrow spectrum antibiotics, acts on only a specific group of organism. The widespread use of antibiotics has increased the number of pathogenic microorganisms that display antibiotic resistance.

Results and Discussion

The antimicrobial activity of aminoimidazoliones containing phenyl groups was studied by Shafi and Basheer[113] and they found these compounds to be moderately active against bacteria. Therefore we expected better results for the aminoimidazolinones containing pyridyl groups.

Two aminoimidazolinones 4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one (C_1) and 4-[amino,(4-pyridyl) methylene]-2-(4-pyridyl)-2-imidazolin-5-one) and their hydrochloride (C_3 & C_4) were tested for antimicrobial activity. Four Gram-positive bacterial strains (*Staphylococcus aureus, Bacillus subtilis, Streptococcus faecalis* and *Staphylococcus albus*) four Gram-negative bacterial strains (*Escherichia coli, Pseudomonas aeruginosa, Protieus vulgaris* and *Klebsiella aerogenes*) and two fungi (*Candida albicans* and *Aspergillus niger*) were the microorganisms tested against the compounds under study.

The experimental results revealed that the maximum activity was shown by the hydrochloride of 4-[amino(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one. But this compound was not active against the Gram-negative bacteria, *Escherichia coli*. All the compounds were active against one Gram-positive bacteria, *Staphylococcus albus* and one Gram-negative bacteria *Pseudomonas aeruginosa* at all concentrations tried (1 mg/ml, 2.5

mg/ml and 5 mg/ml). But the extent of activity of the aminoimidazolinones depends on their concentrations.

The results obtained for the studies of the compounds C_1, C_2, C_3 and C_4 at different concentrations on different bacteria are tabulated in Tables V.1, V.2, V.3 and V.4 respectively and the results obtained for these compounds at different concentrations on different fungi are tabulated in Tables V.5, V.6, V.7 and V.8. The activity was measured in terms of the diameter of the zone of inhibition.

Ciprofloxacin (2μg/disc) was used as standard for bacteria and clotrimazole (10 μg/disc) was used as standard for fungi. DMSO was used as the solvent and it showed no effect against the microorganisms under test (No inhibitory effect is indicated by NI).

Table V.1

Antibacterial activity of C_1 at different concentrations

Sl. No.	Name of Bacteria	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1	*Staphylococcus aureus*	NI	NI	16	20
2	*Bacillus subtilis*	NI	10	12	19
3	*Streptococcus faecalis*	NI	NI	NI	19
4	*Staphylococcus albus*	11	12	12	18
5	*Escherichia coli*	NI	NI	NI	18
6	*Pseudomonas aeruginosa*	12	12	13	19
7	*Klebsiella aerogenes*	NI	NI	10	19
8	*Protieus vulgaris*	NI	NI	NI	19

Table V.2

Antibacterial activity of C_2 at different concentrations

Sl. No.	Name of Bacteria	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1	*Staphylococcus aureus*	NI	8	13	20
2	*Bacillus subtilis*	NI	NI	NI	19
3	*Streptococcus faecalis*	NI	NI	NI	19
4	*Staphylococcus albus*	10	10	14	18
5	*Escherichia coli*	NI	NI	NI	18
6	*Pseudomonas aeruginosa*	10	10	12	19
7	*Klebsiella aerogenes*	NI	NI	NI	19
8	*Protieus vulgaris*	NI	NI	NI	19

Table V.3

Antibacterial activity of C_3 at different concentrations

Sl. No.	Name of Bacteria	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1	*Staphylococcus aureus*	10	10	16	20
2	*Bacillus subtilis*	NI	11	13	19
3	*Streptococcus faecalis*	NI	10	13	19
4	*Staphylococcus albus*	12	12	13	18
5	*Escherichia coli*	NI	NI	NI	18
6	*Pseudomonas aeruginosa*	12	12	12	19
7	*Klebsiella aerogenes*	NI	NI	11	19
8	*Protieus vulgaris*	NI	NI	15	19

Table V.4

Antibacterial activity of C_4 at different concentrations

Sl. No.	Name of Bacteria	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1	*Staphylococcus aureus*	NI	9	15	20
2	*Bacillus subtilis*	NI	NI	NI	19
3	*Streptococcus faecalis*	NI	NI	NI	19
4	*Staphylococcus albus*	11	12	12	18
5	*Escherichia coli*	NI	NI	NI	18
6	*Pseudomonas aeruginosa*	10	10	10	19
7	*Klebsiella aerogenes*	NI	NI	12	19
8	*Protieus vulgaris*	NI	NI	NI	19

Table V.5

Antifungal activity of C_1 at different concentrations

Sl. No.	Name of Fungi	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1	*Candida albicans*	NI	NI	9	12
2	*Aspergillus niger*	NI	NI	NI	12

Table V.6

Antifungal activity of C_2 at different concentrations

Sl. No.	Name of Fungi	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1.	*Candida albicans*	NI	NI	9	12
2	*Aspergillus niger*	NI	NI	NI	12

Table V.7

Antifungal activity of C_3 at different concentrations

Sl. No.	Name of Fungi	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1.	*Candida albicans*	NI	NI	11	12
2	*Aspergillus niger*	NI	NI	NI	12

Table V.8

Antifungal activity of C_4 at different concentrations

Sl. No.	Name of Fungi	Diameter of zone of inhibition (mm) at different concentrations			
		1 mg/ml	2.5 mg/ml	5 mg/ml	STD
1.	*Candida albicans*	NI	NI	9	12
2	*Aspergillus niger*	NI	NI	NI	12

The hydrochlorides of the aminoimidazolinones were more active on both bacteria and fungi when compared with the activity of the aminoimidazolinones as such. This can be due to the greater solubility of the hydrochlorides in aqueous medium. Gram-positive bacteria were found to be more susceptible to the action of these compounds than Gram-negative bacteria.

The biological activity of this type of compounds has been established from the study of Maneesh Kumar and Silpee.[147] They carried out a dose dependent antiproliferative activity study of 4-[amino,(2-pyridyl) methylene]-2-(2-pyridyl)-2-imidazolin-5-one and its hydrochloride on mitogen induced human peripheral lymphocyte culture. The compound showed promising potential in arresting lymphocyte reproduction.

Experimental

Materials and Methods

Microorganisms

The test microorganisms of Gram-positive bacteria namely *Staphylococcus aureus, Bacillus subtilis, Streptococcus faecalis* and *Staphylococcus aureus* and Gram-negative bacteria *Escherichia coli, Pseudomonas aeruginosa, Protieus vulgaris, Klebsiella aerogenes* and fungi *Candida albicans, Aspergillus niger* were obtained from National Chemical Laboratory (NCL), Pune and maintained by periodical sub culturing on

nutrient agar and dextrose medium for bacteria and fungi respectively.

The antimicrobial activity of the compounds under study against the selected microorganisms were done by disc diffusion technique.[148-150]

Preparation of chemical extracts

The amino imidazolinones under investigation were dissolved in DMSO and solutions of different concentrations (1 mg/ml, 2.5 mg/ml and 5 mg/ml) were used to check the antibacterial and antifungal activity.

Detection of Antimicrobial activity

The petri plates were streaked with the microbes. For this bacterial strains grown on nutrient agar slants and fungi grown on dextrose were used. As soon as the filter paper disc impregnated with the antimicrobial agent comes in contact with the moist agar surface, water is absorbed into the filter paper and the antibiotic diffuses into the surrounding medium. The rate of extraction of the antibiotic out of the disc is greater than its outward diffusion into the medium, so that the concentration immediately adjacent to the disc may exceed that in the disc itself. As the distance from the disc increased, there was a reduction in the antibiotic concentration. Sensitive organisms were inhibited by the antibiotic diffused into the plate and no growth was seen at the points of inoculation. Resistant organisms appeared as distinct colonies of microbial growth. The edges of the inhibitory zones were clear and easy to measure. The zone diameter was measured in mm.

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