SYNTHESIS OF SOME IMIDAZOLE DERIVATIVES AND THE STUDY OF THEIR CHEMICAL AND PHOTOCHEMICAL REACTIONS

Thesis submitted to the University of Calicut in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry

By

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Kerala - 2001

To my beloved father
who cared for my education

Dr. P. Mohamed Shafi, M.Sc. Ph.D.,
Professor,
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CERTIFICATE

This is to certify that this thesis entitled **"Synthesis of some imidazole derivatives and the study of their chemical and photochemical reactions"** is an authentic record of the research work carried out by Mr. P.A. Mohamed Basheer, under my supervision in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry of the University of Calicut, and further that no part thereof has been presented before for any other degree.

Department of Chemistry,
11-01-2001.

Dr. P.MOHAMED SHAFI
(Supervising Teacher)

DECLARATION

I hereby declare that the thesis bound herewith is an authentic record of the research work carried out by me under the supervision of Dr. P. Mohamed Shafi, M.Sc., Ph.D., Professor, Department of Chemistry, University of Calicut in the partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry of the University of Calicut, and further that no part thereof has been presented before for any other degree.

P.A. MOHAMED BASHEER

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Above all the blessings bestowed by the Almighty God is gratefully acknowledged and I pray for His mercy further.

P.A. Mohamed Basheer.

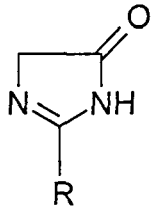
CONTENTS

PREFACE

The Chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. With the number of organic compounds approaching five million more than half of them are heterocyclics. It is equally interesting for its theoretical implications, for the diversity of its synthetic procedures and for the physiological and industrial significance.

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 genetic material DNA, the essential amino acid proline, histidine, tryptophan, the vitamin and co-enzyme precursors thiamin, riboflavin, pyridoxin, folic acid, the B_{12} and E families of vitamin, the photo synthesising pigment chlorophyll, the oxygen transporting pigment haemoglobin and its breakdown products the bile pigments are heterocyclic compounds. Majority of synthetic heterocyclics have found widespread use as anticancer agents, analgesics, hypnotics, pesticides, weed killers and rodenticides. There are also a large number of synthetic heterocyclics with other practical applications as dyestuffs, copolymers, solvents, photographic sensitizers, developers, antioxidants and vulcanization accelerators in rubber industry.

Debus discovered the parent compound imidazole from glyoxal and ammonia and to indicate its source proposed the name 'glyoxaline'. The name imidazole is due to Hantzsch. The first chemical study of imidazole 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 imidazolinone (I) can further react with another molecule of imidic acid ester to give aminoimidazolinones. 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.

In the present work 1,2,4-trisubstituted imidazolinones with carbethoxymethyl group at position -1 were synthesised and is discussed in chapter I. Reaction of azlactones with glycine ethyl ester followed by vacuum heating of the amide formed yielded 2-aryl-4-arylidene-1-(carbethoxy methyl)-2-imidazolin-5-ones. These imidazolinones underwent hydrolysis with a weak base, sodium carbonate solution, yielding the corresponding acids. Based on this an article entitled "**Synthesis and reactions of 1,2,4-trisubstituted-2-imidazolin-5-ones**" has been submitted for publication in Indian Journal of Hetrocyclic Chemistry.

In chapter II synthesis of some spiro imidazolinones are discussed. The reaction between (I) and divinylketones yielded hitherto unreported spiro imidazolinones by the double Michael addition. Spiro compounds containing imidazolinone ring are not many and by this approach novel spiro imidazolinones could be prepared.

Chapter III describes reactions of spiro imidazolinones. Spiro imidazolinones underwent thermal decomposition by heating just above 300°C yielding one molecule of 3-aryl substituted cyclobutanone and one molecule of 2-aryl-4-arylidene-2-imidazolin-5-one. As these spiro compounds contained a carbonyl group in the cyclohexane ring undergo condensation with 2,4-dinitrophenylhydrazine and also with (I) yielding new spiro compounds. Based on the works presented in chapter II and III an article

entitled "**Synthesis and reactions of some novel spiro compounds**" has been sent for publication in Indian Journal of Chemistry.

Reaction between glycine ethyl ester and excess imidic acid ester in toluene at the reflux temperature gave 4-(Amino,arylmethylene)-2-aryl-2-imidazolin-5-ones. The benzoylation of this amino imidozolinone gave hitherto unreported compounds. Spectral studies of their acetyl derivatives also forms the topics of discussion of chapter IV. This work is part of an article entitled "**Synthesis of 4-(Amino, aryl methylene)-2-aryl-2-imidazolin-5-one and their reactions**" presented for publication in Indian Journal of Chemistry.

Imidazolinones possess various biological properties. The antibacterial and antifungal study of some 1,2,4-trisubstituted imidazolinones and spiro imidazolinones were conducted and are discussed in Chapter V.

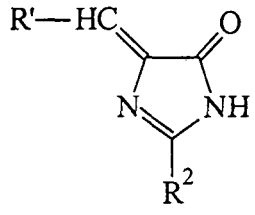
The photochemical reactions of 2-imidazolin-5-ones are discussed in Chapter VI. The compounds photoirradiated were 2-aryl-4-cyclohexylidene-2-imidazolin-5-one and 2-aryl-4-arylidene-2-imidazolin-5-one.

REVIEW

The work presented in this thesis deals with the synthesis and reactions including photochemical reactions 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-disubtituted imidazolin-5-ones.

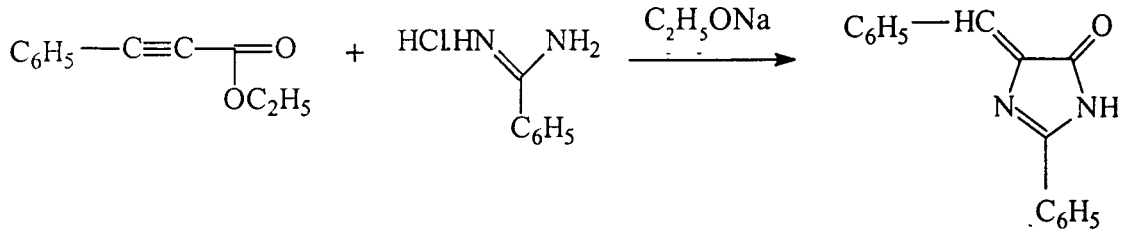
SYNTHESIS OF UNSATURATED 2-IMIDAZOLIN-5-ONES

Imidazolinones with an exocyclic double bond at the 4th position is usually called unsaturated 2,4 disubstituted-2-imidazolin-5-ones. They are also known as unsaturated 2,4 disubstituted 5(4H)-imidazolones and unsaturated 2,4 disubstituted 5-Keto dihydro 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[1,2]. 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.



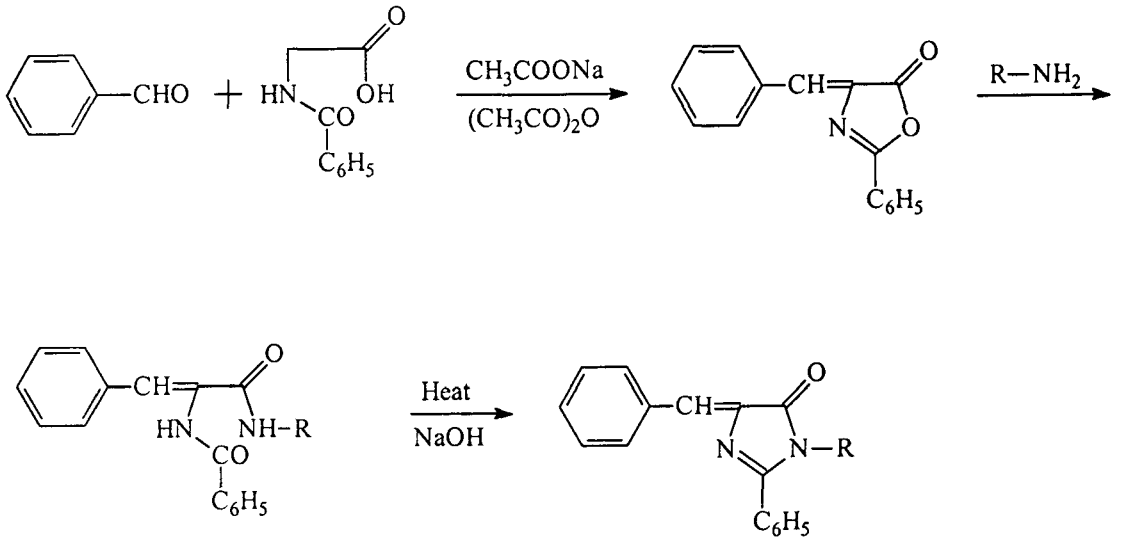
At present there are four general methods for the synthesis of unsaturated 2-imidazolin -5- ones namely azlactone, amidine-glyoxal, imidic acid ester- glycine ester and amidine - haloacetic ester method.

AZLACTONE METHOD

Azlactones may be considered as anhydrides of alpha-acylamino acids. Plochl [3] in 1883 prepared the first unsaturated azlactone by the condensation of benzaldehyde with hippuric acid in presence of acetic anhydride.

Erlenmeyer[4-12] 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.

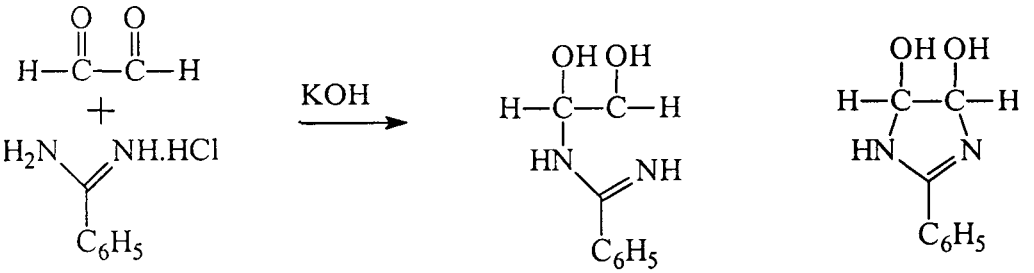
This method was further extended by various workers[13-33] to synthesise 1,2,4 trisubstituted -2-imidazolin-5-ones.



(R=H , alkyl , aryl etc.)

AMIDINE-GLYOXAL METHOD

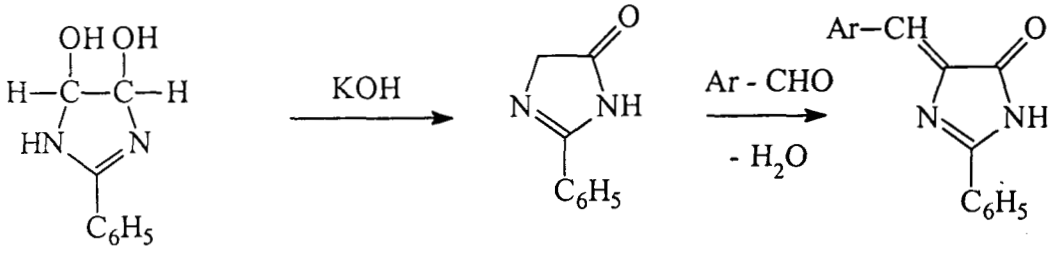
In 1935 Ekeley and Ronzio[2,34] developed a method for the synthesis of 2-aryl-4-arylidene-2-imidazolin-5-one by condensing aromatic aldehydes with aromatic amidine-glyoxal addition products. Actually they thought that the condensation products obtained were either diaryl pyrimidones or 2-aryl-4-aroyl glyoxalones. 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 sodium hydroxide or potassium hydroxide good yields of 2-phenyl-4-arylidene-2-imidazolin-5-ones are obtained.

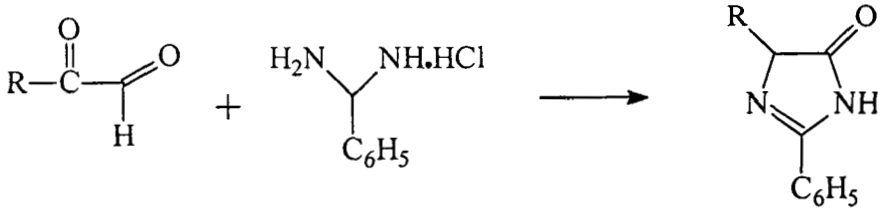
The reaction may be formulated in the manner illustrated below using the more plausible 4,5-dihydroxy-2-imidazoline structure for the benzamidine-glyoxal complex. It is assumed that the dihydroxy imidazoline loses a molecule of water under the influence of the base to form 2-phenyl-2-imidazolin-5-one 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[34-35] 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.

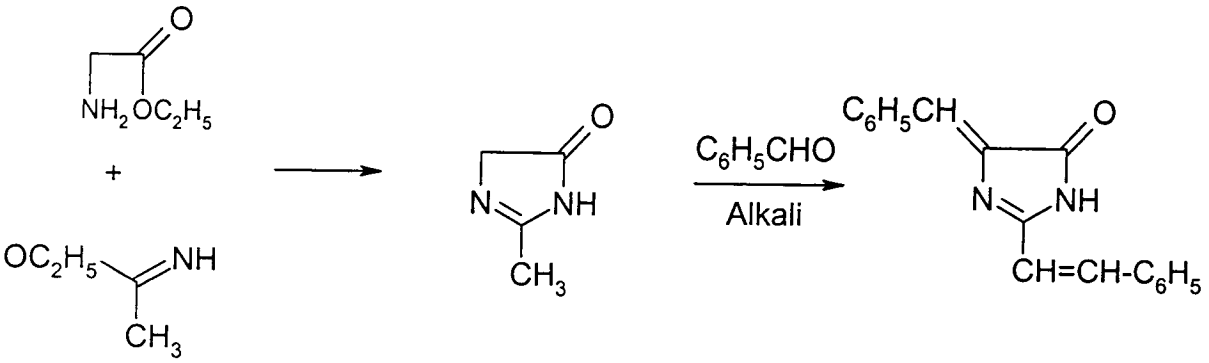
In 1948 Cornforth[36,37] prepared 5-imidazolones by the reaction between Benzamidine hydrochloride and monosubstituted glyoxals.



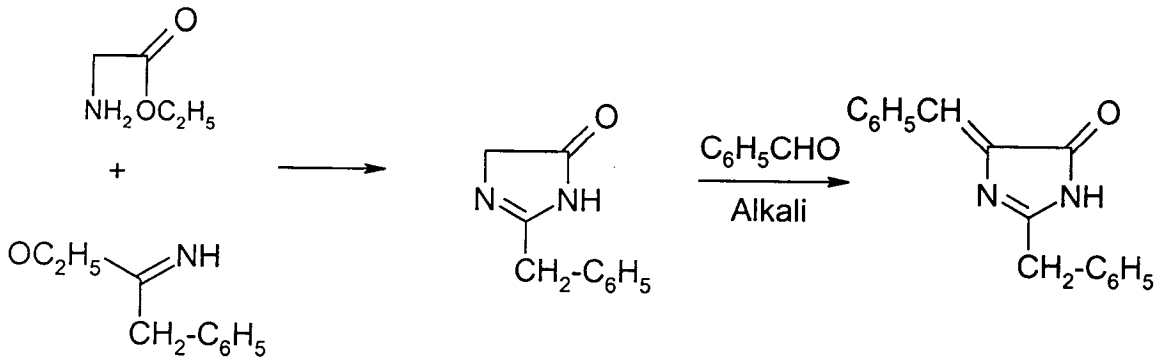
The 4(5) imidazolones which have a methylene group adjacent to the carbonyl group form[38] benzylidene derivatives and also couple with diazonium salts.

IMIDIC ACID ESTER - GLYCINE ESTER METHOD

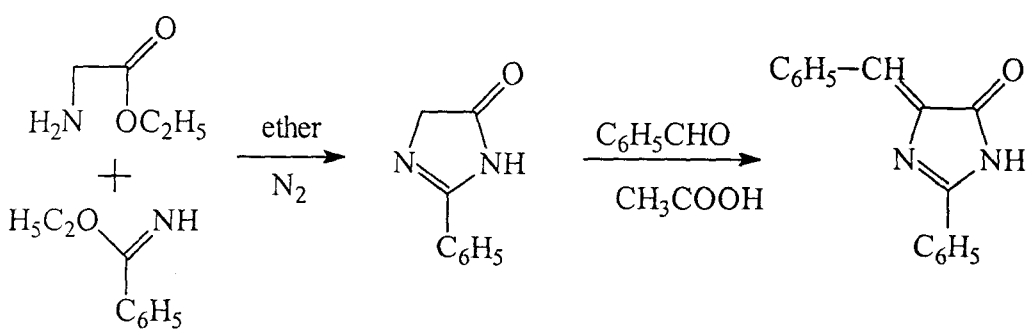
In 1907 Finger[38] obtained 2-methyl-2-imidazolin-5-one by condensing glycine ester with acetimidic acid ester at room temperature. The 2-methyl-2-imidazolin-5-one condensed with two molecules of benzaldehyde to form 2-benzylidene methyl-4-benzylidene-2-imidazolin-5-one.



Finger and Zeh[39] prepared 2-benzyl-2-imidazolin-5-one by condensing phenyl acetimidic ester and glycine ester. This imidozolone condenses with C_6H_5-CHO in presence of alkali to give 2-benzyl-4-benzylidene-2-imidazolin -5-one.

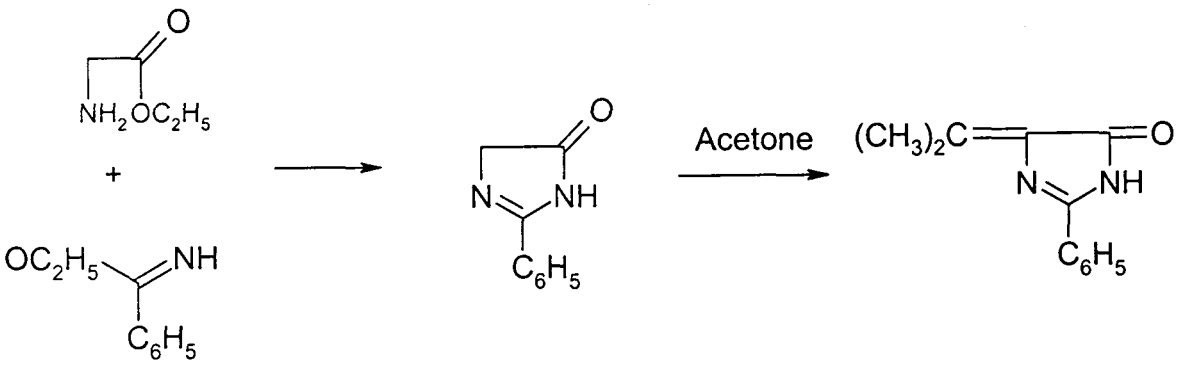


In 1953 Kjaer[40] prepared 2-phenyl-2-imidazolin-5-ones in 18.8% yield by condensing benzimidic acid ester with glycine ester in presence of anhydrous ether in nitrogen atmosphere. The product was recrystallised from benzene in an oxygen free atmosphere followed by sublimation. He obtained 2-phenyl-4-benzylidene-2-imidazolin-5-one by condensing benzaldehyde with 2-phenyl-2-imidazolin-5-one.



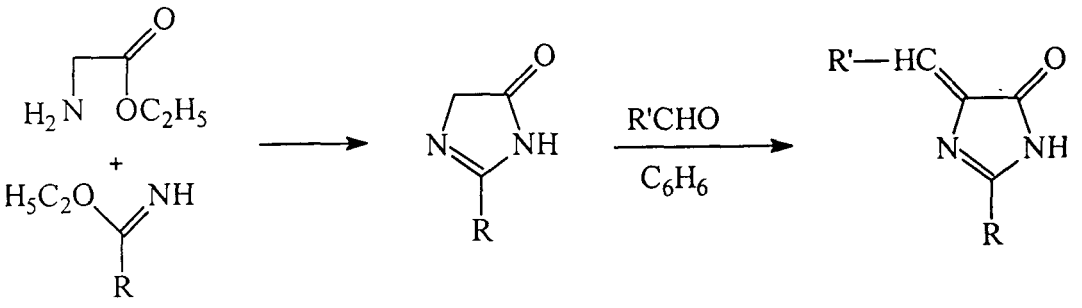
1- Naphthaldehyde, furfuraldehyde, isatin and pyruvic acid were also condensed with 2-phenyl-2-imidazolin-5-one and obtained the corresponding unsaturated 2-imidazolin-5-ones.

In 1953 Lehr and coworkers[41] obtained 2-substituted 4-isopropylidene -2-imidazolin-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.

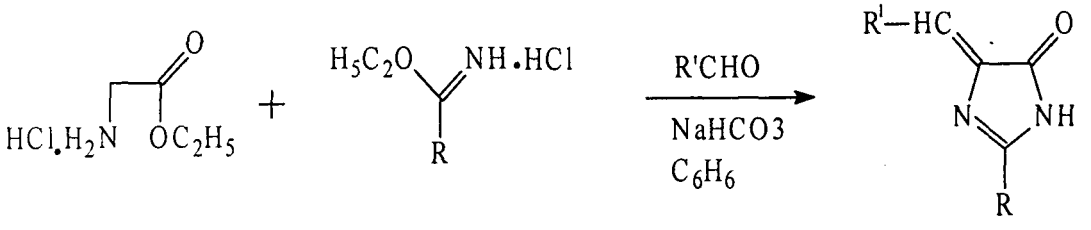


Lehr and coworkers[41] prepared a large number of unsaturated 2-imidazolin-5-ones by refluxing aliphatic and aromatic ketones, acetoacetic ester, levulinic ester and acetophenone with a mixture of imidic acid ester and glycine ester. Benzene was used as solvent in the case of high boiling ketones while 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[42] prepared a number of unsaturated 2-imidazolin-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-arylidine-2-imidazolin-5-ones. Phenylacetimidic acid ester and acetimidic acid ester are other imidic acid esters used by them.

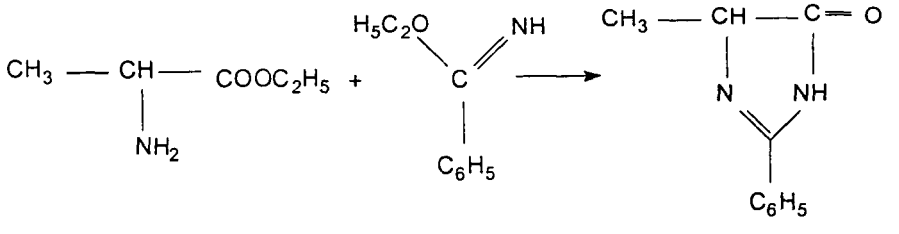


They further improved this method by condensing aromatic aldehydes directly with a mixture of the hydrochlorides of an imidic acid ester and glycine ester in presence of sodium bicarbonate in benzene at 72°C. Thus they prepared a few 2-phenyl-4-arylidene-2-imidazolin-5-ones in very high yields.



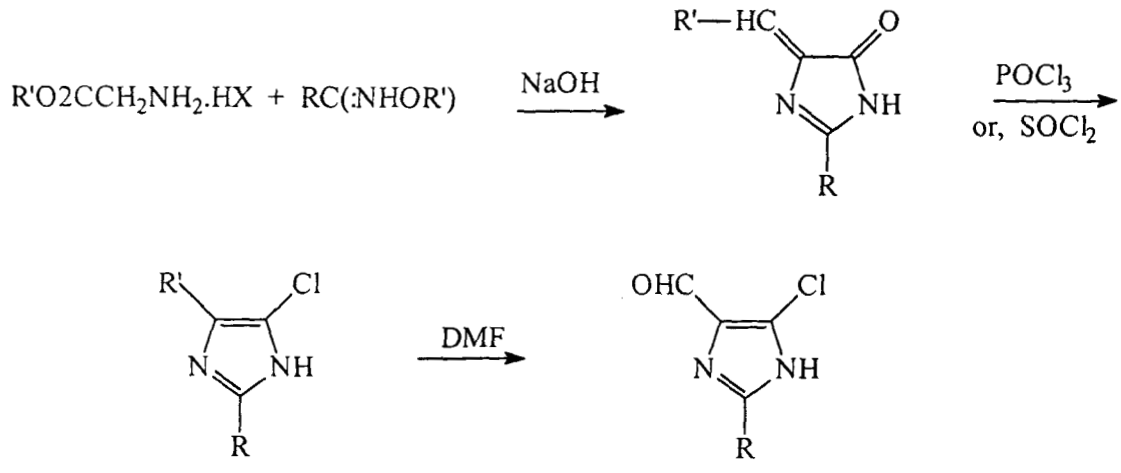
In 1975 Devasia and Pillai[43] prepared a few 2-phenyl-4-arylidene-2-imidazolin-5-ones employing the above methods of Kidwai and Devasia.

It is relevent to mention here that saturated 2,4-disubstituted-2-imidazolin-5-ones were prepared by condensing benzimidic acid ester with amino acid esters.[14,44]



Imidazolinones having hypotensive activity were synthesised[45] by cyclocondensation of various imidic acid esters with glycine ethyl ester.

In 1994 Griffiths and coworkers[46] prepared imidazolones by the cyclocondensation of glycine ester hydrohalide (e.g. glycine methyl ester hydrochloride) with imidic ester (e.g. pentanimidic acid methylester) in presence of a base (e.g. sodium hydroxide). These imidazolones were chlorinated with phosphorous oxychloride or thionyl chloride to get their chloro derivatives which on treatment with DMF and $POCl_3$ yielded their formyl derivatives.

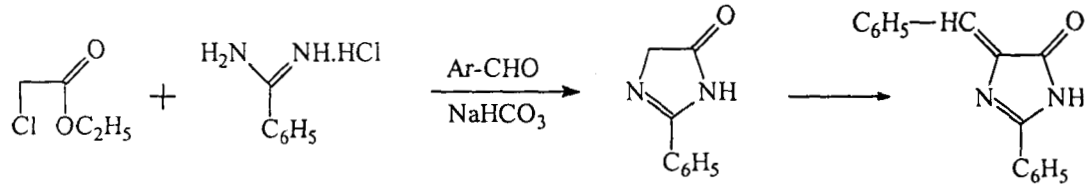


These compounds are useful as pharmaceutical and agrochemical intermediates.

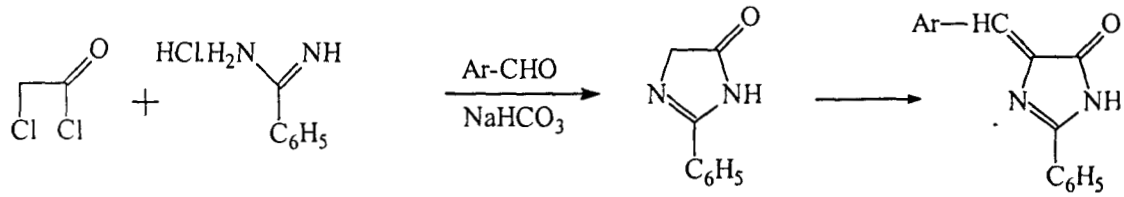
AMIDINE-HALOACETIC ESTER METHOD

In 1976 Devasia[47] 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-glyoxal 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.



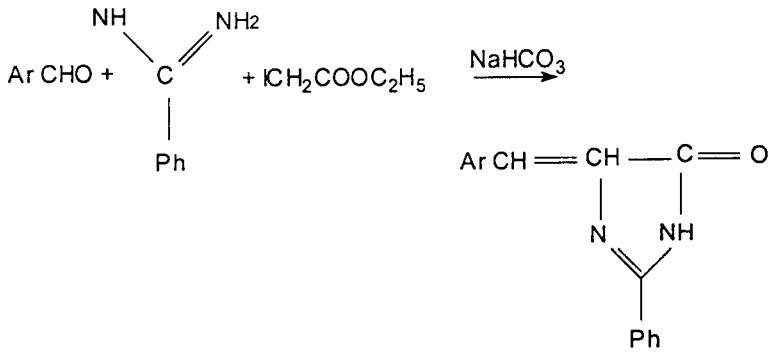
Devasia and Shafi[48] synthesised 4-arylidene-2-phenyl-2-imidazolin-5-ones by condensing aromatic aldehydes with a mixture of chloroacetyl chloride and benzamidine in presence of sodium bicarbonate.



Devasia and Shafi[49] prepared a large number of unsaturated 2,4-disubstituted-2-imidazolin-5-ones employing the known amidine-haloacetic ester method.

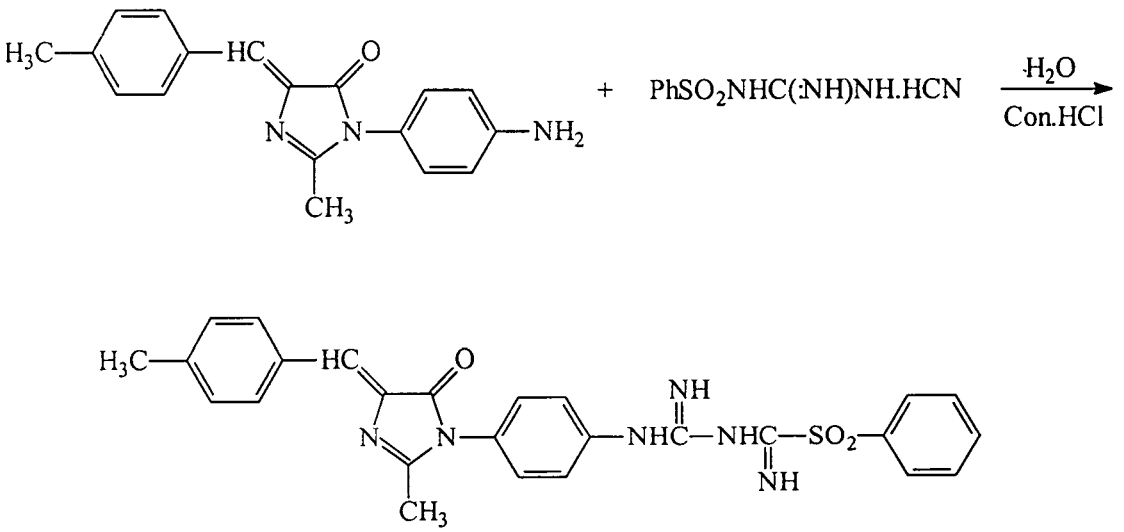
In 1985 Shafi[50] prepared 2-Aryl-4-arylidene-2-imidazolin-5-ones in

quantitative yield by condensing aromatic aldehydes with benzamidine and ethyl iodoacetate in presence of sodium bicarbonate.

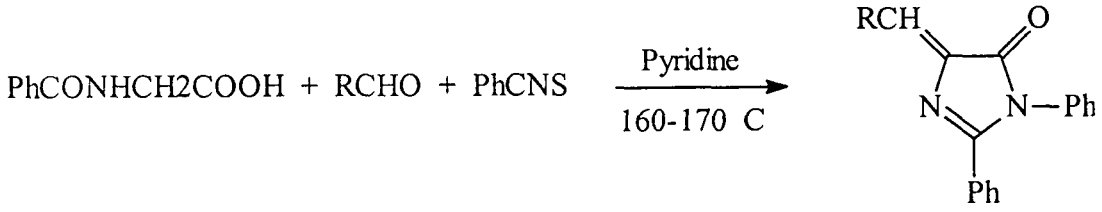


OTHER METHODS

Husain and coworkers[51] synthesised new imidazolinones by heating amine with $PhSO_2NHC$ (:NH) NHCN, water and concentrated hydrochloric acid at 130-140°C

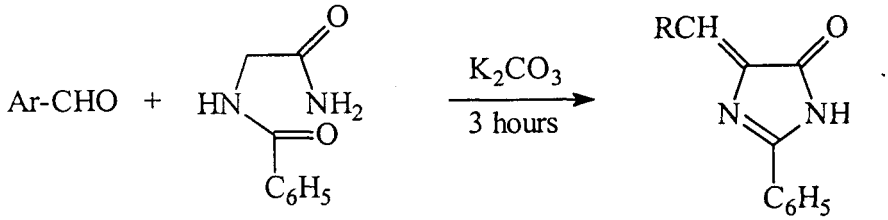


In 1985 Ashare and coworkers[52] synthesised-4-(arylmethylene)-1,2-diphenyl-2-imidazolin-5-ones by the reaction between hippuric acid, phenyl isothiocyanate and aromatic aldehydes.



In 1991 Saxena and coworkers[53] prepared novel imidazole congeners as anti-inflammatory 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 Shafi and Sobha[55] synthesised 2-imidazolin-5-ones by heating benzoylglycine amide and aromatic aldehyde with saturated aqueous potassium carbonate solution for 3 hours. They got 2-imidazolin-5-ones in 44-60% yields.



CHAPTER I

SYNTHESIS OF 1,2,4-TRISUBSTITUTED -2-IMIDAZOLIN-5-ONES

Imidazolinones are found to have several pharmacological activities[56-59]. The benzylidene imidazolinone chemistry with its diverse biological properties like central nervous system depressant[60], anticonvulsant[61], and monoamine oxidase inhibitor[57] has received importance in recent years. Amino acids are the precursers of various macro molecules in the biological system and they play a prominent role in the pathophysiology of inflammation[62-63]. With a view to extend the scope and validity of these observations, it is worthwhile to synthesise and characterise new imidazolinones containing both these moities. In this chapter the synthesis of 1,2,4-trisubstituted-2-imidazolin-5-ones containig both these moieties is presented.

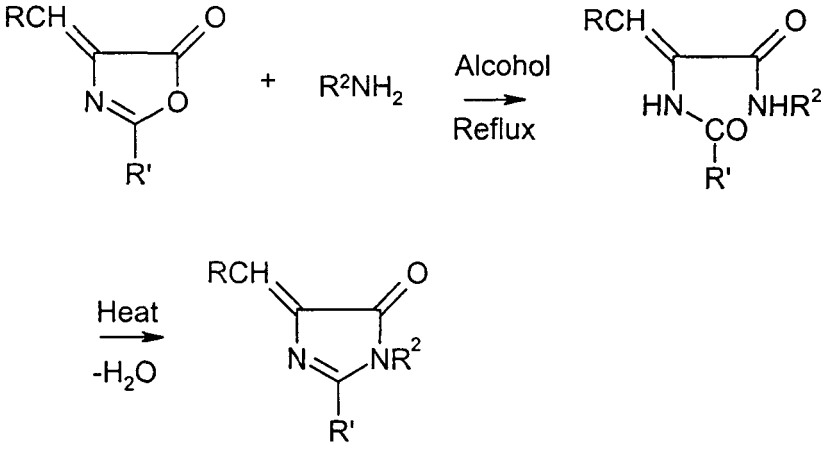
A. Synthesis of 2-aryl-4-arylidene-1- (carbethoxymethyl) -2-imidazolin-5-ones

Results and discussion

4-Arylidene-2-phenyl-2-oxazolin-5-ones (azalactones) undergo ring opening at C-5 by the interaction with amines to yield α–benzoylamino

cinnamic acid amides[64]. These amides under suitable conditions undergo cyclisation to give 2-aryl-4-arylidene-2-imidazolin-5-ones[65].

The reaction can be dipicted as follows.



In this work azlactones were heated with glycine ethyl ester and the amides formed were converted into imidazolinones by heating in vacuum for 2 hours.

In the general procedure the oxazolinone and glycine ethyl ester in equimolar amounts were heated under reflux in ethanol for 2 hours. Within a few minutes of boiling the solid compound dissolved to give a practically colourless solution. After 2 hours of refluxing, it was poured into cold water and the amide precipitated was filtered, washed and dried. The dried amide on heating in vacuum[64,66] for 2 hours yielded 2-aryl-4-arylidene -1-(carbethoxymethyl)-2-imidazolin-5-ones. The compounds thus prepared are given in Table-1.1

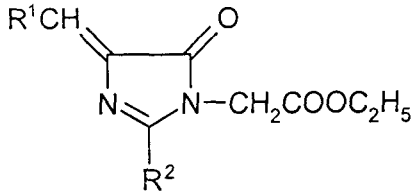


Table 1.1

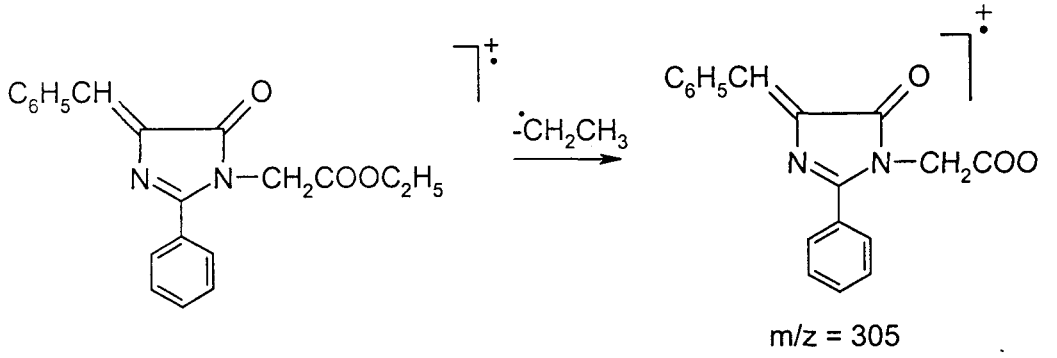
2-Aryl-4-arylidene-1-(carbethoxymethyl)-2-imidazolin-5-ones

No.	R^1	R^2	M.P (°C)	Yield (%)	λ_{max} (nm)	Molecular Formula
1.	phenyl	Phenyl	108	71	409	$C_{20}H_{18}N_2O_3$
2.	p-chlorophenyl	Phenyl	105	70	404	$C_{20}H_{17}N_2O_3Cl$
3.	o-chlorophenyl	Phenyl	93	65	408	$C_{20}H_{17}N_2O_3Cl$
4.	p-methoxyphenyl	Phenyl	125	74	414	$C_{21}H_{20}N_2O_4$
5.	o-hydroxyphenyl	Phenyl	165	65	414	$C_{20}H_{18}N_2O_4$
6.	p-dimethylamino phenyl	Phenyl	130	62	513	$C_{22}H_{23}N_3O_3$
7.	furfuryl	Phenyl	117	50	416	$C_{18}H_{16}N_2O_4$
8.	p-tolyl	p-chlorophenyl	150	64	408	$C_{21}H_{19}N_2O_3Cl$
9.	p-methoxyphenyl	o-chlorophenyl	143	61	396	$C_{21}H_{19}N_2O_4Cl$
10.	p-tolyl	o-chlorophenyl	115	64	404	$C_{21}H_{19}N_2O_3Cl$
11.	phenyl	methyl	228	69	407	$C_{15}H_{16}N_2O_3$

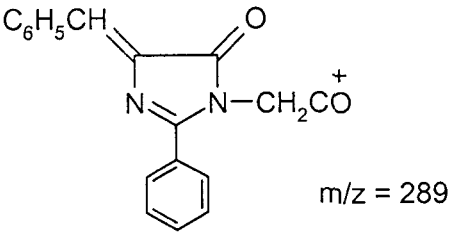
The identity of all the compounds were confirmed by elemental analysis. The mass spectrum and ^1H nmr spectrum of one of the compounds, 4-Benzylidene-1-(carbethoxymethyl)-2-phenyl-2-imidazolin-5-one was recorded. The structure was arrived at as follows.

The mass spectrum has M^+ peak at 334 corresponding to the proposed structure. The even mass justified the presence of two nitrogen atoms. Other important peaks in the mass spectrum were at m/z = 305, 261, 233, 204, 247, 130, 117, 105 and 77 which further supported the proposed structure.

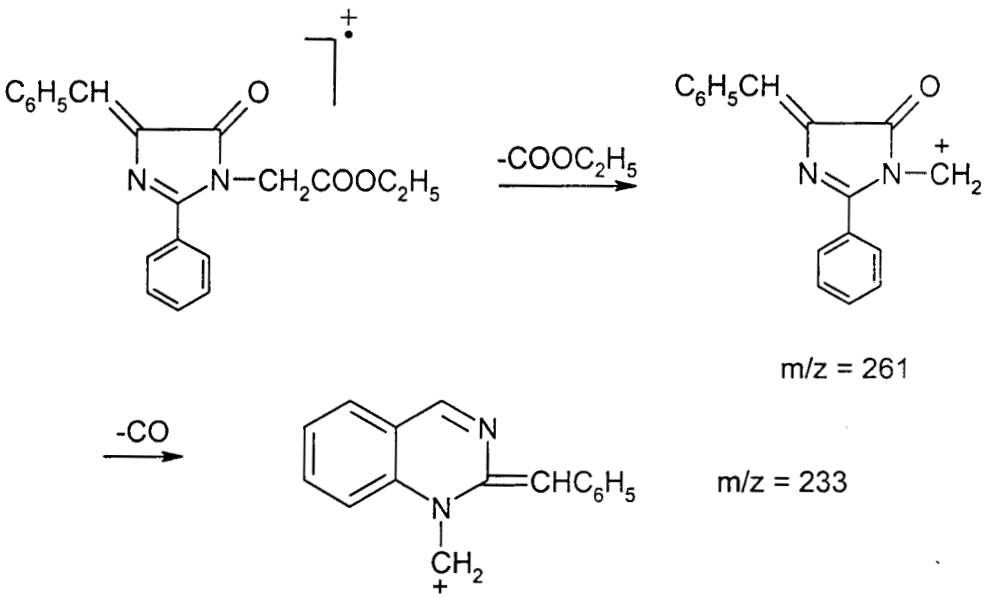
The fragment at m/z = 305 is formed by the elimination of an ethyl radical.



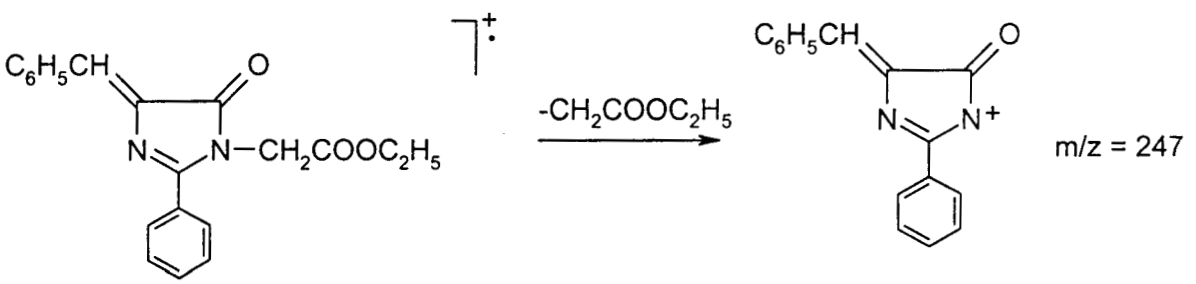
An ion with m/z = 289 is due to the removal of ethoxy group.



The ion with m/z = 261 correspond to the radical ion formed by the elimination of the radical $\dot{C}OOC_2H_5$ which further eliminates one CO molecule giving the fragment with m/z = 233.

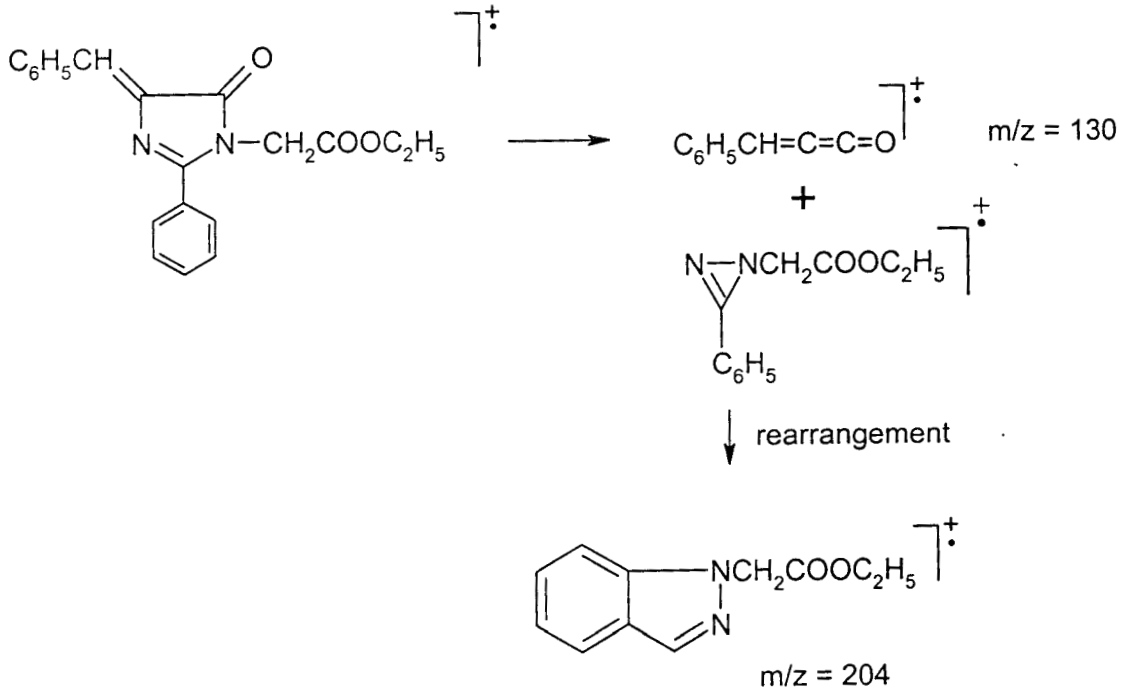


An alternate fragmentation pathway give rise to the peak at m/z = 247. It is due to the removal of $\dot{C}H_2COOC_2H_5$ from the molecular ion.

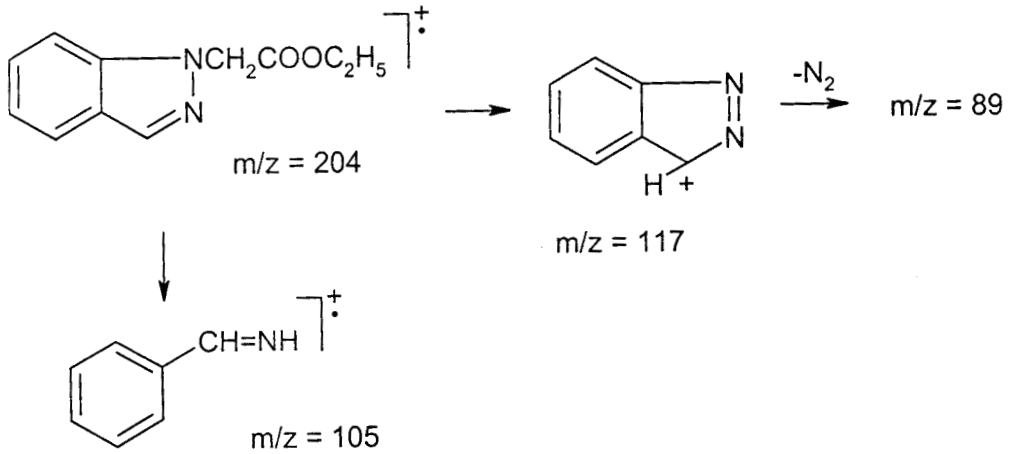


The highly intense peak at m/z = 130 is formed by the following fragmentation of the molecular ion. In this fragmentation both the

fragments can be formed either as a neutral molecule or as a radical ion. The high intensity of the ion at m/z 130 proves its higher stability than the one at m/z 204.



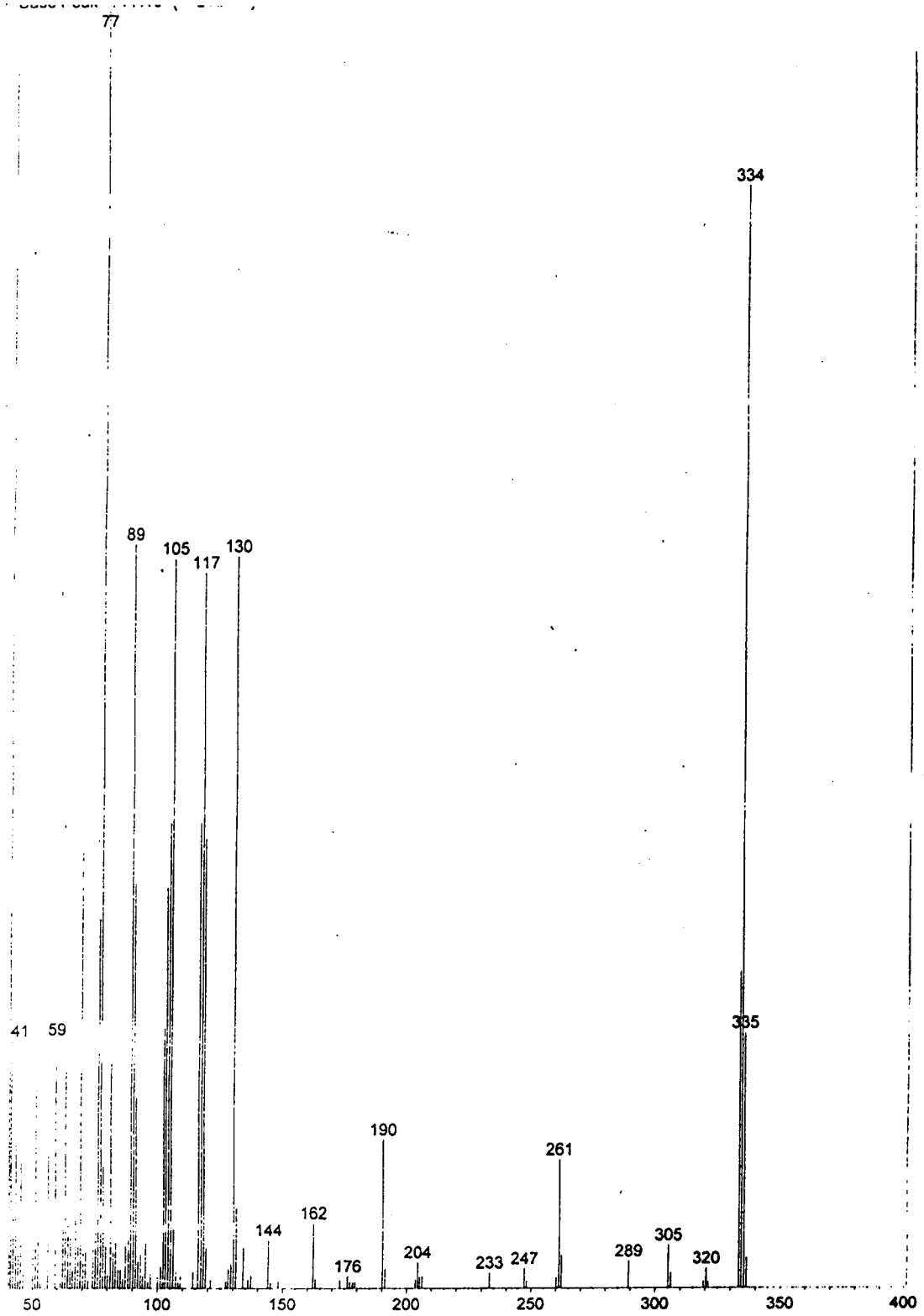
Intense peaks at m/z = 117, 105 and 89 are due to the fragments given below.



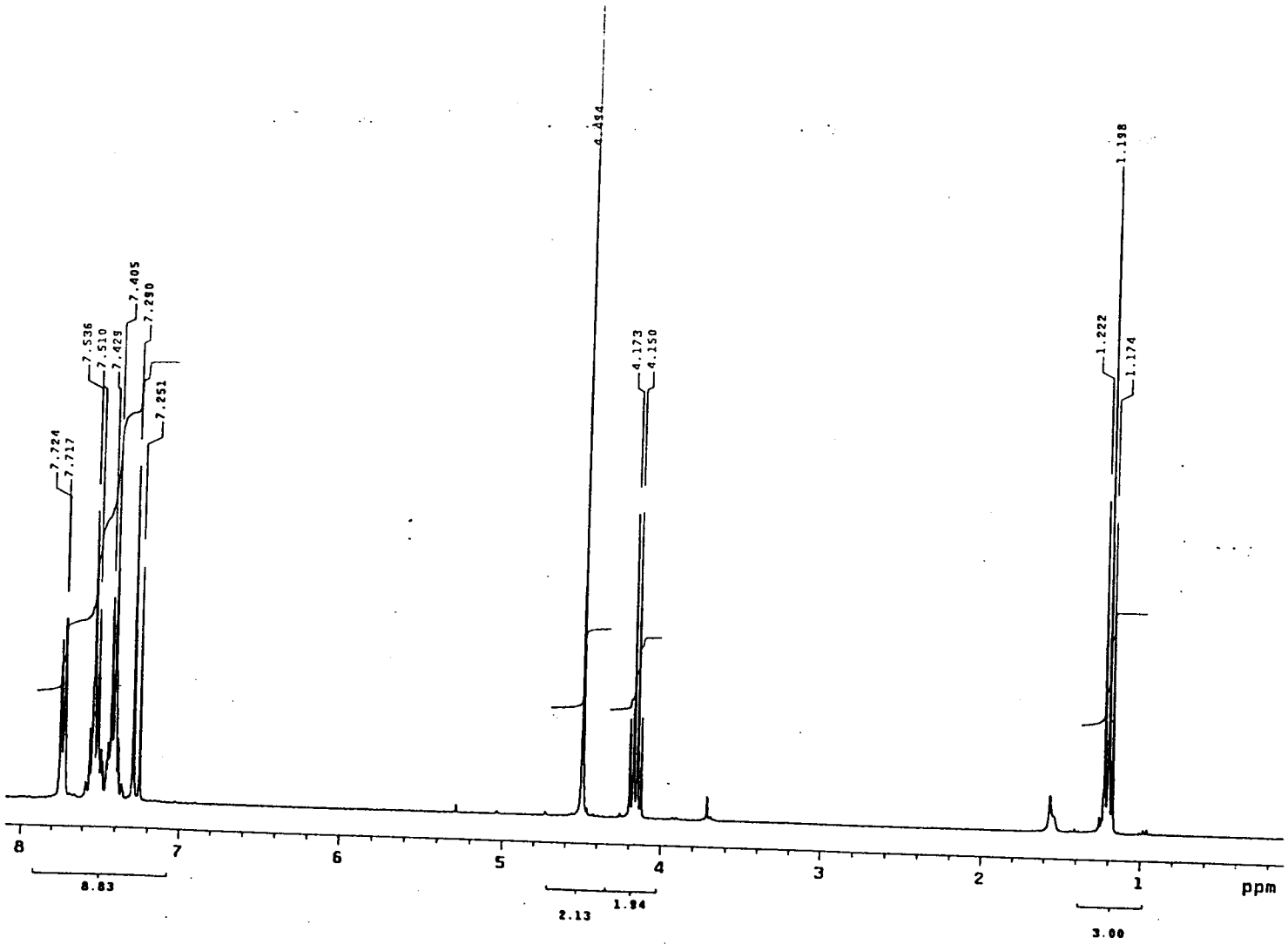
The ^1H nmr spectrum also supported this structure. The CH_2 proton (methylene group attached to nitrogen) absorbed at a highfield of $\delta = 4.49$(Singlet). This is reasonable as CH_2 group is flanked by the carbonyl group of the ester on one side and nitrogen on the other. It also showed absorptions due to ten aromatic protons and the -CH= proton in the region 7.25- 7.72. The $-CH_2-$group in the ethoxy moiety absorbed at $\delta = 4.16$ (quartet). A triplet at $\delta = 1.19$ is due to CH_3 group of the ethoxy moiety.

The UV-visible spectra of these compounds had an absorption maximum in the range of 396-513 nm. Comparison of these values with those of 4-arylidene-2-phenyl-2-imidazolin-5-ones[134] showed that introduction of carbethoxymethyl group at position-1 of the imidazolinone ring has very little influence on the absorption maximum of these compounds. This can be justified on the basis that the absorption is due to the n-π^* transition of the carbonyl group perturbed by the intramolecular charge transfer from arylidene residue to the polarised carbonyl group[128]. The lone pair electron on the adjacent nitrogen can influence the electronic environment of the carbonyl group. The availability of the electron pair on the nitrogen at position-1 of the imidazolinone ring for conjugation with the C=O bond can be practically the same in the unsubstituted and substituted imidazolinones.

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

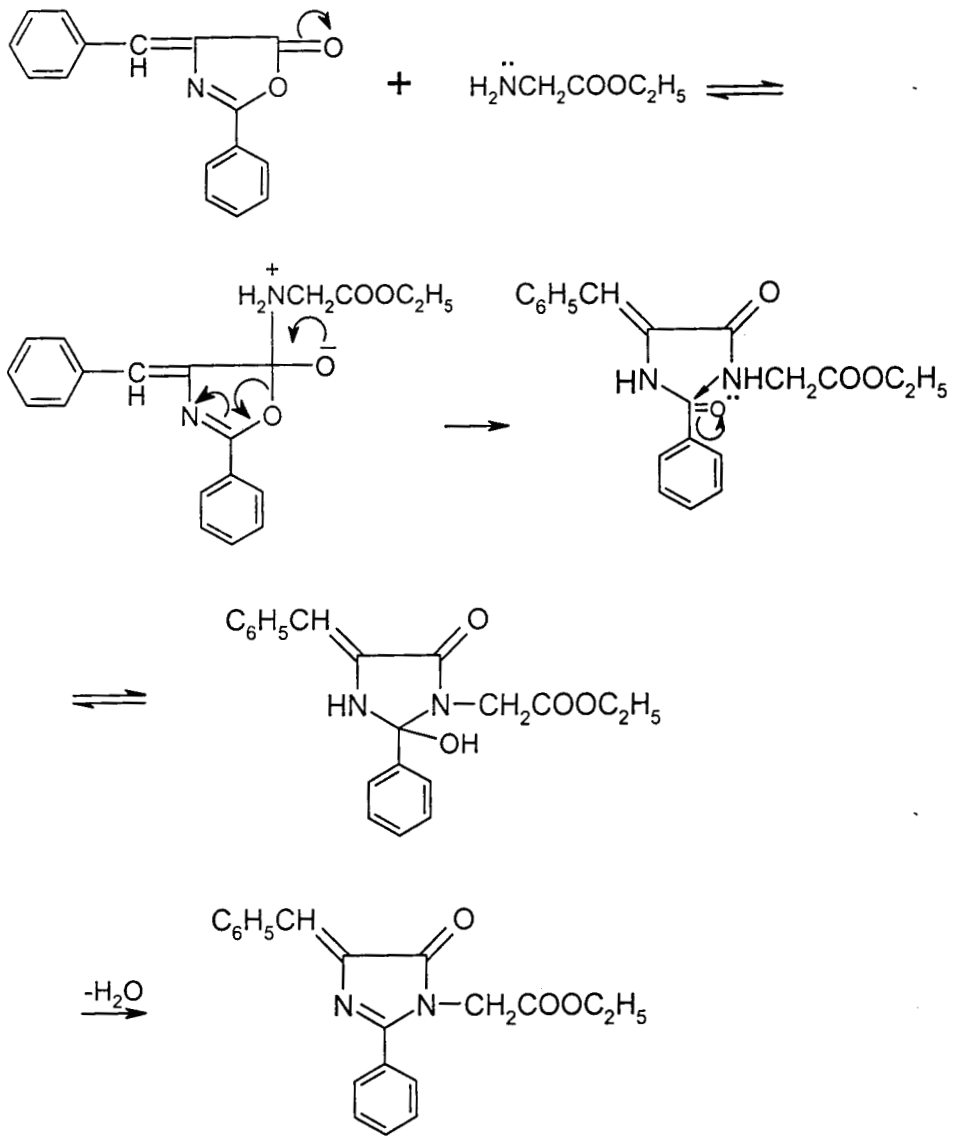


EI-MS of 4-Benzylidene-1-(carbethoxymethyl)-2-phenyl-2-imidazolin-5-one.



^{1}H nmr spectrum of of 4-Benzylidene-1-(carbethoxymethyl)-2-phenyl-2-imidazolin-5-one.

Mechanism



B. Hydrolysis of the ester group in 2-Aryl-4-arylidene -1-(carbethoxymethyl)-2-imidazolin-5-one

Results and Discussion

In an attempt to synthesise and characterise new imidazolinones the ester group in 2-aryl-4-arylidene-1-(carbethoxymethyl)-2-imidazolin-5-one was hydrolysed using strong alkali and dilute mineral acids. In both cases the reaction mixture turned red and we could not separate any solid product probably due to breaking of the imidazolinone ring. In the presence of strong bases the enolate formation also is possible as the methylene group is flanked by the ester carbonyl on one side and nitrogen on the other. However the esters could be hydrolysed using sodium- or potassium carbonate solution.

In every case 2g of the imidazolinone was dissolved in ethanol (10 mL) and refluxed with saturated sodium carbonate solution (15 mL) for one hour. After refluxing, the reaction mixture was cooled and acidified with dilute hydrochloric acid. The solidified product was filtered, washed with water and dried. The compounds thus prepared are given in Table I.2.

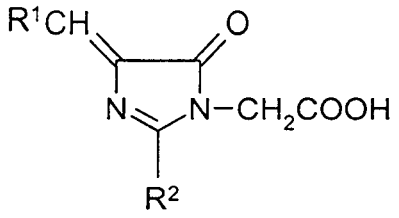


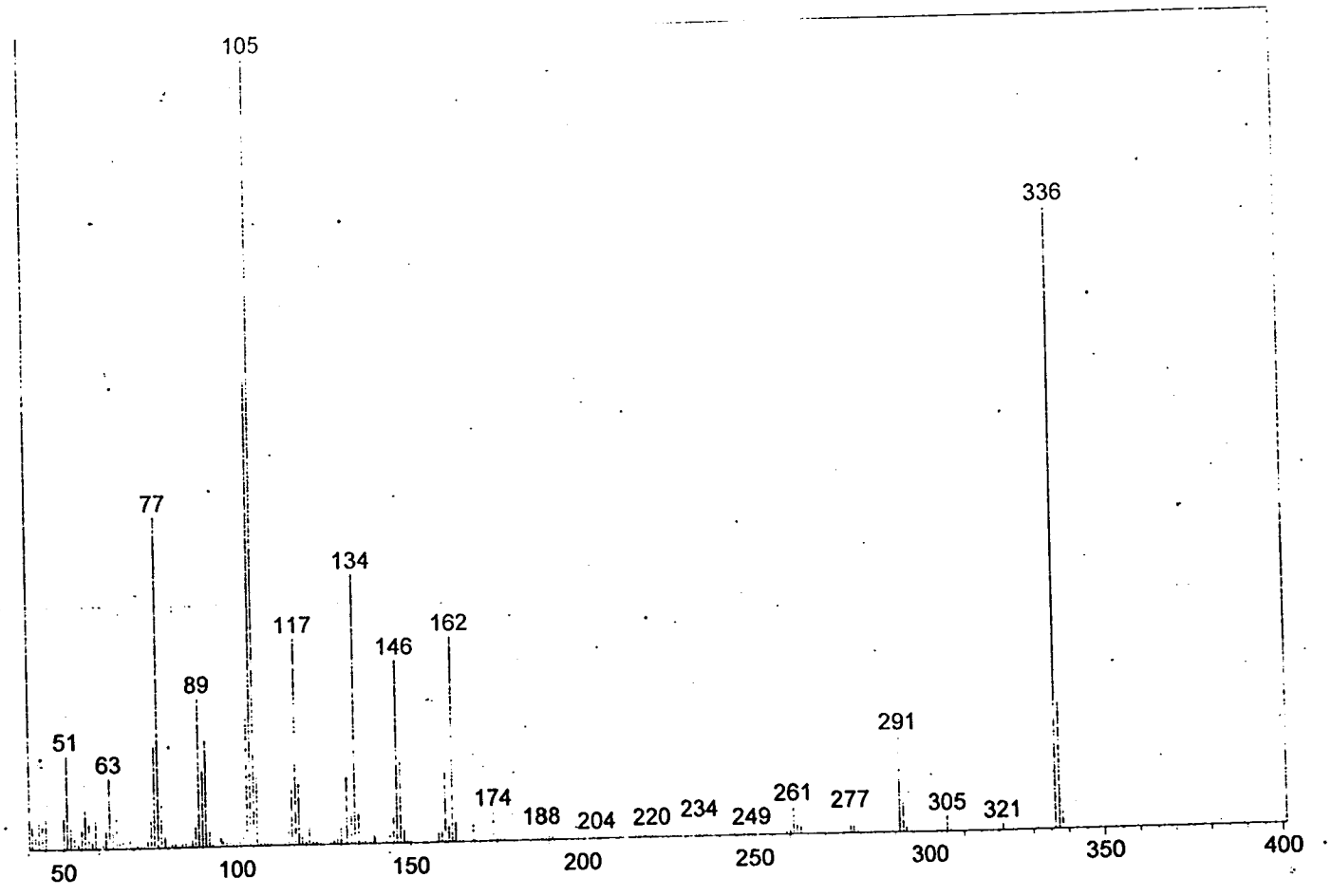
Table 1.2

2-Aryl-4-arylidene-1-carboxymethyl-2-imidazolin-5-ones

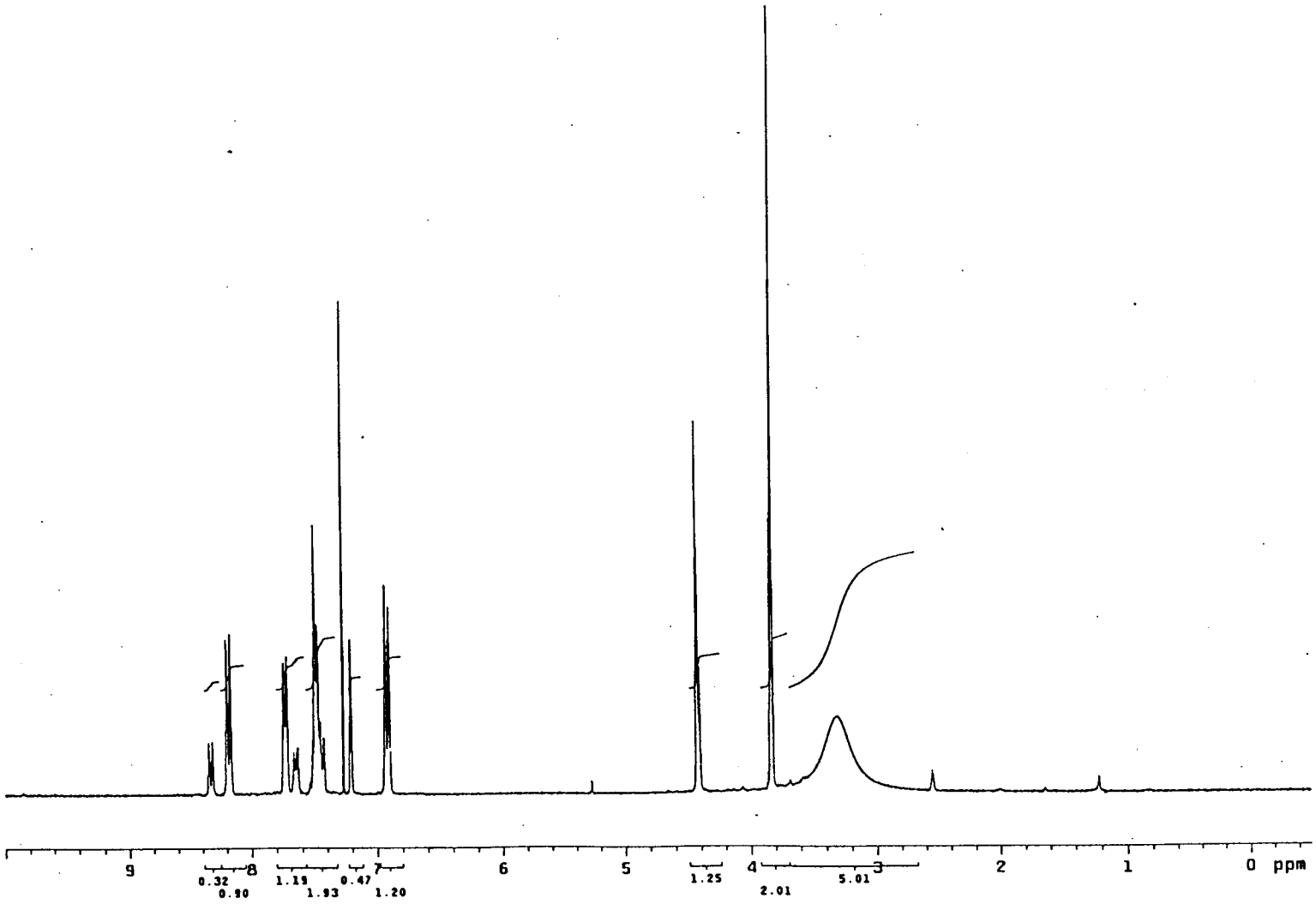
No	R^1	R^2	MP (°C)	λ(max) (nm)	N (%)	Molecular formula
1	phenyl	phenyl	198	412	9.2	$C_{18}H_{14}O_3N_2$
2	p-chlorophenyl	phenyl	216	408	8.3	$C_{18}H_{13}O_3N_2Cl$
3	p-methoxyphenyl	phenyl	195	415	8.4	$C_{19}H_{16}O_4N_2$
4	o-chlorophenyl	phenyl	198	416	8.3	$C_{18}H_{13}O_3N_2Cl$
5	p-tolyl	p-chlorophenyl	190	396	7.8	$C_{19}H_{15}O_3N_2Cl$
6	phenyl	methyl	250	410	11.3	$C_{13}H_{12}O_3N_2$

All the acid synthesised above gave satisfactory analytical result for nitrogen. The mass spectrum of 1-(carboxymethyl)-4-(p-methoxybenzylidene)-2-phenyl-2-imidazolin-5-one was recorded. It had M^+ peak at m/z = 336 (76%) in accordance with the structure proposed. Other peaks present were 305, 291, 277, 162, 146, 134, 117, 105 and 77 which further supported its structure.

The ^1H nmr spectrum also supported this structure. The methoxy protons absorbed at δ=3.8. The methylene group protons attached to nitrogen absorbed at δ=4.49. It also showed absorptions due to nine aromatic protons and the -CH= proton in the region 6.9 - 8.2.



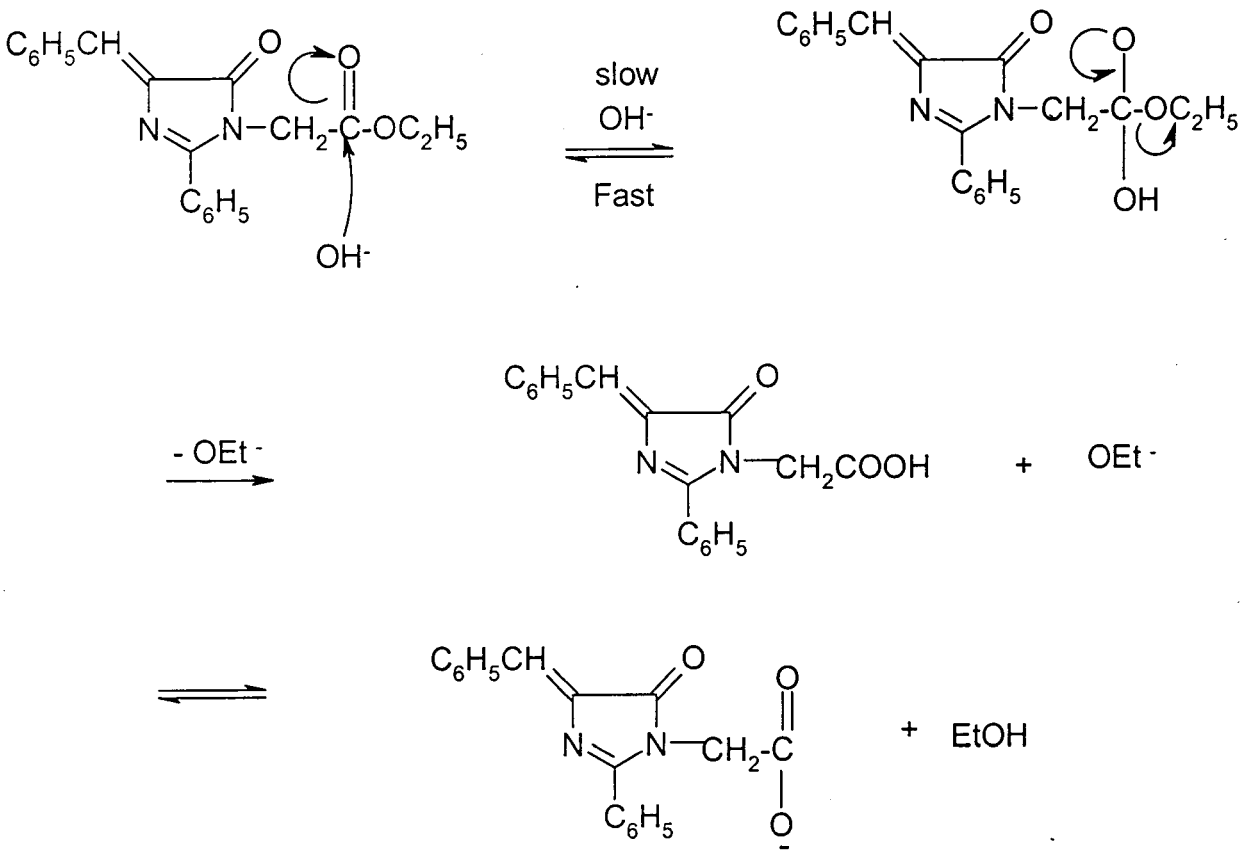
EI-MS of 1-(Carboxymethyl)-4-(p-methoxybenzylidene)-2-phenyl-2-imidazolin-5-one.



^{1}H nmr spectrum of 1-(Carboxymethyl)-4-(p-methoxybenzylidene)-2-phenyl-2-imida zolin -5-one.

The UV-visible absorption maxima of these acids are very close to their ester precursors (Table I.1) showing a negligible influence on esterification.

Mechanism of Hydrolysis



EXPERIMENTAL

Melting points recorded on Toshniwal capillary melting point apparatus are uncorrected. The mass spectrum was recorded on Finnigan MAT 8200 spectrometer. The ^1H nmr spectrum were recorded on Unity plus 300 Varian spectrometer using TMS as internal standard. UV - visible spectra were recorded in ethanol on a Shimadzu 1601- UV - visible spectrometer.

SYNTHESIS OF STARTING MATERIALS

N-Acetylglycine

N-Acetylglycine (Aceturic acid) is prepared by known method[67]. Glycine (75g) was dissolved in 300 mL of water and stirred while 95% acetic anhydride (215g) was added in one portion. The mixture became warm and stirred for further 15-20 minutes. The crystallisation that has begun is completed by external cooling. The product was collected next day. Washed with cold water and dried at 100-110°. It melted at (207 - 208°C)[67].

Benzoyl glycine

Benzoyl glycine was prepared by benzoylating glycine. Glycine (25g, 0.33 mole) was dissolved in 250mL of 10% sodium hydroxide solution contained in a conical flask. Added 45mL (0.385 mole) of benzoylchloride in five portions to this solution, stoppered the vessel and shook vigorously

after each addition until all the chloride has reacted. Transferred the solution to a beaker and rinsed the conical flask with a little water. A few grams of crushed ice was put in the solution and added con. HCl slowly and with stirring until the mixture was acidic to congo red. The crystals formed were filtered on a buchner funnel and air dried. The melting point was found to be 188°C. The reported[68] m.p. is 187°C.

p-Chlorobenzoylglycine

Dry powdered p-chlorobenzoic acid (38.4g, 0.246 mole) was placed in a 250 -mL round bottomed flask fitted with a condenser. Thionyl chloride (22mL. 0.306 mole) was added and heated the flask on a boiling water bath for one hour until the evolution of HCl stopped. The contents were left to cool and transferred into a separatory funnel. Ice-cold water (50mL) and solvent ether (100mL) were added into the funnel and shaken well. The ether layer was separated and dried using anhydrous sodium sulphate. Ether was removed by distillation and the crude product again distilled to get pure p-chlorobenzoylchloride.[69]

Glycine (12g, 6.16 mole) was dissolved in 150 mL of 10% sodium hydroxide solution contained in a conical flask, added the p-chlorobenzoyl chloride prepared in five portions to this solution, stoppered the vessel and shook vigorously after each addition until all the chloride had reacted. Transferred the solution to a beaker and rinsed the conical flask with a little water. A few grams of crushed ice was put in the solution and added

conc. HCl slowly and with stirring until the mixture was acidic to congo red. The crystals formed were filtered on a buchner funnel and air dried. The melting point was found to be 142°C. The reported[70] melting point is 143°C.

Azlactones

Azlactones were prepared following the known method[71]. Aromatic aldehyde and benzoylglycine were taken in a dry 250 mL conical flask in equimolar proportions (0.04 mole). Twelve mL of acetic anhydride and 3.5g of anhydrous sodium acetate were also added and the mixture heated over a flame with shaking. When the mixture liquified it was transferred over to a boiling water bath and heated. After one hour, 20 mL of alcohol was added to the flask and allowed the mixture to stand for one and half hours. The crystalline product formed was filtered, washed with 5mL portions of cold alcohol, small portions of boiling water and dried at 100°C. The different azactones thus prepared are given in table 1.3

For the preparation of azlactone of aceturic acid, warmed a mixture of 29g (0.25 mole) of acetylglycine, 39.5g (37.5 mL, 0.37 mole) of redistilled benzaldehyde, 15 g (0.183 mole) anhydrous sodium acetate and 63.5 g (59 mL) acetic anhydride in a 500 mL flask with a reflux condenser on a water bath with occational sturring until the solution is complete (10 - 20 minutes). Boiled the resulting solution for one hour. Cooled and left in a fridge over night. Stired the solid mass of yellow crystals with 60 mL cold water. Filtered washed with cold water and dried. It was recrystallised fromethylacetate.

Table 1.3

2-Aryl-4-arylidene-2-oxazolin-5-ones

	Name	MP(°C)	Yield(%)	N%	
				Found	Calculated
1.	4-Benzylidene-2-phenyl -2-oxazolin-5-one	169	56	5.5	5.6
2.	4-(p-Methylbenzylidene) -2-phenyl-2-oxazolin-5-one	203	46	5.1	5.3
3.	4-(o-Chlorobenzylidene)-2-phenyl-2-oxazolin-5-one	195	52	4.7	4.94
4.	4-(p-Chlorobenzylidene)-2-phenyl-2-oxazolin-5-one	145	49	4.81	4.94
5.	4-(p-Methoxybenzylidene)-2-phenyl-2-oxazolin-5-one	164	48	5.0	5.03
6.	4-Benzylidene-2-(p-chlorophenyl)-2-oxazolin-5-one	163	45	4.9	4.94
7.	4-(p-Methylbenzylidene)-2-(p-Chlorophenyl)-2-oxazolin-5-one	133	48	4.6	4.71
8.	4-(p-Chlorobenzylidene)-2-(p-chlorophenyl)-2-oxazolin -5-one	199	47	4.4	4.41
9.	4-(o-Chlorobenzylidene)-2-(p-chlorophenyl)-2-oxazolin -5-one	202	49	4.3	4.41
10	4-(p-Methoxybenzylidene)-2-(p-chlorophenyl)-2-oxazolin -5-one	117	41	4.5	4.47
11	4-Benzylidene-2-methyl-2-oxazolin-5-one.	149	60	7.4	7.5

Glycine ethyl ester hydrochloride

Glycine ethyl ester hydrochloride was prepared according to the method developed by Curtius and Goebel[72] and improved by others[42,73,74].

In a 2 litre round bottomed flask with ground glass joint was placed a mixture of glycine (75g, 1 mole) and absolute ethanol (750 mL) and the flask was fitted with a rubber cork carrying an inlet tube and a calcium chloride guard tube. Hydrogen chloride gas dried by bubbling through concentrated sulphuric acid was passed into the mixture till 100g (2.7 mole) 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[42] reported m.p. 144 - 145°C for this compound.

Glycine ethyl ester

Glycine ethyl ester hydrochloride was converted to glycine ethyl ester according to the method developed by Fischer[75-76] and improved by Kidwai and Devasia[42].

A saturated solution of glycine ethyl ester hydrochloride (25g, 0.18 mole) in 30mL of water was placed in a 500 mL conical flask. To this solution was added ether (100 mL) and the mixture was cooled in icebath and neutralised with 20 mL of ice cold sodium hydroxide solution (40%). The aqueous layer was saturated with potassium carbonate by keeeping the flask in icebath. The contents of the flask was transferred into a separatory funnel, shaken well and the ether layer was collected in a 500 mL conical flask. The aqueous layer was extracted twice more with 50 mL portions of ether. To dry the combined ether extracts anhydrous potassium carbonate was added, the flask was stoppered and placed in refrigerator for 6 hours. The ether solution of glycine ester was filtered through a fluted filter paper by decantation and the residue was washed with dry ether. The ether was evaporated under reduced pressure from a cold water bath. The yield of colourless glycine ethyl ester thus obtained was 16.1 g (87%)

Synthesis of 1,2,4-trisubstituted-2-imidazolin-5-ones

4-Benzylidene-1-(carbethoxymethyl)-2-phenyl-2-imidazolin-5-one

4-Benzylidene-2-phenyl-2-oxazolin-5-one (4g 0.016 mole), glycine ethyl ester (1.65g, 0.016 mole) and ethanol (15mL) were taken in a round bottomed flask and heated under reflux on a water bath. Within few minutes the yellow solution turned colourless. After a refluxing of 2 hours, it was added to cold water. The white solid formed was filtered, washed with water and dried. The dried amide was then heated at 170°C in vacuum for 2 hours in an oil bath. It was then cooled and dissolved in benzene and Petroleum ether added. The pale yellow solid formed was filtered, washed and dried. The yellow product weighed 3.8g. (71%) which melted at 107°C. The reported melting point is 108 - 110°C[64].

The unsaturated 2-imidazolin-5-one was recrystallised from ethanol. The yellow crystals melted at 108°C.

Analysis

N%

Found : 8.3

Calculated : 8.4

$C_{20}H_{18}N_2O_3$

UV - Visible λ_{max} : 409 nm

1-(Carbethoxymethyl)-4-(p-chlorobenzylidene)-2-phenyl -2-imidazolin-5-one

4-(p-chloro benzylidene)-2-phenyl-2-oxazolin-5-one (2g.0.007 mole), glycine ethyl ester (0.7g. 0.007mole) and ethanol (15 mL) were taken in a round bottomed flask and heated under reflux for two hours. It was cooled and added to cold water. The white residue formed was filtered, washed with water and dried. The dried amide was then heated at 180°C in vacuum for 2 hours in an oil bath. It was then cooled and dissolved in benzene and petroleum ether added. The pale yellow solid formed was filtered, washed and dried. The yellow product weighed 1.81g (70%) which melts at 105°C.

The unsaturated 2-imidazolin-5-one was recrystallised from ethanol. The yellow crystals melted at 105°C.

Analysis

N%

Found : 7.48

Calculated : 7.6

$C_{20}H_{17}N_2O_3Cl$

UV-Visible λ_{max} = 404 nm

1-(Carbethoxymethyl)-4-(o-chlorobenzylidene)-2-phenyl -2-imidazolin-5-one

4-(o-chlorobenzylidene)-2-phenyl-2-oxazolin-5-one (2g 0.007 mole), glycine ethyl ester (0.7g 0.007 mole) and alcohol (15 mL) were heated under reflux in a water bath for 2 hours. It was then cooled and added to water. The white residue formed was filtered, washed with water and dried. The dried product was then heated at 180 ^{0}C in vacuum for 2 hours. It was then cooled and dissolved in benzene. Petroleum ether was added and the yellow solid formed was filtered, washed and dried. The yellow product weighed 1.5g (65%) which melted at 91°C.

The unsaturated 2-imidiazolin-5-one was recrystallised from ethanol. The yellow crystals melted at 93°C.

Analysis

N%

Found	: 7.5
Calculated	: 7.6
$C_{20}H_{17}N_2O_3Cl$	
UV-Visible	λ_{max} = 408 nm

1-(Carbethoxymethyl)-4-(p-methoxybenzylidene)-2-phenyl -2-imidazolin-5-one

4-(p-methoxybenzylidene)-2-phenyl-2-oxazolin-5-one (3g 0.01 mole), glycine ethyl ester (1.1g. 0.01mole) and alcohol (15 mL) were heated under reflux in a waterbath. After a total refluxing of 2 hours, it was cooled and added to cold water. The white residue formed was filtered, washed with water and dried. The dried product was heated at 180°C in vacuum for 2 hours. It was then cooled and dissolved in benzene and petroleum ether was added and the yellow crystalline product formed was filtered, washed and dried. The yellow product weighed 2.9g (74%) and melted at 124°C.

The unsaturated imidazolinone was recrystallised from ethanol. The yellow crystals melted at 125°C.

Analysis

N%

Found	: 7.8
Calculated	: 7.7
$C_{21}H_{20}O_4N_2$	
UV-Visible	$\lambda_{max} = 414$ nm

1-(Carbethoxymethyl)-2-(p-chlorophenyl)-4-(p-methylbenzylidene) -2-imidazolin-5-one

2-(p-chlorophenyl)-4-(p-methylbenzylidene)-2-oxazolin-5-one (3g 0.01 mole), glycine ethyl ester (1g 0.01 mole) and ethanol (15mL) were heated under reflux in a water bath for 2 hours. It was then cooled and added to water. The white residue of the amide formed was filtered, washed with water and dried. The dried product was then heated at 180°C in vacuum for 2 hours in an oil bath. It was dissolved in benzene and petroleum ether was then added. The yellow solid formed was filtered, washed and dried. The yellow product weighed 2.5g (64%) and melteds at 149°C.

The unsaturated imidazolinone was recrystallised from ethanol. The yellow crystals melted at 150°C.

Analysis

N%

Found	: 7.5
Calculated	: 7.3

$C_{21}H_{19}O_3N_2Cl$

UV-Visible λ_{max} = 408 nm

(1-Carbethoxymethyl)-2-(o-chlorophenyl)-4-(p-methoxybenzylidene) -2-imidazolin-5-one

2-(o-chlorophenyl)-4-(p-methoxybenzylidene)-2-oxazolin-5-one (2g, 0.006 mole), glycine ethyl ester (0.65g, 0.006 mole) and ethanol (15mL) were heated under reflux in a water bath for 2 hours. It was then cooled and added to cold water. The white residue formed was filtered, washed with cold water and dried. The dried product was then heated at 180°C in vacuum for 2 hours. It was then cooled and dissolved in benzene. Petroleum ether was added and the yellow solid formed was filtered, washed and dried. The yellow product weighed 1.6g (61%) which melted at 140°C.

The unsaturated imidazolinone was recrystallised from ethanol. The yellow crystals melted at 143°C.

Analysis

N%

Found	: 7.15
Calculated	: 7
$C_{21}H_{19}N_2O_4Cl$	
UV-Visible	λ_{max} = 396 nm

1-(Carbethoxymethyl)-4-(furfurylidene)-2-phenyl-2-imidazolin-5-one

4-Furfurylidene-2-phenyl-2-oxazolin-5-one (3g, 0.01 mole), glycine ethyl ester (1.3g, 0.01 mole) and alcohol (15 mL) were heated under reflux in a water bath for 2 hours. It was then cooled and added to cold water. The white residue formed was filtered, washed with water and dried. The dried product was heated at 180^{0}C in vacuum for 2 hours. It was then cooled, dissolved in benzene and petroleum ether was added. The yellow solid separated was filtered, washed and dried. The yellow product weighed 2g. (50%) and melted at 116^{0}C.

The unsaturated imidazolinone was recrystallised from ethanol. The yellow crystals melted at 117^0 C

Analysis

N(%)

Found	: 8.4
Calculated	: 8.6
$C_{18}H_{16}N_2O_4$	
UV-vis.	λ_{max} = 416 nm

4-Benzylidene-1-(carbethoxymethyl)-2-methyl-2-imidazolin-5-one

4-Benzylidene-2-methyl-2-oxazolin-5-one (2g, 0.01 mole), glycine ethyl ester (1.1g, 0.01 mole) and alcohol (15 mL.) were heated under reflux in a water bath. After a total refluxing of 2 hours it was cooled and added to cold water. The white residue formed was filtered, washed with water and dried. The dried product was heated at 180^{0}C in vacuum for 2 hours in an oil bath. It was cooled and dissolved in benzene. Petroleum ether was added and the yellow solid formed was filtered and dried. The yellow product of the imidazolinone weighed 2g (69%) which melted at 226^{0}C.

The unsaturated imidazolinone was recrystallised from ethanol and the yellow crystals melted at 228^{0}C.

Analysis

N(%)

Found : 10.45

Calculated : 10.3

$C_{15}H_{16}N_2O_3$

UV-vis. λ_{max} = 407 nm

1-(carbethoxymethyl)-4-(o-hydroxybenzylidene)-2-phenyl -2-imidazolin-5-one

4-(o-hydroxybenzylidene)-2-phenyl-2-oxazolin-5-one (2g, 0.0075 mole), glycine ethyl ester (0.8g, 0.0075 mole), and ethanol (15 mL) were heated under reflux for 2 hours. It was added to cold water and the white residue formed was filtered washed with water and dried. The dried product was heated at 180^0 C in vacuum for 2 hours in an oil bath. It was then dissolved in benzene and petroleum ether added. The yellow solid formed weiged 1.7g (65%) which melted at 164^0 C.

The unsaturated imidazolinone was recrystallised from ethanol. It melted at 165^0C.

Analysis

N(%)

Found : 7.8

Calculated : 8

$C_{20}H_{18}N_2O_4$

UV-vis. $\lambda_{max} = 414$ nm

1-(carbethoxymethyl)-4-(p-dimethylaminobenzylidene)-2-phenyl -2-imidazolin-5-one

4-(p-Dimethylaminobenzylidene)-2-phenyl-2-oxazolin-5-one (1g, 0.0034 mole), glycine ethyl ester (0.35g 0.0034 mole), ethanol (15 mL) were heated under reflux for 2 hours. It was then cooled and added to cold water. The amide formed was filtered, washed with water and dried. The dried product was heated at 190^{0}C in vacuum for 2 hours. It was then cooled and dissolved in benzene. Petroleum ether was added and the brown solid formed was filtered, washed and dried. The reddish brown solid of the imidazolinone weighed 0.8g (62%) which melted at 128 ^{0}C.

The unsaturated imidazolinone was recrystallised from ethanol and melted at 130 ^{0}C.

Analysis

N(%)

Found : 11

Calculated : 11.1

$C_{22}H_{23}N_3O_3$

UV-vis. λ_{max} = 513 nm

1-(carboxymethyl)-4-(p-methoxybenzylidene)-2-phenyl-2-imidazolin-5one

1-(carbethoxymethyl)-4-(p-methoxybenzylidene)-2-phenyl-2-imidazolin-5-one (2g, 0.005 mole) was dissolved in 10mL alcohol and refluxed with saturated sodium carbonate solution (15 mL) for 1 hour. After cooling, it was acidified with dilute hydrochloric acid. The yellow product formed was filtered, washed with warm water and dried.

The unsaturated imidazolinone was recrystallised from alcohol. The yellow crystals of 1-(carboxymethyl)-4-(p-methoxybenzylidene)-2-phenyl-2-imidazolin-5-one melted at 195°C.

Analysis

N%

Found	: 8.4
Calculated	: 8.3
$C_{19}H_{16}O_4N_2$	
UV-vis	λ_{max} = 415 nm

4-Benzylidene-1-(carboxymethyl)-2-phenyl-2-imidazolin-5-one

4-Benzylidene-1-(carbethoxymethyl)-2-phenyl-2-imidazolin-5-one (2g, 0.006 mole) was dissolved in 10 mL. alcohol and refluxed with saturated sodium carbonate solution (15 mL). After a refluxing of 1 hour, it ws cooled and acidified with dilute hydrochloric acid. The orange red product formed was filtered, washed with hot water and dried.

The unsaturated imidazolinone was recrystallised from ethanol. The orange red crystals melted at 198°C.

Analysis

N(%)

Found : 9.2

Calculated : 9.15

$C_{18}H_{14}O_3N_2$

UV-vis. $\lambda_{max} = 412$ nm

All the other 2-aryl-4-arylidene-1-carboxymethyl-2-imidazolin-5-ones were prepared according to the above method.

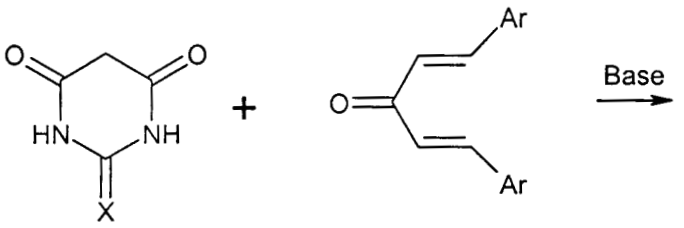
CHAPTER II

SYNTHESIS OF SPIRO IMIDAZOLINONES

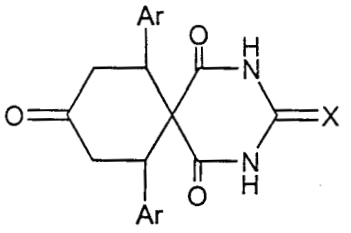
Spiro compounds are polycyclic compounds possessing the structural characteristics in which one carbon atom is a member of two different rings. The spiro compounds containing imidazolinone ring are not many and has generated considerable interest in recent years due to their pharmacological activities. The aim of the present investigation was to prepare new class of spiro compounds; spiro imidazolinones.

Certain spiro compounds can be prepared by various methods[77-85]. But the reaction of dibenzalacetone with a compound having active methylene group yielding double Michael adduct would be an interesting subject of investigation.

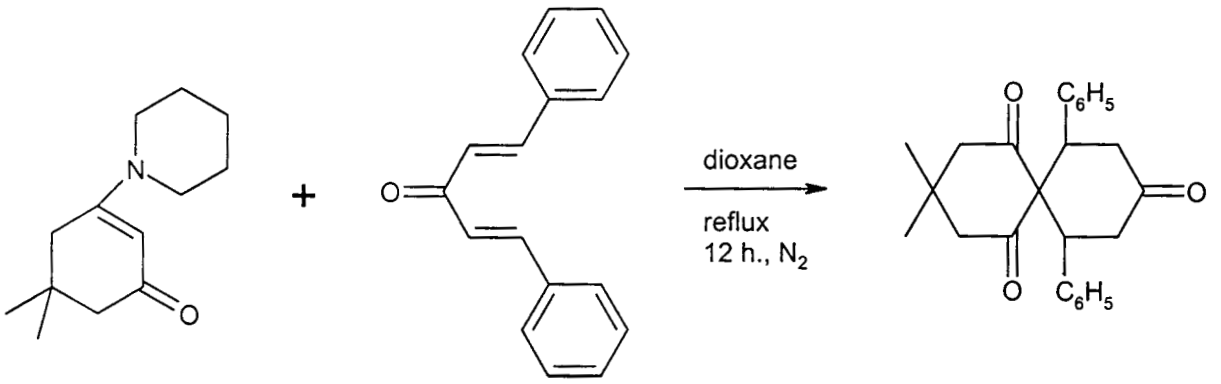
Kandeel[86] and coworkers prepared spiro compounds by the Michael reaction of divinyl ketones with barbituric acid or thiobarbituric acids in ethanol-dioxane mixture in presence of triethylamine. These spiro compounds showed anticonvulsant activity in frogs against pentylene tetrazol induced convulsions in comparison to phenobarbitone as reference drug.



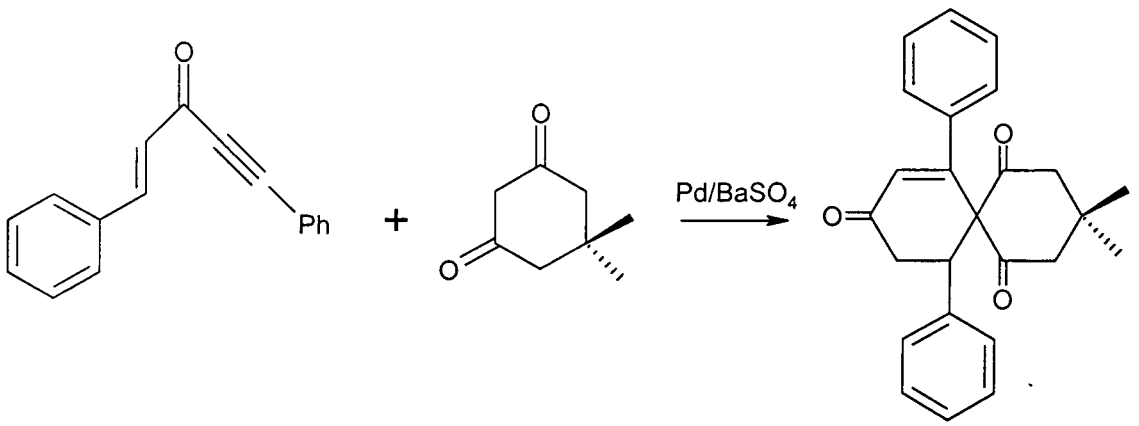
(X = O or S)



Trivedi[87] and coworkers 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[88] by the double Michael addition of cross conjugated enyone with dimedone in presence of $Pd/BaSO_4$ in methylene chloride.



Certain spiro compounds show anticancer[89], narcotic[90-91], anti-inflammatory [92] and analgesic[93] properties. Some new spiro heterocycles are found to have activity as herbicides and pesticides[94]. Imidazolinones have been found to be associated with several pharma cological[95-98] properties and cyclohexanone derivatives possess analgesic properties. In view of the above data the present investigation was undertaken in which new spiro compounds containing the above active nuclei have been synthesised.

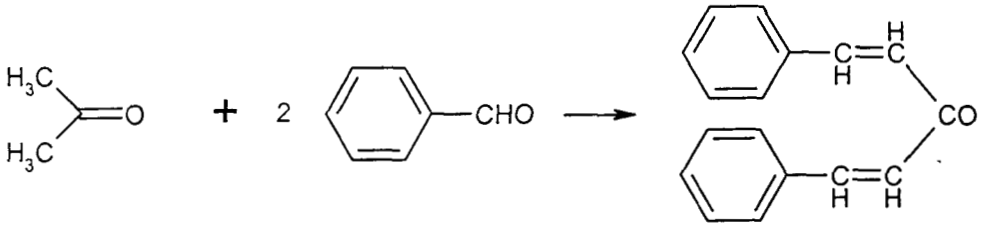
Present Work

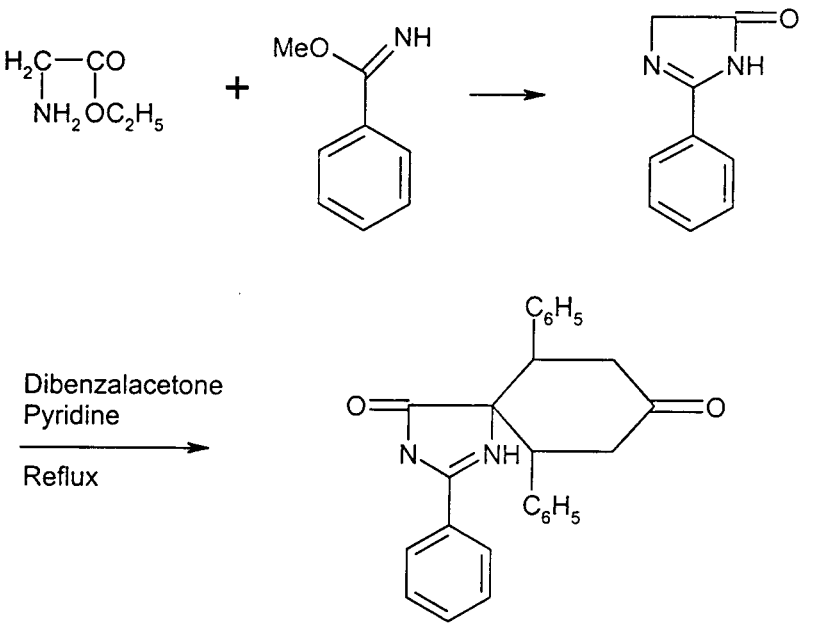
The Michael reaction of 1,5 diaryl-1,4- pentadien–3-ones with active methylene compounds has long been employed to prepare substituted cyclohexanones[99-102]. The product of these reactions are of interest in terms of their stereochemistry and as starting materials for the synthesis of compounds with possible biological activity [(88,103)]. The reaction of a cross conjugated olefin, dibenzalacetone and a

compound having an active methylene group resulted in the formation of some novel spiro imidazolinones containing cyclohexanone moiety. Spiro annulated cyclohexanones are biologically important but at the same time are difficult to synthesise.

Results and discussion

The base catalysed condensation of acetone was carried out with aromatic aldehydes to get the corresponding divinyl ketones[104-107]. This divinyl ketones on Michael addition with 2-aryl-2- imidazolin -5-ones, which in turn is formed by the reaction between glycine ethyl ester and benzimidic acid methyl ester or substituted benzimidic acid ester in presence of pyridine, yielded spiro imidazolinones.





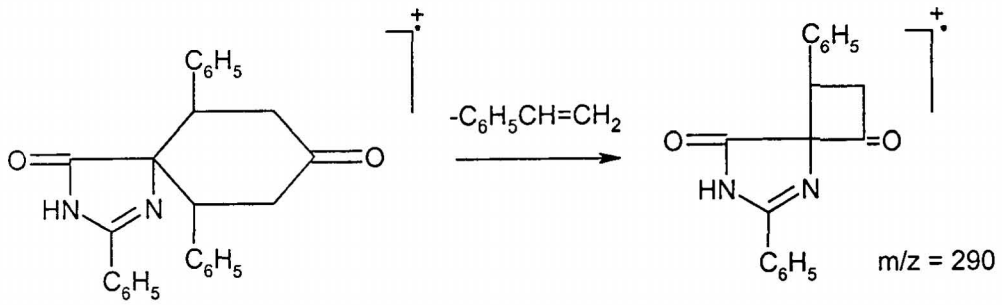
The active methylene group of 2-phenyl-2-imidazolin –5-one condense with carbonyl compounds to give 4-arylidene/alkylidene-2-phenyl-2- imidazolin-5-ones[41]. But dibenzalacetone did not undergo this type of condensation. This observation is not at all unsual as the carbonyl group of dibenzalacetone is 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.(Chapter III)

The IR spectrum is in consistance with the above observations. The IR spectrum of the compound showed two carbonyl absorption frequencies. The absorption frequency of 1722.6cm^{-1} is due to the carbonyl group of imidazolinone ring and the other at 1716.9 cm^{-1} is due to a cyclohexanone ring. If the carbonyl group of dibenzalacetone condense with active

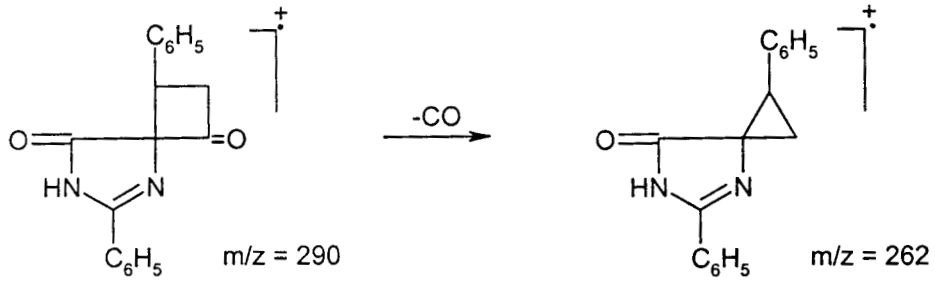
methylene group of 2-phenyl-2-imidazolin-5-one, the product should contain only one carbonyl group. This shows that dibenzalacetone underwent a double Michael addition with 2-phenyl-2-imidazolin-5-one yielding a spiro imidazolinone containing cyclohexanone-moiety. This fact is further supported by other spectral studies.

The structure was arrived at as follows. Its mass spectrum had M^+ peak at 394 corresponding to the proposed structure. The even mass justified the presence of even nitrogen atoms. Other important peaks in the mass spectrum were at m/z = 290, 262, 248, 233, 131, 117, 104, 91 and 77 which further supported the proposed structure.

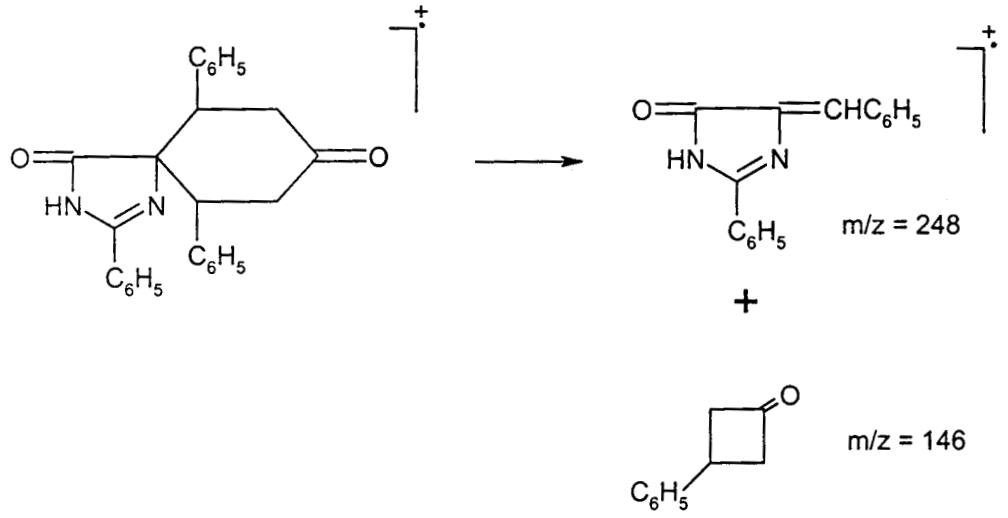
The mass spectral fragmentations of spiro ketones was found to differ widely from those of the corresponding cycloalkanes[108] or cycloalkanones. The fragment at m/z 290 is formed by the elimination of a styrene molecule[108] with m/z 104 from the molecular ion.



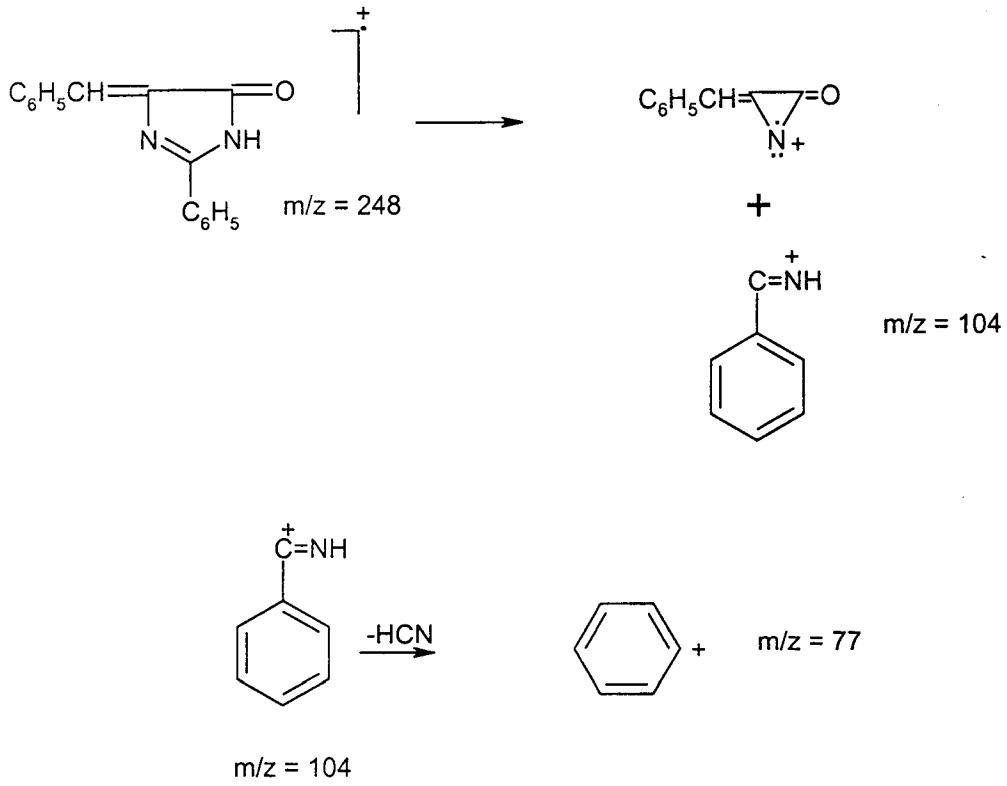
The mass peak at 262 unit corresponds to the radical ion formed by the elimination of a neutral molecule of CO from the above ion.



An alternate pathway gave rise to the peak of m/z 248. It is due to the removal of one molecule of 3-phenylcyclobutanone[108] with m/z 146



The peaks at m/z 104 and 77 are due to the fragmentations given below.



The ^{1}H nmr spectrum of the spiroimidazolinone showed absorption corresponding to the 15 aromatic protons in the range of δ 7–7.6. The NH proton was in the downfield at δ 9.3. The two methine protons and the four methylene protons appeared as six doublet of doublets in the region δ 2.9-3.8. They form two ABX systems and are marked as AA', BB' and 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 ^1H 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[109]. 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 13Hz and 9.4Hz respectively. The bulky phenyl groups occupying the equitorial positions, these two hydrogens should be axial. A coupling constant of 13Hz is typical of axial protons(X). But X' has a lower coupling constant of 9.4Hz which can be due to some twist in the conformation that makes it not exactly axial (i.e., Dihedral angle less than 180^0 with the axial hydrogen of the neighbouring methylene group).

As B and B' also exhibit coupling constants of 13Hz and 9.4Hz 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[110].

The coupling pattern of the six protons can be summarised as follows.

$J_{AB} = J_{A'B'} = 16.8Hz$

$J_{BX} = 13Hz$

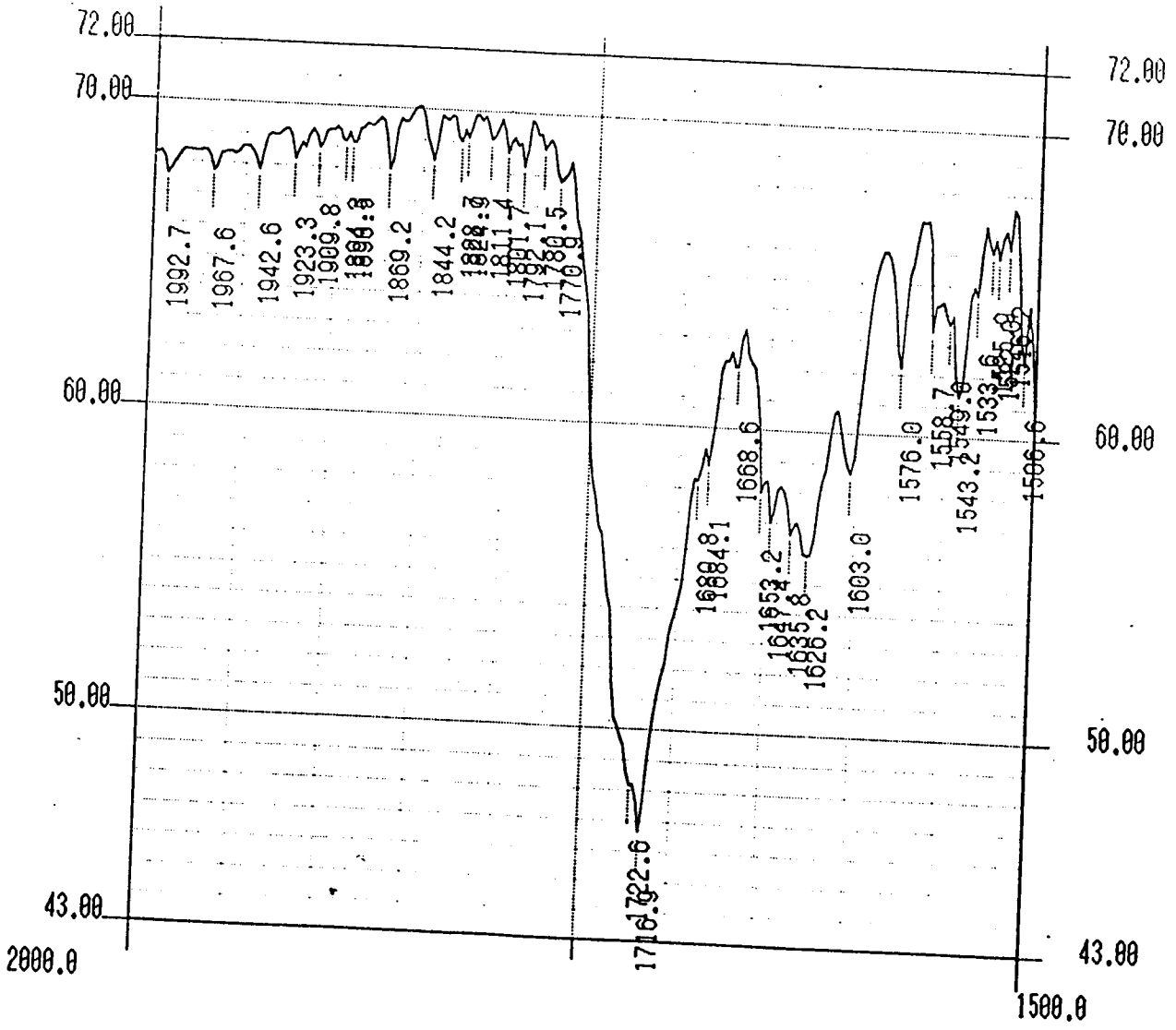
$J_{B'X'} = 9.4\ Hz$

$J_{AX} = 3.75\ Hz$

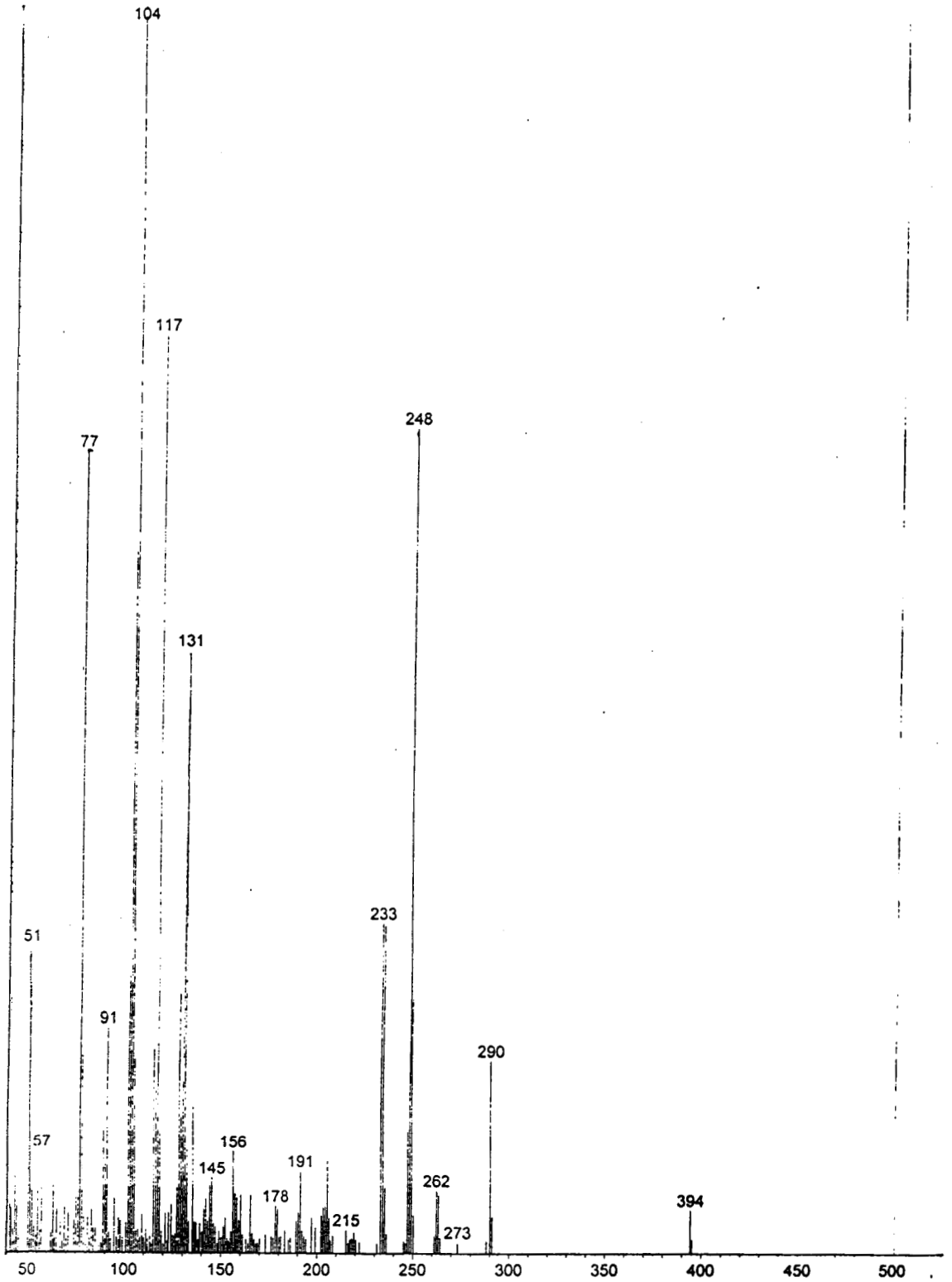
The appearance of sharp peaks for all the six protons of the cyclohexanone ring proved its fairly rigid conformation . The difference in chemical shifts of X and X' may be due to the influence of the imidazolinone ring with its carbonyl group having a major influence.

The ^{13}C nmr spectrum also were in consistance with the proposed structure. Absorption at δ 42.58, 43.25, 45.19 and 47.24 are represented by the four carbon atoms other than the carbonyl and spiro carbon atom of the cyclohexanone moiety. The carbonyl group of this part absorbed at δ 211.1 while carbonyl group of the imidazolinone ring absorbed at 185.66. The N=C carbon of the imidazolinone ring absorbed at δ 158.14. The absorptions corresponding to the three phenyl carbons were in the region δ 127-138. The spiro carbon absorbed at δ 77.6 and is observed among the solvent ($CDCl_3$) peaks.

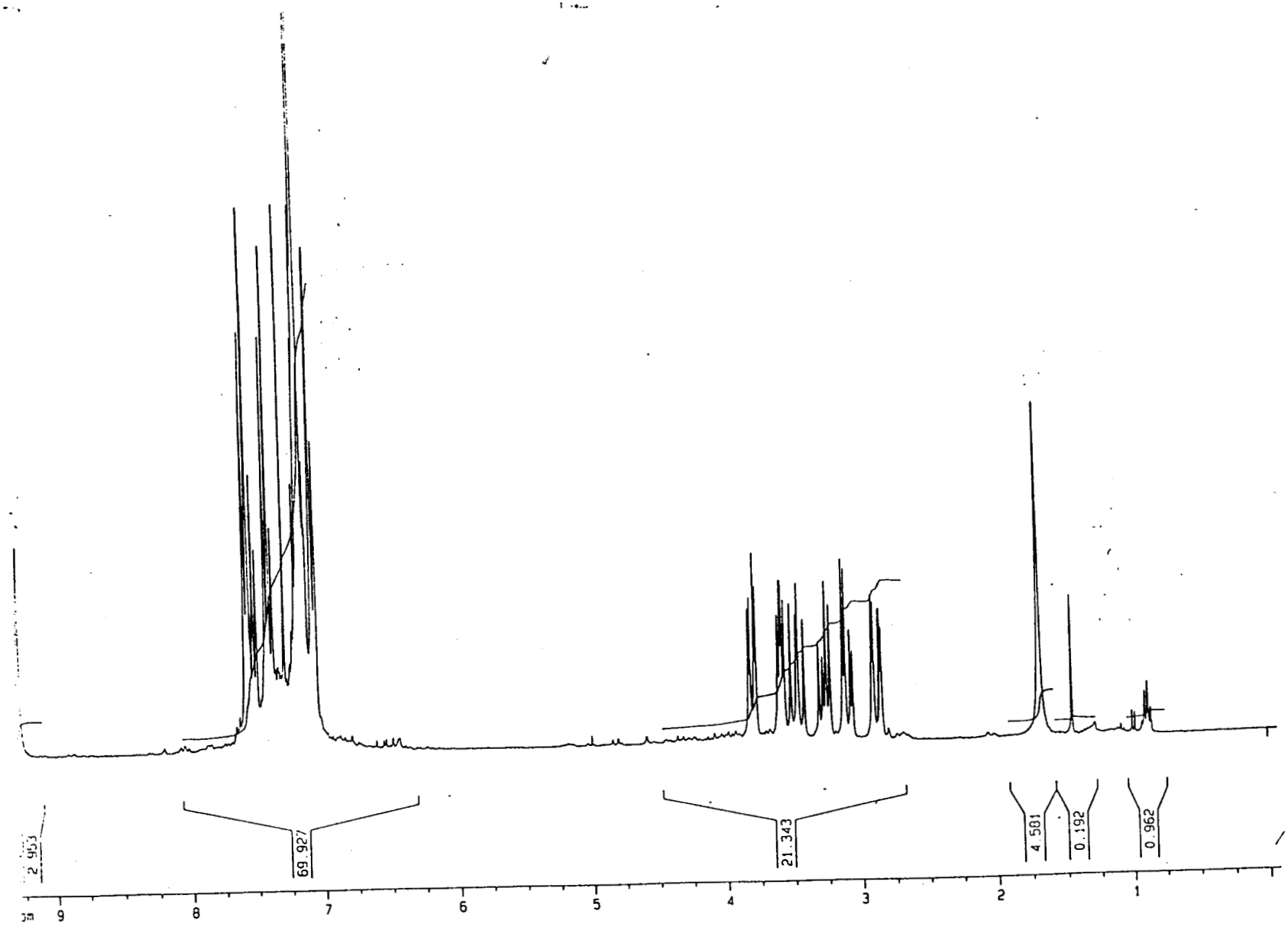
The UV absorption maximum of of these spiro compounds were in the range 313-340 nm except for the dimethylaminophenyl derivatives. This absorption can be attributed to the n-π* transitions in the chromophores including the imidazolinone carbonyl and the adjacent nitrogen that can contribute its lone pair electron for conjugation with the carbonyl group.



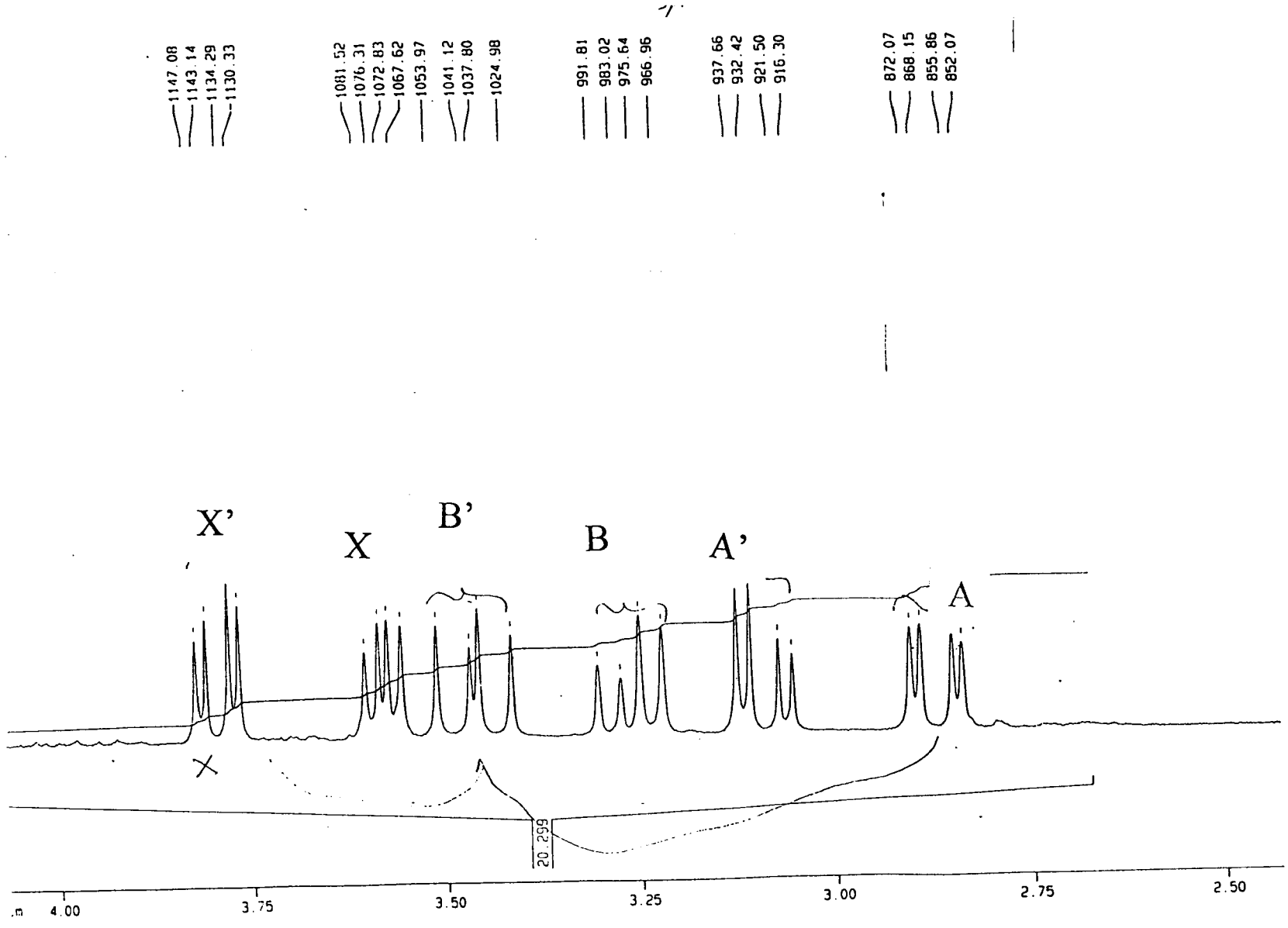
IR spectrum of 3,6,10-Triphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione.



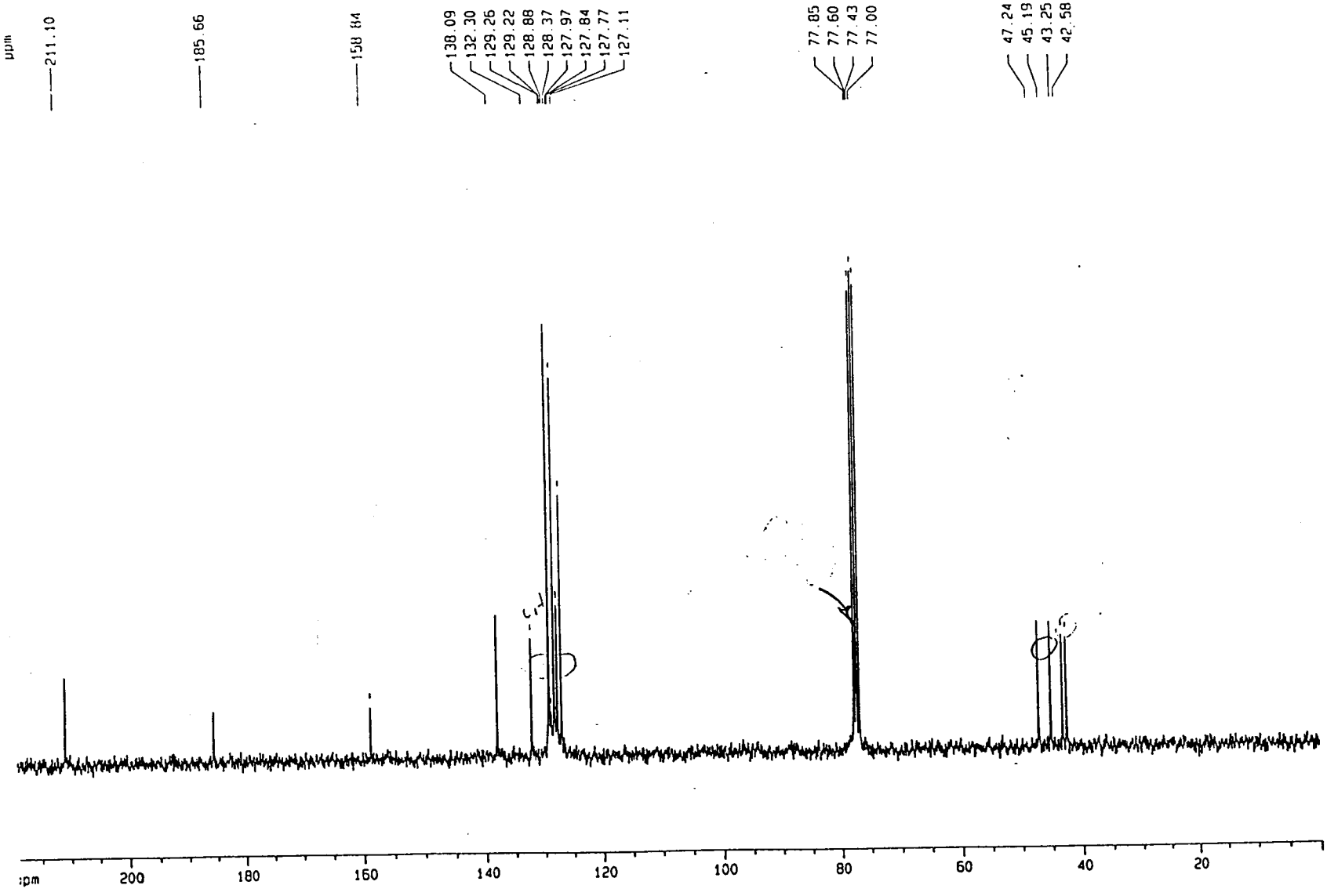
EI-MS of 3,6,10-Triphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione



^{1}H nmr spectrum of 3,6,10-Triphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione

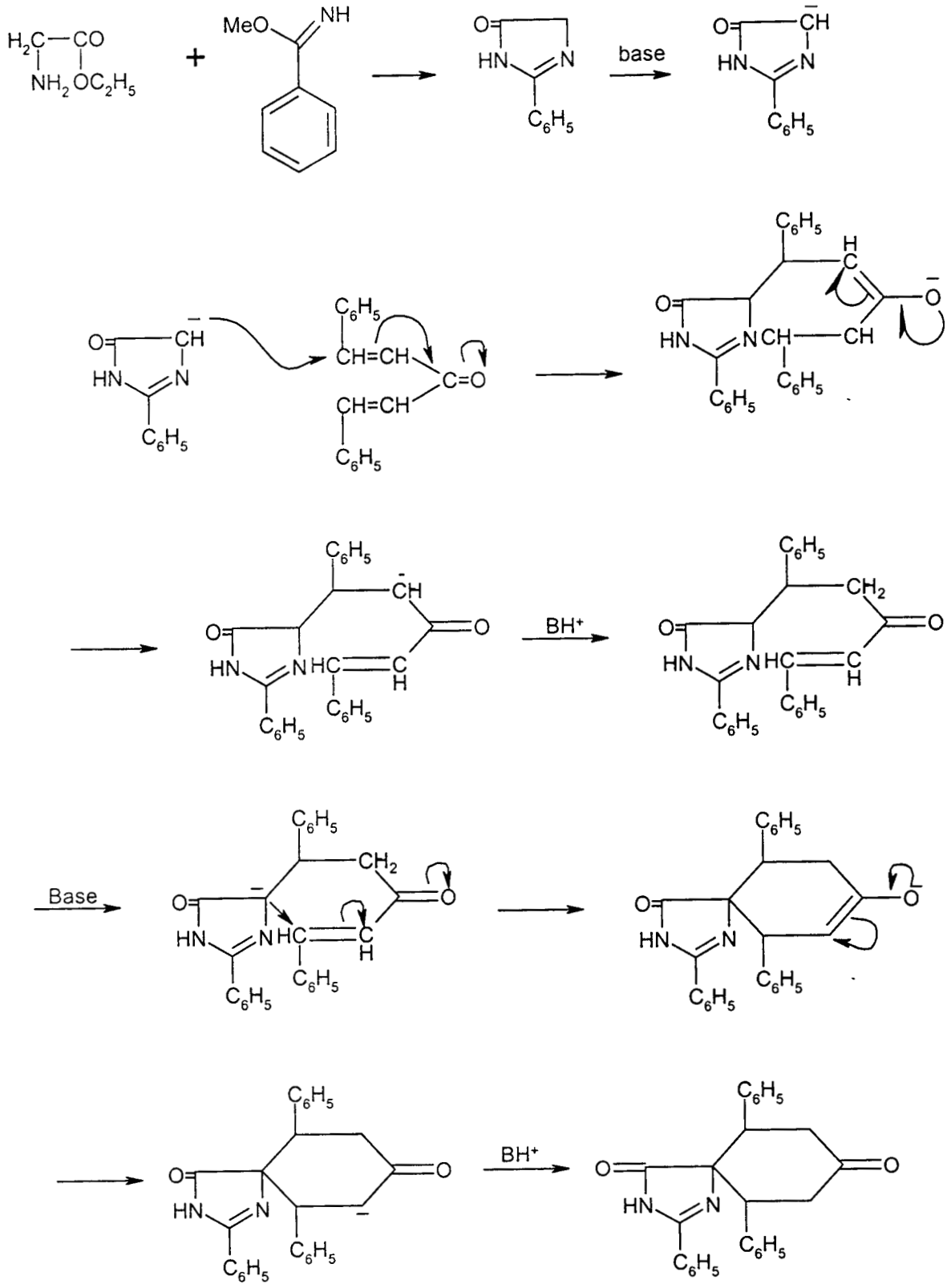


^{1}H nmr spectrum of 3,6,10-Triphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione.(Expanded)



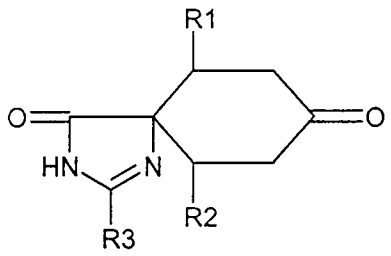
^{13}C nmr spectrum of 3,6,10-Triphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione.

Mechanism



In the synthesis of spiro imidazolinones pyridine acts as a base. In order to increase the yields of the products the general procedure was modified as follows.

Imidic acid ester, glycine ethyl ester and the 1,5 diaryl-1,4- penta dien-3-ones are taken in equimolar ratio and heated under reflux in pyridine. After 3 hours the mixture was added to cold water and acidified with dilute HCl to increase the dissolution of pyridine in water. The solid imidazolinone was then filtered, washed and dried. It was then recrystallised from suitable solvents and further purified by column chromatography. The spiro imidazolinones thus prepared are given in Table - II.1. All the compounds gave satisfactory analytical data for nitrogen.



(R1 = R2)

Table II.1

No.	$R^1=R^2$	R^3	Yield %	MP(°C)	λ_{max} (nm)
1.	phenyl	phenyl	76	140	328
2.	p- chlorophenyl	phenyl	87	178	340
3.	o- chlorophenyl	phenyl	61	140	323
4.	p-dimethylaminophenyl	phenyl	86	267	468
5.	phenyl	p- tolyl	68	174	308
6.	p-chlorophenyl	p-tolyl	74	175	330
7.	o-chlorophenyl	p-tolyl	68	172	309
8.	p-dimethylaminophenyl	p-Tolyl	81	170	457
9.	phenyl	m-Tolyl	71	145	321
10.	p-chlorophenyl	m-Tolyl	80	165	313
11.	o-chlorophenyl	m-Tolyl	79	180	331
12.	p-dimethylaminophenyl	m-Tolyl	81	147	462

EXPERIMENTAL

Melting points recorded are un corrected and carried on a Toshniwal capillary melting point apparatus. The mass spectra were recorded on Finnigan MAT 8200 Spectrometer. All the ^1H nmr were recorded on a Brucker AM 360 spectrometer using TMS as reference standard. ^{13}C nmr spectrum were recorded on Bruker AC 250 spectroscope at 90.5MHz. IR spectra were recorded as KBr pellets using Shimadzu 8101 AFT IR equipment.

UV-vis Spectra were recorded in ethanol on a Shimadzu 1601 UV-Vis Spectrometer. All the compounds were purified by column chromatography on silica gel (60-120 mesh) using benzene-ethyl acetate mixture.

SYNTHESIS OF STARTING MATERIALS

Glycine ethyl ester hydrochloride and glycine ethyl ester are prepared as described in chapter I.

Benzimidic acid methyl ester hydrochloride

Imidic acid ester hydrochlorides were prepared according to the method suggested by Pinner[111] and improved by others.[112-114]

In a 500 mL filter flask a cork carrying an inlet tube was placed a mixture of benzonitrile (51 mL, 0.5 mole) and absolute methanol (22 mL, 0.54 mole). A calcium chloride guard tube was attached to the side arm and the flask was cooled in freezing mixture of ice and salt. Dry hydrogen chloride gas was passed into the mixture till 22g(0.6 mole)of the gas was absorbed. The flask was stoppered and left in the freezing mixture. The reaction mixture solidified within 3 hours into a colourless crystalline mass. The flask was placed in the refrigerator overnight. The hard solid mass of the product was carefully broken up, transferred in to a dry mortar, quickly powdered and taken in a 500 mL conical flask. Dry ether (150mL) was added and the flask was stoppered and allowed to stand in the refrigerator overnight. The imidic acid ester hydrochloride was collected in a sintered

glass funnel and washed with two 50 mL portions of dry ether. It was dried in a vacuum desiccator over potassium hydroxide pellets and phosphorous pentoxide.The benzimidic acid methyl ester hydrochloride weighed 82.5 g (96%) and melted at 98-99° C. with decomposition. It was tightly stoppered in a bottle and kept in the refrigerator.

Benzimidic acid methyl ester

Benzimidic acid methyl ester hydrochloride was converted in to free ester according to the method employed by Lehr[41] and coworkers and improved by Kidwai and Devasia[42].

A solution of benzimidic acid methyl ester hydrochloride (22.2g, 0.13 mole) in 30 mL of water was placed in a 500 mL conical flask. To this 60 mL ether added, cooled in ice bath and neutralised it by slowly adding 16 mL of icecold 40% sodium hydroxide solution. The aqueous layer was saturated with potassium carbonate by keeping the flask in ice bath. The contents of the flask was transferred in to a seperating funnel, shaken well and the ether layer was collected. The aqueous layer was extracted twice more with 50 mL. portions of ether. The combined ether extracts were dried using anhydrous potassium carbonate. The flask was stoppered and placed in the refrigerator for 6 hours. The ether solution of the benzimidic acid methyl ester was filtered and the residue washed with dry ether. The ether was evaporated under reduced pressure from a cold water bath. The yield of benzimidic acid methyl ester was 17.4 g (100%).

p-Toluimidic acid methyl ester hydrochloride

A mixture of p-tolunitrile (35.8 mL 0.3 mole) and absolute methanol (13.3 mL 0.33 mole) was taken in a 250 mL filter flask fitted with a cork carrying an inlet tube. A calcium chloride guard tube was attached to the side arm of the flask and the mixture was cooled in cold water. Dry hydrogen chloride gas was passed into the mixture till 14g(0.38 mole) of the gas was absorbed. The flask was closed and kept in cold water. Within 30 minutes the reaction mixture solidified in to a colourless crystalline mass. The flask was then allowed to stand in the refrigerator over night. The hard solid mass of the product was powdered and transferred in to a 250 mL conical flask. Dry ether (100mL) was added, the flask was stoppered and placed in the refrigerator overnight. The imidic acid methyl ester hydrochloride was filtered on a sintered glass funnel and washed twice with 25 mL portions of dry ether. It was dried in a vacuum desiccator over solid potassium hydroxide and phosphorous pentoxide. The colourless p-toluimidic acid methyl ester hydrochloride melting at 164-65°C weighed 55g (99%).

p-Toluimidic acid methyl ester

A saturated solution of p-toluimidic acid methyl ester hydrochloride (5g, 0.027 mole) in 6 mL water, was placed in a 250 mL conical flask. To this ether (12 mL) was added, cooled in icebath and neutralised by slowly adding 4 mL of ice cold 40 % sodium hydroxide solution. The contents of the flask was transferred in to a seperatory funnel, shaken well and the ether layer was collected. The aqueous layer was saturated with potassium

carbonate and extracted twice more with 6 mL portions of ether. The combined ether extracts were dried with anhydrous potassium carbonate by keeping the flask in the refrigerator for 6 hours. The ether solution of p-toluimidic acid methyl ester was filtered through a fluted filter paper by decantation and the residue was washed with dry ether. The ether was evaporated under reduced pressure from a cold water bath. The yield of slightly coloured p-toluimidic acid methyl ester was 4g (100%).

m-Toluimidic acid ethyl ester hydrochloride

A mixture of m-tolunitrile (29.85 mL, 0.025 mole) and absolute ethanol (15.75 mL, 0.027 mole) was placed in a filter flask with a cork carrying an inlet tube. A calcium chloride guard tube was attached to the side arm and the flask was cooled in freezing mixture of ice and salt. Dry hydrogen chloride gas was passed into the mixture until (11 g, 0.3 mole) of the gas was absorbed. The flask was stoppered and left in the freezing mixture. After six hours the imidic acid ester hydrochloride began to separate as colourless crystals. Then the flask was placed in the refrigerator for one day. The hard solid mass of imidic acid ethyl ester hydrochloride formed was powdered and filtered. It was then washed twice with 25 mL portions of the dry ether and dried in a vacuum desiccator over solid sodium hydroxide. The colourless m-toluimidic acid ethyl ester hydrochloride melting143-44°C weighed 45g (89%). Since it is not very stable at room temperature it was stored in the refrigerator.

m-Toluimidic acid ethyl ester

A saturated solution of the m-toluimidic acid ethyl ester hydrochloride (5g, 0.025 mole) in 6 mL of water was placed in a conical flask. To this 12 mL ether was added, cooled in ice bath and neutralised by slowly adding 4 mL of ice cold 40% NaOH solution. The contents of the flask was transferred in to a seperating funnel, shaken well and ether layer was collected. The aqueous layer was saturated with potassium carbonate and extracted twice more with 6 mL portions of dry ether. The combined ether exracts were dried with anhydrous potassium carbonate by keeping the flask in the refrigerator for 6 hours. The ether solution of m-toluimidic acid ethyl ester was filtered and the residue was washed with dry ether. The ether solution of the ester was evaporated under reduced pressure from a cold water bath. The yield of slightly coloured m-toluimidic acid ethyl ester was 4.1 g (100 %).

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

Dibenzylidene acetone was prepared by known method[104-107,115]

In 500 mL R.B flask place cold solution of 25 g of sodium hydroxide in 250mL water and 200 mL ethanol. Equip the flask with a mechanical stirrer and surround with bath of water. Maintain the temperature of the solution 20-25^{0}C. Stir vigorously and add one half of the previously prepared mixture of 26.5g (25.5 mL, 0.25 mole) of pure benzaldehyde and 7.3g (9.3mL, 0.125 mole) acetone. A flocculent ppt. forms in two to three minutes. After 15 minutes added 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 27g (93%) melting at 105°-107°C.

The crude sample was recrystallised from ethyl acetate (2.5 mL per g) and melted at 112°C.

SYNTHESIS OF SPIROIMIDAZOLINONES

3,6,10-Triphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione

Benzimidic acid methyl ester (1.4g, 0.01 mole), glycine ethyl ester (1.1g, 0.01 mole), dibenzal acetone (2.5g, 0.01 mole) and pyridine (10 mL) were taken in a 100 mL round bottomed flask and heated under reflux on a sand bath. The yellow colour of the solution gradually turns to brown. After refluxing of 3 hours, it was cooled, added to ice cold water and acidified using dilute hydrochloric acid. The dull yellow coloured residue formed was filtered, washed with cold water and dried in the oven at 80°C for one hour. The pale yellow solid of the spiro imidazolinone weighed 3.2 g (76%) and melted at 138°C.

Recrystallisation of the spiro imidazolinone from benzene petroleum ether mixture gave pale yellow crystals melting at 140°C.

Analysis

N %

Found	: 7.15
Calculated	: 7.1
$C_{26}H_{22}O_2N_2$	
UV - Vis	λ_{max} - 328 nm.

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

Benzimidic acid methyl ester (0.7g, 0.005 mole), glycine ethyl ester (0.5g, 0.005 mole), di(p-chlorobenzal) acetone (1.1g, 0.005 mole) and pyridine (10 mL) were heated under reflux for 3 hours. The yellow colour of the solution gradually turned brown. After refluxing it was cooled and added to ice cold water. It was then acidified using dilute hydrochloric acid. The pale yellow coloured residue formed was filtered, washed twice with cold water and dried at 80°C for one hour. The pale yellow solid of spiro imidazolinone weighed 2g (87%) and melted at 178°C

Recrystallisation of the spiro imidazolinone from benzene petroleum ether mixture gave dull yellow crystals melting at 180°C.

Analysis

N %

Found	: 6.15
Calculated	: 6
$C_{26}H_{20}O_2N_2Cl_2$	
UV - Vis.	λ_{max} - 340 nm

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

Benzimidic acid methyl ester (0.7g, 0.005 mole) glycine ethyl ester (0.5g, 0.005 mole), di(o-chlorobenzal)acetone (1.1g, 0.005 mole), and pyridine (10 mL) were heated under reflux for 3 hours. After refluxing it was cooled and added to ice cold water. It was then acidified and the dull yellow coloured residue formed was filtered, washed with cold water and dried at 80°C for one hour. The dull yellow solid of the spiro imidazolinone weighed 1.4 (61%) and melted at 139°C.

Recrystallisation of the spiro imidazolinone from benzene petroleum ether mixture gave yellow crystals melting at 140°C.

Analysis

N %

Found : 6.15

Calculated : 6

$C_{26}H_{20}O_2N_2Cl_2$

UV - Vis. λ_{max} - 323 nm

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

Benzimidic acid methyl ester (0.5g, 0.003 mole), glycine ethyl ester (0.3g, 0.003 mole), di(p-dimethylaminobenzal) acetone (1g, 0.003 mole) and pyridine (10 mL) were taken in a 100 mL round bottomed flask and heated under reflux for 3 hours. It was then cooled, added to ice cold water and acidified using dilute hydrochloric acid. The red coloured residue formed was filtered, washed twice with cold water and dried. The product weighed 1.3g (86%) and melted at 265°C.

Recrystallisation of the spiro imidazolinone from ethanol gave red crystals melting at 267°C.

Analysis

N %

Found	: 11.75
Calculated	: 11.67
$C_{30}H_{32}O_2N_4$	
UV - Vis.	λ_{max} - 468 nm

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

Dibenzalacetone (2g, 0.0085 mole), para toluimidic ester (1.3g, 0.0085 mole), glycine ethyl ester (0.9 gr, 0.0085mole) and pyridine (10 mL) were refluxed on a sand bath. The yellow colour of the solution gradually turned brown. After refluxing for 3 hours, it was cooled and added to ice cold water. It was then acidified using dilute hydrochloric acid. The dull yellow coloured residue formed was filtered, washed twice with cold water and dried in the oven at 80°C for one hour. The pale yellow solid of the spiro imidazolinone weighed 2.4 g. (68%) and melted at 174°C.

Recrystallisation of the spiro imidazolinone from alcohol gave pale yellow crystals melting at 175°C.

Analysis

N %

Found	: 6.79
Calculated	: 6.86
$C_{27}H_{24}N_2O_2$	
UV - Vis.	λ_{max} - 308 nm

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

p-Toluimidic ester (1g, 0.0067 mole) glycine ethyl ester (0.68g, 0.0066 mole),di (p- chlorobenzal) acetone (2g, 0.0066 mole) and pyridine (10 mL) were heated under reflux for 3 hours. The yellow colour of the solution gradually turned brown. It was then cooled, added to cold water and acidified with dilute hydrochloric acid. The pale yellow coloured residue was filtered, washed with cold water and dried at 80°C for one hour. The pale yellow solid of the spiro imidazolinone weighed 2.3g (74%) add melted at 173°C.

Recrystallisation of the spiro imidazolinone from alcohol gave pale yellow crystals melting at 175°C.

Analysis

N %

Found : 5.82

Calculated : 5.9

$C_{27}H_{22}N_2O_2Cl_2$

UV - Vis λ_{max} - 391 nm

3-(p-tolyl)-6,10-di(o-chloro phenyl)-2,4-diazaspiro [4.5]deca-2-en-5,8-dione

p-Toluimidic ester (1g, 0.0067 mole),glycine ethyl ester (0.68g, 0.006 mole), di(o-chlorobenzal) acetone (2g, 0.006 mole) and pyridine (10 mL) were heated under reflux for 3 hours. It was then cooled and added to cold water and acidified. The pale yellow coloured residue formed was filtered, washed with cold water and dried at 80°C for one hour. The pale yellow solid of the spiro imidazolinone weighed 2.1g (68%) and melted at 170°C.

Recrystallisation of the spiro imidazolinone from benzene-petroleum ether mixture gave pale yellow crystals melting at 172°C.

Analysis

N %

Found	: 5.79
Calculated	: 5.9
$C_{27}H_{22}N_2O_2Cl_2$	
UV - Vis.	λ_{max} - 309 nm

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

p-Toluimidic ester (0.9g, 0.00625),glycine ethyl ester (0.6g, 0.00625 mole), di(p-dimethylaminobenzal) acetone (2g, 0.00625 mole) pyridine (10 mL) were refluxed on a sand bath. After refluxing of 3 hours, it was cooled, added to cold water and acidified with dilute hydrochloric acid. The red coloured residue was filtered, washed with cold water and dried at 80°C for 1 hour. The red solid of the spiro imidazolinone weighed 2.5g (81%) and melted at 169°C.

Recrystallisation of spiro imidazolinone from alcohol gave reddish yellow crystals melting at 170°C.

Analysis

N %

Calculated	: 11.33
Found	: 11.5
$C_{31}H_{34}N_4O_2$	
UV - Vis.	λ_{max} - 457 nm

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

m-Toluimidic ester (1.1g. 0.0070 mole), glycine ethyl ester (0.8g, 0.007 mole), di(p-chlorobenzal) acetone (2.1g. 0.007 mole) and pyridine (10 mL) were refluxed on a sand bath for 3 hours. It was then cooled,

added to ice cold water and acidified with dilute hydrochloric acid. The pale yellow coloured solid was filtered, washed with cold water and dried in the oven at 80°C for one hour. The pale yellow solid of the spiro imidazolinone weighed 2.5g. (80%) and melted at 162°C.

Recrystallisation of the spiro imidazolinone from benzene- petroleum ether mixture gave pale yellow crystals melting at 165°C.

Analysis

N %

Found	: 5.81
Calculated	: 5.9
$C_{27}H_{22}N_2O_2Cl_2$	
UV - Vis.	λ_{max} - 313 nm

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

Dibenzalacetone (2g, 0.0085 mole),m-toluimidic ester (1.27g, 0.0085mole), glycine ethyl ester (0.9g, 0.0085 mole), and pyridine (10 mL) were refluxed on a sand bath. The yellow colour of the solution turned brown. After refluxing for 3 hours, it was cooled and added to ice cold water. It was then acidified using dilute hydrochloric acid. The pale yellow coloured solid of the spiro imidazolinone was filtered, washed with cold water and dried in the oven at 80°C for one hour. The spiro imidazolinone weighed 2.5g. (71%) and melted at 144°C.

Recrystallisation of the spiro imidazolinone from benzene petroleum ether mixture gave pale yellow crystals melting at 145°C.

Analysis

N %

Found	: 6.92
Calculated	: 6.86
$C_{27}H_{24}N_2O_2$	
UV - Vis	λ_{max} - 321 nm

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

m-Toluimidic ester (1.1g. 0.007 mole), glycine ethyl ester (0.8g, 0.007 mole), di(o-chlorobenzal) acetone (2.1g, 0.007 mole) and pyridine (10 mL) were refluxed on a sand bath for 3 hours. It was then cooled, added to ice cold water and acidified with dilute hydrochloric acid. The pale yellow coloured solid was filtered, washed with cold water and dried in the oven at 80°C for one hour. The pale yellow solid of the spiro imidazolinone weighed 2.5g. (79%) and melted at 177°C.

Recrystallisation of spiro imidazolinone from benzene-petroleum ether mixture gave pale yellow crystals melting at 180°C.

Analysis

N %

Found	: 5.80
Calculated	: 5.9
$C_{27}H_{22}N_2O_2Cl_2$	
UV-vis.	λ_{max} - 331 nm

3-(m-tolyl)-6,10-di(p-dimethylaminophenyl)-2,4-diazaspiro [4.5]deca-2-en-5,8-dione

m-Toluimidic ester (0.9g, 0.00625mole),glycine ethyl ester (0.6g, 0.00625 mole), di(p-dimethylaminobenzal)acetone (2g. 0.00625 mole) pyridine (10 mL) were refluxed on a sand bath. After refluxing of 3 hours, it was cooled, added to cold water and acidified with dilute hydrochloric acid. The red coloured residue was filtered, washed with cold water and dried at 80°C for one hour. The red solid of the spiro imidazolinone weighed 2.5. (81%) and melted at 146°C.

Recrystallisation of spiro imidazolinone from alcohol gave red yellow crystals melting at 147°C.

Analysis

N %

Found	: 11.45
Calculated	: 11.33
$C_{31}H_{34}N_4O_2$	
UV-Vis.	λ_{max} - 462 nm

CHAPTER III

REACTIONS OF SPIRO IMIDAZOLINONES

The double Michael reaction between 2-aryl-2-imidazolin-5-one and bis-benzalacetone yields spiro imidazolinones (Chapter II). The mass spectral studies of these spiro imidazolinones showed the formation of aryl substituted cyclobutanone fragments. Since spiro imidazolinones contain a free carbonyl group, it can react with 2,4-dinitrophenylhydrazine yielding the corresponding phenylhydrazones. The free carbonyl group of spiro imidazolinone can further condense with the active methylene group of 2-phenyl-2-imidazolin-5-one yielding hitherto unreported spiro imidazolinones. In this chapter studies of these reactions of spiro imidazolinones are presented.

Thermal decomposition of spiro imidazolinones

Introduction

Thermal decomposition is the breaking apart of chemical bonds by the use of thermal energy only. The analysis of these process and fragments tells much about the nature and identity of the original larger molecule. The production of a variety of smaller molecules from larger original molecule

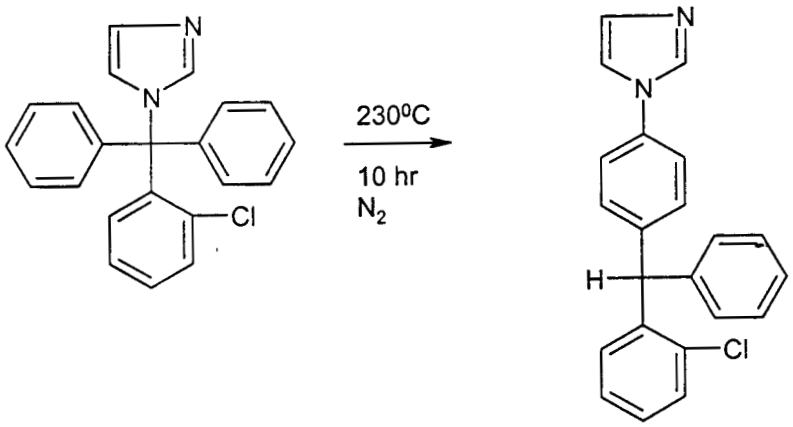
has fostered the use of pyrolysis as a simple preparative technique.

The fragmentation which occurs during thermal decomposition is analogous to the process that occur during the production of a mass spectrum. Energy is put in to the system and as a result the molecule breaks apart in to stable fragments. If the energy parameters are controlled in a reproducible way, this fragmentation is characteristic of the original molecule based on the relative strengths of the bonds between atoms. The degradation of a molecule which occurs during pyrolysis is caused by the dissociation of the chemical bond and production of free radicals.

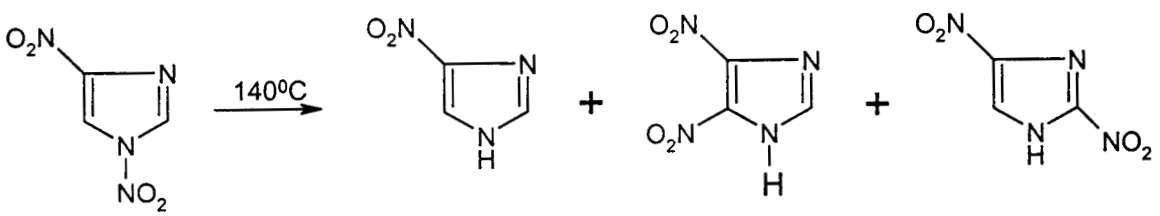
Imidazoles in general are very stable to heat. The parent molecule is said to decompose at 590°C by an unknown process which may be similar to the mass spectral fragmentation since HCN has been identified among the reaction products.

In 1883 Wallach discovered that when 1-methylimidazole was heated, he obtained 2-methylimidazole and some HCN. The reaction now appears to be much more general[116] and of some synthetic importance since it can give rise to a fairly wide variety of 2-substituted imidazoles.

1-Tritylimidazoles undergo isomerisation on melting to 2-and 4-Tritylimidazoles. But recent reports shows that at 230°C 1-tritylimidazoles rearrange in a rather different fashion without the migration to 2 or 4–position.



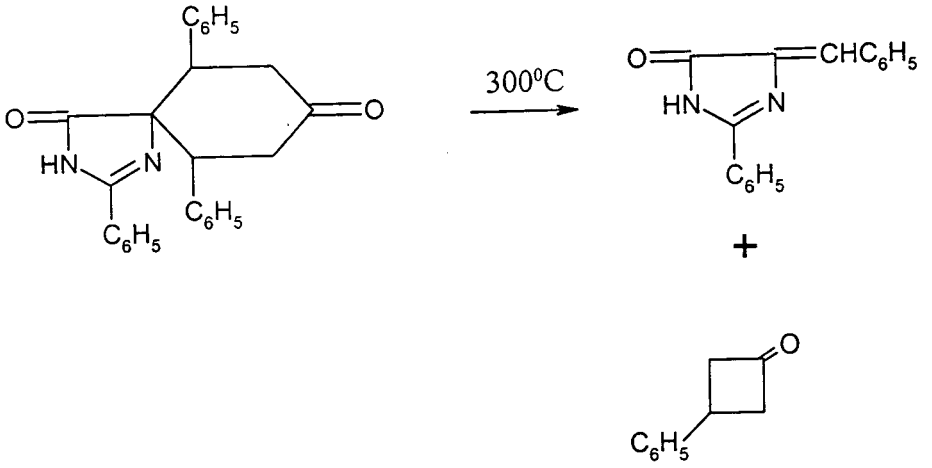
When 1,4-dinitroimidazole is heated at 140°C in chlorobenzene, benzonitrile or anisole there is conversion into 2,4- and 4,5-dinitroimidazoles but considerable denitration can also occur giving 4-nitroimidazole.



Present work

The thermal decomposition of spiro imidazolinones obtained by the double Michael addition of bis-benzalacetone with 2-phenyl-2-imidazolin-5-one gave interesting products. They were thermally decomposed by heating just above 300°C and the resulting products on purification yielded 3-aryl substituted cyclobutanones and 2-aryl-4-arylidene-2-imidazolin-5-ones. Two spiroimidazolinones 3-(p-tolyl)-6,10-di(p-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione and 3-(p-tolyl)-6,10-diphenyl-2,4-

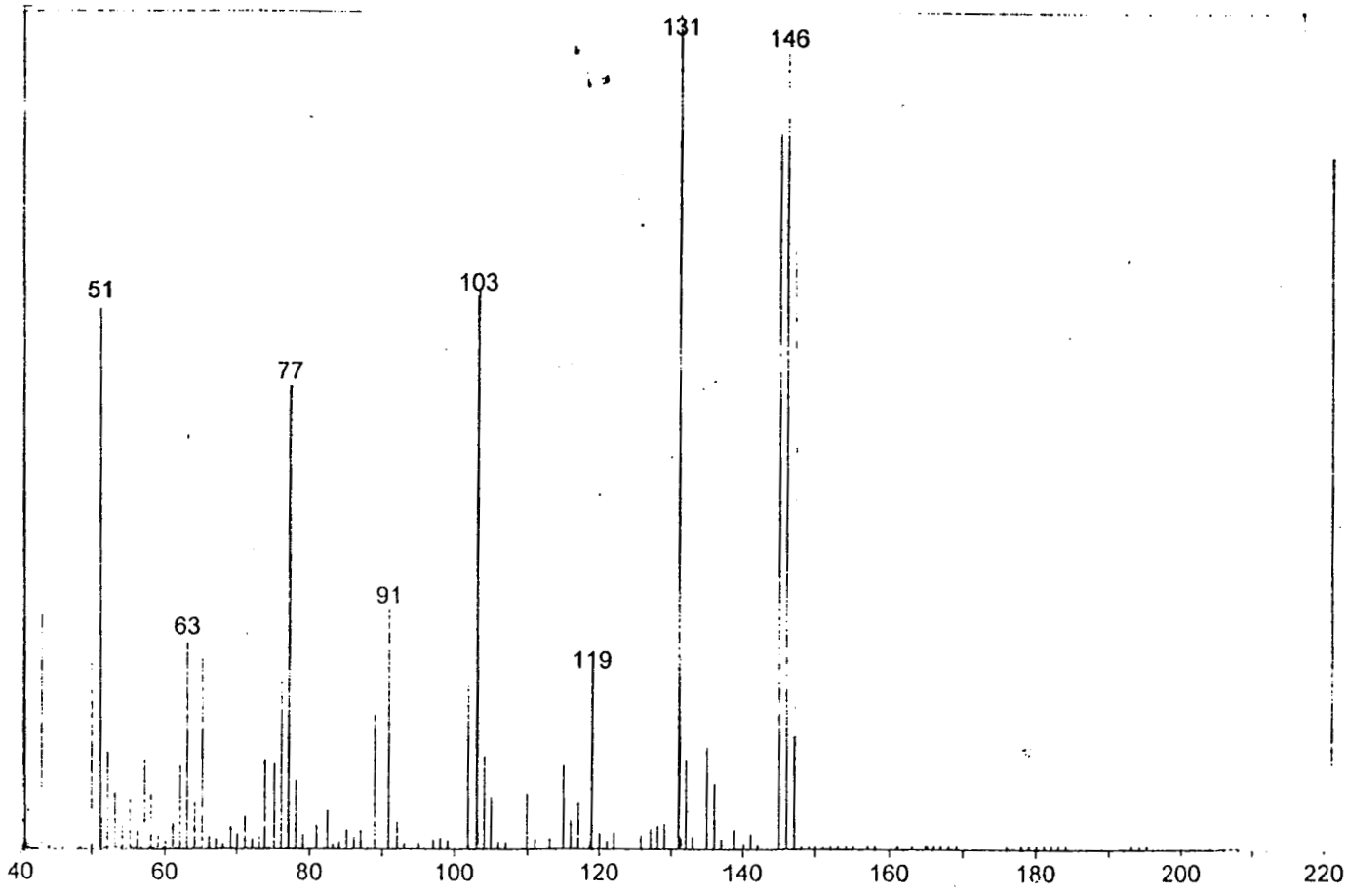
diazaspiro[4.5]deca-2-en-5,8-dione were subjected to thermal decomposition.



The structures of 3-arylcyclobutanones formed were arrived at from their mass spectra. They also gave the corresponding 2,4-dinitrophenylhydrazone derivatives. The structures of 2-aryl-2-imidazolin-5-ones were confirmed by comparison of their melting points with authentic samples[48] and from the undepressed mixed melting points.

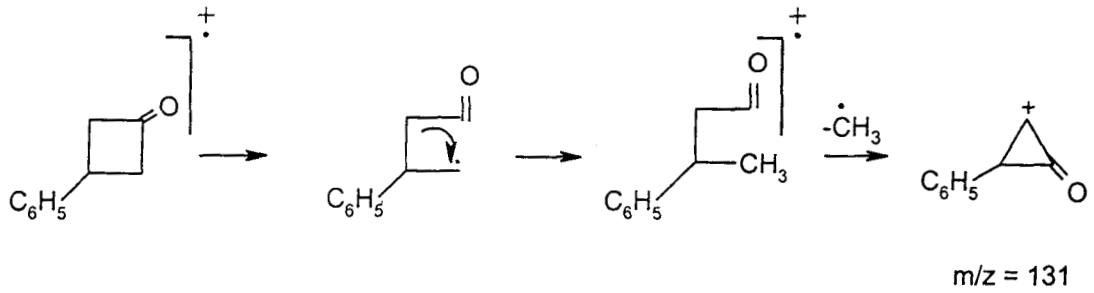
Mass spectral fragmentation of 3-phenylcyclobutanone

The mass spectrum of 3-phenylcyclobutanone had M^+ peak at 146. Other important peaks in the mass spectrum were 131(100%), 103 (65%) 91 (28%) 77 (55%). The fragment at m/z 131 is formed by the breaking of the bond between CH_2 group and carbonyl group. One hydrogen migrates

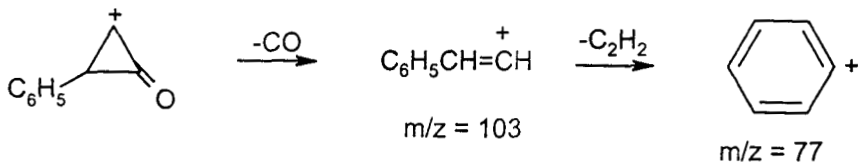


EI-MS of 3-phenyl cyclobutanone

from the second carbon atom to the CH_2 group and the resulting ion eliminates one methyl radical[127].



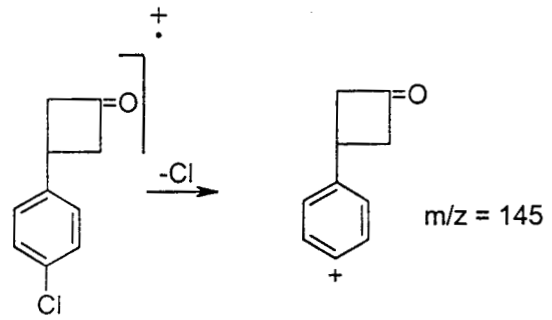
The mass peak at 103 corresponded to the ion formed by the elimination of a neutral molecule of CO.



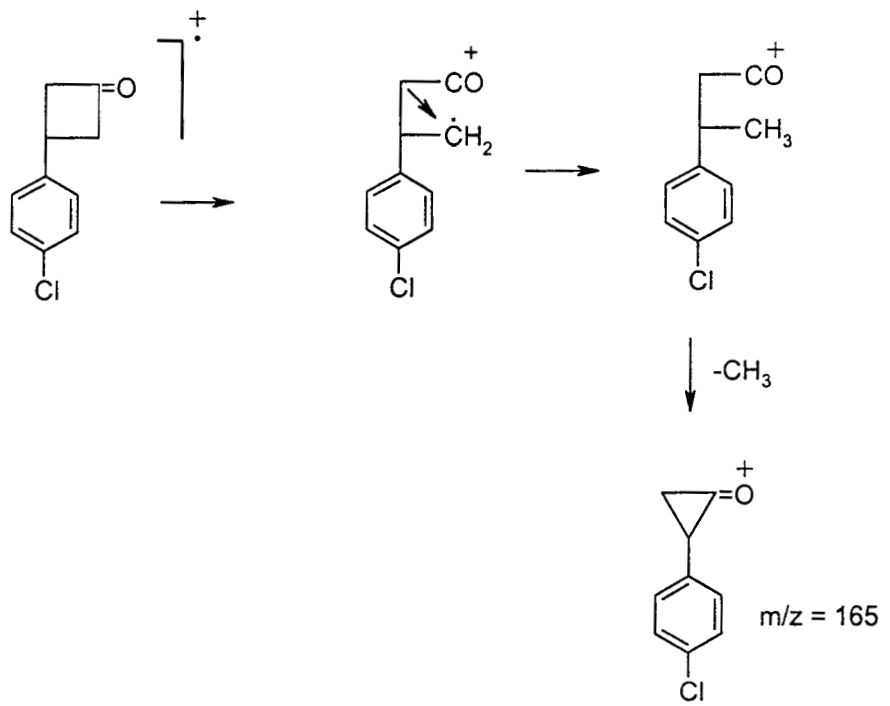
Mass fragmentation of 3-(p- chlorophenyl)cyclobutanone

The mass spectrum of 3-(p- chlorophenyl)cyclobutanone had M^+ peak at 180. The other important peaks in the mass spectrum were 165(100%), 145 (53%), 137 (43%) 102 (35%) , 75 (26%)

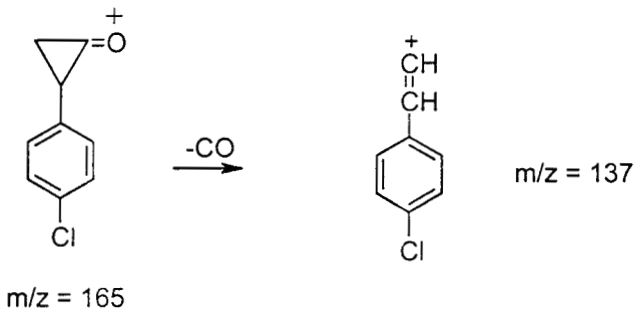
The mass peak at 145 units corresponds to the ion formed by the elimination of chlorine atom.



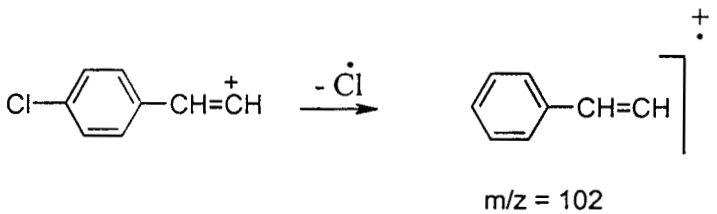
By an alternate fragmentation pathway it gave rise to ion at m/z = 165. This ion is formed by the breaking of a bond adjacent to the carbonyl group and simultaneous migration of a hydrogen followed by elimination of a methyl radical[127].



Removel of a neutral CO molecule from the above fragment gave the daughter ion at m/z = 137.

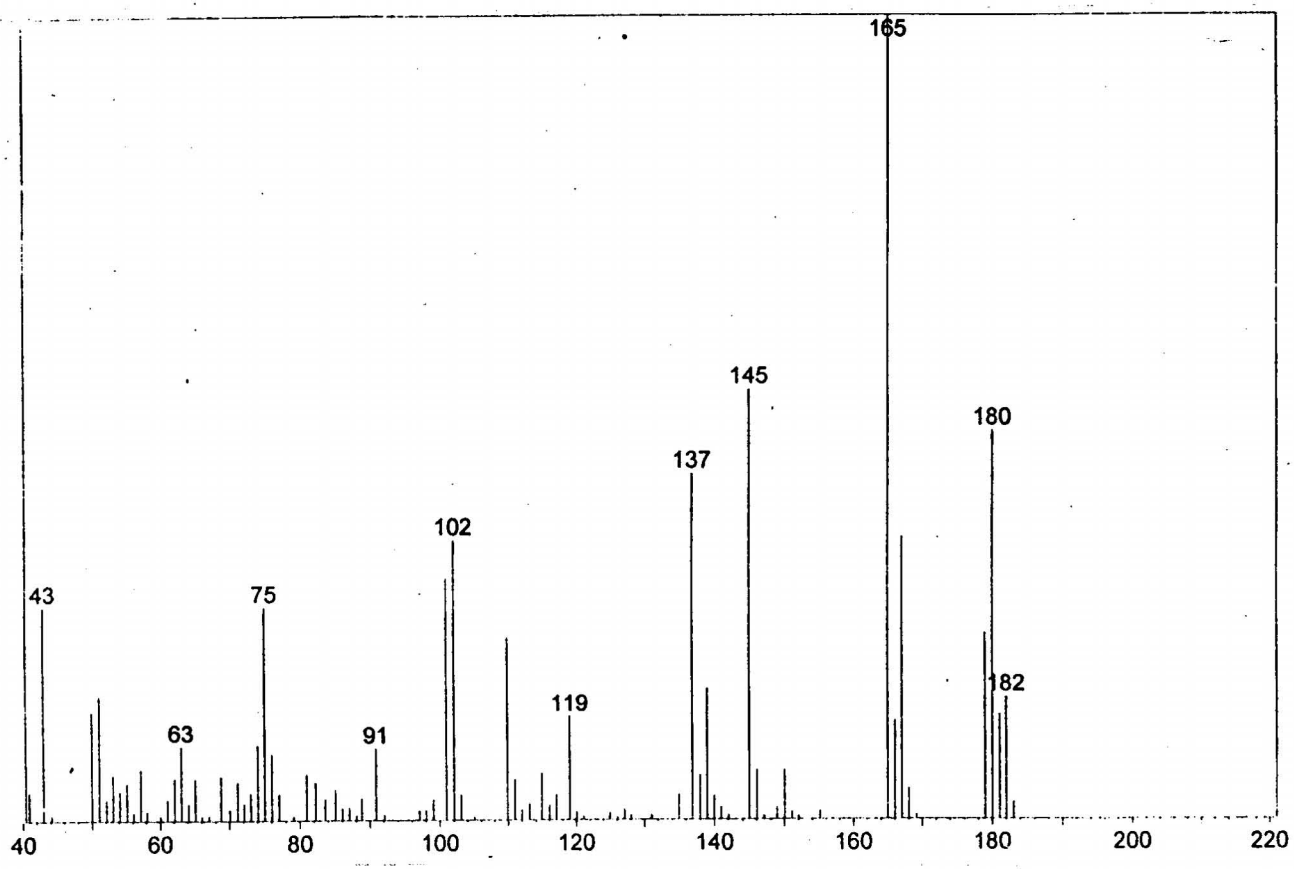


The peaks at m/z 102 is due to the following fragmentation.



All the chlorine containing fragments were accompanied by the corresponding +2 peaks in the intensity ratio 3:1 as is common with compounds containing one chlorine atom.

Usually four membered rings are more difficult to prepare by the direct cyclisation of straight chain intermediates. This is partly because atoms which must combine unlike those which join to give a three membered ring, can alter their relative positions considerably under the influence of thermal motion. It is only when the cyclising atoms happen to be suitably oriented and the appropriate stimulus applied that the ring can form. The rate of such cyclisations should therefore be much less than those of the corresponding three membered ring[117-118].



EI-MS of 3-(p-chlorophenyl) cyclobutanone

Cyclobutanone derivatives can be prepared by various methods[119-126]. Spiro imidazolinones on thermal decomposition yield 3-arylcyclobutanones and therefore this method can be used for the preparation of 3-arylcyclobutanones with desirable aryl group at position three.

Thermal decomposition of 3-p-tolyl-6,10-di(p-chlorophenyl)-2,4-diazaspiro [4.5] deca-2-en-5,8-dione

The spiroimidazolinone 3-(p-tolyl)-6,10-di (p-chlorophenyl)-2,4-diazaspiro [4.5] deca-2-en-5,8-dione (3g) was taken in a dry hard glass test tube. It was heated just above 300^{0}C in an electric bunsen for 10 minutes. A thermometer was suspended using a thread inside the test tube. The oily liquid which rose through the sides of the test tube was absorbed in cotton attached at the end of a glass rod. The product absorbed in cotton was washed with ether and the ether evaporated. Purification by preparative TLC eluting with benzene-ethylacetate (1:1) mixture gave 3-(p-chlorophenyl)cylcobutanone. The residue in the test tube was boiled with 5mL of isobutanol and filtered hot. On cooling 4-(p-chlorophenyl)-2-(p-tolyl)-2-imidazolin-5-one crystallised. It was filtered and dried. The identity of this compound was proved by comparing its melting point with authentic sample[48] and the undippressed mixed melting point.

Thermal decomposition of 3-(p-tolyl)-6,10-diphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione

The spiroimidazolinone 3-(p-tolyl)-6,10-diphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione (3g) was taken in a dry hard glass test tube. It was heated just above 300^{0}C in an electric bunsen for 30 minutes. A thermometer was suspended using a thread inside the test tube. The oily liquid which rose through the sides of the test tube was absorbed in cotton attached at the end of a glass rod. The product absorbed in cotton was washed with ether and the ether evaporated. Purification by preparative TLC using benzene-ethylacetate (1:1) mixture gave 3-phenylcyclobutanone. The residue in the test tube was boiled with 5mL of isobutanol and filtered hot. On cooling 4-Benzylidene-2-(p-tolyl)-2-imidazolin-5-one crystallised. It was filtered and dried. The identity of this compound was proved by comparing its melting point with authentic sample[48] and the undippressed mixed melting point.

2,4-Dinitrophenylhydrazine derivative of spiro imidazolinones

In an attempt to synthesize and characterise new imidazolinones, the free keto group in the spiroimidazolinones were reacted with 2,4-dinitro-phenylhydrazine to yeild the respective hydrazones which were sparingly soluble in alcohol.

For the synthesis of the new derivatives of spiroimidazolinones the following procedure was followed. In each case the spiroimidazolinone (100 mg) was dissolved in ethanol and added calculated amounts of 2,4-dinitrophenylhydrazine reagent. The mixture was shaken well and kept for a day. The reddish crystalline product formed was filtered, washed with ethanol and dried. The compounds thus prepared are given in the table III.1. All the compounds synthesised gave satisfactory analytical data for nitrogen. The UV-visible absorption maxima of these compounds were found to be in the range of the 2,4-dinitrophenylhydrazones of ketones.

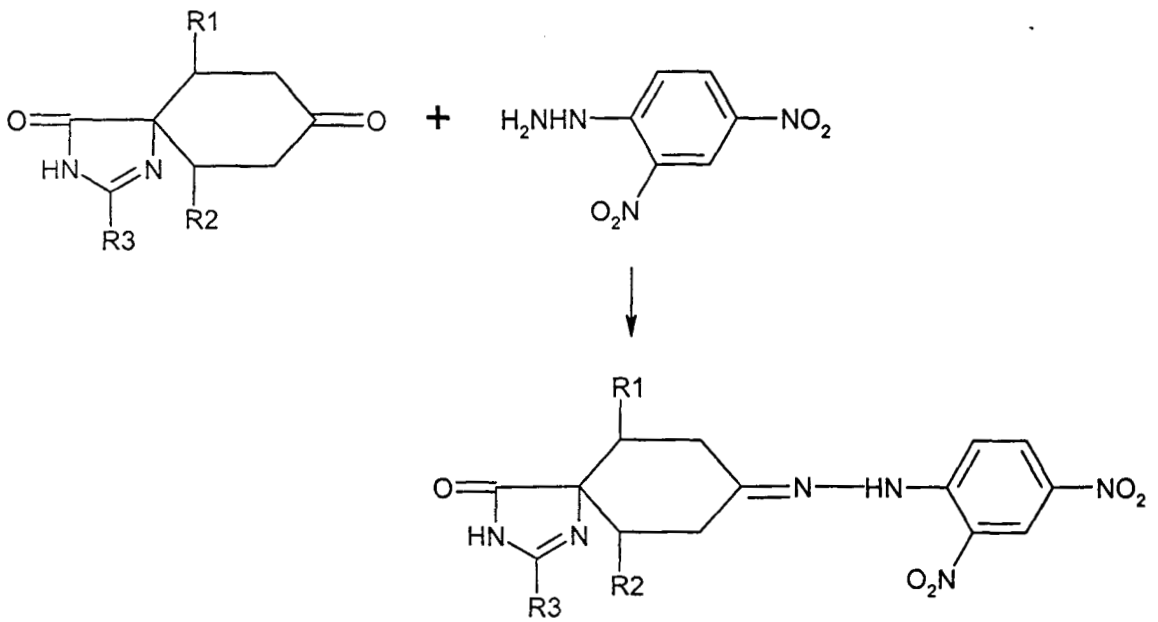


Table III.1

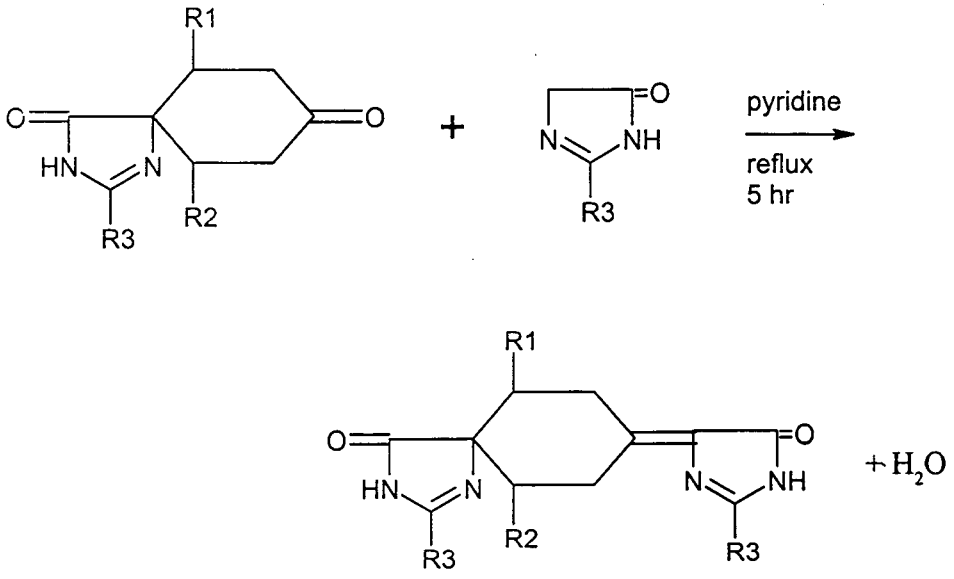
2,4-dinitrophenylhydrazone derivatives of spiroimidazolinones

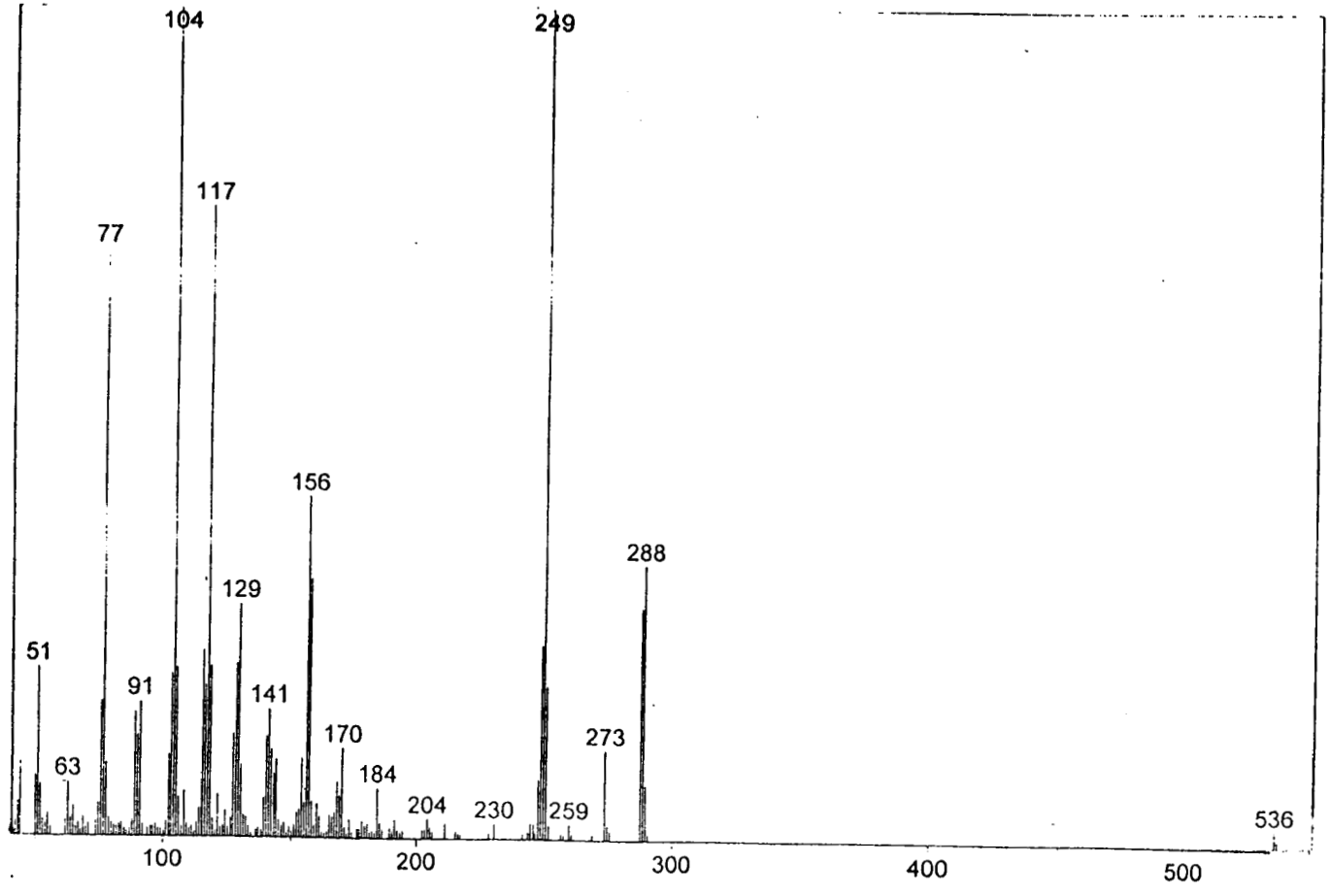
No.	$R^1=R^2$	R^3	MP.(°C)	λ_{max}(nm)	N(%)	
					calculated	Found
1.	phenyl	phenyl	170	416	14.6	14.2
2.	phenyl	p-tolyl	238	364	14.3	14
3.	phenyl	m-tolyl	120	391	14.3	14.1
4.	p-chlorophenyl	phenyl	132	392	13	13.2
5.	p-chlorophenyl	p-tolyl	148	360	12.8	12.6
6.	p-chlorophenyl	m-tolyl	193	364	12.8	12.9
7.	o-chlorophenyl	phenyl	125	387	13	13.2
8.	o-chlorophenyl	p-tolyl	147	361	12.8	12.9
9.	o-chlorophenyl	m-tolyl	130	364	12.8	12.7

Condensation of spiroimidazolinones

The spiro imidazolinones formed by the double Michael reaction between glycine ethyl ester, benzimidic ester and dibenzal acetone contain a free carbonyl group. This carbonyl group underwent condensation with 2-phenyl-2-imidazolin-5-ones when excess of glycine ethyl ester and benzimidic ester were used. This resulted in the synthesis of four new compounds.

In the general procedure the di-benzylideneacetone, glycine ethyl ester and benzimidic ester in the ratio 1:2:2 were refluxed in pyridine for 5 hours. After refluxing it was cooled and poured to cold water and acidified with dilute hydrochloric acid. The condensed products of spiroimidazolinones formed were filtered, washed with ethanol and dried.





EI-MS of 3,6,10 –Triphenyl-8-(5-oxo-2-phenyl-1,3-diazacyclopenta–2-en-4-ylidene)-2,4-diazaspiro[4.5]deca-2-en-5-one.

The mass spectrum of 3,6,10-Triphenyl(5-oxo-2-phenyl-1,3-diazacyclopenta-2-en-4-ylidene)-2,4-diazaspiro [4.5] deca-2-en-5-one was recorded. It had M^+ peak at m/z = 536 in accordance with the structure proposed. Other peaks present are 288(16%), 249(52%), 156(21%), 117(38%), 104(100%) and 77(35%) which further supported its structure. The compounds thus prepared are given in the table III.2. All the compounds gave satisfactory analytical data for nitrogen.

Table III.2

Characterisation data of the compounds prepared

No.	$R^1=R^2$	R^3	Yield (%)	MP (°C)	(λ_{max}) (nm)	N_2 (%)		Molecular formula
						cacul.	Found	
1.	phenyl	phenyl	87	175	351	10.45	10.6	$C_{35}H_{28}N_4O_2$
2.	p-chloro Phenyl	phenyl	79	210	336	9.26	9.1	$C_{35}H_{26}N_4O_2Cl_2$
3.	o-chloro phenyl	phenyl	76	198	337	9.26	9.3	$C_{35}H_{26}N_4O_2Cl_2$
4.	p-dimethylamino phenyl	phenyl	70	290	467	13.5	13.27	$C_{39}H_{38}N_6O_2$

SYNTHESIS OF CONDENSED SPIRO IMIDAZOLINONES

3,6,10-Triphenyl-8-(5-oxo-2-phenyl-1,3-diazacyclopenta-2-en-4-ylidene)-2,4-diazaspiro [4.5] deca-2-en-5-one

Benzimidic acid methyl ester (0.6g. 0.0044 mole) glycine ethyl ester (0.46g. 0.0044 mole) dibenzal acetone (0.5 g. 0.0021 mole)and pyridine (10 mL) were taken in a 100 mL. round bottomed flask and heated under

reflux for 5 hours. It was then cooled and added to cold water and acidified with dilute hydrochloric acid. The yellow coloured solid formed was filtered, washed and dried. The solid weighed 1g. (87%) which melted at 174°C.

Recrystallisation of the imidazolinone from benzene petroleum ether mixture gave yellow crystals melting at 175°C.

Analysis

N %

Calculated : 10.45

Found : 10.6

$C_{35}H_{28}N_4O_2$

UV-Vis. λ_{max} = 351nm

3-Phenyl-6,10-(p-chlorophenyl)-8-(5-oxo-2-phenyl-1,3-diazacyclopenta-2-en-4-ylidene)-2,4-diazaspiro [4.5] deca-2-en-5-one

Benzimidic acid methyl ester (0.5, 0.0037) glycine ethyl ester (0.40g. 0037 mole), di(p-chlorobenzylidene) acetone (0.6g, 0.002 mole) and pyridine (10mL) were taken in a 100 mL. round bottomed flask and heated under reflux for 5 hours. It was then cooled, added to cold water and acidified with dilute hydrochloric acid. The yellow coloured solid formed was filtered, washed with water and dried. The solid weighed 0.95g, (79%) which melted at 207°C.

Recrystallisation of the imidazolinone from benzene gave yellow crystals melting at 210°C.

Analysis

N %

Calculated	: 9.26
Found	: 9.1
$C_{35}H_{26}N_4O_2Cl_2$	
UV-Vis.	λ_{max} = 336 nm

3-Phenyl-6,10-(o-chlorophenyl)-8-(5-oxo-2-phenyl-1,3-diazacyclopenta-2-en-4-ylidene)-2,4-diazaspiro [4.5] deca-2-en-5-one

Benzimidic acid methyl ester (0.5g, 0.0037 mole) glycine ethyl ester (0.4g, 0.0037), di(o-chlorobenzylidene)acetone (0.6g, 0.002 mole) and pyridine (10mL) were taken in a 100 mL round bottomed flask and heated under reflux for 5 hours. It was then cooled, added to cold water and acidified with dilute hydrochloric acid. The yellow coloured solid weighed 0.920 g, (76%) which melts at 196°C.

Recrystallisation of the imidazolinone from benzene - petroleum ether gave yellow crystals melting at 198°C.

Analysis

N %

Calculated	: 9.26
Found	: 9.3
$C_{35}H_{26}O_2N_4Cl_2$	
UV-Vis.	λ_{max} = 337nm

3-Phenyl-6,10-(p-dimethylaminophenyl)-8-(5-oxo-2-phenyl-1,3-diazacyclopenta-2-en-4-ylidene)-2,4-diazaspiro [4.5] deca-2-en-5-one

Benzimidic acid methylester (0.5g, 0.0037 mole) glycine ethyl ester (0.38g, 0.0037 mole), di(p-dimethylaminobenzylidene) acetone (0.6g, 0.00187 mole) and pyridine (10 mL) were refluxed for 5 hours. It was then cooled, added to cold water and acidified. The red coloured solid was filtered, washed and dried. The solid weighed 0.95g, (70%) and melted at 288°C.

Recrystallisation of the imidazolinone from benzene gave red crystals melting at 290°C.

Analysis

N %

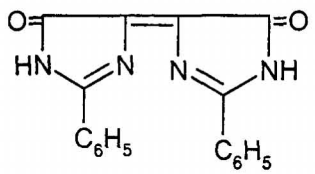
Calculated	: 13.5
Found	: 13.27
$C_{39}H_{38}N_6O_2$	
UV-Vis.	λ_{max} = 467nm

CHAPTER IV

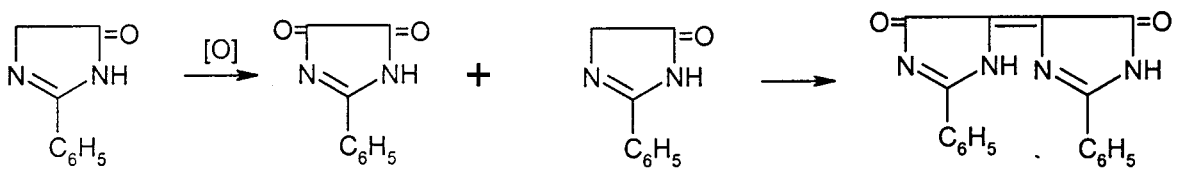
SYNTHESIS AND SPECTRAL STUDIES OF DERIVATIVES OF 4-(Amino, arylmethylene)-2-aryl-2-imdazolin-5-ones

The reaction between benzimidic acid ester and glycine ester yielding red coloured products have been thoroughly investigated[129-130]. Wieland and Biener[131] pherographically 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.

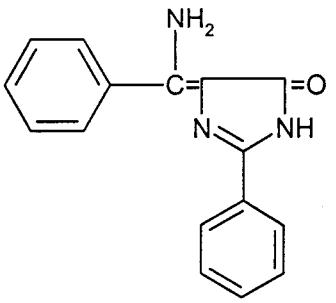
Ekeley and Ronzio[132-133] suggested that the red colour is due to the formation of glyoxaline red with the following structure.



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[134] resulted in the isolation and structutal elucidation of 4-(Amino, arylmethylene)-2-aryl-2-imidazolin-5-one and they prepared their acetylated products[134]. 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. After spectral studies they assigined the structure[134].



The aminoimidazolinones prepared by them are given below.

1. 4-(Amino, phenylmethylene)-2-phenyl-2-imidazolin-5-one
2. 4-(Amino, p-methylphenylmethylene)-2-(p-methylphenyl)-2-imidazolin-5-one.

3. 4-(Amino, m-methylphenylmethylene)-2-(m-methylphenyl)-2-imidazolin-5-one.

As amino group can be easily acetylated by reacting with acetic anhydride they prepared the acetylated derivatives[134]. The amino imidazolinone (2g) was stirred with acetic anhydride (2mL) and pyridine (10mL) for six hours, and poured in to cold water. The product was filtered, washed with water and dried. The acetyl derivatives prepared by them are given below.

1. 4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one.
2. 4-(Acetylamino, p-methylphenylmethylene)-2-(p- methylphenyl)-2-imidazolin-5-one.
3. 4-(Acetylamino, m-methylphenylmethylene)-2-(m-methylphenyl)-2-imidazolin-5-one.

Benzoylation of 4-(Amino, arylmethylene)-2-aryl-2-imidazolin-5-one

As amino groups can be benzoylated by reacting with benzoylchloride it was proposed to attempt it on 4-(amino, arylmethylene)-2-aryl-2-imidazolin-5-one. This resulted in the synthesis of three more new compounds.

Results and discussion

In each case 2g of the amino imidazolinone was dissolved in pyridine (10mL) and to this, freshly distilled benzoyl chloride (0.8mL) in pyridine

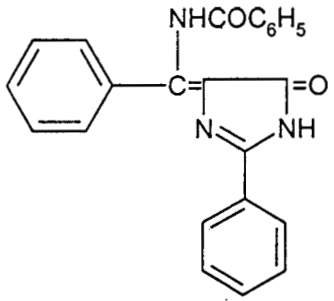
was added and stirred for 5 hours. The product was poured into water filtered, washed with water and dried. The benzoyl derivatives synthesised are given in table IV.I. All the compounds synthesised gave satisfactory analytical data for nitrogen.

Table IV.I

4-(benzoylamino, arylmethylene)-2-aryl-2-imidazolin-5-one

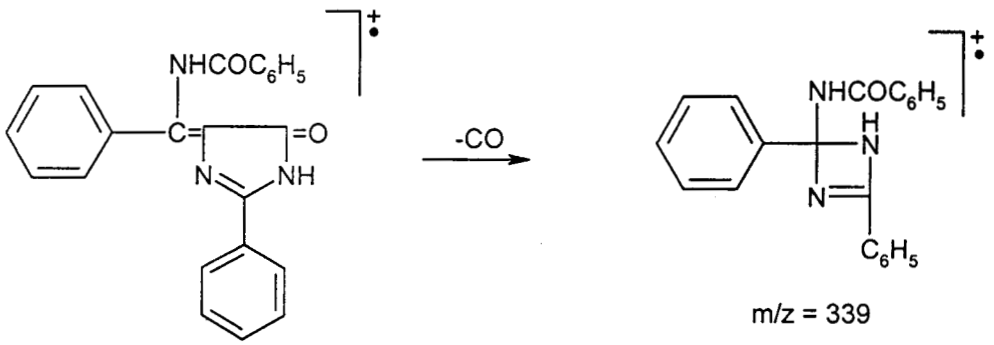
No.	Name of benzoyl derivative	Yield(%)	MP (°C)	λ_{max} (nm)
1.	4-(benzoylamino, phenylmethylene) -2-phenyl-2-imidazolin-5-one.	75	234	395
2.	4-(benzoylamino, p-methylphenyl methylene)-2-(p-methylphenyl) -2-imidazolin-5-one	65	221	388
3.	4-(benzoylamino, m-methylphenyl methylene)-2-(m-methylphenyl) -2-imidazloin-5-one	63	217	383

The structure of the benzoyl derivative was elucidated from its spectral data. The mass spectrum of 4-(benzoylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one gave M^+ peak at m/z = 367, corresponding to the expected structure.

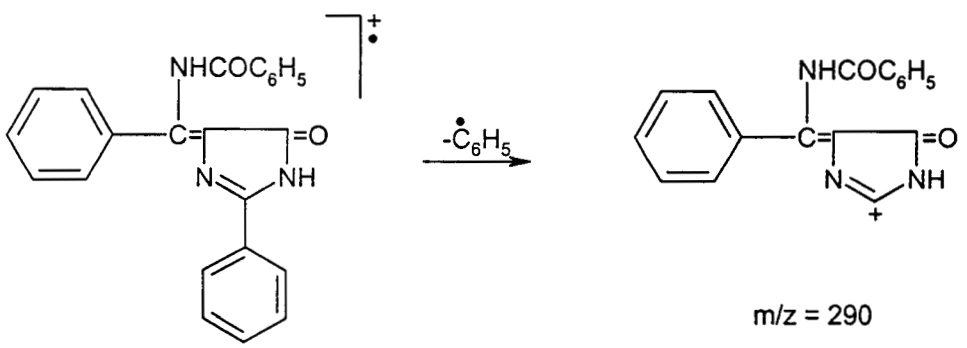


Other peaks were at m/z = 339, 290, 264, 235, 105 and 77. which further supported the proposed structure.

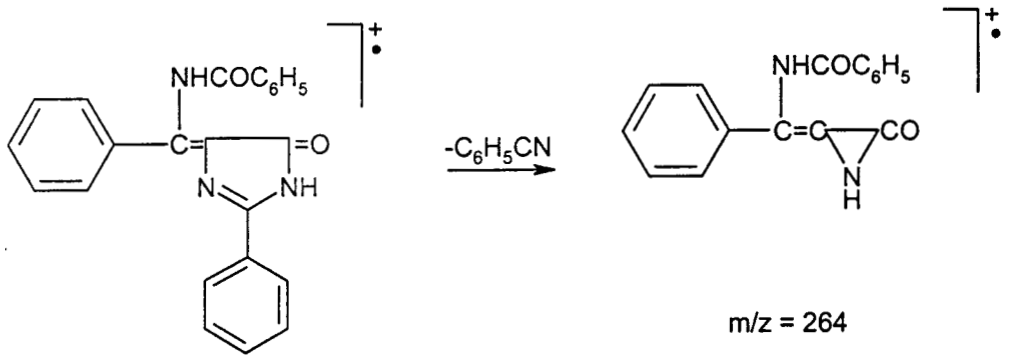
The mass peak at m/z = 339 correspond to the radical ion formed by the elimination of the neutral molecule of CO from molecular ion.



Another fragmentation pathway give rise to the peak at m/z = 290. It is due to the removal of a phenyl radical.

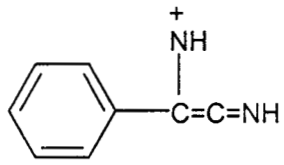


The mass peak at m/z = 264 is formed by the removal of a neutral benzonitrile molecule from the molecular ion.

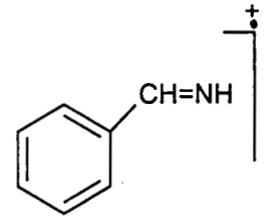


m/z = 264

The mass peak at m/z = 131and 105 are formed due to the following fragments.

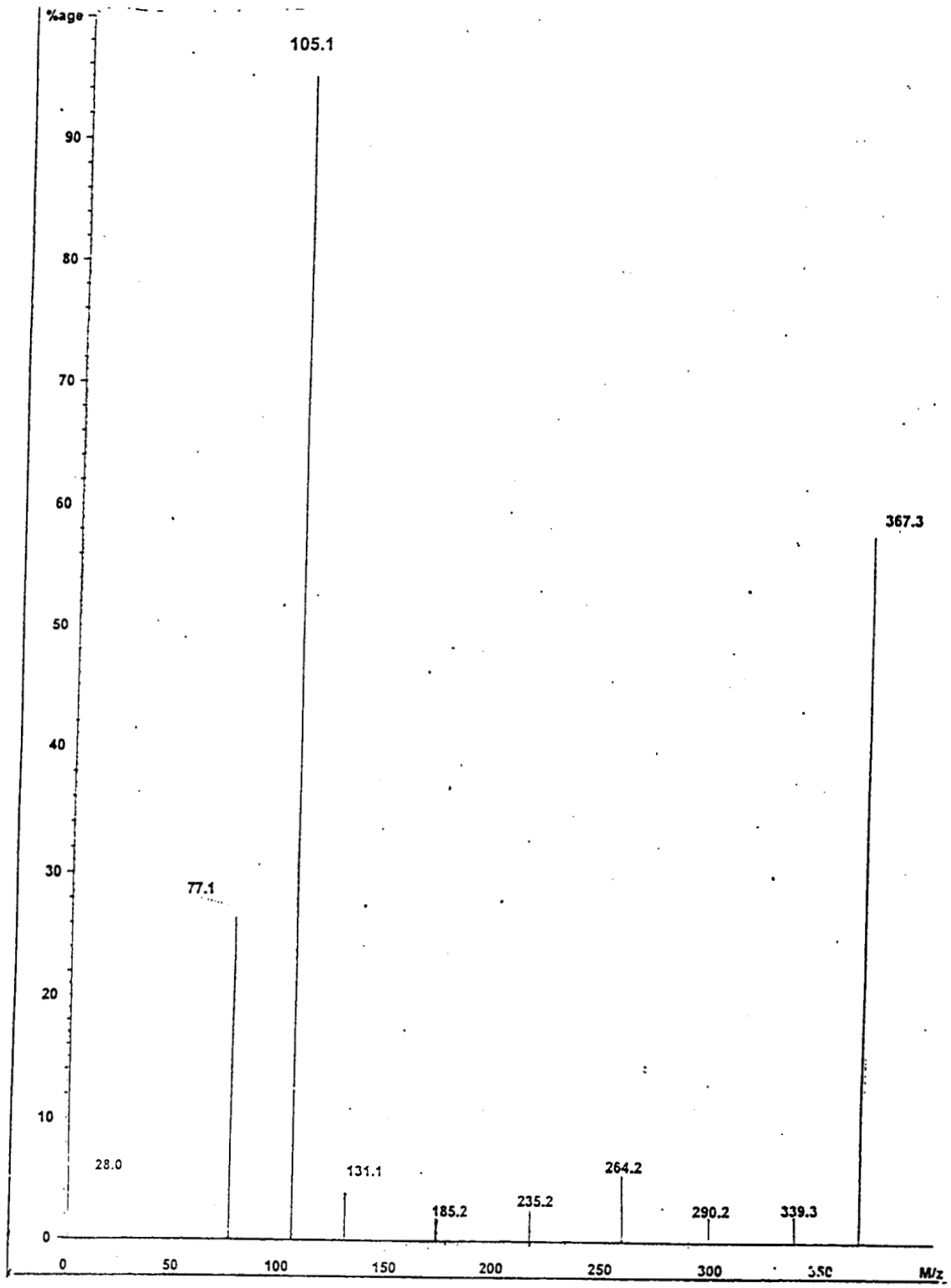


m/z = 131

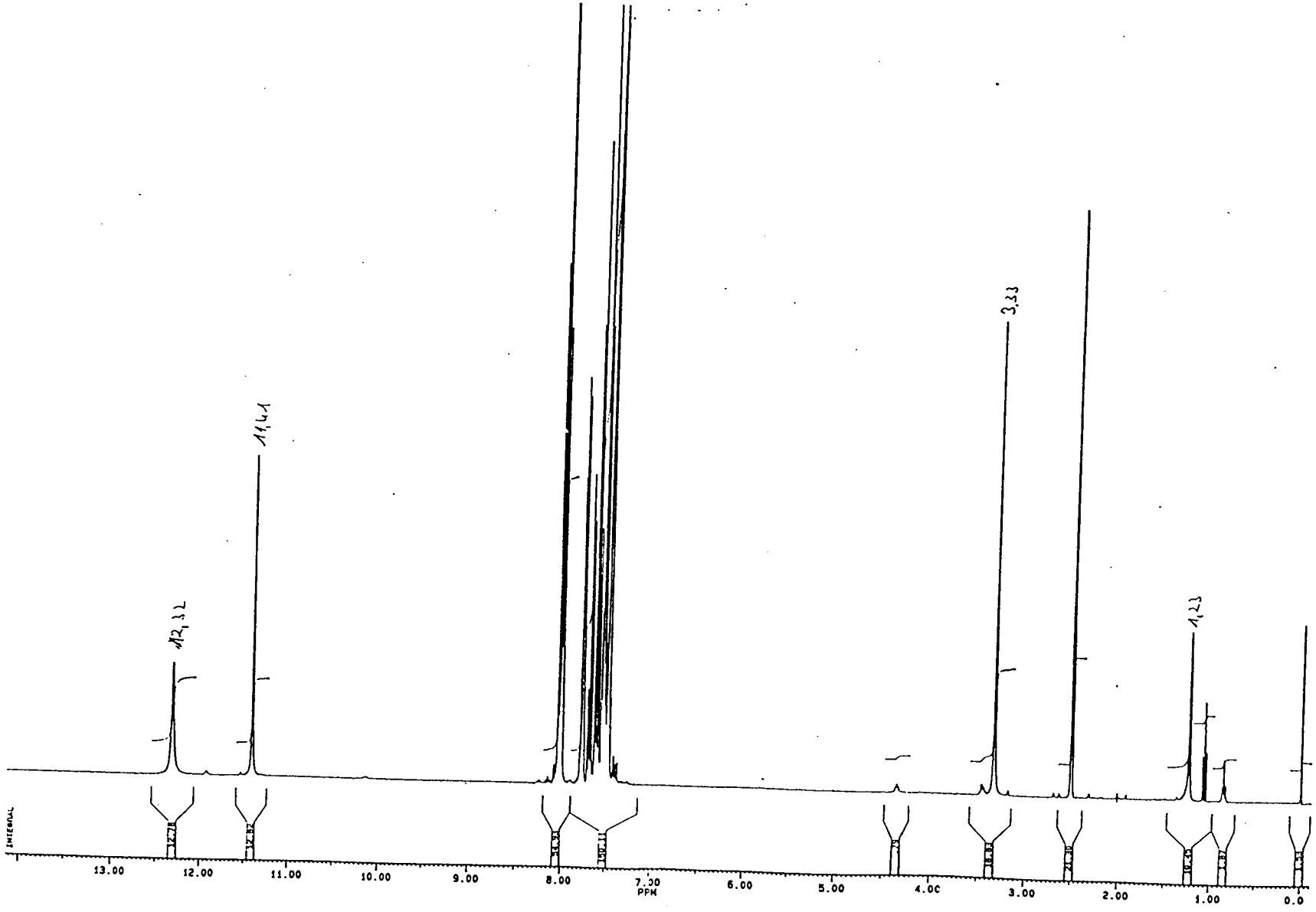


m/z = 105

The ^{1}H nmr spectrum also was in agrement with the proposed structure. The N-H proton in the heterocyclic ring absorbed at low field of δ = 11.41. The amino proton absorbed at δ = 12.32 which is a higher value than the N-H proton of the acetyl derivative. This is reasonable as the benzoyl group is more electron withdrawing than acetyl group. It also showed absorptions due to 15 aromatic protons in the region δ = 7.4 - 8 ppm.



EI-MS of 4-(Benzoylamino, phenylmethylene)-2-phenyl-2-imidazolin -5-one.

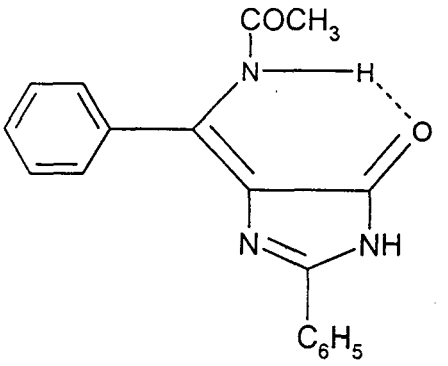


^{1}H nmr spectrum of 4-(Benzoylamino,phenylmethylene)-2-phenyl-2-imidazolin -5-one.

SPECTRAL STUDIES ON

4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one

4-(Amino, phenylmethylene)-2-phenyl-2-imidazolin-5-one on reaction with acetic anhydride in pyridine the corresponding acetyl derivative 4-(acetylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one was formed. Its mass spectrum gave M^+ peak at m/z = 305. Other important peaks, at m/z = 263, 160, 132, 105, 104 and 77 corresponds to the expected structure.



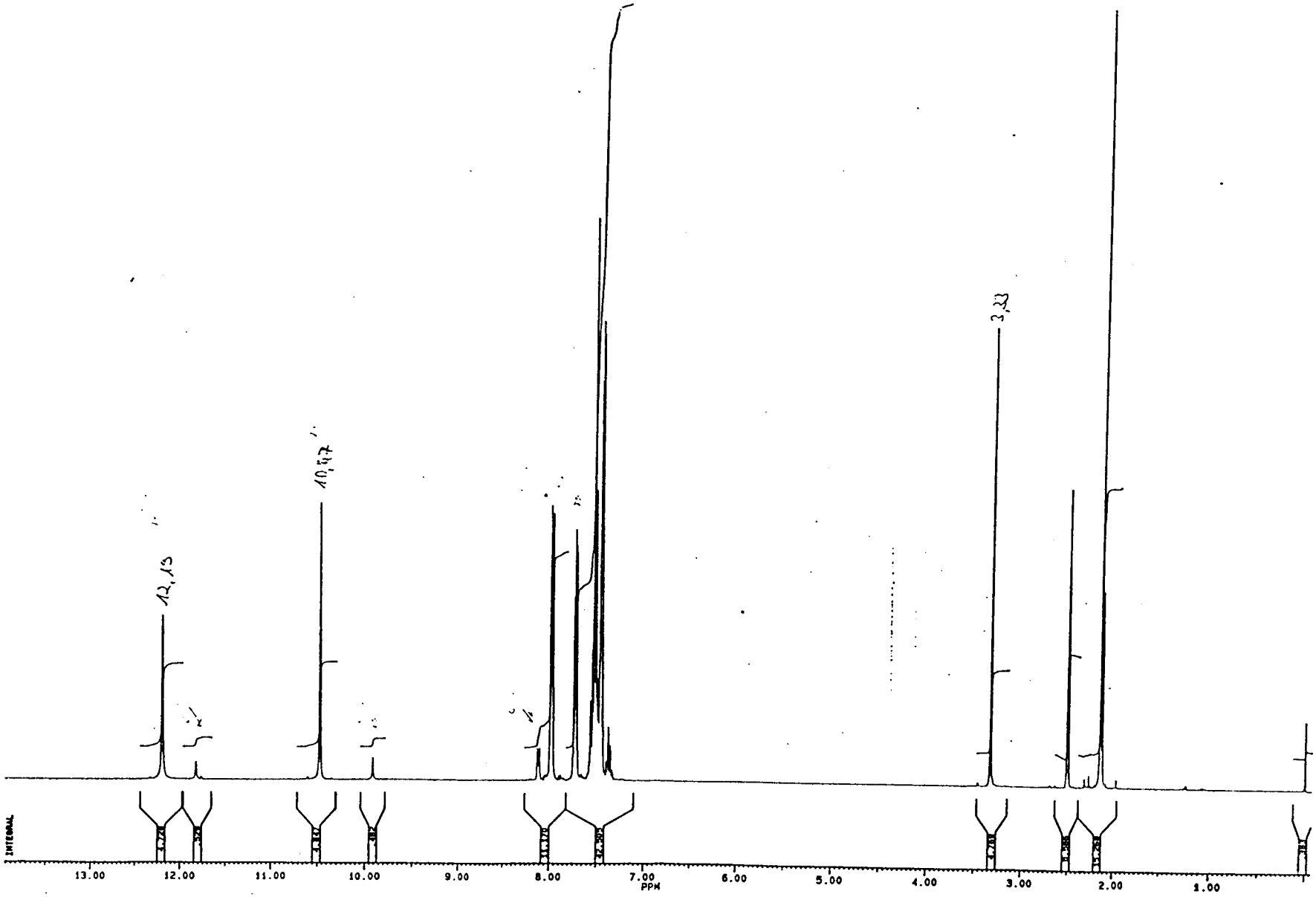
The proton nmr spectrum of this acetyl derivative showed absorptions due to ten aromatic protons in the region δ = 7.4-8. There is a three proton singlet at δ = 2.14 which corresponds to the methyl group of the acetyl moiety. The proton bonded to the ring nitrogen absorbs at δ =12.13. The proton on the amino nitrogen absorbs at δ = 10.47, since it is hydrogen bonded to the carbonyl oxygen. Two doublets at δ = 7.75 (J = 6Hz) and at δ = 8 (J = 6 Hz) correspond to the two orthophenyl protons. The remaining six protons appeared at $\delta \approx 7.5$.

The hydrogen at δ = 10.47 was confirmed to be one on the acetylated amino group as it gave cross peak with the carbon absorbing at δ =169.68 in the HMBC (Hetero nuclear multiple bond correlation) spectrum. HMBC spectrum gives cross peaks between hydrogen and C^{13} separated by two bonds and three bonds.

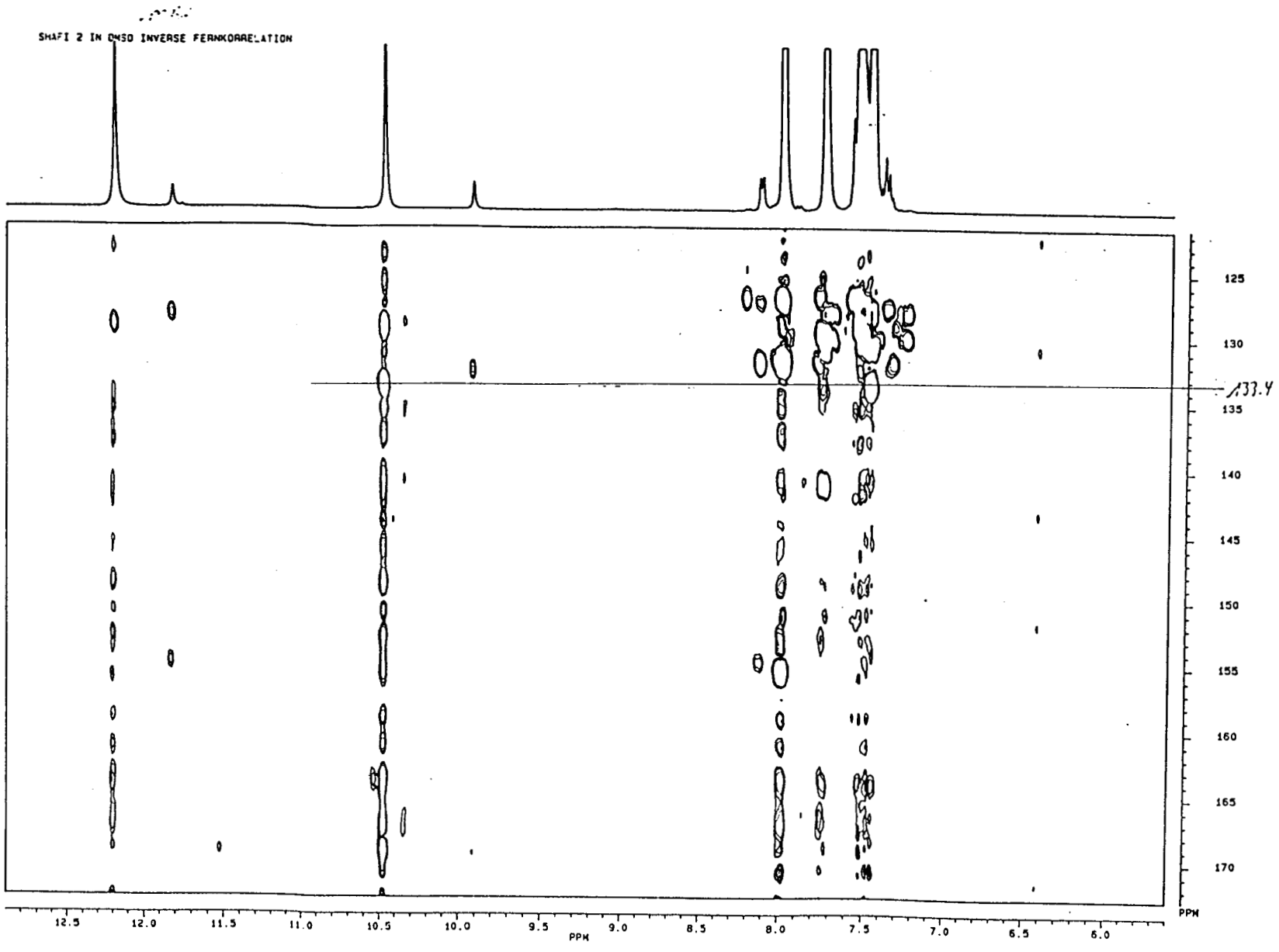
Further the ^{13}C assignments of some other carbon atoms in the molecule were also done by the help of different nmr experiments like Heteronuclear Muliple Bond Correlation (HMBC) and Heteronuclear Multiple Quantum Correlation (HMQC) experiments.

The HMQC specturm give cross peaks between the protons absorbing at δ =2.14 and the carbon at δ =24.36 which is the $-CH_3$ carbon of acetyl group.(HMQC spectrum gives cross peaks for directly bonded carbon and hydrogen). The same set of protons give cross peaks with the carbon at δ =169.68 in the HMBC spectrum. This carbon is therefore the carbonyl carbon of the acetyl group. This information confirms the identity of the other carbonyl carbon (that of the imidazolinone ring) which absorbs at δ = 171.18.

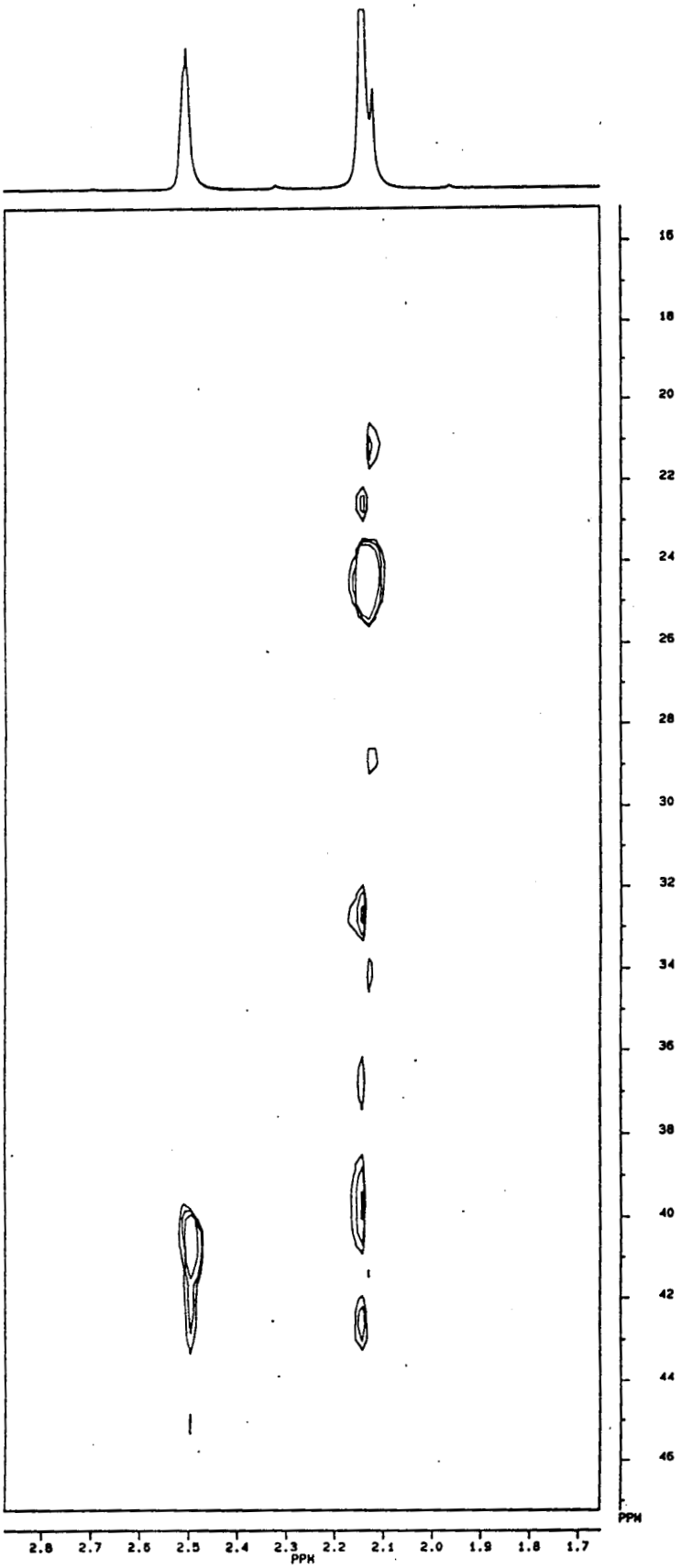
In the HMQC spectrum cross peaks were observed between the proton doublet at δ =7.75 and carbon at δ =130.7 and between proton doublet δ =8 and carbon at δ =127. These two carbons are the ortho carbons of the two phenyl rings. But sufficient data is not available to confirm to which



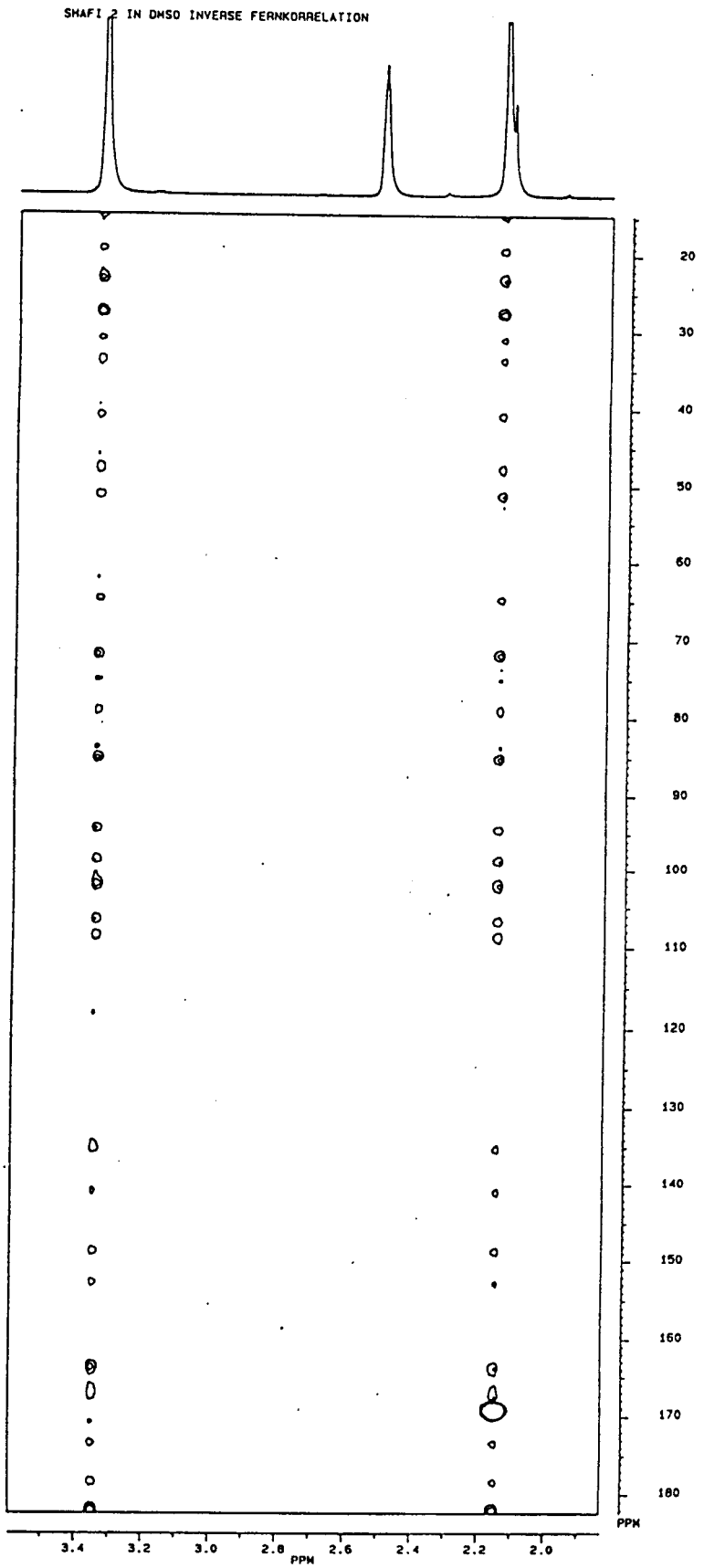
^{1}H nmr spectrum of 4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one.



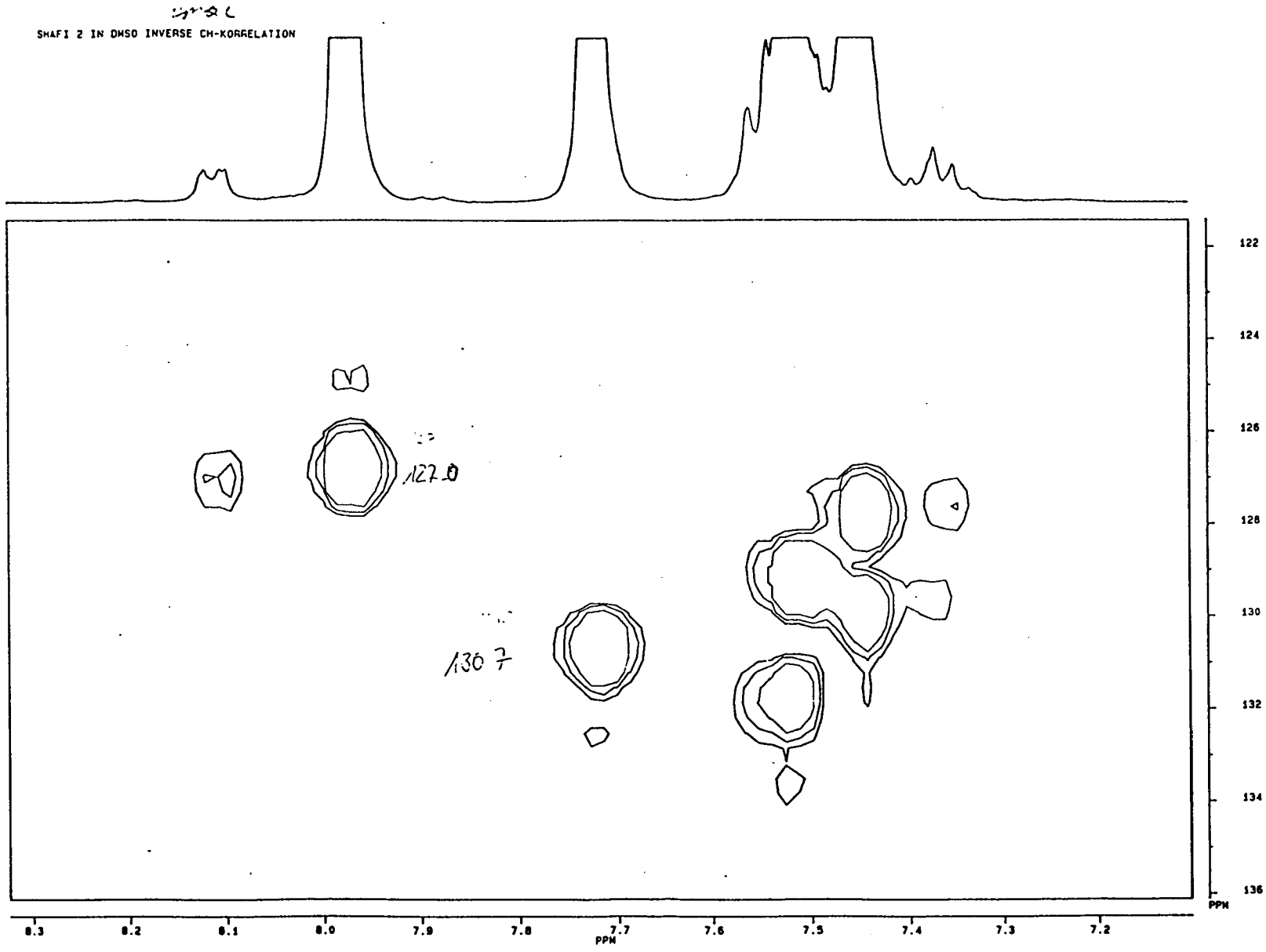
HMBC spectrum of 4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin -5-one.



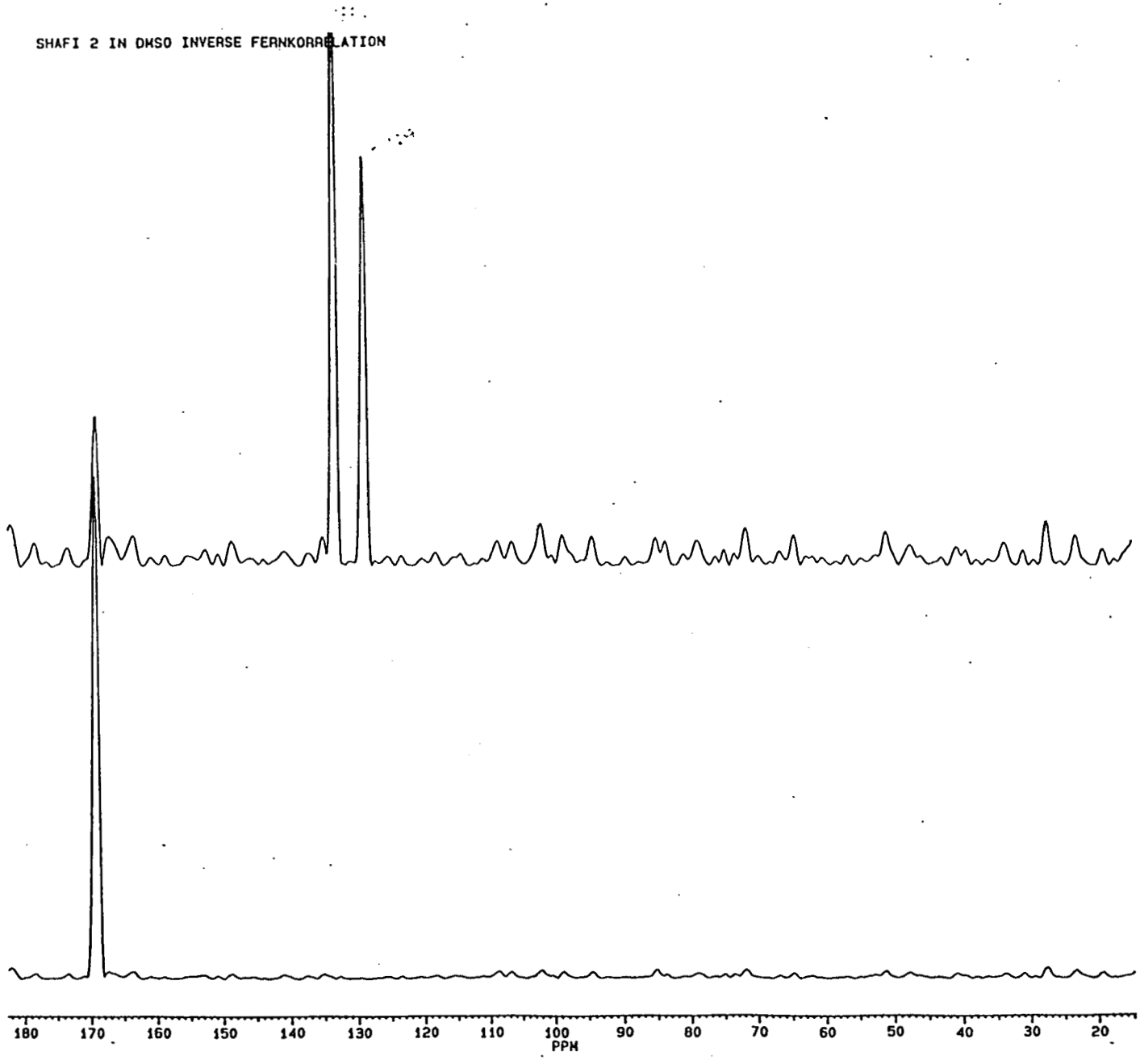
HMQC spectrum of 4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin -5-one.



.HMBC spectrum of 4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin -5-one



HMQC spectrum of 4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin -5-one-



.HMBC spectrum of 4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin -5-one.

benzene ring these carbons belong.

The HMBC spectrum shows cross peaks between amino proton and carbons absorbing at δ =129, 133.4 and 169.68. The carbon at δ =169.68 is assigned as the acetyl carbonyl. Therefore olefinic carbon to which the amino group is bonded absorbs at δ =129 or 133.4.

EXPERIMENTAL

Melting points are recorded using open capillary are uncorrected. All the ^{1}H nmr spectra were recorded on a Brucker AM 360 spectroscope. ^{13}C nmr (broad band decoupled) spectra were recorded on Bruker AC 250 spectroscope at 62.5 MHz. All the other nmr experiments were conducted using Bruker AM 360 at 360 MHz for ^{1}H and 90.5 MHz for ^{13}C (Compounds dissolved in $DMSO.d_6$). The mass spectra were recorded on Finnigan MAT 8200 spectrometer.

SYNTHESIS OF STARTING MATERIALS

Glycine ethyl ester hydrochloride, Glycine ethyl ester, benzimidic acid methyl ester hydrochloride, benzimidic acid methyl ester, Toluimidic acid ethyl ester hydrochloride, and toluimidic acid ethyl ester were prepared as described in chapter I and II.

4-(Amino, phenylmethylene)-2-phenyl-2-imidazolin-5-one

Benzimidic acid methyl ester (3.9g, 0.26 mole), glycine ethyl ester (1.5g, 0.0145 mole), anhydrous sodium acetate (3g, 0.0037 mole) and

toluene (10 mL) were taken in a 100 mL round bottomed flask, heated under reflux for 5 hours. It was kept as such for a day and filtered, washed twice with 20 mL portions of water and then with 10 mL of ether and dried in the oven at 90°C. The yellow crystals of 4-(amino, phenyl methylene)-2-phenyl-2-imidazolin-5-one weighed 2.3g (62%) and melted at 197°C.

Recrystallisation of the amino imidozolinone from ethanol gave yellow crystals melting at 201°C.

4-(Amino, p-methylphenylmethylene)-2-(p-methylphenyl)-2-imidazolin-5-one

p-Toluimidic acid methyl ester (4.73g, 0.029 mole), glycine ethyl ester (1.49g, 0.0145 mole), Sodium acetate (3g, 0.037 mole) and toluene (15 mL) were heated under reflux for 5 hours. The product formed was kept for a day, filtered, washed with water and then with ether. It was then dried at 90° for one hour. The yellow crystals of 4-(Amino, p-methylphenylmethylene)-2-(p-methylphenyl)-2-imidazolin-5-one weighed 2.7g (65%) and melts at 258°C.

Recrystallisation of unsaturated 2-imidazolin-5-one from alcohol gave yellow crystals melting at 260°C.

TH
NB4309 546 MOH/S

4-(Amino, m-methylphenylmethylene)-2-(m-methylphenyl)-2-imidazolin-5-one

m-Toluimidic acid ethyl ester (4.73g , 0.029 mole), glycine ethyl ester (1,49g, 0.0145 mole), Sodium acetate (3g, 10.037 mole)and toluene (15 mL) were taken in a 100 mL round bottomed flask, heated under reflux for 5 hours. The product formed was kept for a day, filtered, washed twice with 20 mL portions of water and then with 10 mL of ether and dried at 90°C for one hour. The yellow crystals of 4-(amino, m-methyl phenyl methylene)-2-(m-methyl phenyl)-2-imidazolin-5-one weighed 2.9g, (69%).

The unsaturated 2-imidazolin-5-one was recrystallised from ethanol. The yellow crystals melted at 257°C.

4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one

4-(Amino, phenylmethylene)-2-phenyl-2-imidazolin-5-one (2g , 0.0076 mole) was taken in a 100 mL conical flask. To this pyridine (10 mL) and acetic anhydride (2 mL 0.02 mole) were added and stirred using a magnetic stirrer for 6 hours and then poured in to ice cold water and kept in refrigerator for 4 hours. The product formed was filtered, washed with water and dried. The yellow crystals of 4-(acetyl amino, phenyl methylene)-2-phenyl-2-imidzolin-5-one weighed 1.65g (71%).

The unsaturated 2-imidzolin-5-one was recrystallised from ethanol to give yellow crystals melting at275°C.

Synthesis of 4-(Benzoylamino, arylmethylene)-2-aryl -2-imidazolin-5-one

4-(Benzoylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one

4-(Amino, phenylmethylene)-2-phenyl-2-imidazolin-5-one was (2g, 0.0076mole) dissolved in 10 ml pyridine. To this freshly distilled benzoyl chloride (1.07g (0.9 mL) 0.0076 mole) in 5 mL pyridine was added and stirred for 5 hours. It was then added to cold water, filtered, washed with cold water and dried. The yellow crystals of 4-(Benozylamino phenylmethylene)–2-phenyl-2-imidazoline-5-one weighed 2.1g(75%) and melted at 233°C.

The benzoyl derivative of the imidazolinone was recrystallised from ethanol to give yellow crystals melting at 234°C.

Analysis

N (%)

Calculated : 11.44

Found : 11.3

$C_{23}H_{17}O_2N_3$

UV – Vis. λ_{max} = 395 (nm)

4-(Benzoylamino, p-methyl phenylmethylene)-2-(p-methylphenyl)-2-imidazolin-5-one

4-(Amino, p-methylphenylmethylene)-2(p-methylphenyl)-2-imidazolin -5-one (2g, 0.0069 mole) dissolved in 10 mL pyridine. To this freshly distilled benzoylchloride (1g, 0.8 mL 0.0076 mole) in 5 mL pyridine was added and stirred for 5 hours. It was then added to cold water. The solid formed was filtered, washed with cold water and dried. The yellow crystals of 4-(Benozylamino, p-methylphenylmethylene)-2-(p-methylphenyl)-2-imidazolin-5-one weighed 1.76g (65%) and melted at 219°C.

The unsaturated imidazolinone was recrystallised from ethanol to give yellow crystals melting at 221°C.

Analysis

N (%)

Calculated : 10.6

Found : 10.45

$C_{25}H_{21}O_2N_3$

UV – Vis. λ_{max} = 388 nm

4-(Benzoylamino, m-methylphenylmethylene)-2-(m- methylphenyl)-2-imidazolin-5-one

4-(Amino, m-methylphenylmethylene)-2-(m-methylphenyl)-2-imidazolin-5-one (2g, 0.0069 mole) was dissolved in 10 mL pyridine. To this freshly distilled benzoyl chloride (1g, 0.8 mL 0.0076 mole) in 5 mL pyridine was added and stirred for 5 hours. It was then added to cold water and the solid formed was filtered, washed with cold water and dried. The yellow crystals of 4-(Benozylamino, m- methyl phenyl methylene)-2-(m-methyl phenyl)-2-imidazolin-5-one weighed 1.7g (63%) and melted at 215°C.

The yellow coloured imidazolinone was recrystallised from ethanol to give yellow crystals melting at 217°C.

Analysis

N (%)

Calculated : 10.6

Found : 10.40

$C_{25}H_{21}O_2N_3$

UV – Vis. λ_{max} = 383 (nm)

CHAPTER V

ANTIMICROBIAL ACTIVITY OF SOME IMIDAZOLINONES

Introduction

The interactions between microorganisms, plants, and animals are natural and constant. The ecological role of microorganisms and their importance in all the geochemical cycles in nature is well documented. Since the human food supply consists basically of plants and animals or products derived from them, it is understandable that our food supply can contain microorganisms in interaction with the food.

When the microorganisms involved are pathogenic their association with our food supply is critical from a public health point of view. Many of our foods will support the growth of pathogenic microorganism or at least serve as a vector of them.

Microorganisms, the forms of life so small that can be seen only with a high power microscope, also influence human life in many ways. These minute things are present almost every where, in the air, in the soil and in the water and on the surfaces of all kinds of plants and animals and occasionally in the tissues of their bodies. They are a heterogeneous group of several classes of living things. They were originally classified under

the plant and animal kingdoms. As this proved unsatisfactory, a third kingdom known as protista was assigned for them. Based on the difference in cellular organisation and biochemistry the kingdom protista has been divided into two groups, prokaryotes and eukaryotes. Fungi, algae, and protozoa are microorganisms with eukaryotic cells. The cells of these organisms are structurally similar to those of plants and animals which are multicellular organisms with eukaryotic cells and differentiated tissues. Bacteria and blue-green algae are prokaryotes.

As a group fungi are microorganisms that obtain their nutrition from organic compounds. Their cells are usually surrounded by protectine cell walls composed of chitin or other polysaccharides. They produce spores which are specialized cells involved in reproduction, dissemination and survival. Some fungi called yeasts are unicellular. Other fungi called molds or filamentous fungi form multicellular filaments called hyphae. 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. They can be observed growing fuzzy mats on rotting bread, fruits and vegetables and various other plant materials. The simplest type of fungus is the unicellular yeast. Fungi which form mycelia are called moulds. Depending on the cell morphology, fungi can be divided

into four classes yeast, yeast like fungi, moulds and dimorphic fungi. The only pathogenic yeast is cryptococcus neoformans. Fungi had been recognised as causative agents of human disease earlier than bacteria. Fungal infections are extremely common and some of them are serious and even fatal.

Protozoa are unicellular, nonphotosynthetic eukaryotic micro organisms. Various groups of protozoa exhibit differing strategies of locomotion. Some such as Amoeba can change their cell shape, extending the cell so that it migrates along whereas others such as paramecium are propelled by numerous beating structures called cilia.

Viruses which traditionally are considered microorganisms, lack the fundamental structure of living organisms. 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.

Control of microbial growth

Control of microbial growth equals with preventing microbial reproduction. This is accomplished by killing microorganisms or creating conditions under which they cannot grow. Exposure to high temperatures, ionizing radiation, and various chemicals are routinely employed to kill microorganisms. Low temperatures, high solute concentrations and

desiccation are employed to prevent microbial growth. Killing and limiting growth of microorganisms is especially important in preserving and maintaining the safety of foods. It is also key to modern medical practice and the use of antimicrobics to treat infectious diseases. Antimicrobial agents that exhibit toxicities to microorganisms have greatly reduced death rates from such diseases.

The process of killing, inactivating or removing pathogenic micro organisms from an environment is called disinfection. An agent that is used to carryout disinfection is called disinfectant. Most disinfectants are chemicals. They are generally too harsh to be applied to body tissues and are strictly applied to inanimate objects. Although disinfectants can remove pathogens from an environment, they may have no effect on spores and viruses. Chemicals that control microorganisms on body tissues are called antiseptics.

Chemical control of microorganisms

It is well known that the majority of the spices used in food seasoning have a broad spectrum of antimicrobial activity and are potential inhibitors of lipid auto oxidation. Thus spices considerably enhances the keeping quality of processed food stuffs, apart from imparting their characteristic aroma flavour and colour.

Many chemicals kills or prevent growth of microorganisms. Such

chemicals have been called antimicrobial agents. Concentrations and contact time are critical factors that determine the effectiveness of an antimicrobial agent against a particular microorganism. Microorganisms vary in their sensitivity to particular antimicrobial agents. Many antimicrobial agents block active metabolism and prevent the organism from generating the macro molecular constituents needed for reproduction. Because resting stages are metabolically dormant and are not reproducing, they are not affected by such antimicrobial agents. Similarly viruses are more resistant than other microorganisms to antimicrobial agents because they are metabolically dormant outside host cells.

Antimicrobial agents are classified according to their application and spectrum of action. Agents that kill microorganisms are given the suffix-cide (Latin caedere, meaning to kill). Germicides are antimicrobial agents that kill microorganisms but not necessarily bacterial endospores. Such chemicals may exhibit selective toxicity and depending as their spectrum of action, may act as viricides (killing viruses), bactericides (killing bacteria), algicides (killing algae) or fungicides (killing fungi).

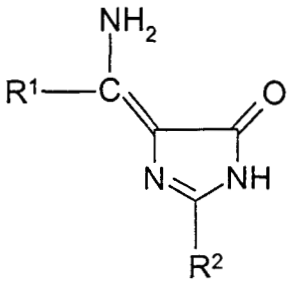
A major break through in the development of an antimicrobial drugs occured in 1929 when the scotish bacteriologist Alexander Fleming reported on the antibacterial action of cultures of a Penicillium species. His publication on the active ingradient which he called penicillin was the first report of the

production of an antibiotic. Narrow spectrum antibiotics are targeted at particular pathogens or particular bacterial species. Broad spectrum antibiotics inhibit a relatively wide range of bacterial species.

Result and discussion

The experimental result revealed that most of the compounds under study showed antibacterial activity. The compounds showed strong activities (10-50 mm zone of inhibition) against *E. coli*. Under identical conditions the compounds showed only moderate activity (10-21 mm zone of inhibition) against *salmonella typhimurium*. Th antibiotic chloramphenicol showed a zone of inhibition of 24mm & 28 mm against *E.coli. and salmonella typhimurium* respectively at a concentration of 30 microgram. Inhibition zones greater than 18 mm are considered as sensitive. The low activity of the imidazolinones against *salmonella* at low concentration (100 ppm) can be increased by increasing the concentration. The amino imidazolinones [1,4 and 5in table V.1] showed the highest activity against *E. coli* probably due to the presence of an amino group. The sharp decrease in the activity of its acetylated and benzoylated derivatives justified it. The spiro imidazolinones also showed moderate activity against *E.coli*.

Preliminary studies revealed that most of these imidazolinones are active towards the two bacterial strains. In this context a lead molecule of the following structure is worth for further studies.



Introduction of different groups in place of R^1 and R^2 may lead to more active derivatives. Hence a detailed study in this regard will be fruitful and interesting. The mechanism involving the inhibition will also require detailed investigation.

EXPERIMENTAL

Materials and Methods

Bacterial Strains

Human pathogens such as *Escherichia coli* and *Salmonella typhimurium* were collected from the Department of Aquaculture and Fishery Microbiology, M.E.S. Ponnani College, Ponnani. Cultures were serotyped at National Salmonella and Escherichia centre, Kasauli, Himachal Predesh. Cultures were maintained on nutrient agar slants. The other materials like peptone and agar were of bacteriological grade. Acetone was used as solvent for preparing solutions of imidazolinones. The other chemicals sodium chloride and D-glucose were of Analar grade.

The antibacterial activity of compounds under study against the two selected bacterial strains were done using the cup-plate method[135-139] The medium used for testing antibacterial activity was Nutrient agar containing.

Peptone	= 5g	D- glucose	= 4g
NaCl	= 5g	Beef extract	= 1.5g
Yeast extract	= 1.5g	Agar	= 15g
Distilled water	=1000mL		

P^H was adjusted to 7.4 ± 0.2

The medium after autoclaving at 15 lb pressure for 15 minutes was poured in to Petri dishes (9cm). The media (25 mL.) was poured into each Petri plates and allowed to cool.

Preparation of inoculam

Escherichia coli and *salmonella typhimurium* were enriched in nutrient broth for 16-18 hours and these young cultures were used as inoculum.

Preparation of Chemical extracts

The imidazolinones under study were dissolved in acetone and 100 microliters of 100 ppm concentration solution were used to check the antibacterial activity.

Detection of antibacterial activity

The Petri plates were streaked with two bacterial strains; *Escherichia*

coli and *Salmonella typhimurium*. For this each bacterial strain grown on nutrient agar slants were used.

To prepare a mat growth of bacteria on the Petridishes, young cultures of *Escherichia coli* and *Salmonella typhimurium* were swabbed over sterile nutrient agar plates using sterile cotton swabs. Using a sterile cork boarer, wells (10 mm) were made on these plates. In each well 100 μL (100 ppm) of the compounds in acetone were added. Each plate was having a well for the control; the solvent acetone. The wells were properly labelled and the plates were prepared in triplicate and incubated at 37°C for 24 hours. The antibacterial activity was detected by measuring the diameter of the inhibitory zone around each well. The diameters of inhibition zones were measured and recorded.

Detection of anti-fungal activity

The imidazolinones were screened for their anti-fungal activity at different concentrations using cup-plate method. The fungus used was *Aspergillus niger*. No compound showed activity against the fungus showing that the compounds under study are not anti-fungal.

Table V.I
Antibacterial activity of imidazolinones

Sl No.	Name of the Compound	Diameter of inhibition zone in (mm)	
		Escherichia coli	Salmonella typhimurium
1	4-(Amino, phenylmethylene) -2-phenyl-2-imidazolin-5-one	50	20
2	4-(Acetylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one	32	11
3	4-(Benzoylamino, phenylmethylene)-2-phenyl-2-imidazolin-5-one	30	16
4	4-(Amino, p-methylphenylmethylene)-2-(p-methylphenyl)-2-imidazolin-5-one	47	21
5	4-(Amino, m-methylphenylmethylene)-2-(m-methylphenyl)-2-imidazolin-5-one	48	20
6	3,6,10-Triphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione	36	10
7	3-(p-tolyl)-6,10-diphenyl-2,4-diazaspiro [4.5] deca-2-en-5,8-dione	38	12
8	3-(m-tolyl)-6,10-di(p-chlorophenyl)-2,4-diazaspiro[4.5]deca-2-en-5,8-dione	35	10
9	1-(carbethoxymethyl)-4-(p-chloro benzylidene)-2-phenyl-2-imidazolin-5-one.	16	14
10	1-(carbethoxymethyl)-4-(p-methoxy benzylidene)-2-phenyl-2-imidazolin-5-one	28	10
11	Chloramphenicol (Standard)	24	28

CHAPTER VI

PHOTOCHEMISTRY OF IMIDAZOLINONES

Introduction and Scope

In the last 50 years photochemistry has seen a tremendous upsurage of interest and activity. In recent years the growth of photochemistry has been stimulated anew by the keen interest of not only the physical chemists but also the physical organic, organic and inorganic chemists, molecular spectroscopists, kineticists and photobiologists.

Rapidly increasing number of investigations since 1960 have shown that many novel and synthetically useful reactions including oxidation, reduction, dimerisation, cycloaddition, rearrangement substitution and elimination may be consequent upon the absorption of light by organic molecules. Many chemical transformations can be effected photochemically which would otherwise require a large number of steps by standard chemical procedures. Now a days the study of organic photochemical reactions has become an inevitable tool for the understanding of a number of biological transformations. Heterocyclic ring systems which are the constituents of almost all of the biological systems, play an important role in the interaction of light with biological materials.

The study of photochemistry deals with a unique type of chemical reaction. It is concerned with the "bimolecular" interaction of light quantum and a molecule and subsequent chemical and physical changes which result from the interactions. Light is always one of the reactants in photochemical reactions.

The current interest in organic photochemistry is reflected in the increase in the number of publications[140-143] concerned with the photochemistry of heterocyclic systems. Photo-oxidation of heterocyclic compounds is important in a number of photobiological and photomedical phenomena.[144] Photo oxygenation reactions of nitrogen heterocyclics have been the subject of recent review[145].

Many heterocyclics including drugs are responsible for phototoxic or photo allergic behaviour due to photo oxidation[146]. Formation of heterocyclics both by photo addition and photo cyclisation has become a preferable method for their synthesis in a number of cases[147].

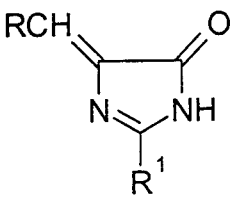
The relevance of photochemistry also lies in its varied applications in science and technology. Synthetic organic photochemistry has provided methods for the manufacture of many chemicals which could not be produced by dark reactions. Some industrially viable photo chemical syntheses are the synthesis of vitamin D_2 from ergosterol isolated from certain yeasts, synthesis of

cubanes which are antiviral agents, industrial synthesis of caprolactam the monomer of Nylon-6, and synthesis of antioxidants by photo sulphonation. Photo initiated polymerisation is used in photography, lithoprinting and manufacture of printed circuits for the electronic industry. The destructive effects of sunlight on coloured cotton fabrics is of everyday experience, the worst sufferer being window curtains. The light absorbed by dyes used for colouring fabrics initiates oxidative chain reaction to cellulose fibres. This causes the tendering of cotton. The photo physical phenomenon of fluorescence and phosphorescence have found varied applications in fluorescent tube lights, X-ray and T.V screens as lummescent dials, as optical brightners in white dress materials, as paints in advertisement boardings which show enhanced brilliance by utilizing fluorescence.

Photo oxidation reactions play a significant role in the chemistry and biology of a number of naturally occuring system containing the imidazole[148] ring.

The photo reactions of substituted imidazoles are also important in the study of chemiluminescence[149]. Great interest has centered on the involvement of 2,4,5-triphenyl imdazole (lophine) and similar compounds in the phenomenon of chemiluminescence[150].

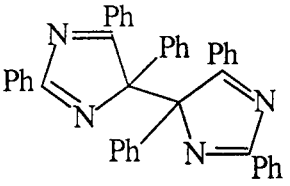
The work presented in this thesis deals with the photochemical reactions of some 2,4-disubstitued imidazolin-5-ones of the type.



As a back ground to these investigations a survey of the literature of photochemical reactions of imdazoles is presented below.

Photochemistry of imdazoles - A Review

In 1877 Radziszewski[151] observed the emission of light when 2,4,5- triphenyl imidazole (lophine) was decomposed with alcoholic potash in presence of light. In presence of potassium ferricyanide lophine give rise to a piezochromic dimer (1) which gives an intensely violet solution of the radical (2) in organic solvents. Other dimeric species (3), (4) have also been reported[152-155].



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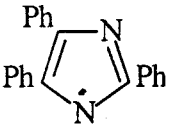

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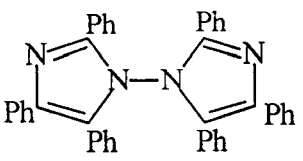

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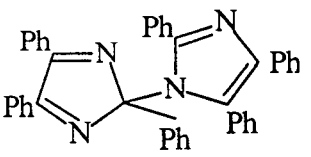
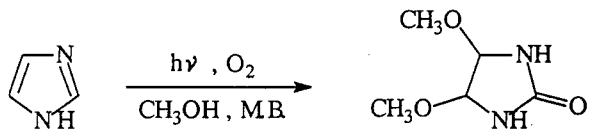


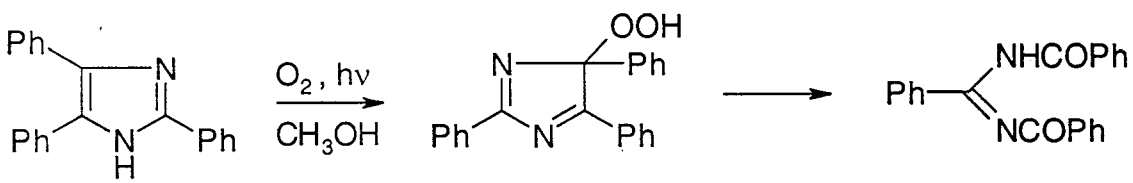
4

In 1953 Weil, James Buchert[156] noticed the loss of biological activity during photolysis of the enzyme Ribonuclease is due to the disappearence of histidine residues and accordingly with the oxidative destruction of the imidazole fragment. The oxidative degradation was also found to be responsible for the loss of biological activity of insulin on photolysis[157].

Wasserman[158-163] and coworkers observed that irradiation of imidazole with UV-visible light in methanol in presence of methylene blue as sensitizer results in the formation of dimethoxy hydantoin.



In a study of photsensitized oxygenation of imidazoles Wasserman[158] found that 2,4,5-triphenyl imidazole reacts with singlet oxygen to yield an N,N[1]-diaroyl benzamidine probably through hydroperoxide.



They also found that 4,5-diphenylimidazole on photooxygenation under similar conditions yields 5-methoxy-4,5-diphenylimidazolin -2-one and 4,5-dimethoxy-4,5-diphenylimidazolidin-2-one.

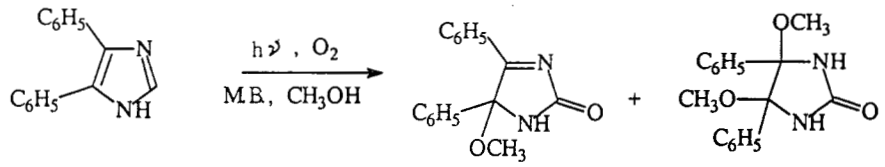
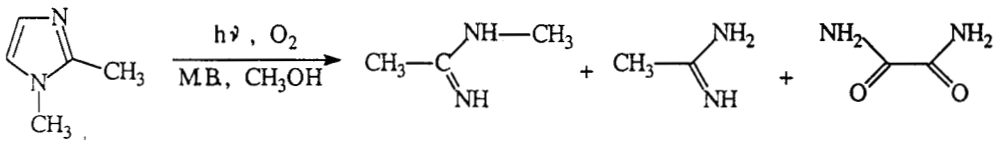
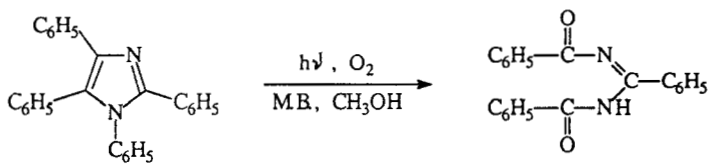


Photo-oxidation of alkyl imidazoles under similar conditions gave degraded products like acetamidines and oxamide.[164]

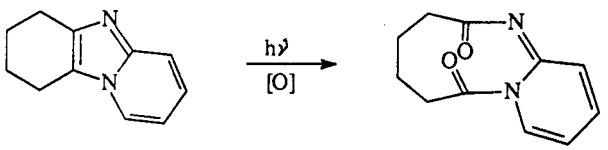


Wasserman and coworkers[158-160] reported the formation of N-phenyl N,N[1]-dibenzoyl benzamidine by the photooxygenation of tetraphenyl imidazole.

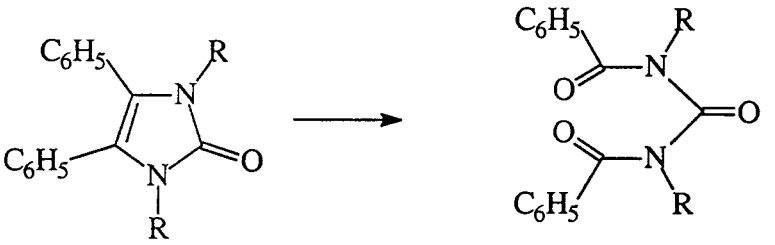


2,5 substitued imidazoles undergo cleavage at the enamine double bond yielding products similar to that of dioxetane intermediates. The

photooxidation of fused ring imidazole gave corresponding diamide in good yield[165]

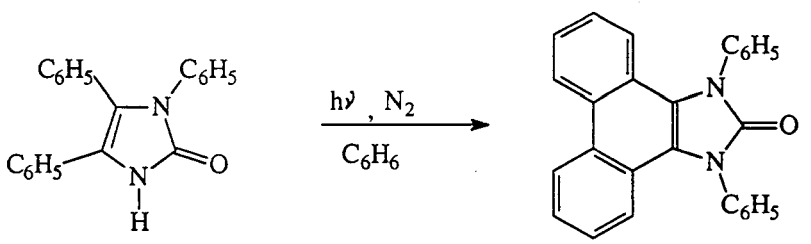


The photosensitized reactions of imidazolones and imidazoline derivatives are less available.[166-167] Phenyl substituted imidazolones were found to undergo thermal singlet oxygenation to give N,N^1-diacyl ureas.[162]

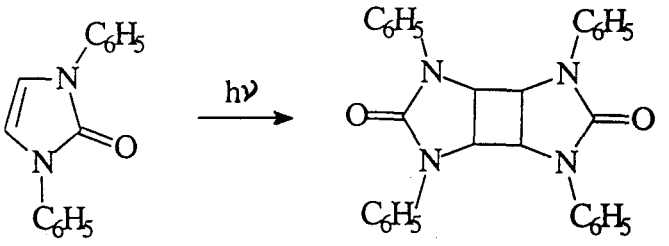


a: R = CH_3
b: R = C_6H_5

Irradiation 1,3,4,5-tetraphenyl imidazolin-2-one in benzene under nitrogen atmosphere gave N-substituted phenanthrimidazolone.[166]

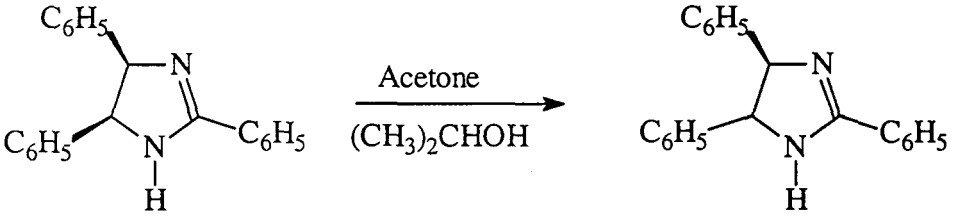


1,3 diphenyl imidazolin-2-one undergoes photodimerisation giving cyclobutane system.

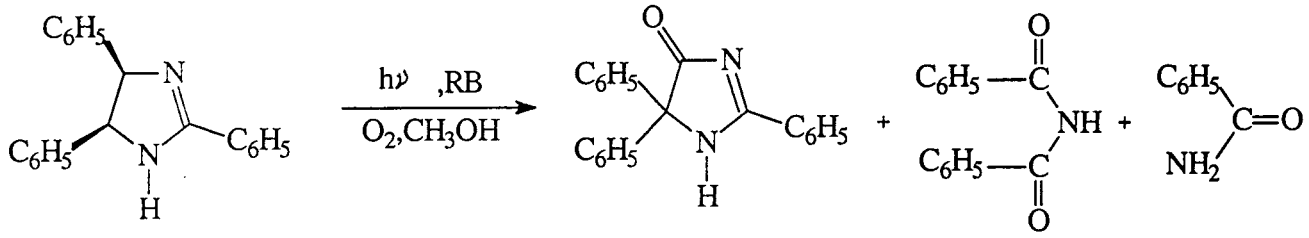


Synthesis of (±) biotin is based on photochemical cycloadditon[168] reaction of 1,3 diacetyl-imidazolin-2-one.

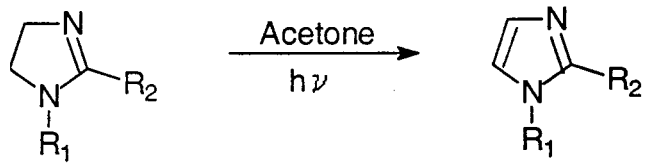
Imidazolines were found to undergo photosensitized cis-trans isomerisation between amarine and isoamarine[169].



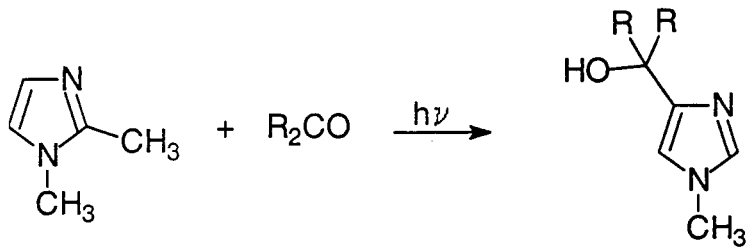
The rose bengal sensitized photo-oxygenation of cis-2,4,5-triphenyl imidazoline has been found to give a mixture of products[170]. The products are 2,5,5-triphenyl imidazolin-4-one, dibenzamide and benzamide.



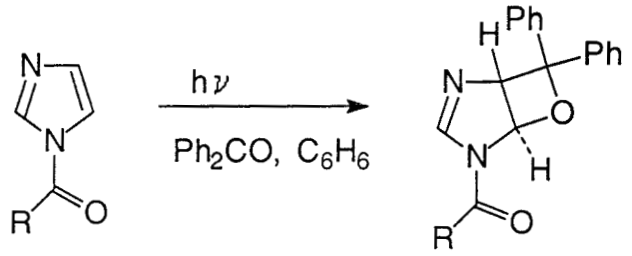
1,2-disubstituted imidazoline in presence of acetone or benzophenone undergoes photodehydrogenation to form imidazole.[171]



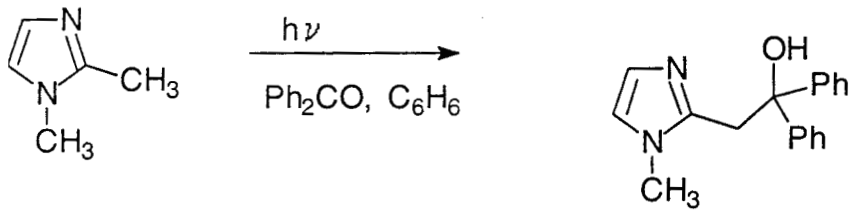
The photoaddition of acetone to 1,2-dimethyl imidazole gives α-hydroxy alkyl imidazoles[172] which results from selective attack of excited carbonyl oxygen at C-5.

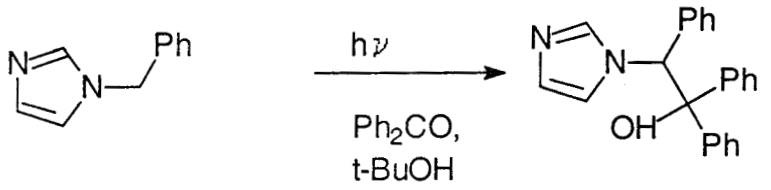


Benzophenone forms oxetanes across the 4,5 bond in its photo-addtion[173] to 1-acyl imidazoles.

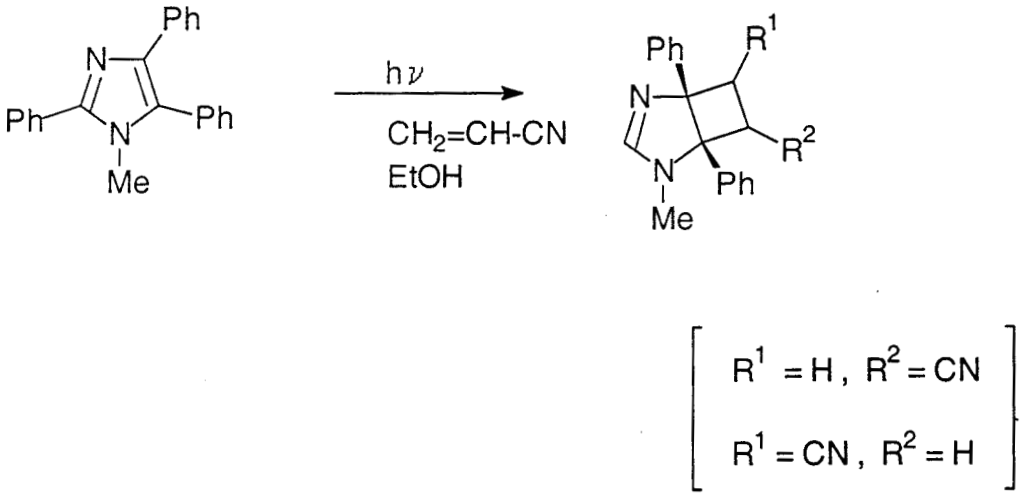


1,2-dimethyl imidazole adds benzophenone at the 2-methyl group but with 1-benzylimidazole, the methylene group is also involved.[173]

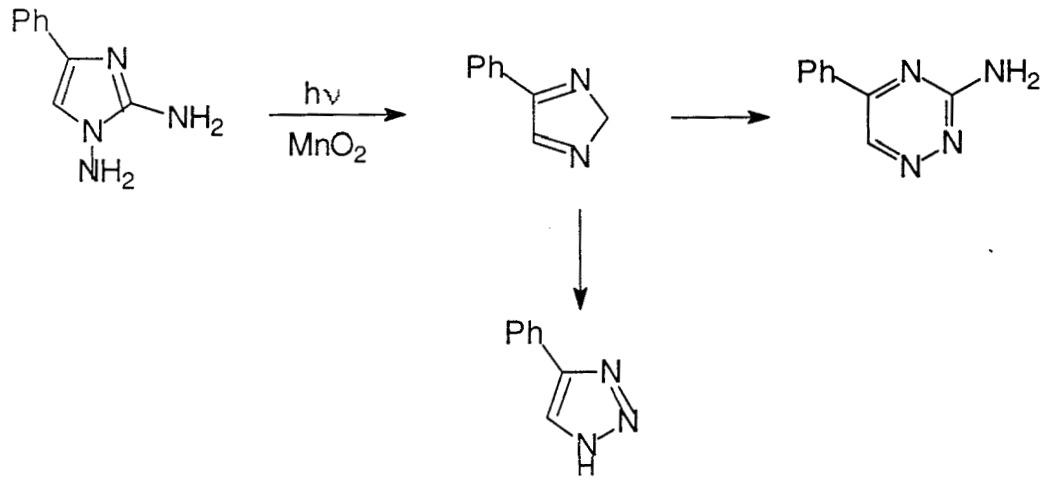




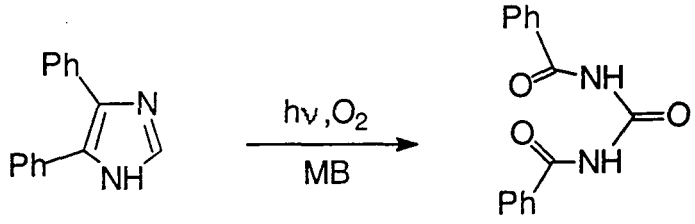
Photoaddition of 1-methyl-2,4,5-triphenylimidazole with acrylonitrile forms an addition product across 4,5 bond. [168-170]



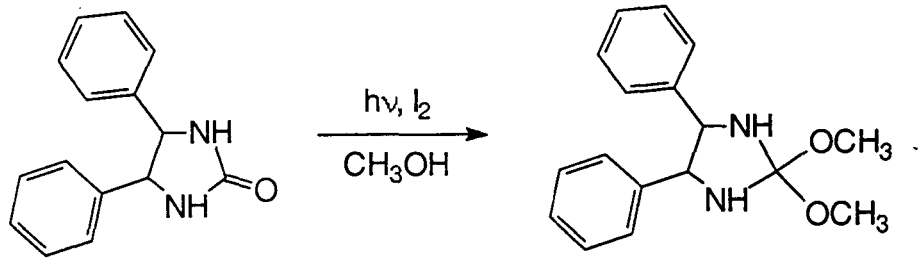
Imidazole 3-oxides when photolyzed gives unsymmetrical benzil diimines. Photooxidation of diaminoimidazole gives a mixture of triazine and triazole.[172-173]



4,5-diaryl imidazoles undergo singlet oxygenation[174] and cleavage to give N,N[1] diaroyl ureas. On irradiation with alcoholic solution in presence of methylene blue as sensitizer.

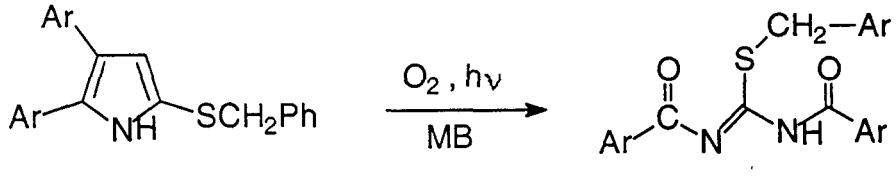


1,3-dihydro-4,5- diphenyl -2H-imidazole-2-one undergo[175] conversion to 2,2-dialkoxy-4,5-diaryl-2H-imidazolines by a charecteristic solvent interaction of the carbonyl group on irradiation in alcoholic solvents.



UV induced trifluoromethylation[176] of 1-methyl-2-(methylthio) imidazole using CF_3I give 1.5% 1-methyl-2-methylthio -4-(trifluoromethyl) imidazole and 25% 1-methyl -2-(methylthio) -5-(trifluoromethyl) imidazole.

Photolysis[177] of imidazole (R=Ph,ClC_6H_4, $CH_3C_6H_4$) in ethanol in presence of methylene blue and oxygen give photo oxidation product N,N^1-dibenzoyl-S-benzyl isothio ureas in 35-65% yeild.



4,5-Diaryl imidazolin-2-thiones have been converted to bis-(4,5-diarylimidazol-2-yl) sulphides by photolysis in ethanolic solution[178].

PRESENT WORK

Photoirradiation of 4-Cyclohexylidene-2-(p-methylphenyl)-2-imidazolin-5-one

A solution of 4-Cyclohexylidene-2-(p-methylphenyl)-2-imidazolin -5-one (1.25g) in benzene (300 mL) was irradiated with 125 W Philips mercury quartz lamp in a water cooled photochemical reactor of 500 mL capacity. The lamp was surrounded by a jacket containing the solution to be irradiated. The reaction was monitered by TLC. On completion of the reaction (34 hours) the brown coloured product formed at the sides of the reactor was removed, washed with benzene and dried. The melting point was 144-48°C. TLC of this product showed a number of spots and it was subjected to column chromatography using benzene-ethylacetate mixture. The silica gel used was BDH sample

(60 - 120 mesh). But the compound was not obtained in the pure form even after repeated chromatography.

The solvent in the photochemical reactor was distilled out. The concentrated solution showed a number of spots in the TLC and therefore subjected to column chromatography. But any single compound in the pure form could not be separated. So spectral study was not done and thereby the structure elucidation of photoirradiated product was not possible.

The photoirradiation was repeated using 4-Cyclohexylidene-2-(m-methylphenyl)-2-imidazolin-5-one and 4-Cyclohexylidene-2-phenyl -2-imidazolin-5-one. In these cases also the result was same and could not separate any single compound in pure form.

4-Cyclohexylidene-2-aryl-2-imidazolin-5-one was prepared[41] by refluxing benzimidic ester, glycine ester and cyclohexanone for 5 hours.

Photoirradiation of 4-Benzylidene-2-phenyl-2-imidazolin-5-one

A solution of 4-Benzylidene-2-phenyl-2-imidazolin-5-one (100 mg) in benzene (300 mL) was irradiated with 125 W philips mercury quartz lamp in a water cooled photochemical reactor of 500 mL capacity. The lamp was surrounded by a jacket containing the solution to

be irradiated. But even after irradiation of 50 hours the TLC examination of the reaction mixture showed that no reaction had taken place. The experiment was further repeated in isopropanol as the solvent. After irradiation of 50 hours no change in the reaction mixture was noted by TLC examination.

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