2-Imidazolines in Annulation Studies

A thesis submitted for the degree of

Doctor of Philosophy in Chemistry

To

The Open University

Milton Keynes

Paschalis A. Dimopoulos

December 1999

DATE OF SUBMISSION: 2 DECEMBER 1999
DATE OF AWARD: 8 MARCH 2000

Department of Chemistry
The Open University
Walton Hall
Milton Keynes
MK7 6AA
UNITED KINGDOM
Declaration

I declare that the work presented in this thesis is the result of my own investigations, and where the work of others is cited, it is fully acknowledged. The material embodied in the thesis has not been submitted, nor is currently submitted for any other degree.

Paschalis A. Dimopoulos

Prof. R.C.F. Jones
Supervisor
Acknowledgements

I am eternally grateful to my parents and my brother who have supported me both emotionally and financially throughout all of my years of studies. I would like to thank my supervisor, Professor Ray Jones, for his help, guidance and encouragement throughout my Ph.D. studies. I would also like to thank Pravin Patel for his help and for driving me to the University, and the rest of the Chemistry department technical staff for their help.
Abstract

This thesis will describe attempts to use suitably substituted 2-imidazolines in Diels-Alder reactions. In order to synthesise these target 2-imidazolines a new and reliable method for the synthesis of 2-alkyl and 2-alkenyl-2-imidazolines has been developed. Metallation at C(2α) of 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline, followed by reaction with a range of electrophiles and deprotection with TFA reliably afforded N(1)- unsubstituted 2-substituted 2-imidazolines; P- or Se-electrophiles led to 2-alkenyl-2-imidazolines via Wadsworth-Emmons reaction or selenoxide elimination.

In an attempt to prepare N-butadienyl-2-imidazolines via the reaction of 2-alkyl-2-imidazolines and α,β-unsaturated aldehydes or ketones, tetrahydroimidazo[1,2-a]pyridines have been synthesised via conjugate addition of the heterocycle N(1) nitrogen atom followed by enamine–aldol condensation at C(2α).

2-Imidazolines reacted with β-ketoesters to give tetrahydroimidazo[1,2-a]pyridin-5-ones. It has also been shown that 2-imidazolines undergo conjugate additions with other unsaturated compounds with electron withdrawing groups.

Whilst examining the reactions of 2-alkyl-2-imidazolines with alkyne diesters, a new annulation was uncovered that is based on N(1) conjugate addition followed by C(2α)-acylation. The reaction of 2-imidazolines with dialkyl acetylenedicarboxylate afforded tetrahydropyrrolo[1,2-α]imidazole-5,6-diones.

None of the 2-imidazolines synthesised that contained diene functionalities underwent either intra or intermolecular Diels-Alder reactions.
## Abbreviations used in the Thesis

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIBN</td>
<td>$\alpha,\alpha'$-Azoisobutyronitrile</td>
</tr>
<tr>
<td>$n$-BuLi</td>
<td>$n$-Butyllithium</td>
</tr>
<tr>
<td>sec-BuLi</td>
<td>sec-Butyllithium</td>
</tr>
<tr>
<td>Boc</td>
<td>tert-Butoxycarbonyl</td>
</tr>
<tr>
<td>Bn</td>
<td>Benzyl</td>
</tr>
<tr>
<td>Cbz</td>
<td>Benzyloxycarbonyl</td>
</tr>
<tr>
<td>m-CPBA</td>
<td><em>meta</em>-Chloroperbenzoic acid</td>
</tr>
<tr>
<td>DBU</td>
<td>1,8-Diazabicyclo[5.4.0]undec-7-ene</td>
</tr>
<tr>
<td>DCC</td>
<td>1,3-Dicyclohexylcarbodiimide</td>
</tr>
<tr>
<td>DMF</td>
<td>N,N-Dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>Dimethylsulfoxide</td>
</tr>
<tr>
<td>LDA</td>
<td>Lithium diisopropylamide</td>
</tr>
<tr>
<td>Ph</td>
<td>Phenyl</td>
</tr>
<tr>
<td>TBDMS</td>
<td>tert-Butyldimethylsilyl</td>
</tr>
<tr>
<td>TFA</td>
<td>Trifluoroacetic acid</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran</td>
</tr>
<tr>
<td>TMEDA</td>
<td>Tetramethylenediamine</td>
</tr>
<tr>
<td>TMS</td>
<td>Trimethylsilyl</td>
</tr>
<tr>
<td>Tr</td>
<td>Trityl</td>
</tr>
<tr>
<td>Ts</td>
<td>$p$-Toluenesulfonyl</td>
</tr>
<tr>
<td>Z</td>
<td>Benzyloxycarbonyl</td>
</tr>
</tbody>
</table>
Table of Contents

Chapter 1

1.0 Introduction 1
1.1 2-Imidazolines 2
1.2 Biological activity of 2-imidazolines 2
1.3 2-Imidazolines: Tools to synthetically useful compounds 6
  1.3.1 Carboxylic acids 6
  1.3.2 Ketones 7
  1.3.3 Aldehydes 8
  1.3.4 Diaminoesters, acids and amino alcohols 9
  1.3.5 β-Hydroxy-α-amino acids 11
  1.3.6 Chiral diamines 11
  1.3.7 Amidoamines 12
  1.3.8 Imidazoles from 2-imidazolines 13
1.4 2-Imidazolines as synthetic intermediates 14
  1.4.1 As nucleophilic transfer reagents 14
  1.4.2 As reagents 15
  1.4.3 As metallation directing groups 17
  1.4.4 2-Imidazolines as spin labels 20
1.5 2-Imidazolines as mimics 22
  1.5.1 2-Imidazolines azaprostanoids 22
  1.5.2 2-Imidazoline analogues of Kainoid family 23
  1.5.3 2-Imidazolines as C-protected β-enamino acid derivatives 24
  1.5.4 2-Imidazolines as pseudopeptides 25
1.6 2-Imidazolines in annulations 27
  1.6.1 Guanidine units from 2-imidazolines 27
  1.6.2 Synthesis of pyrimidones 30
  1.6.3 Reactions of 2-aminomethyl-2-imidazolines with double electrophiles 31
  1.6.4 Triazinones 33
  1.6.5 Triazines from 2-imidazolines 33
  1.6.6 Imidazo[1,2-b]thiazinones and thiazolones 34
  1.6.7 2,4,6-Trisubstituted pyrimidines 35
  1.6.8 Homochiral piperidines from 2-imidazolines 35
1.7 2-Imidazolines in cycloadditions

1.7.1 2-Imidazolines in 2+2 cycloadditions 36
1.7.2 2-imidazolines in 1,3-dipolar cycloadditions 37

1.8 Strategy

1.8.1 The Diels-Alder approach to the target molecules 39
1.8.2 Intramolecular approach 40
1.8.3 Intermolecular approach 41

Chapter 2

2.0 Discussion

2.1 A new protocol for the synthesis of 2-substituted 2-imidazolines 43

2.1.1 Studies on 2-imidazole dianions 43
2.1.2 N-Benzyl protected 2-imidazolines 47
2.1.3 2-Alkyl-2-imidazolines 51
2.1.4 Synthesis of 2-(oxoalkyl)-2-imidazolines 57
2.1.5 Synthesis of 2-alkenyl-2-imidazolines 60

2.2 Reactions of 2-imidazolines with double electrophiles 67

2.2.1 Synthesis of tetrahydroimidazo[1,2-a]pyridines 67
2.2.2 2-Imidazolines in conjugate additions 73
2.2.3 Tetrahydroimidazo[1,2-a]pyridin-5-ones 75

2.3 Imidazolines in Diels-Alder studies

2.3.1 Studies towards the synthesis of N-butadienyl-2-imidazolines 82
2.3.2 The intermolecular approach to N-Butadienyl-2-imidazolines 85
2.3.3 2-Imidazolines in intramolecular Diels-Alder studies 88
2.3.4 Molecular modelling studies 91
2.3.5 Alternative systems for intramolecular Diels-Alder reaction 93
2.3.6 2-Imidazolines in intermolecular Diels-Alder studies 96
2.3.7 Templates for the synthesis of 5,5,6-systems 101
2.3.8 Conclusion 105

2.4 Reactions of 2-imidazolines with acetylenic esters 106

2.4.1 Reactions with non-terminal propynoates 106
2.4.2 Reactions with dialkyl acetylene dicarboxylates 109
2.4.3 2-Imidazolines in radical reactions 116

Chapter 3

3.0 Experimental 119

4.0 References 227

Appendix
Chapter 1

1.0 Introduction

As organic chemists attempt syntheses of increasingly complex molecules, the need for efficient, mild, and selective functional group transformation and elaboration becomes even more apparent. The ability of heterocycles to act as vehicles to assist in meeting these requirements is not a new idea,¹ and this concept has been generally accepted for synthesis. The introduction and rapid acceptance of dithianes,² dihydroxazines,³ isoxazoles,⁴ 2-oxazolines⁵ and other heterocycles as versatile tools for the synthetic chemist results predominantly from their ability 1) to remain inert to a variety of commonly used reagents, 2) to act as a platform on which to perform a desired transformation efficiently and under mild conditions, and 3) to be available for further modification via mild or neutral "releasing" conditions. These properties, commonly identified with latent functionality, provide a flexibility which is both rare and valuable to the chemist involved in synthesis.

2-Imidazolines (1.1), although well known compounds, are newcomers to this elite group of molecules. It was of great interest to us to use 2-imidazolines in our synthetic methodology.

![2-Imidazoline Ring](image)

The 2-imidazoline ring has long been recognised as having potential by interesting biological and synthetically useful properties.⁶ This introduction has been restricted to the synthetic utility of the 2-imidazoline system as a template in the synthesis of other organic molecules and to its involvement in annulation reactions. No attempt has been made to survey preparations of 2-imidazolines; these are many and well documented.⁷
1.1 2-Imidazolines

The 2-imidazoline (or 4,5-dihydroimidazole) nucleus (1.1) has a numbering system derived from the imidazoles (1.2) (Scheme 1.1).

![Diagram of 2-imidazolines](image)

Scheme 1.1

The nitrogen atom connected to the two adjacent ring atoms via single bonds is assigned position 1. The second nitrogen atom in the 5-membered ring is therefore assigned position 3, and is connected to C(2) by a double bond and to C(4) by a single bond.

1.2 Biological activity of 2-imidazolines

The nitrogen atoms of the 2-imidazoline ring are arranged in the form of a cyclic amidine and therefore constitute nitrogen analogues of carboxylic acids. Amidines and hence 2-imidazolines possess pharmaceutical properties and have been the subject of many studies in the search for drugs to be used in both man and domestic animals.

Nature uses a 2-imidazoline in 5,10-methenyl-5,6,7,8-tetrahydrofolate (1.3), one of the tetrahydrofolate family of coenzymes, which plays an important role in one-carbon transfers in purine biosynthesis. It is required for the insertion of C(8) and indirectly for the insertion of C(2) into the purine ring. An enzyme, 5,10-methenyl-5,6,7,8-tetrahydrofolate hydrolase catalyses the hydrolysis of 5,10-methenyl-5,6,7,8-tetrahydrofolate to N\(^{10}\)-formyl-5,6,7,8-tetrahydrofolate which then acts as a donor and effects formylation of the amino function on compound (1.4). The reaction of (1.5) is catalysed by the enzyme 10-formyl-
5,6,7,8-tetrahydrofolate:5-amino-1-ribosyl-4-imidazole-carboxamide-5'-phosphate transformylase and lies on the pathway for biosynthesis of the purine nucleotides (1.6) (Scheme 1.2).^{11}

Many 2-imidazolines substituted in the 2-position by either alkyl, aryl or even arylalkyl groups show pharmacological activity. 2-Benzyl-2-imidazoline (1.7), known as Priscol, is an important vasodilator and is used in the treatment of peripheral circulatory disorders.\textsuperscript{12} Replacement of the phenyl group by a naphthyl group reverses the effects, so that Pivine (1.8) is a potent vasoconstrictor.\textsuperscript{13} Phentolamine (1.9) is also used for the treatment of circulatory disorders, and blocks the pressor action of noradrenaline and adrenaline.\textsuperscript{14} Structural modification of these drugs led to the discovery of clonidine (1.10), a molecule that is used for the treatment of hypertension (Scheme 1.3).\textsuperscript{15}
Other 2-imidazolines have properties and uses in the control of cardiac arrhythmias. Antazoline (1.11) has the properties of an antihistamine drug and also possesses local anaesthetic and anticholinergic properties. Structural modification of antazoline led to the discovery of compounds (1.12) and (1.13) that have antifibrillatory effects on aconitine-induced cardiac arrhythmias (Scheme 1.4).

Structurally more complex 2-imidazolines such as (1.14), which contains two 2-phenyl-2-imidazolines linked through a *meta* urea bridge, has found use in the treatment of babesiasis in domestic animals whereas (1.15) has been shown to be active against transplantable leukemia L1210 (Scheme 1.5).
A number of other simpler compounds have shown biological activities. The 2-amino-4-aryl-2-imidazolines (1.16) have been reported to have antihypertensive activity and several members of that series also exhibited central nervous system activity through prevention of reserpine-induced ptosis. 20 2-(Methoxycarbonylamino)-4-phenyl-2-imidazolines (1.17), on the other hand, demonstrated an antidepressant profile. 21 A recent report documented that compound (1.18) has been shown to be a potent cholesterol acyltransferase inhibitor and antihypercholesterolemic agent (Scheme 1.6). 22

It is not only the 2-substituted 2-imidazolines that are biologically active. N-Substituted 2-imidazolines have also been shown to exhibit biological activity. Compounds (1.19a) and (1.19b) were reported to inhibit $\alpha$ and $\beta$-adrenergic receptors (Scheme 1.7). 23
The biological activity shown by a large number of 2-imidazolines and the ease of their synthesis explains the extensive use of the imidazoline ring in synthetic organic chemistry.

1.3 2-Imidazolines: Tools to synthetically useful compounds

1.3.1 Carboxylic acids

The labile nature of the α-hydrogen atoms in 2-substituted 2-imidazolines was recognised early\textsuperscript{24} and was utilised by Jones \textit{et al.} in reports of C(2α) metallation of 2-alkyl-2-imidazolines.\textsuperscript{25} This property proved valuable because it allowed the synthesis of more elaborate 2-imidazolines.

The simple N-benzyl-2-methyl-2-imidazoline (1.20) may be metallated with \textit{n}-butyllithium at -78°C and treated with alkyl halides to afford the elaborated imidazolines (1.21) in excellent yields. Acidic hydrolysis afforded the homologated carboxylic acids. A second metallation followed by addition of alkyl halide furnished the 2-dialkylmethylimidazolines (1.22) which were likewise hydrolysed with aqueous H\textsubscript{2}SO\textsubscript{4} to give the disubstituted carboxylic acids (Scheme 1.8).\textsuperscript{26,25}
1.3.2 Ketones from 2-imidazolines

1-Benzyl-2-alkyl or 2-dialkylmethyl-2-imidazolines can be used to synthesise ketones efficiently. 2-Imidazolines (1.22) can be easily and quantitively converted into the more electrophilic methiodide salts (1.23) by reaction with methyl iodide (neat, 2 equiv.). Grignard reagents (3 equiv. in THF) can be added to these salts to produce the presumed 2,2-disubstituted imidazolidines (1.24) which were not isolated but instead were decomposed on mild acidic work up (2M hydrochloric acid at 0°C). The ketones were obtained in good yields on simple extraction with diethyl ether (Scheme 1.9). This method gave satisfactory results with primary organomagnesium halides and alkyl lithiurns; secondary organomagnesium reagents added slowly and gave low yields.
1.3.3 Aldehydes

A mild methodology to transform 2-imidazolines to aldehydes has also been developed recently. The aldehyde was obtained in a "one-pot" three step sequence (Scheme 1.10). Imidazoline (1.25) was N-permethylated using excess of methyl iodide and the resulting imidazolinium derivative was in turn reduced with sodium borohydride. The aminal was obtained and without isolation was converted to the aldehyde (1.26) using 0.5M HCl.

An alternative synthetic methodology was also reported for the conversion of 2-imidazolines to aldehydes. The 2-substituted-2-imidazolines (1.27) were reduced to the 2-
substituted imidazolidines with Na in ethanol. It was found that the best results were obtained when the reduction was performed at 0-5°C using 2.5 equiv. of sodium. The 2-substituted imidazolidines were then subjected to acidic cleavage in aqueous oxalic acid. The aldehydes derived from the hydrolysis were isolated after distillation in good yields (Scheme 1.11).

\[
\text{Scheme 1.11}
\]

\[\text{Scheme 1.11} \]

**1.3.4 2,3-Diaminoesters, acids and amino alcohols**

Optically active 2-imidazolines (1.28) have been synthesised by stereoselective aldol-type reaction of N-sulfonylimines with ethyl isocyanoacetate catalysed by a gold (I) complex having a chiral ferrocenyl phosphine ligand (1.29).\(^{30}\)
The 2-imidazolines (1.28) could easily be ring opened to produce a variety of synthetically useful compounds. The 2,3-diamino ester (1.30) was obtained from the chiral imidazoline by treatment with conc. HCl in ethanol. Reduction of the ester produced the chiral amino alcohol (1.31). Hydrolysis of the ester followed by removal of the tosyl group in a refluxing solution of HBr/AcOH in the presence of phenol afforded the free 2,3-diamino acid (1.33).
1.3.5 Synthesis of \( \beta \)-hydroxy-\( \alpha \)-amino acids

The use of 2-imidazolines as templates has been extended even further to the synthesis of \( \beta \)-hydroxy-\( \alpha \)-amino acids.\(^{32}\) Imidazolines (1.34) reacted with aldehydes in dimethylformamide to give the corresponding products by an aldol type reaction (Scheme 1.13).

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{ZHN} & \quad \text{ZHN}
\end{align*}
\]

\( \text{i) } R\text{CHO} \quad \text{DMF} \quad \text{ii) } \text{PhSO}_2\text{Cl} \quad \text{iii) } \text{HCl}, 110^\circ\text{C} \quad \text{R} \quad \text{CH} \quad \text{CH} \quad \text{CO}_2\text{H}
\]

\( \text{R= Me, Et, Ph} \)

Scheme 1.13

Hydrolysis of the benzenesulfonyl derivatives of (1.35) with 1M HCl at 110\(^\circ\)C gave the \( \beta \)-hydroxy-\( \alpha \)-amino acids (1.36) in 5:1 ratio of threo and erythro forms.

1.3.6 Chiral Diamines

Imidazolines have also been used as intermediates in the conversion of diols to diamines.\(^{33}\) Enantiomerically enriched diols (1.37) were converted into the cyclic sulphates (1.38). The sulfates (1.38) reacted with the amidines (1.39) in DME to give the zwitterionic intermediates (1.40) which underwent cyclisation to afford the imidazolines (1.41) in a stereocontrolled sequence. Acetylation of (1.41) followed by hydrolysis in refluxing aq. HBr/AcOH afforded the enantiomerically pure diamines (1.42) (Scheme 1.14).
The ready availability of enantiomerically pure diols\(^{34}\) coupled with the versatile electrophilic behaviour of the derived cyclic sulfates\(^{35}\) provided an efficient route to chiral 1,2-diamines.

**1.3.7 Amidoamines**

Hydrolysis of N-unsubstituted 2-imidazolines requires rather harsh conditions, such as concentrated acids and elevated temperatures.\(^{36}\) E. Korshin *et al.* have discovered that N-benzoylated 2-imidazolines (1.43) can be easily hydrolysed when boiled for 3 hours in aqueous acetone, to give amido amines (1.44).\(^{37}\) The replacement of the benzoyl group by the p-nitrobenzoyl group had an incredible effect. The hydrolysis occurred at 10°C in aqueous acetone (Scheme 1.15).
1.3.6 Imidazoles from 2-imidazolines

The dehydrogenation of 2-imidazolines to imidazoles (1.45) has recently attracted a lot of attention. An efficient method for this conversion using commercially available Pd-C has been reported (Scheme 16).\(^{38}\)

The 2-substituted or 2,4-disubstituted-2-imidazolines were heated to reflux in toluene in the presence of 10% Pd/C to give the corresponding imidazoles (1.45) in good yields.
1.4 2-Imidazolines as synthetic intermediates

1.4.1 As nucleophilic transfer reagents

The 2-imidazoline subunit was utilised as a nucleophilic carbon reagent in order to mimic biological processes mediated by the tetrahydrofolate coenzymes. The simple 1-benzyl-2-imidazoline (1.46) was metallated with n-butyllithium in THF at -78°C and the 2-lithio derivative was treated with a variety of aldehydes to give 2-(1-hydroxyalkyl)-2-imidazolines (1.47) in 60-70% yield. Oxidation of the resulting alcohols (MnO₂, CH₂Cl₂) produced the corresponding 2-(1-oxoalkyl)-2-imidazolines (1.48). An alternative approach to these 2-acyl-2-imidazolines was via the direct acylation of the lithio derivative of (1.46) with carboxylic acids ethyl esters. Ketones (1.48) were treated with organometallic reagents to give tertiary alcohols (1.49) in moderate to good yields (34-92%). These alcohols were also obtained via direct reaction of the lithio derivative of imidazoline (1.46) with ketones in slightly lower yields.

Compounds (1.49) collapsed to the corresponding ketones (1.50) upon heating in chloroform containing a catalytic amount of conc. hydrochloric acid. It was suggested that the reaction proceeds via protonation of the amidine at N(3) and elimination to give the ketone and the imidazolinium ylide (1.52; R=H) that then protonates at C(2). In support of this proposal, treatment of the tertiary alcohols (1.49) with an excess of methyl iodide led to the crystalline 1-benzyl-3-methyl-2-imidazolinium iodide, presumably via the ylide (1.52), where R=Me, and a mother liquor that contained the desired ketones (1.50) (Scheme 1.17).
Ketone (1.48), \(R^1=\text{Ph}\), was treated with an excess of iodomethane and the salt was reacted with nucleophiles to afford benzoic acid (NaOH), ethyl ester (EtOH reflux), ethyl thioester (EtSH, THF reflux) and benzyl or butyl amides (Ph\(\text{CH}_2\text{NH}_2\) or Bu\(\text{NH}_2\), THF reflux). In all the above cases the 2-imidazoline proved to be a good nucleophilic \(C_1\)-transfer reagent and a useful leaving group.

1.4.2 As reagents

It is known that alcohols can be converted to alkyl halides with a number of reagents. Japanese researchers have developed an imidazoline reagent\(^40\) that transforms alcohols to alkyl halides. 2-Chloro-1,3-dimethylimidazolinium chloride (1.53) was found to be an extremely useful reagent. Chloroalkanes (1.54) were obtained from alcohols by
reaction with (1.53) in the presence of triethylamine (1 equiv.) in good yields (Scheme
1.18).

\[
RCH_2OH + \begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2 \quad \text{1.53}
\xrightarrow{1 \text{ eq Et}_3\text{N}}
\begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2
\rightarrow
RCH_2Cl \quad \text{1.54}
\]

Scheme 1.18

When the same reaction was carried out in the presence of carboxylic acids the
acylated alcohols (1.55) were obtained (Scheme 1.19).

\[
R'CH_2OH + \begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2 \quad \text{1.53}
\xrightarrow{1 \text{ eq Et}_3\text{N}}
\begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2
\rightarrow
R'CH_2OCOR^2 \quad \text{1.55}
\]

Scheme 1.19

Vinylogous acid chlorides (1.56) were also efficiently synthesised under the same
conditions when diketones were used as starting materials (Scheme 1.20).

\[
\begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2 \quad \text{1.53}
\xrightarrow{1 \text{ eq Et}_3\text{N}}
\begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2
\rightarrow
R^1CH_2OCOR^2 \quad \text{1.56}
\]

Scheme 1.20

This imidazoline reagent (1.53) was shown to have the ability to oxidise secondary
alcohols to ketones (1.57) in the presence of 2 equiv. of triethylamine when 1 equiv. of
DMSO was used as co-additive. The ketones were obtained in good yields (71-92%)
(Scheme 1.21).

\[
\begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2 \quad \text{1.53}
\xrightarrow{2 \text{ eq Et}_3\text{N} \ \text{1 eq DMSO}}
\begin{array}{c}
\text{Me}^+ \ \text{N}^- \ \text{Me}^+ \ \text{N}^-
\end{array}
\text{Cl}_2
\rightarrow
R^1COOR^2 \quad \text{1.57}
\]

Scheme 1.21
Aromatic aldehydes were also obtained from benzyl alcohols in moderate yields of 47-63%, when the reaction was carried out in the presence of hexamethylenetetramine, in place of DMSO, followed by the hydrolysis of an intermediate with 50% aqueous acetic acid. DMSO was found to give a mixture of chlorinated (major) and oxidised products (minor).

A Lossen-type rearrangement was observed when (1.53) was reacted with hydroxamic acids (Scheme 1.22) to produce isocyanates (1.58). Urea derivatives (1.59) were obtained in good to moderate yields by trapping the intermediate isocyanates (1.58) with primary amines. The use of either alcohols or thiols in place of amines afforded carbamates (1.60) or thiocarbamates (1.61) (Scheme 1.22).

1.4.3 As metellation directing groups

The presence of the two nitrogen atoms in the imidazoline ring appealed to researchers that investigated the ability of the imidazoline ring to act as a metellation directing group. Studies of the metellation characteristics of 2-arylimidazolines and of their
heteroaromatic analogues have been reported. Houlihan and Parrino reported ortho (and N-1) lithiation in 2-phenyl-2-imidazoline to afford (1.62), and lithiation of the methyl group (and of N-1) in 2-(2-methylphenyl)-2-imidazoline to give (1.63) (Scheme 1.23).

The ortho lithiated imidazoline (1.62), generated with 3 equiv. of n-butyllithium in hexane at 50°C, reacted with methyl 4-chlorobenzoate to form 5-(4-chlorophenyl)-2,3-dihydro-5H-imidazo[2,1-a]isoindol-5-ol (1.64) in 60% yield (Scheme 1.24).

When the dilithio derivative (1.63) formed from 2-(2-methylphenyl)-2-imidazoline was reacted with methyl 4-chlorobenzoate at 50°C, the compound (1.65) was isolated, incorporating two molecules of the ester. In contrast, the 'simple' acylation product (1.66) was produced when the reaction was performed at -25°C (Scheme 1.25).
The 2-imidazoline moiety has also been studied as a director of 3-metallation in heteroaromatic rings such as pyrroles, furans and thiophenes (Scheme 1.26). The dilithio intermediate (1.67) was generated using n-butyllithium (2.2 equiv.) in either THF or DME at -78°C for 2 hours. A high level of metallation was achieved after that period, and the intermediate (1.67) was reacted with a range of electrophiles leading to the 2,3-disubstituted heterocycles (1.68). In cases where excess butyllithium was added 5-substitution was also observed.

These metallations directed by 2-imidazolines presumably occur via an initial complex formation between the directing group and the incoming metallation agent, with subsequent delivery of the metal to an adjacent ortho-position (Figure 1.1).
1.4.4 2-Imidazolines as spin labels

An elegant route to a series of useful biological probes and paramagnetic ligands in coordination compounds was developed by Russian researchers. The reaction of $\alpha$-hydroxylamino oxime (1.69) with aldehydes in an ethanolic solution led to the corresponding 3-imidazoline-3-oxides (1.70) (Scheme 1.28). Oxidation with PdO$_2$ in chloroform afforded $4H$-imidazole-1,3-dioxides (1.71). Further oxidation with PdO$_2$ in methanol led to nitronylnitroxy radicals (1.73). When the oxidation was performed in ethanol saturated with ammonia, compound (1.72) was obtained containing an amino group at the carbon atom $\alpha$ to the nitroxyl group. The conjugation with the double bond at the C(2) position favours addition of methanol and ammonia at C(4). In the reaction of $4H$-imidazole dioxide (1.71) with excess phenyllithium the addition of only one molecule was observed; this addition occurred preferentially at the arylnitrone group and gave the nitronylnitroxy radical (1.74) on subsequent oxidation (Scheme 1.28). This reaction route correlates with the ability of the alkylnitrone to be metallated at the C(2) position thus preventing the phenyllithium from adding at the C(2) position.
Scheme 1.28
1.5 2-Imidazolines as mimics

1.5.1 2-Imidazoline azaprostanoids

The doubly nucleophilic character of 2-methyl-2-imidazoline has been utilised for the synthesis of 2-imidazoline azaprostanoids.\textsuperscript{45} N-Alkylation of 2-methyl-2-imidazoline (1.75) with n-butyllithium at 20°C and bromo-orthoester (1.76) to give imidazoline (1.77), followed by a second C-alkylation with 1-iodoheptane afforded the orthoester (1.78). Conversion of the orthoester to the methyl ester with H\textsubscript{2}SO\textsubscript{4}-MeOH and then K\textsubscript{2}CO\textsubscript{3} provided the first analogues (1.79) of the primary prostaglandins to contain the 2-imidazoline moiety (Scheme 1.29).

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\textbf{1.75}};
\node (b) at (1.5,0) {\textbf{1.76}};
\node (c) at (3,0) {\textbf{1.77}};
\node (d) at (4.5,0) {\textbf{1.78}};
\node (e) at (6,0) {\textbf{1.79}};
\draw[->] (a) -- (b) node[midway,above] {i) n-BuLi, 20°C};
\draw[->] (b) -- (c) node[midway,above] {ii) Br(CH\textsubscript{2})\textsubscript{6}};
\draw[->] (c) -- (d) node[midway,above] {iii) n-BuLi, -78°C, iv) I(CH\textsubscript{2})\textsubscript{6}CH\textsubscript{3}};
\draw[->] (d) -- (e) node[midway,above] {v) MeOH, H\textsubscript{2}SO\textsubscript{4}, vi) K\textsubscript{2}CO\textsubscript{3}};
\end{tikzpicture}
\end{center}

Scheme 1.29
1.5.2 2-Imidazoline analogues of the Kainoid family

In an effort to mimic the anthelmintic and insecticidal activities of “kainoid” (1.80) with compounds of simpler structure and much easier accessibility, O’Sullivan et al. synthesised functionalised imidazolines (1.83a), (1.83b) and (1.83c) (Scheme 1.30).46

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad \text{CO}_2\text{Me} \\
\text{+H}_3\text{N} \quad \text{NHPh} \\
\text{i) RC(O\text{Me})}_3 \quad \text{ii) Na}_2\text{CO}_3 \\
\text{MeO}_2\text{C} & \quad \text{CO}_2\text{Me} \\
\text{1.81} & \quad \text{1.82} \\
\text{HO}_2\text{C} & \quad \text{CO}_2\text{H} \\
\text{HN.} & \quad \text{HN.} \\
\text{MeO}_2\text{C} & \quad \text{NHPh} \\
\text{N^s^s^s^s^N—Ph} \\
\text{R} & \quad \text{R} \\
\text{1.83a R= H} \\
\text{1.83b R= Me} \\
\text{1.83c R= Bu} \\
\end{align*}
\]

Scheme 1.30

The condensation reactions of the diamine salt (1.81) with orthoesters were performed under acidic conditions and imidazolines (1.82) were obtained in moderate yields. After hydrolysis of the esters, the desired diacids (1.83) were isolated.

The diamine salt (1.81) was used because it was found that the free base was unstable and underwent a facile ring closure to form the butyrolactam (1.84) (Scheme 1.31).

\[
\begin{align*}
\text{MeO}_2\text{C} & \quad \text{CO}_2\text{Me} \\
\text{+H}_3\text{N} \quad \text{NHPh} \\
\text{neutralisation} & \quad \text{MeOOC} \\
\text{N^s^s^s^s} & \quad \text{NHPh} \\
\text{1.81} & \quad \text{1.84} \\
\end{align*}
\]

Scheme 1.31
These cyclic glutamate analogues (1.83a-c) showed no anthelmintic or insecticidal activity despite the fact that the glutamic acid subunit in these imidazolines is held by the planar imidazoline ring in a conformation similar to that found in the crystal structure of kainic acid.

1.5.3 2-Imidazolines as C-protected β-enamino acid derivatives

The imidazoline heterocycle has been employed as the masked carboxyl functionality in the synthesis of C-protected β-enamino acids\textsuperscript{47} which are potential precursors to β-amino acids.

The 1-benzyl-2-alkyl-2-imidazolines (1.85) were treated with 1.25 equiv. of \textit{n}-butyllithium in THF at -78°C. The lithiated imidazolines (1.86) were then reacted with nitriles to give the anionic intermediate (1.87) after short reaction times (2-5 h). After quenching with saturated aqueous NH\textsubscript{4}Cl, the intermediates (1.87) evolved to the single reaction products (1.88) that were isolated in the β-tautomeric form, due to the additional stabilisation resulting from delocalisation and the possibility of intramolecular hydrogen bonding (Scheme 1.32). The configuration of the double bond was confirmed as Z by n.O.e. experiments.
1.5.4 Imidazolines as pseudopeptides

The imidazoline ring contains an amidine that has similar resonance structures to those of the parent amide bond and may be viewed as a mimic of many of the features of the amide bond. The similarities include the presence of two heteroatoms, similar configuration of double bonds, similar hydrogen bonding possibilities and similar steric properties. On the other hand the basicity of an amidine is much greater than that of an amide, a property that retards hydrolysis under the conditions likely to prevail in biological systems. Jones et al. capitalised on these advantages and similarities to the amide bond and synthesised 2-imidazolines as pseudopeptides (Scheme 1.33).
The S-methylthioimidate salt (1.89) was treated directly with the homochiral R-
diaminoester (1.90) to give the protected pseudopeptide (1.91) as inseparable mixture of
diastereoisomers. After protection of the amidine ring as the tert-butyloxycarbonyl amide
chromatographic separation of the two diastereoisomers (1.92a) and (1.92b) was achieved.
Basic hydrolysis at the C-terminus, followed by activation as the pentafluorophenyl ester
and coupling with Asp-Phe-NH₂ afforded the separate protected pseudotetrapeptide
diastereoisomers. Deprotection by hydrogenolysis and trifluoroacetic acid treatment
afforded the separate pseudopeptide isomers (1.93a) and (1.93b) as trifluoroacetate salts.
Unfortunately these compounds showed minimal binding activity when tested against the rodent CCK-A and CCK-B.

1.6 2-Imidazolines in annulations

1.6.1 Guanidine units from 2-imidazolines

The nucleophilic character exhibited by 2-imidazolines has been explored by a number of chemists that have used this molecule in ring forming reactions. Compounds containing the guanidine unit are of considerable biological interest due to the hydrogen-bond mediated interactions of guanidinium ions with phosphate-containing biomolecules and to their large range of biological activities, including hypotensive and adrenergic neuron-blocking effects. The synthesis of acylguanidines from suitable 2-amino-2-imidazolines has been the subject of a number of reports. 2-Amino-2-imidazoline (1.94), for example reacted directly with ethyl acrylate to give exclusively the product (1.95) (Scheme 1.34).

![Scheme 1.34](image)

The other possible regioisomeric product (1.97) was prepared by ring closure of suitably 2-substituted-2-imidazoline (1.96a) (Scheme 1.35). This was achieved by refluxing in mineral acid. The guanidinium ion is sufficiently nucleophilic to react with the protonated carboxylic acid group. In the case of the N-methyl-2-imidazoline (1.96b), compound (1.98) was obtained (Scheme 1.35).
The N(1)-methyl derivative (1.99) reacted similarly to give compound (1.100) (Scheme 1.36).  

2-Methylamino-2-imidazoline (1.101) on the other hand gave only the acyl guanidine (1.102) in refluxing ethyl acrylate. However when the reaction was carried out in ethanol at 5°C, it afforded 61% of (1.102) accompanied by a 21% yield of compound (1.103) (Scheme 1.37).
Compound (1.105), prepared from the reaction of 2-methylthio-2-imidazoline (1.104) and \( \gamma \)-aminobutyronitrile, underwent cyclisation to form the imine (1.106) which was hydrolysed to give (1.97). Conversion of the acid (1.107) to the methyl ester resulted in a spontaneous alternative cyclisation to give pyrroline (1.108) (Scheme 1.38). The formation of the five membered pyrroline ring in (1.108) appears to be more favourable than the seven membered ring fused to the imidazoline.

![Chemical structures and reactions](image)

Scheme 1.38

These imidazo[1,2-\(a\)]pyrimidine molecules can be regarded as analogous to many of the nucleotides.

In a similar way chiral 2-imidazolines have been employed as starting materials in the synthesis of chiral bicyclic guanidines (Scheme 1.39).
Thiourea (1.109) was transformed with 2 equiv. of methyl iodide in methanol into the isothiouronium iodide (1.110), which was then heated in DMF at 120°C to produce bicyclic guanidine (1.111).

1.6.2 Synthesis of pyrimidones

The double nucleophilic character of 2-amino-2-imidazolines has been used by other researchers in order to synthesise heterocyclic molecules. 2-Anilino-2-imidazolines (1.112a) when treated with β-ketoesters produced tetrahydroimidazopyrimid-7-ones (1.113). In particular 2-(2-amino-anilino)-2-imidazoline (1.112b) reacted with ethyl benzoylacetae to give compound (1.114) as an intermediate which eliminated one molecule of water spontaneously to give benzimidazole derivative (1.115) (Scheme 1.40).
These 2-anilino-2-imidazolines (1.116) also reacted with propiolate esters to give pyrimidones (1.117) of the opposite regiochemistry (Scheme 1.41).\textsuperscript{52}

1.6.3 Reaction of 2-aminomethyl-2-imidazolines with double electrophiles

The ability of 2-aminomethyl-2-imidazolines to act as binucleophiles has been explored even further by Korshin \textit{et al.}\textsuperscript{56} The reaction of 2-arylaminomethyl-2-imidazolines (1.118) with oxalyl chloride in the presence of 2 equiv of triethylamine gave hexahydro-5,6-dioxoimidazo[1,2-\(\alpha\)]pyrazines (1.119), while the reaction with phosgene
under the same conditions resulted in 5-oxo-5H-tetrahydroimidazo[1,2-a]imidazole (1.120) in 60% yield. A possible acylation reaction at the highly nucleophilic N(1) atom of the imidazoline ring takes place first followed by cyclisation to afford the compounds (1.119) and (1.120). Imidazoline (1.118) also reacted with methylbromoacetate to give the bicyclic compound (1.121) in 27% yield (Scheme 1.42).

![Scheme 1.42](image)

The reactions of these 2-arylaminomethyl-2-imidazolines with MeOP(O)Cl₂ and diamides of phosphinic acids in the presence of triethylamine afforded (1.122) in only 24% yield and the bicyclic diamidophosphinates (1.123) (Scheme 1.43) in 58 and 70% yields, respectively.

![Scheme 1.43](image)
1.6.4 Triazinones

In a similar fashion to the 2-amino-2-imidazolines, 2-hydrazino-2-imidazoline hydrides (1.124) reacted with dimethyl acetylenedicarboxylate in methanol in the presence of triethylamine to give the 1,2,4-triazin-5-ones (1.125) (Scheme 1.44).\(^{57}\)

\[
\begin{align*}
\text{R} &= \text{H, Me} \\
\text{1.124} & \quad \text{CO}_2\text{CH}_3 \\
\quad \text{CO}_2\text{CH}_3 & \quad \text{R} = \text{H, Me} \\
\text{1.125} & \quad \text{N} \\
\end{align*}
\]

Scheme 1.44

1.6.5 Triazine derivatives from 2-imidazolines

2-Methyl-2-imidazolines bearing a hydrogen or a methyl group at the amidine nitrogen have been shown to react smoothly with 2 equivalents of methyl isothiocyanate in anhydrous DMF, yielding condensed 1,3,5-triazine derivatives (1.126) (Scheme 1.45).\(^{58}\)

\[
\begin{align*}
\text{N} & \quad \text{CH}_3\text{N=C=S} \\
\text{R}^1 &= \text{H, Me} \\
\text{1.126} & \quad \text{N} \\
\end{align*}
\]

Scheme 1.45
Phenyl isothiocyanate on the other hand reacted to give only the N-thiocabamyl derivatives (1.127) but did not proceed to form the cycloadduct. This reaction appears to depend on the R group of the isothiocyanate.

### 1.6.6 Imidazo[2,1-b]thiazinones and imidazo[2,1-b]thiazolones

Imidazoline (1.128) reacted with chloroacetic acid and 3-bromopropanoic acid in acetic acid and sodium acetate to give the 2-substituted sulfanyl derivatives (1.129) and (1.131) which were cyclised by polyphosphoric acid to give imidazo[2,1-b]thiazolones (1.130) and imidazo[2,1-b][1,3]thiazinone (1.132) (Scheme 1.46). Imidazoline-2-thiol (1.128) also reacted with dimethyl acetylenedicarboxylate (Scheme 1.46) to give the bicyclic compound (1.133). The sulfur atom added to the triple bond followed by cyclisation of the NH group onto the non-conjugated ester to give the isolated product.

$$\begin{align*}
\text{CICH}_2\text{CO}_2\text{H} & \quad \text{BrCH}_2\text{CH}_2\text{CO}_2\text{H} \\
\text{AcOH} & \quad \text{AcOH} \\
\text{PPA} & \quad \text{PPA}
\end{align*}$$

Scheme 1.46
1.6.7 2,4,6-Trisubstituted pyrimidines from 2-imidazolines

C-Alkyl and C-arylpyrimidines were synthesised by a rearrangement of 4-functionalised 2-imidazoline derivatives. 4-(1-Chloroalkyl)-2-imidazoline derivatives (1.134) were treated with 2 equiv. of NaH and underwent intramolecular alkylation to give aziridino[1,2-c]-2-imidazolines (1.135). These aziridine derivatives were subsequently treated with 1 equiv. of NaH in dimethylformamide which resulted in a base induced β-eliminative ring expansion to the dihydropyrimidines (1.136). Air oxidation of (1.136) produces the aromatic pyrimidines (1.137) (Scheme 1.47).

![Scheme 1.47](image)

1.6.8 Homochiral piperidines from 2-imidazolines

The chiral enaminoester (1.138) has been reported by Jones et al. to undergo a conjugate addition to pent-1-enone to give the imidazoline adducts (1.139). Reduction of imidazoline (1.139) with diborane followed by H₂SO₄ work up afforded the octahydroimidazopyridines (1.140) as a single enantiomer. Further reduction of the aminal,
with NaBH₃CN at pH 3, and hydrogenolysis of the benzylic C-N bond (H₂, Pd-C, MeOH) produced a single enantiomer of the volatile 2-substituted piperidines which were isolated as their N-tosyl derivatives (1.141) (Scheme 1.48). The other enantiomer of the enaminoester (1.138) led to piperidines of the opposite stereochemistry.

![Scheme 1.48](image)

Other anulations involving imidazoline enaminoesters of the type (1.138) will be referred to during the discussion of our own studies.

### 1.7 2-Imidazolines in cycloaddition reactions

#### 1.7.1 Imidazolines in 2+2 cycloadditions

2-Imidazolines have been involved in the synthesis of azapenams. An earlier attempt to synthesise azapenams from the reaction of azidoketene with 2-imidazolines was not successful.³³ Azapenams were detected as intermediates, but not isolated. Recent reports of the photolytic reaction of chromium carbene complexes (1.142) with
imidazolines (1.143) have shown that the synthesis of azapenams is possible (Scheme 1.49).\textsuperscript{64}

Protection of the imidazoline NH group was deemed essential to prevent its reaction with the photogenerated ketene, so the easily removed Cbz group was appended to the imidazoline. In all cases a single diastereoisomer of the Cbz protected azapenams (1.144) was detected. Removal of the Cbz group by hydrogenolysis at 45 psi in methanol and triethylamine occurred in 4 min and produced azapenams (1.145). When the deprotection of the Cbz-azapenams was carried out under acidic conditions, hexahydrodiazepinones (1.146) were produced (Scheme 1.49).

\subsection*{1.7.2 Homochiral imidazolines in 1,3-dipolar cycloadditions}

Optically active 2-imidazolines (1.147) have also been employed as templates for the synthesis of chiral pyrrolidines by using the 1,3-dipolar cycloaddition reaction.\textsuperscript{65}
N-Alkylation of 1-benzyl-4-phenyl-2-imidazoline (1.147) with bromoesters and addition of DBU to these quaternary salts generates the azomethine ylides (1.148). Ylides (1.148) were shown to undergo diastereoselective 1,3-dipolar cycloaddition with a variety of electron-deficient electrophiles to afford hexahydropyrrolo[1,2-a]imidazole cycloadducts (1.149) as single enantiomers, and generating three of the five bonds of the new pyrrolidine ring in one-pot. Further reduction with NaBH₃CN followed by hydrogenolysis, led to the formation of optically active pyrrolidines (1.150) (Scheme 1.50). The 4-phenyl substituent provides facial selectivity in the cycloaddition and facilitates the removal of the templating atoms. The other imidazoline enantiomer produced pyrrolidines of the opposite stereochemistry.
1.8 Strategy

1.8.1 The Diels-Alder approach to the target molecules

The original aim of this project was to extend the idea of employing 2-imidazolines as templates in order to synthesise the optically active hydroquinoline unit found in many alkaloids such as lycoricidine (1.151) and narciclasine (1.152), compounds that have attracted considerable interest due to their range of biological effects and antitumour activity. Pumiliotoxin C (1.153) is an alkaloid, produced by poison frogs native to South and Central America, that also contains the hydroquinoline moiety. Aloperine (1.154) has been isolated from seeds and leaves of Sophora alopecuroides L. These plants have been long used in the treatment of inflammation in traditional Chinese medicine (Scheme 1.51).

![Chemical structures](image)

**Scheme 1.51**

One possible way to access these compounds could be by designing imidazoline templates that could undergo either inter or intramolecular Diels-Alder reactions.

The Diels-Alder reaction was chosen as a possible method for the synthesis of the hydroquinolines because it accomplishes the union of a $4\pi$ electron system with a $2\pi$
electron system creating two new carbon-carbon bonds, a six-membered ring and up to four contiguous stereocentres in one efficient step. The Diels-Alder cycloaddition is indeed a most productive process because it involves a simple summation of the reaction partners; all the atoms that constitute the diene and the dienophilic components are expressed in the [4+2] cycloaddition, and none are wasted.

Even more substantial structural changes can be brought about when the Diels-Alder reaction is intramolecular, where the probability is enhanced that the diene and dienophile will react with each other. When the reactive components are themselves cyclic and/or have ring substituents, complex multicyclic arrays such as those contained in drugs and natural products, can be constructed in a single step (Scheme 1.52).

Scheme 1.52

Those advantages and the fact that the Diels-Alder reaction offers a good control of the stereochemistry of the final products led us to investigate this approach to the synthesis of those molecules.

1.8.2 The intermolecular Diels-Alder approach

Retrosynthetic analysis of a target hydroquinoline such as (1.155) (retrosynthetic analysis 1) reveals that an intermolecular Diels-Alder reaction between the electron-rich imidazoline (1.158) and the electron-deficient methyl acrylate would lead to cyclohexene (1.157). Ring closure could be forced by addition of a base to give the tricycle (1.156). Reduction of the carbonyl group and cleavage of the imidazoline will provide the target molecule (1.155). The presence of the double bond could be used for further manipulation.
The original imidazoline (1.158) should be available in principle by reaction of a ring nitrogen atom with 2-butenal.

Retrosynthetic analysis 1

1.8.3 The intramolecular Diels-Alder approach

Another possible route to the target hydroquinolines could be from 2-imidazoline templates designed to undergo intramolecular Diels-Alder reactions. Retrosynthetic analysis suggests two possible templates (retrosynthetic analyses 2 and 3).
As can be seen from retrosynthetic analysis 2, the imidazoline (1.159) contains an electron-rich diene attached to the ring nitrogen, and the dienophile at the C(2) position. Disconnection of the dienamine (1.159) reveals that it could in principle be formed from 2-butenal and 2-(but-3-enyl)-2-imidazoline (1.160) which would be synthesised from N,C(2α) dianion (1.161) and 3-bromopropene.

A different disconnection reveals that an isomeric target molecule (1.162) could also be synthesised from an imidazoline (1.163) which contains a diene at the C(2) position and the dienophile now attached at N(1). The enamine could be synthesised from imidazoline nucleophile (1.164) and a suitable partner; use of methyl propiolate or ethyl acetoacetate would provide an electron withdrawing dienophile substituent, for example. The second disconnection shows that the diene could be introduced by generation of the N,C(2α) dianion (1.161) and 5-bromopenta-1,3-diene.

Retrosynthetic analysis 3

In both cases the analysis leads to a doubly nucleophilic synthon (1.161) which is the key for the synthesis of the proposed imidazoline templates. This synthon is equivalent to the 2-methyl-2-imidazoline reagent, which is a commercially available material.
2.0 Discussion

2.1 A new protocol for the synthesis of 2-substituted-2-imidazolines

2.1.1 Studies on 2-imidazoline dianions

In considering assembly of the target Diels-Alder templates of dienamine (1.159) or enamine (1.163), it was felt that enamines would be unstable under lithiation conditions. It was therefore decided that the enamine functionality should be introduced at a later stage. C(2α)-alkylation had to be completed first which implied that N(1)-protection could be necessary in order to prepare those target molecules, unless a different method for their synthesis was devised.

If the double anion that was suggested as the key synthon (1.161) for the synthesis of the target imidazoline could actually be generated, the least stable anion at the C(2α) position would be expected to react first with the electrophile to give the C(2)-substituted 2-imidazoline. If this methodology proved successful there would be no need for an N(1) protecting group, therefore the synthesis of the target imidazoline templates would become shorter.

![Scheme 2.1.1](image)

Dianions derived from C(2α)-disubstituted chiral 2-imidazolines (2.1.1) have been reported to undergo diastereoselective alkylation in the presence of 1.1 equiv. of alkyl halides to afford the corresponding quaternary substituted imidazolines (2.1.2) in good...
yields (Scheme 2.1.2). These presumed dianions benefit from the extra stabilisation provided by the aryl substituent.

Scheme 2.1.2

On the other hand, earlier efforts in our group to create the dimetallated species (1.161) from 2-methyl-2-imidazoline with 2.2 equiv. of n-butyllithium in THF at -78°C, had failed to demonstrate formation of a dianion. Quenching with 1.1 equiv. of benzyl bromide afforded only the N-benzylated-2-methyl-2-imidazoline. In contrast to this, when we attempted to form the dianion (1.161) by double deprotonation of 2-methyl-2-imidazoline (2.1.3) with 2.0 equiv. of n-butyllithium in tetrahydrofuran at 0°C, quenching with 1.0 equiv. of 3-bromopropene did afford the desired C-allylated compound (2.1.4) but only in a 10% yield (Scheme 2.1.3).

Scheme 2.1.3

Despite efforts to optimise the yield by pre-drying the 2-methyl-2-imidazoline (2.1.3) in a vacuum oven over phosphorous pentoxide, compound (2.1.4) could not be obtained in more than 10% yield. No unchanged starting material was recovered due to its water solubility. The presence of a phenyl ring at the C(2α)-position does indeed appear to
stabilise the anion more than in the case of 2-methyl-2-imidazoline, which could explain
the difference in yield.

It was not clear at this point whether complete formation of the dianion (1.161) had
been achieved. In order to understand whether the dianion formation was possible, the
question of the C- versus N-lithiation behaviour was addressed in more detail. When 1.0
equiv. of n-butyllithium was added to 2-methyl-2-imidazoline at 0°C, a yellow solution of
the anion was produced and on quenching with 1.1 equiv. of 3-bromopropene the N-prop-
3-enyl-2-methyl-2-imidazoline (2.1.5) was obtained in 44% yield, along with 10% of the
diallylated compound (2.1.6). This result confirms that the NH is the most acidic site on
the molecule and that this is the first proton that is abstracted (Scheme 2.1.4).

![Scheme 2.1.4](image)

A different experiment was carried out to investigate whether the N(1) and C(2)
doubly alkylated species can be formed. 2 Equiv. of n-butyllithium were added to a
solution of 2-methyl-2-imidazoline in THF at 0°C and to the yellow suspension formed
was added 2.2 equiv. of 3-bromopropene. The disubstituted 2-imidazoline (2.1.6) was
obtained in 45% yield (Scheme 2.1.5).

![Scheme 2.1.5](image)

It is not clear whether the NH and C(2α) protons are abstracted together or
sequentially. In the latter case N-alkylation would be followed by C-deprotonation by the
excess base, and then C-alkylation. The yellow suspension observed when the 2 equiv. of
$n$-butyllithium added is possibly an indication (yellow solution formed when 1 equiv. of $n$-butyllithium was added) that the dianion is actually formed. The negative charge in the mono-anions is delocalised in the imidazoline ring in both cases (Scheme 2.1.6).

![Scheme 2.1.6](image)

Similar experiments were carried out with 2-benzyl-2-imidazoline (2.1.7). 2 Equiv. of $n$-butyllithium were added to a solution of 2-benzyl-2-imidazoline in THF at 20°C and 2.2 equiv. of 3-bromopropene was added to the white suspension that was formed at 0°C. The dialkylated product (2.1.8) was obtained in 91% yield (Scheme 2.1.7). This difference in yields is an indication of the difference in the stability and reactivity of the two dianions.

![Scheme 2.1.7](image)

When 2-benzyl-2-imidazoline was treated with 2.1 equiv. of $n$-butyllithium at 20°C followed by 1.0 equiv. of 3-bromopropene produced a mixture of diallylated, N-allylated and C(2)-alkylated compounds was produced. Although this experiment was carried out under different conditions to those described by Langlois, it proves that C(2)-substituted imidazolines could be obtained. In any case, we can conclude that efficient N,C(2α)-dianion formation and reaction is limited to the 2-aryl cases, where extra delocalisation is available.

It is evident therefore that this approach to the C(2)-alkylated imidazolines is not very useful for the 2-methyl substrate, and a good imidazoline N(1) protecting group that
could be easily removed at a later stage, was required in order to synthesise the proposed imidazoline templates.

2.1.2 N-Benzyl protected 2-imidazolines

An alternative approach to the synthesis of 2-substituted 2-imidazolines involved the utilisation of 1-benzyl-2-methyl-2-imidazoline (2.1.9) as a starting material. It has been reported earlier by our group that 1-benzyl-2-methyl-2-imidazoline can be metallated at the C(2α)-position by treatment with n-butyllithium (1 equiv.) in tetrahydrofuran to afford, after addition of an alkyl halide, the 2-substituted N-benzyl-2-imidazoline (2.1.10).\textsuperscript{72} Debenzylation of the N-benzyl-2-imidazoline (2.1.10) with sodium in liquid ammonia/ethanol has also been reported to give the 2-substituted 2-imidazoline (2.1.11) (Scheme 2.1.8).\textsuperscript{45}

![Scheme 2.1.8](image)

This already existing methodology was an attractive one for the synthesis of 2-substituted-2-imidazolines that contained the required diene and dienophile functionalites at the C(2)-position.

47
1-Benzyl-2-methyl-2-imidazoline (2.1.9) was easily synthesised (Scheme 2.1.9).

\[
\begin{array}{c}
\text{Ph} \\
\text{NH} \\
\text{OEt} \\
\end{array}
\quad + 
\begin{array}{c}
\text{NH}_2 \\
\text{NH}_2 \\
\end{array}
\quad \rightarrow 
\begin{array}{c}
\text{Ph} \\
\text{NH} \\
\text{HCl.HN} \\
\text{OEt} \\
\end{array}
\]

Scheme 2.1.9

Ethyl acetimidate hydrochloride (2.1.13) was prepared by addition of acetyl chloride (1 equiv.) to ethanol (2 equiv.) followed by treatment with dry acetonitrile at 5°C. Storage at 0°C for 12 h and addition of dry diethyl ether afforded the imidate salt as a white solid in 32% yield. N-Alkylation of an excess of 1,2-diaminoethane with benzyl chloride at gentle reflux afforded a crude product from which N-benzyl-1,2-diaminoethane (2.1.12) was isolated after distillation as a colourless liquid in 72% yield. N-Benzyl-1,2-diaminoethane and ethyl acetimidate hydrochloride were heated at reflux for 3 h under nitrogen to afford after work up, the 1-benzyl-2-methyl-2-imidazoline (2.1.9) as a colourless liquid in 70% yield.

1-Benzyl-2-methyl-2-imidazoline (2.1.9) was lithiated with n-butyllithium in THF at -78°C and the orange anion was quenched with 1.1 equiv. of 3-bromopropene to give 1-benzyl-2-(but-3-enyl)-2-imidazoline (2.1.14) after work up and chromatography, as a colourless liquid (72%) (Scheme 12).
When methyl 4-bromobut-2-enoate was used as the electrophile the reaction did not produce the expected compound (2.1.15) (Scheme 2.1.11). This target imidazoline was selected because it would have contained an electron-deficient dienophile at C(2), which is important in Diels-Alder reactions.

\[
\text{Scheme 2.1.10}
\]

1H NMR spectroscopy showed traces of the desired product but purification and isolation of the pure material proved difficult. The presence of three electrophilic centres on methyl 4-bromobut-2-enoate and its ability to act as a proton source could be responsible for the poor reaction. The lithiated 2-imidazoline has the choice of attacking the ester carbonyl, the bromide or the conjugated double bond.

1-Benzyl-2-(but-3-enyl)-2-imidazoline (2.1.14) was subjected to the Birch reduction conditions using 8 equiv. of sodium in liquid ammonia/ethanol as described in the literature\textsuperscript{73} which resulted in unidentified products without any of the desired material being isolated. When the amount of sodium was reduced to 2.6 equiv., an inseparable 3:2 mixture of the unsaturated 2-(but-3-enyl)-2-imidazoline (2.1.4) and the saturated 2-butyl-2-imidazoline (2.1.16) was obtained in 31 % yield (Scheme 2.1.12). The saturated compound is probably produced via an intramolecular electron transfer from the benzene ring to the double bond of the side chain. Only when the amount of sodium was reduced to 1.95 equiv. was the desired 2-(but-3-enyl)-2-imidazoline (2.1.4) obtained but unfortunately in a
disappointing 21% yield (Scheme 2.1.12). Attempts to optimise the yield proved unsuccessful.

\[
\begin{array}{ccc}
\text{Ph} & \xrightarrow{2.6 \text{ equiv. Na/liq NH}_3} & \text{2.1.14} \\
& (31\%) & \text{2.1.14}+\text{2.1.16} \\
\text{2.1.14} & \xrightarrow{1.95 \text{ equiv. Na/liq NH}_3} & \text{2.1.16} \\
& (21\%) & \text{2.1.16} \\
\end{array}
\]

Scheme 2.1.12

In order to understand whether it is the presence of the double bond in the side chain that interferes with the debenzylation or whether the debenzylation is not generally useful, 1-benzyl-2-butyl-2-imidazoline was prepared. 1-Benzyl-2-methyl-2-imidazoline (2.1.9) was lithiated using n-butyllithium in THF at -78°C and C-alkylation was carried out by addition of 1.1 equiv of 1-iodopropane to produce compound (2.1.17) in 96% yield (Scheme 2.1.13). Imidazoline (2.1.17) was subjected to a Birch reduction using 2.5 equiv. of sodium in liquid ammonia/ethanol to give a yellow oil which solidified after column chromatography. \(^1\)H, \(^13\)C and DEPT NMR spectroscopy suggest it may be compound (2.1.18) (Scheme 2.1.13). Although mass spectroscopy showed that the molecular ion of (2.1.18) was present (M\(^+\) 218), high resolution mass spectroscopy (which was done a few months later) suggested that facile oxidation back to the starting material (2.1.14) may have taken place upon standing.
It is evident from these results that the benzyl group is not the ideal protecting group and another more general N(1)-protection should be found.

2.1.3 2-Alkyl-2-imidazolines

During our search for a better N-protecting group for 2-imidazolines we were aware of a report from our group that silyl-protected imidazolines had been found to be unstable and moisture sensitive, and that C-lithiation and alkylation of these compounds did not occur cleanly. The use of the tert-butyloxycarbonyl (Boc) group as 2-imidazoline N-protection, has been reported for pseudopeptide imidazolines and for 2-imidazolines used in chromium mediated 2+2 cycloaddition reactions, but had not been reported as an imidazoline protecting group in lithiation reactions, so its application seemed attractive.

1-tert-Butyloxycarbonyl-2-methyl-2-imidazoline (2.1.19) was easily prepared from the commercially available 2-methyl-2-imidazoline (2.1.3) and di-tert-butyl dicarbonate in the presence of triethylamine in dichloromethane at 20°C, and was isolated as a colourless low melting solid in 72% yield after distillation (Scheme 2.1.14). The compound is stable and can be stored at room temperature for long periods of time.
In an initial attempt to form the anion, 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (2.1.19) was treated at -78°C in dry THF with 1.1 equiv. of n-butyllithium to give a brown solution. Quenching with 1.2 equiv. of 3-bromopropene and stirring overnight did not produce the desired C(2α)-alkylated compound. The same procedure was repeated with lithium diisopropylamide (LDA) as base and a brown solution was again produced but no product was isolated after quenching with 3-bromopropene. In both cases starting material was recovered. The brown colour could suggest aggregation of the base which may inhibit anion formation.

The effect of a stronger base was investigated in the hope that this would facilitate the anion formation. 1-Boc-2-methyl-2-imidazoline was treated at -78°C in dry THF with 1.1 equiv. of sec-butyllithium. A bright yellow solution was obtained which was maintained at this temperature for 20 min. The 2-lithiomethyl-1-Boc-2-imidazoline (2.1.20) may be stabilised by interaction with the carbamate carbonyl forming a six-membered intermediate (Scheme 2.1.15).\textsuperscript{76} 3-Bromopropene was then added and the reaction mixture was allowed to warm to 20°C overnight, as it was found that shorter times resulted in lower yields. Aqueous work up, followed by purification using column chromatography on silica gel produced the desired 1-Boc-2-(but-3-enyl)-2-imidazoline (2.1.21a) as a colourless oil in 82% yield (Scheme 2.1.15). 3-Bromopropene was the first electrophile to be used because the resulting product would be useful for another part of the project.

The same brown colour seen previously when n-butyllithium or LDA were used as bases, was observed on some occasions with sec-butyllithium. Addition of
tetramethylethanediamine (TMEDA) solved the problem. TMEDA proved to be an essential additive in this reaction because it leads to higher yields. Presumably the TMEDA deaggregates the sec-butyllithium producing the monomeric species and hence strengthening the base.

In order to investigate the scope and limitations of the Boc moiety as a replacement for the benzyl group in imidazoline N-protection, it was decided to prepare a number of 2-substituted-2-imidazolines using the chemistry described in Scheme 2.1.15.

![Scheme 2.1.15](image)

**Scheme 2.1.15**

Metallation of 1-Boc-2-methyl-2-imidazoline in the usual way (sec-butyllithium, THF/TMEDA, -78°C) was followed by addition of alkyl halides (3-bromoprop-1-ene, 1-iodopropane, 4-bromobut-1-ene, benzyl bromide, 2-(phenyl)benzyl bromide, furfuryl chloride, 1-bromohexa-2,4-diene and 5-bromopenta-1,3-diene) to afford after work up and purification the 1-Boc-2-alkyl-2-imidazolines (2.1.21a-h), respectively in good yields (Table 2.1.1). Furfuryl chloride was prepared from furfuryl alcohol, pyridine and thionyl chloride using the method described by W. Kimer. 1-Bromohexa-2,4-diene was synthesised from commercial hexa-2,4-dien-1-ol and phosphorous tribromide. The reaction with 1-bromohexa-2,4-diene initially produced the desired product in low yield probably due to the poor quality of the bromide. When pure bromide was obtained by
careful distillation the yield of (2.1.21g) increased significantly. 5-Bromopenta-1,3-diene was made from commercial penta-1,4-dien-3-ol and phosphorous tribromide using the method described by Prevost and Bidon. The alkylation reaction proceeded well and the desired compound was obtained in 60% yield. Imidazolines (2.1.21f), (2.1.21g) and (2.1.21h) all contain diene functionalities that could potentially undergo intermolecular or intramolecular Diels-Alder reactions.

When methyl 4-bromobut-2-enoate and 3-chloroprop-1-ynel were used as electrophiles no reaction was observed. In the case of 3-chloroprop-1-ynel the reaction mixture turned brown when the chloride was added and starting material was recovered. It is possible that the chloride polymerises under the strongly basic reaction conditions.

Table 2.1.1

<table>
<thead>
<tr>
<th>compound</th>
<th>R^1</th>
<th>yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.21a</td>
<td>CH₂CH=CH₂</td>
<td>82%</td>
</tr>
<tr>
<td>2.1.21b</td>
<td>CH₂CH₂CH₃</td>
<td>86%</td>
</tr>
<tr>
<td>2.1.21c</td>
<td>CH₂CH₂CH=CH₂</td>
<td>64%</td>
</tr>
<tr>
<td>2.1.21d</td>
<td>CH₂Ph</td>
<td>92%</td>
</tr>
<tr>
<td>2.1.21e</td>
<td>CH₂(2-Ph)Ph</td>
<td>81%</td>
</tr>
<tr>
<td>2.1.21f</td>
<td>CH₂Furyl</td>
<td>71%</td>
</tr>
<tr>
<td>2.1.21g</td>
<td>CH₂CH=CHCH=CHCH₃</td>
<td>81%</td>
</tr>
<tr>
<td>2.1.21h</td>
<td>CH₂CH=CHCH=CH₂</td>
<td>70%</td>
</tr>
</tbody>
</table>

Deprotection of the 2-alkyl-1-tert-butyloxycarbonyl-2-imidazolines was achieved with excess of neat trifluoroacetic acid (Scheme 2.1.15). The Boc group is cleaved within 20 min. under these conditions. When the reaction was completed the trifluoroacetic acid was removed under reduced pressure and the imidazoline trifluoroacetate salt was
dissolved in dichloromethane. The free imidazolines were liberated by washing the organic layer with a 10% solution of aqueous NaOH (Table 2.1.2).

<table>
<thead>
<tr>
<th>compound</th>
<th>R¹</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.4</td>
<td>CH₂CH=CH₂</td>
<td>82%</td>
</tr>
<tr>
<td>2.1.15</td>
<td>CH₂CH₂CH₃</td>
<td>87%</td>
</tr>
<tr>
<td>2.1.22a</td>
<td>CH₂Ph</td>
<td>73%</td>
</tr>
<tr>
<td>2.1.22b</td>
<td>CH₂(2-Ph)Ph</td>
<td>87%</td>
</tr>
<tr>
<td>2.1.22c</td>
<td>CH₂Furyl</td>
<td>65%</td>
</tr>
<tr>
<td>2.1.22d</td>
<td>CH₂CH=CHCH=CHCH₃</td>
<td>67%</td>
</tr>
</tbody>
</table>

Imidazolines (2.1.22a), (2.1.22b) and (2.1.22c) were synthesised because of the reported hypoglycemic activity exhibited by 2-imidazoline derivatives with bulky aryl and heterocyclic groups located at a distance of two carbon units from position 2 in the imidazoline ring.⁸⁰ Compounds (2.1.22c) and (2.1.22d) contain diene functionalities at C(2) and are precursors to the proposed templates for intramolecular Diels-Alder reactions.

A small amount of the dialkylated imidazoline (2.1.23a) was isolated when excess (1.3 equiv.) of sec-butyllithium was added to 1-Boc-2-methyl-2-imidazoline (2.1.19), followed by 3-bromopropene. In order to exploit this result and to test whether formation of C(2α)-dialkylated 2-imidazolines can be achieved in one pot, a reaction was carried out with 1-Boc-2-methyl-2-imidazoline using 2.2 equiv. of sec-butyllithium under the usual conditions followed by quenching with 2.2 equiv. of 3-bromopropene. The reaction produced the dialkylated compound (2.1.23a) in 22% yield and the monoalkylated product (2.1.21a) in 56% yield. The overall yield for the dialkylated imidazoline (2.1.23a) was increased when it was synthesised in two steps from the 2-methyl compound, by
metallation of (2.1.21a) with sec-butyllithium in THF/TMEDA at -78°C and quenching with freshly distilled 3-bromopropene (Scheme 2.1.16).

![Scheme 2.1.16](image)

Compound (2.1.23c) was prepared in the same way from (2.1.21a) and benzyl bromide. Imidazoline (2.1.23b) was again synthesised from (2.1.21b) and 3-bromopropene in good yield over two steps. Attempts to introduce a third group onto C(2α) in imidazoline (2.1.23a) failed. Presumably the C(2α) position is now too hindered and the electrophile cannot approach. Table 2.1.3 shows the dialkylated 1-Boc-2-imidazolines (2.1.23a-c).

<table>
<thead>
<tr>
<th>compound</th>
<th>R^1</th>
<th>R^2</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.23a</td>
<td>CH2CH=CH2</td>
<td>CH2CH=CH2</td>
<td>22% one pot</td>
</tr>
<tr>
<td>2.1.23a</td>
<td>CH2CH=CH2</td>
<td>CH2CH=CH2</td>
<td>84%</td>
</tr>
<tr>
<td>2.1.23b</td>
<td>CH2CH=CH2</td>
<td>CH2=CH2</td>
<td>87%</td>
</tr>
<tr>
<td>2.1.23c</td>
<td>CH2CH=CH2</td>
<td>CH2Ph</td>
<td>76%</td>
</tr>
</tbody>
</table>

Deprotection of the 2-(α-dialkyl)-1-tert-butyloxycarbonyl-2-imidazolines (2.1.23a-c) with trifluoroacetic acid followed by washing with a 10% w/v solution of aqueous NaOH affords the C(2α)-dialkylated-2-imidazolines (2.1.24a-c) (Table 2.1.4).
The Boc group thus provides a general and robust solution to the N-protection of 2-imidazolines during lithiation-alkylation studies.

2.1.4 Synthesis of 2-(2-oxoalkyl)-2-imidazolines

The varied biological activities shown by many 2-imidazolines and the possible uses of the 1-Boc-2-lithiomethyl-2-imidazoline in carbon-carbon forming processes led us to explore the C-acylation which would provide a route to the synthesis of 2-(2-oxoalkyl)-2-imidazolines. 2-(2-oxoalkyl)-2-imidazolines have been synthesised by treatment of ketene N,O-acetals, or imino esters derived from benzoyl, and ester-substituted acetonitriles, with 1,2-diamines (Scheme 2.1.17).\textsuperscript{81}

\[
\text{ArCOCH}_2\text{NH.HCl} \quad \text{H}_2\text{N} \quad \rightarrow \quad \text{HN} \quad \text{O} \quad \text{Ar}
\]

\[\text{2.1.26} \quad \text{2.1.27} \quad \text{2.1.28}\]

Scheme 2.1.17

Related compounds had been previously made in our group by reaction of C(2\(\alpha\))-metallated 1-benzyl-2-imidazolines with carboxylic acid esters, but the N-benzyl group was
These compounds were assigned to exist as their imino-enol tautomer (2.1.29b). An X-ray structure in this series, however, was unable to locate the exchangeable hydrogen atom.

The use of the Boc group as 2-imidazoline N-protection should allow the synthesis of 2-(2-oxoalkyl)-2-imidazolines with no N-substituent and provide an alternative route to such compounds. In an initial attempt to synthesise these compounds, the reaction of 1-Boc-2-lithiomethyl-2-imidazoline with propenoyl chloride was investigated. This produces a yellow polymeric material due to the extreme reactivity of propenoyl chloride, which appears to undergo polymerisation under the reaction conditions. In order to circumvent this problem the reaction was repeated and this time the 1-Boc-2-lithiomethyl-2-imidazoline was quenched with methyl propenoate to afford the desired 2-(2-oxoalkyl)-2-imidazoline (2.1.30c) in 42% yield (Scheme 2.1.19). It is possible that the presence of the double bond in methyl propenoate could be responsible for the low yield obtained. On the other hand the reaction of 1-Boc-2-methyl-2-imidazoline with ethyl acetate and methyl benzoate proceeded smoothly to give compounds (2.1.30a) and (2.1.30b) in 72% and 64% yield respectively as white crystalline solids (Scheme 2.1.19).
It appears that these compounds (2.1.30a-c) exist in their enaminoketone form based on evidence from IR, $^1H$ and $^{13}C$ NMR spectra. Both compounds displayed in their I.R. spectra (KBr discs) sharp bands corresponding to a hydrogen bonded NH (3253 and 3245 cm$^{-1}$) and carbonyl stretching bands at around 1600 cm$^{-1}$ characteristic of a vinylogous amide. The $^1H$ NMR spectra exhibited a one proton vinyl resonance and a broad one proton signal (NH) at 9.5 ppm typical of hydrogen bonded NH. The $^{13}C$ NMR spectra showed signals at 186.3 and 195.6 ppm which correspond to two carbonyl groups.

To support these conclusions a crystal structure was obtained on compound (2.1.30b), which was recrystallised from hexane-methanol, and confirmed the proposed structure (Figure 2.1.1). For x-ray bond lengths and angles of compound (2.1.30b) see appendix.
It can be seen from the crystal structure that the compound exists in its enamine form with one vinyl hydrogen and an NH. Intramolecular hydrogen bonding is indicated by the proximity (1.94 Å) of the NH and keto carbonyl. This sets the enamine with the bulky phenyl and Boc groups anti to each other. The spectral data obtained are very similar to the 1-benzyl compounds (2.1.29) and the structures formerly assigned as enol-imines should probably be revised to the enamino-ketones tautomers.\textsuperscript{82}

Deprotection of (2.1.30a) and (2.1.30b) using acidic conditions (TFA) proceeded smoothly to give the desired products (2.1.31a) and (2.1.31b) in 81% and 89% yields, respectively. They also exist in their enamine form (Scheme 2.1.19) based on the evidence from \textsuperscript{1}H and \textsuperscript{13}C NMR spectroscopy. Hydrogen bonding between the carbonyl oxygen and an NH is also present.

2.1.5 Synthesis of 2-alkenyl-2-imidazolines

We wished to extend this work to produce 2-alkenyl-2-imidazolines in order to examine their potential as acceptors in conjugate additions,\textsuperscript{83} and as dienes and dienophiles in Diels-Alder reactions. They were also of interest to us because of their reported
biological activities, e.g. anthelmintic\textsuperscript{84} or hypoglycemic.\textsuperscript{85} It was anticipated that the incorporation of a heteroatom at the $\alpha$-carbon of 1-Boc-2-methyl-2-imidazoline would provide a good route to the desired 2-alkenyl-2-imidazolines. Other methods used for the synthesis of 2-alkenyl-2-imidazolines were long and the conditions used were rather harsh (high temperatures).\textsuperscript{86}

1-Boc-2-Methyl-2-imidazoline (2.1.19) was treated with 1.1 equiv of sec-butyllithium followed by diethyl chlorophosphate (1.1 equiv.) and quenching with water afforded phosphonate (2.1.32) in 50\% yield. The pure compound was isolated after column chromatography along with some unidentified impurities. Attempts to improve the yield and quality of (2.1.32) proved unsuccessful. The phosphonylated compound (2.1.32) was then lithiated with 1.1 equiv. of sec-butyllithium and the phosphonate salt produced was quenched at -78\degree C with butanal, 2-butenal and benzaldehyde. After allowing the reaction to warm up to 25\degree C overnight, the 2-alkenyl-1-Boc-2-imidazolines (2.1.33a-c) were isolated after column chromatography on silica gel in 67\%, 65\% and 66\% yield (Scheme 2.1.20). Benzaldehyde and 2-butenal gave only the $E$ alkenes whereas when butanal was the carbonyl component both $E$ and $Z$ isomers were obtained initially in a 2:1 ratio. The $Z$ isomer slowly converts to the thermodynamically more stable $E$ isomer upon standing at 25\degree C for a few days. The preparation of 2-alkenyl-1-Boc-2-imidazolines (2.1.33a-c) was also carried out in one pot from 1-Boc-2-methyl-2-imidazoline (2.1.19), thus making the synthesis even shorter. sec-Butyllithium (1.1. equiv.) was added to 1-Boc-2-methyl-2-imidazoline (2.1.19) followed by addition of diethyl chlorophosphate at -78\degree C and the reaction mixture was stirred at that temperature for 1h. A further 1.1 equiv. of sec-butyllithium was injected at -78\degree C and the orange anion produced was quenched with freshly distilled aldehydes. Work up and column chromatography afforded the desired compounds (2.1.330a-c) in comparable overall yields (33\%, 32\% and 40\%) to the two-step sequence.
When deprotection of (2.1.33a), (2.1.33b) and (2.1.33c) with trifluoroacetic acid was followed by chromatography on silica gel the reactions failed to produce the desired products (2.1.34a), (2.1.34b) and (2.1.34c), respectively. Aqueous work up also led to decomposition of the material and was therefore avoided. It is suspected that one mode of decomposition is addition of water taking place on the column followed by a retro-aldol reaction possibly via the "retro-ene" pathway drawn in Scheme 2.1.21, as has been suggested earlier, although this is not proven.
This problem was overcome by carrying out the chromatography on alumina (activation grade III) eluting with 3:97 v/v isopropylamine:ethyl acetate. The basic conditions that were used to carry out the column are also sufficient to liberate the free imidazoline from the trifluoroacetate salt. The desired products (2.1.34a-c) were obtained in 82%, 64% and 91% yield respectively. 2-(Pent-1-enyl)-2-imidazoline (2.1.34a) is extremely hygroscopic and appears to be decomposing at room temperature. 2-(2-Phenylethenyl)-2-imidazoline (2.1.34c) appears to be the most stable. The conjugation through the phenyl group presumably provides extra stability.

A second approach to 2-alkenyl-2-imidazolines was also investigated. It was anticipated that the insertion of a sulfur or selenium atom at the α-carbon atom of 1-Boc-2-methyl-2-imidazoline, followed by C-alkylation, selenium or sulfur oxidation and elimination would produce the desired 2-alkenyl-2-imidazolines. This approach had been unsuccessful in the N-benzyl series.

The reaction of the 2-lithiomethyl-1-Boc-2-imidazoline (2.1.19) with diphenyl disulfide produced both monosulfenated and disulfenated products (2.1.36) and (2.1.37) in 38% and 28% yield, respectively (Scheme 2.1.22). The monosulfenated imidazoline was deprotected using the usual conditions (TFA) to give (2.1.37), which is a compound that has been tested for activity in mice against the nematode *Nematospordoides dubius*.
Consistent with this result, the reaction of the 2-methyl-1-Boc-2-imidazoline (2.1.19) with diphenyl diselenide produced phenylselenenomethyl derivative (2.1.38) in 52% yield and diselenenated product (2.1.39) in 8% yield (Scheme 2.1.23). The disubstituted products could be formed because the insertion of one heteroatom makes the α carbon more acidic and proton exchange between the 2-lithiomethyl compound and the monosubstitution product allows a second substitution to compete.
The ability of selenium to stabilise adjacent negative charges and the weakness of the Se-C bond, as well as the ease with which selenides undergo oxidation to selenoxides with subsequent facile selenoxide syn-elimination (often at room temperature or below), compared to the more vigorous conditions required for sulfoxide elimination (often at reflux in toluene), directed our attention towards the monoselenenated compound (2.1.38) as our starting material for the synthesis of 2-alkenyl-2-imidazolines.

Insertion of an alkyl group onto (2.1.38) at the α-carbon was easily achieved. Lithiation of (2.1.38) in the usual way (sec-BuLi, THF/TMEDA, -78°C) gave the lithio(phenylselenenomethyl)-2-imidazoline; addition of an alkyl halide (benzyl bromide, 1-iodopropane and 3-bromopropene) produced compounds (2.1.40a-c) in good yields.
(79%, 80%, 90%) (Scheme 2.1.23). The $^1$H NMR spectra of all these compounds (2.1.40a-c) show a CH signal which appears to exist as a broad singlet rather than a triplet or double doublet.

Oxidation of compound (2.1.40a) was attempted with 3-chloroperbenzoic acid in dichloromethane at 0°C, in order to generate a selenoxide and hence achieve selenoxide elimination. This produced only starting material and some unidentified impurities.

Instead deprotection (removal of the Boc group) with neat trifluoroacetic acid produced the 2-imidazolines (2.1.41a), (2.1.41b) and (2.1.41c) in 71%, 91%, and 80% yield, respectively (Scheme 2.1.23). Oxidation with 3-chloroperbenzoic acid in dichloromethane at 0°C followed by column chromatography on alumina now produced the desired 2-alkenyl-2-imidazolines (2.1.42a-c) in 90%, 92% and 92% yield, respectively (Scheme 2.1.23), presumably via selenoxide formation and spontaneous elimination. Aqueous work up and chromatography on silica gel were again avoided to prevent hydrolysis of these compounds.

When we attempted to introduced a second alkyl group onto imidazoline (2.1.40c) by treatment with 1.1. equiv of sec-butyllithium followed by addition of 3-bromopropene, the dialkylated imidazoline (2.1.24a) was obtained in 60% yield (Scheme 2.1.24). No trace of the expected product (2.1.43) was observed. A transmetallation reaction of the selenide must have occurred. The resulting lithioalkylimidazoline (2.1.44) was then trapped with 3-bromoprop-1-ene to give the observed compound (2.1.24a). Such transmetallation reactions of selenides have been reported in the literature. 88
This concluded our survey of the reactivity of 1-Boc-2-methyl-2-imidazoline in lithiation reactions.

### 2.2 Reactions of 2-imidazolines with double electrophiles

#### 2.2.1 Synthesis of tetrahydroimidazo[1,2-\(a\)]pyridines

A new and reliable protocol has been developed for the synthesis of 2-substituted 2-imidazolines that contain a diene or a potential dienophile at the C(2)-position for the proposed Diels-Alder reactions. A method to introduce a diene onto the nitrogen centre was needed in order to synthesise the target template (1.159) which was expected to undergo intramolecular Diels-Alder reaction. This system, if it were to undergo Diels-Alder reaction could, after cleavage of the imidazoline template, provide the tetrahydroquinoline moiety.
It was anticipated that 2-(but-3-enyl)-2-imidazoline (2.1.4) when heated with 2-butenal in toluene at reflux, under Dean-Stark conditions for water removal, would provide the dienamine (1.159).

\[
\begin{align*}
\text{N} & \quad \text{NH} \\
\text{2.1.4} & \quad \begin{array}{c}
\text{Toluene} \\
\text{Reflux}
\end{array}
\end{align*}
\]

Scheme 2.2.1

A reaction was indeed observed but no trace of the expected compound was isolated. The only product that was isolated was the tetrahydroimidazo[1,2-\(\alpha\)]pyridine (2.2.1) in 36% yield.

\[
\begin{align*}
\text{N} & \quad \text{NH} \\
\text{2.1.4} & \quad \begin{array}{c}
\text{Toluene} \\
\text{Reflux}
\end{array}
\end{align*}
\]

Scheme 2.2.2

The structure of bicycle (2.2.1) is supported by \(^1\)H and \(^13\)C NMR spectra; for example there are signals consistent with the C=CH (doublet of doublets) and NCH fragments, that would not be present in alternative isomers arising from the reaction of (2.1.4) with but-2-enal with the opposite regiochemistry that would contain two alkenic signals and no NCH signal.

The most likely mechanism for the formation of the annulation products (2.2.5) is conjugate addition of the imidazoline NH to the aldehyde double bond, followed by an enamine-aldol reaction of C(2\(\alpha\)) as a nucleophile, with dehydration (Scheme 2.2.3).
The opposite order of bond formation could not be ruled out at this stage, although results reported later in this thesis support initial conjugate addition by the nitrogen atom. It is possible that the enamine does a nucleophilic attack on the carbonyl group to initiate the annulation but dehydration would have to occur at this stage to allow subsequent N(1) addition on the double bond. It seems unlikely that the reaction proceeds via the latter route.

The reaction can be rationalised if we consider the terms “hard” and “soft” acids and bases. The 2-alkyl-2-imidazolines are soft bases as the lone pair of electron is delocalised between the two nitrogen atoms (Scheme 2.2.4). α,β-Unsaturated carbonyl compounds have a hard electrophilic centre at the carbonyl carbon and a soft electrophilic centre at the β-carbon. Soft bases such as imidazolines react with soft electrophiles in a Michael-type addition.
Due to the pharmaceutical activities displayed by many heteropolycyclic compounds, it was of interest to us to investigate the applicability of the observed reaction. It was therefore repeated with a range of 2-alkyl-2-imidazolines, namely 2-butyl, 2-(but-3-enyl), 2-(2-phenylethyl), 2-[2-(2-phenyl)phenylethyl] and 2-benzyl-2-imidazolines. The \(\alpha,\beta\)-unsaturated aldehydes were 2-butenal, pent-2-enal and 3-phenylprop-2-enal. The same annulation reaction was observed in all cases to afford tetrahydroimidazopyridines (2.2.5; \(R^2=H\)) (Table 2.2.1). 3-Phenylprop-2-enal reacted with 2-(but-3-enyl)-2-imidazoline to some extent to give the tetrahydroimidazo[1,2-\(a\)]pyridines (2.2.5b) in only 13% yield. The bulky phenyl group could be held responsible for the low yield by hindering the approach of the 2-imidazoline to the double bond.

2-Benzyl-2-imidazoline reacted with but-2-enal under the same conditions to produce a 2:1 mixture of the tetrahydroimidazo[1,2-\(a\)]pyridines (2.2.5l) and the alcohol (2.2.6a) in 46% yield (Scheme 2.2.5). Some of the pure alcohol was isolated after careful chromatography in 37% yield. The stereochemistry of alcohol (2.2.6a) has not been determined. The tetrahydroimidazo[1,2-\(a\)]pyridine (2.2.5l) was isolated after extended reflux in toluene in 33% yield. Although compound (2.2.5l) appeared to be pure by \(^1\)H and \(^{13}\)C NMR spectroscopy, mass spectroscopy showed a higher molecular weight impurity that did not allow us to fully characterised the compound. Extended reflux appears lead to slow decomposition of the compound. The conjugation with the phenyl ring stabilises the enamine form and inhibits the elimination of water that was proposed as the final step of the annulation (Scheme 2.2.3), making the synthesis of (2.2.5l) more difficult.
2-Benzyl-2-imidazoline reacted with pent-2-enal under extensive reflux to give only the tetrahydroimidazo[1,2-α]pyridine (2.2.5) in 15% yield. The intermediate alcohol was never isolated in this particular case. The extended reflux led to slow decomposition of the compound which could explain the low yield obtained.

The reaction of the 2-alkyl-2-imidazolines with α,β-unsaturated ketones was also investigated. But-3-en-2-one and pent-3-en-2-one reacted with 2-alkyl-2-imidazolines in the same fashion (Scheme 2.2.3, \( R^3 \neq H \)) to produce tetrahydroimidazo[1,2-α]pyridines (2.2.5) (Table 2.2.1).

Table 2.2.1

<table>
<thead>
<tr>
<th>imidazoline</th>
<th>( R^1 )</th>
<th>( R^2 )</th>
<th>( R^3 )</th>
<th>Imidazo[1,2-α]pyridine (yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.15</td>
<td>CH(_2)CH(_2)CH(_3)</td>
<td>Me</td>
<td>H</td>
<td>2.2.5a 64%</td>
</tr>
<tr>
<td>2.1.4</td>
<td>CH(_2)CH=CH(_2)</td>
<td>Me</td>
<td>H</td>
<td>2.2.1 36%</td>
</tr>
<tr>
<td>2.1.4</td>
<td>CH(_2)CH=CH(_2)</td>
<td>Ph</td>
<td>H</td>
<td>2.2.5b 13%</td>
</tr>
<tr>
<td>2.1.4</td>
<td>CH(_2)Ph</td>
<td>Me</td>
<td>H</td>
<td>2.2.5c 85%</td>
</tr>
<tr>
<td>2.1.22a</td>
<td>CII(_2)Ph</td>
<td>CH(_2)Me</td>
<td>H</td>
<td>2.2.5d 91%</td>
</tr>
<tr>
<td>2.1.22a</td>
<td>CH(_2)Ph</td>
<td>H</td>
<td>Me</td>
<td>2.2.5e 38%</td>
</tr>
<tr>
<td>2.1.22b</td>
<td>2-PhC(_6)H(_4)CH(_2)</td>
<td>Me</td>
<td>H</td>
<td>2.2.5f 90%</td>
</tr>
<tr>
<td>2.1.22b</td>
<td>2-PhC(_6)H(_4)CH(_2)</td>
<td>CH(_2)Me</td>
<td>H</td>
<td>2.2.5g 85%</td>
</tr>
<tr>
<td>2.1.22b</td>
<td>2-PhC(_6)H(_4)CH(_2)</td>
<td>H</td>
<td>Me</td>
<td>2.2.5h 66%</td>
</tr>
<tr>
<td>2.1.22b</td>
<td>2-PhC(_6)H(_4)CH(_2)</td>
<td>Me</td>
<td>Me</td>
<td>2.2.5i 55%</td>
</tr>
<tr>
<td>2.1.7</td>
<td>Ph</td>
<td>CH(_2)Me</td>
<td>H</td>
<td>2.2.5j 15%</td>
</tr>
<tr>
<td>2.1.7</td>
<td>Ph</td>
<td>H</td>
<td>Me</td>
<td>2.2.5k 88%</td>
</tr>
<tr>
<td>2.1.7</td>
<td>Ph</td>
<td>Me</td>
<td>H</td>
<td>2.2.5l 33%</td>
</tr>
<tr>
<td>2.1.7</td>
<td>Ph</td>
<td>Me</td>
<td>Me</td>
<td>2.2.5m 86%</td>
</tr>
</tbody>
</table>
In order to further investigate the sequence of bond formations in this annulation, some more experiments were carried out. 2-(But-3-enyl)-2-imidazoline was treated with but-2-enal in dichloromethane at 20°C in the presence of MgSO₄ and the intermediate alcohol (2.2.4a) was isolated in 27% yield which appears to exist in the imine form (Scheme 2.2.3). Similarly when 2-benzyl-2-imidazoline was reacted with but-3-en-2-one at 20°C in dichloromethane the intermediate alcohol (2.2.4) precipitated out of solution as a white solid (42%). The white solid was filtered and the reaction mixture was purified by column chromatography to give only the dehydration product (2.2.5m) (21%). This alcohol is only soluble in warm methanol and ¹H NMR spectroscopy suggests that exists in equilibrium between its imine and enamine form (2.2.4a) and (2.2.4b). The equilibrium changes with time and the dehydrated product (2.2.5m) begins to form. Taken with the earlier findings using 2-benzyl-2-imidazolines, these results are supportive of the initially proposed mechanism but not conclusive.

This cyclocondensation reaction of 2-alkyl-2-imidazolines with α,β-unsaturated aldehydes and ketones has not been reported before. It is in contrast with the reactions of enaminoester (2.2.7) with α,β-unsaturated aldehydes and ketones. This enaminoester can be regarded as an imidazoline carrying an activating ethoxycarbonyl group at C(2α). With α,β-unsaturated aldehydes and ketones the reactivity of (2.2.7) is dominated by conjugate addition of the enamine C(α) carbon atom to the carbonyl component (Scheme 2.2.6). α,β-Enals afford the imidazo[1,2-a]pyridines (2.2.8),⁸⁹ enones give the Michael adducts (2.2.9) but do not proceed to cyclisation.⁹⁰ The regiochemistry of the initial reaction and eventual annulation with the enaminoester is thus opposite to that observed with simple 2-alkyl-2-imidazolines.
2.2.2 2-Imidazolines in conjugate additions

As supportive evidence to the mechanism proposed above for the reaction with $\alpha,\beta$-unsaturated aldehydes and ketones, the reaction of 2-imidazolines with other unsaturated compounds conjugated with electron withdrawing groups was also investigated. 2-Benzyl-2-imidazoline (2.1.7) and methyl propenoate react to give the conjugate addition product (2.2.10) in 82% yield, when mixed in a concentrated solution of dichloromethane (Scheme 2.2.7). In a similar fashion 2-benzyl and 2-(but-3-enyl)-2-imidazolines react with phenyl vinyl sulfonate and phenyl vinyl sulfone in dichloromethene to give the conjugate addition products (2.2.11a-d) as colourless oils in 89%, 75%, 70% and 57% yield, respectively (Scheme 2.2.7).
The above observations reinforce the proposed annulation mechanism that the 2-imidazoline adds first via a nitrogen atom to the double bond of the \( \alpha,\beta \)-unsaturated carbonyls. Related results using alkynes conjugated to withdrawing groups have also been observed; these results are discussed separately, later in this thesis (Section 2.4).

It was anticipated that the ester (2.2.10) might undergo cyclisation (via enamine formation) upon heating in the presence of p-toluenesulfonic acid to give bicycle (2.2.12) (Scheme 2.2.7). Unfortunately the reverse of the conjugate addition reaction was observed after heating to reflux in toluene. 2-Benzyl-2-imidazoline was the only product isolated in a very low yield. The effect of base on the ester (2.2.10) was also studied. Sodium methoxide (2 equiv.) was added to a solution of (2.2.10) in dry methanol but again no cyclised product was observed. A stronger base such as sec-butyllithium (1 equiv.) was used which also failed to give the desired compound. Only when 2 equiv. of sec-butyllithium were added to (2.2.12) was cyclisation achieved, but in only 34% yield. This compound appears to exist in its enamine form. A broad NH peak at 4.85 ppm and the disappearance of the \( \alpha \)-CH in the \( ^1 \)H NMR spectrum suggest the compound favours the enamine form. Evidence from the I.R. spectrum (KBr disc) that shows a broad NH peak at 3200 cm\(^{-1} \) and the broad
vinyllogous amide CO stretching band at 1563 cm\(^{-1}\), combined with that from the \(^{13}\)C NMR spectrum that exhibits a carbonyl carbon resonance at 185.7 ppm, characteristic of a carbonyl group rather than an enol, indicates that the enaminoketone form is predominant. The result agrees with the tautomer observed in the 2-(oxoalkyl)-2-imidazolines (Section 2.1.4).

The presence of the ester functionality on imidazoline (2.2.10) and the desire to form a variety of fused 2-imidazolines prompted us to reduce the ester to the alcohol (2.2.13). Treatment of (2.2.10) with 2-equiv. of LiAlH\(_4\) afforded the alcohol (2.2.13) in 55\% yield (Scheme 2.2.8).

The alcohol was then converted into the mesylate (2.2.14) using triethylamine and methanesulfonyl chloride (1.1 equiv.) compound at 20°C in 52\% yield. This conversion proved to be problematic since it produced unidentified mixtures when excess of methanesulfonyl chloride was used, or when aqueous work up was carried out. Although the \(^1\)H NMR spectrum supported the structure, mass spectroscopy did not show the expected molecular ion; we did not pursue cyclisation of the putative mesylate (2.2.14).

2.2.3 Tetrahydroimidazo[1,2-a]pyridin-5-ones

The cyclisation reported in the previous section 2.2.1 prompted us to study the reaction of 2-alkyl-2-imidazolines with different 1,3-bis-electrophiles such as \(\beta\)-ketoesters in order to gain a better understanding of the behaviour of 2-imidazolines and their
synthetic utility for the synthesis of heterocyclic systems such as those containing the reduced pyridine moiety. Dihydropyridines have shown coronary vasodilator activity\textsuperscript{91} and are the most potent calcium channel blockers\textsuperscript{92} and it was in our interest to incorporate the reduced pyridine moiety on the 2-imidazoline molecule in an effort to combine their biological properties.

It was initially expected that the reaction between a 2-imidazoline and \( \beta \)-ketoester would proceed via formation of the intermediate enaminoketone (2.2.15) which could tautomerise to the enediamine (2.2.16). The intramolecular acylation of (2.2.16) accompanied by loss of ethoxide and a proton shift (2.2.17) would have resulted in the formation of the tetrahydroimidazo[1,2-\( a \)]pyridin-7-ones (2.2.18) (Scheme 2.2.9).\textsuperscript{93}

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) \{\includegraphics[width=\textwidth]{scheme.png}\};
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.2.9}

A number of 2-alkyl-2-imidazolines, prepared using the method described in Section 2.1.3, were reacted with ethyl acetoacetate, ethyl benzoylacacetate and ethyl cyclohexanone-2-carboxylate in refluxing toluene using a Dean-Stark trap to give what were initially thought to be tetrahydroimidazo[1,2-\( a \)]pyridin-7-ones (2.2.18) as high melting solids. In fact it was found that the reaction proceeds via the alternative
regiochemistry to afford 1,2,3,5-tetrahydroimidazo[1,2-a]pyridin-5-ones (2.2.19) and (2.2.20) (Table 2.2.2 and Scheme 2.2.10).

![Scheme 2.2.10](image)

**Table 2.2.2**

<table>
<thead>
<tr>
<th>Imidazoline</th>
<th>R¹</th>
<th>R²</th>
<th>Imidazo[1,2-a]pyridin-5-one 2.2.19 or 2.2.20 (%yield)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.4</td>
<td>CH₂CH=CH₂</td>
<td>Me</td>
<td>2.2.19a (44%)</td>
</tr>
<tr>
<td>2.1.4</td>
<td>CH₂CH=CH₂</td>
<td>Ph</td>
<td>2.2.19b (86%)</td>
</tr>
<tr>
<td>2.1.22a</td>
<td>CH₂Ph</td>
<td>Ph</td>
<td>2.2.19c (75%)</td>
</tr>
<tr>
<td>2.1.7</td>
<td>Ph</td>
<td>Me</td>
<td>2.2.19d (56%)</td>
</tr>
<tr>
<td>2.1.7</td>
<td>Ph</td>
<td>Ph</td>
<td>2.2.19e (58%)</td>
</tr>
<tr>
<td>2.1.22a</td>
<td>CH₂Ph</td>
<td></td>
<td>2.2.20a (75%)</td>
</tr>
<tr>
<td>2.1.22b</td>
<td>2-PhC₆H₄CH₂</td>
<td></td>
<td>2.2.20b (88%)</td>
</tr>
<tr>
<td>2.1.7</td>
<td>Ph</td>
<td></td>
<td>2.2.20c (66%)</td>
</tr>
</tbody>
</table>

It is not clear whether N-acylation occurs first followed by enamine-aldol condensation or *vice versa*. Enamine or imine formation is generally a reversible process and although in this case it may be the kinetic pathway (a), under the reaction conditions it
may be reversed and the imidazoline NH react with the ester to form the more stable amide bond (pathway b) (Scheme 2.2.11). Intramolecular enamine-aldol condensation would then give then the 1,2,3,5-tetrahydroimidazo[1,2-\(a\)]pyridin-5-ones (2.2.19). No intermediates have been isolated to support either of the two pathways.

Scheme 2.2.11

The regiochemical assignment of (2.2.19a-e) and (2.2.20a-c) was based on \(^1\)H n.O.e experiments carried out on molecules (2.2.19a) and (2.2.19d). In both cases irradiation of the alkenyl-\(\text{CH}_3\) gave enhancement of the pyridone alkenyl CH and a smaller enhancement of the adjacent vinyl or aromatic group.
Irradiation of the pyridone alkenyl CH in compound (2.2.19a) gave enhancement of the methyl signal (3.4%) (Figure 2.2.1). Irradiation of the alkenyl CH$_3$ in compound (2.2.19a) produced a 1.9% enhancement of the pyridone alkenyl CH signal and a 1.4% enhancement of the CH$_2$ of the adjacent allyl group. When the allyl CH$_2$ was irradiated enhancement of 3.2% of the methyl group was observed. These results prove that the allyl and methyl groups are adjacent to each other. The irradiation of each of the "diaminoethane" backbone methylene signals resulted in enhancement of the other (7.9% and 6.8%).

In agreement with these results, the $^1$H n.O.e.experiments carried out on imidazo[1,2-a]pyridin-5-one (2.2.19c) revealed the same interactions and support the same regiochemistry (Figure 2.2.2).

Irradiation of the alkenyl CH$_3$ in compound (2.2.19c) produced a 3.3% enhancement of the alkenyl CH signal and a 2.8% enhancement of the aromatic protons, confirming that the methyl and phenyl substituents are adjacent, which would not be the case in the 7-keto regioisomer. Irradiation of the alkenyl CH gave enhancement of the methyl signal (6.2%). The irradiation of each of the backbone methylene signals resulted in enhancement of the other (7.3% and 6.5%). Nonetheless no enhancement of the methyl
signal was observed upon irradiation of the backbone methylene signals, something that would have been expected if the opposite regiochemistry was present.

<table>
<thead>
<tr>
<th>Irradiated</th>
<th>Enhanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH</td>
<td>Me (6.2%)</td>
</tr>
<tr>
<td>Me</td>
<td>CH (3.3%), Ph(CHs) (2.8%)</td>
</tr>
<tr>
<td>HNCH₂</td>
<td>NCH₂ (7.3%), NH (2.1%)</td>
</tr>
<tr>
<td>NCH₂</td>
<td>HNCH₂ (6.5%)</td>
</tr>
</tbody>
</table>

**Figure 2.2.2**

In addition compounds (2.2.19) and (2.2.20) exhibit more extended conjugation in the UV spectrum ($\lambda_{\text{max}}=330-340$ nm). The possible paths for delocalisation of the electrons (a and b) around the ring gives these molecules a pseudoaromatic character (Scheme 2.2.12) and higher $\lambda_{\text{max}}$ than would be expected for the 7-keto regioisomers.

**Scheme 2.2.12**

A single crystal X-ray diffraction study was performed on the tricyclic compound (2.2.20c) which was recrystallised from water-ethanol (Figure 2.2.3). The crystal structure confirmed the regiochemistry that had been deduced from the spectroscopic data. The amide bond is present as predicted from the n.O.e. studies reported above. The bond lengths and angles for the x-ray are given in the appendix.
The regiochemistry of these tetrahydroimidazo[1,2-a]pyridin-5-ones (2.2.19a-e) and (2.2.20) is the same as that reported for the major product (2.2.21) from the reaction of the enaminoester (2.2.7) with β-ketoesters (Scheme 2.2.13).94

![Reaction Scheme](image)

Scheme 2.2.13

Reduction of compounds (2.2.20a-c) would provide the hydroisoquinoline moiety that occurs in the yohimbine alkaloids (Scheme 2.2.14).95 Attempts to hydrogenate compound (2.2.20c) produced starting material. Treatment with excess LiAlH₄ failed to reduced the amide bond even in THF at reflux. The pseudoaromatic character exhibited by compounds (2.219a-e) and (2.2.20) makes their reduction difficult. Alternative ways to reduce this system were not pursued due to lack of time.
2.3 Imidazolines in Diels-Alder reactions studies

2.3.1 Studies towards the synthesis of N-butadienyl-2-imidazolines and their use in intramolecular Diels-Alder reactions

When the approach to dienamine (1.159) from 2-(but-3-enyl)-2-imidazoline (2.1.4) and butenal failed, an alternative route was attempted. The reaction of (2.1.4) and 4,4-diethoxy-1-butene could produce the desired product (1.159). Unfortunately when the two materials were heated to reflux in toluene in the presence of p-toluenesulfonic acid under Dean-Stark conditions no product was isolated but only starting material (Scheme 2.3.1).

A different method for the synthesis of N-butadienyl-2-imidazolines had to be devised. The addition of primary or secondary amines to ethynyl ketones (2.3.1) is a well reported reaction in the literature. This smooth reaction which occurs at room temperature leads to β-aminoethylenic ketones (2.3.2) (Scheme 2.3.2.)
Even in compounds in which the double and triple bonds are cross conjugated with the carbonyl group such as in (2.3.3) the addition reaction is restricted solely to the triple bond even with excess of amine (Scheme 2.3.3).96

This reaction was an attractive alternative for the synthesis of the target dienamine. In a similar fashion 2-(but-3-enyl)-2-imidazoline (2.1.4) reacted with butynone in dry methanol at room temperature to produce solely the $E$-isomer of imidazoline (2.3.4) in 89% yield (Scheme 2.3.4).

Imidazoline (2.3.4) could in principle undergo a hetero-Diels-Alder reaction under the right conditions. The compound was heated in toluene for 48 h, but no cyclisation was observed (Scheme 2.3.5). The effect of a Lewis acid such as BF$_3$-etherate was briefly investigated but this appeared to have no particular effect. It possible that elevated temperatures or high pressure could facilitate cyclisation but the lack of suitable local facilities prohibited such investigations.
The conversion of the vinylogous amide (2.3.4) into the corresponding silyl enol ether (2.3.6) was attempted as it was felt this would lead to a very electron-rich diene. Lithium diisopropylamide (1.2 equiv), freshly prepared from n-butyllithium and diisopropylamine, was added to imidazoline (2.3.4) in THF at -78°C under nitrogen. The resulting suspension was quenched with trimethylsilyl chloride. Aqueous work up followed by chromatography did not produce the expected silyl enol ether (2.3.6) (Scheme 2.3.6) and starting material was recovered.

The reaction was repeated using 2.2 equiv. of LDA and 2 equiv. of trimethylsilyl chloride in an attempt to ensure enol ether formation. The aqueous work up was avoided in order to ensure that hydrolysis of the enol ether (2.3.6) did not occur. The solvent was removed under reduced pressure and the crude reaction mixture was dissolved in toluene and heated to reflux for 36 h. Consumption of the starting material occurred and the crude reaction mixture was purified by chromatography only to afford the 2-(but-3-enyl)-2-imidazoline (2.1.4) in 22% yield. No evidence of a Diels-Alder reaction was observed. In order to test whether the silyl enol ether was actually formed, an attempt was made to trap it with an electron-deficient dienophile such as methyl propenoate, but no Diels-Alder adduct was observed.
Disappointed by this result, it was decided to carry out some model studies on a more easily accessible molecule, in order to find out whether the synthesis of the target dienamine is possible and if so to investigate its reactivity. 2-Benzyl-2-imidazoline (2.1.7), a commercially available material, was reacted with butynone in dry methanol to give the \( E \)-vinylogous amide (2.3.7) as a white solid in 79% yield. This is an exothermic reaction and the temperature was kept below 40°C.

\[ \text{2.1.7} \rightarrow \text{2.3.7} \]

**Scheme 2.3.7**

We again attempted to form the silyl enol ether (2.3.8), under similar conditions, using 2.2 equiv. of LDA and quenching with 2.2 equiv. of TBDMS-Cl at -78°C. The crude \(^1\)H NMR spectrum showed consumption of the starting material but attempts to isolate the compound by carrying out chromatography on the crude reaction mixture, produced starting material (30%). Methyl propenoate was added to a solution of the reaction mixture in toluene and was heated to reflux in an attempt to trap the expected diene but also proved unsuccessful, resulting in starting material. It was not clear whether diene formation was achieved.

\[ \text{2.3.7} \rightarrow \text{X} \]

**Scheme 2.3.8**
An alternative approach to the diene was pursued. A possible Emmons-Wadsworth reaction between the vinylogous amide (2.3.7) and diethyl methylphosphonate would lead to the target dienamine. When 1 equiv. of diethyl methylphosphonate was used with sec-butyllithium as a base to generate the phosphonate anion (THF, -78°C), starting material was isolated. It was felt that the Emmons-Wadsworth reagent may be basic enough to abstract the proton at the C(2) position before reacting with the carbonyl group to give the desired dienamine (2.3.9). The reaction was repeated using 2 equiv. of diethyl methylphosphonate and 2.0 equiv. of n-butyllithium in order to ensure C(2) deprotonation as well as phosphonate anion formation. This resulted in disappearance of the starting material. Column chromatography of the crude reaction mixture produced a less polar spot. The \(^1H\) NMR spectrum revealed a mixture of materials that contained no new olefinic signals. The starting material signals were no longer observed, with the CH\(_3\) and PhCH\(_2\) signals disappearing and the alkenyl CH\(_2\)’s moving upfield. It was impossible to deduce the outcome of that reaction but it was clear that the expected diene was not produced.

Scheme 2.3.9

Addition of an organolithium reagent to the carbonyl group of (2.3.7) would produce an intermediate alcohol that could undergo dehydration to give the target dienamine. This type of addition to vinylogous amides has been reported to give in some cases 1,2-addition\(^97\) and in other cases 1,4-additions.\(^98\) When imidazoline (2.3.7) was treated with 2 equiv. of MeLi in THF at -78°C, the tertiary alcohol (2.3.10) was isolated as an impure material in 26% yield (Scheme 2.3.10). No further attempts were carried out to increase the yield.
Reduction of the carbonyl would provide an alternative approach to the target diename (2.3.12). Reductions of such vinylogous amides have been reported to give in some cases allylic alcohols and in other cases resulted in reduction of the double bond. In our case reduction of the imidazoline (2.3.7) with 2 equiv. of LiAlH$_4$ in THF proceeded smoothly and afforded the allyl alcohol (2.3.11) in 75% yield (Scheme 2.3.11). In an attempt to force the alcohol (2.3.11) to undergo dehydration, it was heated to reflux in toluene in the presence of p-toluenesulfonic acid. Consumption of the starting material occurred and a less polar spot appeared on the TLC plate. The only product isolated after column chromatography was 2-benzyl-2-imidazoline (2.1.7). The presence of water in the reaction mixture, either from the p-toluenesulfonic acid monohydrate or that produced from the dehydration of the alcohol (2.3.11), could be responsible for the enamine hydrolysis. It appears from that result that the allylic alcohol (2.3.11) is unstable under acidic conditions and easily hydrolyses to the starting material in the presence of water.
Frustrated by this result and being one step away from the desired N-butadienyl-2-imidazoline (2.3.12), an alternative synthesis was investigated. Conversion of the alcohol (2.3.11) to the mesylate (2.3.13) and elimination of the mesyl group would produce the desired product (2.3.12). When compound (2.3.11) was treated with triethylamine and methanesulfonyl chloride in dichloromethane, the reaction unfortunately proved problematic and did not produce the expected product (Scheme 2.3.11). Instead a complex mixture was obtained that had no signal resembling either the starting material, the expected product or the N-butadienyl-2-imidazoline (2.3.12). This result was consistent with the previous effort to form an imidazoline mesylate in Section 2.2.2. No other approach to the dienamine was pursued due to lack of time.

2.3.3 2-Imidazolines in intramolecular Diels-Alder studies

The previous section has focussed on attempts to connect a diene at N(1) of an imidazoline, to partner a dienophile at C(2). Frustrations in those attempts led to an alternative approach to substrates for intramolecular Diels-Alder reactions. It has been shown in Section 2.1.3 that a diene can be easily introduced at C(2). A method for the introduction of a dienophile at N(1) was required. Amines have been found to undergo conjugate additions to activated acetylenic esters to give either transoid or cisoid products. This reaction, if applicable to 2-imidazolines, could prove synthetically useful for the introduction of the required dienophile at N(1) and therefore make the synthesis of the imidazoline templates (1.163) possible.

A model reaction was carried out, using 2-benzyl-2-imidazoline (2.1.7) as a starting material in order to test whether 2-imidazolines can undergo conjugate additions to acetylenic esters. Indeed when methyl propynoate was added to a solution of 2-benzyl-2-imidazoline in dry methanol, an exothermic reaction occurred and the temperature was kept
below 40°C. The conjugate addition product (2.3.14) was isolated from the reaction mixture as a 2:1 ratio of separable Z:E geometric isomers in 65% yield.

![Scheme 2.3.12](attachment:image.png)

This model experiment proved that 2-imidazolines could easily undergo conjugate additions to the triple bond of alkynyl esters and produce the target templates. The main disadvantage of such systems is the ability of the imidazoline nitrogen to donate electrons to the double bond, deactivating the dienophile (Figure 2.3.1).

![Figure 2.3.1](attachment:image.png)

In a similar way imidazoline (2.1.22c), which contains a furan ring at C(2) that may be considered to be an electron-rich diene, reacted with methyl propynoate in dry methanol, to give compound (2.3.15) in a 2:1 ratio of separable Z:E isomers in 60% yield.

![Scheme 2.3.13](attachment:image.png)

This compound has the general structure of the initially proposed imidazoline templates that were suggested should undergo intramolecular Diels-Alder reaction. In an initial attempt to persuade these isomers (2.3.15) to undergo Diels-Alder reaction, they were heated to reflux in toluene for 18 h. No Diels-Alder adducts were observed but under
these conditions conversion of the Z-isomer to the thermodynamically more stable E-isomer occurred. Starting materials were also isolated when the reaction was carried out in a sealed tube at 150°C. It has been reported in the literature that Diels-Alder reactions of the furan ring are best performed under pressure.\textsuperscript{101} Experiments were performed at the University of Reading on both Z- and E-isomers of compound (2.3.15) at 19 kBar in dichloromethane which resulted in recovered starting materials unchanged except for the Z to E isomerisation.

The failure of that system to undergo intramolecular Diels-Alder reaction was attributed, at that particular time, to the ability of the furan cycloadducts to undergo retro-Diels-Alder reaction and revert to the starting material.

The introduction of an acyclic diene at the C(2) position would avoid this problem and enhance the possibility of a Diels-Alder reaction occurring. Imidazoline (2.1.22d) was reacted with methyl propynoate in dry methanol to give compound (2.3.16) as the separate Z:E isomers in a 2:1 ratio in 50% yield. Both Z- and E-isomers exist as a 3:1 mixture of heptadienyl-E,E,E,Z-isomers.

![Scheme 2.3.13](image)

The possibility of these two compounds (2.3.16a-b) undergoing Diels-Alder reaction under thermal conditions was investigated. When heated to reflux in toluene in a sealed tube at 150°C no reaction was observed. Lewis acids such as BF\textsubscript{3} or AlCl\textsubscript{3} were also added but they led to diene polymerisation. No cycloadducts were isolated in either cases.
2.3.4 Molecular modelling studies

In an attempt to understand why these systems could not undergo intramolecular Diels-Alder reaction some simple molecular modelling was carried out. Typical minimum energy conformations for isomeric compounds (2.3.16a) and (2.3.16b) were calculated using Spartan 5.1 as the molecular modelling program and the semi-empirical routine and are shown in (Figure 2.3.2). These two conformations were obtained by simply drawing the two starting materials and minimising their energy.

![Figure 2.3.2](image)

A different approach was also taken in order to access what other minimum energy conformation for compounds (2.1.16a) and (2.3.16b). The minimum energy conformation for the proposed cycloaddition products (2.3.17a) and (2.3.17b) were calculated. These two compounds were then disconnected at the bonds expected to be formed during the cycloaddition and the double bonds were introduced at the appropriate places. The minimum energy conformations were recalculated and are shown in Figure 2.3.3. It can be seen in this case that although the dienes fold in a slightly different way from the previous two conformations shown in Figure 2.3.2, they are pointing away from the dienophile which lies absolutely flat.
It was concluded from both efforts on the modelling that the dienophile moiety is flat and the diene appears to fold in such way that is actually pointing away from the dienophile. Although other minimum energy conformation may exist, it was not our target to establish that conformation, but to get a general idea how these molecules may like to fold in three dimensions.

An essential requirement for Diels-Alder reaction to take place is for the p-orbitals to approach each other head on, as shown in Figure 2.3.4. In the transition structure the p-orbitals have to be very close for the new σ-bonds to be formed.
In our case the chances of the diene and dienophile sitting above each other are limited. The lack of flexibility from the dienophile makes the Diels-Alder reaction transition state difficult to access.

2.3.5 Alternative systems for intramolecular Diels-Alder reactions

It was suggested that the introduction of a CH$_2$ group between the dienophile and the nitrogen would provide more flexibility and allow the diene and dienophile to approach in order to react. This system would not afford the original target molecules, but this approach was nevertheless of interest, since it would result in 5,7,6-tricyclic molecules.

N-Lithiation of 2-benzyl-2-imidazoline (2.1.7) with 1.1 equiv of sec-butyllithium and reaction with methyl 4-bromobut-2-enoate unfortunately did not produce the desired compound (2.3.18) and only starting material was isolated. This compound would have contained an electron-deficient dienophile on the nitrogen atom separated by a CH$_2$ group from the ring rather than having the dienophile directly attached to the imidazoline nitrogen. In this case the electron donating effect of the nitrogen that was deactivated would also be eliminated.

![Diagram](image.png)

Figure 2.3.4

Scheme 2.3.15
It has been shown in Section 2.1.1 that N-allylated 2-imidazolines could be easily synthesised. 2-Benzyl-2-imidazoline was treated with 2.2 equiv. of sec-butyllithium in THF at 0 °C and the dianion was quenched with 1.1 equiv. of 1,3-dibromopropane to give the 1-(prop-2-enyl)-2-benzyl-2-imidazoline (2.3.19) in 48% yield as the product of N-alkylation and elimination. 1,3-Dibromopropane was used as the double electrophile in order to investigate whether doubly N- and C(2α) lithiated 2-imindazolines would be able to react twice and produce a new six membered bicyclic 2-imidazoline. Compound (2.3.19) was lithiated again with 1 equiv. of n-butyllithium and addition of 1-bromohexa-2,4-diene produced the desired template (2.3.20) in 50% yield. This system contained the dienophile one carbon atom away from the nitrogen atom although the absence of the conjugating ester group would reduce the reactivity of the system. There have been reports of the same dienophile undergoing Diels-Alder reaction under thermal conditions. Nevertheless this molecule was heated in a sealed tube as a solution in toluene at 240°C for 48 h (Scheme 2.3.16). No significant change was observed after that period and no indication that the cyclic product (2.3.21) was formed. The starting material remained unreacted.

\[
\begin{align*}
\text{N} & \text{H} \quad \text{Ph} \\
\text{N} & \text{H} \\
\text{Ph} & \quad \text{i) 2.2 equiv. n-BuLi} \\
\text{Ph} & \quad \text{ii) BrCH}_2\text{CH}_2\text{CH}_2\text{Br} \\
\text{Ph} & \quad 2.3.19 \\
\text{BrCH}_2\text{CH} & \quad \text{i) n-BuLi} \\
\text{CH} & \quad \text{ii) BrCH}_2\text{CH=CH=CH}_3 \\
\text{Ph} & \quad 2.3.20 \\
\text{Ph} & \quad 2.3.21
\end{align*}
\]

Scheme 2.3.16
It was decided to see whether any change in reactivity would be observed if the diene was placed on the nitrogen atom and the dienophile at the C-2 position. 2-Benzyl-2-imidazoline was lithiated in the usual way, 1.1 equiv. of n-butyllithium, and alkylated with 1-bromohexa-2,4-diene to afford imidazoline (2.3.22) in 54% yield (Scheme 2.3.17). The resulting compound was alkylated at C(2α), by treatment with sec-butyllithium and 3-bromopropene to give the template (2.3.23) in 49% yield. The possibility of this system undergoing Diels-Alder reaction was investigated by heating a solution of (2.3.23) in toluene in a sealed tube at 240°C. Unfortunately the starting material remained unchanged and no cycloadduct (2.3.24) was observed.

The lack of activation on the dienophile and the presence of the methyl group on the diene (1,4-disubstitution) was thought to be possibly slowing the reaction down. Higher temperature and/or pressure may be required for the above systems to undergo cycloadditions. These conditions are less synthetically viable and were not explored here.
Our interest in forming rings associated with the imidazoline moiety and the lack of success with the intramolecular Diels-Alder approach directed our studies towards the intermolecular Diels-Alder reaction. It has been shown in Sections 2.1.3, 2.1.5 and 2.3.5 that dienes can be easily introduced either at C(2) or at N(1) and was decided to investigate whether possible intermolecular Diels-Alder reaction would take place.

The first experiments were carried out on imidazoline (2.1.21f). Compounds containing furan rings have been reported to undergo Diels-Alder reactions, sometimes reversibly. An initial experiment was carried out by mixing imidazoline (2.1.21f) with methyl propenoate and stirring at 20°C for 24 h, which did not produce any cycloadducts but only starting material. Then the effect of higher temperatures was investigated. Methyl propenoate was added to a solution of compound (2.1.21f) in toluene and the resulting mixture was heated in a sealed tube at 120°C for 18 h. No reaction was observed under these conditions. Change of dienophile to dimethyl maleate did not prove successful. Dimethyl maleate is a good dienophile for undergoing Diels-Alder reactions with the furan ring. Addition of a catalytic amount of BF₃-etherate and heating of the mixture in a sealed tube at 160°C resulted in cleavage of the tert-butyloxy group to give imidazoline (2.1.22c) and no cycloaddition products.
The furan ring was then introduced onto the nitrogen, in order to establish whether there would any effect in the reactivity of the furan ring. This was easily achieved by lithiation of 2-benzyl-2-imidazoline with 1.2 equiv of sec-butyllithium and addition of 1.2 equiv. of freshly prepared furfuryl chloride produced the desired compound (2.3.26) in 60% yield along with the disubstituted imidazoline (2.3.27) in 9% yield (Scheme 2.3.19). Imidazoline (2.3.26) was heated in a sealed tube with ethyl propenoate and dimethyl maleate, in the absence or presence of either BF₃-etherate or Et₂AlCl but no cycloadducts (2.3.28) were obtained.
Directing our studies to the acyclic diene (2.1.21g) was thought to be more hopeful since the problem of cycloaddition reversibility would be eliminated. This type of diene has been repeatedly reported in the literature to undergo Diels-Alder reaction.\textsuperscript{105} A large number of experiments were carried out on imidazoline (2.1.21g) with a variety of dienophiles in attempts to generate adducts (2.3.29) (Scheme 2.3.20). These experiments are summarised in Table 2.3.1.

![Scheme 2.3.20](image)

Table 2.3.1

<table>
<thead>
<tr>
<th>Dienophile</th>
<th>Solvent</th>
<th>Lewis-acid</th>
<th>Temperature/°C</th>
<th>time/ h</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>methyl propenoate</td>
<td>toluene</td>
<td>No</td>
<td>120°C</td>
<td>18 h</td>
<td>No reaction</td>
</tr>
<tr>
<td>methyl propenoate</td>
<td>toluene</td>
<td>No</td>
<td>180/sealed tube</td>
<td>24</td>
<td>No reaction</td>
</tr>
<tr>
<td>methyl propenoate</td>
<td>toluene</td>
<td>BF₃OEt₂</td>
<td>180/sealed tube</td>
<td>24</td>
<td>polymerisation</td>
</tr>
<tr>
<td>methyl propenoate</td>
<td>toluene</td>
<td>Et₂AlCl</td>
<td>120</td>
<td>24</td>
<td>polymerisation</td>
</tr>
<tr>
<td>methyl propenoate</td>
<td>trichlorobenzene</td>
<td>No</td>
<td>200/sealed tube</td>
<td>48</td>
<td>No reaction</td>
</tr>
<tr>
<td>ethyl propenoate</td>
<td>toluene</td>
<td>No</td>
<td>120/sealed tube</td>
<td>48</td>
<td>No reaction</td>
</tr>
<tr>
<td>Maleic anhydride</td>
<td>toluene</td>
<td>no</td>
<td>160/sealed tube</td>
<td>24</td>
<td>polymerisation</td>
</tr>
<tr>
<td>tetracyanoethylene</td>
<td>toluene</td>
<td>BF₃ and Et₂AlCl</td>
<td>180/sealed tube</td>
<td>24</td>
<td>polymerisation</td>
</tr>
<tr>
<td>Dimethyl maleate</td>
<td>toluene</td>
<td>BF₃/SO₂</td>
<td>120/sealed tube</td>
<td>24</td>
<td>polymerisation</td>
</tr>
</tbody>
</table>
Tetracyanoethylene was also used as a dienophile, because it is a very electron deficient reagent due to the electron withdrawing ability of the four cyano groups on the double bond, but the diene polymerised and failed to undergo cycloaddition. A recent report that 2,3-disubstituted-3-sulfolenes have been used as diene precursors in Diels-Alder reactions attracted our attention. In an attempt to form the 2,3-disubstituted-3-sulfolene we bubbled sulfur dioxide through a solution of diene (2.1.21g) in toluene at 0°C. A premixed solution of dimethyl maleate and BF₃-etherate was added to the reaction mixture which was sealed and heated in a tube at 120°C. Removal of the solvent showed that the diene had polymerised.

Disappointed by the above results, we decided to introduce the diene onto the nitrogen atom, in the usual way, from 2-benzyl-2-imidazoline, sec-butyllithium and 1-bromohexa-2,4-diene, compound (2.3.22) was obtained as a yellow oil in 54% yield (Scheme 2.3.17). Attempted Diels-Alder reaction with methyl propenoate in the absence or presence of BF₃-etherate did not give the cycloadduct (2.3.30). The Lewis acid catalyst again in this case caused diene polymerisation but no sensible cycloadduct was isolated.

Unable to explain these negative results, it was suggested that the presence of the methyl group on the diene could be causing the problem by reducing the rate of the cycloaddition significantly and allowing polymerisation. The introduction of a diene that did not contain the methyl group could result in increase in reactivity and produce a cycloadduct.

It has been shown in Section 2.1.3 that imidazoline 2.1.21h, which contained a monosubstituted diene moiety at C(2), could be easily synthesised. Our studies were then
directed towards compound (2.1.21h). This particular type of diene has been used very
often in both intermolecular or intramolecular Diels-Alder reactions. In an initial attempt
to obtain a Diels-Alder cycloadduct a solution of imidazoline (2.1.21h) in toluene and ethyl
propenoate (20 equiv.) was stirred at 20°C overnight but no reaction was observed. The
solution was then heated in a sealed tube at 200°C but this resulted in polymerisation of the
diene. When a premixed solution of BF₃-etherate in 20 equiv. of ethyl propenoate was
added to a solution of imidazoline (2.1.21h) in toluene and the mixture was heated to
200°C, a possible Diels-Alder product (2.3.31) was isolated as a BF₃ complex (Scheme
2.3.29). Attempts to increase the yield of the reaction proved unsuccessful and small
amounts of the cycloadduct were obtained as a mixture with diene rearrangement-
polymerisation products. It was also found that the reaction was not reproducible. There
appeared to be competition between diene polymerisation and cycloaddition.

When the reaction was carried out in the presence of BF₃-etherate at 20°C, it has
been possible to detect by TLC a very strong U.V. active less polar spot appeared. Column
chromatography was carried out in order to isolate that newly formed material and a very
small amount of the imidazoline BF₃ complex was isolated. It appears that the particular
complex breaks down in the column which explains the very small amount obtained. This
observation suggested that Lewis-acids prefer to form stronger complexes with 2-
imidazolines rather than coordinating with the dienophile which would result in
acceleration of the Diels-Alder reaction.

\[
\text{Scheme 2.3.29}
\]

\[
\begin{align*}
\text{N} & \quad \text{Boc} \\
\text{CO}_2\text{Et} & \\
\text{Heat} & \\
\text{BF}_3\text{OEt}_2 & \\
\text{2.1.21h} & \\
\text{N} & \quad \text{NHCO}_2\text{Et} \\
\text{2.3.31} & \\
\end{align*}
\]
The diene was then attached on the nitrogen atom in the usual way, by lithiation of 2-benzyl-2-imidazoline with $n$-butyllithium followed by addition of 5-bromohexa-1,3-diene, to afford imidazoline (2.3.32) in 57% yield (Scheme 2.3.27). The reactivity of compound (2.3.32) towards dienophiles was explored by carrying out some preliminary experiments. Ethyl propenoate and dimethyl maleate were used as dienophiles. Reactions carried out at 20°C in the absence of BF$_3$ produced unreacted material. Heating the reaction mixture in toluene in a sealed tube at 200°C resulted in polymerisation of the diene even in the presence of catalytic amount of quinol as inhibitor. When BF$_3$ was present diene polymerisation or products were obtained but in all cases no sign of any of the desired cycloaddition products (2.3.33) were observed.

\[
\begin{align*}
\text{2.1.7} & \quad n \text{-BuLi} \\
\text{2.3.32} & \quad \text{ii) BrCH}_2\text{CH=CHCH=CH}_2 \\
\text{2.3.33} & \quad \text{Heat BF}_3\text{OEt}_2
\end{align*}
\]

Scheme 2.3.23

2.3.7 2-Imidazoline templates for the synthesis of 5,5,6-systems

As was shown in Section 2.1.5, the introduction of a heteroatom such as phosphorus or selenium at the C(2α)-position of the imidazoline allows the creation of
double bonds directly attached to the imidazoline ring at C(2), and therefore makes the synthesis of alternative imidazoline Diels-Alder templates possible.

Initial attempts to introduce a dienophile onto imidazolines (2.1.34b) and (2.1.42c) at N(1) by metellation with n-butyllithium at 0°C in THF, followed by addition of 1.1 equiv. of 3-bromopropene did not proceed cleanly, producing traces of impure compounds (2.3.34a-b) that could not be utilised further (Scheme 2.3.24). It is possible that these 2-alkenyl-2-imidazolines are unstable under these metellation conditions.

![Scheme 2.3.24](image)

An alternative approach to these systems was devised by utilising the 2-(1-phenylselenenobut-3-enyl)-2-imidazoline (2.1.41c), whose synthesis has been described in Section 2.1.4. 2-(1-Phenylselenenobut-3-enyl)-2-imidazoline (2.1.41c) was treated with 1.0 equiv. of sec-butylithium in THF at 20°C, and the lithioimidazoline salt was quenched with 1.0 equiv. of 3-bromopropene to give the 2-(1-phenylselenenobut-3-enyl)-1-(prop-2-enyl)-2-imidazoline (2.3.35) in 47% yield, based on recovered material. Oxidation of the selenium with 3-chloroperbenzoic acid in dichloromethane at 20°C, followed by spontaneous selenoxide elimination afforded the desired template (2.3.34b) in quantitative yield (Scheme 2.3.25).
It was felt that this synthesis could be made shorter by applying the dianion chemistry that had been effective in the dialkylation of 2-benzyl-2-imidazoline (Section 2.1.1). 2-Phenylselenenomethyl-2-imidazoline (2.3.36), which was obtained by deprotection of the parent compound (2.1.38) with trifluoroacetic acid in 77% yield, was lithiated with 2.1 equiv of n-butyllithium followed by addition of 2.2 equiv of 3-bromo-propene to give compound (2.3.35) which was oxidised as before to obtain the compound (2.3.34b) (Scheme 2.3.26).
In order to make the synthesis of compounds like (2.3.34b) even shorter, we attempted to introduce the selenium atom at C(2a) of 2-methyl-1-(prop-2-enyl)-2-imidazoline (2.1.5) (Scheme 2.3.27) but treatment with sec-butyllithium and diphenyldiselenide failed to produce the expected compound (2.3.37), in accord with the result reported earlier in the N-benzyl series. The presence of the N-Boc group appears to be essential for the introduction of the selenium.

\[
\text{N} \quad \text{SeO}_{\text{BuLi}} \quad \text{PhSeSePh} \quad \text{N}
\]

A solution of compound (2.3.34b) in dry toluene was then heated in a sealed tube at 140°C. Removal of the solvent and crude \(^1\)H NMR spectroscopy showed that the compound had decomposed and that no cycloadducts (2.3.38) had been formed. We also investigated whether imidazoline (2.3.34b) could undergo intermolecular Diels-Alder reaction with an electron-rich dienophile, ethyl vinyl ether, at high temperatures. These experiments showed that the starting material had decomposed. It appears from the results obtained that compounds such as (2.3.34b) are unstable at high temperatures.
2.3.8 Conclusions

Despite our efforts to utilise imidazoline templates that contained diene and dienophile functionalities in either intramolecular or intermolecular Diels-Alder reactions, for reasons we do not understand, no cycloadducts were obtained. Lack of sufficient conformational flexibility in the substrates may hinder intramolecular reaction, but this would not account for the failure to observe intermolecular cycloadditions. In only one case a cycloadduct was isolated but that was obtained as a complex and the result was not reproducible. It was found that the imidazoline molecule formed strong complexes with Lewis-acids therefore inhibiting any complexation with the dienophiles which could accelerate the reaction and reduce activation energies.
2.4 Reactions of 2-imidazolines with acetylenic esters

2.4.1 Reactions with non terminal propynoates

It has been shown in Section 2.3.3 that 2-imidazolines react readily with activated acetylenes to give the conjugate addition products. This ability of 2-imidazolines to add to the triple bond of activated acetylenic compounds was explored further. Using 2-benzyl-2-imidazoline (2.1.7) as a model substrate, two experiments were carried out in order to understand the behaviour of 2-imidazolines in the presence of non-terminal alkynyl esters. When ethyl pent-2-ynoate was added to a solution of 2-benzyl-2-imidazoline in methanol, the conjugate addition product (2.4.1a) was obtained after a week in 19% yield. Only one geometric isomer was obtained but we have been unable to deduce which one. Ester exchange also occurred and afforded the methyl ester. In a similar way, compound (2.4.1b) was isolated as a single isomer in 52%, when ethyl 3-phenylpropynoate was added to a solution of 2-benzyl-2-imidazoline in dry methanol (Scheme 2.4.1). Ester exchange occurred again and the methyl ester was isolated. In both cases only one isomer was isolated but it has been difficult to determine the stereochemistry of the double bond. It is most probable that it is the thermodynamically most stable E-isomer that has been isolated in both cases.

![Scheme 2.4.1](image)

The proposed mechanism for these additions involves an initial attack by the imidazoline on the β-carbon of the acetylenic ester with initial formation of an intramolecurarly stabilised Z-intermediate (2.4.2a). This intermediate can then proceed to
the Z-adduct (2.4.3a) by protonation (kinetic control) or isomerize to the E-intermediate (2.4.2b). Protonation of the E-intermediate leads to the E-adduct (2.4.3b) (Scheme 2.4.2).110

Other researchers have proposed that the solvent controls the stereochemistry of the products in the addition of amines onto activated acetylenic esters. It has been suggested that the methanol molecule (which was used as solvent in our case) functions as a proton donor in the six-membered transition state (2.4.4) to give predominantly E-isomers.111 This does not agree with our results obtained with the terminal alkyne methyl propynoate where 2:1 mixtures of Z:E isomers were isolated.
Further experiments are required in order to confirm that these yields obtained are
the optimum and to understand the effect of the \( R^2 \) group on the 2-imidazoline conjugate
additions.

Keteneaminals (2.4.5) containing the imidazolidine ring have been reported to react
in completely the opposite way to the 2-imidazolines (Scheme 2.4.4).\(^{112}\) The \( \alpha \)-carbon
atom of these compounds possesses higher electron density and they act as C-nucleophiles
which could attack electron-deicient compounds. Aminals (2.4.5) react smoothly with
methyl propynoate in dioxane at ambient temperature to give the C-alkylated products
(2.4.6) as their \( E \)-isomer. Where \( R^1=H \), Huang \textit{et al.} have concluded that the reaction proceeds \textit{via} an aza-ene mechanism\(^{113}\) When the reaction is carried out in methanol at
reflux, the C-adducts are converted into fused heterocycles (2.4.7) (Scheme 2.4.4).

\[
\begin{align*}
\text{HN}\_ & \text{N} \\
\text{CO}_\text{Et} & \\
\text{Dioxane} & \\
\text{NH} & \\
\text{CO}_\text{Me} \\
\text{2.4.5} & \\
\end{align*}
\]

\[
\begin{align*}
\text{HN} & \\
\text{CO}_\text{Me} & \\
\text{Dioxane} & \\
\text{NH} & \\
\text{CO}_\text{Et} & \\
\text{2.4.6} & \\
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 & = H, \text{Me}, \text{PhCH}_2 \\
\text{R}^2 & = \text{Ar}, \text{EtO} \\
\text{2.4.7} & \\
\end{align*}
\]

Scheme 2.4.4

Cyclisation products similar to those isolated in the case of keteneaminals, have
never been observed from the reaction of 2-alkyl-2-imidazolines and propynoates. The
delocalisation of the pair of electrons from the ring nitrogen across the double bond in the
initial adducts could be responsible for deactivating the ester functionality and inhibiting cyclisation (Scheme 2.4.5).

![Scheme 2.4.5](image)

2.4.2 Reactions of 2-imidazolines with dialkyl acetylenedicarboxylate

Due to our interest in studying reactions of 2-imidazolines with electrophiles we investigated the behaviour of 2-alkyl-2-imidazolines with dialkyl acetylenedicarboxylates in order to utilise the outcome of those reactions in the synthesis of new heterocycles. Dialkyl acetylenedicarboxylates are more active electrophilic reagents than the activated acetylenic esters and were expected to react easily with 2-imidazolines.

2-Benzyl-2-imidazoline (2.1.7) was reacted with diethyl acetylenedicarboxylate in dry dichloromethane at 20°C. An exothermic reaction took place and the temperature was held below 30°C. The red solution that was produced was stirred overnight at 20°C and an orange precipitate was formed which was filtered immediately. This orange precipitate was found to be the cyclisation product (2.4.9). The mother liquor was concentrated and NMR spectroscopy showed that it contained the conjugate addition product (2.4.8) (Scheme 2.4.6). The geometry of the conjugate addition product was assigned as $E$ by comparison of chemical shifts of the olefinic CH ($\delta = 5.05$ ppm) of (2.4.8) with that of (2.4.13) ($\delta = 4.91$ ppm) that was established by X-ray crystallography to be $E$ (see later).
Scheme 2.4.6

Compound (2.4.9) was recrystallised from methanol to give orange orthorhombic crystals which were submitted to X-ray crystallography. This confirmed the structure of the recrystallised bicyclic compound, which exists as the Z-isomer (Figure 2.4.1). (see appendix for bond lengths and angles).

Figure 2.4.1
When a solution of adduct (2.4.8) in THF was added to a solution of potassium tert-butoxide in THF at 0°C, the cyclised products (2.4.9) and (2.4.10) were obtained as the separate Z and E-isomers in a 5:2 ratio in 67% yield (Scheme 2.4.6).

The same reaction was repeated, this time using 2-benzyl-2-imidazoline and dimethyl acetylenedicarboxylate (Scheme 2.4.6). The reaction was stirred at 20°C for 72 h. In agreement to the previous result the Z-isomer of the cyclised product (2.4.11) precipitated out of the reaction mixture as an orange solid. The residue from the filtrate was recrystallised from methanol/hexane to give the E-isomer (2.4.12) as an orange solid. No conjugate addition products were isolated this time, just the cyclisation products in 57% combined yield. It appears that longer reaction times produce solely the cyclised compounds. The stereochemistry of the double bond was assigned by comparison of the chemical shifts of the olefinic CHs for (2.4.11) (δ = 5.49 ppm) and for (2.4.12) (δ = 4.98 ppm) with those of (2.4.9) (δ = 5.48 ppm) and (2.4.10) (δ = 5.06 ppm), respectively.

The observed reaction proceeds via an initial conjugate addition of the imidazoline onto the triple bond followed by enamine attack on the carbonyl of the α-ester to give the observed pyrroloimidazoles (Scheme 2.4.7). The enamine has the choice of attacking the carbonyl of both esters but the delocalisation of the electrons across the double bond deactivates the β-ester (described in section 2.4.1) and cyclisation occurs only at the α-ester.
Scheme 2.4.7

The presence of the phenyl group at C(2) position plays an important role in the formation of those cyclic pyrroloimidazoles (2.4.9), (2.4.10), (2.4.11) and (2.4.12). The conjugation with the benzene ring stabilises the formation of the enamine which can act as a nucleophile and attack the ester carbonyl.

The reaction of other 2-alkyl-2-imidazolines with diethyl acetylenedicarboxylate was also investigated. 2-[(2-Phenyl)phenylethyl]-2-imidazoline (2.1.22b) was also reacted with diethyl acetylenedicarboxylate to give the conjugate addition product as the two isomers $E$ (2.4.13) and $Z$ (2.4.14) in a 3:1 ratio in 65%. The $E$-isomer was the less polar compound and was obtained as a white crystalline solid which was recrystallised from hexane/ethyl acetate and geometry was assigned by obtaining an X-ray crystal structure (Figure 2.4.2). No cyclised products were isolated this time. The more polar material that was obtained as a yellow oil was assigned as the $Z$-isomer (2.4.14). The $E$-isomer of (2.4.13) was treated in THF at 0°C with potassium tert-butoxide to give the pyrroloimidazole (2.4.15) in 54% yield. The geometry of the double bond appears to be $Z$.
by comparison of the chemical shift of the CH (\(\delta = 5.77\) ppm) of (2.4.15) with that of (2.4.9) (\(\delta = 5.48\) ppm) and of (2.4.17) (\(\delta = 5.83\) ppm).

\[
\begin{align*}
\text{N} & \text{VN} & \text{H} \\
\text{EtO}_2\text{C} = & \text{CO}_2\text{Et} & \text{S}_{\text{XY}} & \text{N} & \text{C}_2 \text{O}_2 \text{Et} \\
\text{Ph} & & & & \\
\end{align*}
\]

Scheme 2.4.8

The stereochemistry of the double bond of (2.4.13) was determined by X-ray crystallography (Figure 2.4.2) and confirmed as the E-isomer.

\[
\begin{align*}
\text{N} & \text{VN} & \text{H} \\
\text{EtO}_2\text{C} = & \text{CO}_2\text{Et} & \text{S}_{\text{XY}} & \text{N} & \text{C}_2 \text{O}_2 \text{Et} \\
\text{Ph} & & & & \\
\end{align*}
\]

Figure 2.4.2
The above crystal structure shows that the system is well set for cyclisation, with the C(2) carbon and α-ester being very close to each other, whereas the β-ester is coplanar with the N-C=C double bond, so conjugated and deactivated (see appendix for bond lengths and angles). The crystal structure also supports the result obtained from the molecular modelling (Section 2.34) that suggested that the dienophile was flat and lacked flexibility.

2-(But-3-enyl)-2-imidazoline was reacted in a similar way with diethyl acetylenedicarboxylate in dry dichloromethane at 20°C for 7 days to give after column chromatography the conjugate addition product (2.4.16) in 17% yield and the cyclisation compound (2.4.17) in 6% yield (Scheme 2.4.9). The low yields obtained were attributed to the poor quality of the starting material. The stereochemistry of these compounds was assigned based on comparison with the previous compounds. It appears that the conjugate addition product is the E-isomer based again on the chemical shift of the CH (δ = 5.02 ppm) and the cyclised product is the Z-isomer (for CH, δ = 5.83 ppm) (Scheme 2.4.9).

Scheme 2.4.9

This reaction of 2-alkyl-2-imidazolines with diethyl acetylenedicarboxylate proceeds via a completely different route to the reported reaction of keteneaminals (2.4.5) with dimethyl acetylenedicarboxylate. Keteneaminals reacted with 1 molecule of dimethyl acetylenedicarboxylate to give imidazo[1,2-a]pyridin-5-ones (2.4.19). The reaction
proceeds via C-alkylation to give the addition product (2.4.18) followed by the amide bond formation to afford the compound (2.4.19) (Scheme 2.4.10).\(^\text{114}\)

![Scheme 2.4.10](image)

Hydrogenation of the bicyclic Z-isomers, compounds (2.4.9) and (2.4.11), using 10% Pd/C as catalyst in methanol under an atmosphere of hydrogen resulted in reduction of the vinylogous urethane bond and gave compounds (2.4.20) and (2.4.21) in 69 and 92% yield, respectively (Scheme 2.4.11). The vinylogous amide bond remained untouched.

![Scheme 2.4.11](image)

This difference in the reactivity of the two double bonds in the system is possibly caused by the aromatic character acquired in the pyrrole substructure upon reduction of the vinylogous urethane bond. Keto-enol tautomerisation gives the molecule a degree of aromatic character making the further hydrogenation of the system more difficult (Scheme...
2.4.12. In addition the trisubstituted exocyclic double bond is expected to be reduced easier than the endocyclic tetrasubstituted double bond, could explain the observed result.

\[
\begin{align*}
\text{HN} & \quad \text{CO}_2\text{R} \\
\text{Ph} & \quad \text{HN} \\
\text{CO}_2\text{R}
\end{align*}
\]

Scheme 2.4.12

2.4.3 2-Imidazolines in radical reactions

The possibility of forming rings fused to the 2-imidazoline nucleus by radical chemistry was investigated briefly. It has been shown in Section 2.3.5 that a selenium atom can be introduced at the C(2α)-position. Alkyl selenides are well known for their ability to form free radicals and undergo radical reactions. Introduction of a carbon chain containing a double bond functionality on the N(1) of imidazoline (2.3.36) should allow the formation of a second ring under radical conditions.

Phenylselenenomethyl-2-imidazoline (2.3.36) was lithiated with 1.1 equiv. of n-butyllithium at 0°C followed by addition of 1.1 equiv. of 3-bromopropene to give an inseparable mixture of the N-alkylated (2.3.37) and C-alkylated (2.1.41c) products with the N-alkylated material being the major product. The insertion of the selenium atom at C(2α) makes that position more acidic and there now appears to be only a very small difference in acidity of the NH and C(2α) positions. Nevertheless the mixture was reacted under the standard radical conditions with Bu₃SnH (0.2 equiv.) and AIBN (catalytic amount) in toluene at reflux, using a syringe pump for the tin hydride addition. Unfortunately no cyclised products were obtained, only a 3:2 mixture of the reduced uncyclised materials (2.1.5) and (2.1.4) in 34% yield (Scheme 2.4.13).
Similar studies were carried out by Bowman et al. on the imidazole nucleus. These researchers have found that imidazole (2.4.22a) yielded no 5-membered ring cyclisation to (2.4.23a) and gave only reduction to 1-propylimidazole-5-carbaldehyde (2.4.24a), whereas (2.4.22b) gave the cyclised imidazole (2.4.23b) selectively with no uncyclised product (2.4.24b) (Scheme 2.4.14). This difference in reactivity is due to the fact that 6-exo cyclisation is more favourable than 5-exo cyclisation, which is disfavoured due to ring strain.

It was felt that this could also be the reason for not observing any cyclised products in our case. The introduction of a longer chain on the nitrogen should answer that particular question. Attempts to introduced a butenyl chain on the nitrogen by lithiation of (2.3.36)
with 1.0 equiv of n-butylithium or sec-butyllithium at -78°C, 0°C or 20°C and addition of 4-bromobut-1-ene did not prove successful and the desired product (2.4.25) was not obtained (Scheme 2.4.15). Starting material was isolated in all cases. The lithiated 2-imidazoline (2.3.36) is now too bulky and sterically hindered to act as a nucleophile and behaves like LDA, acting as a base rather than a nucleophile. It is also possible that the bromide is not reactive enough and acts as a proton donor. Perhaps conversion to the iodide could provide the desired compound. No other approaches were pursued due to lack of time but the possibility of radical cyclisation merits further investigation.

Scheme 2.4.15
Chapter 3

Experimental

**General:** Melting points were determined using an electrochemical digital melting point apparatus and are uncorrected. Infra-red spectra were recorded on a Perkin-Elmer 1710 FTIR spectrometer. Ultraviolet spectra were recorded on a contron Uvikon 860 spectrophotometer in ethanol. $^1$H NMR spectra were recorded in deuteriochloroform (unless otherwise stated) on JEOL LAMBDA300 or JEOL EX400 spectrometers at 300 or 400 MHz and chemical shifts are quoted in parts per million (p.p.m) from tetramethylsilane as internal standard. Coupling constants ($J$), where appropriate, are quoted in Hz with multiplicities; $s$-singlet, $d$-doublet, $t$-triplet, $q$-quartet and $m$-multiplet. The prefix br-broad is used where applicable. $^{13}$C spectra were recorded at 75 MHz or 100 MHz, respectively, in deuteriochloroform (unless otherwise stated) and chemical shifts are quoted in parts per million (p.p.m) from tetramethylsilane as internal standard or from tetramethylsilane using CDCl$_3$ as internal standard. Low resolution mass spectra were obtained using an AEI MS902 spectrometer in EI-positive mode. High resolution EI/CI mass spectra were performed by the EPSRC National Mass Spectrometry Sevice. Microanalytical data were obtained from Medac LTD Analytical and Chemical Consultancy Services. Solvents were dried and distilled before use: chloroform and dichloromethane from CaH$_2$; tetrahydrofuran (THF) and toluene from K; methanol and ethanol from Mg turnings and iodine immediately before use. n- and sec-Butyllithium were titrated with diphenylacetic acid before use. Column chromatography was performed under medium pressure using silica gel (Kieselgel 60; 220-440 mesh) or neutral alumina (150 mesh) as indicated. Organic extracts were dried over anhydrous MgSO$_4$. 
2-(But-3-enyl)-2-imidazoline (2.1.4)

\[
\begin{align*}
\text{N}^s-NH & \rightarrow \text{N}^s,NH
\end{align*}
\]

\(n\)-Butyllithium (9.52 cm\(^3\) of a 2.5M solution in hexanes, 23.80 mmol) was injected to a stirred solution of 2-methyl-2-imidazoline (1.00 g, 11.90 mmol) in dry THF (119 cm\(^3\)) at 20°C under nitrogen. The yellow suspension that was formed was stirred at 20°C for 50 min. The reaction mixture was cooled to 0°C and 3-bromopropene (1.02 cm\(^3\), 11.90 mmol) was injected to it. The reaction mixture was stirred at 0°C for 15 min. and at 20°C overnight. The reaction was quenched with water (100 cm\(^3\)) and the organic layer was extracted with diethyl ether (3 x 100 cm\(^3\)). The combined organic extracts were washed with brine (100 cm\(^3\)) and water (100 cm\(^3\)), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→5:97 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (0.15 g, 10%) (Found: MH\(^+\) 124.1000. C\(_7\)H\(_{12}\)N\(_2\) requires: M 124.1000); \(v\)\(_{\text{max}}\) (film)/cm\(^{-1}\) 3200, 2934, 1610, 1540, 1369, 754,h (400 MHz) 2.37-2.45 (4H, br m, \(\text{CH}_2\text{CH}2\text{CH}2\text{CH}2\)), 3.72 (4H, s, \(\text{NCH}_2\text{CH}2\text{N}\)), 4.89 (1H, br s, \(\text{NH}\)), 5.00-5.11 (2H, m, \(\text{CH}_2\text{CH}2\text{CH}2\text{CH}2\)), 5.78-5.87 (1H, m, \(\text{CH}_2\text{CH}2\text{CH}2\text{CH}2\)), \(\delta\)\(_C\) (100 MHz) 28.6 (\(\text{CH}_2\text{CH}2\text{CH}2\text{CH}2\)), 30.5 (\(\text{CH}_2\text{CH}2\text{CH}2\text{CH}2\)), 49.7 (\(\text{NCH}_2\text{CH}2\text{N}\)), 115.4 (\(\text{CH}_2\text{CH}2\text{CH}2\text{CH}2\)), 137.3 (\(\text{CH}_2\text{CH}2\text{CH}2\text{CH}2\)), 167.2 (N=C-N); \(m/z\) 124 (M\(^+\), 2%) 123 (87), 113 (22), 109 (9), 84 (21), 67 (24), 55 (49), 43 (51).

1-(Prop-2-enyl)-2-methyl-2-imidazoline (2.1.5)

\[
\begin{align*}
\text{N}^s-NH & \rightarrow \text{N}^s,NH
\end{align*}
\]

\(n\)-Butyllithium (14.28 cm\(^3\) of a 2.0M solution in hexanes, 28.57 mmol) was injected to a stirred solution of 2-methyl-2-imidazoline (2.00 g, 23.80 mmol) in dry THF (150 cm\(^3\)) at
20°C under nitrogen. The yellow suspension that was formed was stirred at 20°C for 50 min. The reaction mixture was cooled to 0°C and 3-bromopropene (2.47 cm³, 28.57 mmol) was injected to it. The reaction mixture was stirred at 0°C for 15 min. and at 20°C overnight. The reaction was quenched with water (100 cm³) and the organic layer was extracted with diethyl ether (3 x 100 cm³). The combined organic extracts were washed with brine (100 cm³) and water (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100—3:97 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (1.30 g, 44%) (Found: M⁺ 124.0999. C₇H₁₂N₂ requires: M 124.1000); νmax (film)/cm⁻¹ 2934, 2866, 1616, 1490, 1420, 1258, 934; δH (400 MHz) 1.93 (3H, s, CH₃), 3.26-3.31 (2H, t, J 9.8, NCH₂CH₂N), 3.63-3.68 (2H, t, J 9.8, NCH₂CH₂N), 3.72 (2H, d, J 5.8, NCH₂CH=CH₂), 5.17-5.22 (2H, m, NCH₂CH=CH₂), 5.72-5.82 (1H, m, NCH₂CH=CH₂); δC (100 MHz) 13.9 (CH₃), 49.4 (NCH₂CH₂N), 49.9 (NCH₂CH=CH₂), 51.9 (NCH₂CH₂N), 117.1 (NCH₂CH=CH₂), 133.1 (NCH₂CH=CH₂), 164.3 (N=C=N); m/z 124 (M⁺, 27%), 110 (1), 97 (5), 83 (24), 67 (19), 54 (100), 42 (30), 28 (17).

2-(But-3-enyl)-1-(prop-2-enyl)-2-imidazoline (2.1.6)

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{CH} & \quad \text{CH} \\
\text{N} & \quad \text{N} \\
\text{CH} & \quad \text{CH} \\
\end{align*}
\]

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{CH} & \quad \text{CH} \\
\text{N} & \quad \text{N} \\
\text{CH} & \quad \text{CH} \\
\end{align*}
\]

n-Butyllithium (25.88 cm³ of a 1.8 M solution in pentane, 46.62 mmol) was injected to a stirred solution of 2-methyl-2-imidazoline (1.78 g, 21.19 mmol) in dry THF (150 cm³) at 20°C under nitrogen. The milky suspension that was formed was stirred at 20°C for 1 h. The reaction mixture was cooled to 0°C and 3-bromopropene (4.00 cm³, 46.62 mmol) was injected to it. The suspension slowly disappeared and the reaction mixture was stirred at 0°C for 15 min and at 20°C for 48 h. The reaction was quenched with water (100 cm³) and
the organic layer was extracted with diethyl ether (3 x 100 cm³). The combined organic extracts were washed with brine (100 cm³) and water (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→4:96 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (1.56 g, 45%) (Found: MH⁺ 165.1391. C₁₀H₁₆N₂ requires: MH 165.1391); νmax (film)/cm⁻¹ 2977, 2932, 2862, 1642, 1615, 1486, 1418, 1258, 1213, 995, 915; δH (300 MHz) 2.24-2.29 (2H, m, CH₂CH₂CH=CH₂), 2.37-2.44 (2H, m, CH₂CH₂CH=CH₂), 3.27 (2H, t, J 9.7, NCH₂CH₂N), 3.69 (2H, t, J 9.7, NCH₂CH₂N), 3.71 (2H, d, J 4.0, NCH₂CH=CH₂), 4.97-5.10 (2H, m, CH₂CH₂CH=CH₂), 5.15-5.22 (2H, m, NCH₂CH₂CH₂), 5.71-5.92 (2H, m, NCH₂CH=CH₂ and CH₂CH₂CH=CH₂); δC (75 MHz), 27.1 (CH₂CH₂CH=CH₂), 30.4 (CH₂CH₂CH=CH₂), 49.2 (NCH₂CH₂N), 50.1 (NCH₂CH=CH₂), 52.2 (NCH₂CH₂N), 115.1 (CH₂CH₂CH=CH₂), 117.0 (NCH₂CH=CH₂), 133.8 (NCH₂CH=CH₂), 137.5 (CH₂CH₂CH=CH₂), 166.5 (N=C-N); m/z 164 (M⁺, 1%), 163 (4), 149 (4), 135 (2), 123 (10), 109 (3), 98 (2), 83 (32), 70 (100), 55 (29), 41 (65).

2-[(1-Phenyl)but-3-enyl]-1-(prop-2-enyl)-2-imidazoline (2.1.8)

\[\text{Ph} \quad \text{NHC} \quad \text{CH} \quad \text{N} \quad \text{He} \quad \text{CH} \quad \text{N} \quad \text{H} \quad \text{Ph} \]

n-Butyllithium (15.70 cm³ of a 2.5 M solution in hexanes, 39.37 mmol) was injected to a stirred solution of 2-benzyl-2-imidazoline (3.00 g, 18.75 mmol) in dry THF (188 cm³) at 20 °C under nitrogen. The yellow suspension that was formed was stirred at 20°C for 50 min. The reaction mixture was cooled to 0°C and 3-bromopropene (3.40 cm³, 39.37 mmol) was injected to it. The reaction mixture went clear yellow when 3-bromopropene was added and was stirred at 0°C for 15 min. and at 20°C overnight. The reaction was quenched with water (100 cm³) and the organic layer was extracted with diethyl ether (3 x 100 cm³).
combined organic extracts were washed successively with brine (100 cm$^3$) and water (100 cm$^3$), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→3:97 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (4.10 g, 91%) (Found: C, 78.72; H, 8.36; N, 11.41%; (M-H)$^+$ 239.1545. C$_{16}$H$_{20}$N$_2$·0.2H$_2$O requires: C, 78.81; H, 8.37; N, 11.49%; M-H 239.1548); $\nu$max (film)/cm$^{-1}$ 2932, 2862, 1641, 1611, 1416, 1210, 11074, 917, 702; $\delta_h$ (400 MHz) 2.49-2.56 (1H, m, PhCHCH$_2$H), 2.84-2.91 (1H, m, PhCHCH$_2$H), 3.13-3.21 (1H, dd, $J$ 8.8 and 17.1, NCH$_2$CH=CH$_2$), 3.26-3.33 (1H, dd, $J$ 8.8 and 17.6, NCHHCH=CH$_2$), 3.43-3.49 (2H, m, NCH$_2$CH$_2$N), 3.60-3.65 (1H, dd, $J$ 5.9 and 15.2, PhCHCH$_2$CH=CH$_2$), 3.69-3.84 (2H, m, NCH$_2$CH$_2$N), 4.92-4.97 (2H, m, PhCHCH$_2$CH=CH$_2$), 5.01-5.07 (2H, m, NCH$_2$CH=CH$_2$), 5.40-5.50 (1H, m, PhCHCH$_2$CH=CH$_2$), 5.69-5.75 (1H, m, NCH$_2$CH=CH$_2$), 7.20-7.32 (5H, m, Ar-H); $\delta_c$ (100 MHz) 39.8 (PhCHCH$_2$), 44.5 (PhCHCH$_2$), 49.1 (NCH$_2$CH$_2$N), 50.2 (NCH$_2$CH=CH$_2$), 52.6 (NCH$_2$CH$_2$N), 116.5 (PhCHCH$_2$CH=CH$_2$), 117.1 (NCH$_2$CH=CH$_2$), 127.1, 128.2 and 128.8 (Ar-CH), 134.0 (PhCHCH$_2$CH=CH$_2$), 136.7 (NCH$_2$CH=CH$_2$), 140.6 (Ar-C), 167.3 (N=C=N); $m/z$ 240 (M$^+$, 51%), 226 (5), 211 (11), 199 (43), 184 (5), 170 (8), 156 (17), 149 (31), 135 (9), 129 (13), 121 (14), 103 (13), 91 (24), 82 (15), 77 (23).

### Ethyl acetic acid (2.1.13)

![Chemical structure of Ethyl acetic acid](attachment:image.png)

Freshly distilled acetic acid (41.57 cm$^3$, 0.58 mol) was added dropwise to dry ethanol (25 cm$^3$) at 0°C under nitrogen. A solution of acetonitrile (25.44 cm$^3$, 0.48 mol) in dry ethanol (25 cm$^3$) was added via cannula to the mixture at 0°C under nitrogen. The reaction mixture was stored at 0°C for 48 h. Dry diethyl ether (50 cm$^3$) was added to it and the title compound precipitated out of solution as a white solid (19.18 g, 32%) $\delta_h$ (400 MHz) 1.46
A solution of 1-benzyl-1,2-diaminoethane (23.33 g, 0.15 mol) in dry ethanol (50 cm³) was added to a stirred suspension of ethyl acetimidate hydrochloride (19.18 g, 0.15 mol) in dry ethanol (150 cm³) at 20°C under nitrogen. The resulting mixture was heated at reflux for 3 h. The ethanol was removed under reduced pressure and the residue was partitioned between diethyl ether (100 cm³) and water (100 cm³). The aqueous layer was basified to pH 11 with 50% aq. NaOH and was extracted with chloroform (5 x 100 cm³). The combined organic extracts were dried and concentrated. The residue was distilled under reduced pressure and the *title compound* was obtained as a colourless liquid (19.02 g, 70%), b.p. 92-94°C at 0.05 mmHg (lit. b.p. 102-106°C at 1 mmHg); δH (400 MHz) 2.02 (3H, s, CH₃), 3.24 (2H, t, J 9.8, NCH₂), 3.68 (2H, t, J 9.8, NCH₂), 4.30 (2H, s, PhCH₂), 7.22-7.37 (5H, m, Ar-H).

*n*-Butyllithium (14.04 cm³ of a 1.8M solution in hexanes, 25.28 mmol) was injected to a stirred solution of 1-benzyl-2-methyl-2-imidazoline (4.00 g, 23.00 mmol) in dry THF (80 cm³) at -78°C under nitrogen. The solution was stirred at -78°C for 30 min and 3-
bromopropene (2.18 cm³, 25.28 mmol) was injected to it. The reaction mixture was stirred at -78°C for 4 h. and at 20°C for 1.5 h. Wet diethyl ether (50 cm³) was added and followed by water (100 cm³). The organic layer was extracted with diethyl ether (3 x 100 cm³) and the combined organic extracts were washed with brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:99 v/v isopropylamine:chloroform) to give the title compound as a yellow oil (3.85 g, 78%) (Found: (M-H)+ 213.1392. C14H18N2 requires: (M-H) 213.1392); νmax (film)/cm⁻¹ 3065, 2934, 2863, 1612, 1496, 1453, 1274, 737; δH (300 MHz) 2.39-2.49 (4H, br m, CH₂CH₂CH=CH₂), 3.20 (2H, t, J 9.7, NCH₂CH₂N), 3.69 (2H, t, J 9.7, NCH₂CH₂N), 4.28 (2H, s, PhCH₂), 4.98-5.10 (2H, m, CH=CH₂), 5.82-5.93 (1H, m, CH=CH₂), 7.22-7.37 (5H, m, Ar-H); δC (75 MHz; CDCl₃) 27.3 (CH₂CH₂CH=CH₂), 30.5 (CH₂CH₂CH=CH₂), 50.3 (NCH₂CH₂N), 50.7 (PhCH₂), 53.5 (NCH₂CH₂N), 115.4 (CH₂CH₂CH=CH₂), 127.2, 127.4 and 128.8 (Ar-CH), 137.4 (CH₂CH₂CH=CH₂), 137.8 (Ar-C), 166.4 (N=C=N), m/z 214 (M⁺, 1%), 213 (2), 203 (1), 190 (1), 174 (3), 160 (1), 149 (2), 133 (41), 120 (59), 106 (21), 91 (100), 77 (3), 65 (15).

2-(But-3-enyl)-2-imidazoline (2.1.4) and 2-butyl-2-imidazoline (2.1.16)

A solution of 1-benzyl-2-(but-3-enyl)-2-imidazoline (1.00 g, 4.67 mmol) in dry diethyl ether (1.5 cm³) and ethanol (0.68 cm³, 11.68 mmol) was added to freshly distilled liquid ammonia (47 cm³) at -78°C. Freshly cut sodium (0.27 g, 11.68 mmol) was added in small portions over a period of 10 min. A blue colour was produced after each addition. When all the sodium was added the blue colour persisted for 15 min and the reaction was stirred at -78°C for a further 15 min. The ammonia was then allowed to evaporate at 20°C overnight.
and diethyl ether (50 cm³) was added to the white solid. The ether layer was washed with water (50 cm³), dried and concentrated. The yellow oil was purified by column chromatography on silica gel (1:99→5:95 v/v isopropylamine:chloroform) to give an inseparable 2:1 mixture of 2-(but-3-enyl)-2-imidazoline and 2-butyl-2-imidazoline as a yellow oil (0.18 g, 32%). For 2-(but-3-enyl)-2-imidazoline: δ_H (400 MHz) 2.37-2.45 (4H, br m, CH₂CH₂CH=CH₂), 3.72 (4H, s, NCH₂CH₂N), 4.89 (1H, br s, NH), 5.00-5.11 (2H, m, CH₂CH₂CH=CH₂), 5.78-5.87 (1H, m, CH=CH₂), δ_C (75 MHz; CDCl₃) 28.6 (CH₂CH₂CH=CH₂), 30.5 (CH₂CH₂CH=CH₂), 49.7 (NCH₂CH₂N), 115.4 (CH=CH₂), 137.3 (CH=CH₂), 167.2 (N=C-N). For 2-(butyl)-2-imidazoline: δ_H (400 MHz; CDCl₃) 0.92 (3H, t, J 7.2, CH₂CH₂CH₃), 1.31-1.41 (2H, m, CH₂CH₂CH₂CH₃), 1.57-1.64 (2H, m, CH₂CH₂CH₂CH₃), 2.32 (2H, t, J 7.8, CH₂CH₂CH₂CH₃), 3.70 (4H, s, NCH₂CH₂N); δ_C (75 MHz) 13.8 (CH₂CH₂CH₂CH₃), 22.5 (CH₂CH₂CH₂CH₃), 28.8 (CH₂CH₂CH₂CH₃), 29.2 (CH₂CH₂CH₂CH₃), 49.9 (NCH₂CH₂N), 168.1 (N=C-N).

2-(But-3-enyl)-2-imidazoline (2.1.4)

\[
\begin{align*}
\text{N}^\text{s} / \text{N H} \\
\text{Ph} & \quad \rightarrow \quad \text{N}^\text{N} \text{NH} \\
\end{align*}
\]

A solution of 1-benzyl-2-(but-3-enyl)-2-imidazoline (1.00 g, 4.67 mmol) in dry diethyl ether (1.5 cm³) and ethanol (0.68 cm³, 9.34 mmol) was added to freshly distilled liquid ammonia (47 cm³) at -78°C. Freshly cut sodium (0.27 g, 9.34 mmol) was added in small portions over a period of 10 min. A blue colour was produced after each addition. When all the sodium was added the blue colour persisted for 15 min. and the reaction was stirred at -78°C for a further 15 min. The ammonia was then allowed to evaporate at 20°C overnight and diethyl ether (50 cm³) was added to the white solid. The ether layer was washed with water (50 cm³), dried and concentrated. The yellow oil was purified by column
chromatography on silica gel (1:99→5:99 v/v isopropylamine:chloroform) to give the *title compound* as a yellow oil (0.12 g, 21%); data identical to those reported before.

**1-Benzyl-2-butyl-2-imidazoline (2.1.17)**

![Chemical Structure](image)

*n*-Butyllithium (1.91 cm³, of a 1.8M solution in hexanes, 3.44 mmol) was injected to a stirred solution of 1-benzyl-2-methyl-2-imidazoline (0.50 g, 2.87 mmol) in dry THF (28 cm³) at -78°C under nitrogen. The solution was stirred at -78°C for 30 min and 1-iodopropane (0.34 cm³, 3.44 mmol) was injected to it. The reaction mixture was stirred at -78°C for 4 h and at 20°C for 1.5 h. Wet diethyl ether (20 cm³) was added and followed by water (50 cm³). The organic layer was extracted with diethyl ether (3 x 50 cm³) and the combined organic extracts were washed with brine (50 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:99 v/v isopropylamine:chloroform) to give the *title compound* as a yellow oil (0.60 g, 97%); δ_H (400 MHz) 0.87 (3H, t, J 7.3, CH2CH2CH2CH3), 1.25-1.40 (2H, m, CH2CH2CH2CH3), 1.53-1.63 (2H, m, CH2CH2CH2CH3), 2.15-2.25 (2H, t, J 7.80, CH2CH2CH2CH3), 3.07-3.15 (2H, t, J 9.8, NCH2CH2N), 3.59 (2H, t, J 9.8, NCH2CH2N), 4.20 (2H, s, NCH2Ph), 7.10-7.30 (5H, m, Ar-H).
A solution of 1-benzyl-2-butyl-2-imidazoline (0.50 g, 2.31 mmol) in dry diethyl ether (1.5 ml) and ethanol (0.31 cm³, 5.32 mmol) was added to freshly distilled liquid ammonia (23 cm³) at -78°C. Freshly cut sodium (0.12 g, 5.32 mmol) was added in small portions over a period of 10 min. A blue colour was produced every time a small portion of sodium was added. When all the sodium was added the blue colour persisted for 15 min. and the reaction was stirred at -78°C for a further 15 min. The ammonia was then allowed to evaporate at 20°C overnight and diethyl ether (20 cm³) was added to the white solid. The ether layer was washed with water (20 cm³), dried and concentrated. The yellow oil was purified by column chromatography on silica gel (1:99-3:97 v/v isopropylamine:chloroform) to give the title compound as a white solid (0.25 g, 50%), m.p. 35-37°C δH (400 MHz) 0.92 (3H, t, J 7.2, CH₂CH₂CH₂CH₃), 1.22-1.38 (2H, m, CH₂CH₂CH₂CH₃), 1.58-1.65 (2H, m, CH₂CH₂CH₂CH₃), 2.18 (2H, t, J 7.8, CH₂CH₂CH₂CH₃), 2.60-2.75 (6H, m, NCH₂ and 2 x cyclohexadiene CH₂), 3.12 (2H, s, NCH₂Cyclohexadiene), 3.34 (2H, m, NCH₂CH₂CH₃), 5.62 (1H, s, C=CH), 5.69-79 (2H, m, CH₂CH=CHCH₂); δC (100 MHz) 13.8 (CH₃), 22.3 (CH₂CH₃), 26.5 (CH₂CH₂CH₃), 27.5 and 27.8 (CH₂), 36.5 (CH₂CH₂CH₂CH₃), 38.9 (NCH₂Cyclohexadiene), 47.8 and 55.2 (NCH₂), 120.3, 124.0 and 124.1 (CH), 133.2 (NCH₂C), 173.3 (N-C=N).
Triethylamine (19.78 cm³, 0.14 mol) was added dropwise to a solution of 2-methyl-2-imidazoline (10.00 g, 0.12 mol) in dichloromethane (120 cm³) at 0°C. Di-tert-butyl dicarbonate (31.11 g, 0.14 mol) was added to the solution in small portions and the reaction mixture was stirred at 0°C for 10 min. The ice bath was removed and the reaction was stirred at 20°C overnight. Water was added and the organic layer was extracted with dichloromethane (3 x 100 cm³). The combined organic extracts were washed with saturated aq. NaHCO₃ (100 cm³), dried and concentrated. The crude product was distilled under reduced pressure and the title compound was obtained as a white solid (16.75 g, 77%) b.p 82-86°C at 0.15 mmHg, m.p 44-46°C (Found: M⁺ 184.1212. C₉H₁₆N₂O₂ requires: M⁺ 184.1212); v_max (film)/cm⁻¹ 2995, 1714; δ_H (400 MHz) 1.45 (9H, s, [C(CH₃)₃], 2.28 (CH₃), 3.68 (4H, s, NCH₂CH₂N); δ_C (100 MHz) 17.9 (CH₃), 28.1 [C(CH₃)₃], 46.4 and 51.7 (NCH₂), 81.4 [C(CH₃)₃], 150.9 (CO), 158.1 (N=C-N); m/z 184 (M⁺, 7%), 128 (7), 84 (20), 70 (24), 57 (100).

**General method for the synthesis of 2-substituted 1-tert-butyloxy carbonyl-2-imidazolines (2.1.21)**

Sec-Butyllithium (1.3M solution in hexanes) was injected into a solution of 1-tert-butyloxy carbonyl-2-methyl-2-imidazoline in dry THF/TMEDA (25-30:1 v/v; 0.1M in imidazoline) at -78°C under nitrogen. The bright yellow solution produced was stirred for
20 min at -78°C. The organohalide was injected (when liquid) or added by cannula as a solution in THF (when solid) to the reaction mixture at -78°C under nitrogen. The reaction was allowed to warm to 20°C overnight. It was then quenched with water (100 cm³) and the organic layer was extracted with diethyl ether (3 x 100 cm³) and the combined extracts were washed with saturated aq. NaHCO₃ (100 cm³), water (100 cm³) and brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica (1:9→2:3 v/v ethyl acetate:hexane) to give the product imidazoline.

**2-(But-3-enyl)-1-tert-butyloxycarbonyl-2-imidazoline (2.1.21a)**

![Chemical structure](image)

This compound was prepared by the general method, using 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (4.00 g, 21.74 mmol), sec-butyllithium (26.08 cm³ of a 1M solution in hexanes, 26.08 mmol) and 3-bromopropene (2.25 cm³, 26.08 mmol). The title compound was obtained as a colourless oil (4.00 g, 82%) (Found: C, 63.20; H, 8.78; N, 12.72%; MH⁺ 225.1603. C₁₂H₂₀N₂O₂·0.2H₂O requires: C, 63.24; H, 9.02; N, 12.29%; M H⁺ 225.1603; νmax (film)/cm⁻¹ 2960, 2934, 1720, 1640. 1369, 1150, 754; δH (400 MHz) 1.50 (9H, s, [C(CH₃)₃]), 2.40 (2H, q, J 8.0, CH₂CH₂CH=CH₂), 2.78 (2H, t, J 8.0, CH₂CH₂CH=CH₂), 3.77 (4H, s, NCH₂CH₂N), 5.00-5.10 (2H, m, CH₂CH₂CH=CH₂), 5.84 (1H, m, CH₂CH₂CH=CH₂); δC (100 MHz) 27.9 [C(CH₃)₃], 30.0 (CH₂CH₂CH=CH₂), 30.4 (CH₂CH₂CH=CH₂), 46.6 (NCH₂CH₂N), 51.8 (NCH₂CH₂N), 81.4 [C(CH₃)₃], 114.8 (CH₂CH₂CH=CH₂), 137.3 (CH₂CH₂CHII=CH₂), 150.7 (CO), 160.57 (N=C-N); m/z 225 (MH⁺, 0.9%), 208 (1), 169 (17), 124 (12), 97 (4), 84 (5), 58 (16)
2-Butyl-1-tert-butyloxycarbonyl-2-imidazolme (2.1.21b)

This compound was prepared by the general method, using 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (2.00 g, 10.86 mmol), sec-butyllithium (9.19 cm$^3$ of a 1.3M solution in hexanes, 11.95 mmol) and 1-iodopropane (1.16 cm$^3$, 11.95 mmol). The title compound was obtained as a colourless oil (2.10 g, 86%), (Found: C, 63.29; H, 9.42; N, 12.29%; M$^+$ 226.1681. C$_{12}$H$_{22}$N$_2$O$_2$ requires: C, 63.69; H, 9.80; N, 12.38%; M 225.1681); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2960, 2875, 1722, 1642, 1369, 1322, 1151, 1004; $\delta_H$ (400 MHz) 0.92 (3H, t, $J$ 7.3, CH$_2$CH$_2$CH$_2$CH$_3$), 1.40 (2H, m, CH$_2$CH$_2$CH$_2$CH$_3$), 1.50 [9H, s, C(CH$_3$)$_3$], 1.63 (2H, m, CH$_2$CH$_2$CH$_2$CH$_3$), 2.72 (2H, t, $J$ 7.8, CH$_2$CH$_2$CH$_2$CH$_3$). 3.75 (4H, s, NCH$_2$CH$_2$N); $\delta_C$ (75 MHz) 13.9 (CH$_2$CH$_2$CH$_2$CH$_3$), 22.5 (CH$_2$CH$_2$CH$_2$CH$_3$), 28.2 [C(CH$_3$)$_3$], 28.7 (CH$_2$CH$_2$CH$_2$CH$_3$), 30.6 (CH$_2$CH$_2$CH$_2$CH$_3$), 46.7 (NCH$_2$CH$_2$N), 51.80 (NCH$_2$CH$_2$N), 81.5 [C(CH$_3$)$_3$], 150.8 (CO), 161.6 (N=C-N); $m/z$ 226 (M$^+$, 0.8%), 184 (1), 171 (2), 128 (2), 85 (3), 58 (8).

1-tert-butyloxycarbonyl-2-(pent-4-enyl)-2-imidazolme (2.1.21c)

This compound was prepared by the general method, using 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (1.50 g, 8.15 mmol), sec-butyllithium (6.89 cm$^3$ of a 1.3M solution in hexanes, 8.96 mmol) and 4-bromobut-1-ene (0.91 cm$^3$, 8.96 mmol). The title compound was obtained as a colourless oil (1.25 g, 64%) (Found: MH$^+$ 239.1759. C$_{13}$H$_{22}$N$_2$O$_2$ requires: MH 239.1759); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2977, 2934, 1719, 1641, 1369, 1148; $\delta_H$ (400
MHz; CDCl₃) 1.50 [9H, s, C(CH₃)₃], 1.73-1.80 (2H, m, CH₂CH₂CH₂CH=CH₂), 2.13-2.18 (2H, m, CH₂CH₂CH₂CH=CH₂), 2.71 (2H, t, J 7.5, CH₂CH₂CH₂CH=CH₂), 3.73 (4H, s, NCH₂CH₂N), 4.97-5.07 (2H, m, CH₂CH₂CH₂CH=CH₂), 5.78-5.88 (1H, m, CH₂CH₂CH₂CH=CH₂); δC (100 MHz) 25.7 (CH₂CH₂CH₂CH=CH₂), 28.0 [C(CH₃)₃], 30.3 (CH₂CH₂CH₂CH=CH₂), 33.4 (CH₂CH₂CH₂CH=CH₂), 46.6 (NCH₂CH₂N), 51.8 (NCH₂CH₂N), 81.6 [C(CH₃)₃], 114.9 (CH₂CH₂CH₂CH=CH₂), 138.3 (CH₂CH₂CH₂CH=CH₂), 150.9 (CO), 161.5 (N=C-N); m/z 239 (MH⁺, 3%), 201 (9), 183 (26), 157 (16), 140 (26), 129 (10), 88 (18), 57 (100).

1-tert-Butyloxycarbonyl-2-(2-phenylethyl)-2-imidazoline (2.1.21d)

This compound was prepared by the general method, using 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (1.00 g, 5.43 mmol), sec-butyllithium (0.71 cm³ of a 1.3M solution in hexanes, 5.97 mmol) and benzyl bromide (0.71 cm³, 5.97 mmol). The title compound was obtained as a colourless oil (1.36 g, 92%) (Found: C, 70.04; H, 8.07; N, 10.16%; M⁺ 274.1681. C₁₆H₂₂N₂O₂ requires: C, 70.04; H, 8.08; N, 10.21; M 274.1681); ν_max (film)/cm⁻¹ 2977, 2934, 1718, 1644, 1370, 1143; δH (400 MHz) 1.50 [9H, s, C(CH₃)₃], 3.00 (4H, br s, CH₂CH₂Ph), 3.75 (4H, s, NCH₂CH₂N), 7.20-7.50 (5H, m, Ar-H); δC (100 MHz), 28.2 [C(CH₃)₃], 32.5 (CH₂CH₂Ph), 32.6 (CH₂CH₂Ph), 46.8 (NCH₂CH₂N), 52.0 (NCH₂CH₂N), 81.5 [C(CH₃)₃], 125.9, 128.3, 128.4 (Ar-CH), 141.3 (Ar-C), 151.0 (CO), 160.90 (N=C-N); m/z 274 (M⁺, 0.6%), 218 (49), 174 (8), 145 (6), 97 (11).
1-tert-Butyloxycarbonyl-2-[2-(2-phenyl)phenylethyl]-2-imidazoline (2.1.21e)

This compound was prepared by the general method, using 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (1.00 g, 5.43 mmol), sec-butyllithium (5.43 cm³ of a 1.1M solution in hexanes, 5.97 mmol) and 2-phenylbenzyl bromide (1.09 cm³, 5.97 mmol). The title compound was obtained as a colourless oil (1.55 g, 81%) (Found: C, 74.79; H, 7.52; N, 7.53%; M⁺ 350.1994. C₂₂H₂₆N₂O₂ requires: C, 75.00; H, 7.44; N, 7.95%; M 350.1994); v_max (film)/cm⁻¹ 2977, 2934, 1718, 1642 1480, 1370, 1145; δ_H (400 MHz) 1.47 [9H, s, C(CH₃)₃], 2.85 (2H, t, J 8.0, CH₂CH₂Ar), 2.98 (2H, t, J 8.0, CH₂CH₂Ar), 3.65 (4H, s, NCH₂CH₂N), 7.15-7.40 (9H, m, Ar-H); δ_C (100 MHz) 28.0 [C(CH₃)₃], 29.5 (CH₂CH₂Ar), 32.3 (CH₂CH₂Ar), 46.6 (NCH₂CH₂N), 51.9 (NCH₂CH₂N), 81.4 [C(CH₃)₃], 125.9, 126.7, 127.5, 128.1, 129.2, and 130.1 (Ar-CH), 138.7, 141.7 and 141.9 (Ar-C), 150.8 (CO), 160.7 (N=C-N); m/z 350 (M⁺, 9%), 294 (48), 249 (60), 217 (12), 165 (39), 115 (97), 97 (11), 71 (14), 57 (100).

1-tert-Butyloxycarbonyl-2-[2-(2-furyl)ethyl]-2-imidazoline (2.1.21f)

This compound was prepared by the general method, using 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (2.00 g, 10.86 mmol), sec-butyllithium (14.94 cm³ of a 0.8M in hexanes, 11.95 mmol) and furfuryl chloride (1.20 g, 11.97 mmol). The title compound was
obtained as a colourless oil (2.03 g, 71%) (Found: C, 60.88; H, 7.48; N, 10.08%; M+ 264.1474. C_{14}H_{20}N_{2}O_{2} requires: C, 60.34; H, 7.18, N,10.05%; M 264.1473); ν_{max} (film)/cm⁻¹ 2977, 2934, 1718, 1644, 1479, 1369, 1331, 1222, 1147, 1000; δ_{H} (400 MHz) 1.45 [9H, s, C(CH₃)₃], 2.92-3.02 (4H, br m, CH₂CH₂Furyl), 3.68 (4H, s, NCH₂CH₂N), 5.95 (1H, d, J 2.9, Fuiyl-4H), 6.18 (1H, dd, J 2.0 and 2.9, Fuiyl-3H), 7.28 (1H, d, J 1.5, Fuiyl-2H); δ_{C} (100 MHz) 25.0 (CH₂CH₂Furyl), 28.2 [C(CH₃)₃], 29.5 (CH₂CH₂Furyl), 46.8 (NCH₂CH₂N), 51.9 (NCH₂CH₂N), 81.8 [C(CH₃)₃], 105.0, 110.1 and 140.9 (Fuiyl-C), 150.8 (CO), 154.9 (Fuiyl-C), 160.4 (N=C-N); m/z 264 (M+, 2%), 208 (68), 191 (16), 163 (41), 135 (55), 121 (24), 94 (17), 84 (15), 81 (33), 70 (14), 58 (100).

1-tert-Butyloxy carbonyl-2-(hepta-3,5-dienyl)-2-imidazoline (2.121g)

This compound was prepared by the general method, using 1-tert-butyloxy carbonyl-2-methyl-2-imidazoline (1.50 g, 8.15 mmol), sec-butyllithium (6.89 cm³ of a 1.3 M solution in hexanes, 8.96 mmol) and 6-bromohexa-2,4-diene (1.44 g, 8.96 mmol). The compound was obtained as a colourless oil, 4:1 mixture of E,E:E,Z isomers (1.55 g, 81%), (Found: M+ 264.1474. C_{15}H_{24}N_{2}O_{2} requires: M 264.1473); ν_{max} (film)/cm⁻¹ 2977, 2934, 1718, 1644, 1479, 1369, 1331, 1222, 1147, 1000; for E,E isomer: δ_{H} (400 MHz) 1.50 [9H, s, C(CH₃)₃], 1.71 (3H, d, J 6.8, CH₃CH=CH), 2.33 (2H, q, J 7.6, CHCH=CHCH₂CH₂), 2.73 (2H, t, J 7.6, CH=CHCH₂CH₂), 3.72 (4H, s, NCH₂CH₂N), 5.58-5.63 (2H, m, CH₃CH=CHCH₂CH₂), 5.98-6.10 (2H, m, CH₃CH=CHCH=CHCH₂CH₂); δ_{C} (100 MHz) 17.9 (CH₃CH=), 28.2 [C(CH₃)₃], 29.3 CH=CHCH₂CH₂), 30.6 (CH=CHCH₂CH₂), 46.7 (NCH₂CH₂N), 51.9 (NCH₂CH₂N), 81.5 [C(CH₃)₃], 127.2 (CH₃CH=CHCH=CH), 130.2 (CH₃CH=CHCH=CH), 130.8 (CH₃CH=CHCH=CH), 131.4
(CH$_3$CH=CHCH=CHCH$_2$CH$_2$), 150.8 (CO), 160.7 (N=C-N); for $E:Z$ isomer $\delta_H$ (400 MHz)
1.11 (3H, d, $J$ 6.8, CH$_3$CH=CH), 1.50 [9H, s, C(CH$_3$)$_3$], 2.42 (2H, q, $J$ 7.6, CH=CHCH$_2$CH$_2$), 2.76 (2H, t, $J$ 7.6, CH=CHCH$_2$CH$_2$), 3.72 (4H, s, NCH$_2$CH$_2$N), 4.97 (1H, dd, $J$ 1.7 and 10.2, CH$_3$CH=CHCH=CHCH$_2$), 5.12 (1H, dd, $J$ 1.7 and 17.1, CH$_3$CH=CHCH=CHCH$_2$), 5.98-6.10 (1H, m, CH$_3$CH=CHCH=CHCH$_2$2) 6.28-6.35 (1H, m, CH$_3$CH=CHCH=CHCH$_2$); $\delta_C$ (100 MHz) 17.9 (CH$_3$CH=CH), 28.2 [C(CH$_3$)$_3$], 34.3 CH=CHCH$_2$CH$_2$), (CH=CHCH$_2$CH$_2$), 46.7 (NCH$_2$CH$_2$N), 51.9 (NCH$_2$CH$_2$N), 81.5 [C(CH$_3$)$_3$], 127.1 (CH$_3$CH=CHCH=CH), 128.5 (CH$_3$CH=CHCH=CH), 137.6 (CH$_3$CH=CHCH=CHCH$_2$CH$_2$), 139.1 (CH$_3$CH=CHCH=CHCH$_2$CH$_2$), 150.8 (CO), 160.7 (N=C-N); $m/z$ 264 (M+, 0.7%), 208 (65), 193 (35), 179 (23), 149 (33), 135 (19), 123 (20), 109 (48), 83 (39), 57 (100).

1-*tert*-Butyloxy carbonyl-2-(hexa-3,5-dienyl)-2-imidazoline (2.1.21b)

This compound was prepared by the general method, from 1-**tert**-butyloxy carbonyl-2-methyl-2-imidazoline (1.20 g, 6.52 mmol), sec-butyllithium (6.01 cm$^3$ of a 1.3M solution in hexanes, 7.82 mmol) and 5-bromopenta-1,3-diene (1.15 cm$^3$, 7.82 mmol). The title compound was obtained as a colourless oil (1.09 g, 67%) (Found: C, 65.70; H, 8.84; N, 10.94%; MH$^+$ 251.1755. C$_{14}$H$_{22}$N$_2$O$_2$·0.4H$_2$O requires: C, 65.42; H, 8.86; N, 10.88%; MH 251.1579); $v_{max}$ (film)/cm$^{-1}$ 2977, 1718, 1643, 1369, 1317, 1256, 1143, 1005, 768; $\delta_H$ (300 MHz) 1.50 [9H, s, C(CH$_3$)$_3$], 2.48 (2H, q, $J$ 7.6, CH=CHCH$_2$CH$_2$), 2.79 (2H, t, $J$ 7.6, CH=CHCH$_2$CH$_2$), 3.74 (4H, s, NCH$_2$CH$_2$N), 4.97 (1H, m, CH=CHH), 5.10 (1H, dd, $J$ 1.1 and 16.8 CH=CHH), 5.72-5.81 (1H, m, CH=CHCH=CH$_2$), 6.05-6.14 (1H, m, CH=CH-CH=CH$_2$), 6.10-6.34 (1H, m, CH=CH-CH=CH$_2$); $\delta_C$ (75 MHz) 28.2 [C(CH$_3$)$_3$], 29.4...
General method for the synthesis of 2-substituted 2-imidazolines (2.1.22)

Trifluoroacetic acid (5 cm³) was added to the 2-substituted 1-tert-butyloxycarbonyl-2-imidazolines and the resulting solution was stirred at 20°C for 20–60 min. The trifluoroacetic acid was removed under reduced pressure and the imidazoline trifluoroacetate salt was dissolved in dichloromethane (100 cm³). The solution was then washed with aq. NaOH (10% w/v; 100 cm³) and the organic layer was dried and concentrated. The crude product was then purified by column chromatography on silica gel (0:100→4:96 v/v isopropylamine:ethyl acetate) to give the desired imidazoline.

2-(But-3-enyl)-2-imidazoline (2.1.4)

This compound was prepared by the general method, using 2-(but-3-enyl)-1-tert-butyloxycarbonyl-2-imidazoline (1.45 g, 6.47 mmol) and TFA (3 cm³). The title compound was obtained as a white solid (0.66 g, 82%), m.p. 29-31 °C (Found: MH⁺ 124.1000. C₇H₁₂N₂ requires: M 124.1000); ν max (film)/cm⁻¹ 3200, 2934, 1610, 1540, 1369, 1150, 754; δH (400 MHz) 2.37-2.45 (4H, br m, CH₂CH₂CH=CH₂), 3.72 (4H, s, NCH₂CH₂N), 4.89 (1H, br s, NH), 5.00-5.11 (2H, m, CH₂CH₂CH=CH₂), 5.78-5.87 (1H, m,
CH₂CH₂CH=CH₂; δC (75 MHz) 28.6 (CH₂CH₂CH=CH₂), 30.5 (CH₂CH₂CH=CH₂), 49.7 (NCH₂), 115.4 (CH=CH₂), 137.3 (CH=CH₂), 167.2 (N=C-N); m/z 124 (M⁺, 2%) 123 (87), 113 (22), 109 (9), 84 (21), 67 (24), 55 (49), 43 (51).

2-Butyl-2-imidazoline (2.1.15)

This compound was prepared by the general method, using 2-butyl-1-tert-butylxoycarbonyl-2-imidazoline (1.25 g, 5.53 mmol) and TFA (3 cm³). The title compound was obtained as a white crystals (0.61 g, 87%), m.p 39-41 °C (Found: C, 66.32; H, 10.94; N, 21.96%; MH⁺ 127.1235. C₇H₁₄N₂ requires: C, 66.62; H, 11.18; N, 22.20%; M 127.1235); νmax (KBr)/cm⁻¹ 3230, 2958, 2871, 1615, 1495, 1467, 1289, 1268; δH (400 MHz) 0.92 (3H, t, J 7.2, CH₂CH₂CH₂CH₃), 1.31-1.41 (2H, m, CH₂CH₂CH₂CH₃), 1.57-1.64 (2H, m, CH₂CH₂CH₂CH₃), 2.32 (2H, t, J 7.8, CH₂CH₂CH₂CH₃), 3.70 (4H, s, NCH₂CH₂N); δC (75 MHz) 13.8 (CH₂CH₂CH₂CH₃), 22.5 (CH₂CH₂CH₂CH₃), 28.8 (CH₂CH₂CH₂CH₃), 29.2 (CH₂CH₂CH₂CH₃), 49.9 (NCH₂), 168.1 (N=C-N); m/z 127 (M⁺, 80%), 115 (5), 98 (8), 84 (100), 73 (15), 69 (11), 57 (15), 44 (23).

2-(2-Phenylethyl))-2-imidazoline (2.1.22a)

This compound was prepared by the general method, from 1-tert-butyloxycarbonyl-2-(2-phenylethyl)-2-imidazoline (2.00 g, 7.29 mmol) and TFA (4 cm³). The title compound was obtained as a white solid (0.93 g, 73%), m.p. 102-104 ºC (Found: C, 75.83; H, 8.12; N,
15.86%; $M^+$ 174.1146. $C_{11}H_{14}N_2$ requires: C, 75.82; H, 8.10; N, 16.07%; $M$ 174.1157; $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3158, 3059, 3001, 2926, 2859, 1606, 1498, 1286; $\delta_H$ (400 MHz) 2.52-2.56 (2H, t, $J$ 8.0, $CH_2CH_2$Ph), 2.94-2.98 (2H, t, $J$ 7.8, $CH_2CH_2$Ph), 3.56 (4H, br s, NCH$_2$CH$_2$N), 7.20-7.50 (5H, m, Ar-H), $\delta_C$ (100 MHz) 31.1 ($CH_2CH_2$Ph), 32.8 ($CH_2CH_2$Ph), 49.4 (NCH$_2$), 126.2, 128.2 and 128.4 (Ar-CH), 141.1 (Ar-C), 167.2 (N=C-N); $m/z$ 174 ($M^+$, 33%), 173 (100), 144 (8), 117 (16), 97 (38), 91 (25), 84 (10), 65 (33).

2-[(2-Phenyl)phenylethyl]-2-imidazoline (2.1.22b)

This compound was prepared by the general method, from 2-[2-(2-phenyl)phenylethyl]-1-tert-butyloxycarbonyl-2-imidazoline (1.38 g, 3.94 mmol) and TFA (3 cm$^3$). The title compound was obtained as a white solid (0.79 g, 80%), m.p. 118-120 °C (Found: C, 81.68; H, 7.25; N, 11.17%; (M-H)$^+$ 249.1382. $C_{22}H_{26}N_2O_2$ requires: C, 81.56; H, 7.25; N, 11.18%; $M-H$ 249.1392); $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3152, 3104, 2932, 1608, 1558, 1538, 1505, 1479, 1310, 1279; $\delta_H$ (400 MHz) 2.30-2.33 (2H, t, $J$ 8.0, $CH_2$Ar), 2.92-2.95 (2H, t, $J$ 8.0, $CH_2$Ar), 3.47 (4H, s, NCH$_2$CH$_2$N), 4.11 (1H, br s, NH), 7.15-7.40 (9H, m, Ar-H); $\delta_C$ (100 MHz) 30.2 ($CH_2$Ar), 30.7 ($CH_2$Ar), 50.2 (NCH$_2$), 126.3, 127.0, 127.6, 128.2, 129.1, 129.2 and 130.2 (Ar-CH), 138.3, 141.5 and 141.8 (Ar-C), 167.1 (N=C-N); $m/z$ 250 ($M^+$, 33%), 249 (100), 173 (30), 165 (40), 152 (13), 115 (10), 97 (25), 71 (22).
2-[2-(2-Furyl)ethyl]-2-imidazoline (2.1.22c)

This compound was prepared by the general method, from 1-tert-butyloxycarbonyl-2-[2-(2-furyl)ethyl]-2-imidazoline (0.30 g, 1.13 mmol) and TFA (2 cm³). The title compound was obtained as a white solid (0.12 g, 65%), m.p. 98-100 °C (Found: M⁺ 164.0950. C₉H₁₂N₂ requires: M⁺ 164.0949); vₘₐₓ(KBr)/cm⁻¹ 3165, 3118, 2927, 2862, 1606, 1511, 1377, 1289, 1001; δₛ (400 MHz) 2.48-2.52 (2H, t, J 7.8, OCH₂Furyl), 2.88-2.93 (2H, t, J 7.8, C₅H₂CH₂Furyl), 3.48 (4H, s, NCH₂CH₂N), 4.31 (1H, br s, NH), 5.95 (1H, d, J 3.0, Furyl-3H), 6.21 (1H, dd, J 2.0 and 3.0, Furyl-4H), 7.29 (1H, d, J 2.0, Furyl-5H); δₛ (100 MHz) 25.1 (CH₂CH₂Furyl), 27.8 (OCH₂Furyl), 49.8 (NCH₂), 105.3, 110.2, 141.1 and 154.6 (Furyl-C), 166.7 (N=C-N); m/z 164 (M⁺, 100%), 135 (92), 121 (40), 110 (11), 94 (17), 84 (65), 54 (37).

2-(Hepta-3,5-dienyl)-2-imidazoline (2.1.22d)

This compound was prepared by the general method, from 1-tert-butyloxycarbonyl-2-(hepta-3,5-dienyl)-2-imidazoline (1.20 g, 4.54 mmol) and TFA (3 cm³). The title compound was obtained as a 4:1 mixture of geometric isomers E,E:E,Z as a white solid (0.50 g, 67%), m.p. 68-70 °C (Found: M⁺ 164.1317. C₁₀H₁₆N₂ requires: M⁺ 164.1313); νₘₐₓ(KBr)/cm⁻¹ 3154, 3017, 2932, 2862, 1606, 1505, 1475, 1451, 1376, 1284, 1146, 987; data for E:E isomer δₛ (400 MHz) 1.73 (3H, d, J 6.8, CH₃CH=CH), 2.28-2.42 (4H, m, CH=CHCH₂CH₂), 3.58 (4H, s, NCH₂CH₂N), 3.80 (1H, br s, NH), 5.52-5.68 (2H, m,
CH$_3$CH=CH=CHCH$_2$), 5.98-6.10 (2H, m, CH$_3$CH=CH=CHCH$_2$CH$_2$); $\delta_C$ (100 MHz), 18.0 (CH$_3$), 29.2 (CH=CHCH$_2$CH$_2$), 29.4 (CH=CHCH$_2$CH$_2$), 49.9 (NCH$_2$), 127.9, 130.3, 131.3 and 136.9 (CH), 167.4 (N=C-N); data for E:Z isomer Sh (400 MHz) 1.08 (3H, d, f J 6.8, CH$_3$), 2.28-2.42 (4H, m, CH=CHCH$_2$CH$_2$), 3.58 (4H, s, NCH$_2$CH$_2$N), 3.80 (1H, br s, NH), 5.04-5.52-5.68 (1H, dd, J 1.7 and 10.2, CH$_3$CH=CH=CH=CH), 5.12 (1H, dd, J 1.7 and 17.2, CH$_3$CH=CH=CH=CH), 5.98-6.10 (1H, m, CH$_3$CH=CH=CHCH$_2$CH$_2$), 6.24-6.34 (1H, m, CH$_3$CH=CH=CH=CHCH$_2$CH$_2$); $\delta_C$ (100 MHz) 20.1 (CH$_3$), 29.2 (CH=CHCH$_2$CH$_2$), 29.4 (CH=CHCH$_2$CH$_2$), 49.9 (NCH$_2$), 115.9, 130.3, 131.3 and 139.1 (CH), 166.5 (N=C-N); $m/z$ 164 (M$^+$, 57%), 149 (93), 135 (57), 123 (25), 97 (22), 84 (100), 79 (44), 54 (35).

**General method for the synthesis of 2-disubstituted 1-tert-butyloxycarbonyl-2-imidazoline (2.1.23)**

Sec-Butyllithium (1.3M solution in hexanes) was injected to a solution of 1-tert-butyloxycarbonyl-2-substituted-2-imidazoline in dry THF/TMEDA (25-30:1 v/v; 0.1M in imidazoline) at -78°C under nitrogen. The bright yellow solution produced was stirred for 20 min at -78°C. The organohalide electrophile was injected (when liquid) or added by cannula as a solution in THF (when solid) to the reaction mixture at -78°C under nitrogen. The reaction was allowed to warm to 20°C overnight. The reaction was quenched with water (100 cm$^3$) and the organic layer was extracted with diethyl ether (3 x 100 cm$^3$) and the combined extracts were washed with saturated aq. NaHCO$_3$ (100 cm$^3$), water (100 cm$^3$) and brine (100 cm$^3$), dried and concentrated. The crude product was purified by column
chromatography on silica gel (1:9→4:6 v/v ethyl acetate:hexane) to give the product imidazoline.

1-tert-Butyloxycarbonyl-2-[1-(prop-2-enyl)but-3-enyl]-2-imidazoline (2.1.23a)

\[
\text{Boc} \quad \text{Boc}
\]

This compound was prepared by the general method, from 2-(but-3-enyl)-1-tert-butyloxycarbonyl-2-imidazoline (0.60 g, 2.67 mmol), sec-butyllithium (2.67 cm\(^3\) of a 1.1M solution in hexanes, 2.94 mmol) and 3-bromopropene (0.25 cm\(^3\), 2.94 mmol). The title compound was obtained as a colourless oil (0.59 g, 84%) (Found: MH\(^+\) 265.1916. C\(_{15}\)H\(_{24}\)N\(_2\)O\(_2\) requires: MH\(^+\) 265.1916); \(\nu_{\text{max}}\) (film)/cm\(^{-1}\) 2996, 2972, 1720, 1644, 1483, 1369, 1329, 1149, 1010, 915; \(\delta_{\text{H}}\) (400 MHz) 1.52 [9H, s, C(CH\(_3\))\(_3\)], 2.29-2.35 (2H, m, 2 x CHCH\(_2\)CH=CH\(_2\)), 2.40-2.50 (2H, m, 2 x CHCH\(_2\)CH=CH\(_2\)), 3.58 (1H, t, \(J\) 6.6, CHCH\(_2\)CH=CH\(_2\)), 3.77 (4H, s, NCH\(_2\)CH\(_2\)N), 4.98-5.08 (4H, m, 2 x CH\(_2\)CH\(_2\)CH=CH\(_2\)), 5.75-5.86 (2H, m, 2 x CH\(_2\)CH\(_2\)CH=CH\(_2\)); \(\delta_{\text{C}}\) (75 MHz) 28.3 [C(CH\(_3\))\(_3\)], 36.6 [CH(CH\(_2\)CH=CH\(_2\))\(_2\)], 37.8 [CH(CH\(_2\)CH=CH\(_2\))\(_2\)], 47.1 (NCH\(_2\)CH\(_2\)N), 51.9 (NCH\(_2\)CH\(_2\)N), 81.7 [C(CH\(_3\))\(_3\)], 116.6 [CH(CH\(_2\)CH=CH\(_2\))\(_2\)], 136.1 6 [CH(CH\(_2\)CH=CH\(_2\))\(_2\)], 150.8 (CO), 163.6 (N=C-N); \(m/z\) 265 (MH\(^+\), 2%), 209 (19), 191 (5), 165(27), 154 (14), 149 (14), 123 (25), 108 (8), 83 (3), 57 (100).
This compound was prepared by the general method, from \textit{1-tert-butyloxy carbonyl-2-(pent-4-enyl)-2-imidazoline} (0.77 g, 3.23 mmol), \textit{sec}-butyllithium (2.73 cm$^3$ of a 1.3M solution in hexanes, 3.55 mmol) and 3-bromopropene (0.31 cm$^3$, 3.55 mmol). The title compound was obtained as a yellow oil (0.78 g, 87%), (Found: C, 67.14; H, 9.18, N, 9.81%; \textit{MH}$^+$ 279.2084. C$_{16}$H$_{26}$N$_2$O$_2$0.5H$_2$O requires: C, 66.89, H, 9.05, N, 9.75%; \textit{MH}$^+$ 279.2072); $\nu$$_{\text{max}}$ (film)/cm$^{-1}$ 3076, 2977, 2933, 2878, 1718, 1640, 1479, 1455, 1363, 1321, 1215, 1175, 1157, 1005; $\delta$$_H$ (400 MHz) 1.50 [9H, s, C(CH$_3$)$_3$], 1.60-1.70 (1H, m, CHCHHCH$_2$CH=CH$_2$), 1.77-1.84 (1H, m, CHCHHCH$_2$CH=CH$_2$), 2.03-2.15 (2H, m, CHCH$_2$CH$_2$CH=CH$_2$), 2.26-2.34 (1H, m, CHCHHCH=CH$_2$), 2.39-2.49 (1H, m, CHCHHCH=CH$_2$), 3.50-3.58 (1H, m, CHCH$_2$CH=CH$_2$), 3.77 (4H, s, NCH$_2$CH$_2$N), 4.90-5.07 (4H, m, CH$_2$CH$_2$CH=CH$_2$ and CHCH$_2$CH=CH$_2$), 5.75-5.86 (2H, m, CHCH$_2$CH$_2$CH=CH$_2$ and CHCH$_2$CH=CH$_2$); $\delta$$_C$ (100 MHz) 28.5 [C(CH$_3$)$_3$], 31.4 (CHCH$_2$CH$_2$CH=CH$_2$), 31.5 (CHCH$_2$CH$_2$CH=CH$_2$), 37.4 (CHCH$_2$CH=CH$_2$), 37.7 (CHCH$_2$CH=CH$_2$), 47.2 (NCH$_2$CH$_2$N), 51.9 (NCH$_2$CH$_2$N), 114.7 (CHCH$_2$CH$_2$CH=CH$_2$), 116.7 (CHCH$_2$CH=CH$_2$), 136.1 (CHCH$_2$CH=CH$_2$), 138.9 (CHCH$_2$CH$_2$CH=CH$_2$), 151.0 (CO), 164.1 (N=C-N), \textit{m/z} 279 (MH$^+$, 12%), 223 (82), 179 (14), 168 (12), 137 (8), 123 (9), 97 (13), 67 (11), 57 (100).
1-tert-Butyloxy carbonyl-2-[(1-phenylmethyl)but-3-enyl]-2-imidazoline (2.1.23c)

This compound was prepared by the general method, from 2-(but-3-enyl)-1-tert-butyloxy carbonyl-2-imidazoline (0.30 g, 1.34 mmol), sec-butyllithium (1.47 cm$^3$ of a 1.0M in hexanes, 1.47 mmol) and benzyl bromide (0.18 cm$^3$, 1.47 mmol). The title compound was obtained as a yellow oil (0.32 g, 76%) (Found: C, 71.82; H, 8.38; N, 9.45 %; M$^+$ 314.1995. C$_{14}$H$_{18}$N$_2$ requires: C, 71.49; H, 8.67; N, 9.26%; M 314.1994); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2976, 1669, 1610, 1296, 1178, 1130; $\delta$H (400 MHz) 1.50 [9H, s, C(CH$_3$)$_3$], 2.27-2.34 (1H, m, CHCHHCH=CH$_2$), 2.40-2.47 (1H, m, CHCHHCH=CH$_2$), 2.78-2.84 (1H, dd, J 7.8 and 13.6, CHCHHPH), 3.02-3.07 (1H, dd, J 7.6 and 13.6, CHCHHPH), 3.60-3.77 (4H, m, NCH$_2$CH$_2$N), 3.87-3.92 (1H, m, CHCHPh), 5.00-5.05 (2H, m, CHCH$_2$CH=CH$_2$), 5.65-5.75 (1H, m, CHCH$_2$CH=CH$_2$), 7.15-7.28 (5H, m, Ar-H); $\delta$C (100 MHz) 28.2 [C(CH$_3$)$_3$], 36.6 (CHCH$_2$CH=CH$_2$), 38.8 (ClClCl$_2$Ph), 39.6 (CHCH$_2$Ph), 46.9 (NCH$_2$CH$_2$N), 51.8 (NCH$_2$CH$_2$N), 81.5 [OC(CH$_3$)$_3$], 116.6 (CHCH$_2$CH=CH$_2$), 126.0, 128.1 and 129.3 (Ar-CH), 135.9 (CHCH$_2$CH=CH$_2$), 139.9 (Ar-C), 150.6 (CO), 163.5 (N=C-N); m/z 315 (MH$^+$, 2%), 259 (24), 217 (26), 213 (15), 173 (24), 167 (28), 123 (26), 91 (21), 57 (100).

General method for the synthesis of 2$\alpha$-disubstituted 2-imidazolines (2.1.24)

Trifluoroacetic acid (5 cm$^3$) was added to the 2$\alpha$-disubstituted 1-tert-butyloxy carbonyl-2-imidazolines and the resulting solution was stirred at room temperature for 20–60 min. The trifluoroacetic acid was removed under reduced pressure and the imidazoline salt was...
dissolved in dichloromethane (50 cm³). The solution was then washed with a 10% w/v solution of aq.NaOH (50 cm³) and the organic layer was dried and concentrated. The crude product was then purified by column chromatography on silica gel (0:100→4:96 v/v isopropylamine:ethyl acetate) to give the 2-disubstituted 2α-imidazolines.

2-[1-(Prop-2-enyl)but-3-enyl]-2-imidazoline (2.1.24a)

\[
\text{NHBoc} \quad \text{H} \quad \text{N} \\
\text{CHCH=CH} \quad \text{CHCH=CH} \\
\text{NHBoc} \quad \text{H} \quad \text{N}
\]

This compound was prepared by the general method, from 1-tert-butyloxycarbonyl-2-[1-(prop-2-enyl)but-3-enyl]-2-imidazoline (1.20 g, 4.54 mmol) and TFA (3 cm³). The title compound was obtained as a yellow oil (0.50 g, 67%) (Found: M⁺ 165.138. C₁₀H₁₆N₂ requires: MH 165.139); v_max (film)/cm⁻¹ 3196, 3077, 2977, 2864, 1642, 1612, 1495, 1472, 1452, 1288, 994, 914; δ_H (400 MHz) 2.25-2.35 (4H, m, 2 x CHCH₂CH=CH₂), 2.46 (1H, m, CHCH₂CH=CH₂), 3.52 (4H, s, NCH₂CH₂N), 3.95 (1H, br s, NH), 4.95-5.10 (4H, m, 2 x CH=CH₂), 5.70-5.86 (2H, m, 2 x CH=CH₂); δ_C (100 MHz), 36.9 (CHCH₂CH=CH₂), 39.7 (CHCH₂CH=CH₂), 49.5 (NCH₂), 116.8 (CH=CH₂), 135.9 (CH=CH₂), 169.9 (N=C-N); m/z 165 (MH⁺, 100%), 149 (14), 135 (14), 121 (34), 110 (10), 94 (4), 82 (9), 67 (6).

2-[1-(Prop-2-enyl)pent-4-enyl]-2-imidazoline (2.1.24b)

\[
\text{NHBoc} \quad \text{H} \quad \text{N} \\
\text{CHCH=CH} \quad \text{CHCH=CH} \\
\text{NHBoc} \quad \text{H} \quad \text{N}
\]

This compound was prepared by the general method, from 1-tert-butyloxycarbonyl-2-[1-(prop-2-enyl)pent-4-enyl]-2-imidazoline (0.50 g, 1.80 mmol) and TFA (2 cm³). The title compound was obtained as a pale yellow oil (0.26 g, 81%) (Found: MH⁺ 179.1548.
C_{11}H_{18}N_{2} requires: \( MH \) 179.1548; \( \nu_{\text{max}} \) (film)/cm\(^{-1} \) 3176, 3077, 2976, 2933, 2863, 1641, 1611, 1495, 1472, 1455, 1289, 994, 912; \( \delta_{H} \) (400 MHz) 1.58-1.76 (2H, m, CHCH\(_2\)CH\(_2\)CH=CH\(_2\)), 2.05-2.15 (2H, m, CHCH\(_2\)CH\(_2\)CH=CH\(_2\)), 2.26-2.34 (2H, m, CHCH\(_2\)CH=CH\(_2\)), 2.38-2.44 (1H, m, CHCH\(_2\)CH=CH\(_2\)), 3.56 (4H, s, NCH\(_2\)CH\(_2\)N), 4.08 (1H, br s, NH), 4.95-5.10 (4H, m, 2 x CH=CH\(_2\)), 5.72-5.86 (2H, m, 2 x CH=CH\(_2\)); \( \delta_{C} \) (100 MHz) 31.3 (CHCH\(_2\)CH\(_2\)CH=CH\(_2\)), 31.8 (CHCH\(_2\)CH\(_2\)CH=CH\(_2\)), 37.6 (CHCH\(_2\)CH=CH\(_2\)), 39.4 (CHCH\(_2\)CH=CH\(_2\)), 49.6 (NCH\(_2\)), 114.4 and 116.5 (CH=CH\(_2\)), 135.9 and 138.1 (CH=CH\(_2\)), 169.9 (N=C-N); \( m/z \) 1164 (\( M^+ \), 9%), 163 (18), 135 (32), 124 (86), 123 (100), 109 (28), 97 (49), 67 (21).

2-[(1-Phenylmethyl)but-3-enyl]-2-imidazoline (2.1.24c)

![Chemical Structure](image)

This compound was prepared by the general method, from 1-tert-butyloxycarbonyl-2-[(1-phenyl)methylbut-3-enyl]-2-imidazoline (0.20 g, 0.64 mmol) and TFA (1 cm\(^3\)). The title compound was obtained as a white solid (0.09 g, 67%), m.p. 76-78 °C (Found: \( M^+ \) 214.1470). C\(_{14}\)H\(_{18}\)N\(_2\) requires: \( M \) 214.1470; \( \nu_{\text{max}} \) (KBr)/cm\(^{-1} \) 3120, 2976, 1669, 1610, 1296, 1200, 1178, 1130; \( \delta_{H} \) (400 MHz) 2.35-2.41 (1H, m, CHCH\(_2\)CH=CH\(_2\)), 2.48-2.56 (1H, m, CHCH\(_2\)CH=CH\(_2\)), 2.91-2.98 (1H, dd, \( J \) 7.6 and 13.6, CHCH\(_2\)Ph), 3.02-3.09 (1H, dd, \( J \) 7.6 and 13.6, CHCH\(_2\)Ph), 3.20-3.30 (1H, m, CHCH\(_2\)Ph), 3.99-3.87 (4H, m, NCH\(_2\)CH\(_2\)N), 5.05 (1H, d, \( J \) 10.2, CHCH\(_2\)CH=CH\(_2\)), 5.12 (1H, d, \( J \) 17.1, CHCH\(_2\)CH=CH\(_2\)), 5.65-5.75 (1H, m, CHCH\(_2\)CH=CH\(_2\)), 7.15-7.30 (5H, m, Ar-II), \( \delta_{C} \) (100 MHz) 36.1 (CHCH\(_2\)CH=CH\(_2\)), 37.8 (CHCH\(_2\)Ph), 40.2 (CHCH\(_2\)Ph), 44.7 (NCH\(_2\)), 118.2 (CHCH\(_2\)CH=CH\(_2\)), 126.9, 128.6 and 128.9 (Ar-CH), 133.8 (CHCH\(_2\)CH=CH\(_2\)), 137.4 (Ar-...
General method for the synthesis of 1-tert-butyloxycarbonyl-2-(2-oxoalkylidene)imidazolidines (2.1.30)

Sec-Butyllithium (1.3M solution in hexanes) was injected to a solution of 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline in dry THF/TMEDA (25:1 v/v; 0.1M in imidazoline) under nitrogen at -78°C. The bright yellow solution produced was stirred for 20 min at -78°C. The freshly distilled ester electrophile was injected to the reaction mixture at -78°C under nitrogen and the mixture was allowed to warm to 20°C overnight. The reaction was quenched with water (100 cm³) and the organic layer was extracted with diethyl ether (3 x 50 cm³) and the combined extracts were washed successively with saturated aq. NaHCO₃ (100 cm³), water (100 cm³) and brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9→1:1 v/v ethyl acetate:hexane) to give the acylated product.

1-tert-Butyloxy-2-(2-oxopropylidene)imidazolidine (2.1.30a)

This compound was prepared by the general method, from 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (0.55 g, 2.99 mmol), sec-butyllithium (3.58 cm³ of a 1.0 M solution
in hexane, 3.58 mmol) and ethyl acetate (0.70 cm\textsuperscript{3}, 6.00 mmol). The title compound was obtained as white crystals (0.49 g, 72%), m.p. 125-127°C (Found: C, 58.12; H, 8.11; N, 12.11%; M 226.1317. C\textsubscript{11}H\textsubscript{18}N\textsubscript{2}O\textsubscript{3} requires: C, 58.39; H, 8.02; N, 12.37%; M 226.1317); v\textsubscript{max} (KBr)/cm\textsuperscript{-1} 3253, 2976, 2936, 1725, 1622, 1557, 1318, 1253, 1149; \delta\textsubscript{H} (400 MHz) 1.45 [9H, s, C(CH\textsubscript{3})\textsubscript{3}], 2.03 (3H, s, CH\textsubscript{3}), 3.57 and 3.80 (each 2H, t, J 9.0, NCH\textsubscript{2}CH\textsubscript{2}N), 5.92 (1H, s, CH), 9.96 (1H, br s, NH); \delta\textsubscript{C} (100 MHz) 28.0 [C(CH\textsubscript{3})\textsubscript{3}], 29.3 (CH\textsubscript{3}), 41.1 and 44.9 (NCH\textsubscript{2}), 81.6 (CH), 82.7 [C(CH\textsubscript{3})\textsubscript{3}], 150.4 (CO), 157.6 (N=C-N), 195.2 (CH\textsubscript{3}CO); m/z 226 (M\textsuperscript{+}, 10%), 170 (32), 153 (10), 126 (31), 111 (68), 84 (41), 70 (12) 57 (100) 43 (29).

1-tert-Butyloxy-2-(2-oxo-2-phenylethylidene)imidazolidine (2.1.30b)

This compound was prepared by the general method, from 1-tert-butyloxy carbonyl-2-methyl-2-imidazoline (2.00 g, 10.86 mmol), sec-butyllithium (10.86 cm\textsuperscript{3} of a 1.1M solution in hexane, 11.95 mmol) and methyl benzoate (1.48 cm\textsuperscript{3}, 11.95 mmol) in THF (108 cm\textsuperscript{3}) and TMEDA (4 cm\textsuperscript{3}). The title compound was obtained as white crystals (2.00 g, 64%), m.p 170-172 °C (Found: C, 66.50; H, 7.00; N, 9.63%; MH\textsuperscript{+} 289.1545; C\textsubscript{16}H\textsubscript{20}N\textsubscript{2}O\textsubscript{3} requires: C, 66.65; H, 6.99; N, 9.71%; MH 289.1552); v\textsubscript{max} (KBr)/cm\textsuperscript{-1} 3253, 2979, 1733, 1608, 1557, 1581, 1532, 1358, 1317, 1146; \delta\textsubscript{H} (300 MHz) 1.57 [9H, s, C(CH\textsubscript{3})\textsubscript{3}], 3.67 and 3.88 (each 2H, t, J 8.5, NCH\textsubscript{2}CH\textsubscript{2}N), 6.69 (1H, s, CH), 7.86-7.95 (5H, m, Ar-H) 10.47 (1H, br s, NH); \delta\textsubscript{C} (75 MHz) 28.1 [C(CH\textsubscript{3})\textsubscript{3}], 41.2 and 45.1 (NCH\textsubscript{2}), 78.8 (C=CH), 82.9 [C(CH\textsubscript{3})\textsubscript{3}], 126.9, 128.1, 130.4 (Ar-CH), 140.5 (Ar-C), 150.5 (CO), 159.1 (NCN), 188.2 (PhCO); m/z 288 (M\textsuperscript{+}, 11%), 232 (22), 215 (8), 204 (7), 187 (100), 159 (24), 146 (3), 131 (8), 111 (41), 105 (33), 77 (34).
**1-tert-Butyloxy-2-(2-oxobut-3-enylidene)imidazolidine (2.1.30c)**

This compound was prepared by the general method, from 1-tert-butyloxy carbonyl-2-methyl-2-imidazoline (2.00 g, 10.86 mmol), sec-butyl lithium (11.95 cm³ of a 1.0M solution in hexane, 11.95 mmol) and methyl propenoate (1.86 cm³, 11.95 mmol). The **title compound** was obtained as white crystals (1.05 g, 42%), m.p 145-147 °C (Found: C, 60.63; H, 7.69; N, 11.77%; MH⁺ 239.1383. C₁₂H₁₇N₂O₃ requires: C, 60.74; H, 7.22; N, 11.80%; MH⁺ 239.1396); νmax (KBr/cm⁻¹) 3245, 2971, 2930, 1732, 1601, 1541, 1514, 1476, 1313, 1250, 1151; 1040; δH (400 MHz) 1.55 [9H, s, C(CH₃)₃], 3.67 and 3.88 (each 2H, t, J 7.8 NCH₂CH₂ N), 5.44-5.47 (1H, dd, J 2.0 and 10.4, CH=CH₂), 6.06 (1H, s, C=CHCO), 6.11-6.16 (1H, dd, J 2.0 and 17.2, CH=CH₂), 6.34-6.41 (1H, dd, J 10.4, and 17.2, CH=CH₂), 10.48 (1H, br s, NH); δC (100 MHz) 28.0 [C(CH₃)₃], 41.3 and 44.0 (NCH₂), 81.9 (CHCO), 83.0 [C(CH₃)₃], 122.1 (CH=CH₂), 138.3 (CH=CH₂), 150.4 (CO), 159.1 (N-C-N), 186.3 (C=CHCO); m/z 239 (M⁺, 5%), 183 (12), 165 (3), 149 (5), 139 (12), 123 (2), 108 (6), 87 (5) 57 (100).

**2-(2-Oxopropylidene)imidazolidine (2.1.31a)**

Trifluoroacetic acid (1 cm³) was added to 1-tert-butyloxy-2-(2-oxopropylidene)imidazolidine (0.20 g, 088 mmol) and the resulting solution was stirred at 20°C for 1h. The trifluoroacetic acid was removed under reduced pressure and the
imidazolidine trifluoroacetate salt was dissolved in dichloromethane (20 cm³). The solution was then washed with aq. NaOH (20 cm³, 10 % w/v) and the organic layer was dried and concentrated. The crude product was then purified by column chromatography on silica gel (0:100→3:97 v/v isopropylamine:chloroform) to give the title compound as a yellow solid (0.09 g, 81 %), m.p. 157-159 °C (Found: M⁺ 126.0793. C₆H₁₀N₂O requires: M⁺ 126.0793); νₘₐₓ (KBr)/cm⁻¹ 3279, 3116, 1605, 1557, 1490, 1323; δ_H (400 MHz) 1.98 (3H, s, CH₃), 3.55 and 3.70 (each 2H, t, J 7.8, NCH₂CH₂N), 4.77 (1H, s, CH), 5.40 (1H, br s, NH), 9.20 (1H, br s, NH); δ_C [100 MHz; (CD₃)₂SO] 28.5 (CH₃), 41.8 and 43.5 (NCH₂), 76.0 (CH), 164.4 (N-C-N), 188.1 (CO); m/z 126 (M⁺, 44%), 111 (100) 97 (12), 84 (39), 70 (23), 54 (40) 43 (73).

2-(2-Oxo-(3-phenyl)ethylidene)imidazolidine (2.1.3lb)

Trifluoroacetic acid (4 cm³) was added to 1-tert-butyloxy-2-(2-oxo-3-phenylethylidene)imidazolidine (1.20 g, 4.16 mmol) and the resulting solution was stirred at 20°C for 40 min. The trifluoroacetic acid was removed under reduced pressure and the imidazolidine salt was dissolved in dichloromethane (20 cm³). The solution was then washed with a solution of aq. NaOH (20 cm³, 10% w/v) and the organic layer was dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→3:97 v/v isopropylamine:ethyl acetate) to give the title compound as white crystals (0.70 g, 90 %), m.p. 203-205°C (lit., 116 208°C) (Found: C, 69.88; H, 6.48; N, 14.73%; (M-H)⁺ 187.0864. C₁₁H₁₂N₂O requires: C, 70.19; H, 6.43; N, 14.88%; M-H 187.0871); νₘₐₓ (KBr)/cm⁻¹ 3310, 2987, 2860, 1603, 1582, 1554, 1503, 1477, 1451, 1332, 1290, 1213,
1054, 720; δ$_H$ [300 MHz; (CD$_3$)$_2$SO] 3.45 and 3.59 (each 2H, t, J 8.0, NCH$_2$), 5.54 (1H, s, CH), 7.30-7.39 (3H, m, Ar-H), 7.69-7.75 (2H, m, Ar), 9.28 (1H, br s, NH); δ$_C$ [75 MHz; (CD$_3$)$_2$SO] 41.8 and 43.5 (NCH$_2$), 73.1 (CH), 126.1, 127.9 and 129.4 (Ar-CH), 141.5 (Ar-C), 165.4 (N-C-N), 181.9 (CO); m/z 188 (M$,^+$, 67%), 159 (30), 131 (18), 111 (100), 105 (37), 81 (8), 77 (85).

1-tert-Butyloxycarbonyl-2-(diethylphosphonomethyl)-2-imidazoline (2.1.32)

Sec-Butyllithium (18.39 cm$^3$ of a 1.3M solution in cyclohexane, 23.91 mmol) was injected to a solution of 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (4.00 g, 21.74 mmol) in dry THF (200 cm$^3$) and TMEDA (5 cm$^3$) at -78°C under nitrogen. The bright yellow solution produced was stirred for 20 min at -78°C under nitrogen before diethyl chlorophosphate (3.45 cm$^3$, 23.91 mmol) was injected into the reaction mixture. The mixture was allowed to warm to 20°C overnight and the reaction was quenched with water (100 cm$^3$). The organic layer was extracted with diethyl ether (3 x 100 cm$^3$) and the combined organic extracts were washed successively with saturated aq. NaHCO$_3$ (100 cm$^3$), water (50 cm$^3$) and brine (50 cm$^3$), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→1:99 v/v isopropylamine:chloroform) to give the title compound as a yellow oil (3.56 g, 51%) (Found: C, 45.14; H, 7.86; N, 7.90%, M$^+$ 320.1501. C$_{13}$H$_{25}$N$_2$O$_5$P·1.5H$_2$O requires: C, 44.95; H, 8.07; N, 8.07%; M 320.1501); v$_{max}$ (film)/cm$^{-1}$ 2981, 2935, 1713, 1639, 1371, 1254, 1165, 1028, 971; δ$_H$ (400 MHz) 1.31-1.34 (6H, t, J 7.2, CH$_3$CH$_2$), 1.50 [9H, s, C(CH$_3$)$_3$], 3.56-3.62 (2H, d, J 22.0, CH$_2$P(O)(OEt)$_2$), 3.80 (4H, s, NCH$_2$CH$_2$N), 4.14-4.21
General method for the synthesis of 1-tert-butyloxycarbonyl-2-(1-alkenyl)-2-imidazolines (2.1.33)

Sec-Butyllithium (solution in cyclohexane, 1.1 equiv.) was added dropwise to a stirred solution 1-tert-butyloxycarbonyl-2-(diethylphosphonomethyl)-2-imidazoline in dry THF/TMEDA (25:1 v/v; 0.1M in imidazoline) at -78°C under nitrogen. The red solution produced was stirred for 20 min at -78°C. Freshly distilled aldehyde electrophile (1.1 equiv.) was injected rapidly to the reaction mixture at -78°C under nitrogen and the stirred reaction mixture was allowed to warm to 20°C overnight. It was then quenched with water (100 cm³). The organic layer was extracted with diethyl ether (3 x 100 cm³) and the combined organic extracts were washed successively with saturated aq. NaHCO₃ (100 cm³) and brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9→2:3 ethyl acetate/hexane) to give the 1-Boc-2-(1-alkenyl)-2-imidazoline.
1-\textit{tert}-Butyloxycarbonyl-2-(pent-1-enyl)-2-imidazoline (2.1.33a)

The compound was synthesised by the general method, from 1-\textit{tert}-butyloxycarbonyl-2-(diethylphosphonomethyl)-2-imidazoline (0.50 g, 1.56 mmol), \textit{sec}-butyllithium (1.72 cm$^3$ of a 1M solution in cyclohexane, 1.72 mmol) and butanal (0.15 cm$^3$, 1.72 mmol). The title compound was obtained after column chromatography on silica gel (1:9→1:1 v/v ethyl acetate:hexane) as a colourless oil (0.25 g, 67%; 0.19 g of \textit{E}-isomer and 0.06 g of \textit{Z}-isomer). The \textit{Z}-isomer converts to the \textit{E}-isomer upon standing; (Found: C, 63.51; H, 9.22; N, 11.74%; MH$^+$ 239.1760. C$_{13}$H$_{22}$N$_2$O$_2$·0.4H$_2$O requires: C, 63.31; H, 9.25; N, 11.36%; MH$^+$ 239.1759); $\nu$ max (film)/cm$^{-1}$ 2961, 2932, 1718, 1654, 1614, 1370, 1149, 1014; data for \textit{E}-isomer: $\delta_H$ (400 MHz) 0.93 (3H, t, J 7.2, CH$_3$CH$_2$CH$_2$), 1.48-1.53 (2H, m, CH$_3$CH$_2$CH$_2$), 1.52 [9H, s, C(CH$_3$)$_3$], 2.15-2.20 (2H, dt, J 7.2 and 7.6, CH$_3$CH$_2$CH$_2$CH=CH), 3.78 (4H, s, NCH$_2$CH$_2$N), 6.72 (2H, s, CH=CH); $\delta_C$ (100 MHz) 13.9 (CH$_3$CH$_2$), 21.7 (CH$_3$CH$_2$CH$_2$), 28.2 [C(CH$_3$)$_3$], 35.3 (CH$_3$CH$_2$CH$_2$), 46.8 and 52.0 (NCH$_2$), 81.6 [C(CH$_3$)$_3$], 119.6 (CH$_2$CH=CH), 141.8 (CH$_2$CH=CH), 151.1 (CO), 157.3 (N=C-N); m/z 239 (MH$^+$, 100%), 183 (84), 167 (16), 139 (39), 123 (14), 109 (25), 84 (5), 81 (11), 57 (99). Data for \textit{Z}-isomer: $\delta_H$ (400 MHz) 0.92 (3H, t, J 7.2, CH$_3$CH$_2$), 1.48-1.53 (2H, m, CH$_3$CH$_2$), 1.52 [9H, s, C(CH$_3$)$_3$], 2.42-2.47 (2H, dt, J 7.2 and 7.6, CH$_3$CH$_2$CH$_2$CH=CH), 3.71-3.76 and 3.86-3.90 (each 2H, t, J 9.2, NCH$_2$CH$_2$N), 5.92 (1H, m, CH$_2$CH=CH), 6.42 (1H, d, J 11.6, CH$_2$CH=CH); $\delta_C$ (100 MHz) 13.9 (CH$_3$CH$_2$), 22.5 (CH$_3$CH$_2$CH$_2$), 28.2 [C(CH$_3$)$_3$], 31.4 (CH$_3$CH$_2$CH$_2$CH=CH), 45.9 and 52.8 (NCH$_2$), 81.6 [C(CH$_3$)$_3$], 118.8 and 141.3 (CH=CH), 151.1 (CO), 155.8 (N=C-N).
The compound was synthesised by the general method, from 1-<em>tert</em>-butyloxycarbonyl-2-(diethylphosphonomethyl)-2-imidazoline (1.42 g, 4.44 mmol), sec-butyllithium (6.10 cm$^3$ of a 0.8M solution in cyclohexane, 4.48 mmol) and but-2-enal (0.40 cm$^3$, 4.48 mmol). The title compound was obtained after column chromatography on silica gel (1:9→2:8 v/v ethyl acetate:hexane) as an orange solid (0.68 g, 65%), m.p 58-60$^\circ$C (Found: C, 65.82; H, 8.56; N: 11.43%; $M/H^+$ 237.1603. $C_{13}H_{20}N_2O_2$ requires: C, 66.07; H, 8.53; N, 11.85%; $M/H$ 237.1603); $\nu_{\max }$ (KBr/cm$^{-1}$) 2977, 2934, 1714, 1646, 1617, 1596, 1375, 1166, 1140, 1011; $\delta_H$ (400 MHz) 1.52 [9H, s, C(CH$_3$)$_3$], 1.83 (3H, d, $J$ 6.8, CH$_3$CH), 3.80 (4H, s, NCH$_2$CH$_2$N), 5.96-6.01 (1H, m, CH$_3$CH), 6.20 (1H, dd, $J$ 13.0, 13.2, CH$_3$CH=CHCH=CH), 6.78-6.82 (1H, d, $J$ 15.6, CH$_3$CH=CHCH=CH), 7.15-7.21 (1H, dd, $J$ 13.2 and 15.6, CH$_3$CH=CHCH=CH); $\delta_C$ (100 MHz) 18.5 (CH$_3$), 28.3 [C(CH$_3$)$_3$], 46.9 and 52.1 (NCH$_2$), 81.7 [C(CH$_3$)$_3$], 117.9, 131.1, 135.7 and 139.3 (CH), 151.2 (CO), 157.5 (N=C-N); $m/z$ 237 ($M/H^+$, 18%), 221 (49), 181 (38), 165 (100), 135 (17), 121 (52), 107 (12), 83 (92), 57 (100).
1-tert-Butyloxycarbonyl-2-(2-phenylethenyl)-2-imidazoline (2.1.33c)

The compound was synthesised by the general method, from 1-tert-butyloxycarbonyl-2-(diethylphosphonomethyl)-2-imidazoline (0.50 g, 1.56 mmol), sec-butyllithium (1.72 cm³ 1M of a solution in cyclohexane, 1.72 mmol) and benzaldehyde (0.17 cm³, 1.72 mmol). Column chromatography on silica gel (1:9–2:3 v/v ethyl acetate:hexane) afforded the title compound as a white solid (0.28 g, 66%), m.p. 63–65°C (Found: C, 69.90; H, 7.45; N, 9.89%; M⁺ 272.1525. C₁₆H₂₀N₂O₂·0.1H₂O requires: C, 70.08; H, 7.37; N, 10.22%; M 272.1525); v max (KBr)/cm⁻¹: 2979, 1713, 1641, 1608, 1371, 1316, 1148, 1015, 756; δ H (400 MHz) 1.50 [9H, s, C(CH₃)₃], 3.80 (4H, s, NCH₂CH₂N), 7.22–7.32 (4H, m, PhC=CH, and 3 x Ar-H), 7.47 (3H, m PhCH=CH and 2 x Ar-H); δ C (100 MHz) 28.2 [C(CH₃)₃], 46.9 and 52.1 (NCH₂), 81.7 [C(CH₃)₃], 117.2 (PhCH=CH), 127.5, 128.6 and 128.9 (Ar-CH), 135.9 (Ar-C), 138.2 (PhCH=CH), 151.1 (CO), 157.4 (N=C-N); m/z 272 (M⁺, 13%), 244 (13), 215 (100), 199 (25), 171 (100), 143 (29), 115 (55), 107 (62), 91 (73) 79 (71) 57 (100).

General method for the one pot synthesis of 1-tert-butyloxycarbonyl-2-(1-alkenyl)-2-imidazolines (2.1.33)

Sec-Butyallithium (1.3M solution in cyclohexane) was injected to a stirred solution of 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline in dry THF/TMEDA (25:1 v/v; 0.1M in
imidazoline) stirred at -78°C under nitrogen. The bright yellow solution produced was stirred for 20 min at -78°C, when diethyl chlorophosphate (1.1 equiv.) was injected a pale yellow solution was produced that was stirred at -78°C for 1h and at 20°C for 4 h under nitrogen. The reaction mixture was cooled to -78°C and a second equiv. of sec-butyllithium (1.3M solution in cyclohexane) was added. The bright red solution produced was stirred at -78°C for 20 min and freshly distilled aldehyde (1.1 equiv.) was injected to it. The stirred reaction mixture was allowed to warm to 20°C overnight. It was then quenched with water (100 cm³), the organic layer was extracted with diethyl ether (3 x 100 cm³) and the combined organic extracts were washed successively with saturated aq. NaHCO₃ (100 cm³), water (50 cm³) and brine (50 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:4→2:3 v/v ethyl acetate:hexane) to give the 1-tert-butyloxycarbonyl-2-(1-alkenyl)-2-imidazoline.

One pot synthesis of 1-tert-butyloxycarbonyl-2-(pent-1-enyl)-2-imidazoline (2.1.33a)

The compound was synthesised by the general method, from 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (2.00 g, 10.86 mmol), sec-butyllithium (2 x 9.19 cm³ of a 1.3M solution in cyclohexane, 11.95 mmol), diethyl chlorophosphate (1.32 cm³, 10.86 mmol) and butanal (1.05 cm³, 11.95 mmol) in THF (108 cm³) and TMEDA (3 cm³). The title compound was obtained as a yellow oil (0.85 g, 33%), (0.68 g of E-isomer and 0.17 g of Z-isomer). They have data identical to those reported for the two-stage synthesis.
One pot synthesis of 1-tert-butyloxycarbonyl-2-(pent-1,3-dienyl)-2-imidazoline (2.1.33b)

![Chemical structure](image)

The compound was synthesised by the general method, from 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (4.00 g, 21.70 mmol), sec-butyllithium (2 x 18.4 cm$^3$ of a 1.3 M solution in cyclohexane, 2 x 23.90 mmol), diethyl chlorophosphate (3.45 cm$^3$, 23.90 mmol) and 2-butenal (1.98 cm$^3$, 23.90 mmol) in THF (217 cm$^3$) and TMEDA (3 cm$^3$). The title compound was obtained as a white solid (1.75 g, 33%), m.p 58-60 °C, having data identical to those reported for the two-stage synthesis.

One pot synthesis of 1-tert-butyloxycarbonyl-2-(2-phenylethenyl)-2-imidazoline (2.1.33c)

![Chemical structure](image)

The compound was synthesised by the general method, from 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (2.00 g, 10.86 mmol), sec butyllithium (2 x 9.19 cm$^3$ of a 1.3 M solution in cyclohexane, 2 x 11.95 mmol), diethyl chlorophosphate (1.32 cm$^3$, 10.86 mmol) and benzaldehyde (1.21 cm$^3$, 11.95 mmol) in THF (108 cm$^3$) and TMEDA (3 cm$^3$). The title compound was obtained as a white solid (1.20 g, 40%), m.p. 63-65 °C, having data identical to those reported for the two-stage synthesis.
General method for the synthesis of 2-(1-alkenyl)-2-imidazolines from 1-tert-butyloxycarbonyl-2-(1-alkenyl)-2-imidazolines (2.1.34)

Trifluoroacetic acid (1 cm³) was added to the 1-tert-butyloxycarbonyl-2-(1-alkenyl)-2-imidazoline and the resulting solution was stirred at 20 °C for 20–60 min. The trifluoroacetic acid was removed under reduced pressure and the crude product was then purified by column chromatography on neutral alumina (activation grade III) (0:100→2:98 v/v isopropylamine:ethyl acetate) to give the 2-(1-alkenyl)-2-imidazoline.

2-(Penta-1-enyl)-2-imidazoline (2.1.34a)

The compound was synthesised by the general method, from 1-tert-butyloxycarbonyl-2-(penta-1-enyl)-2-imidazoline (0.20 g, 0.84 mmol) and trifluoroacetic acid (1 cm³). The title compound was obtained as a white gum (0.095 g, 82%) (Found: M⁺ 138.1157. C₈H₁₄N₂ requires: M⁺, 138.1157); νₘₐₓ (film)/cm⁻¹ 3197, 2956, 2932, 2871, 1699, 1603, 1580, 1500, 1470, 1278, 973; δH (400 MHz) 0.85 (3H, t, J 7.2, CH₃), 1.37-1.43 (2H, m, CH₂CH₂CH₂), 2.07-2.13 (2H, dt, J 7.2 and 7.6, CH₃CH₂CH₂CH=CH), 3.60 (4H, s, NCH₂CH₂N), 5.95-6.00 (1H, d, J 16.1, CH₂CH=CH), 6.17-6.24 (1H, m, CH₂CH=CH); δC (100 MHz) 13.6 (CH₃), 21.7 (CH₃CH₂), 34.6 (CH₂CH=CH), 50.0 (NCH₂), 120.9 and 139.9 (CH=CH),
164.2 (N-C=N); m/z 138 (M⁺, 61%), 123 (31), 109 (100), 94 (37), 81 (96), 67 (26), 56 (34), 41(48).

2-(Penta-1,3-dienyl)-2-imidazoline (2.1.34b)

The compound was synthesised from 1-tert-butyloxycarbonyl-2-(penta-1,3-dienyl)-2-imidazoline (0.54 g, 2.28 mmol) and trifluoroacetic acid (1 cm³) using the general method described before. The title compound was obtained as a white solid (0.20 g, 64%), m.p 112-114 °C (Found: M⁺ 136.1000. C₈H₁₂N₂ requires: M 136.1000); νmax (KBr)/cm⁻¹ 3178, 2936, 2870, 1651, 1630, 1475, 1276, 988; δH (400 MHz) 1.83 (3H, d, J 6.8 Hz, CH₃CH=CHCH=CH), 3.68 (4H, s, NCH₂CH₂N), 4.40 (1H, br s, NH), 5.95-6.00 (1H, m, CH₃CH=CHCH=CH), 6.02-6.06 (1H, d, J 15.6, CH₃CH=CHCH=CH), 6.14-6.20 (1H, dd, J 13.2 and 13.0, CH₃CH=CHCH=CH), 6.72-6.68 (1H, dd, J 13.2 and 15.6, CH₃CH=CHCH=CH); δC (100 MHz) 18.5 (CH₃CH=CHCH=CH), 49.6 (NCH₂CH₂N), 118.4, 130.5, 135.8 and 138.0 (CH), 164.3 (N-C-N); m/z 136 (M⁺, 100%), 135 (64), 121 (49), 106 (66), 92 (26), 79 (38), 66 (22), 41 (18), 18 (16).
The compound was synthesised from 1-tert-butyloxycarbonyl-2-(2-phenylethenyl)-2-imidazoline (0.17 g, 0.62 mmol), and trifluoroacetic acid (2 cm³) using the general method. The title compound was obtained as a white solid (0.098 g, 91%), m.p 154-156 °C (Found: M⁺ 172.1000. C₁₁H₁₂N₂ requires: M 172.1000); νmax (KBr/cm⁻¹ 3171, 2926, 2867, 1651, 1597, 1581, 1501, 1292, 982, 760; δH (400 MHz) 3.70 (4H, s, NCH₂CH₂N), 4.32 (1H, br s, NH), 6.68 and 7.05 (each 1H, d, J 16.6, CH=CH), 7.30 (3H, m, Ar-H), 7.46 (2H, m, Ar-H), δC (100 MHz) 50.0 (NCH₂), 118.3 (CH), 127.2, 128.8, 128.9 and 135.4 (Ar-C), 136.7 (CH), 164.1 (N=C-N); m/z 172 (M⁺, 65%), 171 (79), 143 (23), 128 (13), 115 (100), 103 (8), 77 (17), 57 (36).

1-tert-Butyloxycarbonyl-2-phenylthiomethyl-2-imidazoline (2.1.35) and 1-tert-butyloxycarbonyl-2,2-bis(phenylthiomethyl)-2-imidazoline (2.1.36)

Sec-Butyllithium (4.97 cm³ of a 1.2M solution in cyclohexane, 5.97 mmol) was injected to a stirred solution of 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (1.00 g, 5.43 mmol) in dry THF (54 cm³) and TMEDA (2 cm³) at -78°C under nitrogen. The bright yellow solution produced was stirred for 20 min at -78°C when diphenyl disulphide (1.30 g, 5.97 mmol) in THF (20 cm³) was added via cannula to the reaction mixture at -78°C under nitrogen and the mixture was allowed to warm to 20°C overnight. The reaction was
quenched with water (100 cm$^3$), the organic layer was extracted with diethyl ether (3 x 100 cm$^3$) and the combined organic extracts were washed successively with aq. NaHCO$_3$ (100 cm$^3$), water (50 cm$^3$) and brine (50 cm$^3$), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9→2:3 v/v ethyl acetate:hexane) to give the **monosulphenated 2-imidazoline** as a white solid (0.60 g, 38%), m.p. 77-79 °C (Found: C, 61.55; H, 6.98; N, 9.50%; M$^+$ 292.1245. C$_{15}$H$_{20}$N$_2$O$_2$S requires: C, 61.62; H, 6.89; N, 9.58%; $M$ 292.1245); $\nu$$_{\text{max}}$ (KBr)/cm$^{-1}$ 2974, 1703, 1635, 1483, 1379, 1142, 737; $\delta$$_{\text{H}}$ (400 MHz) 1.46 [9H, s, C(CH$_3$)$_3$], 3.70 (4H, s, NCH$_2$CH$_2$N), 4.07 (2H, s, PhSCH$_2$), 7.22-7.35 (3H, m, Ar-H), 7.38-7.42 (2H, m, Ar-H); $\delta$$_{\text{C}}$ (100 MHz) 28.1 [C(CH$_3$)$_3$], 34.0 (PhSCH$_2$), 46.8 and 52.2 (NCH$_2$), 82.2 [C(CH$_3$)$_3$], 126.4, 128.9 and 129.8 (Ar-CH), 136.0 (Ar-C), 150.6 (CO), 157.7 (N=C-N); m/z 292 (M$^+$, 8%), 236 (41), 219 (5), 203 (14), 191 (13), 159 (22), 123 (12), 109 (10), 57 (100), and the **disulphenated 2-imidazoline** as a white solid (0.65 g, 28%), m.p. 91-93 °C (Found: C, 62.93; H, 6.13; N, 7.03%; $M$ 400.1279. C$_{15}$H$_{20}$N$_2$O$_2$S requires: C, 62.97; H, 6.04; N, 6.99%; $M$ 400.1279); $\nu$$_{\text{max}}$ (KBr)/cm$^{-1}$ 2977, 1698, 1634, 1482, 1364, 1133, 1006, 739; $\delta$$_{\text{H}}$ (400 MHz; CDCl$_3$) 1.52 [9H, s, C(CH$_3$)$_3$], 3.66-3.68 and 3.74-3.77 (each 2H, t, $J$ 8.0, NCH$_2$CH$_2$N), 6.20 (1H, br s, CH), 7.31-7.35 (6H, m, Ar-H), 7.48-7.51 (4H, m, Ar-H); $\delta$$_{\text{C}}$ (100 MHz) 28.7 [C(CH$_3$)$_3$], 47.5 and 52.4 (NCH$_2$), 54.5 ((PhS)$_2$CH), 82.7 [C(CH$_3$)$_3$], 128.6, 129.2 and 132.7 (Ar-CH), 134.4 (Ar-C), 150.7 (CO), 157.8 (N=C-N); m/z 400 (M$^+$, 2%), 291 (19), 235 (100), 191 (38), 139 (43), 121 (27), 110 (21), 97 (80), 77 (18), 70 (23), 57 (85).
Trifluoroacetic acid (2 cm³) was added to 1-tert-butyloxycarbonyl-2-phenylthiomethyl-2-imidazoline (0.30 g, 1.02 mmol) and the resulting solution was stirred at 20°C for 1 h. The trifluoroacetic acid was removed under reduced pressure and the imidazoline salt was dissolved in chloroform (10 cm³). The solution was then washed with aq. NaOH (10% w/v; 10 cm³) and the organic layer was dried and concentrated. The crude product was purified by column chromatography on neutral alumina (activation grade III) (0:100→1:99 v/v isopropylamine:chloroform) to give the title compound as a white solid (0.16 g, 81%), m.p. 83-85 °C (Found: C, 62.38; H, 6.37; N, 14.51%; M⁺ 192.0721. C₁₀H₁₂N₂S requires: C, 62.47; H, 6.29; N, 14.56%; M 192.0721); νmax (KBr)/cm⁻¹ 3207, 3057, 2928, 1613, 1482, 1464, 1448, 1439, 1292, 1278, 1094, 980, 734; δH (400 MHz) 3.57 (4H, s, NCH₂CH₂ N), 3.75 (2H, s, PhSCTf₂), 4.58 (1H, br s, NH), 7.22-7.35 (3H, m, Ar-H), 7.42-7.45 (2H, m, Ar-H); δC (100 MHz) 31.9 (PhSCH₂), 50.2 (NCH₂), 126.5, 128.8, 129.3 (Ar-CH), 135.0 (Ar-C), 164.3 (N=C-N); m/z 192 (M⁺, 100%), 177 (5), 159 (55), 123 (9), 109 (39), 81 (50), 65 (25), 54 (74).

1-tert-Butyloxycarbonyl-2-phenylselenenomethyl-2-imidazoline (2.1.38) and 1-tert-butyloxycarbonyl-2,2-bis(phenylseleneno)methyl-2-imidazoline (2.1.39)

Sec-Butyllithium (12.32 cm³, of a 1.3M solution in cyclohexane, 16.02 mmol) was injected to a stirred solution of 1-tert-butyloxycarbonyl-2-methyl-2-imidazoline (2.95 g,
16.02 mmol) in dry THF (100 cm$^3$) and TMEDA (0.5 cm$^3$) at -78°C under nitrogen. The bright yellow solution produced was stirred for 20 min at -78°C, when diphenyl diselenide (5.00 g, 16.02 mmol) in THF (60 cm$^3$) was added via cannula and the mixture was allowed to warm to 20°C overnight. The reaction was quenched with water (100 cm$^3$), the organic layer was extracted with diethyl ether (3 x 100 cm$^3$) and the combined organic extracts were washed successively with saturated aq. NaHCO$_3$ (100 cm$^3$), water (50 cm$^3$) and brine (50 cm$^3$), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9→2:3 v/v ethyl acetate:hexane) to give the monoselenated 2-imidazoline as a white solid (2.86 g, 52%), m.p. 76-78 °C (Found: C, 53.13; H, 6.03; N, 8.29%, $M^+$ 340.0689. C$_{15}$H$_{20}$N$_2$O$_2$Se requires: C, 53.10; H, 5.94; N, 8.25%; $M$ 340.0689); $v_{\text{max}}$ (KBr)/cm$^{-1}$ 2974, 1702, 1636, 1480, 1380, 1141, 732; $\delta_H$ (400 MHz) 1.55 [9H, s, C(CH$_3$)$_3$], 3.76 (4H, s, NCH$_2$CH$_2$N), 4.05 (2H, s, PhSeCH$_2$), 7.25 (3H, m, Ar-H), 7.60 (2H, m, Ar-H); $\delta_C$ (100 MHz) 26.2 (PhSeCH$_2$), 28.5 [C(CH$_3$)$_3$], 46.6 and 52.2 (NCH$_2$CH$_2$N), 82.2 [C(CH$_3$)$_3$], 127.5, 128.7 and 130.6 (Ar-CH), 133.3 (Ar-C), 150.7 (CO), 159.1 (N=C=N); $m/z$ 340 ($M^+$, 1.5%), 282 (12), 215 (17), 203 (11), 159 (45), 127 (7), 91 (8), 57 (100); and the diselenenated 2-imidazoline as a yellow oil (0.63 g, 8%) (Found: C, 51.58; H, 4.85; N, 5.59%; $M^+$ 496.0163. C$_{16}$H$_{20}$N$_2$O$_2$ requires: C, 51.01; H, 4.85; N, 5.66%; $M$ 496.0168); $v_{\text{max}}$ (film)/cm$^{-1}$ 2977, 2930, 1708, 1628, 1477, 1371, 1141, 1002; $\delta_H$ (300 MHz) 1.47 [9H, s, C(CH$_3$)$_3$], 3.63 and 3.68 (each 2H, t, $J$ 7.0, NCH$_2$CH$_2$N), 6.14 (1H, br s, CH), 7.25-7.29 (6H, m, Ar-H), 7.59-7.71 (4H, m, Ar-H); $\delta_C$ (75 MHz) 28.2 [C(CH$_3$)$_3$], 37.5 (CH), 47.3 and 51.9 (NCH$_2$), 82.1 [C(CH$_3$)$_3$], 128.7, 129.1, 135.1 (Ar-CH), 131.5 (Ar-C), 150.4 (CO), 159.1 (N=C=N); $m/z$ 494 ($M^+$, 2%), 439 (1), 397 (1), 395 (1), 339 (2), 314 (12) 283 (11), 234 (7), 157 (100), 130 (8), 117 (21), 97 (18), 77 (100).
Sec-Butyllithium (0.62 cm³ of a 1.2M solution in cyclohexane, 0.74 mmol) was injected to a solution of 1-tert-butyloxy carbonyl-2-phenylselenenomethyl-2-imidazoline (0.21 g, 0.62 mmol) in dry THF (7 cm³) and TMEDA (0.5 cm³) at -78°C under nitrogen. The dark orange solution produced was stirred for 20 min at -78°C, when benzyl bromide (0.09 cm³, 0.74 mmol) was injected into the reaction mixture under nitrogen and the mixture was allowed to warm to 20°C overnight. The reaction was quenched with water (100 cm³), the organic layer was extracted with diethyl ether (3 x 100 cm³) and the combined organic extracts were washed successively with saturated aq. NaHCO₃ (100 cm³), water (100 cm³) and brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9→2:3 v/v ethyl acetate:hexane) to give the title compound as a yellow oil (0.21 g, 79%) (Found: C, 60.66; H, 6.27; N, 6.33%; M⁺ 430.1159. C₂₂H₂₆N₂O₂Se 0.2H₂O requires: C, 60.86; H, 6.08; N, 6.45%; M 430.1159); νmax (film)/cm⁻¹ 2977, 1713, 1370, 1144, 999, 766, 696; δH (400 MHz) 1.48 [9H, s, CF₃CH₂]; 3.10-3.18 (1H, dd, J 6.8 and 13.8, CHPh); 3.38-3.48 (1H, dd, J 6.8 and 13.8, CH₂Ph); 3.60-3.77 (4H, m, NCH₂CH₂N); 5.15 (1H, br s, CH); 7.15-7.40 (8H, m, Ar-H); 7.53 (2H, m, Ar-H); δC (100 MHz) 28.2 [C(CH₃)$_3$], 39.0 (CH₂Ph), 39.2 (CH), 46.8 and 51.8 (NCH₂), 81.8 [C(CH₃)$_3$], 126.3, 128.1 128.4, 128.6, 128.8 and 136.5 (Ar-CH), 137.1 and 139.4 (Ar-C), 150.5 (CO), 160.8 (N=C-N); m/z 430 (M⁺, 1%), 374 (5), 324 (5), 293 (3), 217 (32), 173 (24), 141 (19), 123 (31), 77 (18), 57 (100).
Sec-Butyllithium (5.38 cm³ of a 1.3M solution in cyclohexane, 7.00 mmol) was injected to a solution of 1-tert-butyloxycarbonyl-2-phenylselenenomethyl-2-imidazoline (2.00 g, 5.89 mmol) in dry THF (59 cm³) and TMEDA (2 cm³) at -78°C under nitrogen. The brown solution produced was stirred for 20 min at -78°C when 1-iodopropane (0.70 cm³, 7.00 mmol) was injected to the reaction mixture. The reaction was allowed to warm to 20°C overnight and was quenched with water (100 cm³). The organic layer was extracted with diethyl ether (3 x 100 cm³) and the combined organic extracts were washed successively with saturated aq. NaHCO₃ (100 cm³), water (100 cm³) and brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9-2:3 v/v ethyl acetate:hexane) to give the title compound as a yellow oil (1.80 g, 80%) (Found: C, 56.98; H, 7.23; N, 7.48%; M⁺ 382.1158. C₁₅H₂₈N₂O₂Se requires: C, 56.69; H, 6.87; N, 7.34; M 382.1158); νmax (film)/cm⁻¹ 2960, 1713, 1613, 1368, 1146; δH (400 MHz) 0.82 (3H, t, J 7.2, CH₃CH₂), 1.45 (2H, m, CH₃CH₂), 1.52 (9H, s, [C(CH₃)₃], 1.68-1.75 (1H, m, CH₃CH₂CHHCH), 1.83-1.91 (1H, m, CH₃CH₂CHHCH), 3.57-3.80 (4H, m, NCH₂CH₂N), 4.71 (1H, br s, CH), 7.25 (3H, m, Ar-H), 7.53 (2H, m, Ar-H); δC (100 MHz) 13.6 (CH₃CH₂), 21.0 (CH₃CH₂), 28.2 [C(CH₃)₃], 33.6 (PhSeCHCH₂), 38.8 (PhSeCH), 46.8 and 51.8 (NCH₂), 81.8 [C(CH₃)₃], 128.4, 128.5 and 128.8 (Ar-CH), 136.8 (Ar-C), 150.68 (CO), 161.3 (N=C-N); m/z 382 (M⁺, 7%), 326 (33), 284 (15), 245 (32), 201 (27), 169 (30), 141 (14), 125 (58), 123 (13), 78 (9), 57 (100).
Sec-Butyllithium (3.09 cm³ of a 1.1M solution in cyclohexane, 3.4 mmol) was injected to a stirred solution of 1-tert-butyloxycarbonyl-2-phenylselenomethyl-2-imidazoline (1.05 g, 3.09 mmol) in dry THF (31 cm³) and TMEDA (1 cm³) at -78°C under nitrogen. The dark orange solution produced was stirred for 20 min at -78°C. 3-Bromopropene (0.29 cm³, 3.40 mmol) was injected to the reaction mixture at -78°C under nitrogen and the mixture was allowed to warm to 20°C overnight. The reaction was quenched with water (100 cm³), the organic layer was extracted with diethyl ether (3 x 100 cm³) and the combined organic extracts were washed successively with saturated aq. NaHCO₃ (50 cm³) and brine (50 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9–2:3 v/v ethyl acetate:hexane) to give the title compound as a yellow oil (1.06 g, 90%) (Found: M₁ 380.1002. requires: M₁ 380.1002); νmax (film)/cm⁻¹ 2977, 1714, 1631, 1478, 1147; δH (400 MHz) 1.52 [9H, s, C(CH₃)₃], 2.45-2.52 (1H, m, CHHCH=CH₂), 2.67-2.74 (1H, m, CHHCH=CH₂), 3.60-3.80 (4H, m, NCH₂CH₂N), 4.75 (1H, br s, PhSeCH₂), 5.00-5.09 (2H, m, CH=CH₂), 5.80-5.90 (1H, m, CH=CH₂), 7.25 (3H, m, Ar-H), 7.55 (2H, m, Ar-H); δc (100 MHz) 28.2 [C(CH₃)₃], 37.7 (CH₂CH=CH₂), 38.3 (ArSeCH), 46.9 and 51.8 (NCH₂), 81.8 [C((CH₃)₃], 116.6 (CH=CH₂), 128.2, 128.4, and 128.5 (Ar-CH), 135.8 (CH=CH₂), 136.8 (Ar-C), 150.6 (CO), 160.6 (N=C-N); m/z 380 (M⁺, 1%), 243 (10), 224 (6), 169 (49), 141 (16), 123 (56), 78 (8), 70 (10) 57 (100).
2-(1-Phenylseleneno-2-phenylethyl)-2-imidazoline (2.1.41a)

Trifluoroacetic acid (4 cm$^3$) was added to 1-tert-butyloxycarbonyl-2-(1-phenylseleneno-2-phenylethyl)-2-imidazoline (1.25 g, 2.91 mmol) and the resulting solution was stirred at 20°C for 1 h. The trifluoroacetic acid was removed under reduced pressure and the imidazoline salt was dissolved in dichloromethane (20 cm$^3$). The solution was then washed with aq.NaOH (10% w/v; 20 cm$^3$) and the organic layer was dried and concentrated. The crude product was then purified by column chromatography on silica gel (ethyl acetate) to give the title compound as a white solid (0.68 g, 71%), m.p 103-105 °C (Found: C, 61.27; H, 5.53; N, 8.91%; M$^+$ 330.0634. $C_{17}H_{18}N_{2}Se$·0.2H$_2$O requires: C, 61.14; H, 5.51; N, 8.39%; $M$ 330.0634); $\nu_{max}$ (film)/cm$^{-1}$ 3061, 2926, 1601, 1498, 1270, 740, 693; $\delta$H (400 MHz) 3.00-3.10 (1H, dd, $J$ 6.8 and 13.7, CH$\beta$Ph), 3.26-3.35 (1H, dd, $J$ 6.8 and 13.7, CH$\alpha$Ph), 3.42 (4H, m, NCH$_2$CH$_2$N), 4.03 (1H, t, $J$ 6.8, PhSeCH), 7.10-7.28 (8H, m, Ar-CH), 7.48 (2H, m, Ar-CH); $\delta$C (100 MHz) 39.3 (CH$_2$Ph), 42.1 (PhSeCH), 50.1 (NCH$_2$), 126.7, 128.2, 128.4, 128.9, 129.0 and 134.4 (Ar-CH), 134.9, 138.7 (Ar-C), 167.4 (N=C-N); m/z 330 (M$^+$, 6%), 249 (62), 239 (26), 173 (100), 158 (12), 132 (14), 115 (15), 105 (26), 91 (22), 77 (22).

2-(2-Phenylselenenobutyl)-2-imidazoline (2.1.41b)

Trifluoroacetic acid (3 cm$^3$) was added to 1-tert-butyloxycarbonyl-2-(1-phenylselenenobutyl)-2-imidazoline (1.50 g, 3.93 mmol) and the resulting solution was stirred at room
temperature for 1 h. The trifluoroacetic acid was removed under reduced pressure and the imidazoline salt was dissolved in dichloromethane (20 cm³). The solution was then washed with of aq.NaOH (10% w/v; 30 cm³) and the organic layer was dried and concentrated. The crude product was then purified by column chromatography on silica gel (ethyl acetate) to give the title compound as a yellow solid (1.00 g, 91 %), m.p 67-69 °C (Found: C, 55.55; H, 6.56; N, 9.96%; M⁺ 282.0635. C₁₃H₁₈N₂Se requires: C, 55.52; H, 6.45; N, 9.96%; M 282.0635); νmax (KBr/cm⁻¹ 3176, 2955, 1605, 1495, 1466, 1276, 978, 746, 694; δH (400 MHz) 0.87 (3H, t, J 7.4, CH₃CH₂CH₂), 1.34-1.52 (2H, m, CH₃CH₂CH₂), 1.70-1.80 (1H, m, CH₃CH₂CHHCH), 1.86-1.96 (1H, m, CH₃CH₂CHHCH), 3.45 (4H, s, NCH₂CH₂N), 3.85 (1H, t, J 6.8, CH₂CH), 4.40 (1H, br s, NH), 7.28 (3H, m, Ar-CH), 7.52 (2H, m, Ar-CH); δC (100 MHz) 13.5 (CH₃CH₂CH₂), 21.4 (CH₃CH₂CH₂), 35.1 (CH₃CH₂CH₂CH), 41.0 (CHSePh), 50.1 (NCH₂), 127.9, 128.5 and 128.9 (Ar-CH), 134.5 (Ar-C), 167.8 (N=C-N); m/z 282 (M⁺, 3.5%), 253 (2), 240 (2), 201 (11), 160 (7), 125 (5), 97 (7), 84 (9).

2-(1-Phenylselenenobut-3-nyl)-2-imidazoline (2.1.41c)

Trifluoroacetic acid (1 cm³) was added to 1-tert-butyloxycarbonyl-2-(1-phenylselenenobut-3-nyl)-2-imidazoline (0.29 g, 0.76 mmol) and the resulting solution was stirred at room temperature for 20-60 min. The trifluoroacetic acid was removed under reduced pressure and the imidazoline salt was dissolved in dichloromethane. (20 cm³). The solution was then washed with aq.NaOH (30 cm³; 10% w/v) and the organic layer was dried and concentrated. The crude product was then purified by column chromatography on silica gel (0:100→4:96 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (0.17 g, 80 %) which solidified upon standing, m.p. 41-43 °C (Found: C, 55.00; H, 5.72; N,
9.40%; M+ 280.0478. C13H16N2Se·0.2H2O requires: C, 54.99; H, 5.78; N; 9.87%; M 280.0478; v_max (film)/cm⁻¹ 3175, 3073, 2932, 1607, 1477, 1438, 1286, 919, 740; δ_H (400 MHz) 2.55-2.6 (1H, m, CHHCH=CH₂), 2.70-2.80 (1H, m, CHHCH=CH₂), 3.50 (4H, s, NCH₂CH₂N), 3.90 (1H, t, J 6.8, PhSeCH), 4.75 (1H, br s, NH), 5.10-5.20 (2H, m, CH=CH₂), 5.80-5.90 (1H, m, CH=CH₂), 7.26-7.32 (3H, m, Ar-H), 7.57 (2H, m, Ar-H), δ_C (100 MHz) 37.2 (CH₂CH=CH₂), 40.2 (PhSeCH), 50.1 (NCH₂), 117.4 (CH=CH₂), 128.2, 29.1 and 134.9 (Ar-CH), 135.2 (CH=CH₂), 137.5 (Ar-C), 167.4 (N=C-N); m/z 280 (M+, 9%), 279, (17), 239 (13), 199 (61), 157 (12), 123 (100), 97 (14), 77 (19), 67 (16).

General method for the synthesis of 2-(1-alkenyl)-2-imidazolines from 2-(1-phenylselenenoalkyl)-2-imidazolines (2.1.42)

A solution of m-chloroperbenzoic acid (1.1 equiv.) in dry dichloromethane was added via a cannula to a solution of the 2-(1-phenylselenenoalkyl)-2-imidazoline in dry dichloromethane (0.1M in imidazoline) at 0 °C under nitrogen. The resulting yellow solution was stirred at 0 °C for 1 h and further 2 h at room temperature. The dichloromethane was removed under reduced pressure and the crude product was purified by column chromatography on neutral alumina (activation grade III) (0:100→4:96 v/v isopropylamine:ethyl acetate) to give the 2-(1-alkenyl)-2-imidazolines.
2-(2-Phenylethenyl)-2-imidazoline (2.1.42a)

The compound was prepared by the general method, from 2-(1-phenylseleneno-2-phenylethyl)-2-imidazoline (0.30 g, 0.91 mmol) and m-chloroperbenzoic acid (0.17 g, 1.00 mmol). Chromatography on alumina (0:100→3:97 v/v isopropylamine:ethyl acetate) afforded the title compound as a white solid (0.16 g, 90%), m.p 154-156 °C, having data identical to those reported before.

2-(But-1- enyl)-2-imidazoline (2.1.42b)

The compound was prepared by the general method, from 2-(1-phenylselenenobutyl)-2-imidazoline (0.30 g, 1.06 mmol) and m-chloroperbenzoic acid (0.20 g, 1.17 mmol). The product was obtained after chromatography on neutral alumina (0:100→5:95 v/v isopropylamine:ethyl acetate) as a thick colourless oil (0.12 g, 92%) (Found: M⁺ 124.1000. C₇H₁₂N₂ requires: M 124.1000); νₘₐₓ (film)/cm⁻¹ 3197, 2965, 2864, 2873, 1663, 1602, 1500, 1461, 1274, 986; δₜ (400 MHz) 1.00 (3H, t, J 7.2, CH₃CH₂CH=CH), 2.10-2.20 (2H, m, CH₃CH₂CH=CH), 3.60 (4H, s, NCH₂CH₂N), 3.95 (1H, br s, NH), 5.98 (1H, d, J 16.6, CH₃CH₂CH=CH), 6.23-6.32 (1H, m, CH₃CH₂CH=CH); δₑ (100 MHz) 12.6 (CH₃CH₂CH=CH), 25.6 (CH₃CH₂CH=CH), 51.6 (NCH₂CH₂N), 119.9 and 141.3
2-(Buta-1,3-dienyl)-2-imidazoline (2.1.42c)

The compound was prepared from 2-(1-phenylselenenobut-3-enyl)-2-imidazoline (0.30 g, 1.07 mmol) and m-chloroperbenzoic acid (0.22 g, 1.29 mmol) using the general method. Chromatography on neutral alumina (0:100→2:98 v/v isopropylamine:ethyl acetate) afforded the title compound as a white solid (0.12 g, 92%), m.p. 220 °C (decomp.) (Found: M$^+$ 122.0844. C$_7$H$_{10}$N$_2$ requires: M 122.0844); $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3176, 2936, 2864, 1643, 1614, 1566, 1497, 1276, 1000, 982; $\delta_H$ (400 MHz) 3.70 (4H, s, NCH$_2$CH$_2$N), 4.40 (1H, br s, NH), 5.35-5.40 (1H, d, J 10.0, CH=CHCH=CHH), 5.50 (1H, d, J 16.2, CH=CHCH=CHH), 6.20-6.26 (1H, d, J 16.2, CH=CHCH=CH$_2$), 6.43-6.55 (1H, m, CH=CHCH=CH$_2$), 6.71-6.80 (1H, dd, J 10.0 and 16.2, CH=CHCH=CH$_2$); $\delta_C$ (100 MHz) 50.4 (NCH$_2$CH$_2$N), 121.9 (CH=CHCH=CH$_2$), 122.4, 135.7 and 137.0 (CH), 163.8 (N=C-N); m/z 122 (M$^+$, 100%), 121 (52), 106 (16), 93 (75), 66 (57), 53 (23).

1-tert-butyloxycarbonyl-2-[1-(prop-2-enyl)but-3-enyl]-2-imidazoline (2.1.24a)

sec-Butyllithium (1.04 cm$^3$ of a 1.3M solution in hexanes, 1.36 mmol) was injected to a solution of 1-tert-butyloxycarbonyl-2-(phenylselenenomethylbut-3-enyl)-2-imidazoline
(0.47 g, 1.24 mmol) in THF (12 cm³) at −78 C under nitrogen. The yellow solution that was produced was stirred at −78 C for 20 min. 1-Bromopropene (0.12 cm³, 1.36 mmol) was injected to the reaction mixture which was stirred overnight (−78 C→20 C). The reaction was quenched with water (20 cm³) and the organic layer was extracted with diethyl ether (3 x 20 cm³). The combined organic extracts were washed with saturated aq. NaHCO₃ (30 cm³), brine (30 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:9→2:3 v/v ethyl acetate:hexane) to give the title compound as a colourless oil (0.20 g, 61%); data as before.
General method for the synthesis of 2,3,5,6-tetrahydroimidazo[1,2-a]pyridines

The α,β-unsaturated aldehyde or ketone (1.5-2 equiv.) was added to a solution of 2-substituted 2-imidazoline in toluene (20 cm³) at 20°C. The mixture was heated to reflux using a Dean-Stark trap for 12 h. The toluene was removed under reduced pressure and the residue was purified by column chromatography on silica gel (100:0-98:2 v/v ethyl acetate:isopropylamine) to give the 2,3,5,6-tetrahydroimidazo[1,2-a]pyridine.

5-Methyl-8-(prop-2-enyl)-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.2.1)

The compound was synthesised by the general method, from 2-(but-3-enyl)-2-imidazoline (0.10 g, 0.80 mmol) and but-2-enal (0.085 g, 1.2 mmol) in toluene (20 cm³). The title compound was obtained as yellow oil (0.05 g, 36%) (Found: M⁺ 176.1300. C₁₁H₁₆N₂ requires: M 176.1313); νmax (film)/cm⁻¹ 2967, 2929, 2853, 2824, 1654, 1592, 1496, 1454, 1423, 1258, 1199, 1157; δH (400 MHz) 1.18 (3H, d, J 6.4, CH₃), 2.16–2.23 (1H, m, CH₃CHCHHCH=CH), 2.30–2.37 (1H, m, CH₃CHCHHCH=CH), 2.76–2.83 (1H, m, CH₂=CHCH₂), 2.96–3.08 (1H, m, CH₂=CHCH₂), 3.09–3.11 (2H, m, NCH₂CH₂N), 3.51–3.64 (2H, m, NCH₂CH₂N), 3.83–3.89 (1H, m, CH₃CHCH₂), 5.03–5.10 (2H, m, CH=CH₂), 5.85–5.95 (1H, m, CH=CH₂), 6.05 (1H, dd J 3.4 and 1.9, CH=CH₂); δC (100 MHz) 20.7 (CH₃CH), 33.7 (CH₂=CHCH₂), 34.8 (CH₃CHCH₂CH), 50.1 (NCH₂CH₂N), 51.8 (NCHCH₂), 52.8 (NCH₂CH₂N), 116.2 (CH=CH₂), 129.4 (CH₃CHCH₂CH=CH), 131.9
(CH₂CH=C), 135.8 (CH=CH₂), 163.8 (N-C=N); m/z 176 (M⁺, 31%), 175 (100), 161 (34), 147 (18), 133 (17), 119 (19), 106 (9), 92 (7), 79 (11), 77 (9), 65 (11), 53 (15).

5-Methyl-8-propyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.1.5a)

The compound was synthesised from 2-butyl-2-imidazoline (0.10 g, 0.79 mmol) and but-2-enal (0.10 g, 1.19 mmol) in toluene (20 cm³) by the general method and was obtained after purification as yellow oil (0.09 g, 64%) (Found: M⁺ 178.1470. C₁₁H₁₈N₂ requires: M 178.1470); νmax (film)/cm⁻¹ 2965, 2932, 1655, 1589, 1467, 1451, 1425, 1258, 1198, 1154; δH (400 MHz) 0.90 (2H, t, J 7.2, CH₃CH₂CH₂), 1.15 (3H, d, J 6.4, CH₃CHCH₂), 1.45-1.60 (2H, m, CH₃CH₂CH₂), 2.11-2.40 (4H, m, CH₃CH₂CH₂, CH₃CHCH₂CH=C), 2.76-2.82 (1H, m, NCHHCH₂N), 2.96-3.05 (1H, m, NCHHCH₂N), 3.51-3.66 (2H, m, NCH₂CH₂N), 3.85-3.90 (1H, m, NCHHCH₂), 6.05 (1H, dd, J 3.4 and 1.9, CH₃CHCH₂CH=C); δC (100 MHz) 14.0 (CH₃CH₂), 20.6 (CH₃CHCH₂), 21.5 (CH₃CH₂CH₂), 33.0 (CH₃CH₂CH₂), 33.6 (CH₃CHCH₂CH=CH), 49.9 (NCH₂CH₂N), 51.8 (CH₃CHCH₂CH=C), 52.6 (NCH₂CH₂N), 130.1 (CH₃CHCH₂CH=C), 131.0 (CH₃CHCH₂CH=C), 164.0 (N-C=N); m/z 178 (M⁺, 57%), 163 (100), 149 (100), 135 (74), 121 (32), 108 (6), 106 (5), 94 (12), 79 (8), 70 (19), 65 (11), 53 (11), 42 (24).
The compound was synthesised by the general method, from 2-but-3-enyl-2-imidazoline (0.20 g, 1.60 mmol) and 3-phenylprop-2-enal (0.30 cm³, 2.41 mmol) in toluene (20 cm³).

The title compound was obtained after purification as a thick yellow oil (0.05 g, 13%) (Found: M⁺ 238.1470. C₁₆H₁₈N₂ requires: M 238.1470); νₘₐₓ (KBr)/cm⁻¹ 2968, 2932, 2855, 2824, 1657, 1592, 1454, 1423, 1257, 1223, 1199, 1157; δ_H (400 MHz) 2.54-2.60 (2H, m, CH₂=CHCH₂C=CH), 2.68-2.76 (1H, m, PhCHCHHCH=CH), 3.15-3.20 (2H, m, NCH₂CH₂N), 3.21-3.25 (1H, m, PhCHCHHCH=CH), 3.58-3.67 (1H, m, NCH₂CH₂N), 3.80-3.90 (1H, m, NCH₂CH₂H), 3.99 (1H, t, J 7.8, PhCH₂H), 5.10-5.20 (2H, m, CH₂=CHCH₂), 5.90-6.00 (1H, m, CH₂=CHCH₂), 6.12 (1H, dd J 3.4 and 1.9, CH₂CH=CH), 7.30-7.42 (5H, m, Ar-H); δ_C (100 MHz) 34.9 (PhCHCH₂CH=CH), 35.4 (CH₂=CHCH₂C=CH), 51.3 and 52.7 (NCH₂), 61.9 (PhCHCH₂CH=CH), 116.5 (CH₂=CHCH₂), 127.2, 128.3 and 128.9 (Ar-CH), 129.0 (PhCHCH₂CH=CH), 131.5 (PhCHCH₂CH=CH), 135.8 (CH₂=CHCH₂), 142.1 (Ar-C), 163.7 (N-C=N); m/z 238 (M⁺, 46%), 237 (100), 2.09 (10), 173 (8), 161 (17), 147 (6), 145 (8), 133 (8), 119 (11), 115 (12), 105 (22), 91 (28), 84 (15), 78 (14), 63 (7), 51 (19).
8-Benzyl-5-methyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.2.5c)

The compound was synthesised from 2-(2-(phenylethyl)-2-imidazoline (0.23 g, 1.32 mmol) and but-2-enal (0.15 cm$^3$, 1.84 mmol) in toluene (20 cm$^3$) by the general method and was obtained after purification as yellow oil (0.24 g, 80%) (Found: C, 78.57; H, 8.02; N, 12.11%; (M-H)$^+$ 225.1390. C$_{13}$H$_{18}$N$_2$·0.2H$_2$O requires: C, 78.39; H, 7.83; N, 12.19%; M-H 225.1392); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2967, 2929, 2853, 2824, 1654, 1592, 1496, 1454, 1423, 1258, 1199, 1157; $\delta_H$ (400 MHz) 1.11 (3H, d, $J = 6.4$, CH$_3$CHCH$_2$), 2.08-2.16 (1H, m, CH$_3$CHCHHCH=CH), 2.19-2.26 (1H, m, CH$_3$CHCHHCH=CH=C), 2.70-2.81 (1H, m, NCHHCH$_2$N), 2.90-3.00 (1H, m, NCHHCH$_2$N), 3.48-3.58 (2H, m, NCH$_2$CH$_2$N), 3.60 (2H, s, PhCH$_2$), 3.80-3.87 (1H, m, NCHCH$_2$CH=C), 5.67 (1H, dd, $J = 1.9$ and 3.4, CH$_3$CHCH$_2$CH=CH), 7.10-7.18 (3H, m, Ar-H), 7.20-7.25 (2H, m, Ar-H); $\delta_C$ (100 MHz) 20.6 (CH$_3$CHCH$_2$), 33.7 (CH$_3$CHCH$_2$CH=CH), 36.5 (PhCH$_2$), 50.1 (NCH$_2$CH$_2$N), 51.8 (NCHCH$_2$), 52.9 (NCH$_2$CH$_2$N), 126.0 (CH=C), 128.2, 129.4 (Ar-C), 130.7 (CH=C), 132.7 and 139.2 (Ar-C), 164.0 (N-C=N); m/z 225 (M+, 100%), 211 (15), 184 (3), 149 (4), 133 (3), 128 (5), 119 (7), 105 (13), 91 (16), 70 (6), 65 (6), 56 (3).

8-Benzyl-5-ethyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.2.5d)

The compound was synthesised by the general method, from 2-(2-(phenylethyl)-2-imidazoline (0.15 g, 0.86 mmol) and pent-2-enal (0.17 cm$^3$, 1.72 mmol) in toluene (20
cm\(^3\)). The \textit{title compound} was obtained as a pale yellow oil (0.19 g, 91%) (Found: C, 78.54; H, 8.34; N, 11.43%; (M-H\(^+\)) 239.1542. C\(_{16}H_{20}N_2\cdot0.2\text{H}_2\text{O}\) requires: C, 78.81; N, 8.37; N, 11.49%; \textit{M-H} 239.1548); \(v_{\text{max}}\) (film)/cm\(^{-1}\) 2966, 2933, 2858, 1656, 1593, 1495, 1454, 1426, 1249, 1192, 1158; \(\delta_H\) (400 MHz) 0.83 (3H, t, \textit{J} 7.3, \text{CH}_3\text{CH}_2), 1.35-1.44 (1H, m \text{CH}_3\text{CHH}), 1.57-1.64 (1H, m \text{CH}_3\text{CHH}), 2.07-2.14 (1H, m, \text{CHCH}_2\text{HCH=C}), 2.19-2.26 (1H, m, CHCH\_CH\_CH=C), 2.73-2.83 (2H, m, N\text{CH}_2\text{CH}_2\text{N}), 3.46-3.57 (2H, m, N\text{CH}_2\text{CH}_2\text{N}), 3.60 (2H, s, Ar\text{CH}_2), 3.82-3.86 (1H, m, C\text{H}_3\text{CH}_2\text{CH}_2\text{N}), 5.68 (1H, dd, \textit{J} 1.9 and 5.4, CH=C), 7.11-7.23 (5H, m, Ar-H), \(\delta_C\) (100 MHz) 8.7 (CH\(_3\)), 26.9 (CH\(_3\)CH\(_2\)), 29.9 (CH\(_3\)CH\(_2\)CH=CH), 36.5 (PhCH\(_2\)), 50.1 and 52.9 (N\text{CH}_2), 57.0 (N\text{CHCH}_2), 126.0 (CH=C), 128.5, 129.5 and 130.7 (Ar-CH), 132.6 (CH=C), 139.2 (Ar-C), 164.2 (N-C=N); \(m/z\) 240 (M\(^+\), 35%), 239 (100), 225 (10), 211 (52), 197 (3), 155 (3), 140 (3), 119 (21), 105 (15), 91 (28).

7-Methyl-8-phenylmethyl-2,3,5,6-tetrahydroimidazo[1,2-\(\alpha\)]pyridine (2.2.5e)

\[
\begin{align*}
\text{Ph} & \quad \text{NH} \\
\text{N} & \quad \text{NH}
\end{align*}
\]

The compound was synthesised by the general method, from 2-(2-phenylethyl)-2-imidazoline (0.11 g, 0.63 mmol) and but-2-en-3-one (0.10 cm\(^3\), 1.26 mmol) in toluene (20 cm\(^3\)). The \textit{title compound} was obtained as a yellow oil (55 mg, 38%) (Found: (M-H\(^+\)) \textit{M-H} 225.1389. C\(_{15}H_{18}N_2\) requires: \textit{M-H} 225.1392); \(v_{\text{max}}\) (film)/cm\(^{-1}\) 2921, 2852, 2823, 1650, 1586, 1494, 1454, 1419, 1279, 1238, 1210, 1057, 1031, 1015, 754, 737, 700; \(\delta_H\) (400 MHz) 1.77 (3H, s, CH\(_3\)), 2.39-2.43 (2H, t, \textit{J} 6.6, CH\(_3\)C\text{CCH}_2\text{CH}_2\text{N}), 2.99-3.02 (2H, t, \textit{J} 6.6, CH\(_3\)C\text{CCH}_2\text{CH}_2\text{N}), 3.12-3.17 (2H, t, \textit{J} 8.8, N\text{CH}_2\text{CH}_2\text{N}), 3.65-3.70 (2H, t, \textit{J} 8.8, N\text{CH}_2\text{CH}_2\text{N}), 3.76 (2H, s, CH\(_3\)=C\text{CCH}_2\text{Ph}), 7.13-7.19 (5H, m, Ar-H); \(\delta_C\) (100 MHz) 20.1
(CH$_3$), 31.8 (CH$_3$CCH$_2$CH$_2$N), 32.2 (CH$_3$C=CCH$_2$Ph), 45.5 and 53.0 (NCH$_2$CH$_2$N), 53.2 (CH$_3$CCH$_2$CH$_2$N), 123.9 (CH$_3$C=CCH$_2$Ph), 125.5, 128.1 and 128.2 (Ar-CH), 140.4 (CH$_3$C=CCH$_2$Ar), 142.6 (Ar-C), 164.6 (N-C=N); m/z 226 (M$^+$, 28%), 225 (100), 199 (5), 171 (3), 149 (9), 128 (4), 115 (4), 105 (3), 91 (9), 56 (4).

5-Methyl-8-[(2-phenyl)phenylmethyl]-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.2.5f)

![Chemical structure diagram]

The compound was synthesised from 2-[2-(2-phenyl)phenylethyl]-2-imidazoline (0.16 g, 0.62 mmol) and but-2-enal (0.10 cm$^3$, 1.25 mmol) in toluene (20 cm$^3$) using the general method. The title compound was obtained after purification as a colourless oil (0.17 g, 90%) (Found: C, 81.47; H, 7.24; N, 9.05%; (M-H)$^+$ 301.1701. C$_{21}$H$_{22}$N$_2$·0.4H$_2$O requires: C, 81.50; H, 7.37; N, 9.05%; M-H 301.1701); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2968, 2930, 2855, 2825, 1655, 1592, 1479, 1425, 1258, 1200, 1157; $\delta_\text{H}$ (400 MHz) 1.06 (3H, d, J 6.4, CH$_3$CHCH$_2$), 1.99-2.07 (1H, m, CH$_3$CHCHHCH=CH), 2.12-2.20 (1H, m, CH$_3$CHCHHCH=CH=C), 2.67-2.74 (1H, m, NCHHCH$_2$N), 2.83-2.83 (1H, m, NCHHCH$_2$N), 3.41-3.55 (2H, m, NCH$_2$CH$_2$N), 3.60 (2H, s, ArCH$_2$), 3.72-3.78 (1H, m, NCH$_2$CH$_2$N), 5.47 (1H, dd, J 1.9, 3.4, CH$_2$CH=C), 7.16-7.28 (9H, m, Ar-H); $\delta_\text{C}$ (100 MHz) 20.5 (CH$_3$CH), 33.7 (CH$_3$CH=CH), 33.8 (ArCH$_2$), 50.1 (NCH$_2$CH$_2$N), 51.7 (NCH), 52.8 (NCH$_2$CH$_2$N), 126.2 (CH$_2$CH=C), 126.7, 127.2, 128.0, 128.8, 130.1, 130.9, 131.0 (Ar-CH), 132.6 (CH$_2$CH=C), 136.3, 141.5 and 142.6 (Ar-C), 163.9 (N-C=N); m/z 302 (M$^+$, 43%), 301
5-Ethyl-8-[(2-phenyl)phenylmethyl]-2,3,5,6-tetrahydroimidazo[1,2-\text{a}]pyridine (2.2.5g)

The compound was synthesised by the general method, from 2-[2-(2-phenyl)phenylethyl]-2-imidazoline (0.13 g, 0.52 mmol) and pent-2-enal (0.10 cm$^3$, 1.04 mmol) in toluene (20 cm$^3$). The title compound was obtained as a pale yellow oil (0.14 g, 85%) (Found: (M-H)$^+$ 315.1861. C$_{22}$H$_{24}$N$_2$ requires: M-H 315.1865; $\nu$$_{\text{max}}$ (film)/cm$^{-1}$ 2965, 2933, 2862, 1656, 1594, 1479, 1451, 1435, 1247, 1194, 1158 703; $\delta$$_{\text{H}}$ (400 MHz) 0.80 (3H, t, $J$ 7.3, CH$_3$CH$_2$CH), 1.31-1.37 (1H, m CH$_3$CH$H$CH), 1.52-1.60 (1H, m CH$_3$CHHCH), 2.02-2.07 (1H, m, CH$_3$CH$_2$CHCH$H$CH=C), 2.13-2.20 (1H, m, CH$_3$CH$_2$CHCH$H$CH=C), 2.67-2.74 (2H, m, NCH$_2$CH$_2$N), 3.40-3.53 (2H, m, NCH$_2$CH$_2$N), 3.60 (2H, s, ArCH$_2$), 3.72-3.75 (1H, m, CH$_3$CH$_2$CHCH$_2$), 5.49 (1H, dd, $J$ 1.9 and 5.4, CH=C), 7.19-7.26 (9H, m, Ar-H); $\delta$$_{\text{C}}$ (100 MHz) 8.7 (CH$_3$), 26.7 (CH$_3$CH$_2$CH), 29.9 (CH$_2$CH$_2$CH=CH), 36.7 (ArCH$_2$), 50.1 and 52.8 (NCH$_2$), 56.9 (NCH$_2$CH$_2$), 126.2 (CH=C), 126.3, 126.7, 127.2, 127.9, 128.1, 128.8, 130.0 and 130.9 (Ar-CH), 132.5 (CH=C), 136.4, 141.5 and 142.6 (Ar-C), 164.0 (N-C=N); m/z 316 (M$^+$, 56%), 315 (75), 287 (60), 239 (100), 225 (11), 165 (31), 142 (22), 127 (7), 84 (5), 44 (10).
The compound was synthesised by the general method, from 2-[2-(2-phenyl)phenylethyl]-2-imidazoline (0.11 g, 0.44 mmol) and but-2-en-3-one (77 μcm³, 0.88 mmol) in toluene (20 cm³). The title compound was obtained as a white solid (0.09 g, 66%), m.p. 111-113°C (Found: (M-H)+ 301.1705. C₂₁H₂₂N₂ requires: M-H 301.1705); ν max (film)/cm⁻¹ 2956, 2917, 2859, 2820, 1651, 1588, 1476, 1431, 1279, 754; δH (400 MHz) 1.42 (3H, s, CH₃), 2.31-2.35 (2H, t, J 6.3, CH₃CH=C=CH₂), 2.95-2.98 (2H, t, J 6.3, CH₃CH₂CH₂N), 3.12-3.17 (2H, t, J 8.8, NCH₂CH₂N), 3.66-3.69 (2H, t, J 8.8, NCH₂CH₂N), 3.70 (2H, s, CH₂Ar), 7.06-7.32 (9H, m, Ar-H); δC (100 MHz) 20.0 (CH₃), 30.2 (ArCH₂), 31.7 (CH₃CH₂CH₂N), 45.5 and 53.0 (NCH₂CH₂N), 53.3 (CH₃CCH₂CH₂N), 124.3 (CH₃C=CH₂Ar), 125.4, 126.7, 127.6, 128.0, 129.3, 129.3, 137.8 (Ar-CH), 141.5 (CH₃C=CH₂Ar), 141.8 and 142.0 (Ar-C), 165.1 (N-C=N); m/z 302 (M⁺, 25%), 301 (53), 287 (19), 225 (100), 165 (9), 149 (11), 115 (3), 105 (2), 91 (5), 56 (5).
5,7-Dimethyl-8-[(2-phenyl)phenylmethyl]-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.5.5i)

The title compound was synthesised by the general method, from 2-[2-(2-phenyl)phenylethyl]-2-imidazoline (0.11 g, 0.43 mmol) and pent-2-en-3-one (84 μm³, 0.86 mmol) in toluene (20 cm³) described before and was obtained after purification as a colourless oil (75 mg, 55 %), (Found: (MH)+ 317.2005. C22H24N2 requires: MH 317.2017); νmax (film)/cm⁻¹ 2968, 2852, 1651, 1588, 1478, 1416, 1329, 1281, 1209, 750, 704; δH (300 MHz) 1.17 (3H, d, J 6.2, CH3CH), 1.47 (3H, s, CH3C=CCH2Ar), 2.13-2.32 (2H, m, CH3CHCH2C), 2.79-2.86 (1H, m, NCHHCH2N), 2.95-3.02 (1H, m, NCHHCH2N), 3.53-3.59 (2H, m, NCH2CH2N), 3.75 (2H, s, ArCH2), 3.80-3.91 (1H, m, CH3CHCH2C), 7.12-7.41 (9H, m, Ar-H); δc (75 MHz) 19.7 (CH3CH), 20.6 (CH3C=CCH2Ar), 30.4 (CH3CHCH2C), 40.3 (CH2Ar), 50.8 (NCH2CH2N), 51.4 (NCH2CH2N), 53.2 (CH3CH), 124.1, 125.3, 126.7, 127.6 and 129.3 (Ar-C), 128.0 (CH3C=CCH2Ar), 137.9 (CH3C=CCH2Ar), 141.4, 141.8 and 142.5 (Ar-C), 165.5 (N-C=N); m/z 316 (M⁺, 34%), 315 (55), 301 (28), 239 (100), 165 (33), 152 (17), 135 (12) 115 (8), 77 (20).
5-Ethyl-8-phenyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.2.5j)

\[ \text{N} \quad \text{Ph} \quad \text{N} \quad \text{Ph} \]

The compound was synthesised by the general method, from 2-benzyl-2-imidazoline (0.55 g, 3.44 mmol) and pent-2-enal (0.67 cm\(^3\), 6.88 mmol). The title compound was obtained after purification as a dark yellow oil (0.12 g, 15 %) (Found: \(\text{M-H}^+\) 227.1540. \(\text{C}_{13}\text{H}_{18}\text{N}_2\) requires: \(\text{M-H}^+\) 227.1548); \(\nu_\text{max}\) (film)/cm\(^{-1}\) 2966, 2936, 1619, 1586, 1495, 1448, 1423, 1282, 1246, 1180, 996, 753; \(\delta_\text{H}\) (400 MHz) 0.97 (3H, t, \(J\ 7.8\), \(\text{CH}_3\text{CH}_2\text{CHCH}_2\)), 1.46-1.59 (1H, m, \(\text{CH}_3\text{CHHCH}\)), 1.71-1.80 (1H, m, \(\text{CH}_3\text{CHHCH}\)), 2.37-2.44 (1H, m, \(\text{CHCHHCH}=\text{C}\)), 2.50-2.57 (1H, m, \(\text{CHCHHCH}=\text{C}\)), 2.85-2.95 (1H, m, \(\text{NCHCH}_2\text{N}\)), 2.98-3.05 (1H, m, \(\text{NCHCH}_2\text{N}\)), 3.57-3.68 (2H, m, \(\text{NCH}_2\text{N}\)), 3.91-3.95 (1H, m, \(\text{NCHCH}_2\)), 6.38 (1H, dd, \(J\ 2.1\) and 6.1, \(\text{CH}=\text{C}\)), 7.26-7.50 (5H, m, \(\text{Ar-H}\)); \(\delta_\text{C}\) (100 MHz) 8.8 (\(\text{CH}_3\)), 27.1 (\(\text{CH}_3\text{CH}_2\text{CH}\)), 30.5 (\(\text{CHCH}_2\text{CH}=\text{CH}\)), 49.9 and 53.3 (\(\text{NCH}_2\)), 56.8 (\(\text{NCII}\)), 127.4 (\(\text{CH}=\text{C}\)), 127.9, 128.2, 128.7 (Ar-CH), 134.7 (\(\text{CH}=\text{C}\)), 137.8 (Ar-C), 163.1 (N-C=N); \(m/z\) 227 (MH\(^+\), 100%), 197 (6), 171 (3), 159 (6), 91 (2), 71 (2).

7-Methyl-8-phenyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.2.5k)

\[ \text{N} \quad \text{Ph} \quad \text{N} \quad \text{Ph} \]

The compound was synthesised by the general method, from 2-benzyl-2-imidazoline (0.50 g, 3.12 mmol) and but-2-en-3-one (0.50 cm\(^3\), 6.24 mmol) in toluene (30 cm\(^3\)). The title compound was obtained after purification as a yellow oil (0.65 g, 98 %) (Found: C, 77.14; H, 7.69; N, 13.16%; (M-H\(^+\)) 211.1234. \(\text{C}_{14}\text{H}_{16}\text{N}_2\cdot0.3\text{H}_2\text{O}\) requires: C, 77.27; H, 7.63; N,
12.88%; $M-H$ 211.1235; $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2918, 2851, 2821, 1636, 1587, 1494, 1466, 1442, 1418, 1285, 1229, 1190, 1168, 978; $\delta_H$ (400 MHz) 1.65 (3H, s, CH$_3$), 2.48-2.51 (2H, t, $J$ 6.6, CH$_3$CCH$_2$CH$_2$N), 3.06-3.10 (2H, t, $J$ 6.6, CH$_3$CCH$_2$CH$_2$N), 3.11-3.16 (2H, t, $J$ 8.8, NCH$_2$CH$_2$N), 3.62-3.67 (2H, t, $J$ 8.8, NCH$_2$CH$_2$N), 7.10-7.28 (5H, m, Ar-H); $\delta_C$ (100 MHz) 20.9 (CH$_3$), 31.5 (CH$_3$CCH$_2$CH$_2$N), 45.4 (NCH$_2$CH$_2$N), 52.8 (NCH$_2$CH$_2$N), 53.6 (NCH$_2$CH$_2$C), 126.8 (CH$_3$C=CPh), 127.7, 127.8, 129.8 (Ar-CH), 136.6 (CH$_3$C=CPh), 142.5 (Ar-C), 164.3 (N-C=N); m/z 212 (M+, 56%), 211 (100), 195 (5), 183 (2), 154 (2), 128 (6), 115 (7), 105 (5), 69 (3), 56 (4).

5-Methyl-8-phenyl-2,3,5,6-tetrahydroimidazo[1,2-a]pyridine (2.2.51)

![Diagram of the compound]

The compound was synthesised by the general method, from 2-benzyl-2-imidazoline (0.50 g, 3.12 mmol) and but-2-enal (0.28 g, 3.43 mmol) in toluene (31 cm$^3$). The title compound was obtained as yellow oil (0.22 g, 33%), $\nu_{\text{max}}$ (film/cm$^{-1}$) 2967, 2936, 1619, 1586, 1495, 1495, 1448, 1282, 1246, 1180, 996; $\delta_H$ (400 MHz) 1.23 (3H, d, $J$ 6.4, CH$_3$), 2.30-2.41 (1H, m, CH$_3$CHCHHCH=CH), 2.47-2.55 (1H, m, CH$_3$CHCHHCH=CH=C), 2.82-2.91 (1H, m, NCHHCH$_2$N), 3.09-3.19 (1H, m, NCHHCH$_2$N), 3.55-3.70 (2H, m, NCH$_2$CH$_2$N), 3.51-3.64 3.87-3.96 (1H, m, NCHCH$_2$), 6.32 (1H, dd $J$ 3.4 and 1.9, CH=H), (7.25-7.38 (3H, m, Ar-H), 7.45-7.49 (2H, m, Ar-H); $\delta_C$ (100 MHz) 20.7 (CH$_3$), 34.1 (NCHCH$_2$CH), 49.8 (NCH$_2$CH$_2$N), 51.5 (NCHCH$_2$), 53.2 (NCH$_2$CH$_2$N), 127.8, 128.1 and 128.7 (Ar-CH), 132.4 (CH=H), 134.5 (CH=H), 137.6 (Ar-C), 162.8 (N-C=N).
5,7-Dimethyl-8-phenylmethyl-2,3,5,6-tetrahydroimidazo[1,2-α]pyridine (2.2.5m)

The compound was synthesised by the general method, from 2-benzyl-2-imidazoline (1.00 g, 6.25 mmol) and pent-2-en-3-one (1.20 cm³, 12.5 mmol) in toluene (62 cm³). The title compound was obtained as a yellow oil (1.22 g, 86 %) (Found: (M-H)⁺ 225.1393; C₁₅H₁₈N₂ requires: M-H 225.1392); νmax (film)/cm⁻¹ 2967, 2930, 2851, 1642, 1590, 1495, 1443, 1411, 1378, 1282, 1252, 1229, 1177, 990, 700; λmax/nm 219 (εmax/mol.dm⁻³ 13092); δH (400 MHz) 1.23 (3H, d, J 6.2, CH₃CHCH₂), 1.72 (3H, s, CH₃C=CPh), 2.39-2.43 (2H, m, NCHCH₂), 2.78-2.87 (1H, m, NCHHCH₂N), 3.11-3.20 (1H, m, NCH₂CH₂N), 3.53-3.66 (2H, m, NCH₂CH₂N), 3.80-3.90 (1H, m, NCH), 7.16-7.37 (5H, m, Ar-H); δC (100 MHz) 20.8 (CH₃C=CPh), 21.0 (CH₃CH), 40.2 (CH₃CHCH₂C), 50.4 (NCH₂CH₂N), 51.4 (NCH₂CH₂N), 53.8 (CH₃CHCH₂), 127.7, 128.4 and 129.9 (Ar-CH), 128.1 and 136.9 (C=C), 142.4 (Ar-C), 164.8 (N-C=N); m/z 226 (M⁺, 75%), 225 (100), 211 (21), 195 (10), 183 (4), 166 (5), 154 (4), 128 (9), 115 (10), 91 (4), 70 (9), 42 (10).

7-Hydroxy-5-methyl-8-phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-α]pyridine (2.2.6a)

But-2-enal (0.19 cm³, 2.34 mmol) was added in a solution of 2-benzyl-2-imidazoline (0.25 g, 1.56 mmol), in toluene (30 cm³) and the resulting solution was heated to reflux for 12 h. The toluene was removed and the crude reaction mixture was purified with column chromatography on silica gel (0:100→1:99 isopropylamine:chloroform) to give the title
compound as a yellow oil (0.13 g, 37%) (Found M$^+$ 230.1419. C$_{14}$H$_{18}$N$_2$O requires: M, 230.1419); $\nu_{\text{max}}$ (film) 3401, 2968, 2931, 2851, 1636, 1585, 1494, 1249, 1196, 990, 774; $\delta_H$ (400 MHz) 1.12 (3H, d, J 6.4, CH$_3$CH), 1.88-1.93 (1H, dd, J 10.9 and 15.6, NCHCH$_2$H), 2.28-2.34 (2H, dt, J 3.6 and 10.9, NCHCHH), 2.80-2.92 (1H, m, NCH$_2$CH$_2$N), 2.98-3.08 (1H, m, NCH$_2$CH$_2$N), 3.28 (1H, m, NCH$_2$), 3.50-3.60 (2H, m, NCHH and NCHCH$_3$), 3.74 (1H, t, J 10.9, CHO), 7.20-7.35 (3H, m, Ar), 7.40 (2H, m Ar); $\delta_C$ (100 MHz) 20.7 (CH$_3$), 32.9 (NCHCH$_2$), 46.6 (NCH), 49.8 and 52.6 (NCH$_2$), 56.2 (NC=CPh), 61.3 (CHOH), 126.6, 127.9 and 128.1 (Ar-CH), 135.8 (Ar-C), 163.9 (NC=CPh); $m/z$ 230 (M$^+$, 16%), 213 (29), 199 (26), 185 (46), 170 (5), 157 (25), 143 (7), 129 (14), 115 (12), 105 (38), 91 (12), 77 (31).

7-Hydroxy-5-methyl-8-(prop-2-enyl)-2,3,5,6,7,8-hexahydroimidazo[1,2-a]pyridine (2.2.4a)

\[
\begin{align*}
\text{But-2-enal (47 mg, 0.67 mmol) was added in a solution of 2-(but-3-enyl)-2-imidazoline (70 mg, 0.56 mmol), in anhydrous dichloromethane (6 cm}^3). A small amount of MgSO$_4$ was added to the reaction mixture and the reaction was stirred at 20°C for 12 h. The MgSO$_4$ was filtered and the dichloromethane was removed under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel eluting (0:100→ 3:97 isopropylamine:chloroform) to give the title compound as a white solid (30 mg, 27%) (Found: M$^+$ 194.1419. C$_{11}$H$_{18}$N$_2$O requires: M 194.1491); $\nu_{\text{max}}$ (film) 3100, 2972, 2936, 1612, 1424, 1346, 1277, 1139; $\delta_H$ (400 MHz) 1.18 (3H, d, J 6.4, CH$_3$CH), 1.60-1.69 (1H, dd, J 11.2 and 24.4, NCHCHH), 2.06-2.11 (2H, dt, J 3.6 and 11.2, CHCHH), 2.34-2.37
(1H, m, CHHCH=CH2), 2.56-2.62 (1H, m CHHCH=CH2), 2.79-2.86 (3H, m, NCH2CH2N and CHCH2CH=CH2), 3.55-3.60 (2H, m, NCH2CH2N), 3.69-3.75 (1H, m, NCH), 3.85 (1H, t, J 11.2, CHOH), 5.05 (1H, m, CH=CHH), 5.17-5.21 (1H, m, CH=CHH), 6.00-6.07 (1H, m, CH=CH2); δc (100 MHz) 22.7 (CH3), 33.0 (NCHCH2), 40.8 (CH2CH=CH2), 44.5 (CHCH2CH=CH2) 50.3 and 51.6 (NCH2), 53.0 (NCHCH3), 69.9 (CHOH), 116.7 (CH=CH2), 137.5 (CH=CH2), 166.9 (NC=CH=O); mlz 194 (M+, 24%), 176 (80), 161 (32), 150 (28), 137 (21), 132 (17), 121 (34), 109 (15), 106 (11), 94 (100), 81 (16), 67 (17).

7-Hydroxy-7-methyl-8-phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridine (2.2.4b) and 7-hydroxy-5-methyl-8-phenyl-2,3,5,6,7,8-hexahydroimidazo[1,2-a]pyridine (2.2.4b)

But-3-en-2-one (1.97 cm3, 23.77 mmol) was added to a solution of 2-benzyl-2-imidazoline (3.17 g, 19.81 mmol), in dichloromethane (100 cm3) and the resulting solution was stirred at 20°C for 12 h. The title compound precipitate out of solution as a white solid (1:1 mixture of regioisomers) which was filtered (1.93 g, 42%), m.p. 141-143°C (Found: C, 72.57; H, 7.84; N, 12.03%; M+ 230.1419. C14H18N2O requires: C, 73.01; H, 7.88; N, 12.16%; M, 230.1417); νmax (film) 3435, 3083, 3063, 2970, 1616, 1495, 1424, 1344, 1276, 1139, 704; δh (400 MHz, CD3OD) 1.01 and 1.14 (3H, s, CH3), 1.63-1.72 [1H, m, NCH2CHHC(OH)], 1.88-1.93 [1H, m, NCH2CHHC(OH)], 1.98-2.03 [1H, m, NCH2CHHC(OH)], 2.05-2.09 [1H, m, NCH2CHHC(OH)], 3.09-3.21 (4H, m, NCH2), 3.28-3.42 (4H, m, 2x NCH2CH2N and 2x NCH2CH2CCH3), 3.53-3.63 (4H, m, 2x NCH2CH2N and 2x NCH2CH2CCH3), 3.69-3.72 (1H, m, PhCH), 7.22-7.36 (10H, m, Ar-H); δH (100 MHz, CD3OD) 27.7 and 28.0 (CH3), 32.2 and 32.4 [NCH2CH2C(OH)], 44.8 and 48.1
Methyl 3-(2-benzylimidazolin-1-yl)propenoate (2.2.10)

Methyl propenoate (3.37 cm³, 37.5 mmol) was injected to a solution of 2-benzyl-2imidazoline (3.00 g, 18.75 mmol) in dry dichloromethane (18 cm³). The resulting solution was refluxed overnight under nitrogen. The dichloromethane was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (100:0-99:1 ethyl acetate:isopropylamine) to give the title compound as a yellow oil (3.75 g, 81%) (Found: C, 64.12; H, 7.39; N, 11.11%; (M-H)+ 245.1288. C_{14}H_{18}N_{2}O_{2}-0.8H_{2}O requires: C, 64.51; H, 6.91; N, 10.75%; M-H 245.1290); v_{\text{max}} (film)/cm^{-1} 2951, 2862, 1737 (CO), 1615 (C=N), 1496, 1456, 1437, 1271, 1175, 1007; δ_{H} (400 MHz) 2.33 (2H, t, J 6.8, NCH_{2}CH_{2}CO_{2}CH_{3}), 3.28 (2H, t, J 9.0, NCH_{2}CH_{2}N), 3.32 (2H, t, J 6.8, NCH_{2}CH_{2}CO_{2}CH_{3}), 3.64 (3H, s, CO_{2}CH_{3}), 3.65 (2H, s, PhCH_{2}), 3.70 (2H, t, J 9.0, NCH_{2}CH_{2}N), 7.21-7.33 (5H, m, Ar-H); δ_{C} (75 MHz; CDCl_{3}), 33.5 (NCH_{2}CH_{2}CO_{2}CH_{3}), 34.5 (PhCH_{2}), 42.9 (CO_{2}CH_{3}), 50.1, 51.7 and 52.4 (NCH_{2}), 126.7, 128.6 and 128.7 (Ar-CH), 135.9 (Ar-C), 165.2 (N=C-N), 171.9 (CO_{2}Me); m/z 246 (M⁺, 38%), 187 (95), 173 (28), 158 (20), 130 (12), 117 (10), 115 (10), 103 (7), 92 (7), 83 (35), 56 (100), 42 (23).
The phenyl vinylsulfonate (1.2 equiv.) was added to a solution of the 2-alkyl-2-imidazoline (1 equiv) in dichloromethane (10 cm³). The reaction mixture was stirred at 20°C overnight. The dichloromethane was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (0:100→3:97 v/v isopropylamine:ethyl acetate) to give the desired compounds.

**Phenyl 2-(2-benzylimidazolin-1-yl)ethyl sulfonate (2.2.11b)**

Prepared by the general method, using 2-benzyl-2-imidazoline (0.25 g, 1.56 mmol) and phenyl vinylsulfonate (0.31 g, 1.71 mmol) to give the title compound as a yellow oil (0.40 g, 75%) (Found: (M-H)+ 343.1122. C_{18}H_{20}N_{2}O_{3}S requires: (M-H) 343.1116); ν_{max} (film)/cm⁻¹ 2936, 1618, 1488, 1366, 1263, 1170, 1145, 866; δ_{H} (300 MHz) 3.05 (2H, t, J 7.2, NCH_{2}CH_{2}SO_{3}Ph), 3.34 (2H, t, J 9.6 NCH_{2}CH_{2}N), 3.63 (2H, J 7.2, NCH_{2}CH_{2}SO_{3}Ph), 3.69 (2H, s, PhCH_{2}), 3.79 (2H, t, J 9.6 NCH_{2}CH_{2}N), 7.13-7.43 (10H, m, Ar-H); δ_{C} (75 MHz) 34.7 (PhCH_{2}), 41.7 (NCH_{2}CH_{2}SO_{3}Ph), 48.5 (NCH_{2}CH_{2}N), 50.2 (NCH_{2}CH_{2}SO_{3}Ph), 52.6 (NCH_{2}CH_{2}N), 121.9, 127.1 127.4, 128.6, 128.9 and 130.0 (Ar-CH), 135.4 and 148.5 (Ar-C), 164.4 (N-C=N); m/z 343 [(M-H)^{+}, 4%), 279 (2), 203 (3), 187 (100), 159 (21), 131 (9), 117 (7), 103 (7), 91 (100), 77 (18), 65 (54).
Phenyl 2-[2-(but-3-enyl)imidazolin-1-yl]ethyl sulfonate (2.2.11d)

Prepared by the general method, using 2-(but-3-enyl)-2-imidazoline (0.37 g, 2.98 mmol) and phenyl vinylsulfonate (0.66 g, 3.58 mmol) to give the title compound as a colourless oil (0.52 g, 57%), (Found: $M^+$ 308.1189. C$_{15}$H$_{20}$N$_2$O$_3$S requires: $M$ 308.1195); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2936, 1618, 1489, 1366, 1191, 1170, 1145, 867; $\delta_H$ (300 MHz) 2.30 (2H, t, $J$ 7.8, CH$_2$CH$_2$CH), 2.41 (2H, m, CH$_2$CH$_2$CH=CH$_2$), 3.30 (2H, t, $J$ 9.6 NCH$_2$CH$_2$N), 3.44 (2H, t, $J$ 7.3, NCH$_2$CH$_2$SO$_3$Ph), 3.68-3.75 (4H, m NCH$_2$CH$_2$N and NCH$_2$CH$_2$SO$_3$Ph), 4.98-5.11 (2H, m, CH=CH$_2$), 5.82-5.91 (1H, m, CH=CH$_2$), 7.25-7.46 (5H, m, Ar-H); $\delta_C$ (75 MHz) 27.0 (CH$_2$CH$_2$CH=CH$_2$), 30.3 (CH$_2$CH$_2$CH=CH$_2$), 41.7 (NCH$_2$CH$_2$SO$_3$Ph), 49.0 (NCH$_2$CH$_2$N), 50.2 (NCH$_2$CH$_2$N), 52.5 (NCH$_2$CH$_2$SO$_3$Ph), 115.5 (CH=CH$_2$), 121.8, 127.5 and 130.1 (Ar-CH), 137.1 (CH=CH$_2$), 148.9 (Ar-C), 165.4 (N-C=N); $m/z$ 308 ($M^+$, 8%), 297 (1), 284 (2), 268 (4), 243 (2), 233 (2), 215 (11), 204 (3), 184 (2), 175 (4), 167 (5), 151 (23), 123 (100), 109 (14), 97 (5), 94 (10), 84 (14), 67 (30).

General method for the synthesis of phenyl 2-(2-alkylimidazolin-1-yl) sulfones

The phenyl vinylsulfone (1.2 equiv.) was added to a solution of the 2-alkyl-2-imidazoline (1 equiv) in dichloromethane (10 cm$^3$). The reaction mixture was stirred at 20°C overnight. The dichloromethane was removed under reduced pressure and the crude product was purified by column chromatography on silica gel eluting with 0:100→3:97 v/v isopropylamine:ethyl acetate to give the title compounds.
Phenyl 2-(benzylimidazolin-1-yl)ethyl sulfone (2.2.11a)

\[
\begin{align*}
\text{Ph} & \quad \text{N} \quad \text{Ph} \\
\text{N} & \quad \text{N} \quad \text{Ph}
\end{align*}
\]

Prepared by the general method, using 2-benzyl-2-imidazoline (0.58 g, 3.62 mmol) and phenyl vinylsulfone (0.73 g, 4.35 mmol) to give the title compound as a colourless oil (1.05 g, 89%), (Found: (M-H)\(^{-}\) 327.1173. \(\text{C}_{19}\text{H}_{20}\text{N}_{2}\text{O}_{2}\text{S}\) requires: (M-H) 327.1167); \(\nu_{\max}\) (film)/cm\(^{-1}\) 2934, 2866, 1615, 1585, 1495, 1447, 1304, 1148, 1087, 1005, 726, 691; \(\delta_{\text{H}}\) (300 MHz) 2.97 (2H, t, \(J\ 7.7, \text{NCH}_{2}\text{CH}_{2}\text{SO}_{2}\text{Ph}\)), 3.10 (2H, t, \(J\ 9.8 \text{NCH}_{2}\text{CH}_{2}\text{N}\)), 3.44 (2H, \(J\ 7.2, \text{NCH}_{2}\text{CH}_{2}\text{SO}_{2}\text{Ph}\)), 3.58 (2H, s, PhCH\(_2\)), 3.61 (2H, t, \(J\ 9.8 \text{NCH}_{2}\text{CH}_{2}\text{N}\)), 7.17 (2H, m, Ar-H), 7.23-7.31 (3H, m, Ar-H), 7.56 (2H, m, Ar-H), 7.68 (2H, m, Ar), 7.79 (1H, m, Ar); \(\delta_{\text{C}}\) (75 MHz) 34.6 (PhCH\(_2\)), 41.1 (NCH\(_2\)CH\(_2\)SO\(_2\)Ph), 49.9 (NCH\(_2\)CH\(_2\)N), 52.4 (NCH\(_2\)CH\(_2\)N), 54.0 (NCH\(_2\)CH\(_2\)SO\(_2\)Ph), 127.0 127.9, 128.6, 128.9 and 133.9 (Ar-CH), 135.5 and 139.3 (Ar-C), 164.4 (N-C=N); \(m/z\) 327 [(M-H)\(^{-}\), 7%], 187 (100), 171 (13), 159 (11), 141 (2), 131 (8), 125 (9), 103 (8), 91 (100), 77 (67).

2-(But-3-enyl)-1-(2-phenyl)ethylsulfonyl)-2-imidazoline (2.2.11c)

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{CH} & \quad \text{Ph}
\end{align*}
\]

Prepared by the general method, using 2-(but-3-enyl)-2-imidazoline (0.25 g, 2.01 mmol) and phenyl vinylsulfone (0.40 g, 2.41 mmol) to give the title compound as a colourless oil (0.41 g, 70%) (Found: (M-H)\(^{+}\) 291.1173. \(\text{C}_{15}\text{H}_{20}\text{N}_{2}\text{O}_{2}\text{S}\) requires: M-H 291.1167); \(\nu_{\max}\) (film)/cm\(^{-1}\) 2932, 2863, 1641, 1616, 1447, 1305, 1146, 1087, 1005, 730; \(\delta_{\text{H}}\) (300 MHz) 2.20 (2H, t, \(J\ 7.6, \text{CH}_{2}\text{CH}_{2}\text{CH}\)), 2.34 (2H, m, CH\(_2\)CH\(_2\)CH=CH\(_2\)), 3.04 (2H, t, \(J\ 9.5 \text{NCH}_{2}\text{CH}_{2}\text{N}\)), 3.30 (2H, \(J\ 7.3, \text{NCH}_{2}\text{CH}_{2}\text{SO}_{2}\text{Ph}\)), 3.50-3.57 (4H, m NCH\(_2\)CH\(_2\)N and
NCH₂CH₂SO₂Ph), 4.96-5.08 (2H, m, CH=CH₂), 5.76-5.90 (1H, m, CH=CH₂), 7.55-7.71 (3H, m, Ar-H), 7.88-7.92 (2H, m, Ar-H); δC (75 MHz) 26.8 (CH₂CH₂CH=CH₂), 30.1 (CH₂CH₂CH=CH₂), 40.9 (NCH₂CH₂SO₂Ph), 49.6 (NCH₂CH₂N), 52.1 (NCH₂CH₂N), 54.4 (NCH₂CH₂SO₂Ph), 115.4 (CH=CH₂), 127.7 129.3 and 133.9 (Ar-CH), 137.1 (CH=CH₂), 139.3 (Ar-C), 165.4 (N-C=N); m/z 291 [(M-H)⁺, 23%], 198 (3), 165 (2), 151 (100), 137 (8), 123 (76), 109 (17), 97 (9), 94 (10), 82 (13), 77 (88).

8-Phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-a]pyridin-7-one (2.2.12)

sec-Butyllithium (4.43 cm³ of a 1.1M solution in hexanes, 4.87 mmol) was injected to a solution methyl 3-(2-benzylimidazolin-1-yl)propenoate (0.60 g, 2.48 mmol) in dry THF (25 cm³) at -78°C under nitrogen. The yellow suspension that was produced was stirred at -78°C for 1 h and was allowed to warm up to 20°C where it was stirred for further 1 h. The reaction was quenched with water (25 cm³) and the organic layer was extracted with diethyl ether (3 x 50 cm³). The combined organic extracts were washed successively with saturated aq. NaHCO₃ (100 cm³), water (100 cm³) and brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (1:99→4:96 v/v isopropylamine:ethyl acetate) to give the title compound as a white solid (0.18 g, 34%), m.p 139-141°C (Found: M⁺ 214.1103. C₁₃H₁₄N₂O requires: M 214.1106); ν max (KBr)/cm⁻¹ 3111 (NH), 2975, 2868, 1563, 1548, 1532, 1505, 1479, 1441, 1319, 1301, 1279, 1101; δH (300 MHz) 2.56 (2H, t, J 7.1, NCH₂CH₂CO), 3.28 (2H, t, J 7.1, NCH₂CH₂CO), 3.40 (2H, m, NCH₂CH₂N), 3.48 (2H, m, NCH₂CH₂N), 4.85 (1H, br s, NH), 7.00-7.28 (5H, m, Ar-H); δC (75 MHz) 35.4 (NCH₂CH₂CO), 43.1 (NCH₂CH₂N), 45.2
(NCH₂CH₂CO), 50.6 (NCH₂CH₂N), 94.5 (PhC=CN), 125.8, 128.4 and 130.6 (Ar-CH),
135.0 (Ar-C), 164.6 (PhC=CN), 185.7 (CO); m/z 214 (M⁺, 100%), 185 (92), 171 (6), 157
(18), 129 (35), 115 (15), 103 (24), 89 (16), 77 (19), 63 (9).

2-Benzyl-1-(3-hydroxypropyl)-2-imidazoline (2.2.13)

\[
\text{Ph} \quad \text{p} \quad \text{Ph}
\]

\[
\text{OH}
\]

A solution of methyl 3-(2-benzylimidazolin-1-yl)propenoate (5.20 g, 21.13 mmol) in dry
THF (150 cm³) was added via cannula to a solution of LiAlH₄ (38.42 cm³ of a 1.1M
solution in THF, 42.27 mmol) in THF (100 cm³) at -78°C under nitrogen. The resulting
yellow solution was stirred overnight (-78°C to 20°C). The reaction mixture was then
cooled down to at 0°C and the excess LiAlH₄ was destroyed by addition of ethyl acetate
(50 cm³). The solvent was removed under reduced pressure and the crude product was
purified by column chromatography on silica gel (1:2:97→5:20:75 v/v
isopropylamine:methanol:ethyl acetate) to give the title compound as a yellow oil (2.52 g,
55%) (Found: (M-H)⁺ 217.1339. C₁₃H₁₈N₂O requires: M-H 217.1341); ν_max (film)/cm⁻¹
3187 (OH), 2934, 2864, 1600 (C=N), 1496, 1455, 1280, 1169, 1063, 723; δ_H (300 MHz)
1.54-1.57 (2H, m, NCH₂CH₂CH₂OH), 2.43 (1H, br s, OH), 3.09 (2H, t, J 6.7,
NCH₂CH₂CH₂OH), 3.27 (2H, t, J 9.4, NCH₂CH₂N), 3.41 (2H, t, J 5.9, NCH₂CH₂CH₂OH),
3.57 (2H, s, PhCH₂), 3.66 (2H, t, J 9.4, NCH₂CH₂N) 7.16-7.28 (5H, m, Ar-H); δ_C (75
MHz) 31.0 (NCH₂CH₂CH₂OH), 34.5 (PhCH₂), 43.1 (NCH₂CH₂N), 50.0
(NCH₂CH₂CH₂OH), 51.9 (NCH₂CH₂N), 59.2 (NCH₂CH₂CH₂OH), 126.8, 128.5 and 128.6
(Ar-CH), 136.1 (Ar-C), 166.1 (N-C=N); m/z 218 (M⁺, 10%), 201 (4), 187 (43), 173 (35),
159 (10), 131 (7), 117 (9), 101 (20), 91 (100), 77 (7), 65 (21), 56 (54).
General method for the synthesis of 1,2,3,5-tetrahydroimidazo[1,2-a]pyridin-5-one (2.2.19) and (2.2.20)

\[
\begin{align*}
\text{R}^1 & \quad \text{N} & \quad \text{NH} & \quad + & \quad \text{O} & \quad \text{OEt} \\
\text{R}^2 & \quad \text{O} & \quad \text{O} & \quad \text{R}^3
\end{align*}
\]

The β-ketoester (2 equiv.) was injected into a solution of the 2-substituted 2-imidazoline (1 equiv.) in toluene (30 cm\(^3\)) and the solution was heated to reflux using a Dean-Stark trap for 12 h. The toluene was then removed under reduced pressure and the crude product was purified by column chromatography on silica gel (98:1:1 → 85:10:5 v/v ethyl acetate:methanol:isopropylamine) to give the 1,2,3,5-tetrahydroimidazo[1,2-a]pyridin-5-one.

7-Methyl-8-(prop-2-enyl)-1,2,3,5-tetrahydroimidazo[1,2-a]pyridin-5-one (2.2.19a)

The compound was synthesised by the general method, from 2-(but-3-enyl)-2-imidazoline (0.20 g, 1.61 mmol) and ethyl acetoacetate (0.41 cm\(^3\), 3.22 mmol) in toluene (20 cm\(^3\)). The title compound was obtained as yellow solid (0.14 g, 44%), m.p 147-149°C, (Found: M\(^+\) 190.1102. C\(_{11}\)H\(_{14}\)N\(_2\)O requires: M\(^+\) 190.1106; \(\nu_{\text{max}}\) (KBr)/cm\(^{-1}\) 3215 (NH), 3006, 2977, 1657 (NCO), 1545, 1467, 1421, 1399, 1288, 1202, 1106, 994, 909, 809; \(\delta_{\text{H}}\) (400 MHz) 2.09 (3H, s, CH\(_3\)), 3.04-3.06 (2H, m, CH\(_2\)CH=CH\(_2\)), 3.71 (2H, t, J 8.6, NCH\(_2\)CH\(_2\)N), 4.20 (2H, t, J 8.6, NCH\(_2\)CH\(_2\)N), 4.66 (1H, br s, NH), 4.98-5.08 (2H, m, CH\(_2\)CH=CH\(_2\)), 5.77 (1H, s, CH=CH\(_3\)), 5.76-5.86 (1H, m, CH=CH\(_2\)); \(\delta_{\text{C}}\) (75 MHz) 19.8 (CH\(_3\)), 30.3 (CH\(_2\)CH=CH\(_2\)), 192
The compound was synthesised by the general method, from 2-(but-3-enyl)-2-imidazoline (0.20 g, 1.61 mmol) and ethyl benzoylacetate (0.55 cm³, 3.22 mmol) in toluene (20 cm³).

The title compound was obtained as a yellow solid (0.35, 86%), m.p. 152-154°C (Found: M⁺ 252.1267. C₁₆H₁₆N₂O requires: M 252.1263); λmax/µm 343 (εmax/mol.dm⁻³ 34980); νmax (KBr)/cm⁻¹ 3170 (NH), 2981, 2924, 1656 (NCO), 1547, 1475, 1417, 1375, 1181, 781, 708; δH (300 MHz) 2.87-2.91 (2H, m, CH₂CH=CH₂), 3.70 (2H, t, J 8.6, NCH₂CH₂N), 4.20 (2H, t, J 8.6, NCH₂CH₂N), 4.75 (1H, br s, NH), 4.91-5.04 (2H, m, CH=CH₂), 5.77 (1H, s, CH=CPh), 5.55-5.81 (1H, m, CH=CH₂), 7.15-7.21 (2H, m, Ar-H), 7.24-7.33 (3H, m, Ar-H); δC (75 MHz) 31.1 (CH₂=CHCH₂), 42.9 (NCH₂CH₂N), 44.6 (NCH₂CH₂N), 92.7 (CH₂C≡CN), 107.2 (CH=CPh), 115.5 (CH=CH₂), 127.8, 127.9 and 128.1 (Ar-CH), 136.1 (CH=CH₂), 139.3 (Ar-C), 151.4 (CH=CPh), 157.2 (NC=CCH₂), 160.2 (NCO); m/z 252 (M⁺, 100%), 225 (59), 197 (10), 152 (14), 127 (19), 115 (15), 102 (11), 77 (18).
7-Phenyl-8-phenylmethyl-1,2,3,5-tetrahydroimidazo[1,2-a]pyridin-5-one (2.2.19c)

The compound was synthesised by the general method, from 2-phenylethyl-2-imidazoline (0.10 g, 0.57 mmol) and ethyl benzoyleacetate (0.20 cm$^3$, 1.14 mmol) in toluene (20 cm$^3$). The title compound was obtained after purification as a white solid (0.13 g, 75%), m.p 210-212°C (Found: M$^+$ 302.1423. C$_{20}$H$_{18}$N$_2$O requires: M 302.1419); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 3246 (NH), 1667 (NCO), 1546, 1526, 1468, 1415, 1289, 1237, 699; $\delta_{\text{H}}$ (400 MHz) 3.60 (2H, s, PhCH$_2$), 3.64 (2H, t, $J$ 8.3, NCH$_2$CH$_2$N), 4.23 (2H, t, $J$ 8.3, NCH$_2$CH$_2$N), 4.38 (1H, br s, NH), 5.89 (1H, s, NCOC$/\equiv$/CPh), 7.08-7.36 (10H, m, Ar-H); $\delta_{\text{C}}$ (100 MHz) 32.4 (PhCH$_2$), 42.9 (NCH$_2$CH$_2$N), 44.6 (NCH$_2$CH$_2$N), 93.9 (PhCH$_2$/C=CN), 107.3 (NCOCH=CPh), 126.4, 127.7, 127.7, 127.9, 128.2 and 128.8 (Ar-CH), 139.2 and 139.5 (Ar-C), 151.45 (NCOCH=CPh), 157.4 (NC=CCH$_3$Ph), 160.3 (NCO); m/z 302 (M$^+$, 13%), 273 (2), 225 (14), 202 (2), 167 (2), 154 (2), 140 (2), 127 (5), 105 (5), 91 (19), 77 (19).

6-Methyl-7-phenyl-1,2,3,5-tetrahydroimidazo[1,2-a]pyridin-5-one (2.2.19d)

The compound was synthesised by the general method, from 2-benzyl-2-imidazoline (0.90 g, 5.62 mmol) and ethyl acetoacetate (1.43 cm$^3$, 11.25 mmol). The title compound was obtained after purification as a white solid (0.72 g, 56%), m.p. 161-163°C (Found: M$^+$ 226.1107. C$_{14}$H$_{14}$N$_2$O requires: M 226.1106); $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3145 (NH), 1657 (NCO), 1559, 1519, 1493, 1439, 1296, 702; $\delta_{\text{H}}$ (400 MHz) 1.95 (3H, s, CH$_3$), 3.66 (2H, t, $J$ 8.2,
7,8-Diphenyl-1,2,3,5-tetrahydroimidazol[1,2-a]pyridin-5-one (2.2.19e)

![Diagram of the compound]

The compound was synthesised by the general method, from 2-benzyl-2-imidazoline (1.10 g, 6.25 mmol) and ethyl benzoylacetate (2.16 cm³, 12.50 mmol) in toluene (62 cm³). The title compound was obtained as a yellow solid (1.05 g, 58%), m.p 279-281 °C (Found: M⁺ 288.1259. C₁₉H₁₆N₂O requires: M⁺ 288.1263); νmax (KBr)/cm⁻¹ 3234 (NH), 1646 (NCO), 1586, 1531, 1500, 1487, 1469, 1420, 1282, 768, 699; δ H (400 MHz) 3.69 (2H, t, J 8.3, NCH₂CH₂N), 4.20 (2H, t, J 8.3, NCH₂CH₂N), 4.98 (1H, br s, NH), 5.95 (1H, s, COCH=CPh), 7.05-7.28 (10H, m, Ar-H); δ C (100 MHz) 42.8 and 44.9 (NCH₂), 98.3 (PhC=CN), 107.4 (NCOCH=CPh), 126.7, 127.8, 128.0, 128.6, 128.9, and 130.6 (Ar-CH), 135.3 and 139.0 (Ar-C), 151.0 (NCOCH=CPh), 155.5 (NC=CPh), 160.5 (NCO); m/z 288 (M⁺, 6%), 242 (2), 223 (3), 210 (3), 190 (4), 162 (4), 120 (16), 91 (24), 57 (18).
10-Phenylmethyl-1,2,3,5,6,7,8,9-octahydroimidazo[1,2-b]isoquinolin-5-one (2.2.20a)

The compound was synthesised by the general method, from 2-phenylethyl-2-imidazoline (0.10 g, 0.57 mmol) and ethyl 2-cyclohexanone carboxylate (0.18 cm³, 1.15 mmol) in toluene (20 cm³). The title compound was obtained as a white solid (0.12 g, 75%), m.p 231-233°C (Found: C, 76.49; H, 7.18; N, 9.78%; M⁺ 280.1575 C₁₈H₂₀N₂O·0.1H₂O requires: C, 76.65; H, 7.16; N, 9.93%; M 280.1576); νmax (film)/cm⁻¹ 3240 (NH), 2927, 1652 (NCO), 1533, 1494, 1481, 1290, 1228, 740; δH (400 MHz) 1.65-1.70 (4H, m, CH₂CH₂CH₂CH₂), 2.42 (2H, t, J 4.8, CH₂CH₂CH₂CH₂), 2.53 (2H, t, J 4.8, CH₂CH₂CH₂CH₂), 3.57 (2H, t, J 8.3, NCH₂CH₂N), 3.68 (2H, s, PhCH₂), 4.20 (2H, t, J 8.3, NCH₂CH₂N), 4.30 (1H, br s, NH), 7.10-7.30 (5H, m, Ar-H); δC (100 MHz) 22.2, 22.5, 23.5 and 26.9 (CH₂), 31.2 (PhCH₂), 42.7 (NCH₂CH₂N), 44.8 (NCH₂CH₂N), 94.2 (PhCH₂C=CN), 115.4 (NCOC=CN), 126.3, 127.6 and 128.7 (Ar-CH), 139.6 (Ar-C), 147.6 (NCOC=CN), 149.2 (NC=C(CH₃)₂Ph), 160.2 (NCO); m/z 280 (M⁺, 100%), 265 (26), 251 (29), 236 (5), 203 (29), 189 (10), 175 (6), 152 (3), 115 (5), 91 (14), 69 (15).
10-[(2-Phenyl)phenylmethyl]-1,2,3,5,6,7,8,9-octahydroimidazo[1,2-b]isoquinolin-5-one
(2.2.20b)

The compound was synthesised by the general method, from 2-[(2-phenyl)phenylethyl]-2-imidazoline (0.50 g, 2.00 mmol) and ethyl 2-cyclohexanone carboxylate (0.64 cm³, 4.00 mmol) in toluene (20 cm³). The title compound was obtained after purification as a white solid (0.63 g, 88%), m.p 251-253°C (Found: C, 79.88; H, 6.70; N, 7.78%; M⁺ 356.1889. C₂₄H₂₄N₂O O.15H₂O requires: C, 80.28; H, 6.77; N, 7.80%; M 356.1889); ν_max (film)/cm⁻¹ 3208 (NH), 2928, 1657 (NCO), 1533, 1494, 1476, 1450, 1288, 1230, 1154, 751; δH (300 MHz) 1.61-1.66 (4H, m, CH₂CH₂CH₂CH₂), 2.25 (2H, t, J 4.8, CH₂CH₂CH₂CH₂), 2.49 (2H, t, J 4.8, CH₂CH₂CH₂CH₂), 3.51 (2H, t, J 8.3, NCH₂CH₂N), 3.59 (2H, s, ArCH₂), 3.86 (1H, br s, NH), 4.17 (2H, t, J 8.3, NCH₂CH₂N), 7.18-7.46 (9H, m, Ar-H); δC (75 MHz) 22.2, 22.5, 23.4 and 26.8 (CH₂), 29.6 (ArCH₂), 42.7 (NCH₂CH₂N), 44.8 (NCH₂CH₂N), 94.4 (ArCH₂C=CN), 115.6 (NCOC=O), 126.3, 127.2, 127.4, 127.9, 128.3, 129.1 and 136.7, (Ar-CH), 139.6, 141.4 and 142.2 (Ar-C), 147.6 (NCOC=O), 149.2 (NC=CHCH₂Ar), 160.2 (NCO); m/z 356 (M⁺, 100%), 355 (28), 341 (11), 327 (7), 313 (4), 277 (4), 251 (3), 215 (4), 203 (71), 189 (20), 175 (15), 165 (33), 152 (21), 128 (5), 115 (6), 91 (6), 77 (16) 44 (23).
The compound was synthesised by the general method, from 2-benzyl-2-imidazoline (5.00 g, 31.25 mmol) and ethyl 2-cyclohexanonecarboxylate (9.98 cm³, 62.50 mmol) in toluene (150 cm³). The title compound was obtained as a yellow solid (5.48 g, 66%), m.p 223-235°C (Found: C, 76.50; H, 6.81; N, 10.50%; M⁺ 266.1417. C₁₇H₁₈N₂O requires: C, 76.66; H, 6.81; N, 10.50%; M 266.1419); νₘₚ (film)/cm⁻¹ 3127 (NH), 2935, 1650 (NCO), 1563, 1523, 1491, 1436, 1096, 698; δₜ (400 MHz) 1.56-1.62 (2H, m, CH₂CH₂CH₂CH₂), 1.67-1.72 (2H, m, CH₂CH₂CH₂CH₂), 2.22 (2H, t, J 4.8, CH₂CH₂CH₂CH₂), 2.53 (2H, t, J 4.8, CH₂CH₂CH₂CH₂), 3.59 (2H, t, J 8.3, NCH₂CH₂N), 4.11 (1H, br s, NH), 4.22 (2H, t, J 8.3, NCH₂CH₂N), 7.19-7.30 (5H, m, Ar-H); δₜ (100 MHz) 22.3, 22.5, 23.4 and 28.5 (CH₂) 42.7 (NCH₂CH₂N), 44.9 (NCH₂CH₂N), 98.9 (PhC=CN), 114.9 (NOCOC=C), 127.3, 128.9 and 130.8 (Ar-CH), 135.2 (Ar-C), 146.8 (NOCOC=C), 148.3 (NC=CPH), 160.3 (NCO); m/z 266 (M⁺, 52%), 251 (14), 237 (28), 206 (11), 191 (19), 149 (71), 115 (12), 105 (13), 91 (53), 77 (15).
2-(But-3-enyl)-1-(3-oxo)but-1-enyl)-2-imidazoline (2.3.4)

3-Butyn-2-one (0.47 cm³, 5.33 mmol) was injected into a solution of 2-(but-3-enyl)-2-imidazoline (0.63 g, 5.08 mmol) in dry methanol (50 cm³) at 20°C under nitrogen. The reaction mixture was stirred at 20°C for 14 h. The methanol was then removed under reduced pressure and the residue was purified by column chromatography on silica gel (0.25:99.75→2:98 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (0.81 g, 83%) (Found: (M-H)+ 191.1184. C_{11}H_{16}N_{2}O requires: M-H 191.1184); ν_{max} (film)/cm⁻¹ 2950, 1642, 1572, 1479, 1405, 1354, 1257, 1201, 1005, 964, 927; δ_{H} (400 MHz) 2.20 (3H, s, COCH₃), 2.47-2.52 (4H, m, CH₂CH₂CH=CH₂), 3.57 (2H, t, J 9.2, NCH₂CH₂N), 3.95 (2H, t, J 9.2, NCH₂CH₂N), 5.00-5.15 (2H, m, CH=CH₂), 5.30 (1H, d, J 13.2, NCH=CHCOMe), 5.85-5.94 (1H, m, CH=CH₂), 7.75 (1H, d, J 13.2, NCH=CHCOMe); δ_{C} (100 MHz) 26.6 (CH₂CH₂CH=CH₂), 28.7 (COCH₃), 29.5 (CH₂CH₂CH=CH₂), 46.3 (NCH₂CH₂N), 53.3 (NCH₂CH₂N), 103.6 (NCH=CHCOMe), 116.0 (CH=CH₂), 136.5 (CH=CH₂), 137.7 (NCH=CHCOMe), 160.2 (N=C-N), 196.6 (COMe); m/z 192 (M⁺, 27%) 177 (6), 149 (89), 135 (6), 121 (17), 111 (80), 96 (78), 83 (48), 68 (44), 55 (100), 43 (100).

2-Benzyl-1-(3-oxobut-1-enyl)-2-imidazoline (2.3.7)

3-Butyn-2-one (1.45 cm³, 18.75 mmol) was injected into a solution of 2-benzyl-2-imidazoline (2.50 g, 15.62 mmol) in dry methanol (20 cm³) at 0°C. The reaction mixture
was stirred at 0°C for 30 min and at 20°C for 4 h. The methanol was then removed under reduced pressure and the crude product was purified by column chromatography on silica gel (0.25:99.75→2-98 v/v isopropylamine:ethyl acetate) to give the *title compound* as a yellow solid (2.56 g, 72%), m.p. 104-106°C (Found: C, 71.43; H, 7.09; N, 11.93%; M⁺ 228.1263. C₁₄H₁₆N₂O·0.4H₂O requires: C, 71.39; H, 6.79; N, 11.89%; M 228.1262); ν_max (KBr)/cm⁻¹ 2995, 2919, 1606, 1457, 1360, 1249, 1167, 1001, 942; δH (400 MHz) 2.10 (3H, s, COCH₃), 3.56 (2H, t, J 9.3, NCH₂CH₂N), 3.88 (2H, s, PhCH₂), 4.02 (2H, t, J 9.3, NCH₂CH₂N), 5.20 (1H, d, J 13.2, NCH=CHCOMe), 7.20-7.35 (5H, m, Ar-H), 7.67 (1H, d, J 13.2, NCH=CHCOMe); δC (100 MHz) 28.2 (COCH₃), 34.3 (PhCH₂), 46.6 (NCH₂CH₂N), 53.7 (NCH₂CH₂N), 104.5 (NCH=CHCOMe), 127.7, 128.7 and 129.1 (Ar-CH), 134.3 (Ar-C), 138.6 (NCH=CHCOMe), 159.7 (N=C-N), 196.7 (COMe); m/z 228 (M⁺, 29%), 213 (3), 185 (12), 171 (5), 159 (2), 117 (8), 111 (98), 96 (100), 91 (52), 83 (42), 70 (22).

2-Benzyl-1-(3-hydroxybut-1-enyl)-2-imidazoline (2.3.11)

A solution of 2-benzyl-1-(3-(oxo)but-1-enyl)-2-imidazoline (.48 g, 2.10 mmol) in THF (21 cm³) was added via cannula to LiAlH₄ (2.10 cm³ of a 1M solution in THF, 2.10 mmol) at -78°C under nitrogen. The resulting yellow solution was stirred at -78°C for 1 h and was then allowed to warm up to 20°C. The reaction was quenched with ethyl acetate (5 cm³) and stirred the mixture for 30 min. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (2.98 v/v isopropylamine:ethyl acetate) to give the *title compound* as a thick yellow oil (0.36 g, 75%) (Found: M⁺ 230.1419. C₁₄H₁₈N₂O requires: M 320.1419); ν_max (film)/cm⁻¹ 3294 (OH), 2966, 2874, 1661, 1617, 1456, 1417, 1280, 1144, 1010, 927, 725; δH (400 MHz;
CDCl₃ 1.21 (3H, d, J 6.2, CH₃), 2.78 (1H, br s, OH), 3.46 (2H, t, J 10.0 NCH₂), 3.68 (2H, s, PhCH₂), 3.82 (2H, t, J 10.0, NCH₂), 4.17-4.23 (1H, m, CH₃CHOH), 4.53-4.59 (1H, dd, J 7.5 and 13.1, NCH=CH), 6.56 (1H, d, J 13.1, NCH=CH), 7.20-7.35 (5H, m, Ar-H); δC (100 MHz) 24.2 (CH₃), 34.0 (PhCH₂), 46.5 and 53.2 (NCH₂), 67.2 (CH₃CHOH), 109.4 (NCH=CH), 126.1 (NCH=CH), 127.1, 128.4 and 128.9 (Ar-CH), 134.9 (Ar-C), 160.3 (N-C=N); m/z 230 (M⁺, 7%), 211 (45), 197 (5), 171 (7), 159 (18), 131 (5), 115 (6), 103 (5), 98 (18), 91 (49), 77 (7), 67 (11).

**General method for the synthesis of methyl 3-(2-alkylimidazolin-1-yl)propenoates**

![Diagram of general method](attachment:image.png)

Methyl propenoate was injected to a solution of the 2-alkyl-2-imidazoline in dry methanol at 20 °C under nitrogen. The resulting yellow solution was stirred overnight at 20 °C. Methanol was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (3:7→10:0 v/v ethyl acetate:hexane) to give the products.

**Z and E Methyl 3-(2-benzylimidazolin-1-yl)propenoate (2.3.14)**

![Diagram of Z and E isomers](attachment:image.png)

These compounds were prepared by the general method, from 2-benzyl-2-imidazoline (2.00 g, 12.48 mmol) and methyl propynoate (1.10 cm³, 18.67 mmol) in methanol (62 cm³). The *title compounds* were obtained after purification in a 2:1 ratio Z:E isomers (1.95 g, 65%). Data for Z isomer: (Found: C, 66.49; H, 6.73; N, 10.74%; M⁺ 244.1212.

201
$C_{14}H_{16}N_2O_2\cdot 0.4H_2O$ requires: C, 66.84; H, 6.36, N, 11.14%; $M \ 244.1212$; $\nu_{\text{max}}$ (film)/cm$^{-1}$ 1 2948, 1704 (CO), 1610 (C=N), 1357, 1268, 1153, 1011, 718; $\delta_H$ (400 MHz) 3.62 (3H, s, CO$_2$CH$_3$), 3.81 (2H, s, PhCH$_2$), 3.97 (2H, t, $J$ 8.8, NCH$_2$CH$_2$N), 4.04 (2H, t, $J$ 8.8, NCH$_2$CH$_2$N), 4.65 (1H, d, $J$ 10.0, NCH=CHCO$_2$Me), 4.57 (1H, d, $J$ 10.0, NCH=CHCO$_2$Me), 7.20-7.34 (5H, m, Ar-H); $\delta_C$ (100 MHz) 34.5 (PhCH$_2$), 49.4 (NCH$_2$CH$_2$N), 50.9 (CO$_2$CH$_3$), 54.1 (NCH$_2$CH$_2$N), 90.9 (NCH=CHCO$_2$Me), 127.2, 128.7, 128.9 (Ar-CH), 134.2 (Ar-C), 136.0 (NCH=CHCO$_2$Me), 160.5 (N=C-N), 165.9 (CO$_2$Me); $m/z$ 244 (M$^+$, 52%), 229 (3), 213 (20), 185 (84), 171 (64), 159 (8), 128 (34), 117 (16), 105 (20), 91 (100), 77 (19). Data for the $E$-isomer: m.p 74-76°C, (Found: C, 67.51; H, 6.59; N, 11.24%; M$^+$ 244.1212. $C_{14}H_{16}N_2O_2\cdot 0.2H_2O$ requires: C, 67.81; H, 6.45; N, 11.30%; M $244.1212$; $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2935, 1693 (CO), 1607 (C=N), 1408, 1315, 1261, 1192, 1170, 718; $\delta_H$ (400 MHz) 3.57 (2H, t, $J$ 8.8, NCH$_2$CH$_2$N), 3.68 (3H, s, CO$_2$CH$_3$), 3.94 (2H, s, PhCH$_2$), 3.97 (2H, t, $J$ 8.8, NCH$_2$CH$_2$N), 4.82 (1H, d, $J$ 13.2, NCH=CHCO$_2$Me), 7.20-7.34 (5H, m, Ar-H), 7.78 (1H, d, $J$ 13.2, NCH=CHCO$_2$Me); $\delta_C$ (100 MHz) 34.0 (PhCH$_2$), 46.3 (NCH$_2$CH$_2$N), 51.1 (CO$_2$CH$_3$), 53.2 (NCH$_2$CH$_2$N), 93.2 (NCH=CHCO$_2$Me), 127.4, 128.9 and 129.1 (Ar-CH), 134.1 (Ar-C), 139.1 (NCH=CHCO$_2$Me), 159.5 (N=C-N), 168.6 (CO$_2$Me); $m/z$ 244 (M$^+$, 36%), 213 (25), 185 (50), 171 (30), 159 (10), 128 (40), 117 (20), 105 (17), 91 (100), 77 (26).

$Z$ and $E$ Methyl 3-[2-(furylethylimidazolin-1-yl)propenoate (2.3.15)

These compounds were prepared by the general method, from 2-[2-(2-furyl)ethyl]-2-imidazoline (0.21 g, 1.28 mmol) and methyl propynoate (0.17 cm$^3$, 1.92 mmol) in methanol (1.2 cm$^3$). The title compounds were obtained as white solids (0.19 g, 60%). Data
for Z-isomer: m.p. 58-60°C (Found: C, 62.70; H, 6.54; N, 11.14%; M+ 248.1160. C13H18N2O3 requires: C, 62.89; H, 6.50, N,11.28%; M 248.1160); νmax (KBr)/cm⁻¹ 2949, 1699 (CO), 1611 (C=N), 1474, 1378, 1335, 1213, 1173, 997, 924; δH (400 MHz) 2.69 (2H, t, J 7.8, CH₂CH₂Furyl), 2.99 (2H, t, J 7.8, CH₂CH₂Furyl), 3.59 (3H, s, CO₂CH₃), 3.83 (2H, t, J 9.0, NCH₂CH₂N), 3.93 (2H, t, J 9.0, NCH₂CH₂N), 4.67 (1H, d, J 10.0, NCH=CHCO₂Me), 5.98 (1H, d, J 2.9, Furyl-4H), 6.21 (1H, dd, J 1.9 and 2.9, Furyl-3H), 6.52 (1H, d, J 10.0, NCH=CHCO₂Me), 7.24 (1H, d, J 1.9, Furyl-2H); δC (100 MHz) 24.5 (CH₂CH₂Furyl), 26.6 (CH₂CH₂Furyl), 49.4 (NCH₂CH₂N), 50.9 (CO₂CH₃), 54.0 (NCH₂CH₂N), 90.9 (NCH=CHCO₂Me), 105.6, 110.2 and 141.3 (Furyl-CH), 135.6 (NCH=CHCO₂Me), 153.9 (Furyl-C), 160.9 (N=C=N), 165.9 (CO₂Me); m/z 248 (M⁺, 25%), 233 (6), 217 (10), 189 (100), 161 (10), 135 (10), 121 (10), 109 (36), 96 (24), 81 (32), 68 (9). Data for E-isomer: m.p. 96-98 °C (Found: C, 62.74; H, 6.54; N, 11.01%; M⁺ 248.1160. C₁₃H₁₈N₂O₃ requires: C, 62.89; H, 6.50, N,11.28%; M 248.1160); νmax (KBr)/cm⁻¹ 2958, 1693 (CO), 1634 (C=N), 1315, 1286, 1217, 1168, 793, 740; δH (400 MHz) 2.66 (2H, t, J 7.8, CH₂CH₂Furyl), 3.01 (2H, t, J 7.8, CH₂CH₂Furyl), 3.48 (2H, t, J 9.0, NCH₂CH₂N), 3.65 (3H, s, CO₂CH₃), 3.87 (2H, t, J 9.0, NCH₂CH₂N), 4.79 (1H, d, J 13.2, NCH=CHCO₂Me), 6.00 (1H, d, J 3.1, Furyl-4H), 6.21 (1H, dd, J 2.0 and 3.1, Furyl-3H), 7.25 (1H, d, J 2.0, Furyl-2H), 7.65 (1H, d, J 13.2, NCH=CHCO₂Me); δC (100 MHz) 24.5 (CH₂CH₂Furyl), 26.2 (CH₂CH₂Furyl), 46.6 (NCH₂CH₂N), 51.4 (CO₂CH₃), 53.3 (NCH₂CH₂N), 93.6 (NCH=CHCO₂Me), 105.9, 110.5 and 141.6 (Furyl-CH), 138.8 (NCH=CHCO₂Me), 154.1 (Furyl-C), 160.1 (N=C-N), 168.9 (CO₂Me); m/z 248 (M⁺, 23%), 233 (5), 217 (9), 205 (5), 189 (100), 175 (2), 161 (8), 135 (6), 121 (8), 109 (36), 96 (21), 81 (27), 68 (8).
Z and E methyl 3-[2-(hepta-3,5-dienyl imidazolin-1-yl]propenoate (2.316a-b)

The compounds were synthesised from 2-(hepta-3,5-dienyl)-2-imidazoline (0.31 g, 1.93 mmol) and methyl propenoate (0.30 cm³, 2.89 mmol) in methanol (10 cm³) using the general method. The title compound was obtained after purification as 2:1 mixture of propenoate Z:E isomers as yellow oils (each a 3:1 mixture of E,E:E,Z isomers) (0.24 g, 50%); Data for propenoate Z-isomer (Found: C, 66.95; H, 8.10; N, 11.03%; M⁺ 248.1534. C₁₄H₂₀N₂O₂·0.1H₂O requires C, 67.21; H, 8.08; N, 11.20%; M 248.1525); νmax (film)/cm⁻¹ 2949, 1707 (CO), 1653, 1610 (C=N), 1364, 1160, 994, 922; data for heptadienyl E:E isomer δH (400 MHz) 1.73 (3H, d, J 6.8, CH3), 2.37-2.45 (4H, m, CH=CHCH₂CH₂), 3.66 (3H, s, CO₂CH₃), 3.88 (2H, t, J 8.8, NCH₂CH₂N), 3.98 (2H, t, J 8.8, NCH₂CH₂N), 4.74 (1H, d, J 10.0, NCH=CHCO₂Me), 5.56-5.66 (2H, m, CH₃CH=CHCH=CH₂), 6.00-6.10 (2H, m, CH₃CH=CHCH=CH₂), 6.61 (1H, d, J 10.0, NCH=CHCO₂Me), δC (100 MHz) 18.1 (CH₃), 27.9 (CH=CHCH₂CH₂), 28.8 (CH=CHCH₂CH₂), 49.4 (NCH₂CH₂N), 50.9 (CO₂CH₃), 54.1 (NCH₂CH₂N), 90.6 (NCH=CHCO₂Me), 128.2, 129.2, 131.2 and 131.6 (CH), 135.9 (NCH=CHCO₂Me), 161.3 (N=C-N), 166.1 (CO₂Me); data for heptadienyl E:Z isomer δH (400 MHz) 1.11 (3H, d, J 6.8, CH3CH), 2.37-2.45 (4H, m, CH₂CH₂), 3.66 (3H, s, CO₂CH₃), 3.88 (2H, t, J 8.8, NCH₂CH₂N), 3.98 (2H, t, J 8.8, NCH₂CH₂N), 4.74 (1H, d, J 10.0, NCH=CHCO₂Me), 5.01 (1H, dd, J 1.7 and 10.2, CH₃CH=CHCH=CH), 5.14 (1H, d, J 1.7 and 17.1, CH₃CH=CHCH=CHCH₂), 5.61-5.66 (1H, m, CH₃CH=CHCH=CHCH₂), 6.25-6.32 (1H, m, CH₃CH=CHCH=CHCH₂), 6.61 (1H, d, J 10.3, NCH=CHCO₂Me); δC (100 MHz) 20.0 (CH₃), 33.8 (CH₂CH₂), 34.9 (CH₂CH₂), 49.4 (NCH₂CH₂N), 50.9 (CO₂CH₃), 54.1 (NCH₂CH₂N), 90.6 (NCH=CHCO₂Me), 116.1, 129.9, 136.9 and 138.5 (CH), 136.0 (NCH=CHCO₂Me), 161.3 (N=C-N), 166.1 (CO₂Me); m/z 248 (M⁺, 56%), 233
Data for propenote E-isomer (Found: M+ 248.1523. C14H20N2O2 requires: M 248.1525); νmax (film)/cm⁻¹ 2950, 1703 (CO), 1615 (C=N), 1410, 1315, 1256, 1197, 1163, 994; data for heptadienyl-E,E isomer δH (400 MHz) 1.73 (3H, d, J 6.8, CH₃), 2.41-2.51 (4H, m, CH₂CH₂), 3.53 (2H, t, J 9.0, NCH₂CH₂N), 3.72 (3H, s, CO₂CH₃), 3.93 (2H, t, J 9.0, NCH₂CH₂N), 4.85 (1H, d, J 13.2, NCH=CHCO₂Me), 5.58-5.69 (2H, m, CH₃CH=CHCH=CHCH₂), 5.98-6.10 (2H, m, CH₃CH=CHCH=CHCH₂), 7.74 (1H, d, J 13.2, NCH=CHCO₂Me); δC (100 MHz) 18.5 (CH₃), 27.3 (CH₂CH₂), 28.5 (CH₂CH₂), 46.2 (NCH₂CH₂N), 50.9 (CO₂CH₃), 53.1 (NCH₂CH₂N), 92.9 (NCH=CHCO₂Me), 128.2, 129.0, 131.6 and 131.7 (CH), 138.9 (NCH=CHCO₂Me), 160.1 (N=C-N), 168.7 (CO₂Me); m/z 248 (M⁺, 28%), 233 (22), 217 (9), 205 (6), 189 (100), 175 (16), 161 (10), 149 (14), 134 (17), 121 (15), 109 (32), 96 (23), 79 (26), 67 (16); Data for heptadienyl E:Z-isomer δC (400 MHz) 1.13 (3H, d, J 6.8, CH₃), 2.40-2.51 (4H, m, CH₂CH₂), 3.53 (2H, t, J 9.0, NCH₂CH₂N), 3.66 (3H, s, CO₂CH₃), 3.95 (2H, t, J 9.0, NCH₂CH₂N), 4.74 (1H, d, J 10.2, NCH=CHCO₂Me), 5.01 (1H, dd, J 1.7 and 9.8, CH₃CH=CHCH=CHCH₂), 5.14 (1H, d, J 1.7 and 17.1, CH₃CH=CHCH=CHCH₂), 5.65-5.70 (1H, m, CH₃CH=CHCH=CHCH₂), 6.24-6.31 (1H, m, CH₃CH=CHCH=CHCH₂), 6.61 (1H, d, J 10.2, NCH=CHCO₂Me); δC (100 MHz) 20.2 (CH₃), 27.9 (CH₂CH₂), 28.8 (CH₂CH₂), 49.3 (NCH₂CH₂N), 51.1 (CO₂CH₃), 54.1 (NCH₂CH₂N), 90.6 (NCH=CHCO₂Me), 116.1, 131.1, 135.9 and 138.3 (CH), 138.8 (NCH=CHCO₂Me), 160.1 (N=C-N), 168.7 (CO₂Me).
General method for the synthesis of 1-alkyl-2-benzyl-2-imidazolines

sec-Butyllithium (1.3M solution in hexanes, 1.2 mol equiv.) was injected dropwise to a solution of 2-benzyl-2-imidazoline in dry THF/TMEDA (25:1 v/v) at -78 °C. The yellow solution that was produced was stirred at -78 °C for 20 minutes, the alkyl halide (1.2 equiv) was injected rapidly and the reaction mixture was stirred overnight (-78 °C to 20 °C). The reaction was quenched with water (100 cm³) and the organic layer was extracted with diethyl ether (3 x 50 cm³). The combined organic extracts were washed successively with water (100 cm³) and brine (100 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→2:98 v/v isopropylamine:ethyl acetate) to give the 1-alkyl-2-benzyl-2-imidazoline.

2-Benzyl-1-(prop-2-enyl)-2-imidazoline (2.3.19)

Prepared by the general method from 2-benzyl-2-imidazoline (2.00 g, 12.5 mmol), sec-butyllithium (10.57 cm³ of a 1.3M solution in hexanes, 13.75 mmol), and 1,3-dibropropane (1.39 cm³, 13.75 mmol) to give the title compound as a yellow oil (1.2 g, 48%) (Found: (M-H)+ 199.1234. C13H16N2 requires: M-H 199.1235); ν_max (film)/cm⁻¹ 2933, 2865, 1644, 1611, 1417, 1211, 1074, 917; δ_H (300 MHz) 3.28 (2H, t, J 9.8, NCH₂CH₂N), 3.63-3.68 (4H, m, PhC=N 2 and NCH₂CH=CH₂) 3.74 (2H, t, J 9.8, NCH₂CH₂N), 5.07-5.14 (2H, m, NCH₂CH=CH₂), 5.52-5.62 (1H, m, NCH₂CH=CH₂), 7.19-7.34 (5H, m, Ar-H); δ_C (75 MHz) 34.6 (PhCH₂), 49.3, 50.0 and 52.3 (NCH₂), 117.1 (NCH₂CH=CH₂), 126.7, 128.6 and
2-(2-Phenylhepta-3,5-dienyl)-1-(prop-2-enyl)-2-imidazoline (2.3.20)

\[
\begin{array}{c}
\text{Ph} \\
\text{N}<x \text{/N} \\
\text{Ph}
\end{array}
\xrightarrow{\text{N-butyllithium}}
\begin{array}{c}
\text{Ph} \\
\text{N}<x \text{/N} \\
\text{Ph}
\end{array}
\]

n-Butyllithium (1.24 cm\(^3\) of a 1.1M solution in hexanes, 1.36 mmol) was injected to a stirred solution of 2-benzyl-1-(prop-2-enyl)-2-imidazoline (0.249 g, 1.24 mmol) in dry THF (12 cm\(^3\)) at 20°C under nitrogen. The yellow suspension that was formed was stirred at 20°C for 50 min. The reaction mixture was cooled to 0°C and 1-bromohexa-2,4-diene (0.22 g, 1.36 mmol) was injected to it as a solution in THF (3 cm\(^3\)). The reaction mixture was stirred at 0°C for 15 min and at 20°C overnight. The reaction was quenched with water (20 cm\(^3\)) and the organic layer was extracted with diethyl ether (3 x 20 cm\(^3\)). The combined organic extracts were washed with brine (50 cm\(^3\)) and water (50 cm\(^3\)), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→3:97 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (0.30 g, 49%) (Found: M\(^+\) 280.1937. C\(_{19}\)H\(_{24}\)N\(_2\) requires: M 280.1939); \(\nu_{\text{max}}\) (film)/cm\(^{-1}\) 3018, 2932, 2859, 1610, 1455, 1416, 1213, 991, 702; \(\delta_H\) (300 MHz) 1.69 (3H, d, J 6.2, CH\(_3\)), 2.48-2.55 (1H, m, PhCHCH\(_2\)H), 2.82-2.92 (1H, m, PhCHCH\(_2\)H), 3.14-3.30 (2H, m, NCH\(_2\)CH\(_2\)N), 3.40-3.48 (2H, m, NCH\(_2\)CH=CH\(_2\)), 3.58-3.62 (1H, m, PhCHCH\(_2\)), 3.72-3.82 (2H, m, NCH\(_2\)CH\(_2\)N), 5.00-5.07 (2H, m, NCH\(_2\)CH=CH\(_2\)), 5.40-5.57 (3H, m, CH\(_3\)CH=CH=CHCH\(_2\) and NCH\(_2\)CH=CH\(_2\)), 5.93-6.01 (2H, m, CH\(_3\)CH=CH=CHCH\(_2\)), 7.20-7.33 (5H, m, Ar-H); \(\delta_C\) (75 MHz) 18.0 (CH\(_3\)), 38.7 (PhCHCH\(_2\)), 44.9 (PhCHCH\(_2\)), 48.9 (NCH\(_2\)CH\(_2\)N), 50.1 (NCH\(_2\)CH=CH\(_2\)), 52.3 (NCH\(_2\)CH\(_2\)N), 117.0 (NCH\(_2\)CH=CH\(_2\)), 126.9 (Ar-CH), 127.5 (CH), 128.0 and 128.6 (Ar-CH), 129.3, 131.6,
132.0, 133.9 (CH), 140.6 (Ar-C), 167.1 (N=C-N); m/z 280 (M⁺, 85%), 265 (32), 251 (26), 239 (58), 225 (28), 211 (17), 197 (39), 183 (13), 157 (36), 130 (20), 121 (17), 103 (21), 91 (18), 81 (80), 65 (19).

2-Benzyl-1-(hexa-2,4-dienyl)-2-imidazoline (2.3.22)

This compound was prepared by the general method, using n-Butyllithium (8.25 cm³ of a 2.5M solution in hexanes, 20.62 mmol), 2-benzyl-2-imidazoline (3.00 g, 18.75 mmol) and 1-bromohexa-2,4-diene (3.32 g, 20.62 mmol). The title compound was obtained as a yellow oil (2.45 g, 54%) (Found: (M-H)⁺ 239.1546. C₁₆H₂₀N₂ requires M-H 239.1548); νmax (film)/cm⁻¹ 3022, 2932, 2860, 1623, 1495, 1455, 1436, 1262, 1179, 991, 722; δH (300 MHz) 1.74 (3H, d, J 6.4, CH₃), 3.32 (2H, t, J 10.0, NCH₂CH₂N), 3.61-3.63 (3H, m, NCH₂CH=CHCH=CHCH₃ and PhCH₂), 3.69 (2H, t, J 10.0, NCH₂CH₂N), 5.18-5.35 (1H, m, NCH₂CH=CHCH=CHCH₃ and PhCH₂), 5.69 (2H, t, J 10.0, NCH₂CH₂N), 5.96-6.06 (2H, m, 2 x CH), 7.20-7.33 (5H, m, Ar-H); δC (75 MHz) 18.1 (CH₃), 34.7 (PhCH₂), 48.5 (NCH₂CH₂N), 50.0 (NCH₂CH=CH), 52.3 (NCH₂CH₂N), 125.7 (CH), 126.7, 128.5 and 128.6 (Ar-CH), 129.9, 130.5, 132.8 (CH), 136.1 (ArC), 165.3 (N=C-N); m/z 240 (M⁺, 19%), 225 (12), 211 (8), 197 (3), 185 (14), 171 (8), 159 (29), 131 (8), 117 (8), 91 (85), 81 (100), 65 (24).
n-Butyllithium (2.19 cm$^3$ of a 1.1M solution in hexanes, 2.41 mmol) was injected to a stirred solution of 2-benzyl-1-(hexa-2,4-dienyl)-2-imidazoline (0.57 g, 2.41 mmol) in dry THF (22 cm$^3$) at 20°C under nitrogen. The yellow suspension that was formed was stirred at 20°C for 50 min. The reaction mixture was cooled to 0°C and 3-bromoprop-1-ene (0.21 cm$^3$, 2.41 mmol) was injected to it. The reaction mixture was stirred at 0°C for 15 min and at 20°C overnight. The reaction was quenched with water (50 cm$^3$) and the organic layer was extracted with diethyl ether (3 x 50 cm$^3$). The combined organic extracts were washed successively with brine (50 cm$^3$) and water (50 cm$^3$), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100→3:97 v/v isoproplamine:ethyl acetate) to give the title compound as a yellow oil (0.30 g, 49%) (Found: (M-H)$^+$ 279.1860. C$_{19}$H$_{24}$N$_2$ requires M-H 279.1861); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 3022, 2932, 1640, 1455, 1437, 1251, 1207, 991, 702; $\delta_{\text{H}}$ (300 MHz) 1.72 (3H, d, $J$ 6.2, CH$_3$), 2.50-2.57 (1H, m, PhCHCHH), 2.82-2.89 (1H, m, PhCHCHH), 3.13-3.32 (2H, m, NCH$_2$CH$_2$N), 3.42-3.49 (2H, dd 6.4 and 13.5, NCH$_2$CH), 3.59-3.67 (1H, dd, $J$ 6.0 and 15.6, PhCHCH$_2$), 3.69-3.79 (2H, m, NCH$_2$CH$_2$N), 4.91-5.01 (2H, m, CH$_2$CH=CH$_2$), 5.02-5.14 (1H, m, CH), 5.58-5.79 (2H, m, 2 x CH), 5.91-5.96 (2H, m, 2 x CH), 7.21-7.33 (5H, m, Ar-H); $\delta_{\text{C}}$ (75 MHz) 18.0 (CH$_3$), 39.8 (PhCHCH$_2$), 48.1 (NCH$_2$CH$_2$N), 50.1 (NCH$_2$CH=CH), 52.3 (NCH$_2$CH$_2$N), 116.2 (CH=CH$_2$), 125.9 (CH), 126.9, 128.0 and 128.6 (Ar-CH), 129.7, 130.5, 132.7 and 136.6 (CH), 140.5 (Ar-C), 167.1 (N=C-N); $m/z$ 240 (M$^+$, 24%), 265 (13), 251 (13), 239 (9), 225 (13), 211 (16), 199 (84), 171 (11), 157 (30), 130 (20), 116 (24), 103 (12), 91 (31), 77 (39), 65 (15), 53 (50).
2-Benzyl-1-(2-furylmethyl)-2-imidazoline (23.26) and 2-[1-phenyl-2-(2-furyl)ethyl]-1-(2-furylmethyl)-2-imidazoline (23.27)

This compound was prepared by the general method, using 2-benzyl-2-imidazoline (5.00 g, 31.25 mmol), sec-butyllithium (26.43 cm$^3$ of a 1.3M solution in hexanes, 34.37 mmol) and furfuryl chloride (4.00 g, 34.37 mmol). The title compound was obtained as a yellow liquid (4.52 g, 60%) (Found: C, 73.87; H, 6.84; N, 11.54%; M$^+$ 240.1266. C$_{15}$H$_{16}$N$_2$O-0.2H$_2$O requires: C, 73.85; H, 6.72; N, 11.48%; $M$ 240.1263); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2935, 2865, 1617, 1496, 1456, 1432, 1265, 1147, 1010, 722; $\delta_\text{H}$ (300 MHz) 3.25 (2H, t, $J$ 9.5, NCH$_2$), 3.70 (2H, s, PhCH$_2$), 4.14 (2H, s, NCH$_2$Furyl), 5.82 (1H, d, J 2.0, Furyl-3H), 6.05 (1H, dd, J 2.0 and 3.3, Furyl-4H), 7.21-7.33 (1H, Furyl-5H and 5H, m, Ar-H); $\delta_C$ (75 MHz) 34.5 (PhCH$_2$), 43.2 (NCH$_2$Furyl), 49.7 (NCH$_2$), 52.3 (NCH$_2$), 107.8, 110.1 (Furyl-C), 126.6, 128.5 and 128.6 (Ar-CH), 135.9 (Ar-C), 142.1 (Furyl-CH), 150.6 (Furyl-C), 165.0 (N=C-N); $m/z$ 240 ($M^+$, 39%), 223 (2), 211 (28), 197 (6), 185 (4), 171 (3), 157 (18), 131 (6), 121 (7), 117 (7), 102 (5), 91 (83), 81 (100), 65 (21); and 2-[1-phenyl-2-(2-furyl)ethyl]-1-(2-furylmethyl)-2-imidazoline as a pale yellow oil (0.92 g, 9%) (Found: C, 74.82; H, 6.27; N, 8.85%; $M^+$ 320.1529. C$_{20}$H$_{20}$N$_2$O requires: C, 74.98; H, 6.28; N, 8.74%; $M$ 320.1525); $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2933, 2864, 1613, 1505, 1456, 1426, 1178, 1148, 1012, 736; $\delta_\text{H}$ (300 MHz) 3.05-3.13 (1H, dd, J 8.7 and 15.0, PhCHCHHFur), 3.18-3.29 (2H, m, NCH$_2$CH$_2$N), 3.47-3.54 (1H, dd, J 6.2 and 15.0 PhCHCHHFur), 3.67-3.81 (2H, m, NCH$_2$), 3.90 (1H, d, J 16.0, NCHHFuryl), 4.05 (1H, dd, J 6.2 and 8.7, PhCHCH$_2$Furyl), 4.24 (1H, d, J 16.1 NCHHFuryl), 5.80 (1H, d, J 3.1, Furyl-3H), 5.91 (1H, d, J 3.3 NCH$_2$Furyl-3H), 6.18 (1H, dd, J 2.0 and 3.1, CHCH$_2$Furyl-4H), 6.25 (1H, dd, J 2.0 and 3.3, NCH$_2$Furyl-4H), 7.21-7.33 (2H, m Furyl-5H and 5H, m, Ar-H); $\delta_C$ (75 MHz) 34.1
(PhCHCH₂), 43.0 (PhCHCH₂), 43.2 (NCH₂Furyl), 50.1 and 52.4 (NCH₂), 106.7, 107.6, 110.1 and 110.2 (Furyl-CH), 127.9, and 128.6 (Ar-CH), 140.8 (Ar-C), 140.8 and 142.2 (Furyl-CH), 150.8 and 153.6 (Furyl-C), 166.6 (N=C-N); \( m/z \) 320 (\( \text{M}^+ \), 29%), 291 (14), 122 (3), 263 (1), 239 (540, 211 (8), 195 (6), 171 (3), 158 (2), 141 (7), 128 (9), 115 (9), 103 (11), 91 (12), 81 (100).

2-Benzyl-1-(penta-2,4-dienyl)-2-imidazoline (2.3.32)

Prepared by the general method, from 2-benzyl-2-imidazoline (0.72 g, 4.51 mmol), \( n \)-butyllithium (1.98 cm\(^3\) of a 1.3M solution in hexanes 4.96 mmol) and 1-bromopenta-2,4-diene (0.73 g, 4.96 mmol). The title compound was obtained as a yellow oil (0.58 g, 57%) \( \nu_{\text{max}} \) (film)/cm\(^{-1}\) 3023, 2930, 1624, 1495, 1456, 1264, 1175, 722; \( \delta_H \) (300 MHz) 3.29 (2H, t, 9.9, NCH₂), 3.61-3.64 (4H, m, NCH₂CH=CH and PhCH₂), 3.74 (2H, t, \( J \) 9.9, NCH₂CH₂N), 5.05-5.23 (2H, m, CH=CH₂), 5.37-5.47 (1H, m, CH), 5.97-6.12 (1H, m, CH), 6.18-6.32 (1H, m, CH), 7.20-7.35 (5H, m, Ar-H); \( \delta_C \) (100 MHz) 34.7 (PhCH₂), 48.4 and 52.3 (NCH₂CH₂N), 50.1 (NCH₂CH=CH), 117.5 (CH=CH₂), 126.7, 128.5 and 128.6 (Ar-CH), 129.2, 133.1 and 135.9 (CH), 136.0 (Ar-C), 165.2 (N=C-N); \( m/z \) 226 (\( \text{M}^+ \), 28%), 211 (18), 197 (7), 184 (16), 171 (9), 159 (36), 148 (7), 135 (13), 121 (7), 108 (12), 96 (43), 91 (91).
sec-Butyllithium (1.72 cm³ of a 1.0M solution in cyclohexane, 1.72 mmol) was added dropwise to a solution of 2-(phenylselenenobut-3-enyl)-2-imidazoline (0.48 g, 1.72 mmol) in dry THF (17 cm³) at 20°C under nitrogen. The resulting yellow solution was stirred for 45 min. 3-Bromoprop-1-ene (0.15 cm³, 1.72 mmol) was injected and the reaction mixture was stirred overnight at 20°C. Water (20 cm³) was added and the organic layer was extracted with diethyl ether (3 x 50 cm³). The combined organic extracts were washed successively with water (50 cm³) and brine (50 cm³), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100–2:98 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (0.13 g, 23%) and 0.24 g, of starting material, 47% yield based on recovered starting material, (Found: M⁺ 320.0792. C₁₆H₂₀N₂Se requires: M 320.0792); νmax (film)/cm⁻¹ 2931, 2860, 1641, 1603, 1477, 1437, 1416, 1248, 1205, 1001, 918, 740; δH (400 MHz) 2.62-2.70 (1H, m, PhSeCHCH₂), 2.87-2.97 (1H, m PhSeCHCH₂), 3.23-3.35 (2H, m, NCH₂CH₂N), 3.55-3.64 (1H, m, PhSeCH), 3.67-3.74 (2H, m, NCH₂CH₂N), 3.77-3.88 (2H, m, NCH₂CH=CH₂), 5.06-5.24 (4H, m, 2 x CH=CH₂), 5.70-5.82 (1H, m, CH₂CH=CH₂), 5.83-5.90 (1H, m, NCH₂CH=CH₂), 7.28-7.33 (3H, m, Ar-H), 7.62 (2H, m, Ar-H); δC (100 MHz) 37.4 (PhSeCH), 38.0 (PhSeCHCH₂), 49.3 (NCH₂CH₂N), 50.1 (NCH₂CH=CH₂), 51.9 (NCH₂CH₂N), 117.1 (CH=CH₂), 117.2 (CH=CH₂), 128.5, 128.7 and 128.9 (Ar-CH), 131.5 (Ar-C), 133.9 (CH=CH₂), 136.2 (CH=CH₂), 165.6 (N=C=N); m/z 320 (M⁺, 11%), 279 (2), 239 (57), 225 (3), 211 (3), 197 (12), 163 (100), 149 (13), 135 (6), 121 (36), 107 (5), 93 (8), 82 (9), 77 (17).
2-Phenylselenenomethyl-2-imidazoline (2.3.36)

\[
\begin{align*}
\text{PhSe} & \quad \text{Boc} \\
\text{N} & \quad \text{N} \\
\text{PhSe} & 
\end{align*}
\]

Trifluoroacetic acid (3 cm³) was added to 1-tert-butyloxycarbonyl-2-phenylselenenomethyl-2-imidazoline (2.10 g, 6.19 mmol) and the resulting solution was stirred at 20°C for 30 min. The trifluoroacetic acid was removed under reduced pressure and the imidazoline salt was dissolved in dichloromethane (20 cm³). The solution was then washed with aq. NaOH (10% w/v; 50 cm³) and the organic layer was dried and concentrated. The crude product was then purified by column chromatography on silica gel (1:99→4:96 v/v isopropylamine:ethyl acetate) to give the title compound as a white solid (1.15 g, 77%), m.p. 42-44°C (Found: M⁺ 240.0154. C₁₀H₁₂N₂Se requires: M 240.0166); ν max (KBr)/cm⁻¹ 3177, 2932, 2868, 1601, 1577, 1496, 1477, 1438, 1292, 1267, 740; δ H (400 MHz) 3.55 (4H, s, NCH₂CH₂N), 3.64 (2H, s, PhSeCH₂), 4.20 (1H, br s, NH), 7.26-7.29 (3H, m, Ar-H), 7.52-7.54 (2H, m, Ar-H), δ C (100 MHz) 24.2 (PhSeCH₂), 50.8 (NCH₂CH₂N), 127.9, 129.4, 132.9 and 134.7 (Ar-C), 165.3 (N=C-N); m/z 240 (M⁺, 25%), 239 (34), 179 (100), 132 (8), 117 (11), 104 (5), 91 (18), 81 (13), 77 (30), 54 (41).

2-(1-Phenylseleneno)but-3-enyl)-1-(prop-2-enyl)-2-imidazoline (2.3.35)

\[
\begin{align*}
\text{PhSe} & \quad \text{N} & \quad \text{N} \\
\text{SePh} & \quad \text{N} \\
\text{PhSe} & 
\end{align*}
\]

n-Butyllithium (3.23 cm³ of a 2.5 M solution in hexanes, 8.08 mmol) was injected to a solution of 2-phenylselenenomethyl-2-imidazoline (0.92 g, 3.85 mmol) in dry THF (38 cm³) at -78°C under nitrogen. The yellow suspension produced was stirred at -78°C for 20
min. 3-Bromopropene (0.70 cm$^3$, 8.08 mmol) was injected rapidly to the reaction mixture and was stirred overnight (-78°C to 20°C). Water (50 cm$^3$) was added to it and the organic layer was extracted with diethyl ether (3 x 50 cm$^3$). The combined organic extracts were washed successively with water (50 cm$^3$) and brine (50 cm$^3$), dried and concentrated. The crude product was purified by column chromatography on silica gel (0:100—3:98 v/v isopropylamine:ethyl acetate) to give the title compound as a yellow oil (0.61 g, 50%). Data identical to those reported earlier.

2-(Buta-1,3-dienyl)-1-(propen-2-enyl)-2-imidazoline (2.3.34b)

A solution of m-chloroperbenzoic acid (0.24 g, 1.36 mmol) (58%) in dry dichloromethane (5 cm$^3$) was added via a cannula to a solution of 2-(1-phenylselenobut-3-enyl)-1-(propen-2-enyl)-2-imidazoline (0.20 g, 0.62 mmol) in dry dichloromethane (15 cm$^3$), at 0°C under nitrogen. The reaction mixture was stirred at 0°C for 1 h and at 20°C for a further 1 h. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (0:100→3:97 isopropylamine:ethyl acetate) to give the title compound as a yellow oil (0.10 g, 100%) (Found: C, 71.35; H, 8.45; N, 17.12%, (M-H)$^+$ 161.1079. C$_{10}$H$_{14}$N$_2$ requires: C, 71.63; H, 8.71; N, 16.71%; $M-H$ 161.1076), $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2933, 2859, 1645, 1603, 1582, 1429, 1402, 1285, 1266, 1221, 1009, 918; $\delta_{\text{H}}$ (400 MHz) 3.35 (2H, t, $J$ 10.0 NCH$_2$), 3.75-3.80 (4H, m, NCH$_2$ and NCH$_2$CH=CH$_2$), 5.17-5.23 (2H, m, NCH$_2$CH=CH$_2$), 5.30-5.5.34 (1H, m, CHCH=CHH), 5.46 (1H, d, $J$ 17.1, CH-CH=CHH), 5.74-5.82 (1H, m, NCH$_2$CH=CH$_2$), 6.03 (1H, d, $J$ 15.6, CH=CH-CH=CH$_2$).
6.38-6.47 (1H, m, CH-CH=CH₂), 7.11-7.18 (1H, dd J 10.7 and 15.6, CH=CH-CH=CH₂); δ c (100 MHz) 50.0 (NCH₂CH₂N), 50.7 (NCH₂CH=CH₂), 52.4 (NCH₂CH₂N), 117.1 (NCH₂CH=CH₂), 118.9 (CH-CH=CH₂), 122.3, 133.8, 135.8 and 139.0 (CH), 163.3 (N=C-N); m/z 162 (M⁺, 58%), 159 (6), 147 (7), 135 (6), 121 (24), 107 (7), 93 (68), 80 (10), 66 (26), 54 (17).

Methyl (E)-3-(2-benzylimidazolin-1-yl)pent-2-enoate (2.4.1a)

Prepared by the general method from 2-benzyl-2-imidazoline (0.30 g, 1.88 mmol) and ethyl 2-pentynoate (0.30 cm³, 2.25 mmol) to give the title compound as a yellow oil (0.08 g, 15%). (Found: C, 68.27; H, 7.59; N, 10.10%; MH⁺ 273.1605. C₁₆H₂₀N₂O₂·0.5H₂O requires: C, 68.32; H, 7.47, N, 9.96%; MH 273.1603); νmax (film)/cm⁻¹ 2973, 2947, 2874, 1708 (CO), 1620 (C=N), 1456, 14166, 1384, 1268, 1224, 1169, 1006, 714; δH (300 MHz) 0.72 (3H, t, J 7.4, CH₃CH₂), 2.03 (2H, q, J 7.4, CH₃CH₂), 3.55 (2H, s, PhCH₂), 3.63 (2H, t, J 9.6, NCH₂CH₂N), 3.73 (3H, s, CO₂CH₃), 3.83 (2H, t, J 9.6, NCH₂CH₂N), 5.45 (1H, s, NCEt=CHCO₂Me), 7.15-7.34 (5H, m, Ar-H); δC (75 MHz) 11.1 (CH₃CH₂), 29.1 (CH₃CH₂), 34.8 (PhCH₂), 51.2 (CO₂CH₃), 50.2 and 53.0 (NCH₂), 106.2 (NCEt=CHCO₂Me), 126.7, 128.3 and 129.1 (Ar-CH), 136.4 (Ar-C), 156.7 (NC(Et)=CHCO₂Me), 163.4 (N=C-N), 166.1 (CO₂Me); m/z 272 (M⁺, 13%), 257 (4), 241 (3), 213 (38), 199 (9), 184 (1), 156 (12), 140 (2), 130 (7), 124 (39), 116 (25), 96 (43), 91 (100), 68 (25).
Methyl (E)-3-(2-benzylimidazolin-1yl)-3-phenylpropenoate (2.4.1b)

\[
\begin{align*}
\text{Prepared by the general method from 2-benzyl-2-imidazoline (0.46 g, 2.87 mmol) and ethyl phenyl propynoate (0.71 cm}^3, 4.31 mmol) to give the title compound as a yellow oil (0.48 g, 52\%) \text{ (Found: } C, 74.13; H, 6.39; N, 8.57%; M^+ 320.1525. C_{20}H_{20}N_{2}O_{2} \cdot 0.2H_2O \text{ requires: } C, 74.13; H, 6.30, N, 8.64%; M 320.1525); \nu_{max} \text{ (film)/cm}^{-1} 2948, 2872, 1708 \text{ (CO), 1600, } 1574, 1406, 1276, 1153, 1007, 777; \delta_{H} (300 \text{ MHz}) 3.40 (2H, s, PhCH$_2$), 3.62 (2H, t, J 9.6, NCH$_2$CH$_2$N), 3.79 (3H, s, CO$_2$CH$_3$), 3.93 (2H, t, J 9.6, NCH$_2$CH$_2$N), 5.75 (1H, s, NC$_2$Ph=CHC$_2$O), 7.12-7.43 (10H, m, Ar-H); \delta_{C} (100 \text{ MHz}) 35.2 (PhCH$_2$), 51.2 (CO$_2$CH$_3$), 52.1 (NCH$_2$CH$_2$N), 53.6 (NCH$_2$CH$_2$N), 106.5 (NC$_2$Ph=CHCO$_2$Me), 126.6, 128.1 128.3, 128.6, 129.4 and 130.6 (Ar-CH), 136.0 and 1369 (Ar-C), 152.8 (NC$_2$Ph=CHCO$_2$Me), 163.4 (N=C-N), 165.4 (CO$_2$Me); m/z 320 (M$^+$, 20\%), 305 (2), 289 (6), 261 (65), 247 (18), 229 (2), 204 (25), 191 (2), 174 (14), 158 (12), 144 (57), 57, 130 (34), 115 (27), 103 (42), 91 (100), 77 (41), 65 (24)).
\end{align*}
\]
General method for the synthesis of diethyl 2-(alkylimidazolin-1-yl)-1,4-butenedionate

\[
\begin{align*}
\text{Diethyl acetylene dicarboxylate} (1.2 \text{ mol equiv.}) & \text{ was injected to a solution of 2-alkyl-2-imidazoline (1 equiv.) in dry dichloromethane (1M in imidazoline) at 0°C. The reaction was allowed to warm up to 20°C and was stirred for 8 h. The dichloromethane was removed and the crude product was chromatographed on silica gel eluting with 3:7 v/v ethyl acetate:hexane to give the title compound.}
\end{align*}
\]

Diethyl (E)-2-(2-benzylimidazolin-1-yl)-1,4-butenedionate (2.4.8)

\[
\begin{align*}
\text{Prepared by the general method from 2-benzyl-2-imidazoline (2.00 g, 12.5 mmol) and ethyl acetylene dicarboxylate (2.40 cm}^3, 15.00 \text{ mmol) to give compound (2.4.9) (see later) and the title compound as an orange gum, (1.42 g, 34%) } & \text{ as a film/cm}^{-1} \text{ 2982, 1739 (CO}_2\text{Et), 1704 (CO}_2\text{Et), 1577, 1416, 1366, 1161, 1021, 756; } \delta_H (300 \text{ MHz}) 1.23-1.33 (6H, m, 2 x CH}_3\text{CH}_2, 3.64 (2H, t, 9.6, NCH}_2\text{CH}_2\text{N), 3.69 (2H, s, PhCH}_2, 3.84 (2H, t, J 9.6, NCH}_2\text{CH}_2\text{N), 4.14 (2H, q, J 7.2, CH}_3\text{CH}_2, 4.30 (2H, q, J 7.2, CH}_3\text{CH}_2), 5.05 (1H, s, CHCO}_2\text{Et), 7.18-77.34 (5H, m, Ar-H); } \delta_C (75 \text{ MHz}) 13.5 \text{ and 14.2 (CH}_3\text{CH}_2, 34.7 (PhCH}_2, 50.1 \text{ and 52.0 (NCH}_2, 62.0 \text{ and 62.7 (CH}_3\text{CH}_2, 96.9 [NCCO}_2\text{Et=}CHCO}_2\text{Et], 126.9, 128.4 \text{ and 129.1 (Ar-CH), 134.9 (Ar-C), 144.2 [NC(CO}_2\text{Et=}CHCO}_2\text{Et], 158.8 (N=-C-N), 164.4 and 166.2 (CO}_2\text{Et}; m/z 331 (MH}^+, 2\%), 303 (1), 289 (2), 257 (23), 238 (16), 229 (7), 213 (47), 200 (10), 183 (7), 162 (9), 140 (32), 126 (28), 91 (100).}
\end{align*}
\]
Diethyl (E) and (Z) 2-[2-(2-phenyl)phenylethylimidazolin-1-yl]-1,4-butenoate (2.4.13) and (2.4.14)

Prepared by the general method, from 2-[2-(2-phenyl)phenylethyl]-2-imidazoline (0.47 g, 1.88 mmol) and ethyl acetylene dicarboxylate (0.36 cm³, 2.22 mmol) to give the E-isomer of the title compound as a yellow gum, which was recrystallised from hexane/ethyl acetate, as a white crystalline solid (0.43 g, 54%), m.p. 85-87°C (Found: C, 71.20; H, 6.70; N, 6.64%; (M-H)⁺ 419.1974. C₂₅H₂₈N₂O₄ requires: C, 71.41; H, 6.71; N, 6.64%; M-H 419.1971); ν_max (film)/cm⁻¹ 2981, 1741 and 1703 (CO₂Et), 1641, 1575, 1479, 1197, 1156, 1046, 752; δ_H (300 MHz) 1.19 (3H, t, J 7.2, CH₃CH₂), 1.26 (3H, t, J 7.2, CH₃CH₂), 2.41 (2H, t, J 8.0, CH₂CH₂Ar), 3.00 (2H, t, J 8.0, CH₂CH₂Ar), 3.56 (2H, t, J 9.0, NCH₂), 3.79 (2H, t, J 9.0, NCH₂), 4.12 (2H, q, J 7.2, CH₃CH₂), 4.20 (2H, q, J 7.2, CH₃CH₂), 4.91 (1H, s, CHC₀₂Et), 7.18-7.43 (9H, m, Ar-H); δ_C (75 MHz) 13.4 and 14.2 (CH₃CH₂), 29.4 (ArCH₂CH₂), 30.1 (ArCH₂CH₂), 49.8 and 51.9 (NCH₂), 60.0 and 62.6 (CH₃CH₂), 96.0 [NC(CO₂Et)=CHCO₂Et], 126.3, 127.0, 127.6, 128.3, 129.1, 130.3, 138.3 (Ar-CH), 141.4 and 141.9 (Ar-C), 144.4 [NC(CO₂Et)=CHCO₂Me], 159.1 (N-C=N), 164.4 and 166.4 (CO₂Et); m/z 421 [(MH)⁺, 2%], 375 (3), 347 (100), 319 (21), 273 (9), 213 (6), 191 (5), 178 (15), 165 (72), 152 (33), 139 (7), 126 (6), 94 (7), 68 (15); and the Z-isomer of the title compound as a thick yellow oil (0.12 g, 15%) (Found: M⁺ 420.2052. C₂₅H₂₈N₂O₄ requires: M 420.2049); ν_max (film) 2981, 2939, 1729, 1610, 1480, 1368, 1259, 1172, 1033, 753; δ_H (300 MHz) 1.24-2.31 (6H, m 2 x CH₃), 2.12 (2H, t, J 8.3, CH₂CH₂Ar), 2.88 (2H, t, J 8.3, CH₂CH₂Ar), 3.62 (2H, t, J 9.9, NCH₂), 3.81 (2H, t, J 9.9, NCH₂), 4.14 (2H, q, J 7.2,
CH$_3$CH$_2$, 4.20 (2H, q, $J$ 7.2, CH$_3$CH$_2$), 6.30 (CH), 7.14-7.40 (9H, m, Ar-H); $\delta_C$ 14.1 and 14.2 (CH$_3$), 29.8 and 30.6 (CH$_2$CH$_2$Ar), 51.5 and 53.7 (NCH$_2$), 60.9 and 62.3 (CH$_3$CH$_2$), 118.5 (CH), 126.1, 126.9, 127.6, 128.2, 129.0, 129.4, 130.2, (Ar-CH), 138.4, 141.5 and 141.8 (Ar-C), 140.0 (NC=CH), 163.4 (N-C=N), 163.9 and 164.0 (CO); m/z 420 (M$^+$, 2%), 391 (1), 375 (2), 364 (1), 34 (100), 319 (20), 275 (6), 249 (5), 238 (2), 178 (7), 165 (29), 152 (12), 128 (3), 115 (2), 91 (5).

Diethyl (E)-2-[2-(but-3-enyl)imidazol-1-yl]-1,4-butenedionate (2.4.16)

Prepared by the general method from 2-(but-3-enyl)-2-imidazoline (0.83 g, 6.69 mmol) and ethyl acetylene dicarboxylate (1.28 cm$^3$, 8.03 mmol) to give the title compound as a yellow oil (0.34 g, 17%) (Found: C, 60.24; H, 7.46; N, 9.03%; M$^+$ 294.1574. C$_{15}$H$_{22}$N$_2$O$_4$·0.3H$_2$O requires: C, 60.08; H, 7.54, N, 9.35%; M 294.1579); $\nu_{max}$ (film)/cm$^{-1}$ 2983, 1737 (CO$_2$Et), 1694 (CO$_2$Et), 1639 (C=N), 1577, 1421, 1372, 1337, 1160, 1096, 1027, 915, 800; $\delta_H$ (300 MHz) 1.27 (3H, t, $J$ 7.2, CH$_3$CH$_2$), 1.38 (3H, t, $J$ 7.3, CH$_3$CH$_2$), 2.42 (4H, m, CH$_2$CH$_2$CH=CH$_2$), 3.62 (2H, t, $J$ 8.9, NCH$_2$CH$_2$N), 3.86 (2H, t, $J$ 8.9, NCH$_2$CH$_2$N), 4.12 (2H, q, $J$ 7.2, CH$_3$CH$_2$), 4.35 (2H, q, $J$ 7.3, CH$_3$CH$_2$), 5.02 (1H, s, CHCO$_2$Et), 5.02-5.15 (2H, m, CH=CH$_2$), 5.78-5.88 (1H, m, CH=CH$_2$); $\delta_C$ (75 MHz) 13.7 and 14.3 (CH$_3$CH$_2$), 25.4 (CH$_2$CH$_2$CH=CH$_2$), 30.1 (CH$_2$CH$_2$CH=CH$_2$), 50.0 and 51.9 (NCH$_2$), 60.1 and 62.8 (CH$_3$CH$_2$), 96.2 [NC(CO$_2$Et)=CHCO$_2$Et], 115.5 (CH=CH$_2$), 136.9 (CH=CH$_2$), 144.5 [NC(CO$_2$Et)=CHCO$_2$Et], 159.3 (N-C=N), 164.5 and 166.4 (CO$_2$Et); m/z 294 (M$^+$, 7%), 265 (3), 249 (9), 221 (100), 193 (45), 175 (8), 147 (18), 126 (24), 98 (18), 82 (14).
General method for the synthesis of 5-ethoxycarbonylmethylene-1,2,3,6-tetrahydro-5\(H\)-pyrrolo[1,2-\(a\)]imidazol-6-one

Diethyl acetylene dicarboxylate (1.2 mol equiv.) was injected to a solution of 2-alkyl-2-imidazoline (1 equiv.) in dry dichloromethane (1M solution) at 0\(^\circ\)C. The reaction was allowed to warm up to 20\(^\circ\)C and was stirred for 8 h. The dichloromethane was removed and the crude product was chromatographed on silica gel (3:7-10:0 v/v ethyl acetate:hexane to give the title compound.

\[(Z)-5\text{-Ethoxycarbonylmethylene-7-phenyl-1,2,3,6-tetrahydro-5\(H\)-pyrrolo[1,2-\(a\)]imidazol-6-one \(2.4.9\)}\]

Prepared by the general method from 2-benzyl-2-imidazoline (2.00 g, 12.5 mmol) and ethyl acetylenedicarboxylate (2.40 cm\(^3\), 15.00 mmol) to give the \(Z\)-isomer of the title compound as an orange solid that precipitated out of solution and was recrystallised from methanol (1.50 g, 42%), m.p. 230-232\(^\circ\)C (Found: C, 67.55; H, 5.64; N, 9.84%; \(M^+\) 284.1155. \(C_{16}H_{16}N_2O_3\) requires: C, 67.59; H, 5.67, N, 9.85%; \(M\) 284.1161); \(\nu\) max (KBr)/cm\(^{-1}\) 3291 (NH), 2984, 1712 (CO\(_2\)Et), 1655,1603, 1559, 1515, 1482, 1447, 1307, 1189, 1154, 1105, 701; \(\delta\)\(_\text{H}\) [300 MHz; (CD\(_3\))SO] 1.21 (3H, t, \(J\) 7.2, CH\(_3\)CH\(_2\)), 4.00 (2H, t, \(J\) 7.5, NCH\(_2\)CH\(_2\)N), 4.10-4.17 (4H, m, CH\(_3\)CH\(_2\) and NCH\(_2\)CH\(_2\)N), 5.48 (1H, s, CHCO\(_2\)Et), 7.05 (1H, t, \(J\) 7.5, Ar-H), 7.28 (2H, t, \(J\) 7.5, Ar-H), 7.69 (2H, d, \(J\) 7.5, Ar-H); \(\delta\)\(_C\) [75 MHz; (CD\(_3\))SO] 14.1
(CH₃CH₂), 44.8 and 48.0 (NCH₂), 59.8 (CH₃CH₂), 88.4 (PhC=CN), 90.9 (CHCO₂Et),
123.7, 124.2 and 128.1 (Ar-CH), 132.5 (Ar-C), 144.0 (NC=CHCO₂Et), 165.4 (NC=CPh),
168.8 (CO₂Et), 180.8 (CO); m/z 284 (M⁺, 47%), 238 (42), 211 (28), 183 (32), 168 (9), 154
(27), 143 (27), 128 (48), 115 (88), 103 (31), 89 (100), 77 (48), 63 (35).

(Z) and (E)-5-Ethoxycarbonylmethylene-7-phenyl-1,2,3,6-tetrahydro-5H-pyrrolo[1,2-
a]imidazol-6-one (2.4.9) and (2.4.10)

A solution of diethyl 1-[(1-carboxylate)prop-1-enolate]-2-(phenylmethyl)-2-imidazoline
(1.20 g, 3.63 mmol) in THF (30 cm³) was added to a solution of potassium tert butoxide
(0.81 g, 7.27 mmol). The orange solution produced was stirred at 20 C for 12 h and the
solvent was removed. The crude product was purified by column chromatography on silica
gel (0:3:7→5:95:0 methanol:ethyl acetate:hexane) to give the Z-and E-isomers of the title
compound in a 5:1 ratio as an orange and yellow solids (0.69 g, 67%); Data for E-isomer
(less polar material) yellow solid, m.p. 172-174 C (Found: M⁺ 284.1161. C₁₆H₁₆N₂O₃
requires: M 284.1161); νmax (KBr) 3436 (NH), 1636, 1610, 1543, 1495, 1233, 1216, 1186,
780; δH (300 MHz) 1.36 (3H, t, J7.2, CH₃), 3.49 (2H, t, J7.2, NCH₂), 4.25 (2H, q, J7.2,
CH₃CH₂), 4.43 (2H, t, J7.2, NCH₂), 5.06, (1H, s, CH), 7.26 (1H, t, J7.8, Ar-H), 7.39 (2H,
t, J 7.8, Ar-H), 8.22 (2H, d, J 7.8, Ar-H), 13.82 (1H, br s, NH); δC (100 MHz) 14.2 (CH₃),
41.1 and 41.5 (NCH₂CH₂N), 61.1 (NC=CPh), 61.7 (CH₃CH₂), 88.4, (NC=CH), 127.1,
127.4, 128.3, (Ar-CH), 130.8 (Ar-C), 148.7 (NC=CH), 159.3 (NC=CPh), 164.2 (CO₂Et),
172.7 (CO); m/z 284 (M⁺, 17%), 238 (100), 209 (15), 181 (10), 167 (1), 153 (5), 143 (6),
128 (6), 115 (17), 103 (4), 89 (7), 77 (4); data for Z isomer as reported earlier.
(Z) and (E)-5-Methoxycarbonylmethylene-7-phenyl-1,2,3,6-tetrahydro-5H-pyrrolo[1,2-a] imidazol-6-one (2.4.11) and (2.4.12)

Prepared by the general method from 2-benzyl-2-imidazoline (3.05 g, 19.06 mmol) and dimethyl acetylene dicarboxylate (2.81 cm³, 22.87 mmol) to give the the Z-isomer of the title compound as an orange precipitate that was recrystallised from methanol, (1.24 g, 24%), m.p 236-238°C (Found: C, 66.17; H, 5.14; N, 10.25%; M⁺ 270.1002. C₁₅H₁₄N₂O₃ requires: C, 66.66; H, 5.22; N, 10.36%; M 270.1004); νmax (KBr)/cm⁻¹ 3255, (NH), 1717, (CO₂Me), 1674, 1604, 1562 (CO), 1514, 1309, 1189, 1169, 1154, 1105; δH [300 MHz; (CD₃)SO] 3.66 (3H, s, CH₃), 4.00 (2H, t, J 7.2, NCH₂CH₂N), 4.13 (2H, t, J 7.2, NCH₂CH₂N), 5.49 (1H, s, C=CO₂Me), 7.05 (1H, t, J 7.5, Ar-H), 7.28 (2H, t, J 7.5, Ar-H), 7.67 (2H, d, J 7.5, Ar-H), 9.58 (1H, br s, NH); δC [75 MHz; (CD₃)SO] 44.8 and 47.9 (NCH₂), 51.2 (CH₃), 88.4 (PhC=CN), 90.6 (CHCO₂Me), 123.7, 124.2 and 128.1 (Ar-CH), 132.4 (Ar-C), 144.1 (NC=CHCO₂Me), 165.8 (NC=CPh), 168.2 (CO₂Me), 180.8 (CO); m/z 270 (M⁺, 86%), 238 (100), 209 (29), 181 (26), 168 (4), 153 (14), 143 (14), 129 (10), 115 (34), 103 (12), 89 (38), 77 (19) and the E isomer of the title compound was recrystallised out of the reaction mixture from methanol/hexane as an orange solid (1.70 g, 33%), m.p. 161-163°C (Found: M⁺ 270.1020. C₁₅H₁₄N₂O₃ requires: M 270.1004); νmax (KBr) 3251 (NH), 1716, 1614, 1550, 1511, 1494, 1443, 1421, 1233, 1218, 1183, 797, 776; δH (300 MHz) 3.38 (2H, t, J 7.2, NCH₂), 3.78 (3H, s, CH₃), 4.36 (2H, t, J 7.2, NCH₂), 4.98, (1H, s, CH), 7.26 (1H, t, J 7.6, Ar-H), 7.39 (2H, t, J 7.6, Ar-H), 8.22 (2H, d, J 7.6, Ar-H), 13.72 (1H, br s, NH); δC (100 MHz) 41.3 (NCH₂CH₂N), 51.9 (CH₃), 61.2 (NC=CPh), 87.8, (NC=CH), 127.1, 127.4 and 128.3 (Ar-CH), 130.8 (Ar-C), 148.6 (NC=CH), 159.3
A solution of diethyl 1-[(1-carboxylate)prop-1-enolate]-2-(2-phenylphenylmethyl)-2-imidazoline (68 mg, 0.16 mmol) in THF (3 cm$^3$) was added to a solution of potassium tert-butoxide (35 mg, 0.31 mmol) in THF (3 cm$^3$). The resulting yellow solution was stirred at 20°C for 12 h, the solvent was removed under reduced pressure and the residue was chromatographed on silica gel (0:3:7→5:95:0 methanol:ethyl acetate:hexane) to give the title compound as a yellow oil (32 mg, 54%), (Found: M$^+$ 374.1627. C$_{23}$H$_{22}$N$_2$O$_3$ requires: M 374.1630); $\nu_{\max }$ (film)/cm$^{-1}$ 3404 (NH), 1712 (CO$_2$Et), 1659 (CO), 1568, 1480, 1369, 1163; $\delta_H$ (300 MHz) 1.27 (3H, t, $J$ 7.1, CH$_3$CH$^2$), 3.55 (2H, s, CH$_2$Ar), 3.63 (2H, t, $J$ 7.4, NCH$_2$), 4.09 (2H, t, $J$ 7.4, NCH$_2$), 4.14 (2H, q, $J$ 7.1, CH$_3$CH$_2$), 5.77 (1H, s, CH), 7.20-7.47 (9H, m, Ar-H); $\delta_C$ (75 MHz) 14.2 (CH$_3$CH$_2$), 25.0 (ArCH$_2$), 45.3 and 47.3 (NCH$_2$), 60.2 (CH$_3$CH$_2$), 88.1 (PhC=CN), 93.9 [NC(CO$_2$Et)=CHCO$_2$Et], 126.4, 127.1, 127.9, 128.3, 129.5, 130.3, 137.6 (Ar-CH), 141.2 and 141.8 (Ar-C), 143.6 [NC(CO$_2$Et)=CHCO$_2$Et], 166.5 (NC=CPh), 169.4 (CO$_2$Et), 184.4 (CO); $m/z$ 374 (M$^+$, 17%), 345 (3), 328 (2), 317 (2), 299 (9), 271 (22), 247 (2), 221 (2), 203 (11), 189 (8), 178 (16), 165 (100), 152 (66), 128 (9), 115 (13), 94 (8), 7 (42).
(Z)-5-Ethoxycarbonylmethylene-7-(prop-2-enyl)-1,2,3,6-tetrahydro-5H-pyrrolo[1,2-a]imidazol-6-one (2.4.17)

Prepared by the general method from 2-(but-3-enyl)-2-imidazoline (0.83 g, 6.69 mmol) and ethyl acetylene dicarboxylate (1.28 cm³, 8.03 mmol) to give the title compound as a yellow solid (0.10 g, 6%), m.p 162-164°C (Found: C, 60.36; H, 6.40; N, 10.30%; MH⁺ 249.1239. C₁₃H₁₆N₂O₃·0.5H₂O requires: C, 60.70; H, 6.61, N, 10.89%; MH 249.1235); νmax (KBr/cm⁻¹) 3391 (NH), 3317, 2981, 1714 (CO₂Et), 1658 (CO), 1554, 1494, 1321, 1150; δH (300 MHz) 1.29 (3H, t, J 7.1, CH₂CH₂), 2.97 (2H, d, J 6.4, CH₂CH=CH₂), 3.94 (2H, t, J 7.4, NCH₂CH₂N), 4.14-4.26 (4H, m, CH₃CH₂ and NCH₂CH₂N), 5.01-5.13 (2H, m, CH=CH₂), 5.78-5.88 (1H, m, CH=CH₂), 5.83 (1H, s, CHCO₂Et); δC (75 MHz) 14.3 (CH₃CH₂), 25.4 (CH₂CH=CH₂), 45.4 and 47.6 (NCH₂), 60.2 (CH₃CH₂), 85.9 (PhC=CN), 93.9 [NC(CO₂Et)=CHCO₂Et], 115.1 (CH=CH₂), 136.6 (CH=CH₂), 144.1 (NC(CO₂Et)=CHCO₂Et), 166.5 (NC=CPh), 168.8 (CO₂Et), 181.3 (CO); m/z 248 (M⁺, 15%), 219 (4), 202 (10), 191 (13), 173 (15), 161 (14), 147 (17), 135 (5), 121 (8), 105 (12), 84 (62).
5-Ethoxycarbonylmethyl-7-phenyl-1,2,3,6-pentahydro-5H-pyrrolo[1,2-a]imidazol-6-one (2.4.21)

A solution of 5-ethoxycarbonylmethylene-7-phenyl-1,2,3,6-tetrahydro-5H-pyrrolo[1,2-a]imidazol-6-one (0.80 g, 2.81 mmol) in methanol (28 cm³) containing 10% Pd/C (0.03 g, 0.28 mmol) was stirred under an atmosphere of hydrogen for 24 h. The catalyst was filtered and the residue was recrystallised from hexane/methanol to give the title compound as white crystals (0.56 g, 69%), m.p. 119-121°C (Found: C, 67.00; H, 6.29; N, 9.70%; M⁺ 286.1317. C₁₆H₁₈N₂O₃ requires: C, 67.12; H, 6.34, N, 9.78%; M 286.1317); vₘₐₓ (KBr)/cm⁻¹ 3282 (NH), 1724 (CO₂Et), 1607, 1548, 1516, 1305, 1160, 1189; δH (300 MHz) 1.27 (3H, t, J 7.1, CH₃CH₂), 2.33-2.43 (1H, dd, J 10.6 and 17.2, CHHC0₂Et), 3.02-3.08 (1H, dd, J 2.6 and 17.2, CHCH₂CO₂Et), 3.13-3.22 (1H, dd, J 8.2 and 17.2, CHCHHCO₂Et), 3.59-3.70 (1H, m, NCHH), 3.74-3.93 (3H, m, NCHH, and NCH₂), 4.21 (2H, q, J 7.2, CH₃CH₂), 6.54 (1H, br s, NH), 7.01 (1H, t, J 7.3, Ar-H), 7.22 (2H, t, J 7.3, Ar-H), 7.55 (2H, d, J 7.3, Ar-H); δC (75 MHz) 14.2 (CH₃CH₂), 36.4 (NCHCH₂), 46.5 and 47.2 (NCH₂), 60.8 (CH₃CH₂), 62.5 (NCH), 92.2 (PhC=CN), 12.2, 124.9 and 128.5 (Ar-CH), 132.9 (Ar-C), 172.2 (NC=CPh), 174.6 (CO₂Et), 193.0 (CO); m/z 286 (M⁺, 73%), 257 (3), 241 (8), 213 (100), 199 (13), 185 (36), 171 (7), 156 (5), 143 (7), 128 (6), 115 (20), 103 (6), 89 (22).
A solution of 5-methoxycarbonylmethylene-7-phenyl-1,2,3,6,-tetrahydro-5H-pyrrolo[1,2-α]imidazol-6-one (0.76 g, 2.81 mmol) in methanol (28 cm³) was stirred in the presence of 10% Pd/C (0.03 g, 0.028 mmol) under an atmosphere of hydrogen for 12 hours. The catalyst was filtered and the methanol was removed under reduced pressure. The yellow gum that was produced was recrystallised from hexane/methanol to give the title compound as a white solid (0.70 g, 92%), m.p. 171-174°C (Found: M 272.1160. C₁₅H₁₆N₂O₃ requires: M 272.1161); ν max 3257 (NH), 1729 (CO₂Me), 1607 (CO), 1549, 1516, 1477, 1442, 1381, 1306, 1197, 1167, 762; δ H (300 MHz, CD₃OD) 2.44-2.52 (1H, dd, J 9.8 and 16.7, CHHCO₂Me), 2.96-3.03 (1H, dd, J 3.2 and 16.7, CHCH₂CO₂Me), 3.23-3.34 (1H, dd, J 9.8 and 18.3, CHHCO₂Me), 3.61-3.69 (1H, m, NCH₂CH₂N), 3.71 (3H, s, CH₃), 3.74-3.95 (1H, m, NCHHCH₂N), 7.06 (1H, t, J 7.4, Ar-H), 7.29 (2H, t, J 7.4, Ar-H), 7.56 (2H, d, J 7.4, Ar-H); δ C (100 MHz; CD₃OD) 36.8 (CH₂CO₂Me), 47.8 and 48.1 (NCH₂CH₂N), 52.4 (CH₃), 63.5 (CH), 93.9 (NC=CH), 125.5, 126.4, 129.3, (Ar-CH), 133.9 (Ar-C), 173.6 (NC=CH), 176.1 (CO₂Et), 194.2 (CO); m/z 272 (M⁺, 72%), 241 (6), 238 (3), 225 (2), 213 (100), 199 (10), 185 (26), 171 (7), 157 (5), 142 (8), 128 (9), 115 (18), 96 (9), 91 (14), 89 (14).
4.0 References


114 a) Z.R. Liu, *Heterocycles*, 1986, 24, 2247;  


Appendix
2-(2-Oxo-(3-phenyl)ethylidene)imidazolidine (2.1.31b)

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C_{16}H_{20}N_{2}O_{3}</td>
</tr>
<tr>
<td>Formula weight</td>
<td>288.34</td>
</tr>
<tr>
<td>Temperature</td>
<td>150 (2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>Pbca</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>10.6561 (2) Å</td>
</tr>
<tr>
<td>α</td>
<td>90</td>
</tr>
<tr>
<td>b</td>
<td>15.5737 (3) Å</td>
</tr>
<tr>
<td>β</td>
<td>90</td>
</tr>
<tr>
<td>c</td>
<td>17.8997 (3) Å</td>
</tr>
<tr>
<td>γ</td>
<td>90</td>
</tr>
<tr>
<td>Volume</td>
<td>2970.54 (9) Å</td>
</tr>
<tr>
<td>Z</td>
<td>8</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.289 Mg / m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.090 mm⁻¹</td>
</tr>
<tr>
<td>F (000)</td>
<td>1232</td>
</tr>
<tr>
<td>Crystal</td>
<td>Bipyramid; colourless</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.20 x 0.20 x 0.20 mm³</td>
</tr>
<tr>
<td>θ range for data collection</td>
<td>2.58 - 26.00</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-12 ≤ h ≤ 13, -19 ≤ k ≤ 19, -22 ≤ l ≤ 22,</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>23802</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>2910 [R_{int} = 0.0565]</td>
</tr>
<tr>
<td>Completeness to θ = 27.47</td>
<td>99.9%</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.9823 and 0.9823</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>2910 / 0 / 270</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.048</td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>R1 = 0.0356, wR2 = 0.0893</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0467, wR2 = 0.0947</td>
</tr>
<tr>
<td>Largest diff. Peak and hole</td>
<td>0.168 and -0.211 e Å⁻³</td>
</tr>
</tbody>
</table>
Bond lengths [Å] and angles [°] for 2-(2-oxo-3-phenyl)ethylidene)imidazoline (2.1.31b)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2576(14)</td>
<td>1.2050(14)</td>
<td>1.3333(14)</td>
<td>1.4889(16)</td>
<td>1.3852(13)</td>
<td>1.3916(13)</td>
<td>1.4781(15)</td>
<td>1.3339(15)</td>
<td>1.4474(17)</td>
<td>0.885(16)</td>
<td>1.5254(19)</td>
<td>0.957(14)</td>
<td>0.983(15)</td>
<td>0.962(16)</td>
<td>0.992(15)</td>
<td>1.3855(16)</td>
<td>1.4162(17)</td>
<td>0.962(13)</td>
<td>1.5072(16)</td>
<td>1.3929(17)</td>
<td>1.3828(18)</td>
<td>0.955(14)</td>
<td>1.3938(17)</td>
<td>1.3855(18)</td>
<td>0.934(15)</td>
<td>1.383(19)</td>
<td>0.980(14)</td>
<td>1.3873(18)</td>
<td>0.972(15)</td>
<td>0.942(15)</td>
<td>1.5133(19)</td>
<td>1.5138(18)</td>
<td>1.5176(17)</td>
</tr>
</tbody>
</table>

Bond length [Å] and angle [°] for the hydrogen bond

<table>
<thead>
<tr>
<th>D-H-A</th>
<th>d(D-H)</th>
<th>d(H-A)</th>
<th>(D-A)</th>
<th>(D-HA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N2-H2N-O1</td>
<td>0.883(16)</td>
<td>1.939(15)</td>
<td>2.6264(14)</td>
<td>133.3(13)</td>
</tr>
<tr>
<td>Property</td>
<td>Value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>--------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C₁₇H₁₈N₂O</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formula weight</td>
<td>266.33</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>150 (2) K</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Space group</td>
<td>P-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 8.831 (2) Å  alpha = 90.34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>b = 11.534 (2) Å  beta = 92.49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>c = 13.182 (3) Å  gamma = 90.79</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>13441.3 (5) Å³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.319 Mg/m³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.083 mm⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F (000)</td>
<td>568</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.5 x 0.2 x 0.1 mm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>theta range for data collection</td>
<td>1.77 to 24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index ranges</td>
<td>-10 ≤ h ≤ 10, -13 ≤ k ≤ 13, -15 ≤ l ≤ 15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reflections collected / unique</td>
<td>21333 / 4182 [R (int) = 0.1113]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completeness to theta = 24.00</td>
<td>99.5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least squares on F²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>4182 / 0 / 378</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.213</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>R1 = 0.0661, wR2 = 0.1715</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0906, wR2 = 0.1873</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Largest diff. Peak and hole</td>
<td>0.282 and −0.341 e Å⁻³</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Bond lengths [Å] and angles [°] for 10-phenyl-1,2,3,5,6,7,8,9-octahydroimidazo[1,2-b]isoquinolin-5-one (2.2.20c)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length</th>
<th>Bond</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(1)-C(13)</td>
<td>1.252(3)</td>
<td>O(2)-C(30)</td>
<td>1.255(3)</td>
</tr>
<tr>
<td>N(1)-C(3)</td>
<td>1.390(3)</td>
<td>N(1)-C(2)</td>
<td>1.670(3)</td>
</tr>
<tr>
<td>N(2)-C(3)</td>
<td>1.360(3)</td>
<td>N(2)-C(13)</td>
<td>1.385(3)</td>
</tr>
<tr>
<td>N(2)-C(1)</td>
<td>1.469(3)</td>
<td>N(3)-C(20)</td>
<td>1.393(3)</td>
</tr>
<tr>
<td>N(3)-C(29)</td>
<td>1.470(3)</td>
<td>N(4)-C(20)</td>
<td>1.375(3)</td>
</tr>
<tr>
<td>N(4)-C(30)</td>
<td>1.388(3)</td>
<td>N(4)-C(18)</td>
<td>1.466(3)</td>
</tr>
<tr>
<td>C(1)-C(2)</td>
<td>1.538(3)</td>
<td>C(3)-C(4)</td>
<td>1.371(4)</td>
</tr>
<tr>
<td>C(4)-C(11)</td>
<td>1.438(4)</td>
<td>C(4)-C(5)</td>
<td>1.495(3)</td>
</tr>
<tr>
<td>C(5)-C(10)</td>
<td>1.389(4)</td>
<td>C(5)-C(6)</td>
<td>1.392(4)</td>
</tr>
<tr>
<td>C(6)-C(7)</td>
<td>1.390(4)</td>
<td>C(7)-C(8)</td>
<td>1.378(4)</td>
</tr>
<tr>
<td>C(8)-C(9)</td>
<td>1.386(4)</td>
<td>C(9)-C(10)</td>
<td>1.381(4)</td>
</tr>
<tr>
<td>C(11)-C(12)</td>
<td>1.377(3)</td>
<td>C(11)-C(17)</td>
<td>1.505(4)</td>
</tr>
<tr>
<td>C(12)-C(13)</td>
<td>1.427(4)</td>
<td>C(12)-C(14)</td>
<td>1.516(3)</td>
</tr>
<tr>
<td>C(14)-C(15)</td>
<td>1.515(4)</td>
<td>C(15)-C(16)</td>
<td>1.508(4)</td>
</tr>
<tr>
<td>C(16)-C(17)</td>
<td>1.533(4)</td>
<td>C(18)-C(19)</td>
<td>1.532(4)</td>
</tr>
<tr>
<td>C(20)-C(21)</td>
<td>1.365(4)</td>
<td>C(21)-C(22)</td>
<td>1.393(4)</td>
</tr>
<tr>
<td>C(21)-C(22)</td>
<td>1.393(4)</td>
<td>C(22)-C(23)</td>
<td>1.392(4)</td>
</tr>
<tr>
<td>C(24)-C(25)</td>
<td>1.375(4)</td>
<td>C(25)-C(26)</td>
<td>1.393(4)</td>
</tr>
<tr>
<td>C(26)-C(27)</td>
<td>1.384(4)</td>
<td>C(27)-C(28)</td>
<td>1.379(4)</td>
</tr>
<tr>
<td>C(28)-C(29)</td>
<td>1.310(4)</td>
<td>C(29)-C(30)</td>
<td>1.424(4)</td>
</tr>
<tr>
<td>C(31)-C(32)</td>
<td>1.553(3)</td>
<td>C(32)-C(33)</td>
<td>1.522(5)</td>
</tr>
<tr>
<td>C(33)-C(34)</td>
<td>1.518(6)</td>
<td>C(32')-C(33')</td>
<td>1.586(7)</td>
</tr>
<tr>
<td>C(33')-C(34)</td>
<td>1.466(14)</td>
<td>C(33)-C(34)</td>
<td>1.466(14)</td>
</tr>
</tbody>
</table>

[Table continues with bond angles and distances for all bonds in the molecule, providing a complete set of bond lengths and angles.]
**Empirical formula** | \( \text{C}_{16}\text{H}_{16}\text{N}_{2}\text{O}_{3} \)  
---|---  
**Formula weight** | 284.32  
**Temperature** | 150 (2) K  
**Wavelength** | 0.71073 Å  
**Crystal system** | Orthorhombic  
**Space group** | \( \text{P}b\text{ca} \)  
**Unit cell dimensions**  
\( a = 7.1760 (10) \) Å  \( \alpha = 90 \)  
\( b = 17.805 (4) \) Å  \( \beta = 90 \)  
\( c = 20.947 (4) \) Å  \( \gamma = 90 \)  
**Volume** | 2676.4 (9) Å³  
**Z** | 8  
**Density (calculated)** | 1.411 Mg/m³  
**Absorption coefficient** | 0.099 mm⁻¹  
**F (000)** | 1200  
**Crystal** | Needle; orange  
**Crystal size** | 0.4 x 0.25 x 0.25 mm³  
**θ range for data collection** | 1.94 – 27.47  
**Index ranges** | \(-7 \leq h \leq 9, -19 \leq k \leq 23, -27 \leq l \leq 27,\)  
**Reflections collected** | 16412  
**Independent reflections** | 3062 \( [R_{\text{int}} = 0.1168]\)  
**Completeness to θ = 27.47** | 99.9%  
**Absorption correction** | Semi-empirical from equivalents  
**Max. and min. transmission** | 1.0 and 0.935  
**Refinement method** | Full-matrix least-squares on \( F^2 \)  
**Data / restraints / parameters** | 3062 / 0 / 191  
**Goodness-of-fit on \( F^2 \)** | 0.815  
**Final R indices [I>2σ(I)]** | \( R1 = 0.0576, wR2 = 0.1218 \)  
**R indices (all data)** | \( R1 = 0.1387, wR2 = 0.1595 \)  
**Largest diff. Peak and hole** | 0.246 and -0.260 e Å⁻³
<table>
<thead>
<tr>
<th>Bond Lengths [Å]</th>
<th>Angles [°]</th>
</tr>
</thead>
<tbody>
<tr>
<td>01-C12</td>
<td>1.241(3)</td>
</tr>
<tr>
<td>02-C14</td>
<td>1.217(3)</td>
</tr>
<tr>
<td>03-C14</td>
<td>1.332(3)</td>
</tr>
<tr>
<td>03-C15</td>
<td>1.455(3)</td>
</tr>
<tr>
<td>N1-C8</td>
<td>1.322(2)</td>
</tr>
<tr>
<td>N1-C9</td>
<td>1.468(3)</td>
</tr>
<tr>
<td>N2-C11</td>
<td>1.379(3)</td>
</tr>
<tr>
<td>N2-C8</td>
<td>1.383(3)</td>
</tr>
<tr>
<td>N2-C10</td>
<td>1.470(3)</td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.390(3)</td>
</tr>
<tr>
<td>C1-C6</td>
<td>1.391(3)</td>
</tr>
<tr>
<td>C2-C3</td>
<td>1.383(5)</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.378(4)</td>
</tr>
<tr>
<td>C4-C5</td>
<td>1.382(3)</td>
</tr>
<tr>
<td>C5-C6</td>
<td>1.407(3)</td>
</tr>
<tr>
<td>C6-C7</td>
<td>1.464(3)</td>
</tr>
<tr>
<td>C7-C8</td>
<td>1.394(3)</td>
</tr>
<tr>
<td>C7-C12</td>
<td>1.423(3)</td>
</tr>
<tr>
<td>C9-C10</td>
<td>1.530(3)</td>
</tr>
<tr>
<td>C11-C13</td>
<td>1.341(3)</td>
</tr>
<tr>
<td>C11-C12</td>
<td>1.534(3)</td>
</tr>
<tr>
<td>C13-C14</td>
<td>1.457(3)</td>
</tr>
<tr>
<td>C15-C16</td>
<td>1.497(4)</td>
</tr>
<tr>
<td>C14-C3-C15</td>
<td>117.42(19)</td>
</tr>
<tr>
<td>C8-N1-C9</td>
<td>112.2(2)</td>
</tr>
<tr>
<td>C11-N2-C8</td>
<td>109.6(2)</td>
</tr>
<tr>
<td>C11-N2-C10</td>
<td>138.6(2)</td>
</tr>
<tr>
<td>C8-N2-C10</td>
<td>111.27(19)</td>
</tr>
<tr>
<td>C3-C1-C6</td>
<td>121.0(2)</td>
</tr>
<tr>
<td>C3-C2-C1</td>
<td>120.5(3)</td>
</tr>
<tr>
<td>C4-C3-C2</td>
<td>119.3(2)</td>
</tr>
<tr>
<td>C5-C4-C5</td>
<td>120.8(2)</td>
</tr>
<tr>
<td>C6-C5-C6</td>
<td>120.8(2)</td>
</tr>
<tr>
<td>C1-C6-C5</td>
<td>117.7(2)</td>
</tr>
<tr>
<td>C1-C6-C7</td>
<td>122.6(2)</td>
</tr>
<tr>
<td>C5-C6-C7</td>
<td>119.7(2)</td>
</tr>
<tr>
<td>C8-C7-C12</td>
<td>105.0(2)</td>
</tr>
<tr>
<td>C8-C7-C6</td>
<td>127.0(2)</td>
</tr>
<tr>
<td>C12-C7-C6</td>
<td>128.0(2)</td>
</tr>
<tr>
<td>N1-C8-N2</td>
<td>109.4(2)</td>
</tr>
<tr>
<td>N1-C2-C7</td>
<td>137.4(2)</td>
</tr>
<tr>
<td>N2-C8-C7</td>
<td>113.2(2)</td>
</tr>
<tr>
<td>N1-C9-C10</td>
<td>103.86(19)</td>
</tr>
<tr>
<td>N2-C10-C9</td>
<td>102.35(19)</td>
</tr>
<tr>
<td>C13-C11-N2</td>
<td>134.9(2)</td>
</tr>
<tr>
<td>C13-C11-C12</td>
<td>120.4(2)</td>
</tr>
<tr>
<td>N2-C11-C12</td>
<td>104.7(2)</td>
</tr>
<tr>
<td>O1-C12-C7</td>
<td>130.5(2)</td>
</tr>
<tr>
<td>O1-C12-C11</td>
<td>121.7(2)</td>
</tr>
<tr>
<td>C7-C12-C11</td>
<td>107.8(2)</td>
</tr>
<tr>
<td>C11-C13-C14</td>
<td>130.9(2)</td>
</tr>
<tr>
<td>O2-C14-O3</td>
<td>123.3(2)</td>
</tr>
<tr>
<td>O2-C14-C13</td>
<td>123.1(2)</td>
</tr>
<tr>
<td>O3-C14-C13</td>
<td>113.7(2)</td>
</tr>
<tr>
<td>O3-C15-C16</td>
<td>106.9(2)</td>
</tr>
</tbody>
</table>
### Crystallographic Data

**Empirical formula**  
\(C_{25}H_{28}N_{2}O_{4}\)

**Formula weight**  
420.49

**Temperature**  
298 (2) K

**Wavelength**  
0.71073 Å

**Crystal system**  
Triclinic

**Space group**  
\(P-1\)

**Unit cell dimensions**  
\(a = 11.0117 (5) \text{ Å}, \alpha = 65.331 (3)\)  
\(b = 10.6661 (8) \text{ Å}, \beta = 65.329 (4)\)  
\(c = 12.2753 (9) \text{ Å}, \gamma = 62.908 (3)\)

**Volume**  
1119.42 (13) \(\text{Å}^3\)

**Z**  
2

**Density (calculated)**  
1.248 Mg/m³

**Absorption coefficient**  
0.085 mm⁻¹

**\(F(000)\)**  
448

**Crystal**  
Colourless plates

**Crystal size**  
0.10 x 0.10 x 0.02 mm³

**\(\theta\) range for data collection**  
3.26-23.25

**Index ranges**  
\(-11 \leq h \leq 12, -11 \leq k \leq 11, -13 \leq l \leq 13\)

**Reflections collected**  
8067

**Independent reflections**  
3169 \([R_{int} = 0.0767]\)

**Completeness to \(\theta = 23.25\)**  
98.4 %

**Absorption correction**  
Empirical, SORTAV

**Max. and min. transmission**  
0.9983 and 0.9916

**Refinement method**  
Full-matrix least-squares on \(F^2\)

**Data / restraints / parameters**  
3169 / 0 / 283

**Goodness-of-fit on \(F^2\)**  
0.931

**Final \(R\) indices \([I>2\sigma(I)]\)**  
\(R1 = 0.0558, wR2 = 0.1103\)

**\(R\) indices (all data)**  
\(R1 = 0.1396, wR2 = 0.1373\)

**Extinction coefficient**  
0.013 (3)

**Largest diff. Peak and hole**  
0.217 and -0.207 e \(\text{Å}^3\)
### Bond lengths [Å] and angles [°] for (E)-Diethyl 2-[2-(2-phenyl)phenylethylimidazolin-l-yl]-1,4-butenoate (2.4.13)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length</th>
<th>Bond</th>
<th>Length</th>
<th>Bond</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>O1–C20</td>
<td>1.351(4)</td>
<td>C14–C15</td>
<td>1.497(4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O1–C21</td>
<td>1.446(4)</td>
<td>C14–C13</td>
<td>1.519(4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1–C18</td>
<td>1.373(4)</td>
<td>C13–C12</td>
<td>1.522(4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1–C15</td>
<td>1.417(4)</td>
<td>C7–C8</td>
<td>1.395(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1–C17</td>
<td>1.466(4)</td>
<td>C7–C12</td>
<td>1.403(4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O4–C23</td>
<td>1.202(4)</td>
<td>C19–C20</td>
<td>1.457(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O3–C23</td>
<td>1.331(4)</td>
<td>C12–C11</td>
<td>1.388(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O3–C24</td>
<td>1.470(4)</td>
<td>C1–C2</td>
<td>1.385(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2–C15</td>
<td>1.261(4)</td>
<td>C11–C10</td>
<td>1.384(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N2–C16</td>
<td>1.473(4)</td>
<td>C10–C9</td>
<td>1.371(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O2–C20</td>
<td>1.199(4)</td>
<td>C8–C9</td>
<td>1.372(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C6–C1</td>
<td>1.387(5)</td>
<td>C21–C22</td>
<td>1.500(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C6–C5</td>
<td>1.394(5)</td>
<td>C5–C4</td>
<td>1.378(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C6–C7</td>
<td>1.489(5)</td>
<td>C2–C3</td>
<td>1.369(6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C18–C19</td>
<td>1.350(4)</td>
<td>C3–C4</td>
<td>1.358(6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C18–C23</td>
<td>1.499(5)</td>
<td>C24–C25</td>
<td>1.432(5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C17–C16</td>
<td>1.531(4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>C20–O1–C21</td>
<td>117.0(3)</td>
<td>N2–C15–N1</td>
<td>114.9(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C18–N1–C15</td>
<td>132.4(3)</td>
<td>N2–C15–C14</td>
<td>122.5(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C18–N1–C17</td>
<td>119.8(2)</td>
<td>N1–C15–C14</td>
<td>122.6(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C15–N1–C17</td>
<td>107.5(3)</td>
<td>C2–C1–C6</td>
<td>120.4(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C23–O3–C24</td>
<td>119.3(3)</td>
<td>C2–C1–C6</td>
<td>120.4(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C15–N2–C16</td>
<td>108.8(3)</td>
<td>C10–C11–C12</td>
<td>121.8(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C1–C6–C5</td>
<td>117.5(4)</td>
<td>C9–C10–C11</td>
<td>119.4(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C1–C6–C7</td>
<td>122.3(4)</td>
<td>C9–C8–C7</td>
<td>121.5(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C5–C6–C7</td>
<td>120.1(4)</td>
<td>O2–C20–O1</td>
<td>123.2(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C19–C18–N1</td>
<td>121.8(3)</td>
<td>O2–C20–C19</td>
<td>127.5(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C19–C18–C23</td>
<td>119.5(3)</td>
<td>O1–C20–C19</td>
<td>109.3(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N1–C18–C23</td>
<td>118.7(3)</td>
<td>O1–C21–C22</td>
<td>106.4(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N1–C17–C16</td>
<td>102.2(2)</td>
<td>C4–C5–C6</td>
<td>121.1(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C15–C14–C13</td>
<td>112.1(3)</td>
<td>C3–C2–C1</td>
<td>121.0(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C14–C13–C12</td>
<td>114.7(3)</td>
<td>C4–C3–C2</td>
<td>119.3(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C8–C7–C12</td>
<td>118.8(3)</td>
<td>C10–C9–C8</td>
<td>120.0(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C8–C7–C6</td>
<td>117.6(3)</td>
<td>C3–C4–C5</td>
<td>120.7(5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C12–C7–C6</td>
<td>123.6(3)</td>
<td>O4–C23–O3</td>
<td>125.5(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C18–C19–C20</td>
<td>123.5(3)</td>
<td>O4–C23–C18</td>
<td>124.0(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C11–C12–C7</td>
<td>118.5(3)</td>
<td>O3–C23–C18</td>
<td>110.5(4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C11–C12–C13</td>
<td>120.3(3)</td>
<td>C25–C24–O3</td>
<td>110.9(3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C7–C12–C13</td>
<td>121.2(3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>