NEW ROUTES FOR THE SYNTHESIS OF AZIRIDINES, OXAZOLINES AND THIAZOLINES

by

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Thesis presented towards the degree of

DOCTOR OF PHILOSOPHY

University of St Andrews

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DECLARATION

I, Steven McGill, hereby certify that this thesis, which is of approximately 40000 words in length has been written by me, that it is the record of work carried out by me and that it has not been submitted in any previous application for a higher degree.

date 9th Dec 2004 signature of candidate

I was admitted as a research student in October 2000 and as a candidate for the degree of Doctor of Philosophy in October 2001; the higher study for which this is a record was carried out in the University of St. Andrews between 2000 and 2004.

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I hereby certify that the candidate has fulfilled the conditions of the Resolution and Regulations appropriate for the degree of Doctor of Philosophy in the University of St. Andrews and that the candidate is qualified to submit this thesis in application for that degree.

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LECTURE COURSES ATTENDED

The following is a statement of lecture courses attended during the period of study

Organic Research Seminars	3 years attendance
School Colloquia	3 years attendance
Organic Problem Solving	Prof. D. O'Hagan Dr. N. P. Botting
Molecular Rearrangements in Organic Chemistry	Prof. J. C. Walton
The Chemistry of Sulfur and Related Elements	Dr. R. A. Aitken
The Chemistry of Phosphorus and Related Elements	Dr. R. A. Aitken

ABSTRACT

A range of *N*-acyloxazolidin-5-ones have been synthesised from readily available α-amino acids and their behaviour under conditions of Flash Vacuum Pyrolysis (FVP) has been examined for the first time. Several of the oxazolidinones were previously unknown compounds and were fully characterised including an X-ray structure determination of one example. In all cases the NMR spectra were complicated by restricted rotation of the *N*-acyl groups and this was quantified in one case by a variable temperature NMR study. In general FVP of the *trans* oxazolidinones at 450°C resulted in loss of carbon dioxide to give *cis N*-acylaziridines. Many of these possessed non-zero optical rotations. FVP at 550°C produced mainly *cis* 2-oxazolines and in some cases a *N*-(1-phenyalkenyl)benzamide. The stereochemistry of these new heterocyclic reactions is considered in terms of frontier molecular orbital theory.

Alkylation of one example at the 4-position resulted in a change in the pyrolysis behaviour to give exclusively the alkenylamide product, *N*-(1,3-diphenyl-2-methylprop-2-enyl)benzamide.

In an attempt to learn more about the processes a range of chiral *N*-thioacyloxazolidin-5-ones were synthesised from *N*-acyloxazolidin-5-ones using Lawesson's reagent. This class of compounds is previously unknown in the literature and they were fully chacterised including X-ray structure determinations in two cases. Their FVP between 450°C and 550°C again resulted in loss of carbon dioxide this time yielding 2-thiazolines. No *N*-thioacylaziridines were observed.

In an attempt to extend the approach to synthetically useful bis(oxazoline) ligands, bis(oxazolidinones) were synthesised from α-amino acids and characterised. Their FVP at 550°C is expected yield bis(oxazolines) although there was not enough time to fully investigate this.

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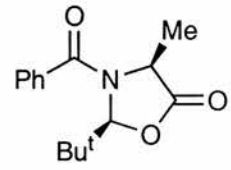
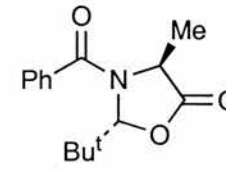
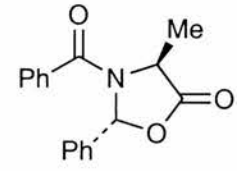
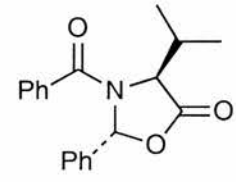
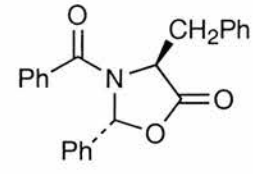
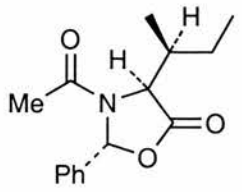


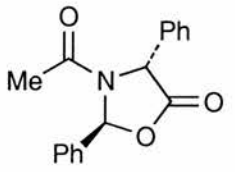


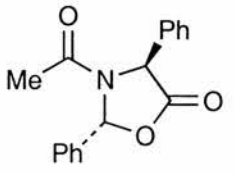


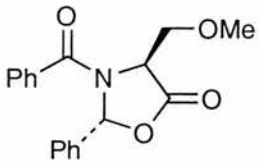


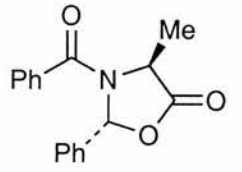


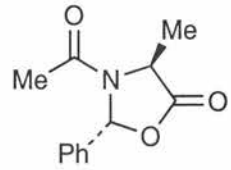




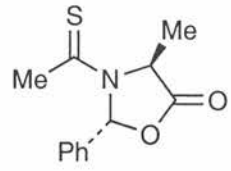




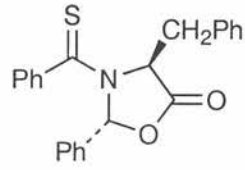




2. (*2R,4S*)-4-methyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one **485** 107



3. (*2R,4S*)-4-benzyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one **483** 107



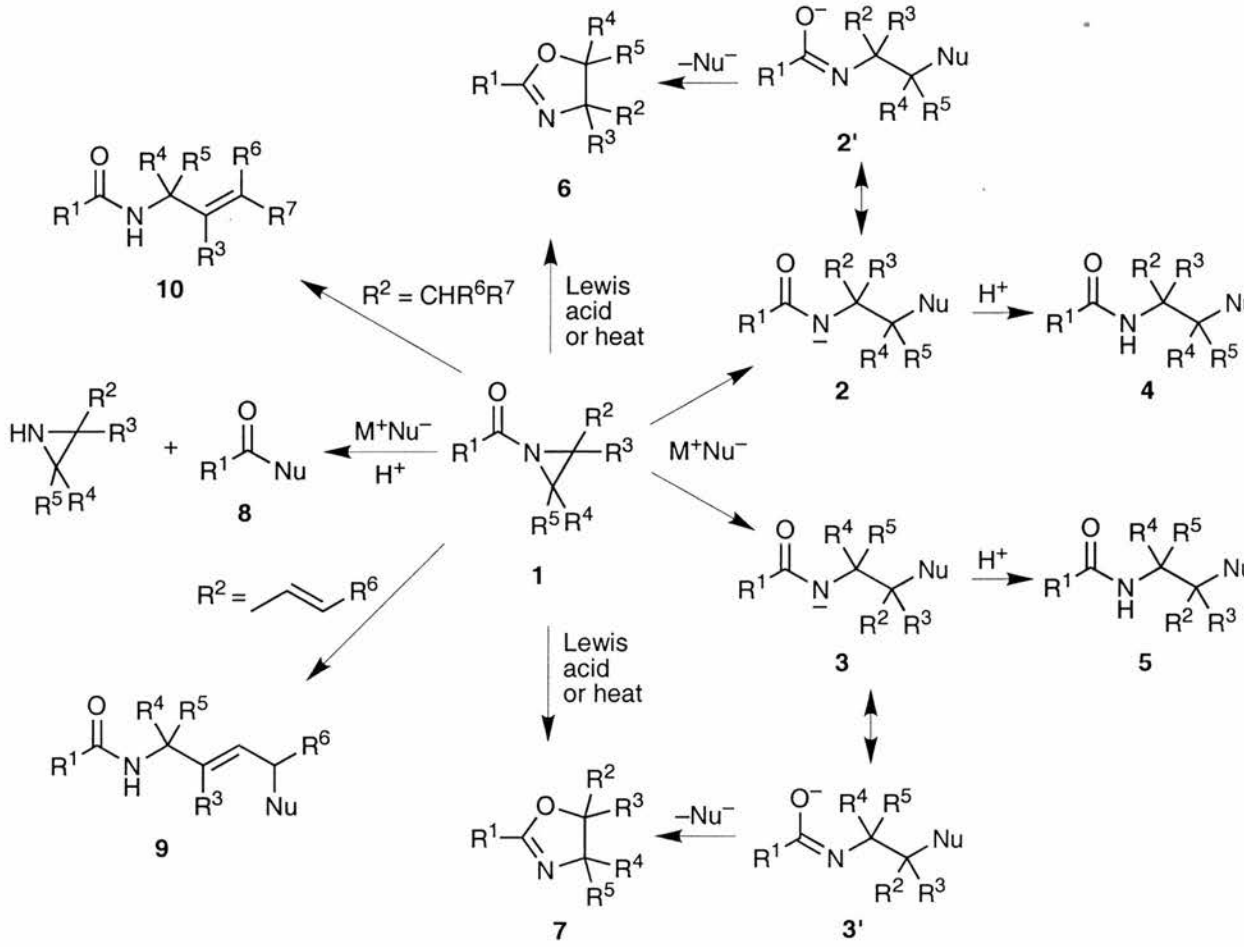
Discussion

Appendix

INTRODUCTION

A. Scope and general principles

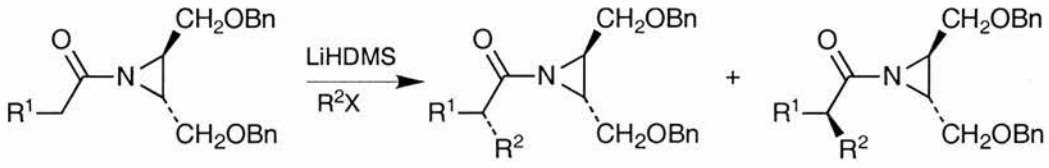
Although there have been several previous reviews on the chemistry of aziridines, these have either been general,[1-4] or focused on particular aspects such as nucleophilic ring-opening,[5] a comparison between aziridines and epoxides,[6] or use of chiral aziridines in asymmetric synthesis.[7] As far as we are aware the reactions of *N*-acylaziridines have not been specifically reviewed before. This is unfortunate since, as summarised in Scheme 1, these simple starting materials can react in many different ways to give a variety of useful products.



For a general *N*-acylaziridine **1** nucleophilic attack can result in ring opening by attack at a ring carbon and for unsymmetrical aziridines this may occur in either regiochemical sense to give, after protonation, the functionalised amides **4** or **5**. Alternatively the initially formed anions **2** or **3** may react in their azaenolate forms **2'** or **3'**

and cyclise with loss of Nu^- to give oxazolines **6** or **7**. The overall rearrangement to the regiomeric oxazolines may also be brought about thermally or by Lewis acid catalysis. Of course, not only the regioselectivity but also the diastereo- and enantioselectivity of this process is highly relevant when it cames to chiral aziridines. An alterative mode of nucleophilic attack is at the carbonyl carbon in **1** leading to products **8** in which the *N*-acylaziridine has acted as an acylating agent. Where we have an unsaturated substituent on the aziridine ring, nucleophilic ring opening may occur in an S_N' sense to give functionalised allylamides **9**. Allylamides **10** also result from thermal rearrangement of compounds **1** with a hydrogen atom on one substituent.

In the following sections these processes are considered in turn and all the important reactions of the *N*-acylaziridine function are surveyed. It should be noted that reactions such as asymmetric alkylation of the *N*-acyl group in **11** to give **12** and **13**, in which the acylaziridine moiety remains intact have been investigated recently,[8] but these are not considered further in this review.



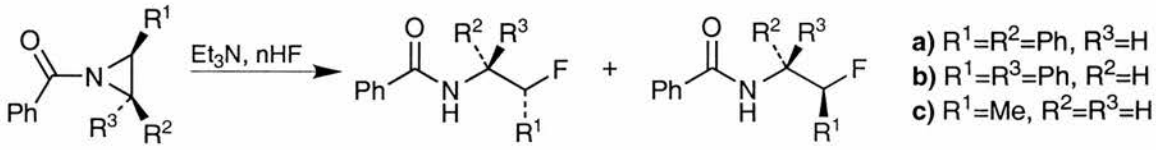
11 **12** **13**

B. Nucleophilic ring opening

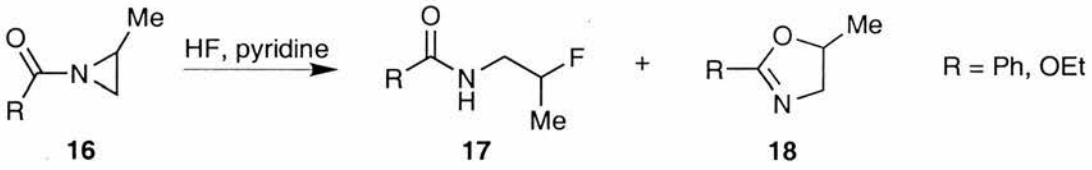
1. Addition of hydrogen halides and halide anions

Synthesis of fluoroamides **15** by ring-opening of *N*-benzoylaziridines **14** with hydrogen fluoride, Olah's reagent (hydrogen fluoride and pyridine) or its analogues has been attempted.[9] In order to improve the fluoroamide yields the ring nitrogen needs to be activated. A less acidic and more nucleophilic agent than Olah's was required to decrease the

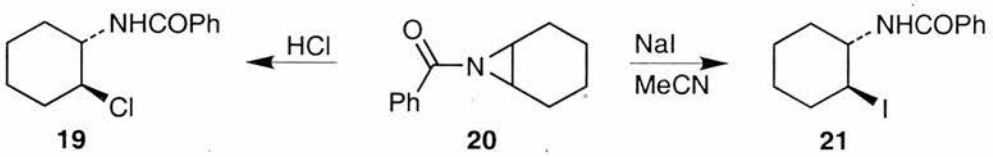
oxazoline yields. *N*-benzoylaziridines when treated with Et_3N and HF give predominantly fluoroamides. Compound **14a** was ring opened using 2.5 equivalents of HF to produce threo fluoroamide **15t** (69%) and erythro fluoroamide **15e** (17%). Aziridine **14b** gave poorer yields of 5 and 25% for **15t** and **15e** respectively. A single isomer of compound **15** was obtained from the reaction of compound **14c** (85%). Its stereochemistry was not determined.



N-benzoyl-2-methyl-3-phenylaziridine **16** gave only 46% of the desired *N*-benzoylfluoroamine **17** and 2-phenyl-2-oxazolines **18** in 47% yield when reacted with Olah's reagent.[10] However the *N*-ethoxycarbonyl derivative rearranged quantitatively to **17** under the same conditions.



An iodoamide was suggested as a possible intermediate in the formation of 2-oxazolines from *N*-acylaziridines.[11] Treatment of *N*-benzoylcyclohexenimine **20** with sodium iodide in acetonitrile or acetone indeed gives the ring-opened iodoamide, **21**. The analogous *p*-nitrobenzoyl derivative was treated with sodium iodide in acetone to give primarily the oxazoline and very little of the iodo amide. In acetonitrile the oxazoline was the sole product (95%).

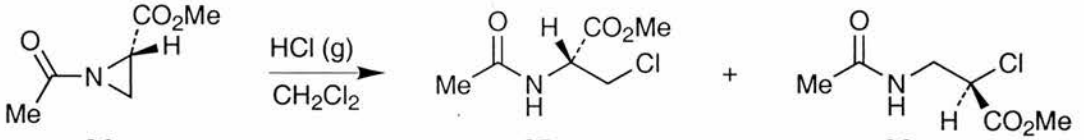


Attack of chloride ion from hydrogen chloride[12] has the same effect as iodide, opening the ring to yield the *N*-(*trans*-2-chlorocyclohexyl)benzamide **19**.

The *N*-acety1-3-*n*-hexylaziridine ester **22** gave a single diastereomer of the product **23** upon treatment with various nucleophiles including Cl^-.[13] Reacting **22** with ethereal hydrogen chloride gave the ring opened product arising from nucleophilic reaction at C-3. Catalysis by protonation at nitrogen or oxygen will cause attack at C-3. The positive charge cannot be stabilized at C-2 due to the electron-withdrawing ester group.

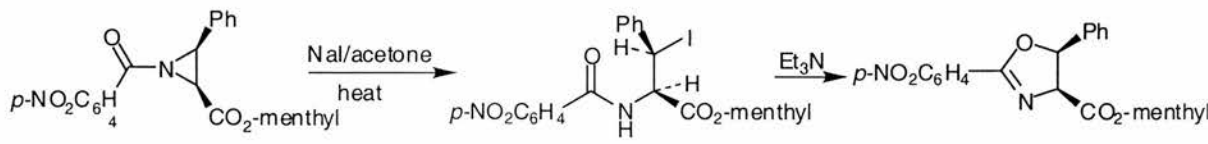
22 **23**

The ring-opening at C-3 of (*S*)-(–)-*N*-acetyl-2-methoxycarbonylaziridine **24** by hydrogen chloride afforded the unnatural α-amino acid derivative **25**.[14] The reaction of chloride at the C-2 ring carbon gives rise to the β-amino acid derivative **26**. Compounds **25** and **26** were produced in a 1:1 ratio showing the reaction was not regioselective. The total yield was 80%.



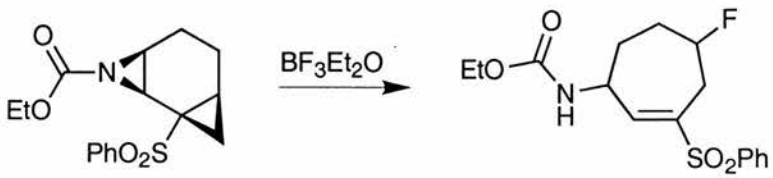
24 **25** **26**

Unusually, reaction of the *l*-menthyl aziridine-2-carboxylate **27** and sodium iodide gave iodoalkylamide **28**.[15] Normally this would not be observed, but would be considered an intermediate in the formation of the corresponding 2-oxazoline. The isolation of the intermediate β-haloamide in the rearrangement of aziridines is rare. Ring closure to the expected oxazoline product **29** is achieved by addition of triethylamine.



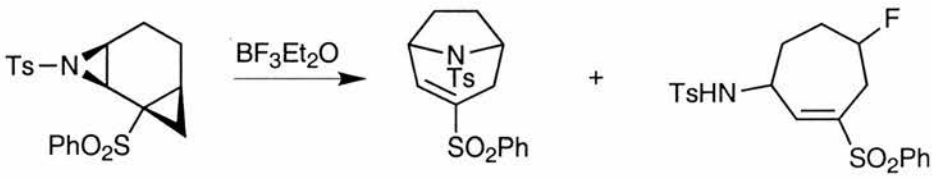
27 **28** **29**

The cyclic fluoroamidosulfone **31** was formed as the sole product of the reaction between *N*-ethoxycarbonyl aziridine **30** and boron trifluoride etherate.[16]



30 **31**

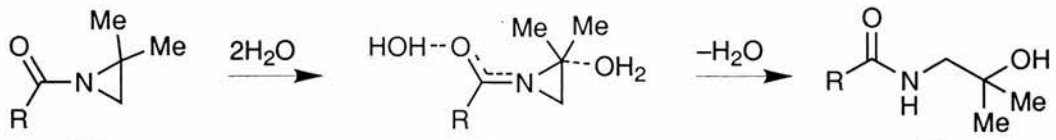
The low nucleophilicity of the carbamate nitrogen allows fluoride attack as opposed to the expected attack of N^- at C-6 to form a bicylic pyrrolidine analogous to **33**. In contrast the *N*-tosylaziridine **32** forms both the pyrrolidine **33** and the cyclic fluoroamidosulfone **34** in a ratio of 60:40. No yields are given. Varying the amount of Lewis acid used and the temperature had no effect on the ratio of **33**:**34**. Using a 9:1 mixture of dichloromethane and nitromethane as solvent gave **33** and an unidentified product in a ratio of 65:35.



32 **33** **34**

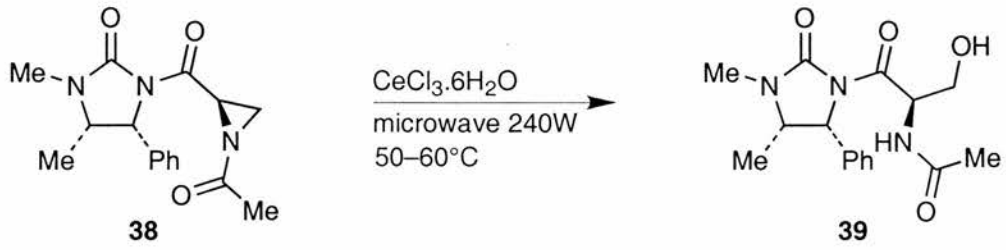
2. Addition of water, alcohols and carboxylic acids

Reaction of *N*-acyl-2,2-dimethylaziridines **35** with water gave the hydroxyethylamides **37**. The presence of two methyl groups at C-2 of the aziridines accelerated the hydrolysis[17] of the aziridine (3 days compared to 11 for unsubstituted) and considerably increased the yields. The authors suggest the possibility of hydrogen bonding between the acyl oxygen atom and a hydrogen atom of the first water molecule. This weakens the N-C-2 bond and the donor inductive effect of two methyl groups makes attack of a second water molecule more facile (see **36**). The author concludes that water attacks the more positive carbon atom of the aziridine ring.



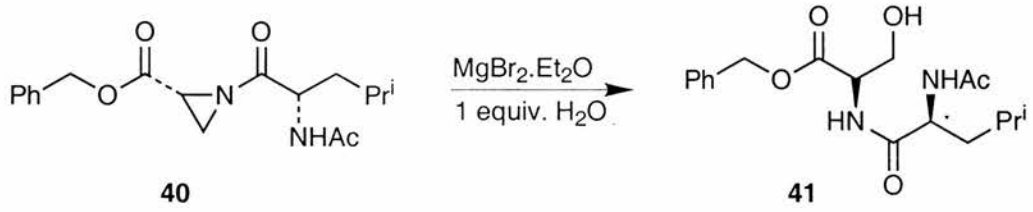
35 36 37

The acylaziridine **38** was irradiated with cerium chloride hexahydrate in toluene for 10 minutes to form compound **39** as the sole product in quantitive yield.[18] The oxazoline that would arise from ring expansion of **38** also provides **39** under the same conditions.



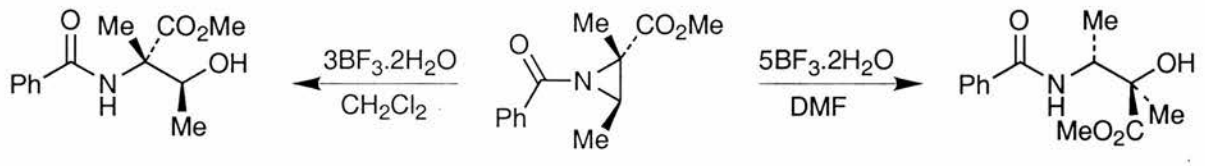
38 39

In a similar example (*R*)-aziridine-2-ester dipeptide **40** reacted with $MgBr_2.Et_2O$ and one equivalent of water in THF to give a D-serine-containing dipeptide **41**.[19] However, as in the previous example it is not clear whether an isomerisation to the oxazoline occured before the addition of H_2O.



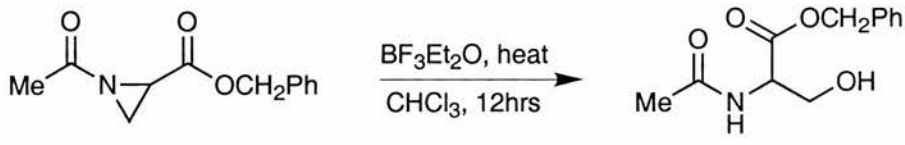
40 41

The reaction of the *N*-benzoylaziridinecarboxylate **42** with BF_32H_2O is solvent dependant.[20] In DMF an α-hydroxy-β-amino acid derivative **44** is formed while in dichloromethane the β-hydroxy-α-amino acid derivative **43** is the product.



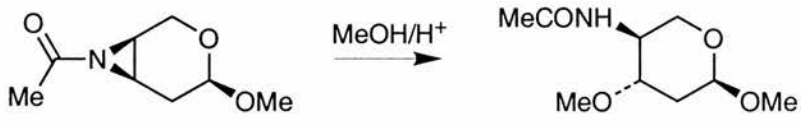
43 42 44

In the presence of $BF_3.Et_2O$, the 2-acetylamino-3-hydroxypropionate **46** is isolated from the *N*-acetylaziridine-2-carboxylate **45** after 12 hours in quantitative yield.[21] There is no mention of the source of the water in the paper.



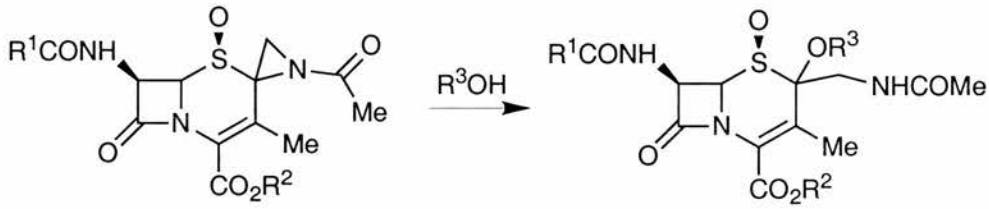
45 **46**

The enantiomerically pure, activated aziridine **47** was treated with methanol under acid conditions to give the dimethoxy amide **48** (91%).[22] Attack of the nucleophile (MeOH) on the protonated aziridine occurs regio and stereoselectively as shown.



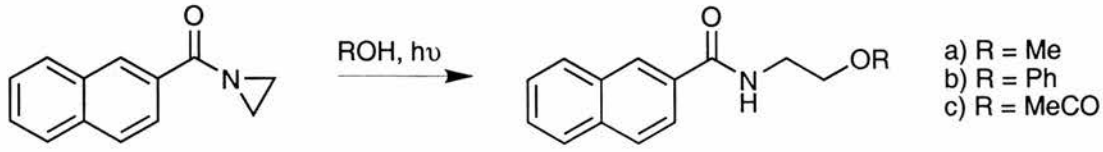
47 **48**

The cephalosporin spiro-*N*-acylaziridines **49** can undergo ring opening reactions with alcohols to give 2-alkoxy-2-acetylaminomethyl derivatives **50** in yields of 38-84%.[23]



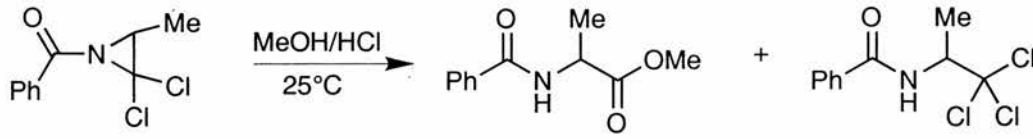
49 **50**

The photo-irradiation of *N*-(2-naphthoyl)aziridine **51** in methanol afforded *N*-(2-methoxyethyl)-2-naphthamide **52a** (31%).[24] Hydrogen bonding of methanol to the acyl oxygen would make the nucleophilic attack easier. The photochemical reaction of **51** in phenol afforded *N*-(2-phenoxyethyl)-2-naphthamide **52b** (42%) but also phenyl 2-naphthoate resulting from attack at the carbonyl group (23%) and an oligomer (35%). In the acidic medium of acetic acid, the quantitative acetolysis of **51** was observed to afford *N*-(2-acetoxyethyl)-2-naphthamide **52c**.



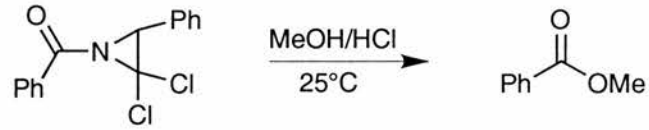
51 **52**

Treatment of the 2,2-dichloro-3-methylaziridine **53** with methanolic hydrogen chloride at room temperature for one week gave two products:[25] *N*-benzoylalanine methyl ester **54** (39%) and trichloroisopropylamide **55** from the nucleophilic attack of chloride at C-2 (13%).



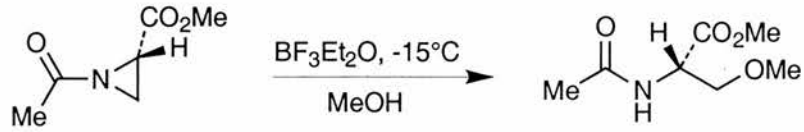
53 **54** **55**

Similar treatment of the 2,2-dichloro-3-phenylaziridine **56** resulted in a more destructive reaction, which produced methyl benzoate **57** in 90% yield from attack at the benzoyl group. In the absence of acid, the phenylaziridine **56** was stable in methanol.



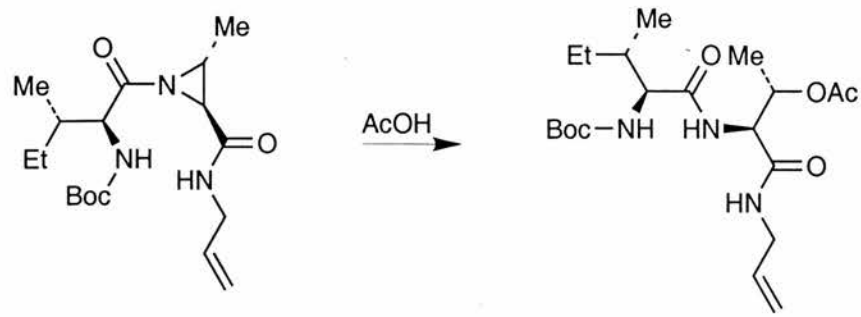
56 **57**

The reaction of methanol with (*S*)-(–)-*N*-acetyl-2-methoxycarbonylaziridine **24** in the presence of boron trifluoride etherate furnished the unnatural α-amino acid derivative **58** in 55% yield.[14] No products derived from attack at C-2 were observed.



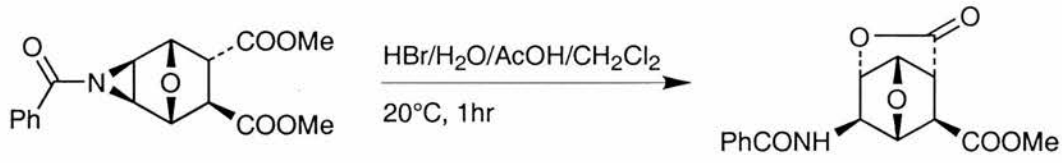
24 **58**

As part of the synthesis of a tripeptide,[26] the (2*S*,3*R*)-aziridine **59** was opened by acetic acid to give the (2*S*,3*S*)- *allo*-threonine derivative **60** in 95% yield.



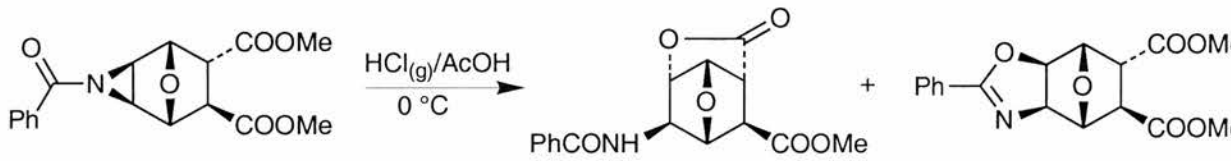
59 **60**

Treatment of the tricyclic aziridine **61** with $HBr/H_2O/AcOH$ (20°C, 1 hr) gave the lactone **62** as the sole product (65%).[27] This is due to removal of the carboxylate methyl group by the nucleophile (H_2O, HBr), followed by attack of the resulting carboxylate anion



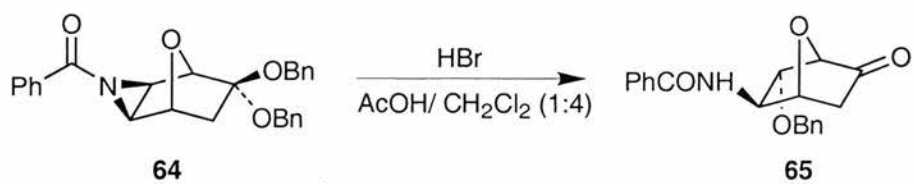
61 **62**

on an aziridine ring carbon. However, in a less nucleophilic medium ($CF_3CH(OH)CF_3$) the *N*-benzoylaziridine **61** was rearranged readily and quantitatively to the oxazoline **63** (77%). These conditions allow more time for the cationic intermediate to undergo an intramolecular process. A 2.3:1 mixture of **62**:**63** was obtained by bubbling dry hydrogen chloride gas through a solution of **61** in dichloromethane.



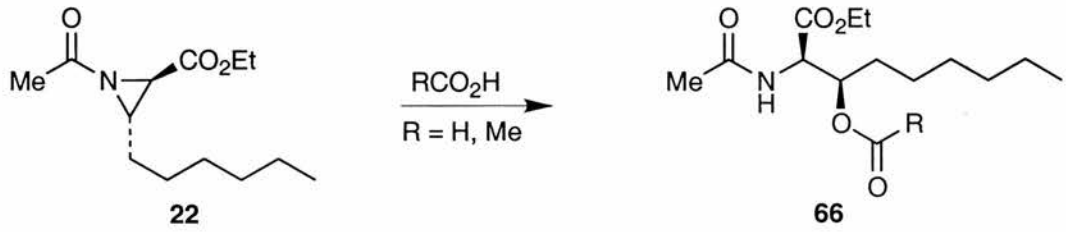
61 **62** **63**

Treatment of the tricyclic *N*-benzoylaziridine **64** with hydrogen bromide in a solution of acetic acid and dichloromethane was shown to yield the corresponding benzamide **65** with high stereoselectivity.[28]



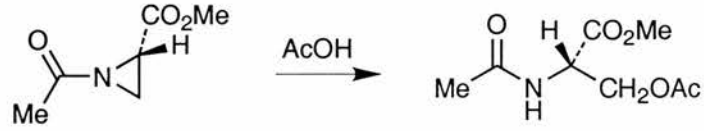
64 **65**

The *N*-acetyl-3-*n*-hexylaziridine ester **22** gave a single diastereomer of the products **66** upon treatment with acetic acid (78%) and neat formic acid (91%).[13] Compound **22** ring-opens by nucleophilic reaction at C-3.



22 **66**

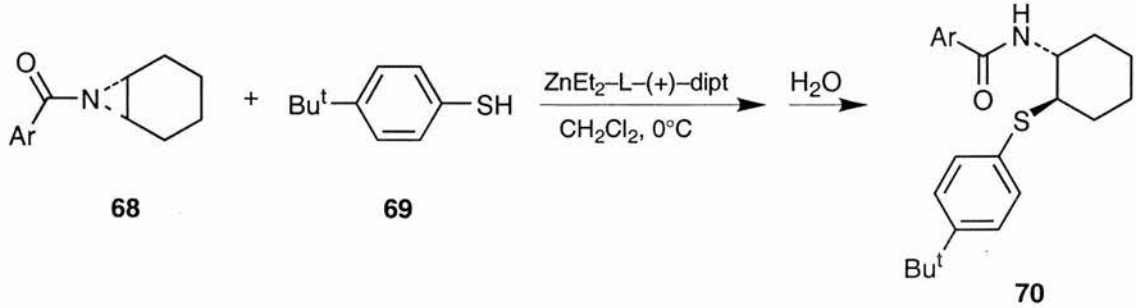
The reaction of (*S*)-(–)-*N*-acetyl-2-methoxycarbonylaziridine **24** in acetic acid gave the unnatural α-amino acid derivative **67** in 55% yield.[14] No amino acid derivatives formed from attack at C-2 were observed in this case.



24 **67**

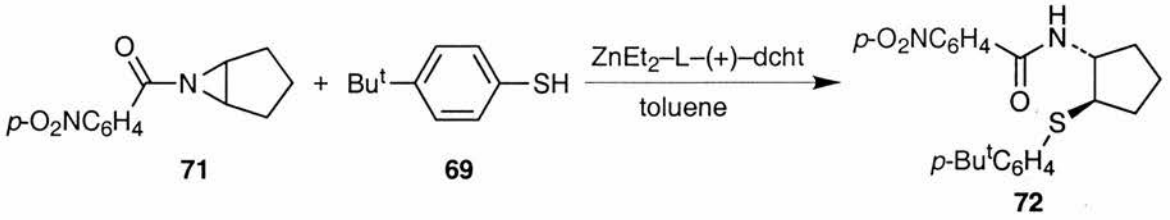
3. Additions of thiols

In a short communication,[29] Hayashi *et al.* carried out the ring opening of bicyclo *N*-benzoyl and *N*-*p*-nitrobenzoylaziridines **68** with *p tert* butylbenzenethiol **69** using chiral zinc complexes. They found that the enantioselectivity of the reaction was influenced by the molar ratio of the reactants, i.e. substrate, Et_2Zn, tartrate and thiol. Using a ratio of 1:3:1:4.8 produced the desired sulfide **70** in a yield of 98% and 88% e.e. In a further publication,[30] range of chiral additives were investigated including L-(+)-diethyl, diisopropyl, diisobutyl,



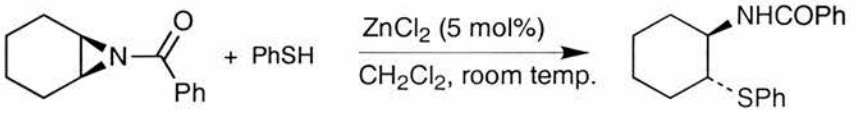
68 **69** **70**

dicyclohexyl and di-*tert*-butyl tartrates. Generally, diethyl zinc/dicyclohexyl tartrate complex gave the best results. The reaction also proceded with a cyclopentane ring fused to the aziridne. Compound **71** afforded the sulfide **72** in 89% yield and 85% e.e.



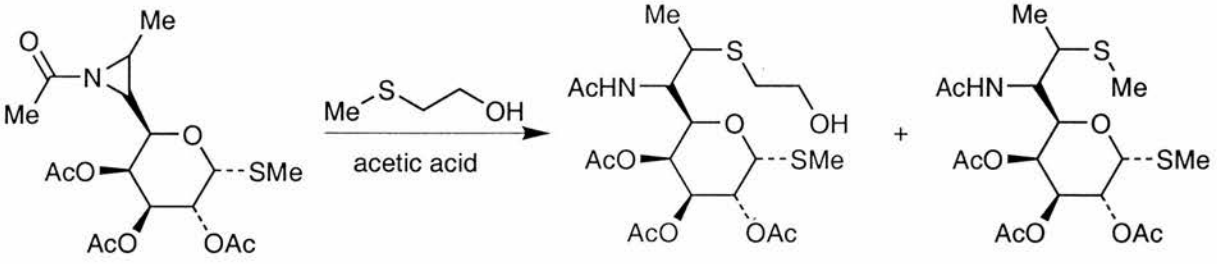
71 **69** **72**

The ring opening of *N*-benzoylcyclohexenimine **20** proceeded smoothly under mild conditions to afford the desired β-amino sulfides **73** in high yields.[31] Softer Lewis acids gave better results. Coordination of the Lewis acid to form a highly reactive intermediate is an important prequisite for the reaction.



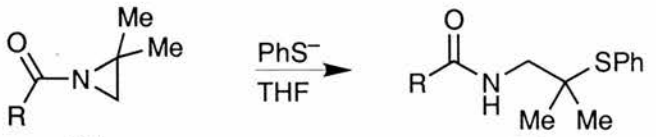
20 **73**

The formation of sulfides **75** and **76** must involve nucleophilic attack by the sulfur atom of 2-hydroxyethyl methyl sulfide at C-3 of the *N*-acetylaziridine **74** once it has been protonated.[32] This produces a sulfonium salt that undergoes nucleophilic attack by acetate ion mainly at the methyl group removing it. Attack by an acetate ion at the more hindered carbon gives the *S*-methyl (minor) product.



74 **75** **76**

There are many other examples using dialkyl sulfides, dialkyl disulfides and dialkyl trisulfides.[32]

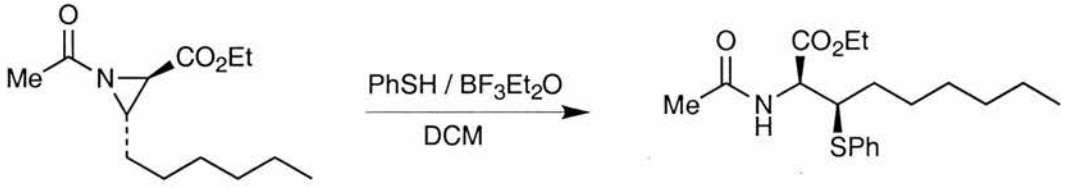


37 **77**

The reaction of *N*-acyl-2,2-dimethylaziridine **37** with thiophenoxide gave mainly the sulfide **77** resulting from attack by the nucleophile at C-2.[33] The yields were mostly 50-70% with two other possible products, the opposite regioisomers and an unsaturated amide in yields of 1-3 and 2-21% respectively. Thiophenoxide was prepared by adding thiophenol to a solution of sodium naphthalenide. Use of methanol as the solvent gave more by-products since it acted as a competing nucleophile.

78 **79**

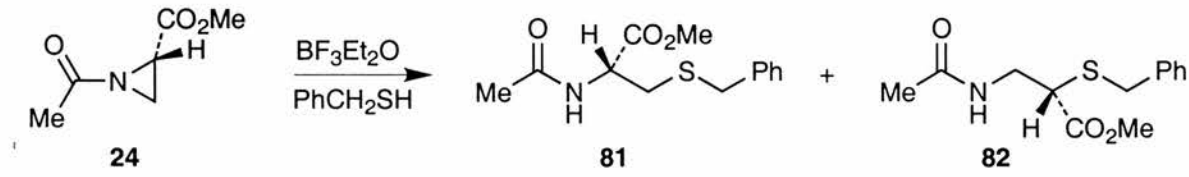
Reaction of the aziridine lactone **78** with ethanethiol in the presence of a Lewis acid gave the 3-acetamido-4-ethylthio ring opened **79** resulting from nucleophilic attack at C-2 of the aziridine ring.[34]



22 **80**

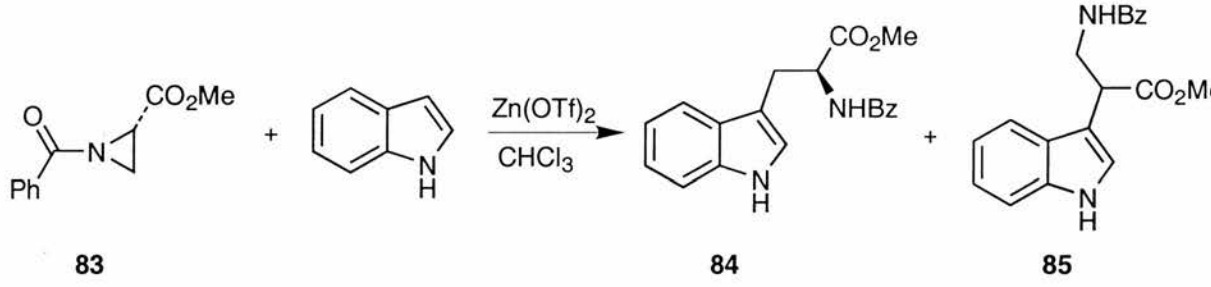
The *N*-acety1-3-*n*-hexylaziridine ester **22** gave a single diastereomer of the product **80** (38%) upon reaction with thiophenol in the presence of a boron trifluoride etherate.[13]

The ring-opening at C-3 and C-2 of (*S*)-(-)-*N*-acetyl-2-methoxycarbonylaziridine **24** by benzyl thiol in the presence of boron trifluoride etherate provided the unnatural α- and β-amino acid derivatives **81** (41%) and **82** (10%) respecively.[14]

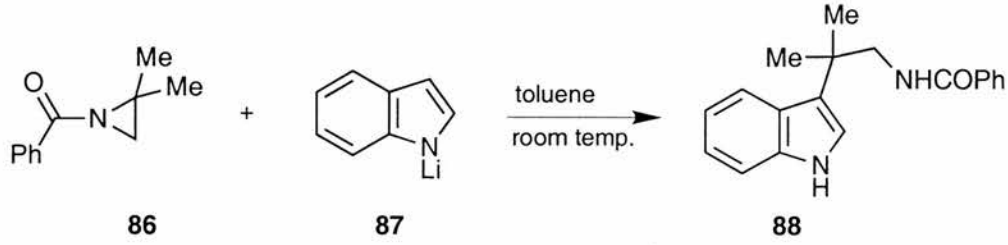


4. Addition of amines and amide anions

Sato and Kozikowski became interested in making tryptophan derivatives from indoles and 2-aziridinecarboxlyates, but only a single example was reported using *N*-benzoyl-2-methoxycarbonylaziridine **83** and indole to produce the 3-substituted indoles **84** (38%) and **85** (14%).[35] The stereochemistry of compound **85** was not determined. We might have predicted compound **85** to be the main product as it is formed via attack of the carbon next to an electron withdrawing group.

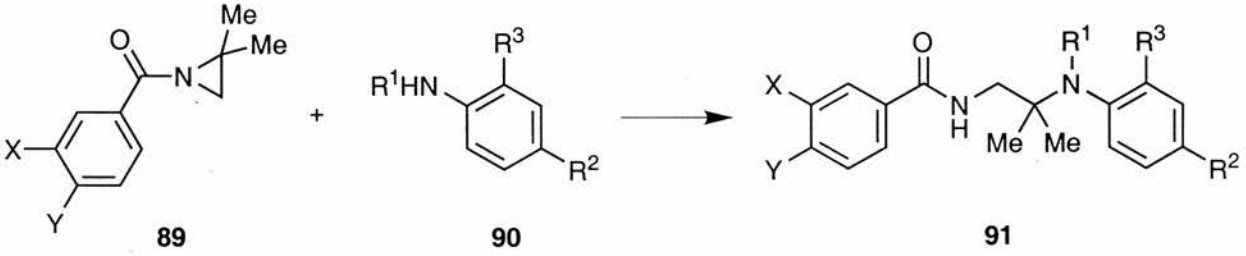


In another method, the indole was lithiated in ether then the solvent was replaced by toluene. The lithiated indole **87** was then reactive enough for the nucleophilic attack on the acylaziridine **86** solely at C-2 to afford the amide **88**[36] in 80% yield. The reaction does not proceed with 2,2-dimethyl-*N*-pivaloylaziridine or in tetrahydrofuran.



Strangely the reaction takes place at the more sterically hindered of the two aziridine ring carbons. This carbon is also the more electron rich of the two.

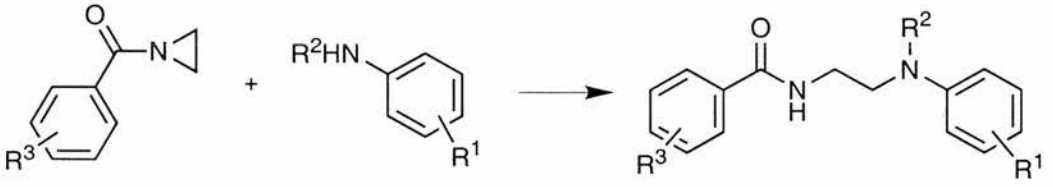
The *N*-benzoyl-2,2-dimethylaziridines **89** are also opened by nucleophilic attack at the dimethyl carbon atom of the ring by substituted anilines **90** to give **91** in high yields.[37] There are nine examples of this process starting from 2,2-dimethylbenzoylaziridines with various substituents on the benzene ring making this process fairly general. An excess of compounds **90** is used as they are mainly liquids (THF is employed where necessary).



89 **90** **91**

Again, the reaction takes place at the more sterically hindered, more electron rich aziridine ring carbons.

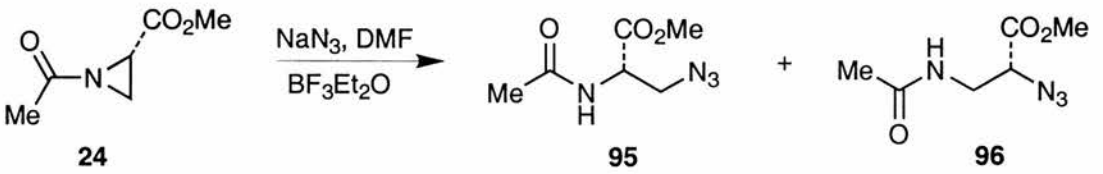
Another similar example using aziridines **92** unsubstituted at C-2 and C-3 and anilines **93** is as shown below.[38] The reaction proceeded for one day at room temperature before the product **94** crystallised out. There were twenty-three examples synthesised in all (mostly 50-80% yield). Most have R^2 and R^3=H and when $R^3 \neq H$, R^1=H.



92 **93** **94**

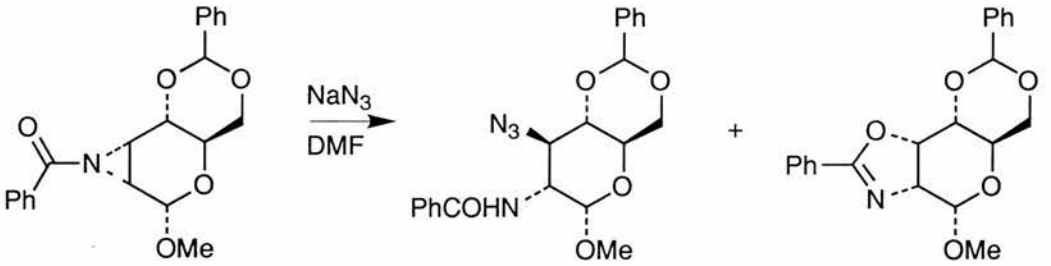
5. Addition of azide and cyanide

In reacting the *N*-acetyl aziridine **24** with sodium azide in DMF and in the presence of boron trifluoride etherate, two ring-opened products **95** and **96** were obtained in a ratio of 1:1 and 50% total yield.[14] The substituent has no effect on the regiochemisrty of the reaction. Nucleophilic attack occurred at C-3 and C-2 affording two regioisomers each with 90% e.e. This occurs in a similar way to an S_N2 reaction with inversion at C-2.



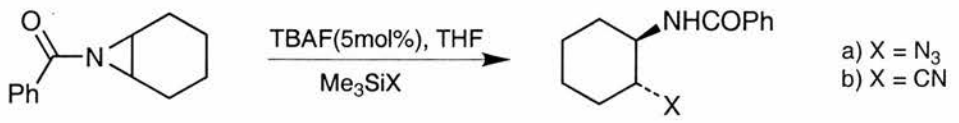
24 **95** **96**

Treatment of the *N*-benzoylaziridinomannoside **97** with sodium azide and ammonium chloride in boiling DMF gave a mixture of oxazoline **99** (36%) and the expected azido amide **98** (20%).[39] This is perhaps because the thermal ring expansion is competing with the nucleophilic ring opening in DMF in the absence of any Lewis acid. When the aziridine ring is on the opposite side of the tetrahydropyran ring only the azido amide is obtained.



97 **98** **99**

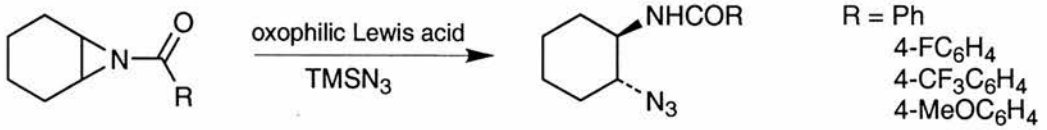
Ring-opening reactions of aziridines with trimethylsilyl compounds can be initiated by tetrabutylammonium fluoride (TBAF).[40] TBAF reacts with Me_3SiX to form the reactive $Bu_4N^+X^-$ species. It was found that electron-withdrawing substituents were necessary and are expected to stabilize the leaving group during nucleophilic attack. Ring opening of the *N*-benzoylcyclohexenimine **20** using TBAF and trimethylsilyl azide or trimethylsilyl cyanide afforded *N*-(2-azidocyclohexyl)benzamide **100a** (82%) and *N*-(2-cyanocyclohexyl)benzamide **100b** (88%) respectively. Apart from supplying the nucleophile, Me_3SiX is also thought to displace Bu_4N^+ from the nitrogen. The reaction does not proceed in the absence of TBAF.



20 **100**

This reaction also proceeds with electron withdrawing groups present on the benzoyl group. *N*-Acylcyclohexenimines **101** were easily ring opened using $TMSN_3$ in the presence

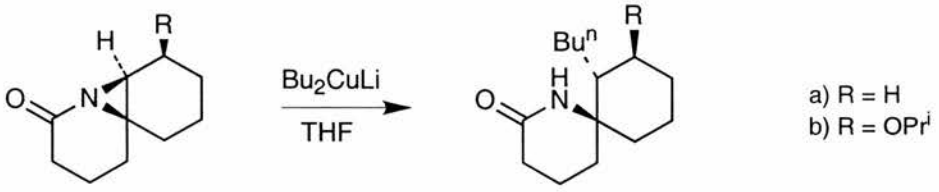
of oxophilic Lewis acids (such as Yb(2,2'-biphenol)OTf) to give *N*-(2-azidocyclohexyl) benzamides **102** as before.[41]



101 **102**

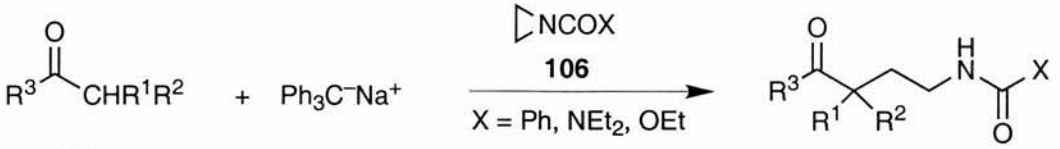
6. Addition of carbanions

The tricyclic acylaziridine **103a** was reacted with lithium dibutylcuprate at room temperature to give the lactam **104a** in approximately 65% yield.[42] The yield was difficult to calculate because of the volatility of the lactam when R=H. As would be predicted the aziridine ring opens via attack of its least hindered, more positive carbon rather than the quaternary one. The yield **104b** is not given.



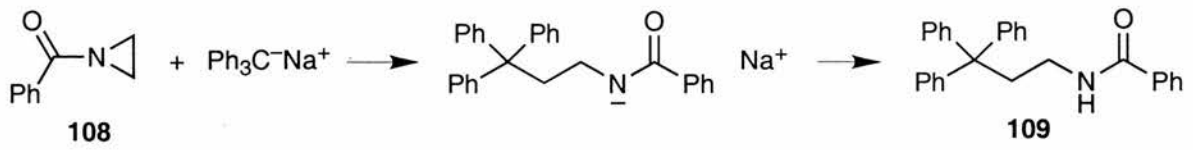
103 **104**

The *C*-amidoethylation of the enolates of simple ketones **105** with *N*-acylaziridines **106** represents a one-step syntheses of *N*-(4-oxoalkyl)-carboxamides **107**,[43] which may be regarded as protected γ-aminoketones. The ketones are deprotonated with tritylsodium in THF then reacted with the aziridine derivatives. Some α,α-bis amidoethylation may occur, usually with methyl ketones. R^1 and R^2 are usually H, Me or Ph.



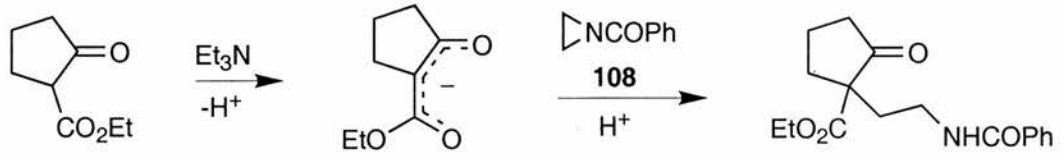
105 **107**

However the trityl anion can itself effect the ring opening by attacking a ring carbon of the aziridine **108** to give the amide **109**.[44]



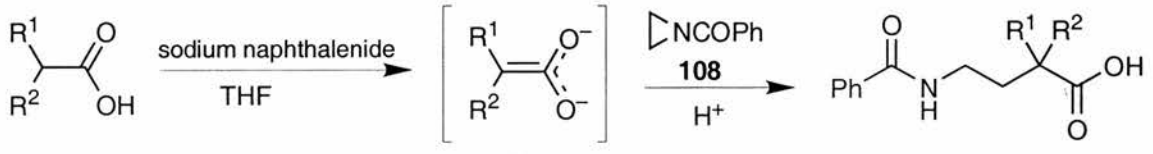
108 **109**

The β-ketoester **110** is firstly partially deprotonated by Et_3N (**111**) without solvent. Since **110** is a β-dicarbonyl compound enolisation occurs more readily at the α-carbon between the two carbonyls. This is then amidoethylated using *N*-benzoylaziridine **108** to give compound **112** in 64% yield.[45]



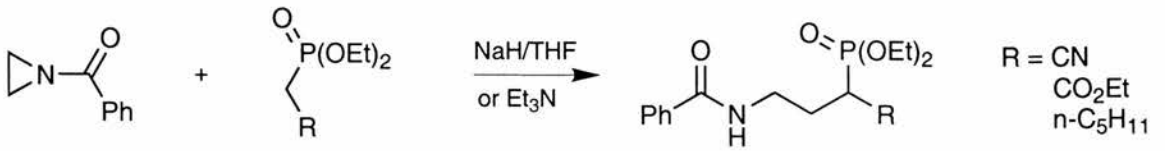
110 **111** **112**

Dianions **114** of carboxylic acids **113** formed by deprotonation using sodium naphthalenide can easily be amidoethylated with *N*-benzoylaziridines **108** yielding the γ-amidobutyric acids **115** (38-76%).[46] R^1 is mainly Ph and R^2 is mainly H or Me.



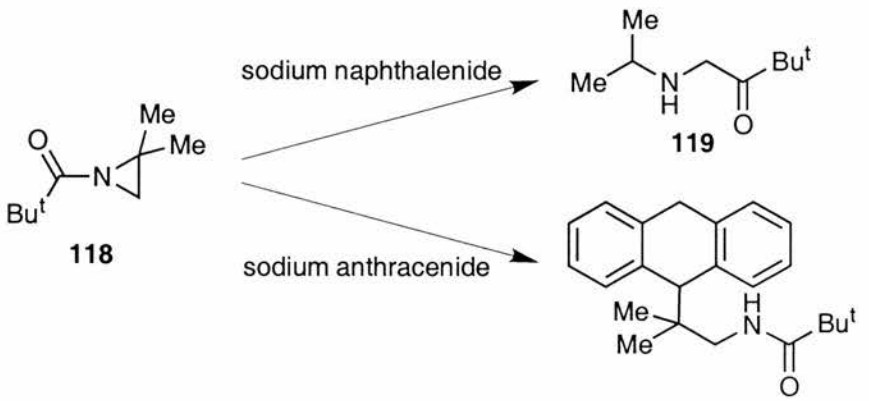
113 **114** **115**

The γ–amidopropanephosphonic esters **117** can be made from *N*-benzoylaziridines **108** in either of the two ways shown below.[47] In the first, the phosphonates **116** were deprotonated with sodium hydride in a suitable solvent (usually THF) and then *N*-benzoylaziridine **108** was added. In the second method triethylamine, aziridine **106** and the phosphonate **116** were mixed, usually without solvent. An excess of **116** was employed to suppress secondary reactions by protonating anionic primary products. The carbon next to phosphorus is deprotonated and attacks at the aziridine ring carbon opening the ring to give **117**.



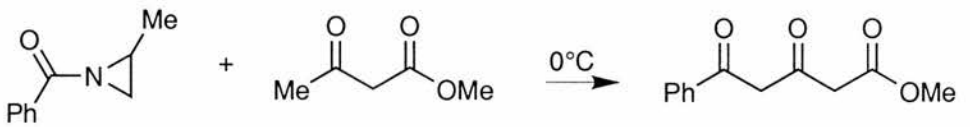
108 **116** **117**

Reaction of sodium naphthalenide with the 2,2-dimethyl-*N*-pivaloylaziridine **118** for one hour provided **119** (43%).[48] With an excess (3:1) of sodium anthracenide only the amidoethylated dihydroanthracene **120** was obtained (75%) after completion of the reaction.



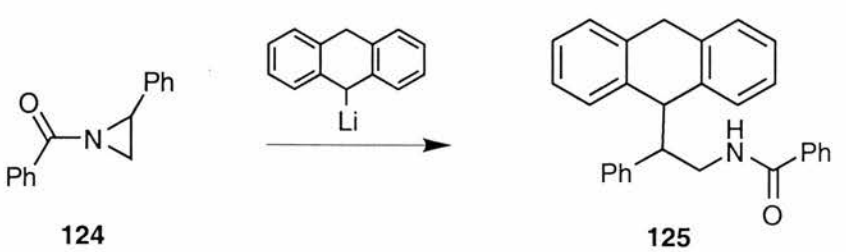
118 **119** **120**

Adding *N*-benzoyl-2-methylaziridine **121** to the carbanion of methyl acetoacetate **122** forms methyl 3,5-dioxo-5-phenylpentanoate **123** in 98% yield.[49] The carbanion is formed from the ester using 2 equivalents of NaH. The carbanion attacks the aziridine at the carbonyl displacing the aziridine ring.



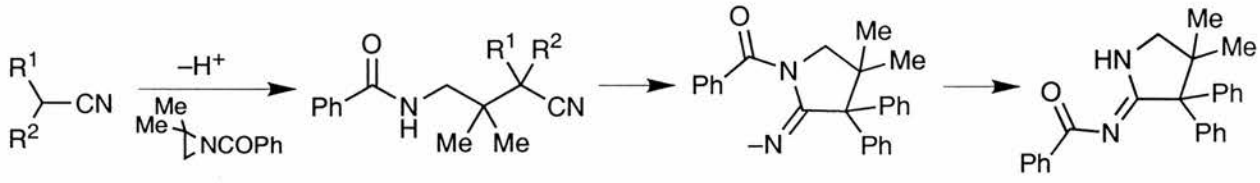
121 **122** **123**

The carbanion of 9,10-dihydroanthracene attacks the *N*-benzoyl-2-phenylaziridine **124** at the most positive ring carbon (next to the phenyl group) opening the ring to give the amide **125**.[50]



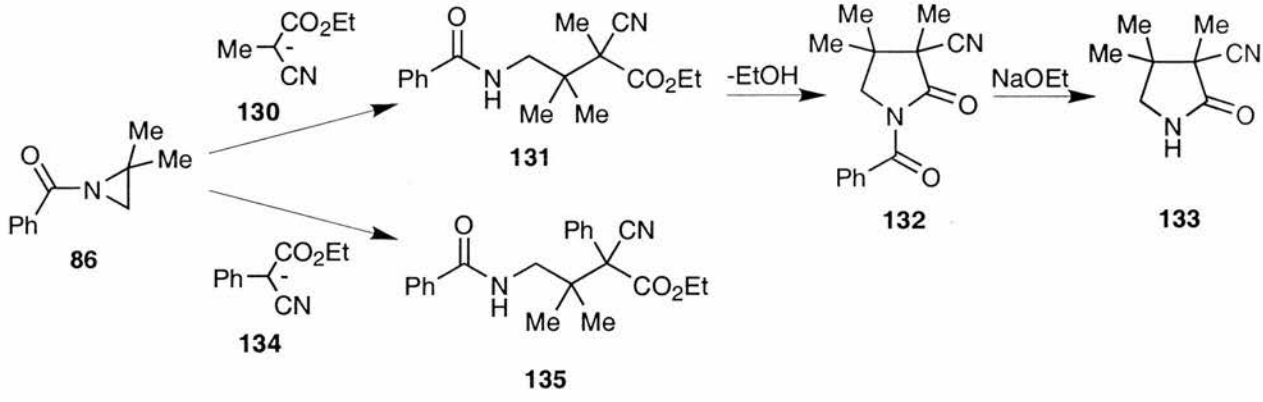
124 **125**

The anion of the nitrile compound **126** attacks the *N*-benzoyl-2,2-dimethylaziridine **86** on the dimethyl carbon to form the ring-opened benzamide **127**.[51] This is an abnormal ring opening i.e. at the most hindered position. All nitriles give mainly the acyclic products except when R^1=R^2=Ph with Ph_3CNa as base when only the cyclised product **129** is formed via **128**.



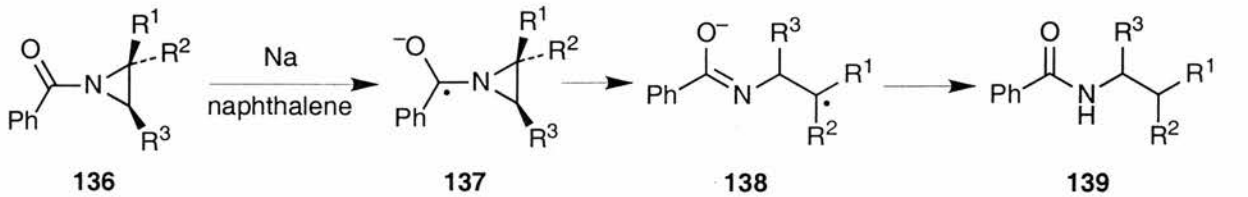
126 **86** **127** **128** **129**

When the aziridine **86** is reacted with ethyl 2-cyanophenylacetate anion the reaction stops at the ring-opened amide **135**. On the other hand, if ethyl 2-cyanopropanionate is employed, the amide **131** cyclises to the pyrrolidin-2-one **132**. Under the conditions of the reaction (NaOEt/EtOH), the benzoyl group is removed to give **132**. In both reactions the ring opening is considered abnormal.[52]



86 **130** **131** **132** **133** **134** **135**

Disubstituted *N*-benzoylaziridines **136** (one of the three R groups is always H) react with sodium and naphthalene in tetrahydrofuran to form the benzamide shown below as the major product.[53] Firstly a ketyl **137** is produced which then undergoes homolytic ring

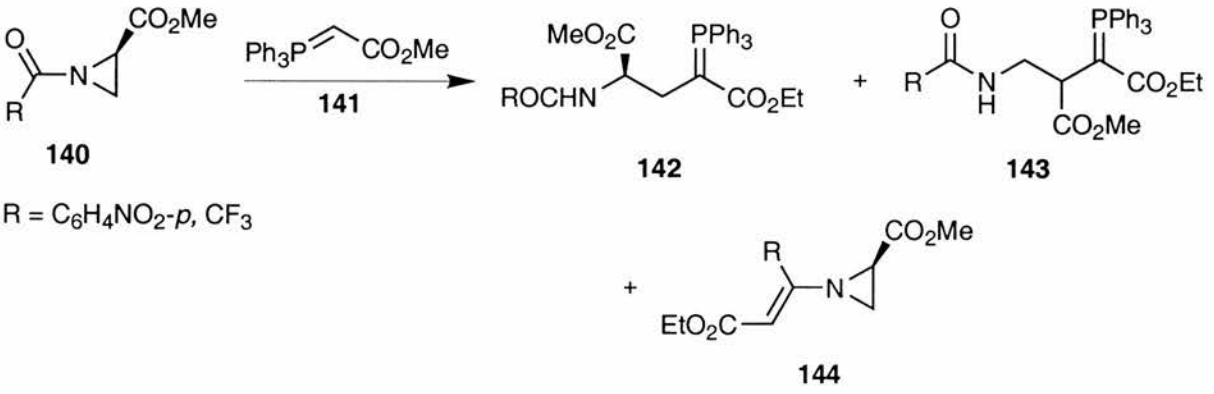


136 **137** **138** **139**

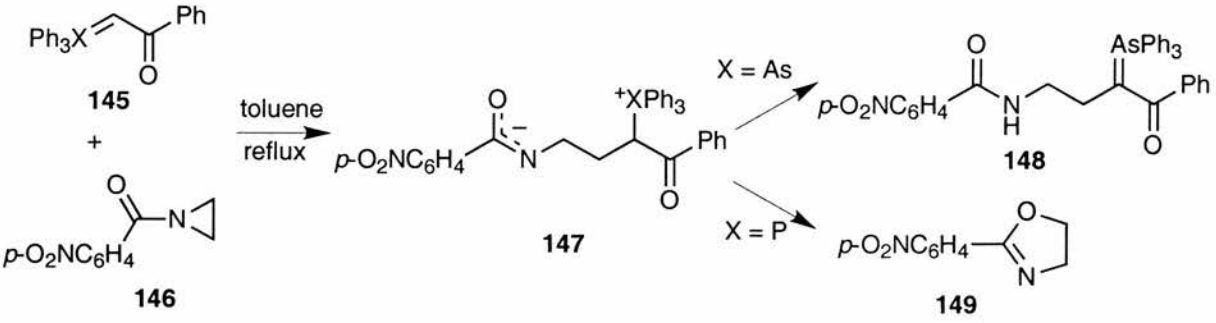
opening to form a more stable radical **138**. The reaction is quenched by hydrogen abstraction from the solvent to give **139**. Other, minor products can arise from dimerisation or disproportionation.

7. Addition of P and As ylides

Reaction of methyl *N*-acylaziridine-(2*S*)-carboxylates **140** with the carbonyl stabilised Wittig reagent methyl (triphenylphosphoranylidene)acetate **139**, provides an isolable optically-pure phosphorus ylide **142** (49%).[54] The opposite regioisomer **143** (12%) plus an unwanted β-aziridinoacrylate **144** (16%) are also formed. When an *N*-trifluoroacetylaziridine was used the sole product was compound **144**.



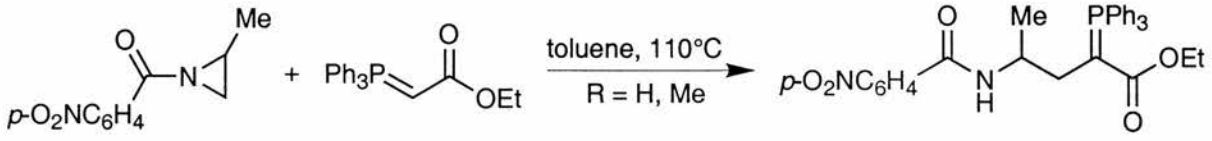
Heating triphenylarsonium phenacylide **145** and *N*-*p*-nitrobenzoylaziridine **146** in toluene gives *N*-(γ-benzoyl-γ-triphenylarsenanylpropyl)-*p*-nitrobenzamide in 41% yield.[55]



Firstly the carbanionic centre attacks the aziridinyl carbon opening the ring to give **147**. Then the arsenic compound **148** is formed via a proton transfer to the nitrogen.

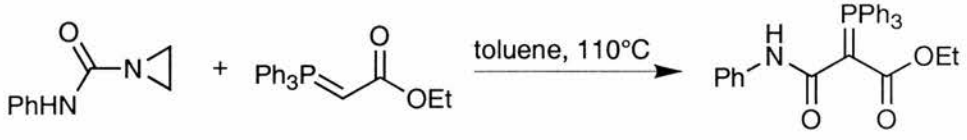
In contrast, the phosphorus analogue catalyses the isomerisation of **146** to 2-*p*-nitrophenyl-2-oxazoline **149**. Heating *N*-*p*-nitrobenzoylaziridine **146** in toluene alone results in complete recovery of the starting material.

The carbanionic centre of the phosphorus ylide **151** attacks the more positive of the ring carbons of the *N*-*p*-nitrobenzoylaziridine **150** to give an ylide amide **152.**[56]



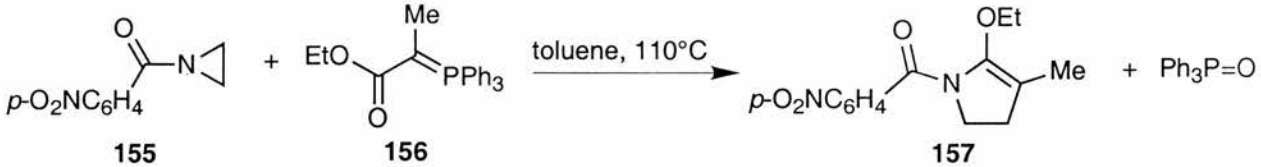
150 **151** **152**

When a carbamoyl aziridine **153** is used, ylide **151** is acylated as it attacks the carbonyl displacing the aziridine ring to produce **154**.



153 **151** **154**

Reaction of aziridine **155** with the ethyl 2-triphenylphosphoranylidenepropionate **156** in boiling toluene gave 1-(*p*-nitrobenzoyl)-2-ethoxy-3-methyl-2-pyrroline **157**. After the initial attack of the ylide, the amide nitrogen could attack the ester group to yield a Wittig intermediate. This would then behave in the usual way to eliminate triphenylphosphine oxide and form the carbon-carbon double bond.

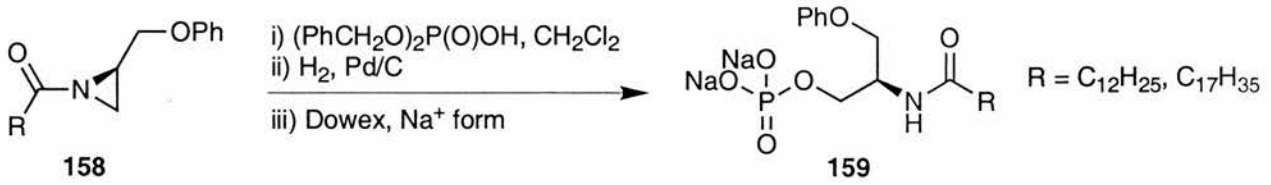


155 **156** **157**

8. Addition of phosphate and other phosphorus nucleophiles

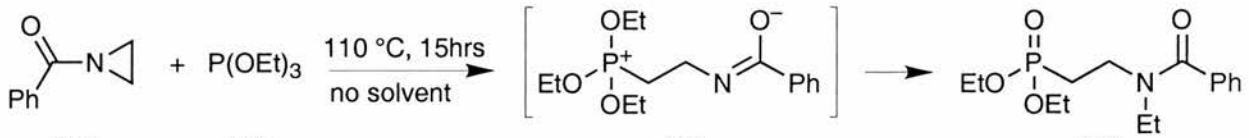
The ring opening of the *N*-acyl-2-phenoxymethylaziridines **158** was performed at 40 °C in a two phase system comprising an aqueous phosphate buffer and an organic layer in which the starting material is present.[57] Using a buffer concentration of 10 mM increased the

rate and gave complete regioselectivity. Due to attack of a phosphate anion on the aziridine ring carbon exposed to the aqueous phase only one isomer is obtained. The reaction that produces compound **159** occurs at the organic-aqueous interface. C-3 is exposed to the aqueous side since the long aliphatic chain and the phenyl ring remain in the organic phase whilst the carbonyl aligns with the hydroxyl of the phosphate.



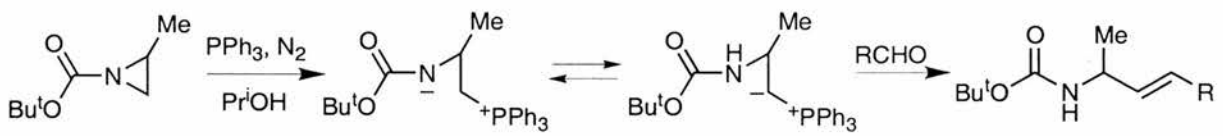
158 **159**

Heating *N*-benzoylaziridine **108** and triethyl phosphite **160** together at 110 °C with no solvent gave the diethyl 2-amidoethylphosphonate **162** in 66% yield (by NMR).[58] Interestingly, one of the phosphite ethyl groups migrates to the nitrogen.



108 **160** **161** **162**

It is possible for aziridines to react with triphenylphosphine to give intermediates which then undergo Wittig type reactions with aldehydes.[59] Thus *N*-Boc aziridine **163** forms a phosphorus ylide **164** and its carbanionic centre attacks the carbonyl of the aldehyde and forms the alkene **165** in the usual way.



163 **164** **165**

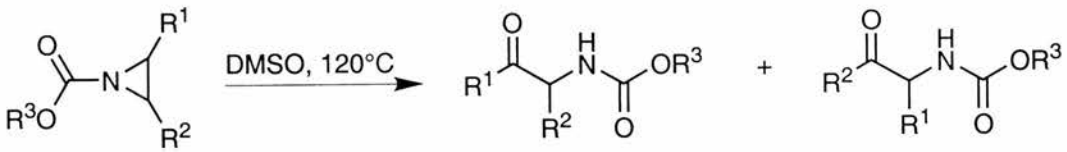
9. Reaction with DMSO

Heating *N*-*p*-nitrobenzoyl-2-phenylaziridine **166** in DMSO at 117 °C produced *N*-phenacyl-*p*-nitrobenzamide **167** in 83% yield.[60] The more positive, phenyl bearing ring

carbon is attacked by the oxygen of DMSO. Rearrangement of the intermediate then results in loss of dimethyl sulfide to yield the product amide.

166 **167**

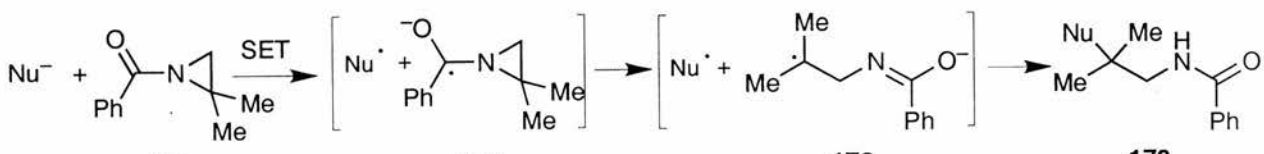
The oxidative ring opening of the *N*-alkoxycarbonylaziridines **168** by dimethyl sulfoxide produces either regioisomer of the alkoxycarbonylamino ketone **169** and **170**.[61] This occurs via an attack of DMSO on either of the aziridine ring carbons. Of the five examples given only one was studied more detail. *Trans*-**168** (R^1 = Ph, R^2 = Me, R^3 = Et) under varying condition gave 93–100% of **169** whereas the *cis*-isomer produced a mixture of both products.



168 **169** **170**

10. S_{RN} Reaction with nucleophiles

The following process is considered to be an abnormal ring opening as a nucleophile would be expected to attack the most positive ring carbon of *N*-benzoyl-2,2-dimethylaziridine **86**.[62] A single electron transfer (SET) mechanism was proposed in view of this anomaly.



86 **171** **172** **173**

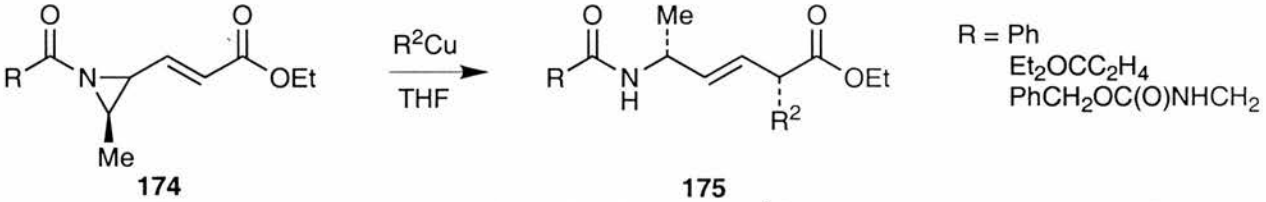
Single electron transfer from the nucleophile gave the ketyl **171**, which rearranges cleaving the ring to give **172**. The radicals then combine to form the product amide **173**. The aziridine is only weakly activated thus slowing down nucleophilic substitution and enabling

SET to occur. (Nu = *p*-$PhC_6H_4CH^-CN$, $EtPhC^-CN$, $PhC^-(CN)CO_2Et$, fluorenyl and piperidine.)

C. S_N' Attack on *C*-vinyl aziridines

1. Intermolecular

There are several electrophilic sites that are potential points of attack on the alkenylaziridines **174** for organocuprate reagents. The desired α-alkylation product **175** was obtained by predominantly *anti* S_N2'-reaction of the organocuprate (>81:19 *anti/syn*).[63] Generally, the formation of (*E*)-alkenyl amides was accompanied by γ-alkylation and reduction products. SET from the copper(I) species followed by hydrogen radical abstraction or enolisation of the α-copper(III) species could account for the reduction product. The



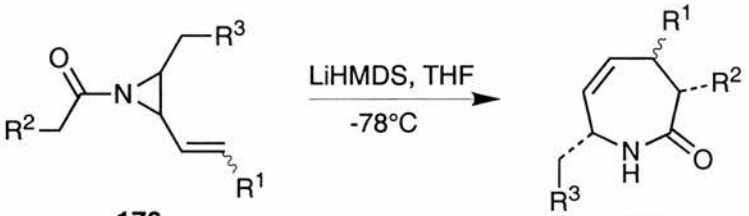
174 **175**

trans-oxazoline was also observed, although only in a significant amount when 3 equivalents $PhCu.BF_3$ in diethyl ether are used. No *O*-alkylation or conjugate addition products were observed. The best results were obtained with alkylcopper reagents R^2Cu in the presence of boron trifluoride etherate. Nucleophilic attack on the *N*-benzoylated substrate led to significant amounts of γ-alkylation. This was not the case with *N*-sulfonated or Boc-protected aziridines and therefore higher yields were observed (70-90%).

2. Intramolecular

When *N*-acetyl vinylaziridine **176** was added to LiHMDS at -78°C followed by a slow warming of the resultant mixture to room temperature, seven membered lactam rings

177 were formed via a highly stereoselective aza-[3,3]-Claisen rearrangement.[64] Bond formation between the enolate and the alkene and opening of the aziridine gives the observed lactam. It is assumed the olefin and enolate moieties involved are *cis* in order to facilitate bond formation and that both these groups adopt an *endo* conformation. Several lactams were synthesised altogether in yields of 73-85%.

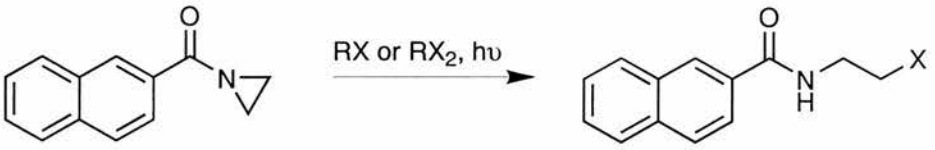


176 **177**

D. Radical Ring Opening

1. Photochemical

The photo-irradiation of *N*-(2-naphthoyl)aziridine **51** in halogenated hydrocarbons resulted in α-cleavage of the aziridine ring to afford halogen substituted secondary amides **178**, *N*-(2-chloroethyl)-2-naphthamide in CCl_4 (57%) and chloroform (55%) or *N*-(2-bromoethyl)-2-naphthamide (84%) in dibromomethane.[24]

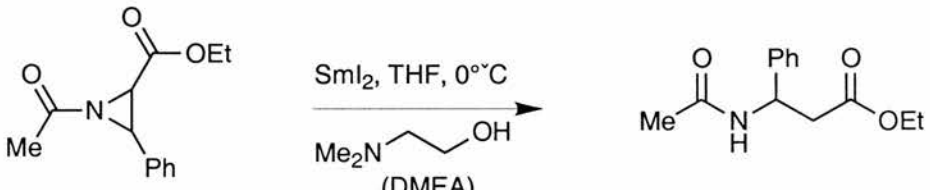


51 **178**

Photolysis of chloroform affords hydrogen chloride. The ring opening by alkyl halide is thought to proceed via an aziridinium salt.

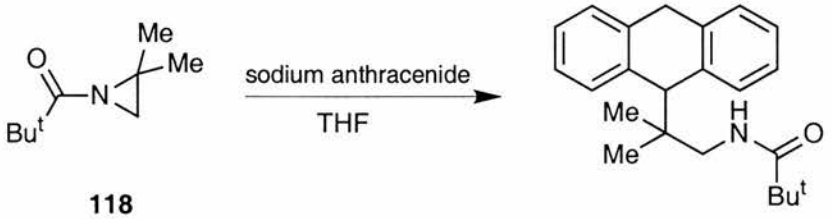
2. Chemically Induced

The *N*-acetyl-2-ethoxycarbonyl-3-phenylaziridine **179** is reduced by samarium iodide, cleaving the ring to give the β-amido ester **180** in 89% yield. Reaction of samarium iodide with the ketone carbonyl generates a ketyl, which is rapidly protonated by DMEA.[65] At this stage cleavage of the nitrogen heterocycle could occur by two diferent pathways. The protonated ketyl could undergo further reduction by the second equivalent of samarium iodide, producing a carbanion. This anion would then induce the ring opening of the aziridine. Tautomerisation of the intermediate enol would provide the observed amino ketone, with loss of stereochemistry adjacent to the carbonyl. Alternatively, the protonated ketyl could undergo a radical ring scission, producing the nitrogen radical. Further reduction of the nitrogen radical to the nitrogen anion by the second equivalent of samarium iodide followed by protonation would lead to the observed product.



179 **180**

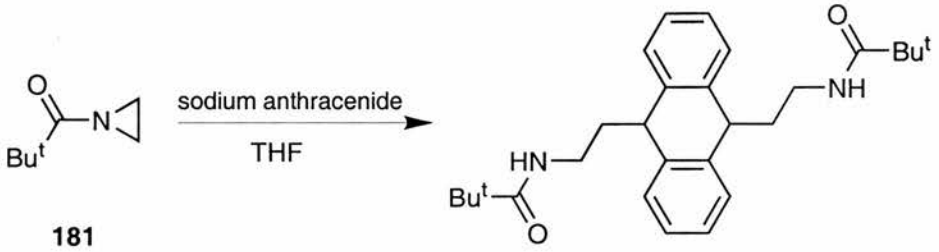
Reacting 2,2-dimethyl-*N*-pivaloylaziridine **118** with an excess (3:1) of sodium anthracenide gave only the monoamidoethylated dihydroanthracene **120** in 75% yield after completion of the reaction (10–20mins) and in 26% yield after a 10 second reaction time.[48]



118 **120**

However, pivaloylaziridine **181** forms a diamide **182** with sodium anthracenide. This is because the intermediate monosubstituted anthracene anion is more reactive than the one generated from the 2,2-dimethylaziridine **118**. Traces of the monosubstituted product are

only detected when a large excess of anthracenide is employed. Both of these reactions proceed via a ketyl which rearranges cleaving the aziridine ring as in earlier examples.

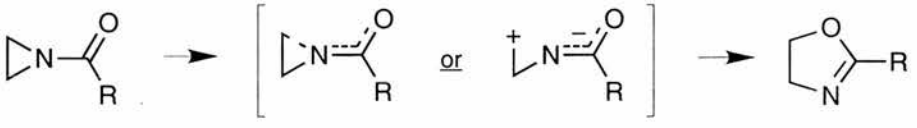


181 182

E. Ring expansion to oxazolines

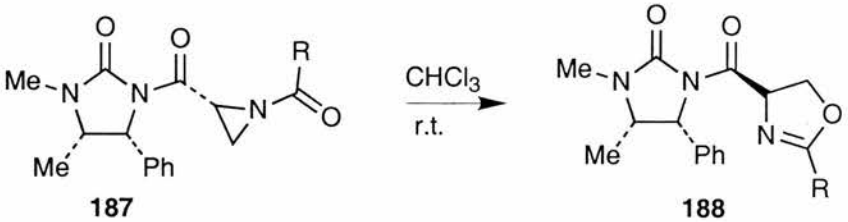
1. Thermal

The rearrangement from *N*-acylaziridine **183** to oxazoline **186** is thought to occur via a four membered transition state.[66] This could be in the form of a tight ion pair intermediate **185** or via a concerted pathway **184** both involving attack of the acyl oxygen on the more positive carbon of the ring.



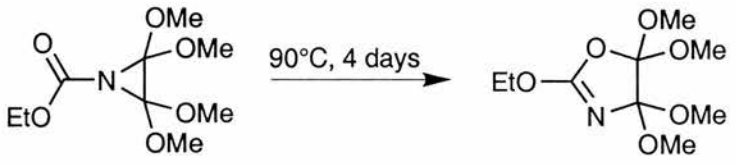
183 184 185 186

The rearrangement from acylaziridine **187** (R = Me, Ph) to oxazoline **188** was found to occur cleanly and regioselectively after stirring the aziridine in chloroform at room temperature for 10 hours (>95%).[21]



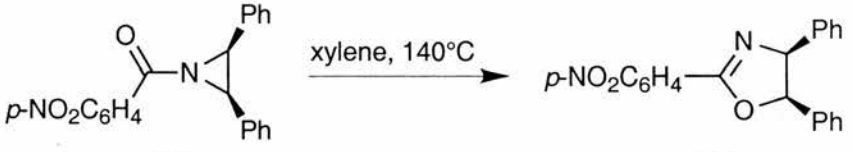
187 188

N-Ethoxycarbonyl-2,2,3,3-tetramethoxyaziridine **189** was heated at 90 °C for 4 days to give entirely the 2-ethoxy-4,4,5,5-tetramethoxyoxazoline **190**.[67] Since all the substituents at C-2 and C-3 are identical there can be no regio or stereoisomers.



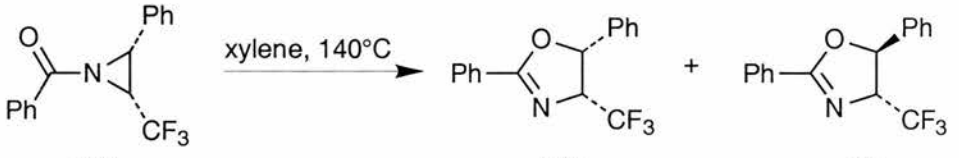
189 **190**

Thermolysis of *cis-N-p*-nitrobenzoyl-2,3-diphenylaziridine **191** gave *cis*-2-*p*-nitrophenyl-4,5-diphenyl-2-oxazoline **192**. Similarly *trans-N-p*-nitrobenzoyl-2,3-diphenylaziridine gave *trans-N*-2-*p*-nitrophenyl-4,5-diphenyl-2-oxazoline.[68] Thermolysis of *cis-N*-benzoyl-2,3-diphenylaziridine gave recovery of the starting material and a residue which could not be characterised. This perhaps suggests that the para-nitro group activates the aziridine towards ring expansion in this case.



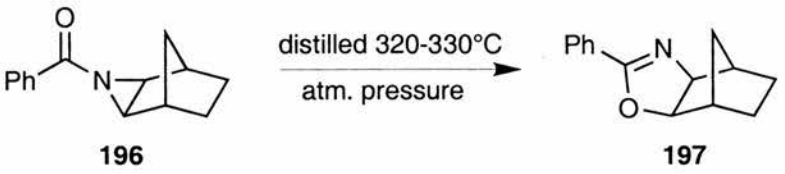
191 **192**

The *N*-benzoyl-3-trifluoromethyl-2-phenylaziridine **193** rearranges when pyrolysed at 140°C for 52 hours to both *cis* and *trans* isomers **194** (21%) and **195** (7%) of the corresponding 2-oxazoline.[69]



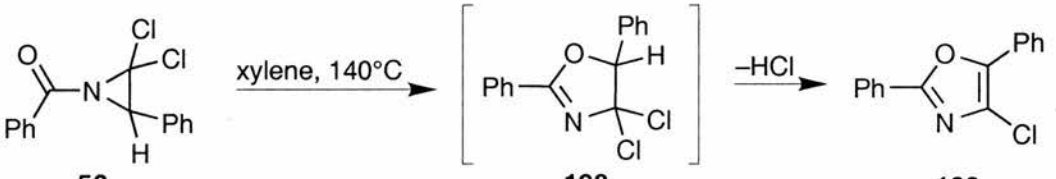
193 **194** **195**

3-Benzoyl-3-azatricyclo[3.2.1.$0^{2,4}$]octane **196** rearranges to 2-phenyl-4,7-methano-hexahydrobenzoxazole **197** when distilled at atmospheric pressure.[70]



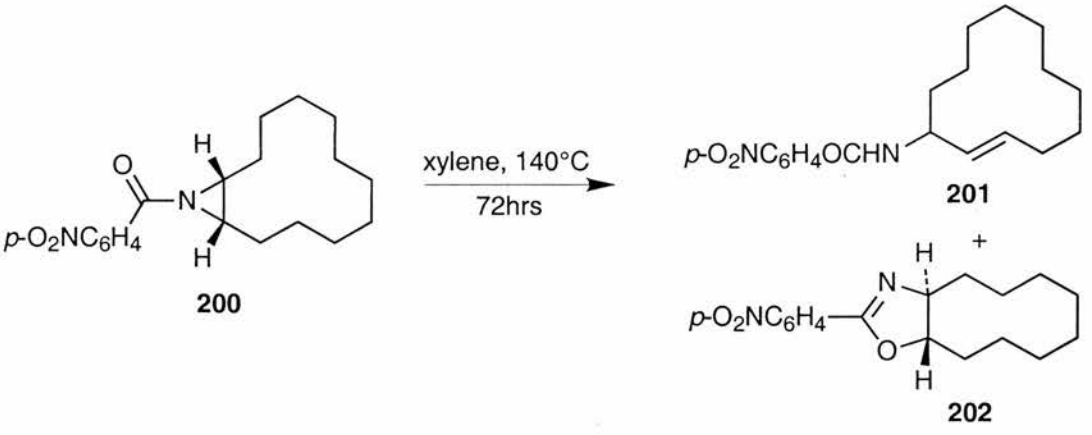
196 197

The thermolysis of *N*-benzoyl-2,2-dichloro-3-phenylaziridine **56** is an interesting example. It rearranges to the oxazoline **198** when heated in boiling xylene, but HCl is then eliminated to give the oxazole **199** in good yield (81%).[25]



56 198 199

Pyrolysis of *cis*-13-*p*-nitrobenzoyl-13-azabicyclo[10.1.0]tridecane **200** in xylene afforded *N*-(*E*-2-cyclododecenyl)-*p*-nitrobenzamide **201** and *trans*-2-*p*-nitrophenylcyclododecano[4,5]oxazoline **202** in a ratio of 7:1 (no yields given).[71] Models have shown that the carbonyl oxygen can approach *cis* or *trans* aziridine hydrogens without much conformational change to the ring.

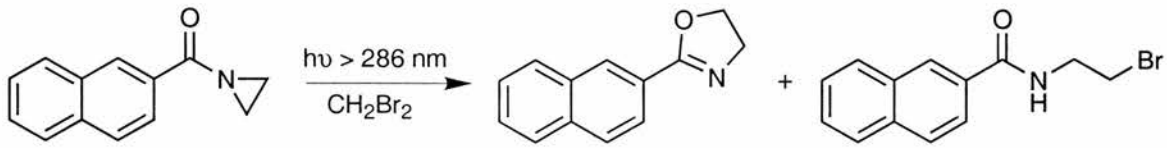


200 201 202

2. Photochemical

The photo-irradiation of *N*-(2-naphthoyl)aziridine **51** at wavelengths of greater than 286 nm in dibromomethane resulted in the formation of 2-(2-naphthyl)-2-oxazoline **203** (52%) along with *N*-(2-bromoethyl)-2-naphthamide **204** (17%).[24] What is not clear is

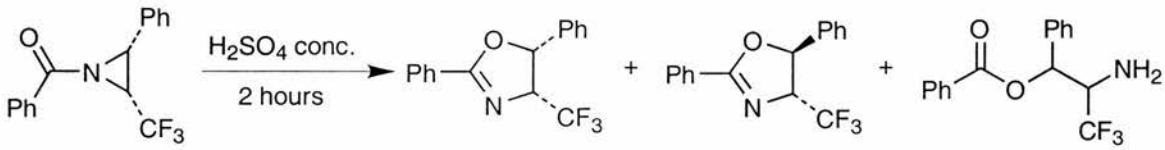
whether this is an acid catalysed reaction since photolysis of dibromomethane gives hydrogen bromide.



51 **203** **204**

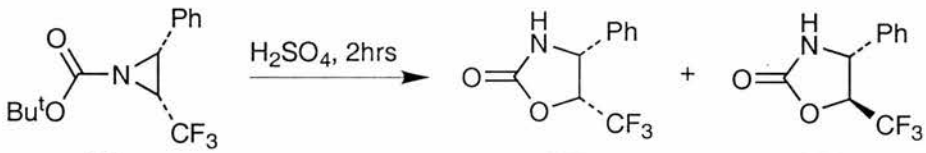
3. Brønsted acid catalysed

The *N*-benzoylaziridine **193** rearranges when reacted with concentrated sulfuric acid at room temperature to both *cis* and *trans* isomers **194** (6%) and **195** (38%) of the corresponding 2-oxazoline along with an amino ester **205** of undetermined stereochemistry.[69]



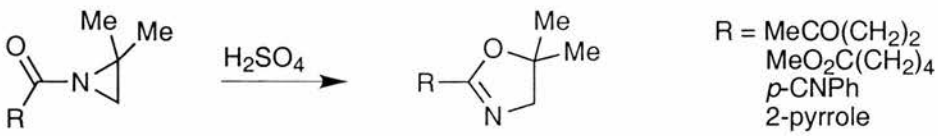
193 **194** **195** **205**

Interestingly, the *N*-Boc derivative **206** forms both *cis* and *trans* oxazolidinones **207** (24%) and **208** (29%) upon treatment with 50% sulfuric acid.[69]



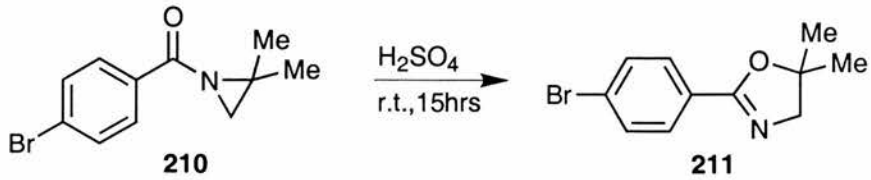
206 **207** **208**

The *N*-acyl-2,2-dimethylaziridines **35** rearrange smoothly to the 5,5-dimethyloxazolines **209** using a catalytic amount of sulfuric acid at room temperature in ether or dichloromethane (50-80%).[72]



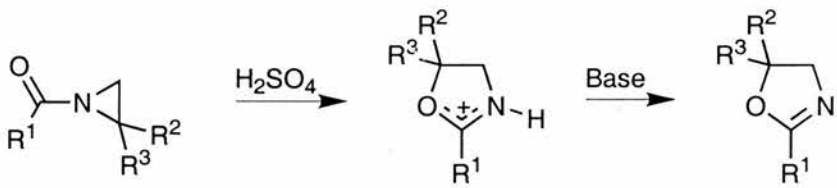
35 **209**

Sulfuric acid also catalyses the rearrangement of *p*-bromobenzoyl-2,2-dimethylaziridine **210** to 2-(4-bromophenyl)-5,5-dimethyl-2-oxazoline **211**.[73]



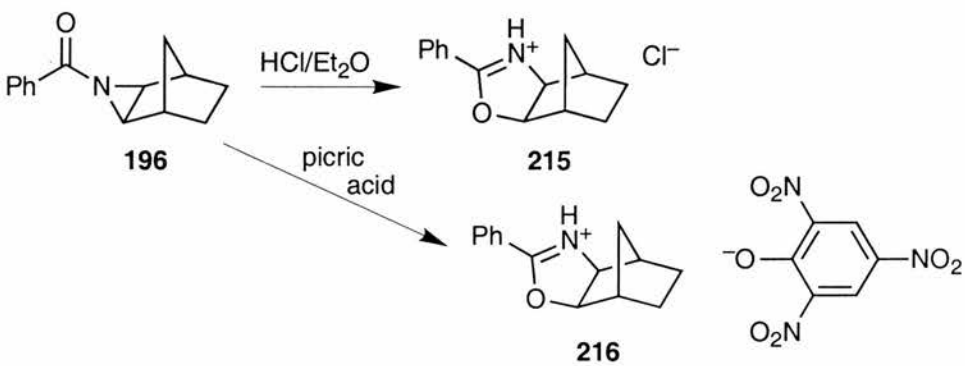
210 **211**

It has been proposed that *N*-acylaziridines **212** rearrange to 2-oxazolines **214** by sulfuric acid via their oxazolinium ions **213**.[74] *O*-Protonated aziridines were not observed. The *N*-protonated species **213** were identified by examination of their NMR spectra, isolation and subsequent identification as 2-oxazolines and the synthesis of the same cationic species from authentic samples of 2-oxazolines.



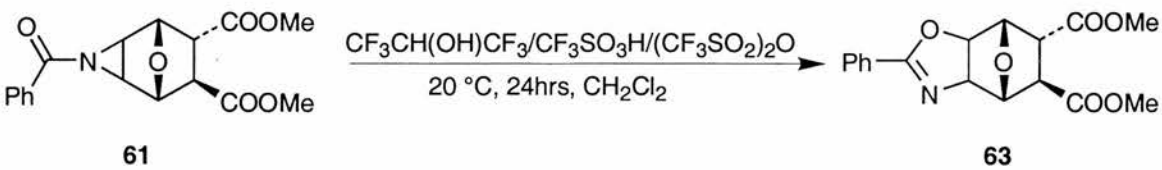
212 **213** **214**

Reacting the tricyclic *N*-benzoylaziridine **196** with hydrochloric acid and picric acid gives the chloride **215** (20%) and the picrate **216** (26%) respectively.[70]



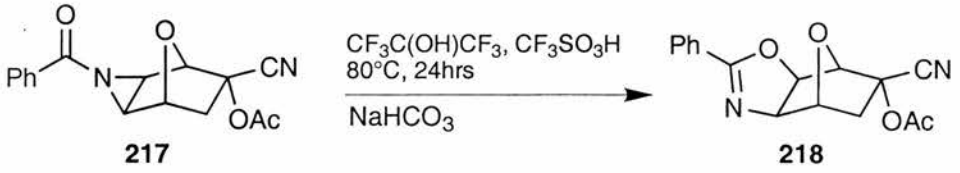
196 **215** **216**

In $CF_3CH(OH)CF_3$ containing triflic acid and triflic anhydride, the dimethyl 3-benzoyl-8-oxa-3-azatricyclo [3.2.1.$0^{2,4}$]octane-6,7-dicarboxylate **61** was rearranged readily and quantitatively to the oxazoline **63** (77%).[27]



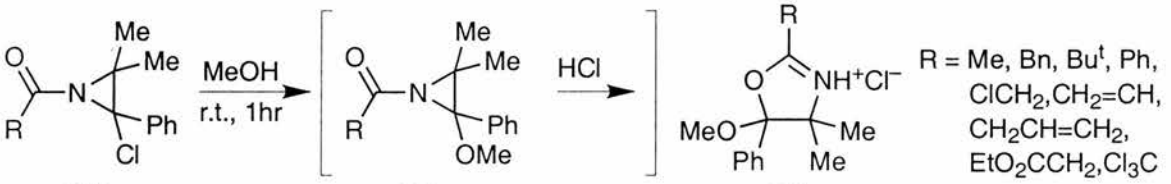
61 **63**

Heating the *N*-benzoylaziridine **217** in $CF_3CH(OH)CF_3$ containing trifluoromethanesulfonic acid at 80°C for 2 hours gave the 2-oxazoline **218** (81%).[75]



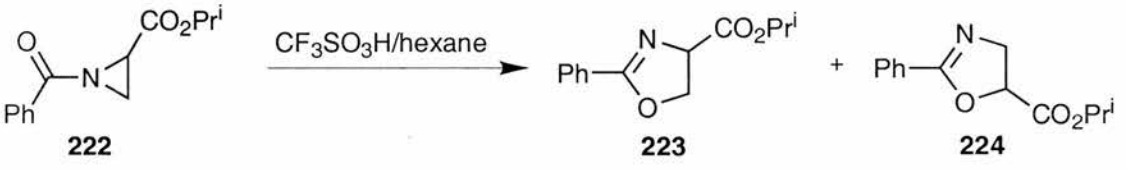
217 **218**

When chloroaziridines **218** were stirred in dry methanol for an hour, quantitative yields of methoxyoxazoline hydrochlorides **221** were obtained.[76] The solvent displaces chlorine generating **220** and HCl which in turn catalyses the ring expansion.



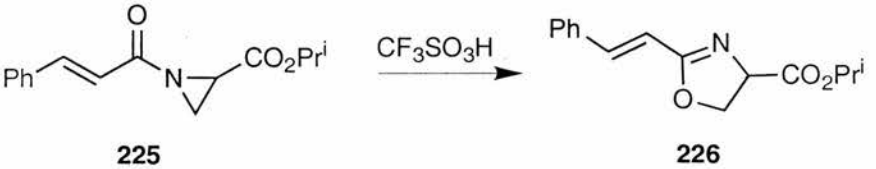
219 **220** **221**

Treatment of the *N*-benzoylaziridine-2-carboxylate **222** with trifluoromethanesulfonic acid gave both regioisomers **223** and **224** of the ring expanded products (~6:1 in favour of the 4-carboxylate **223**).[77] No yields are reported in the paper.



222 **223** **224**

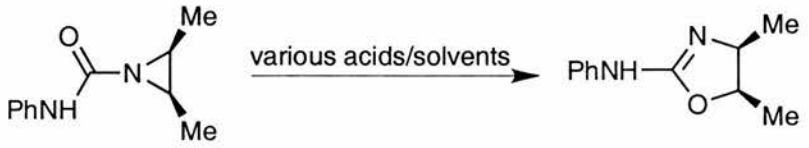
When an allyl group is adjacent to the amido carbonyl as in compound **225**, solely the 4-carboxylate **226** is formed in 78% yield.



225 **226**

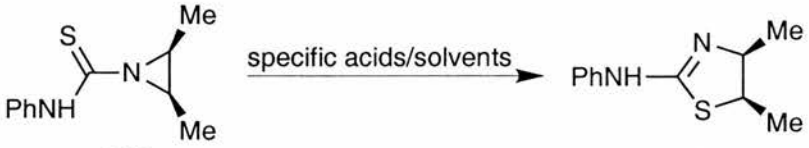
Cis-*N*-phenylcarbamyl-2,3-dimethylaziridine **227** was isomerised to *cis*-2-anilino-4,5-dimethyl-2-oxazoline **228** by *p*-toluenesulfonic acid in benzene (84%), THF (70%), DME (64%), DMF (52%) and nitromethane (76%).[78] This isomerisation can also be carried out

using 2,4,6-trinitrobenzenesulfonic acid in THF (50%) and with picric acid in benzene (74%), THF (82%), DME (72%), DMF (58%) and nitromethane (64%).



227 **228**

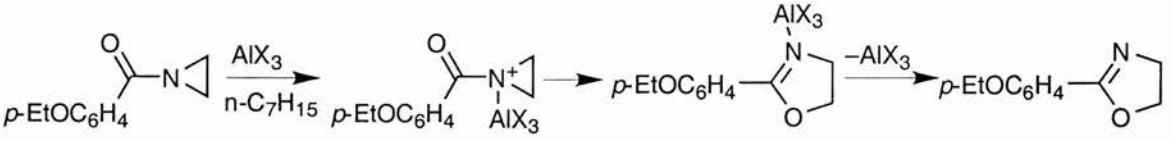
Interestingly, *cis*-*N*-phenylthiocarbamyl-2,3-dimethylaziridine **229** is similarly isomerised to *cis*-2-anilino-4,5-dimethyl-2-thiazoline **230** by *p*-toluenesulfonic acid in benzene (80%), TMF (68%), DME (75%), DMF (78%) and nitromethane (72%).[78] This can also be isomerised using 2,4,6-trinitrobenzenesulfonic acid in THF (70%) and picric acid using THF (72%) and DMF (83%). Using 2,4-dinitrophenol or trifluoroacetic acid in DMF gives only 42% and 40% yields respectively.



229 **230**

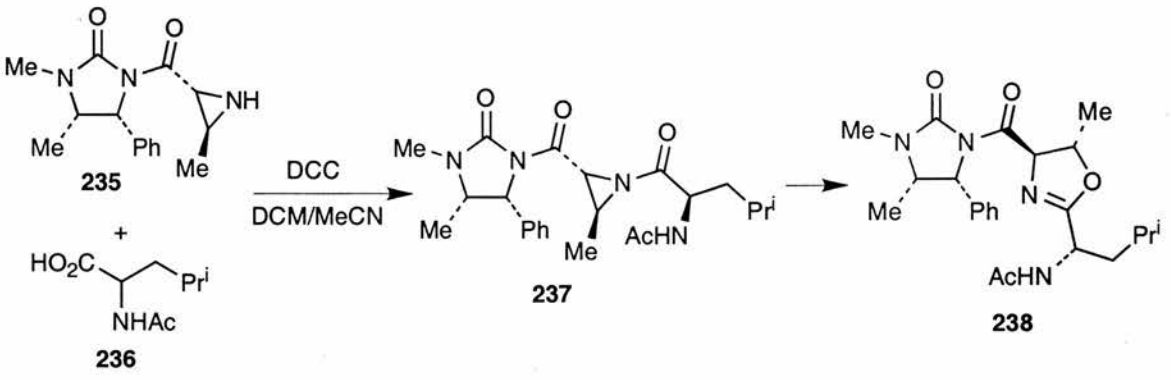
4. Lewis acid catalysed

N-*p*-Ethoxybenzoylethylenimine **231** was easily isomerised in heptane using aluminium chloride or bromide to give 2-*p*-ethoxyphenyl-2-oxazoline **234** in 97% yield.[79] The reaction proceeds via coordination of aluminium halide to nitrogen producing cation **232** which then rearranges to the oxazolinium salt **233**.

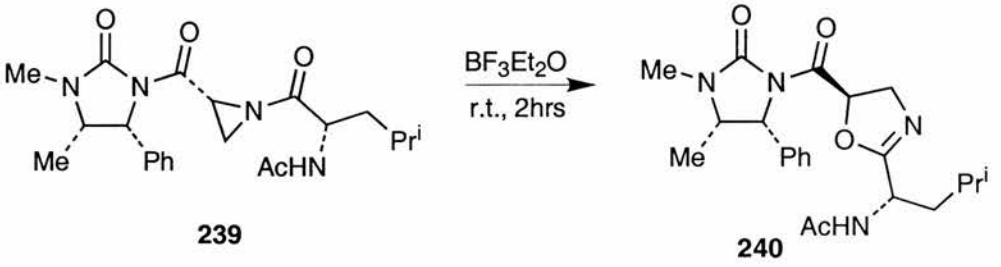


231 **232** **233** **234**

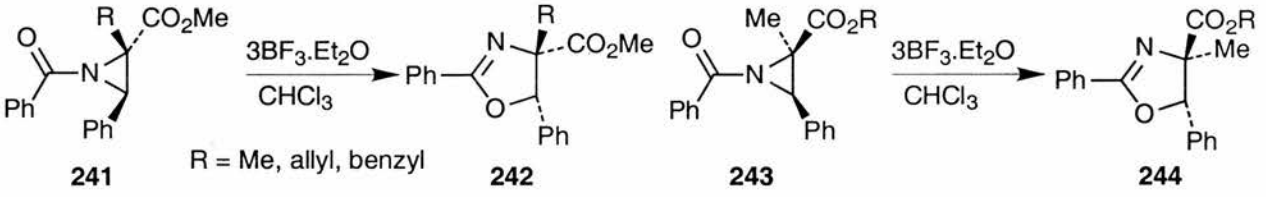
The enantiomerically pure aziridine **235** was treated with *N*-acetylleucine **236** and DCC giving the *N*-acylaziridine **237** in 95% yield. The acylaziridine moiety spontaneously isomerised to the oxazoline **238** in nearly quantitative yield.[80]



The aziridine-dipeptide **239** rearranged quickly upon treatment with $BF_3.Et_2O$ yielding a single regio and stereoisomer of the oxazoline **240**.[19]

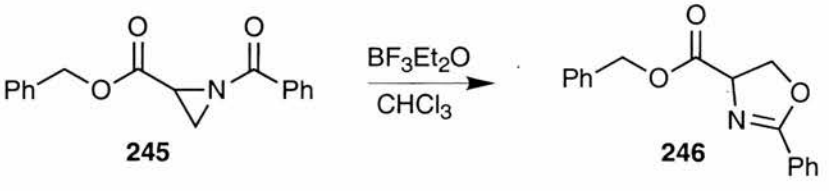


Trans-N-benzoylaziridine carboxylates **241** exclusively ring expanded to the *trans*-4-alkyl-2, 5-diphenyloxazoline-4-carboxylates **242** (>95%) using BF_3.[19] This process was completely regio- and stereoselective.



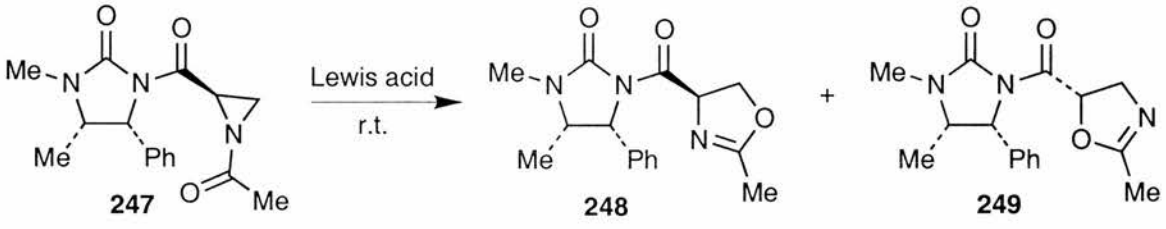
Also, when the carboxylate group is on the opposite face of the aziridine ring as in **243** the reaction proceeds in the same fashion to provide the 2-phenyloxazoline-4-carboxylate (94%) **244**.

Benzyl *N*-benzoylaziridine-2-carboxylate **245** forms the 2-oxazoline **266** as the sole product (no yield given) when treated with $BF_3.Et_2O$ in chloroform.[20]



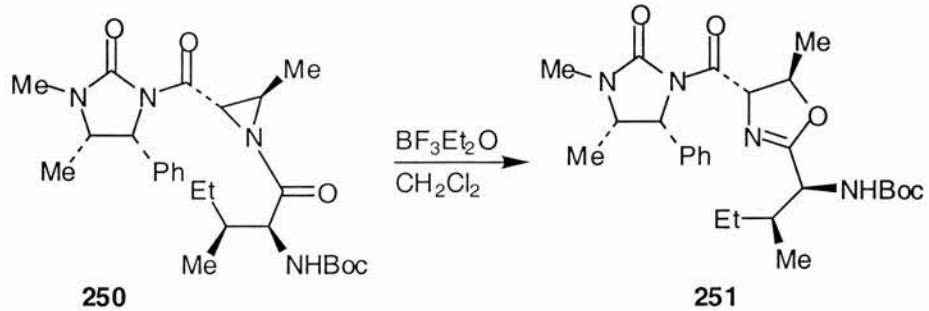
Selectivity studies on the reaction of **247** show that $MgBr_2.Et_2O$ favours the formation of the 4-imidazolidinoyl oxazoline **248**, while $BF_3.Et_2O$ gives the 5-imidazolidinoyl oxazoline **249** as the major product.[18] This result shows that the reaction could occur via attack of the carbonyl oxygen at either C-3 or C-2 on the ring, depending on the Lewis acid. Although all reactions completely convert the aziridine, a detailed analysis showed the presence of regiomeric oxazolines and ring-opened products derived from nucleophilic attack.

Lewis Acid	solvent	**248** : **249**	total yield (%)
$MgBr_2.Et_2O$	THF	85 : 15	95
$MgBr_2.Et_2O$	toluene	70 : 30	70
$BF_3.Et_2O$	THF	1 : 99	95
$BF_3.Et_2O$	toluene	45 : 65	85



247 **248** **249**

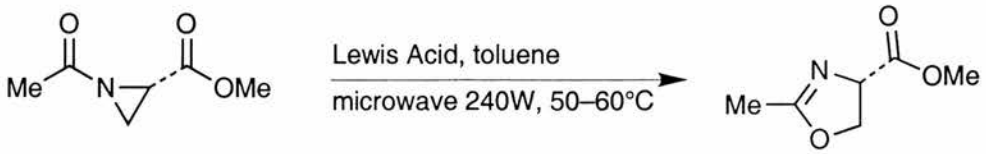
The Lewis acid catalysed ring expansion of aziridine **250** to oxazoline **251** is used here in the synthesis of a dipeptide derivative.[26]



250 **251**

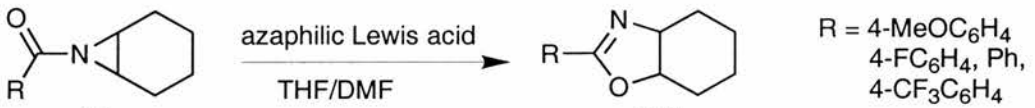
The (2*S*)-*N*-acetylaziridine methyl ester **252** was ring expanded under microwave assisted conditions in toluene and in the presence of various Lewis acids ($MgBr_2.Et_2O$,

$BF_3.Et_2O$, $Cu(OTf)_2$ and $Zn(OTf)_2$) to form (4*S*)-2-methyl-4-methoxycarbonyloxazoline **253** as the major product in yields of 40–75%.[18] Again by products arising from ring opening were observed as well as some unreacted starting material.



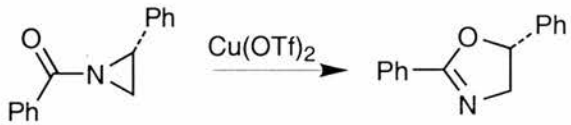
252 **253**

It was thought that more azaphilic salts such as $Zn(OTf)_2$, $Cu(OTf)_2$ and $Sn(OTf)_2$ would increase the chance of *N*-coordination but instead they induced the rearrangement of the aziridines **99** to 2-aryloxazolines **254** in the presence of a variety of nucleophiles.[40]



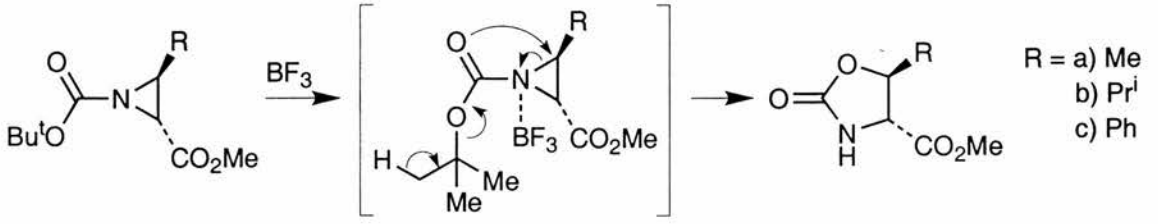
99 **254**

The *N*-benzoyl-2-phenylaziridine **255** is isomerised to the 2,5-diphenyloxazoline **256** induced by $Cu(OTf)_2$. This is the expected product since the carbonyl oxygen attacks the more electrophilic aziridine ring carbon.



255 **256**

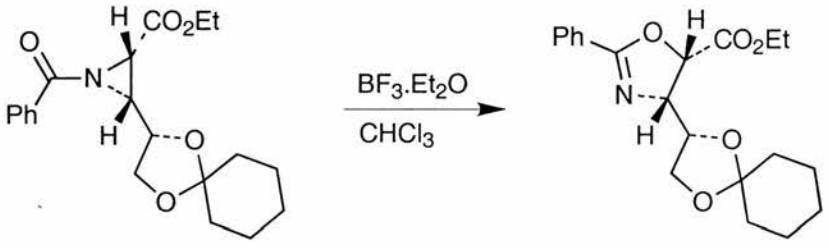
The *trans-N*-Boc aziridines **257** rearrange to the corresponding *trans*-4-methoxycarbonyloxazolidin-2-ones **259** catalysed by N-BF_3 coordination (**258**).[81] Compounds **259a** and **259b** are obtained in yields of 15% and 30% respectively catalysed by $BF_3.Et_2O$. The phenyl compound **259c** is produced in 98% and 92% yield by $BF_3.H_2O$ and $BF_3.Et_2O$ respectively.



257 **258** **259**

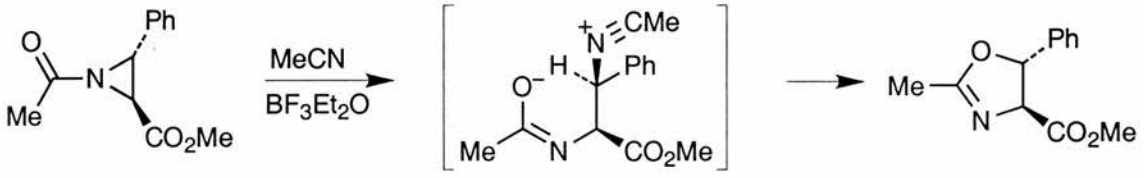
The best results are obtained using $Cu(OTf)_2$ which gives **259a**, **259b** and **259c** in 99, 85 and 98% respectively. In this case the metal coordinates to both nitrogen and the ester carbonyl.

The *cis*-aziridine **260** below also isomerises to the corresponding *cis*-oxazoline **261** using $BF_3.Et_2O$.[82] The oxazoline is obtained in 40% yield after 18 hours at room temperature whereas heating under reflux gave 60% yield after 2 hours.



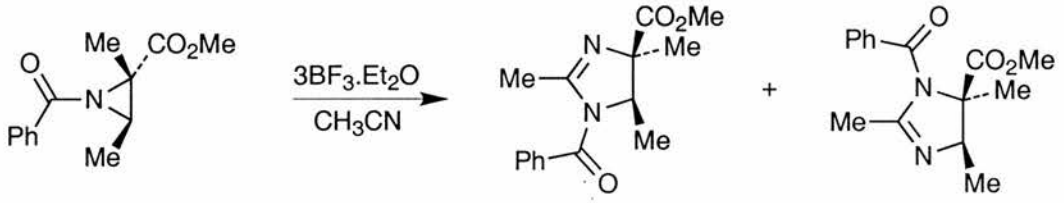
260 **261**

The *N*-acetylaziridinecarboxylate **262** undergoes a ring-expansion reaction to produce a *trans*-oxazoline **264** with a catalytic amount of boron trifluoride etherate in acetonitrile.[83] This reaction resembles the isomerisation of *N*-acylaziridines to oxazolines catalyzed by iodide. Iodide causes initial ring opening, which is followed by nucleophilic ring closure via S_N2 displacement of the iodide ion. This double inversion gives a net retention overall. In this case acetonitrile serves as the nucleophile for the initial ring opening to give a zwitterionic intermediate **263**, which then cyclises to the oxazoline **264** by expulsion of the nitrile unit.



262 **263** **264**

In some cases the use of acetonitrile can cause complications because it behaves as a nucleophile.[19] This was discovered whilst attempting the hydrolytic ring opening of *N*-benzoylaziridinecarboxylate **40** with BF_32H_2O. The acetonitrile competes with the water as



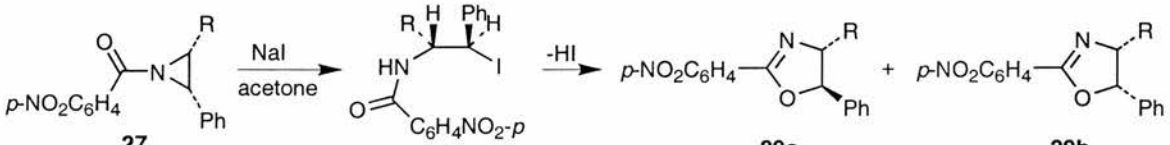
40 **265** **266**

a nucleophile. To investigate this reaction it was repeated using the etherate and both regioisomers of the *N*-benzoyl imidazoles **265** (80%) and **266** (10%) were formed.

5. Catalysed by Anions

a Iodide

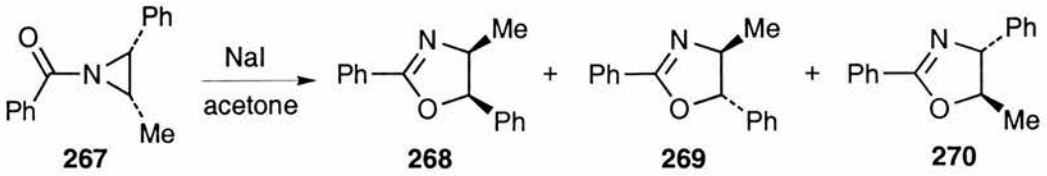
When catalysed by sodium iodide, the *cis*-aziridine **27** ring opens to give a mixture of *trans* and *cis*-*l*-menthyl-2-oxazolines **29a** and **29b** (30:70) in 53% yield.[15] Interestingly isolation of the intermediate, *l*-menthyl-*N*-*p*-nitrobenzoyl-3-iodo-phenylalaninate **27**, was possible in this (rare) case. The ring closure is affected with Et_3N.



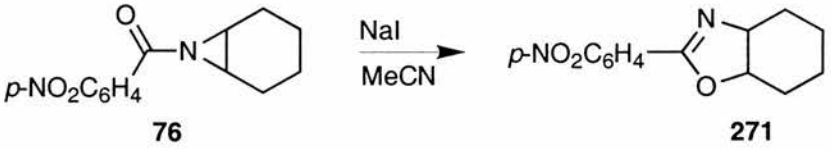
27 **28** **29a** **29b**

R = CO_2-menthyl

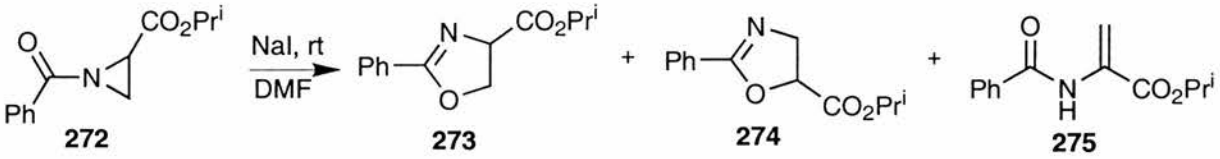
The *N*-benzoyl-3-methyl-2-phenylaziridine **267** ring expands to both *cis*-4-methyl-2,5-diphenyloxazoline **268** (42%) and *trans*-4-methyl-2,5-diphenyloxazoline (29%) **269** plus the opposite regioisomer, *trans*-5-methyl-2,4-diphenyloxazoline **270** (5%).[68]



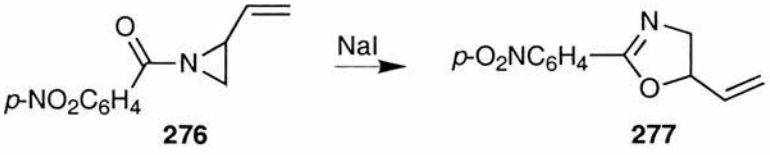
p-Nitrobenzoylcyclohexenimine **76** was treated with sodium iodide in acetone to give mainly the oxazoline **271** and a small amount of iodo amide.[11] In acetonitrile the oxazoline was the sole product (95%). There is no mention of imidazole formation.



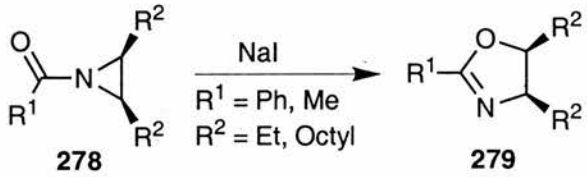
The *N*-benzoylaziridine-2-carboxylate **272**, upon treatment with sodium iodide in DMF gives both regioisomers of the oxazoline **273** (31%) and **274** (45%) plus the unsaturated amide **275** (14%).[76]



N-*p*-Nitrobenzoyl-2-vinylaziridine **276** reacted with iodide ion in acetone solution to give 2-*p*-nitrophenyl-5-vinyl-2-oxazoline **277**.[84]



The iodide ion catalysed isomerisation of *cis*- and *trans*-*N*-acetyl and *N*-benzoyl-2,3-disubstituted aziridines to 2-oxazolines is stereoselective, the selectivity being greater with *trans*-aziridines than with *cis*-aziridines.[85] The *trans*-aziridines yield 90-95% *trans*-oxazolines and 10-5% *cis* while the *cis*-aziridines **278** give 40-90% *cis*-oxazoline **279** and 60-10% *trans*. The selectivity of isomerisation for *cis*-*N*-benzoylaziridines was found to vary with iodide ion concentration and the solvent employed while the ratio of oxazolines formed from the corresponding *trans*-aziridines was unaffected.

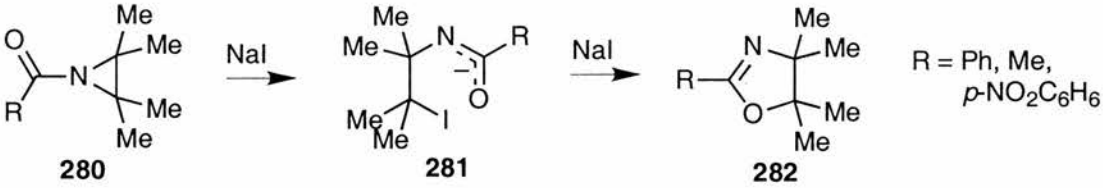


278 279

For *N*-benzoyl-*cis*-2,3-diethylaziridine, the effect of varying concentrations of iodide ion was studied. A pronounced change in the *cis*:*trans* ratio of the oxazoline was observed. At very high concentrations of iodide ion the amount of *cis*-oxazoline falls to a level of about 40%, while at very low concentration the amount of *cis*-oxazoline formed increases asymptotically until nearly total selectivity is observed. As the iodide ion concentration decreased the rate of isomerisation also decreased. At an iodide : aziridine ratio of 1 : 10 less than 50% of the starting aziridine was isomerised after 60 hr of reaction.

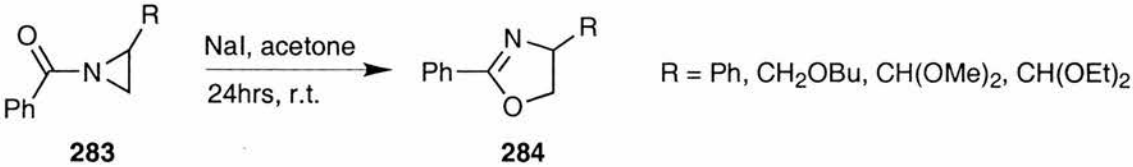
The reaction of *N*-benzoyl-*trans*-2,3-diethylaziridine is unaffected by solvent. However, the reaction of the *cis*-aziridine is affected by using 2% water in acetone (or MeCN) increasing the yield of *cis*-oxazoline to as much as 75%.

It has been proposed that the formation of oxazoline **282** from aziridine **280** occurs via attack of a second iodide ion on the intermediate **281** before ring closure. Although irrelevant in the example below, the retention of relative configuration (*cis* or *trans*) would be achieved because two inversions occur.



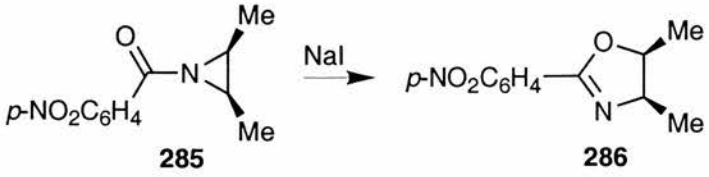
280 281 282

Ring enlargement of *N*-acylaziridines **283** bearing an electron donating substituent at C-2 using sodium iodide in acetone all proceeded with complete regioselectivity, providing 4-substituted oxazolines **284** in good yields (83-98%).[86]



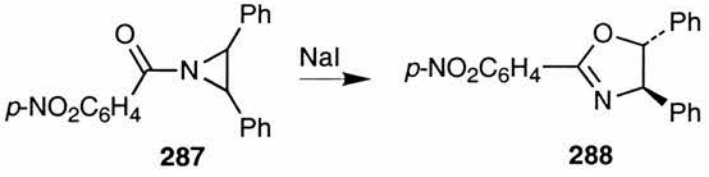
283 284

In acetone the iodide ion catalyses the isomerisation of *cis*-*N*-p-nitrobenzoyl-2,3-dimethylaziridines **285** into *cis*-2-*p*-nitrophenyl-4,5-dimethyl-2-oxazoline **286**.[87] Sodium iodide also catalyses the rearrangement of the *trans*-aziridine into the *trans*-oxazoline.



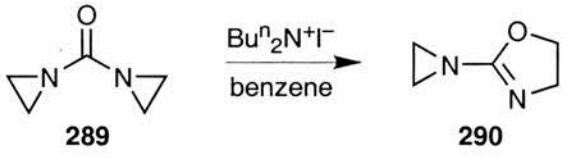
285 **286**

With the same catalyst, *cis*- and *trans*-*N*-*p*-nitrobenzoyl-2,3-diphenylaziridine **287** both rearrange into *trans*-2-*p*-nitrophenyl-4,5-diphenyl-2-oxazoline **288**. This is likely to be due to the steric bulk of the groups at C-2 and C-3 of the aziridine.



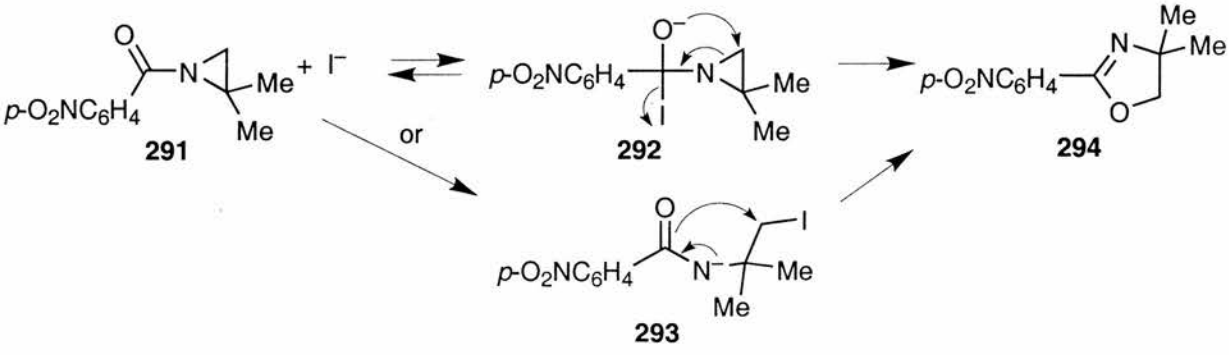
287 **288**

1,1-Carbonylbis(aziridine) **289** was isomerised by tetra-*n*-butylammonium iodide in benzene to 2-aziridinyl-2-oxazoline **290** (79%).[88]



289 **290**

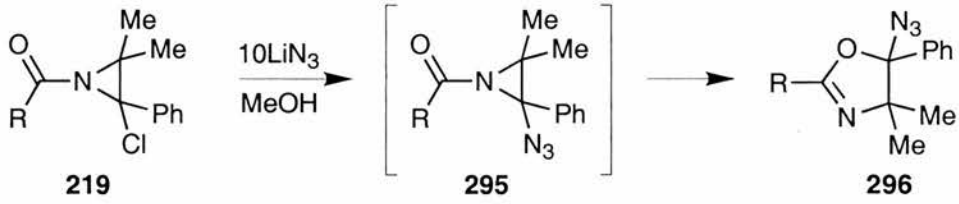
N-*p*-Nitrobenzoyl-2,2-dimethylaziridine **291** was selectively isomerisated into 2-*p*-nitrophenyl-4,4-dimethyl-2-oxazoline **294** by sodium iodide in acetone in 93%.[89] Iodide ion was thought to attack the aziridine at either C-2 of the ring giving **293** or at the carbonyl giving **292**.



291 **292** **294** **293**

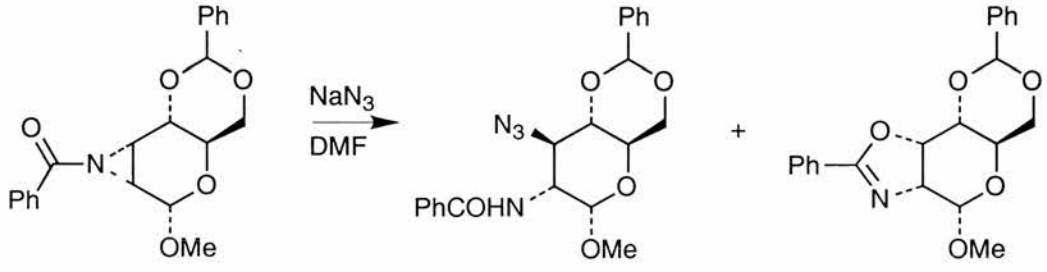
b Azide

Acylaziridines can also be isomerised by lithium azide in methanol.[75] The *N*-acyl-2-chloro-3,3-dimethyl-2-phenylaziridines **219** are isomerised to the azido 2-oxazolines **296** via an azido acylaziridine intermediate **295**. The intermediate could only be isolated for the *N*-benzoyl and *N*-pivaloylaziridines after a few minutes reaction time.



219 **295** **296**

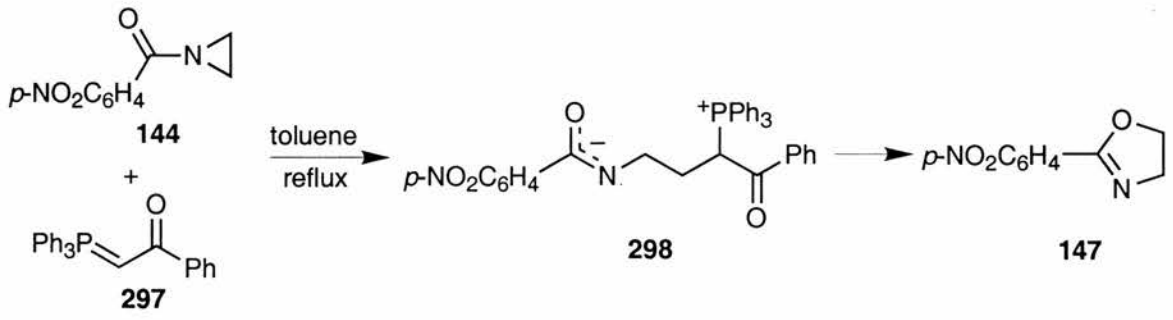
Reaction of the *N*-benzoylaziridino-mannoside **95** with sodium azide and ammonium chloride in boiling DMF gave a mixture of oxazoline **97** (36%) and the expected diaxial azide **96** (20%).[38]



97 **98** **99**

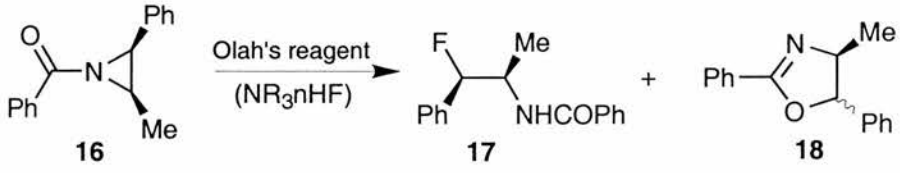
c Phosphorus Ylides

When *N*-*p*-nitrobenzoylaziridine **144** is heated under reflux with a catalytic amount of triphenylphosphonium phenacylide **297** in toluene, it isomerises to 2-*p*-nitrophenyl-2-oxazoline **147**.[54] The ylide is displaced by the benzoyl oxygen when the intermediate **298** cyclises.



d Olah's reagent

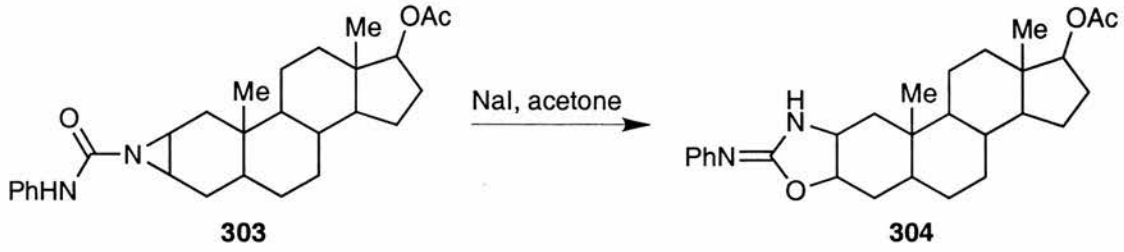
When *N*-benzoyl-3-methyl-2-phenylaziridine **16** reacts with Olah's reagent, the main product isolated is not only the desired *N*-benzoylfluoroamine **17**.[9] The 2-phenyl-2-oxazolines **18** are also formed. The author suggests that Olah's reagent is insufficiently nucleophilic to give entirely the desired product **17**.



6. *N*-Carbamoyl and Thiocarbamoylaziridines

The *N*-phenylthiocarbamoylaziridine **299** is isomerised to *cis*-2-anilino-2-thiazoline **300** exclusively upon interaction with iodide ion.[90] Similarly, the *N,N*-diphenylcarbamoylaziridine **301** is isomerised to 2-anilino-2-oxazoline **302**.

The steroid derived *N*-carbamoylaziridine **303** below can also be isomerised by sodium iodide.[91] Whether it exists as the 2-iminooxazolidine **304** or the 2-oxazoline is not investigated. The yield was calculated at 88%.

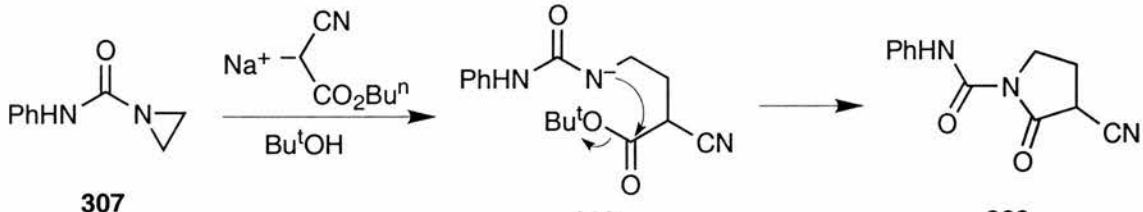


303 304

This can be compared with the behaviour of the corresponding *N*-acetylaziridine **305** which is isomerised in 89% yield by sodium iodide to the 2-methyl-2-oxazoline **306.**

305 306

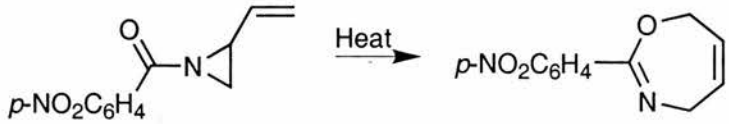
Reaction of *N*-phenylcarbamoylaziridine **307** with the anion of cyanoacetic acid butyl ester gave the pyrrolidin-2-one **309**.[92] Once the aziridine ring has been opened, the intermediate **308** cyclises by attack of the aziridinyl nitrogen at the new carbonyl centre eliminating the butoxy group. There are no ring-opened products observed.



307 308 309

7. Vinylogous ring-expansion to dihydro-1,3-oxazepines

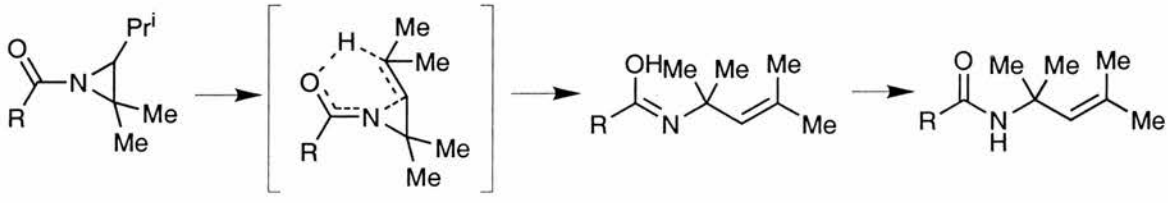
Interestingly, heating *N*-*p*-nitrobenzoyl-2-vinylaziridine **275** in toluene leads to formation of 2-*p*-nitrophenyl-4,7-dihydro-1,3-oxazepine **310**.[84] No mechanism is proposed by the authors but the carbonyl must attack the end of the carbon-carbon double bond to initiate the Cope type cyclisation.



275 310

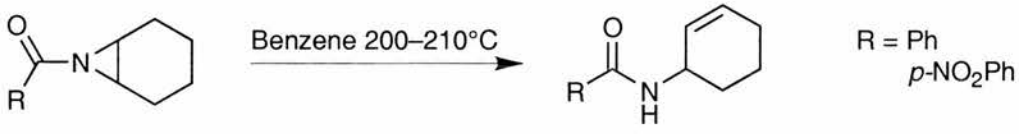
F. Isomerisation to *N*-allylamides

The amides **314** (and all other amides formed from acylaziridines) are thought to form via a six-membered transition state **312** from the *N*-acylaziridine **311**. The tautomer **313** of the amide is formed first.[65]



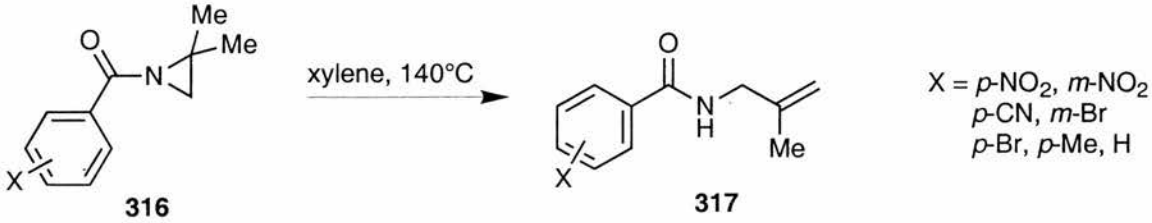
311 312 313 314

In benzene solution at 200-210°C, *N*-acylcyclohexenimine **99** was isomerised to the unsaturated amide **315**.[11]



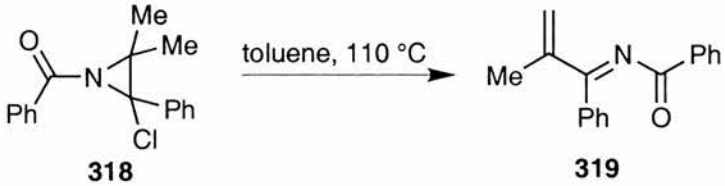
99 315

N-Benzoyl-2,2-dimethylaziridines **316** are isomerised to the *N*-(β-methallyl) benzamides **317** by heatinging in xylene.[93] Significant amounts of oxazoline are detected only when the *p*-toluylaziridine is pyrolysed (33% at 80°C, 13% at 145°C).



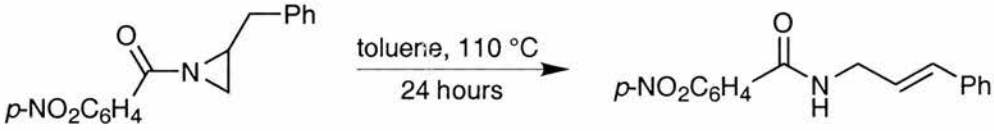
316 317

The pyrolysis of *N*-benzoyl-2-chloro-2-phenyl-3,3-dimethylaziridine **318** in toluene affords *N*-benzoylmethacrylophenone imine **319** (90%).[75] The reaction also proceeds using silver perchlorate in benzene.



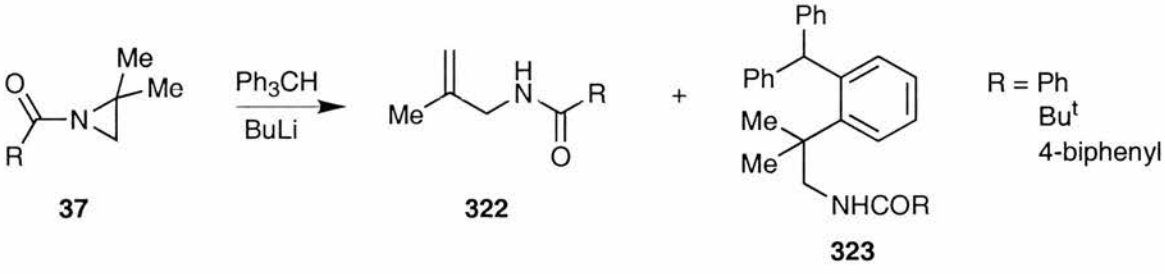
318 **319**

The thermal rearrangement of *N*-(*p*-nitrobenzoyl)-2-benzylaziridine **320** to the benzamide **321** is suggested to be an intramolecular *cis* elimination.[94]



320 **321**

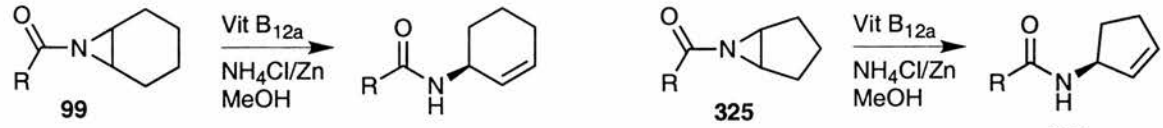
Single electron transfer from the trityl anion to *N*-acyl-2,2-dimethylaziridines **37** yield unsaturated amides **322** and triphenylmethane derived products **323** (plus other minor products).[95] The unsatured amides arise from transfer of a single hydrogen from the second intermediate species to the trityl radical, the triphenylmethanes are formed by combination of these radicals.



37 **322** **323**

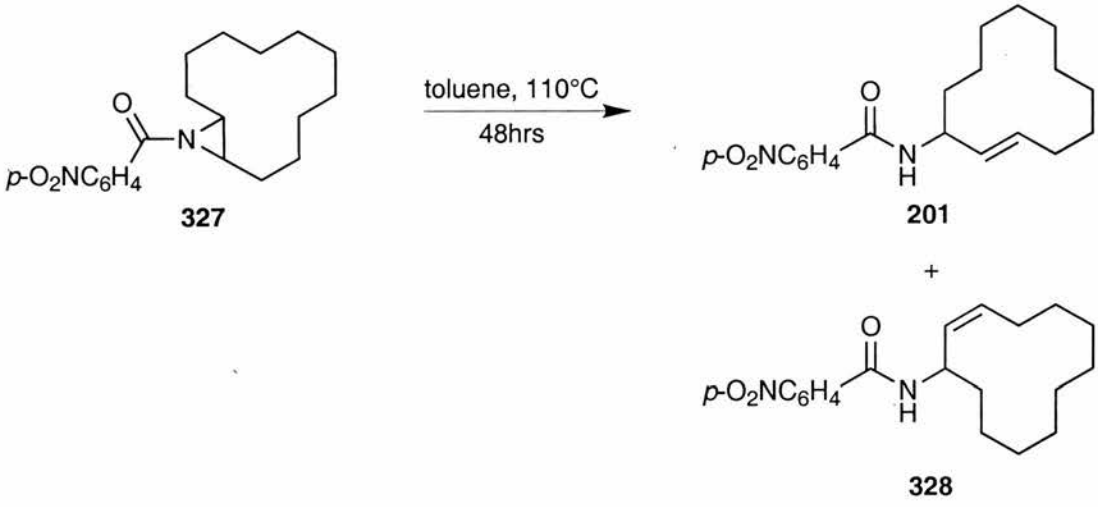
Vitamin B_{12} catalyses the isomerisation of achiral *N*-acylaziridines **99** and **325** to optically active (*R*)-*N*-acyl-*N*-(cycloalk-2-en-1-yl)amines **324** and **326**. This proceeds in two steps.[96] Firstly, the aziridine ring is opened by an S_N^2-type displacement of nitrogen by the chiral cobalt nucleophile to afford a mixture of the diastereoisomeric (1*R*,2*R*)- and (1*S*,2*S*)-

Co-β-(2-(acylaminocycloalkyl)cob(III)alamins in different amounts. The intermediate then decomposes to give the product (plus Co and H^+).



99 R = Et, Ph, t-BuO **324** **325** R = Ph, t-BuO **326**

Heating *trans*-13-*p*-nitrobenzoyl-13-azabicyclo[10.1.0]tridecane **327** under reflux in toluene gave a 2:1 ratio of *E*-*N*-(2-cyclodecenyl)-*p*-nitrobenzamide **201** and its *Z*-isomer **328**.[70] No yields are given.

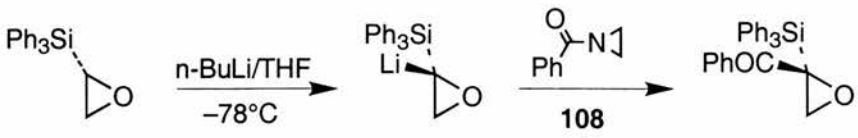


327 **201** **328**

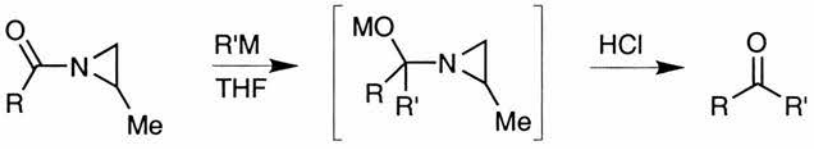
G. Reactions initiated by attack at CO

1. Nucleophilic attack at CO – behaviour as acylating agents

1-triphenylsilyl-1,2-epoxyethyllithium **329** reacts with *N*-benzoylaziridine to form 1-benzoylepoxyethyltriphenysilane **331** in 61% yield.[97] The lithiated epoxide behaves as RLi and R^- attacks the carbonyl group of the benzoylaziridine **108** and thus the epoxide is acylated providing **331**.

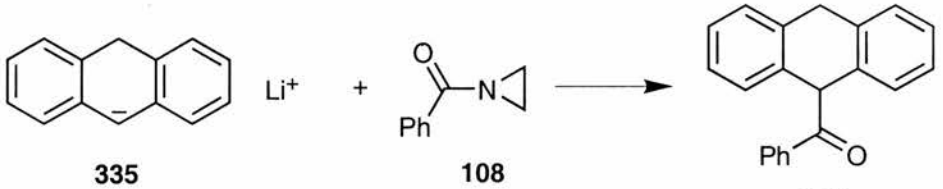


N-acyl-2-methylaziridines **332** react with Grignard reagents and alkyllithiums to give ketones **334**.[98] As above, R^- attacks the carbonyl group and the metal stabilises the charge on oxygen in the intermediate **333**. Addition of acid gives the ketones in yields of over 70%.

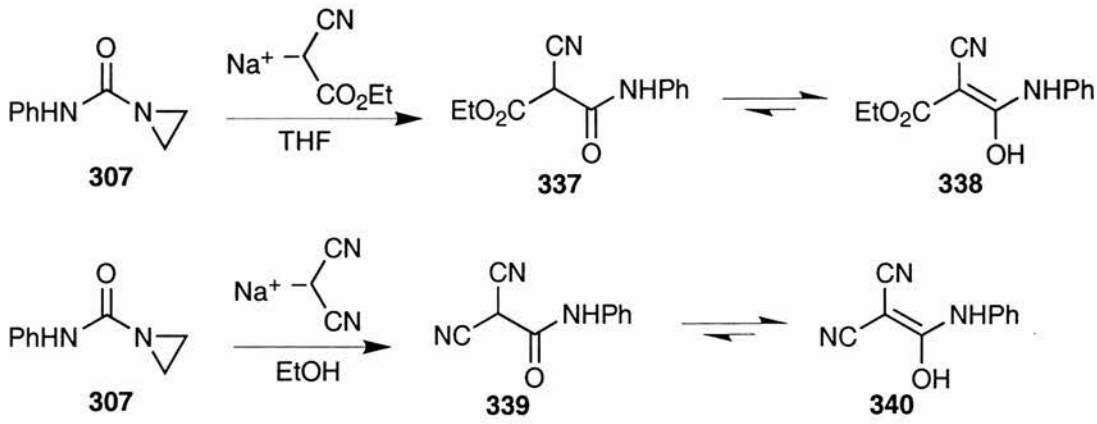


R = Me, Ph, Bu^t

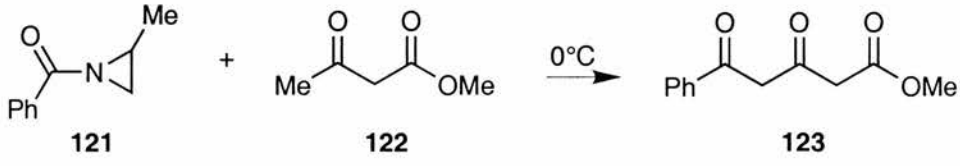
Reaction of *N*-benzoylaziridine **108** with an excess of lithium anthracene hydride **335** gives the mono-acylated anthracene **336** in 93% after one minute.[99] A 4:5 defecit of anthracenide reacted with the same aziridine for twenty minutes gave a yield of only 54%.



Cyanoacetic acid ester anions are acylated when reacted with *N*-phenylcarbamoylaziridine **307**. There is no opening of the aziridine ring observed in this case.[92] The reaction is solvent dependant since use of tertiary butanol yields a pyrrolidine-2-one (see earlier). The resulting products **337** and **339** exist to a significant extent in the enol forms **338** and **340** as shown.

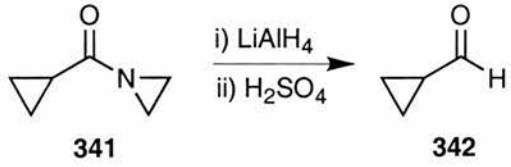


Adding methyl acetoacetate **122** to aziridine **121** forms methyl-3,5-dioxo-5-phenylpentanoate **123** in 98% yield.[48] The carbanion is formed from the ester using 2 equivalents of NaH. The carbanion attacks the aziridine at the carbonyl displacing the aziridine ring.



2. Reduction at CO – aldehyde synthesis

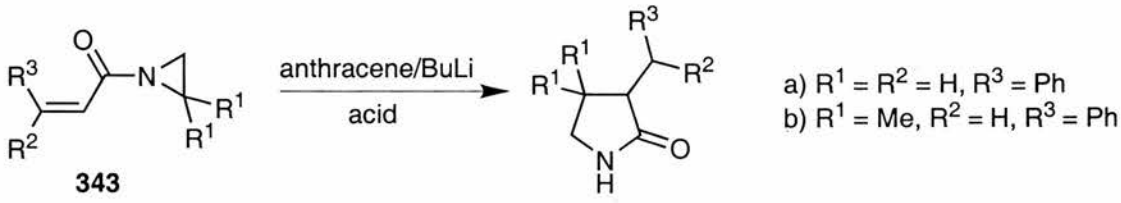
This is essentially the same as the ketone synthesis outlined earlier except that hydride is the nucleophile.[100] Therefore, the hydride anion attacks the carbonyl of compound **341** displacing the aziridine ring. Acid work-up gave the cyclopropanecarboxaldehyde **342** in 60% yield.



3. SET mediated ring-expansion to 2-pyrrolidinones

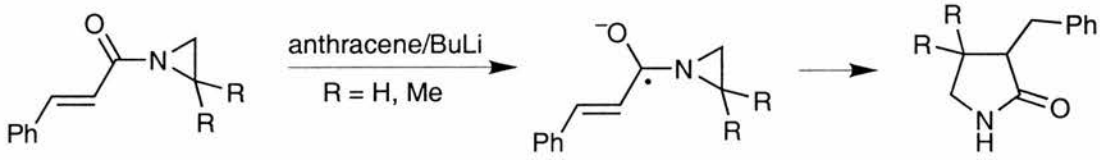
Substituted 2-pyrrolidones **343** are formed by single electron transfer mediated ring-expansion of *N*-cinnamoylaziridines **344**.[101] Firstly addition of an electron forms the ketyl

(metallated - Li^+, Na^+) which rearranges, cleaving the aziridine ring. The acryloyl carbon-carbon double bond then traps the radical. The reaction was quenched with acid to give the 2-pyrrolidones.



343 **344**

Very similar to the previous example, single electron transfer mediated ring-expansion of *N*-cinnamoylaziridines **345** gives the products as 2-pyrrolidones **347** via a metallated ketyl intermediate **346**.[102] Yields of 86 and 78% were reported when R = H and Me respectively.

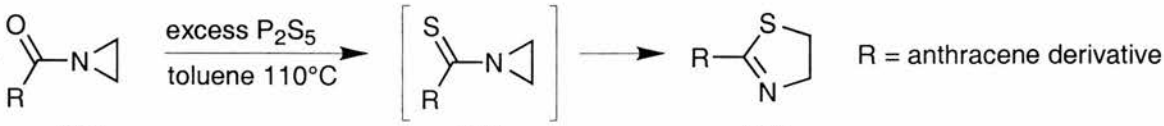


345 **346** **347**

H. Other reactions

1. Conversion to thiazolines

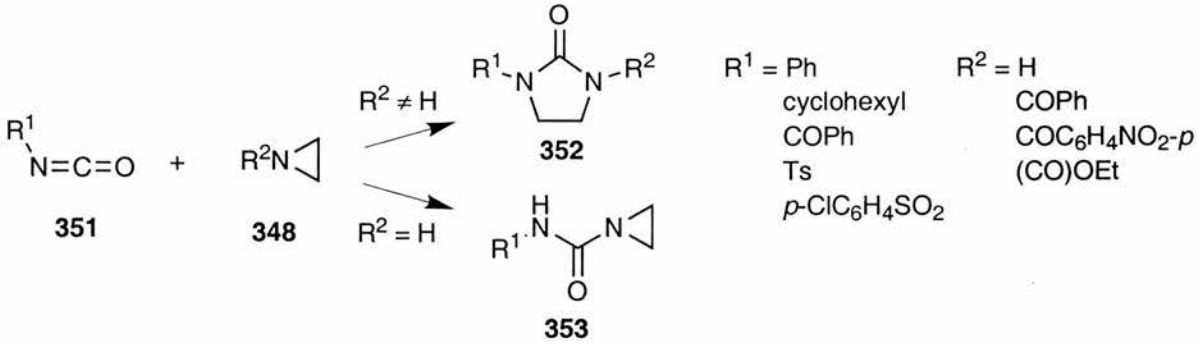
2-alky-2-thiazolines **350** can be prepared by heating *N*-acylaziridines **348** under reflux with an excess of P_2S_5 in toluene.[103] This probably proceeds via a thioacylaziridine intermediate **349** or by a single step concerted mechanism. No intermediates were observed by the author.



348 **349** **350**

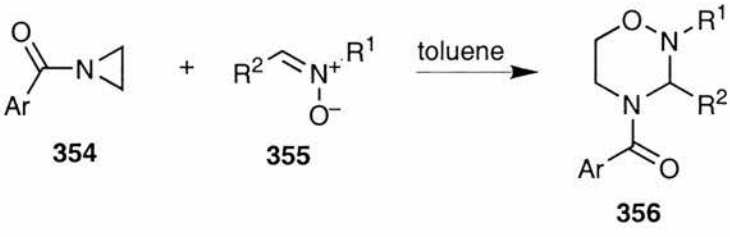
2. Reaction with isocyanates to give imidazolidinones

A variety of imidazolidinones **352** can be formed from *N*-acylaziridines **348** and isocyanates **351**.[104] If only hydrogen is present on nitrogen then *N*-carbamoylaziridines **353** are formed.

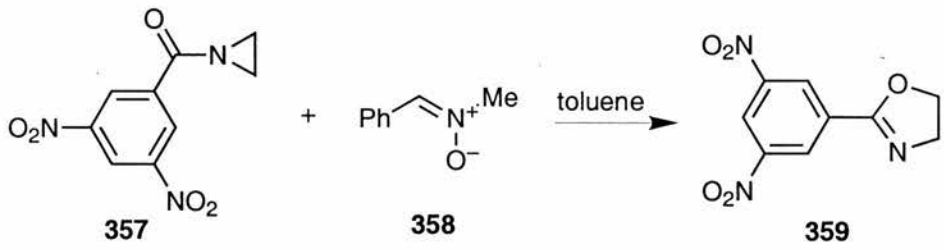


3. Reaction with nitrones

Tetrahydro-1,2,4-oxadiazines **356** can be formed by heaing nitrones **355** with *N*-benzoylaziridines **354** under reflux in either toluene or *m*-xylene.[105] Ten examples were synthesised by Calcagno, Heine, et al starting from nitrobenzoylaziridines. The first step is the attack of the nitrone oxygen the aziridine ring carbon. This could then ring close to the oxadiazine **357**.



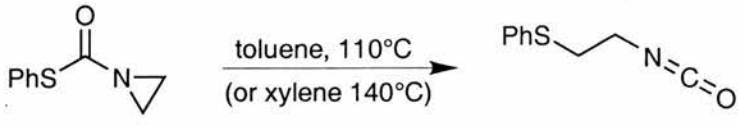
The 2-oxazolines are sometimes observed as a minor product and in some cases there was little or no oxadiazine formed and the oxazoline was the major product. This was the case with *N*-dinitrobenzoylaziridine **357** which gave 2-dinitrophenyl-2-oxazoline **358** (80%) when reacted with nitrone **359**. The 2-oxazoline is formed by expulsion of the nitrone from the intermediate.



357 358 359

4. Conversion of thioacyaziridine to isocyanate

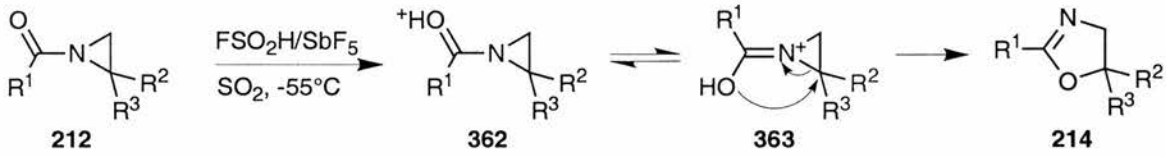
Heating *N*-phenylthiocarbonyl aziridine **360** under reflux in toluene or xylene produced an isocyanate **361** in which the thiophenyl group has attacked one of the aziridine ring carbons.[106] However, no explanation or yield was given.



360 361

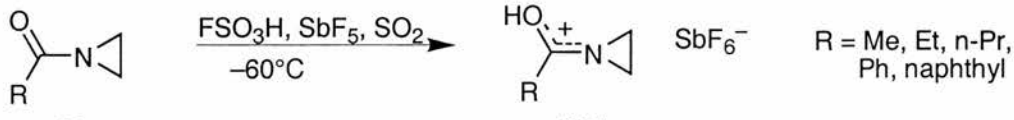
5. Reaction with super acids

In order to isolate the *O*-protonated aziridine species **362** a strong acid, generated from FSO_3H/SbF_5 was added to aziridine **212** at –55 °C.[73] Five examples were made, two *N*-benzoyl and three *N*-acetyl. The *O*-protonated aziridine could rearrange to a short lived *O*-protonated oxazolinium ion which in turn gives the product **214**.



212 362 363 214

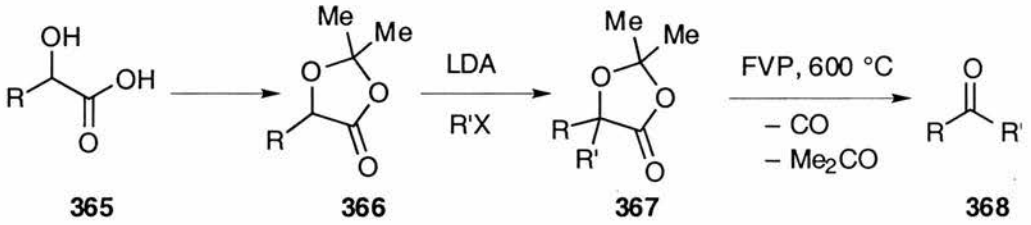
Olah and Szilgyi had previously observed the *O*-protonated *N*-acylaziridines **364** below.[107] ^1H chemical shifts of around 5 ppm were observed for the ring protons.



99 364

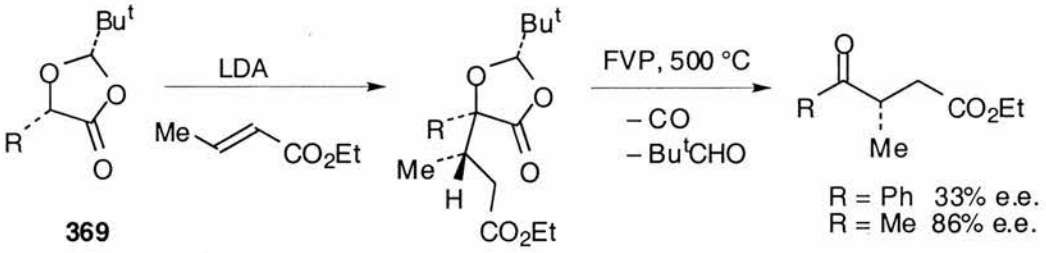
I. Programme of Research

In previous work in this laboratory[108] it was shown that dioxolanones **366** are readily formed from α-hydroxy acids **365**, and they may be alkylated to give **367**. The Flash Vacuum Pyrolysis (FVP) of **367** causes fragmentation to give acetone, carbon monoxide and ketones **368** thus making **366** a new type of acyl anion equivalent. This was further developed to give a



365 **366** **367** **368**

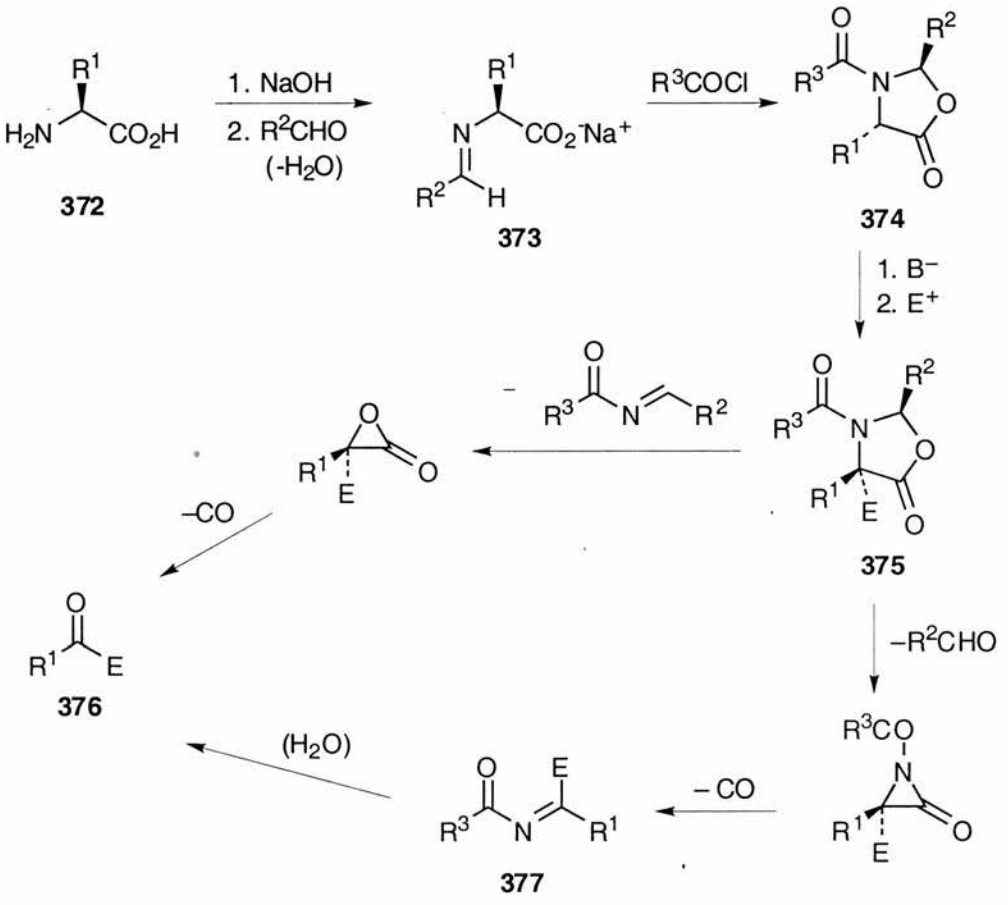
chiral acyl anion equivalent by alkylation of chiral dioxolanones **369** to give chiral products such as **370**. The FVP of the dioxolanones **370** resulted in the loss of carbon monoxide and pivalaldehyde to give the desired chiral product **371** in good enantiomeric excess. One drawback of this method is that there are only a few chiral α-hydroxy acids available (R = Ph, Me). This is unfortunate since it limits the scope of what might otherwise be a versatile new method of obtaining chiral acyl anion equivalents.



369 **370** **371**

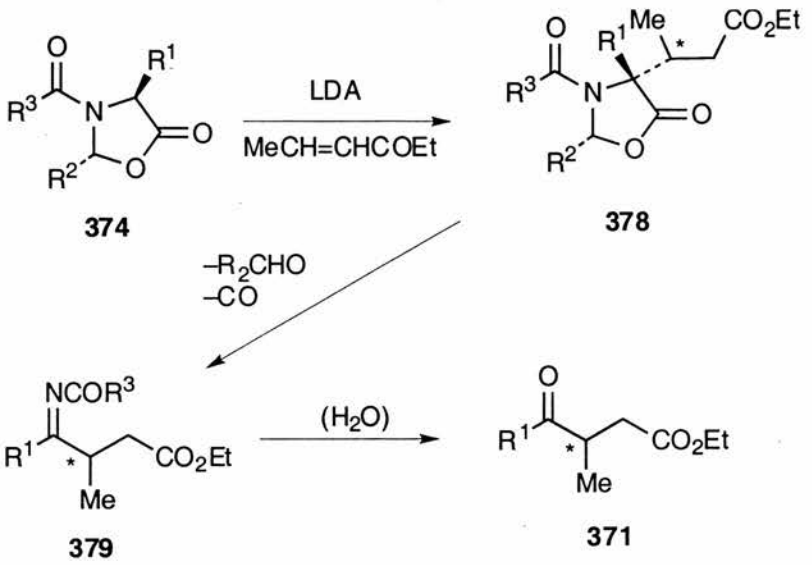
It was now planned to extend this work to functionalised oxazolidin-5-ones **374** and **375** whose synthesis and alkylation at C-4 has already been thoroughly investigated by Seebach.[109] These can be synthesised from any of the 20 readily available α-amino acids **372** via their sodium salts by condensation with an aldehyde and cyclisation of the intermediate **373**

with an acid chloride. A range of these 3-acyloxazolidin-5-ones would be prepared using the literature method shown below.[110] In agreement with previous work these were expected to exist mainly as the 2,4-*trans* isomers taking their stereochemistry at the 2-position from the starting *S*-amino acids.



Apparently, the pyrolytic behaviour of this ring system had not been studied before. The FVP was expected to have the same effect as before (elimination of CO) although the R^1 substituent of interest can now end up either as the ketone **376** or its imine **377** due to the presence of an oxygen and nitrogen in the ring where there were two oxygens previously. This should not be a serious problem however, since **377** should be easily hydrolysed to give **376**.

By alkylation of **374** at the 4-position we would obtain compounds such as **378** (from ethyl crotonate) and upon FVP this might fragment as shown to give either **379** or **380**.



Thus the scope of asymmetric acyl anion chemistry could be greatly extended to a variety of groups R^1. As shown, **379** would be expected to hydrolyse to **371**.

EXPERIMENTAL

A. Abbreviations

4ry	quaternary (in ^{13}C NMR data)
bp	boiling point
br, s, t, q, m	broad, singlet, doublet, triplet, quartet, multiplet
CI	chemical ionisation
δ	chemical shift in parts per million
ether	diethyl ether
FVP	flash vacuum pyrolysis
h, min	hours, minutes
J	spin-spin coupling constant in Hertz
lit.	literature
M^+	mass of the molecular ion
mp	melting point
m/z	mass to charge ratio
pet ether	petroleum ether
NMR	nuclear magnetic resonance
RT	room temperature
TLC	thin layer chromatography
ν_{max}	infra-red absorption wave number
*	signal due to minor isomer (in NMR data)

B. Instrumentation and General Techniques

1. NMR Spectroscopy

Spectra were obtained for ^1H at 200 or 300 MHz on Varian Gemini 200 or 2000 instruments and for ^{13}C NMR at 75 MHz on a Varian Gemini 2000. All spectra were obtained

from solutions in deuteriochloroform unless indicated otherwise and chemical shifts are expressed in ppm to high frequency of internal tetramethylsilane.

2. Mass Spectrometry

Mass spectra were obtained on an A.E.I./ Kratos M.S.-50 spectrometer operated by Mr. C. Millar or Mrs. C. Horsburgh. Unless otherwise indicated the spectra were obtained using impact at 70 eV. Chemical ionisation spectra were obtained using isobutane as the ionising gas and fast atom bombardment spectra were obtained using 3-nitrobenzyl alcohol as the matrix.

3. Elemental Analysis

Microanalysis were carried out for C, H and N using a Carlo-Erba 1106 elemental analyser by Mrs. S. Williamson.

4. Melting Points

Melting points for routine analysis were carried out on a Gallenkamp melting point apparatus. Those for new compounds were determined on a Reichert hot-stage microscope. All melting points are uncorrected.

5. Thin Layer Chromatography

This was carried out using 250μm layers of silica (PE SilG / UV_{254}) on polyester sheets. The products were observed under uv light.

6. Column Chromatography

This was carried out using Fluka silica gel for chromatography (60–120 mesh) or BDH 'flash' grade aluminium oxide (120 mesh) (pH 7.0).

7. Flash Vacuum Pyrolysis

The apparatus used was based on the design of W. D. Crow, Australian National University. A similar set up is illustrated in a recent book by Brown.[111] The essential features of the apparatus are illustrated in Figure 1. The sample was volatilised from a horizontal inlet tube, heated via an external heat source, through a 30 × 2.5 cm silica tube. This was heated at a

temperature of between 400 and 700 °C by a Carbolite Eurotherm Tube Furnace MTF-12/38A, the temperature being measured by a Pt/Pt-13% Rh thermocouple situated in the centre of the furnace. The non-volatile products were collected at the furnace exit and the volatile products collected in a U-shaped trap cooled in liquid nitrogen. The whole system was maintained at a pressure of 10^{-2} to 10^{-3} Torr by an Edwards Model E2M5 high capacity rotary oil pump, the pressure being measured on a Pirani guage situated between the trap and the pump. Under these conditions the contact time in the hot zone was estimated to be in the range 1-10ms.

After pyrolysis the system was isolated from the pump. The products were then dissolved in dichloromethane, which was removed under reduced pressure. The products were then dissolved using deuteriochloroform and analysed using NMR.

Figure 1: Flash vacuum pyrolysis apparatus

8. Optical Rotation

Optical rotation measurements were performed with an Optical Activity AA-1000 polarimeter operating at 589 nm using a 1 cm^3 solution cell with a 20 cm path length. Values for $[\alpha]_D$ are expressed in units of 10^{-1} deg cm^2 g^{-1}.

C. Synthesis of chiral *N*-acyloxazolidin-5-ones

1. Preparation of (*2S,4S*)- and (*2R,4S*)-3-benzoyl-2-t-butyl-4-methyl-1,3-oxazolidin-5-one 381 and 382

Using the literature procedure,[110] (*S*)-alanine (4.45 g, 0.05 mol) was added to $NaOH_{(aq)}$ (1 mol dm^{-3}, 50 cm^3) and ethanol (2-3 cm^3) was also added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Pivalaldehyde (6.45 g, 0.075 mol) and pentane (50 cm^3) were added. The mixture was heated under reflux with azeotropic removal of water (Dean and Stark trap) for 5-8 hours. The solvent was removed and the solid dried overnight. The solid was heated under reflux with CH_2Cl_2 (200 cm^3) and benzoyl chloride (7.0 g, 0.05 mol) in CH_2Cl_2 (40 cm^3) overnight. The resulting cloudy solution was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated. The clear oily substance obtained was shown by ^1H NMR to contain both isomers and so it was subjected to column chromatography [SiO_2, ether-pet ether (1:1)]. This did not give complete separation but the first fraction was mainly the minor, *trans* isomer:

381 δ_H 7.75–7.25 (5 H, m, aromatic H), 6.25 (1 H, s, 2-H), 4.37 (1 H, q, *J* 7, 4-H), 1.11 (3 H, d, *J* 7, 4-Me) and 1.04 (9 H, s, Bu^t).

while the later fractions showed a ratio of about 8:1 in favour of the major *cis* isomer:

382 δ_H 7.45 (5 H, m, aromatic), 6.13 (1 H, s, 2-H), 4.07 (1 H, q, *J* 7, 4-H), 1.5 (3 H, d, *J* 7, 4-Me) and 1.06 (9 H, s, Bu^t).

In the hope of obtaining the isomers pure, the fractions were set aside at RT for a number of weeks but they had still only partly crystallised. In view of the more convenient route to 2-phenyloxazolidinones the pyrolysis of this compound was not examined.

2. Preparation of (*2R,4S*)-3-benzoyl-2-phenyl-4-methyl-1,3-oxazolidin-5-one 383

Following the literature procedure,[112] (*S*)-alanine (4.45 g, 0.05 mol) was added to $NaOH_{(aq)}$ (1 mol dm^{-3}, 50 cm^3) and ethanol (2-3 cm^3) was added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Benzaldehyde (7.95 g, 0.075 mol) and CH_2Cl_2 (300 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5-8 hours. The imine was formed as a white precipitate. The mixture was stirred at 0 °C while a solution of benzoyl chloride (7.0 g, 0.05 mol) in CH_2Cl_2 (40 cm^3) was added and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated and the residue recrystallised [ether-CH_2Cl_2 (3:1)] to give the product **383** (4.72 g, 34%) as colourless crystals, mp 163–165 °C (lit.,[112] 164.8 °C); $[\alpha]_D^{20}$ +216.5 (c 1, $CHCl_3$) (lit.,[112] +225.0); (Found C, 72.3; H, 5.1; N, 5.0. $C_{17}H_{15}NO_3$ requires C, 72.6; H, 5.4; N, 5.0%); δ_H 7.45–7.10 (10 H, m, aromatic), 6.76 (1 H, s, 2-H), 4.84 (1 H, q, *J* 7, 4-H) and 1.50 (3 H, d, *J* 7, 4-Me). This spectrum shows good agreement with the literature[112] in terms of chemical shift but most signals showed considerable broadening presumably due to restricted rotation about the N–COPh group.

3. Preparation of (*2R,4S*)-3-benzoyl-4-isopropyl-2-phenyl-1,3-oxazolidin-5-one 384

This was prepared following the same procedure as for **383** but using (*S*)-valine (5.86 g, 0.05 mol). Recrystallisation gave the product **384** (7.60 g, 49%) as a colourless solid, mp 176.5–178.5 °C (lit.,[112] 178.1 °C); $[\alpha]_D^{20}$ +187.45 (c 1, $CHCl_3$) (lit.,[112] +221.8). (Found C, 73.5; H, 6.1; N, 4.4. $C_{19}H_{19}NO_3$ requires C, 73.8; H, 6.2; N, 4.5%); δ_H (50 °C) 7.6–7.1 (10 H, m, aromatic), 6.62 (1 H, s, 2-H), 4.84 (1 H, br s, 4-H), 2.6–2.1 (1 H, m, CH of Pr^i), 1.15 (3 H, d, *J* 7, Me of Pr^i) and 1.05 (3 H, d, *J* 7, Me of Pr^i). At 25 °C the NMR spectrum showed very broad peaks but these sharpened up considerably when it was recorded at 50 °C. δ_C 170.1

(CO), 169.6 (CO), 136.8 (4ry), 135.6 (4ry), 131.1, 129.8, 128.6 (4 C), 126.9 (2 C), 126.7 (2 C), 91.3 (C-2), 61.6 (C-4), 31.1 (*C*HMe$_2$), 17.9 (CH*Me*$_2$) and 16.7 (CH*Me*$_2$).

4. Preparation of (*2R,4S*)-3-benzoyl-4-benzyl-2-phenyl-1,3-oxazolidin-5-one 385

This was prepared following the same procedure as for **383** using (*S*)-phenylalanine (8.25 g, 0.05 mol). Recrystallisation gave the product **385** (3.9 g, 23%) as colourless needles, mp 183–185 °C (lit.,[112] 184.3 °C); $[\alpha]_D^{20}$ +318.1 (c 1, $CHCl_3$) (lit.,[112] +385.2). (Found C, 77.4; H, 5.3; N, 4.35. $C_{23}H_{19}NO_3$ requires C, 77.3; H, 5.4; N, 3.9%); δ_H 7.45-6.75 (15 H, m, aromatic), 5.83 (1 H, s, 2-H), 5.20 (1 H, m, 4-H) and 3.8–3.3 (2 H, 2 × br s, benzyl CH_2).

5. Preparation of (*2R,4S,2'S*)-3-benzoyl-4-s-butyl-2-phenyl-1,3-oxazolidin-5-one 386

This was prepared following the same procedure as for **383** using (*S,S*)-isoleucine (6.56 g, 0.05 mol). Recrystallisation gave the product **386** (8.14 g, 0.025 mol, 50%) as colourless crystals, mp 168–170 °C; $[\alpha]_D^{20}$ +226.55 (c 1, $CHCl_3$); (Found C, 73.75; H, 6.6; N, 4.35. $C_{20}H_{21}NO_3$ requires C, 74.3; H, 6.5; N, 4.3%); ν_{max}/cm^{-1} 1782, 1638, 1405, 1245, 1176, 1040, 1020 and 697; δ_H (50 °C) 7.5–6.9 (10 H, m, aromatic), 6.64 (1 H, s, 2-H), 4.91 (1 H, br s, 4-H), 1.8–1.65 (1 H, m, CH of Bu^s), 1.55–1.45 (2 H, m, CH_2 of Bu^s), 1.07 (3 H, d, *J* 7, *Me*CH) and 0.90 (3 H, t, *J* 7, *Me*CH_2); δ_C 170.0 (CO), 169.4 (CO) 136.8 (4ry), 135.6 (4ry), 131.1, 129.7, 128.6 (4 C), 126.9 (2 C), 126.7 (2 C), 91.3 (C-2), 60.3 (C-4), 37.8 (Me*C*H), 25.1 (Me*C*H_2), 14.3 (CH*Me*) and 11.7 (CH_2*Me*); *m/z* 323 (M^+, 20%), 189 (10), 174 (12), 161 (19), 145 (5), 117 (10), 105 (100), 77 (38) and 51 (6).

6. Preparation of (*2S,4R*)-3-benzoyl-2,4-diphenyl-1,3-oxazolidin-5-one 387

This was prepared following the same procedure as for **383** using (*R*)-phenylglycine (7.56 g, 0.05 mol). Recrystallisation gave the product **387** (7.04 g, 41%) as colourless crystals,

mp 179–181 °C (lit.,[113] 193–194 °C for opposite enantiomer of "unknown optical purity") (Found C, 76.8; H, 4.8; N, 4.2. $C_{22}H_{17}NO_3$ requires C, 77.0; H, 5.0; N, 4.1%); δ_H 7.5–7.0 (16 H, m, aromatic and 2-H) and 5.65 (1 H, br s, 4-H) [good agreement with lit.[113]].

7. Preparation of (*2R,4S*)-3-acetyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one 388

This was prepared following the same procedure as for **383** using (*S*)-alanine (4.45 g, 0.05 mol) and acetyl chloride (3.92 g, 0.05 mol). The product **388** was obtained as colourless crystals (3.76 g, 34%), mp 106–108 °C; $[\alpha]_D^{20}$ +113.0 (c 1, $CHCl_3$); (Found C, 65.6; H, 6.2; N, 6.4. $C_{12}H_{13}NO_3$ requires C, 65.7; H, 6.0; N, 6.4%); ν_{max}/cm^{-1} 1786, 1652, 1307, 1236, 1169, 1075, 1051, 993, 969, 928, 840, 768, 724, 702, 687 and 655; δ_H 7.55–7.30 (5 H, m, aromatic), 6.66* and 6.58 (1 H, s, 2-H), 4.72 and 4.60* (1 H, q, *J* 7, 4-H), 2.16* and 1.70 (3 H, s, COMe), 1.72 (3 H, d, *J* 7, 4-Me) and 1.59* (3 H, br. s, 4-Me); δ_C 172.1 (CO), 168.1 (CO), 136.4 (4ry), 130.8, 129.5 (2 C), 126.6 (2 C), 90.0 (C-2), 52.6 (C-4), 23.3 (*Me*CO) and 16.7 (4-Me); *m/z* 219 (M^+, 20%), 176 (14), 164 (9), 132 (77), 105 (61), 90 (9), 77 (26) and 51 (12).

8. Preparation of (*2R,4S*)-3-acetyl-4-isopropyl-2-phenyl-1,3-oxazolidin-5-one 389

This was prepared following the same procedure as for **383** using (*S*)-valine (5.86 g, 0.05 mol) and acetyl chloride (3.92 g, 0.05 mol). The crude product (yellow oil) was crystallised from ether to give the product **389** (5.41 g, 44%) as colourless needles, mp 78–80 °C; $[\alpha]_D^{20}$ +53.8 (c 1, $CHCl_3$); (Found C, 68.1; H, 7.0; N, 5.6. $C_{14}H_{17}NO_3$ requires C, 68.0; H, 6.9; N, 5.7%); ν_{max}/cm^{-1} 1785, 1640, 1310, 1260, 1185, 1130, 1060, 860, 780, 730 and 700; δ_H 7.5–7.3 (5 H, m, aromatic), 6.56* and 6.50 (1 H, s, 2-H), 4.68 and 4.49* (1 H, d, *J* 4, 4-H), 2.96–2.84 and 2.48–2.36* (1 H, m, CH of Pr^i), 2.12* and 1.67 (3 H, s, COMe), 1.29* and 1.24 (3 H, d, *J* 7, Me of Pr^i), 1.07* and 1.00 (3 H, d, *J* 7, Me of Pr^i); δ_C 169.6 (CO), 168.1 (CO) 136.8 (4ry), 130.8, 129.5 (2 C), 126.7 (2 C), 90.5 (C-2), 61.6 (C-4), 28.4 (*Me*CO), 23.6

(*CH*Me$_2$), 17.9 (CH*Me*$_2$) and 16.2 (CH*Me*$_2$); *m/z* 247 (M^+, 62%), 162 (61), 145 (8), 117 (32), 107 (20), 90 (9), 77 (15), 71 (8) and 58 (100).

9. Preparation of (*2R,4S*)-3-acetyl-4-benzyl-2-phenyl-1,3-oxazolidin-5-one 390

This was prepared following the same procedure as for **383** using (*S*)-phenylalanine (8.25 g, 0.05 mol) and acetyl chloride (3.92 g, 0.05 mol). Recrystallisation gave the product **390** (7.03 g, 47%) as colourless crystals, mp 150–152 °C (lit.,[114] 148–150 °C for opposite enantiomer); (Found C, 73.4; H, 5.6; N, 4.6. $C_{18}H_{17}NO_3$ requires C, 73.2; H, 5.8; N, 4.6%); ν_{max}/cm^{-1} 1795, 1670, 1350, 1290, 1250, 1180, 1160, 1090, 1020, 920, 735 and 700; δ_H 7.5-7.1 (10 H, m, aromatic), 5.66* and 5.53 (1 H, s, 2-H), 5.20 and 4.88* (1 H, m, 4-H), 3.95-3.81 (1H, A part of ABX, J_{AB} 14, J_{AX} 6, CH_2Ph), 3.38* (2 H, br. s, CH_2Ph); 3.33-3.18 (1H, B part of ABX, J_{AB} 14, J_{AX} 2, CH_2Ph) and 1.58 (3H, s, COMe); δ_C 171.1 (CO), 168.3 (CO), 136.1 (4ry), 134.9 (4ry), 130.8, 129.7 (2 C), 129.4 (2 C), 128.8 (2 C), 127.6, 126.8 (2 C), 90.5 (C-2), 58.6 (C-4), 34.2 (CH_2) and 23.4 (Me); *m/z* 295 (M^+, 53%), 253 (23), 204 (6), 181 (5), 162 (96), 134 (5), 119 (12), 107 (13), 91 (48), 77 (16), 65 (9), 57 (7) and 51 (7).

10. Preparation of (*2R,4S,2'S*)-3-acetyl-4-s-butyl-2-phenyl-1,3-oxazolidin-5-one 391

This was prepared following the same procedure as for **383** using (*S,S*)-isoleucine (6.56 g, 0.05 mol) and acetyl chloride (3.92 g, 0.05 mol). The crude product obtained (10.89 g) crystallised when left overnight. The product **391** (3.77 g, 29%) was obtained by washing this with pet ether and filtering to give colourless crystals, mp 120–122 °C; $[\alpha]_D^{20}$ +122.3 (c 1, $CHCl_3$); (Found C, 68.9; H, 7.6; N, 5.3. $C_{15}H_{19}NO_3$ requires C, 68.9; H, 7.3; N, 5.4%); ν_{max}/cm^{-1} 1795, 1651, 1286, 1252, 1217, 1166, 1133, 1078, 1030, 978, 927, 869, 828, 775, 724, 700 and 647; δ_H 7.44–7.29 (5 H, m, aromatic), 6.49* and 6.42 (1 H, s, 2-H), 4.70 and 4.51* (1 H, d, *J* 4, 4-H), 2.57 (1 H, m, CH of Bu^s), 2.05* and 1.60 (3 H, s, COMe), 1.80–1.40 (2 H, 2 × m, CH_2), 0.97 (3 H, t, *J* 7, CH_2*Me*) and 0.89 (3 H, d, *J* 7, CH*Me*); δ_C 169.7 and 169.7* (CO), 167.9 and 167.6* (CO), 136.8 and 136.5* (4ry), 130.8, 129.8*, 129.5 (2 C), 128.6*, 126.7 (2

C), 126.7*, 91.2* and 90.6 (C-2), 60.5* and 60.5 (C-4), 34.9* and 34.9 (Me*C*H), 25.2* and 25.1 (Me*C*H_2), 23.6 and 22.8* (*Me*CO), 13.8 and 13.8* (CH*Me*), 12.0 and 12.0* (CH_2*Me*); *m/z* 261 (M^+, 31%), 205 (10), 174 (7), 162 (48), 145 (24), 127 (16), 117 (72), 107 (32), 77 (17) and 57 (8) and 43 (100).

11. Preparation of (*2S,4R*)-3-acetyl-2,4-diphenyl-1,3-oxazolidin-5-one 392

This was prepared following the same procedure as for **383** using (*R*)-phenylglycine (7.56 g, 0.05 mol) and acetyl chloride (3.92 g, 0.05 mol). Recrystallisation gave the product **392** (6.21 g, 44%) as colourless crystals, mp 218–220 °C; $[\alpha]_D^{20}$ +165.75 (c 1, $CHCl_3$); (Found C, 70.7; H, 5.2; N, 4.9. $C_{17}H_{15}NO_3$ requires C, 72.6; H, 5.4; N, 5.0%); ν_{max}/cm^{-1} 1778, 1658, 1404, 1353, 1326, 1261, 1241, 1187, 1173, 1006 and 746; δ_H 7.65–7.3 (10 H, m, aromatic), 6.96 and 6.81* (1 H, s, 2-H), 5.68* and 5.45 (1 H, s, 4-H), 1.75 and 1.72* (3H, s, Me); δ_C 169.6 and 169.4* (CO), 168.8 and 168.6* (CO), 136.3 and 136.3* (4ry), 135.5 and 134.9* (4ry), 130.0, 129.8 (2 C), 129.6, 129.3*, 129.0*, 128.8 (2 C), 128.4*, 126.8*, 126.6 (2 C), 126.4 (2 C), 126.0*, 91.1 and 90.8* (C-2), 61.1 and 60.5* (C-4) and 23.6 and 23.3* (Me); *m/z* 281 (M^+, 3%), 237 (2), 194 (100), 175 (49), 165 (7), 147 (11), 89 (10), 77 (16) and 51(7).

12. Preparation of (*2R,4S*)-3-acetyl-2,4-diphenyl-1,3-oxazolidin-5-one 393

This was prepared following the same procedure as for **383** using (*S*)-phenylglycine (7.56 g, 0.05 mol). Recrystallisation gave the product **393** (4.25 g, 30%) as colourless crystals, mp 212–214 °C; $[\alpha]_D^{20}$ +162.9 (c 1, $CHCl_3$); (Found: C, 71.9; H, 5.2; N, 4.9. $C_{17}H_{15}NO_3$ requires C, 72.6; H, 5.4; N, 5.0%); ν_{max}/cm^{-1} 1778, 1659, 1241, 1188, 1007, 745 and 699; δ_H 7.55–7.28 (10 H, m, arom.), 6.96* and 6.81 (1 H, 2 × s, 2-H), 5.68* and 5.45 (1 H, 2 × s, 4-H), 1.75 and 1.72* (3 H, 2 × s, Me); δ_C 169.7 (CO), 168.9(CO), 136.3 (4ry), 135.5 (4ry), 130.4, 130.2 (2 C), 130.1, 129.2 (2 C), 127.0 (2 C), 126.8 (2 C), 91.5 and 91.2* (C-2), 61.5 and 60.9*

(C-4), 24.0 and 23.7* (Me); *m/z* 281 (M^+, 3%), 194 (100), 175 (59), 118 (33), 77 (14) and 43 (22).

13. Attempted Preparation of (*2S,4R*)-3-benzoyl-4-methoxymethyl-2-phenyl-1,3-oxazolidin-5-one 394

Following the literature procedure,[115] benzyl chloroformate (16.0 cm^3, 19.2 g, 112 mmol) and NaOH(aq) (2 mol dm^{-3}, 56 cm^3) were added dropwise simultaneously to a stirred solution of (*S*)-serine (11.8 g, 112 mmol) in NaOH(aq) (2 mol dm^{-3}, 56 cm^3) at 0 °C. The mixture was stirred for 3 hours at 0 °C then washed with ether (20 cm^3). The aqueous phase was acidified with 2M HCl and extracted with ethyl acetate (3 × 50 cm^3). The combined organic phase was dried ($MgSO_4$) and evaporated to give *N*-carbobenzoxy-(*S*)-serine as a colourless solid (12.34 g, 46%); mp 114-116 °C (lit.[115] 115–120 °C).

To a solution of *N*-benzoxycarbonyl-(*S*)-serine (1.72 g, 7.2 mmol) in acetonitrile (150 cm^3) were added successively Ag_2O (8.40 g, 36 mmol) and MeI (4.5 cm^3, 72 mmol) and the mixture was stirred at room temperature for 24 hours according to the literature procedure.[116] The mixture was filtered (through Celite) and evaporated to obtain the crude product, (*S*)-methyl 2-(benzyloxycarbonylamino)-3-methoxypropionate, as an oily residue (1.92 g, 99.7%); δ_H 7.40–7.28 (5 H, m, aromatic), 5.61 (1 H, d, NH, *J* 8), 5.52 (2 H, s, CH_2Ph), 4.49 (1 H, m, CH), 3.83 and 3.62 (2 H, AB pattern of d, *J* 9, 3, *CH*$_2$OMe), 3.68 (3 H, s, CO_2Me) and 3.34 (3 H, s, CH_2O*Me*) [lit.[116] 7.40–7.33 (5 H, m, aromatic), 5.67 (1 H, d, NH, *J* 8), 5.14 (2 H, s, CH_2Ph), 4.46–4.40 (1 H, m, CH), 3.84 and 3.62 (2 H, 2 × dd, *J* 9, 3, *CH*$_2$OMe), 3.78 (3 H, s, CO_2Me) and 3.34 (3 H, s, CH_2O*Me*)].

In accordance with the literature procedure,[116] K_2CO_3 (2.00 g, 14.47 mmol) was added to a solution of (*S*)-methyl 2-(benzyloxycarbonylamino)-3-methoxypropionate (1.92 g, 7.19 mmol) dissolved in MeOH–H_2O (9:1, 40 cm^3) and the mixture stirred at room temperature for 8 hours. The mixture was poured into H_2O (20 cm^3), adjusted to pH 3 and extracted with ethyl acetate (3 × 30 cm^3). The organic extracts were combined, dried and evaporated to give a clear oil, (*S*)-2-(benzyloxycarbonylamino)-3-methoxypropionic acid (1.15 g, 63%); δ_H 8.84 (1 H, s

br, OH), 7.41–7.22 (5 H, m, aromatic), 5.69 (1 H, d, *J* 8, NH), 5.15 (2 H, s, CH_2), 4.52 (1 H, m, CH), 3.86 and 3.64 (2 H, AB pattern of d, *J* 9, 3, CH_2OMe) and 3.36 (3 H, s, CH_2O*Me*) [lit.[116] δ_H 7.47–7.28 (5 H, m, aromatic), 5.78 (1 H, d, *J* 8.4, NH), 5.11 (2 H, s, CH_2), 4.45–4.56 (1 H, m, CH), 3.85 (2 H, dd, *J* 9.3, 3.2, CH_2OMe), 3.61 (2 H, dd, *J* 9.3, 2.7, CH_2OMe) and 3.32 (3 H, s, CH_2O*Me*)].

A solution of (*S*)-2-(benzyloxycarbonylamino)-3-methoxypropionic acid (1.15 g, 4.55 mmol) in methanol (15 cm^3) was hydrogenated in the presence of 10% Pd-C (0.25 g). (Approximately 100 cm^3 of hydrogen was used). The catalyst was removed by filtration through Celite and the filtrate evaporated to give *O*-methyl-(*S*)-serine as a colourless solid (0.48 g, 87%), mp 222–224 °C (decomposed) [lit.[116] 228–230°C (decomposed)]; δ_H (CD_3OD) 3.95–3.75 (3 H, m, $CHCH_2$) and 3.52 (3 H, s, Me) [lit.[116] δ_H (CD_3OD) 3.85–3.65 (3 H, m, $CHCH_2$) and 3.39 (3 H, s, Me)]; δ_C (CD_3COD) 72.0, 59.3 and 56.1 (CO not observed) [lit.[116] 172.2 (CO), 72.2 (CH_2), 59.4 (CH_3) and 56.3 (CH)].

O-methyl-(*S*)-serine (0.48 g, 4.03 mmol) was dissolved in NaOH(aq) (1 mol dm^{-3}, 4 cm^3) and the water evaporated. Benzaldehyde (0.42 g, 4 mmol) and dichloromethane (50 cm^3) were added and the mixture heated under reflux with azeotropic removal of water (inverted Dean and Stark trap) for 5-8 hours. The imine was formed as a white precipitate; δ_H 7.73–6.90 (5 H, m, arom.), 3.92 (1 H, br s, CH), 3.58 (2 H, br d, CH_2) and 3.05 (3 H, s, Me).

The mixture was stirred at 0 °C while a solution of benzoyl chloride (0.57 g, 4 mmol) in dichloromethane (15 cm^3) was added and the mixture was then stirred at room temperature overnight. Analysis of the product by ^1H NMR showed that the desired product **394** had not formed.

D. Flash Vacuum Pyrolysis of *N*-acyloxazolidin-5-ones

1. Pyrolysis of (*2R,4S*)-3-benzoyl-2-phenyl-4-methyl-1,3-oxazolidin-5-one 383

a) at 600 °C

A sample of compound **383** (361 mg) was subjected to FVP at 600 °C and 1×10^{-2} Torr. The crude product (0.263 g) was found by ^{1}H NMR analysis to be a mixture of *cis*-4-methyl-2,5-diphenyloxazoline **268** (56%) and *trans*-4-methyl-2,5-diphenyloxazoline **269** (16%), *N*-(1-phenylprop-2-enyl)benzamide **399** (23%) and propiophenone **400** (3%).

b) at 550 °C

A sample of **383** (1.061 g, 3.776 mmol) was subjected to FVP at 550 °C and 6×10^{-3} Torr. The crude product (890 mg, 99%) was chromatographed [alumina, *n*-hexane-ether (8:2)] to give several fractions. Analysis of these showed the products from the reaction to be *cis*-4-methyl-2,5-diphenyloxazoline **268**, *trans*-4-methyl-2,5-diphenyloxazoline **269**, *N*-(1-phenylprop-2-enyl)benzamide **399** and an isomer of 5-methyl-2,4-diphenyloxazoline **270**.

268; (333 mg, 37%); $[\alpha]_D^{20}$ 0.0 (c 1, $CHCl_3$); (Found: M+H$^+$, 238.1230. $C_{16}H_{16}NO$ requires *M*+H$^+$, 238.1232); ν_{max}/cm^{-1} 2924, 1964, 1905, 1885, 1818, 1719, 1651, 1580, 1493, 1449, 1366, 1211, 1175, 1100, 628 and 549; δ_H 8.05 (2 H, m, aromatic), 7.55–7.18 (8 H, m, aromatic), 5.75 (1 H, d, *J* 10, 5-H), 4.66 (1 H, dq, *J* 10, 7, 4-H) and 0.89 (3 H, d, *J* 7, Me) [lit.[117] δ_H 8.06–8.04 (2 H, m, arom.), 7.53–7.47 (1 H, m, arom.), 7.46–7.42 (2 H, m, arom.), 7.37–7.25 (5 H, m, arom.), 5.76 (1 H, d, *J* 10, 5-H), 4.66 (1 H, dq, *J* 10, 7, 4-H) and 0.88 (3 H, d, *J* 7, Me)]; δ_C 162.5 (CN), 136.7 (4ry), 131.0, 128.0 (2 C), 127.9 (2 C), 127.8 (2 C), 127.4, 127.3 (4ry), 125.7 (2 C), 83.5 (C-5), 65.0 (C-4) and 17.4 (Me) [lit.[117] δ_C 163.0, 137.2, 131.5, 128.4, 128.3, 127.9, 127.7, 126.2, 84.1, 65.5 and 17.8]; *m/z* 238 (M + H$^+$, 100%) and 131 (9).

269; (56 mg, 6%); $[\alpha]_D^{20}$ 0.0 (c 1, $CHCl_3$) [lit.,[118] –60.4 (c 1.01, MeOH)]; (Found: M+H$^+$, 238.1227. $C_{16}H_{16}NO$ requires *M*+H$^+$, 238.1232); ν_{max}/cm^{-1} 2924, 1719, 1647, 1580, 1493, 1449, 1397, 1376, 1326, 1175, 1108, 628 and 545; δ_H 8.02 (2 H, m, aromatic), 7.52–7.22 (8 H, m, aromatic), 5.10 (1 H, d, *J* 8, 5-H), 4.21 (1 H, m, 4-H) and 1.49 (3 H, d, *J* 7, Me) [lit.[118] δ_H

8.06–8.00 (2 H, m, arom.), 7.54–7.30 (8 H, m, arom.), 5.10 (1 H, d, *J* 8, 5-H), 4.21 (1 H, dq, *J* 7, 8, 4-H) and 1.49 (3 H, d, *J* 7, Me)]; δ_C 162.8 (CN), 140.4 (4ry), 131.4, 128.8 (2 C), 128.4 (4 C), 128.3, 127.7 (4ry), 125.6 (2 C), 88.2 (C-5), 70.9 (C-4) and 21.4 (Me) [lit.[118] δ_C 162.6, 140.3, 131.3, 128.7, 128.2, 128.2, 128.2, 127.6, 125.5, 88.1, 70.9, 21.5]; *m/z* 238 (M + H^+, 100%) and 131 (16).

399; (137 mg, 15%); mp 105–107 °C; δ_H 7.79 (2 H, m, aromatic), 7.50–7.22 (8 H, m, aromatic), 6.78 (1 H, br d, NH), 6.08 (1 H, ddd, *J* 17, 10, 5, C*H*=CH_2), 5.82 (1 H, br dd, CH-N), 5.28 (1 H, d, *J* 5, =CH_2) and 5.26 (1 H, d, *J* 17, =CH_2) [good agreement with lit. spectrum of *N*-benzoyl derivative, **404**[119] δ_H 6.78 (ddd), 6.45 (d), 5.45 (d) and 5.41 (d)]; δ_C 166.5 (CO), 140.5 (4ry), 137.2, 134.3 (4ry), 131.6, 128.8 (2 C), 128.6 (2 C), 127.8, 127.3 (2 C), 127.0 (2 C), 116.1 and 55.5 (CHN) [*N*-benzoyl lit.[119] 119.4 and 63.7]; *m/z* 237 (M^+, 26%), 222 (16), 132 (9), 115 (11), 105 (100), 77 (44) and 51 (10).

270; (65 mg, 7%); $[\alpha]_D^{20}$ 0.0 (c 1, $CHCl_3$); (Found: M+H^+, 238.1230. $C_{16}H_{16}NO$ requires *M*+H^+, 238.1232); ν_{max}/cm^{-1} 2924, 1964, 1901, 1818, 1719, 1643, 1580, 1493, 1358, 1334, 1207, 1175, 1005, 933 and 858; δ_H 8.06 (2 H, m, aromatic), 758–7.17 (8 H, m, aromatic), 5.43 (1 H, d, *J* 10, 5-H), 5.09 (1 H, dq, *J*10, 7, 4-H) and 0.97 (3 H, d, *J* 7, Me); δ_C 163.6 (CN), 137.0 (4ry), 130.4, 128.3 (4ry), 127.4 (2 C), 127.3 (2 C), 127.2 (2 C), 126.7 (2 C), 126.4, 78.7 (C-5), 71.4 (C-4) and 15.9 (Me); *m/z* 238 (M + H^+, 100%).

c) at 500 °C

A sample of **383** (106.4 mg, 0.377 mmol) was subjected to FVP at 500 °C and 6–10 × 10^{-3} Torr. The crude product (85.7 mg, 97%) was a mixture of **268**, (30.0 mg, 34%), **399** (15.9 mg, 18%) and *cis*-1-benzoyl-2-methyl-3-phenylaziridine **267**.

267; (16.8 mg, 19%) (Found: M+Na^+, 260.1045. $C_{16}H_{15}NO$ requires *M*+*Na*, 260.1051); δ_H 8.2–8.0 (2 H, m, aromatic), 7.5–7.2 (8 H, m, aromatic), 3.86 (1 H, d, *J* 7, 3-H), 2.97 (1 H, quintet, *J* 7, 2-H) and 1.18 (3 H, d, *J* 7, 2–Me) [lit.[9] 8.15–7.5 (10 H, 2 m), 3.72 (1 H, d, *J* 6), 2.90 (1 H, m, *J* 6) and 1.12 (3 H, d, *J* 6)]; δ_C 179.8 (CO), 134.8 (4ry), 132.8, 129.7 (4ry), 129.1(2 C), 128.4 (2 C), 128.3 (2 C), 127.7 (2 C), 127.5, 44.2 (C-3), 40.1 (C-2) and 12.6 (Me)

[lit.[118] δ_C 179.5, 134.6, 132.8, 132.6, 128.9, 128.3, 128.1, 127.6, 127.4, 44.2, 40.1 and 12.6]; *m/z* (GCMS) 237 (M^+, 3%), 222 (8), 132 (9), 115 (11), 105 (94), 77 (100) and 65 (5).

d) at 450 °C

A sample of **383** (4.70 g, 16.73 mmol) was subjected to FVP at 450 °C and 8–10 × 10^{-3} Torr. The product was chromatographed [alumina, ether-pet ether (1:1)]. Analysis by ^1H NMR showed the products from the reaction to be mainly unreacted **383** (3.38 g, 12.04 mmol). Kugelrohr distillation gave **267** (0.91 g, 23%) and **268** (0.20 g, 5%).

e) at 400 °C

A sample of **383** (196 mg, 0.698 mmol) was subjected to FVP at 400 °C and 6–10 × 10^{-3} Torr. Analysis by ^1H NMR showed the products from the reaction to be mainly unreacted **383** (185 mg, 0.658 mmol) and Kugelrohr distillation gave a small amount of **267** (6.5 mg, 4%).

f) at 700 °C

A sample of **383** was subjected to FVP at 700 °C and 7–10 × 10^{-3} Torr. Surprisingly, the major component of the product was propiophenone **400** (21%) followed by **399** (19%), **268** (14%) and **269** (13%). Yields were calculated from ^1H NMR using acetone as an internal standard.

2. Pyrolysis of (*2R,4S*)-3-benzoyl-4-isopropyl-2-phenyl-1,3-oxazolidin-5-one 384

a) at 550 °C

A sample of **384** (599 mg, 1.939 mmol) was subjected to FVP at 550 °C and 8 × 10^{-3} Torr. The crude product (345 mg, 68%) was a 5:1 mixture (by ^1H NMR integration) of *cis*-4-isopropyl-2,5-diphenyloxazoline **407** to *trans*-4-isopropyl-2,5-diphenyloxazoline **408**. This was chromatographed [alumina, *n*-hexane-ether (9:1)].

407 (170 mg, 32%); (Found: M+H^+, 266.1539. $C_{18}H_{19}NO$ requires *M*+H^+, 266.1545); ν_{max}/cm^{-1} 1963, 1950, 1910, 1896, 1844, 1830, 1806, 1741, 1642, 1578, 1494, 1446, 1334,

1210, 1174, 1061, 1026, 951, 906, 860, 765, 704 and 586; δ_H 8.05 (2 H, m, arom.), 7.55–7.10 (8 H, m, arom.), 5.67 (1 H, d, *J* 10, 5-H), 4.20 (1 H, dd, *J* 10, 8, 4-H), 1.00 (1 H, m, CH of Pr^i), 0.92 (3 H, d, *J* 7, Me of Pr^i) and 0.76 (3 H, d, *J* 7, Me of Pr^i); δ_C 163.9 (C=N), 137.7 (4ry), 131.9, 128.9 (2 C), 128.9, 128.8 (2 C), 128.6 (2 C), 128.3 (4ry), 127.6 (2 C), 84.8 (C-5), 76.9 (C-4), 29.7 (*C*H of Pr^i), 21.6 (Me) and 19.9 (Me); *m/z* 266 (M + H$^+$, 100%).

408 (70 mg, 14%); (Found: M+H$^+$, 266.1541. $C_{18}H_{19}NO$ requires *M*+H$^+$, 266.1545); δ_H 8.06 (2 H, m, arom.), 7.55–7.10 (8 H, m, arom.), 5.26 (1 H, d, *J* 6, 5-H), 4.39 (1 H, t, *J* 6, 4-H), 1.60 (1 H, m, CH of Pr^i), 0.98 (3 H, d, *J* 7, Me of Pr^i) and 0.67 (3 H, d, *J* 7, Me of Pr^i) [lit.[118] δ_H 8.07–8.00 (2 H, m), 7.54–7.27 (8 H, m), 5.28 (1 H, d, *J* 6), 4.04 (1 H, dd, *J* 6, 6), 2.12–1.90 (1 H, m), 1.07 (3 H, d, *J* 7) and 1.01 (3 H, d, *J* 7)]; δ_C 164.6 (C=N), 137.3 (4ry), 131.5 (4ry), 130.3, 129.3, 129.1 (2 C), 128.9 (2 C), 128.6 (2 C), 128.5 (2 C), 90.2 (C-5), 72.3 (C-4), 28.3 (*C*H of Pr^i), 20.3 (Me) and 19.5 (Me) [lit.[118] δ_C 162.2, 141.6, 131.1, 128.6, 128.2, 128.1, 127.9, 127.6, 125.5, 83.2, 81.0, 32.9, 18.6 and 18.2]; *m/z* 266 (M + H$^+$, 100%).

The ^{1}H NMR spectrum of each oxazoline (25 mg, 0.094 mmol) was recorded in the presence of praseodymium tris(heptafluorobutrylcamphorate) (25 mg, 0.028 mmol). Using the doublets at 5.67 and 5.26 ppm the compounds appeared to be racemic in each case.

b) at 450 °C

A sample of compound **384** (2.53 g, 8.20 mmol) was subjected to FVP at 450 °C and 7 × 10^{-3} Torr. The crude product was Kugelrohr distilled to give a colourless liquid (0.502 g, 23%) consisting of a single isomer of 1-benzoyl-2-isopropyl-3-phenylaziridine **409** (0.377 g, 17%) and **407** (0.126 g, 6%).

409; δ_H 8.03 (2 H, m, aromatic), 7.55–7.20 (8 H, m, aromatic), 3.69 (1 H, d, *J* 6, 3-H), 2.68 (1 H, dd, *J* 9, 6, 2-H), 1.70–1.48 (1 H, m, CH of Pr^i), 1.19 (3 H, d, *J* 6, Me) and 0.70 (3 H, d, *J* 6, Me), δ_C 179.7 (CO), 133.1 (4ry), 132.6 (4ry), 130.0, 128.9 (2 C), 128.3 (3 C), 128.2 (2 C), 127.4 (2 C), 50.5 (C-3), 45.6 (C-2), 26.0 (CH of Pr^i), 20.8 (Me) and 18.8 (Me).

3. Pyrolysis of (*2R,4S*)-3-benzoyl-4-benzyl-2-phenyl-1,3-oxazolidin-5-one 385

a) at 600 °C

A sample of compound **385** (103 mg, 0.288 mmol) was subjected to FVP at 600 °C and 6–10 × 10^{-3} Torr. The resulting product was chromatographed [alumina, ether-pet ether (1:1)]. Similar fractions were combined and the solvent was removed. The main fraction (26.5 mg, 26%) appeared to be *cis*-4-benzyl-2,5-diphenyloxazoline **410**, (Found: M+H$^+$, 314.1534. $C_{22}H_{20}NO$ requires *M*+H$^+$, 314.1545); ν_{max}/cm^{-1} 1958, 1812, 1701, 1647, 1580, 1525, 1495, 1334, 1175, 1081, 1026, 910, 844, 782, 706 and 654; δ_H (C_6D_6) 8.55–8.45 (2 H, m, aromatic), 7.35–7.10 (13 H, m, aromatic), 5.57 (1 H, d, *J* 10, 5-H), 4.88 (1 H, t of d, *J* 10, 7, 4-H), 2.87 (1 H, half ABX, *J* 15, 10, $PhCH_2$) and 2.60 (1 H, half ABX, *J* 15, 7, $PhCH_2$); δ_C (C_6D_6) 163.0 (CN), 139.8 (4ry), 137.7 (4ry), signals between 131.5 and 127.0 obscured by solvent, 84.1 (C-5), 71.8 (C-4) and 39.2 (CH_2); *m/z* 314 (M + H$^+$, 100%).

For comparison with a literature spectrum of the *trans* isomer[120] this was also recorded in $CDCl_3$, δ_H 8.1–8.0 (2 H, m, aromatic), 7.50–7.10 (11 H, m, aromatic), 6.95 (2 H, m, aromatic), 5.78 (1 H, d, *J* 10, 5-H), 4.88 (1 H, ddd, *J* 10, 8, 7, 4-H), 2.69 (1 H, dd, *J* 14, 8, CH of CH_2) and 2.40 (1 H, dd, *J* 14, 7, CH of CH_2) [cf. lit.[120] for *trans*, δ_H 8.07–8.02 (2 H), 7.5–7.2 (11 H), 6.95–6.9 (2 H), 5.29 (1 H, d, *J* 6), 4.42 (1 H, ddd, *J* 9, 6, 5), 3.34 (1 H, dd, *J* 14, 5) and 2.84 (1 H, dd, *J* 14, 9)]; δ_C 164.2 (CN), 139.2 (4ry), 137.1 (4ry), 132.1, 129.4 (2 C), 129.0 (2 C), 128.9 (2 C), 128.7 (2 C), 128.6, 128.5 (2 C), 127.9 (4ry), 127.3 (2 C), 126.4, 84.5 (C-5), 71.5 (C-4) and 38.8 (CH_2).

A trace of the *trans* isomer **411** was observed in a ratio of approximately 1:7 (from ^{1}H integration) with the *cis* isomer **410**.

414; δ_H 8.04–8.00 (2 H, m, aromatic), 7.60–7.10 (13 H, m, aromatic), 5.30 (1 H, d, *J* 6, 5-H), 4.47 (1 H, ddd, *J* 9, 6, 5, 4-H), 3.35 (1 H, dd, *J* 14, 5, CH of CH_2) and 2.85 (1 H, dd, *J* 14, 9, CH of CH_2) [good agreement with lit.[120]].

b) at 550 °C

A further sample of compound **385** (550 mg, 1.541 mmol) was subjected to FVP at 550 °C and 6–10 × 10^{-3} Torr. The resulting product was chromatographed [silica,

ether–n-hexane (3:7)]. Similar fractions were combined and the solvent was removed. In this case the products obtained were found to be **410** (168 mg, 38%), *N*-(1,3-diphenylprop-2-enyl)benzamide **412** (97 mg, 22%) and 5-benzyl-2,4-diphenyloxazoline **413** (40 mg, 9%).**412**; (Found: M+H$^+$, 314.1536. $C_{22}H_{19}NO$ requires *M+H*, 314.1545); δ_H 7.34–6.94 (10 H, m, arom.), 6.76 (1 H, br d, *J* 8 NH), 6.60 (1 H, dd, *J* 16, 1, =C*H*Ph), 6.41 (1 H, dd, *J* 16, 6, C*H*=CHPh) and 5.78 (1 H, t, *J* 7, NC*H*Ph); δ_C 167.0 (CO), 141.2 (4ry), 136.8 (4ry), 134.7 (4ry), 132.2, 132.1, 129.3 (2 C), 129.1, 129.0 (2 C), 129.0 (2 C), 128.3, 128.2, 127.7 (2 C), 127.5 (2 C), 127.0 (2 C) and 55.7 (N*C*H); *m/z* 314 (M+H$^+$, 3%), 222 (44) and 193 (100).**413**; δ_H 8.04–8.00 (2 H, m, aromatic), 7.6–7.1 (13 H, m, aromatic), 5.49 (1 H, d, *J* 10, 4-H), 5.11 (1 H, dt, *J* 10, 4, 5-H), 2.54 (1 H, dd, *J* 15, 10, CH of CH_2) and 2.38 (1 H, dd, *J* 15, 4, CH of CH_2); δ_C (identifiable signals) 167.1 (CN), 138.6, (4ry), 138.1 (4ry), 131.2 (4ry), 84.8 (C-5), 72.5 (C-4) and 38.4 (CH_2).

c) at 450 °C

A sample of compound **385** (2.48 g, 6.95 mmol) was subjected to FVP at 450 °C and 8 × 10^{-3} Torr. The crude product (1.69 g) was separated by column chromatography [silica, ether-pet ether (1:1)] to give

cis-1-benzoyl-2-benzyl-3-phenylaziridine **414** (289 mg, 13%); (Found: M+H$^+$, 314.1550. $C_{22}H_{19}NO$ requires *M+H*, 314.1545); δ_H 8.0 (2 H, m, aromatic), 7.5–7.0 (13 H, m, aromatic), 3.78 (1 H, d, *J* 6, 3-H), 3.19 (1 H, q, *J* 6, 2-H), 2.99 (1 H, A part of ABX, J_{AB} 15, J_{AX} 5, CH_2Ph) and 2.64 (1 H, B part of ABX, J_{AB} 15, J_{AX} 8, CH_2Ph) [lit.[121] 8.03–7.97 (ortho H of benzoyl, m), 7.52–7.29 (8 H, m), 7.24–7.14 (3 H, m), 7.00–6.93 (2 H, m), 3.78 (1 H, d, *J* 6, 3-H), 3.19 (1 H, ddd, *J* 8, 6, 5, 2-H), 2.99 (1 H, dd, *J* 15, 5, CH_2), 2.63 (1 H, dd, *J* 15, 8, CH_2)]; δ_C 179.5 (CO), 137.7 (4ry), 134.4 (4ry), 132.7, 129.0 (2 C), 128.7 (2 C), 128.4 (4 C), 128.3 (3 C), 127.8, 127.7 (2 C), 126.3, 44.8 (*C*Ph), 44.7 (*C*Ph) and 32.9 (*CH*CH_2); *m/z* 314 (M+H$^+$, 100%), 208 (16), 122 (7) and 56 (43).

4. Pyrolysis of (*2R,4S,2'S*)-3-benzoyl-4-s-butyl-2-phenyl-1,3-oxazolidin-5-one 386

a) at 550 °C

A sample of compound **386** (1.936 g, 6 mmol) was subjected to FVP at 550 °C and 5×10^{-3} Torr. The crude product (1.69 g) was chromatographed [alumina, ether in pet ether (5–15%)] to give i) both *cis*-diastereomers of 4-isobutyl-2,5-diphenyloxazoline **415** (0.328 g, 20%, 0% d.e.); *m/z* 280 ($M+H^+$, 100%) and 222 (9);

1st diastereomer; δ_H 8.06 (2 H, d, arom.), 7.56–7.22 (8 H, m, arom.), 5.73 (1 H, d, *J* 10, 5-H), 4.28 (1 H, dd, *J* 10, 8, 4-H), 1.22 (1 H, m, CH of Bu^s), 1.10–0.88 (2 H, m, CH_2), 0.63 (3 H, d, *J* 6, CH*Me*) and 0.59 (3 H, t, *J* 7, CH_2*Me*); δ_C 163.9 (CN), 137.9 (4ry), 131.9 (4ry), 131.8, 129.1, 128.9 (2 C), 128.8 (2 C), 128.6 (2 C), 127.7 (2 C), 84.8 (C-5), 76.5 (C-4), 36.0 (*C*HMe), 26.4 (*C*H_2Me), 17.7 (CH*Me*) and 11.6 (CH_2*Me*).

2nd diastereomer; δ_H 8.07 (2 H, d, arom.), 7.56–7.22 (8 H, m, arom.), 5.76 (1 H, d, *J* 10, 5-H), 4.39 (1 H, dd, *J* 10, 7, 4-H), 1.62 (1 H, m, CH_2), 1.03 (1 H, m, CH_2), 1.02 (1 H, m, CH of Bu^s), 0.70 (3 H, d, *J* 7, CH*Me*) and 0.58 (3 H, t, *J* 7, CH_2*Me*); δ_C 163.8 (CN), 137.9 (4ry), 131.9 (4ry), 131.3, 128.9 (2 C), 128.8 (2 C), 128.6 (2 C), 128.5, 127.3 (2 C), 84.7 (C-5), 74.9 (C-4), 36.2 (*C*HMe), 28.4 (*C*H_2Me), 16.0 (CH*Me*) and 12.0 (CH_2*Me*).

ii) both *trans*-diastereomers of 4-isobutyl-2,5-diphenyloxazoline **415** (0.132g, 7%, 12% d.e.); (Found: $M+H^+$, 280.1691. $C_{19}H_{21}NO$ requires $M+H^+$, 280.1701); *m/z* 280 ($M + H^+$, 100%), 193 (23), 123 (16), 58 (48), 57 (62), 56 (44) and 43 (95);

1st diastereomer; δ_H 8.09 (2 H, d, arom.), 7.58–7.09 (8 H, m, arom.), 5.36 (1 H, d, *J* 9, 5-H), 4.59 (1 H, t, *J* 9, 4-H), 1.33 (1 H, m, CH of Bu^s), 1.31 (1 H, m, CH_2), 1.01 (1 H, m, CH_2), 0.95 (3 H, d, *J* 6, CH*Me*), 0.64 (3 H, t, *J* 7, CH_2*Me*); δ_C 165.2 (CN), 138.0 (4ry), 132.1 (4ry), 129.2 (2 C), 128.81 (2 C), 128.78 (2 C), 128.7, 128.5 (2 C), 128.0, 88.4 (C-5), 72.4 (C-4), 34.9 (*C*HMe), 26.5 (*C*H_2Me), 16.0 (CH*Me*) and 11.2 (CH_2*Me*).

2nd diastereomer; δ_H 8.05 (2 H, d, arom.), 7.58–7.09 (8 H, m, arom.), 5.27 (1 H, d, *J* 9, 5-H), 4.50 (1 H, dd, *J* 10, 9, 4-H), 1.78 (1 H, m, CH_2), 1.45 (1 H, m, CH of Bu^s), 1.30 (1 H, m, CH_2), 0.84 (3 H, t, *J* 7, CH_2*Me*) and 0.70 (3 H, d, *J* 6, CH*Me*); δ_C 165.2 (CN), 138.2 (4ry), 131.9, 128.9 (2 C), 128.81 (2 C), 128.78 (2 C), 128.5 (2 C), 128.3 (4ry), 128.1, 88.9 (C-5), 72.6 (C-4), 35.4 (*C*HMe), 26.8 (*C*H_2Me), 15.5 (CH*Me*) and 10.9 (CH_2*Me*).

iii) 2 isomers of *N*-(3-methyl-1-phenylpent-2-enyl)benzamide **416** (0.293 g, 17%); *m/z* 280 (M + H^+, 100%).

1st isomer; δ_H 7.78 (2 H, m, aromatic), 7.55–7.18 (8 H, m, aromatic), 6.45 (1 H, br d, *J* 8, NH), 6.03 (1 H, t, *J* 8, C*H*Ph), 5.36 (1 H, m, =C*H*), 2.26 (1 H, m, CH_2Me), 1.77 (3 H, d, *J* 1, *Me*C=) and 1.04 (3 H, t, *J* 7 CH_2*Me*); δ_C 166.2 (CO), 142.4 (4ry), 142.1 (4ry), 134.4 (*C*=CH), 131.4, 128.6 (2 C), 128.5 (2 C), 127.1, 126.9 (2 C), 126.5 (2 C), 123.8, 51.1 (*C*HPh), 32.2 (*C*H_2Me), 22.9 (=CH*Me*) and 12.8 (CH_2*Me*).

2nd isomer; δ_H 7.78 (2 H, m, aromatic), 7.55–7.18 (8 H, m, aromatic), 6.45 (1 H, br d, *J* 8 NH), 6.03 (1 H, t, *J* 8, C*H*Ph), 5.36 (1 H, m, =C*H*), 2.09 (1 H, q, *J* 8, CH_2Me), 1.93 (3 H, d, *J* 1, *Me*C=) and 1.03 (3 H, t, *J* 8, CH_2*Me*); δ_C 166.3 (CO), 142.4 (4ry), 142.0 (4ry), 134.4 (*C*=CH), 131.4, 128.6 (2 C), 128.5 (2 C), 127.1, 126.9 (2 C), 126.5 (2 C), 122.7, 51.4 (*C*HPh), 25.5 (*C*H_2Me), 16.9 (=CH*Me*) and 12.4 (CH_2*Me*).

There was also a trace of what is likely to be an isomer of 5-isobutyl-2,4-diphenyloxazoline.

b) at 450 °C

A sample of compound **386** (700 mg, 2.167 mmol) was subjected to FVP at 550 °C and 6×10^{-3} Torr. The crude product (640 mg) was distilled to give both diastereomers of 1-acetyl-2-s-butyl-3-phenylaziridine **417** (146 mg, 24%, 18% d.e.); (Found: M+H^+, 280.1709. $C_{19}H_{21}NO$ requires *M+H*, 280.1701); *m/z* 280 (M+H^+, 100%);

1st diastereomer; δ_H 7.91 (2 H, d, arom.), 7.59–7.10 (8 H, m, arom.), 3.60 (1 H, d, *J* 6, 3-H), 3.17 (1 H, dd, *J* 10, 6, 2-H), 1.69 (1 H, m, CH_2), 1.31 (1 H, m, CH_2), 1.10 (1 H, m, CH of Bu^s), 1.08 (3 H, d, *J* 7, CH*Me*) and 0.51 (3 H, t, *J* 7, CH_2*Me*); δ_C 180.4 (CO), 135.4 (4ry), 130.6 (4ry), 130.5, 129.4 (2 C), 129.1, 128.8 (2 C), 128.7 (2 C), 127.9 (2 C), 50.2 (C-3), 46.7 (C-2), 32.6 (*C*HMe), 27.4 (*C*H_2Me), 18.7 (CH*Me*) and 11.7 (CH_2*Me*).

2nd diastereomer; δ_H 7.91 (2 H, d, arom.), 7.59–7.10 (8 H, m, arom.), 3.57 (1 H, d, *J* 6, 3-H), 3.16 (1 H, dd, *J* 10, 6, 2-H), 1.64 (1 H, m, CH_2), 1.40 (1 H, m, CH_2), 1.10 (1 H, m, CH of Bu^s), 0.91 (3 H, t, *J* 7, CH_2*Me*) and 0.55 (3 H, d, *J* 7, CH*Me*); δ_C 180.1 (CO), 135.1 (4ry), 133.2 (4ry), 130.5, 129.4 (2 C), 128.81 (2 C), 128.0 (2 C), 127.9 (2 C), 49.8 (C-3), 45.5 (C-2), 32.1 (*C*HMe), 28.7 (*C*H_2Me), 16.4 (CH*Me*) and 11.5 (CH_2*Me*).

5. Pyrolysis of (*2S, 4R*)-3-benzoyl-2,4-diphenyl-1,3-oxazolidin-5-one 387

a) at 550 °C

A sample of compound **387** (573.9 mg, 1.67 mmol) was subjected to FVP at 550 °C and 8×10^{-3} Torr. ^{1}H NMR of the crude product (410 mg, 82%) showed it to be a mixture of *cis*-2,4,5-triphenyloxazoline **419** and *trans*-2,4,5-triphenyloxazoline **418** in a ratio of approximately 1:2. These were separated by column chromatography [alumina, pet ether-ether (6:4)]. Compound **75** was recrystallised from dichloromethane and ether.

418; (197.6 mg, 40%); $[\alpha]_D^{20}$ 0.0 (c 1, $CHCl_3$); mp 110–112 °C (Found C, 84.1; H, 5.7; N, 4.6. $C_{23}H_{17}NO_3$ requires C, 85.4; H, 5.3; N, 4.3%); ν_{max}/cm^{-1} 3686, 3055, 1649, 1604, 1581, 1495, 1451, 1325, 1261, 1177, 1086, 1065, 969, 894, 765, 752, 736, 724, 705 and 694; δ_H 8.2–8.1 (2 H, m, aromatic), 7.5–6.9 (13 H, m, aromatic), 5.42 (1 H, d, *J* 8, 5-H) and 5.25 (1 H, d, *J* 8, 4-H) [lit.[120] 8.15–8.12 (2 H), 7.49–7.13 (13 H), 5.41 (1 H, d, *J* 8, OCH) and 5.23 (1 H, d, *J* 8, NCH)]; δ_C 164.5 (CN), 142.4 (4ry), 140.9 (4ry), 132.2, 129.4 (2 C), 129.3 (2 C), 129.1 (2 C), 128.9 (2 C), 128.9, 128.2, 127.9 (4ry), 127.2 (2 C), 126.1 (2 C), 89.4 (C-5) and 79.4 (C-4); *m/z* 300 ($M + H^+$, 100%).

419; (58.7 mg, 12%); $[\alpha]_D^{20}$ 0.0 (c 1, $CHCl_3$); δ_H 8.2–8.1 (2 H, m, aromatic), 7.5–6.9 (13 H, m, aromatic), 6.03 (1 H, d, *J* 10, 5-H) and 5.77 (1 H, d, *J* 10, 4-H) [lit.[69] 8.21–8.17 (2 H), 7.55–6.92 (13 H), 6.03 (1 H, d) and 5.76 (1 H, d)]; δ_C 165.4 (CN), 138.1 (4ry), 136.9 (4ry), 136.9 (4ry), 132.2, 129.0 (2 C), 129.0 (2 C), 128.3 (2 C), 128.1 (2 C), 128.1 (2 C), 127.8, 127.4, 126.7 (2 C), 85.7 (C-5) and 74.8 (C-4); *m/z* 300 ($M + H^+$, 100%) and 226 (83).

b) at 500 °C

A sample of compound **387** (101 mg, 0.294 mol) was subjected to FVP at 500 °C and $6–10 \times 10^{-3}$ Torr. The crude product (37 mg, 0.125 mol, 43%) showed ^{1}H NMR signals indicating the presence of four compounds which in decreasing order of amount were **418**, **419**, *cis*-1-benzoyl-2,3-diphenylaziridine **420** and *trans*-1-benzoyl-2,3-diphenylaziridine **421**.

420; δ_H 8.2–6.9 (15 H, m) and 4.08 (2 H, s, CH) [lit.[9] 8.1–7.3 (15 H, m) and 4.10 (2 H, s)].

421; δ_H 8.2–6.9 (15 H, m) and 3.97 (2 H, s, CH) [lit.[9] 8.0–7.4 (15 H, m) and 4.00 (2 H, s)].

c) at 450 °C

A further sample of compound **387** (106 mg, 0.309 mmol) was subjected to FVP at 450 °C and 1×10^{-2} Torr. From ^{1}H integration the resulting crude product (33 mg, 36%) was found to be **418**, **420**, **419** and **421** in a ratio of 4:4:2:1 along with some of starting material, spectra as above.

d) at 400 °C

A sample of compound **387** (122 mg, 0.356 mmol) was subjected to FVP at 400 °C and $6–10 \times 10^{-3}$ Torr. Analysis by ^{1}H NMR showed the products of the reaction to be mainly unreacted **387**, but traces of **420** and **421** were observed.

6. Pyrolysis of (*2R, 4S*)-3-acetyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one 388

a) at 550 °C

A sample of compound **388** (2.00 g, 9.132 mmol) was subjected to FVP at 550 °C and 1×10^{-2} Torr. The resulting crude product was a mixture of *cis*-2,4-dimethyl-5-phenyloxazoline **423** (15%) and *trans*-2,4-dimethyl-5-phenyloxazoline **424** (9%), 3-acetamido-3-phenylprop-1-ene **425** (44%) and a trace of 1-acetyl-2-methyl-3-phenylaziridine **422** (7%). Yields were calculated from ^{1}H NMR using acetone as an internal standard.

423, δ_H 7.5-7.1 (5 H, m, arom.), 5.56 (1 H, d, *J* 10, 5-H), 4.38 (1 H, m, 4-H), 2.08 (3 H, d, *J* 1, 2-Me) and 0.75 (3 H, d, *J* 7, 4-Me) [lit.[122] 7.37–7.26 (3 H, m), 7.20–7.15 (2 H, m), 5.57 (1 H, d, *J* 9.77), 4.45–4.37 (1 H, m), 2.10 (3 H, d, *J* 1.46) and 0.76 (3 H, d, *J* 7.33)]; δ_C 163.7 (CN), 136.4 (4ry), 127.3, 126.9 (2 C), 125.5 (2 C), 83.5 (C-5), 64.3 (C-4), 17.3 (2-Me) and 13.4 (4-Me) [lit.[122] 164.0, 137.1, 128.3, 127.8, 126.1, 84.0, 65.5, 17.8 and 14.1].

424, δ_H 7.5–7.1 (5 H, m, arom.), 4.90 (1 H, d, *J* 8, 5-H), 3.97 (1 H, m, 4-H), 2.05 (3 H, d, *J* 1, 2-Me) and 1.36 (3 H, d, *J* 7, 4-Me) [good agreement with lit.[123]]; δ_C 163.5 (CN), 139.9 (4ry), 128.5 (2 C), 128.2, 125.3 (2 C), 87.7 (C-5), 69.8 (C-4), 20.9 (2-Me) and 12.1 (4-Me) [good agreement with lit.[123]].

425, δ_H 7.5–7.1 (5H, m, arom.), 6.07–5.9 (1 H, ddd, *J* 16, 10, 5, C*H*=CH_2), 5.63 (1 H, t, *J* 5, CH-N), 5.23 (1 H, d, =CH_2) and 5.16 (1 H, d, =CH_2) and 1.96 (3 H, s, *Me*CO) [lit.[124] 7.40–7.22 (5 H), 6.01 (1 H, ddd, *J* 17, 10, 5, CH=CH_2), 5.80 (1 H, br, NH), 5.64 (1 H, m, PhC*H*), 5.26 (1 H, dt, *J* 10, 1, CH=C$H_{(Z)}$), 5.22 (1 H, dt, *J* 17, 1.5, CH=C$H_{(E)}$) and 2.03 (3 H, s, NCOMe)]; δ_C 169.2 (CO), 140.4 (4ry), 137.2 (CH=), 128.0 (2 C), 127.8, 126.8 (2 C), 115.1 (=CH_2), 54.7 (CH) and 22.5 (Me); *m/z* 176 (M + H^+, 66%) and 134 (84).

Chromatographic separation gave **422** (80 mg, 5%), **425** (355 mg, 22%) (Found: M+H^+, 176.1067. $C_{11}H_{14}NO$ requires *M*+H^+, 176.1075); and 2-acetamido-1-phenylpropanol (470 mg, 27%).

major isomer: δ_H 7.35–7.05 (5 H, m, arom.), 6.02 (1 H, d, *J* 9, NH), 4.80 (1 H, d, *J* 3, 1-H), 4.17 (1 H, m, 2-H), 3.60 (1 H, br s, OH), 1.86 (3 H, s, MeCO) and 0.92 (3 H, d, *J* 7, 2-Me); δ_C 170.4 (CO), 141.1 (4ry), 127.6 (2 C), 126.7, 125.7 (2 C), 75.1(*C*HPh), 50.7 (*C*HMe), 22.6 (*Me*CO) and 13.0 (2-Me).

minor isomer: δ_H 7.35–7.05 (5 H, m, arom.), 6.02 (1 H, d, *J* 9, NH), 4.52 (1 H, d, *J* 5, 1-H), 4.11 (1 H, m, 2-H), 3.60 (1 H, br s, OH), 1.80 (3 H, s, MeCO) and 1.05 (3 H, d, 2-Me); δ_C 170.8 (CO), 141.8 (4ry), 127.7 (2 C), 127.0, 126.0 (2 C), 76.2 (*C*HPh), 51.0 (*C*HMe), 22.5 (*Me*CO) and 17.1 (2-Me).

b) at 500 °C

A sample of compound **388** (200 mg, 9.12mmol) was subjected to FVP at 500 °C and 1 × 10^{-2} Torr. The resulting crude product (175mg) was a mixture of **422** (see below for data), **423**, **424**, **425** and starting material **388**.

c) at 450 °C

A sample of compound **388** (2.23 g, 10.18 mmol) was subjected to FVP at 450 °C and 1 × 10^{-2} Torr. The resulting crude product after distillation was found to be the starting material **388** (1.51 g, 64%) and 1-acetyl-2-methyl-3-phenylaziridine **422**; (222 mg, 12%); $[\alpha]_D^{20}$ –22.7 (c 1, $CHCl_3$); δ_H 7.4–7.28 (5 H, m, arom.), 3.62 (1 H, d, *J* 6, 3-H), 2.89 (1 H, quintet, *J* 6, 2-H),

2.21 (3 H, s, MeCO) and 1.02 (3 H, d, *J* 6, 2-Me); δ_C 183.2 (CO), 134.5 (4ry), 128.0 (2 C), 127.3 (2 C), 126.4, 42.7 (C-3), 38.9 (C-2), 23.0 (*Me*CO) and 12.4 (Me).

c) at 600 °C

A sample of compound **388** (100 mg, 0.46 mmol) was subjected to FVP at 450 °C and 5 × 10^{-2} Torr. The resulting crude product (72mg, 89%) was found to be a mixture of **425**, **423** and **424** in a 4 : 3 : 2 ratio.

7. Pyrolysis of (*2R,4S*)-3-acetyl-4-isopropyl-2-phenyl-1,3-oxazolidin-5-one 389

a) at 550 °C

A sample of compound **389** (506 mg) was subjected to FVP at 550 °C and 8 × 10^{-3} Torr. The resulting product was chromatographed [alumina, ether-pet ether (1:1)]. The major product appeared to be a single isomer of 4-isopropyl-2-methyl-5-phenyloxazoline **426** (61.8 mg, 15%), δ_H 7.4–7.2 (5 H, m, aromatic), 5.07 (1 H, d, *J* 8, 5-H), 3.81 (1 H, t, *J* 8, 4-H), 2.08 (3 H, d, *J* 1, 2-Me), 1.82 (1 H, m, C*H*Me_2), 1.01 (3 H, d, *J* 7, CH*Me*$_2$) and 0.95 (3 H, d, *J* 7, CH*Me*$_2$).

b) at 450 °C

A sample of compound **389** (2.75 g, 11.13 mmol) was subjected to FVP at 450 °C and 8 × 10^{-3} Torr. The resulting product was Kugelrohr distilled to give a single isomer of 1-acetyl-2-isopropyl-3-phenylaziridine **427** (517 mg, 23%, 16% ee); $[\alpha]_D^{20}$ –26.3 (c 1, $CHCl_3$) (Found: M+H$^+$, 204.1383. $C_{13}H_{17}NO$ requires *M*+H$^+$, 204.1388); ν_{max}/cm^{-1} 2962, 1700, 1468, 1454, 1427, 1367, 1314, 1269, 1278, 1230, 1090, 1032, 763 and 701; δ_H 7.4–7.2 (5 H, m, aromatic), 3.67 (1 H, d, *J* 6, 3-H), 2.42 (1 H, dd, *J* 9, 6, 2-H), 2.19 (3 H, s, *Me*CO), 1.22–1.08 (1 H, m, *CH*Me_2) 1.12 (3 H, s, *Me*$_2$CH) and 0.70 (3 H, d, *J* 6, *Me*$_2$CH); δ_C 183.8 (CO), 135.3 (4ry), 128.9 (2 C), 127.8, 127.7 (2 C), 51.1 (C-3), 43.6 (C-2) 26.8 (Me_2*CH*), 23.6 (*Me*CO), 21.4 (*Me*$_2$CH) and 19.0 *Me*$_2$CH)); *m/z* 203 (M$^+$, 2%), 160 (67), 146 (7), 114 (51), 106 (14), 100 (11), 91 (20), 77 (15), 72 (100), 55 (23) and 43 (27).

8. Pyrolysis of (*2R, 4S*)-3-acetyl-4-benzyl-2-phenyl-1,3-oxazolidin-5-one 390

a) at 550 °C

A sample of compound **390** (1.01 g, 3.42 mmol) was subjected to FVP at 550 °C and 7 × 10^{-3} Torr. The crude product (0.746. g, 87 %) was found to be a mixture of *cis*-4-benzyl-2-methyl-5-phenyloxazoline **428**, *trans*-4-benzyl-2-methyl-5-phenyloxazoline **429** and *N*-(1,3-diphenylprop-2-enyl)acetamide **430** in a ratio of approximately 10:9:3. Both of these oxazolines hydrolysed during column chromatography [SiO_2, ether-n-hexane (8:92)].

cis-4-benzyl-2-methyl-5-phenyloxazoline **428**; δ_H 7.34–6.94 (10 H, m, arom.), 5.55 (1 H, d, *J* 10, 5-H), 4.62 (1 H, m, 4-H), 2.41 (1 H, A part of ABX, J_{AB} 14, J_{AX} 5, CH_2Ph), 2.30 (1H, B part of ABX, J_{AB} 14, J_{AX} 6, CH_2Ph) and 2.09 (3 H, d, *J* 1, 2-Me) [lit.[125] δ_H (DMSO) 7.50 and 7.40 (10 H, 2 × s, arom.), 5.70 (1 H, d, *J* 7, 5-H), 4.20–3.80 (1 H, m, 4-H), 2.82 (2 H, m, CH_2) and 2.10 (3 H, s, 2-Me)]; δ_C 163.6 (CN), 137.7 (4ry), 135.4 (4ry), 127.5 (2 C), 127.2 (2 C), 127.0 (2 C), 126.7, 126.5, 126.1 (2 C), 82.7 (C-5), 69.7 (C-4), 37.4 (CH_2) and 13.0 (2-Me).

trans-4-benzyl-2-methyl-5-phenyloxazoline **429**; δ_H 7.34–6.94 (10 H, m, arom.), 5.07 (1 H, d, *J* 6, 5-H), 4.20 (1 H, m, 4-H), 3.15 (1 H, A part of ABX, J_{AB} 14, J_{AX} 6, CH_2Ph), 2.75 (1H, B part of ABX, J_{AB} 14, J_{AX} 8, CH_2Ph) and 2.07 (3 H, d, *J* 1, 2-Me); δ_C 163.4 (CN), 139.7 (4ry), 137.3 (4ry), 127.9 (2 C), 127.8 (2 C), 127.4 (2 C), 126.8 (2 C), 126.6, 126.4, 83.9 (C-5), 75.1 (C-4), 40.8 (CH_2) and 13.1 (2-Me).

N-(1,3-diphenylprop-2-enyl)acetamide **430**; δ_H 7.34–6.94 (10 H, m, arom.), 6.47 (1 H, br, NH), 6.41 (1 H, dd, *J* 16, 1, =C*H*Ph), 6.20 (1 H, dd, *J* 16, 6, C*H*=CHPh), 5.78 (1 H, ddd, *J* 8, 6, 1, NC*H*Ph) and 1.97 (3 H, s, MeCO); δ_C 168.3 (CO), 139.8, (4ry), 137.9 (4ry), 130.2, 128.5, 127.70 (2 C), 127.65 (2 C), 125.5 (2 C), 125.4 (2 C), 124.9, 124.0, 53.7 (N*C*HPh) and 22.2 (CO*Me*).

b) at 450 °C

A sample of compound **390** (3.07 g) was subjected to FVP at 450 °C and 1 × 10^{-3} Torr. The crude product was Kugelrohr distilled to give a single isomer of 1-acetyl-2-benzyl-3-phenylaziridine **431** (0.324 g, 12%); $[\alpha]_D^{20}$ –5.7 (c 1, $CHCl_3$); (Found: M+H^+, 252.1380.

$C_{17}H_{17}NO$ requires *M+H*, 252.1388); ν_{max}/cm^{-1} 3317, 3085, 3062, 3029, 1952, 1885, 1801, 1700, 1604, 1544, 1496, 1453, 1369, 1280, 1280, 1230, 1179, 1088, 1030, 966, 918, 748 and 701; *m/z* 252(M + H^+, 100%); δ_H 7.4–7.1 (10 H, m, aromatic), 3.73 (1 H, d, *J* 6, 3-H), 2.97 (1 H, q, *J* 6, 2-H), 2.62 and 2.53 (2 H, AB pattern of d, *J* 12, 6, CH_2Ph) and 2.01 (3 H, s, *Me*CO); δ_C 183.3 (CO), 138.0 (4ry), 134.5 (4ry), 128.7, 128.4, 128.2, 127.7, 127.5, 126.6, 44.7, 43.1, 33.4 (CH_2) and 23.1 (*Me*CO).

9. Pyrolysis of (*2R,4S,2'S*)-3-acetyl-4-s-butyl-2-phenyl-1,3-oxazolidin-5-one 391

a) at 550 °C

A sample of compound **391** (645 mg, 2.471 mmol) was subjected to FVP at 550 °C and 9×10^{-3} Torr. The crude product (445 mg, 83%)was chromatographed [alumina, ether-pet ether (1:1)]. This gave (i) two diastereomers of 4-s-butyl-2-methyl-5-phenyloxazoline **432** (134 mg, 25%) and (ii) *N*-(3-methyl-1-phenylpent-2-enyl)acetamide **433** (120 mg, 22%).

4-s-butyl-2-methyl-5-phenyloxazoline **432**; (134 mg, 25%); *m/z* 217 (M^+, 3%), 174 (100), 146 (23), 128 (6), 118 (11), 106 (46), 91 (55), 86 (11), 77 (10) and 43 (29).

1st diastereomer; δ_H 7.35–7.08 (5 H, m, aromatic), 5.00 (1 H, d, *J* 7, 5-H), 3.850 (1 H, t, *J* 7, 4-H), 2.01 (3 H, d, *J* 1, 2-Me), 1.66–1.08 (3 H, 2 × m, CH_2Me and *CH*Me), 0.83 (3 H, d, *J* 7, CH*Me*) and 0.82 (3 H, t, *J* 7, CH_2*Me*); δ_C 163.4 (CN), 141.6 (4ry), 128.7 (2 C), 128.1 (2 C), 125.8, 83.1 (C-5), 79.3 (C-4), 39.1 (2-Me), 35.8 (*CH*Me), 25.6 (CH_2), 14.5 (CH*Me*) and 11.5 (CH_2*Me*).

2nd diastereomer; δ_H 7.35–7.08 (5 H, m, aromatic), 4.99 (1 H, d, *J* 7, 5-H), 3.854 (1 H, t, *J* 7, 4-H), 2.01 (3 H, d, *J* 1, 2-Me), 1.66–1.08 (3 H, 2 × m, CH_2Me and *CH*Me), 0.87 (3 H, d, *J* 7, CH*Me*) and 0.83 (3 H, t, *J* 7, CH_2*Me*); δ_C 163.6 (CN), 141.6 (4ry), 128.7 (2 C), 128.1 (2 C), 125.8, 84.0 (C-5), 79.3 (C-4), 39.3 (2-Me), 36.3 (*CH*Me), 25.7 (CH_2), 13.9 (CH*Me*), 11.7 (CH_2*Me*).

The diastereomeric excess of the oxazolines was calculated directly from the ^1H NMR spectrum to be 12%.

(*E/Z*)-*N*-(3-methyl-1-phenylpent-2-enyl)acetamide **433**; (120 mg, 22%) (Found: M+Na^+, 240.1358. $C_{14}H_{19}NO$ requires *M* +Na^+, 240.1364); δ_H 7.28–7.06 (5 H, m, aromatic), 6.59 (1

H, d, *J* 8, NH), 5.72 (1 H, t, *J* 8, C*H*Ph), 5.18 (1 H, m, C*H*=C), 2.06* (2 H, m, CH_2), 1.94 (2 H, q, *J* 7, CH_2), 1.83 (3 H, s, 2-Me), 1.82* (3 H, s, 2-*Me*), 1.64 (3 H, d, *J* 1, *Me*C=), 1.63* (3 H, d, *J* 1, *Me*C=), 0.91 (3 H, t, *J* 7, CH_2Me) and 0.89* (3 H, t, *J* 7, CH_2Me); δ_C 169.7 (CO), 169.6* (CO), 143.0* (4ry), 142.9 (4ry), 141.6* (4ry), 141.5 (4ry), 128.9, 127.4, 126.9, 124.5, 123.4, 51.4 (*C*HPh), 51.1* (*C*HPh), 32.6* (CH_2Me), 25.8 (CH_2Me), 23.6 (CO*Me*), 23.3* (=C*Me*), 17.2 (=C*Me*), 13.1* (CH_2Me), and 12.8 (CH_2Me).

After approximately two weeks the oxazolines had begun to hydrolyse to 2-acetamido-3-methyl-1-phenylpentan-1-ol; *m/z* 258 (M + Na^+, 100%).

1st diastereomer; δ_H 7.39–7.21 (5 H, m, aromatic), 5.85 (1 H, d, *J* 9, NH), 4.93 (1 H, d, *J* 4, C*H*Ph), 3.78 (1 H, ddd, *J* 9, 8, 4, C*H*NH), 1.88 (3 H, s, CO*Me*), 1.73 (1 H, m, *CH*Me), 1.56 (1 H, m, CH_2), 1.17 (1 H, m, CH_2), 1.03 (3 H, d, *J* 7, *CHMe*) and 0.89 (3 H, t, *J* 7, CH_2Me).

2nd diastereomer; δ_H 7.39–7.21 (5 H, m, aromatic), 5.82 (1 H, d, *J* 9, NH), 4.79 (1 H, d, *J* 6, C*H*Ph), 3.78 (1 H, dt, *J* 9, 6, C*H*NH), 1.95 (3 H, s, CO*Me*), 1.58 (1 H, m, *CH*Me), 1.54 (1 H, m, CH_2), 1.12 (1 H, m, CH_2), 0.90 (3 H, d, *J* 7, CH*Me*) and 0.88 (3 H, t, *J* 7, CH_2Me).

b) at 450 °C

A sample of compound **391** (2.15 g, 8.24 mmol) was subjected to FVP at 450 °C and 1 × 10^{-3} Torr. The resulting product was Kugelrohr distilled to give 1-acetyl-2-s-butyl-3-phenylaziridine **434** (0.517 g, 29%, d.e. 14%); $[\alpha]_D^{20}$ –30.8 (c 1, $CHCl_3$); (Found: M+H^+, 218.1554. $C_{14}H_{20}NO$ requires *M+H*, 218.1545); ν_{max}/cm^{-1} 2963, 2929, 2876, 1700, 1457, 1426, 1376, 1315, 1279, 1229, 761 and 701; *m/z* 218 (M + H^+, 100%).

1st diastereomer; δ_H 7.4–7.2 (5 H, m, aromatic), 3.66 (1 H, d, *J* 6, 3-H), 2.52–2.44 (1 H, m, 2-H), 2.18 (3 H, s, *Me*CO), 1.25–0.84 (2 H, 2 × m, CH_2Me), 1.07–0.85 (1 H, m, C*H*Me), 0.65 (3 H, d, *J* 7, *Me*CH) and 0.61 (3 H, t, *J* 7, *Me*CH_2); δ_C 183.3 (CO), 134.8 (4ry), 128.0, 127.33 (2 C), 127.29 (2 C), 50.0 (C-3), 43.5 (C-2), 31.9 (Me*C*H), 26.6 (MeCH_2), 23.2 (*Me*CO), 18.2 (CH*Me*) and 11.0 (CH_2Me).

2nd diastereomer: δ_H 7.4–7.2 (5 H, m, aromatic), 3.62 (1 H, d, *J* 6, 3-H), 2.52–2.44 (1 H, m, 2-H), 2.17 (3 H, s, *Me*CO), 1.75–1.62 (1 H, m, CH_2Me), 1.45–1.30 (1 H, m, CH_2Me), 1.10 (3 H,

d, *J* 7, *Me*CH), 1.07–0.85 (1 H, m, C*H*Me) and 0.93 (3 H, t, *J* 7, *Me*CH_2); δ_C 183.1 (CO), 134.8 (4ry), 127.9, 127.33 (2 C), 127.29 (2 C), 49.8 (C-3), 42.5 (C-2), 31.9 (Me*C*H), 28.0 (Me*C*H_2), 23.2 (*Me*CO), 15.3 (CH*Me*) and 10.9 (CH_2*Me*).

10. Pyrolysis of (*2S, 4R*)-3-acetyl-2,4-diphenyl-1,3-oxazolidin-5-one 392

a) at 550 °C

A sample of compound **392** (111 mg, 0.395 mmol) was subjected to FVP at 550 °C and 1×10^{-2} Torr. Initially the crude product (90 mg, 96%) was a mixture of *cis*-2-methyl-4,5-diphenyloxazoline **437** and *trans*-2-methyl-4,5-diphenyloxazoline **438** in a ratio of 1:4, but these were found to slowly hydrolyse in air to 2-acetamido-1,2-diphenylethanols **439** and **440**.

438; δ_H 7.6–6.75 (10 H, m, aromatic), 5.24 (1 H, d, *J* 8, 5-H), 5.02 (1 H, dq, *J* 8, 1, 4-H) and 2.24 (3 H, d, *J* 1, 2–Me) [cf. lit.[126] for *trans*; 7.6–7.2 (10 H, m, arom.), 5.20 (1 H, d, *J* 7.6, CHO), 5.00 (1 H, dq, *J* 7.6, 1.4) and 2.20 (3 H, d, *J* 1.4, Me)].

437; δ_H 7.6–6.75 (10 H, m, aromatic), 5.82 (1 H, d, *J* 10, 5-H), 5.52 (1 H, dq, 10, 1, 4-H) and 2.28 (3 H, d, *J* 1, 2-Me).

(*1R*, 2S**)-2-acetamido-1,2-diphenylethanol **440**; δ_H 7.37–7.12 (10 H, m, aromatic), 6.62 (1 H, d, *J* 8, NH), 5.15 (1 H, dd, *J* 8, 5, 2-H), 4.92 (1 H, d, *J* 5, 1-H), 3.53 (1 H, br s, OH) and 1.88 (3 H, s, *Me*CO) [cf. lit.[126] for (*1R, 2S*) 7.25 (arom.), 5.16 (dd, *J* 7.9, 4.7, CHO), 4.94 (d, *J* 4.7, CHN) and 1.9 (s, Me)].

(*1S*, 2S**)-2-acetamido-1,2-diphenylethanol **439**; δ_H 7.05–6.92 (10 H, m, aromatic), 6.62 (1 H, d, *J* 8, NH), 5.21 (1 H, dd, *J* 8, 3, 2-H), 5.00 (1 H, d, *J* 3, 1-H), 3.53 (1 H, br s, OH) and 1.92 (3 H, s, *Me*CO).

A further sample of **392** (327 mg, 1.164 mmol) was subjected to FVP at 550 °C and 1×10^{-2} Torr. The resulting crude product (257 mg, 93%) was a mixture of *cis*- and *trans*-2-methyl-4,5-diphenyloxazoline in a ratio of 1:4. Disappointingly, column chromatography [alumina, ether-n-hexane (1:1)] resulted in a 2% total yield of the oxazolines.

b) at 450 °C

A sample of compound **392** (112 mg, 0.473 mmol) was subjected to FVP at 450 °C and 1×10^{-2} Torr. The major product appeared to be a mixture of *cis*-1-acetyl-2,3-diphenylaziridine **436** and *trans*-1-acetyl-2,3-diphenylaziridine **435**; (Found: M+H$^+$, 238.1240. $C_{16}H_{15}NO$ requires *M+H*, 238.1232); *m/z* 238 (M + H$^+$, 100%).

436; δ_H 7.5–7.0 (10 H, m, aromatic), 3.95 (2 H, s, CH) and 2.28 (3 H, s, *Me*CO).

435; δ_H 7.5–7.0 (10 H, m, aromatic), 3.78 (2 H, s, CH) and 1.85 (3 H, s, *Me*CO).

There were no literature spectra available for comparison. Small amounts of oxazoline and starting material were also present.

A sample of compound **392** (2.90 g) was subjected to FVP at 450 °C and 1×10^{-2} Torr. The crude product was left for two weeks before analysis and had been hydrolysed by air to give (*1S, 2S*)-2-acetamido-1,2-diphenylethanol **439** (0.29 g, 11%), $[\alpha]_D^{20}$ +18.46° (c 1, $CHCl_3$); δ_C 170.7 (CO), 141.0 (4ry), 139.6 (4ry), 128.5, 128.2, 127.5, 127.0, 126.1, 59.7 (C-2), 53.5 (C-1) and 23.0 (Me).

A sample of compound **392** (2.60 g) was subjected to FVP at 450 °C and 1×10^{-3} Torr. The crude product was Kugelrohr distilled to give a mixture of *trans*-1-acetyl-2,3-diphenyloxazoline **438** (333 mg, 15%), *cis*-1-acetyl-2,3-diphenylaziridine **436** (262 mg, 12%) and *trans*-1-acetyl-2,3-diphenylaziridine **435** (72 mg, 3%) (see above for ^{1}H NMR spectra) .

Identifiable ^{13}C NMR signals:

438, δ_C 162.3 (C=N), 142.3 (4ry), 140.7 (4ry), 89.3 (C-5) and 78.9 (C-4);

436 δ_C 183.5 (CO), 134.1 (4ry) and 46.1 (C-2, C- 3);

435, δ_C 180.1 (CO) and 48.5 (C-2, C- 3).

11. Pyrolysis of (*2R, 4S*)-3-acetyl-2,4-diphenyl-1,3-oxazolidin-5-one 393

a) at 550 °C

A sample of compound **393** (502 mg, 1.92 mmol) was subjected to FVP at 550 °C and 3×10^{-3} Torr. The crude product (390 mg, 86%), a 1:5 mixture of **437** and **438** was separated by column chromatography [alumina, ether-n-hexane (6:4)].

437 (2 mg, 0.5%); δ_H 7.6–6.75 (10 H, m, aromatic), 5.82 (1 H, d, *J* 10, 5-H), 5.52 (1 H, dq, 10, 1, 4-H) and 2.28 (3 H, d, *J* 1, 2-Me).

438 (143 mg, 32%); ν_{max}/cm^{-1} 3434, 3052, 1667, 1496, 1449, 1263 and 1195; δ_H 7.6–6.75 (10 H, m, aromatic), 5.24 (1 H, d, *J* 8, 5-H), 5.02 (1 H, dq, *J* 8, 1, 4-H) and 2.24 (3 H, d, *J* 1, 2–Me) [good agreement with lit.[126]]; δ_C 165.7 (CN), 142.3 (4ry), 140.7 (4ry), 129.3 (2 C), 129.2 (2 C), 128.8, 128.1, 126.9 (2 C), 126.1 (2 C), 89.3 (C-5) 78.9 (C-4) and 23.3 (2-Me); *m/z* 238 ($M+H^+$, 100%) and 57 (44).

E. Hydrolysis of oxazolines to amino alcohols

A sample of compound **383** (202 mg) was subjected to FVP at 500 °C and 1×10^{-2} Torr. The resulting crude product (163 mg) consisting mainly of compounds **268** and **267** (see above) was heated under reflux with HCl (2.3 cm^3 of 3 M, 6.9 mmol) and water (20 cm^3) for 20 mins. The crude product (434 mg, 25%) was a mixture of 2 isomers of 2-benzoylamino-1-phenylpropan-1-ol **472** and **473** in a ratio of approximately 10:1. This was chromatographed [silica, ether–pet ether, 9:1] to give **472** (191 mg, 11%) as colourless crystals; mp 143–145 °C; $[\alpha]_D^{20}$ 0.0 (c 1, CH_2Cl_2) (Found: $M+Na^+$, 278.1152. $C_{16}H_{17}NO_2$ requires *M+Na*, 278.1157); δ_H 7.73 (2 H, d, arom.), 7.54–7.22 (8 H, m, arom.), 6.43 (1 H, d, *J* 10, NH), 4.96 (1 H, d, *J* 2, 1-H), 4.52 (1 H, m, 2-H), 3.61 (1 H, br s, OH) and 1.10 (3 H, d, *J* 10, Me); δ_C 168.5 (CO), 141.1 (4ry), 134.6 (4ry), 132.1, 129.0 (2 C), 128.6 (2 C), 128.0, 127.4 (2 C), 126.7 (2 C), 76.9 (*CH*Ph), 51.8 (*CH*Me) and 14.9 (Me); *m/z* 278 ($M+Na^+$, 100%).

Compound **473** was present in some fractions but never completely separated, δ_H 7.55–7.20 (10 H, m, arom.), 6.45 (1 H, d, *J* 10, NH), 4.73 (1 H, d, *J* 6, 1-H), 4.38 (1 H, m, 2-H) and 1.18 (3 H, d, *J* 10, Me).

F. Attempted reactions of 1-acetyl-2-methyl-3-phenylaziridine

1. with maleic anhydride

A solution of 1-acetyl-2-methyl-3-phenylaziridine **422** [obtained from FVP of **388** as in section D] (0.10 g, 0.57 mmol) and maleic anhydride (0.056 g, 0.57 mmol) in toluene (5 cm^3) was heated under reflux for 72 hours. The solvent was evaporated. ^1H NMR of the resulting product showed that the aziridine had reacted completely. The mass spectrum showed *m/z* 325 whereas 359 was the expected M^+. The aziridine had not reacted in the expected way and the identity of the product needs further study.

2. with DMAD

A solution of **422** (0.10 g, 0.57 mmol) and DMAD (0.081 g, 0.57 mmol) in toluene (5 cm^3) was heated under reflux for 72 hours. The solvent was evaporated and the ^1H NMR spectrum recorded. The aziridine was unreacted.

3. with dimethyl maleate

A solution of **422** (0.0935 g, 0.53 mmol) and dimethyl maleate (0.0795 g, 0.55 mmol) in toluene (5 cm^3) were heated under reflux for 72 hours. The solvent was evaporated. The ^1H NMR spectrum showed that the aziridine was unreacted.

4. with sodium iodide

A solution of **422** (0.1853 g. 1.06 mmol) and sodium iodide (0.1661 g, 1.06 mmol) in acetone (15 cm^3) was heated under reflux for 22 hours. The solvent was evaporated. The ^1H NMR spectrum showed that the aziridine was unreacted.

5. with sulfuric acid

To a solution of **422** (0.0824 g. 0.47 mmol) in ether (20 cm^3) was added sulfuric acid conc. (1 drop). A white precipitate was formed instantly and filtered off. The ^1H NMR

spectrum showed that the aziridine had completely reacted but none of the expected products had formed. The spectrum was too complicated to interpret.

6. with trifluoroacetic acid

A solution of **422** (0.1090 g. 0.61 mmol) and TFA (0.0704 g, 0.61 mmol) in toluene (20 cm^3) was heated under reflux for 2 hours. The solution was evaporated and the residue analysed by NMR. ^1H NMR spectrum showed that the aziridine was completely reacted but none of the desired products had formed. The presence of 2 quartets in the ^{13}C NMR spectrum showed that there has been a trifluoro compound formed, δ_C 162.2 (q, *J* 142) and 116.7 (q, *J* 1154).

7. with *p*-toluenesulfonic acid

A solution of **422** (0.1007 g. 0.57 mmol) and *p*-toluenesulfonic acid (0.0951 g, 0.57 mmol) in toluene (20 cm^3) was heated under reflux for 1 hour. The solution was evaporated and an ^1H NMR spectrum of the residue showed that the aziridine had completely reacted but none of the expected products had formed.

8. by refluxing in xylene

A solution of **422** (0.1007 g. 0.57 mmol) in xylene (10 cm^3) was heated under reflux for 1 hour. There was no reaction by TLC. A further 2 hours heating was required to react the aziridine completely but a ^1H NMR spectrum of the residue upon evaporation showed that none of the desired products had formed.

G. Synthesis of chiral *N*-thioacyloxazolidin-5-ones from thiobenzoyl chloride

1. Preparation of phenylcarbodithioic acid 477[127]

Magnesium turnings (6.2 g, 0.26 mol) were stirred in a dried 3-neck 500 cm^3 flask fitted with a condenser and a dropping funnel under nitrogen with dry ether (150 cm^3). A little of a solution of bromobenzene (40 g, 0.26 mol) in dry ether (50 cm^3) was added. At this point the reaction did not begin so a small single crystal of iodine was added to initiate it. The remainder of the bromobenzene was added at such a rate as to keep the reaction going whilst not allowing it to become too vigorous. The resulting solution was cooled to –20 °C and carbon disulfide (19.3 g, 15.29 cm^3, 0.26 mol) was added dropwise at a rate such that the reaction mixture did not boil. After 30 mins the mixture was slowly allowed to reach room temperature and then stirred for 12 hrs.

The mixture was again cooled to –20 °C and some ice was added. Both layers were transferred to a separating funnel along with some water and washings from the flask. At this stage the magnesium salt is mostly in the aqueous layer although both are a deep red colour. The organic layer was removed and the aqueous layer was washed with ether (2×40 cm^3).

The aqueous layer was acidified with HCl (aq) which led to precipitation of the product **477** as a violet-red, sharp smelling oil. This was extracted with ether (3×100 cm^3) and dried over magnesium sulfate. The solution was not fully evaporated but reduced to 80–100 cm^3 to avoid decomposition. This could then be used directly for the next stage of the reaction.

2. Preparation of thiobenzoyl chloride 478[128]

The solution of carbodithioic acid from part 1 was stirred in a dried 3-neck flask fitted with a condenser and a dropping funnel under nitrogen. Thionyl chloride (80 g, 49 cm^3, 0.67 mol) was added slowly through the dropping funnel and the vigorous reaction began with evolution of hydrogen chloride and sulfur dioxide. The mixture was heated under reflux for 7 hrs. The excess thionyl chloride and ether was evaporated off to give a red-brown liquid.

The liquid was then transferred to a flask for fractional distillation. The liquid was firstly distilled at 50°C under oil pump vacuum to remove any $SOCl_2$ and a little S_2Cl_2. The

temperature was increased to 150°C and vigorous foaming occurred as the compound decomposed to give thiobenzoyl chloride and S_2Cl_2. The thiobenzoyl chloride condensed at room temperature while the S_2Cl_2 condensed separately in a cold trap (liquid N_2). The temperature was then increased to 200°C to distil over the remainder of the product **478** (35 g). Approximately 4 cm^3 of S_2Cl_2 was obtained.

The thiobenzoyl chloride **478** was purified by distilling the product four times at the vacuum pump to give a deep violet, nasty smelling liquid. This was distilled carefully to avoid decomposition of the product to S_2Cl_2 and was stored under nitrogen until further use. The pure thiobenzoyl chloride boiled at 60–65°C and 0.2 mmHg as described in the literature.[128]

3. Attempted preparation of (*2R,4S*)-4-benzyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 483

Following the literature procedure,[112] (*S*)-phenylalanine (5.775 g, 35 mmol) was added to NaOH(aq) (1 mol dm^{-3}, 35 cm^3) and ethanol (1–2 cm^3) was added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Benzaldehyde (3.71 g, 35 mmol) and CH_2Cl_2 (300 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5–8 hours. The imine was formed as a white precipitate. The mixture was stirred at 0 °C while a solution of thiobenzoyl chloride (5.48 g, 35 mmol) in CH_2Cl_2 (40 cm^3) was added and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated under reduced pressure to give a red liquid. The liquid was allowed to stand for 14 hours and a yellow solid (360 mg) precipitated. This solid had a melting point of 114–116 °C and was highly insoluble. This solid was assumed to be sulfur. The ^1H NMR spectrum of the red liquid showed that none of the desired product had formed.

H. Synthesis of chiral *N*-thioacyloxazolidin-5-ones

1. Preparation of (*2R,4S*)-4-methyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 481

A solution of compound **383** (3.00 g, 10.7 mmol) and Lawesson's reagent (2.16 g, 5.3 mmol) in toluene (120 cm^3) was heated under reflux for 3 hours. The solution was allowed to cool and the by-product of Lawesson's reagent precipitated out along with unreacted Lawesson's reagent. The precipitate was filtered off at the water pump and the solvent was removed under reduced pressure. The crude product was recrystallised from CH_2Cl_2 and pet ether to give **481** (2.49 g, 79%) as pale yellow crystals, mp 159–161 °C; $[\alpha]_D^{20}$ +591 (c=1, CH_2Cl_2); (Found C, 67.9; H, 4.6; N, 4.6. $C_{17}H_{15}NO_2S$ requires C, 68.7; H, 5.1; N, 4.7%); ν_{max}/cm^{-1} 1801, 1447, 1415, 1359, 1290, 1278, 1254, 1215, 1191, 1029, 1011, 762, 752, 714 and 693; δ_H 7.60–6.70 (10 H, m, arom.), 7.44* and 6.67 (1 H, 2 × s, 2-H), 5.42* and 4.86 (1 H, 2 × q, *J* 7, 4-H), 1.90* and 1.19 (3 H, 2 × d, *J* 7, 4-Me); δ_C 202.1* and 200.5 (CS), 171.33* and 171.27 (CO), 142.5 and 142.2* (4ry), 135.5 and 134.6* (4ry), 133.2*, 132.1, 130.6*, 129.9* (2 C), 129.8, 128.7 (2 C and 2 C*), 128.6 (2 C), 128.2 (2 C), 127.2* (2 C), 126.5* (2 C), 126.0 (2 C), 93.3 and 92.8* (C-2), 56.8* and 56.3 (C-4) and 18.0* and 15.2 (4-Me); *m/z* 297 (M^+, 55%), 242 (6), 209 (5), 191 (26), 163 (15), 130 (17), 121 (100), 105 (73), 77 (37) and 51 (13).

2. Preparation of (*2R,4S*)-4-isopropyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 482

A solution of compound **384** (3.00 g, 9.7 mmol) and Lawesson's reagent (1.96 g, 4.9 mmol) in toluene (120 cm^3) was heated under reflux for 3 hours. The solution was allowed to cool and the by-product of Lawesson's reagent precipitated out along with unreacted Lawesson's reagent. The precipitate was filtered off at the water pump and the solvent was removed under reduced pressure. The crude product was recrystallised from CH_2Cl_2 and pet

ether to give **482** (1.90 g, 60%) as pale yellow crystals, mp 141–143 °C; $[\alpha]_D^{20}$ +273 (c=1, CH_2Cl_2); (Found C, 70.6; H, 5.5; N, 4.3. $C_{19}H_{21}NO_2S$ requires C, 70.1; H, 5.9; N, 4.3%); ν_{max}/cm^{-1} 1794, 1445, 1422, 1393, 1360, 1346, 1305, 1282, 1264, 1208, 1181, 1145, 1126, 1079, 1021, 1011, 775, 754, 725 and 699; δ_H 7.63–6.70 (10 H, m, arom.), 7.20* and 6.60 (1 H, 2 × s, 2-H), 5.42* and 4.85 (1 H, 2 × d, *J* 7, 4-H), 3.25* and 1.98 (1 H, 2 × m, CH of Pr^i), 1.35* and 0.94 (3 H, 2 × d, *J* 7, Me of Pr^i), 1.19* and 0.97 (3 H, 2 × d, *J* 7, Me of Pr^i); δ_C 202.4* and 201.0 (CS), 169.6* and 169.5 (CO), 143.4* and 142.6 (4ry), 136.3* and 135.4 (4ry), 131.3*, 130.3 (1 C and 1 C*), 130.2, 129.2 (2 C), 129.1 (2 C), 128.7 (2 C and 2 C*), 127.9* (2 C), 127.1 (2 C), 126.6* (2 C), 126.4* (2 C), 94.3* and 94.1 (C-2), 66.4* and 65.7 (C-4), 32.4 and 28.3 (CH of Pr^i), 18.5* and 18.3 (Me of Pr^i), 17.1* and 16.3 (Me of Pr^i); *m/z* 325 (M^+, 64%), 242 (14), 219 (65), 191 (28), 158 (63), 121 (100), 105 (59), 77 (28) and 55 (15).

3. Preparation of *(2R,4S)*-4-benzyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 483

A solution of compound **385** (3.52 g, 9.9 mmol) and Lawesson's reagent (1.99 g, 4.9 mmol) in toluene (120 cm^3) was heated under reflux for 3 hours. The solution was allowed to cool and the by-product of Lawesson's reagent precipitated out along with unreacted Lawesson's reagent. The precipitate was filtered off at the water pump and the solvent was removed under reduced pressure. The crude product was recrystallised from CH_2Cl_2 and ether to give **483** (2.30 g, 62%) as yellow crystals, mp 134–136 °C; $[\alpha]_D^{20}$ +442 (c=1, CH_2Cl_2); (Found C, 68.9; H, 4.8; N, 3.3. $C_{23}H_{19}NO_2S$ requires C, 74.0; H, 5.1; N, 3.8%); ν_{max}/cm^{-1} 1801, 1417, 1360, 1347, 1309, 1290, 1258, 1213, 1185, 1164, 1152, 1042, 1032, 759, 736, 703, 695 and 618; δ_H 7.70–6.90 (11 H, m, arom.), 6.65 (4 H, m, arom.), 6.40* and 5.80 (1 H, 2 × s, 2-H), 5.68* and 5.26 (1 H, 2 × dd, *J* 6, 2, 4-H), 4.34 (1 H, A part of ABX, J_{AB} 14, J_{AX} 6, CH_2Ph), 3.40 (1 H, B part of ABX, J_{AB} 14, J_{AX} 2, CH_2Ph); δ_C 201.6 (C=S), 170.5 (C=O), 142.5 (4ry), 135.3 (4ry), 134.9 (4ry), 130.3 (2 × 2 C), 130.2, 129.4 (3 C), 129.0 (2 C), 128.5 (2

C), 128.4, 127.1 (2 C), 93.9 (C-2), 61.8 (C-4) and 32.6 (CH_2); *m/z* 374 (M + H^+, 100%), 268 (10), 178 (8) and 107 (21).

4. Preparation of (*2R,4S,2'S*)-4-s-butyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 484

A solution of compound **386** (2.5 g, 7.7 mmol) and Lawesson's reagent (2.34 g, 5.8 mmol) in toluene (120 cm^3) was heated under reflux for 3 hours. The solution was allowed to cool and the by-product of Lawesson's reagent precipitated out along with unreacted Lawesson's reagent. The precipitate was filtered off at the water pump and the solvent was removed under reduced pressure. The crude product (4.81 g) was recrystallised from CH_2Cl_2 and pet ether to give **484** (2.49 g, 95%) as yellow crystals, mp 156–158 °C; $[\alpha]_D^{20}$ +240 (c=1, CH_2Cl_2); (Found C, 70.6; H, 6.1; N, 4.1. $C_{20}H_{21}NO_2S$ requires C, 70.8; H, 6.2; N, 4.1%); ν_{max}/cm^{-1} 1812, 1447, 1412, 1365, 1345, 1306, 1292, 1258, 1217, 1174, 1121, 1023, 1003, 920, 763, 729 and 694; δ_H 7.58–6.70 (10 H, m, arom.), 7.18* and 6.59 (1 H, 2 × s, 2-H), 5.52 and 4.93* (1 H, 2 × d, *J* 3, 4-H), 3.00 and 1.62* (1 H, 2 × m, CH of Bu^s), 1.88, 1.70, 1.48* and 1.24* (2 H, 4 × m, CH_2 of Bu^s), 1.18 and 0.95* (3 H, 2 × d, *J* 7, *Me*CH of Bu^s), 1.13 and 0.57* (3 H, 2 × t, *J* 7, *Me*CH_2 of Bu^s); δ_C 201.7 and 200.5* (CS), 169.2* and 169.1 (CO), 143.0 and 142.3* (4ry), 135.9 and 135.0* (4ry), 130.7*, 129.8 (2 C), 129.7* (2 C), 128.7 (4 C), 128.2 (2 C and 1C*), 127.5* (2 C), 126.7* (4 C), 126.3, 126.0, 94.0 and 93.7* (C-2), 64.0 (C-4), 38.9* and 34.2 (CH of Bu^s), 25.3 and 24.9* (CH_2 of Bu^s), 14.6 and 14.3* (*Me*CH of Bu^s) and 11.8 and 11.5* (*Me*CH_2); *m/z* 339 (M^+, 47%), 242 (16), 233 (47), 205 (24), 172 (38), 121 (100), 105 (62), 97 (15), 77(27) and 69 (22).

5. Preparation of (*2R,4S*)-4-methyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one 485

A solution of compound **388** (3.56 g, 16.2 mmol) and Lawesson's reagent (3.28 g, 8.1 mmol) in toluene (120 cm^3) was heated under reflux for 3 hours. The solution was allowed to cool and the by-product of Lawesson's reagent precipitated out along with unreacted

Lawesson's reagent. The precipitate was filtered off at the water pump and the solvent was removed under reduced pressure. The crude product was recrystallised from CH_2Cl_2 and pet ether to give **485** (2.49 g, 65%) as pale yellow crystals, mp 116–118 °C; $[\alpha]_D^{20}$ +120.6 (c 1, CH_2Cl_2); (Found C, 61.0; H, 5.4; N, 5.8. $C_{12}H_{13}NO_2S$ requires C, 61.3; H, 5.6; N, 6.0%); ν_{max}/cm^{-1} 1805, 1429, 1358, 1331, 1310, 1279, 1256, 1202, 1174, 1124, 1062, 1040, 992, 782, 773, 718, 702 and 612; δ_H 7.20–7.25 (5 H, m, arom.), 7.12* and 6.70 (1 H, 2 × s, 2-H), 5.17* and 4.78 (1 H, 2 × q, *J* 7, 4-H), 2.74* and 2.19 (3 H, 2 × s, MeCS), 1.90* and 1.85 (3 H, 2 × d, *J* 7, 4-Me); δ_C 199.643* and 199.636 (CS), 171.2* and 171.0 (CO), 135.5* and 134.9 (4ry), 131.4, 131.2 (2 C), 130.0*, 129.7* (2 C), 128.7* (2 C), 126.9 (2 C), 93.1* and 92.2 (C-2), 56.9* and 56.0 (C-4), 33.9* and 33.5 (MeCS) and 19.2* and 15.5 (4-Me); *m/z* 235 (M^+, 70%), 219 (8), 180 (10), 132 (29), 129 (31), 105 (100), 101 (48), 89 (9), 77 (26), 68 (33), 59 (77), 51 (13) and 43 (29).

6. Attempted Preparation of (*2R,4S*)-4-isopropyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one 486

A solution of compound **389** (3.01 g, 12.2 mmol) and Lawesson's reagent (2.46 g, 6.1 mmol) in toluene (150 cm^3) was heated under reflux for 3 hours. The product (5.20 g) was recrystallised several times but was never pure enough for the messy ^1H NMR to be assigned. The reaction was repeated to no avail.

7. Preparation of (*2R,4S*)-4-benzyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one 487

A solution of compound **390** (3.50 g, 11.9 mmol) and Lawesson's reagent (2.4 g, 5.9 mmol) in toluene (150 cm^3) was heated under reflux for 3 hours. The solution was allowed to cool and the by-product of Lawesson's reagent precipitated out along with unreacted Lawesson's reagent. The precipitate was filtered off at the water pump and the solvent was removed under reduced pressure. The crude product was recrystallised from CH_2Cl_2 and ether

to give **487** (3.03 g, 82%) as yellow crystals, mp 155–157 °C; $[\alpha]_D^{20}$ +223 (c=1, CH_2Cl_2); (Found C, 69.1; H, 5.3; N, 4.4. $C_{18}H_{17}NO_2S$ requires C, 69.4; H, 5.5; N, 4.5%); ν_{max}/cm^{-1} 1802, 1494, 1359, 1350, 1310, 1266, 1199, 1159, 1149, 1121, 1075, 1037, 1023, 988, 769, 738 and 703; δ_H 7.46–7.10 (10 H, m, arom.), 6.06* and 5.60 (1 H, s, 2-H), 5.48* and 5.12 (1 H, dt, *J*, 4-H), 4.49 and 3.57* (1H, A part of ABX, J_{AB} 14, J_{AX} 6 and 5*, CH_2Ph), 3.34* and 3.19 (1H, B part of ABX, J_{AB} 14, J_{AX} 2, CH_2Ph), 2.86* and 2.09 (3 H, s, MeCS); δ_C 199.8 and 198.5* (CS), 169.8 and 169.7* (CO), 135.1 (4ry), 134.7* and 134.5 (4ry), 131.4* (2 C), 130.3* (2 C), 130.1 (2 C), 130.1*, 129.6*, 129.3, 129.0* (2 C), 128.2 (2 C), 128.2 (2 C), 127.5* (2 C), 127.1 (2 C), 126.5, 93.9* and 92.8 (C-2), 62.8 and 62.0* (C-4), 37.8* (CH_2), 33.9* and 33.5 (MeCS) and 32.1 (CH_2); *m/z* 312 ($M + H^+$, 100%), 296 (5), 268 (6), 206 (12), 190 (6), 107 (10) and 57 (32).

I. Flash Vacuum Pyrolysis of *N*-thioacyloxazolidin-5-ones

1. Pyrolysis of (*2R,4S*)-4-methyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 481

a) at 550 °C

A sample of **481** (128 mg, 0.43 mmol) was subjected to FVP at 550 °C and 6×10^{-3} Torr. The crude product was a yellow liquid (98 mg, 90%). ^{1}H NMR analysis showed it to be a mixture of *cis*-4-methyl-2,5-diphenylthiazoline **490** and *trans*-4-methyl-2,5-diphenylthiazoline **491** in a ratio of 5:4.

490; δ_H 7.57–7.02 (10 H, m, aromatic), 4.96 (1 H, d, *J* 8, 5-H), 4.86 (1 H, m, 4-H) and 1.16 (3 H, d, *J* 7, 4-Me); δ_C 167.0 (CN), 138.0 (4ry), 133.0 (4ry), 131.2, 128.44 (2 C), 128.42 (2 C), 128.3 (2 C), 128.2 (2 C), 127.7, 81.1 (C-5), 61.5 (C-4) and 16.5 (Me).

491; δ_H 7.55–7.00 (10 H, m, aromatic), 4.77 (1 H, m, 4-H), 4.61 (1 H, d, *J* 6, 5-H) and 1.45 (3 H, d, *J* 7, 4-Me) [lit.,[129] δ_H 7.88–7.80 (2 H, m), 7.48–7.20 (8 H, m), 4.80–4.78 (1 H, m), 4.61 (1 H, d, *J* 6) and 1.46 (3 H, d, *J* 7)]; δ_C 165.5 (CN), 141.2 (4ry), 131.0 (4ry), 131.1, 128.7 (2 C), 128.3 (2 C), 128.2, 127.7 (2 C), 127.4 (2 C), 76.0 (C-5), 58.4 (C-4) and 20.0 (Me).

The ^{1}H NMR spectrum of this mixture (94 mg, 0.37 mmol) was recorded in the presence of praseodymium tris(heptafluorobutrylcamphorate) (0.154 g, 0.173 mmol). Using the doublets at 4.96 and 4.61 ppm the enantiomeric excess was found to be 9% in each case.

2. Pyrolysis of (*2R,4S*)-4-isopropyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 482

a) at 550 °C

A sample of **482** (758 mg, 2.30 mmol) was subjected to FVP at 550 °C and 3×10^{-3} Torr. The crude product was a yellow liquid (562 mg, 87%). ^{1}H NMR analysis showed it to be a mixture of *cis*-4-isopropyl-2,5-diphenylthiazoline **493** and *trans*-4-isopropyl-2,5-diphenylthiazoline **494**. This was separated by column chromatography [alumina, ether–n-hexane (3:97)] to give:

493; (181 mg, 28%); $[\alpha]_D^{20}$ +11 (c 1, CH_2Cl_2); δ_H 7.85 (2 H, d, *J* 7, aromatic), 7.50–7.05 (8 H, m, aromatic), 4.82 (1 H, d, *J* 7, 5-H), 4.15 (1 H, dd, *J* 10, 7, 4-H), 1.87 (1 H, m, CH of Pr^i), 1.30

(3 H, d *J* 6, Me of Pr^i) and 0.87 (3 H, d, *J* 6, Me of Pr^i); δ_C 167.2 (CN), 140.6 (4ry), 134.0 (4ry), 131.6, 128.9 (2 C), 128.9 (2 C), 128.7 (2 C), 128.6 (2 C), 128.2, 89.1 (C-5), 57.4 (C-4), 29.9 (CH), 23.0 (Me) and 21.0 (Me); *m/z* 282 ($M + H^+$, 100%).

494; (109 mg, 17%); $[\alpha]_D^{20}$ –23 (c 1, CH_2Cl_2); δ_H 7.87 (2 H, m, aromatic), 7.52–7.18 (8 H, m, aromatic), 4.76 (1 H, d, *J* 5, 5–H), 4.67 (1 H, t, *J* 5, 4–H), 2.09 (1 H, m, CH of Pr^i), 1.08 (3 H, d *J* 7, Me of Pr^i) and 1.06 (3 H, d, *J* 7, Me of Pr^i); δ_C 164.1 (CN), 142.7 (4ry), 132.3 (4ry), 130.0, 127.8 (2 C), 127.4 (2 × 2 C), 126.43, 126.39 (2 C), 91.5 (C–5), 55.2 (C–4), 32.3 (CH), 18.5 (Me) and 17.4 (Me); *m/z* 282 ($M + H^+$, 100%).

The ^1H NMR spectrum of this mixture was recorded in the presence of varying amounts of praseodymium tris(heptafluorobutrylcamphorate) and europium tris(heptafluorobutrylcamphorate) but the e.e. could not be determined in either case.

3. Pyrolysis of (*2R,4S*)-4-benzyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 483

a) at 550 °C

A sample of **483** (97 mg, 0.26 mmol) was subjected to FVP at 550 °C and 6 × 10^{-3} Torr. The crude product (71 mg, 86%) was a mixture of *cis*-4-benzyl-2,5-diphenylthiazoline **495** and *trans*-4-benzyl-2,5-diphenylthiazoline **496** in a 65 : 35 ratio, (Found: $M+H^+$, 330.1319. $C_{22}H_{19}NS$ requires $M+H^+$, 330.1316); *m/z* 330 ($M+H^+$, 100%). Attempts to separate these using column chromatography on silica and alumina were both unsuccessful.

495; δ_H 7.92 (2 H, m, aromatic), 7.68–6.95 (13 H, m, aromatic), 4.98 (1 H, q, *J* 8, 4-H), 4.83 (1 H, d, *J* 8, 5-H), 3.22 and 2.71 (2 H, ABX, J_{AB} 14, J_{AX} 8, CH_2Ph); δ_C 167.9 (CN), 139.7 (4ry), 139.2 (4ry), 132.2 (4ry), 131.80, 130.77, 130.0, 129.6 (2 C), 129.0 (2 × 2 C), 128.9 (2 C), 128.8 (2 C), 126.6 (2 C), 82.5 (C-4), 57.7 (C-5) and 37.8 (CH_2).

496; δ_H 7.92 (2 H, m, aromatic), 7.68–6.95 (13 H, m, aromatic), 5.03 (1 H, m, 4-H), 4.69 (1 H, d, *J* 4, 5-H), 3.22 and 2.88 (2 H, ABX, J_{AB} 14, J_{AX} 8, CH_2Ph); δ_C 166.9 (CN), 142.8 (4ry), 138.4 (4ry), 133.7 (4ry), 129.6, 129.4, 129.2 (2 C), 128.9 (2 C), 128.4 (2 C), 128.0 (2 C), 127.5 (2 C), 127.0, 126.6 (2 C), 87.3 (C-4), 57.8 (C-5) and 40.4 (CH_2).

The ^1H NMR spectrum of this mixture was recorded in the presence of varying amounts of praseodymium tris(heptafluorobutrylcamphorate) and europium tris(heptafluorobutrylcamphorate) but the enantiomeric excess could not be determined in either case.

4. Pyrolysis of (*2R,4S,2'S*)-4-s-butyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 484

a) at 550 °C

A sample of **484** (96 mg, 0.28 mmol) was subjected to FVP at 550 °C and 5×10^{-3} Torr. The crude product (73 mg, 88%) was a mixture of *cis*-4-benzyl-2-s-butyl-5-phenylthiazoline **496/497** and *trans*-4-benzyl-2-s-butyl-5-phenylthiazoline **498/499**. This was separated by column chromatography [alumina, ether–n-hexane (6:94)] to give:

i) *cis*-4-s-butyl-2-methyl-5-phenylthiazoline (20 mg, 24%, 0% d.e.), (Found: M+H$^+$, 296.1482. $C_{19}H_{22}NS$ requires *M*+H$^+$, 296.1473); *m/z* 295 (M$^+$, 13%), 264 (10), 238 (100), 210 (28), 180 (64), 165 (22), 158 (15), 144 (80), 105 (10), 91 (25) and 77 (16).

496; δ_H 7.84 (2 H, m, aromatic), 7.48–7.02 (8 H, m, aromatic), 4.79 (1 H, d, *J* 7, 5-H), 4.24 (1 H, dd, *J* 10, 7, 4-H), 1.65 (1 H, m, CH of Bu^s), 1.38 (1 H, m, CH_2), 1.18 (3 H, d, *J* 7, *Me*CH), 1.04 (1 H, m, CH_2) and 0.67 (3 H, t, *J* 7, *Me*CH_2); δ_C 165.4 (CN), 139.3 (4ry), 132.6 (4ry), 127.64 (2 C), 127.57, 127.44 (2 C), 127.39 (2 C), 126.70 (2 C), 126.6, 86.2 (C-5), 56.0 (C-4), 34.6 (CH of Bu^s), 26.0 (CH_2), 17.2 (*Me*CH) and 9.7 (*Me*CH_2).

497; δ_H 7.84 (2 H, m, aromatic), 7.48–7.02 (8 H, m, aromatic), 4.72 (1 H, d, *J* 7, 5-H), 4.16 (1 H, dd, *J* 11, 7, 4-H), 2.12 (1 H, m, CH_2), 1.67 (1 H, m, CH of Bu^s), 1.36 (1 H, m, CH_2), 0.83 (3 H, t, *J* 7, *Me*CH_2) and 0.77 (3 H, d, *J* 7, *Me*CH); δ_C 165.6 (CN), 139.0 (4ry), 132.6 (4ry), 130.1, 127.44 (2 C), 127.30 (2 C), 127.28 (2 C), 127.2 (2 C), 126.65, 85.8 (C-5), 56.0 (C-4), 34.4 (CH of Bu^s), 27.5 (CH_2), 15.6 (*Me*CH) and 9.9 (*Me*CH_2).

ii) *trans*-4-s-butyl-2-methyl-5-phenylthiazoline (16 mg, 19%, 37% d.e.), (Found: M+H$^+$, 296.1473. $C_{19}H_{22}NS$ requires *M*+H$^+$, 296.1473); *m/z* 296 (M+H$^+$, 100%).

498; δ_H 7.79 (2 H, m, aromatic), 7.46–7.04 (8 H, m, aromatic), 4.72 (1 H, s, 5-H), 4.72 (1 H, d, *J* 10, 4-H), 3.05 (1 H, m, CH of Bu^s), 1.88–1.52 (2 H, m, CH_2), 1.42 (3 H, d, *J* 7, *Me*CH) and

0.94 (3 H, t, *J* 7, *Me*CH_2); δ_C (identifiable signals) 164.2 (CN), 143.0 (4ry), 131.4 (4ry), 90.3 (C-5), 55.9 (C-4), 39.2 (CH of Bu^s), 25.7 (CH_2), 13.6 (*Me*CH) and 10.9 (*Me*CH_2).

499; δ_H 7.79 (2 H, m, aromatic), 7.46–7.04 (8 H, m, aromatic), 4.67 (1 H, s, 5-H), 4.66 (1 H, d, *J* 2, 4-H), 1.98 (1 H, m, CH of Bu^s), 1.95–1.64 (2 H, m, CH_2), 1.12 (3 H, d, *J* 7, *Me*CH) and 1.11 (3 H, t, *J* 7, *Me*CH_2); δ_C (identifiable signals) 164.0 (CN), 143.0 (4ry), 134.2 (4ry), 90.4 (C-5), 54.3 (C-4), 39.0 (CH of Bu^s), 24.6 (CH_2), 14.3 (*Me*CH) and 10.8 (*Me*CH_2).

b) at 450 °C

A sample of **484** (100 mg, 0.29 mmol) was subjected to FVP at 550 °C and 3×10^{-3} Torr. The crude product was a yellow solid (90 mg). ^{1}H NMR analysis showed this to consist mainly of the starting material **484** with only a trace of the 2-thiazolines.

5. Pyrolysis of (*2R,4S*)-4-methyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one 485

a) at 550 °C

A sample of **485** (99 mg, 0.42 mmol) was subjected to FVP at 550 °C and 6×10^{-3} Torr. The crude product was a yellow liquid (68 mg, 85%). ^{1}H NMR analysis showed it to be a mixture of *cis*-2,4-dimethyl-5-phenylthiazoline **501**, *trans*-2,4-dimethyl-5-phenylthiazoline **502** and a trace of the vinyl compound **503**. This was separated by column chromatography [alumina, ether–n-hexane (5:95)] to give:

501 (20 mg, 25%); δ_H 7.56–7.02 (5 H, m, arom.), 4.92 (1 H, d, *J* 8, 5-H), 4.62 (1 H, m, 4-H), 2.32 (3 H, s, MeCO) and 1.03 (3 H, d, *J* 7, 4-Me); δ_C 168.3 (CN), 139.1 (4ry), 129.0, 128.7 (2 C), 128.7 (2 C), 75.9 (C-5), 60.1 (C-4), 20.9 (Me) and 16.9 (Me).

502 (12 mg, 15%); δ_H 7.48–7.16 (5 H, m, arom.), 4.65–4.44 (2 H, m, 5-H and 4-H), 2.26 (3 H, s, 2-Me) and 1.37 (3 H, d, *J* 7, 4-Me); δ_C 164.7 (CN), 141.7 (4ry), 129.2 (2 C), 128.1, 127.8 (2 C), 81.4 (C-5), 63.5 (C-4), 20.8 (Me) and 20.5 (Me).

503; δ_H 7.73–6.89 (5 H, m, aromatic), 6.17 (1 H, br d, NH), 5.99 (1 H, ddd, C*H*=CH_2), 5.62 (1 H, t, CH-N), 5.21 (2 H, m, =CH_2) and 1.99 (3 H, s, CO*Me*); δ_C (selected signals) 139.1 (4ry), 137.6 (=CH), 116.2 (CH_2), 23.7 (Me).

The ^{1}H NMR spectra of **501** and **502** were recorded in the presence of varying amounts of praseodymium tris(heptafluorobutrylcamphorate) and europium tris(heptafluorobutrylcamphorate) but the enantiomeric excess could not be determined in either case.

6. Pyrolysis of (*2R,4S*)-4-benzyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one 487

a) at 550 °C

A sample of **487** (100 mg, 0.32 mmol) was subjected to FVP at 550 °C and 4×10^{-3} Torr. The crude product (75 mg, 88%) was assumed to be a mixture of *cis*-4-benzyl-2-methyl-5-phenylthiazoline **504** and *trans*-4-benzyl-2-methyl-5-phenylthiazoline **505**.

504; δ_H 7.53–6.92 (10 H, m, aromatic), 4.77 (1 H, m, 4-H), 4.75 (1 H, d, *J* 7, 5-H), 3.04 and 2.62 (2 H, ABX, J_{AB} 14, J_{AX} 7, CH_2Ph) and 2.32 (3 H, d, *J* 2, 2-Me); δ_C 167.2 (CN), 139.6 (4ry), 139.2 (4ry), 129.9, 128.9 (2 × 2 C), 128.8 (2 C), 128.6 (2 C), 128.4, 82.0 (C-5), 59.2 (C-4), 37.7 (CH_2) and 21.1 (Me).

505; δ_H 7.53–6.92 (10 H, m, aromatic), 4.77 (1 H, m, 4-H), 4.59 (1 H, d, *J* 4, 5-H), 3.09 (1 H, A part of ABX, J_{AB} 14, J_{AX} 5, CH_2Ph), 2.78 (1 H, B part of ABX, J_{AB} 14, J_{AX} 7, CH_2Ph) and 2.28 (3 H, d, *J* 1, 2-Me); δ_C 165.9 (CN), 142.9 (4ry), 138.2 (4ry), 129.5, 128.4, 127.5 (2 C), 127.0 (2 C), 126.6 (2 C), 125.9 (2 C), 87.1 (C-5), 59.2 (C-4), 40.5 (CH_2) and 20.7 (Me).

The ^{1}H NMR spectrum of this mixture was recorded in the presence of varying amounts of praseodymium tris(heptafluorobutrylcamphorate) and europium tris(heptafluorobutrylcamphorate) but the e.e. could not be determined in either case.

J. Preparation of Aziridines from Amino Alcohols

1. Attempted preparation of (*2S*,*3S*)-*2*-methyl-3-phenylaziridine

To a cooled solution (0°C) of (1*R*,2*S*)-(–)-norephedrine (3.00 g, 0.02 mol) and triphenylphosphine (5.25 g, 0.02 mol) in ether (100 cm^3) under nitrogen was slowly added diisopropyl azodicarboxylate (95%, 4.26 g, 4.15 cm^3, 0.02 mol) via a syringe stirring constantly. The ice bath was then removed and the solution was stirred for a further 10 hours. A crystalline precipitate (triphenylphosphine-DIAD complex) was filtered off and washed with n-hexane-ether (1:1, 100 cm^3). The filtrate was evaporated to give 2-methyl-3-phenylaziridine (68 mg, 8%). In light of the poor yield obtained, the following procedure was attempted.

2. Attempted preparation of (*2S*,*3S*)-*2*-methyl-3-phenylaziridine

To a cooled solution (0°C) of (1*R*,2*S*)-(–)-norephedrine (3.00 g, 0.02 mol), triphenylphosphine (5.25 g, 0.02 mol) and triethylamine (8 cm^3) in tetrahydrofuran (60 cm^3) under nitrogen was slowly added diisopropyl azodicarboxylate (95%, 4.26 g, 4.15 cm^3, 0.02 mol) via a syringe stirring constantly. The ice bath was then removed and the solution was stirred for a further 10 hours. The crystalline by-product (triphenylphosphine-DIAD complex) was filtered off and washed with n-hexane–ether (1:1, 100 cm^3). The filtrate was evaporated. A ^1H NMR spectrum showed that none of the correct product had formed.

3. Attempted Preparation of (*2S*)-*2*-benzylaziridine

To a cooled solution (0°C) of (2*S*)-2-amino-3-phenylpropan-1-ol (3.00 g, 0.02 mol), triphenylphosphine (5.25 g, 0.02 mol) and triethylamine (8 cm^3) in ether (100 cm^3) under nitrogen was slowly added diisopropylazodicarboxylate (95%, 4.26 g, 4.15 cm^3, 0.02 mol) via a syringe stirring constantly. The ice bath was then removed and the solution was stirred for a further 2 days. The crystalline by-product (triphenylphosphine-DIAD complex) was filtered

off and washed with n-hexane-ether (1:1, 100 cm^3). The filtrate was evaporated. A ^1H NMR spectrum showed that none of the correct product had formed.

4. Attempted preparation of (*2S*,*3S*)-1-acetyl-*2*-methyl-3-phenylaziridine 425

To a cooled solution (0°C) of (1*R*,2*S*)-(–)-norephedrine (2.00 g, 13.2 mmol) and triethylamine (1.34 g, 1.84 cm^3, 12.3 mmol) in dried dichloromethane was treated dropwise with a solution of acetyl chloride (1.04 g, 13.2 mmol) in dichloromethane (10 cm^3). The ice bath was removed and the solution was stirred for 3 hours. Water (20 cm^3) was added and the organic layer separated and dried over sodium sulfate. Evaporation gave the product as a colourless solid (0.93 g, 37%); δ_H 7.41–7.29 (5 H, m, arom.), 5.85 (1 H, d, *J* 4, C*H*Ph), 5.43 (1 H, d, *J* 9, NH), 4.47 (1 H, m, C*H*Me), 1.98 (3 H, s, *Me*CO) and 1.08 (3 H, d, *J* 7, *Me*CH).

To a solution of (1*R*,2*S*)-(–)-*N*-acetylnorephedrine (0.93 g, 4.82 mmol) and triphenylphosphine (5.25 g, 0.02 mol) in tetrahydrofuran (40 cm^3) under nitrogen was slowly added diisopropylazodicarboxylate (95%, 1.06 g, 1.09 cm^3, 4.82 mmol) via a syringe stirring constantly. The ice bath was then removed and the solution was stirred overnight. The crystalline by-product (triphenylphosphine-DIAD complex) was filtered off and washed with n-hexane–ether (1:1, 100 cm^3). The filtrate was evaporated and column chromatography [silica gel, n-hexane–ether–triethylamine (69:30:1)] of the residue gave not (*2S*,*3S*)-1-acetyl-*2*-methyl-3-phenylaziridine **422**, the expected product, but *trans*-2,4-dimethyl-5-phenyloxazoline **424**, as a colourless oil (443 mg, 52%); $[\alpha]_D^{20}$ –75 (c 1, $CHCl_3$); (Found: M+H$^+$, 176.1070. $C_{11}H_{14}NO$ requires *M*+H$^+$, 176.1075); δ_H 7.5–7.1 (5 H, m, arom.), 4.90 (1 H, d, *J* 8, 5-H), 3.97 (1 H, m, 4-H), 2.05 (3 H, d, *J* 1, 2-Me) and 1.36 (3 H, d, *J* 7, 4-Me) [good agreement with lit.[123]]; δ_C 163.5 (CN), 139.9 (4ry), 128.5 (2 C), 128.2, 125.3 (2 C), 87.7 (C-5), 69.8 (C-4), 20.9 (2-Me) and 12.1 (4-Me); *m/z* 176 (M + H$^+$, 76%) and 134 (87).

K. Alkylation of chiral *N*-acyloxazolidin-5-ones

1. Attempted preparation of (*2R,4S*)-3-benzoyl-4-ethyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one

To a stirred solution of diisopropylamine (1.99 cm^3, 14.2 mmol) in dry THF (125 cm^3) at –78 °C under nitrogen was added n-BuLi (5.68 cm^3 of 2.5 M in hexane, 14.2 mmol). The solution was allowed to warm up to room temperature before re-cooling to –78 °C. A solution of compound **383** (4.00 g, 14.2 mmol) in dry THF (50 cm^3) was added and the solution allowed to warm to room temperature. The solution was cooled to –78 °C and iodoethane (0.99 cm^3 14.2 mmol) was added, the solution allowed to warm to room temperature and stirred overnight. The solution was worked up by adding to a half saturated NH_4Cl solution (75 cm^3). The product was extracted with ether (3 × 30 cm^3). The combined extracts were washed with water (2 × 25 cm^3) and dried over $MgSO_4$. The solvent was evaporated under reduced pressure. An ^1H NMR spectrum of the residue showed that not all of the starting material had reacted and none of the desired product had been formed.

2. Preparation of (*2R,4R*)-3-benzoyl-4-benzyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one 506

To a stirred solution of diisopropylamine (1.99 cm^3, 14.2 mmol) in dry THF 125 cm^3 at –78 °C under nitrogen was added n-BuLi (5.68 cm^3 of 2.5 M in hexane, 14.2 mmol). The solution was allowed to warm up to room temperature before re-cooling to –78 °C. A solution of **385** (5.08 g, 14.2 mmol) in dry THF (50 cm^3) was added and the solution allowed to warm to room temperature. The solution was cooled to –78 °C and iodomethane (0.89 cm^3, 14.2 mmol) was added, the solution allowed to warm to room temperature and stirred overnight. The solution was worked up by adding to a half saturated NH_4Cl solution (75 cm^3). The product was extracted with ether (3 × 30 cm^3). The combined extracts were washed with water (2 × 25 cm^3) and dried over $MgSO_4$. The solvent was evaporated under reduced pressure to give the

product **506** (360 mg, 12%) as a yellow solid; mp 184–186 °C; $[\alpha]_D^{20}$ +3.1 (c 1, CH_2Cl_2) (Found C, 77.2; H, 5.15; N, 3.8. $C_{24}H_{21}NO_3$ requires C, 77.6; H, 5.7; N, 3.8%); ν_{max}/cm^{-1} 1791, 1653, 1401, 1225, 1175, 1016, 880, 742, 697 and 619; δ_H 7.45–6.63 (13 H, m, arom.), 6.19 (1 H, s, 2-H), 5.59 (2 H, d, *J* 8, arom.), 4.08 (1 H, d, *J* 14, 1H of CH_2), 3.43 (1 H, d, *J* 14, 1H of CH_2), 1.95 (3 H, s, Me); δ_C 173.8 (CO), 169.6 (CO), 136.6 (4ry), 136.5 (4ry), 136.1 (4ry), 130.6 (2 C), 129.1 (2 C), 128.9 (2 C), 128.2 (2 C), 127.9 (2 C), 127.5, 127.4 (2 C), 125.0 (2 C), 89.5 (C-2), 65.8 (C-4), 42.1 (CH_2) and 22.3 (Me); *m/z* 394 ($M+Na^+$, 100%), 372 (5) and 222 (14).

3. Pyrolysis of (*2R,4R*)-3-benzoyl-4-benzyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one 506

a) at 550 °C

A sample of compound **506** (89 mg, 0.24 mmol) was subjected to FVP at 550 °C and 5 × 10^{-3} Torr. The resulting crude product was *N*-(1,3-diphenyl-2-methylprop-2-enyl)benzamide **507** (60 mg, 76%); (Found: $M+Na^+$, 350.1514. $C_{23}H_{21}NO$ requires *M*+Na, 350.1521); δ_H 7.82 (2 H, d, arom.), 7.52–7.16 (13 H, m, arom.), 6.64 (1 H, s, =CH), 6.52 (1 H, d, NH), 5.87 (1 H, d, NC*H*) and 1.86 (3 H, s, Me); δ_C 166.4 (CO), 140.5 (4ry), 137.8 (4ry), 137.2 (4ry), 134.8 (4ry), 123.1, 129.5 (2 C), 129.3 (2 C), 129.1 (2 C), 128.5 (2 C), 128.2, 127.9 (2 C), 127.4 (2 C), 127.0, 126.9, 60.7 (N*CH*) and 16.9 (Me); *m/z* 327 (M^+, 3%), 237 (100), 105 (45), 91 (12) and 77 (25); *m/z* 350 ($M + Na^+$, 100%), 328 (6) and 207 (17).

b) at 500 °C

A sample of **506** (90 mg) was subjected to FVP at 500 °C and 5 × 10^{-3} Torr. The resulting crude product was a mixture of **507** and the starting material in a ratio of approx. 1 : 1 from ^1H NMR.

c) at 450 °C

A sample of **506** (96 mg) was subjected to FVP at 450 °C and 5 × 10^{-3} Torr. The ^1H spectrum shows **506** almost completely unreacted, and only a trace of **507** had formed.

L. Preparation of Bisoxazolidin-5-ones

1. Attempted preparation of 3,3'-dimethylmalonylbis((*2R,4S*)-2-methyl-4-phenyl-1,3-oxazolidin-5-one)

Dimethylmalonic acid (6.35 g, 48 mmol) was heated under reflux in an excess thionyl chloride (25 cm^3, 343 mmol) for 2 hours. The remaining thionyl chloride was removed under reduced pressure. The crude product was Kugelrohr distilled at the water pump at around 55 °C to give the dimethylmalonyl chloride as a colourless liquid (4.63 g, 57%).

(*S*)-Alanine (2.22 g, 25 mmol) was added to NaOH(aq) (1 mol dm^{-3}, 25 cm^3) and ethanol (1–2 cm^3) was added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Benzaldehyde (2.65 g, 25 mmol) and CH_2Cl_2 (150 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5–8 hours. The imine was formed as a white precipitate. The mixture was stirred at 0 °C while a solution of dimethyl malonyl chloride (2.11 g, 1.65 cm^3, 12.5 mmol) in CH_2Cl_2 (25 cm^3) was added slowly and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated and the residue recrystallised. ^1H and ^{13}C NMR spectra indicated that the desired product had not formed.

2. Attempted preparation of 3,3'-oxalylbis((*2R,4S*)-2-methyl-4-phenyl-1,3-oxazolidin-5-one)

(*S*)-Alanine (2.22 g, 25 mmol) was added to NaOH(aq) (1 mol dm^{-3}, 25 cm^3) and ethanol (1-2 cm^3) was added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Benzaldehyde (2.65 g, 25 mmol) and CH_2Cl_2 (150 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5–8 hours. The imine was formed as a white precipitate. The mixture was stirred at 0 °C while a

solution of oxalyl chloride (1.59 g, 12.5 mmol) in CH_2Cl_2 (25 cm^3) was added slowly and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated and the residue recrystallised. ^1H NMR indicated that the desired product had not formed.

3. Preparation of 3,3'-malonylbis((*2R,4S*)-2-methyl-4-phenyl-1,3-oxazolidin-5-one) 516

(*S*)-Alanine (1.11 g, 12.5 mmol) was added to NaOH(aq) (1 mol dm^{-3}, 25 cm^3) and ethanol (1-2 cm^3) was added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Benzaldehyde (1.83 g, 12.5 mmol) and CH_2Cl_2 (150 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5–8 hours. The imine was formed as a white precipitate (2.487 g, 12.5 mmol). The mixture was stirred at 0 °C while a solution of malonyl chloride (0.88 g, 0.61 cm^3, 6.3 mmol) in CH_2Cl_2 (5 cm^3) was added slowly and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated and the residue recrystallised to give **516** (1.45 g, 28%) as a colourless solid, mp 198–200 °C; δ_H 7.59–7.13 (10 H, br m, aromatic), 7.00–6.57 (2 H, 4 × br s, 2 × C*H*Ph), 4.95–4.25 (2 H, 4 × br q, 2 × C*H*Me), 3.59–2.88 (2 H, 4 × br s, CH_2) and 1.83–1.42 (6 H, br m, 2 × Me). Variable temperature ^{13}C NMR in $CDBr_3$ indicated restricted rotation around the *N*-acyl bond.

4. Preparation of 3,3'-succinylbis((*2R,4S*)-2-methyl-4-phenyl-1,3-oxazolidin-5-one) 517

(*S*)-Alanine (1.11 g, 12.5 mmol) was added to NaOH(aq) (1 mol dm^{-3}, 25 cm^3) and ethanol (1-2 cm^3) was added to obtain solution. The solvent was evaporated under reduced

pressure until precipitation began. Benzaldehyde (1.11 g, 12.5 mmol) and CH_2Cl_2 (150 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5–8 hours. The imine was formed as a white precipitate. The mixture was stirred at 0 °C while a solution of succinyl chloride (0.97 g, 0.69 cm^3, 6.3 mmol) in CH_2Cl_2 (5 cm^3) was added slowly and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated and the residue recrystallised to give the product **517** (1.74 g, 32%)as a colourless powder; δ_H 7.55–7.14 (10 H, br m, aromatic), 6.74–6.46 (2 H, br m, 2 × C*H*Ph), 4.78–4.49 (2 H, br m, 2 × C*H*Me), 2.88–2.16 (2 H, 2 × br m, CH_2), 1.68 (6 H, br d, 2 × Me) and 1.52–1.22 (2 H, br m, CH_2); δ_C 172.0* and 171.9 (2 CO), 169.7 and 169.4* (CO), 136.4 and 136.1* (4ry), 130.8 and 129.8*, 129.5 and 128.7* (2 C), 126.8 and 126.5* (2 C), 90.4* and 89.6 (2 *C*HPh), 52.8 and 52.0* (2 *C*HMe), 30.4, 30.2* and 30.0* (2 CH_2), 19.4*, 19.3* and 16.2 (2 Me).

5. Preparation of 3,3'-succinylbis((*2R,4S*)-2-isopropyl-4-phenyl-1,3-oxazolidin-5-one) 518

(*S*)-Valine (5.86 g, 50 mmol) was added to $NaOH_{(aq)}$ (1 mol dm^{-3}, 50 cm^3) and ethanol (2-3 cm^3) was added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Benzaldehyde (5.30 g, 50 mmol) and CH_2Cl_2 (300 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5-8 hours. The imine was formed as a white precipitate. The mixture was stirred at 0 °C while a solution of succinyl chloride (3.88 g, 2.76 cm^3, 25 mmol) in CH_2Cl_2 (40 cm^3) was added slowly and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated and the residue recrystallised to give the product **518** as a colourless powder (2.09 g, 17%), mp 219–221 °C; (Found: M+Na^+, 515.2160. $C_{28}H_{32}N_2O_6$ requires *M*+Na^+, 515.2158); ν_{max}/cm^{-1} 1787, 1646, 1404, 1297, 1260, 1222, 1170, 1126, 1088, 1034, 1009, 956, 934, 893, 848 and 830; δ_H

8.14–7.20 (10 H, m. aromatic), 6.68–6.40 (2 H, br m, 2 × C*H*Ph), 4.73–4.48 (2 H, br m, 2 × C*H*Pr^{i}), 2.92–2.08 (4 H, 2 × br m, 2 CH_2) and 1.39–0.42 (12 H, 4 × br d, 4 × Me); *m/z* 515 (M + H^+, 100%).

6. Preparation of 3,3'-succinylbis((*2R,4S*)-2,4-diphenyl-1,3-oxazolidin-5-one) 519

(*R*)-phenylglycine (7.56 g, 50 mmol) was added to NaOH(aq) (1 mol dm^{-3}, 50 cm^3) and ethanol (2–3 cm^3) was added to obtain solution. The solvent was evaporated under reduced pressure until precipitation began. Benzaldehyde (5.30 g, 50 mmol) and CH_2Cl_2 (300 cm^3) were added and the mixture heated with azeotropic removal of water (inverted Dean and Stark trap) for 5-8 hours. The imine was formed as a white precipitate. The mixture was stirred at 0 °C while a solution of succinyl chloride (3.88 g, 2.76 cm^3, 25 mmol) in CH_2Cl_2 (40 cm^3) was added slowly and the mixture was then stirred at room temperature overnight. The turbid mixture was washed successively with water, 5% $NaHCO_3$, 5% $NaHSO_3$ solutions and again with water. The solution was then dried using magnesium sulfate and evaporated and the residue recrystallised to give the product **519** (3.56 g, 26%) as a colourless solid, mp 210–212 °C; (Found: M+H^+, 583.1864. $C_{34}H_{28}N_2O_6$ requires *M*+H^+, 583.1845); ν_{max}/cm^{-1} 1788, 1649, 1587, 1560, 1493, 1420, 1376, 1327, 1301, 1241, 1168, 1075, 1040, 1002, 929, 912, 880 and 834; δ_H 7.74–6.98 (20 H, m, aromatic), 6.96–6.69 (2 H, br m, 2 × C*H*Ph), 5.74–5.29 (2 H, br m, 2 × C*H*Ph) and 2.66–1.34 (4 H, 4 br m, 2 × CH_2); δ_C 170.3 (CO), 169.8 (CO), 136.0 (4ry), 135.8 (4ry), 131.4, 130.4, 130.1, 130.0, 129.2, 128.9, 127.2, 127.1, 126.8, 126.7, 126.6, 126.2, 91.5 and 90.7* (2 *C*HPh), 61.0 and 60.8* (2 *C*HPh) and 30.6 (2 CH_2); *m/z* 583 (M + H^+, 100%).

M. X-Ray Structure Determinations

1. (*2R,4S*) 3-acetyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one 388

Crystal data for $C_{12}H_{13}NO_3$, M = 219.23, colourless prism, crystal dimensions 0.13 × 0.1 × 0.1 mm, orthorombic, space group $P2_12_12_1$, a = 6.568 (16), b = 11.00 (3), c = 15.41 (4) Å, β = 90°, V = 1114(5) Å^3, Z = 4, D_c = 1.308 Mg m^{-3}, T = 293 K, R = 0.0483, R_w = 0.0988 for 1026 reflections with I>2σ(I) and 146 variables. Data were collected on a Bruker SMART diffractometer with graphite-monochromated Mo-Kα radiation (a = 0.71073 Å). The structure was solved by direct methods and refined using full-matrix least squares methods. Atomic coordinates and bond lengths and angles are listed in the Appendix in tables and the structure is shown in the discussion.

2. (*2R,4S*)-4-methyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one 485

Crystal data for $C_{12}H_{13}NO_2S$, M = 235.29, colourless prism, crystal dimensions 0.2 × 0.2 × 0.2 mm, orthorombic, space group $P2_12_12_1$, a = 8.390 (3), b = 9.276 (4), c = 15.439 (6) Å, β = 90°, V = 1201.6(8) Å^3, Z = 4, D_c = 1.301 Mg m^{-3}, T = 293 K, R = 0.0431, R_w = 0.1096 for 1461 reflections with I>2σ(I) and 146 variables. Data were collected on a Bruker SMART diffractometer with graphite-monochromated Mo-Kα radiation (a = 0.71073 Å). The structure was solved by direct methods and refined using full-matrix least squares methods. Atomic coordinates and bond lengths and angles are listed in the Appendix in tables and the structure is shown in the discussion.

3. (*2R,4S*)-4-benzyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one 483

Crystal data for $C_{23}H_{19}NO_2S \cdot 0.75CH_2Cl_2$, M = 437.15, yellow plate, crystal dimensions 0.1 × 0.1 × 0.05 mm, monoclinic, space group $P2_1$, a = 10.4985 (18), b = 9.2896 (16), c = 12.254 (2) Å, β = 104.215(3)°, V = 1158.5(3) Å^3, Z = 2, D_c = 1.253 Mg m^{-3}, T = 293

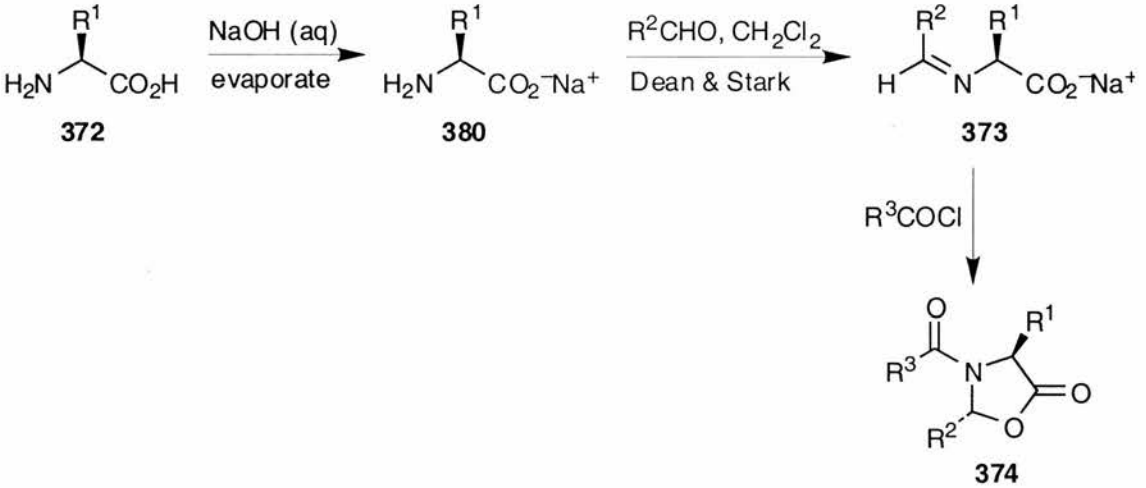
K, R = 0.0717, R_w = 0.1568 for 1941 reflections with $I>2\sigma(I)$ and 272 variables. Data were collected on a Bruker SMART diffractometer with graphite-monochromated Mo-Kα radiation (a = 0.71073 Å). The structure was solved by direct methods and refined using full-matrix least squares methods. Atomic coordinates and bond lengths and angles are listed in the Appendix in tables and the structure is shown in the Discussion.

DISCUSSION

A. Synthesis and Properties of *N*-Acyloxazolidin-5-ones

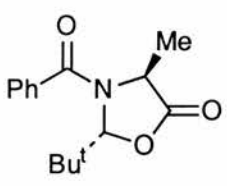
1. Synthesis

A range of oxazolidin-5-ones **374** were prepared starting from amino acids **372** using the route shown below[112]. These can be synthesised from any of the 20 readily available α-amino acids via their sodium salts **380** by condensation with an aldehyde to form the imine **373**. This step is limited to non-enolisable aldehydes. An inverse Dean and Stark trap is employed to remove any water formed since dichloromethane is the solvent here. Cyclisation of the imine with an acid chloride gives the *N*-acyloxazolidin-5-one **374**. The amino acids used were

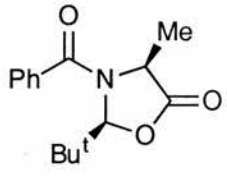


(*S*)-alanine, (*S*)-valine, (*S*,*S*)-isoleucine, (*S*)-phenylalanine and (*R*) and (*S*)-phenylglycine. The aldehyde component was usually benzaldehyde although pivalaldehyde was also examined. Both benzoyl chloride and acetyl chloride were used as the acid chloride component. Although much of Seebach's important work on these systems has used pivalaldehyde,[109] the method for this[110] involved azeotropic distillation with the expensive n-pentane and afforded low-melting products which were a mixture of difficultly separable *cis* and *trans* isomers. In view of this most effort was concentrated on the use of benzaldehyde[112] which involved azeotropic distillation with CH_2Cl_2 and gave higher melting products which were the pure *trans* isomers. The products obtained are shown below.

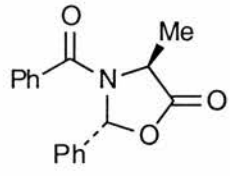
Isomers **381** and **382**,[110] compounds **383–385**,[112] and the opposite enantiomer of **387**[113] are all known compounds and the physical and spectroscopic data obtained were in good agreement with the literature. Compound **390** was already known,[114] but the ^{1}H and ^{13}C NMR spectra had been recorded in DMSO so we characterised **390** in $CDCl_3$ for easier future reference. The previously unknown compounds **386**, **388**, **389**, **391–393** have been fully characterised. The synthesis of **394** from *O*-methyl-(*S*)-serine[115,116] was unsuccessful.



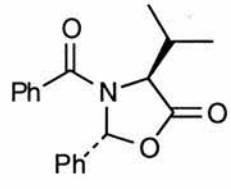
381



382



383



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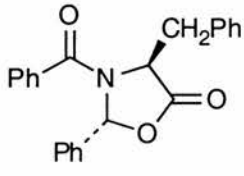

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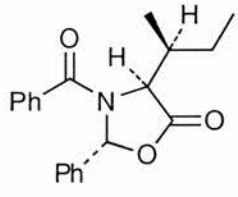

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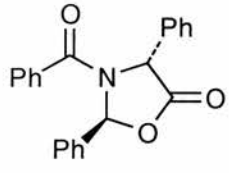

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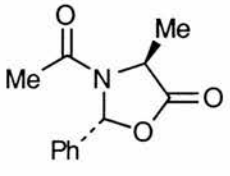
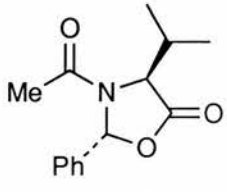
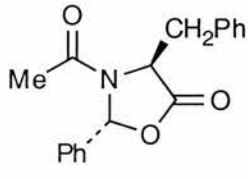


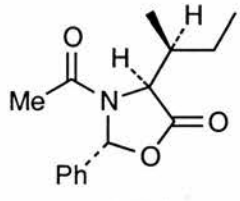
388



389



390



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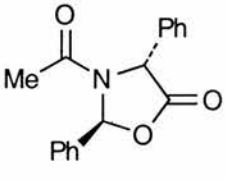
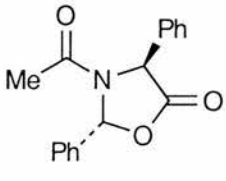
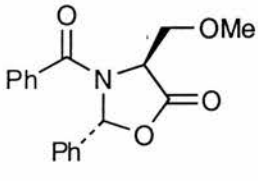


392



393



394

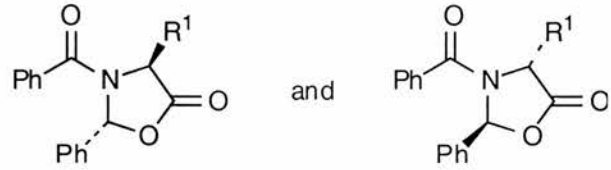
2. Structure and Properties

The ^{1}H NMR spectra (Table 1) of all the *N*-benzoyloxazolidin-5-ones synthesised are in agreement with the literature.[112,113] The previously unknown compound derived from leucine shows values for 2-H and 4-H that are within the expected range for these type of

compounds. Of the *N*-acetyloxazolidin-5-ones formed only the 4-benzyl compound is known.[114] All ^{1}H NMR spectra of the acetyl compounds (Table 2) show two sets of broad peaks due to restricted rotation around the amide bond. With the exception of the 4-phenyl compound all the minor conformers have higher shifts for 2-H and the acetyl group, and lower shifts for 4-H. The pattern of these signals and those for R^1 are also as would be expected. The shifts for 2-H, 4-H and the acetyl groups of these unknown compounds are consistent with each other and known oxazolidinones.

The ^{13}C NMR spectra of the *N*-acetyloxazolidin-5-ones (Table 3) are also consistent with each other and what would be anticipated from literature data[112,114] of their *N*-benzoyl counterparts. What is interesting is that the ^{13}C NMR spectra only show two conformers when R^1 is *s*-butyl or phenyl. Also we can be fairly confident of distinguishing between the aromatic carbons of the benzoyl and R^1 (where they are present).

Table 1: ^{1}H NMR spectra of *N*-benzoyloxazolidin-5-ones

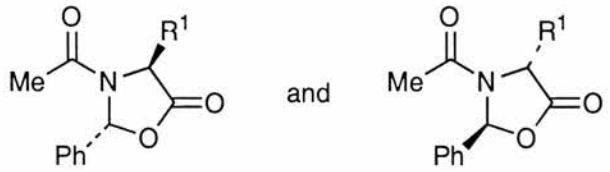


R^1 = Me (**383**), Pr^i (**384**), Bn (**385**), Bu^s (**386**), Ph (**387**)

R^1	Aromatic	2-H	4-H	R^1
Me	7.45-7.10 (10 H, m)	6.76 (s)	4.84 (q, *J* 7)	1.50 (3 H, d, *J* 7)
Pr^i §	7.60-7.10 (10 H, m)	6.62 (s)	4.84 (br s)	2.60-2.1 (1 H, m, CH), 1.15 (3 H, d, *J* 7, Me), 1.05 (3 H, d, *J* 7, Me)
Bn	7.45-6.75 (15 H, m)	5.83 (s)	5.20 (m)	3.80-3.30 (2 H, 2 x br s, CH_2)
Bu^s §	7.50-6.90 (10 H, m)	6.64 (s)	4.91 (br s)	1.73 (1 H, m, CH), 1.50 (2 H, m, CH_2) 1.07 (3 H, d, *J* 7, *Me*CH) 0.90 (3 H, t, *J* 7, *Me*CH_2)
Ph	7.50-7.00 (16 H, m)	in arom.	5.65 (br s)	in aromatic

§ denotes spectrum recorded at 50 °C

Table 2: ^{1}H NMR spectra of *N*-acetyloxazolidin-5-ones



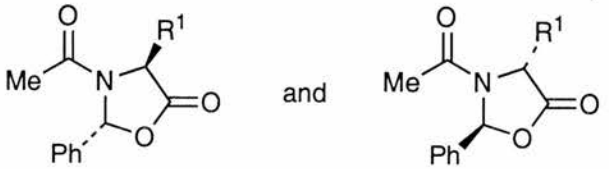
and

R^1 = Me (**388**), Pr^i (**389**), Bn (**390**), Bu^s (**391**), Ph (**392** and **393**)

R^1	Aromatic	2-H	4-H	Acetyl	R^1
Me	7.55–7.30 (5 H, m)	6.58 (s)	4.72 (q, *J* 7)	1.70 (s)	1.72 (3 H, d, *J* 7, Me)
Me*	7.55–7.30 (5 H, m)	6.66 (s)	4.60 (q, *J* 7)	2.16 (s)	1.59 (3 H, br. s, Me)
Pr^i	7.50–7.30 (5 H, m)	6.50 (s)	4.68 (d, *J* 4)	1.67 (s)	2.96–2.84 (1 H, m, CH), 1.24 (3 H, d, *J* 7, Me), 1.00 (3 H, d, *J* 7, Me)
Pr^i*	7.50–7.30 (5 H, m)	6.56 (s)	4.49 (d, *J* 4)	2.12 (s)	2.48–2.36 (1 H, m, CH), 1.29 (3 H, d, *J* 7, Me), 1.07 (3 H, d, *J* 7, Me)
Bn	7.50-7.10 (10 H, m)	5.53 (s)	5.20 (m)	1.58 (s)	3.95-3.80 (1H, dd, *J* 14, 6, CH_2Ph), 3.33-3.18 (1H, dd, *J* 14, 2, CH_2Ph)
Bn*	7.50-7.10 (10 H, m)	5.66 (s)	4.88 (m)	1.58 (s)	3.38 (2 H, br. s, CH_2Ph)
Bu^s	7.44–7.29 (5 H, m)	6.49 (s)	4.70 (d, *J* 4)	1.60 (s)	2.57 (1 H, m, CH), 1.80–1.40 (2 H, m, CH_2), 0.97 (3 H, t, *J* 7, CH_2*Me*), 0.89 (3 H, d, *J* 7, CH*Me*)
Bu^s*	7.44–7.29 (5 H, m)	6.42 (s)	4.51 (d, *J* 4)	2.05 (s)	2.57 (1 H, m, CH), 1.80–1.40 (2 H, m, CH_2), 097 (3 H, t, *J* 7, CH_2*Me*), 0.89 (3 H, d, *J* 7, CH*Me*)
Ph	7.65–7.3 (10 H, m)	6.96 (s)	5.45 (s)	1.75 (s)	
Ph*	7.25 (10 H, m)	6.81 (s)	5.68 (s)	1.72 (s)	

* denotes signals due to minor amide rotomer

Table 3: ^{13}C NMR spectra of *N*-acetyloxazolidin-5-ones



and

R^1 = Me (**388**), Pr^i (**389**), Bn (**390**), Bu^s (**391**), Ph (**392** and **393**)

R^1	C=O	Aromatic	C-2	C-4	*Me*CO	R^1
Me	172.1, 168.1	136.4 (4ry), 130.8, 129.5 (2 C), 126.6 (2 C)	90.0	52.6	23.3	16.7 (Me)
Pr^i	169.6, 168.1	136.8 (4ry), 130.8, 129.5 (2 C), 126.7 (2 C)	90.5	61.6	28.4	23.6 (CH), 17.9 (Me), 16.2 (Me)
Bn	171.1, 168.3	136.1 (4ry), 130.8, 129.7 (2 C), 126.8 (2 C)	90.5	58.6	23.4	134.9 (4ry), 129.4 (2 C), 128.8 (2 C), 127.6, 34.2 (CH_2)
Bu^s	169.7, 167.9	136.8 (4ry), 130.8, 129.5 (2 C), 126.7 (2 C)	90.6	60.5	23.6	34.9 (CH), 25.1 (CH_2), 13.8 (CH*Me*), 12.0 (CH_2*Me*)
Bu^s*	169.7, 167.6	136.5 (4ry), 129.8, 128.6, 126.7	91.2	60.5	22.8	34.9 (CH), 25.2 (CH_2), 13.8 (CH*Me*), 12.0 (CH_2*Me*)
Ph	169.6, 168.8	136.3 (4ry), 130.0, 129.8 (2 C), 126.6 (2 C)	91.1	61.1	23.6	135.5 (4ry), 129.6, 128.8 (2 C), 126.4 (2 C)
Ph*	169.4, 168.6	136.3 (4ry), 130.0, 129.3 (2 C), 126.8 (2 C)	90.8	60.5	23.3	134.9 (4ry), 129.0, 128.4, 126.0

It was noticed that the ^1H NMR spectra of the *N*-benzoyloxazolidin-5-ones displayed extremely broad peaks at 25 °C. By running the spectra at 50 °C the signals were seen to sharpen up considerably. Also, the ^1H and ^{13}C NMR spectra of the *N*-acetyloxazolidin-5-ones showed two sets of broad peaks in most cases and could be mistaken for a mixture of isomers. This behaviour is indicative of restricted rotation of the molecule around the amide bond. This means that the molecule has two conformers **395** and **396** as shown.

395 **396**

Since the conversion between these two conformers is slow in comparison to the time scale of the NMR experiment both are observed. At higher temperatures the interconversion is sufficiently fast that the signal is observed as an "average." At lower temperatures, the spectra due to each of the conformers are recorded. The equilibrium existing between the conformers can be described by the following thermodynamic equations:

$$\Delta G^*/RT_c = 22.96 + \ln(T_c/\delta_\nu) \qquad \text{(Equation 1)}$$

$$n_a/n_b = \exp(\Delta G/RT) \qquad \text{(Equation 2)}$$

where δ_ν is the low temperature separation of the signals of the two conformers, T_c is the coalescence temperature for a given pair of signals (i.e. the temperature at which the signals merge) and ΔG^*, ΔG, T and R have their usual thermodynamic meanings. n_a/n_b is the low temperature ratio of the conformers and can be determined from the integral trace.

In a variable temperature NMR experiment, a spectrum is recorded at a temperature high enough such that only the "average" signal is observed. The temperature is then lowered in increments of 10K and a spectrum recorded at each of these temperatures in order to find T_c for as many of the signals as possible. This is, of course, is limited by the temperature range at which the most suitable solvent is in its liquid state.

This procedure was carried out for (*2R,4S*) 3-acetyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one. The results are shown below.

Signal (ppm)	T_c (K)	δ_v (Hz)	ΔG^* (kJ mol^{-1})	ΔG (kJ mol^{-1})
6.58	325±1	174	63.73	2.47
4.72	328±1	201	63.95	2.47

The energy barrier for rotation, ΔG^*, is determined from the coalescence temperature, T_c using Equation 1. The difference in energy between the two states, ΔG, is calculated from the ratio of the conformers using Equation 2.

The X-ray crystal structure of **388** was determined to confirm the relative position of the substituents at C–2 and C–4 as *trans*. Like other examples synthesised from (*S*)-amino acids by Seebach, the structure of *N*-acetyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one proves the absolute configuration is (*2R,4S*) since the configuration at the 4-position is already known.

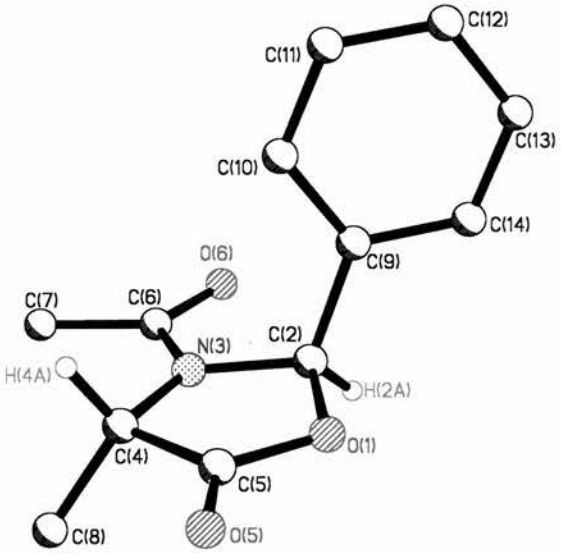


Figure 1: X-ray structure of (*2R,4S*)-3-acetyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one **388** showing the crystallographic numbering scheme. Selected bond lengths and angles; O(1)-C(5) 1.351(6), O(1)-C(2) 1.451(5), C(2)-N(3) 1.464(6), C(2)-C(9) 1.512(7), N(3)-C(6) 1.361(5), N(3)-C(4) 1.453(6), C(4)-C(8) 1.511(6), C(4)-C(5) 1.512(7), C(5)-O(5) 1.194(5), C(6)-O(6) 1.231(5), C(6)-C(7) 1.489(6) Å; C(5)-O(1)-C(2) 111.4(3), O(1)-C(2)-N(3) 103.3(4), O(1)-C(2)-C(9) 107.3(3), N(3)-C(2)-C(9) 115.5(3), C(6)-N(3)-C(4) 130.1(3), C(6)-N(3)-C(2) 118.0(4), C(4)-N(3)-C(2) 111.6(3), N(3)-C(4)-C(8) 116.7(3), N(3)-C(4)-C(5) 102.1(3), C(8)-C(5)-C(4) 108.9(4), O(6)-C(6)-N(3) 119.3(4), O(6)-C(6)-C(7) 122.8(4), O(1)-C(4)-C(5) 110.2(4), N(3)-C(6)-C(7) 117.8(4)°.

For comparison, the reported structure of **397**[130] is shown in Figure 2. It can be seen that the key bond lengths and angles are generally very similar although the length of C(2)-C(9) is substantially greater for our compound than the literature example.

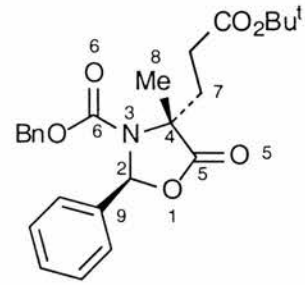


Figure 2: Literature X-ray structure of (2*S*,4*R*)-3-benzoxycarbonyl-4-(2-*t*-butoxycarbonylethyl)-4-methyl-2-phenyl-1,3-oxazolidin-5-one **397** showing the crystallographic numbering scheme. Selected bond lengths and angles; O(1)-C(5) 1.340, O(1)-C(2) 1.444, C(2)-N(3) 1.466, C(2)-C(9) 1.468, N(3)-C(6) 1.388, N(3)-(C4) 1.462, C(4)-C(8) 1.530, C(4)-C(5) 1.526, O(5)-C(5) 1.182, O(6)-C(6) 1.206, C(7)-C(4) 1.533 Å; C(2)-O(1)-C(5) 112.67, N(3)-C(2)-O(1) 102.64, C(9)-C(2)-O(1) 107.77, N(3)-C(2)-C(9) 116.01, C(6)-N(3)-C(4) 121.90, C(6)-N(3)-C(2) 125.18, C(2)-N(3)-C(4) 111.90, N(3)-C(4)-C(8) 113.49, N(3)-C(4)-C(7) 113.26, N(3)-C(4)-C(5) 100.33, C(7)-C(4)-C(5) 108.91, C(8)-C(4)-C(5) 110.85, O(1)-C(5)-O(5) 129.91, O(1)-C(5)-C(4) 111.56, O(5)-C(5)-C(4) 126.50, O(6)-C(6)-N(3) 125.45°.

For comparison, the reported structure of **398**[131] is shown in Figure 3. It can be seen that the key bond lengths and angles are generally very similar although the angle of C(6)-N(3)-C(4) is substantially greater for our compound than the literature example.

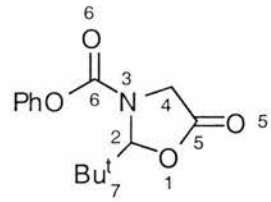
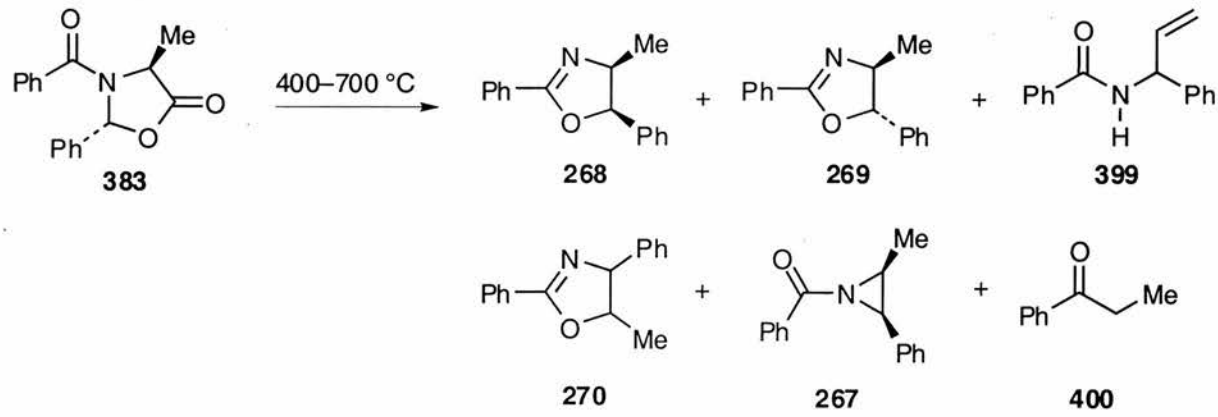


Figure 3: Literature X-ray structure of (2*S*)-2-*t*-butyl-1,3-oxazolidin-5-one **398**[131] showing the crystallographic numbering scheme. Selected bond lengths and angles; O(1)-C(5) 1.345, C(2)-O(1) 1.449, C(2)-N(3) 1.465, C(2)-C(7) 1.529, N(3)-C(6) 1.366, N(3)-C(4) 1.458, C(4)-C(5) 1.497, C(5)-O(5) 1.200, C(6)-O(6) 1.204 Å; C(2)-O(1)-C(5) 110.95, N(3)-C(2)-O(1) 109.21, C(7)-C(2)-O(1) 104.02, N(3)-C(2)-C(7) 115.16, C(6)-N(3)-C(4) 117.71, C(6)-N(3)-C(2) 122.45, C(2)-N(3)-C(4) 109.21, N(3)-C(4)-C(5) 102.72, O(1)-C(5)-O(5) 121.53, O(1)-C(5)-C(4) 110.26, O(5)-C(5)-C(4) 128.21, O(6)-C(6)-N(3) 124.93°.

B. FVP of *N*-acyloxazolidin-5-ones

1. Results

The first compound subjected to FVP was the (*S*)-alanine derived **383**. The experiment was carried out at 50 °C increments between 600 and 400 °C. A summary of the results is shown in the diagram below.

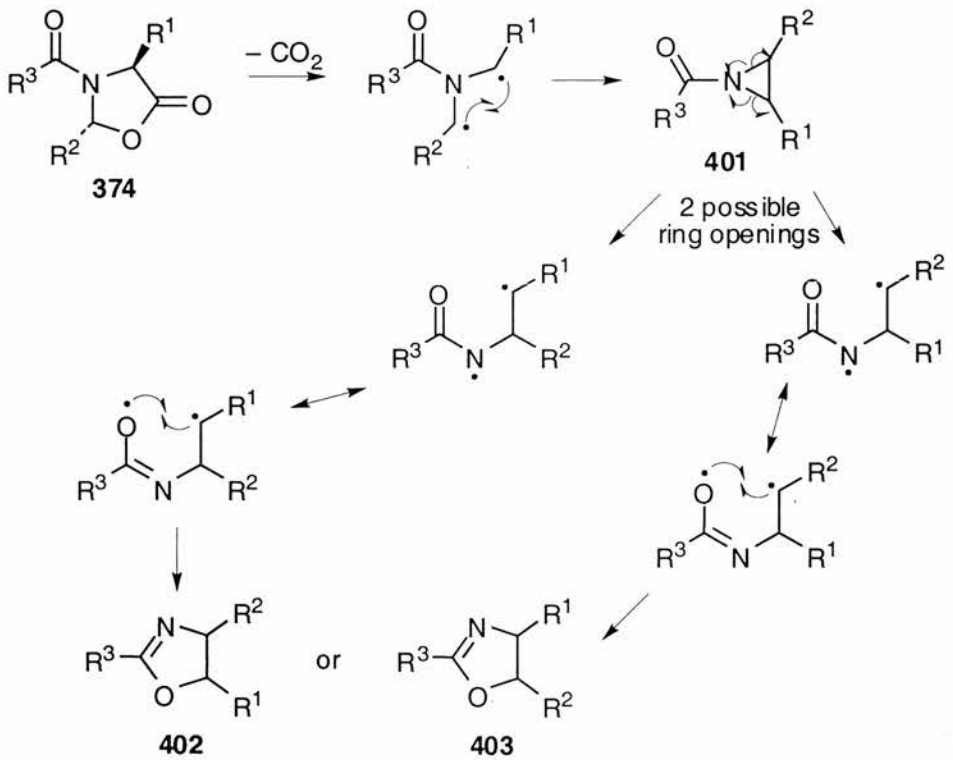


Temperature (°C)	Yield (%) **383**	**267**	**268**	**269**	**399**	**270**	**400**
400	(94)	4	-	-	-	-	-
450	(72)	23	5	-	-	-	-
500	-	19	34	-	18	-	-
550	-	-	37	6	15	7	-
600	-	-	56	16	23	-	3
700	-	-	14	13	19	-	21

Although previous work in this laboratory[108] suggested that carbon monoxide would be expelled from the ring, initial reactions showed that the 3-acyloxazolidin-5-ones did not fragment as expected to give the aldehyde or its imine, which would be required for acyl anion equivalence. In this case it was possible to identify the products as the *cis*- and *trans*-4-methyl-2,5-diphenyloxazolines **268** and **269** and 1-benzoyl-2-methyl-3-phenylaziridine **267** by comparison with literature spectra.[117,118,9] Also a rather interesting by-product **399** was found to form.

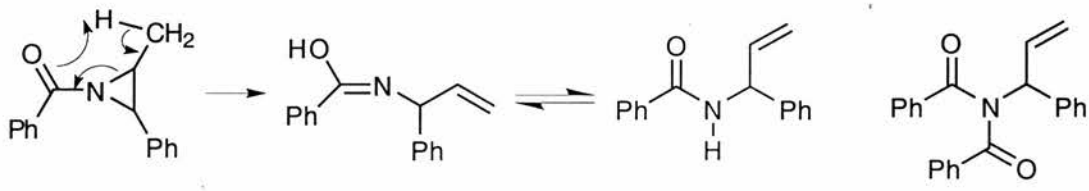
Pyrolysis of the oxazolidinone **383** was first examined at 600 °C. The main product proved to be the *cis* 4-methyl-2,5-diphenyloxazoline **268** (56%) and it showed good agreement of ^{1}H and ^{13}C NMR data with published values.[117] Its *trans*-isomer **269** (16%), *N*-(1-phenylprop-2-enyl)benzamide **399** (23%) and propiophenone **400** (3%) were also formed.

In view of this we proposed the fragmentation pathway below for **374**. Under FVP conditions this ring system loses CO_2 to give the diradical, which ring-closes to the *N*-acylaziridine **401** which under these conditions yields the 2-oxazolines **402** or **403** by a rearrangement of the *N*-acylaziridine as shown.



The nature of the main products was now clear. As shown the aziridine may break open in either way to give isomeric oxazolines. It might be assumed that because the conversion of **374** to **401** to **403** involves two ring cleavages and a diradical mechanism that all stereochemistry would be lost.

In a first large-scale pyrolysis of this compound at 550 °C, chromatographic separation gave the oxazoline **268** (60% yield) and *N*-(1-phenylprop-2-enyl)benzamide **399** (20%). The



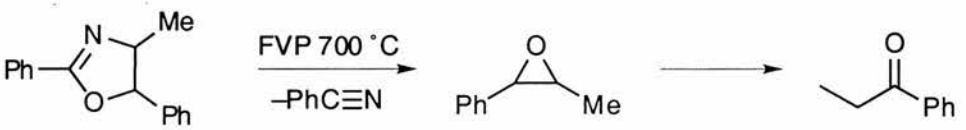
267 **399** **404**

^{1}H and ^{13}C NMR spectra of this showed good agreement with the corresponding *N,N*-dibenzoyl analogue **404** reported by Overman.[119] This is most probably the product of an alternative rearrangement of the aziridine **267** as shown. In a further large scale pyrolysis of **383** at 550 °C, chromatographic separation gave the oxazoline **268** (37%), its *trans* isomer **269** (6%), 1-phenylprop-2-enyl benzamide **399** (15%) and what is presumed to be 5-methyl-2,4-diphenyloxazoline **270** (7%). ^{1}H and ^{13}C NMR data of the *trans*-isomer of **270**[31] are available for comparison but results are not conclusive as to which isomer has formed. The coupling constant of the 4-H doublet in the ^{1}H NMR suggests that it is the *cis*-isomer.

It therefore appeared that the intermediate aziridine fragments almost exclusively by N–CHPh cleavage since only a small amount of the isomeric 5-methyl-2,4-diphenyl product was obtained. Why the rearrangement of the aziridine should give the apparently more sterically hindered *cis*-isomer will be described later.

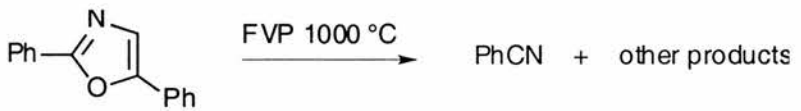
In an attempt to detect the proposed aziridine intermediate the pyrolysis was repeated at 500 °C and this again gave mainly **268** together with NMR signals corresponding to the published data for the *cis* aziridine.[9] We wanted to isolate the *cis* aziridine therefore the experiment was repeated at 400 and 450 °C. Pyrolysis at 400 °C left the starting material almost completely unreacted with only a trace of the *cis* aziridine **267** formed (4%) while at 450 °C the products were **267** (23%), **268** (5%) and starting material **383**.

Our final study on this compound's pyrolytic behaviour was performed at 700 °C. Surprisingly, the major component of the product was propiophenone **400** (21%) followed by **399** (19%), **268** (14%) and **269** (13%). Therefore it was decided that this temperature was of



268 / 269 **405** **400**

no use. The propiophenone **400** probably results from a secondary fragmentation of the oxazoline via **405** as shown. This reaction of oxazolines appears to be new although FVP of an oxazole **406** with loss of PhCN has been reported recently.[132]

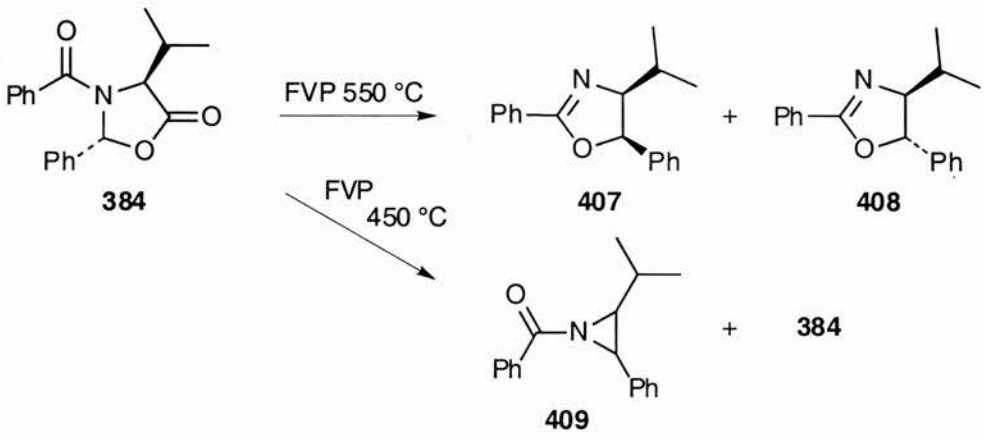


406

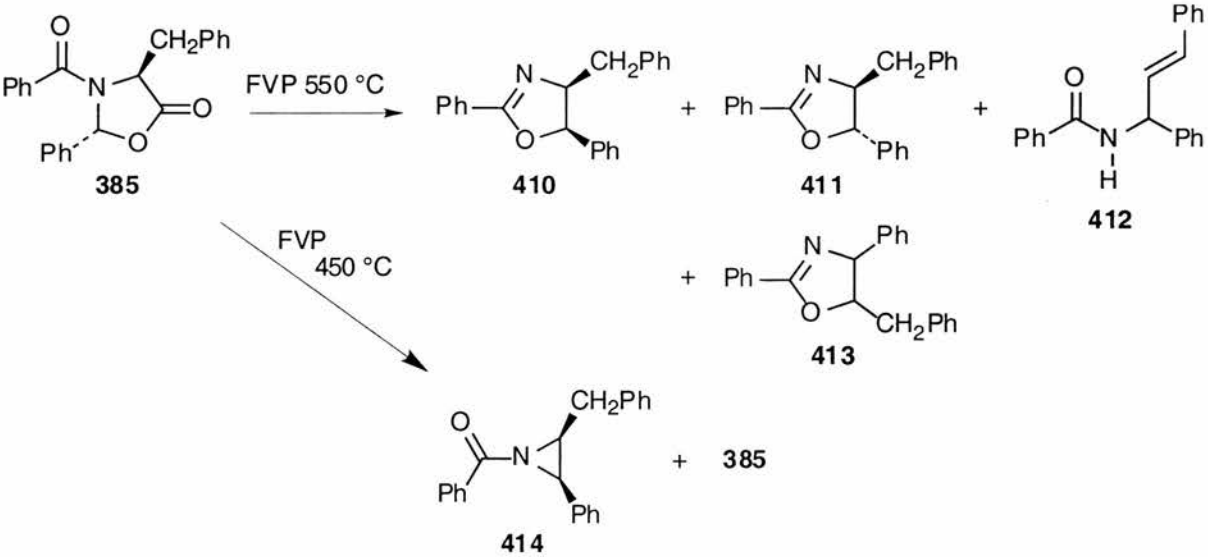
It should be pointed out that at this stage that in all of the pyrolyses an intensely red or purple (in one case blue) colour was formed and the components responsible for this proved to be highly reactive. Since $CDCl_3$ caused almost immediate disappearance of the colour, initial experiments were analysed in C_6D_6. It later became clear that the coloured component (perhaps an azirine or indigo derivative) was only present in trace amounts and the main products were thereafter analysed in $CDCl_3$ to aid comparison with literature spectra where available.

Since conditions of 450 °C and 10^{-2} Torr were found to give good yield of *N*-acyl aziridine **401** while use of 550 °C cleanly gave the oxazolines **403** these two were temperatures focused upon for most of the remaining pyrolyses.

Pyrolysis of the valine-derived compound **384** at 550 °C again gave the *cis* and *trans*-oxazolines **407** and **408** in a ratio of 5:1 from ^{1}H NMR integration. These were isolated in yields of 32% and 14% respectively. There are discrepancies between data for the *trans* isomer **408** and that of the literature[118] which remain unexplained. There was no trace of an analogue of the vinyl compound **399** formed in the pyrolysis of **383**. By carrying out the pyrolysis at 450 °C the aziridine **409** was obtained in 17% yield, together with **407** (6%) and some unreacted starting material.

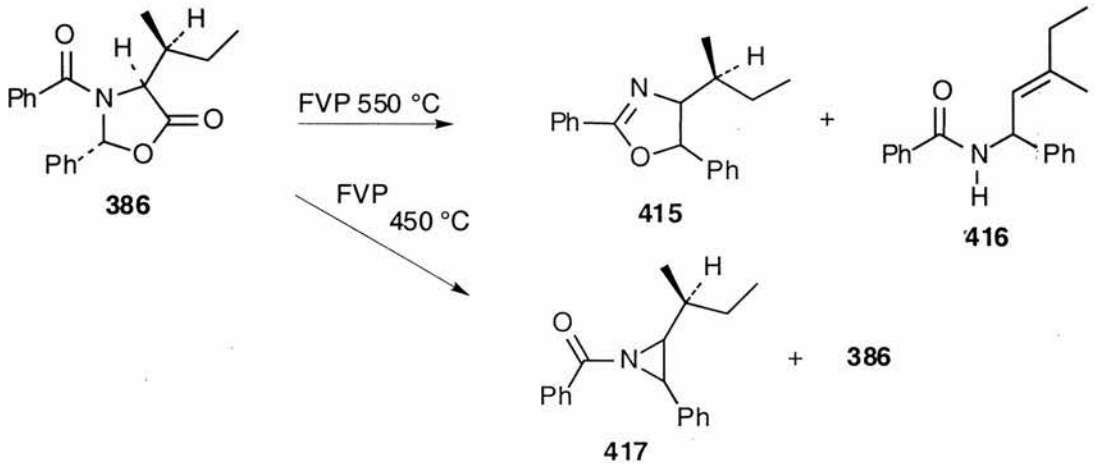


Pyrolysis of **385** at 600 °C gave a single stereoisomer of the oxazoline (26%) and by comparison with the literature data for the *trans* isomer,[7] this was deduced to be the *cis* product **410**. By carrying out this reaction on a large scale at 550 °C and using chromatographic separation, the main product **410** was isolated in 38% yield. A trace of the *trans*-isomer **411** was observed and its ^{1}H NMR data was in good agreement with that of the literature.[120] In addition the previously unknown *N*-(1,3-diphenylprop-2-enyl)benzamide **412** (22%) and what is believed to be an isomer of 5-benzyl-2,4-diphenyloxazoline **413** (9%) were also obtained. In order to obtain the aziridine the experiment was repeated at 450 °C. The products after separation were a single isomer of the *cis*-aziridine **414**[121] (13%), the starting material **385**.



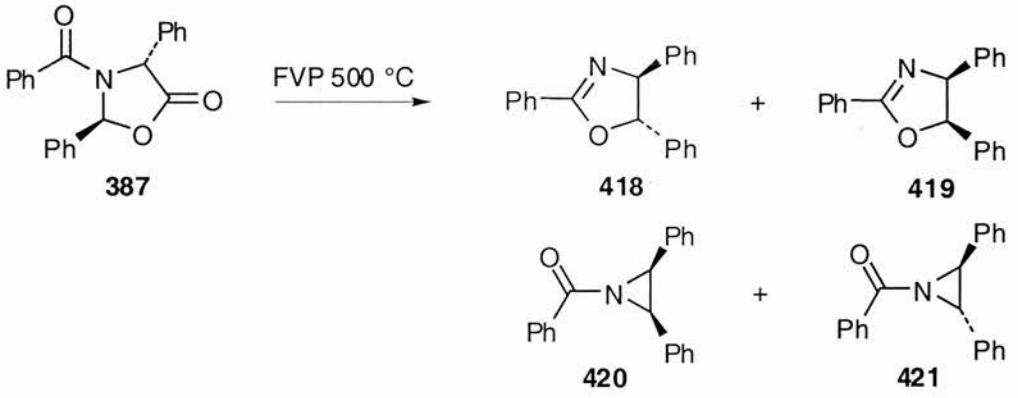
The next compound to be investigated was the (*S*,*S*)-isoleucine derived **386**. As expected FVP of the starting material at 550 °C yields oxazolines and with three stereocentres being present in the molecule all four diastereomers of **415** are identifiable by NMR. Using

column chromatography it was only possible to separate the *cis* isomers (20%) from the *trans* (7%, 12% d.e.). Also, both (*E*) and (*Z*) isomers of *N*-(3-methyl-1-phenylpent-2-enyl)benzamide **416** were formed in the reaction.



On completion of FVP of **386** at 450 °C both diastereomers of the aziridine **417** were formed in 24% yield with a d.e. of 18%. Some unreacted staring material **386** was recovered.

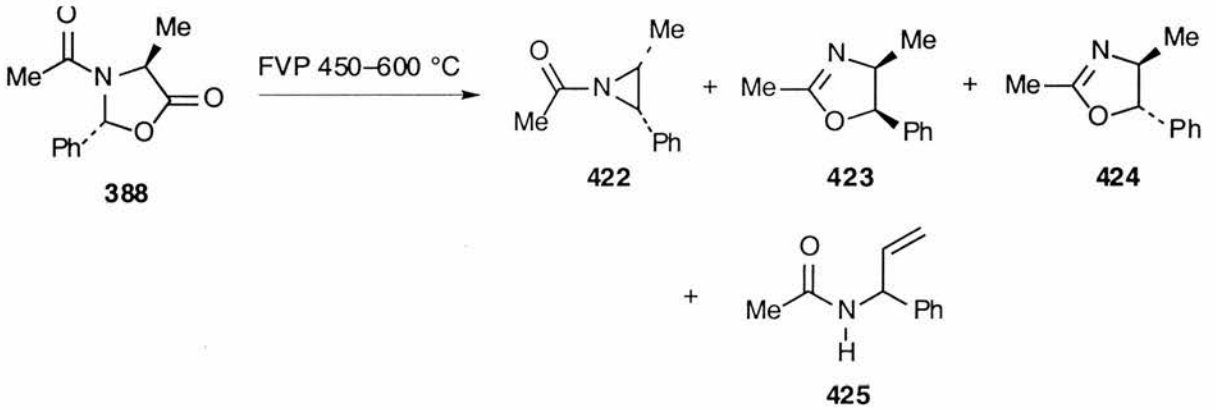
The FVP of the oxazolidinone **387** derived from (*R*)-phenylglycine at 500 °C gave a mixture containing in decreasing order of amount, the *trans*-oxazoline **418**, the *cis*-oxazoline **419**, *cis*-aziridine **420** and *trans*-aziridine **421**. Fortunately all of these could be identified by comparison with published spectroscopic data.[120,69,9]



A sample of **387** was subjected to FVP at 400 °C, the resulting producs were unreacted starting material **387** and traces of the aziridines **420** and **421**. At 450 °C, the products were shown to be **418**, **420**, **419** and **421** in a ratio of 6:3:3:1 (from ^{1}H integration) along with some of starting material. Then at 550 °C the reaction proceeded in 82% yield (crude) to give cleanly the *cis*- and *trans*-oxazolines in a ratio of approximately 1:2. These were isolated by

chromatography in yields of 40 and 12% respectively. There was no sign of an analogue of compound **399** at any temperature.

Pyrolysis of *N*-acetyl-2-methyl-4-phenyloxazolidin-5-one **388** was investigated at 450, 500, 550 and 600 °C. A single isomer of the aziridine **422** (12% yield) and recovered starting material (64 % crude) were obtained at 450 °C. At 500 °C the major products was still the aziridine **422** and *N*-(1-phenylprop-2-enyl)acetamide **425** was identifiable from literature data.[124] Traces of the *cis*- and *trans*-oxazolines **423** and **424** were identifiable from literature data[122,123] as well as a significant amount of starting material. On increasing the furnace temperature to 550 °C the starting material was completely reacted giving the acetamide **425** as

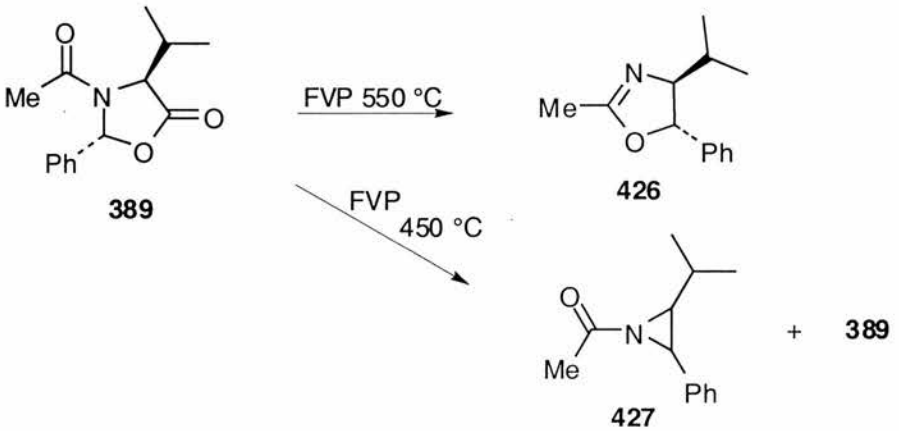


the major product along with the *cis* and *trans*-oxazolines **423** and **424** in NMR yields of 44, 15 and 9% respectively. A trace of the aziridine **422** was also observed.

Any chromatography of the crude products usually resulted in poor yields and hydrolysis of the oxazolines **423** and **424** to amino alcohols. However the allylamide **425** was isolated in 22% yield after chromatography of the products from the pyrolysis at 550°C. At 600°C pyrolysis gave compounds **425**, **423** and **424** in a 4 : 3 : 2 ratio (89% total yield).

Temperature (°C)	Yield **388**	**422**	**423**	**424**	**425**	
450	(64)	12	-	-	-	
500 (from NMR)	√	√√	(√)	(√)	√√	√√ = major
550 (from NMR)	-	7	15	9	44	√ = minor
600 (from NMR)	-	-	√√	√	√√	(√) = trace

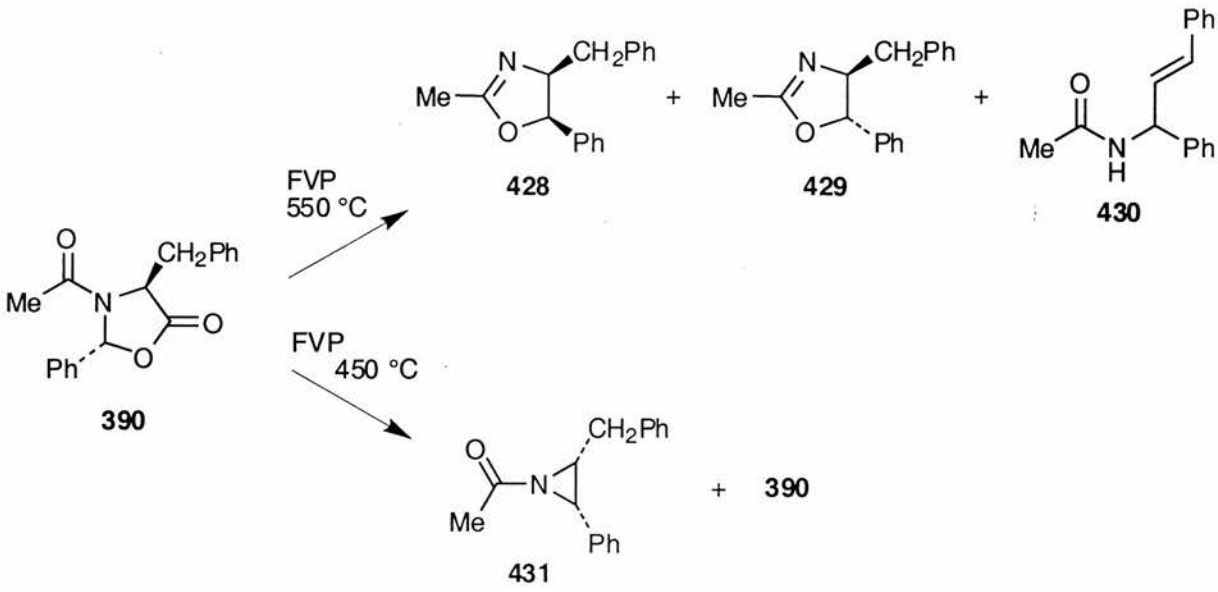
Pyrolysis of the *N*-acetyloxazolidinone **389** was complete at 550 °C to give 2-methyloxazoline **426** resulting from loss of CO_2 in a yield of 15% after chromatographic isolation. Although there is no information as to what the stereochemistry of this might be, it appears from the spectra to be the *trans*-isomer. Determination of which isomer is formed will



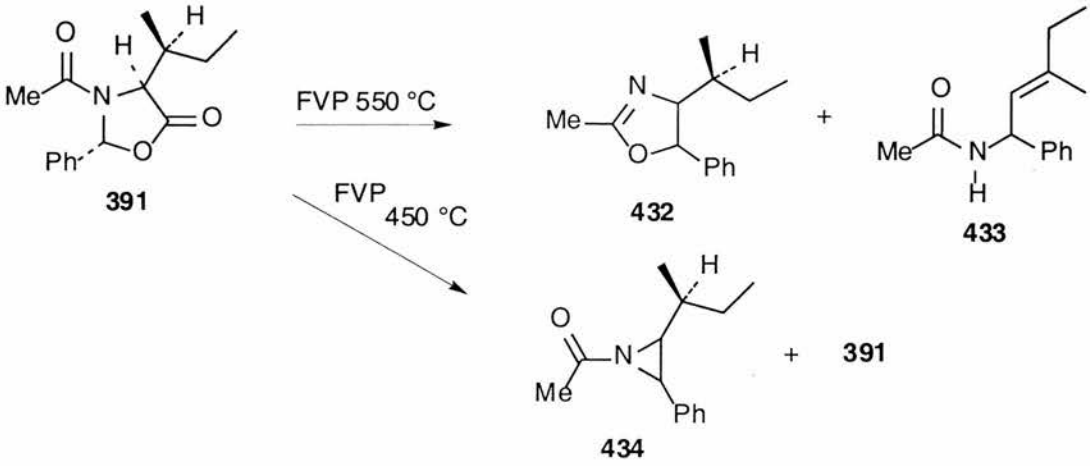
require further investigation. Pyrolysis at 450 °C gives the aziridine **427** as expected. This was present as a single isomer (23%) and with an enantiomeric excess of 16% from the ^{1}H NMR spectrum recorded in the presence of a lanthanide shift reagent. Some starting material **389** was also recovered.

The next compound to be investigated was the (*S*)-phenyalanine derived **390**. At 450 °C reaction yielded the expected aziridine **431** as the *cis*-isomer (12 %). At 550 °C reaction of **390** gave the *cis* and *trans*-oxazolines **428** and **429** along with the elimination product **430**. These products could not be separated using column chromatography after several attempts although

they could be identified clearly by comparison of NMR data. Compound **428** was known in the literature[125] but had been characterised in DMSO.

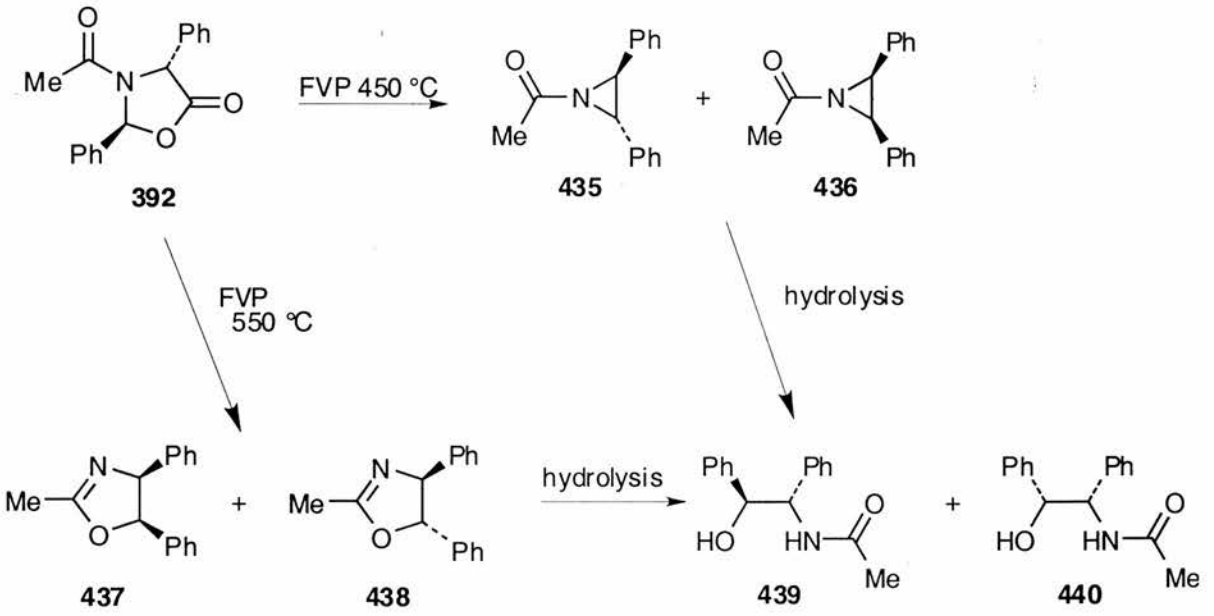


FVP of the (*S*,*S*)-isoleucine derived **391** at 550 °C yielded what appeared to be two diastereoisomers of the oxazoline **432** (25%)although whether they are *cis* or *trans* needs to be ascertained. In this instance the diastereomeric excess was determined as 12% directly from the



^{1}H NMR spectrum without the use of a chiral lanthanide shift reagent. Elimination product **433** (22%) was also formed as a mixture of (*E*) and (*Z*) isomers in a ratio of 55:45. Upon separating these products by column chromatography the oxazolines partially hydrolysed to the corresponding β-acetylamino alcohols. At 450 °C a single isomer of the aziridine **434** (29%) was obtained. Once again the diastereomeric excess could be determined directly from the ^{1}H spectrum without the use of a chiral lanthanide shift reagent. This was calculated as 14%.

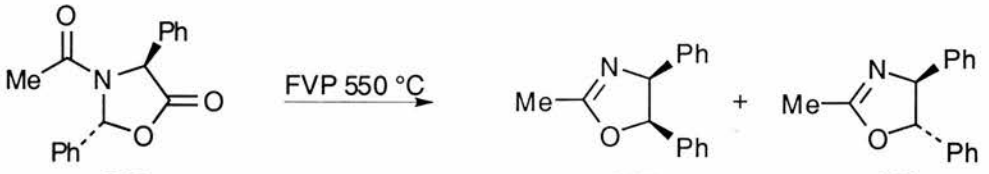
The (*R*)-phenyglycine-derived **392** was also studied. From earlier work the optimum temperatures seemed to be 450 and 550 °C. A small scale pyrolysis were carried out first and these confirmed this as pyrolysis at 450 °C produced the *cis*- and *trans*-aziridines **435**[126] and **436** in a ratio of approximately 5:3. Some starting material **392** and a little of the oxazolines



437 and **438** were also obtained. As with FVP of **387** this suggested that there would be no temperature at which we would obtain purely the aziridines. The experiment was repeated on a larger scale and attempted separation of the products by column chromatography resulted in hydrolysis to the β-acetylamino alcohol **439** as the major product and a trace of the *cis*-isomer **440** (also some starting material **392** was recovered). At 550 °C reaction of **392** gave the oxazolines **437** and **438** in a 1:4 ratio. A white solid crystallised out from NMR samples of both of these products, so both were filtered off and the ^{1}H spectra re-recorded. Both of the samples had hydrolysed either in the air or in $CDCl_3$ to the β-amino alcohol. The oxazolines and the aziridines both hydrolysed to 2-acetamido-1,2-diphenylethanols **439** and **440**.[126]

On completion of pyrolysis at 550 °C on a large scale the results were consistent with the small scale i.e. the crude product was a mixture of *cis*- and *trans*-oxazolines **437** and **438** in a ratio of 1:4 and a yield of 93%. After chromatography the *cis*-isomer was obtained in less than 2% yield. This would imply that most of the oxazoline is reacting on the column and becoming stuck. It seems that column chromatography on alumina is not always efficient in isolating the products.

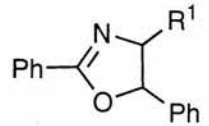
Upon pyrolysis of the (*2R,4S*) isomer of **393** at 550 °C the results were consistent with those of **392** in that the crude product was a mixture of *cis*- and *trans*-oxazolines **437** and **438** in a 1:4 ratio. However chromatography gave these oxazolines in 0.5% and 32% respectively.



393 **437** **438**

Where the oxazolines synthesised were known, their ^{1}H and ^{13}C NMR data are in good agreement with literature values. Where the compounds are unknown their data (Tables 4–7) are consistent with that of similar materials. An exception is the unusually high ^{13}C NMR shift for the 2-Me of the isoleucine derived oxazoline. There is no apparent explanation for this.

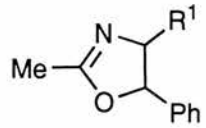
Table 4: ^{1}H NMR spectra of 2-phenyloxazolines



R^1 = Me (**268**, **269**), Pr^i (**407**, **408**), Bn (**410**, **411**), Bu^s (**415**), Ph (**419**, **418**)

R^1	Aromatic	5-H	4-H	R^1
Me (*c*)	8.05 (2 H, m,), 7.55–7.18 (8 H, m)	5.75 (d, *J* 10)	4.66 (dq, *J* 10, 7)	0.89 (3 H, d, *J* 7, Me)
Me (*t*)	8.02 (2 H, m), 7.52–7.22 (8 H, m)	5.10 (d, *J* 8)	4.21 (m)	1.49 (3 H, d, *J* 7, Me)
Pr^i (*c*)	8.05 (2 H, m), 7.55–7.10 (8 H, m)	5.67 (d, *J* 10)	4.20 (dd, *J* 10, 8)	1.00 (1 H, m, CH), 0.92 and 0.76 (2 × 3 H, 2d, *J* 7, 2 × Me)
Pr^i (*t*)	8.06 (2 H, m), 7.55–7.10 (8 H, m)	5.26 (d, *J* 6)	4.39 (t, *J* 6)	1.60 (1 H, m, CH), 0.98 and 0.67 (2 × 3 H, 2d, *J* 7, 2 × Me)
Bn (*c*)	8.05 (2 H, m), 7.50–7.10 (11 H, m), 6.95 (2 H, m)	5.78 (d, *J* 10)	4.88 (ddd, *J* 10, 8, 7)	2.69 (1 H, dd, *J* 14, 8, CH_2) and 2.40 (1 H, dd, *J*14, 7,CH_2)
Bn (*t*)	8.04–8.00 (2 H, m), 7.60–6.95 (13 H, m)	5.30 (d, *J* 6)	4.47 (ddd, *J* 9, 6, 5)	3.35 (1 H, dd, *J* 14, 5, CH_2) and 2.85 (1 H, dd, *J*14, 9,CH_2)
Bu^s (*c*)	8.06 (2 H, d), 7.56–7.22 (8 H, m)	5.73 (d, *J* 10)	4.28 (dd, *J* 10, 8)	1.22 (1 H, m, CH), 1.10–0.88 (2 H, m, CH_2)
				0.63 (3 H, d, *J* 6, CH*Me*), 0.59 (3 H, t, *J* 7, CH_2*Me*)
Bu^s(*c*)*	8.07 (2 H, d), 7.56–7.22 (8 H, m)	5.76 (d, *J* 10)	4.39 (dd, *J* 10, 7)	1.62 and 1.03 (2 × 1 H, 2 × m, CH_2), 1.02 (1 H, m, CH)
				0.70 (3 H, d, *J* 7, CH*Me*), 0.58 (3 H, t, *J* 7, CH_2*Me*)
Bu^s (*t*)	8.09 (2 H, d), 7.58–7.09 (8 H, m)	5.36 (d, *J* 9)	4.59 (t, *J* 9)	1.33 (1 H, m, CH), 1.31 and 1.01 (2 × 1 H, 2 × m, CH_2)
				0.95 (3 H, d, *J* 6, CH*Me*), 0.64 (3 H, t, *J* 7, CH_2*Me*)
Bu^s(*t*)*	8.02 (2 H, d), 7.58–7.09 (8 H, m)	5.27 (d, *J* 9)	4.50 (dd, *J* 10, 9)	1.78 (1 H, m, CH_2), 1.45 (1 H, m, CH), 1.30 (1 H, m, CH_2)
				0.84 (3 H, t, *J* 7, CH*Me*), 0.70 (3 H, d, *J* 6, CH_2*Me*)
Ph (*c*)	8.15 (2 H, m), 7.50–6.90 (13 H, m)	6.03 (d, *J* 10)	5.77 (d, *J* 10)	
Ph (*t*)	8.15 (2 H, m), 7.50–6.90 (13 H, m)	5.42 (d, *J* 8)	5.25 (d, *J* 8)	

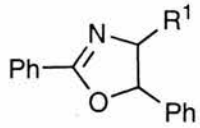
Table 5: ^{1}H NMR spectra of 2-methyloxazolines



R^1 = Me (**423**, **424**), Pr^i (**426**), Bn (**428**, **429**), Bu^s (**432**), Ph (**437**, **438**)

R^1	Aromatic	5-H	4-H	2-Me	R^1
Me (*c*)	7.50-7.10 (5 H, m)	5.56 (d, *J* 10)	4.38 (m)	2.08 (d, *J* 1)	0.75 (3 H, d, *J* 7, Me)
Me (*t*)	7.50–7.10 (5 H, m)	4.90 (d, *J* 8)	3.97 (m)	2.05 (d, *J* 1)	1.36 (3 H, d, *J* 7, Me)
Pr^i	7.40–7.20 (5 H, m)	5.07 (d, *J* 8)	3.81 (t, *J* 8)	2.08 (d, *J* 1)	1.82 (1 H, m, CH), 1.01 (3H, d, *J* 7, Me), 0.95 (3H, d, *J* 7, Me)
Bn (*c*)	7.34–6.94 (10 H, m)	5.55 (d, *J* 10)	4.62 (m)	2.09 (d, *J* 1)	2.41 (1 H, dd, *J* 14, 5, CH_2) and 2.30 (1 H, dd *J* 14, 6, CH_2)
Bn (t)	7.34–6.94 (10 H, m)	5.07 (d, *J* 6)	4.20 (m)	2.07 (d, *J* 1)	3.15 (1 H, dd, *J* 14, 6, CH_2) and 2.75 (1H, dd, *J* 14, 8, CH_2)
Bu^s (t)	7.35–7.08 (5 H, m)	5.00 (d, *J* 7)	3.854 (t, *J* 7)	2.01 (d, *J* 1)	1.66–1.08 (3 H, m, CH and CH_2), 0.83 (3 H, d, *J* 7, CH*Me*)
					0.82 (3 H, t, *J* 7, CH_2*Me*)
Bu^s (t)*	7.35–7.08 (5 H, m)	4.99 (d, *J* 7)	3.850 (t, *J* 7)	2.01 (d, *J* 1)	1.66–1.08 (3 H, m, CH and CH_2), 0.87 (3 H, d, *J* 7, CH*Me*)
					0.83 (3 H, t, *J* 7, CH_2*Me*)
Ph (*c*)	7.60–6.75 (10 H, m)	5.82 (d, *J* 10)	5.52 (dq, *J* 10, 1)	2.28 (d, *J* 1)	
Ph (*t*)	7.60–6.75 (10 H, m)	5.24 (d, *J* 8)	5.02 (dq, *J* 8, 1)	2.24 (d, *J* 1)	

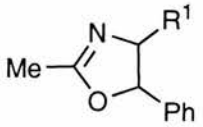
Table 6: ^{13}C NMR spectra of 2-phenyloxazolines



R^1 = Me (**268**, **269**), Pr^i (**407**, **408**), Bn (**410**, **411**), Bu^s (**415**), Ph (**419**, **418**)

R^1	C=N	Aromatic	5-C	4-C	R^1
Me (*cis*)	162.5	136.7 (4ry), 131.0, 128.0 (2 C), 127.9 (2 C) 27.8 (2 C), 1127.4, 127.3 (4ry), 125.7 (2 C)	83.5	65.0	17.4 (Me)
Me (*trans*)	162.8	140.4 (4ry), 131.4, 128.8 (2 C), 128.4 (4 C) 128.3, 127.7 (4ry), 125.6 (2 C)	88.2	70.9	21.4 (Me)
Pr^i (*cis*)	163.9	137.7 (4ry), 131.9, 128.9 (2 C 128.9, 128.8 (2 C) 128.6 (2 C), 128.3 (4ry), 127.6 (2 C)	84.8	76.9	29.7 (CH), 21.6 and 19.9 (2 × Me)
Pr^i (*trans*)	164.6	137.3 (4ry), 131.5 (4ry), 130.3, 129.3 129.1 (2 C), 128.9 (2 C), 128.6 (2 C), 128.5 (2 C)	90.2	72.3	28.3 (CH), 20.3 and 19.5 (2 × Me)
Bn (*cis*)	164.2	139.2 (4ry), 132.1, 129.4 (2 C), 129.0 (2 C) 128.9 (2 C), 128.7 (2 C), 128.6, 127.9 (4ry)	84.5	71.5	137.1 (4ry), 128.5 (2 C), 127.3 (2 C), 126.4, 38.8 (CH_2)
Bu (*cis*)	163.9	137.9 (4ry), 131.9 (4ry), 131.8, 129.1, 128.9 (2 C) 128.8 (2 C), 128.6 (2 C), 127.7 (2 C)	84.8	76.5	36.0 (CH), 26.4 (CH_2), 17.7 (CH*Me*), 11.6 (CH_2*Me*)
Bu (*cis*)*	163.8	137.9 (4ry), 131.9 (4ry), 131.3, 128.9 (2 C) 128.8 (2 C), 128.6 (2 C), 128.5, 127.3 (2 C)	84.7	74.9	36.2 (*C*HMe), 28.4 (*C*H_2Me), 16.0 (CH*Me*), 12.0 (CH_2*Me*)
Bu^s(*trans*)	165.2	138.0 (4ry), 132.1 (4ry), 129.2 (2 C), 128.81 (2 C) 128.78 (2 C), 128.7, 128.5 (2 C), 128.0	88.4	72.4	34.9 (*C*HMe), 26.5 (*C*H_2Me), 16.0 (CH*Me*), 11.2 (CH_2*Me*)
Bu^s(*trans*)*	165.2	138.2 (4ry), 131.9, 128.9 (2 C), 128.81 (2 C) 128.78 (2 C), 128.5 (2 C), 128.3 (4ry), 128.1	88.9	72.6	35.4 (*C*HMe), 26.8 (*C*H_2Me), 15.5 (CH*Me*), 10.9 (CH_2*Me*)
Ph (*cis*)	165.4	138.1 (4ry), 136.9 (4ry), 132.2, 129.0 (2 C) 129.0 (2 C), 128.3 (2 C), 128.1 (2 C), 127.4	85.7	74.8	136.9 (4ry), 128.1 (2 C), 127.8, 126.7 (2 C)
Ph (*trans*)	164.5	142.4 (4ry), 132.2, 129.4 (2 C), 129.3 (2 C) 128.9 (2 C), 128.2, 127.9 (4ry), 127.2 (2 C)	89.4	79.4	140.9 (4ry), 129.1 (2 C), 128.9, 126.1 (2 C)

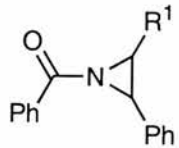
Table 7: ^{13}C NMR spectra of 2-methyloxazolines



R^1 = Me (**423**, **424**), Pr^i (**426**), Bn (**428**, **429**), Bu^s (**432**), Ph (**437**, **438**)

R^1	C=N	Aromatic	C-5	C-4	2-Me	R^1
Me (cis)	163.7	136.4 (4ry), 127.3, 126.9 (2 C), 125.5 (2 C)	83.5	64.3	17.3	13.4 (Me)
Me (trans)	163.5	139.9 (4ry), 128.5 (2 C), 128.2, 125.3 (2 C)	87.7	69.8	20.9	12.1 (Me)
Bn (cis)	163.6	137.7 (4ry), 127.0 (2 C), 126.7, 126.1 (2 C)	82.7	69.7	13.0	135.4 (4ry), 127.5 (2 C), 127.2 (2 C), 126.5, 37.4 (CH_2)
Bn (trans)	163.4	139.7 (4ry), 127.9 (2 C), 126.8 (2 C), 126.6	83.9	75.1	13.1	137.3 (4ry), 127.8 (2 C), 127.4 (2 C), 126.4, 40.8 (CH_2)
Bu^s(trans)	163.4	141.6 (4ry), 128.7 (2 C), 128.1 (2 C), 125.8	83.1	79.3	39.1	35.8 (CH), 25.6 (CH_2), 14.5 (CH*Me*), 11.5 (CH_2*Me*)
Bu^s(trans)*	163.6	141.6 (4ry), 128.7 (2 C), 128.1 (2 C), 125.8	84.0	79.3	39.3	36.3 (CH), 25.7 (CH_2), 13.9 (CH*Me*), 11.7 (CH_2*Me*)
Ph (trans)	165.7	142.3 (4ry), 129.3 (2 C), 128.8, 126.1 (2 C)	89.3	78.9	23.3	140.7 (4ry), 129.2 (2 C), 128.1, 126.9 (2 C)

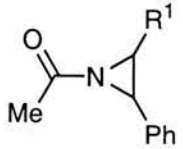
Table 8: ^{1}H NMR spectra of *N*-benzoylaziridines



R^1 = Me (**267**), Pr^i (**409**), Bn (**414**), Bu^s (**417**), Ph (**420** and **421**)

R^1	Aromatic	3-H	2-H	R^1
Me (*c*)	8.10 (2 H, m), 7.50–7.20 (8 H, m)	3.86 (d, *J* 7)	2.97 (quin, *J* 7)	1.18 (3 H, d, *J* 7, Me)
Pr^i	8.03 (2 H, m), 7.55–7.20 (8H, m)	3.69 (d, *J* 6)	2.68 (dd, *J* 9, 6)	1.59 (1 H, m, CH), 1.19 (3 H, d, *J* 6, Me), 0.70 (3 H, d, *J* 6, Me)
Bn (*c*)	8.00 (2 H, m), 7.50–7.00 (13 H, m)	3.78 (d, *J* 6)	3.19 (q, *J* 6)	2.99 (1 H, dd, *J* 15, 5, CH_2), 2.64 (1 H, dd, *J* 15, 8, CH_2)
Bu^s	7.91(2 H, d), 7.59–7.10 (5 H, m)	3.60 (d, *J* 6)	3.17 (dd, *J* 10, 6)	1.69 (1 H, m, CH_2), 1.31 (1 H, m, CH_2), 1.10 (1 H, m, CH) 1.08 (3 H, d, *J* 7, CH*Me*) and 0.51 (3 H, t, *J* 7, CH_2*Me*)
Bu^s*	7.91(2 H, d), 7.59–7.10 (5 H, m)	3.57 (d, *J* 6)	3.16 (dd, *J* 10, 6)	1.64 (1 H, m, CH_2), 1.40 (1 H, m, CH_2), 1.10 (1 H, m, CH) 0.91 (3 H, t, *J* 7, CH_2*Me*) and 0.55 (3 H, d, *J* 7, CH*Me*)
Ph (*c*)	8.20–6.90 (15 H, m)	4.08 (s)	4.08 (s)	
Ph (*t*)	8.20–6.90 (15 H, m)	3.97 (s)	3.97 (s)	

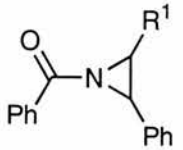
Table 9: ^{1}H NMR spectra of *N*-acetylaziridines



R^1 = Me (**422**), Pr^i (**427**), Bn (**431**), Bu^s (**434**), Ph (**436** and **435**)

R^1	Aromatic	3–H	2–H	Acetyl	R^1
Me	7.40–7.28 (m, 5H)	3.64 (d, *J* 6)	2.89 (quintet, *J* 6)	2.21 (s)	1.04 (3 H, d, *J* 6, Me)
Pr^i	7.40–7.20 (5 H, m)	3.67 (d, *J* 6)	2.42 (dd, *J* 9, 6)	2.19 (s)	1.22–1.08 (1 H, m, *CH*Me), 1.12 (3 H, s, Me) and 0.70 (3 H, d, *J* 6, Me)
Bu^s	7.40–7.20 (5 H, m)	3.66 (d, *J* 6)	2.48 (m)	2.18 (s)	1.25–0.84 (2 H, 2 × m, CH_2), 1.07–0.85 (1 H, m, C*H*Me)
					0.65 (3 H, d, *J* 7, CH*Me*), 0.61 (3 H, t, *J* 7, CH_2*Me*)
Bu^s*	7.40–7.20 (5 H, m)	3.62 (d, *J* 6)	2.48 (m)	2.17 (s)	1.75–1.62 (2 H, m, CH_2), 1.45–1.30 (m, CH_2), 1.10 (3 H, d, *J* 7, CH*Me*)
					1.07–0.85 (1 H, m, C*H*Me), 0.93 (3 H, t, *J* 7, CH_2*Me*)
Bn	7.40–7.10 (10 H, m)	3.73 (d, *J* 6)	2.97 (q, *J* 6)	2.01 (s)	2.62 (1 H, dd, *J* 12, 6, CH_2), 2.53 (1 H, dd, *J* 12, 6, CH_2)
Ph (*c*)	7.50–7.00 (10 H, m)	3.95 (s)	3.95 (s)	2.28 (s)	
Ph (*t*)	7.50–7.00 (10 H, m)	3.78 (s)	3.78 (s)	1.85 (s)	

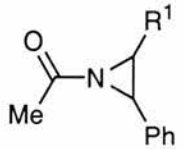
Table 10: ^{13}C NMR spectra of *N*-benzoylaziridines



R^1 = Me (**267**), Pr^i (**409**), Bn (**414**), Bu^s (**417**), Ph (**420** and **421**)

R^1	CO	Aromatic	C-3	C-2	R^1
Me (*cis*)	179.8	134.8, 132.8, 129.7, 129.1(2 C), 128.4 (2 C), 128.3 (2 C), 127.7 (2 C), 127.5	44.2	40.1	12.6 (Me)
Pr^i	179.7	133.1, 132.6, 130.0, 128.9 (2 C), 128.3 (3), 128.2 (2 C), 127.4 (2 C)	50.5	45.6	26.0 (CH), 20.8 (Me), 18.8 (Me)
Bn	179.5	134.4, 132.7, 128.7 (2 C), 128.4 (2 C), 128.3 (2 C), 127.8, 127.7 (2 C), 126.3	44.8	44.7	137.7, 129.0 (2 C), 128.3, 128.4 (2 C) 32.9 (CH_2)
Bu^s	180.4	135.4, 130.6, 130.5, 129.4 (2 C), 129.1, 128.8 (2 C), 128.7 (2 C), 127.9 (2 C)	50.2	46.7	32.6 (CH), 27.4 (CH_2), 18.7 (CH*Me*) 11.7 (CH_2*Me*)
Bu^s*	180.1	135.1, 133.2, 130.5, 129.4 (2 C), 128.81 (2 C), 128.0 (2 C), 127.9 (2 C)	49.8	45.5	32.1 (CH), 28.7 (CH_2), 16.4 (CH*Me*) 11.5 (CH_2*Me*)

Table 11: ^{13}C NMR spectra of *N*-acetylaziridines



R^1 = Me (**422**), Pr^i (**427**), Bn (**431**), Bu^s (**434**), Ph (**436** and **435**)

R^1	CO	Aromatic†	C–3	C–2	*Me*CO	R^1
Me (*cis*)	183.2	134.5, 128.0 (2 C), 127.3 (2 C), 126.4	42.7	38.9	23.0	12.4 (Me)
Pr^i	183.8	135.3, 128.9 (2 C), 127.8, 127.7 (2 C)	51.1	43.6	23.6	26.8 (CH), 21.4 (Me), 19.0 (Me)
Bn	183.3	134.5, 128.7, 127.7, 126.6	44.7	43.1	23.1	138.0, 128.4, 128.2, 127.5, 33.4 (CH_2)
Bu^s	183.3	134.8, 128.0, 127.33 (2 C), 127.29 (2 C)	50.0	43.5	23.2	31.9 (CH), 26.6 (CH_2), 18.2 (CH*Me*), 11.0 (CH_2*Me*)
Bu^s*	183.1	134.8, 127.9, 127.33 (2 C), 127.29 (2 C)	49.8	42.5	23.2	31.9 (CH), 28.0 (CH_2), 15.3 (CH*Me*), 10.9 (CH_2*Me*)

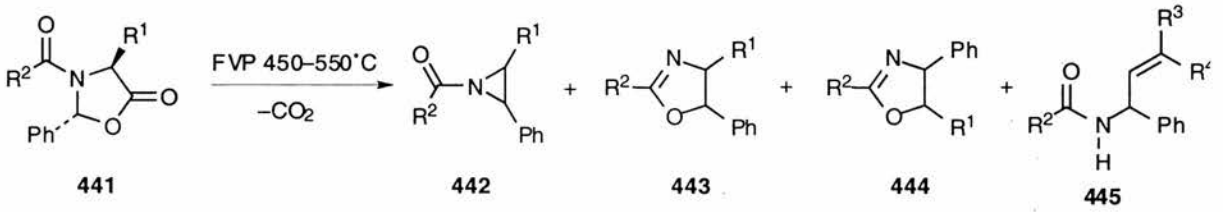
Generally, the literature suggests that the signals for 5-H and 4-H in the *cis*-isomers will have higher chemical shifts than those of the *trans*-isomers. The literature also suggests that the coupling constant for the doublet arising from 5-H will be larger than that of the *trans*-isomer. This seems to be in agreement with the Karplus equation. *Cis* and *trans* isomers for the previously unknown oxazolines have been assigned on this basis.

In the ^{1}H NMR spectra the signal at approximately 8.05 ppm must represent the 2 ortho hydrogens of the phenyl group at the 2-position since no similar signal is observed in the 2-methyloxazolines. Another interesting feature of the ^{1}H NMR spectra is the long range coupling of the 2-methyl group to the 4-H through the C=N bond in the 2-methyloxazolines. What might be expected to give a singlet actually produces a doublet with a 1 Hz coupling.

The amino acid (*S*)-isoleucine was employed in order to give the oxazoline and aziridine products an extra stereocentre. This made it possible to identify all 4 possible diastereomers by NMR. This meant that the diastereomeric excess could be calculated directly from the ^{1}H NMR spectra making the use of lanthanide shift reagents superfluous.

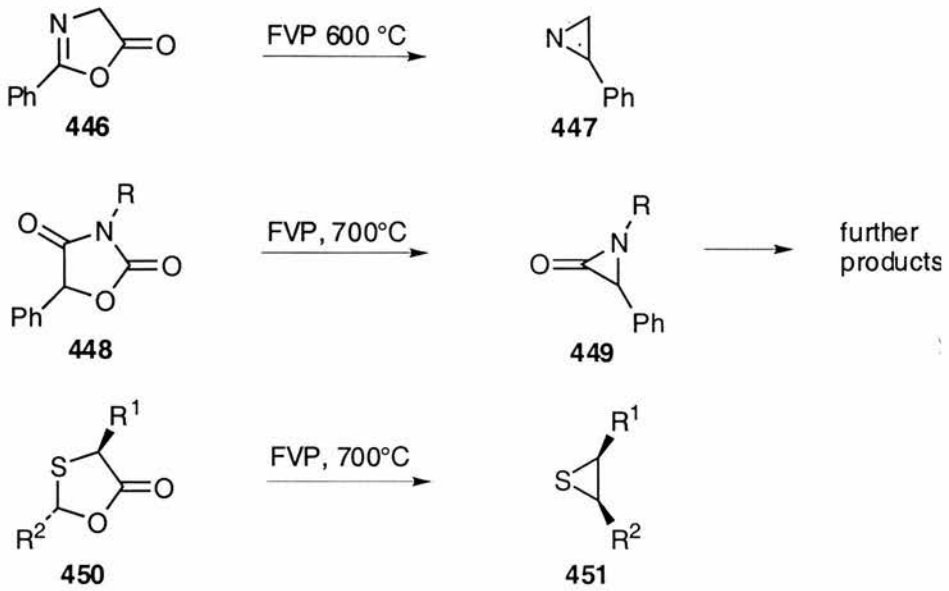
^{1}H and ^{13}C NMR data for the aziridines are presented in Tables 8–11. Where the aziridines synthesised so far are known they are 100% *cis* with exception of aziridines derived from 2,4-diphenyloxazolidinones where a mixture of *cis* and *trans* is obtained. This is presumably due to steric hindrance. In all other cases the unknown single isomer observed is therefore assumed to be the *cis*-aziridine as they also have 3-H signals with similar chemical shifts and couplings. When phenyl groups are present at both C-2 and C-3 the signals arising from these carbons or the attached hydrogens are identical due to the symmetry of the molecule.

Table 12: Summary of Pyrolysis results for *N*-acyloxazolidin-5-ones



441 442 443 444 445

			Yield (%)					
R^1	R^2	T (°C)	aziridine		oxazoline			elimination
			Cis	*Trans*	*Cis*	*Trans*	*Regio*	
Me	Ph	450	23	-	5	-	-	-
		550	-	-	37	6	7	15
Pr^i	Ph	450	17	-	6	-	-	-
		550	-	-	32	14	-	-
Bn	Ph	450	13	-	-	-	-	-
		550	-	-	38	-	9	22
Bu^s	Ph	450	24	-	-	-	-	-
		550	-	-	20	7	-	17
Ph	Ph	450	13	3	7	13	-	-
		550	-	-	12	40	-	-
Me	Me	450	12	-	-	-	-	-
		550					-	22
Pr^i	Me	450	23	-	-	-	-	-
		550	-	-	-	15	-	-
Bn	Me	450	12	-	-	-	-	-
		550	-	-	40	36	-	12
Bu^s	Me	450	29	-	-	-	-	-
		550	-	-	-	25	-	22
Ph	Me	550	-	-	>1	32	-	-

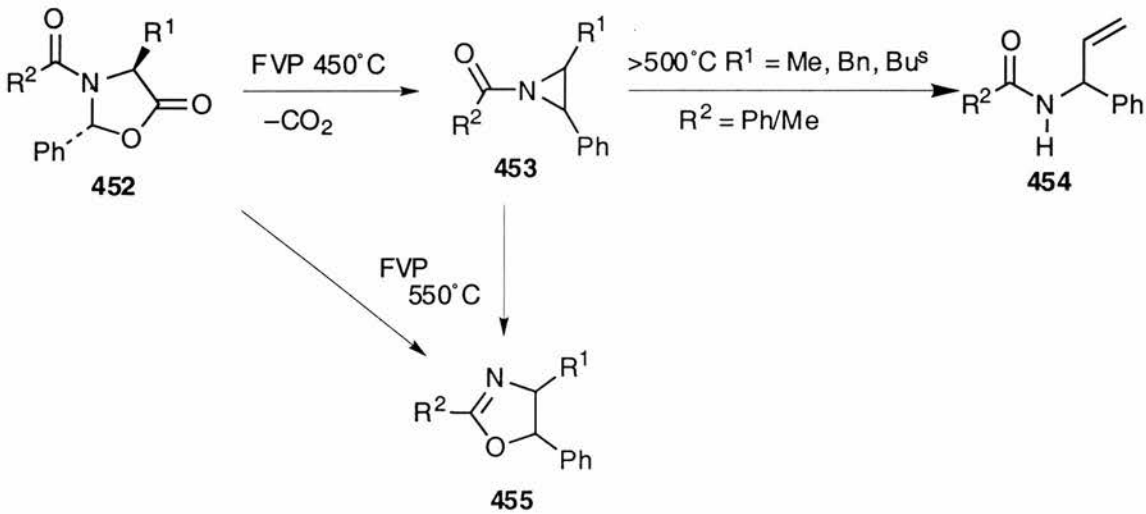


There are a number of precedents for the extrusion of CO_2 under FVP conditions from similar ring systems. The most relevant of these are displayed above. The first shows the pyrolysis of (4*H*)-2-phenyl-1,3-oxazol-5-one **446** which yields 3-phenyl-2*H*-azirine **447** as the only identifiable product in 34% yield.[133] The oxazolidin-2,4-dione **448** eliminates CO_2 to produce a 3-phenyaziridin-2-one **449**.[134] The final example illustrates a useful synthesis of thiiranes **451** from 1,3-oxathiolan-5-ones **450**.[135] This reaction is quite general and involves inversion of relative configuration as shown below as well as giving high yields. It is also thought that the reaction proceeds via a 1,3-diradical.

R^1	R^2	Yield	*cis*:*trans* **450**	*cis*:*trans* **451**
Ph	Ph	91	10:90	92:8
Me	Ph	93	59:41	42:58
Ph	Me	89	67:33	33:67
Me	Pr^n	95	63:37	38:62

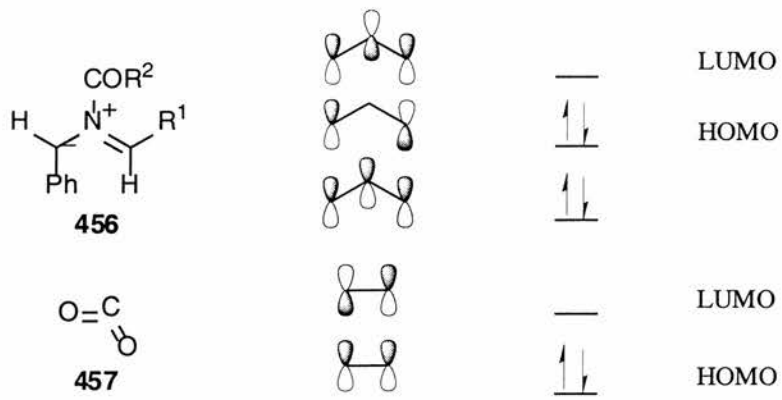
2. Mechanism and Stereochemistry of Products

The results show that using standard FVP equipment, conditions of 450 °C and 10^{-2} Torr were optimum for yielding *N*-acyl aziridines **453** from **452** while use of 550 °C cleanly gave the oxazolines **455**. Although the mechanism described earlier would suggest that any products would be racemic this proved not to be the case. Most of the aziridine products possess non-zero optical rotations or show an enantiomeric excess by way of chiral lanthanide shift reagents. The fact that we have started from enantiomerically pure oxazolidinones makes this result more significant.



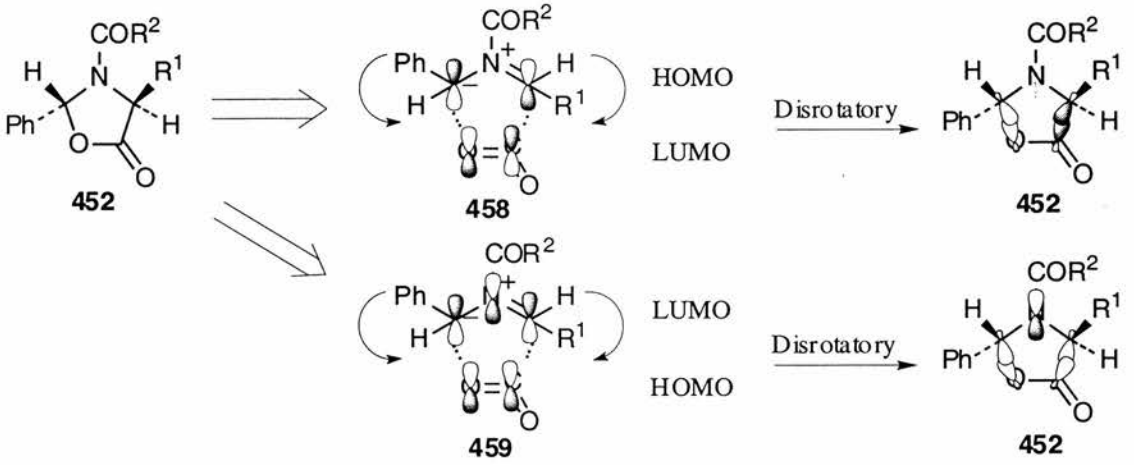
452 **453** **454** **455**

The application of frontier orbital theory to the FVP induced ring opening of the *N*-acyloxazolidin-5-one is quite informative. Below the frontier orbitals of the dipolar, aziridine derived species **456** and carbon dioxide **457** are shown. The dipolar species **456** is treated as an allyl anion.



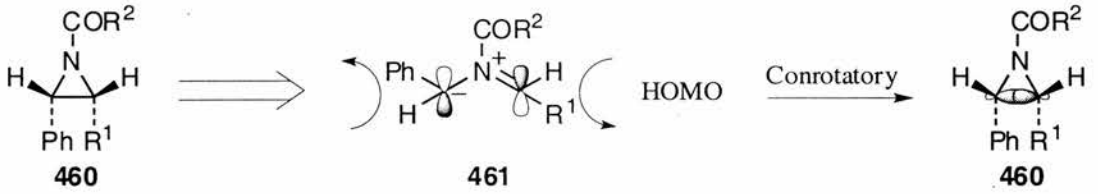
456 **457**

The reaction occurs between the HOMO (highest occupied molecular orbital) of one species and the LUMO (lowest unoccupied molecular orbital) of the other. The ring opening will happen in the same way as the ring closure (which is easier to visualise), so the ring closure was examined. Two possible modes of closure are below. The HOMO of the dipolar species

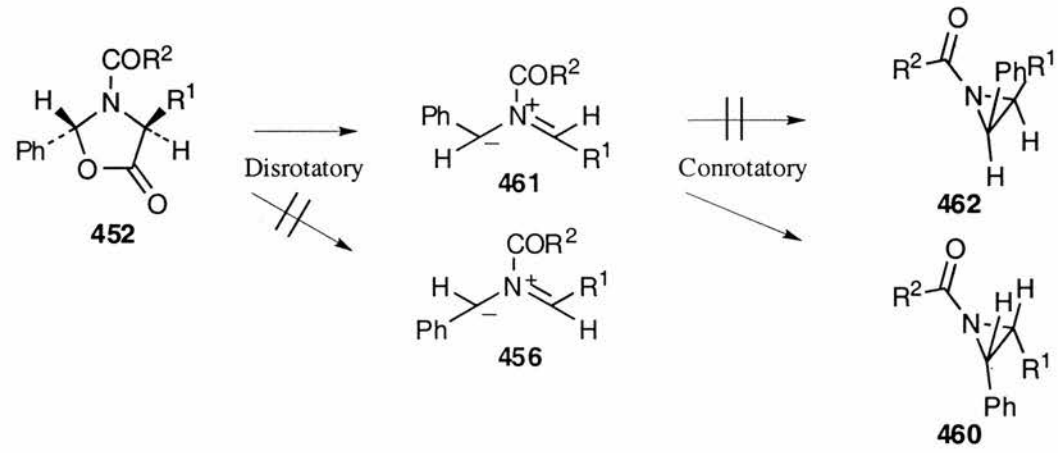


and the LUMO of the carbon dioxide **458** or the LUMO of the dipolar species and the HOMO of the carbon dioxide **459** may combine as shown. Both are disrotatory as the orbitals involved (on the dipolar species) must rotate in different directions (one clockwise and one anti-clockwise) to form the bonds therefore the ring opening is disrotatory as well.

The intramolecular ring closure of the aziridine **460** takes place in the HOMO **461** and therefore must be conrotatory as the orbitals must both turn in the same direction to form the bond.

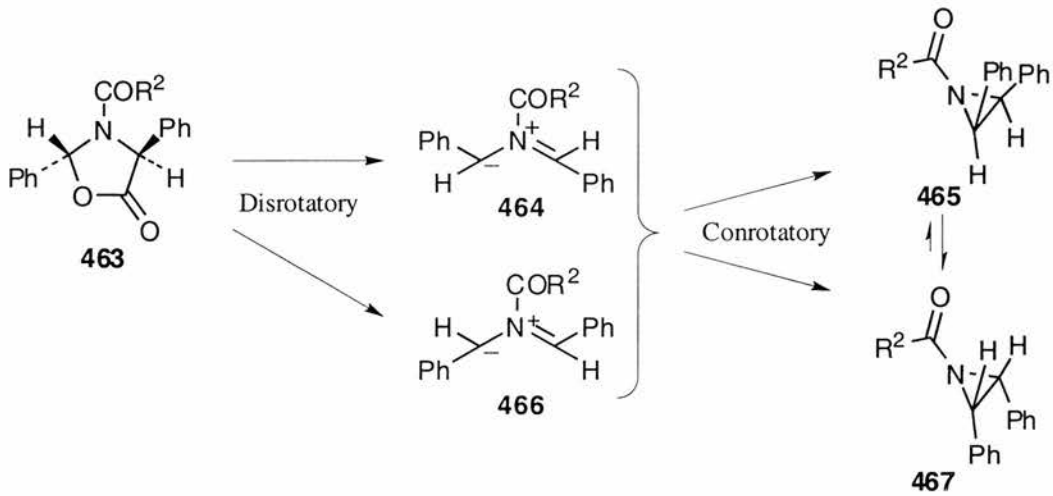


Of the products of pyrolysis tested so far many have non-zero optical rotations so some speculation is needed as to how this could be so. Nearly all of the aziridines synthesised up until now (with one exception) show a definite preference for the *cis*-isomer. The outline below shows a route to one particular stereoisomer. To arrive at this isomer we must first suppose that when the oxazolidinone opens to the dipolar intermediate that it retains a little of the

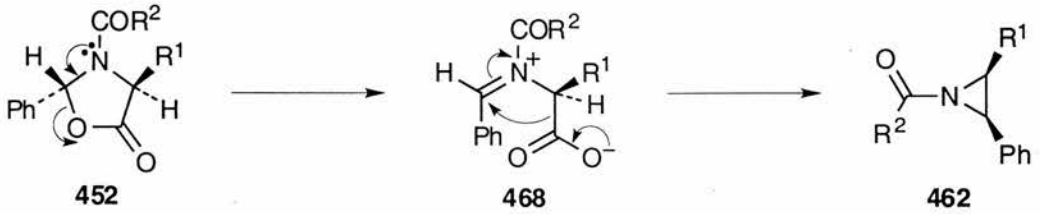


pyramidal shape at the nitrogen (**461**). Next we must suggest that the preferred ring closure of the aziridine would occur such as to place the *N*-acyl group as far away from Ph- and R^1 as possible producing the least sterically hindered product **460**. Without these suppositions we would expect the products to be racemic but a non-zero optical rotation means they are not racemic.

Something that cannot be explained so easily is the mechanism for the 2,4-diphenyloxazolidin-5-ones **463**. Since there are two phenyl groups the two possible ring opened products **464** and **466** are symmetrical and therefore identical to each other. Now there are only two possible stereoisomers (as opposed to the above case with $R^1 \neq Ph$ where four are possible) and again we would expect the sterically less hindered aziridine **467** to be favoured.

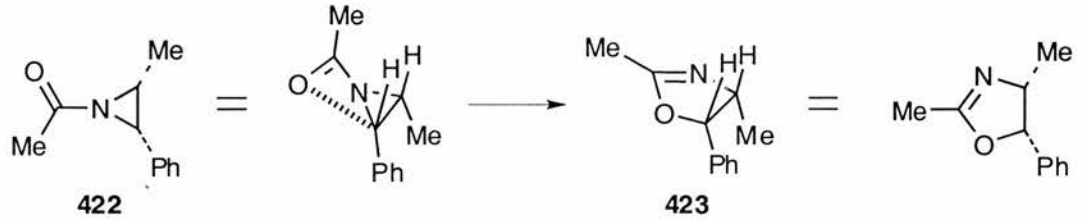


An alternative explanation for the retention of the stereochemistry in the aziridines is that the ring closure begins before the CO_2 has been fully lost in an intermediate such as **468**



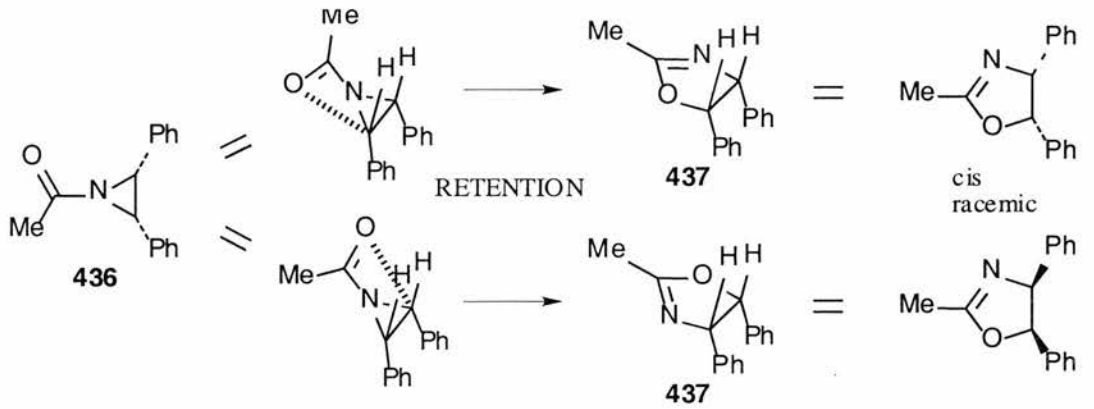
shown. Although this has the advantage of readily explaining the retention of chirality since **468** is obviously chiral, it is not so obvious why the *cis* aziridine **462** would be produced.

The next step in the mechanism is the ring expansion. Again this is considered using the *cis*-aziridine **422**, this time as the starting point. From the results so far we know that the oxygen must attack the phenyl bearing carbon so we would expect either the *cis*-oxazoline **423** (retention, see below) or the *trans*-oxazoline (inversion).

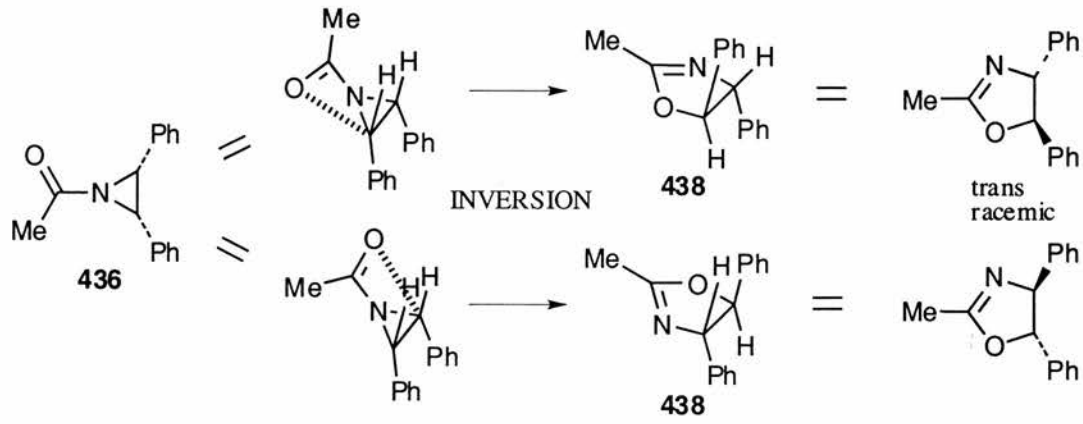


Note that the *cis*-aziridine is now drawn differently in light of our knowledge of how the frontier orbitals must align.

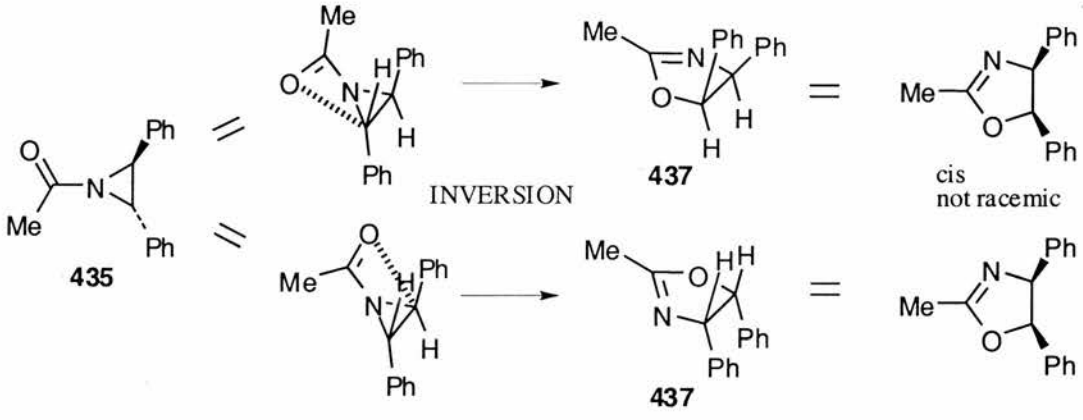
In the case of the 2,3-diphenylaziridine **436** twice as many isomers are possible as the oxygen can attack at either C-2 or C-3. The reaction can take place with either retention or



inversion of configuration leading to a racemic mixture of four isomers. This is in any case obvious as the aziridine is achiral.

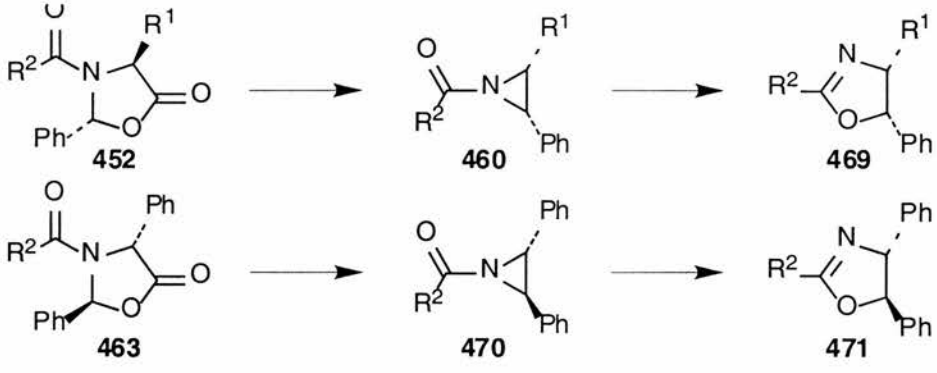


It must therefore be proposed that the non-zero rotation observed for **439** arises because it is formed from hydrolysis of the oxazolines derived from the minor *trans*-aziridine **435** as



these are non racemic. The other *trans*-aziridine would produce the opposite *cis*-oxazoline (non racemic).

Whatever the mechanism involved the relative stereochemistry of the products involved is as shown below.



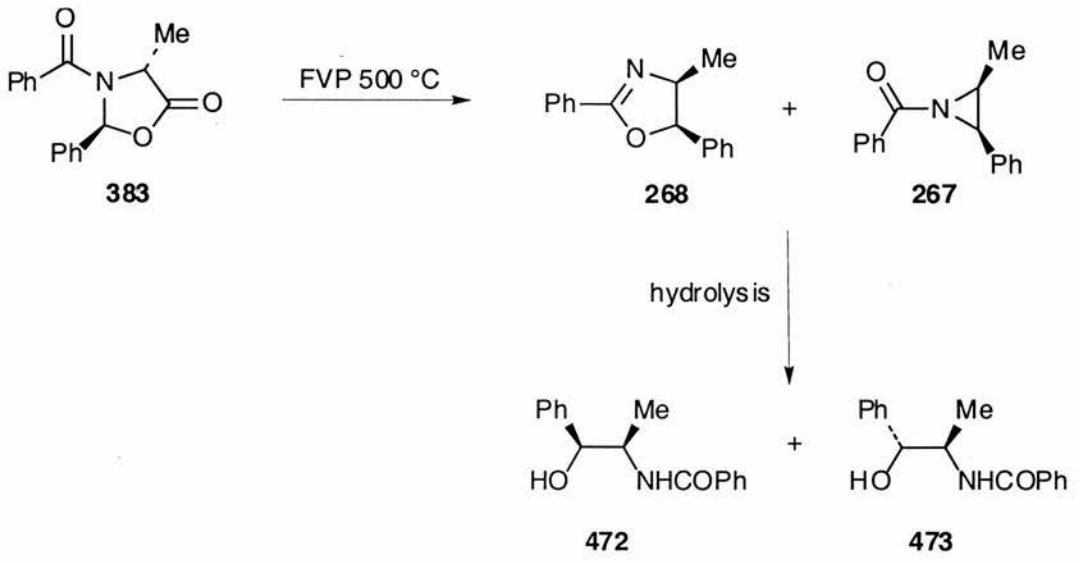
The aziridines formed at 450 °C are confirmed as *cis* where they are known in the literature with the exception of the 2,3-diphenyl examples where both *cis* and *trans* are formed.

Where they are not known it is clear from the trend of the accumulated NMR data that they are also *cis*. Therefore there is an inversion in the relative configuration as we have started from oxazolidinones possessing substituents at positions 2 and 4 that are *trans* to one another. Note that although the yields of aziridine are quite low (<30%) the starting material obtained after FVP can be recrystallised and used again.

In general although not always, FVP of the starting materials at 550 °C with Ph at C-2 give oxazolines with Ph at C-5. This is most probably due to the greater electrophilicity of the carbon adjacent to Ph. In only one case is an *N*-allylamide the major product and this product is formed when R^1 is methyl, benzyl or s-butyl. Results obtained where the oxazolines are known in the literature show a definite preference for the *cis* isomer. Only when phenylglycine is employed the does the *trans*-oxazoline become the major product due to steric factors.

In order to chemically trap the dipolar intermediates proposed for aziridine formation, an aziridine was reacted with various dipolarophiles. Small amounts of 1-acetyl-2-methyl-3-phenylaziridine **422** were heated with maleic anhydride, DMAD, and dimethyl maleate. The aziridine had reacted to form a little of the oxazoline **423** and the rest was unreacted after having been heated with the latter two. This shows that the ring expansion to the oxazoline happens so readily that any alternative process involving a dipolar species cannot compete. The maleic anhydride had reacted with the aziridine (no traces of characteristic peaks in ^{1}H NMR spectrum) but the product could not be identified. The ^{1}H NMR and mass spectra (M^+ 325) did not confirm what was expected (addition across the double bond) and no obvious explanation could be found.

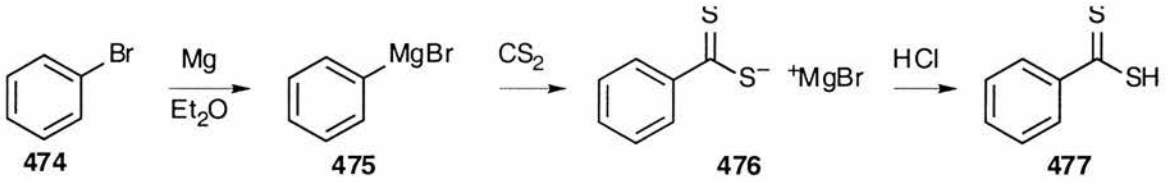
It was noticed earlier that some of the oxazolines hydrolysed upon storage. It was thought that by carrying out this reaction, acylamino alcohols would be obtained whose relative and absolute configuration might be more easily determined. In an attempt to effect the hydrolysis of oxazolines ourselves a pyrolysis of **383** was carried out at 500 °C. The products, mainly **267** and **268**, were hydrolysed by heating under reflux with HCl. The ^{1}H NMR spectrum showed that the threo and erythro isomers **472** and **473** of the acylamino alcohol were present in a ratio of approximately 1:3. The rotation of the acylamino alcohol mixture was measured in the polarimeter and found to be zero; therefore the products were racemic.



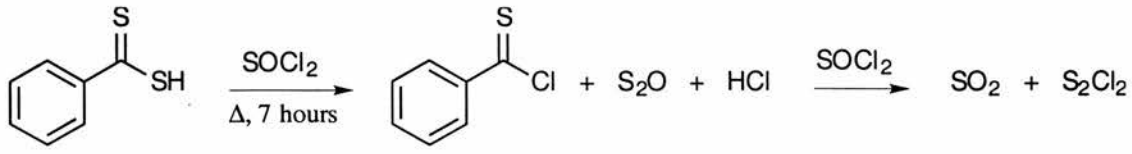
C. Synthesis and Properties of *N*-thioacyloxazolidin-5-ones

1. Synthesis

To extend the chemistry and perhaps learn more about the mechanism of reaction it was decided to synthesise *N*-thioacyloxazolidin-5-ones and subject them to similar FVP conditions. In the first approach the previously used method was employed again but using thiobenzoyl chloride[128] instead of an acid chloride.



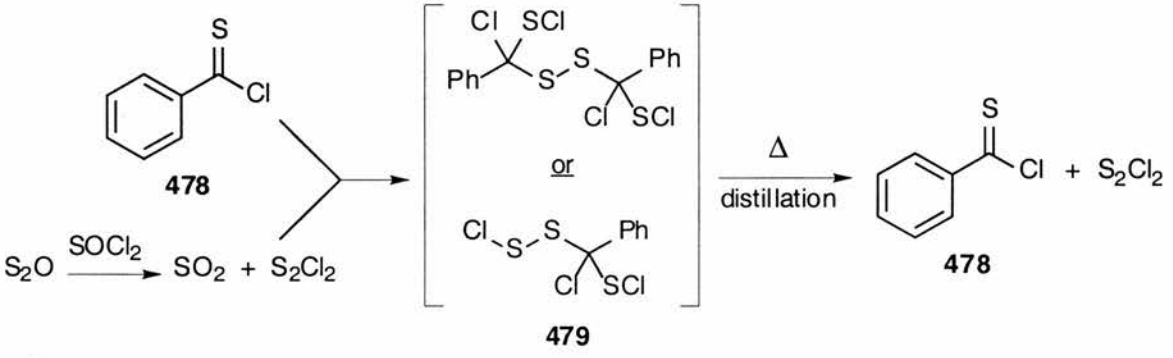
First a Grignard reagent **475** was synthesised from bromobenzene **474** and magnesium and this was used to alkylate carbon disulfide to give the salt **476**. Then the rection mixture was extracted with water and the aqueous layer acidified to precipitate phenylcarbodithioic acid **477**.[127] This was used directly for the next step of the reaction without evaporation or purification due to its instability.



477 **478**

The product **477** was heated with thionyl chloride under nitrogen to convert the thiol group to the chloride giving **478**. The reaction proceeds via PhC(S)S-S(O)Cl and evolves S_2O and hydrogen chloride. The process is complicated by a side reaction where S_2O reacts with excess thionyl chloride to give S_2Cl_2 which then forms a complex **479** with PhC(S)Cl.

Distilling the product at 150°C causes decomposition to thiobenzoyl chloride **478** and S_2Cl_2. The latter is collected in a dry-ice cooled trap whereas the thiobenzoyl chloride condenses at room temperature.



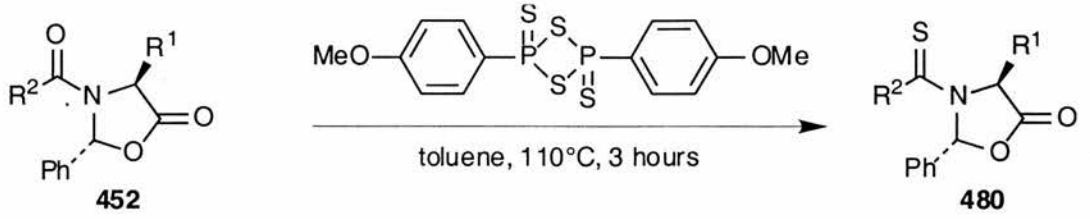
479

Unfortunately the thiobenzoyl chloride was more air and moisture sensitive than was first thought and this made it unsuitable for reaction with the imine as the solvent carried over from the previous stage was not dry. Also, thiobenzoyl chloride was less reactive towards the imine since sulfur is less electronegative than oxygen and the method failed.

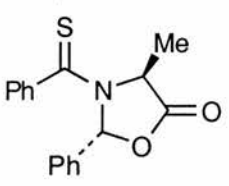
For these reasons it was decided to try an alternative approach using Lawesson's reagent to convert preformed *N*-acyloxazolidin-5-ones to the target compounds. This reacts solely at the amido oxygen making it unnecessary to synthesise thioacyl chlorides.

From the range of oxazolidin-5-ones **452** prepared previously a selection of *N*-thioacyloxazolidin-5-ones **480** were synthesised by heating under reflux with Lawesson's reagent in toluene for approximately 3 hours. Normally, only a quarter of a mole of Lawesson's reagent is required since all four sulfurs are available for reaction. In this case it was found that only two sulfurs were reactive, so a half equivalent of Lawesson's reagent was

used. The by-product derived from Lawesson's reagent is insoluble in toluene at room temperature. Therefore, once the reaction was complete the mixture was allowed to cool and then filtered. The filtrate was evaporated and the residue was recrystallised from dichloromethane and ether to give the product as a yellow crystalline solid.



452 **480**



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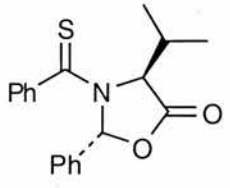

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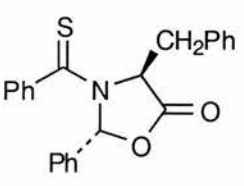

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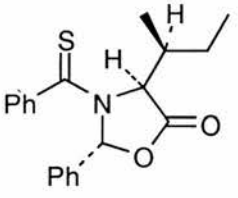

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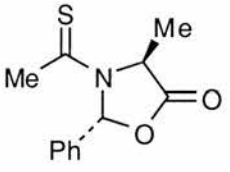

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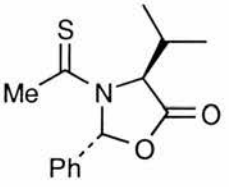

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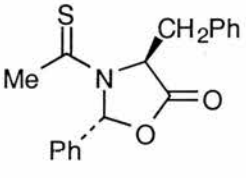

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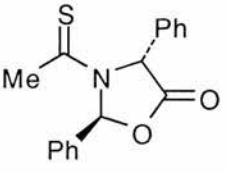

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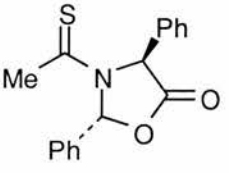


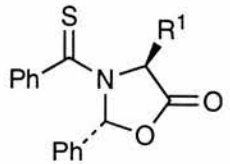
489

The compounds **481–485** and **487** are all unknown compounds in the literature and therefore they were fully characterised. Synthesis of compounds **486**, **488** and **489** was unsuccessful. There was almost no conversion of compounds **389**, **392** and **393**, even when a 100% excess of Lawesson's reagent was employed.

2. Structure and Properties

Since all the *N*-thioacyloxazolidin-5-ones synthesised are previously unknown in the literature their NMR spectra (Tables 13–15) can only be compared with those of the *N*-acyloxazolidin-5-ones. The ^{1}H spectra have values for 2-H and 4-H that are within the expected range for this type of compound. All ^{1}H NMR spectra of these compounds are also shown to have two sets of broad peaks due to conformers and their signals combine and sharpen to a single set at increased temperatures. The *N*-benzoyloxazolidin-5-ones showed only one set of broadened peaks meaning that they are closer to coalescence at room temperature than their sulfur analogues. The pattern of these signals and those for R^1 are also as would be expected. The ^{13}C NMR spectra of the *N*-thioacyloxazolidin-5-ones are also consistent with each other and what would be expected from the data of their *N*-acyl counterparts. The main difference is the presence of a characteristic signal for the C=S carbon at around 200 ppm.

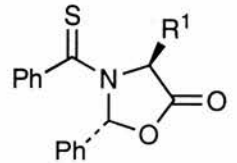
Table 13: ^{1}H NMR spectra of *N*-thiobenzoyloxazolidin-5-ones



R^1 = Me (**481**), Pr^i (**482**), Bn (**483**), Bu^s (**484**)

R^1	Aromatic	2-H	4-H	R^1
Me	7.60–6.70 (10 H, m)	6.76 (s)	4.86 (q, *J* 7)	1.19 (3 H, d, *J* 7, Me)
Me*	7.60–6.70 (10 H, m)	7.44 (s)	5.42 (q, *J* 7)	1.90 (3 H, d, *J* 7, Me)
Pr^i	7.63–6.70 (10 H, m)	6.60 (s)	4.85 (d, *J* 7)	1.98 (1 H, m, CH), 0.94 (3 H, d, *J* 7, Me), 0.97 (3 H, d, *J* 7, Me)
Pr^i *	7.63–6.70 (10 H, m)	7.20 (s)	5.42 (d, *J* 7)	3.25 (1 H, m, CH), 1.35 (3 H, d, *J* 7, Me), 1.19 (3 H, d, *J* 7, Me)
Bn	7.70–6.90 (11 H, m)	5.80 (s)	5.26 (dd, *J* 6, 2)	4.43 (1 H, dd, *J* 14, 6, CH_2Ph), 3.40 (1 H, dd, *J* 14, 2, CH_2Ph), 6.65 (4 H, m)
Bn*	7.70–6.90 (11 H, m)	6.40 (s)	5.68 (dd, *J* 6, 2)	4.43 (1 H, dd, *J* 14, 6, CH_2Ph), 3.40 (1 H, dd, *J* 14, 2, CH_2Ph), 6.65 (4 H, m)
Bu^s	7.58–6.59 (10 H, m)	6.59 (s)	5.52 (d, *J* 3)	3.00 (1 H, m, CH), 1.88 and 1.70 (2 H, 2 × m, CH_2), 1.18 (3 H, d, *J*7, *Me*CH), 1.13 (3 H, t, *J* 7,*Me*CH_2)
Bu^s*	7.58–6.59 (10 H, m)	7.18 (s)	4.93 (d, *J* 3)	1.62 (1 H, m, CH), 1.48 and 1.24 (2 H, 2 × m, CH_2), 0.95 (3 H, d, *J* 7, *Me*CH), 0.57 (3H, t, *J*7, *Me*CH_2)

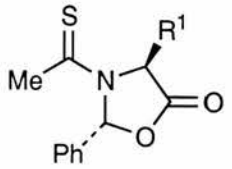
Table 14: ^{13}C NMR spectra of *N*-thiobenzoyloxazolidin-5-ones



R^1 = Me (**481**), Pr^i (**482**), Bn (**483**), Bu^s (**484**)

R^1	C=S	C=O	Aromatic	C-2	C-4	R^1
Me	200.5	171.27	142.5, 135.5, 132.1, 129.8, 128.7 (2 C), 128.6 (2 C), 128.2 (2 C), 126.0 (2 C)	93.3	56.3	15.2
Me*	202.1	171.33	142.2, 134.6, 133.2, 130.6, 129.9 (2 C), 128.7 (2 C), 127.2 (2 C), 126.5 (2 C)	92.8	56.8	18.0
Pr^i	201.0	169.5	142.6, 135.4, 130.3, 130.2, 129.2 (2 C), 129.1 (2 C), 128.7 (2 C), 127.1 (2 C)	94.1	65.7	28.3 (CH), 18.3 (Me), 16.3 (Me)
Pr^i *	202.4	169.6	143.4, 136.3, 131.3, 130.3, 128.7 (2 C), 127.9 (2 C), 126.6 (2 C), 126.4, (2 C)	94.3	66.4	32.4 (CH), 18.5 (Me), 17.1 (Me)
Bn	201.6	170.5	142.5, 135.3, 130.3 (2 C), 130.2, 129.4, 129.0 (2 C), 128.5 (2 C), 127.1 (2 C)	93.9	61.8	134.9, 130.3 (2 C), 129.4 (2C), 128.4 32.6 (CH_2)
Bu^s	201.7	169.1	143.0, 135.9, 129.8 (2 C), 128.7 (4 C), 128.2 (2 C), 126.3, 126.0	94.0	64.0	34.2 (CH), 25.3 (CH_2), 14.6 (*Me*CH) 11.8 (*Me*CH_2)
Bu^s*	200.5	169.2	142.3, 135.0, 130.7, 129.7 (2 C), 128.2, 126.7 (4 C), 127.5 (2 C)	93.7	64.0	38.9 (CH), 24.9 (CH_2), 14.3 (*Me*CH) 11.5* (*Me*CH_2)

Table 15: ^{1}H and ^{13}C NMR spectra of *N*-thioacetyloxazolidin-5-ones



R^1 = Me (**485**), Bn (**487**)

R^1	Aromatic	2-H	4-H	*Me*CS	R^1
Me	7.20–7.25 (5 H, m)	6.70 (s)	4.78 (q, *J* 7)	2.19 (s)	1.85 (3 H, d, *J* 7, Me)
Me*	7.20–7.25 (5 H, m)	7.12 (s)	5.17 (q, *J* 7)	2.74 (s)	1.90 (3 H, d, *J* 7, Me)
Bn	7.46–7.10 (10 H, m)	5.60 (s)	5.12 (dt, *J* 6, 2)	2.09 (s)	4.49 (1H, dd, *J* 14, 6, CH_2Ph), 3.19 (1H, dd, *J* 14, 2, CH_2Ph)
Bn*	7.46–7.10 (10 H, m)	6.06 (s)	5.48 (dt, *J* 5, 2)	2.86 (s)	3.57 (1H, dd, *J* 14, 5, CH_2Ph), 3.34 (1H, dd, *J* 14, 2, CH_2Ph)

R^1	C=S	C=O	Aromatic	C-2	C-4	*Me*CS	R^1
Me	199.636	171.0	134.9, 131.4, 131.2 (2 C), 126.9 (2 C)	92.2	56.0	33.5	15.5 (Me)
Me*	199.643	171.2	135.5, 130.0, 129.7 (2 C), 128.7 (2 C)	93.1	56.9	33.9	19.2 (Me)
Bn	199.8	169.8	135.1, 134.5, 130.1 (2 C), 129.3, 128.2 (2 C), 128.2 (2 C), 127.1 (2 C), 126.5	92.8	62.8	33.5	32.1 (CH_2)
Bn*	198.5	169.7	135.1, 134.7, 131.4 (2 C), 130.3 (2 C), 130.1, 129.6, 129.0 (2 C), 127.5 (2 C)	93.9	62.0	33.9	37.8 (CH_2)

Crystals of the *N*-thioacyloxazolidin-5-one **485** suitable for an X-ray diffraction study were obtained and the resulting structure is shown in Figure 3. As would be expected this shows that the configuration of the ring is unaffected by the action of Lawesson's reagent on the acetyl group and the structure is (*2R,4S*) *N*-thioacetyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one. However, the thioacetyl group is inverted relative to the acetyl group: the sulfur points towards C-4 while for the oxygen analogue the oxygen pointed towards C-2.

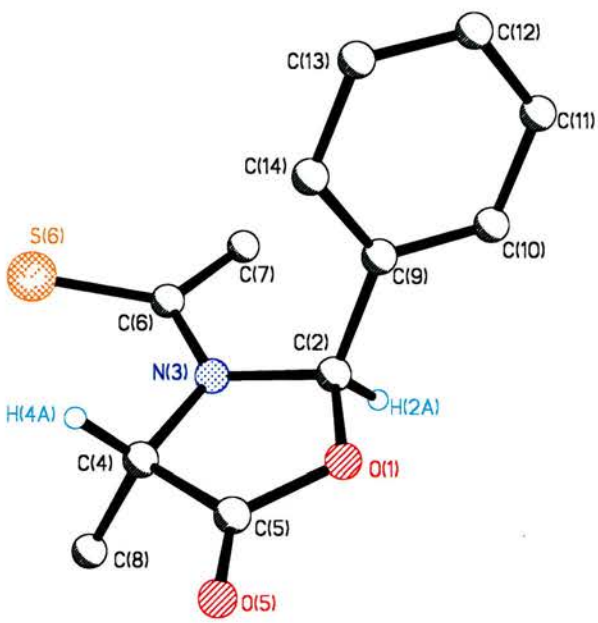


Figure 4: X- ray structure of (*2R,4S*) 4-methyl-2-phenyl-3-thioacetyl-1,3-oxazolidin-5-one **485** showing the crystallographic numbering scheme. Selected bond lengths and angles; O(1)-C(5) 1.358(4), O(1)-C(2) 1.436(3), C(2)-N(3) 1.466(4), C(2)-C(9) 1.493(4), N(3)-C(6) 1.351(4), N(3)-C(4) 1.462(4), C(4)-C(5) 1.502(5), C(4)-C(8) 1.511(4), C(6)-C(7) 1.492(4), C(6)-S(6) 1.661(3) Å; C(5)-O(1)-C(2) 112.4(2), O(1)-C(2)-N(3) 103.5(2), O(1)-C(2)-C(9) 110.0(2), N(3)-C(2)-C(9) 114.8(3), C(6)-N(3)-C(4) 123.1(3), C(6)-N(3)-C(2) 123.8(3), C(4)-N(3)-C(2) 112.0(2), N(3)-C(4)-C(5) 101.9(3), N(3)-C(4)-C(8) 113.6(3), C(5)-C(4)-C(8) 110.6(3), O(5)-C(5)-O(1) 121.8(4), O(5)-C(5)-C(4) 128.0(4), O(1)-C(5)-C(4) 110.2(3), N(3)-C(6)-C(7) 117.2(3), N(3)-C(6)-S(6) 121.6(2), C(7)-C(6)-S(6) 121.1(3)°.

This was thought to be due to sulfur being larger than oxygen. In the light of this the X-ray crystal structure of **483** was determined but this thiobenzoyl compound also shows the same effect.

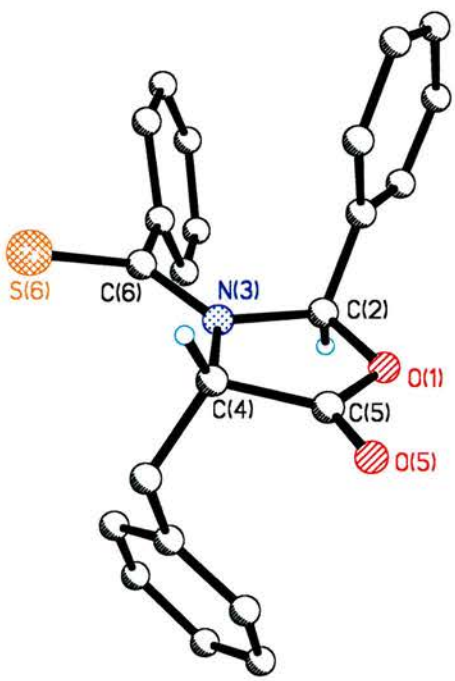
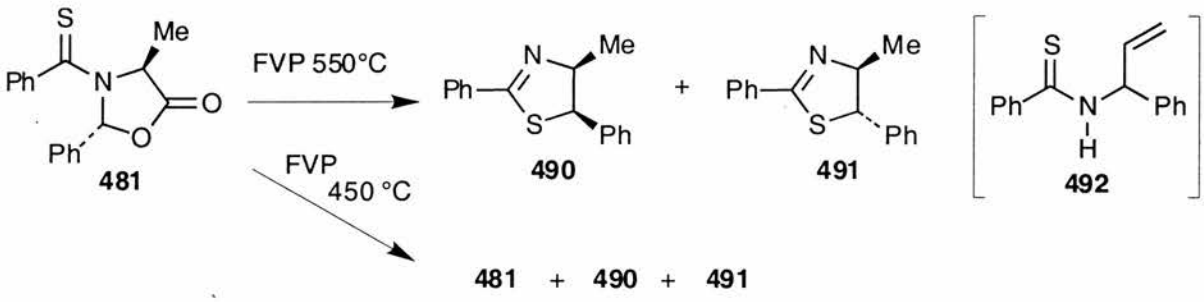


Figure 5: X-ray structure of (*2R,4S*) 4-benzyl-2-phenyl-3-thiobenzoyl-1,3-oxazolidin-5-one **483** showing the crystallographic numbering scheme. Selected bond lengths and angles; O(1)-C(5) 1.323(10), O(1)-C(2) 1.446(9), C(2)-C(13) 1.454(11), C(2)-N(3) 1.488(9), N(3)-C(6) 1.356(8), N(3)-C(4) 1.461(9), C(4)-C(5) 1.504(11), C(4)-C(19) 1.519(11), C(6)-C(7) 1.479(10), C(6)-S(6) 1.640(7) Å; C(5)-O(1)-C(2) 113.5(6), O(1)-C(2)-C(13) 110.6(6), O(1)-C(2)-N(3) 102.2(6), C(13)-C(2)-N(3) 114.5(6), C(6)-N(3)-C(4) 122.9(5), C(6)-N(3)-C(2) 124.1(5), C(4)-N(3)-C(2) 111.6(5), N(3)-C(4)-C(5) 101.7(6), N(3)-C(4)-C(19) 116.3(6), C(5)-C(4)-C(19) 110.5(6), O(5)-C(5)-O(1) 121.2(8), O(5)-C(5)-C(4) 127.8(8), O(1)-C(5)-C(4) 111.0(7), N(3)-C(6)-C(7) 116.0(6), N(3)-C(6)-S(6) 122.1(5), C(7)-C(6)-S(6) 121.8(5)°.

D. FVP of *N*-thioacyloxazolidin-5-ones

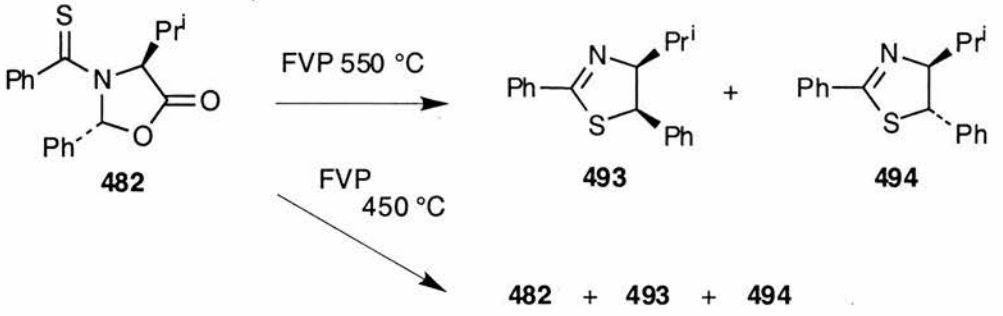
The first of these compounds subjected to FVP was the (*S*)-alanine derived compound **481**. The mass spectrum showed that CO_2 had been lost and the NMR data was consistent with the formation of a 2-thiazoline ring. The ^1H NMR spectrum showed a similar pattern to that of the oxazolines obtained earlier but as would be expected, the doublet arising from the hydrogen at the 5-position is at a lower chemical shift. Compound **491** was known in the literature[129] although which isomer had not been determined. By comparison of the data obtained earlier for the oxazolines we are confident in assigning it as the *trans* isomer. Therefore it appears that the FVP of **481** yields the *cis* and *trans* 2-thiazolines **490** and **491**.



481 + **490** + **491**

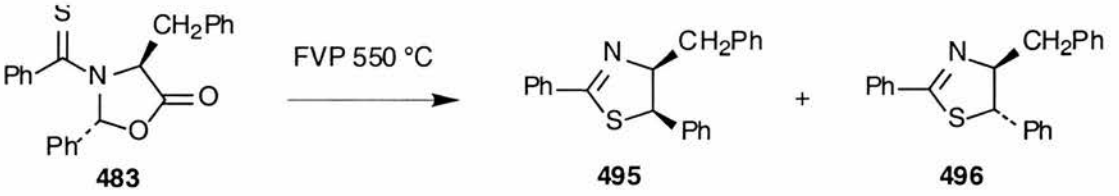
Interestingly at 450 °C, there was no sign of the *N*-thioacylaziridine but there were traces of the thiazolines that were observed at 550 °C. In this case the aziridine must be so reactive once it has formed under these conditions that it immediately ring expands into the thiazoline. There was also no sign of the allylthioamide product **492** corresponding to compound **399** formed from the *N*-benzoyloxazolidinone **383**.

Pyrolysis of the (*S*)-valine derived compound **482** followed the same pattern as the previous reaction. FVP at 550 °C afforded the *cis* and *trans* thiazolines **493** and **494** in yields of 28 and 17% after column chromatography. These both gave non-zero optical rotations, +11 for the *cis* isomer and –23 for the *trans*. What is interesting is that none of the oxazolines synthesized in this way had significant optical rotations.



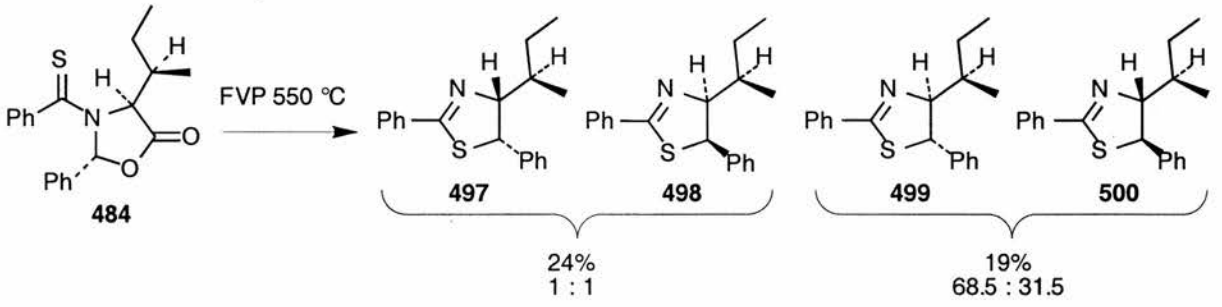
Upon FVP at 450 °C the starting material was only partially reacted and again traces of the thiazolines were apparent. The aziridine is assumed to be an unobserved intermediate in the FVP of *N*-thioacyloxazolidin-5-ones. In light of this the succeeding pyrolyses were carried out at 550 °C only.

Pyrolysis of the (*S*)-phenylalanine derived compound **483** again gave *cis* and *trans* thiazolines. Compounds **495** and **496** were produced in a ratio of approximately 65:35. We were unable to separate these compounds by column chromatography. Interestingly there was no sign of the *N*-allylthioamide product in this case. Its analogue **412** formed in 22% yield by the pyrolysis of *N*-acyloxazolidinone **385**.



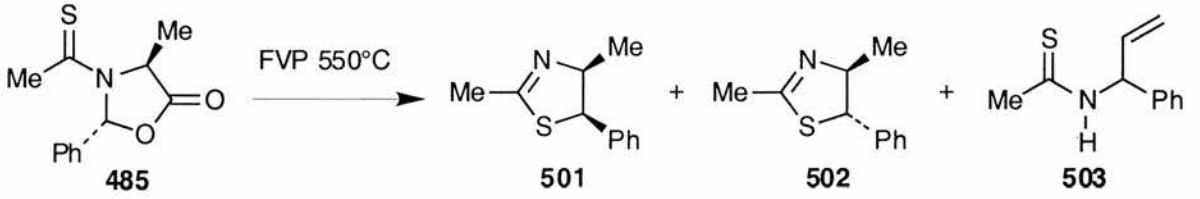
The ^{1}H NMR spectrum of this mixture was recorded in the presence of varying amounts of praseodymium tris(heptafluorobutrylcamphorate) and europium tris(heptafluorobutrylcamphorate). The enantiomeric excess could not be determined in either case as the signals become too broad before the peaks for the different enantiomers separated.

Another oxazolidinone **484** derived from (*S*)-isoleucine was studied at 550 °C. Once again as there are three stereocentres present in the molecule and therefore all four diastereomers are identifiable by NMR. Using column chromatography it was only possible to separate the *cis* isomers from the *trans*. This pyrolysis provides the *cis*-thiazolines **497** and **498**, and *trans*-thiazolines **499** and **500** in almost equal amount. Column chromatography separated these in 24% and 19% yield and in 0% and 37% diastereomeric excess respectively.

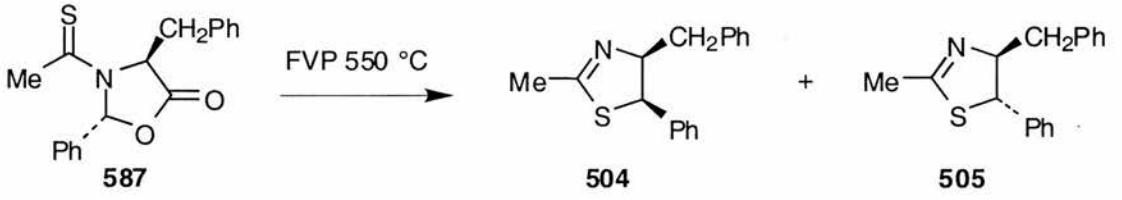


Again there was no sign of an analogue of the allyl compound **416** formed in 17% yield by the pyrolysis compound **386**.

Only two of the three thioacetyloxazolidinones synthesized were subjected to pyrolysis at 550 °C. The first was the (*S*)-alanine derived compound **485**. This reaction produced *cis*- and *trans*-2-thiazolines **501** and **502** isolated in yields of 20% and 12% respectively. A trace of the *N*-thioacetyl analogue of compound **425** was also observed. This in contrast to the pyrolysis of **388** where the *N*-allylamide compound had been the major product.

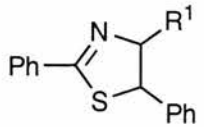


Next the (*S*)-phenyalanine derived compound **487** subjected to pyrolysis at 550 °C. This reaction provided *cis*- and *trans*-2-thiazolines **504** and **505** in yields of 24% and 19% respectively. There was no sign of an analogue of the allyl compound **434** that had formed in the pyrolysis of **390** at 550 °C.



Attempts to establish the enantiomeric excess via the use of lanthanide shift reagents were unsuccessful. Also, since these thiazolines were not separated by column chromatography their optical rotations could not be determined. The ^{1}H and ^{13}C NMR data for all the thiazolines obtained are presented in Tables 16–18 and again these show a highly consistent pattern.

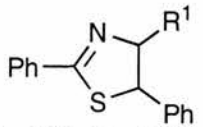
Table 16: ^{1}H NMR spectra of 2-phenylthiazolines



R^1 = Me (**490**, **491**), Pr^i (**493**, **494**), Bn (**495**, **496**), Bu^s (**497**, **498**, **499**, **500**)

R^1	Aromatic	5-H	4-H	R^1
Me (*c*)	7.57–7.02 (10 H, m)	4.96 (d, *J* 8)	4.86 (m)	1.16 (3 H, d, *J* 7, Me)
Me (*t*)	7.55–7.00 (10 H, m)	4.61 (d, *J* 6)	4.77 (m)	1.45 (3 H, d, *J* 7, Me)
Pr^i (*c*)	7.85 (2 H, m), 7.50–7.05 (8 H, m)	4.82 (d, *J* 7)	4.15 (dd, *J* 10, 7)	1.87 (1 H, m, CH), 1.30 (3 H, d, *J* 6, Me), 0.87 (3 H, d, *J* 6, Me)
Pr^i (*t*)	7.87 (2 H, m), 7.52–7.18 (8 H, m)	4.76 (d, *J* 5)	4.67 (t, *J* 5)	2.09 (1 H, m, CH), 1.08 (3 H, d, *J* 7, Me), 1.06 (3 H, d, *J* 7, Me)
Bn (*c*)	7.92 (2 H, m), 7.68–6.95 (13 H, m)	4.83 (d, *J* 8)	4.98 (q, *J* 8)	3.22 (1 H, dd, *J* 14, 8, CH_2), 2.71 (1 H, dd, *J* 14, 8, CH_2)
Bn (*t*)	7.92 (2 H, m), 7.68–6.95 (13 H, m)	4.69 (d, *J* 4)	5.03 (m)	3.22 (1 H, dd, *J* 14, 8, CH_2), 2.88 (1 H, dd, *J* 14, 8, CH_2)
Bu^s(*c*)	7.84 (2 H, m), 7.48–7.02 (8 H, m)	4.97 (d, *J* 7)	4.24 (dd, *J* 10, 7)	1.65 (1 H, m, CH), 1.38 (1 H, m, CH_2), 1.18 (3 H, d *J* 7, CH*Me*)
				1.04 (1 H, m, CH_2), 0.67 (3 H, t, *J* 7, CH_2*Me*)
Bu^s(*c*)*	7.84 (2 H, m), 7.48–7.02 (8 H, m)	4.72 (d, *J* 7)	4.16 (dd, *J* 11, 7)	2.12 (1 H, m, CH_2), 1.67 (1 H, m, CH), 1.36 (1 H, m, CH_2)
				0.83 (3 H, t, *J* 7, CH_2*Me*), 0.77 (3 H, d *J* 7, CH*Me*)
Bu^s(*t*)	7.79 (2 H, m), 7.46–7.04 (8 H, m)	4.72 (s)	4.72 (d, *J* 10)	3.05 (1 H, m, CH), 1.85–1.52 (2 H, m, CH_2), 1.42 (3 H, d *J* 7, CH*Me*)
				0.94 (3 H, t, *J* 7, CH_2*Me*)
Bu^s(*t*)*	7.79 (2 H, m), 7.46–7.04 (8 H, m)	4.76 (s)	4.66 (d, *J* 2)	1.98 (1 H, m, CH), 1.95–1.64 (2 H, m, CH_2), 1.12 (3 H, d *J* 7, CH*Me*)
				1.11 (3 H, t, *J* 7, CH_2*Me*)

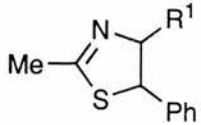
Table 17: ^{13}C NMR spectra of 2-phenylthiazolines



R^1 = Me (**490**, **491**), Pr^i (**493**, **494**), Bn (**495**, **496**), Bu^s (**497**, **498**, **499**, **500**)

R^1	C=N	Aromatic†	5-C	4-C	R^1
Me (*c*)	167.0	138.0, 133.0, 131.2, 128.44 (2 C), 128.42 (2 C), 128.3 (2 C), 128.2 (2 C), 127.7	81.1	61.5	16.5
Me (*t*)	165.5	141.2, 131.0, 131.1, 128.7 (2 C), 128.3 (2 C), 128.2, 127.7 (2 C), 127.4 (2 C)	76.0	58.4	20.0
Pr^i (*c*)	167.2	140.6, 134.0, 131.6, 128.9 (2 C), 128.9 (2 C), 128.7 (2 C), 128.6 (2 C), 128.2	89.1	57.4	29.9 (CH), 23.0 (Me), 21.0 (Me)
Pr^i (*t*)	164.1	142.7, 132.3, 130.0, 127.8 (2 C), 127.4 (2 × 2), 126.43, 126.39 (2 C)	91.5	55.2	32.3 (CH), 18.5 (Me), 17.4 (Me)
Bn (*c*)	167.9	139.7, 132.2, 131.80, 130.0, 129.6 (2 C), 129.0 (2 C), 128.9 (2 C), 128.8 (2 C)	82.5	57.7	139.2, 130.77, 129.0 (2 C), 126.6 (2 C) 37.8 (CH_2)
Bn (*t*)	166.9	142.8, 138.4, 129.6, 128.9 (2 C), 128.4 (2 C), 128.0 (2 C), 127.5 (2 C), 127.0	87.3	57.8	133.7, 129.4, 129.2 (2 C), 126.6 (2 C) 40.4 (CH_2)
Bu^s (*c*)	165.4	139.3, 132.6, 127.64 (2 C), 127.57, 127.44 (2 C), 127.39 (2 C), 126.70 (2 C), 126.6	86.2	56.0	34.6 (CH), 26.0 (CH_2), 17.2 (*Me*CH) 9.7 (*Me*CH_2)
Bu^s (*c*)*	165.6	139.0, 132.6, 130.1, 127.44 (2 C), 127.30 (2 C), 127.28 (2 C), 127.2 (2 C), 126.65	85.8	56.0	34.4 (CH), 27.5 (CH_2), (*Me*CH) 9.9 (*Me*CH_2)
Bu^s (*t*)	164.2	143.0 (4ry), 131.4 (4ry)	90.3	55.9	39.2 (CH), 25.7 (CH_2), 13.6 (*Me*CH) 10.9 (*Me*CH_2)
Bu^s (*t*)*	164.0	143.0 (4ry), 134.2 (4ry)	90.4	54.3	39.0 (CH), 24.6 (CH_2), 14.3 (*Me*CH) 10.8 (*Me*CH_2)

Table 18: ^{1}H and ^{13}C NMR spectra of 2-methylthiazolines



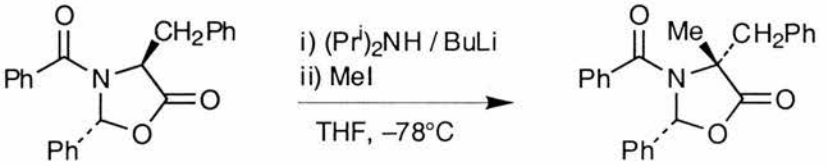
R^1 = Me (**501**, **502**), Bn (**504**, **505**)

R^1	Aromatic	5-H	4-H	2-Me	R^1
Me (*c*)	7.56-7.02 (5 H, m)	4.92 (d, *J* 8)	4.62 (m)	2.32 (s)	1.03 (3 H, d, *J* 7, Me)
Me (*t*)	7.48–7.16 (5 H, m)	4.65–4.44 (2 H, m, 5–H and 4–H)		2.26 (s)	1.37 (3 H, d, *J* 7, Me)
Bn (*c*)	7.53–6.92 (10 H, m)	4.75 (d, *J* 7)	4.77 (m)	2.32 (d, *J* 2)	3.04 (1 H, dd, *J* 14, 7, CH_2), 2.62 (1 H, dd *J* 14, 7, CH_2)
Bn (t)	7.53–6.92 (10 H, m)	4.59 (d, *J* 4)	4.77 (m)	2.28 (d, *J* 1)	3.09 (1 H, dd, *J* 14, 5, CH_2), 2.78 (1 H, dd, *J* 14, 7, CH_2)

R^1	C=N	Aromatic†	5-C	4-C	2-Me	R^1
Me (*c*)	168.3	139.1 (4ry), 129.0, 128.7 (2 C), 128.7 (2 C)	75.9	60.1	20.9	16.9
Me (*t*)	164.7	141.7 (4ry), 129.2 (2 C), 128.1, 127.8 (2 C)	81.4	63.5	20.8	20.5
Bn (*c*)	167.2	139.6 (4ry), 129.9, 128.9 (2 C), 128.8 (2 C)	82.0	59.2	21.1	139.2 (4ry), 128.9 (2 C), 128.6 (2 C), 128.4, 37.7 (CH_2)
Bn (*t*)	165.9	142.9 (4ry), 129.5, 127.5 (2 C), 127.0 (2 C)	87.1	59.2	20.7	138.2 (4ry), 128.4, 126.6 (2 C), 125.9 (2 C), 40.5 (CH_2)

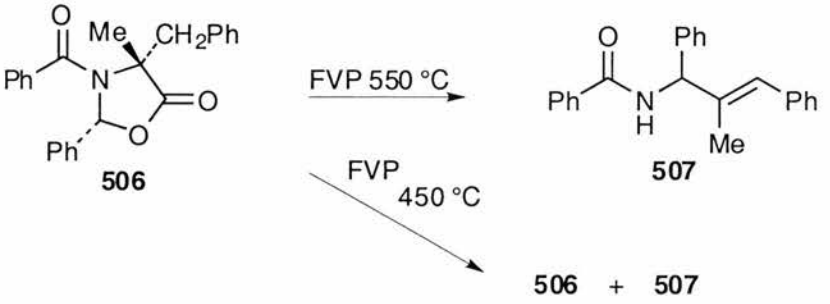
E. Alkylation of chiral *N*-acyloxazolidin-5-ones

Originally the *N*-acyloxazolidin-5-ones were to be alkylated at C-4 in order to extend the acyl anion equivalent chemistry of the dioxolanones. Although the behavior of *N*-acyloxazolidin-5-ones under FVP conditions has turned out to be entirely different to that of the dioxolanones, it was decided to investigate the alkylation briefly. To this end the (*2R,4R*)-3-benzoyl-4-benzyl-4-methyl-2-phenyl-1,3-oxazolidin-5-one **506** was prepared by methylating **385** using LDA. The synthesis of these type of compounds has already been thoroughly investigated by Seebach.[110] However this particular compound was unknown in the literature and was fully characterised with the spectroscopic data confirming the expected structure.



385 **506**

When the FVP of this compound was examined it gave rather surprising results. There is no sign of an aziridine at 450 °C or an oxazoline at 550 °C. As shown below only the ring-opened amide **507** is formed within the temperature range studied. At 550 °C the oxazolidinone **506** is completely reacted to form *N*-(1,3-diphenyl-2-methylprop-2-enyl)benzamide **507** in 76% yield. The reaction was also carried out at 500 °C but the starting material was not fully reacted.

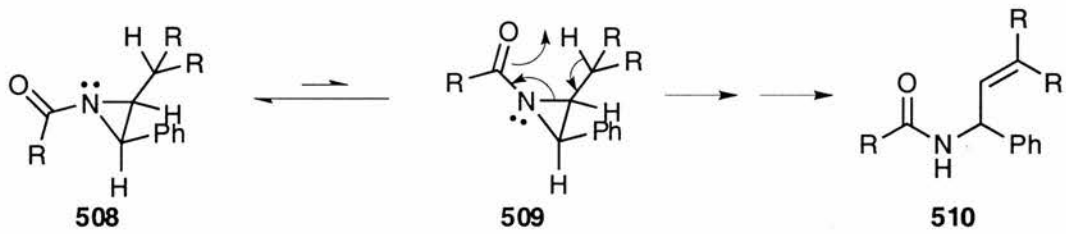


506 **507**

506 + 507

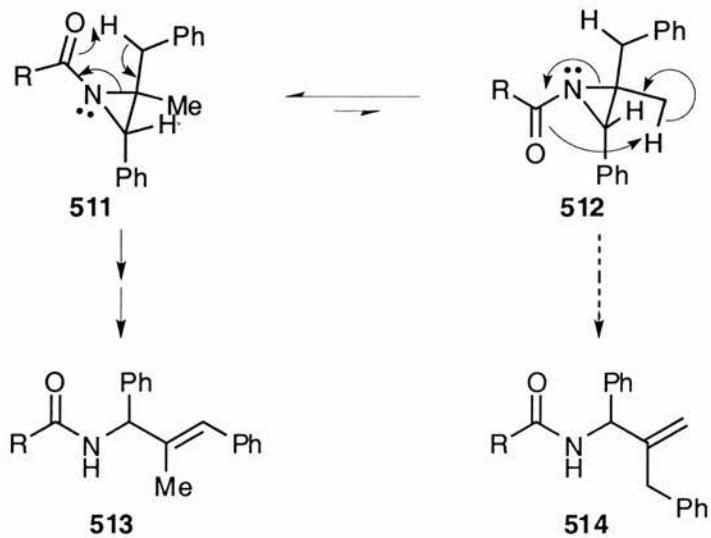
Given the previous examples it is presumed that the aziridine **508** is an unobserved intermediate in this process. The outcome of the experiment can be explained as follows. In the unalkylated examples the *cis*-aziridine intermediate exists predominantly with the *N*-acyl group *trans* to the C-2 and C-3 substituents. The unfavourable all *cis* form **509** required to

allow reaction to give allyl products **510** is only a minor contributor and this means that this is a minor side reaction.



508 **509** **510**

When we come to compound **511** we can first assume that the aziridine is formed with inversion of one centre, as in the other cases, so the benzyl group which was originally *cis* to the phenyl is now *trans* to it. The fact that there is at least one alkyl group on each side of the ring



511 **512** **513** **514**

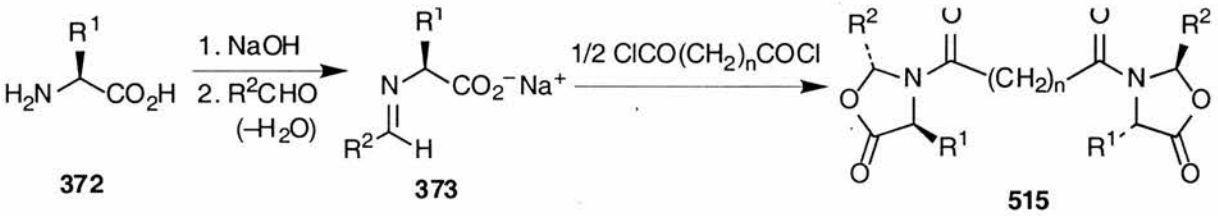
makes the two forms more comparable in energy than before, but the form with benzoyl *trans* to phenyl (**511**) is favoured and this leads to the observed product **513** as shown. This process is apparently more favourable now and overrides any tendency to form oxazolines. The fact that only **513** and not the isomer **514** is formed is in agreement with this explanation.

F. Bis(*N*-acyloxazolidin-5-ones)

Bis(oxazoline) ligands are important in the field of catalytic asymmetric synthesis.[136,137] Bis(oxazoline) ligand-metals catalysts are already employed in a variety of processes including aziridination reactions, oxidations, reductions, hydrosilylations and carbon-carbon forming reactions. Among the carbon-carbon forming reactions are 1,3-dipolar cycloadditions, [2+2] photochemical cycloaddition, aldol reactions, Diels-Alder and hetero Diels-Alder reactions to name a few.

The C_2 axis of symmetry in bis(oxazolines) limits the number of potential transitions states in a given reaction. The donor nitrogens are close to the chiral centres producing a strong directing effect. Also, the bis(oxazoline) can be synthesised with variety of spacers between the rings. Therefore, the size can of the space between rings can be adjusted to allow for the best ligand geometry.

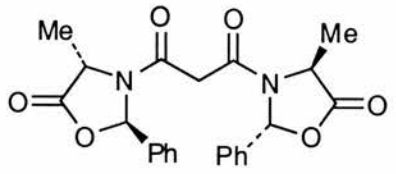
Bis(oxazolidin-5-ones) **515** were prepared starting from amino acids **372** using the route shown previously. The aldehyde component was benzaldehyde. The acid chlorides



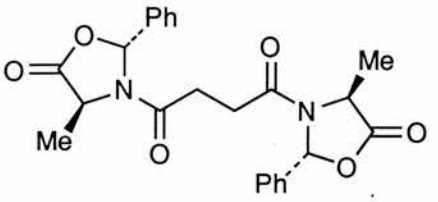
372 **373** **515**

employed were malonyl and succinyl chloride. Only half as many moles are required since we have two reactive sites on these acid chlorides. Syntheses with dimethylmalonyl and oxalyl chlorides failed due to steric factors. The reaction to form the bis(oxazolidinone) **516** from malonyl chloride and (*S*)-alanine was successful giving a yield of 28%. Unfortunately this product could not be obtained in a suitable form for X-ray diffraction.

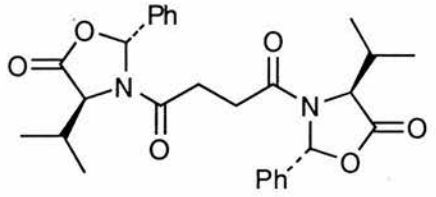
It was then decided that succinyl chloride would be used in order to improve the yields. It was thought that increasing the length of the chain between the carbonyl groups of the acid would reduce steric hindrance. The amino acids used were (*S*)-alanine, (*S*)-valine, and (*S*)-phenylglycine and this gave compounds **517**, **518** and **519** in yields of 32%, 26% and 17% respectively.



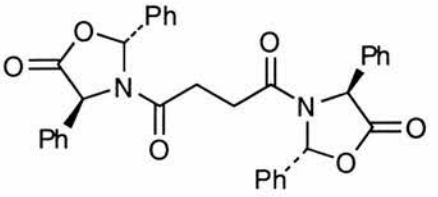
516



517



518



519

The ^{1}H and ^{13}C NMR spectra of the bis(oxazolidin-5-ones) displayed extremely broad peaks at 25 °C. As many as four rotamers are observed at room temperature because there are two possible rotamers for each end of the molecule. By running the spectra at 50 °C the signals were seen to sharpen up considerably. Therefore these oxazolidinones also display restricted rotation of the molecule around the amide bond. This means that the molecule has two or more conformers. The energy barrier for rotation, ΔG^* and the difference in energy between the two states, ΔG, are calculated from the thermodynamic equations 1 and 2 (see earlier).

This procedure was carried out for 3,3'-succinylbis-(*2R,4S*)-2-methyl-4-phenyl-1,3-oxazolidin-5-one **517**. The results are shown below.

Signal (ppm)	T_c (K)	δ_ν (Hz)	ΔG^* (kJ mol^{-1})	ΔG (kJ mol^{-1})
16.2	328±1	226	63.32	3.46
30.4	305±1	29	64.13	3.46
52.8	318±1	57	65.24	3.46
89.6	315±1	57	64.57	3.46

The values of ΔG^* and ΔG are very similar to those obtained earlier for the mono oxazolidinones.

Improved analytical and spectroscopic data is required for these compounds. Also, a wider variety of acids need to be examined in order to broaden their applications and improve yields.

Due to time constraints and the need for a larger catalogue of bis(oxazolidinone) precursors, the subsequent FVP of these compounds to produce the synthetically valuable bis(oxazoline) compounds has not yet been investigated but this is a promising area for future work.

APPENDIX

X-Ray Structural Data

Compound **388** Tables 19–22

Compound **485** Tables 23–26

Compound **483** Tables 27–30

Table 19 Atomic coordinates and U(eq) for **388**

Atom	x	y	z	U(eq)
O(1)	10193(5)	9506(2)	1729(2)	52(1)
C(2)	8642(6)	10263(4)	1332(3)	40(1)
N(3)	9571(5)	11473(3)	1331(2)	40(1)
C(4)	11720(6)	11420(3)	1550(3)	40(1)
C(5)	11990(8)	10097(4)	1788(3)	47(1)
O(5)	13506(5)	9605(3)	2032(2)	66(1)
C(6)	8414(7)	12428(4)	1062(3)	43(1)
O(6)	6613(4)	12258(2)	877(2)	58(1)
C(7)	9417(6)	13638(4)	985(3)	52(1)
C(8)	12416(7)	12200(4)	2301(3)	64(2)
C(9)	8187(6)	9734(3)	448(3)	38(1)
C(10)	9251(6)	10091(4)	-288(3)	46(1)
C(11)	8963(7)	9504(4)	-1064(3)	56(1)
C(12)	7603(7)	8565(4)	-1126(3)	61(1)
C(13)	6493(7)	8227(4)	-401(4)	62(2)
C(14)	6775(6)	8809(4)	378(3)	48(1)
H(2A)	7409	10265	1690	48
H(4A)	12537	11608	1035	48
H(7A)	8440	14228	791	77
H(7B)	10512	13588	574	77
H(7C)	9944	13877	1540	77
H(8A)	12250	13042	2155	96
H(8B)	13825	12038	2420	96
H(8C)	11616	12014	2805	96
H(10A)	10168	10733	-254	55
H(11A)	9696	9746	-1551	67
H(12A)	7425	8159	-1649	73
H(13A)	5549	7600	-442	75
H(14A)	6013	8580	859	58

Table 20 Bond lengths (Å) for **388**

Atom	Atom	Distance	Atom	Atom	Distance
O(1)	C(5)	1.351(6)	C(6)	C(7)	1.489(6)
O(1)	C(2)	1.451(5)	C(6)	O(6)	1.231(5)
C(2)	N(3)	1.464(6)	C(9)	C(14)	1.381(6)
C(2)	C(9)	1.512(7)	C(9)	C(10)	1.389(6)
N(3)	C(6)	1.361(5)	C(10)	C(11)	1.372(7)
N(3)	C(4)	1.453(6)	C(11)	C(12)	1.369(6)
C(4)	C(8)	1.511(6)	C(12)	C(13)	1.385(7)
C(4)	C(5)	1.512(7)	C(13)	C(14)	1.373(7)
C(5)	O(5)	1.194(5)			

Table 21 Bond angles (°) for **388**

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C(5)	O(1)	C(2)	111.4(3)	O(1)	C(5)	C(4)	110.2(4)
O(1)	C(2)	N(3)	103.3(4)	O(6)	C(6)	N(3)	119.3(4)
O(1)	C(2)	C(9)	107.3(3)	O(6)	C(6)	C(7)	122.8(4)
N(3)	C(2)	C(9)	115.5(3)	N(3)	C(6)	C(7)	117.8(4)
C(6)	N(3)	C(4)	130.1(3)	C(14)	C(9)	C(10)	118.8(4)
C(6)	N(3)	C(2)	118.0(4)	C(14)	C(9)	C(2)	119.2(4)
C(4)	N(3)	C(2)	111.6(3)	C(10)	C(9)	C(2)	121.9(4)
N(3)	C(4)	C(8)	116.7(3)	C(11)	C(10)	C(9)	120.7(4)
N(3)	C(4)	C(5)	102.1(3)	C(12)	C(11)	C(10)	120.3(5)
C(8)	C(4)	C(5)	108.9(4)	C(11)	C(12)	C(13)	119.4(5)
O(5)	C(5)	O(1)	122.2(4)	C(14)	C(13)	C(12)	120.6(5)
O(5)	C(5)	C(4)	127.6(4)	C(13)	C(14)	C(9)	120.2(4)

Table 22 Torsion angles [°] for **388**

Atom	Atom	Atom	Atom	Angle
C(5)	O(1)	C(2)	N(3)	-12.1(4)
C(5)	O(1)	C(2)	C(9)	110.5(4)
O(1)	C(2)	N(3)	C(6)	-174.5(3)
C(9)	C(2)	N(3)	C(6)	68.7(4)
O(1)	C(2)	N(3)	C(4)	11.1(4)
C(9)	C(2)	N(3)	C(4)	-105.8(4)
C(6)	N(3)	C(4)	C(8)	61.5(6)
C(2)	N(3)	C(4)	C(8)	-124.9(4)
C(6)	N(3)	C(4)	C(5)	-179.8(4)
C(2)	N(3)	C(4)	C(5)	-6.2(4)
C(2)	O(1)	C(5)	O(5)	-174.0(4)
C(2)	O(1)	C(5)	C(4)	8.8(4)
N(3)	C(4)	C(5)	O(5)	-178.6(4)
C(8)	C(4)	C(5)	O(5)	-54.5(6)
N(3)	C(4)	C(5)	O(1)	-1.5(4)
C(8)	C(4)	C(5)	O(1)	122.5(4)
C(4)	N(3)	C(6)	O(6)	177.2(4)
C(2)	N(3)	C(6)	O(6)	4.0(5)
C(4)	N(3)	C(6)	C(7)	-1.3(6)
C(2)	N(3)	C(6)	C(7)	-174.6(4)
O(1)	C(2)	C(9)	C(14)	85.6(4)
N(3)	C(2)	C(9)	C(14)	-159.8(4)
O(1)	C(2)	C(9)	C(10)	-89.7(4)
N(3)	C(2)	C(9)	C(10)	24.9(5)
C(14)	C(9)	C(10)	C(11)	-2.5(6)
C(2)	C(9)	C(10)	C(11)	172.9(4)
C(9)	C(10)	C(11)	C(12)	0.7(7)
C(10)	C(11)	C(12)	C(13)	1.1(7)
C(11)	C(12)	C(13)	C(14)	-1.2(7)
C(12)	C(13)	C(14)	C(9)	-0.6(7)
C(10)	C(9)	C(14)	C(13)	2.4(6)
C(2)	C(9)	C(14)	C(13)	-173.1(4)

Table 23 Atomic coordinates and U(eq) for **485**

Atom	x	y	z	U(eq)
O(1)	5544(3)	3475(3)	-997(1)	55(1)
C(2)	6489(4)	3802(3)	-247(2)	41(1)
N(3)	6755(3)	5359(3)	-318(2)	40(1)
C(4)	5988(4)	5969(4)	-1085(2)	44(1)
C(5)	5232(4)	4661(4)	-1484(2)	52(1)
O(5)	4454(3)	4595(3)	-2128(2)	78(1)
C(6)	7363(3)	6177(3)	327(2)	42(1)
S(6)	7043(1)	7941(1)	375(1)	60(1)
C(7)	8365(4)	5432(4)	989(2)	60(1)
C(8)	7142(5)	6662(4)	-1711(2)	64(1)
C(9)	5635(4)	3337(3)	554(2)	41(1)
C(10)	6053(4)	2052(4)	941(2)	63(1)
C(11)	5260(6)	1607(6)	1684(3)	88(2)
C(12)	4076(7)	2411(7)	2022(3)	87(2)
C(13)	3618(5)	3691(5)	1633(2)	70(1)
C(14)	4412(4)	4151(4)	899(2)	52(1)
H(2A)	7513	3297	-286	49
H(4A)	5166	6663	-913	53
H(7A)	8419	4422	857	90
H(7B)	7901	5562	1552	90
H(7C)	9420	5833	983	90
H(8A)	7610	7497	-1446	96
H(8B)	6584	6943	-2227	96
H(8C)	7965	5985	-1857	96
H(10A)	6860	1487	706	75
H(11A)	5548	746	1951	105
H(12A)	3561	2103	2522	104
H(13A)	2787	4234	1863	83
H(14A)	4121	5014	636	62

Table 24 Bond lengths [Å] for **485**

Atom	Atom	Distance	Atom	Atom	Distance
O(1)	C(5)	1.358(4)	C(6)	C(7)	1.492(4)
O(1)	C(2)	1.436(3)	C(6)	S(6)	1.661(3)
C(2)	N(3)	1.466(4)	C(9)	C(14)	1.381(4)
C(2)	C(9)	1.493(4)	C(9)	C(10)	1.379(5)
N(3)	C(6)	1.351(4)	C(10)	C(11)	1.389(6)
N(3)	C(4)	1.462(4)	C(11)	C(12)	1.347(7)
C(4)	C(5)	1.502(5)	C(12)	C(13)	1.385(7)
C(4)	C(8)	1.511(4)	C(13)	C(14)	1.383(5)
C(5)	O(5)	1.190(4)			

Table 25 Bond angles (°) for **485**

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C(5)	O(1)	C(2)	112.4(2)	O(1)	C(5)	C(4)	110.2(3)
O(1)	C(2)	N(3)	103.5(2)	N(3)-	C(6)	C(7)	117.2(3)
O(1)	C(2)	C(9)	110.0(2)	N(3)	C(6)	S(6)	121.6(2)
N(3)	C(2)	C(9)	114.8(3)	C(7)	C(6)	S(6)	121.1(3)
C(6)	N(3)	C(4)	123.1(3)	C(14)	C(9)	C(10)	119.6(3)
C(6)	N(3)	C(2)	123.8(3)	C(14)	C(9)	C(2)	121.2(3)
C(4)	N(3)	C(2)	112.0(2)	C(10)	C(9)	C(2)	119.1(3)
N(3)	C(4)	C(5)	101.9(3)	C(9)	C(10)	C(11)	119.6(4)
N(3)	C(4)	C(8)	113.6(3)	C(12)	C(11)	C(10)	120.5(4)
C(5)	C(4)	C(8)	110.6(3)	C(13)	C(12)	C(11)	120.8(4)
O(5)	C(5)	O(1)	121.8(4)	C(12)	C(13)	C(14)	119.1(4)
O(5)	C(5)	C(4)	128.0(4)	C(13)	C(14)	C(9)	120.4(4)

Table 26 Torsion angles [°] for **485**

Atom	Atom	Atom	Atom	Angle
C(5)	O(1)	C(2)	N(3)	-0.3(3)
C(5)	O(1)	C(2)	C(9)	122.7(3)
O(1)	C(2)	N(3)	C(6)	168.4(2)
C(9)	C(2)	N(3)	C(6)	48.5(4)
O(1)	C(2)	N(3)	C(4)	0.3(3)
C(9)	C(2)	N(3)	C(4)	-119.6(3)
C(6)	N(3)	C(4)	C(5)	-168.3(3)
C(2)	N(3)	C(4)	C(5)	-0.2(3)
C(6)	N(3)	C(4)	C(8)	72.7(4)
C(2)	N(3)	C(4)	C(8)	-119.1(3)
C(2)	O(1)	C(5)	O(5)	-179.5(3)
C(2)	O(1)	C(5)	C(4)	0.2(4)
N(3)	C(4)	C(5)	O(5)	179.7(3)
C(8)	C(4)	C(5)	O(5)	-59.2(5)
N(3)	C(4)	C(5)	O(1)	0.0(3)
C(8)	C(4)	C(5)	O(1)	121.1(3)
C(4)	N(3)	C(6)	C(7)	-169.2(3)
C(2)	N(3)	C(6)	C(7)	24.0(4)
C(4)	N(3)	C(6)	S(6)	9.7(4)
C(2)	N(3)	C(6)	S(6)	-157.2(2)
O(1)	C(2)	C(9)	C(14)	-78.4(3)
N(3)	C(2)	C(9)	C(14)	37.7(4)
O(1)	C(2)	C(9)	C(10)	99.8(3)
N(3)	C(2)	C(9)	C(10)	-144.0(3)
C(14)	C(9)	C(10)	C(11)	-1.4(5)
C(2)	C(9)	C(10)	C(11)	-179.7(3)
C(9)	C(10)	C(11)	C(12)	0.8(6)
C(10)	C(11)	C(12)	C(13)	0.5(6)
C(11)	C(12)	C(13)	C(14)	-1.2(6)
C(12)	C(13)	C(14)	C(9)	0.6(5)
C(10)	C(9)	C(14)	C(13)	0.6(5)
C(2)	C(9)	C(14)	C(13)	178.9(3)

Table 27 Atomic coordinates and U(eq) for **483**

Atom	x	y	z	U(eq)
O(1)	-2862(6)	411(7)	11582(5)	84(2)
C(2)	-2936(7)	1447(8)	10688(6)	65(2)
N(3)	-1531(5)	1622(6)	10676(5)	56(2)
C(4)	-673(7)	734(8)	11536(6)	65(2)
C(5)	-1650(10)	-20(9)	12052(7)	70(2)
O(5)	-1436(7)	-922(7)	12780(5)	99(2)
C(6)	-1116(7)	2269(8)	9833(6)	57(2)
S(6)	392(2)	2094(2)	9698(2)	76(1)
C(7)	-2087(6)	3198(7)	9072(6)	54(2)
C(8)	-2357(8)	2938(8)	7902(7)	66(2)
C(9)	-3263(10)	3788(10)	7176(8)	83(2)
C(10)	-3873(9)	4895(10)	7577(8)	82(3)
C(11)	-3570(8)	5187(9)	8719(8)	73(2)
C(12)	-2688(7)	4322(8)	9464(6)	64(2)
C(13)	-3774(7)	915(8)	9640(6)	61(2)
C(14)	-3445(9)	-294(9)	9107(7)	78(3)
C(15)	-4229(12)	-828(12)	8110(9)	113(4)
C(16)	-5412(13)	-64(16)	7663(9)	116(4)
C(17)	-5767(10)	1125(14)	8166(10)	104(3)
C(18)	-4969(8)	1608(10)	9107(8)	84(3)
C(19)	337(8)	1531(8)	12433(7)	75(2)
C(20)	-184(7)	2785(9)	12972(6)	66(2)
C(21)	-130(8)	4206(9)	12562(7)	78(2)
C(22)	-607(10)	5328(10)	13045(10)	95(3)
C(23)	-1107(10)	5090(11)	13965(10)	94(3)
C(24)	-1181(10)	3754(13)	14364(8)	98(3)
C(25)	-715(8)	2580(10)	13873(7)	82(2)
C(30)	2789(11)	4023(15)	5155(10)	88(3)
Cl(1)	3489(4)	2499(4)	4736(3)	113(1)
Cl(2)	3415(4)	5599(4)	4813(3)	122(1)
H(2A)	-3289	2381	10896	78

Table 27 Atomic coordinates and U(eq) for **483** (Cont'd)

Atom	x	y	z	U(eq)
H(4A)	-216	8	11164	79
H(8A)	-1919	2184	7617	79
H(9A)	-3465	3600	6390	100
H(10A)	-4505	5466	7072	99
H(11A)	-3968	5983	8993	88
H(12A)	-2500	4511	10249	77
H(14A)	-2646	-778	9439	94
H(15A)	-3990	-1654	7749	135
H(16A)	-5981	-396	6983	139
H(17A)	-6573	1602	7849	124
H(18A)	-5208	2457	9439	101
H(19A)	743	837	13031	90
H(19B)	1039	1886	12091	90
H(21A)	244	4372	11942	93
H(22A)	-596	6272	12750	114
H(23A)	-1406	5883	14324	113
H(24A)	-1554	3610	14988	117
H(25A)	-765	1639	14163	98
H(30A)	1832	4007	4807	106
H(30B)	2911	3989	5982	106

Table 28 Bond lengths [Å] for **483**

Atom	Atom	Distance	Atom	Atom	Distance
O(1)	C(5)	1.323(10)	C(11)	C(12)	1.386(11)
O(1)	C(2)	1.446(9)	C(13)	C(14)	1.385(11)
C(2)	C(13)	1.454(11)	C(13)	C(18)	1.418(11)
C(2)	N(3)	1.488(9)	C(14)	C(15)	1.387(12)
N(3)	C(6)	1.356(8)	C(15)	C(16)	1.418(16)
N(3)	C(4)	1.461(9)	C(16)	C(17)	1.361(16)
C(4)	C(5)	1.504(11)	C(17)	C(18)	1.325(13)
C(4)	C(19)	1.519(11	C(19)	C(20)	1.506(11)
C(5)	O(5)	1.204(9)	C(20)	C(25)	1.367(11)
C(6)	C(7)	1.479(10)	C(20)	C(21)	1.418(11)
C(6)	S(6)	1.640(7)	C(21)	C(22)	1.354(12)
C(7)	C(12)	1.367(10)	C(22)	C(23)	1.372(13)
C(7)	C(8)	1.412(10)	C(23)	C(24)	1.343(15)
C(8)	C(9)	1.380(11)	C(24)	C(25)	1.392(13)
C(9)	C(10)	1.365(12)	C(30)	Cl(2)	1.699(13)
C(10)	C(11)	1.383(12)	C(30)	Cl(1)	1.730(14)

Table 29 Bond angles (°) for **483**

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C(5)	O(1)	C(2)	113.5(6)	C(9)	C(10)	C(11)	120.0(8)
O(1)	C(2)	C(13)	110.6(6)	C(10)	C(11)	C(12)	120.2(7)
O(1)	C(2)	N(3)	102.2(6)	C(7)	C(12)	C(11)	120.2(7)
C(13)	C(2)	N(3)	114.5(6)	C(14)	C(13)	C(18)	116.4(8)
C(6)	N(3)	C(4)	122.9(5)	C(14)	C(13)	C(2)	121.7(7)
C(6)	N(3)	C(2)	124.1(5)	C(18)	C(13)	C(2)	121.9(8)
C(4)	N(3)	C(2)	111.6(5)	C(13)	C(14)	C(15)	122.9(9)
N(3)	C(4)	C(5)	101.7(6)	C(14)	C(15)	C(16)	115.8(10)
N(3)	C(4)	C(19)	116.3(6)	C(17)	C(16)	C(15)	122.9(10)

Table 29 Bond angles (°) for **483** (Cont'd)

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
C(5)	C(4)	C(19)	110.5(6)	C(18)	C(17)	C(16)	118.9(10)
O(5)	C(5)	O(1)	121.2(8)	C(17)	C(18)	C(13)	123.1(9)
O(5)	C(5)	C(4)	127.8(8)	C(20)	C(19)	C(4)	115.5(6)
O(1)	C(5)	C(4)	111.0(7)	C(25)	C(20)	C(21)	118.4(8)
N(3)	C(6)	C(7)	116.0(6)	C(25)	C(20)	C(19)	120.7(7)
N(3)	C(6)	S(6)	122.1(5)	C(21)	C(20)	C(19)	121.0(7)
C(7)	C(6)	S(6)	121.8(5)	C(22)	C(21)	C(20)	120.7(9)
C(12)	C(7)	C(8)	119.5(7)	C(21)	C(22)	C(23)	119.5(9)
C(12)	C(7)	C(6)	122.0(7)	C(24)	C(23)	C(22)	121.1(9)
C(8)	C(7)	C(6)	118.4(6)	C(23)	C(24)	C(25)	120.6(9)
C(9)	C(8)	C(7)	119.5(7)	C(20)	C(25)	C(24)	119.8(9)
C(10)	C(9)	C(8)	120.6(8)	Cl(2)	C(30)	Cl(1)	114.5(6)

Table 30 Torsion angles [°] for **483**

Atom	Atom	Atom	Atom	Angle
C(5)	O(1)	C(2)	C(13)	121.6(7)
C(5)	O(1)	C(2)	N(3)	-0.7(7)
O(1)	C(2)	N(3)	C(6)	166.2(6)
C(13)	C(2)	N(3)	C(6)	46.7(9)
O(1)	C(2)	N(3)	C(4)	-0.5(7)
C(13)	C(2)	N(3)	C(4)	-120.1(7)
C(6)	N(3)	C(4)	C(5)	-165.6(6)
C(2)	N(3)	C(4)	C(5)	1.4(7)
C(6)	N(3)	C(4)	C(19)	74.3(9)
C(2)	N(3)	C(4)	C(19)	-118.7(7)
C(2)	O(1)	C(5)	O(5)	-177.2(7)
C(2)	O(1)	C(5)	C(4)	1.6(9)
N(3)	C(4)	C(5)	O(5)	176.9(8)
C(19)	C(4)	C(5)	O(5)	-59.0(11)
N(3)	C(4)	C(5)	O(1)	-1.8(8)
C(19)	C(4)	C(5)	O(1)	122.3(7)
C(4)	N(3)	C(6)	C(7)	-176.6(6)
C(2)	N(3)	C(6)	C(7)	18.1(9)
C(4)	N(3)	C(6)	S(6)	0.7(9)
C(2)	N(3)	C(6)	S(6)	-164.7(5)
N(3)	C(6)	C(7)	C(12)	56.2(9)
S(6)	C(6)	C(7)	C(12)	-121.1(7)
N(3)	C(6)	C(7)	C(8)	-126.2(7)
S(6)	C(6)	C(7)	C(8)	56.5(9)
C(12)	C(7)	C(8)	C(9)	-2.5(10)
C(6)	C(7)	C(8)	C(9)	179.8(7)
C(7)	C(8)	C(9)	C(10)	1.6(12)
C(8)	C(9)	C(10)	C(11)	0.9(13)
C(9)	C(10)	C(11)	C(12)	-2.6(12)
C(8)	C(7)	C(12)	C(11)	0.9(10)
C(6)	C(7)	C(12)	C(11)	178.5(7)

Table 30 Torsion angles [°] for **483** (Cont'd)

Atom	Atom	Atom	Atom	Angle
C(10)	C(11)	C(12)	C(7)	1.7(11)
O(1)	C(2)	C(13)	C(14)	-64.7(9)
N(3)	C(2)	C(13)	C(14)	50.0(9)
O(1)	C(2)	C(13)	C(18)	115.5(7)
N(3)	C(2)	C(13)	C(18)	-129.7(7)
C(18)	C(13)	C(14)	C(15)	-0.6(12)
C(2)	C(13)	C(14)	C(15)	179.7(8)
C(13)	C(14)	C(15)	C(16)	-0.5(14)
C(14)	C(15)	C(16)	C(17)	0.3(16)
C(15)	C(16)	C(17)	C(18)	1.0(17)
C(16)	C(17)	C(18)	C(13)	-2.1(15)
C(14)	C(13)	C(18)	C(17)	2.0(12)
C(2)	C(13)	C(18)	C(17)	-178.3(8)
N(3)	C(4)	C(19)	C(20)	48.4(9)
C(5)	C(4)	C(19)	C(20)	-66.8(9)
C(4)	C(19)	C(20)	C(25)	86.1(9)
C(4)	C(19)	C(20)	C(21)	-94.3(9)
C(25)	C(20)	C(21)	C(22)	-0.7(12)
C(19)	C(20)	C(21)	C(22)	179.6(8)
C(20)	C(21)	C(22)	C(23)	2.2(13)
C(21)	C(22)	C(23)	C(24)	-2.8(15)
C(22)	C(23)	C(24)	C(25)	1.8(15)
C(21)	C(20)	C(25)	C(24)	-0.2(12)
C(19)	C(20)	C(25)	C(24)	179.5(8)
C(23)	C(24)	C(25)	C(20)	-0.3(14)

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