Synthesis of *N*-amino compounds and C2 symmetric *N*-amino compounds and transformation into aziridines using olefins

Dissertation

zur Erlangung des akademischen Grades
Doktor der Naturwissenschaften (Dr. rer. nat.)
am Fachbereich Naturwissenschaften, Institut für Chemie,
an der Universität Kassel

Vorgelegt von

M.Sc. Chemiker
Anil Kumar Tripathi
Organische Chemie
Universität Kassel
Fachbereich 18: Naturwissenschaften

Kassel, November 2008

This work was performed in the work group of Mr. Prof. Dr. H. Frauenrath, Department of Organic Chemistry, FB18: Natural Sciences, University of Kassel, Germany, since February 2004 to November 2008.

I am very much thankful to Mr. Prof. Dr. H. Frauenrath for providing me the interesting theme, day to day interactions as well as kind discussions.

I am very much thankful to Dr. M. Maurer for NMR measurements and helping me for solving the NMR spectroscopic problems and computer problems as well.

I am very much thankful to Dr. C. Bruhn for single crystal XRD measurements.

I am very much thankful to Dr. S. Fürmeier for MS measurements.

I am very much thankful to Dr. S. Flock and Dr. M. Maurer for reading the manuscript and discussion as well.

I am very much thankful to Mrs. S. Schneider for helping the administrative work.

Furthermore, I am very much thankful to Dr. D. Brethauer, Mr. D. Dittmann, Mr. T. Newrkla, and Mrs. B. Diwisch, Mr. I. Graf, Mr. E. Tatarov, and late Mrs. G. Fischer for their kind help.

Tag der Disputation: 1. Juli 2009

1. Gutachter: Prof. Dr. H. Frauenrath
2. Gutachter: Prof. em. Dr. H. Follmann

Selected parts of this work were published in:

A. K. Tripathi, C. Bruhn, S. Flock, H. Frauenrath, *Acta Cryst.* (2005), **C61**, 705.

My wife Mahima and son Shashank

Table of contents

1 Introduction

1.1 Structure, chemical and physical data of aziridines

Aziridines are the nitrogen analogues of epoxides and show similar reactivity patterns as electrophilic reagents.[1] They undergo highly regio- and stereoselective ring opening reactions, which provides them a great value as building blocks in organic synthesis.[2] The first synthesis of an aziridine was disclosed by Gabriel in 1888 by chlorination of ethanolamines with thionyl chloride and then cyclization in the presence of alkali.[3] Aziridine **1**, also known as azaethylene or ethyleneimine, is a three-membered saturated nitrogen-containing heterocycle. It is a water-soluble, colourless liquid (b.p. 57 °C). The compound easily undergoes polymerization *via* nucleophilic ring-opening, explosively so when treated with acids.

1

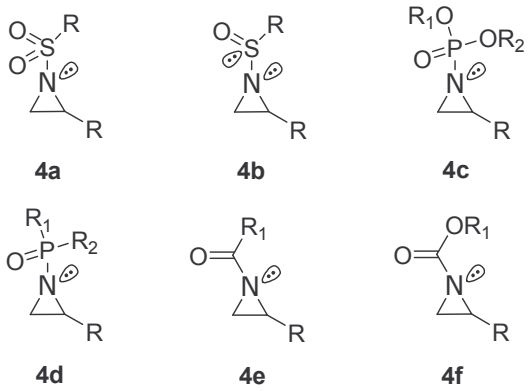
Scheme 1: *Aziridine (**1**).*

Aziridines are less basic than acyclic amines, but more basic than arylamines (the aziridinium ion has p*K*a = 7.98), and reacts in a similar fashion to acyclic secondary amines with alkylating agents. Aziridines differ from other acyclic secondary amines; due to additional bond strain caused by ring makes the barrier to inversion at nitrogen considerably higher.[3] Thus, the activation enthalpy of the *N*-inversion of 2-methylaziridine is approximately 70 kJ mol^{-1}, considerably higher than secondary amine, but it is not sufficient to prevent racemization at room temperature. However, if an electronegative substituent is present on nitrogen, the inversion barrier is enhanced to such an extent, that, for instance, 1-chloro-2-methylaziridine (**2**) (in which the inversion barrier $\Delta G^{\ddagger}$ = 112 kJ mol^{-1}) can be separated into diastereomers, which are stable at room temperature. (+)-(*S*)-1-Chloro-2,2-bis(methoxycarbonyl)aziridine can be prepared by enzymatic hydrolysis of the racemic compound. Moreover, the amide derivative of this compound exists only in (*Z*)-conformation (**3**) (**Scheme 2**).[3]

2 **3**

Scheme 2: *1-Chloro-2-methylaziridine (**2**) and (-)-E-1-Chloro-2-methoxycarbonyl-2-methyl-carbamoylaziridine (**3**).*[3]

The chemistry of aziridines is more complicated in comparision to epoxides because of additional valency on the heteroatom. Aziridines may be broadly divided into two groups of compounds based on their reactivity toward nucleophile: a) activated aziridines which contain substituents capable of stabilizing a negative charge, which is formed on the aziridine nitrogen in the transition state when the compound reacts with a nucleophile; b) non activated aziridines, which contain no such substituents, e.g. ethyleneimine, or compounds containing a basic aziridine nitrogen.[5] Activating groups usually comprise oxygenated substituents such as sulfonyl (**4a**), sulfinyl (**4b**), phosphoryl (**4c**), phosphinyl (**4d**) or carbonyl (**4e**, **4f**) functional groups (**Scheme 3**).

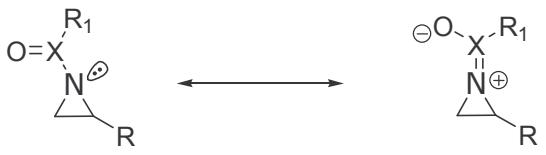


4a **4b** **4c**

4d **4e** **4f**

Scheme 3: *Activated aziridines (**4**).*[5]

In the activated aziridines, there is little resonance interaction between the *N* non bonded electron pairs and the X=O bond, due to the large increase in ring-strain which would be associated with the amidate-like resonance isomers (**5a**) and (**5b**). The X may be sulphur, phosphorus or carbon (**Scheme 4**).[5]

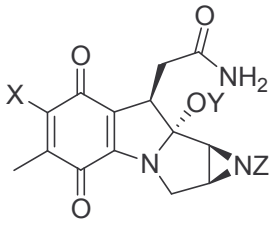


5a **5b**

Scheme 4: *Resonance isomer of aziridine (**5a,5b**).*[5]

1.2 Biologically active aziridines

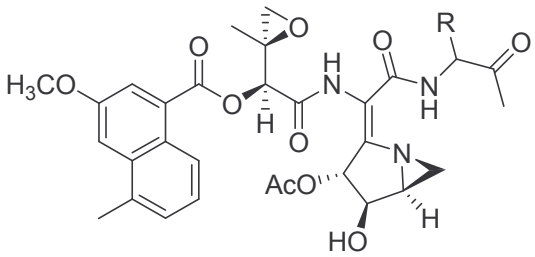
Aziridines are having *in vivo* potency because of their toxicity.[3] The most important class of aziridines are mitosanes, which were first isolated from soil extracts of *streptomyces verticillatus*. They exhibit both anti tumor and antibiotic activity. A lot of research is focused on making derivatives to get increased antitumor activity. The mitomycines (**6**) are naturally occurring antitumor antibiotics, which exhibit *in vivo* and *in vitro* activity (**Scheme 5**).[6]



6a: Mitomycin A, X= OMe, Y= Me, Z= H
6b: Mitomycin B, X= OMe, Y= H, Z= Me
6c: Mitomycin C, X= NH_2, Y= Me, Z= H
6d: Porfiromycin, X= NH_2, Y= Me, Z= Me

Scheme 5: *Mitomycines (**6**).*[3,6]

The azinomycines (**7**), isolated from *Streptomyces grieseofusus S42227,* exhibit antitumor and antibiotic activity.[7] The actvity of azinomycine is based on cross linking with DNA *via* nucleophilic ring opening of the aziridine and epoxide moiety by purine (**Scheme 6**).

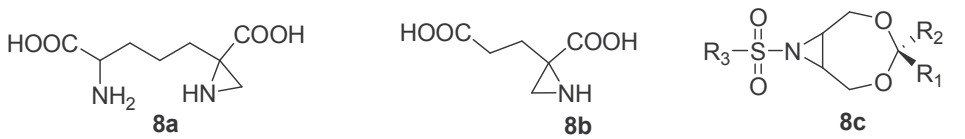


7a: Azinomycin A, R= H
7b: Azinomycin B, R= CHO

Scheme 6: *Azinomycine A (7**a**) and Azinomycin B (7**b**).*[7]

There are several other compounds like azicemicin, ficellomycin, maduropeptin and epothilone containg aziridine moieties, which are biologically active.[8,9]

A number of synthetic aziridines have shown to exhibit useful biological properties. For example, 2-(4-amino-4-carboxybutyl)aziridine-2-carboxylic acid (**8a**) is a potent irrervesible inhibitor of the bacterial enzyme diaminopimelic acid epimerase,[10] 2-(3-carboxypropyl) aziridine-2-carboxylic acid (**8b**) an irreversible inhibitor of glutamate racemase,[11] and dioxipinoaziridine (**8c**) antihyperglycemic activity,[12] benzamide aziridines[13] are having cytotoxic activity (**Scheme 7**).



R_1,R_2 = H, alkyl
R_3 = Alkyl, aryl

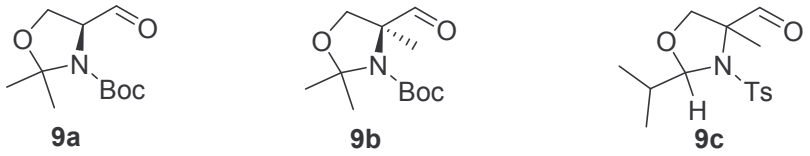
Scheme 7: *Biologically active synthetic aziridines (**8a,8b,8c**).*[11-13]

1.3 Use of aziridines

The C_2-symmetric bis(aziridine) ligands have been used in a variety of metal-mediated asymmetric reactions using osmium (dihydroxylation), palladium (allylic alkylation) and copper (cyclopropanation and catalysts).[14] Aziridines were also used in the synthesis of α-amino acids,[15] *N*-protected β-amino ester,[16] β-amino acids,[17] β-lactones,[18,19] and in the synthesis of biologically active compounds such as feldamycin,[20] which exhibits antibacterial and antibiotic activity. They have also found application in synthesis of the tumor and *GSK-3*β inhibiting alkaloid, (-)-agelastatin A,[21] in the synthesis of ustiloxin-D,[22] ustiloxin-F,[23] a

potent antimitotic agents, in the synthesis of L-epicapreomycidine,[24] and in the stereoselective synthesis of (+)-bromoxone,[25] which shows potent antitumor activity.

(*S*)-*N*-Boc-*N,O*-isopropylidene serinal (**9a**) is known as Garner aldehyde and its methyl homologue (**9b**) is established as versitile chiral building block in organic synthesis.[26] (*S*)-as far as (*R*)- (**9b**) have proved to be valuable starting materials in the approach of the synthesis of (*S*)-and (*R*)-2-amino-2-methylbutanoic acids (*Iva*).[27] They are used in the synthesis of *meso*-2,3-diaminoglutaric acid,[28] analogues of dihydrosphingosine,[29] asymmetric synthesis of all isomers of *α*-methyl-*β*-phenylserine,[30] synthesis of both enantiomers of *α*-vinylalanine and *α*-ethynylalanine.[31] A direct aziridination process was described for the synthesis of *N*-tosyl-4-methyl-*N,O*-isobutyrylideneserinal (**9c**), an important building block for the synthesis of *α*-vinylalanine (**Scheme 8**).[32]



Scheme 8: *Garner's aldehyde* (***9a***)*,* (***9b***) *and N-tosyl-4-methyl-N,O-isobutyrylideneserinal (**9c**).*

1.4 Methods of preparation of aziridines

1.4.1 Method A: Transition metal catalysed nitrogen transfer to alkenes

1.4.1.1 Aziridinations using isolated [*N*-(arenesulfonyl)imino]phenyliodinanes

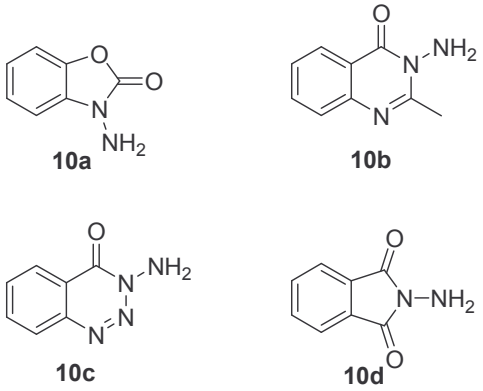
Transition metal catalyzed aziridinations using alkenes and [*N*-(arenesulfonyl)imino] phenyliodinanes as nitrogen sources have intensively been studied.[33,34] To obtain optimal yields, these reactions are often performed with a large excess of alkenes, and they are also often accompanied by insertion of a nitrene into activated C-H bonds.[35]

1.4.1.2 Aziridinations using in situ generated phenyliodinanes

The preparation of aziridines using alkenes and *in situ* generation of PhI=NTs and [*N*-(alkenesulfonyl)imino]phenyliodinanes have been reported, which avoid the tedious preparation of PhI=NTs and extend the scope of this type of aziridinations.[36-37]

1.4.1.3 Method B: Preparation of aziridines using *N*-amino compounds as nitrogen source

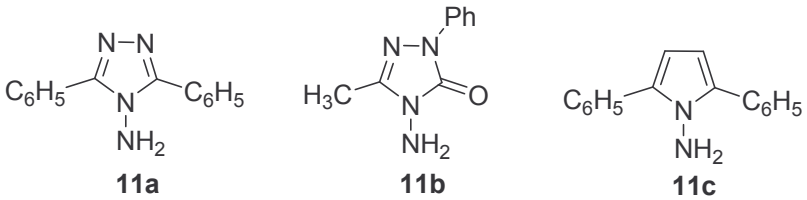
A useful method involves *in situ* generation of nitrenes by means of oxidation of hydrazine derivatives.[38] Rees and co workers described the method of the preparation of *N*-amino aziridine derivatives by reactions of the corresponding hydrazine derivatives (**10**) with alkenes in the presence of lead tetraacetate as oxidising agent (**Scheme 9**).[39,40]



Scheme 9: *N-Amino compounds (**10**) used for the preparation of aziridines.*[38-40]

Electrochemical aziridination methods are also described in the literature with electron rich and electron deficient olefins and *N*-aminophthalimide as nitrene source, lead tetraacetate,[41] and iodbenzenediacetate[42] as oxidising agent.

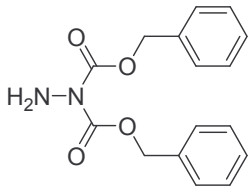
Other *N*-amino heterocycles, e.g. substituted *N*-amino triazoles (**11a**, **11b**) and pyrrole (**11c**) have been reacted with a large excess of olefins and lead tetraacetate as oxidising agents to get good to excellent yields of aziridines (**Scheme 10**).[43] These nitrogen sources have disadvantages, since the olefins were used as solvent.



Scheme 10: *N-Amino heterocycles (**11**) used for the aziridination reactions with $Pb(OAc)_4$ as oxidising agent.*[43]

The preparation of aziridines was also achieved using *N,N*-dibenzyloxycarbonyl hydrazine (**12**) as nitrogen source, which requires a large excess of olefins and oxidation with $Pb(OAc)_4$.

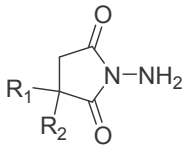
The advantage of using the Cbz protected hydrazine as nitrogen source is, that the protecting group can be easily removed under neutral conditions by hydrogenation in presence of catalytic amounts of Pd on activated charcoal. An alternative procedure to remove the Cbz protecting group by refluxing aziridine in cyclohexene in presence of Pd on calcium carbonate to form *N*-amino aziridine was also reported. [44]



12

Scheme 11: *N,N-Dibenzyloxycarbonyl hydrazine (**12**).*[44]

Foucaud and coworkers generated nitrenes by lead tetraacetate oxidation of disubstituted *N*-aminosuccinimides (**13**) and alkenes (**Scheme 12**). The *singlet* nitrene react stereospecifically with *trans*-methyl cinnamate to form aziridines.[45]



13

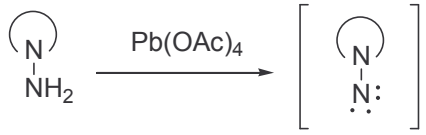
R_1 = H, Me, Ph and CH_2Ph
R_2 = Ph, CH_2Ph

Scheme 12: *Substituted N-aminosuccinimides (**13**).*[45]

The above nitrogen sources have limitation, since in most of the aziridination reactions the nitrogen sources requires large amounts of olefins to get good yields. This leads to a great waste of olefins. To address this problem, there are urgent needs to develop efficient nitrogen sources to make the aziridination process more effective and economical.

1.4.2 Mechanism of the synthesis of aziridines

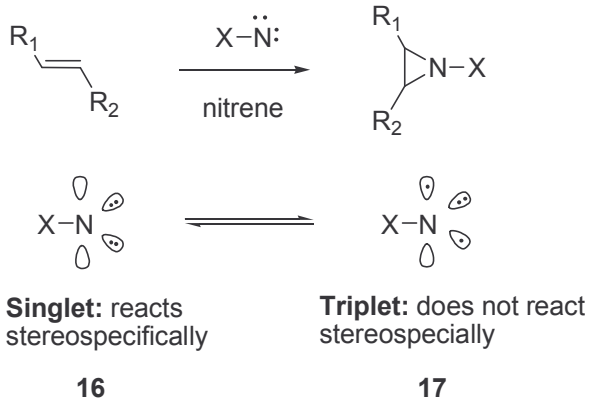
In the classical approach, the aziridination reactions believed to proceed through the generation of nitrenes.[38-42] Typically, nitrenes (**15**) were generated by thermal or photochemical decomposition of the corresponding azides[46] or oxidation of *N*-amino heterocycles (**14**) with lead tetraacetate (**Scheme 13**).[42]



14 **15**

Scheme 13: *Generation of nitrenes (**15**) by oxidation of N-amino heterocycles (**14**) with Pb(OAc)4.*[42-46]

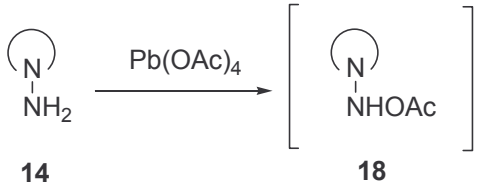
In the aziridination reactions, nitrenes were generated by oxidation of *N*-amino heterocycles with lead tetraacetate (**Scheme 14**), which give the mixtures of more reactive *singlet* (**16**) and more stable *triplet* (**17**) nitrenes. The *singlet* nitrenes, in which nitrogen may be imagined to retain its non-bonded electrons in *two* orbitals, each containing an *anti*-parallel electron pair, may react stereospecifically with 1,2-disubstituted alkenes.[3] Moreover, *triplet* nitrenes (having non-bonded electrons in *three* orbitals, one filled with an antiparallel electron-pair and two others being *semi*-filled with one electron each with parallel spin) may react in a two-step process with alkenes in which a N–C bond is formed in step wise process whereas *singlet* nitrenes may form both new bonds in a concerted process.[3]



16 **17**

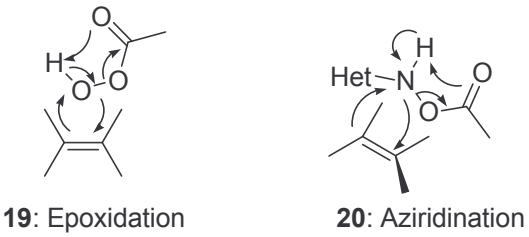
Scheme 14: *Singlet (**16**) and triplet (**17**) nature of nitrene.*[3]

Atkinson has further described that oxidation of *N*-amino heterocycles (**14**) with lead tetraacetate at -20 °C yield acetoxyaminoimides (**18**), not nitrenes as intermediate (**Scheme 15**).[47]



Scheme 15: *Generation of acetoxyaminoimides (**18**) as aziridinating agent.*[47]

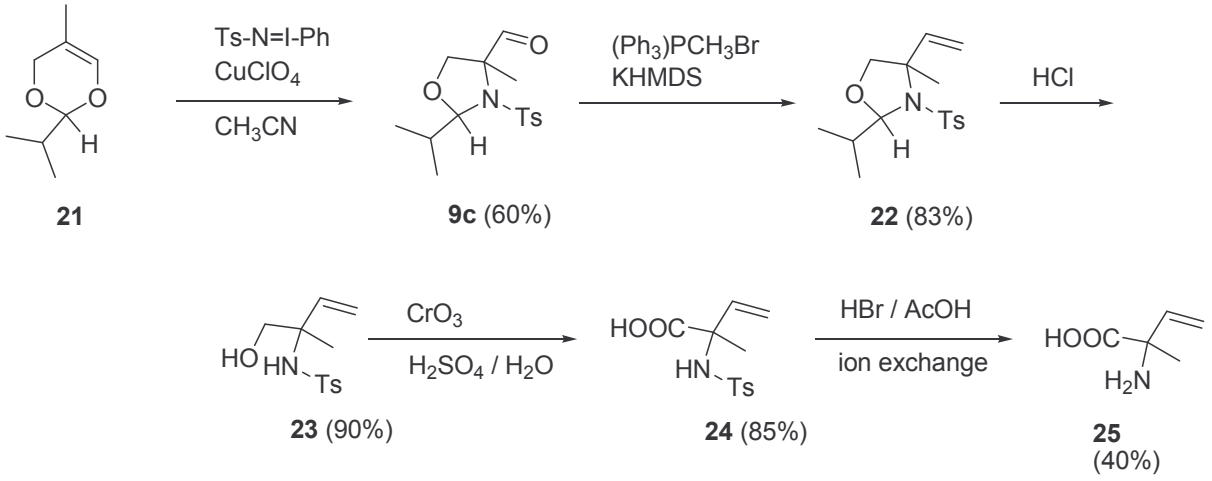
Atkinson further described that acetoxyaminoimide nitrogen equivalents of peroxyacetic acids are potential aziridinating agents which react *via* Bartlett mechanism comparable to the epoxidation (**Scheme 16**).[48]



Scheme 16: *Mechanism of epoxidation (**19**) and aziridination (**20**) reactions.*[48]

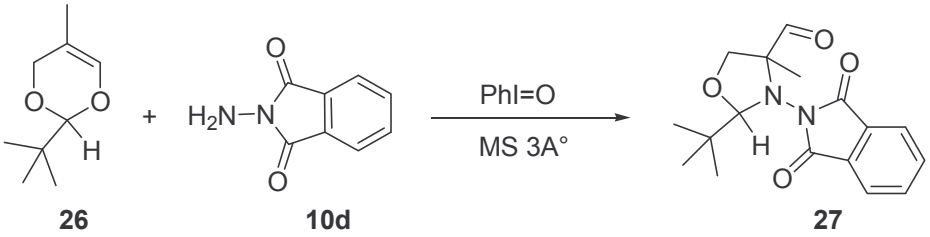
1.5 Task

In the group of Prof. H. Frauenrath aziridination reactions starting from functionalized olefins as 5-methyl-4*H*-1,3-dioxins have been investigated. For example the metal induced aziridination of 2-isopropyl-5-methyl-4*H*-1,3-dioxin (**21**) with nitrenes generated from *N*-(*p*-toluenesulfonyl)iminophenyliodinane (PhI=NTs) leads to the *N*-tosyl protected 4-methyl-l,3-oxazolidincarbaldehyde (**9c**). An intermediate formation of an aziridine and subsequent rearrangement to **9c** was suggested in the reaction mechanism. The oxazolidincarbaldehyde (**9c**) can be used as building block for the synthesis of unnatural amino acids, e.g. α-vinylalanine (**25**) as shown in (**Scheme 17**).[32]



Scheme 17: *Preparation of α-vinylalanine (**25**).*[32]

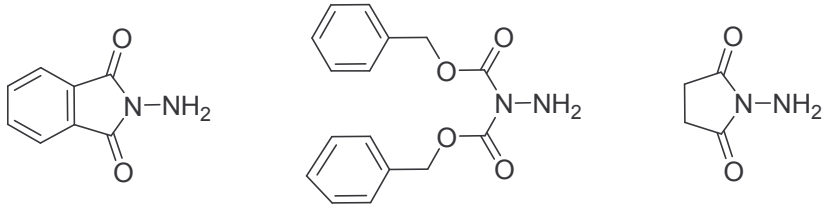
Furthermore another applied method of direct aziridination of the dioxin (**26**) yielding possible starting compounds for α-hydrazino acids was succeeded by the use of hydrazin derivatives like *N*-aminophthalimide (**10d**) after oxidation with the hypervalent iodine compound iodosyl benzene (Ph-I=O) (**Scheme l8**).[49]



Scheme 18: *Preparation of 2-tert-butyl-4-methyl-3-(1,3-dioxoisoindolin-2-yl)oxazolidine-4-carbaldehyde (**27**).*[49]

Associated with this aziridination method is the formation of phthalimide as byproduct; the removal is a tedious processes.[49] Similar observations were also described in the literature.[42] Regarding this background the question rises if nitrogen sources with reduced molecule architecture are basically applicable in the aziridination of olefins. Therefore hydrazine derivatives without an aromatic subunit and open chained instead of cyclic imine derivatives are in the focus of the following work.

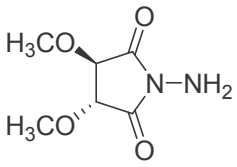
One related but non-aromatic hydrazine derivative of *N*-aminophthalimide (**10d**) is *N*-aminosuccinimide (**28**). Several methods of the synthesis of (**10d**) are known in the literature.[50] Aziridination reactions using **28** as a nitrogen source are unknown in the literature. Moreover, open chained, e.g. *N,N*-dibenzyloxycarbonylhydrazine (**12**) as a nitrogen source is rarely described (**Scheme 19**).[44]



10d **12** **28**

Scheme 19: *N-Aminophthalimide* (**10d**), *N,N-dibenzyloxycarbonyl hydrazine (12) and N-aminosuccinimide (28)*.

Optically active aziridines set themselves apart as versatile chiral building blocks that have found widespread use in the asymmetric organic synthesis because ring opening can be performed under high regio-and stereoselectlity (**Scheme 20**).[51]



(3*R*,4*R*)-**29**

Scheme 20: *(3R,4R)-(+)-N-amino-3,4-dimethoxysuccinimide (29)*

Based on the simple architecture of *N*-aminosuccinimide (**28**) the synthesis and the application in aziridinations of the C_2 symmetric modified (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxysuccinimide (**29**) with prochiral olefins are planned.

2 Theoretical section

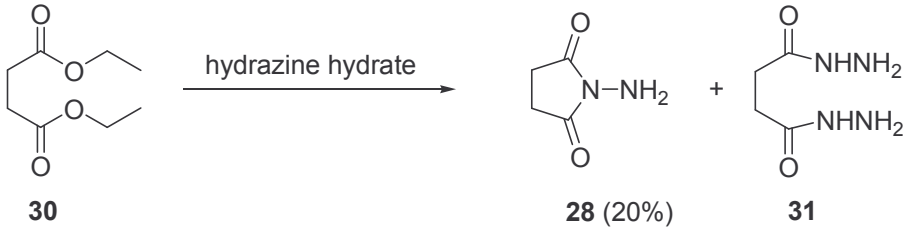
2.1 Synthesis of nitrogen sources for the aziridination of alkenes

N-Amino heterocycles like *N*-aminophthalimide (**10d**) and related compounds have been established in their use as nitrene sources for the transformation of alkenes to aziridines. Typically, these compounds are containing an *N*-amino imide moiety and prepared by reaction of hydrazine hydrate with anhydrides,[52] dicarboxylic acids,[53] and dicarboxylic esters compounds.[54,55] *N*-Aminophthalimide (**10d**) was prepared by reaction with phthalimide and hydrazine hydrate,[50] which has been extensively used in aziridination reactions. Further research was directed towards protected hydrazines for the preparation of *N*-amino heterocycles. For example Krause and coworkers[52] described the synthesis of various *N*-amino compounds by reaction of Boc-protected hydrazine with anhydrides to yield Boc-protected *N*-amino compounds. These compounds were deprotected under acidic conditions, e.g. hydrochloric acid, to form the hydrochloride salts, which give the free *N*-amino compounds in good to excellent yields when treated with alkali. Aziridination reactions using *N*-aminosuccinimide (**28**) are unknown in the literature.

2.1.1 Synthesis of *N*-aminosuccinimide

2.1.1.1 Literature methods for the preparation of *N*-aminosuccinimide

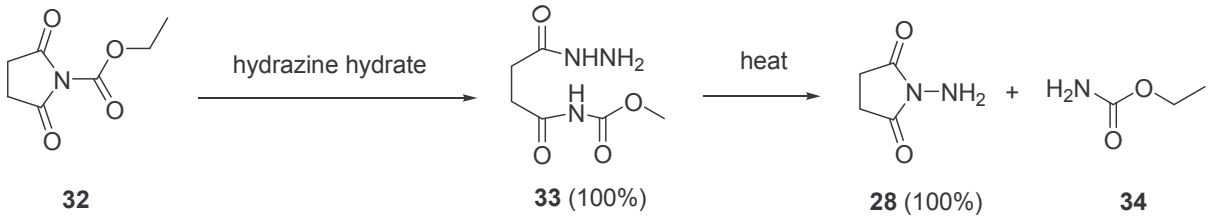
In 1915 Curtius[57] disclosed a method for the preparation of *N*-aminosuccinimide (**28**). Diethyl succinate (**30**) was reacted with hydrazine hydrate to give succindihydrazide (**31**), *N*-aminosuccinimide (**28**) and a lot of unknown side products (**Scheme 21**). The yield of *N*-aminosuccinimide was very low.



Scheme 21: *Curtius method for the preparation of N-aminosuccinimide **28**.*[57]

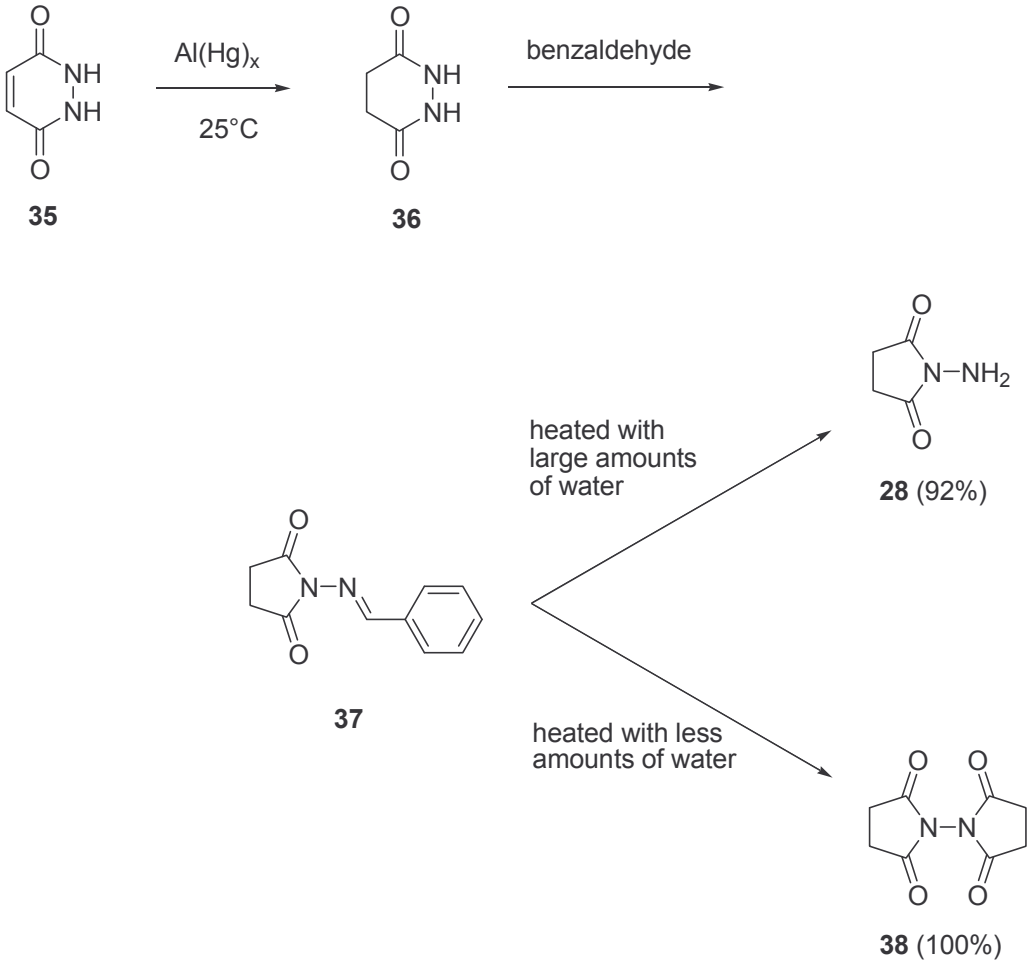
Later on Hedaya *et al.*[58] used the method of the Gabriel synthesis by reaction of *N*-carbethoxysuccinimide (**32**) with hydrazine hydrate to give *N*-amino-*N´*-

carbethoxysuccinimide (**33**), which was further reacted by heating on a sand bath to give *N*-aminosuccinimide (**28**) in molar yields, most likely as hydrate (**Scheme 22**).



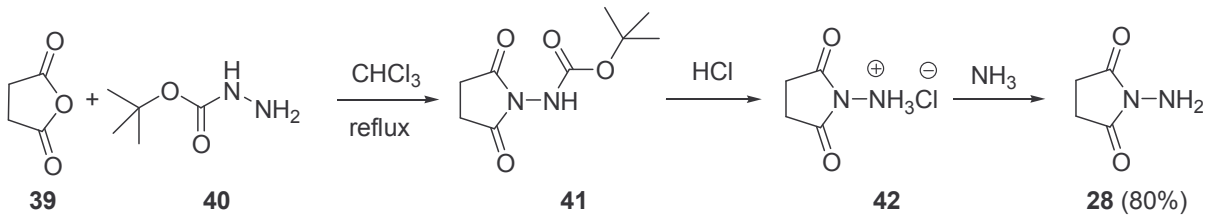
Scheme 22: *Hedaya method for the preparation of N-aminosuccinimide **28**.*[58]

According to the method from Feuer and Gut, the cyclic succinhydrazide (**36**) was prepared from maleic hydrazide (**35**) in presence of aluminum amalgam, and was reacted with benzaldehyde to form *N*-benzylideneamino succinimide (**37**). In the suspension of *N*-benzylideneamino succinimide (**37**), a large excess of water was added, and water was removed to give an oily *N*-amino succinimide (**28**) with 92% yield (**Scheme 23**).[59,60] When lower amounts of water were used, bisuccinimyl (**38**) was obtained as byproduct. Hence this method has disadvantages, because there are possibilities to give bisuccinimyl (**38**) as side product. Moreover, concentration of water is always a tedious process.



Scheme 23: *Feuer and Gut method for the preparation of N-aminosuccinimide (**28**)*[59,60]

The apparently most practical method for the preparation of (**28**) was described by Krause *et al.*[56] (**Scheme 24**). **28** was prepared from the HCl salt (**42**) with ammonia with 80% yield. The salt (**42**) could be obtained by reaction of equal molar amounts of succinic anhydride (**39**) and *tert*-butyl carbazate (**40**) in chloroform. The deprotection of Boc group was performed using HCl to give salt (**42**).



Scheme 24: *Krause method for the preparation of N-aminosuccinimide (**28**).*[56]

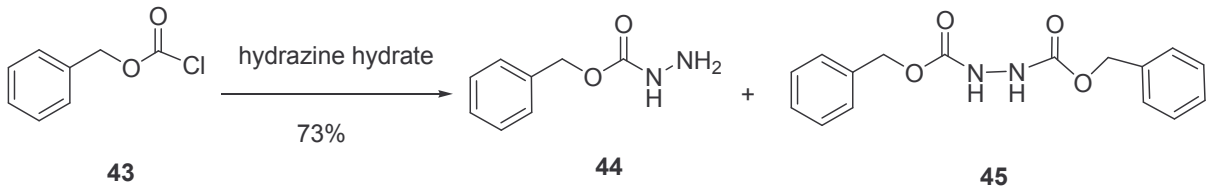
Portoghese modified Krause's method by reaction of succinic anhydride (**39**) and *tert*-butyl carbazate (**40**) in presence of DCC (*N,N´*-dicyclohexyl carbodiimide) to form Boc protected

N-aminosuccinimide (**41**). Subsequent deprotection was performed in the presence of HCl to give *N*-aminosuccinimide hydrochloride salt (**42**) with 82% yield.[61]

In the synthesis of *N*-aminosuccinimide (**28**), *N*-aminosuccinimide hydrochloride salt (**42**) was prepared by using Portoghese *et al.* method.[61] However, further transformation of (**42**) to (**28**) by treatment with ammonia (Krause method[56]) yields a solid, whose structure could not be assigned. Therefore, the synthesis of *N*-aminosuccinimide (**28**) by using Cbz protected hydrazine has been planned. It was expected that Cbz protected hydrazine could be easily deprotected under neutral condition by hydrogenation in presence of catalytic amounts of Pd on activated charcoal.

2.1.1.2 Synthesis of Cbz protected hydrazine

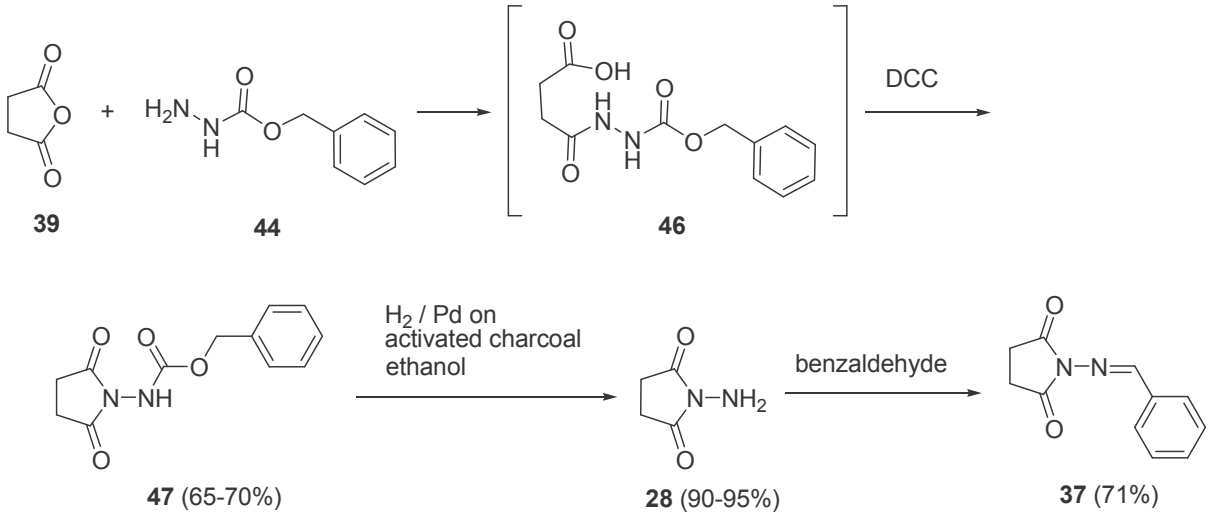
The mono-Cbz-protected hydrazine, i.e. benzyl carbazate, can be prepared from the literature known methods.[1] Benzyl chloroformate (**43**) was reacted with excess of hydrazine hydrate to form benzyl carbazate (**44**). The HCl generated during the reaction was trapped by excess of hydrazine hydrate. When the literature procedure for the preparation of benzyl carbazate was used, the GC purity of the reaction mixture was approximately 75 to 80%. The main impurity formed in the reaction was isolated by column chromatography and characterised as *N,N′*-dibenzyloxycarbonylhydrazine (**45**). However, the modified procedure by lowering the temperature (Lit.[62] described temperature is -5 °C) of the reaction mixture to -20 °C and increasing the addition time of benzyl chloroformate 5 to 6 h (Lit.[62] addition time 1 h) produced the benzyl carbazate (**44**) in 73% yield and *N,N′*-dibenzyloxycarbonylhydrazine (**45**) was formed < 5% (**Scheme 25**).



Scheme 25: *Modified method of Merkley and Warkentin[62] for the preparation of benzyl carbazate (44).*

2.1.1.3 Synthesis of *N*-aminosuccinimide using Cbz protected hydrazine

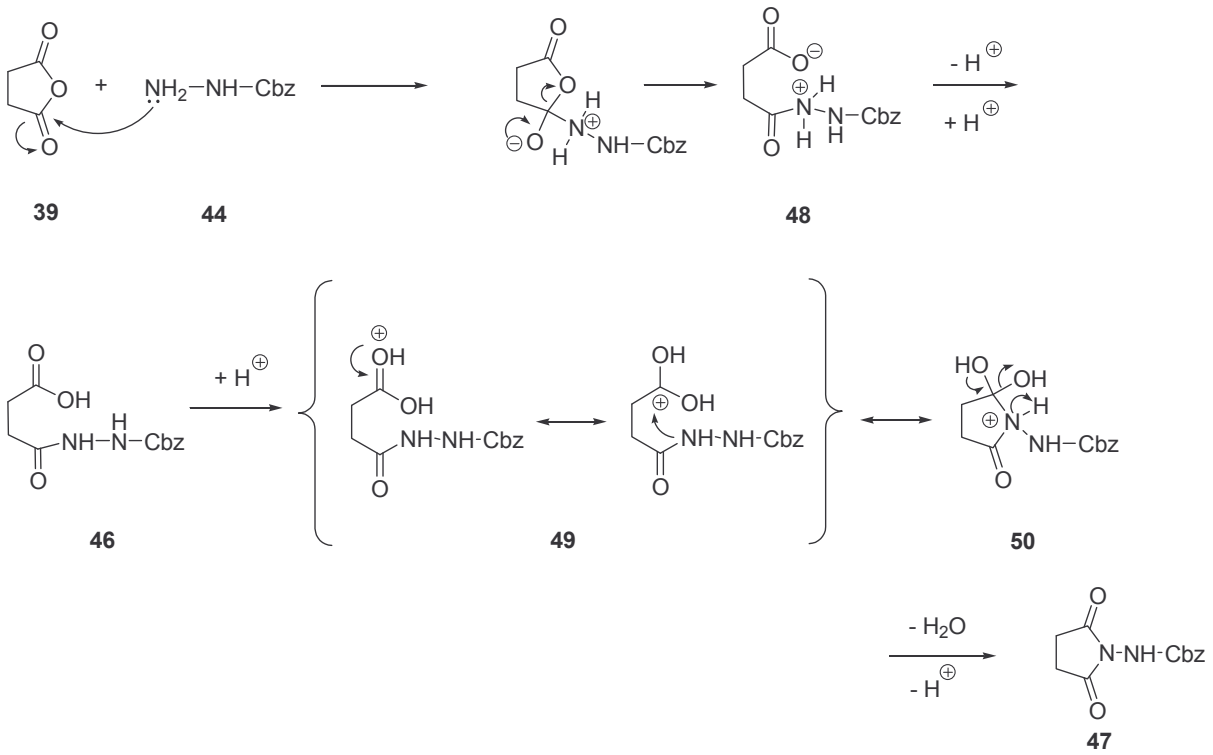
N-Aminosuccinimide (**28**) was prepared by reaction with equal amounts of succinic anhydride (**39**) and benzyl carbazate (**44**). In the first step, nucleophilic attack of benzyl carbazate (**44**) on **39** give monohydrazide acid (**46**). The cyclisation was performed in the presence of one equivalent of *N,N'*-dicyclohexylcarbodiimide (DCC) to give Cbz-protected *N*-aminosuccinimide (**47**) with 65-70% yield. Deprotection was achieved by hydrogenation using Pd on activated charcoal as a catalyst to give *N*-aminosuccinimide (**28**) as colourless oil in 90-95% yield. Compound **28** was further treated with benzaldehyde to form Schiff's base (**37**) with 71% yield, whose analytical data were identical with Lit[57] (**Scheme 26**).



Scheme 26: *Preparation of N-aminosuccinimide (**28**) and conversion to Schiff's base (**37**).*

2.1.1.4 Mechanism of the reaction of succinic anhydride and benzylcarbazate

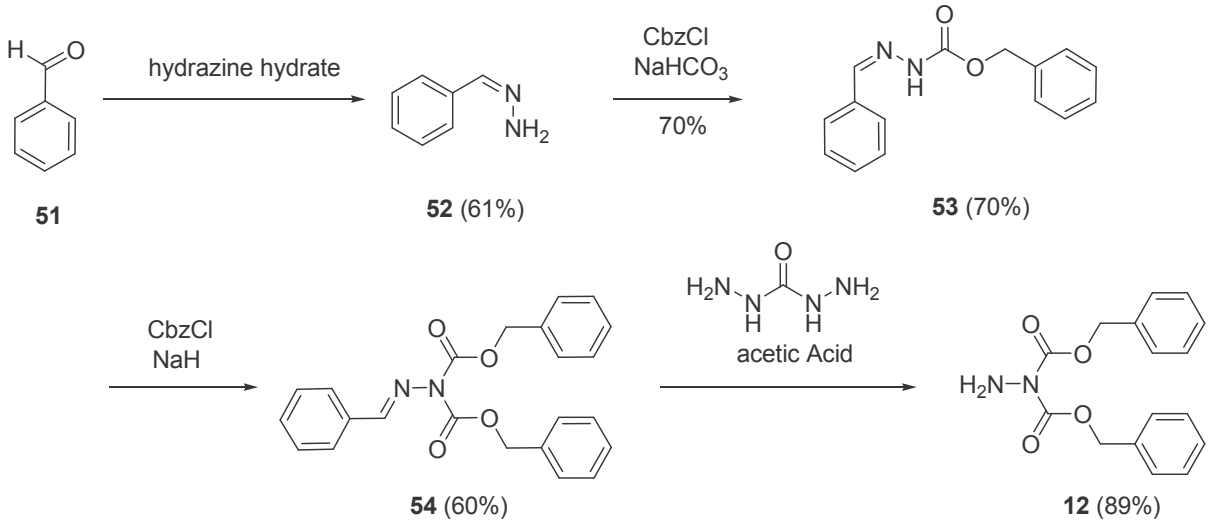
Nucleophilic attack of benzyl carbazate (**44**) on the carbonyl group of succinic anhydride (**39**) primarly leads to an intermediate (**48**), which after proton exchange give the acid (**46**). The acid was probably further protonated at the carbonyl oxygen to give the carboxonium ion as an intermediate (**49**). Attack of the lone pair electron of the nitrogen atom on the carboxonium ion leads to the ring closure. Elimination of water and deprotonation then leads to the Cbz protected *N*-aminosuccinimide (**47**) (**Scheme 27**).



Scheme 27: *Mechanism of the preparation of (2,5-dioxo-pyrrolidine)-carbamic acid benzyl ester (47).*

2.1.2 Synthesis of *N,N*-dibenzyloxycarbonylhydrazine

Benzylidene hydrazine (**52**) was prepared according to the method of Milcent by reaction with benzaldehyde (**51**) and hydrazine hydrate,[63] which was reacted with benzyl chloroformate in presence of a base to form mono-Cbz-protected Schiff's base (**53**). Furthermore, **53** was treated with benzylchloroformate in presence of sodium hydride to yield (**54**). The cleavage of Schiffs base was performed using carbohydrazide under acidic conditions, e.g. in presence of acetic acid to obtain *N,N*-dibenzyloxycarbonylhydrazine (**12**) (**Scheme 28**).[44]

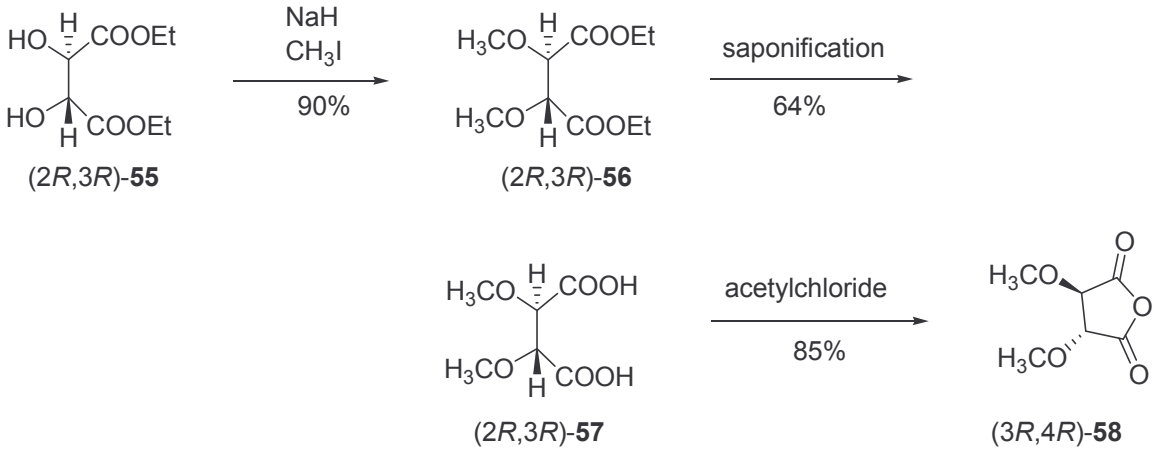


Scheme 28: *Milcent et al. method for the preparation of N,N-dibenzyloxycarbonylhydrazine (**12**).*[44]

2.1.3 Synthesis of optically active *N*-aminosuccinimides

2.1.3.1 Literature synthesis of (3*R*,4*R*)-(+)-3,4-dimethoxy succinic anhydride

(3*R*,4*R*)-(+)-3,4-Dimethoxy succinic anhydride (**58**) was prepared by using Felner and Schenker's method[64] (**Scheme 29**). Diethyl L-(+)-tartrate (**55**) was di-*O*-methylated with methyl iodide in presence of sodium hydride to yield di-*O*-methyl-L-(+) tartaric acid diethyl ester (**56**). Di-*O*-methyl-L-(+) tartaric acid (**57**) was obtained by saponification of (**56**), which was further cyclised with acetylchloride to form (3*R*,4*R*)-(+)-3,4-dimethoxysuccinic anhydride (**58**).

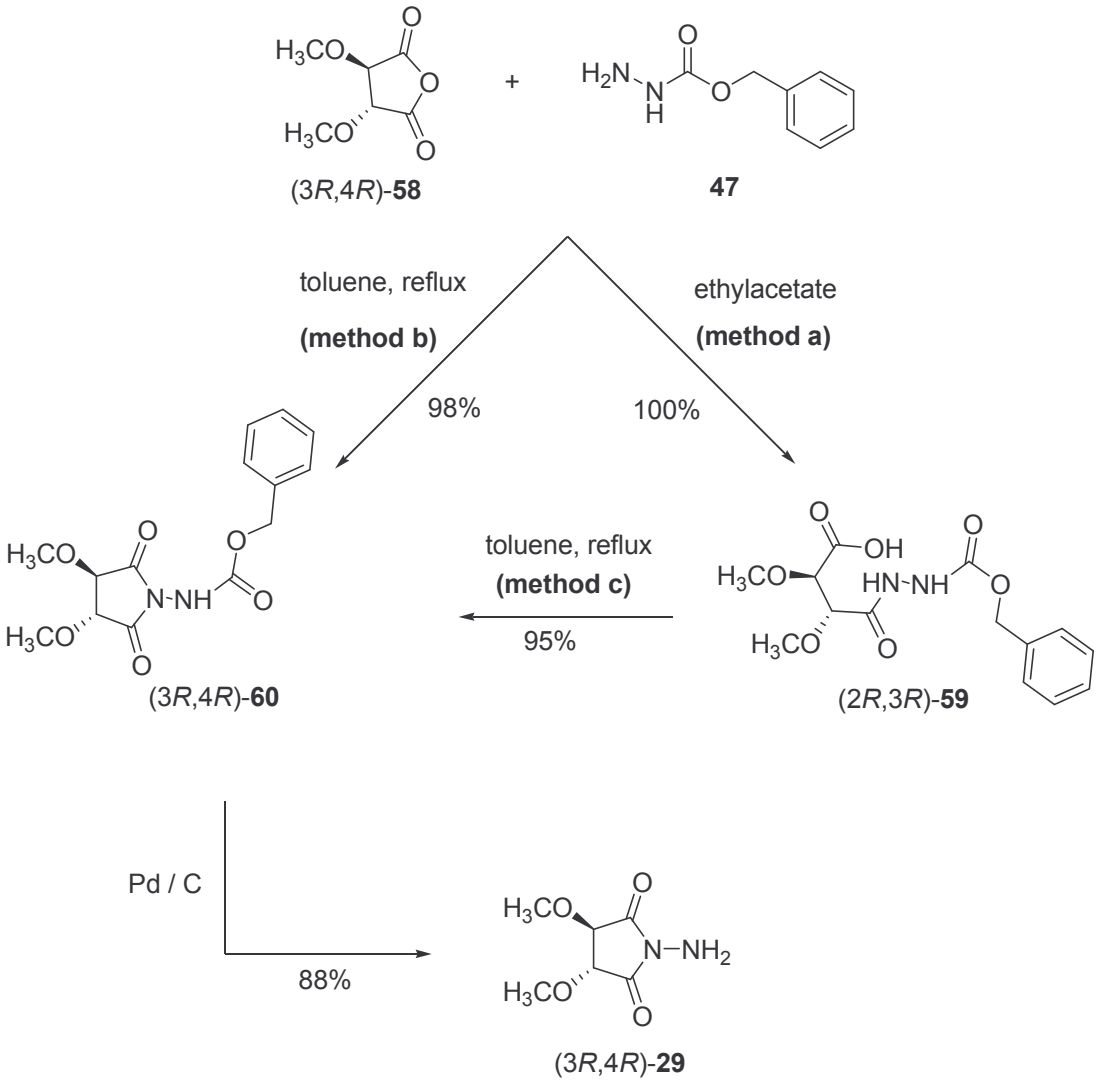


Scheme 29: *Felner and Schenker's method for the preparation of (3R,4R)-(+)-3,4-dimethoxy succinic anhydride (**58**).*[64]

2.1.3.2 Synthesis of (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide

The synthesis of (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succcinimide (**29**) could be achieved by treatment of (3*R*,4*R*)-(+)-3,4-dimethoxy succinic anhydride (**58**) with benzyl carbazate (**47**). Equal amounts of (3*R*,4*R*)-(+)-3,4-dimethoxy succinic anhydride (**58**) and benzyl carbazate (**47**) were reacted at room temperature to give acid **59** in quantitative yield (**Method a, scheme 30**). The cyclisation of **59** was achieved by refluxing the acid in toluene to yield Cbz protected (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**60**) (**Method c, scheme 30**) in 95% yield. Moreover, (**60**) can also be prepared in single step by reaction with equal amounts of (3*R*,4*R*)-(+)-3,4-dimethoxy succinic anhydride (**58**) and benzyl carbazate (**47**) in toluene as solvent. The reaction was driven to completion by azeotropic removal of water to give 98% yield (**Method b, scheme 30**). The deprotection of Cbz group was performed by

hydrogenation in presence of catalytic amounts of Pd on activated charcoal to give (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) in 88% yield.



Scheme 30: *Preparation of (3R,4R)-(+)-N-amino-3,4-dimethoxy succcinimide (**29**).*

2.2 Use of iodosylbenzene as oxidising agent

The aziridines are usually prepared by insertion of nitrenes in to the π bond of olefin. The nitrenes are generated by oxidation of *N*-amino imide moiety using several oxidising reagents. Rees and coworkers[65] and subsequently Atkinson[66] described the preparation of aziridines using lead tetra acetate (LTA) as oxidising agent of *N*-amino compounds. However, the LTA is known to be highly toxic and its storage as well as its use are troublesome. Similar in chemical properties and reactivity to Pb(IV) oxidising agents are iodine (III) species but without the toxic and environmental problems. The iodosylbenzene, PhI=O, is the most

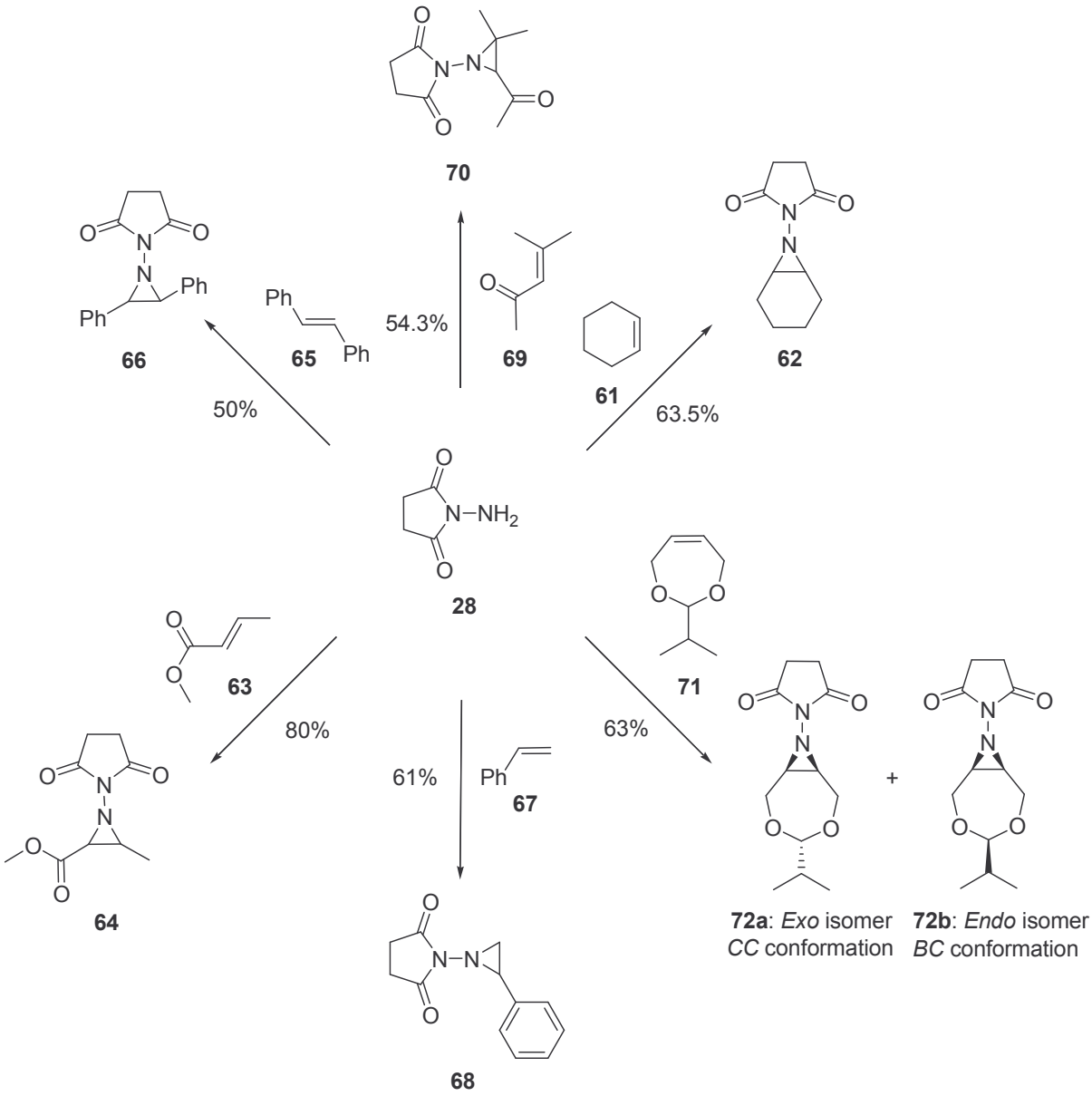
important and best investigated member of the family of iodosyl compounds. It is prepared by hydrolysis of $PhI(OAc)_2$ with aqueous NaOH.[67] Iodosylbenzene is a yellowish amorphous powder, which cannot be recrystallized due to its polymeric nature. Heating or extended storage at room temperature results in disproportionation of iodosylbenzene to PhI and colorless, explosive iodylbenzene, $PhIO_2$. Drying of PhI=O at elevated temperatures should be avoided because of the possibility of severe explosion.[68] However, handling of even large amounts of PhI=O at room temperature is relatively safe. Recent X-ray powder diffraction and EXAFS analysis of amorphous PhI=O clearly indicated a linear polymeric, asymmetrically bridged structure in the solid state having the expected T-shaped geometry around the iodine centers.[69]

2.3 Synthesis of aziridines using alkenes and *N*-amino succinimide as nitrogen source

2.3.1 Synthesis of aziridines using non functionalized alkenes and *N*-aminosuccinimide as nitrogen source

2.3.1.1 General aspects

The synthesis of aziridines has received much attention in recent years. Rees et al.[38] and others[70] demonstrated the oxidation of *N*-amino phthalimide (**10d**) with lead tetraacetate in presence of alkenes yield aziridines. The disadvantage of the above nitrogen source is that it often during aziridination reaction generates the *N*-amino phthalimide (**10d**) as by-product which makes the work-up troublesome. Moreover the molecular weight of the *N*-amino phthalimide (**10d**) is much more than the *N*-amino succinimide (**28**), so a smaller amounts of (**28**) is required to generate the aziridines. To explore further aziridination reactions, the reaction conditions were optimized for the synthesis of aziridines using cyclohexene (**61**) as a model substrate, *N*-amino succinimide (**28**) as nitrogen source in polar aprotic solvent, e.g. acetonitrile as well as dichloromethane. The yield of aziridine (**62**) was good when PhI=O was used as oxidising source in presence of activated molecular sieves (**Scheme 31**, **table 1**, **entry 1**), however the lower yield was observed when $PhI(OAc)_2$ was used as oxidising source (**Scheme 31**, **table 1**, **entry 2**). The roles of the molecular sieves are depending on reacton conditions. The molecular sieves may serve to trap water,[71] or as a sources of limited amounts of water.[72] The structure and the water content of molecular sieves may affect the yields and reproducibility of the reactions.[73]



Scheme 31: *Aziridination reactions using olefins and N-amino succinimide (**28**) as nitrogen source.*

Encouraged by the results of cyclohexene (**61**) as substrate further aziridination reactions using the functionalised as well as non functionalized olefins have been planned. When methyl crotonate (**63**) was used as substrate, $PhI(OAc)_2$ as oxidising source, the aziridine (**64**) was obtained in 80% yield (**Scheme 31**, **table 1**, **entry 4**). However, using mesityl oxide (**69**) as substrate gives aziridine **70** in moderate yields (**Scheme 31**, **table 1**, **entry 9**). In general yields are better when $PhI(OAc)_2$ was used as oxidising source. Moreover, the yields of aziridine (**70**) are better when $PhI(OAc)_2$ was used as oxidising source (**Scheme 31**, **table 1**, **entry 10**). Furthermore, when electron rich olefins, e.g. *trans*-stilbene (**65**) and styrene (**67**)

were used as substrates (**Scheme 31, table 1, entry 5-8**) moderate yield of aziridines **66** and **68** were observed.

Table 1: Preparation of aziridines using non functionalized olefins and *N*-aminosuccinimide (**28**) as nitrogen source.

Entry	Substrate	Solvent	Oxidising agent	Yield (%) [b]	Product
1	Cyclohexene (**61**)	CH_3CN	PhI=O, MS 3Å [a]	63.5 % [c]	**62**
2	Cyclohexene (**61**)	CH_2Cl_2	$PhI(OAc)_2$	48 % [c]	
3	Methyl crotoate (**63**)	CH_3CN	PhI=O, MS 3Å	66.5% [d]	**64**
4	Methyl crotoate (**63**)	CH_3CN	$PhI(OAc)_2$	80% [d]	
5	*trans*-Stilbene (**65**)	CH_3CN	PhI=O, MS 3Å	50% [e]	**66**
6	*trans*-Stilbene (**65**)	CH_3CN	$PhI(OAc)_2$	40% [e]	
7	Styrene (**67**)	CH_3CN	PhI=O, MS 3Å	55% [f]	**68**
8	Styrene (**67**)	CH_3CN	$PhI(OAc)_2$	61% [f]	
9	Mesityl oxide (**69**)	CH_3CN	PhI=O, MS 3Å	49% [f]	**70**
10	Mesityl oxide (**69**)	CH_3CN	$PhI(OAc)_2$	54.3% [f]	

a) In the case of PhI=O as oxidising agent, activated mol sieve 3Å was added to the reaction mixture.

b) Yields were determined after purification by column chromatography.

c) Conditions for column chromatography silica / cyclohexane / ethyl acetate (3:1).

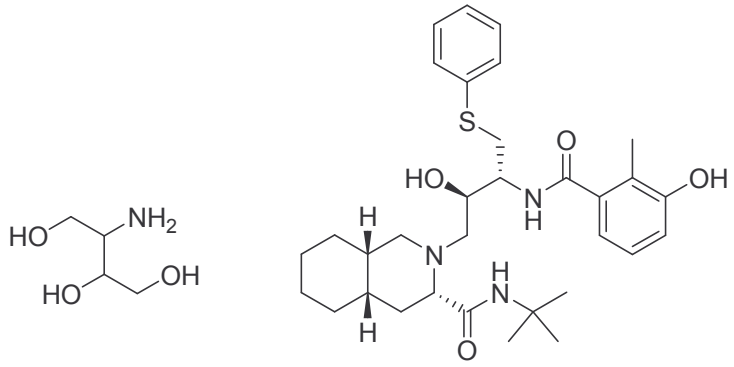
d) Conditions for column chromatography silica / petrol ether / ethyl acetate (4:1).

e) Conditions for column chromatography silica / petrol ether / ethyl acetate (4:1).

f) Conditions for column chromatography silica petrol ether / ethyl acetate (3:1)

2.3.1.2 Preparation of dioxepino aziridine using *N*-amino succinimide as nitrogen source

The dioxepino aziridines are very useful building blocks, since they are used in the synthesis of 2-amino-1,3,4-butanetriol (ABT-**73**) is a versatile building block for the preparation of nelfinavir (**74**), a potent *HIV-Protease Inhibitor* (**Scheme 32**).[74] Sharpless asymmetric aminohydroxylation has been utilized for the preparation of ABT equivalents employing 2-butene-1,4-diol derivatives as substrates.[75] The catalytic asymmetric aminolysis of 3,5,8-trioxabicyclo[5.1.0]octane provides optically pure 2-amino-1,3,4-butanetriol (**73**).[76]



73 **74**

Scheme 32 : *2-Amino-1,3,4-butanetriol (**73**) and nelfinavir (**74**).* [74-76]

Potential precursor of ABT, 1-(4-isopropyl-3,5-dioxa-8-aza-bicyclo[5.1.0]-pyrrolidine-2,5-dione (**72**) was prepared in a single step by aziridination of 4,7-dihydro-2-isopropyl-1,3-dioxepine (**71**) and *N*-aminosuccinimide (**28**) in aprotic polar solvents, e.g. acetonitrile and PhI=O as well as $PhI(OAc)_2$ were used as oxidising agents. The yields are better when $PhI(OAc)_2$ was used as oxidising agent. The crude mixture was purified by column chromatography and isomers (**72a**) and (**72b**) were separated (**Scheme 31, table 2**).

Table 2: Preparation of aziridines using 4,7-dihydro-2-isopropyl-1,3-dioxepine (**71**) and *N*-aminosuccinimide (**28**) as nitrogen source.

Entry [a]	Substrate	Oxidising agent	Yield (%) [b]	(d.r.) [c]	Product
1	4,7-dihydro-2-isopropyl-1,3-dioxepine (**71**)	PhI=O, MS 3Å	60% [d]	1:1.2	**72**
2	4,7-Dihydro-2-isopropyl-1,3-dioxepine (**71**)	$PhI(OAc)_2$	63% [e]	1:1	

a) MeCN was used as solvent.

b) Yields were determined after purification by column chromatography.

c) Diastereomeric ratio (d.r.) of the crude reaction mixture was determined by GC.

d) Conditions for column chromatography silica / petrol ether / ethyl acetate (1: 4).

e) Conditions for column chromatography silica / cyclohexane / ethyl acetate (1: 4).

In both the isomers, the isopropyl substituent at the acetalic unit was found in a *quasi equatorial* position. The single crystal XRD studies of isomer (**72b**) reveals that the dioxepanoaziridine moiety adopts a boat chair (*BC*) conformation (**Scheme 31**, **figure 2**), while for the *exo* isomer, (**72a**), the preferred conformation in the solid state is chair-chair

(*CC*) conformation (**Scheme 31**, **figure 1**). The substituent on the aziridine *N* atom occupies, in both cases, the *anti* position with respect to the dioxepane ring.[77]

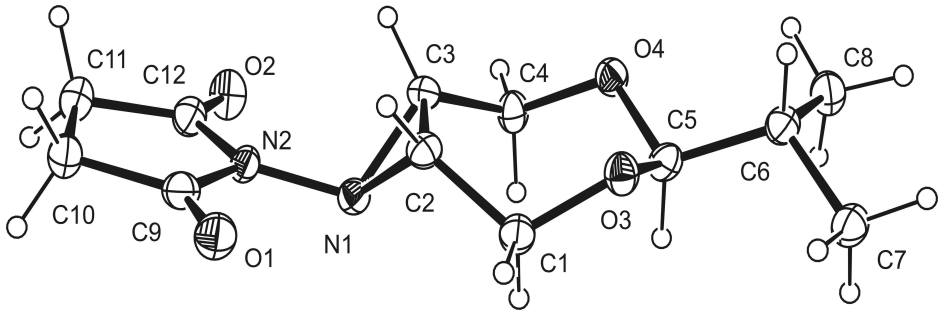


Figure 1: *Single crystal XRD exo isomer (**72a**) (CC conformation).*

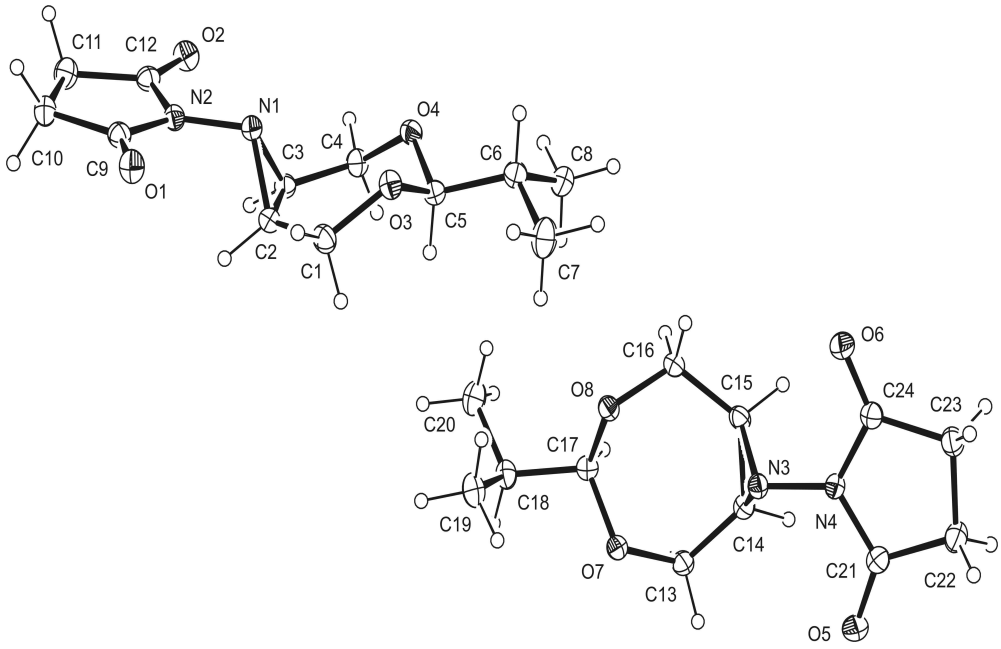


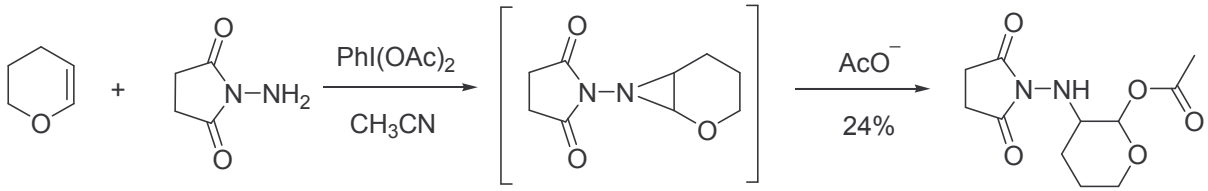
Figure 2: *Single crystal XRD of endo isomer (**72b**) (BC conformation).*

2.3.2 Synthesis of aziridines using functionalized alkenes and *N*-aminosuccinimide as nitrogen source

2.3.2.1 Synthesis of acetic acid 3-(2,5-dioxo-pyrrolidin-1-ylamino)-tetrahydro-pyran-2-yl ester

The aziridination reactions of functionalized olefins like enol ether are rarely described in the literature. When the aziridination reaction was performed using DHP (**75**) as substrate, *N*-aminosuccinimide (**28**) as nitrogen source and iodosylbenzene as oxidising agent (**Table 3**, **entry 2**), a polymerization take place, and probably the aziridine ring was very strained because of neighbouring oxygen atom present on the six membered ring, leads to polymerization. In contrast, aziridination reactions in presence of nucleophile have been investigated by using iodosylbenzenediacetate as oxidising agent (**Table 3**, **entry 1**). Probably the *in situ* generated nucleophile AcO^- attacks on the intermediate aziridine ring (**76**) to form the ring opened diastereomers (**77**) with diastereomeric ratio in the crude reaction mixture is 1:2.4, which was determined by GC. The similar observation was also described in the literature.[78]

Table 3: Aziridination reactions using 3,4-dihydro-2*H*-pyran (**75**) as substrate and *N*-aminosuccinimide (**28**) as nitrogen source and PhI=O as well as $PhI(OAc)_2$ as oxidising agent.



75 **28** **76** intermediate **77**

Entry [a]	Solvent	Oxidising agent	Yield [b]
1	CH_3CN	$PhI(OAc)_2$ [c]	24% [c]
2	CH_3CN	PhI=O/ MS 3Å	-

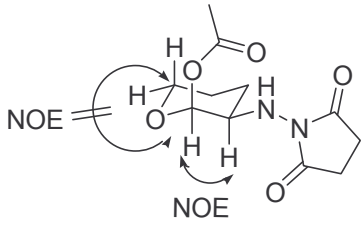
a) 2 eqivalents of 3,4-dihydro-2*H*-pyran was used.

b) Yield was determined after purification by column chromatography.

c) Conditions for column chromatography alox basic / ethyl acetate /petrol ether (1: 4).

The purifications of the crude product by bulb to bulb distillation, crystallization as well as column chromatography using silica gel as stationary phase were unsuccessful. Moreover, the purification was performed by column chromatography using alox basic as stationary phase

and ethylacetate: petrol ether mixture (1:4) as mobile phase to give the major diastereomers (**77**). The relative conformation of the major diastereomer was established by NOE. The NOE was observed between proton at C2 and C3, however, no NOE were observed among proton at C2 and protons (ax. and eq.) at C6. This indicates that the proton at 2 is in equatorial position. However, the relative configuration of proton at C3 could not be assigned by NOE (**Scheme 33**). Neverthless, the relative conformation was established by single crystal XRD, which indicated that the proton at C2 occupies the equatorial position and proton at C3 occupies the axial position. Hence the relative conformation in the solid state of major diastereomer is cis (**Figure 3**). Furthermore, the single crystal XRD has indicated that the hydrogen bonding among the molecules between nitrogen of NH group and proton of NH group of other molecules (**Figure 4**).



Scheme 33: *NOE interpretation of major diastereomer (77).*

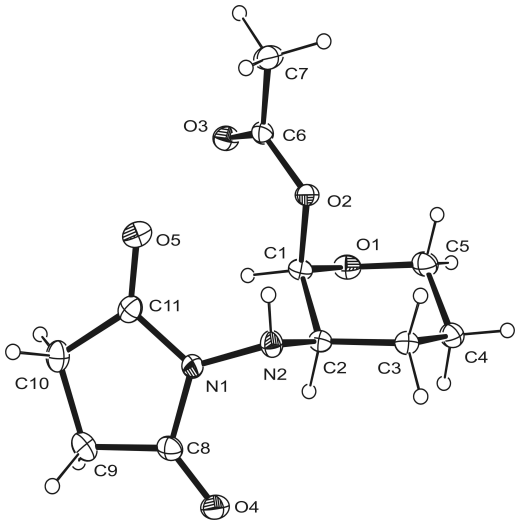


Figure 3: *Single crystal XRD of major diastereomer (77) is cis.*

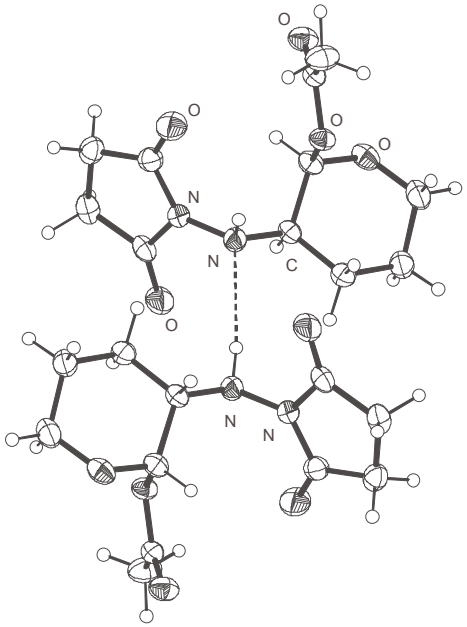


Figure 4: *Single crystal XRD of major diastereomer (77) (the hydrogen bonding among the molecules).*

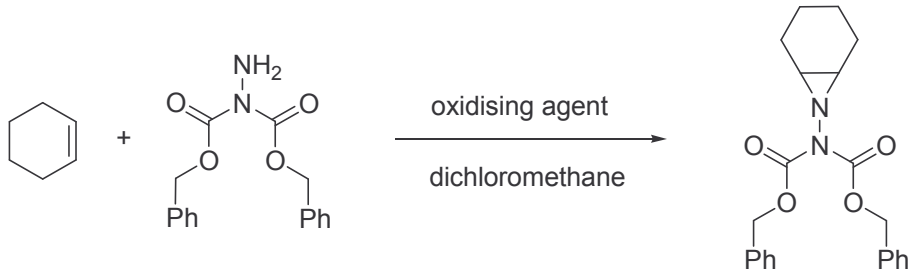
2.4 Aziridination reactions using *N,N*-dibenzyloxycarbonylhydrazine as nitrogen source

2.4.1 Synthesis of *N*-(dibenzyloxycarbonylamino)-7-azabicyclo[4.1.0]heptane

Milcent and coworkers[44] described the preparation of aziridines using *N,N*-dibenzyloxycarbonylhydrazine (**12**) as nitrogen source, lead tetraacetate was serving as oxidising agent at -20 °C and alkenes were used as solvent. The *N,N*-dibenzyloxycarbonylhydrazine (**12**) was prepared by literature known procedure.[44] However,

the modified aziridination procedure using 2 equivalents of cyclohexene (**61**) as a model substrate and $PhI(OAc)_2$ as oxidising agent at room temperature forms aziridine **78** in 60% yield (**Table 4**, **entry 1**). The use of PhI=O as oxidising agent in presence of molecular sieves 3Å leads to lower yields of aziridine **78** (**Table 4**, **entry 2**).

Table 4: Aziridination reactions using cyclohexene (**61**) as substrate and *N*,*N*-dibenzyloxycarbonylhydrazine (**12**) as nitrogen source, PhI=O as well as $PhI(OAc)_2$ as oxidising agent.

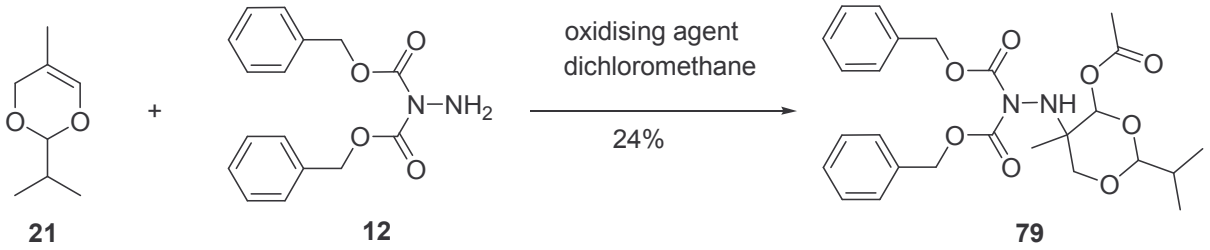


61 **12** **78**

Entry	Oxidising agent	Yield
1	$PhI(OAc)_2$	60%
2	PhI=O/ MS 3Å	52%

2.4.2 Synthesis of acetic acid 5-(*N*,*N*-dibenzylcarbonly-hydrazino)-2-isopropyl-5-methyl-1,3-dioxan-4-yl ester

To extend further strategy, we performed aziridination reactions using **12** as nitrogen source together with the cyclic vinyl acetal **21**, where the aziridination reactions were carried out using 2 equivalents of 2-isopropyl-5-methyl-4*H*-[1,3]dioxine (**21**) as substrate and PhI=O as oxidising agent in dichloromethane as solvent under inert atmosphere, the polymerization reaction took place. When the aziridnation reaction was performed using 2-isopropyl-5-methyl-4*H*-[1,3]dioxine (**21**), *N,N*-dibenzyloxycarbonylhydrazine (**12**) as nitrogen source and iodbenzenediacetate as oxidising agent in dichloromethane as solvent gave ring opened diastereomers 5-(*N,N*-dibenzyloxycarbonyl-hydrazino)-2-isopropyl-5-methyl-[1,3]dioxin-4-yl ester (**79**). The diastereomeric ratio in the crude reaction mixture was 1:1.8, determined by ^{1}H NMR. The crude product was purified by extraction with diethyl ether, chilled to -20 °C for 12 h. The solid was filtered and dried under vacuum to get 24% yield. The major diastereomer was lost during the work-up (**Scheme 34**).



21 12 79

Scheme 34: *Aziridination reaction using 2-isopropyl-5-methyl-4H-1,3-dioxine (**21**) as substrate, N,N-dibenzyloxycarbonylhydrazine (**12**) as nitrogen source and PhI(OAc)$_2$ as oxidising agent.*

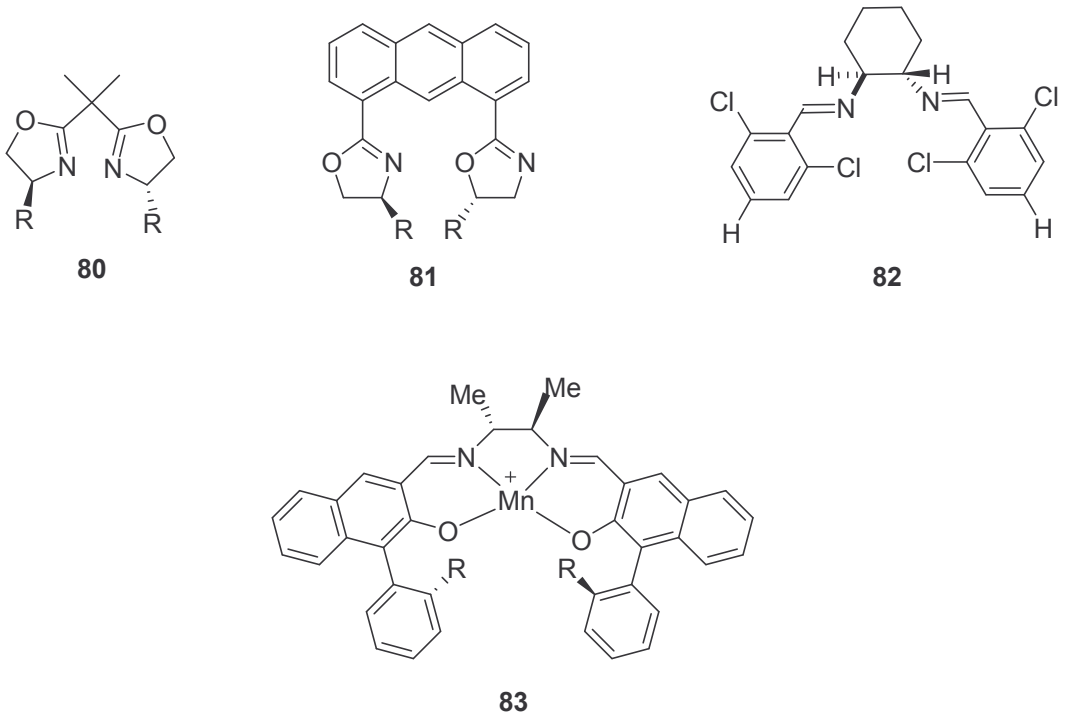
Table 5: Aziridination reactions using 2-isopropyl-5-methyl-4*H*-1,3-dioxine (**21**) as substrate, *N,N*-dibenzyloxycarbonylhydrazine (**12**) as nitrogen source and PhI=O as well as PhI(OAc)$_2$ as oxidising agent.

Entry	Oxidising agent	Yield
1	PhI=O	-
2	PhI(OAc)$_2$	24%

2.5 Asymmetric aziridination reactions

2.5.1 Literature procedures for the aziridination reactions using optically pure ligands

The synthesis of optically pure aziridines has received much attention in recent years. They are not only attractive intermediates in organic synthesis, but also can serve as useful chiral auxiliaries, chiral reagents and chiral ligands in asymmetric synthesis.[11,79] The asymmetric epoxidations[80] are much described in the literature, however counter part of asymmetric epoxidations, asymmetric aziridinations are little known. Evans,[81] Xu,[82] Jacobsen[83] and Katsuki[84] have described the preparation of optically active aziridines using chiral ligands, e.g. bis-oxazolins (**80**), 1,8-anthracene linked bis-oxazolines (**81**), salens (**82**) and magnesium salen complex (**83**) respectively, PhI=NTs as nitrene source and transition metal as catalyst (**Scheme 35**). However, these ligands are effective to a very limited number of olefins. Furthermore, the disadvantage of this aziridination reactions are the necessity of using the expensive and inconvenient PhI=NTs as nitrene source.[85]

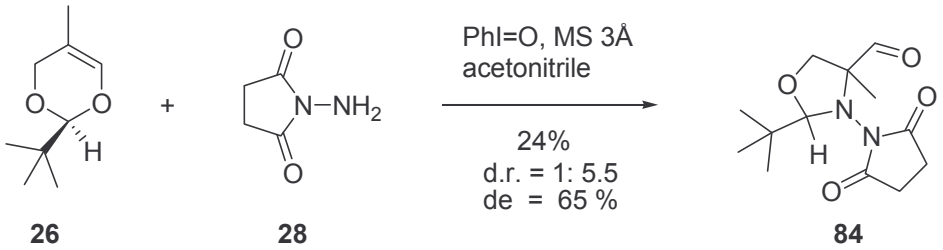


Scheme 35: *Optically active ligands used for asymmetric aziridination reactions.* [81-84]

2.5.2 Asymmetric aziridination reactions using optically active alkenes

2.5.2.1 Synthesis of 2-*tert*-butyl-4-methyl 3-(2,5-dioxopyrrolidin-1-yl)oxazolidine-4-carbaldehyde (84)

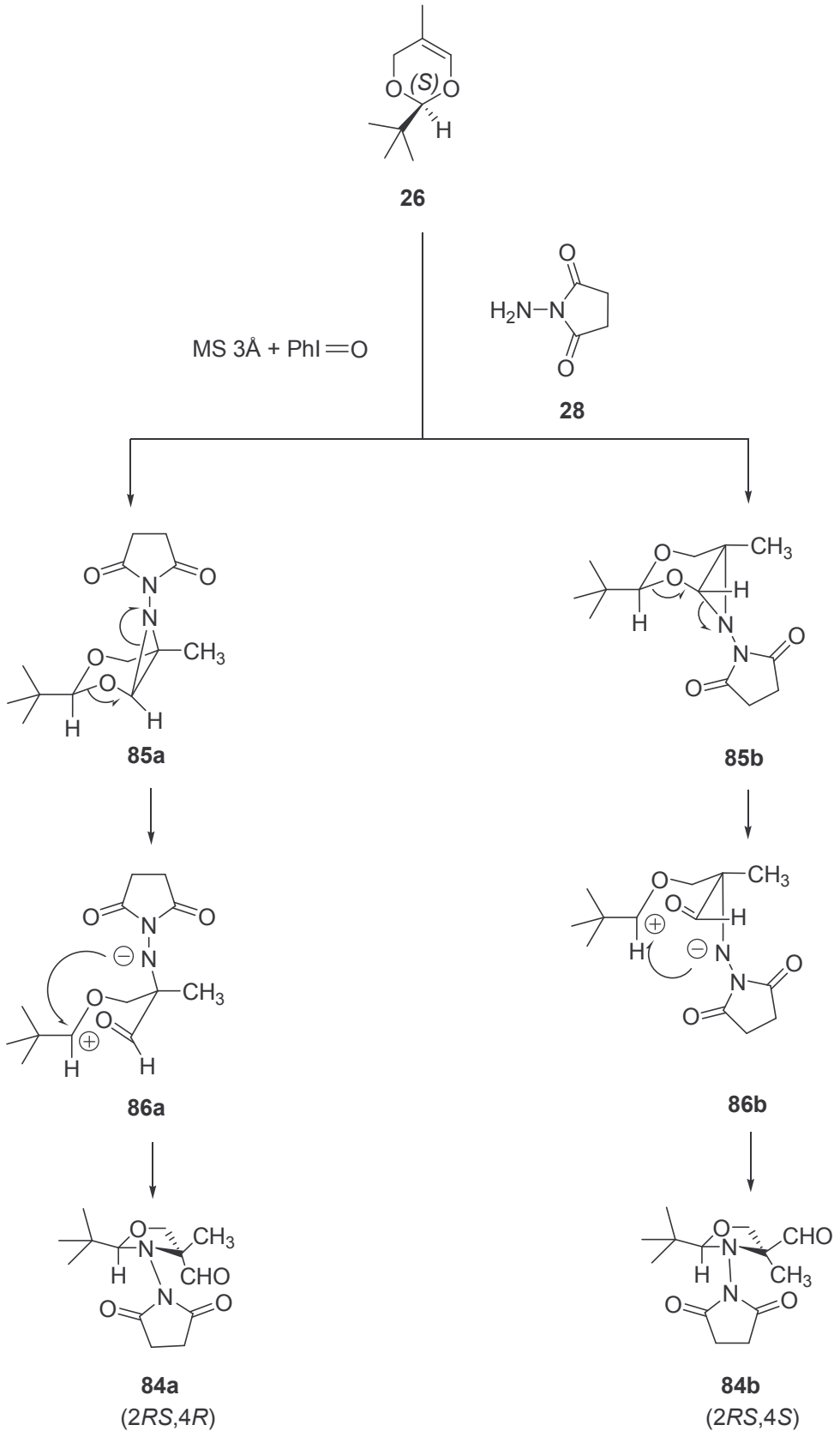
The literature references indicate that asymmetric aziridination reactions using optically active ligands have often limited success.[81-84] To address the problem of asymmetric aziridination reactions, the use of optically pure olefins has been planned. *N*-Amino succinimide (**28**) is a very useful nitrogen source for the aziridination reaction using functionalised as well as non functionalized olefins. In the work group of Prof. H. Frauenrath, *S*-(-)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (**26**) was synthesised with 85-92% ee.[86,87] Asymmetric aziridination reactions using *S*-(-)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (**26**) as substrate and *N*-aminosuccinimide (**28**) as nitrogen source and PhI=O as oxidising agent in presence of molecular sieves 3Å yield diastereomeric oxazolidinecarbaldehydes (**84**) (**Scheme 36**). The diastereomeric ratio in the crude reaction mixture is 1:5.5, determined by GC. The crude mixture was purified by column chromatography using silica gel as stationary phase and ethylacetate: cyclohexane mixture (1:4) as mobile phase gives **84** in 24% yield as white solid.



Scheme 36: *Aziridination reactions using S-(-)-2-tert-butyl-5-methyl-4H-1,3-dioxine (**26**) as substrate and N-aminosuccinimide (**28**) as nitrogen source and PhI=O as oxidising agent.*

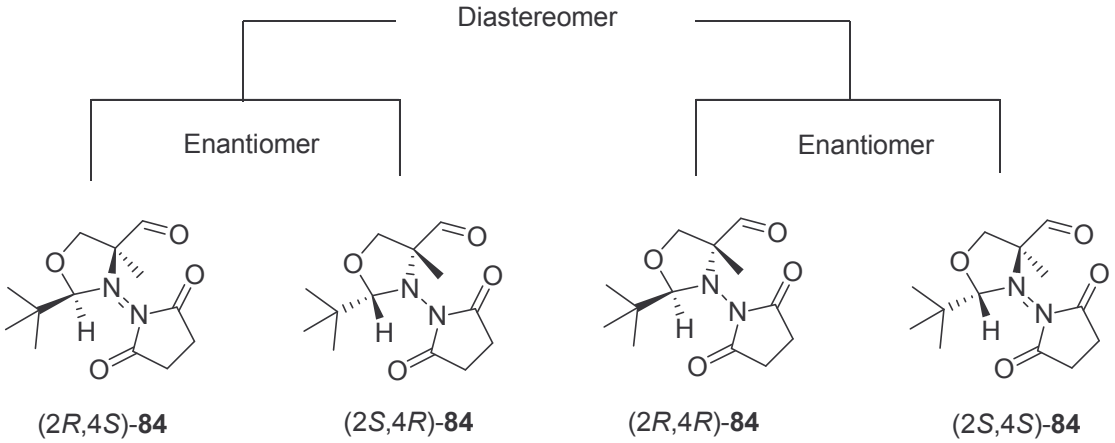
2.5.3 General aspects of the aziridination of enantiomeric enriched dioxin (26)

Oxazolidine-4-carbaldehyde (**84**) was prepared by aziridination reaction using *S*-(-)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (**26**), *N*-aminosuccinimide (**28**) as nitrogen source in presence of molecular sieves 3Å using PhI=O as oxidising agent. *S*-(-)-2-*tert*-Butyl-5-methyl-4*H*-1,3-dioxine (**26**) was prepared with 92% ee by literature known methods.[86,87] Theoretically, there are two possible sides of attack of nitrene on the π-bond of dioxine, i.e., one is upper side and other down side which leads in the formation of two new stereocenters to the diastereomeric aziridines (**85a**,**85b**) as intermediates (**Scheme 37**). The following rearrangement occurs probably in two steps. In the first the opening of aziridine (**85**) leads to intermediate (**86**) associated with the destruction of one of the new stereocenters at C3. The second ring contraction step to (**84**) forms a new stereocenter at the *O*/*N*-acetalic unit at C2, independent of stereo information of (**26**) which were rearranged by ring opening and ring contractions (**85a**,**85b**) to give 2-*tert*-butyl-4-methyl 3-(2,5-dioxopyrrolidin-1-yl)oxazolidine-4-carbaldehydes (**84a**,**84b**).



Scheme 37: *Proposed mechanism of aziridination reaction using S-(-)-2-tert-butyl-5-methyl-4H-1,3-dioxine (**26**) as substrate and N-aminosuccinimide (**28**) as nitrene source leads to the formation of diastereomeric oxazolidinecarbaldehydes (**84a**,**84b**).*

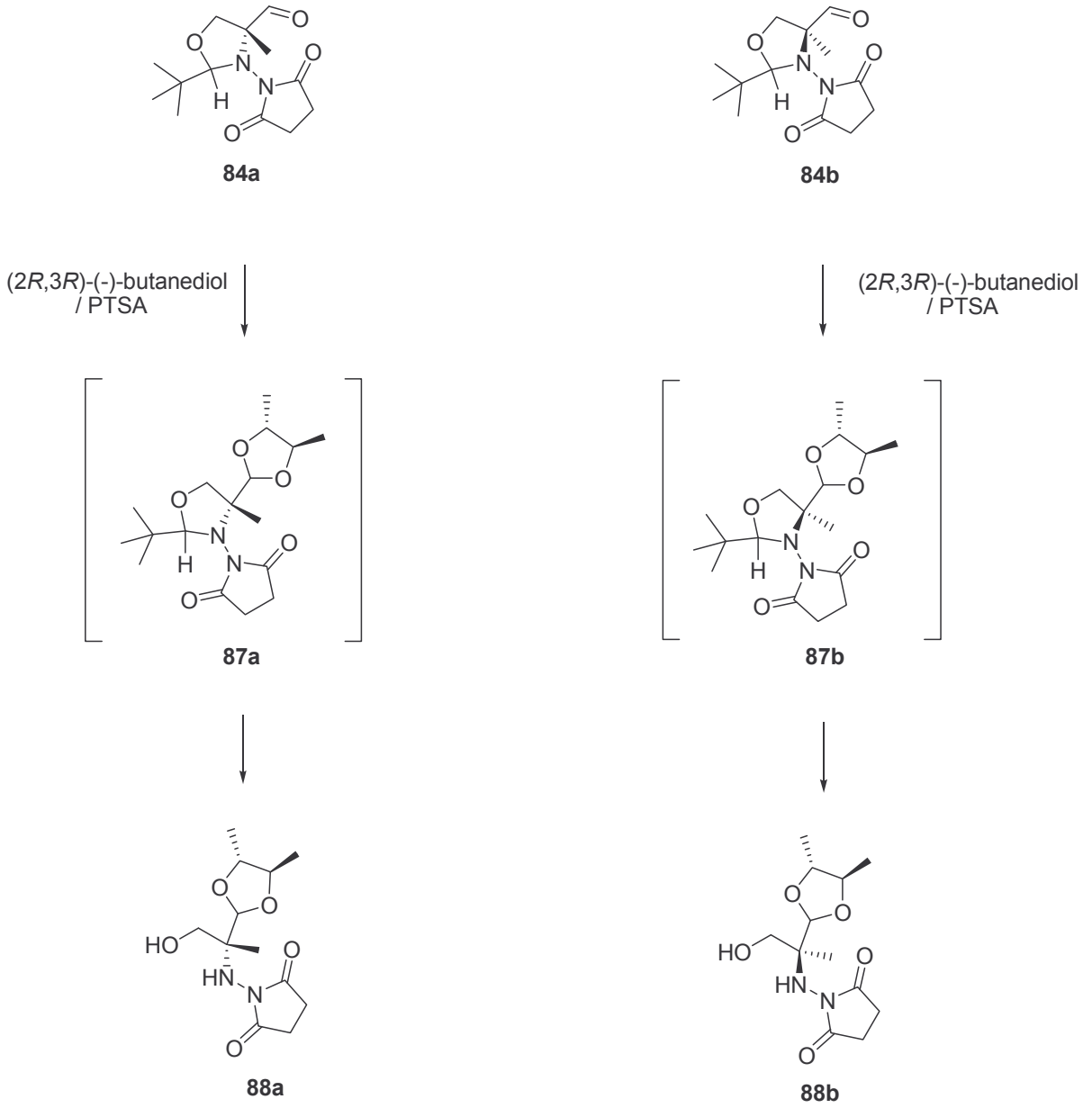
The 2-*tert*-butyl-4-methyl 3-(2,5-dioxopyrrolidin-1-yl)oxazolidine-4-carbaldehyde (**84**) has two chiral centers. The following figure shows the possible stereoisomers (**Scheme 38**).



Scheme 38: *The four stereoisomers of 2-tert-butyl-4-methyl 3-(2,5-dioxopyrrolidin-1 yl)oxazolidine-4-carbaldehyde (**84**).*

2.5.3.1 Determination of diastereomeric excess (de) of 2-*tert*-butyl-4-methyl 3-(2,5-dioxopyrrolidin-1-yl)oxazolidine-4-carbaldehyde (84)

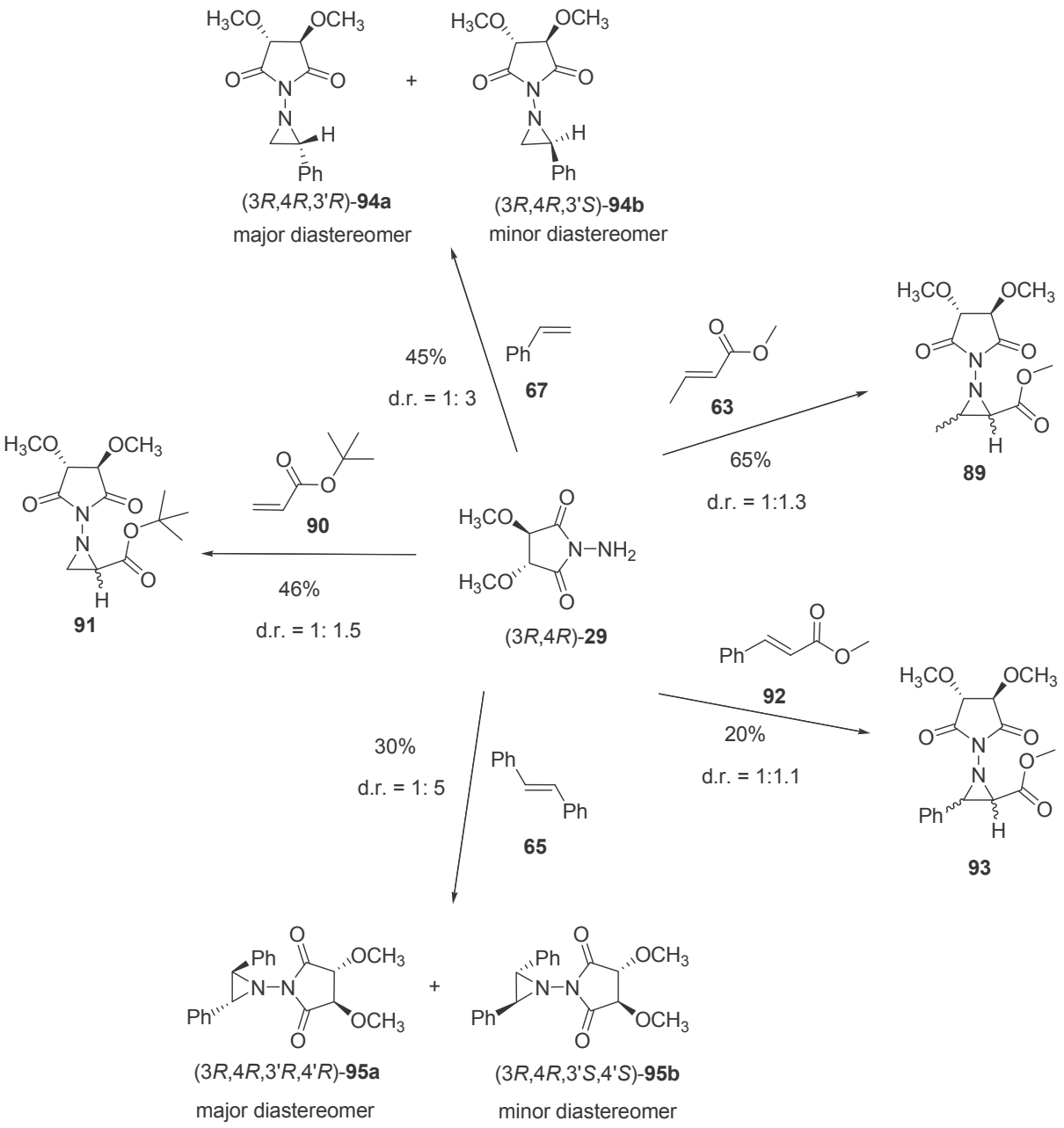
To determine the stereochemical course of the aziridination enantiomerically enriched dioxins (92% ee) the enantiomeric excess of the aziridination products **84** were determined by treatment with 3 equivalents of (2*R*,3*R*)-(-)-2,3-butandiol[88] in the presence of catalytic amounts of *p*-toluenesulfonic acid. This led to a mixture of dioxolanes **87** (**Scheme 39**). As the stereocenters in the 2-position of oxazolidinecarbaldehydes **84** are destroyed by transacetalization, the diastereomeric ratio of **88** together with the enantiomeric ratio of the starting material reflects the diastereomeric ratio of the intermediate aziridination step of **26 → 84**. (**Scheme 36**). Calculated from the 4:1 ratio of **88** the diastereoselectivity of the aziridination of (*S*)-(–)-**26** was 65% de.



Scheme 39: *Determination of diastereomeric excess (de) of 2-tert-butyl-4-methyl 3-(2,5-dioxopyrrolidin-1-yl)oxazolidine-4-carbaldehyde (**84**).*

2.5.4 Diastereoselective aziridination reactions using alkenes and optically active (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide as nitrogen source

Atkinson and coworkers described the reaction of optically pure 3-acetoxyaminoquinazolinone derivatives with alkenes in the presence of Lewis acid providing aziridines with good diastereoselectivities.[89] Chen and coworkers disclosed the reaction of *N*-enoyl oxazolidinones with *N*-aminophthalimide and lead tetraacetate in the presence of camphor derived chiral ligands providing the desired *N*-phthalimidoaziridines with moderate to good enantioselectivities.[90] The aziridination reactions of various chiral auxiliaries' derived *N*- and *O*-enones with *N*-aminophthalimide in presence of lead tetraacetate have been demonstrated with good diastereoselectivities.[91] Atkinson further described reagent-controlled diastereoselectivity in aziridination of prochiral alkenes with optically active nitrogen sources, where asymmetric induction arises from a chiral center present in the reagent. There is a preferred transition state geometry leading to high diastereoselectivity.[48,92] The high and low diastereoselectivity from the aziridines are not only the steric effects arising from the substituents from the chiral center. The conformational preference may account for the diastereoselectivity of addition reactions to the double bond; moreover there are always possibilities that the reacting conformations are not stable.[93] The nitrene was generated by oxidation of an optically pure *N*-aminoimide compound, (i) have singlet ground states and consequently always insert stereospecifically into π-bonds, (ii) show selectivity in competitive insertion into different π-bonds, (iii) insert into π-bonds substituted either by electron-donating or electronwithdrawing groups (or both), and (iv) show stereospecific formation of a single pyramid at the aziridine ring nitrogen in their addition to mono substituted alkenes.[94] The aziridination reactions using *N*-amino succinimide (**28**) and functionalised as well as non functionalized olefins yield moderate to good results. Furthermore, extending the same strategy the diastereoselective aziridination reactions using prochiral olefins and optically active, C_2 symmetric (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) as nitrogen source and PhI=O, $PhI(OAc)_2$ as oxidising agents, as well as study of steric and electronic effect of olefins have been planned.



Scheme 40: *Diastereoselective aziridination reactions using olefins and (3R,4R)-(+)-N-amino-3,4-dimethoxy succinimide (**29**) as nitrogen source.*

Table 6: Diastereoselective aziridination reactions using prochiral alkenes and (3*R*,4*R*)-(+)-*N*-amino-3,4 dimethoxy succinimide (**29**) as nitrogen source.

Entry	Substrate	Oxidising agent	Yield[b]	Aziridine	d.r.	Absolute configuration[d]
1[a]	*tert*-Butyl acrylate (**90**)	PhI=O, MS 3Å,3 eq. MgO	46%	(**91**)	1:1.5[c]	n.d.
2[a]	*tert*-Butyl acrylate (**90**)	$PhI(OAc)_2$	-	(**91**)[e]	-	-
3[a]	Methyl crotonate (**63**)	PhI=O, MS 3Å	65%	(**89**)	1:1.3[c]	n.d.
4[a]	Methyl cinnamate (**92**)	PhI=O, MS 3Å	20%	(**93**)	1:1.1[c]	n.d.
5[a]	Styrene (**67**)	PhI=O, MS 3Å	35%	(**94a**+**94b**)	1:3[c]	(3*R*,4*R*,3´*R*)
6[a]	Styrene (**67**)	PhI=O, MS 3Å, 3eq. MgO	45%	(**94a**+**94b**)	1:3[c]	(3*R*,4*R*,3´*R*)
7[f]	*trans*-stilbene (**65**)	PhI=O, MS 3Å	30%	(**95a**+**95b**)	1:5[g]	(3*R*,4*R*,3´*R*,4´*R*)

a) Acetonitrile was used as solvent.

b) Yields were determined after purification by column chromatography.

c) Diastereomeric ratio (d.r.) of the crude reaction mixture was determined by ^{13}C NMR, by taking the mean value of the reporter groups.

d) Absolute configuration of major diastereomer was determined by single crystal XRD.

e) Reaction mixture was polymerized.

f) DMF was used as solvent.

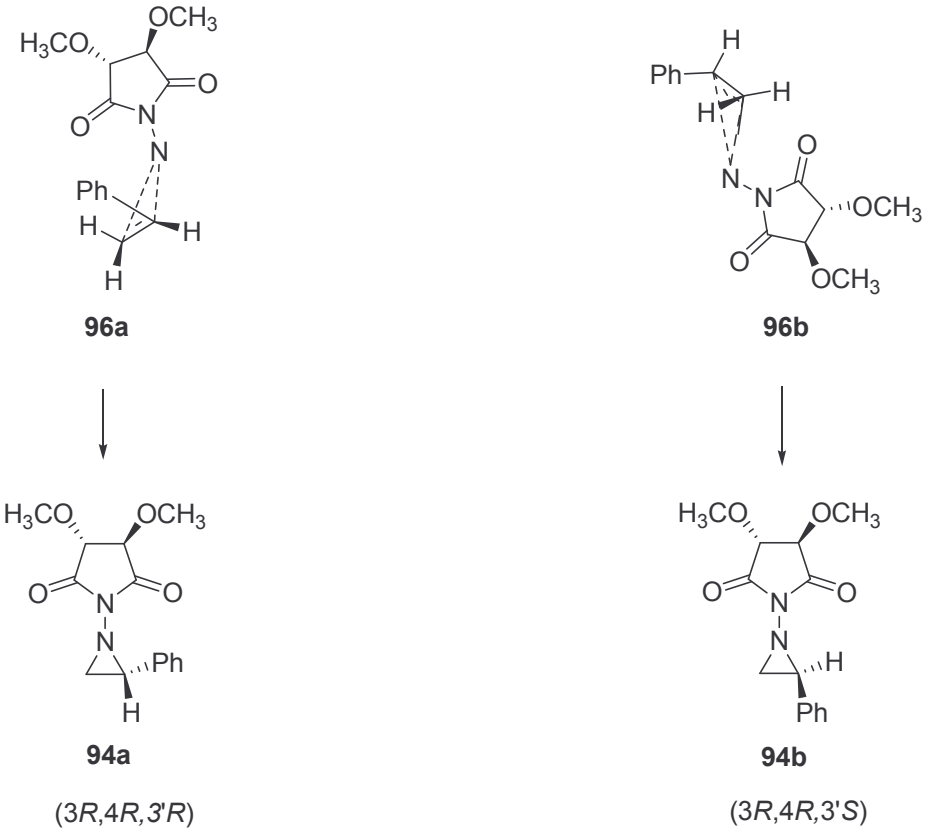
g) The diastereomeric ratio (d.r.) of the crude reaction mixture was determined by ^{1}H NMR by taking the mean value of the reporter groups.

The diastereoselective aziridination reactions were investigated using 10 equivalents of *tert*-butyl acrylate (**90**) and optically active (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) in anhydrous acetonitrile at room temperature. When $PhI(OAc)_2$ was used as oxidising agent, the reaction mixture was polymerized, whereas the use of PhI=O as oxidising agent in presence of MgO (**Scheme 40**, **table 6**, **entry 1**) yields aziridine (**91**). The work-up was done by removing the solvent under vacuum and the crude reaction mixture was purified by column chromatography using silica gel as stationary phase and petrol ether: diethyl ether mixture (1:3) as mobile phase yielding 46% of **91** as colourless viscous oil. The diastereomeric ratio of **91** in the crude reaction mixture was 1:1.5, determined by ^{13}C NMR. The low diastereomeric ratio of **91** revealed that the aziridination was not stereoselective even though the substrate is containing a bulky *tert*-butyl group. However, the role of MgO is not

clear; probably maintaing pH basic during the aziridination reaction to prevent polymerization. Furthermore, aziridination reactions were performed using two equivalents of methyl crotonate (**63**), (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) as nitrogen source and iodbenzenediacetate as oxidising agent give aziridine (**89**). The crude reaction mixture was purified by column chromatography using silica gel as stationary phase and ethylacetate: petrol ether mixture (1:3) as mobile phase give (**89**) in 65% yield. The diastereomeric ratio in the crude reaction mixture was 1:1.3 (**Scheme 40**, **table 6**, **entry 3**). From the results described above it was concluded, that attack of a nitrene or nitrenoid species genertaed by oxidation of optically active (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**), there are no discrimination between the two phases of π-bonds of (**63**) and (**90**). Hence, aziridines **89** and **91** could not yielded to a good diastereomeric ratios (dr). When methyl cinnamate (**92**) was used as substrate, (**29**) as nitrogen source and iodosylbenzene as oxidising agent, the diastereomeric ratio in the crude reaction mixture was 1:1.1. The crude reaction mixture was purified by column chromatography using silica gel as stationary phase and petrol ether: diethyl ether mixture (1:1) as mobile phase to give aziridine **93** in 20% yields (**Scheme 40**, **table 6**, **entry 4**). This observation leads to the conclusion that the diastereoselectivities of the aziridination reactions are not only depending on the bulky substituent present in the substrates but also the relative conformation of the diastereomers. The bulky group, e.g. phenyl group has no influence on the diastereoselectivity using substrate **92** probably the conformational preferences with the ester group in olefins as reducing effect to diastereoselectivity. Since the above diastereoselective aziridination reactions using substrates (**63**), (**90**) and (**92**) were not promising, hence further aziridination reactions using electron rich alkenes have been planned.

The diastereoselective aziridination reactions were performed using ten equivalents of styrene (**67**) and optically active (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxysuccinimide (**29**) as nitrogen source and PhI=O as oxidising agent, acetonitrile as solvent give aziridine (**94**) in 35% yield as a white amarphous solid (**Scheme 40**, **table 6**, **entry 5**). When the above experiment was repeated in presence of six equivalents of MgO, the yield of isolated aziridine **94** was enhanced to 45% (**Scheme 40**, **table 6**, **entry 6**). The diastereomeric ratio in the crude reaction mixtures were similar i.e. 1:3. This reveals that the nitrene generated by oxidation of optically active (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) is trapped by styrene (**67**) in diastereoselective manner. There are two possible sides of attack on the π-bond of (**67**). Moreover, using a transition state geometry (TSG) for nitrene insertion to styrene (**67**) may leads to asymmetric induction due to chiral centers at position 2 and 3 were able to

bring about discrimination in the addition of nitrene between two faces of styrene (**67**). There are two possible sides for nitrene attack on the styrene (**67**), i.e. two diastereoisomeric transition states are illustrated in (**96a**, **96b**), from which the chiral induction may be depend on the better fit of the chiral substituents with the aromatic ring. There may be secondary interaction possible between the aromatic ring and nitrogen or electronegative substituent present on **29**. In the transition state geometry (**96a**) was favoured over (**96b**). Thus the two diastereomers (**94a**, **94b**) were formed (**Scheme 41**).



Scheme 41: *Proposed transition state geometry for the aziridination reactions using styrene (**67**) as substrate with optically active (3R,4R)-(+)-N-amnio-3,4-dimethoxysuccinimide (**29**) as nitrene source.*

The absolute configuration of major diastereomer (3*R*,4*R*)-3,4-dimethoxy-1-((*R*)-2-phenylaziridin1-yl)pyrrolidine-2,5-dione (**94a**) was established by single crystal XRD (**Figure 5**). This indicates that the transition state geometry (**96a**) is favoured over (**96b**).

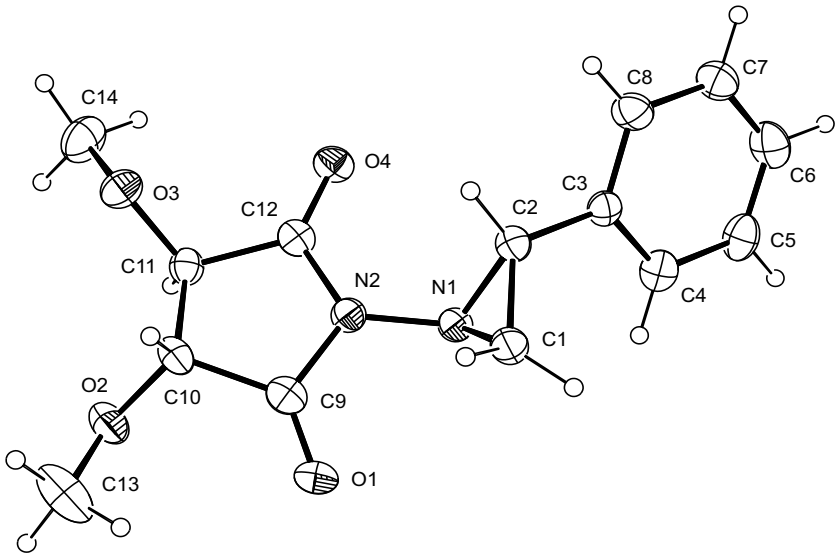


Figure 5: *Single crystal XRD of major diastereomer (3R,4R)-3,4-dimethoxy-1-((R)-2-phenylaziridin1-yl)pyrrolidine-2,5-dione (**94a**).*

Encouraged by the diastereoselective aziridination reactions using styrene (**67**) as substrate, the study was further extended to use the more sterically hindered substrate, e.g. 2 equivalent of *trans*-stilbene (**65**) as substrate and **29** as nitrogen source, 3 equivalent of magnesium oxide as additive, hypervalent PhI=O as oxidising agent, in presence of molecular sieves 3Å yielding diastereoselective aziridines (**95a**, **95b**). When the acetonitrile was used as solvent, the aziridines (**95**) were not formed. However, when the reactions were carried out using anhydrous DMF as solvent, diastereoselective aziridinations occurred. The work-up was done by removing the solvent under vacuum and crude product was purified by column chromatography using silica gel as stationary phase and petrol ether: diethyl ether mixture (1:1) as mobile phase give **95** in 30% yield. The diastereomeric ratio in the crude reaction mixture was 1:5, determined by ^{1}H NMR. This indicates that there were enough discrimination during nitrene trap between the two phases of the prochiral *trans*-stilbene (**65**), resulted diastereoselective aziridine **95a**. The absolute configuration of major diastereomer was determined by single crystal XRD as (3*R*,4*R*)-3,4-dimethoxy-1-((2*R*,3*R*)-2,3-diphenylaziridin-1-yl)pyrrolidine-2,5-dione (**95a**) (**Figure 6**).

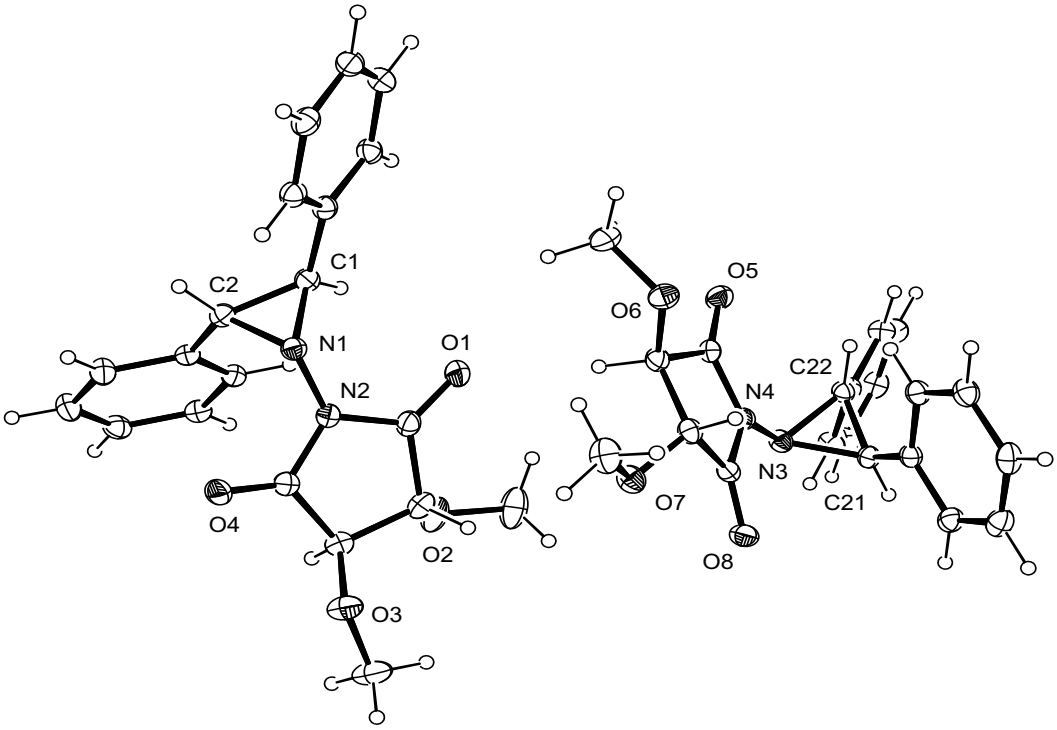
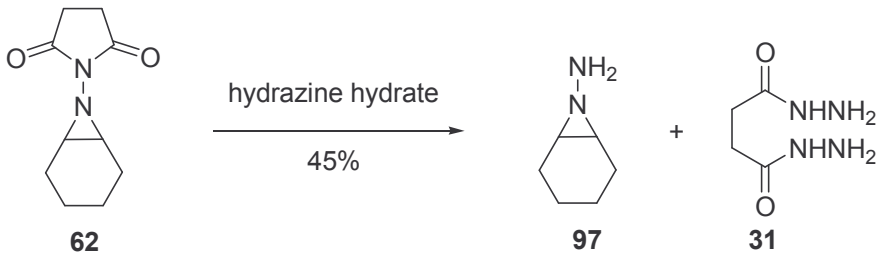


Figure 6: *Single crystal XRD of (3R,4R)-3,4-dimethoxy-1-((2R,3R)-2,3-diphenylaziridin-1-yl)pyrrolidine-2,5-dione (**95a**).*

2.6 Synthesis of *N*-amino aziridines by cleavage of protecting group with hydrazine hydrate.

2.6.1 Synthesis of 7-aza-bicyclo[4.1.0]hept-7-ylamine (97)



Scheme 42: *Preparation of N-amino aziridine (**97**) by cleavage of protecting group of aziridine (**62**) with hydrazine hydrate .*

1-(7-aza-bicyclo[4.1.0]hept-7-yl)-pyrrolidine-2,5-dione (**62**) was treated with hydrazine hydrate in methanol as solvent give *N*-amino aziridine (**97**) as well as succindihydrazide (**31**). The work-up was done by filtering the reaction mixture to remove the dihydrazide and mother

liquor was concentrated on reduced pressure to obtain the crude product. The crude mass was extracted in pentane and solvent was removed under reduced pressure to give (**97**) in 45% yield. The analytical data of (**97**) is in full agreement with literature.[95]

3 Conclusion

A straight forward novel process for the synthesis of *N*-aminosuccinimide (**28**) was developed with excellent yield, moreover which can be scaled up. It has been shown very detailed in the theoretical section (**Scheme 26**).

A method was devised for the generation of new optically pure C_2 symmetric (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) with excellent a yield. It has been shown very detailed in the theoretical section (**Scheme 30**).

The applicality of *N*-aminosuccinimide (**28**) as nitrogen source was demonstrated in reactions with alkenes leading to corresponding aziridines with good to excellent yields. The details are summarized in the theoretical section (**Scheme 31**).

The aziridination reaction using 2-isopropyl-5-methyl-4*H*-[1,3]dioxine (**21**) with *N,N*-dibenzyloxycarbonylhydrazine (**12**) as nitrogen source and iodbenzenediacetate as oxidising agent in dichloromethane as solvent yield 5-(*N,N*-dibenzoloxycarbonyl-hydrazino)-2-isopropyl-5-methyl-[1,3]dioxin-4-yl ester (**79**) with diastereomeric ratio 1:1.8 (determined by NMR). The crude product was purified in petrol ether with 24% yield (**Scheme 34**).

Aziridination reactions using *S*-(-)-2-*tert*-butyl-5-methyl-4*H*-1,3-dioxine (**26**) as substrate and *N*-aminosuccinimide (**28**) as nitrogen source and PhI=O as oxidising agent in presence of molecular sieves yield diastereomeric oxazolidinecarbaldehydes (**84**). The diastereomeric ratio in the crude reaction mixture was 1:5.5. The crude product was purified by column chromatography give 24% yield and 65% de (**Scheme 36**).

The successful use of optically active (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) as nitrogen source was demonstrated with reactions using prochiral alkenes leading to corresponding optically active aziridines in moderate to good yields and with moderate to good diastereoselectivities. The aziridines (**94**) derived from styrene (**67**) and (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) as nitrogen source, the diastereomeric ratio was 1:3. The diastereomeric ratios were better when a bulky group like phenyl group were present in

the olefins. The absolute configuration of major diastereomer (**94a**) was unambiguously established by single crystal XRD as (3*R*,4*R*)-3,4-dimethoxy-1-((*R*)-2-phenylaziridin-1-yl)pyrrolidine-2,5-dione. However little asymmetric induction were observed in the aziridines (**89**), (**91**) and (**93**), which were obtained from the corresponding prochiral alkenes, e.g. methyl crotonate (**63**), *tert*-butylacrylate (**90**), and methyl cinnamate (**92**) (**Scheme 40**). Moreover, aziridines (**95**) derived from *trans*-stilbene (**65**), shown very good diastereomeric ratio (1:5). The absolute configuration of major diastereomer was determined by single crystal XRD as (3*R*,4*R*)-3,4-dimethoxy-1-((2*R*,3*R*)-2,3-diphenylaziridin-1-yl)pyrrolidine-2,5-dione (**95a**).

In conclusion, the *N*-aminosuccinimide **(28)** is a very versatile nitrogen source for the transformation of alkenes to corresponding aziridines. Furthermore, deprotection of succinimido aziridine with hydrazine hydrate afforded to yield *N*-amino aziridine (**Scheme 42**) with moderate yield. Until a few years ago, the field of asymmetric aziridinations were less known in comparison to asymmetric epoxidation. The aziridination reactions using new optically pure nitrogen source, e.g. (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29)** have been demonstrated using prochiral alkenes. The excellent diastereoselectivity were obtained using *trans*-stilbene **(65)** and styrene (**67)**.

4 Experimental Section

4.1 General

NMR spectroscopy

Varian Unity INOVA 500, ^{1}H (500 MHz) in indirect dectection method with internal standard used as TMS. ^{13}C (125 MHz) with bright band testing method.

GC (Gas chromatography)

Varian Star 3400C, column 25m×0.25mm ID, FS-OV-1-CB, carrier gas: N_2, detector-FID.

ee-Determination

CE instruments, GC 8000 top serie, column 30m×0.32mm ID, Rt-βDEXcst^{TM}, RESTEK GmbH, carrier gas H_2, detector- FID.

Röntgen-crystal structure analysis (Single crystal X-Ray analysis)

Mesasurements, CAD4 express (Enraf-Nonius, data reduction: XCAD4 (Harms, 1993), Structur solution: SHELXS (Sheldrick, 1990), structure refine: SHELX-93 (Sheldrick, 1993), graphic representation: SCHAKAL 92 (Keller, 1993), ORTEX (P. Mc Ardle, 1993).

Polarimeter

Perkin- Elmer Polarimeter 241, glass cuvette 10 and 1 cm with iternal water circulation provision, sodium lamp.

CHN analyser

Vario E. L. Elementar Analysensysteme GmbH.

Kryomat

Huber Kältmaschinenbau GmbH; Cooling medium: methanol

Oil pump

Vacuubrand type RZ 5

Capacity: 0.0004 mbar

Melting point

Prof. Tottoli apparatus (manufacturer: Büchi).

Melting points are measured in open capillary and uncorrected.

Thin layer chromatography (TLC)

Merck silica gel plate coated with 60F254, 5×10 cm. UV (λ=254 nm), iodine, vanillin and phosphomolybdic acid was used for detection.

Column chromarography

Merck silica gel, mesh size 0.060-0.200 mm (70 to 230 mesh ASTM) and Merck aluminium oxide 150 basic (type T).

Nitrogen

Nitrogen gas 5.0 was used during the reaction when ever necessary.

Mass spectrometer

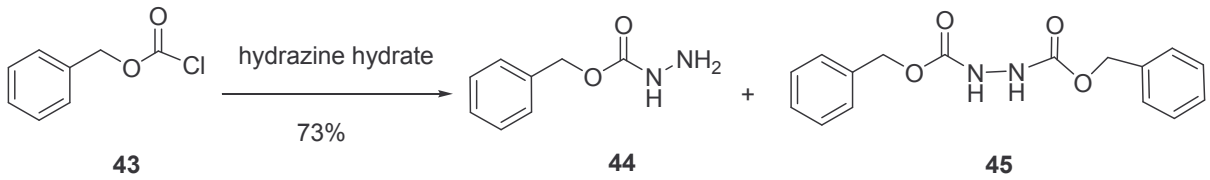
(i) Finnigin LCQ^{DECA} from Thermoquest
Ionisation technique
Electrospray-ionisation (ESI).
Atmospheric pressure chemical ionisation (APCI).

(ii) micrOTF from Brucker Daltonics

Ionisations techniques.
Electrospray-ionisation ESI.
Exact mass measurement with < 3 ppm (RMS) difference.

4.2 Synthesis of *N*-aminosuccinimide (28)

4.2.1 Synthesis of benzyl carbazate (44)



20.0 ml, 0.142 mol benzylchloroformate (**43**) were mixed in 144 ml ether and slowly added to a stirred solution of 34 ml, 0.67 mol hydrazine hydrate in 20 ml ether at -20 °C over a period of 5 h. The reaction mixture was further stirred for 1 h. The reaction was monitored by GC. The work-up was done by addition of 50 ml water in the reaction mixture and extracted the product with 3×50 ml ether, wash the organic layer with 3×50 ml water, dried over magnesium sulphate. The solvent was removed under vacuum and product was recrystallized with petrol ether and product was dried in high vacuum to obtain solid.

The main impurity formed in the reaction mixture was isolated by column chromatography and characterized as *N,N′*-dibenzyloxycarbonylhydrazine (**45**). The modified procedure by lowering the reaction temperature (Lit.[62] described temperature is -5 °C) to -20 °C and increasing the addition time 5 h (Lit.[62] described time 1h) of benzyl chloroformate (**43**) yield the formation of impurity < 5%.

Colourless solid; 17 g (yield 73%)

The m.p.; ^{1}H NMR; ^{13}C NMR and mass are in good agreement with Lit. data.[62]

***N,N′*-Dibenzyloxycarbonylhydrazine (45)**

White crystalline powder; m.p. 104-107 °C. (Lit.[96] m.p. 105 °C)

^{1}H NMR (500 MHz, $CDCl_3$)

δ=5.11 (s, 4H, C<u>H</u>$_2$Ph); 7.24 (s, 2H, N<u>H</u>); 7.30 (m, 10H, CH arom).

^{13}C NMR (125 MHz, $CDCl_3$)

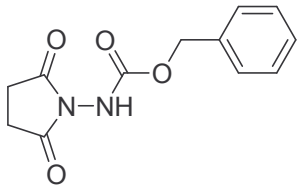
δ=67.8 (2C, (O<u>C</u>H$_2$Ph)$_2$); 128.2 (2C, arom); 128.3 (4C, arom); 128.5 (4C, arom); 135.4 (1C, arom); 156.6 (2C, <u>C</u>O).

MS/ESI (+):

m/z (%) = 318 (100) $[M+H+H_2O]^+$, 323 (26) $[M+Na]^+$.

m/z (%) = 319 (100) $[C_{16}H_{19}N_2O_5]^+$, 323(26) $[C_{16}H_{16}N_2O_4Na]^+$.

4.2.2 Synthesis of (2,5-dioxo-pyrrolidine)-carbamic acid benzyl ester (47)



7.53 g, 75.30 mmol Succinic anhydride (**39**) were added to a stirred solution of 12.5 g, 75.30 mmol benzyl carbazate (**44**) in 500 ml ethylacetate at 4 °C. The reaction mixture was further stirred at 0 to 4 °C for 30 minutes, then allowed to reach the ambient temperature and stirred for 2h to form hydrazine acid (**46**) as an intermediate. The reaction mixture was again chilled to 4 °C and 15.55 g, 75.36 mmol of *N,N'*-dicyclohexylcarbodiimide (DCC) was added to form cyclized product (**47**) and stirred for 30 minutes. The ice bath was removed and temperature of the reaction mixture was allowed to reach to ambient and further stirred for 24 h. The reaction mixture was filtered and solid was washed with 250 ml ethyl acetate. To isolate the product (**47**), the solvent was removed in vacuum and recrystallized with diethyl ether.
Colourless solid, 13 g (yield 70%), m.p. 132-133 °C.

^{1}H NMR (500 MHz, $CDCl_3$)

δ= 2.67 (s, 4H, $CO(C\underline{H}_2)_2CO$); 5.12 (s, 2H, $OC\underline{H}_2Ph$); 7.38 (m, 5H, CH arom); 7.49 (br s, 1H, N<u>H</u>).

^{13}C NMR (125 MHz, $CDCl_3$)

δ= 26.2 (2C, $CO(\underline{C}H_2)_2CO$); 68.4 (1C, $O\underline{C}H_2Ph$); 128.3 (2C, arom);
128.5 (2C, arom); 128.5 (1C, arom); 134.9 (1C, arom); 154.2 (1C, NH<u>C</u>OO); 173.9 (2C, $\underline{C}O(CH_2)_2\underline{C}O$).

MS/APCI (+):

m/z (%) = 249 (100) $[M+H]^+$, 267 (38) $[M+H+H_2O]^+$.

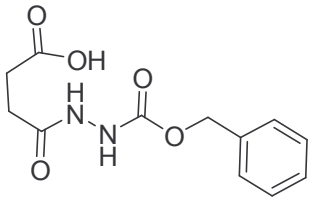
m/z (%) = 249 (100) $[C_{12}H_{13}N_2O_4]^+$, 267 (38) $[C_{12}H_{15}N_2O_5]^+$.

MS/ESI (+):

m/z (%) = 255 (100) $[M+Li]^+$, 361 (11) $[M+Li+LiClO_4]^+$, 503 (5) $[2M+Li]^+$.

m/z (%) = 255 (100) $[C_{12}H_{12}LiN_2O_4]^+$, 361 (11) $[C_{12}H_{12}ClLi_2N_2O_8]^+$, 503 (5) $[C_{24}H_{24}LiN_4O_8]^+$.

4-(*N′*-Benzyloxycarbonyl-hydrazino)-4-oxo-butyric acid (intermediate) (46)



Colourless solid; mp 134-136 °C.

^{1}H NMR (500 MHz, $CDCl_3$)

δ=2.83 (m, 2H, CO(C<u>H</u>$_2$)$_2$CO); 3.00 (m, 2H, CO(C<u>H</u>$_2$)$_2$CO); 2.51 (s, 2H, OC<u>H</u>$_2$Ph); 7.33 (m, 5H, CH arom); 8.08 (br s, 2H, CON<u>H</u>N<u>H</u>CO).

^{13}C NMR (125 MHz, $CDCl_3$)

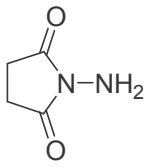
δ=23.92 (1C, CO(<u>C</u>H$_2$)$_2$CO); 27.25 (1C, CO(<u>C</u>H$_2$)$_2$CO); 67.48 (1C, O<u>C</u>H$_2$Ph); 128.22 (2C, arom); 128.33 (1C, arom); 128.48 (2C, arom); 135.55 (1C, arom); 145.04 (1C, <u>C</u>OOCH$_2$Ph); 153.01 (1C, NH<u>C</u>OCH$_2$); 170.33 (1C, <u>C</u>OOH).

MS/APCI (+)

m/z (%) = 267 (100) $[M+H]^+$

m/z (%) = 267 (100) $[C_{12}H_{15}N_2O_5]^+$.

4.2.3 Synthesis of *N*-aminosuccinimide (28)



To a magnetically stirred solution of 5.0 g, 20 mmol of (2,5-dioxo-pyrollidine-1-yl)-carbamicacidbenzyl ester (**47**) in 225 ml ethanol, 1.0 g 10% of Pd on activated charcoal was added. The hydrogen was bubbled at room temperature till complete deprotection of Cbz group. The reaction was monitored by ^{1}H NMR. After complete conversion to **28**, the reaction mixture was filtered through a celite bed and the solvent was removed under vacuum to obtain **28** as a colourless viscous oil.

Colourless viscous oil, which solidifies on standing; 2.160 g (yield 93%).

^{1}H NMR (500 MHz, CD_2Cl_2)

δ=2.66 (s, 4H, $CO(C\underline{H}_2)_2CO$); 4.43 (br s, 2H, NH_2).

^{13}C NMR (125 MHz, CD_2Cl_2)

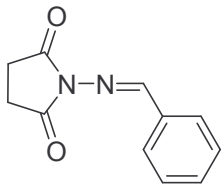
δ=26.7 (2C, $CO(\underline{C}H_2)_2CO$); 174.4 (2C, $\underline{C}O(CH_2)_2\underline{C}O$).

MS/APCI (+):

m/z (%) = 115 (100) $[M+H]^+$.

m/z (%) = 115 (100) $[C_4H_7N_2O_2]^+$.

4.2.4 Synthesis of 1-(benzylidene-amino)-pyrrolidine-2,5-dione (37)



To a stirred solution of 0.5 g, 4.4 mmol *N*-aminosuccinimide (**28**), 50 mg *p*-toluenesulphonic acid and 1.4 g, 13 mmol benzaldehyde, 50 ml dichloromethane were heated to reflux for 24 h. The reacton mixture was cooled to room temperature and treated with 5 ml 10% sodium carbonate solution to make pH ~10. The organic layer was separated and washed with 3×5 ml water. The combined organic extracts were dried over magnesium sulphate and solvent was removed under reduced pressure. The crude product was recrystallized with 35 ml of diethyl ether, the mixture was chilled at -18 °C for 16 h. **37** was isolated by filteration and dried in high vacuum.

Colourless solid; 621 mg (yield 71%); m.p. 170-172 °C. (Lit.[57] m.p. 172-173 °C).

^{1}H NMR (500 MHz, $CDCl_3$)

δ= 2.82 (s, 4H, $CO(C\underline{H}_2)_2CO$); 7.46 (m, 3H, CH arom); 7.84 (m, 2H, CH arom); 9.12 (s, 1H, C<u>H</u>Ph).

^{13}C NMR (125 MHz, $CDCl_3$)

δ= 26.7 (2C, $CO(\underline{C}H_2)_2CO$); 128.7 (2C, arom); 128.8 (2C, arom); 132.2 (1C, arom); 132.8 (1C, arom); 162.0 (1C, <u>C</u>HPh); 173.1 (2C, $\underline{C}O(CH_2)_2\underline{C}O$).

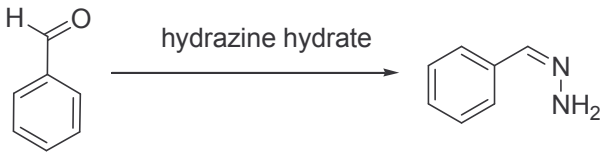
MS/APCI (+):

m/z (%) = 203 (100) $[M+H]^+$.

m/z (%) = 203 (100) $[C_{11}H_{11}N_2O_2]^+$.

4.3 Synthesis of *N,N*-dibenzyloxycarbonylhydrazine (12)

4.3.1 Synthesis of benzylidene hydrazine (52)



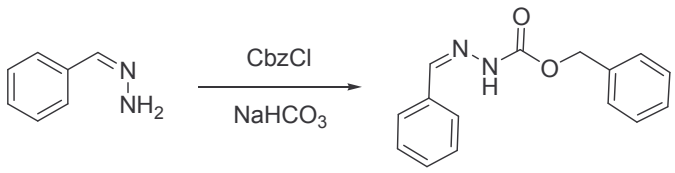
15.75 g, 0.15 mol Benzaldehyde (**51**) was added dropwise to a stirred mixture of 16.4 g, 0.33 mol hydrazine hydrate, 10 g magnesium sulphate and 250 ml diethyl ether over a period of 1 h at 38 to 40 °C under inert atmosphere and further stirred for 4 h. The reaction was monitored by GC. After completion conversion, the reaction mixture was filtered; organic layer was dried over potassium hydroxide. The solvent under removed under reduced pressure and product was distilled in high vacuum to obtain (**52**) as light yellow liquid.
Light yellow liquid; 10.9 g (yield 61.3%); b.p. 75 to 78 °C / 1 mbar pressure (Lit.[63] b.p. 115-120 °C / 8 mbar).

^{1}H NMR (500 MHz, $CDCl_3$)
δ=5.52 (br s, 2H, N<u>H</u>$_2$); 7.31 (m, 3H, CH arom); 7.53 (m, 2H, CH arom); 7.71 (s, 1H, PhC<u>H</u>=N).

^{13}C NMR (125 MHz, $CDCl_3$)
δ=126.1 (1C, arom); 128.5 (2C, arom); 128.6 (2C, arom); 135.0 (1C, arom); 142.1 (1C, Ph<u>C</u>H=N-NH$_2$).

MS/APCI (+):
m/z (%) = 121 (90) $[M+H]^+$.
m/z (%) = 121 (90) $[C_7H_9N_2]^+$.

4.3.2 Synthesis of *N´*-benzylidene-hydrazine carboxylic acid benzylester (53)



57 g, 0.34 mol Benzylchloroformate was added drop wise to a solution of 40 g, 0.33 mol benzylidene hydrazine (**52**) in 250 ml *N,N*-dimethylformamide at -20 °C. The 67 g, 0.8 mol $NaHCO_3$ was added over a period of 1.5 h. The reaction mixture was further stirred at -20 °C for 1 h. The reaction was monitored by GC. The crude product was isolated by quenching the reaction mixture in 800 g ice, filtered and washed the solid with water till pH neutral and dried in high vacuum. The crude product was recrystallised with 600 ml (300 ml benzene and 300 ml cyclohexane) mixture and solid was dried in high vacuum to obtain **53**.

Colourless solid; 50 g (yield 70%).

The m.p. and ^{1}H NMR are in good agreement with Lit.[44] data.

^{13}C NMR (125 MHz, $CDCl_3$)

δ=65.9 (1C, O<u>C</u>H_2Ph); 126.6 (3C, arom); 127.9 (1C, arom); 128.0 (1C, arom); 128.4 (2C, arom); 128.71 (2C, arom); 129.5 (C, arom); 134.3 (1C, arom); 136.5 (1C, arom); 144.2 (1C, arom); 153.2 (1C, O<u>C</u>ONH).

MS/APCI (+):

m/z (%) = 255 (100) $[M+H]^+$.

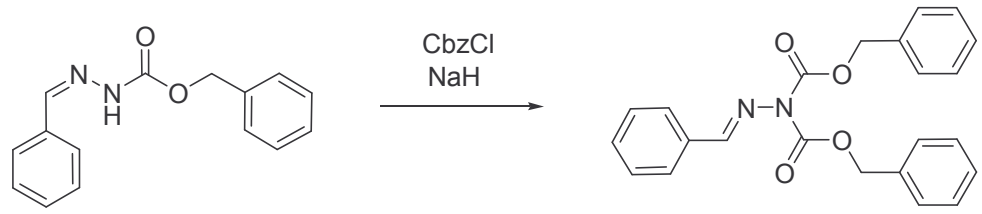
m/z (%) = 255 (100) $[C_{15}H_{15}N_2O_2]^+$.

MS/ESI (+):

m/z (%) = 255 (54) $[M+H]^+$; 277 (43) $[M+Na]^+$.

m/z (%) = 255 (100) $[C_{15}H_{15}N_2O_2]^+$; 277 (43) $[C_{15}H_{14}N_2O_2Na]^+$.

4.3.3 Synthesis of benzaldehyde dibenzyloxycarbonyl hydrazone (54)



8.815 g, 0.22 mol Sodium hydride was added to a stirred solution of 28 g, 0.11 mol *N´*-benzylidene-hydrazine carboxylic acid benzyl ester (**53**) and 500 ml dried *N,N*-dimethylformamide over a period of 10 minutes at 0 to 5 °C and further stirred for 2 h. The reaction mixture was cooled to -20 °C, 37.4 g, 0.22 mol benzyl chloroformate was mixed with 41 ml toluene and added drop wise to the cooled mixture over a period of 1 h and further stirred for 1 h. The reaction mixture was further stirred at 0 °C to 2 °C for 17 h. The reaction was monitored by TLC. After complete conversion, reaction mixture was quenched in to 2000 gm ice, filtered and washed the solid with water till pH neutral and dried in high vacuum. The crude product was recrystallized in isopropanol to get pure **54**.

Off white powder; 25.8 g (yield 60.3%).

The m.p. and ^{1}H NMR are in good agreement with lit.[44] data.

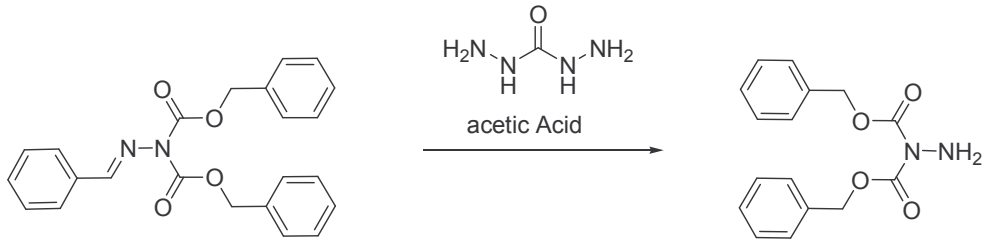
^{13}C (125 MHz, DMSO-d_6)

δ=68.5 (2C, O<u>C</u>H$_2$Ph); 127.9 (2C, arom); 128.2 (2C, arom); 128.3 (2C, arom); 128.4 (2C, arom); 129.0 (2C, arom); 132.0 (2C, arom); 132.6 (1C, arom); 135.2 (1C, arom).

HRMS/ESI (+)

m/z = 395.1577 $[M+Li]^+$, measured value and calculated value 395.1578, $[C_{23}H_{20}LiN_2O_2]^+$.

4.3.4 Synthesis of *N,N*-dibenzyloxycarbonylhydrazine (12)



To a magnetically stirred mixture of 61 g, 157 mmol *N,N*-dibenzyloxycarbonyl benzylidene hydrazine (**54**), 600 ml ethanol, 7.3 g, 81 mmol carbohydrazide and 9.8 ml, 170 mmol acetic acid were heated to reflux for 16 h. Reaction was monitored by TLC. The work-up was done by removing the solvent under reduced pressure and residue was refluxed with 600 ml toluene, cooled to room temperature, filter and mother liquer was concentrated under reduced pressure. The cude product was recrystallised with 400 ml water: ethanol (1:1) mixture. The solid was filtered and solid was dried in high vacuum.
Colourless solid; 47.14 g (yield 89%).

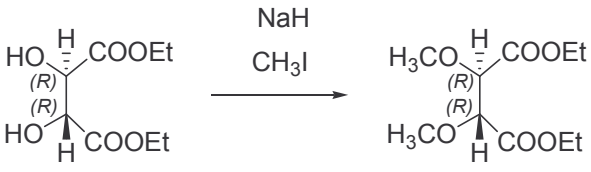
The m.p. and ^{1}H NMR is in good agreement with the lit.[44] data.

^{13}C NMR (125 MHz, DMSO-d_6)
δ=67.8 (2C, N(COO<u>C</u>H_2Ph)$_2$; 127.8 (4C, arom); 128.1 (2C, arom); 128.4 (4C, arom); 135.8 (2C, arom); 153.7 (2C, <u>C</u>O).

HRMS/ESI (+):
m/z = 307.1264 $[M+Li]^+$ measured value and calculated value 307.1265 $[C_{16}H_{16}LiN_2O_4]^+$.

4.4 Synthesis of (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (29)

4.4.1 Synthesis of di-*O*-methyl-L-(+)-tartaric acid diethyl ester (56)



To a magnetically stirred suspension of 9.0 g, 0.225 mol sodium hydride and 400 ml anhydrous diethyl ether (dried over sodium and benzophenone), 25 g, 121 mmol L-(+)-tartaric acid diethyl ester (**55**) was mixed with 125 ml anhydrous diethyl ether and added over a period of 3 h at room temperature and subsequently heated to reflux for 2 h and allowed to reach to ambient. The reaction mixture was further stirred at room temp. for 16 h and filtered under nitrogen atmosphere. The solid was washed with 9×70 ml anhydrous diethyl ether. The solid was transfered in to flask containg 200 ml anhydrous diethyl ether and stirred under nitrogen atmosphere. 58 ml, 920 mmol methyl iodide was mixed with 150 ml diethyl ether and drop wise added to the slurry under stirring over a period of 2 h at room temperature and further stirred for 18 h. The reaction was monitored by GC. After completion of reaction, the reaction mixture was filtered and solid was washed with 200 ml anhydrous diethylether. The mother liquor was concentrated on rotary and product was distilled in high vacuum.

Colourless oil; 15 g (yield 53%); b.p. 95 to 98 °C / 0.1 mbar pressure.

The $[\alpha]_D^{20}$ and ^{1}H NMR are in good agreement with lit.[64,97] data.

^{13}C NMR (125 MHz, $CDCl_3$)

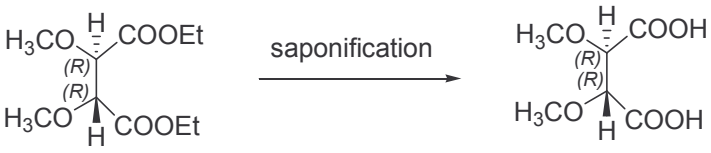
δ=14.2 (2C, $\underline{C}H_3$); 59.5 (2C, O$\underline{C}H_3$); 61.2 (2C, $\underline{C}H_2CH_3$), 81.1 (2C, $\underline{C}H$), 169.1 (2C, $\underline{C}O$).

MS/ESI (+):

m/z (%) = 235 (11) $[M+H]^+$, 257 (100) $[M+Na]^+$.

m/z (%) = 235 (11) $[C_{10}H_{19}O_6]^+$, 257 (54) $[C_{10}H_{18}NaO_6]^+$.

4.4.2 Synthesis of di-*O*-methyl-L-(+)-tartaric acid (57)



8.6 g, 0.215 mol NaOH was dissolved in to 217 ml water and added to a stirred solution of 25 g, 108 mmol di-*O*-methyl-L-(+)-tartaric acid diethyl ester (**56**) in 115 ml ethanol over a period of 1 h at 5 to 10 °C. The reaction mixture was further stirred at 5 to 10 °C for 1 h. 22.5 ml of conc. HCl was added to the reaction mixture over a period of 30 minutes at 5 to 10 °C and further stirred for 10 minutes. The reaction mixture was concentrated under reduced pressure to get solid. The solid was extracted with 3×500 ml hot ethylacetate, treated with charcoal and filtered. The solvent was removed under vacuum and the crude product was crystallized from ethyl acetate.

Colourless crystalline solid; 10.0 g (yield 52.6%); m.p. 152-154 °C;

$[\alpha]_D^{20}$ +89° (c=2.30 in acetone).

^{1}H NMR (500 MHz, DMSO-d_6)

δ=3.29 (s, 6H, OC<u>H</u>$_3$); 4.12 (s, 2H, C<u>H</u>); 12.84 (br s, 1H, COO<u>H</u>).

^{13}C NMR (125 MHz, DMSO-d_6)

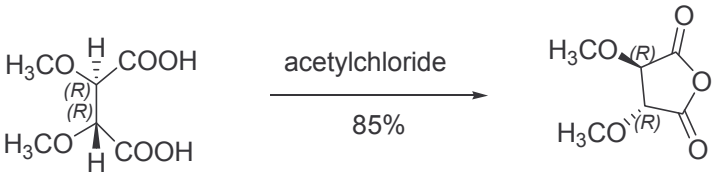
δ=58.6 (2C, O<u>C</u>H$_3$); 80.5 (2C, <u>C</u>H); 170.4 (2C, <u>C</u>OOH).

MS/ESI (-)

m/z (%) = 177 (100) $[M-H]^-$; 355 (10) $[2M-H]^-$.

m/z (%) = 177.05 (100) $[C_6H_9O_6]^-$; 355 (10) $[C_{12}H_{19}O_{12}]^-$.

4.4.3 Synthesis of (3*R*,4*R*)-(+)-3,4-dimethoxy succinic anhydride (58)



To a stirred suspension of 9.5 g, 53.32 mmol di-*O*-methyl-L-(+)-tartaric acid (**57**) and 50 ml acetylchloride were heated to reflux for 2 h until the evolution of HCl was stopped. The excess of acetylchloride was distilled under reduced pressure. In the concentrated mass 2×50 ml toluene was added and solvent was distilled under reduced pressure to remove the traces of acetylchloride. Crude product was stirred with 100 ml diethylether: petrol ether (1:1) mixture at room temperature for 15 minutes, filtered and dried in high vacuum.

Colourless solid; 6.8 g (yield 80%).

m.p. and ^{1}H NMR are in good agreement Lit.[64] data.

^{13}C NMR (125 MHz, Acetone-d_6)

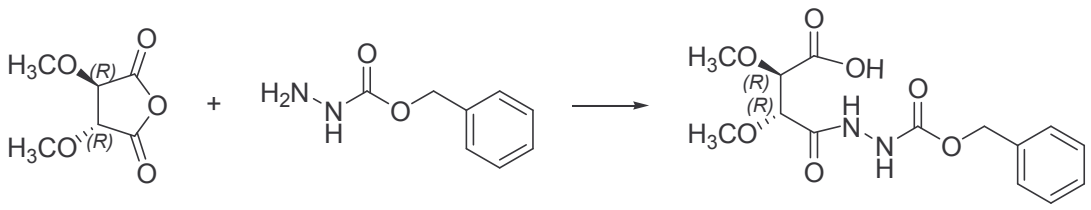
δ=59.5 (2C, O<u>C</u>H$_3$); 81.5 (2C, <u>C</u>H); 167.7 (2C, <u>C</u>O).

MS/APCI (-)

m/z (%) = 159 (10) $[M-H]^-$, 177 (100) $[M-H+H_2O]^-$.

m/z (%) = 159 (10) $[C_6H_7O_5]^-$, 177 (10) $[C_6H_9O_6]^-$.

4.4.4 Synthesis of 4-(*N´*-benzyloxycarbonyl-hydrazino)-2,3-dimethoxy-4-oxo-butyric acid (Method a) (59)



To a magnetically stirred solution of 3.321 g, 20 mmol benzyl carbazate (**47**) in 100 ml ethylacetate at room temperature, 3.202 g, 20 mmol of (3*R*,4*R*)-(+)-3,4-dimethoxy succinic anhydride (**58**) was added and stirred for 2 h. The reaction was monitored by GC. After complete conversion, solvent was removed in vacuum and dried in high vacuum to afford (**59**) as colourless solid.

Colourless solid; 6.5 g (yield 100%); m.p. 67-70 °C; $[\alpha]_D^{20}$ +81.3° (c=2.14 in acetone).

^{1}H NMR (500 MHz, DMSO-d_6)

δ=3.28 (s, 3H, OC<u>H</u>$_3$); 3.33 (s, 3H, OC<u>H</u>$_3$); 4.07 (br s, 2H, C<u>H</u>); 5.08 (s, 2H, C<u>H</u>$_2$); 7.368 (br s, 5<u>H</u>, CH arom); 7.27 (s, 1H, N<u>H</u>); 9.84 (s, 1H, N<u>H</u>); 12.65 (br s, 1H, COO<u>H</u>).

^{13}C NMR (125 MHz, DMSO-d_6)

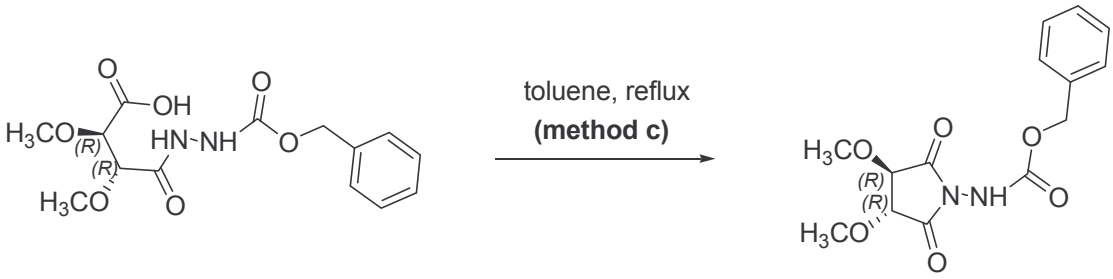
δ=58.7 (C, O<u>C</u>H$_3$); 59.2 (C, O<u>C</u>H$_3$); 65.8 (1C, O<u>C</u>H$_2$Ph); 79.8 (1C, <u>C</u>H); 82.2 (1C, <u>C</u>H); 127.8 (2C, C_3+C_5 arom); 127.9 (1C, C_4 arom); 128.3 (2C, C_2+C_6 arom); 136.6 (1C, C_1 arom); 155.8 (1C, NH<u>C</u>OOR); 168.3 (1C, NH<u>C</u>OCH); 170.8 (1C, COOH).

MS/APCI (-):

m/z (%) = 325 (100) $[M-H]^-$.

m/z (%) = 325 (100) $[C_{14}H_{17}N_2O_7]^-$.

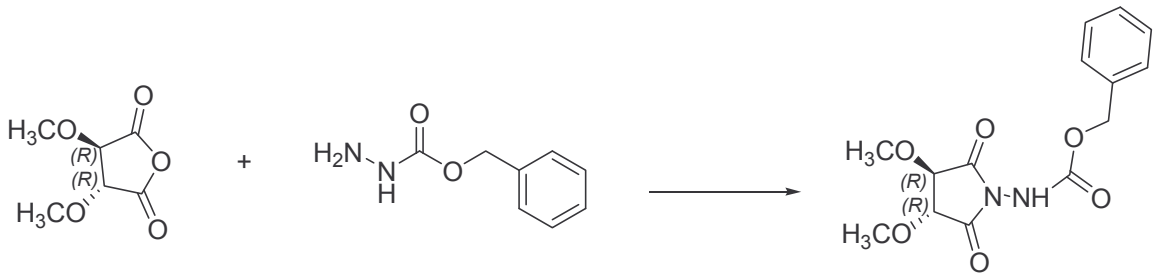
4.4.5 Synthesis of (3*R*,4*R*)-(+)-(3,4-dimethoxy-2,5-dioxo-pyrrolidin-1-yl)-carbamic acid benzyl ester (Method c) (60)



To a magnetically stirred suspension of 6.0 g, 18.4 mmol 4-(*N'*-benzyloxycarbonyl-hydrazino)-2,3-dimethoxy-4-oxo-butyric acid (**59**) in 100 ml toluene was heated to reflux for 17 h. The reaction was monitored by ^{1}H NMR. After complete conversion, solvent was removed in reduced pressure and dried in high vacuum to afford (**60**) as colourless solid.

Colourless solid; 5.4 g (yield 95 %); m.p. 112-115 °C.

4.4.6 Synthesis of (3*R*,4*R*)-(+)-(3,4-dimethoxy-2,5-dioxo-pyrrolidin-1-yl)-carbamic acid benzyl ester (Method b) (60)



To a suspension of 8.1 g, 0.051 mol (3*R*,4*R*)-(+)-3,4-dimethoxy succinic anhydride (**58**), 8.4 g, 0.051 mol, benzyl carbazate (**47**) in 100 ml toluene were heated to reflux for 24 h. The reaction water was removed using Dean and Stark apparatus. The reaction was monitored by ^{1}H NMR. After complete conversion, solvent was removed in vacuum and dried in high vacuum to afford (**60**) as colourless solid.

Colourless solid; 15.5 g (yield 98%); m.p. 112-115 °C, $[\alpha]_D^{20}$ +133.2° (c=2.78 in acetone).

^{1}H NMR (500 MHz, Acetone-d_6)

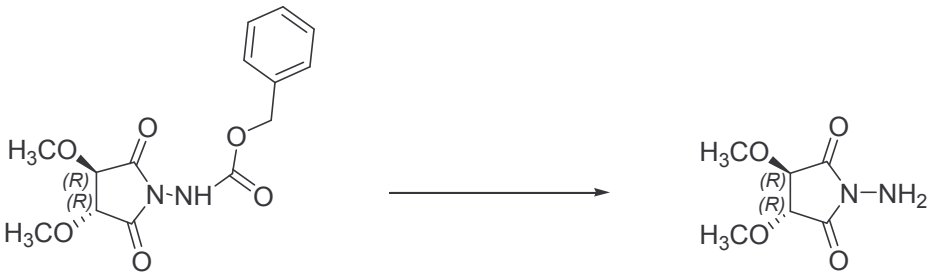
δ=3.67 (s, 6H, OC<u>H</u>$_3$), 4.42 (s, 2H, C<u>H</u>OCH$_3$), 5.19 (s, 2H, C<u>H</u>$_2$Ph), 7.38 (m, 5<u>H</u>, CH arom), 9.16 (br s, 1H, N<u>H</u>).

^{13}C NMR (125 MHz, Acetone-d_6)

δ=59.3 (2C, O<u>C</u>H$_3$); 68.2 (1C, O<u>C</u>H$_2$Ph); 80.4 (2C, <u>C</u>HOCH$_3$); 128.8 (2C, C$_3$+C$_5$ arom); 128.9 (1C, C$_4$ arom); 129.1 (2C, C$_2$+C$_6$ arom); 136.6 (1C, C$_1$ arom); 155.0 (1C, NH<u>C</u>OOR); 170.4 (2C, N<u>C</u>OCH).

MS/APCI (-):
m/z (%) = 307 (100) [M-H]$^-$.
m/z (%) = 307 (100) [$C_{14}H_{15}N_2O_6$]$^-$.

4.4.7 Synthesis of (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (29)



To a stirred solution of 4.0 g, 129.74 mmol (3*R*,4*R*)-(+)-(3,4-dimethoxy-2,5-dioxo-pyrrolidin-1-yl)-carbamic acid benzyl ester (**60**) in 300 ml ethanol at room temperature, 0.8 g, 10% Pd on activated charcoal was added and hydrogen was passed till complete deprotection of Cbz group. The reaction was monitored by ^{1}H NMR. After complete conversion, reaction mixture was filtered and solvent was removed in reduced pressure and dried in high vacuum to afford (**29**) as colourless oil.

Colourless oil (solidified on standing), 2.0 g (yield 88%); $[\alpha]_D^{20}$ +219° (c=1.86 in ethanol).

^{1}H NMR (500 MHz, DMSO-d$_6$)
δ=3.54 (s, 6H, OC<u>H</u>$_3$); 4.36 (s, 2H, C<u>H</u>); 5.02 (s, 2H, N<u>H</u>$_2$).

^{13}C (125 MHz, DMSO-d$_6$)
δ=58.2 (2C, CHO<u>C</u>H$_3$); 79.1 (2C, <u>C</u>HOCH$_3$); 170.7 (2C, <u>C</u>O).

MS/APCI (+)
m/z (%) = 175 (100) [M+H]$^+$.
m/z (%) = 175 (100) [$C_6H_{11}N_2O_4$]$^+$.

4.5 Synthesis of hypervalent iodine compounds

4.5.1 Synthesis of iodbenzenediacetate

To a stirred solution of 104 ml aceticanhydride, 24 ml 35% hydrogenperoxide was added drop wise over a period of 20 minutes at room temperature. The temperature of reaction mixture was further raised to 40 °C and maintained for 4 h. The reaction mixture was cooled to room temperature and 9.24 ml, 83 mmol iodbenzene was added dropwise over a period of 10 minutes and further stirred at room temperature for 17 h. 100 g crushed ice was added in the reaction mixture to obtain white solid. The product was isolated by filtration, washed with 200 ml water and 100 ml diethyl ether. The solid was dried in high vacuum at 50 °C for 5 h. Colourless solid; 17 g (yield 60%); m.p. 160-164 °C.

4.5.2 Synthesis of iodosylbenzene

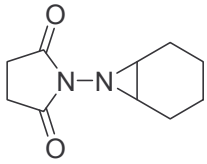
7.0 g, 125 mmol of KOH was dissolved in to 160 ml water and added to 16.1 g, 50 mmol iodbenzenediacetate at 0 to 10 °C under stirring over a perod of 10 minutes, allowed the temperature of reaction mixture to reach ambient and further stirred for 3 h. The reaction mixture was filtered, washed the solid with water till pH neutral and finally with 50 ml acetone. The solid was dried in high vacuum at 40 °C for 5 h. Light yellow powder; 10.0 g (yield 91%).

4.6 General procedure for the Synthesis of aziridines

4.6.1 General procedure for the Synthesis of aziridines using *N*-amino succinimide (28) as nitrogen source

To a stirred suspension of 20 mmol olefins, 10 mmol of *N*-amino sucinimide (**28**), 5 g molecular sieves in 30 ml dry solvent were added under inert atmosphere, 12 mmol of the oxidising agent in small portions over a period of 2.5 h at room temperature. The reaction mixtures were further stirred for 17 h. After complete conversion (monitored by GC or TLC). The reaction mixtures were filtered if necessary and residue was washed with 50 ml ethyl acetate. To obtain the crude product, the solvent was removed under vacuum. When the $PhI(OAc)_2$ was used as oxidising agent, the solvent was removed under vacuum without filtering the reaction mixtures. The crude products were purified by crystallisations, column chromatography using silica gel as well as alox basic as stationary phase and eluted with appropriate solvents, as when required.

4.6.1.1 Synthesis of 1-(7-aza-bicyclo[4.1.0]hept-7-yl)-pyrrolidine-2,5-dione (62)



The crude product was purified by using column chromatography, silica as stationary phase and cyclohexane: ethyl acetate (3:1) as mobile phase. The solvent was removed in vacuum to get (**62**) as colourless solid.
Colourless solid; 1.23 g (yield 63.5%); m.p. 107-110 °C.

^{1}H NMR (500 MHz, CD_2Cl_2)
δ=1.26 (m, 2H, C$\underline{H}_2$); 1.36 (m, 2H, C$\underline{H}_2$); 1.92 (m, 2H, C$\underline{H}_2$); 2.12 (m, 2H, C$\underline{H}_2$); 2.51 (m, 2H, C$\underline{H}$); 2.55 (s, 4H, CO(C$\underline{H}_2$)$_2$CO).

^{13}C NMR (125 MHz, CD_2Cl_2)

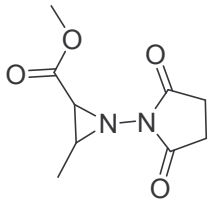
δ=20.3 (2C, $\underline{C}H_2$); 23.3 (2C, $\underline{C}H_2$); 27.0 (2C, $CO(\underline{C}H_2)_2CO$); 43.7 (2C, $\underline{C}H$); 173.4 (2C, $\underline{C}O(CH_2)_2\underline{C}O$).

MS/ESI (+)

m/z (%) = 195 (100) $[M+H]^+$.

m/z (%) = 195 (100) $[C_{10}H_{15}N_2O_2]^+$.

4.6.1.2 Synthesis of 1-(2,5-dioxo-pyrrolidin-1-yl)-3-methyl-aziridine-2-carboxylic acid methyl ester (64)



The crude product was purified by using column chromatography, silica as stationary phase and petrol ether: ethyl acetate (4:1) as mobile phase. The solvent was removed in vacuum to get (**64**) as colourless solid.

Colourless solid; 1.70 g (yield 80%); m.p. 125-127 °C.

^{1}H NMR (500 MHz, $CDCl_3$)

δ=1.43 (3H, d, J= 5.7, $NCHC\underline{H}_3$); 2.63 (m, 4H, $CO(C\underline{H}_2)_2CO$); 2.98 (d, J=5.3, 1H, $NC\underline{H}CO$); 3.12 (dq, J=5.7, J=5.3, $NCHCH_3$); 3.68 (s, 3H, OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$)

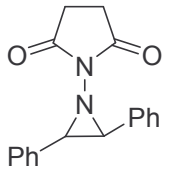
δ=16.2 (1C, $NCH\underline{C}H_3$); 26.5 (2C, $CO(\underline{C}H_2)_2CO$); 44.5 (1C, $N\underline{C}HCO$); 44.7 (1C, $N\underline{C}HCH_3$); 52.6 (1C, $O\underline{C}H_3$); 167.5 (1C, $CH\underline{C}OOCH3$); 172.9 (2C, $\underline{C}O(CH_2)_2\underline{C}O$).

MS/APCI (+)

m/z (%) = 213 (100) $[M+H]^+$.

m/z (%) = 213 (100) $[C_9H_{13}N_2O_4]^+$.

4.6.1.3 Synthesis of 1-(2,3-diphenyl-aziridin-1-yl)-pyrrolidine-2,5-dione (66)



The crude product was purified by using column chromatography, silica as stationary phase and petrol ether: ethyl acetate (4:1) as mobile phase. The solvent was removed in vacuum to get (**66**) as colourless solid.

Colourless solid; yield 1.46 g (yield 50%); m.p. 128-130 °C.

^{1}H NMR (500 MHz, $CDCl_3$)

δ=2.40 (m, 4H, CO(C<u>H</u>$_2$)$_2$CO); 3.93 (d, 1H, J= 5.8, PhC<u>H</u>CHPh); 4.86 (d, 1H, J= 5.8, PhCHC<u>H</u>Ph); 7.33 (m, 8H, CH arom), 7.49 (m, 2H, CH arom).

^{13}C NMR (125 MHz, $CDCl_3$)

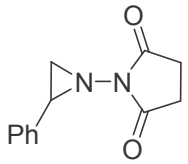
δ=26.2 (1C, CO(<u>C</u>H$_2$)$_2$CO); 26.2 (1C, CO(<u>C</u>H$_2$)$_2$CO); 45.6 (1C, Ph<u>C</u>HCHPh); 53.6 (1C, PhCH<u>C</u>HPh); 127.0 (1C, arom); 128.1 (1C, arom); 128.1 (2C, arom); 128.5 (3C, arom); 128.9 (1C, arom); 129.2 (2C, arom); 130.9 (1C, arom), 136.3 (1C, arom); 173.3 (1C, <u>C</u>O); 174.4 (1C, <u>C</u>O).

MS/APCI (+)

m/z (%) = 293 (100) $[M+H]^+$, 585 (10) $[2M+H]^+$.

m/z (%) = 293 (100) $[C_{18}H_{17}N_2O_2]^+$, 585 (10) $[C_{36}H_{33}N_4O_4]^+$.

4.6.1.4 Synthesis of 1-(2-phenyl-aziridin-1-yl)-pyrrolidine-2,5-dione (68)



The crude product was purified by using column chromatography, silica as stationary phase and petrol ether: ethyl acetate (3:1) as mobile phase. The solvent was removed in vacuum to get (**68**) as solid.

Colourless solid; 1.32 g (yield 61%); m.p. 104-106 °C.

^{1}H NMR (500 MHz, $CDCl_3$)

δ=2.63 (s, 4H, CO($C\underline{H}_2$)$_2$CO); 2.68 (m, 2H, PhCHC$\underline{H}_2$); 3.42 (dd, J=7.9, 6.0, NC$\underline{H}$Ph); 7.31 (m, 10H, CH arom).

^{13}C NMR (125 MHz, $CDCl_3$)

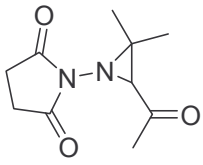
δ=26.5 (2C, CO($\underline{C}H_2$)$_2$CO); 39.5 (1C, $\underline{C}H_2$CHPh); 44.1 (1C, $CH_2\underline{C}$HPh); 127.0 (1C, arom); 128.0 (2C, arom); 128.4 (2C, arom); 136.2 (1C, arom); 172.8 (2C, $\underline{C}$O(CH$_2$)$_2\underline{C}$O).

MS/APCI (+)

m/z (%) = 217 (100) $[M+H]^+$, 433 (29) $[2M+H]^+$.

m/z (%) = 217 (100) $[C_{12}H_{13}N_2O_2]^+$, 433 (29) $[C_{24}H_{25}N_4O_4]^+$.

4.6.1.5 Synthesis of 1-(3-acetyl-2,2-dimethyl-aziridin-1-yl)-pyrrolidine-2,5-dione (70)



The crude product was purified by using column chromatography, silica as stationary phase and petrol ether: ethyl acetate (3:1) as mobile phase. The solvent was removed in vacuum to obtain (**70**).

Colourless solid; 1.14 g (yield 54.3%); m.p. 126-128 °C.

^{1}H NMR (500 MHz, $CDCl_3$)

δ=1.29 (s, 3H, $C(C\underline{H}_3)_2$); 1.33 (s, 3H, $C(C\underline{H}_3)_2$); 2.29 (s, 3H, $COC\underline{H}_3$); 2.67 (s, 4H, $CO(C\underline{H}_2)_2CO$); 3.17 (s, 1H, $NC\underline{H}COCH_3$).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=19.8 (1C, $C(\underline{C}H_3)_2$); 20.1 (1C, $C(\underline{C}H_3)_2$); 26.7 (2C, $CO(\underline{C}H_2)_2CO$); 29.3 (1C, $\underline{C}(CH_3)_2$); 50.6 (1C, $N\underline{C}HCOCH_3$); 55.9 (1C, $CO\underline{C}H_3$); 173.2 (2C, $\underline{C}O(CH_2)_2\underline{C}O$);
203.4 (1C, $\underline{C}OCH_3$).

MS/APCI (+)

m/z (%) = 211 (100) $[M+H]^+$.

m/z (%) = 211 (100) $[C_{10}H_{15}N_2O_3]^+$.

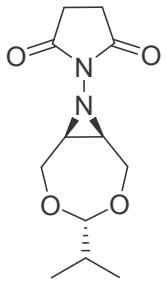
4.6.1.6 Synthesis of 1-(4-isopropyl-3,5-dioxa-8-aza-bicyclo[5.1.0]-octan-8-yl)-pyrrolidine-2,5-dione (72a)

The crude product was purified by using column chromatography, silica as stationary phase and cyclohexane: ethyl acetate (1: 4) as mobile phase. The solvent was removed in vacuum to obtain isomers (**72**).

Colourless solid, 1.52 g (yield 63%).

Isomer (**72a**)

Colourless solid; m.p. 140-142 °C.



^{1}H NMR (500 MHz, CD_2Cl_2)

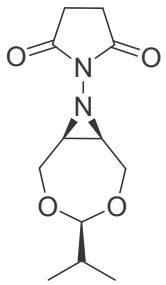
δ= 0.90 (d, J= 6.84, 6H, CH(C$\underline{H}_3$)$_2$); 1.84 (m, 1H, CH(C$\underline{H}_3$)$_2$); 2.63 (s, 4H, CO(C$\underline{H}_2$)$_2$CO); 2.82 (m, 2H, C$\underline{H}$N); 3.84 (m, 2H, OC$\underline{H}_2$); 4.12 (d, J= 6.84, 1H, OC$\underline{H}$RO); 4.56 (m, 2H, OC$\underline{H}_2$).

^{13}C NMR (125 MHz, $CDCl_3$)

δ= 17.74(2C, CH(C$\underline{H}_3$)$_2$); 26.46 (2C, CO(C$\underline{H}_2$)$_2$CO); 31.56 (1C, C$\underline{H}$(CH$_3$)$_2$); 47.46 (2C, C$\underline{H}$N); 66.64 (2C, OC$\underline{H}_2$); 112.42 (1C, OC$\underline{H}$RO); 172.45 (2C, C$\underline{O}$).

Isomer (**72b**)

Colourless solid; m.p. 142-144 °C.



^{1}H NMR (500 MHz, CD_2Cl_2)

δ= 0.88 (d, J= 6.88, 6H, CH(C<u>H</u>$_3$)$_2$); 1.83 (m, 1H, CH(C<u>H</u>$_3$)$_2$); 2.62 (s, 4H, CO(C<u>H</u>$_2$)$_2$CO); 2.71 (m, 2H, C<u>H</u>-N); 3.94 (d, J= 6.83, 1H, O-C<u>H</u>R-O); 3.98 (m, 2H, OC<u>H</u>$_2$); 4.62 (m, 2H, OC<u>H</u>$_2$).

^{13}C NMR (125 MHz, $CDCl_3$)

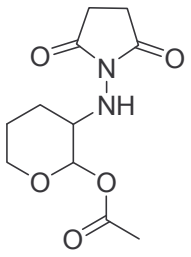
δ= 17.72(2C, CH(<u>C</u>H$_3$)$_2$); 26.60 (2C, CO(<u>C</u>H$_2$)$_2$CO); 32.23 (1C, <u>C</u>H(CH$_3$)$_2$); 48.15 (2C, <u>C</u>H-N); 65.36 (2C, O-<u>C</u>H$_2$); 111.28 (1C, O<u>C</u>HRO); 172.70 (2C, <u>C</u>O).

MS/APCI (+)

m/z (%) = 255 (100) $[M+H]^+$, 287 (21) $[M+H+MeOH]^+$.

m/z (%) = 255 (100) $[C_{12}H_{19}N_2O_4]^+$, 287 (21) $[C_{13}H_{23}N_2O_5]^+$.

4.6.1.7 Synthesis of acetic acid 3-(2,5-dioxo-pyrrolidin-1-ylamino)-tetrahydro-pyran-2-yl ester (77)



The crude product was purified by using column chromatography, alox basic as stationary phase and ethylacetate: petrol ether mixture (1:4) as mobile phase. The solvent was removed in vacuum to get (**77**).

Colourless sticky solid; 650 mg (yield 24%); dr 1:2.4.

Major diastereomer

Colourless solid; m.p. 130-132 °C.

^{1}H NMR (500 MHz, CD_2Cl_2)

δ=1.66 (m, 3H, NHCHC<u>H</u>C<u>H</u>$_2$); 1.92 (m, 1H, NHCHC<u>H</u>); 2.12 (s, 3H, OCOC<u>H</u>$_3$); 2.64 (s, 4H, CO(C<u>H</u>$_2$)$_2$CO); 3.27 (m, 1H, NHC<u>H</u>CH$_2$); 3.62 (m, 2H, OC<u>H</u>$_2$); 4.79 (d, 1H, J=9.9, OC<u>H</u>OAc); 5.86 (br s, 1H, N<u>H</u>).

^{13}C NMR (125 MHz, CD_2Cl_2)

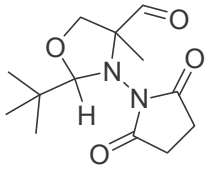
δ=21.1 (1C, $COCH_3$); 23.6 (1C, $OCH_2\underline{C}H_2$); 24.4 (1C, $NHCH\underline{C}H_2$); 26.6 (2C, $CO(\underline{C}H_2)_2CO$); 56.0 (1C, $NH\underline{C}HCH_2$); 61.0 (1C, $O\underline{C}H_2$); 90.0 (1C, $O\underline{C}HOAc$); 170.2 (1C, $O\underline{C}OCH_3$); 174.2 (2C, $\underline{C}O(CH_2)_2\underline{C}O$).

MS/ESI (+)

m/z (%) = 263 (100) $[M+Li]^+$, 519 (72) $[2M+Li]^+$.

m/z (%) = 263 (100) $[C_{11}H_{16}LiN_2O_5]^+$, 519 (72) $[C_{22}H_{32}LiN_4O_{10}]^+$.

4.6.1.8 Synthesis of 2-*tert*-butyl-4-methyl 3-(2,5-dioxopyrrolidin-1-yl)oxazolidine-4-carbaldehyde (84)



To a stirred suspension of 0.342 g, 3 mmol *N* -aminosuccinimide (**28**) and 0.844 g, 5.4 mmol 2-*tert*-butyl-5-methyl-4H-[1,3]dioxine (**26**), 2 g, 3Å molecular sieves in 6 ml dry acetonitrile, 0.792 g, 3.6 mmol iodosylbenzene was added over a period of 3 h under argon atmosphere. Stirred the reaction mixture for 15 h. The reaction was monitored by GC. The work-up was done by filtering the reaction mixture and solvent was removed in vacuum. The crude product was purified by column chromatography using silicagel as stationary phase and ethylacetate cyclohexane mixture (1:3) as mobile phase to obtain 0.216 g diastereomrs (**84**) as colourless solid.

Colourless solid; 0.216 g (yield 26.7%); d.r. 1: 5.5; de = 65%.

Major diastereomer

Colourless solid; $[\alpha]_D^{20}$ = + 51.05 (C= 2.2 in CH_2Cl_2); m.p. 120-122 °C.

^{1}H NMR (500 MHz, CD_2Cl_2)

δ=0.90 (s, 9H, $C(C\underline{H}_3)_3$); 0.96 (s, 3H, $C\underline{H}_3$); 2.70 (m, 4H, $CO(C\underline{H}_2)_2CO$); 3.85 (d, J=8.3,1H, $OC\underline{H}_2$); 4.50 (d, J=8.3, 1H, $OC\underline{H}_2$); 4.84 (s, 1H, $OC\underline{H}RN$); 9.56 (s, 1H, $C\underline{H}O$).

^{13}C NMR (125 MHz, CD_2Cl_2)

δ=12.2 (1C, $\underline{C}H_3$); 24.4 (3C, $C(\underline{C}H_3)_3$); 26.5 (1C, $CO(\underline{C}H_2)_2CO$); 26.8 (1C, $CO(\underline{C}H_2)_2CO$); 35.3 (1C, $\underline{C}(CH_3)_3$); 71.5 (1C, $N\underline{C}(CH_3)$; 72.6 (1C, $O\underline{C}H_2$); 99.0 (1C, $O\underline{C}HRN$); 175.5 (1C, $CO(CH_2)_2\underline{C}O$); 176.9 (1C, $\underline{C}O(CH_2)_2CO$); 200.8 (1C, $\underline{C}HO$).

Minor diastereomer- oil.

^{1}H NMR (500 MHz, CD_2Cl_2)

δ=0.86 (s, 9H, $C(C\underline{H}_3)_3$); 1.18 (s, 3H, $C\underline{H}_3$); 2.64 (m, 4H, $CO(C\underline{H}_2)_2CO$); 3.95 (d, J=9.3,1H, OCH_2); 4.27 (d, J=9.3, 1H, OCH_2); 5.03 (s, 1H, $OC\underline{H}RN$); 9.72 (s, 1H, $C\underline{H}O$).

^{13}C NMR (125 MHz, CD_2Cl_2)

δ=16.4 (1C, $\underline{C}H_3$); 24.4 (3C, $C(\underline{C}H_3)_3$); 26.8 (1C, $CO(\underline{C}H_2)_2CO$); 27.2 (1C, $CO(\underline{C}H_2)_2CO$); 36.7 (1C, $\underline{C}(CH_3)_3$); 71.3 (1C, $N\underline{C}(CH_3)$; 72.7 (1C, $O\underline{C}H_2$); 96.1 (1C, $O\underline{C}HRN$); 175.1 (1C, $\underline{C}O(CH_2)_2\underline{C}O$); 176.7 (1C, $\underline{C}O(CH_2)_2\underline{C}O$); 197.9 (1C, $\underline{C}HO$).

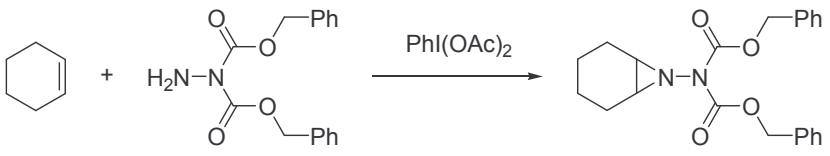
MS/APCI (+)

m/z (%) = 269 (100) $[M+H]^+$

m/z (%) = 269 (100) $[C_{13}H_{21}N_2O_4]^+$.

4.7 Synthesis of aziridines using *N,N*-dibenzyloxycarbonylhydrazine (12) as nitrogen source

4.7.1 Preparation of *N*-(dibenzyloxycarbonylamino)-7-azabicyclo[4.1.0]heptane (78)



To a stirred mixture of 3.0 g, 10 mmol *N,N*-dibenzyloxycarbonyl hydrazine (**12**), 1.648 g, 20 mmol cyclohexene (**61**) and 50 ml dichloromethane under nitrogen atmosphere at room temperature, 3.864 g, 12 mmol iodobenzenediacetate was added portion wise over a period of 3 h at an interval of 15 minutes and further stirred for 15 h. The solvent was removed in vaccum and crude product was purified by column chromatography using silica gel as

stationary phase and 10% ethylacetate: petrol ether as mobile phase. The eluted fractions containing the product were concentrated on rotatory and dried in high vacuum to obtain 3.6 g as a colourless solid.

Colourless solid; 3.8 g (yield 60%).

The m.p. and ^{1}H NMR are in good agreement with the lit.[44] data.

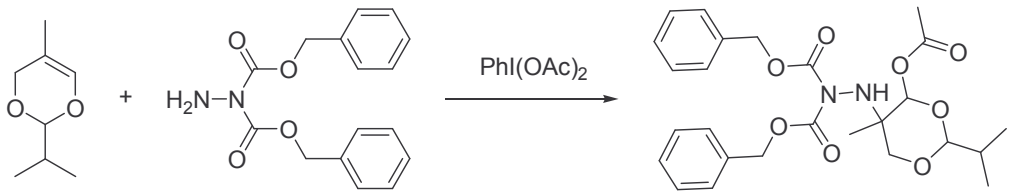
^{13}C NMR (125 MHz, $CDCl_3$)

δ=22.0 (2C, $NHCH_2\underline{C}H_2$); 22.7 (2C, $NH\underline{C}H_2$); 44.9 (2C, $N\underline{C}H$); 69.0 (2C, $O\underline{C}H_2Ph$); 128.5 (2C, C_4 arom); 128.5 (4C, C_3+C_5 arom); 128.5 (4C, C_2+C_6 arom); 134.9 (2C, C_1 arom); 152.3 (2C, CO).

HRMS/ESI (+)

m/z (%) = 403.1628 $[M+Na]^+$ measured value and calculated value 403.1634 $[C_{22}H_{24}N_2NaO_4]^+$.

4.7.2 Synthesis of acetic acid 5-(*N,N*-dibenzyloxycarbonyl-hydrazino)-2-isopropyl-5-methyl-[1,3] dioxin-4-yl ester (79)



To a stirred mixture of 3.0 g *N,N*-dibenzyloxycarbonylhydrazine (**12**), 2.84 g, 20 mmol 2-isopropyl-5-methyl-4*H*-[1,3]dioxine (**21**) and 50 ml dichloromethane at room temperature, 3.86 g, 12 mmol iodobenzenediacetate was added portion wise over a period of 3 h under nitrogen atmosphere at room temperature and further stirred for 17 h. The solvent was removed under vacuum to get oil. In the oily mass 25 ml diethyl ether was added, heated to reflux for 5 minutes, cooled to room temperature and put at -20 °C for 12 h for crystallisation. The solid was isolated by filteration and dried in high vacuum. The diastereomeric ratio of **79** in the crude reaction mixture was 1:1.8, determined by ^{1}H NMR. Major diastereomer was lost during the work-up.

Colourless solid; 1.3 g (yield 26%); m.p. 78-79 °C.

^{1}H NMR (500 MHz, $CDCl_3$)

δ=0.78 (s, 3H, C<u>H</u>$_3$); 0.87 (d, J= 6.8, 2H, CHC<u>H</u>$_3$); 0.89 (d, J= 6.8, 2H, CHC<u>H</u>$_3$); 1.78 (dqq, J=6.8, J=6.8, J=4.9, 1H, OC<u>H</u>R); 2.11 (s, 3H, OC<u>H</u>$_3$); 3.74 (d, J=11.6, O-C<u>H</u>$_2$, ax); 3.87 (d, J=11.6, ^{4}J=1.6, O-C<u>H</u>$_2$, eq); 4.65 (d, J=4.8, OC<u>H</u>R); 5.27 (s, 4H,OC<u>H</u>$_2$Ph); 6.06 (s, 1H, OC<u>H</u>OAc); 7.35 (m, 10H, CH arom).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=14.8 (1C, <u>C</u>H$_3$); 16.3 (1C, CH<u>C</u>H$_3$)$_2$; 16.7 (1C, <u>C</u>HCH$_3$)$_2$; 21.0 (1C, CO<u>C</u>H$_3$); 55.7 (C, CH$_3$<u>C</u>HNH); 69.4 (2C, O-<u>C</u>H$_2$Ph); 70.3 (1C, O-<u>C</u>H$_2$CHCH$_3$); 93.5 (1C, O-<u>C</u>H-R); 98.5 (1C, O<u>C</u>HCNH); 128.4 (4C, C_3+C_5 arom); 128.4 (2C, C_4 arom); 128.5 (4C, C_2+C_6 arom); 134.8 (2C, C_1 arom), 154.6 (2C, <u>C</u>OCH$_2$Ph), 168.7 (1C, O-<u>C</u>OCH$_3$).

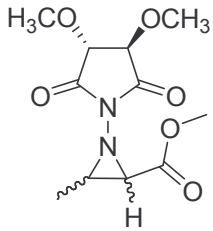
MS/ESI (+)

m/z (%) = 501 (6) $[M+H]^+$, 523 (100) $[M+Na]^+$.

m/z (%) = 501 (6) $[C_{26}H_{33}N_2O_8]^+$, 523 (100) $[C_{26}H_{32}N_2O_8Na]^+$.

4.8 Synthesis of diastereoselective aziridines using (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (29) as nitrogen source and prochiral alkenes

4.8.1 Synthesis of methyl 1-((3*R*,4*R*)-3,4-dimethoxy-2,5-dioxopyrrolidin-1-yl)-3-methylaziridine-2 carboxylate (89)



To a stirred suspension of 2.0 g (20 mmol) of methyl crotonate (**63**), 1.74 g (10 mmol) (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) in 50 ml dry acetonitrile and 5 g activated molecular sieves 3Å, 2.64 g (12 mmol) iodosylbenzene was added portion wise over a period of 3 h at room temperature under nitrogen atmosphere. The reaction mixture was further stirred for 17 h. The reaction was monitored by GC. The reaction mixture was filtered

through sintered funnel and washed the molecular sieves with 50 ml acetonitrile. To obtain the crude product, the solvent was removed under vacuum. Crude product was purified using column chromatography on silica gel using ethyl acetate: perol ether (1:5) yielded (**89**) as a colourless oil.

Colourless oil; 1.77 g (yield 65%); d.r. 1:1.34.

Major diastereomer

^{1}H NMR (500 MHz, $CDCl_3$)

δ=1.41 (d, J=6, 3H, NCHC$\underline{H}_3$); 2.99 (d, J=4.9, 1H, NC$\underline{H}$CO); 3.13 (m, 1H, NC$\underline{H}$CH$_3$); 3.63 (s, 6H, OC$\underline{H}_3$); 3.68 (s, 3H, COOC$\underline{H}_3$); 4.12 (s, 2H, C$\underline{H}$OCH$_3$).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=16.0 (1C, NCH$\underline{C}$H$_3$); 44.2 (1C, N$\underline{C}$HCH$_3$); 45.3 (1C, $\underline{C}$HCOOCH$_3$); 52.8 (1C, COO$\underline{C}$H$_3$); 59.3 (2C, CHO$\underline{C}$H$_3$); 79.8 (2C, $\underline{C}$HOCH$_3$); 167.4 (1C, $\underline{C}$OOCH$_3$); 168.6 (2C, N$\underline{C}$O).

Minor diastereomer

^{1}H NMR (500 MHz, $CDCl_3$)

δ=1.43 (d, J=5.7, 3H, NCHC$\underline{H}_3$); 2.95 (d, J=5.3, 1H, NC$\underline{H}$CO); 3.13 (m, 1H, NC$\underline{H}$CH$_3$); 3.64 (s, 6H, OC$\underline{H}_3$); 3.68 (s, 1H, COOC$\underline{H}_3$); 4.07 (s, 2H, C$\underline{H}$OCH$_3$).

^{13}C (125 MHz, $CDCl_3$)

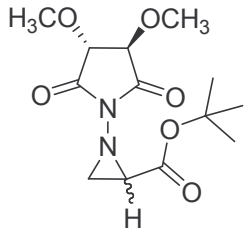
δ=16.1 (1C, NCH$\underline{C}$H$_3$); 44.0 (1C, N$\underline{C}$HCH$_3$); 45.3 (1C, $\underline{C}$HCOOCH$_3$); 52.7 (1C, COO$\underline{C}$H$_3$); 59.3 (2C, CHO$\underline{C}$H$_3$); 79.8 (2C, $\underline{C}$HOCH$_3$); 167.1 (1C, $\underline{C}$OOCH$_3$); 168.5 (2C, N$\underline{C}$O).

MS/ESI (+):

m/z (%) = 295 (100) $[M+Na]^+$, 567 (10) $[2M+Na]^+$.

m/z (%) = 295 (100) $[C_{11}H_{16}N_2NaO_6]^+$, 567 (10) $[C_{22}H_{32}N_4NaO_{12}]^+$.

4.8.2 Synthesis of 2-*tert*-butyl-1-((3*R*,4*R*)-3,4-dimethoxy-2,5-dioxopyrrolidin-1-yl)-2-methylaziridine-2-carboxylate (91)



To a stirred suspension of 12.8 g (100 mmol) of *tert*-butyl acrylate (**90**), 1.74 g (10 mmol) (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**) in 50 ml dry acetonitrile and 5 g activated molecular sieves 3Å, 2.64 g (12 mmol) iodosylbenzene was added portion wise over a period of 3 h at room temperature under nitrogen atmosphere. The reaction mixture was further stirred for 17 h. The reaction was monitored by GC. The reaction mixture was filtered through sintered funnel and washed the molecular sieves with 50 ml acetonitrile. To obtain the crude product, the solvent was removed under vacuum. Crude product was purified using column chromatography on silica gel using perol ether: ether (1:1) yielded (**91**) as a colourless oil.

Colourless oil; 1.1 g (yield 36**%)**; d.r. 1:1.5.

Major diastereomer

^{1}H NMR (500 MHz, $CDCl_3$)

δ=1.49 (s, 9H, C($C\underline{H}_3$)$_3$); 2.63 (dd, J=7.8, 2.0, 1H, NC$\underline{H}_2$); 2.74 (dd, J=5.2, 2.0, 1H, NC$\underline{H}_2$); 2.84 (dd, J=7.8, 5.2, 1H, NC$\underline{H}$); 3.66 (s, 6H, OC$\underline{H}_3$); 4.01 (s, 2H, C$\underline{H}$OCH$_3$).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=27.60 (3C, C($\underline{C}H_3$)$_3$); 36.68 (1C, N$\underline{C}H_2$); 40.39 (1C, N$\underline{C}$H); 59.75 (2C, CHO$\underline{C}H_3$); 80.00 (2C, $\underline{C}$HOCH$_3$); 82.78 (1C, O$\underline{C}$(CH$_3$)$_3$); 165.52 (1C, $\underline{C}$OOC(CH$_3$)$_3$); 168.10 (2C, N$\underline{C}$O).

Minor diastereomer

^{1}H NMR (500 MHz, $CDCl_3$)

δ=1.425 (s, 9H, C($C\underline{H}_3$)$_3$); 2.45 (dd, J=7.8, 2.0, 1H, NC$\underline{H}_2$); 2.72 (dd, J=5.7, 2.0, 1H, NC$\underline{H}_2$); 2.96 (dd, J=7.8, 5.7, 1H, NC$\underline{H}$); 3.67 (s, 6H, OC$\underline{H}_3$); 4.03 (s, 2H, C$\underline{H}$OCH$_3$).

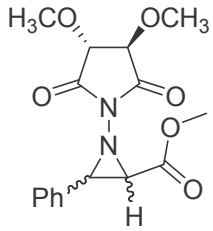
^{13}C NMR (125 MHz, $CDCl_3$)

δ=27.90 (3C, C($\underline{C}H_3)_3$); 35.92 (1C, N$\underline{C}H_2$); 41.24 (1C, N$\underline{C}$H); 59.74 (2C, CHO$\underline{C}H_3$); 79.9 (2C, $\underline{C}$HOCH$_3$); 82.74 (1C, O$\underline{C}(CH_3)_3$); 166.47 (1C, $\underline{C}$OOC$(CH_3)_3$); 168.06 (2C, N$\underline{C}$O).

HRMS/ESI (+):

m/z (%)= 322.1213 $[M+Na]^+$ measured value, and calculated value 322.1213 $[C_{13}H_{20}N_2NaO_6]^+$.

4.8.3 Synthesis of methyl-1-((3*R*,4*R*)-3,4-dimethoxy-2,5-dioxopyrrolidin-1-yl)-3-phenylaziridine-2 carboxylate (93)



To a stirred suspension of 3.24 g (20 mmol) of *trans*-methyl cinnamate (**92**), 1.74 g (10 mmol) (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**), 1.2 g (30 mmol) MgO in 50 ml dry acetonitrile and 5 g activated molecular sieves 3Å, 2.64 g (12 mmol) iodosylbenzene was added portion wise over a period of 3 h at room temperature under nitrogen atmosphere. The reaction mixture was further stirred for 17 h. The reaction was monitored by GC. The reaction mixture was filtered through sintered funnel and washed the molecular sieves with 50 ml acetonitrile. To obtain the crude product, the solvent was removed under vacuum. Crude product was purified using column chromatography on silica gel using ether: perol ether (1:1) yielded (**93**) as a colourless oil.

Colourless oil; 0.67 g (yield 20%); d.r. 1:1.1.

^{1}H NMR (500 MHz, $CDCl_3$)

δ=3.45/3.49 (d, J=5.4, 1H, C$\underline{H}$COOMe); 3.68/3.69 (s, 6H, OC$\underline{H}_3$); 3.76/3.76 (s, 3H, COOC$\underline{H}_3$); 4.14/4.20 (s, 2H, C$\underline{H}$OCH$_3$); 4.17/4.18 (d, J=4.9, 1H, C$\underline{H}$Ph); 7.35 (m, 5H, C$\underline{H}$ arom).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=45.1/46.4 (1C, N<u>C</u>HCOOMe); 49.0/50.0 (1C, N<u>C</u>HPh); 53.0/53.1 (1C, COO<u>C</u>H$_3$); 59.4/59.5 (2C, CHO<u>C</u>H$_3$); 79.9/80.0 (2C, <u>C</u>HOCH$_3$); 127.0/127.1 (2C, arom); 128.6/128.8 (2C, arom); 133.8/133.9 (1C, arom); 166.5/ 166.8 (1C, <u>C</u>OOCH$_3$); 168.4/168.6 (2C, <u>C</u>O).

HRMS/ESI (+):

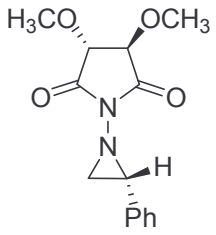
m/z (%)= 357.1057 $[M+Na]^+$ measured value and calculated value 357.1063 $[C_{16}H_{18}N_2NaO_6]^+$.

4.8.4 Synthesis of (3*R*,4*R*)-3,4-dimethoxy-1-((*R*)-2-phenylaziridin-1-yl)pyrrolidine-2,5-dione (94a)

To a stirred suspension of 10.40 g (100 mmol) of styrene (**67**), 1.74 g (10 mmol) (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**), 1.2 g (30 mmol) MgO in 50 ml dry acetonitrile and 5 g activated molecular sieves 3Å, 2.64 g (12 mmol) iodosylbenzene was added portion wise over a period of 3 h at room temperature under nitrogen atmosphere. The reaction mixture was further stirred for 17 h. The reaction was monitored by GC. The reaction mixture was filtered through sintered funnel and washed the molecular sieves with 50 ml acetonitrile. To obtain the crude product, the solvent was removed under vacuum. Crude product was purified using column chromatography on silica gel using ether: perol ether (1:3) yielded (**94**) as a colourless solid.

Colourless solid; 1.24 g (yield 45%); m.p. 108-110 °C; d.r. 1:3.

Major diastereomer (**94a**)



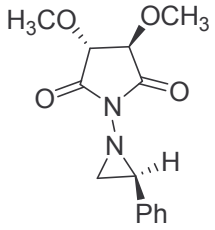
^{1}H NMR (500 MHz, $CDCl_3$)

δ=2.61 (dd, J=8.1, 2.7, 1H, NC<u>H</u>$_2$); 2.71 (dd, J=6.0, 2.7, 1H, NC<u>H</u>$_2$); 3.49 (dd, J=8.1, 6.0, 1H, NC<u>H</u>); 3.68 (s, 6H, OC<u>H</u>$_3$); 4.06 (s, 2H, C<u>H</u>OCH$_3$), 7.37 (m, 5H, CH arom).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=39.17 (1C, N<u>C</u>H_2); 45.02 (1C, N<u>C</u>H); 59.71 (2C, CHO<u>C</u>H_3); 80.10 (2C, <u>C</u>HOCH_3); 127.05 (2C, arom); 128.17 (1C, arom); 128.49 (2C, arom); 135.68 (1C, arom); 168.55 (2C, <u>C</u>O).

Minor diastereomer (**94b**); colourless oil.



^{1}H NMR (500 MHz, $CDCl_3$)

δ=2.72 (dd, J=5.9, 2.6, 1H, NC<u>H</u>$_2$); 2.77 (dd, J=8.0, 2.6, 1H, NC<u>H</u>$_2$); 3.37 (dd, J=8.0, 5.9, 1H, NC<u>H</u>); 3.67 (s, 6H, OC<u>H</u>$_3$); 4.05 (s, 2H, C<u>H</u>OCH_3), 7.5 (m, 5H, CH arom).

^{13}C NMR (125 MHz, $CDCl_3$)

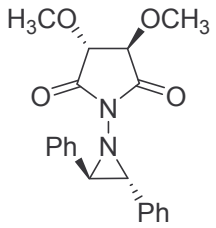
δ=39.95 (1C, N<u>C</u>H_2); 44.14 (1C, N<u>C</u>H); 59.66 (2C, CHO<u>C</u>H_3); 79.98 (2C, <u>C</u>HOCH_3); 127.09 (2C, arom); 128.15 (1C, arom); 128.47 (2C, arom); 135.65 (1C, arom); 168.65 (2C, <u>C</u>O).

HRMS/ESI (+)

m/z (%)= 299.1002 $[M+Na]^+$ measured value and calculated value 299.1002

$[C_{14}H_{16}N_2NaO_6]^+$.

4.8.5 Synthesis of (3*R*,4*R*)-3,4-dimethoxy-1-((2*R*,3*R*)-2,3-diphenylaziridin-1-yl)pyrrolidine-2,5 dione (95a)



To a stirred suspension of 3.60 g (20 mmol) of *trans*-stilbene (**65**), 1.74 g (10 mmol) (3*R*,4*R*)-(+)-*N*-amino-3,4-dimethoxy succinimide (**29**), 1.2 g (30 mmol) MgO in 50 ml dry DMF and 5 g activated molecular sieves 3Å, 2.64 g (12 mmol) iodosylbenzene was added portion wise over a period of 3 h at room temperature under nitrogen atmosphere. The reaction mixture was further stirred for 17 h. The reaction was monitored by GC. The reaction mixture was filtered through sintered funnel and washed the molecular sieves with 50 ml DMF. To obtain the crude product, the solvent was removed under vacuum. Crude product was purified using column chromatography on silica gel using ether: perol ether (1:1) yielded (**95**) as a colourless solid.

Colourless solid; 1.07 g (yield 30%); m.p. 112-114 °C; d.r. 1: 5.

Major diastereomer (**95a**)

^{1}H NMR (500 MHz, $CDCl_3$)

δ=3.56 (s, 6H, $OC\underline{H}_3$); 3.69 (s, 2H, $C\underline{H}OCH_3$), 3.94 (d, J= 5.2, 1H, $C\underline{H}$Ph); 4.83 (d, J= 5.2, 1H, $C\underline{H}$Ph); 7.35 (m, 8H, C<u>H</u> arom); 7.50 (m, 2H, C<u>H</u> arom).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=46.2 (1C, N<u>C</u>HPh); 53.3 (1C, N<u>C</u>HPh); 59.3 (2C, CHO<u>C</u>H$_3$); 79.6 (2C, <u>C</u>HOCH$_3$); 127.0 (2C, arom); 128.2 (2C, arom); 128.5 (2C, arom); 129.0 (2C, arom); 129.3 (2C, arom); 130.2 (1C, arom); 135.7 (1C, arom); 169.1 (2C, <u>C</u>O).

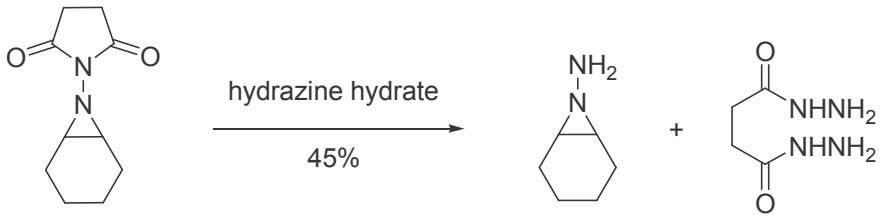
HRMS/ESI (+):

m/z (%)= 375.1315 $[M+Na]^+$ measured value and calculated value 375.1321

$[C_{20}H_{20}N_2NaO_4]^+$.

4.9 Synthesis of *N*-amino aziridine

4.9.1 Synthesis of 7-aza-bicyclo[4.1.0]hept-7-ylamine (97)



1.774 g, 9 mmol 1-(7-aza-bicyclo[4.1.0]hept-7-yl)-pyrrolidine-2,5-dione (**62**), 6.58 g, 131 mmol hydrazine hydrate and 50 ml methanol were stirred and subsequently heated to reflux for 1 h, then cooled to room temperature. The reaction mixture was filtered to remove succindihydrazide and mother liquor was concentrated under reduced pressure to obtain an oil. The oil was extracted 10×100 ml pentane and solvent was removed to obtain (**97**) as an oil.

Viscous oil, 0.772 g (yield 44.5%).

^{1}H NMR (500 MHz, $CDCl_3$)

δ=4.20 (m, 4H, NCH($C\underline{H}_2$)$_2$); 4.51 (m, 6H, $C\underline{H}_2$($C\underline{H}$)$_2C\underline{H}_2$); 5.53 (br s, NH_2).

^{13}C NMR (125 MHz, $CDCl_3$)

δ=20.4 (2C, $CHCH_2(\underline{C}H_2)_2$); 23.2 (2C, $\underline{C}H_2(CH)_2\underline{C}H_2$); 42.5 (2C, $\underline{C}H\underline{C}H$).

MS/APCI (+):

m/z (%) = 113 (100) $[M+H]^+$.

m/z (%) = 113 (100) $[C_6H_{13}N_2]^+$.

Succindihydrazide (31)

Colourless solid; m.p. 160-162 °C (Lit.[57] m.p. 167 °C).

^{1}H NMR (500 MHz, DMSO-d_6)

δ=2.24 (4H, s, CO(C<u>H</u>$_2$)$_2$CO); 3.67 (br s, 4H, NHN<u>H</u>$_2$); 8.99 (br s, 2H, N<u>H</u>NH$_2$).

^{13}C NMR (125 MHz, DMSO-d_6)

δ=29.0 (2C, CO(<u>C</u>H$_2$)$_2$CO); 170.9 (2C, <u>C</u>O(<u>C</u>H$_2$)$_2$<u>C</u>O).

MS/APCI (+):

m/z (%) = 147 (100) $[M+H]^+$.

m/z (%) = 147 (100) $[C_4H_{11}N_4O_2]^+$.

5 Abbreviation

Abs.	Absolute
Ac	Acetyl
ACN	Acetonitrile
Acac	Acetylacetonate
Ar	Aryl
ax	axial
B	Base
Boc	*tert*-Butyloxycarbonyl
bp	Boiling point
Cat.	Catalyst
Cbz	*tert*-Benzyloxycarbonyl
d	Doublet
de	Diastereomeric excess
dr	Diastereomeric ratio
δ	Chemical shift
DABCO	1,4-Diazabicyclo[2.2.2]octane
DBU	1,8-Diazabicyclo[5.4.0]undeca-7-ene
DCC	*N,N'*-dicyclohexyl carbodiimide
DIOP	4,5-Bis-(diphenylphosphinomethyl)-2,2-dimethyl-(1,3)-dioxolan
DMAP	4-(Dimethylamino)pyridine
DMF	*N,N*-Dimethylformamide
DMSO	*N,N*-Dimethylsulfoxide
DuPHOS	1,2-Bis(2,5-dimethylphospholanyl)benzene
ee	enantiomeric excess

eq	equatorial
eV	Electron volt
EDTA	Ethylenediamine-*N,N,N′,N′*-tetraacetate
Et	Ethyl
et al	and other
Et_2O	Diethylether
FID	Flame ionisation detecto
GC	Gas chromatography
h	Hour
IPA	*iso*-Propyl alcohol
HMPA	Hexamethylphosphorictriamide
Hz	Hertz
IR	Infrared spectroscopy
J	Coupling constant
KHMDS	Calcium-bis-(trimethylsilyl)-amide
L*	Chiral ligand
LDA	Lithium diisopropylamide
LTA	Lead tetraacetate
*m*CPBA	*m*-Chloroperbenzoic acid
m	Multiplet
m	meta
Me	Methyl
mol%	mol percent
MOM	Methoxymethyl
m.p.	Melting point
MS	Molecular sieve
NOE	Nuclear Overhauser Effect

Ns	*p*-Nitrobenzene sulfonyl
OTf	Trifluoromethanesulfonate
PG	Protecting group
Ph	Phenyl
ppm	Relative chemical shift
PTAB	Phenyltrimethyl ammoniumtribromide
PTSA	*p*-Toluenesulfonic acid
$Py.Br_3$	Pyridinehydrobromide perbromide
q	Quartet
Q	Quinazolinone
quin	Quintet
RT	Room temperature
s	Singlet
sep	Septet
SES	2-(Trimethylsilyl)ethanesulfonyl
Sext.	Sextet
t	Triplet
TBME	*tert*-Butyl methyl ether
TEA	Triethyl amine
TMSOTf	Trimethylsilyl triflate
temp.	Temperature
tert	Tertiary
TASF	Tris-(dimethylamino)-sulfonium-difluorotrimethylsilicate
TBAF	Tetrabutylammoniumfluoride
tfacam	trifluoroacetamide
THF	Tetrahydrofuran
TLC	Thin layer chromatography

TPP	Tetraphenylporphyrin
Ts	*p*-Toluenesulfonyl
UV	Ultra violet

6 References

1. (a) A. Padwa, S. S. Murphree, In *Progress in Het. Chem.*, G.W. Gribble, T. L. Gilchrist, Eds., Elsevier Science: Oxford **2000**, Vol. 12, Chapter 4.1, p 57.
(b) A. Padwa, A. D. Woolhouse, W. Lwowski, In *Comp. Het. Chem.*, Ed., Pergamon Press: Oxford **1984**, Vol. 7, pp 47-93.

2. (a) X. E. Hu, *Tetrahedron* **2004**, *60*, 2701.
(b) W. McCoull, F. A. Davis, *Synthesis* **2000**, 1347.

3. J. B. Sweeney, *Chem. Soc. Rev.* **2002**, 31, 247.

4. L. Antolini, M. Bucciarelli, A. Forni, I. Moretti and F. Prati, *J. Chem. Soc., Chem. Commun.*, **1991**, 538.

5. G. E. Ham, *J. Org. Chem.* **1964**, 29, 3052.

6. (a) K. R. Kunz, B. S. Iyengar, R. T. Dorr, D. S. Alberts, W. A. Remers, *J. Med. Chem.* **1991**, 34, 2281.
(b) S. Kinoshita, K. Uzu, K. Nakano, M. Shimizu, T. Takahasahi, *J. Med. Chem.* **1971**, 14 (2), 103.
(c) I. Han, H. Kohn, *J. Org. Chem*. **1991**, 56, 4648.

7. R. S. Coleman, A. J. Carpenter, *J. Org. Chem.* **1992**, 57, 5813.

8. I. D. Watson, L.Yu, A. K. Yudin, *Acc. Chem. Res*. **2006**, 39, 194.

9. R. Ren, R. M. Borzilleri, X. Zheng, S. H. Kim, J. A. Johnson, C. R. Fairchild, F. Y. Lee, B. H. Long, G. D. Vite, *Org. Lett.* **2001**, 2693.

10. F. Gerhart, W. Hinggins, C. Tardif, J. Ducep, *J. Med. Chem*. **1990**, 33, 2157.

11. M. E. Tanner, S. Miao, *Tetrahedron: Lett.* **1994**, 35, 4073.

12. M. Dumić, M.Vinković, D. Filić, B. Jamnicky, M. Eškinja, B. Kamenar, *J. Med. Chem.* **1995**, 38, 3034.

13. (a) N. A. Helsby, G. J. Atwell, S. Yang, B. D. Palmer, R. F. Anderson, S. M. Pullen,

D. M. Ferry, A. Hogg, W. R. Wilson, W. A. Denny, *J. Med. Chem.* **2004**, *47,* 3295.
(b) P. Kestell, F. B. Pruijn, B. G. Siim, B. D. Palmer, W. R. Wilson,
Cancer Chemother Pharmacol **2000**, 46, 365.

14. D. Tanner, F. Johansson, A. Hardenb, P. G. Andersson, *Tetrahedron* **1998**, 54, 15731.

15. N. J. Church, D. W. Young, *Tetrahedron Lett.* **1995**, 36 (1), 151.

16. P. Dauban, R. H. Dodd, *Tetrahedron Lett.* **1998**, 39, 5739.

17. R. S. Atkinson, R. D. Draycott, D. J. Hirst, M. J. Parratt,
T. M. Raynham, *Tetrahedron Lett.* **2002**, 43, 2083.

18. S. M. Lu, H. Alper, *J. Org. Chem.* **2004**, *69*, 3558.

19. (a) D. Tanner, P. Somfai, *Tetrahedron Lett.* **1987**, 28 (11), 1211.
(b) D. Tanner, P. Somfai, *Tetrahedron* **1988**, 44 (2), 619.

20. K. Imae, H. Kamachi, H. Yamashita,T. Okita, S. Okuyama, T. Tsuno, T. Yamasaki, Y. Sawada, M. Ohbayashi, T. Naito, T. Oki, *J. Antibiotics* **1991**, 76.

21. K. J. Hale, M. M. Domostoj, D. A. Tocher, E. Irving, F. Scheinmann,
Org. Lett. **2003**, 5 (16), 2927.

22. P. Li, C. D. Evans, M. M. Joullie, *Org. Lett.* **2005**, 7 (23), 5325.

23. P. Li, C. D. Evans, E. M. Forbeck, H. Park, R. Bai, E. Hamel, M. M. Joullie,
Bioorg. & Med. Chem. Lett. **2006**, 16, 4804.

24. T. Teshima, K. Konishi, T. Shiba, *Bull. Chem. Soc. Jpn*. **1980**, 53, 508.

25. M. T. Barros, P. M. Matias, C. D. Maycock, M. R. Ventura,
Org. Lett. **2003**, 5 (23), 4322.

26. P. Garner, J. M. Park, *J. Org. Chem.* **1987**, 52, 2361.

27. Avenoza, C. Cativiela, F. Corzana, J. M. Peregrina, M. M. Zurbano,
J. Org. Chem. **1999**, *64,* 8220.

28. Avenoza, C. Cativiela, J. M. Peregrina, M. M. Zurbano, *Tetrahedron: Asymmetry* **1996**, 7, 1555.

29. R. Villard, F. Fotiadu, G. Buono, *Tetrahedron: Asymmetry* **1998**, 9, 607.

30. Avenoza, C. Cativiela, F. Corzana, J. M. Peregrina, M. M. Zurbano, *Tetrahedron: Asymmetry* **2000**, 11, 2195.

31. Avenoza, C. Cativiela, J. M. Peregrina, D. Sucunza, M. M. Zurbano, *Tetrahedron: Asymmetry* **1999**, 10, 4653.

32. S. Flock, H. Frauenrath, *Synlett* **2001**, No. 6, 839.

33. (a) R. A. Abramovitch, T. D. Bailey, T. Takaya, V. J. Uma, *Org. Chem.* **1974**, *39*, 340.
(b) Y. Yamada, T. Yamamoto, M. Okawara, *Chem. Lett*. **1975**, 361.
(c) D. A. Evans, M. M. Faul, M. T. Bilodeau, *J. Org. Chem.* **1991***,* 56 (24), 6744.

34. (a) P. J. Pérez, M. Brookhart, J. L. Templeton, *Organometallics* **1993**, *12*, 261.
(b) J. G. Knight, M. P. Muldowney, *Synlett* **1995**, 949.
(c) P. Müller, C. Baud, Y. Jacquier, *Tetrahedron* **1996**, *52*, 1543.
(d) I. Nägeli, C. Baud, G. Bernardinelli, Y. Jacquier, M. Moran, P. Müller, *Helv. Chim. Acta* **1997**, *80*, 1087.
(e) M. J. Södergren, D. Alonso, A. V. Bedekar, P. G. Andersson, *Tetrahedron Lett.* **1997**, *38*, 6897.
(f) D. Macikenas, B. V. Meprathu, J. D. Protasiewicz, *Tetrahedron Lett.* **1998**, *39*, 191.

35. P. Müller, C. Baud, I. Nägeli, *J. Phys. Org. Chem.* **1998**, *11*, 597.

36. (a) B. D. Heuss, M. F. Mayer, S. Dennis, M. M. Hossain, *Inorg. Chim. Acta* **2003**, *342*, 301.
(b) S. Taylor, J. Gullick, P. McMorn, D. Bethell, P. Bulman, C. Philip, F. E. Hancock, F. King, G. J. Hutchings, *Top. Catal.* **2003**, *24*, 43.

37. (a) P. Dauban, L. Saniere, A. Tarrade, R. H. Dodd, *J. Am. Chem. Soc.* **2001**, *123*, 7707
(b) K. Guthikonda, J. Du Bois, *J. Am. Chem. Soc.* **2002**, *124*, 13672.
(c) H. Han, I. Bae, E. J. Yoo, J. Lee, Y. Do, S. Chang, *Org. Lett.* **2004**, *6*, 4109.
(d) H. L. Kwong, D. Liu, K. Y. Chan, C. S. Lee, K. H. Huang, C. M. Che, *Tetrahedron Lett.* **2004**, 45, 3965.

38. D.J. Anderson, T.L. Gilchrist, D.C. Horwell, C.W. Rees, *J. Chem. Soc., Chem. Commun.* **1970**, 576.

39. D. J. Anderson, T. L. Gilchrist, D. C. Horwell, C. W. Rees, *Chem. Commun.,* **1969**, 146.

40. C. W. Rees, M. Yelland, *J. Chem. Soc. Perkin I, Commun.* **1972**, 77.

41. (a) T. Siu, A. K. Yudin, *J. Am. Chem. Soc.* **2002**, 124 (4), 530.
(b) T. Siu, C. J. Picard, A. K. Yudin, *J. Org. Chem.* **2005**, *70*, 932.
(c) R. S. Atkinson, E. Barker, *Chem. Commun*., **1995**, 819.

42. L. B. Krasnova, R. M. Hili, O. V. Chernoloz, A. K. Yudin, *ARKIVOC* **2005**, (iv), 26.

43. K. K. Mayer, F. Schröppel, J. Sauer, *Tetrahedron Lett.* **1972**, No. 29, 2899.

44. R. Milcent, M. G. Soghomoniantz, G. Barbier, *J. Het. Chem.* **1986**, 23, 1845.

45. M. Baudru, A. Foucaud, *Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques* **1970**, 270(1), 104.

46. H. Kwart, A. A. Kahn, *J. Chem. Soc.* **1967**, 89, 1950.

47. (a) R.S. Atkinson, K.L. Skinner, *J. Chem. Soc., Chem. Commun.* **1983**, 22.
(b) R. S. Atkinson, M. J. Grimshire, J. B. Kelly, *Tetrahedron* **1989**, 2875.

48. R. S. Atkinson, A. P. Ayscough, W. T. Gattrell, T. M. Raynham, *J. Chem. Soc., Perkin Trans. 1*. **1998**, 2783.

49. D. Dittmann, University of Kassel, unpublished work.

50. H. D. K. Drew, H. H. Hatt, *J. Chem. Soc*. **1937**, 16.

51. (a) Y. Arroyo, A. Meana, J.F. Rodríguez, M. Santos, M. A. S. Tejedor, J. L. G. Ruano, *Tetrahedron* **2006**, 62, 8525.
(b) E. K. Dolence, J. B. Roylance, *Tetrahedron: Asymmetry* **2004**, 15, 3307.
(c) C. S. Park, H. G. Choi, H. Lee, W. K. Lee, H. J. Ha*,* *Tetrahedron: Asymmetry* **2000**, 11, 3283.

52. (a) W. H. Schuller, R. V. Lawrence, *J. Chem. Eng. Data* **1967**, 12, 267.
(b) C. Li, X. Pan, C. Hua, J. Su, H. Tian, *European Polymer Journal* **2003**, 39, 1091.
(c) Z. Wang, J. Zhu, K. Chen, H. Tian, *J. Chem. Research (S)* **1999**, 438.
(d) K. R Scott, P. G. Kennedy, M. Kemp, V. G, Telang, W. H. Matthews, *J. Pharmaceutical Sciences* **1983**, 72(2), 183.
(e) J. Lange, S. Rump, G. Borkowska, M. Kowalczyk, J. Lapszewicz, B. Miagaj, K. Walczyna, *Pharmazie* **1984**, 39, 318.
(f) L. I. Kas'yan, I. N. Tarabara, Y. S. Bondarenko, S. V. Shishkina, O. V. Shishkin, V. I. Musatov, *Russian J. Org. Chem.* **2005***,* 41 (8), 1122.

53. M. G. Rowlands, M. A. Bunnett, A. B. Foster, M. Jarman, J. Stanek, E. Schweizer, *J. Med. Chem.* **1988**, 31, 971.

54. J. Bergman, T. Janosik, E. Koch, B. Pelcman, *J. Chem. Soc. Perkin Trans. 1*, **2000**, 2615.

55. W. Saal, R. Reinhardt, H. M. Seidenspinner, J. Stawitz, H. Quast, *Liebigs Ann. Chem*. **1989**, 703.

56. J. G. Krause, S. Kwon, B. George, *J. Org. Chem.* **1972**, 37 (12), 2040.

57. T. Curtius, *J. für Praktische Chemie (Leipzig)* **1915**, 92, 102.

58. E. Hedaya, R. L. Hinman, V. Schomaker, S. Theodoropulos, L. M. Kyle, *J. Am. Chem. Soc.* **1967**, 4876.

59. H. Feuer, G. B. Bachman, E. H. White, *J. Am. Chem. Soc.* **1951**, 4716.

60. J. Gut, A. Novacek, P. Fiedler, *Coll. Cz. Chem. Commun.* **1968**, 33(7), 2087.

61. P. S. Portoghese, H. Nagase, A. W. Lipkowski, D. L. Larson, A. E. Takemori, *J. Med. Chem.* **1988**, 31(10), 2056.

62. N. Merkley, J. Warkentin, *Can. J. Chem.* **2000**, 78 (7), 942.

63. G. B. Kline, S. H. Cox, *J. Org. Chem.*, **1961**, 26, 1854.

64. I. Felner, K. Schenker, *Helv. Chim. Acta* **1970**, 53, 754.

65. D. J. C. Adams, S Bradburdy, D. *C* . Horwelml, M. Keating, C .W. Rees, and R. C. Storr, *Chem. Commun.* **1971**, 828.

66. R. S. Atkinson, M. P. Coogan and C. L. Cornell, *J. Chem.* Soc. *Perkin Trans. I, **1996,*** 157.

67. H. Saltzman, J. G. Sharefkin, *Org. Syn.* **1963**, *43*, 60.

68. P. J. Stang, V. V. Zhdankin, *Chem. Rev.* **1996**, 96, 1123.

69. C. J. Carmalt, J. G. Crossley, J. G. Knight, P. Lightfoot, A. Martin, M. P. Muldowney, N. C. Norman, A. G. Orpen, *J. Chem. Soc., Chem. Commun.* **1994**, 2367.

70. (a) J. T. Kapron, B. D. Santarsiero, J. C. Vederas, *J. Chem. Soc., Chem. Commun.,* **1993**, 1074.
(b) K. S. Yang, K. Chen, *Org. Lett*. **2002**, *4*, 1107.
(c) J.-F. Pan, K. Chen, *Tetrahedron Lett.* **2004**, (45), 2541.

71. R. M. Hanson, K.B. Sharpless, *J. Org. Chem*. **1986**, *51*, 1922.

72. M. Terada, Y. Matsumoto, Y. Nakamura, K. Mikami, *Chem. Commun*. **1997**, 281.
(b) M. Shimizu, T. Ogawa, T. Nishi, *Tetrahedron Lett.* **2001**, *42*, 5463.
(c) J. Casas, C. Nájera, J. M. Sansano, J. M. Saá, J. M. *Org. Lett*. **2002**, *4*, 2589.

73. G. H. Posner, H. Dai, D. S. Bull, J. -K. Lee, F. Eydoux, Y. Ishihara, W. Welsh, N. Pryor, J. S. Petr *J. Org. Chem*. **1996**, *61*, 671.

74. T. Inaba, Y. Yamada, H. Abe, S. Sagawa, H. Cho, *J. Org. Chem.* **2000,** *65,* 1623.

75. H. Han, C. W. Cho, K. D. Janda, *Chem. Eur. J.* **1999**, *5*, 1565.

76. S. Sagawa, H. Abe, Y. Hase, T. Inaba, *J. Org. Chem.* **1999**, 64, 4962.

77. A. K. Tripathi, C. Bruhn, S. Flock, H. Frauenrath, *Acta Cryst.* **2005**, C061, o705.

78. A. Padwa, A. C. Flick, C. A. Leverett, T. Stengel, *J. Org. Chem.* **2004**, 69, 6377.

79. D. Tanner, *Angew. Chem. Int. Ed. Eng.* **1994**, 33, 599.

80. H. Zhang, C. Li, *Tetrahedron* **2006**, 62, 6640.
(b) W. Zhang, H. Yamamoto, *J. Am. Chem. Soc*. **2007**, 129, 286.

81. D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson, D. M. Barnesl, *J. Am. Chem. Soc*. **1993**, 115, 5328.

82. L. Ma, P. Jiao, Q. Zhang, J. Xu, *Tetrahedron: Asymmetry* **2005**, 16, 3718.

83. Z. Li, K. R. Conser, E. N. Jacobsen, *J. Am. Chem. Soc*. **1993**, 115, 5326.

84. (a) T. Katsuki, *Synlett* **2003**, 281.
(b) H. Nishikori, T. Katsuki, *Tetrahedron Lett.* **1996**, *37*, 9245.
(c) K. Noda, N. Hosoya, R. Irie, Y. Ito, T. Katsuki, *Synlett* **1993**, 469.

85. M. J. Sodergren, D. A. Alanso, P. G. Anderson, *Tetrahedron: Asymmetry* **1997**, 9, 3563.

86. H. Frauenrath, S. Reim, A. Wiesner, *Tetrahedron: Asymmetry* **1998**, 9, 1103.

87. S. Flock, H. Frauenrath, C. Wattenbach, *Tetrahedron: Asymmetry* **2005**, 16, 3394.

88. S. Flock, Dissertation, University of Kassel, **2003**.

89. R. S. Atkinson, W. T. Gattrell, A. P. Ayscough, T. M. Raynham, *J. Chem. Soc., Chem. Commun*. **1996**, 1935.

90. K. -S. Yang, K. Chen, *Org. Lett.* **2002**, 7, 1107.

91. P. -W. Duan, C. -C. Chiu, W.-D. Lee, L. S. Pan, U. Venkatesham, Z. -H. Tzeng, K. Chen, *Tetrahedron: Asymmetry*, **2008**, 19, 682.

92. R. S. Atkinson, M. P. Coogan, I. S. T. Lochrie, *Tetrahedron Lett.* **1986**, 37 (29), 5179.

93. (a) B. Gung, J.P. Melnick, M.A. Wolf , A. King, *J. Org. Chem.* **1995***,* 60, 1947.
(b) B. Gung, M.B. Francis, *Tetrahedron Lett.* **1995**, 36, 2579.

94. R. S. Atkinson, G. Tughan, *J. Chem. Soc., Chem. Commun.* **1997**, 2787.

95. D. Felix, J. Schreiber, K. Piers, U. Horn, A. Eschenmoser *Helv. Chim. Acta*, **1968**, 51, 1461.

96. H. Böshagen und J. Ullrich, *Chemische Berichte* **1959**, 92, 1478.

97. D. Seebach, H. O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Dorr, N. P. D. Preez, V. E. W. Langer, C. Niissler, H. A. Oei und M. Schmidt, *Helv. Chim. Acta* **1977**, 60, 301.

7 Appendix

7.1 Single crystal XRD of acetic acid 3-(2,5-dioxo-pyrrolidin-1-ylamino)-tetrahydro-pyran-2-yl ester (77)

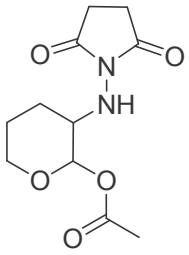


Table 1.

Empirical formula	$C_{11}H_{16}N_2O_5$
Formula weight	256.26
Temperature	153(2) K
Wavelength	0.71073 A
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 9.8852(14) alpha = 9°
	b = 12.9356(16) = 114.856(10)°
	c = 10.3206(14) = 90°.
Volume	1197.5(3) A^3 Z4
Density (calculated)	1.421 Mg/m^3
Absorption coefficient	0.113 mm^-1
F(000)	544
Crystal size	0.243 x 0.193 x 0.145 mm
Theta range for data collection	2.69 to 25.00 deg.
Index ranges	-11<=h<=11, -14<=k<=15, -12<=l<=12

Reflections collected	13209
Independent reflections	2096 [R(int) = 0.0532]
Reflections observed	1641
Absorption correction	Numerical
Max. and min. transmission	0.99 and 0.97
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2096 / 0 / 172
Goodness-of-fit on F^2	0.971
Final R indices [I>2sigma(I)]	R1 = 0.0294, wR2 = 0.0701
R indices (all data)	R1 = 0.0402, wR2 = 0.0723
Largest diff. peak and hole	0.166 and -0.170 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	7179(2)	-843(1)	1211(1)	26(1)
C(2)	8090(2)	-879(1)	2830(1)	25(1)
C(3)	9444(2)	-1579(1)	3255(1)	28(1)
C(4)	8969(2)	-2635(1)	2550(1)	33(1)
C(5)	8091(2)	-2499(1)	958(2)	36(1)
C(6)	7286(2)	205(1)	-648(1)	26(1)
C(7)	8297(2)	801(1)	-1102(2)	39(1)
C(8)	6781(2)	606(1)	4441(1)	29(1)
C(9)	5544(2)	1370(1)	4107(1)	34(1)
C(10)	5526(2)	2006(1)	2849(1)	33(1)

C(11)	6752(2)	1564(1)	2519(1)	29(1)
N(1)	7381(1)	749(1)	3449(1)	25(1)
N(2)	8576(1)	157(1)	3450(1)	27(1)
O(1)	6821(1)	-1835(1)	628(1)	33(1)
O(2)	8063(1)	-299(1)	607(1)	26(1)
O(3)	5956(1)	156(1)	-1295(1)	34(1)
O(4)	7253(1)	-28(1)	5389(1)	40(1)
O(5)	7176(1)	1841(1)	1630(1)	42(1)

Table 3. Bond lengths [A] and angles [deg] for.

C(1)-O(1)	1.3985(16)
C(1)-O(2)	1.4502(15)
C(1)-C(2)	1.5303(17)
C(1)-H(1A)	1.0000
C(2)-N(2)	1.4753(17)
C(2)-C(3)	1.5191(18)
C(2)-H(2A)	1.0000
C(3)-C(4)	1.5264(18)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.5117(19)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-O(1)	1.4385(18)

C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-O(3)	1.2005(17)
C(6)-O(2)	1.3626(15)
C(6)-C(7)	1.4846(19)
C(7)-H(7C)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7A)	0.9800
C(8)-O(4)	1.2102(17)
C(8)-N(1)	1.3945(16)
C(8)-C(9)	1.495(2)
C(9)-C(10)	1.531(2)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(11)	1.503(2)
C(10)-H(10B)	0.9900
C(10)-H(10A)	0.9900
C(11)-O(5)	1.2115(16)
C(11)-N(1)	1.3855(17)
N(1)-N(2)	1.4078(15)
N(2)-H(12A)	0.87(3)
N(2)-H(12B)	0.92(3)
O(1)-C(1)-O(2)	110.49(10)
O(1)-C(1)-C(2)	111.58(10)
O(2)-C(1)-C(2)	107.45(10)
O(1)-C(1)-H(1A)	109.1
O(2)-C(1)-H(1A)	109.1

C(2)-C(1)-H(1A)	109.1
N(2)-C(2)-C(3)	109.22(11)
N(2)-C(2)-C(1)	112.35(10)
C(3)-C(2)-C(1)	112.08(10)
N(2)-C(2)-H(2A)	107.7
C(3)-C(2)-H(2A)	107.7
C(1)-C(2)-H(2A)	107.7
C(2)-C(3)-C(4)	109.81(11)
C(2)-C(3)-H(3A)	109.7
C(4)-C(3)-H(3A)	109.7
C(2)-C(3)-H(3B)	109.7
C(4)-C(3)-H(3B)	109.7
H(3A)-C(3)-H(3B)	108.2
C(5)-C(4)-C(3)	109.55(11)
C(5)-C(4)-H(4A)	109.8
C(3)-C(4)-H(4A)	109.8
C(5)-C(4)-H(4B)	109.8
C(3)-C(4)-H(4B)	109.8
H(4A)-C(4)-H(4B)	108.2
O(1)-C(5)-C(4)	111.86(11)
O(1)-C(5)-H(5A)	109.2
C(4)-C(5)-H(5A)	109.2
O(1)-C(5)-H(5B)	109.2
C(4)-C(5)-H(5B)	109.2
H(5A)-C(5)-H(5B)	107.9
O(3)-C(6)-O(2)	123.48(12)
O(3)-C(6)-C(7)	125.23(12)

O(2)-C(6)-C(7)	111.29(12)
C(6)-C(7)-H(7C)	109.5
C(6)-C(7)-H(7B)	109.5
H(7C)-C(7)-H(7B)	109.5
C(6)-C(7)-H(7A)	109.5
H(7C)-C(7)-H(7A)	109.5
H(7B)-C(7)-H(7A)	109.5
O(4)-C(8)-N(1)	123.05(13)
O(4)-C(8)-C(9)	129.36(12)
N(1)-C(8)-C(9)	107.58(11)
C(8)-C(9)-C(10)	105.53(11)
C(8)-C(9)-H(9A)	110.6
C(10)-C(9)-H(9A)	110.6
C(8)-C(9)-H(9B)	110.6
C(10)-C(9)-H(9B)	110.6
H(9A)-C(9)-H(9B)	108.8
C(11)-C(10)-C(9)	105.37(11)
C(11)-C(10)-H(10B)	110.7
C(9)-C(10)-H(10B)	110.7
C(11)-C(10)-H(10A)	110.7
C(9)-C(10)-H(10A)	110.7
H(10B)-C(10)-H(10A)	108.8
O(5)-C(11)-N(1)	123.52(13)
O(5)-C(11)-C(10)	128.90(13)
N(1)-C(11)-C(10)	107.58(11)
C(11)-N(1)-C(8)	113.84(11)
C(11)-N(1)-N(2)	123.15(11)

C(8)-N(1)-N(2)	122.91(11)
N(1)-N(2)-C(2)	111.95(10)
N(1)-N(2)-H(12A)	105.0(18)
C(2)-N(2)-H(12A)	114.0(17)
N(1)-N(2)-H(12B)	113.5(17)
C(2)-N(2)-H(12B)	114.0(17)
H(12A)-N(2)-H(12B)	97(2)
C(1)-O(1)-C(5)	114.08(10)
C(6)-O(2)-C(1)	116.10(10)

Table 4. Anisotropic displacement parameters (A^2 x 10^3). The anisotropic displacement factor exponent takes the form -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	26(1)	31(1)	23(1)	-1(1)	13(1)	-4(1)
C(2)	27(1)	26(1)	22(1)	-1(1)	12(1)	-2(1)
C(3)	31(1)	31(1)	25(1)	1(1)	13(1)	1(1)
C(4)	41(1)	29(1)	33(1)	-1(1)	20(1)	2(1)
C(5)	50(1)	29(1)	33(1)	-5(1)	23(1)	-3(1)
C(6)	28(1)	30(1)	22(1)	0(1)	11(1)	4(1)
C(7)	35(1)	49(1)	35(1)	15(1)	17(1)	2(1)
C(8)	36(1)	26(1)	26(1)	-7(1)	15(1)	-6(1)
C(9)	34(1)	35(1)	36(1)	-9(1)	18(1)	-2(1)
C(10)	30(1)	28(1)	37(1)	-5(1)	10(1)	1(1)
C(11)	31(1)	26(1)	27(1)	-1(1)	9(1)	-2(1)
N(1)	27(1)	26(1)	23(1)	0(1)	11(1)	3(1)

N(2)	25(1)	27(1)	27(1)	-3(1)	9(1)	1(1)
O(1)	36(1)	34(1)	26(1)	-6(1)	12(1)	-9(1)
O(2)	25(1)	33(1)	22(1)	3(1)	11(1)	0(1)
O(3)	27(1)	45(1)	27(1)	3(1)	9(1)	0(1)
O(4)	58(1)	35(1)	33(1)	5(1)	25(1)	2(1)
O(5)	53(1)	40(1)	40(1)	11(1)	25(1)	4(1)

Table 5. Hydrogen coordinates (x10^4) and isotropic displacement parameters (A^2 x 10^3).

	x	y	z	U(eq)
H(1A)	6238	-449	992	31
H(2A)	7435	-1171	3261	29
H(3A)	9923	-1660	4306	34
H(3B)	10177	-1264	2952	34
H(4A)	9861	-3065	2740	40
H(4B)	8348	-2993	2954	40
H(5A)	8747	-2201	548	43
H(5B)	7747	-3183	511	43
H(7C)	7721	1100	-2048	47
H(7B)	9064	339	-1143	47
H(7A)	8772	1356	-413	47
H(9A)	5731	1820	4941	41
H(9B)	4580	1011	3843	41
H(10B)	4552	1941	2014	40

H(10A)	5714	2745	3111	40
H(12A)	8960(30)	530(20)	2990(30)	20(7)
H(12B)	9390(30)	150(20)	4320(30)	24(7)

7.2 Single crystal XRD of 1-(4-isopropyl-3,5-dioxa-8-aza-bicyclo[5.1.0]-pyrrolidine-2,5-dione (isomer I) (72a)

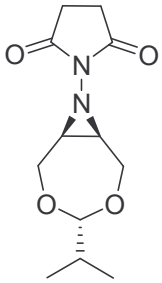


Table 1

Empirical formula	$C_{12}H_{18}N_2O_4$
Formula weight	254.28
Temperature	153(2) K
Wavelength	0.71073 A
Crystal system	Monoclinic
Space group	P21
Unit cell dimensions	a = 6.1449(11) A alpha = 90 deg.
	b = 7.8343(10) A beta = 100.250(15) deg.
	c = 13.080(3) A gamma = 90 deg.
Volume	619.6(2) A^3 Z 2
Density (calculated)	1.363 Mg/m^3
Absorption coefficient	0.103 mm^-1 F(000) 272
Crystal size	0.47 x 0.41 x 0.05 mm
Theta range for data collection	1.58 to 25.48 deg.
Index ranges	-7<=h<=7, -9<=k<=9, -15<=l<=15

Reflections collected	8393
Independent reflections	1244 [R(int) = 0.0574]
Reflections observed	998
Absorption correction	Integration
Max. and min. transmission	0.9951 and 0.9535
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1244 / 1 / 165
Goodness-of-fit on F^2	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0359, wR2 = 0.0731
R indices (all data)	R1 = 0.0468, wR2 = 0.0764
Largest diff. peak and hole	0.144 and -0.208 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for i0070. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	1562(5)	8397(4)	6551(2)	36(1)
C(2)	1003(5)	8771(4)	7606(2)	31(1)
C(3)	-1000(4)	8033(4)	7901(2)	31(1)
C(4)	-2544(5)	6976(4)	7130(2)	35(1)
C(5)	-1931(4)	7912(4)	5452(2)	31(1)
C(6)	-3220(5)	8561(4)	4427(2)	34(1)
C(7)	-1823(5)	8357(4)	3577(2)	40(1)
C(8)	-5429(5)	7652(4)	4124(2)	42(1)
C(9)	3970(5)	8568(4)	9687(2)	36(1)
C(10)	4386(5)	8615(4)	10854(2)	40(1)

C(11)	2335(5)	7804(4)	11162(2)	40(1)
C(12)	983(5)	7156(4)	10165(2)	35(1)
N(1)	1217(4)	7252(3)	8309(2)	31(1)
N(2)	2005(4)	7706(3)	9362(2)	30(1)
O(1)	5120(3)	9170(3)	9107(2)	45(1)
O(2)	-704(4)	6317(3)	10044(2)	45(1)
O(3)	-102(3)	9024(3)	5729(1)	35(1)
O(4)	-3350(3)	7922(3)	6202(1)	34(1)

Table 3. Bond lengths [A] and angles [deg] for isomer II.

C(1)-O(3)	1.432(3)
C(1)-C(2)	1.509(4)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.472(4)
C(2)-N(1)	1.495(3)
C(2)-H(2A)	1.0000
C(3)-N(1)	1.502(4)
C(3)-C(4)	1.504(4)
C(3)-H(3A)	1.0000
C(4)-O(4)	1.434(3)
C(4)-H(4B)	0.9900
C(4)-H(4A)	0.9900
C(5)-O(3)	1.417(3)

C(5)-O(4)	1.423(3)
C(5)-C(6)	1.519(4)
C(5)-H(5A)	1.0000
C(6)-C(8)	1.521(4)
C(6)-C(7)	1.529(4)
C(6)-H(6A)	1.0000
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-H(8C)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8A)	0.9800
C(9)-O(1)	1.219(3)
C(9)-N(2)	1.382(4)
C(9)-C(10)	1.503(4)
C(10)-C(11)	1.528(4)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-C(12)	1.504(4)
C(11)-H(11B)	0.9900
C(11)-H(11A)	0.9900
C(12)-O(2)	1.213(3)
C(12)-N(2)	1.385(4)
N(1)-N(2)	1.422(3)
O(3)-C(1)-C(2)	111.8(2)
O(3)-C(1)-H(1A)	109.3
C(2)-C(1)-H(1A)	109.3

O(3)-C(1)-H(1B)	109.3
C(2)-C(1)-H(1B)	109.3
H(1A)-C(1)-H(1B)	107.9
C(3)-C(2)-N(1)	60.83(18)
C(3)-C(2)-C(1)	120.0(2)
N(1)-C(2)-C(1)	113.4(2)
C(3)-C(2)-H(2A)	116.8
N(1)-C(2)-H(2A)	116.8
C(1)-C(2)-H(2A)	116.8
C(2)-C(3)-N(1)	60.33(17)
C(2)-C(3)-C(4)	119.8(2)
N(1)-C(3)-C(4)	116.0(2)
C(2)-C(3)-H(3A)	116.3
N(1)-C(3)-H(3A)	116.3
C(4)-C(3)-H(3A)	116.3
O(4)-C(4)-C(3)	111.4(2)
O(4)-C(4)-H(4B)	109.3
C(3)-C(4)-H(4B)	109.3
O(4)-C(4)-H(4A)	109.3
C(3)-C(4)-H(4A)	109.3
H(4B)-C(4)-H(4A)	108.0
O(3)-C(5)-O(4)	112.1(2)
O(3)-C(5)-C(6)	106.6(2)
O(4)-C(5)-C(6)	108.6(2)
O(3)-C(5)-H(5A)	109.8
O(4)-C(5)-H(5A)	109.8
C(6)-C(5)-H(5A)	109.8

C(5)-C(6)-C(8)	112.0(2)
C(5)-C(6)-C(7)	109.6(2)
C(8)-C(6)-C(7)	110.7(2)
C(5)-C(6)-H(6A)	108.2
C(8)-C(6)-H(6A)	108.2
C(7)-C(6)-H(6A)	108.2
C(6)-C(7)-H(7A)	109.5
C(6)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(6)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(6)-C(8)-H(8C)	109.5
C(6)-C(8)-H(8B)	109.5
H(8C)-C(8)-H(8B)	109.5
C(6)-C(8)-H(8A)	109.5
H(8C)-C(8)-H(8A)	109.5
H(8B)-C(8)-H(8A)	109.5
O(1)-C(9)-N(2)	124.7(3)
O(1)-C(9)-C(10)	127.5(3)
N(2)-C(9)-C(10)	107.8(2)
C(9)-C(10)-C(11)	104.9(2)
C(9)-C(10)-H(10A)	110.8
C(11)-C(10)-H(10A)	110.8
C(9)-C(10)-H(10B)	110.8
C(11)-C(10)-H(10B)	110.8
H(10A)-C(10)-H(10B)	108.8

C(12)-C(11)-C(10)	105.5(2)
C(12)-C(11)-H(11B)	110.7
C(10)-C(11)-H(11B)	110.7
C(12)-C(11)-H(11A)	110.7
C(10)-C(11)-H(11A)	110.7
H(11B)-C(11)-H(11A)	108.8
O(2)-C(12)-N(2)	124.2(3)
O(2)-C(12)-C(11)	128.6(3)
N(2)-C(12)-C(11)	107.3(3)
N(2)-N(1)-C(2)	112.0(2)
N(2)-N(1)-C(3)	111.9(2)
C(2)-N(1)-C(3)	58.84(17)
C(9)-N(2)-C(12)	114.1(2)
C(9)-N(2)-N(1)	123.2(2)
C(12)-N(2)-N(1)	122.3(2)
C(5)-O(3)-C(1)	114.2(2)
C(5)-O(4)-C(4)	114.8(2)

Table 4. Anisotropic displacement parameters (A^2x10^3) for isomer II. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	30(1)	46(2)	32(1)	-1(1)	6(1)	0(1)
C(2)	34(2)	28(2)	32(1)	0(1)	7(1)	0(1)

C(3)	30(1)	34(2)	30(1)	1(1)	6(1)	5(1)
C(4)	35(2)	42(2)	26(2)	6(1)	6(1)	-4(1)
C(5)	31(1)	35(2)	30(1)	-1(1)	10(1)	-4(1
C(6)	39(2)	33(2)	31(1)	-1(1)	7(1)	0(1)
C(7)	49(2)	39(2)	34(2)	1(1)	11(1)	1(2)
C(8)	40(2)	48(2)	36(2)	2(2)	3(1)	-1(2)
C(9)	33(2)	35(2)	39(2)	-4(1)	6(1)	2(1)
C(10)	42(2)	44(2)	33(2)	-3(2)	1(1)	0(2)
C(11)	49(2)	39(2)	31(1)	-3(1)	4(1)	-5(2)
C(12)	45(2)	9(2)	31(2)	2(1)	5(1)	1(2)
N(1)	36(1)	29(1)	29(1)	-1(1)	5(1)	2(1)
N(2)	35(1)	31(1)	24(1)	-3(1)	3(1)	0(1)
O(1)	35(1)	61(1)	42(1)	-3(1)	11(1)	-4(1)
O(2)	49(1)	46(1)	40(1)	4(1)	6(1)	-15(1)
O(3)	35(1)	39(1)	30(1)	4(1)	6(1)	-3(1)
O(4)	31(1)	43(1)	30(1)	5(1)	7(1)	2(1)

Table 5. Hydrogen coordinates (x10^4) and isotropic displacement parameters (A^2 x 10^3) for isomer II.

	x	y	z	U(eq)
H(1A)	2998	8933	6500	43
H(1B)	1719	7149	6472	43
H(2A)	1520	9890	7930	37
H(3A)	-1692	8701	8411	38

H(4B)	-1758	5945	6951	41
H(4A)	-3809	6599	7448	41
H(5A)	-1396	6725	5364	38
H(6A)	-3517	9805	4504	41
H(7A)	-1594	7141	3457	48
H(7B)	-389	8916	3796	48
H(7C)	-2592	8885	2933	48
H(8C)	-6164	8051	3439	51
H(8B)	-6364	7902	4639	51
H(8A)	-5180	6418	4100	51
H(10A)	4573	9805	11109	48
H(10B)	5731	7958	11143	48
H(11B)	2757	6853	11656	48
H(11A)	1492	8658	11490	48

7.3 Single crystal XRD of 1-(4-isopropyl-3,5-dioxa-8-aza-bicyclo[5.1.0]-pyrrolidine-2,5-dione (isomer II) (72b)

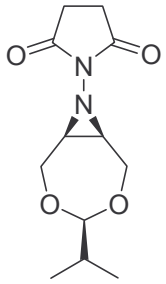


Table 1.

Empirical formula	C12 H18 N2 O4
Formula weight	254.28
Temperature	153(2) K
Wavelength	0.71073 A
Crystal system	Monoclinic
Space group	P21/c
Unit cell dimensions	a = 24.470(3) A alpha = 90 deg.
	b = 8.8444(8) A beta = 97.119(9) deg.
	c = 11.8252(14) A gamma = 90 deg.
Volume	2539.6(5) A^3
Z	8
Density (calculated)	1.330 Mg/m^3
Absorption coefficient	0.100 mm^-1
F(000)	1088
Crystal size	0.66 x 0.65 x 0.25 mm
Theta range for data collection	1.68 to 25.00 deg.
Index ranges	-29<=h<=29, -10<=k<=10, -13<=l<=14
Reflections collected	18062
Independent reflections	4465 [R(int) = 0.0332]
Reflections observed	2623

Absorption correction	Integration
Max. and min. transmission	0.9717 and 0.9137
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4465 / 0 / 330
Goodness-of-fit on F^2	0.895
Final R indices [I>2sigma(I)]	R1 = 0.0312, wR2 = 0.0783
R indices (all data)	R1 = 0.0595, wR2 = 0.0843
Extinction coefficient	0.0028(4)
Largest diff. peak and hole	0.208 and -0.154 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for i0084. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U (eq)
C(1)	1385(1)	1498(2)	3797(1)	34(1)
C(2)	829(1)	2206(2)	3781(1)	28(1)
C(3)	645(1)	3303(2)	4594(1)	27(1)
C(4)	982(1)	3966(2)	5619(1)	30(1)
C(5)	1828(1)	2665(2)	5487(1)	27(1)
C(6)	2365(1)	2446(2)	6259(2)	34(1)
C(7)	2823(1)	1981(2)	5565(2)	50(1)
C(8)	2527(1)	3879(2)	6935(1)	40(1)
C(9)	-219(1)	449(2)	3250(1)	29(1)
C(10)	-836(1)	481(2)	2988(1)	33(1)

C(11)	-1033(1)	1549(2)	3865(1)	35(1)
C(12)	-521(1)	2109(2)	4577(1)	29(1)
C(13)	4003(1)	8873(2)	4333(1)	30(1)
C(14)	4332(1)	8240(2)	5382(1)	27(1)
C(15)	4145(1)	7121(2)	6184(1)	28(1)
C(16)	3598(1)	6350(2)	6145(1)	32(1)
C(17)	3163(1)	7553(2)	4463(1)	27(1)
C(18)	2620(1)	7386(2)	3696(2)	32(1)
C(19)	2609(1)	5990(2)	2942(1)	41(1)
C(20)	2141(1)	7386(2)	4404(2)	44(1)
C(21)	5512(1)	7140(2)	5480(1)	29(1)
C(22)	6021(1)	6605(2)	6217(2)	36(1)
C(23)	5821(1)	5510(2)	7068(1)	34(1)
C(24)	5206(1)	5437(2)	6770(1)	28(1)
N(1)	475(1)	1677(1)	4642(1)	26(1)
N(2)	-77(1)	1475(1)	4130(1)	26(1)
N(3)	4519(1)	6631(1)	5345(1)	26(1)
N(4)	5066(1)	6463(1)	5889(1)	26(1)
O(1)	111(1)	-283(1)	2795(1)	36(1)
O(2)	-482(1)	2965(1)	5384(1)	37(1)
O(3)	1696(1)	1304(1)	4892(1)	31(1)
O(4)	1411(1)	3029(1)	6165(1)	29(1)
O(5)	5476(1)	8015(1)	4681(1)	37(1)
O(6)	4877(1)	4677(1)	7201(1)	36(1)
O(7)	3584(1)	7908(1)	3786(1)	29(1)
O(8)	3286(1)	6182(1)	5049(1)	29(1)

Table 3. Bond lengths [A] and angles [deg].

C(1)-O(3)	1.4279(18)
C(1)-C(2)	1.497(2)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.475(2)
C(2)-N(1)	1.4908(19)
C(2)-H(2A)	1.0000
C(3)-N(1)	1.499(2)
C(3)-C(4)	1.499(2)
C(3)-H(3A)	1.0000
C(4)-O(4)	1.4277(18)
C(4)-H(4B)	0.9900
C(4)-H(4A)	0.9900
C(5)-O(4)	1.4101(18)
C(5)-O(3)	1.4115(18)
C(5)-C(6)	1.517(2)
C(5)-H(5A)	1.0000
C(6)-C(8)	1.524(2)
C(6)-C(7)	1.525(2)
C(6)-H(6A)	1.0000
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800

C(8)-H(8C)	0.9800
C(9)-O(1)	1.2125(18)
C(9)-N(2)	1.392(2)
C(9)-C(10)	1.504(2)
C(10)-C(11)	1.525(2)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-C(12)	1.506(2)
C(11)-H(11B)	0.9900
C(11)-H(11A)	0.9900
C(12)-O(2)	1.2129(19)
C(12)-N(2)	1.384(2)
C(13)-O(7)	1.4259(18)
C(13)-C(14)	1.501(2)
C(13)-H(13A)	0.9900
C(13)-H(13B)	0.9900
C(14)-C(15)	1.481(2)
C(14)-N(3)	1.497(2)
C(14)-H(14A)	1.0000
C(15)-N(3)	1.4928(19)
C(15)-C(16)	1.499(2)
C(15)-H(15A)	1.0000
C(16)-O(8)	1.4276(17)
C(16)-H(16B)	0.9900
C(16)-H(16A)	0.9900
C(17)-O(8)	1.4108(18)
C(17)-O(7)	1.4149(18)

C(17)-C(18)	1.521(2
C(17)-H(17A)	1.0000
C(18)-C(19)	1.521(2)
C(18)-C(20)	1.522(2)
C(18)-H(18A)	1.0000
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-H(20C)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20A)	0.9800
C(21)-O(5)	1.2161(19)
C(21)-N(4)	1.383(2)
C(21)-C(22)	1.506(2)
C(22)-C(23)	1.521(2)
C(22)-H(22A)	0.9900
C(22)-H(22B)	0.9900
C(23)-C(24)	1.504(2)
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
C(24)-O(6)	1.2109(18)
C(24)-N(4)	1.3915(19)
N(1)-N(2)	1.4215(17)
N(3)-N(4)	1.4205(17)
O(3)-C(1)-C(2)	116.29(13)
O(3)-C(1)-H(1A)	108.2
C(2)-C(1)-H(1A)	108.2

O(3)-C(1)-H(1B)	108.2
C(2)-C(1)-H(1B)	108.2
H(1A)-C(1)-H(1B)	107.4
C(3)-C(2)-N(1)	60.72(10)
C(3)-C(2)-C(1)	128.17(14)
N(1)-C(2)-C(1)	117.71(13)
C(3)-C(2)-H(2A)	113.2
N(1)-C(2)-H(2A)	113.2
C(1)-C(2)-H(2A)	113.2
C(2)-C(3)-N(1)	60.16(10)
C(2)-C(3)-C(4)	127.00(13)
N(1)-C(3)-C(4)	118.14(12)
C(2)-C(3)-H(3A)	113.6
N(1)-C(3)-H(3A)	113.6
C(4)-C(3)-H(3A)	113.6
O(4)-C(4)-C(3)	116.04(13)
O(4)-C(4)-H(4B)	108.3
C(3)-C(4)-H(4B)	108.3
O(4)-C(4)-H(4A)	108.3
C(3)-C(4)-H(4A)	108.3
H(4B)-C(4)-H(4A)	107.4
O(4)-C(5)-O(3)	109.90(12)
O(4)-C(5)-C(6)	108.69(13)
O(3)-C(5)-C(6)	108.63(13)
O(4)-C(5)-H(5A)	109.9
O(3)-C(5)-H(5A)	109.9
C(6)-C(5)-H(5A)	109.9

C(5)-C(6)-C(8)	111.03(14)
C(5)-C(6)-C(7)	110.45(14)
C(8)-C(6)-C(7)	110.25(15)
C(5)-C(6)-H(6A)	108.3
C(8)-C(6)-H(6A)	108.3
C(7)-C(6)-H(6A)	108.3
C(6)-C(7)-H(7A)	109.5
C(6)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(6)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(6)-C(8)-H(8A)	109.5
C(6)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(6)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
O(1)-C(9)-N(2)	124.16(15)
O(1)-C(9)-C(10)	128.77(15)
N(2)-C(9)-C(10)	107.06(14)
C(9)-C(10)-C(11)	105.41(13)
C(9)-C(10)-H(10A)	110.7
C(11)-C(10)-H(10A)	110.7
C(9)-C(10)-H(10B)	110.7
C(11)-C(10)-H(10B)	110.7
H(10A)-C(10)-H(10B)	108.8

C(12)-C(11)-C(10)	105.81(13)
C(12)-C(11)-H(11B)	110.6
C(10)-C(11)-H(11B)	110.6
C(12)-C(11)-H(11A)	110.6
C(10)-C(11)-H(11A)	110.6
H(11B)-C(11)-H(11A)	108.7
O(2)-C(12)-N(2)	124.45(15)
O(2)-C(12)-C(11)	128.59(15)
N(2)-C(12)-C(11)	106.96(13)
O(7)-C(13)-C(14)	115.66(13)
O(7)-C(13)-H(13A)	108.4
C(14)-C(13)-H(13A)	108.4
O(7)-C(13)-H(13B)	108.4
C(14)-C(13)-H(13B)	108.4
H(13A)-C(13)-H(13B)	107.4
C(15)-C(14)-N(3)	60.17(10)
C(15)-C(14)-C(13)	127.08(13)
N(3)-C(14)-C(13)	117.74(12)
C(15)-C(14)-H(14A)	113.6
N(3)-C(14)-H(14A)	113.6
C(13)-C(14)-H(14A)	113.6
C(14)-C(15)-N(3)	60.43(10)
C(14)-C(15)-C(16)	128.99(13)
N(3)-C(15)-C(16)	117.77(13)
C(14)-C(15)-H(15A)	112.9
N(3)-C(15)-H(15A)	112.9
C(16)-C(15)-H(15A)	112.9

O(8)-C(16)-C(15)	116.74(12)
O(8)-C(16)-H(16B)	108.1
C(15)-C(16)-H(16B)	108.1
O(8)-C(16)-H(16A)	108.1
C(15)-C(16)-H(16A)	108.1
H(16B)-C(16)-H(16A)	107.3
O(8)-C(17)-O(7)	110.08(12)
O(8)-C(17)-C(18)	109.06(13)
O(7)-C(17)-C(18)	109.13(13)
O(8)-C(17)-H(17A)	109.5
O(7)-C(17)-H(17A)	109.5
C(18)-C(17)-H(17A)	109.5
C(17)-C(18)-C(19)	112.30(13)
C(17)-C(18)-C(20)	110.36(14)
C(19)-C(18)-C(20)	111.29(14)
C(17)-C(18)-H(18A)	107.6
C(19)-C(18)-H(18A)	107.6
C(20)-C(18)-H(18A)	107.6
C(18)-C(19)-H(19A)	109.5
C(18)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(18)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(18)-C(20)-H(20C)	109.5
C(18)-C(20)-H(20B)	109.5
H(20C)-C(20)-H(20B)	109.5

C(18)-C(20)-H(20A)	109.5
H(20C)-C(20)-H(20A)	109.5
H(20B)-C(20)-H(20A)	109.5
O(5)-C(21)-N(4)	124.22(15)
O(5)-C(21)-C(22)	128.67(16)
N(4)-C(21)-C(22)	107.11(13)
C(21)-C(22)-C(23)	105.75(13)
C(21)-C(22)-H(22A)	110.6
C(23)-C(22)-H(22A)	110.6
C(21)-C(22)-H(22B)	110.6
C(23)-C(22)-H(22B)	110.6
H(22A)-C(22)-H(22B)	108.7
C(24)-C(23)-C(22)	105.49(13)
C(24)-C(23)-H(23A)	110.6
C(22)-C(23)-H(23A)	110.6
C(24)-C(23)-H(23B)	110.6
C(22)-C(23)-H(23B)	110.6
H(23A)-C(23)-H(23B)	108.8
O(6)-C(24)-N(4)	124.22(14)
O(6)-C(24)-C(23)	128.66(15)
N(4)-C(24)-C(23)	107.10(13)
N(2)-N(1)-C(2)	110.51(12)
N(2)-N(1)-C(3)	110.94(11)
C(2)-N(1)-C(3)	59.12(10)
C(12)-N(2)-C(9)	114.50(13)
C(12)-N(2)-N(1)	122.38(12)
C(9)-N(2)-N(1)	122.46(13)

N(4)-N(3)-C(15)	110.54(11)
N(4)-N(3)-C(14)	111.20(11)
C(15)-N(3)-C(14)	59.40(9)
C(21)-N(4)-C(24)	114.33(13)
C(21)-N(4)-N(3)	122.52(12)
C(24)-N(4)-N(3)	122.54(12)
C(5)-O(3)-C(1)	114.39(12)
C(5)-O(4)-C(4)	114.79(11)
C(17)-O(7)-C(13)	114.12(12)
C(17)-O(8)-C(16)	114.48(12)

Table 4. Anisotropic displacement parameters (A^2 x 10^3). The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	33(1)	43(1)	26(1)	-4(1)	3(1)	0(1)
C(2)	28(1)	32(1)	25(1)	2(1)	3(1)	-2(1)
C(3)	27(1)	25(1)	28(1)	2(1)	2(1)	-1(1)
C(4)	29(1)	30(1)	32(1)	-2(1)	3(1)	3(1)
C(5)	27(1)	28(1)	28(1)	2(1)	3(1)	-2(1)
C(6)	32(1)	33(1)	35(1)	6(1)	1(1)	-2(1)
C(7)	31(1)	55(1)	62(1)	-6(1)	0(1)	7(1)
C(8)	32(1)	48(1)	40(1)	0(1)	2(1)	-9(1)
C(9)	33(1)	27(1)	27(1)	1(1)	2(1)	-2(1)
C(10)	29(1)	35(1)	35(1)	-1(1)	-1(1)	-2(1)

C(11)	29(1)	34(1)	43(1)	-2(1)	2(1)	3(1)
C(12)	30(1)	27(1)	31(1)	3(1)	5(1)	1(1)
C(13)	31(1)	28(1)	29(1)	2(1)	3(1)	-3(1)
C(14)	27(1)	26(1)	28(1)	-4(1)	4(1)	-1(1)
C(15)	30(1)	33(1)	21(1)	-1(1)	3(1)	2(1)
C(16)	28(1)	44(1)	23(1)	3(1)	2(1)	-2(1)
C(17)	28(1)	26(1)	28(1)	-2(1)	5(1)	1(1)
C(18)	30(1)	30(1)	35(1)	1(1)	-3(1)	1(1)
C(19)	39(1)	43(1)	39(1)	-7(1)	-6(1)	-2(1)
C(20)	29(1)	46(1)	56(1)	-4(1)	2(1)	2(1)
C(21)	29(1)	27(1)	31(1)	-4(1)	5(1)	-2(1)
C(22)	27(1)	37(1)	43(1)	1(1)	2(1)	-3(1)
C(23)	30(1)	36(1)	34(1)	2(1)	-1(1)	1(1)
C(24)	29(1)	28(1)	29(1)	-2(1)	3(1)	0(1)
N(1)	25(1)	28(1)	26(1)	1(1)	2(1)	-1(1)
N(2)	25(1)	27(1)	27(1)	0(1)	0(1)	0(1)
N(3)	24(1)	27(1)	25(1)	-2(1)	2(1)	0(1)
N(4)	23(1)	26(1)	27(1)	-1(1)	2(1)	-2(1)
O(1)	33(1)	37(1)	38(1)	-8(1)	3(1)	3(1)
O(2)	39(1)	35(1)	36(1)	-6(1)	6(1)	4(1)
O(3)	30(1)	30(1)	31(1)	-1(1)	0(1)	1(1)
O(4)	28(1)	35(1)	25(1)	1(1)	4(1)	1(1)
O(5)	38(1)	37(1)	36(1)	5(1)	7(1)	-5(1)
O(6)	33(1)	37(1)	38(1)	8(1)	3(1)	-4(1)
O(7)	29(1)	33(1)	25(1)	-1(1)	2(1)	-4(1)
O(8)	29(1)	30(1)	26(1)	3(1)	0(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for.

	x	y	z	U(eq)
H(1A)	1338	495	3427	41
H(1B)	1604	2128	3327	41
H(2A)	625	2297	2997	34
H(3A)	343	3984	4248	32
H(4B)	1149	4918	5387	36
H(4A)	732	4228	6186	36
H(5A)	1868	3502	4934	33
H(6A)	2313	1617	6811	40
H(7A)	2880	2782	5020	60
H(7B)	2719	1043	5152	60
H(7C)	3164	1818	6078	60
H(8A)	2229	4171	7372	48
H(8B)	2594	4696	6409	48
H(8C)	2863	3692	7458	48
H(10A)	-992	-543	3057	40
H(10B)	-948	859	2205	40
H(11B)	-1242	2404	3482	42
H(11A)	-1274	1009	4344	42
H(13A)	3829	9826	4541	35
H(13B)	4260	9128	3776	35
H(14A)	4622	8944	5743	32

H(15A)	4339	7225	6975	33
H(16B)	3660	5331	6484	38
H(16A)	3372	6924	6636	38
H(17A)	3132	8384	5025	32
H(18A)	2577	8290	3185	39
H(19A)	2618	5080	3417	49
H(19B)	2930	5999	2522	49
H(19C)	2271	5993	2402	49
H(20C)	1794	7304	3898	53
H(20B)	2144	8329	4840	53
H(20A)	2178	6525	4930	53
H(22A)	6218	7467	6616	43
H(22B)	6274	6090	5749	43
H(23A)	5988	4499	7000	40
H(23B)	5919	5881	7857	40

5.4 Single crystal XRD of (3*R*,4*R*)-3,4-dimethoxy-1-((*R*)-2-phenylaziridin-1 yl)pyrrolidine-2,5-dione (94a)

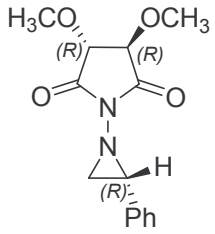


Table 1.

Empirical formula	$C_{14} H_{16} N_2 O_4$
Formula weight	276.29
Temperature	153(2) K
Wavelength	0.71073 A
Crystal system	Tetragonal
Space group	I 41
Unit cell dimensions	a = 15.2912(13) A alpha = 90 deg.
	b = 15.2912(13) A beta = 90 deg.
	c = 12.2961(11) A gamma = 90 deg.
Volume	2875.1(4) A^3Z8
Density (calculated)	1.277 Mg/m^3
Absorption coefficient	0.095 mm^-1
F(000)	1168
Crystal size	0.59 x 0.20 x 0.16 mm
Theta range for data collection	1.88 to 25.50 deg.
Index ranges	-18<=h<=18, -18<=k<=18, -14<=l<=13
Reflections collected	9850
Independent reflections	1398 [R(int) = 0.0791]
Reflections observed	983

Absorption correction	Integration
Max. and min. transmission	0.9860 and 0.9395
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1398 / 1 / 183
Goodness-of-fit on F^2	0.888
Final R indices [I>2sigma(I)]	R1 = 0.0357, wR2 = 0.0786
R indices (all data)	R1 = 0.0516, wR2 = 0.0816
Largest diff. peak and hole	0.493 and -0.154 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	4605(2)	1042(2)	6438(3)	46(1)
C(2)	4432(2)	1995(2)	6350(3)	40(1)
C(3)	5147(2)	2638(2)	6128(3)	38(1)
C(4)	5847(2)	2425(2)	5476(3)	49(1)
C(5)	6519(2)	3020(3)	5323(3)	56(1)
C(6)	6507(3)	3807(3)	5848(3)	61(1)
C(7)	5812(3)	4025(2)	6508(4)	62(1)
C(8)	5121(2)	3443(2)	6635(3)	51(1)
C(9)	2968(2)	370(2)	5267(3)	45(1)
C(10)	1974(2)	455(2)	5217(3)	45(1)
C(11)	1842(2)	1395(2)	4855(3)	43(1)
C(12)	2681(2)	1860(2)	5166(2)	40(1)
C(13)	1410(4)	-967(3)	4947(5)	105(2)

C(14)	647(3)	2375(3)	4661(3)	68(1)
N(1)	4205(2)	1394(2)	5431(2)	41(1)
N(2)	3294(2)	1215(2)	5388(2)	38(1)
O(1)	3406(2)	-280(1)	5236(2)	59(1)
O(2)	1592(2)	-132(2)	4479(2)	59(1)
O(3)	1102(1)	1790(1)	5354(2)	50(1)
O(4)	2819(1)	2639(1)	5201(2)	47(1)

Table 3. Bond lengths [A] and angles [deg]

C(1)-N(1)	1.481(4)
C(1)-C(2)	1.484(4)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.497(4)
C(2)-N(1)	1.497(4)
C(2)-H(2A)	1.0000
C(3)-C(4)	1.377(5)
C(3)-C(8)	1.380(5)
C(4)-C(5)	1.384(5)
C(4)-H(4A)	0.9500
C(5)-C(6)	1.366(6)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.378(6)
C(6)-H(6A)	0.9500

C(7)-C(8)	1.389(5)
C(7)-H(7A)	0.9500
C(8)-H(8A)	0.9500
C(9)-O(1)	1.199(4)
C(9)-N(2)	1.393(4)
C(9)-C(10)	1.527(5)
C(10)-O(2)	1.404(4)
C(10)-C(11)	1.519(4)
C(10)-H(10A)	1.0000
C(11)-O(3)	1.422(4)
C(11)-C(12)	1.516(4)
C(11)-H(11A)	1.0000
C(12)-O(4)	1.209(4)
C(12)-N(2)	1.386(4)
C(13)-O(2)	1.428(5)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-O(3)	1.417(4)
C(14)-H(14C)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14A)	0.9800
N(1)-N(2)	1.422(3)
N(1)-C(1)-C(2)	60.64(19)
N(1)-C(1)-H(1A)	117.7
C(2)-C(1)-H(1A)	117.7
N(1)-C(1)-H(1B)	117.7

C(2)-C(1)-H(1B)	117.7
H(1A)-C(1)-H(1B)	114.8
C(1)-C(2)-C(3)	121.9(3)
C(1)-C(2)-N(1)	59.6(2)
C(3)-C(2)-N(1)	115.8(3)
C(1)-C(2)-H(2A)	115.9
C(3)-C(2)-H(2A)	115.9
N(1)-C(2)-H(2A)	115.9
C(4)-C(3)-C(8)	119.8(3)
C(4)-C(3)-C(2)	121.3(3)
C(8)-C(3)-C(2)	118.9(3)
C(3)-C(4)-C(5)	120.1(3)
C(3)-C(4)-H(4A)	120.0
C(5)-C(4)-H(4A)	120.0
C(6)-C(5)-C(4)	120.3(4)
C(6)-C(5)-H(5A)	119.9
C(4)-C(5)-H(5A)	119.9
C(5)-C(6)-C(7)	120.2(4)
C(5)-C(6)-H(6A)	119.9
C(7)-C(6)-H(6A)	119.9
C(6)-C(7)-C(8)	119.8(4)
C(6)-C(7)-H(7A)	120.1
C(8)-C(7)-H(7A)	120.1
C(3)-C(8)-C(7)	119.9(3)
C(3)-C(8)-H(8A)	120.1
C(7)-C(8)-H(8A)	120.1
O(1)-C(9)-N(2)	125.0(3)

O(1)-C(9)-C(10)	128.7(3)
N(2)-C(9)-C(10)	106.3(3)
O(2)-C(10)-C(11)	111.1(3)
O(2)-C(10)-C(9)	112.7(3)
C(11)-C(10)-C(9)	103.0(3)
O(2)-C(10)-H(10A)	109.9
C(11)-C(10)-H(10A)	109.9
C(9)-C(10)-H(10A)	109.9
O(3)-C(11)-C(12)	111.4(3)
O(3)-C(11)-C(10)	112.4(3)
C(12)-C(11)-C(10)	104.9(3)
O(3)-C(11)-H(11A)	109.3
C(12)-C(11)-H(11A)	109.3
C(10)-C(11)-H(11A)	109.3
O(4)-C(12)-N(2)	125.1(3)
O(4)-C(12)-C(11)	128.2(3)
N(2)-C(12)-C(11)	106.7(2)
O(2)-C(13)-H(13A)	109.5
O(2)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
O(2)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
O(3)-C(14)-H(14C)	109.5
O(3)-C(14)-H(14B)	109.5
H(14C)-C(14)-H(14B)	109.5
O(3)-C(14)-H(14A)	109.5

H(14C)-C(14)-H(14A)	109.5
H(14B)-C(14)-H(14A)	109.5
N(2)-N(1)-C(1)	111.5(2)
N(2)-N(1)-C(2)	111.9(2)
C(1)-N(1)-C(2)	59.8(2)
C(12)-N(2)-C(9)	113.4(2)
C(12)-N(2)-N(1)	122.2(2)
C(9)-N(2)-N(1)	122.2(2)
(10)-O(2)-C(13)	113.1(3)
C(14)-O(3)-C(11)	113.5(3)

Table 4. Anisotropic displacement parameters (A^2x10^3). The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	48(2)	40(2)	52(2)	7(2)	-7(2)	-1(2)
C(2)	43(2)	40(2)	38(2)	1(2)	-1(2)	-1(1)
C(3)	38(2)	38(2)	39(2)	6(2)	-4(2)	1(1)
C(4)	45(2)	55(2)	47(2)	8(2)	2(2)	-3(2)
C(5)	45(2)	69(2)	53(2)	12(2)	6(2)	-5(2)
C(6)	56(2)	60(3)	66(3)	20(2)	-7(2)	-16(2)
C(7)	64(2)	40(2)	83(3)	2(2)	-5(2)	-10(2)
C(8)	53(2)	42(2)	58(2)	3(2)	2(2)	-2(2)
C(9)	55(2)	41(2)	40(2)	-2(2)	2(2)	-1(2)
C(10)	51(2)	42(2)	41(2)	-4(2)	-4(2)	-12(2)
C(11)	40(2)	52(2)	36(2)	1(2)	-3(1)	0(2)
C(12)	48(2)	39(2)	32(2)	3(2)	-2(2)	-2(2)
C(13)	133(5)	75(3)	108(4)	-7(3)	-11(3)	-51(3)
C(14)	57(2)	86(3)	59(2)	-1(2)	-13(2)	14(2)
N(1)	39(1)	40(1)	42(2)	0(1)	1(1)	-1(1)
N(2)	38(1)	38(1)	40(2)	2(1)	1(1)	-2(1)
O(1)	61(2)	37(1)	78(2)	-7(1)	-4(2)	3(1)
O(2)	61(2)	53(1)	63(2)	-9(1)	-4(1)	-17(1)
O(3)	49(1)	58(1)	44(1)	2(1)	4(1)	8(1)
O(4)	59(1)	37(1)	45(1)	6(1)	-7(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3).

	x	y	z	U(eq)
H(1A)	5221	845	6401	56
H(1B)	4227	696	6930	56
H(2A)	3927	2219	6786	48
H(4A)	5870	1870	5130	59
H(5A)	6991	2880	4851	67
H(6A)	6979	4204	5759	73
H(7A)	5805	4571	6876	75
H(8A)	4632	3599	7069	61
H(10A)	1718	368	5958	54
H(11A)	1771	1412	4047	51
H(13A)	942	-909	5486	126
H(13B)	1939	-1192	5301	126
H(13C)	1226	-1374	4375	126
H(14C)	164	2645	5061	81
H(14B)	415	2052	4035	81
H(14A)	1049	2830	4405	81

5.5 Single crystal XRD of (3*R*,4*R*)-3,4-dimethoxy-1-((2*R*,3*R*)-2,3-diphenylaziridin-1-yl)pyrrolidine-2,5-dione (95a)

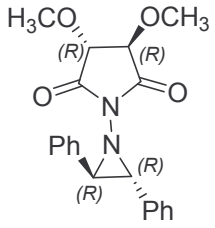


Table 1.

Identification code	
Empirical formula	$C_{20} H_{20} N_2 O_4$
Formula weight	352.38
Temperature	153(2) K
Wavelength	0.71073 A
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 10.7924(10) A alpha = 90 deg.
	b = 10.8421(11) A beta = 90 deg.
	c = 30.851(3) A gamma = 90 deg.
Volume	3610.0(6) A^3Z8
Density (calculated)	1.297 Mg/m^3
Absorption coefficient	0.091 mm^-1
F(000)	1488
Crystal size	0.59 x 0.31 x 0.29 mm
Theta range for data collection	1.99 to 25.50 deg.
Index ranges	-13<=h<=12, -13<=k<=13, -37<=l<=37
Reflections collected	24744
Independent reflections	3804 [R(int) = 0.0663]
Reflections observed	3436

Absorption correction	Integration
Max. and min. transmission	0.9809 and 0.9625
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3804 / 0 / 473
Goodness-of-fit on F^2	1.068
Final R indices [I>2sigma(I)]	R1 = 0.0314, wR2 = 0.0806
R indices (all data)	R1 = 0.0355, wR2 = 0.0821
Largest diff. peak and hole	0.410 and -0.228 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3). U (eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
C(1)	3465(2)	4717(2)	2295(1)	28(1)
C(2)	4373(2)	4289(2)	1964(1)	30(1)
C(3)	5473(2)	5015(2)	1824(1)	28(1)
C(4)	5915(2)	6051(2)	2044(1)	30(1)
C(5)	6957(2)	6672(2)	1899(1)	33(1)
C(6)	7573(2)	6277(2)	1528(1)	36(1)
C(7)	7136(2)	5262(2)	1302(1)	40(1)
C(8)	6102(2)	4638(2)	1449(1)	36(1)
C(9)	2121(2)	4394(2)	2262(1)	29(1)
C(10)	1232(2)	5303(2)	2333(1)	32(1)
C(11)	-13(2)	5040(2)	2271(1)	38(1)
C(12)	-387(2)	3870(2)	2144(1)	38(1)

C(13)	494(2)	2958(2)	2085(1)	37(1)
C(14)	1741(2)	3214(2)	2142(1)	32(1)
C(15)	5186(2)	4610(2)	3074(1)	33(1)
C(16)	6445(2)	4571(2)	3298(1)	33(1)
C(17)	7277(2)	3849(2)	2990(1)	32(1)
C(18)	6420(2)	3391(2)	2633(1)	28(1)
C(19)	6615(4)	6378(3)	3731(1)	63(1)
C(20)	8944(3)	3171(3)	3423(1)	54(1)
C(21)	4188(2)	8007(2)	5421(1)	28(1)
C(22)	3509(2)	8931(2)	5155(1)	28(1)
C(23)	3797(2)	10269(2)	5199(1)	30(1)
C(24)	5011(2)	10693(2)	5235(1)	36(1)
C(25)	5251(2)	11930(2)	5312(1)	40(1)
C(26)	4284(2)	12757(2)	5358(1)	39(1)
C(27)	3082(2)	12345(2)	5323(1)	39(1)
C(28)	2834(2)	11107(2)	5241(1)	34(1)
C(29)	3585(2)	6895(2)	5609(1)	29(1)
C(30)	4215(2)	6260(2)	5934(1)	34(1)
C(31)	3667(2)	5282(2)	6148(1)	39(1)
C(32)	2480(2)	4910(2)	6039(1)	39(1)
C(33)	1849(2)	5523(2)	5708(1)	36(1)
C(34)	2393(2)	6509(2)	5496(1)	31(1)
C(35)	3080(2)	7152(2)	4382(1)	29(1)
C(36)	3148(2)	5912(2)	4145(1)	31(1)
C(37)	3874(2)	5092(2)	4459(1)	31(1)
C(38)	4605(2)	6006(2)	4731(1)	29(1)
C(39)	1481(2)	5854(3)	3642(1)	51(1)

C(40)	4100(3)	3165(2)	4115(1)	47(1)
N(1)	4300(2)	3664(2)	2404(1)	28(1)
N(2)	5292(2)	3976(2)	2685(1)	28(1)
N(3)	4482(2)	8148(2)	4940(1)	29(1)
N(4)	4008(2)	7133(2)	4697(1)	27(1)
O(1)	4262(2)	5112(2)	3202(1)	51(1)
O(2)	6963(2)	5758(2)	3355(1)	47(1)
O(3)	7879(2)	2821(2)	3174(1)	42(1)
O(4)	6653(1)	2653(1)	2349(1)	35(1)
O(5)	2377(2)	7990(2)	4312(1)	38(1)
O(6)	1965(1)	5443(2)	4051(1)	41(1)
O(7)	4699(1)	4242(1)	4275(1)	37(1)
O(8)	5520(1)	5818(2)	4945(1)	36(1)

Table 3. Bond lengths [A] and angles [deg].

C(1)-C(2)	1.491(3)
C(1)-N(1)	1.493(3)
C(1)-C(9)	1.496(3)
C(1)-H(1A)	1.0000
C(2)-C(3)	1.488(3)
C(2)-N(1)	1.521(3)
C(2)-H(2A)	1.0000
C(3)-C(4)	1.398(3)
C(3)-C(8)	1.402(3)
C(4)-C(5)	1.386(3)

C(4)-H(4A)	0.9500
C(5)-C(6)	1.392(3)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.385(3)
C(6)-H(6A)	0.9500
C(7)-C(8)	1.381(3)
C(7)-H(7A)	0.9500
C(8)-H(8A)	0.9500
C(9)-C(10)	1.392(3)
C(9)-C(14)	1.395(3)
C(10)-C(11)	1.388(3)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.387(4)
C(11)-H(11A)	0.9500
C(12)-C(13)	1.384(3)
C(12)-H(12A)	0.9500
C(13)-C(14)	1.384(3)
C(13)-H(13A)	0.9500
C(14)-H(14A)	0.9500
C(15)-O(1)	1.203(3)
C(15)-N(2)	1.387(3)
C(15)-C(16)	1.525(3)
C(16)-O(2)	1.415(3)
C(16)-C(17)	1.522(3)
C(16)-H(16A)	1.0000
C(17)-O(3)	1.409(3)
C(17)-C(18)	1.523(3)

C(17)-H(17A)	1.0000
C(18)-O(4)	1.212(3)
C(18)-N(2)	1.383(3)
C(19)-O(2)	1.392(3)
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
C(20)-O(3)	1.435(3)
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-C(29)	1.488(3)
C(21)-C(22)	1.489(3)
C(21)-N(3)	1.525(3)
C(21)-H(21A)	1.0000
C(22)-C(23)	1.490(3)
C(22)-N(3)	1.504(3)
C(22)-H(22A)	1.0000
C(23)-C(28)	1.387(3)
C(23)-C(24)	1.393(3)
C(24)-C(25)	1.386(3)
C(24)-H(24A)	0.9500
C(25)-C(26)	1.383(3)
C(25)-H(25A)	0.9500
C(26)-C(27)	1.377(4)
C(26)-H(26A)	0.9500
C(27)-C(28)	1.391(3)

C(27)-H(27A)	0.9500
C(28)-H(28A)	0.9500
C(29)-C(30)	1.393(3)
C(29)-C(34)	1.396(3)
C(30)-C(31)	1.383(3)
C(30)-H(30A)	0.9500
C(31)-C(32)	1.384(4)
C(31)-H(31A)	0.9500
C(32)-C(33)	1.396(3)
C(32)-H(32A)	0.9500
C(33)-C(34)	1.385(3)
C(33)-H(33A)	0.9500
C(34)-H(34A)	0.9500
C(35)-O(5)	1.203(3)
C(35)-N(4)	1.397(3)
C(35)-C(36)	1.533(3)
C(36)-O(6)	1.404(3)
C(36)-C(37)	1.529(3)
C(36)-H(36A)	1.0000
C(37)-O(7)	1.401(2)
C(37)-C(38)	1.520(3)
C(37)-H(37A)	1.0000
C(38)-O(8)	1.205(2)
C(38)-N(4)	1.385(3)
C(39)-O(6)	1.437(3)
C(39)-H(39A)	0.9800
C(39)-H(39B)	0.9800

C(39)-H(39C)	0.9800
C(40)-O(7)	1.424(3)
C(40)-H(40C)	0.9800
C(40)-H(40B)	0.9800
C(40)-H(40A)	0.9800
N(1)-N(2)	1.418(2)
N(3)-N(4)	1.425(2)
C(2)-C(1)-N(1)	61.31(13)
C(2)-C(1)-C(9)	121.17(18)
N(1)-C(1)-C(9)	114.95(17)
C(2)-C(1)-H(1A)	116.0
N(1)-C(1)-H(1A)	116.0
C(9)-C(1)-H(1A)	116.0
C(3)-C(2)-C(1)	123.94(18)
C(3)-C(2)-N(1)	122.39(17)
C(1)-C(2)-N(1)	59.42(12)
C(3)-C(2)-H(2A)	113.6
C(1)-C(2)-H(2A)	113.6
N(1)-C(2)-H(2A)	113.6
C(4)-C(3)-C(8)	118.1(2)
C(4)-C(3)-C(2)	123.82(18)
C(8)-C(3)-C(2)	118.11(19)
C(5)-C(4)-C(3)	120.69(19)
C(5)-C(4)-H(4A)	119.7
C(3)-C(4)-H(4A)	119.7
C(4)-C(5)-C(6)	120.3(2)
C(4)-C(5)-H(5A)	119.9

C(6)-C(5)-H(5A)	119.9
C(7)-C(6)-C(5)	119.8(2)
C(7)-C(6)-H(6A)	120.1
C(5)-C(6)-H(6A)	120.1
C(8)-C(7)-C(6)	119.9(2)
C(8)-C(7)-H(7A)	120.0
C(6)-C(7)-H(7A)	120.0
C(7)-C(8)-C(3)	121.3(2)
C(7)-C(8)-H(8A)	119.4
C(3)-C(8)-H(8A)	119.4
C(10)-C(9)-C(14)	119.3(2)
C(10)-C(9)-C(1)	119.45(19)
C(14)-C(9)-C(1)	121.2(2)
C(11)-C(10)-C(9)	120.0(2)
C(11)-C(10)-H(10A)	120.0
C(9)-C(10)-H(10A)	120.0
C(12)-C(11)-C(10)	120.6(2)
C(12)-C(11)-H(11A)	119.7
C(10)-C(11)-H(11A)	119.7
C(13)-C(12)-C(11)	119.3(2)
C(13)-C(12)-H(12A)	120.3
C(11)-C(12)-H(12A)	120.3
C(14)-C(13)-C(12)	120.6(2)
C(14)-C(13)-H(13A)	119.7
C(12)-C(13)-H(13A)	119.7
C(13)-C(14)-C(9)	120.2(2)
C(13)-C(14)-H(14A)	119.9

C(9)-C(14)-H(14A)	119.9
O(1)-C(15)-N(2)	125.2(2)
O(1)-C(15)-C(16)	127.03(19)
N(2)-C(15)-C(16)	107.76(17)
O(2)-C(16)-C(17)	108.23(18)
O(2)-C(16)-C(15)	112.53(19)
C(17)-C(16)-C(15)	104.90(16)
O(2)-C(16)-H(16A)	110.3
C(17)-C(16)-H(16A)	110.3
C(15)-C(16)-H(16A)	110.3
O(3)-C(17)-C(16)	115.35(17)
O(3)-C(17)-C(18)	108.22(17)
C(16)-C(17)-C(18)	105.15(17)
O(3)-C(17)-H(17A)	109.3
C(16)-C(17)-H(17A)	109.3
C(18)-C(17)-H(17A)	109.3
O(4)-C(18)-N(2)	124.75(19)
O(4)-C(18)-C(17)	127.79(19)
N(2)-C(18)-C(17)	107.46(17)
O(2)-C(19)-H(19A)	109.5
O(2)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
O(2)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
O(3)-C(20)-H(20A)	109.5
O(3)-C(20)-H(20B)	109.5

H(20A)-C(20)-H(20B)	109.5
O(3)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(29)-C(21)-C(22)	122.99(18)
C(29)-C(21)-N(3)	123.43(17)
C(22)-C(21)-N(3)	59.85(12)
C(29)-C(21)-H(21A)	113.5
C(22)-C(21)-H(21A)	113.5
N(3)-C(21)-H(21A)	113.5
C(21)-C(22)-C(23)	120.09(17)
C(21)-C(22)-N(3)	61.29(13)
C(23)-C(22)-N(3)	116.41(17)
C(21)-C(22)-H(22A)	116.0
C(23)-C(22)-H(22A)	116.0
N(3)-C(22)-H(22A)	116.0
C(28)-C(23)-C(24)	118.8(2)
C(28)-C(23)-C(22)	119.34(19)
C(24)-C(23)-C(22)	121.66(19)
C(25)-C(24)-C(23)	120.5(2)
C(25)-C(24)-H(24A)	119.7
C(23)-C(24)-H(24A)	119.7
C(26)-C(25)-C(24)	120.3(2)
C(26)-C(25)-H(25A)	119.9
C(24)-C(25)-H(25A)	119.9
C(27)-C(26)-C(25)	119.5(2)
C(27)-C(26)-H(26A)	120.3

C(25)-C(26)-H(26A)	120.3
C(26)-C(27)-C(28)	120.6(2)
C(26)-C(27)-H(27A)	119.7
C(28)-C(27)-H(27A)	119.7
C(23)-C(28)-C(27)	120.3(2)
C(23)-C(28)-H(28A)	119.9
C(27)-C(28)-H(28A)	119.9
C(30)-C(29)-C(34)	118.7(2)
C(30)-C(29)-C(21)	117.83(19)
C(34)-C(29)-C(21)	123.33(19)
C(31)-C(30)-C(29)	121.0(2)
C(31)-C(30)-H(30A)	119.5
C(29)-C(30)-H(30A)	119.5
C(30)-C(31)-C(32)	120.2(2)
C(30)-C(31)-H(31A)	119.9
C(32)-C(31)-H(31A)	119.9
C(31)-C(32)-C(33)	119.3(2)
C(31)-C(32)-H(32A)	120.3
C(33)-C(32)-H(32A)	120.3
C(34)-C(33)-C(32)	120.4(2)
C(34)-C(33)-H(33A)	119.8
C(32)-C(33)-H(33A)	119.8
C(33)-C(34)-C(29)	120.3(2)
C(33)-C(34)-H(34A)	119.8
C(29)-C(34)-H(34A)	119.8
O(5)-C(35)-N(4)	126.07(19)
O(5)-C(35)-C(36)	127.42(18)

N(4)-C(35)-C(36)	106.51(17)
O(6)-C(36)-C(37)	112.70(18)
O(6)-C(36)-C(35)	111.83(17)
C(37)-C(36)-C(35)	103.48(16)
O(6)-C(36)-H(36A)	109.6
C(37)-C(36)-H(36A)	109.6
C(35)-C(36)-H(36A)	109.6
O(7)-C(37)-C(38)	108.79(16)
O(7)-C(37)-C(36)	116.91(17)
C(38)-C(37)-C(36)	103.71(17)
O(7)-C(37)-H(37A)	109.0
C(38)-C(37)-H(37A)	109.0
C(36)-C(37)-H(37A)	109.0
O(8)-C(38)-N(4)	124.84(19)
O(8)-C(38)-C(37)	128.2(2)
N(4)-C(38)-C(37)	106.98(16)
O(6)-C(39)-H(39A)	109.5
O(6)-C(39)-H(39B)	109.5
H(39A)-C(39)-H(39B)	109.5
O(6)-C(39)-H(39C)	109.5
H(39A)-C(39)-H(39C)	109.5
H(39B)-C(39)-H(39C)	109.5
O(7)-C(40)-H(40C)	109.5
O(7)-C(40)-H(40B)	109.5
H(40C)-C(40)-H(40B)	109.5
O(7)-C(40)-H(40A)	109.5
H(40C)-C(40)-H(40A)	109.5

H(40B)-C(40)-H(40A)	109.5
N(2)-N(1)-C(1)	114.20(16)
N(2)-N(1)-C(2)	113.60(15)
C(1)-N(1)-C(2)	59.27(12)
C(18)-N(2)-C(15)	113.63(17)
C(18)-N(2)-N(1)	118.91(16)
C(15)-N(2)-N(1)	125.79(16)
N(4)-N(3)-C(22)	114.67(15)
N(4)-N(3)-C(21)	111.08(15)
C(22)-N(3)-C(21)	58.86(12)
C(38)-N(4)-C(35)	113.54(16)
C(38)-N(4)-N(3)	118.36(15)
C(35)-N(4)-N(3)	127.66(17)
C(19)-O(2)-C(16)	115.9(2)
C(17)-O(3)-C(20)	112.08(19)
C(36)-O(6)-C(39)	113.54(19)
C(37)-O(7)-C(40)	113.01(17)

Table 4. Anisotropic displacement parameters (A^2 x 10^3). The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	29(1)	28(1)	28(1)	2(1)	1(1)	1(1)
C(2)	30(1)	31(1)	29(1)	-1(1)	-2(1)	-1(1)

C(3)	27(1)	30(1)	28(1)	2(1)	-2(1)	3(1)
C(4)	30(1)	30(1)	29(1)	0(1)	-1(1)	2(1)
C(5)	32(1)	33(1)	35(1)	0(1)	-3(1)	0(1)
C(6)	29(1)	41(1)	40(1)	6(1)	4(1)	-2(1)
C(7)	38(1)	44(1)	37(1)	-4(1)	9(1)	1(1)
C(8)	37(1)	37(1)	33(1)	-4(1)	4(1)	-3(1)
C(9)	29(1)	33(1)	26(1)	3(1)	1(1)	-1(1)
C(10)	33(1)	34(1)	30(1)	2(1)	3(1)	0(1)
C(11)	29(1)	49(1)	38(1)	-1(1)	3(1)	4(1)
C(12)	28(1)	55(2)	33(1)	2(1)	2(1)	-8(1)
C(13)	40(1)	40(1)	31(1)	2(1)	0(1)	-8(1)
C(14)	35(1)	33(1)	29(1)	3(1)	0(1)	0(1)
C(15)	42(1)	31(1)	26(1)	1(1)	1(1)	6(1)
C(16)	43(1)	29(1)	28(1)	2(1)	-6(1)	-5(1)
C(17)	32(1)	29(1)	34(1)	2(1)	-3(1)	-3(1)
C(18)	29(1)	27(1)	30(1)	3(1)	1(1)	-2(1)
C(19)	96(2)	53(2)	40(1)	-16(1)	7(2)	-20(2)
C(20)	48(2)	54(2)	61(2)	0(1)	-25(1)	7(1)
C(21)	30(1)	29(1)	26(1)	-5(1)	0(1)	1(1)
C(22)	26(1)	29(1)	28(1)	-4(1)	1(1)	0(1)
C(23)	31(1)	31(1)	26(1)	-2(1)	1(1)	-1(1)
C(24)	31(1)	35(1)	43(1)	-5(1)	3(1)	-1(1)
C(25)	36(1)	38(1)	45(1)	-3(1)	2(1)	-11(1)
C(26)	52(1)	29(1)	36(1)	-2(1)	1(1)	-7(1)
C(27)	44(1)	30(1)	43(1)	-3(1)	-2(1)	3(1)
C(28)	33(1)	31(1)	38(1)	-1(1)	-2(1)	-1(1)
C(29)	30(1)	29(1)	26(1)	-6(1)	2(1)	3(1)

C(30)	38(1)	34(1)	30(1)	-4(1)	-2(1)	3(1)
C(31)	52(1)	34(1)	31(1)	-1(1)	-2(1)	5(1)
C(32)	52(1)	32(1)	32(1)	-2(1)	9(1)	-2(1)
C(33)	37(1)	36(1)	35(1)	-6(1)	4(1)	-5(1)
C(34)	33(1)	31(1)	30(1)	-4(1)	2(1)	2(1)
C(35)	28(1)	33(1)	24(1)	2(1)	4(1)	0(1)
C(36)	28(1)	38(1)	28(1)	-5(1)	1(1)	-3(1)
C(37)	32(1)	29(1)	31(1)	-4(1)	3(1)	-1(1)
C(38)	25(1)	32(1)	29(1)	-3(1)	3(1)	2(1)
C(39)	41(1)	73(2)	41(1)	-13(1)	-14(1)	7(1)
C(40)	59(2)	32(1)	49(1)	-12(1)	5(1)	-7(1)
N(1)	28(1)	29(1)	28(1)	1(1)	-1(1)	0(1)
N(2)	31(1)	28(1)	25(1)	-1(1)	0(1)	0(1)
N(3)	28(1)	28(1)	31(1)	-4(1)	2(1)	-1(1)
N(4)	27(1)	28(1)	27(1)	-4(1)	0(1)	0(1)
O(1)	51(1)	72(1)	31(1)	-8(1)	1(1)	26(1)
O(2)	75(1)	34(1)	33(1)	-5(1)	-2(1)	-11(1)
O(3)	41(1)	35(1)	50(1)	-1(1)	-15(1)	3(1)
O(4)	35(1)	34(1)	36(1)	-8(1)	1(1)	6(1)
O(5)	43(1)	39(1)	33(1)	1(1)	-5(1)	9(1)
O(6)	35(1)	48(1)	40(1)	-6(1)	-7(1)	-6(1)
O(7)	40(1)	30(1)	41(1)	-8(1)	3(1)	2(1)
O(8)	29(1)	38(1)	41(1)	-7(1)	-4(1)	6(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3)

	x	y	z	U(eq)
H(1A)	3661	5519	2440	34
H(2A)	3988	3797	1725	36
H(4A)	5496	6333	2297	36
H(5A)	7253	7371	2054	40
H(6A)	8290	6701	1430	44
H(7A)	7547	4996	1046	47
H(8A)	5812	3940	1293	43
H(10A)	1479	6103	2424	39
H(11A)	-615	5666	2316	46
H(12A)	-1240	3697	2098	46
H(13A)	242	2151	2005	44
H(14A)	2339	2583	2098	39
H(16A)	6379	4136	3583	40
H(17A)	7909	4418	2863	38
H(19A)	6769	5849	3983	75
H(19B)	5731	6581	3717	75
H(19C)	7099	7138	3758	75
H(20A)	8690	3732	3656	65
H(20B)	9544	3588	3235	65
H(20C)	9325	2433	3549	65

H(21A)	4829	8381	5615	34
H(22A)	2630	8723	5083	33
H(24A)	5681	10130	5207	43
H(25A)	6082	12210	5334	48
H(26A)	4449	13604	5412	47
H(27A)	2416	12910	5356	47
H(28A)	2001	10835	5213	41
H(30A)	5033	6503	6009	40
H(31A)	4106	4864	6371	47
H(32A)	2100	4243	6189	46
H(33A)	1040	5262	5628	43
H(34A)	1954	6924	5273	37
H(36A)	3628	6011	3870	37
H(37A)	3277	4642	4650	37
H(39A)	1989	5519	3407	62
H(39B)	1499	6757	3631	62
H(39C)	626	5566	3610	62
H(40C)	4722	2593	4000	56
H(40B)	3521	3394	3884	56
H(40A)	3645	2764	4351	56

Erklärung

Hiermit versichere ich, dass ich die vorliegende Dissertation selbständig und ohne unerlaubte Hilfe angefertigt und andere als in der Dissertation angegebenen Hilfsmittel nicht benutzt habe. Alle Stellen, die wörtlich oder sinngemäß aus veröffentlichten oder unveröffentlichten Schriften entnommen sind, habe ich als solche kenntlich gemacht. Kein Teil dieser Arbeit ist in einem anderen Promotions- oder Habilitationsverfahren verwendet worden.

Kassel, den 01.07.2009