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APPLICATIONS OF OXAZIRIDINES IN ORGANIC SYNTHESIS

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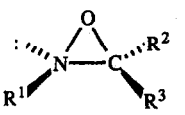
CONTENTS

1. INTRODUCTION

Oxaziridines **1**, heterocyclic compounds containing oxygen, nitrogen and carbon atoms in a three-membered ring, were first reported in the mid-fifties by Krimm,[1] Emmons[2] and Horner and Jurgens.[3] Extensive investigations of these compounds have revealed their unusual reactivity, undoubtedly related to the presence of the strained three-membered ring and a relatively weak N—O bond. A consequence of these features is the low basicity of the oxaziridine nitrogen compared to amines. Another remarkable property of some oxaziridines is that they possess a configurationally stable nitrogen atom at ordinary temperatures. For the N-alkyl oxaziridines the experimentally determined inversion barriers are in the range of 24 to 31 kcal mol^{-1}.[4] Optically active oxaziridines the asymmetry of which is due solely to nitrogen have been reported.[4] The area of oxaziridines has been the subject of several general reviews.[4–6] The focus of this Report is on those reactions of oxaziridines that are useful synthetically.



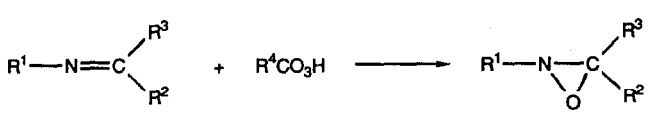
1

R^1= H, R, Ar, RC(O), RSO_2

2. SYNTHESIS OF OXAZIRIDINES

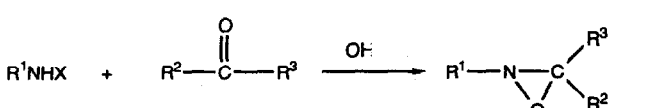
2.1. N—H, N-*alkyl- and* N-*aryloxaziridines*

The two principal routes to N—H, N-alkyl and N-aryloxaziridines are: (i) the oxidation of imines with peracids eqn (1); and (ii) the amination of carbonyl compounds with NH_2-X derivatives eqn (2). Detailed discussions of the mechanism, scope and selectivity of these methods are found in several excellent reviews.[5,6] The synthesis of a variety of N-alkyl-3-aryl oxaziridines, including those where R^2 is heteroaromatic, via peracid oxidation of the corresponding imine, has recently been reported.[7]



(1)

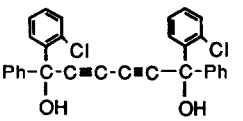
R^1, R^2, R^3= Alkyl, Aryl



(2)

R^1= H, CH_3
X = Cl, OSO_3H

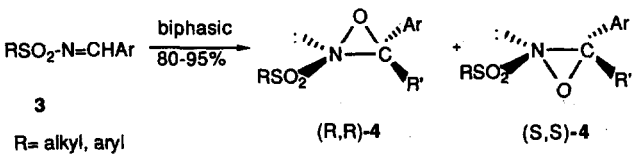
The oxidation of chiral imines with peracids and the oxidation of achiral imines with chiral peracids to give optically active N-alkyl and N-aryl oxaziridines have been reviewed.[4] Photolysis of the inclusion complexes of N-alkyl nitrones and the chiral diol, (−)-1,6-di(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**2**), affords optically active oxaziridines in good yield and optical purities up to 100% *ee*.[8]



(-)-**2**

2.2. N-*Sulfonyloxaziridines*

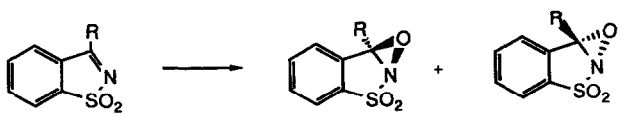
Biphasic buffered oxidation of sulfonimines **3** with *m*-chloroperbenzoic acid (*m*-CPBA) and the phase transfer catalyst benzyltriethylammonium chloride affords racemic *trans*-N-sulfonyloxaziridines **4** in excellent yields, eqn (3).[9,10] The Baeyer–Villiger type oxidation of the sulfonimine affords only the thermodynamically more stable *trans* oxaziridines. A recent improvement in the synthesis of these compounds uses buffered potassium peroxymonosulfate (Oxone) in place of expensive and now less readily accessible *m*-CPBA.[11] Preparation of **4** (R = Ph) from **3** using Oxone was complete and quantitative within 15 min. A phase transfer catalyst was not required. Similar oxidation of 3-alkyl or 3-aryl-1,2-benzisothiazole-1,1-dioxides **5** affords racemic bicyclic oxaziridines **6**, also in high yield eqn (4).[12]



3

R= alkyl, aryl

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

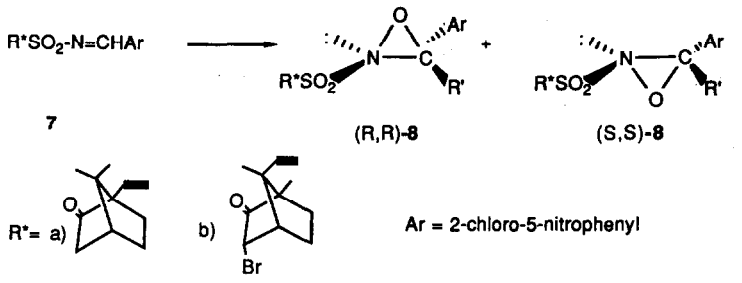


5 (2S,3R)-**6** (2R,3S)-**6** (4)

Jennings *et al.* have reported the first examples of 3,3-dialkyl N-sulfonyloxaziridines.[13a] In one method they were prepared in low yield (15%) by treatment of the oxaziridine derived from cyclohexanone and hydroxylamine-O-sulfonic acid with aryl sulfonyl chlorides. The second method involves the biphasic oxidation of 3,3-dialkyl sulfonimines.[13b]

Generally, N-sulfonyloxaziridines are isolated as stable crystalline solids. However, when Ar in **4** is a *p*-methoxyphenyl, the oxaziridines were too unstable to be isolated.[12] On the other hand, *trans*-2-(phenylsulfonyl)-3-phenyloxaziridine **4** (R = Ar = Ph) has been prepared on the molar scale in greater than 80% isolated yield.[10]

Sulfonimines **3** are prepared by heating sulfonamides (RSO_2NH_2) with aromatic aldehydes in the presence of an ion exchange acid catalyst,[10] or with titanium tetrachloride–triethylamine,[13c] and by heating at 150–180°C with the diethyl acetals of aromatic aldehydes.[12] The related 3,3-dialkyl sulfonimines have been prepared by reaction of sulfinyl chlorides (RS(O)Cl) with oximes.[13b] Treatment of saccharin with lithium reagents (RLi), described by Abromovitch *et al.* gives **5**.[12,14]



Sulfonimine	Ratio of (R,R)/(S,S)
7a	35:65
7b	50:50

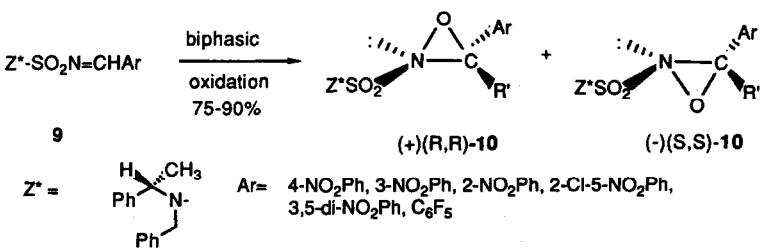
Scheme 1.

2.2.1. *Optically active* N-*sulfonyloxaziridines.* The nitrogen inversion barrier in 3,3-dialkyl N-sulfonyloxaziridines is estimated to be 20–21 kcal mol^{-1} at 62°C using DNMR techniques. This result suggests that racemization could be rapid at 25°C for such oxaziridines.[13] The *cis* to *trans* inversion barrier for N-sulfonyloxaziridines **4** derived from aromatic aldehydes is unknown, but is expected to be higher due to reduced steric interactions between the N-sulfonyl group and the *syn* ring hydrogen atom.

Optically active N-sulfonyloxaziridines **4** have been prepared by oxidation with chiral peracids.[15] Repeated crystallizations from ethyl ether give **4** (R = Ph, Me; Ar = Ph) in greater than 95% optical purity.

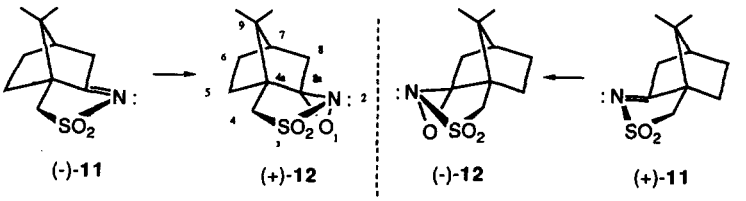
A more convenient route to optically active N-sulfonyloxaziridines, developed by Davis *et al.*, entails oxidation of optically active sulfonimines **7a** and **7b** to give mixtures of oxaziridine diastereoisomers, (+)(R,R)-**8** and (−)(S,S)-**8** (Scheme 1).[16] The R,R and S,S configurations assigned to the oxaziridine three-membered ring atoms were determined by X-ray crystallography and chemical correlation techniques. These oxaziridine diastereoisomers could only be separated into their optically pure forms by crystallization when the aryl group in **8** was the 2-chloro-5-nitrophenyl group. Chromatography resulted in decomposition.

2.2.2. *Diastereomeric* N-*sulfamyloxaziridines.* Biphasic oxidation of sulfamimines **9** affords diastereomeric 2-sulfamyloxaziridine (+)(R,R)-**10** and (−)(S,S)-**10** in a 1 : 1 ratio (Scheme 2).[17] These diastereoisomers are stable to chromatography and were separated into their optically pure forms by crystallization or by preparative HPLC. The requisite sulfamines **9** are prepared by the acid catalyzed condensation of homochiral sulfamides ($Z^*NSO_2NH_2$) with aromatic aldehydes.



Scheme 2.

2.2.3. *(Camphorylsulfonyl)oxaziridines.* Both isomeric forms of (+)- and (−)-(camphorylsulfonyl)oxaziridines **12** are available by oxidation of the corresponding sulfonimines **11** with buffered potassium peroxymonosulfate (Oxone) (Scheme 3).[18,19] Since oxidation can only take place from the endo-face of the C–N double bond due to steric blocking of the exo-face, a single oxaziridine isomer is obtained. The enantiomerically pure sulfonimines **11** can be prepared in three steps (>80% yield) from inexpensive (+) and (−)-camphor-10-sulfonic acids.[19] Alternatively they are commercially available from Aldrich.



Scheme 3.

3. REACTIONS OF OXAZIRIDINES

Ring opening of the strained oxaziridine three-membered ring is the key to all of the synthetically useful reactions of oxaziridines discussed in this Report. An unusual property of oxaziridines is their ability to react as both aminating and oxygenating reagents with nucleophiles. The site of nucleophilic attack at the oxaziridine three-membered ring is determined by the substitution pattern at nitrogen.[20] For example, Hata and Watanabe demonstrated that oxaziridines act as aminating reagents when the groups attached to the oxaziridine nitrogen in **1** are small (i.e. R^1 = H, Me). As R^1 becomes larger, the site of attack is shifted from nitrogen to oxygen. In contrast to oxiranes and aziridines, nucleophiles generally do not react at the oxaziridine carbon atom. To date the N-sulfonyloxaziridines **4** act exclusively as oxidizing reagents with nucleophiles.

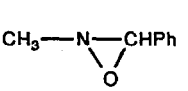
3.1. *Reactions of* N—H, N-*alkyl and* N-*aryloxaziridines*

3.1.1. *Nitrogen-transfer reactions.* A number of nucleophiles attack oxaziridines **1** (R^1 = H, Me) at the ring nitrogen atom to give carbonyl compounds and ylide intermediates eqn (5).[20] Depending on the nucleophile, the intermediate ylide may rearrange to hydrazines, aziridines, sulfenamides or fragment to azo compounds and alkenes.

(5)

1

3.1.1.1. *Reaction with nitrogen nucleophiles. Synthesis of hydrazines.* The reaction of *cis*-2 and *trans*-2-methyl-3-phenyloxaziridine (**13**) and 1-oxa-2-aza-spiro[2.5]octane (**14**) with amines has been explored by Hata and Watanabe[20] and by Schmitz[21] (Table 1). Triethylamine reacts with **13** (4 days) to give hexamethylenetetramine via condensation of the methylimine (HN = CH_2) formed by fragmentation of the ylide (Et_3N^+-N^--Me). Hydrazines are formed in good yield on treatment of secondary amines with oxaziridines **13** or **14**. Primary amines react with **13** to give azo compounds which are thought to result from oxidation of the initially formed hydrazine by the oxaziridine.[20]



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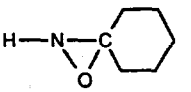

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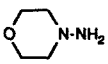
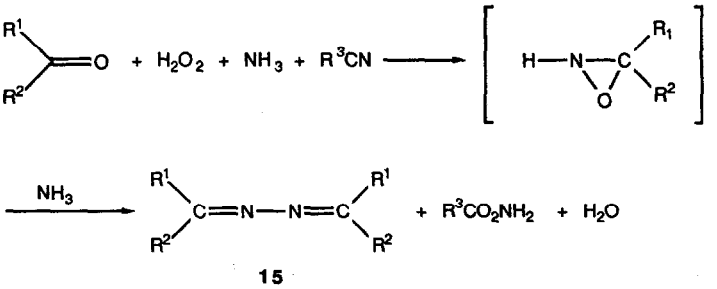
Table 1: Reaction of Amines with Oxaziridines 13 and 14.

Oxaziridine	Amine	Product	(% Yield)
cis-13 *trans*-13	Et_3N	hexamethylenetetramine	(64.6)[a] (78)
cis-13 *trans*-13	Me_2NH	Me_2N-NHMe	(71.6)[a] (85.3)
14	Et_2NH	Et_2N-NH_2	(>90)[b]
14			(>90)[b]
cis-13 *trans*-13	$MeNH_2$	MeN=NMe	(72)[a] (50)
trans-13	$PhNH_2$	PhN=NMe	(26)[a]

a) Reference 20.
b) Reference 21.

Amination of an *in situ* generated oxaziridine appears to be the key step in the process leading to the synthesis of hydrazine by oxidation of ammonia with hydrogen peroxide in the presence of carbonyl compounds and a nitrile (Scheme 4).[22] Yields vary from a low of 12% [**15**, $R^1 = R^2 =$ $-(CH_2)_{11}-$] to a high yield of 78% (**15**, $R^1 = R^2 =$ Me). A modification of this method is used to prepare hydrazine industrially.[23]



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Scheme 4.

3.1.1.2. *Reactions with sulfur nucleophiles. Synthesis of sulfenamides and alkenes.* Thiols, sulfinates and thiocyanates react with oxaziridines **13** and **14** according to eqn (5) to give sulfenamides, sulfonamides and NH_2—SCN respectively; yields are good to excellent (Table 2). However, dimethyl

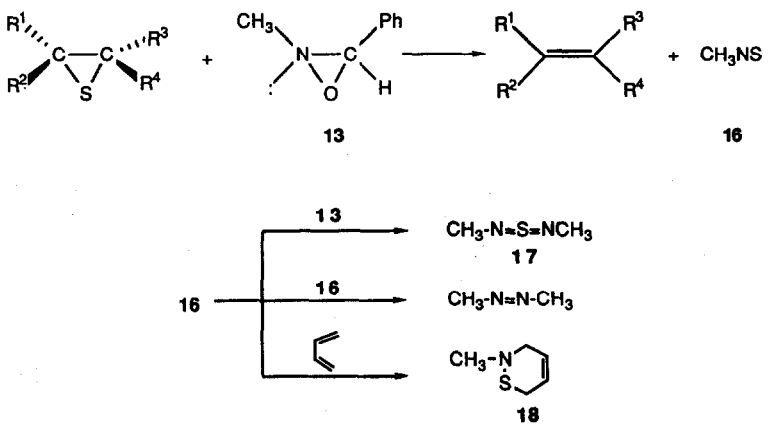
Table 2: Reaction of Oxaziridines 13 and 14 with Organosulfur Compounds.

Organosulfur Compound	Oxaziridine	Product	(% Yield)
PhSH	*cis*-13	PhSNHMe	(99)[a]
PhSH	*cis*-13 (Me=i-Pr)	PhSNHPr-i	(97)[a]
p-MePhSO$_2$Na	14	p-MePhSO$_2$NH$_2$	(84)[b]
NaSCN	14	NCS-NH$_2$	(91)[b]
Me$_2$S	*cis*-13	MeN=NMe	(72)[a]

a) Reference 20.
b) Reference 21.

sulfide gives azomethane (MeN = NMe) via attack of the initially formed ylide Me_2S^+-NMe on **13**.[20]

At room temperature episulfides react with two equivalents of *cis*-2-methyl-3-phenyloxaziridine (**13**) to give alkenes, dimethylsulfur diimide (**17**) and azomethane (Scheme 5).[25] The desulfurization of episulfides to alkenes by **13** appears to be a general reaction. The alkenes, which are formed with retention of configuration, are obtained in good to excellent yield (80–90%). Thionitrosomethane (**16**) reacts with **13** to give **17**. Compound **17** was trapped with 2,3-butadiene to give the cyclic sulfenamide **18** in 23–33% yield.



Scheme 5.

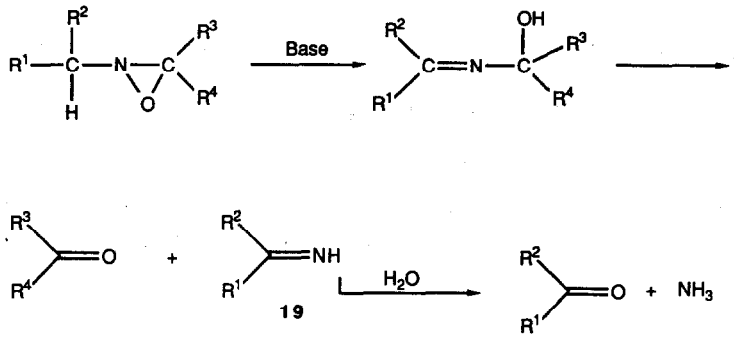
3.1.1.3. *Reactions with alkenes. Synthesis of aziridines.* Oxaziridines are reported to be able to transfer nitrogen to certain alkenes affording aziridines. Heating oxaziridine **14** with styrene, α-methylstyrene or indene in toluene for 3 h gave the corresponding aziridines in yields up to 46%.[26] The reaction is reported to be stereospecific, but yields are poor with aliphatic alkenes.

3.1.2. *Oxygen-transfer reactions.* Although NH, N-alkyl and aryl oxaziridines **1** oxidize I^- to I_2 and phosphines to phosphine oxides, they are poor reagents for the epoxidation of alkenes or for the oxidation of sulfides to sulfoxides.[2–6,20] For example, a bis-oxaziridine oxidizes thiacycloalkanes to the corresponding sulfoxides in only 5–7% yield at ambient temperature.[27] However, N-*tert*-butyloxaziridine (**1**, R^1 = *t*-Bu, $R^2 = R^3$ = H) is reported to give a quantitative yield of dimethyl

sulfoxide on heating with dimethyl sulfide (80°C for 10 h),[20h] while N-(trifluoromethyl-3,3-difluoro-oxaziridine (**1**, $R^1 = CF_3$, $R^2 = R^3 = F$) epoxidizes alkenes at low temperatures.[28] Boyd and Jennings recently described the synthesis of N-phosphinoyloxaziridines **1** ($R^1 = Ph_2P(O)$-).[29] These oxaziridines are reported to epoxidize alkenes and oxidize sulfides to sulfoxides.[29]

3.1.3. *Base-catalyzed eliminations.*

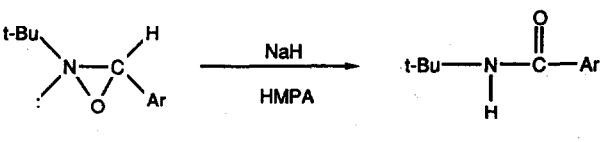
3.1.3.1. *Synthesis of carbonyl compounds.* The oxaziridine ring itself is generally inert towards bases.[30] However, oxaziridines bearing an α-hydrogen atom on the N-alkyl group isomerize to carbinolimines which, on hydrolysis, give ketones or aldehydes and ammonia (Scheme 6). A concerted E_2 elimination mechanism has been proposed for this transformation.[31,32] Boyd *et al.* described the synthesis of N—H substituted aldimines and ketimines **19** ($R_2C = NH$) in good yield (52–90%) by treating the fluorenone and *p*-nitrobenzaldehyde derived N-alkyl oxaziridines with hindered bases (DABCO, DBN and KO*t*-Bu) in anhydrous solvents.[32]



Scheme 6.

Methodology for the oxidative deamination of amines to ketones, mediated by oxaziridines, has been described by Dinizo and Watt.[33a] Toward this end, amines were transformed into their respective imines using 2-pyridinecarboxyaldehyde followed by oxidation to oxaziridines **20**. Treatment of **20** with KOH in aqueous acetone solutions containing methanol or N,N-dimethylformamide gave the corresponding ketones. 2-Pyridinecarboxyaldehyde is trapped by acetone, preventing its condensation with the product ketone (R^1R^2CO). Yields are moderate to good (Table 3). In a similar way benzylamine derivatives are transformed into ketones.[33b]

3.1.3.2. *Synthesis of amides.* Treatment of *E-tert*-butyl-3-(*p*-nitrophenyl)oxaziridine (**21**) with NaH in HMPA gave an 83% yield of amide **22**.[34] Dinizo and Watt also observed the formation of amides when LDA was used to effect the ring opening of oxaziridine **20**.[33a] However, deoxygenation is the principal product on treatment of oxaziridine **21** (Ar = Ph) with LDA giving the imine ($Me_3CN = CHPh$).[35] This imine is thought to be formed via an initial electron transfer reaction from the base to oxaziridine.



21 **22**

Ar= p-nitrophenyl

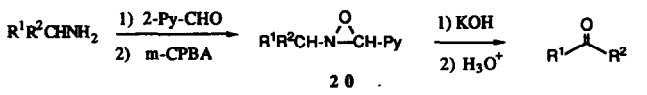
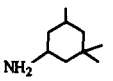
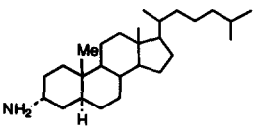


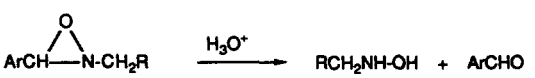
Table 3. Oxaziridine Mediated Oxidative Deamination of Amines into Ketones.[33a]

Amine ($R^1R^2CHNH_2$) R^1	R^2	Cosolvent	% Yield of Ketone ($R^1C(O)R^2$)
n-C_5H_{11}	n-C_5H_{11}	DMF	73
n-C_6H_{13}	n-C_6H_{13}	DMF	73
-$CH_2(CH_2)_4$	CH_2-	MeOH	64
- C_2H_5	CH_2CH_2Ph	MeOH	74
		MeOH	47
		DMF	77

3.1.4. *Reactions with acids. Synthesis of hydroxylamines.* Acid-catalyzed hydrolysis of N-aryloxaziridines may proceed via cleavage of either the C—O or N—O bonds, depending upon the ring substitution pattern.[36] Isomerization to the nitrone has also been reported.[36]

Hydrolysis of 3-aryl oxaziridines **1** (R^2 = aryl) generally takes place with exclusive N—O bond cleavage to give hydroxylamines in 70–85% yield eqn (6).[36] This is particularly true when the C–Ar group in **1** is a *p*-MeOPh which is able to stabilize the developing carbocation on the oxaziridine carbon atom.[37] A series of biologically active N-hydroxyamino acid derivatives were prepared by transforming amino acids into oxaziridines, followed by acid catalyzed hydrolysis (Table 4).[37–39]

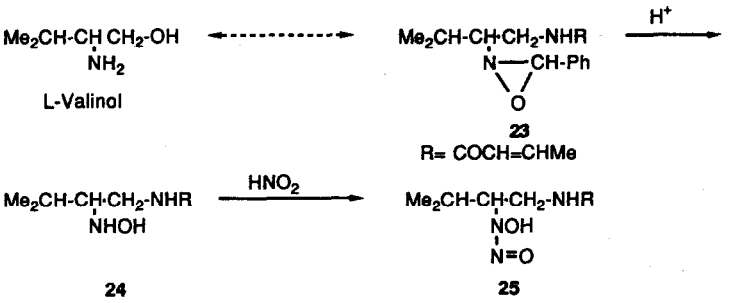
Dopastin **25**, a dopamine β-hydroxylase inhibitor, was prepared in eight steps from L-valinol by treating hydroxyl amine **24** with HNO_2.[39] An acidic ion exchange resin effected hydrolysis of optically active **23** to **24**.



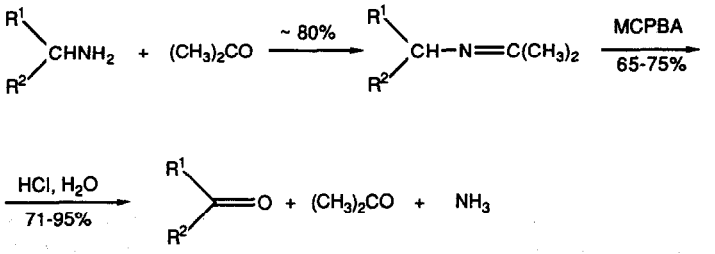
(6)

Table 4: Synthesis of N-Hydroxyamino Acids from Oxaziridines.[37a]

R-CH-CO_2R' NHOH R	R'	% Yield
i-Pr	H	30
$PhCH_2$	H	42
$PhCH_2$	CH_3	30
$CH_2CH_2CO_2Me$	CH_3	42

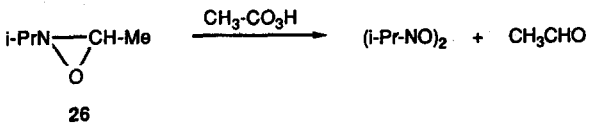


Oxaziridines derived from acetone give carbonyl compounds on treatment with dilute acids (Scheme 7). Black and Blackman used this reaction to convert a number of primary and secondary amines to aldehydes and ketones.[40] This method is an alternative to the base catalyzed rearrangement of oxaziridines to ketones discussed earlier (see Section 3.1.3.1.).



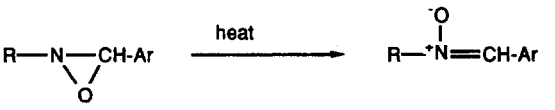
Scheme 7.

Aliphatic nitroso compounds have been prepared by treatment of oxaziridines such as **26** with peracids.[36] The initial site of oxidation is believed to be the oxaziridine nitrogen.



3.1.5. *Thermal and photochemical isomerizations.* A large number of thermal and photochemical reactions of N-alkyl and N-aryl oxaziridines have been reported.[4-6] The possible involvement of unstable oxaziridine intermediates in the photochemical reactions of aromatic N-oxides has also appeared.[41] The most useful of the thermal and photochemical transformations of oxaziridines are their rearrangement to nitrones and amides. While there are some general empirical guidelines for predicting the oxaziridine substitution pattern likely to give amides or nitrones, this aspect of oxaziridine chemistry is not well understood.

3.1.5.1. *Rearrangement to nitrones.* Thermal rearrangement of oxaziridines to nitrones, which involves cleavage of the C—O bond, appears to be limited to oxaziridines having an aryl substituent on the ring carbon eqn (7). This suggests that C—O bond cleavage is heterocyclic, involving a developing positive charge on the oxaziridine carbon.[42] Indeed, this rearrangement is particularly

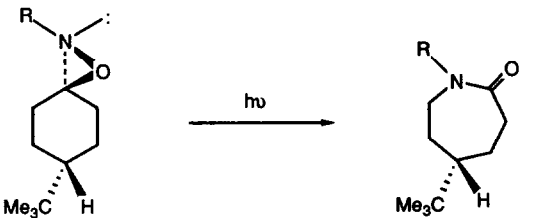


(7)

efficient when the C-aryl moiety contains an electron releasing substituent.[43] Rearrangement of oxaziridines to nitrones is a non-stereoselective process with *cis*- or *trans*-oxaziridines affording mixtures of the *cis*- and *trans*-nitrones.[44] Yields however are good to excellent.

Some optically active oxaziridines are thought to racemize upon irradiation via nitrone intermediates.[45]

3.1.5.2. *Rearrangement to amides.* The thermal and photochemical isomerization of oxaziridines to amides [$R^2C(O)NR^1R^3$] takes place with concomitant cleavage of the N—O bond and migration of one of the substituents on carbon to nitrogen.[46] Oliveros *et al.* demonstrated that the group that migrates is the one that is anti to the nitrogen lone pair.[47] They showed that photolysis of (2R,αS)-6(*e*)-*tert*-butyl-2(α-methylbenzyl)-1,2-oxazaspiro[2.5]octane **27** afforded a single lactam **28** in 80% yield having the (S)-configuration at the ring *tert*-butyl substituted carbon.

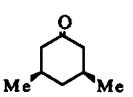


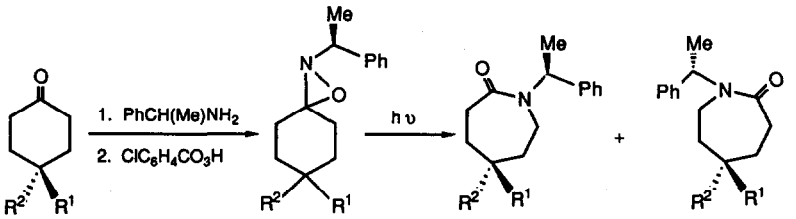
27 **28**

R= (S)-Ph-CH-CH_3

Aube *et al.* extended these studies to the synthesis of a number of chiral lactams.[48] The prochiral cyclohexanone derivatives **29** were converted into mixtures of oxaziridine isomers **30**. On irradiation at 2537 Å the isomeric mixture gives lactams **31** and **32** (Table 5).

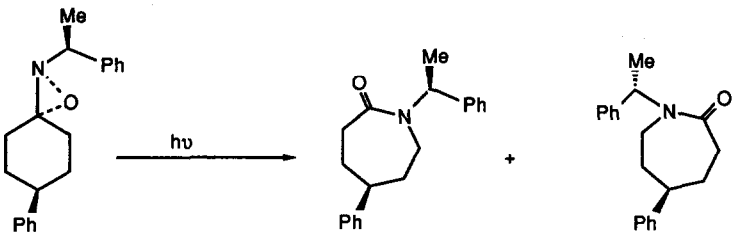
Table 5: Photolysis of Oxaziridine 29.[48]

Entry	Ketone 29 R^1	R^2	Lactones (31:32) % Yield
1	CH_3	H	62 (3.8:1)
2	CH_3CH_2	H	69 (3.8:1)
3	CMe_3	H	69 (6.0:1)
4	Ph	H	59 (4.7:1)
5	Ph	Me	83 (1.5:1)
6			68 (5.4:1)



29 30 31 32

As expected, the selectivity is much higher when a single oxaziridine isomer **30** is photolyzed. Irradiation of **33** gave **34** and **35** (94 : 6) in 59% overall yield from 4-phenylcyclohexanone. Lactams such as **34** have potential application in the enantioselective synthesis of benzomorphinan class of analgesics.

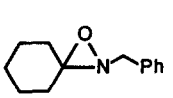
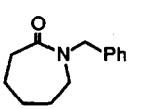
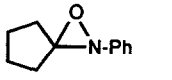
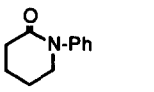
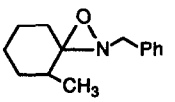
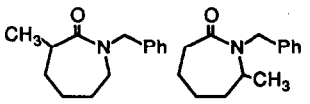


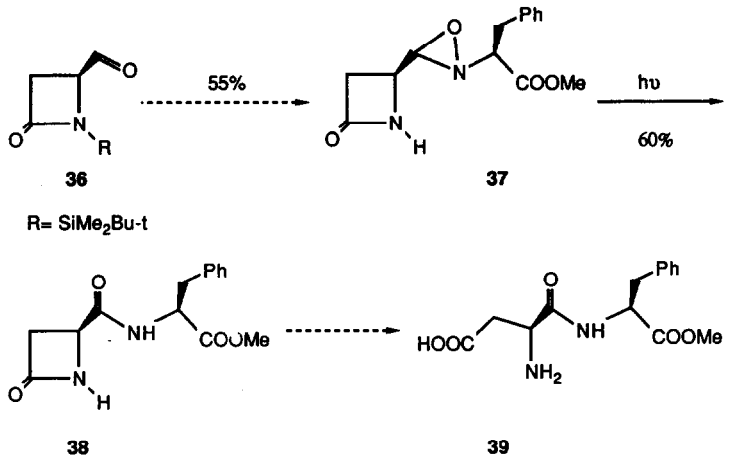
33 34 35

The oxaziridine to amide isomerization of spiro oxaziridines has been used in the synthesis of medium to large lactams.[49–51] Some representative examples are given in Table 6.

Duhamel *et al.* recently reported the synthesis of the dipeptide sweetener aspartame **39** using the oxaziridine–amide rearrangement (Scheme 8).[52] More specifically, the optically active azetidinone **36** was converted into the imine by reaction with (*S*)-methylphenylalaninate followed by oxidation to

Table 6: Rearrangement of of Spirooxaziridines to Lactams[27]

Oxaziridine	Conditions	Products	(% Yield)
	heat hυ		(55) (85)
	heat hυ		(75) (28)
	heat hυ	 (65:35) (95:5)	(60) (80)

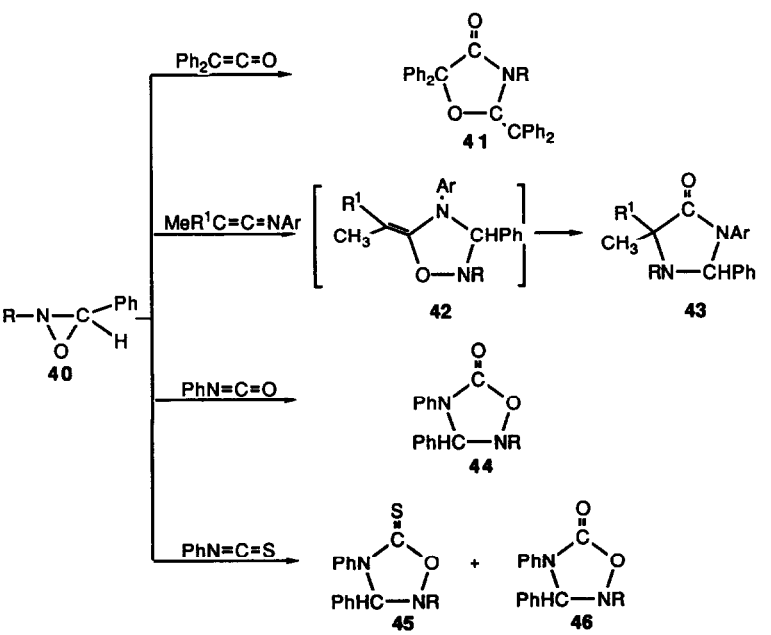


Scheme 8.

oxaziridine **37** in 65% yield. Photolysis of **37** gave **38**, which had previously been converted into aspartame **39** by Pietsch.[53]

3.1.6. *Cycloaddition reactions.* Oxaziridines **40** undergo a number of addition and cycloaddition reactions on heating with heterocumulenes to afford various types of heterocyclic compounds (Scheme 9). These investigations, primarily carried out by Agawa *et al.*,[54–57] have recently been reviewed by Haddadin and Freeman.[6] Only those reactions that are potentially useful synthetically will be discussed here.

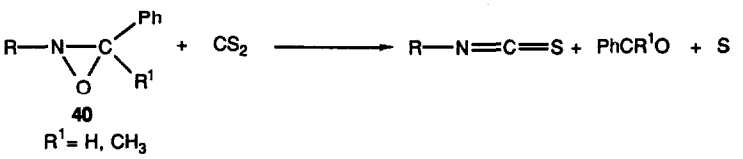
Two molecules of diphenylketene react with **40** on heating to give oxazolidinones **41** in yields up to 68% (R^1 = isopropyl).[54] Ketenimines react with **40** (R = *t*-butyl) to give **43** (40–60%) via rearrangement of **42**.[56] Oxadiazolidinones **44** are obtained in 36–95% yield on heating **40** (R =



Scheme 9.

n-Bu, *i*-Pr, *t*-Bu) with phenylisocyanate.[54] For example, phenyl isothiocyanate and **40** (R = *t*-butyl) gave heterocyclic compounds **45** and **46** in 68 and 19% yield, respectively.[55,57] While the mechanistic details for these transformations remain unclear, they have been discussed in terms of nucleophilic attack by either the oxaziridine nitrogen or oxygen atoms at the central carbon of the heterocumulene.[54]

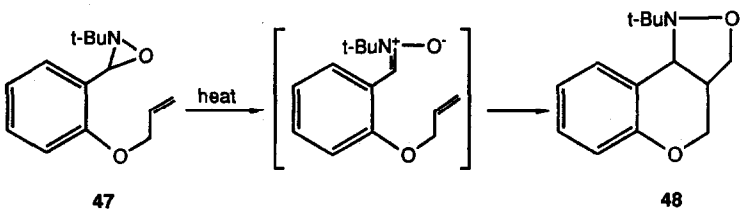
Heating N-alkyl-3-phenyloxaziridines **40** with excess carbon disulfide gives excellent yields of the corresponding alkyl isothiocyanates eqn (8).[55] A mechanism involving attack of the nitrogen lone pair of electrons on CS_2 to give an intermediate thione thiaziridine has been proposed for this transformation.



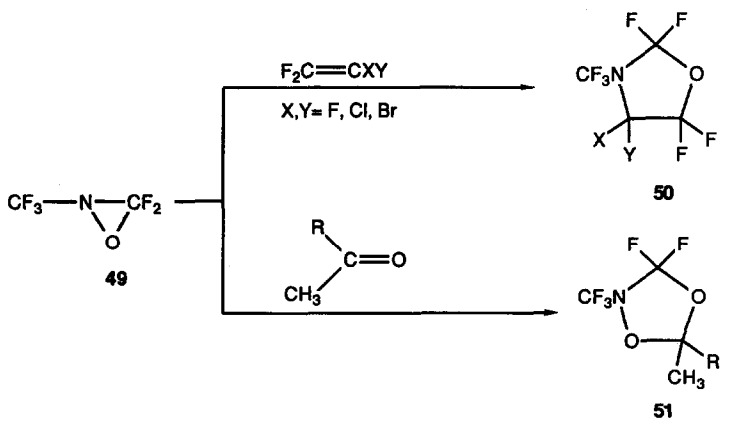
40

R^1 = H, CH_3 (8)

The intramolecular 1,3-dipolar cycloaddition of a nitrone generated from oxaziridine **47** has been used by Padwa and Koehler to prepare isoxazolidine **48** in 86% yield.[58] Cycloaddition of 2-trifluoromethyl-3,3-difluorooxaziridine **49** with various 1,1-difluoroolefins gives 1,3-oxazolidines **50** in 60–85% yield,[59] while ketones react with **49** to give 1,3,4-dioxazolidines **51**.

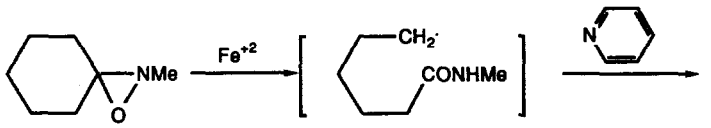


47 **48**

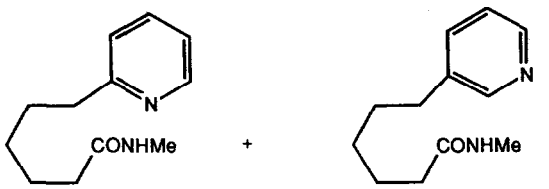


49 **50** **51**

3.1.7. *Homolytic reactions.* Treatment of N-alkyl oxaziridines **1** with ferrous salts leads to products resulting from homolytic opening of the oxaziridine three-membered ring. While this aspect of oxaziridine chemistry has received limited attention, it is potentially useful synthetically. For example, treatment of oxaziridine **52** with ferrous sulfate in the presence of pyridine gave **53a** and **53b** in 80% yield.[60]

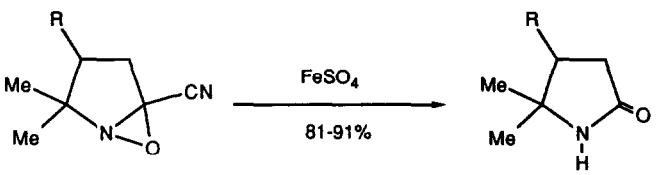


52

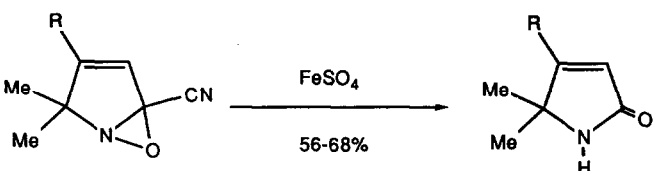


53a 53b

Alternatively, bicyclic oxaziridines such as **54** and **55** afford pyrrolidin-2-ones and 3-pyrrolinones on reaction with Fe(II) salts.[61,62]



54



55
R= H, Me, Ph

3.2. *Oxygen-transfer reactions of* N-*sulfonyloxaziridines*

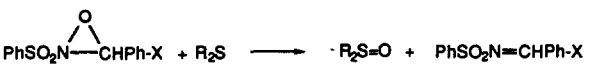
Oxaziridines are members of the general class of oxidizing reagents that have their active site oxygens as part of a three-membered ring.[41,63] Included in this class of reagents are the metal (Cr Mo, W) peroxides and hydroperoxides catalyzed by high-valent d^0 transition-metal complexes (Mo V, Ti) and the dioxiranes. The most well known member of this class of three-membered metal peroxides is the Sharpless reagent for the asymmetric epoxidation of allylic alcohols.[64] The similarities in structures for the metal peroxides, dioxiranes and oxaziridines suggest that they may have a common mechanism of oxygen-transfer. Oxaziridines have been proposed as models for studying the oxygen-transfer reactions of the metal peroxides and dioxiranes which are less easily explored.[63] The driving force for oxygen-transfer by these reagents has been related to relief of ring strain and the enthalpy associated with the formation of strong double bonds in the products.

N-Sulfonyloxaziridines **4** are the only oxaziridines able to oxidize nucleophilic substrates at rates which are comparable to peracids. These oxaziridines are highly chemoselective oxidizing reagents.[41,64] For example, **4** selectively oxidizes sulfides to sulfoxides without over-oxidation to sulfones.[65] Nucleophilic substrates such as sulfides, selenides and amines are oxidized within a few minutes at room temperature, but epoxidation of alkenes requires heating at 60°C for several hours.[66] Alkynes are not oxidized by **4**. Primary, secondary and tertiary amines are oxidized at nitrogen by **4** to give initially hydroxyl amines and amine oxides,[67] but pyridine is unreactive.[68] The closely related (camphorylsulfonyl)oxaziridines **12** effectively oxidize sulfides to sulfoxides, but they do not epoxidize alkenes or oxidize amines even on heating.[19] Since N-sulfonyloxaziridines are neutral, aprotic oxidizing reagents, they are among the few reagents available for the oxidation of carbanions and enolates.

3.2.1. *Oxidation of organosulfur compounds.*

3.2.1.1. *Oxidation of sulfides to sulfoxides.* The oxidation of sulfides to sulfoxides has been widely explored with many different oxidizing reagents; however, very few of these reagents have general application. Many of these reagents are too reactive, over-oxidizing sulfoxides to sulfones, particularly when the reagent is in excess. With other reagents careful control of the reaction parameters is required or chemoselectivity is lost.

Many of these limitations are avoided using N-sulfonyloxaziridines, eqn (9). For example, oxaziridines **56** and **57** quantitatively oxidized a variety of sulfides to sulfoxides within a few minutes at room temperature.[63,65,69–71] Over-oxidation to the corresponding sulfone is very slow even when the oxidizing reagent is present in excess. An S_N2 type mechanism, involving displacement of the sulfonimine from the oxaziridine by the lone pair on sulfur, has been proposed for the oxidation of sulfides to sulfoxides, eqn (9).[63] Representative examples of the oxidation of sulfides to sulfoxides by N-sulfonyloxaziridines are given in Table 7.



$$PhSO_2N\text{—}CHPh\text{-}X + R_2S \longrightarrow R_2S{=}O + PhSO_2N{=}CHPh\text{-}X \quad (9)$$

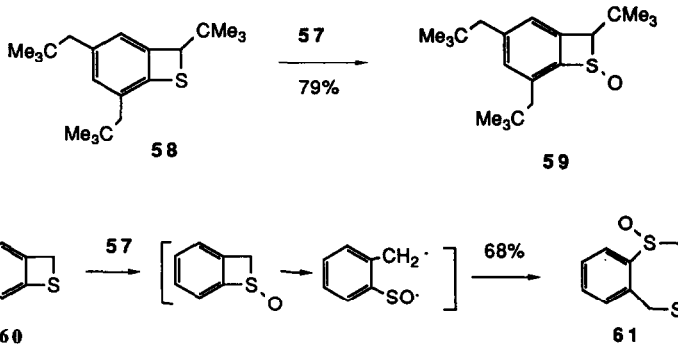
56 X=H
57 X=p-NO_2

Table 7: Oxidation of Sulfides to Sulfoxides by 2-(Phenylsulfonyl)-3-aryloxaziridines **56** and **57** in $CHCl_3$.[65]

Sulfide	Oxaziridine (equiv.)	Time (hr)	Sulfoxide	(% Isolated Yield)
$PhSCH_3$	**56** (1)	fast	$PhS(O)CH_3$	(52)(92)[a]
	56 (2.5)	20	$PhS(O)CH_3$	(20)
			$PhSO_2CH_3$	(80)
Ph_2S	**56** (1)	fast	Ph_2SO	(93)
$(n\text{-}Bu)_2S$	**56** (1)	fast	$(n\text{-}Bu)_2SO$	(89)
	56 (1)	0.5		(81)
$PhSSiMe_3$	**56** (2)	fast	$PhS(O)OSiMe_3$	(63)[b]

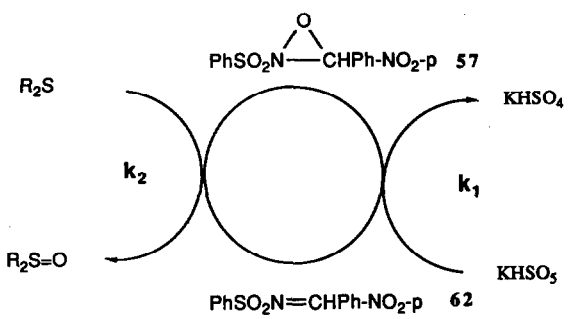
a) Lal, G. S. Unpublished results
b) Reference 69.

The first example of a stable benzo[*b*]thiete sulfoxide **59**, was prepared in 79% yield by oxidation of benzothiete **58** with **57**.[71] By contrast, oxidation of benzo[*b*]thiete **60** gave a diastereomeric mixture of bis-sulfoxide **61** (58 : 42).



2-(Phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine **57** is recommended for sulfide oxidations because the resulting sulfonimine ($PhSO_2N = CHPhNO_2$-*p*) precipitates from the chloroform solution in 70–80% yield.[70] The sulfoxides are then isolated by extraction into *n*-pentane where the sulfonimine is insoluble.

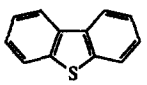
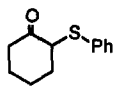
3.2.1.2. *Catalytic oxidation of sulfides to sulfoxides.* A catalytic system for the selective oxidation of sulfides to sulfoxides, which uses N-sulfonyloxaziridines, has been reported by Davis *et al.* (Scheme 10).[65a] Buffered potassium peroxymonosulfate (Oxone) is used to generate **57** from a nonstoichiometric amount of sulfonimine **62**. In the absence of the oxaziridine precursor **62**, sulfoxides are not formed. The system is highly chemoselective affording sulfoxides in excellent isolated yields with only trace amounts of the sulfones being detected in most cases (Table 8). However, sulfides that produce hydrophilic sulfoxides are further oxidized nucleophilically to sulfones by the peroxymonosulfate anion.



Scheme 10.

3.2.1.3. *Asymmetric oxidation of sulfides to sulfoxides.* Prochiral sulfides are oxidized by enantiomerically pure N-sulfonyl and N-sulfamyloxaziridines **8** and **10** to optically active sulfoxides. The asymmetric induction for the N-sulfamyloxaziridines **10** (40–91% *ee*)[17] is better than the camphor based oxaziridines **8** (19–61% *ee*).[16] Of the sulfamyloxaziridines, pentafluorophenyl oxaziridine **63** gives the best results, in part because oxidations take place at −78°C (Table 9). The sulfoxides and the sulfamimine are isolated in high yield >90% yield, with the latter being recycled.

Table 8: Selective Catalytic Oxidation of Sulfides to Sulfoxides Using Buffered Oxone and 0.2 Equivalents of $PhSO_2N{=}CHPhNO_2$-p (62) in CH_2Cl_2 at 25 °C.[65a]

Sulfide	Time (hr)	% Isolate Yields Sulfoxide/Sulfone
p-Tolyl-S-Me	0.5	90/5
Ph-S-Me	0.5	95/0
Ph-S-CH_2Ph	0.5 ($CHCl_3$)	95/0
Ph-S-Ph	0.25	90/0
Ph-S-$CH_2{=}CH_2$	0.25	90/0
PhSCH_2CH_2-OH	0.5	0/95
PhSCH_2CH_2-Cl	0.25	92/0
(s-C_4H_9)$_2$S	0.5	95/0
	3	89/0
	2	90/0

The configuration of the oxaziridine three-membered ring in **8** and **10** controls the stereochemistry of the sulfoxide and can be predicted using steric arguments. In every case oxaziridines (+)(R,R)-**8** and (+)(R,R)-**10** gave the (+)-R sulfoxides, while (−)(S,S)-oxaziridines gave the (−)S-sulfoxides.[16,17] Based on the structure–reactivity trends, the preferred diastereomeric transition state is predicted to be the one where an enantiotopic electron pair on sulfur attacks the active site oxygen

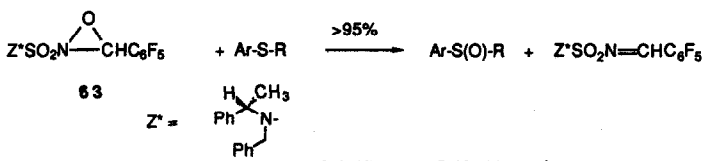
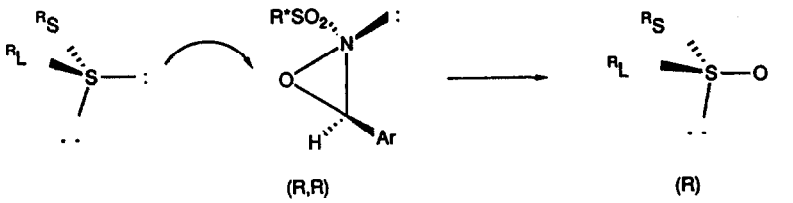


Table 9: Asymmetric Oxidation of Sulfides to Sulfoxides using Pentafluorophenyl Sulfamyloxaziridine **63** in $CHCl_3$.[17]

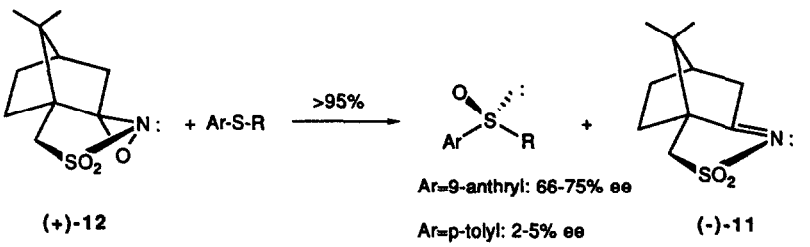
Ar	R	Temp. °C	% ee Sulfoxide (Config.)[a] (+)(R,R)-63	(-)(S,S)-63
p-tolyl	n-Bu	25	34.6 (R)	30.7 (S)
		-22	36.4 (R)	
		-78		53.3 (S)
p-tolyl	i-Pr	25	34.6 (R)	36.6 (S)
		-78		60.3 (S)
9-anthryl	Me	25	50.3 (R)	50.0 (S)
		-22	66.9 (R)	
		-78		90.6 (S)
9-anthryl	i-Pr	25	56.6 (R)	59.9 (S)
		-22	67.7 (R)	
		-78		79.9 (S)

a) Determined using a Pirkle covalent phenyl glycine HPLC column.

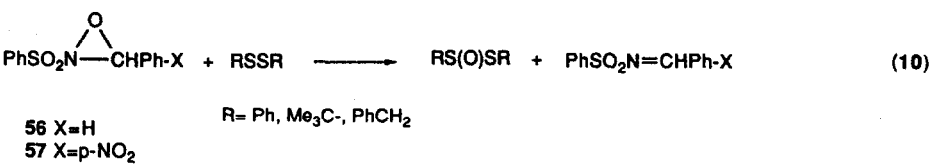
in the plane of the oxaziridine three-membered ring, such that the large (Ar_L) and small (R_S) group of the sulfide (Ar_L-S-R_S) face the small (C-aryl) and large (Z^*SO_2) regions of the oxaziridine three-membered ring, respectively.



Stereoselectivities for the asymmetric oxidation of alkyl 9-anthryl sulfides by (camphoryl-sulfonyl)oxaziridines (**12**) at 25°C are good (66–73% *ee*), but poorer for the alkyl *p*-tolyl sulfides (2–5% *ee*).[19] (+)(2R,8*a*S)-(camphorylsulfonyl)oxaziridine **12** gave (−)-S sulfoxides while (−)-(2S,8*a*R)-**12** gave the (+)-R sulfoxides; chemical yields are excellent (>90%).

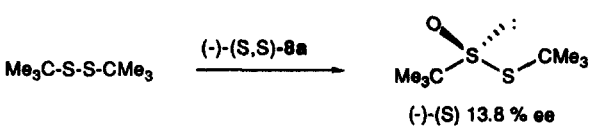


3.2.1.4. *Oxidation of disulfides to thiosulfinates.* Oxidation of disulfides (RSSR) with oxaziridines **56** and **57** affords thiosulfinates (RS(O)SR) within 30 min at 25°C eqn (10).[65b] An advantage of oxaziridines as aprotic and neutral oxidizing reagents is that the acid sensitive thiosulfinates are obtained in higher yield and exhibit better stability than those prepared using *m*-chloroperbenzoic acid.

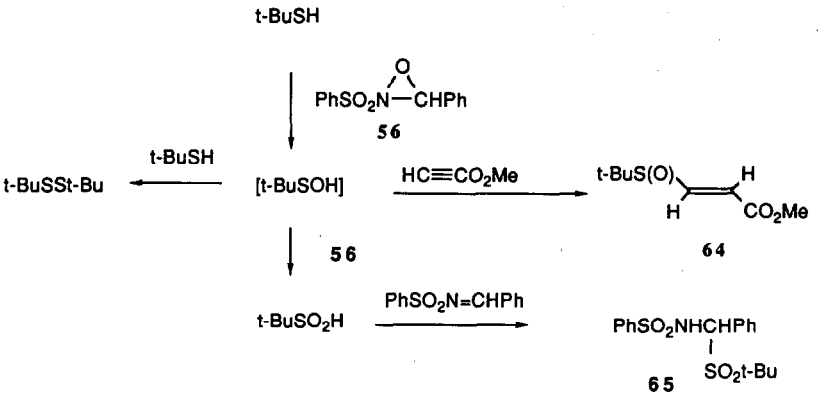


(10)

3.2.1.5. *Asymmetric oxidation of disulfides to thiosulfinates.* Asymmetric oxidation of *p*-tolyl and di-*tert*-butyl disulfides with (−)-(S,S)-**8** gave optically active (−)(S)-*p*-tolyl-*p*-toluene thiosulfinate (2.1% *ee*) and (−)-*tert*-butyl-2-methyl 2-propanethiosulfinate (13.8% *ee*), respectively.[16] The latter thiosulfinate is predicted to have the S-configuration based on the chiral recognition mechanism proposed above for the asymmetric oxidation of sulfides to sulfoxides by optically active sulfonyl-oxaziridines (see Section 3.2.1.3.).

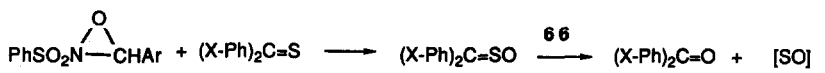


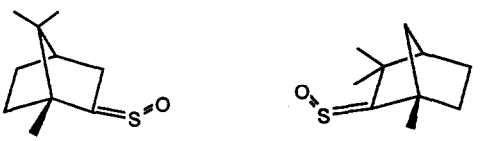
3.2.1.6. *Oxidation of thiols to sulfenic acids.* The biological activity of thiols depends, to a large extent, on the facility with which the SH group is oxidized to high sulfur oxides (RSO_xH) and disulfides (RSSR).[72] Sulfenic acids (RSOH), transient intermediates in many organic and inorganic sulfur reactions, are generally thought to be involved in the oxidation of thiols.[70] Davis and Billmers, making use of the fact that **56** does not oxidize alkynes, were the first to demonstrate that sulfenic acids are involved in the oxidation of thiols (Scheme 10).[72] Oxidation of 2-methyl-2-propanethiol (*t*-BuSH) with **56** in the presence of methyl propiolate gave 2-methyl-2-propanesulfenic acid (*t*-BuSOH), trapped as the vinyl sulfoxide **64**, in 25–47% yield (Scheme 11). Monitoring the reaction by NMR showed that in the absence of the trapping agent, sulfinic acid (*t*-$BuSO_2H$) was the principal product even in the presence of a large excess of thiol. This result is consistent with the fact that sulfenic acids are 'α-effect' or super nucleophiles and are, therefore, oxidized at a faster rate than the thiol. Note that *t*-$BuSO_2H$ is trapped by the sulfonimine to give adduct **65**.



Scheme 11.

3.2.1.7. *Oxidation of thiones to thione* S-*oxides.* Zani *et al.* reported a study of the oxidation of thiones ($Ar_2C=S$) to thione S-oxides ($Ar_2C=S=O$) using N-sulfonyloxaziridines **66**.[73] The oxidation is fast and quantitative, exhibiting second order kinetics. Interestingly, oxidative conversion of the thione S-oxide to the ketone proved to be less selective with **66** than with perbenzoic acid. Thiocamphor S-oxide (**67**) and thiofenchone S-oxide (**68**) were prepared in 91 and 76% yield, respectively by oxidation of the corresponding thiones with **66** (Ar = 3-nitrophenyl). Prior attempts to prepare these thione S-oxides with other oxidants resulted in low yields and products difficult to purify.

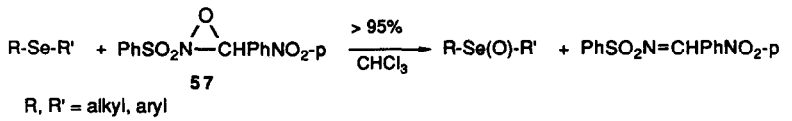




(+)-67 (-)-68

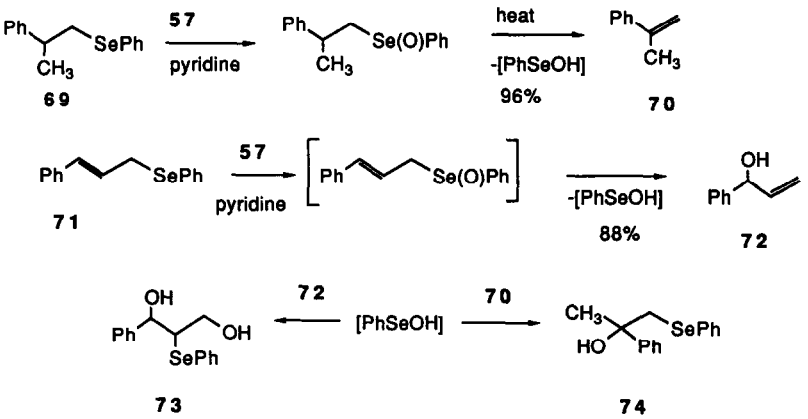
3.2.2. *Oxidation of organoselenium compounds.*

3.2.2.1. *Oxidation of selenides to selenoxides.* Selenides, like sulfides, are quantitatively oxidized to selenoxides in aprotic solvents by 2-(phenylsulfonyl)-3-(*p*-nitrophenyl)oxaziridine (**57**) eqn (11).[68,74] Even in the presence of an excess of **57**, selenones ($ArSeO_2Me$) were not detected.[68] This oxidizing reagent has been used to prepare vinylic selenoxides having different functional groups such as aldehydes.[74] Evidence that diphenyl diselenide (PhSeSePh) is oxidized by **57** to benzeneselenenic anhydride (PhSe(O)O(O)SePh) is suggested by the isolation of phenylselenolethanal on addition of ethyl vinyl ether.[74]

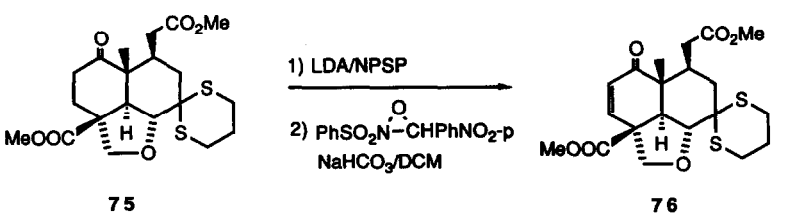


(11)

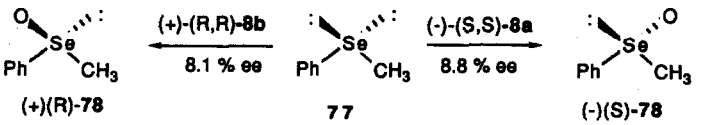
Oxidation of selenides **69** and **71** with oxaziridine **57**, in the presence of 5 molar equivalents of pyridine, gave α-methylstyrene (**70**) and 1-α-phenyl allyl alcohol (**72**) in 96 and 88% isolated yields, respectively.[68] In the absence of pyridine, β-hydroxy selenides **73** and **74** were formed. Pyridine inhibits addition of benzeneselenenic acid (PhSeOH) to olefinic double bonds in **70** and **72** presumably by intercepting the selenic acid.



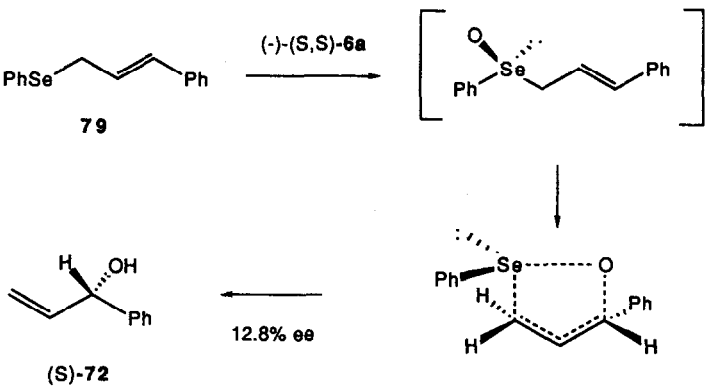
α-Selenylation (LDA, N-phenylselenophthalimide) and oxidative elimination using **57** gave enone **76** in 62% overall yield from **75**.[75]



3.2.2.2. *Asymmetric oxidation of selenides to selenoxides.* The first examples of optically active selenoxides were obtained by asymmetric oxidation of prochiral selenides with optically active N-sulfonyloxaziridines **8**.[76,77] Methyl phenyl selenide (**77**) was oxidized by (−)-(S,S)-**8a** and (+)-(R,R)-**8b** to give (−)-(S)- and (+)-(R)-methyl phenyl selenoxide (**78**) in 8 and 9% *ee*, respectively.[76,77] The absolute configurations were determined using (+)-2,2,2-trifluoro-1-(9-anthryl)ethanol as predicted by the sulfoxide model (Section 3.2.1.3.). The configurational lability of optically active selenoxides, such as **78** ($t_{1/2}$ racemized 10 s), in the presence of water was shown to be the result of acid catalyzed achiral hydrate ($PhSe(OH)_2Me$) formation.



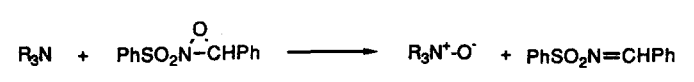
Asymmetric oxidation of *E*-cinnamylphenyl selenide (**79**) gives (+)-(S)-(+)-1-phenylallyl alcohol (**72**) (12.8% *ee*) on oxidation with (−)-(S,S)-**6a**.[77] A concerted [2,3]-sigmatropic rearrangement of an intermediate allylic selenoxide through an exo five-membered cyclic transition state is consistent with the stereochemistry of (+)-**72** (Scheme 12).



Scheme 12.

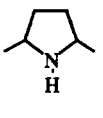
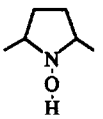
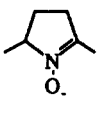
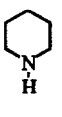
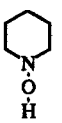
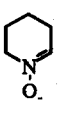
3.2.3. *Oxidation of organonitrogen compounds.*

3.2.3.1. *Oxidation of amines.* A detailed study of oxidation of primary, secondary and tertiary amines by 2-(phenylsulfonyl)-3-phenyloxaziridine (**56**) has been reported by Zajac *et al.*[67] Amines less nucleophilic than pyridine are not oxidized by **56** in accordance with the observation that pyridine does not react with N-sulfonyloxaziridines.[68] Tertiary amines, such as triethylamine, N-methyl piperidine, etc. react within minutes with **56** to give the corresponding tertiary amine oxides (R_3N^+-O^-) and sulfonimine **80** quantitatively eqn (12). Quinine, which has both a quinoline and quinuclidine nitrogen, undergoes oxidation only at the quinuclidine nitrogen atom.[68]



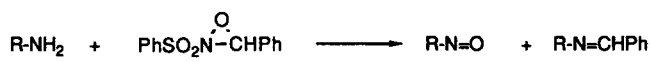
(12)

Table 10: Oxidation of Secondary Amines by 2-(Phenylsulfonyl)-3-phenyloxaziridine (**56**).[68]

Equivalents of **56**	Amine	Products (% yield) Hydroxylamine	Nitrone
	$(PhCH_2)_2NH$	$(PhCH_2)_2N$-OH	$PhCH_2N(O)$=CHPh
1	(10)	(70)	(10)
2	(0)	(0)	(85)
			
1	(5)	(70)	(15)
2	(0)	(0)	(80)
			
1	(5)	(65)	(20)
2	(0)	(0)	(85)

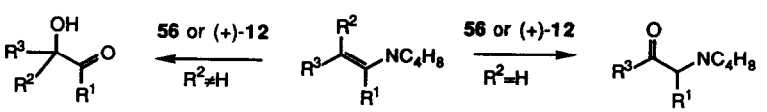
Oxidation of secondary and primary amines with oxaziridines gives complex reaction products. Oxidation of secondary amines with one equivalent of **56** affords both the hydroxylamine (R_2NHOH) and nitrone (Table 10). Nitrones are formed almost exclusively on treatment of the amine with two equivalents of **56** (Table 10). The nitrones are presumably formed by dehydration of the oxidation product of the hydroxylamine, which is formed more rapidly than the hydroxylamine because of the α-effect. Diphenylamine, which is less nucleophilic than pyridine, is not oxidized by **56**.

Aliphatic primary amines gave on oxidation with **56** nitroso compounds (RN = O) in low yields (10–30%) eqn (13). However, the major product (50–65%) is imine **81**, formed by reaction of the primary amine with the sulfonimine **80**.[68]



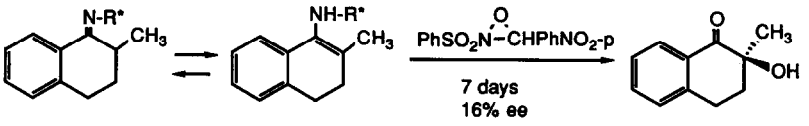
56 **81** (13)

3.2.3.2. *Oxidation of enamines.* The oxidation of enamines by N-sulfonyloxaziridines **56**, **57** and (+)-(camphorylsulfonyl)oxaziridine (**12**) has recently been investigated by Davis and Sheppard.[78] Disubstituted enamines **82** (R^2 = H) are rapidly oxidized (30 min) to α-amino ketones **83** in 50–70% yield, while trisubstituted enamines **82** (R^2 = H) gave, after hydrolysis, α-hydroxy ketones **84** in 70–90% yield. A mechanism involving initial oxidation of **82** to an α-amino epoxide was suggested to account for these products. Racemic α-amino ketones were obtained on oxidation of **82** with (+)-**12**.



84 **82** **83**

The pyrrolidine enamine of 2-methyl-1-tetralone failed to react with (+)-**12** even after 30 h. However, oxidation of imine (+)-**85**, which is in tautomeric equilibrium with its enamine, with oxaziridine **57** gave a 46% isolated yield of (−)-2-hydroxy-2-methyltetralone (**86**) after 7 days.[78]

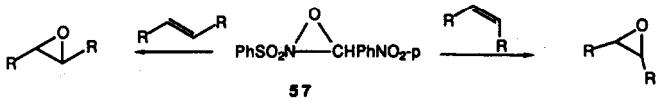


(+)-**85** (-)(S)-**86**

R* = (S)-α-phenylethylamine

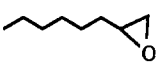
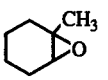
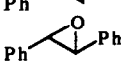
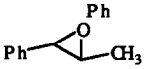
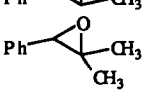
3.2.4. *Oxidation of carbon–carbon double bonds.*

3.2.4.1. *Epoxidation of alkenes.* Like peracids, N-sulfonyloxaziridines **4** epoxidize alkenes in a *syn* stereospecific manner [i.e., *trans* alkenes give *trans* epoxides, while *cis* alkenes give *cis* epoxides, eqn (14)].[66] However, in contrast to peracids, epoxidations using N-sulfonyloxaziridines are slower, requiring 3–12 h at 60°C for satisfactory yields (Table 11). More nucleophilic substrates such as



57 (14)

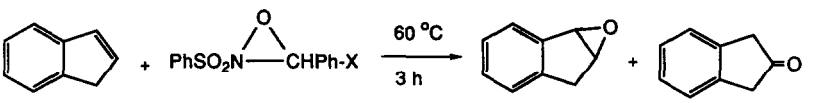
Table 11: Epoxidation of Alkenes at 60 °C Using 2-(Phenylsulfonyl)-3-(p-Nitrophenyl)oxaziridine (**57**) in $CHCl_3$.[66]

Epoxide	Reaction Time (hr)	(% Yield)
	3	(NR)
	72	(42)
	3	(81)
	3	(95)
	3	(74)
	3	(47)
	12	(95)
	3	(72)
	12	(80)
	18	(87)[a]

a) Reference 79.

sulfides, amines, selenides, etc., can therefore be oxidized in the presence of C–C double bonds. Alkynes are not oxidized by **57**.

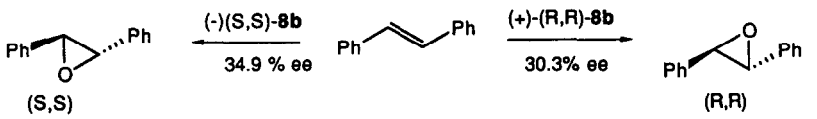
Acid sensitive epoxides are prepared, without special precautions such as buffering, with N-sulfonyloxaziridines **4** because they are aprotic and neutral oxidizing reagents.[66] In this regard, it is important to use the more thermally stable 2-(phenylsulfonyl)-3-(*p*-nitrophenyl)-oxaziridine (**57**) because N-sulfonyloxaziridines on heating give, among other products, benzenesulfonic acid ($PhSO_3H$).[81] Epoxidation of indene, for example, with **56** (60°C for 3 h) gave indene oxide (**87**) and 2-indanone (**88**).[66] 2-Indanone (**88**) is the acid catalyzed rearrangement product of **87** and was not detected when the epoxidation was carried out using **57**.



56	40%	10%
57	63%	0

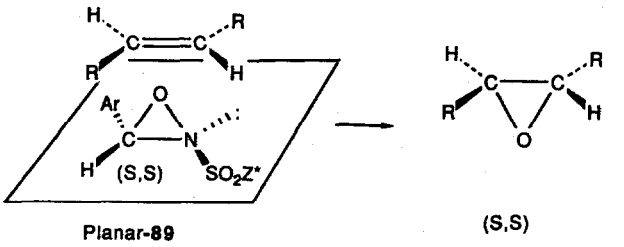
Yauan and Bruice recently described the application of **57** as an oxene transfer reagent to manganes(III) tetraphenylporphyrin chloride in the catalytic epoxidation of alkenes.[82] Yields of epoxides ranged from 5 to 40% after 3 h at 25°C. *cis*-Stilbene gave both *cis* and *trans* stilbene oxides suggesting radical intermediates.

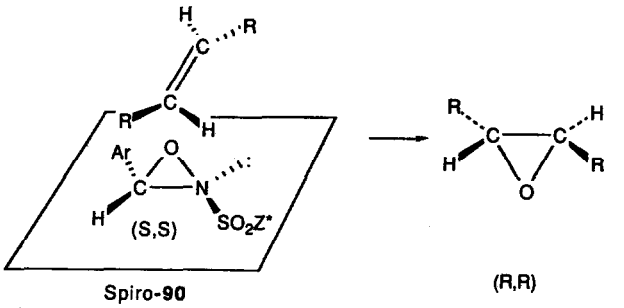
3.2.4.2. *Asymmetric epoxidation of alkenes.* Non-functionalized alkenes are epoxidized asymmetrically at 60°C by bromocamphor oxaziridines (+)(R,R)-**8b**/(−)(S,S)-**8b** in 12–35% *ee* and good chemical yield (80–90%).[83] The highest enantioselectivities were reported for *trans*-stilbene (34% *ee*). As observed for the asymmetric oxidation of sulfides to sulfoxides, the stereochemistry of the product is controlled by the configuration of the oxaziridine three-membered ring.



The highest stereoselectivities reported to date for the asymmetric oxidation of non-functionalized alkenes (13–65% *ee*) are observed with the pentafluorophenyl 2-sulfamyloxaziridines (+)-**63** and (−)-**63** (Table 12).[84] In contrast to asymmetric epoxidations using (+)-**8b** and (−)-**8b** a modest solvent effect was observed with polar solvents resulting in lower enantioselectivities.

For asymmetric epoxidations using homochiral **8** and **63**, the stereochemistry is predicted assuming planar transition state **89**, which minimizes non-bonded steric interactions. Note that if the transition state were spiro **90**, the (S,S)-oxaziridine would afford the (R,R)-epoxide. Molecular orbital calculations (STO-3G/4-31G) carried out by Bach and Wolber are consistent with such transition states suggesting a slight preference for the planar geometry **89**.[85]





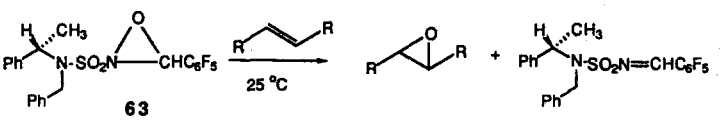
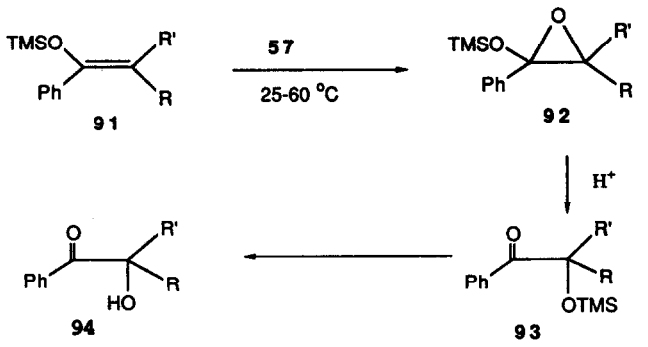


Table 12: Asymmetric Epoxidation of Alkenes by 2-Sulfamyl-3-(pentafluorophenyl)oxaziridines (R,R)-**63**/(S,S)-**63**.[84]

Oxaziridine	Solvent/Temp (°C)	PhCH=CH$_2$	Epoxide % ee (configuration)[a] E-PhCH=CHMe	E-PhCH=CHPh	1-Methyl cyclohexene
(+)(R,R)-**63**	$CHCl_3$ (60)	b	52.5 (R,R)	42.0 (R,R)	
	$CHCl_3$ (25)	44.6 (R)	53.0 (R,R)	49.2 (R,R)	19.4 (1R,2S)
	PhH (25)	c	52.0 (R,R)	c	c
	MeCN (25)	34.2 (R)	32.3 (R,R)	21.0 (R,R)	
(-)(S,S)-**63**	$CHCl_3$ (25)	61.1 (S)	61.0 (S,S)	56.2 (S,S)	14.1 (1S,2R)
	PhH (25)	c	64.7 (S,S)	c	c
	MeCN (25)	27.3 (S)	27.5 (S,S)	28.5 (S,S)	8.1 (1S,2R)

a) % Ee determined using a Daicel Chiral Pak OT (+) HPLC column.
b) Decomposition.
c) No reaction at 25 °C.

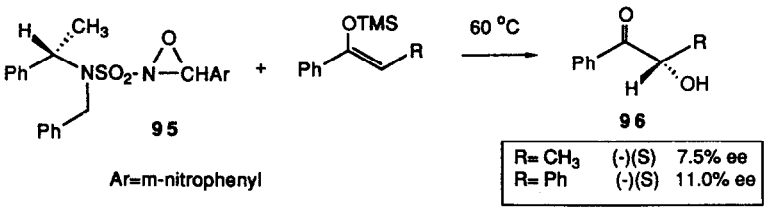
3.2.4.3. *Epoxidation of silyl enol ethers.* Oxidation of silyl enol ethers **91** using **57**, followed by acid hydrolysis, gives good to excellent isolated yields (55–95%) of the corresponding α-hydroxy carbonyl compounds **94** (Scheme 12).[79] Oxaziridine **57** is therefore an alternative to peracids commonly used to effect this rearrangement, known as the Rubottom reaction (Scheme 13). The neutral and aprotic nature of N-sulfonyloxaziridines made possible the isolation of α-siloxy epoxide **92** (R′ = R = Me) in greater than 90% yield. A trace of *p*-toluenesulfonic acid causes the immediate and quantitative rearrangement of **92** to **93** (Scheme 13).



a) R=R'=H b) R=H, R'=Me c) R=R'=Me d) R=H, R'=Ph

Scheme 13.

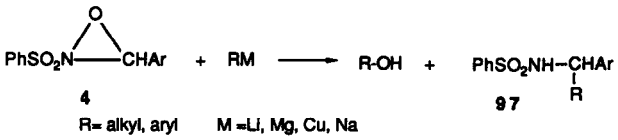
3.2.4.4. *Asymmetric epoxidation of silyl enol ethers.* Asymmetric oxidation of silyl enol ethers at 60°C with enantiomerically pure N-sulfamyloxaziridine (+)(R,R)-**95** gave, after hydrolysis, optically active α-hydroxy carbonyl compounds (−)(S)-**96**.[79] The relatively low stereoselectivities are understandable considering that the steric discrimination between the *re* and *si* faces of the silyl enol ethers is poor.



3.2.5. *Oxidation of organometallic reagents.*

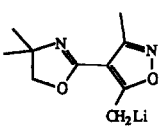
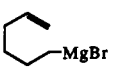
3.2.5.1. *Hydroxylation of lithium and Grignard reagents.* Lithium and Grignard (RM) reagents are hydroxylated by N-sulfonyloxaziridines **4** to alcohols and phenols in good yield eqn (15) (Table 13).[86,87] The product of the addition of RM to the sulfonimine **97** is also obtained. This by-product can be minimized, in the case of alkyl Grignards, by inverse addition (i.e., addition of RM to the oxaziridine).[87] Note that oxidation of phenyl magnesium iodide gives iodobenzene in 84% yield (Table 13, entry 9). Apparently the rate of oxidation of I^- to I_2 is faster than hydroxylation of RM by **4**.

The oxidation of carbanions by N-sulfonyloxaziridines **4** is suggested to involve a stepwise S_N2 mechanism with formation of hemiaminal intermediate **98** which collapses to ROH and the sulfonimine (Scheme 14). This mechanism is supported by the fact that oxidation of 5-hexenyl magnesium bromide, a frequently used probe for radical intermediates, gave the unrearranged alcohol in good yield (Table 13, entry 17).[86] Furthermore, hemiaminal **98** (R = Et) was observed by NMR.[87] Aryl organometallic reagents gave higher yields of **97** than did alkyl Grignard reagents reflecting a longer life-time for **98** when R is alkyl (Table 13). This is probably related to the nucleophilicity of the leaving group (i.e.; RO^- vs ArO^-).

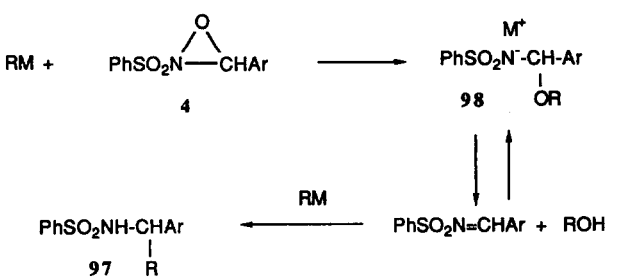


(15)

Table 13: Oxidation of Organometallic Reagents (RM) by N-Sulfonyloxaziridines 4 at -78 °C in THF.[86,87]

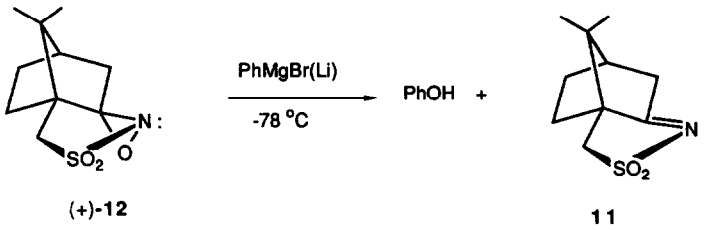
entry	RM[a]	Oxaziridine (4) Ar	% Yield of Products ROH	PhSO2NHCH(R)Ar (97)
1	PhMgBr	p-Tolyl	84	51
2			90[b]	53
3	PhLi	p-Tolyl	55	38
4			62[b]	40
5	p-MeOPhMgBr	p-Tolyl	29	24
6	Ph_2CuLi	p-Tolyl	28	7
7	PhMgBr	2-Cl-5-NO_2-Ph	49[b]	70
8	PhNa	Ph	56	78
9	PhMgI	Ph	0	PhI (84%)
10	o-MeOPhLi		70	78
11	$CH_3(CH_2)_6CH_2MgBr$	Ph	77	32
12			81[b]	2
13	$CH_3(CH_2)_5CH(MgCl)CH_3$	Ph	86[b,c]	trace
14	$C_6H_{11}MgCl$	Ph	95	15
15			72[b]	8
16		Ph	57[d]	
				
17		Ph	65-73	7

a) Ratio of RM to 4 1.5:1.
b) Addition of RM to oxaziridine.
c) Ratio of RM to 4, 3:1.
d) Data from ref. 80.



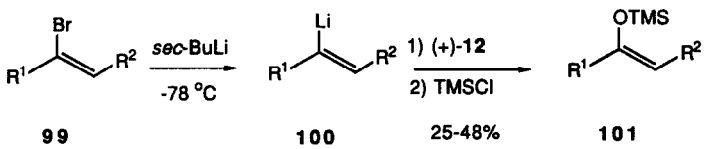
Scheme 14.

Oxidation of phenyl magnesium bromide and phenyllithium with (camphorylsulfonyl)oxaziridine (+)-**12** in both cases gave phenol; the yields were 96% and 41%, respectively. Products of the addition of PhMgBr and PhLi to **11** were not detected.[87]



(+)-12 11

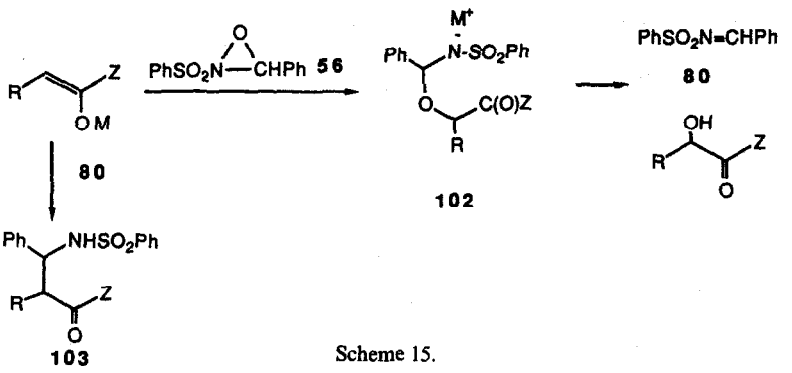
Methodology for the stereo- and regioselective formation of enolates has recently been developed by Davis *et al.*[88] This procedure involves the stereoselective oxidation of *E*- and *Z*-vinyl lithium reagents **99**, generated from the corresponding *E*- and *Z*-vinyl bromides **100** with *sec*-butyllithium. Oxidation of **100** with (+)-**12**, followed by trapping of the enolate with trimethylsilyl chloride (TMSCl), gave the silyl enol ether **101** in moderate yield (25–48%). The oxidation was not entirely stereospecific resulting in 15–20% loss of configuration. Nearly complete retention of configuration and good to excellent yields of **101** are obtained on oxidation of **100** with bis(trimethylsilyl)peroxide ($Me_3SiOOSiMe_3$).[88]



99 100 25-48% 101

R^1=Ph, n-C_5H_{11}, R^2=Me, n-C_5H_{11}

3.2.5.2. *Oxidation of enolates to α-hydroxy carbonyl compounds.* α-Hydroxy carbonyl compounds are valuable intermediates in organic synthesis and are key structural units of many biologically active natural products. This moiety can be prepared in good to excellent yield by oxidation of enolates with N-sulfonyloxaziridine **56** (Table 14).[89] Oxidation is fast (< 15 min) at −78°C, however lithium enolates of esters and ketones generally give lower yields than the potassium or sodium enolates. This result may be related to the counterion dependency of hemiaminal intermediate **102**, thought to be involved in these oxidations (Scheme 15).[89–92] For reasons which are unclear, the lithium hemiaminal **102** (M = Li) is apparently less stable than the sodium or potassium derivatives (i.e., the imino-aldol addition products **103** are isolated in the former case).[89,92] The choice of counterion is evidently less important for oxidation of amide enolates with **56** because similar yields were obtained for the lithium, sodium and potassium amide enolates.[90] Use of (+)-(camphorylsulfonyl)oxaziridine (**12**) for enolate oxidations avoids the imino-aldol type addition products **103** entirely (see Section 3.2.5.5.). Over-oxidation to α-dicarbonyl compounds, an occasional problem with Vedejs' MoOPH reagent,[93] is not observed when **56** is used as the oxidant.



Scheme 15.

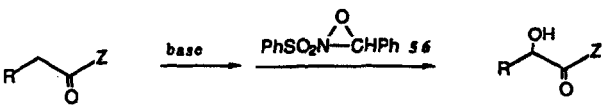
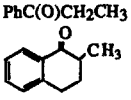
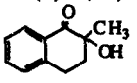
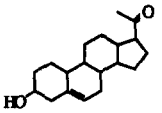
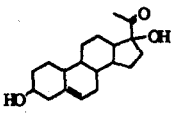
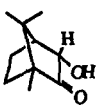
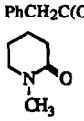
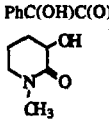


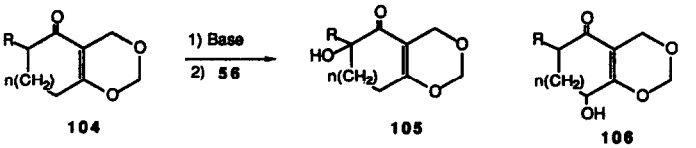
Table 14: Oxidation of Enolates to α-Hydroxy Carbonyl Compounds Using 2-(phenylsulfonyl)-3-phenyloxaziridine (56) in THF at -78 °C.[89]

Ketone/Ester/Amide	Base	α-Hydroxy Carbonyl Compound	(% Yield)[a]
$PhC(O)CH_2Ph$	LDA	$PhC(O)CH(OH)Ph$	(32)[b]
	KHMDS		(75)
$PhC(O)CH_2CH_3$	NHMDS	$PhC(O)CH(OH)CH_3$	(70)
	NHMDS		(57)[c]
	t-BuOK		(53)
	KHMDS		(78)
	LHMDS		(23)
	KHMDS		(85)
$PhCH_2CO_2Et$	LHMDS	$PhCH(OH)CO_2Et$	(40)
	KHMDS		(83)
$PhCHCO_2Me$ (Me)	KHMDS	$PhC(OH)CO_2Me$ (Me)	(68)
	LDA		(51)
$PhCH_2C(O)NC_4H_8$	LDA	$PhCHC(O)NC_4H_8$ (OH)	(74)[d]
	NHMDS		(83)
$PhCH_2C(O)NC_4H_8$ (Me)	NHMDS	$PhC(OH)C(O)NC_4H_8$ (Me)	(74)[d]
	LDA		trace[d]

a) Isolated yields unless otherwise noted.
b) GLC yields.
c) Reference 90.
d) Reference 91.

Smith *et al.* recently reported a study of the oxidation of enolates derived from 1,3-dioxin vinylogous esters **104** using oxaziridine **56**.[94] The regioselectivity was dependent on both the counterion and the ester substitution pattern (Table 15). For example, the lithium enolate of **104** (R = H) gives principally the α-hydroxylated product **105**, while the sodium enolate gave mixtures of both **105** and **106**. When R in **104** ($n = 0$) was CH_3, high stereoselectivity for the formation of **106** was observed for the sodium enolate.

Table 15: Oxidation of Vinylogous Esters **104** using 2-(phenylsulfonyl)-3-phenyloxaziridine (**56**) at -78 °C.[94]

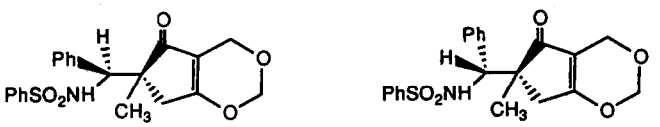


104 **105** **106**

n	R	Base	Solvent	% Isolated Yields of 105/106
0	H	LDA	DME	33/6[a]
0	H	NHMDS	THF	35/36[a]
0	Me	LDA	THF	51/0
0	Me	NHMDS	THF	4/76
1	H	LDA	DME	58/0
1	H	NHMDS	THF	49/37
2	H	LDA	DME	54/0
2	H	NHMDS	THF	51/37

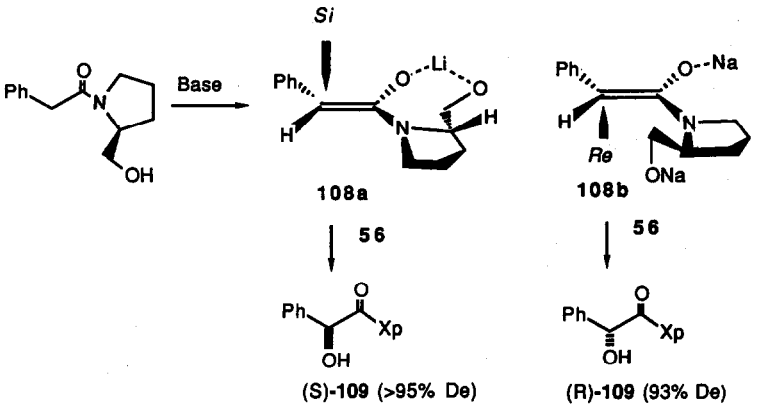
a) Based on recovered starting material.

Oxidation of the lithium enolates of **104** ($n = 0, 1, 2$) with **56** gave, in addition to the hydroxylated products **105**, 18–26% yields of the imino-aldol products **107** as diastereomeric mixtures (*ca* 1 : 1).[94] These products were not detected with the sodium enolates (see also Scheme 15).



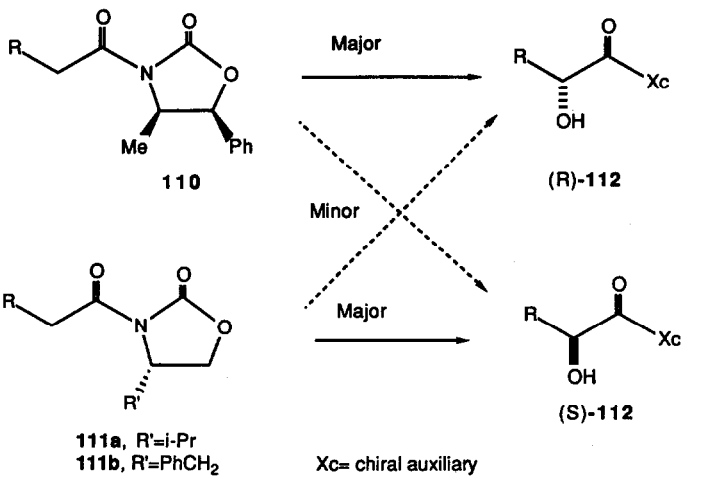
107a **107b**

3.2.5.3. *Oxidation of chiral enolates to α-hydroxy carbonyl compounds.* Oxidation of chiral enolates with N-sulfonyloxaziridines **4** affords diastereomeric α-hydroxy carbonyl compounds. Davis and Vishwakarma reported the hydroxylation of (+)-(S)-2-pyrrolidinemethanol derived chiral enolate **108** with N-sulfonyloxaziridine **56** (Scheme 16).[95] High yields (93–96%) and excellent diastereoselectivities (93–95% *de*) for the α-hydroxy amides were observed. The pyrrolidinemethanol auxiliary was removed by heating with 2 M H_2SO_4 to give optically active mandelic acid **109** without racemization. The stereoselectivity proved to be counterion dependent with the lithium enolate affording (S)-**109** (>95% *de*), while the sodium enolate gave (R)-**109** (93% *de*).[95] The diastereofacial selectivity has been interpreted in terms of a mechanism involving attack of the oxaziridine at the least hindered face of the enolate. This would be the *Si*-face of the intramolecularly chelated lithium enolate **108a** and the *Re*-face of the intermolecular chelated sodium enolate **108b**. It was suggested that intramolecular chelation is inhibited by the larger and more poorly coordinating sodium ion.



Scheme 16.

A more detailed study of the synthesis of optically active α-hydroxy acids using **56** has been reported by Evans *et al.* using optically active carboximides as chiral auxiliaries (Scheme 17).[92] As can be seen from the results summarized in Table 16, oxidation of the sodium enolates of **110** and **111** gives high yields of optically active α-hydroxy amide compounds **112** with good to excellent diastereoselectivity. The chiral auxiliary is removed without concurrent racemization by transesterification with magnesium methoxide in methanol.[92]



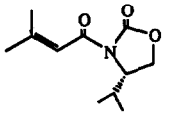
Scheme 17.

α-Benzyloxy aldehydes and α-acetoxy ketones **115**, of high optical purity, are prepared in good overall yield by oxidation of the azaenolates of chiral hydrazone **113** with 2-(phenylsulfonyl)-3-phenyloxaziridine **56**.[96] The chiral auxiliary was removed from the α-hydroxy hydrazone **114** by ozonolysis at −78°C (Table 17).

3.2.5.4. *Diastereoselective oxidation of chiral enolates to optically active α-hydroxy carbonyl compounds.* The α-hydroxylation of enolates using oxaziridine **56** has been employed in the synthesis of a number of natural products.[97–99] The stereochemistry of the α-hydroxy compound, in these examples, can be predicted by assuming that the bulky oxaziridine oxidizing reagent **56** approaches the enolate from the sterically least hindered direction.

In studies directed toward the asymmetric synthesis of the AB ring of alkavinone (+)-**118**. Meyers and Higashiyama reported the isolation of a single diastereomer **117**, in 54% yield on

Table 16: Diastereoselective Hydroxylation of Chiral Carboximide Sodium Enolates Using 2-(Phenylsulfonyl)-3-phenyloxaziridine (56) in THF at -78 °C.[92]

Imide (110/111)		% Yield	% De (Config.)
110	(R=$PhCH_2$)	86	88 (R)
111a	(R=$PhCH_2$)	85	90 (S)
111b	(R=$PhCH_2$)	83	90 (S)
110	(R=Ph)	77	80 (R)
110	(R=Et)	86	88 (R)
110	(R=$CH_2CH=CH_2$)	91	90 (R)
110	(R=CMe_3)	94	98 (R)
111a	(R=$CHMe_2$)	86	98 (S)
110	(R=$MeO_2CCH_2CH_2CH_2$)	68	92 (R)
		75	92 (S)

a) Isolated yields of diastereomerically pure material.

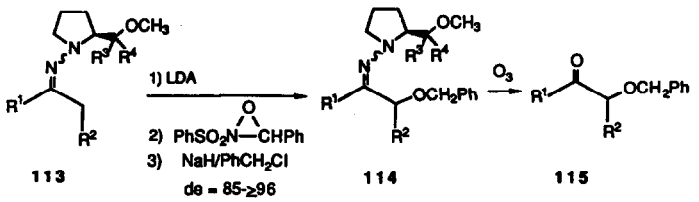
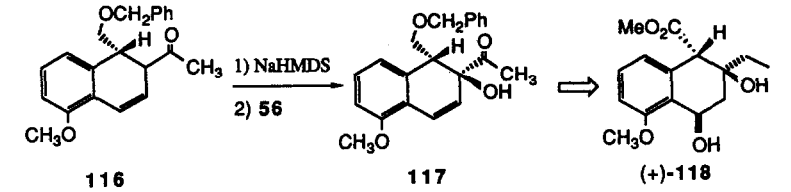


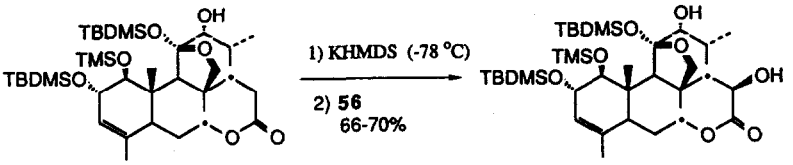
Table 17: Diastereoselective Hydroxylation of Chiral Lithium Azaenolates Using 2-(Phenylsulfonyl)-3-phenyloxaziridine (56) in THF at -86 - 50 °C.[96]

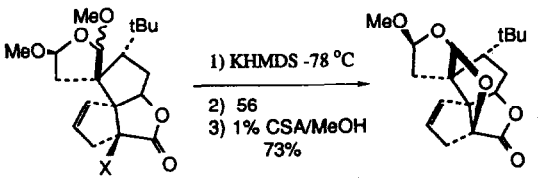
Hydrazone (113)					α-Hydroxy Ketone (115)	
R^1	R^2	R^3	R^4	Base	% Overall	% ee[a] (Config.)
-						
Ph	Me	H	C(O)Me	LDA	51	93 (R)
Ph	Me	Me	C(O)Me	t-BuLi	51	85 (R)
Ph	Me	Me	C(O)Me	LDA	71	88 (R)
Ph	Ph	H	C(O)Me	LDA	74	96(S)[b]
$PhCH_2$	Ph	H	C(O)Me	t-BuLi	48	36 (R)
$PhCH_2$	Ph	Ph	C(O)Me	LDA	62	89 (R)
H	$n\text{-}C_6H_{13}$	H	$PhCH_2$	LDA	63	56 (R)
H	$n\text{-}C_6H_{13}$	Me	$PhCH_2$	LDA	44	96 (S)
H	$n\text{-}C_4H_9$	C_2H_5	$PhCH_2$	LDA	53	96 (S)

a) Determined using the shift reagent Eu(hfc).
b) RAMP used as the chiral auxiliary.

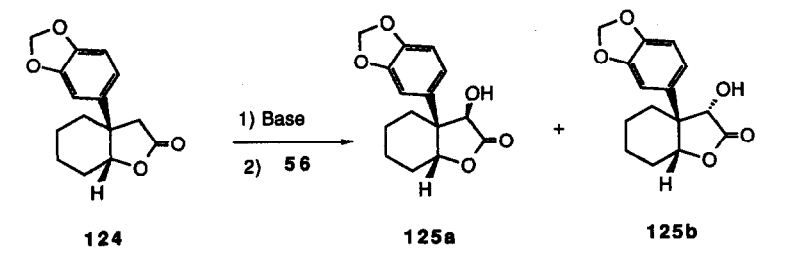
oxidation of the sodium enolate of **116**.[97] The conversion of readily available chaparrin (**119**) into the biologically active α-hydroxy lactones of glaucarubone (**120**) requires introduction of the lactone hydroxy group. Only one isomeric hydroxy lactone **120** was obtained on oxidation of the potassium enolate of **119** with **56**.[98] Oxidation of the enolate with MoOPH results in lower yields (40–45%). A step in the total synthesis of (±)-ginkgolide B, reported by Corey *et al.*, involves generation of the C(4)–C(12) oxygen bridge by deprotonation of bis-acetal **121** with LDA, followed by oxidation with **56**.[99] Treatment of **122** with camphorsulfonic acid afforded **123** in 75% overall yield from **121**.



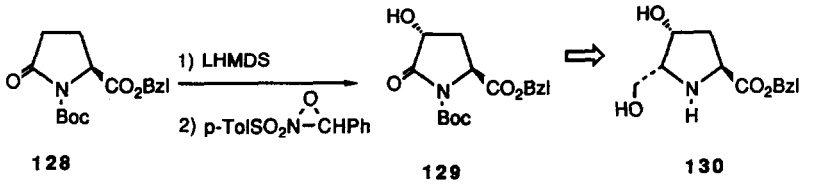




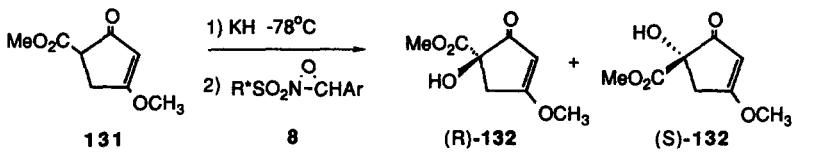
Oxidation of the potassium enolate of lactone **124** with oxaziridine **56** gave only α-hydroxy lactone **125a** in 90% yield. Both **125a** and **125b** (3 : 1) were obtained in low yield on oxidation of the enolate with MoOPH.[89] A 95 : 5 diastereomeric mixture of α-hydroxy esters **127a,b** was produced on oxidation of the potassium enolate of ethyl 3-methyl-4,4,4-trifluorobutyrate **126** with **56**.[100] Similar results were observed with MoOPH.



The lithium enolate of N-*t*-butoxycarbonyl-L-pyroglutamate (**128**) is oxidized with high regio- and diastereoselectivity by 2-(*p*-toluenesulfonyl)-3-phenyloxaziridine to give (+)-4-hydroxypyroglutamate (**129**) in 61% yield.[101] This α-hydroxy amide is an intermediate in the synthesis of (−)-bulgecinine (**130**), a unique glycopeptide isolated from *Pseudomonas acidophila* and *P. mesoacidophila*.



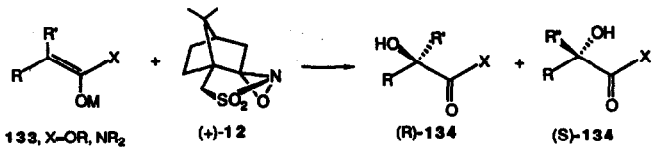
3.2.5.5. *Asymmetric oxidation of enolates to optically active α-hydroxy carbonyl compounds.* The asymmetric oxidation of prochiral enolates to an optically active α-hydroxy carbonyl compound using a homochiral N-sulfonyloxaziridine was first used in the synthesis of the antibiotic (+)(R)-kjellmanianone (**132**) by Smith and Davis.[102] Oxidation of the potassium enolate of **131** by (−)(S,S)-**8a** (Ar = 2-chloro-5-nitrophenyl) gave (+)(R)-**132** in 33% *ee* and 44% yield. The fact that oxaziridines (R,R)-**8a**/(S,S)-**8a** gave higher *ees* (33–37% *ee*) than did (R,R)-**8b**/(S,S)-**8b** (8–12% *ee*) suggests that the camphor carbonyl group plays some role in establishing the transition state for hydroxyl delivery. As noted in other asymmetric oxidations using homochiral N-sulfonyloxaziridines, the configuration of the oxaziridine three-membered ring controls the stereoselectivity.



Oxaziridine	% ee (config.)
(R,R)-**8a**	36.5 (S)
(R,R)-**8b**	12.0 (S)
(S,S)-**8a**	33.0 (R)
(S,S)-**8b**	8.0 (R)

More detailed studies of the oxidation of prochiral enolates to optically active α-hydroxy carbonyl compounds have been carried out using the readily available (camphorylsulfonyl)oxaziridines (+)-**12** and (−)-**12** (Tables 16 and 17).[18,103] Both optical isomers of **134** are readily available because the configuration of the oxaziridine three-membered ring controls the stereochemistry of the product. Oxidation of the lithium enolates of esters and amides **133** with optically active **12** gave the corresponding α-hydroxy carbonyl compounds **134** in up to 85.5% *ee* (Table 18). The sodium and potassium enolates of **133** generally gave lower stereoselectivities.

In contrast to the oxidation of prochiral esters and amides the sodium enolates of ketones gave the highest stereoselectivities with (+)-**12** and (−)-**12** (Table 19).[103] The highest stereoselectivities



133, X=OR, NR_2 (+)-12 (R)-134 (S)-134

Table 18: Asymmetric Oxidation of Lithium Enolates of Esters and Amides using (+)-(Camphorylsulfonyl)oxaziridine (12).[18]

entry	Enolate 133 R	R'	X	Cosolvent	Temp. (°C)	Product 134 %Yield	%ee (Config.)
1	Ph	H	$OCMe_3$	------	-90	82	71.0 (R)
2	$PhCH_2$	H	OMe	------	-90	73	58.0 (R)
				HMPA	-90	63	85.5 (R)
3	Ph	Me	OMe	------	-78	61	45.0 (R)[b]
4	Ph	H	NC_4H_8	------	-78	70	30.0 (S)
				HMPA	-78	74	50.0 (R)
5	Ph	Me	NC_4H_8	------	-78	40	35.0 (S)[b]
				HMPA	-78	35	20.0 (R)

a) Isolated yields.
b) Reference 104.

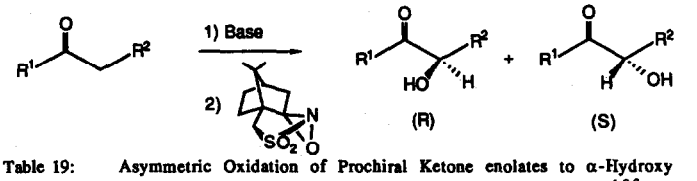
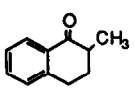
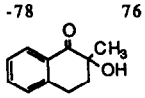
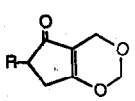
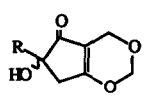
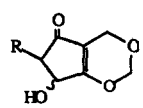
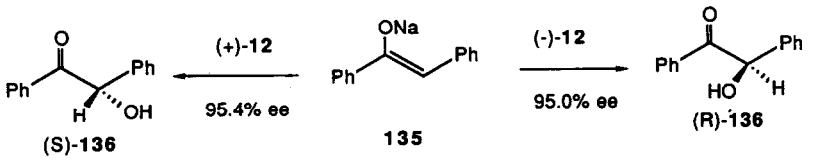


Table 19: Asymmetric Oxidation of Prochiral Ketone enolates to α-Hydroxy Ketones using (+)-(Camphorylsulfonyl)oxaziridine (12).[103]

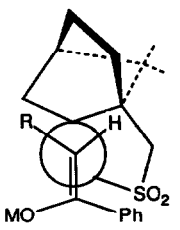
entry	Ketone	Base/Cosolvent	Temp. (°C)	α-Hydroxy Ketone % Yield	% ee (Config).
1	$PhC(O)CH_2Ph$	LDA	0	70	68.0 (S)
2		LDA/HMPA	0	64	6.0 (S)
3		NHMDS	-78	84	95.4 (S)
4	$PhC(O)CH_2Me$	LDA	0	51	43.2 (S)
5		NHMDS	-78	77	68.5 (S)
6	$Me_3C(O)CH_2Me$[a]	LDA	0	55	33 (R)
7		NHMDS	-78	71	90 (R)
8	$PhCH_2C(O)Me$[a]	NHMDS	-78	70	41 (S)
9		NHMDS/HMPA	-78	76	76 (R)
					
10		LDA	0	75	12.3 (R)
11		NHMDS	0	80	16.0 (R)
					
12	R=H[b]	LDA	-45	45	4 c
13	R=Me	LDA	-45	68	4 c
14	R-Me	NHMDS	-45	3	28 c

a) Reference 103b
b) Reference 94.
c) The enantioselectivities are reported to be 10-16% ee.

were observed for oxidation of the sodium enolate of deoxybenzoin, **135**, which gave benzoin (**136**) in >95% optical purity. Compared to acyclic enolates much lower stereoselectivities (12–16% *ee*) were observed for the asymmetric oxidation of cyclic ketone enolates (Table 19, compare entries 1–9 with 10–14). The enantiofacial discrimination between the *re* and *si* faces of the cyclic enolates is likely to be poorer than for the acyclic enolates.



The stereochemistry of α-hydroxy ketones **136** (R = Ph, Me) can be predicted assuming an 'open' planar transition state **137** and that the *Z*-enolates approach the oxaziridine active site oxygen from the least hindered direction.[103]



3.2.5.6. *Asymmetric oxidation of chiral enolates to optically active α-hydroxy carbonyl compounds.* The asymmetric oxidation of tetrasubstituted enolates using homochiral N-sulfonyloxaziridines (+)-**12** and (−)-**12** is poor (Table 18, entries 3 and 5; Table 17, entries 10–14). This would be expected, not only because of the difficulty in forming a specific enolate regioisomer, but also because of the poor enantiofacial discrimination between the *si* and *re* faces of the enolates. The asymmetric oxidation of the chiral amide enolate of **138** with (+)-**12** and (−)-**12**, double asymmetric synthesis, gave acyclic tertiary α-hydroxy amide **139** in high optical purity (Table 20).[104] For the matched

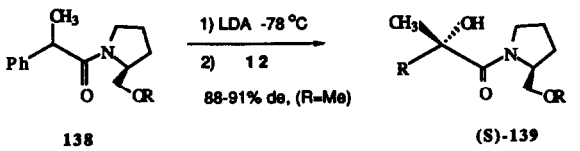


Table 20: Asymmetric oxidation of the Lithium Enolates of 2-Phenylpropanoic amides at -78 °C in THF.[104]

entry	Oxaziridine	138 R	Cosolvent	Product 139 % Yield[a]	% De (Config.)
1	(+)-12	H	---------	25	46.0 (S)
2		H	HMPA	24	50.0 (S)
3	(-)-12	H	---------	30	30.0 (S)
4	(+)-12	Me	---------	60	48.4 (S)
5		Me	HMPA	53	88.7 (S)
6		Me	HMPA[b]	65	89.5 (S)
7	(-)-12	Me	---------	55	88.3 (S)
8		Me	HMPA	55	90.7 (S)
9		Me	HMPA[b]	50	86.2 (S)

a) Isolated yields. b) HMPA added after enolate formation.

pair, **138** (R = Me) and (−)-**12**, the diastereoselectivity was 88–91% *de* (Table 20, entries 7–9). For the mismatched pair, **138** (R = Me) and (+)-**12**, the diastereoselectivity was improved from 48.4 to 89.0% *de* on addition of HMPA (Table 20, entries 4–6). Importantly the pyrrolidine methanol chiral auxiliary could be removed without racemization by basic hydrolysis affording optically active atrolactic acid in 70–89% yield.[104]

4. SUMMARY

Although the N—H, N-alkyl and N-aryl oxaziridines **1** have been known for more than three decades and a number of useful reactions identified, their application in synthesis is much less established than the N-sulfonyloxaziridines **4**. It is hoped that this review will stimulate renewed interest in the development of existing and new applications for oxaziridines in organic synthesis.

Acknowledgements—It is a pleasure to acknowledge the important efforts of my co-workers whose names appear in the references. Our own contributions to this review were supported by the National Science Foundation, the National Institutes of Health, the Petroleum Research Fund administered by the American Chemical Society and Merck Sharp and Dohme. We are grateful to Professors Amos B. Smith III and Walter W. Zajac for helpful discussions. We also thank Professors Jeffrey Aube, Brian B. Jennings, Amos B. Smith III and Walter W. Zajac for manuscripts of their work prior to publication.

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NOTE ADDED IN PROOF

Since submitting this review several papers have appeared which are particularly relevant to the subject.

Mlochowski and co-workers prepared a number of oxaziridinylquinones and oxaziridinylazines as potential antitumor agents by basic *m*-CPBA oxidation of the corresponding imines.[105] The oxidation of sulfides to sulfoxides by a 3,4-dihydroisoquinoline derived oxaziridine in the presence of trifluoroacetic acid has been described by Hanquet, Lusinchi and Milliet.[106] These same workers reported the epoxidation of alkenes using tetrafluoroborate oxaziridinium salts.[107] The asymmetric oxidation of a series of sulfides to sulfoxides (enantiomeric excesses up to 66%) using (+)-(3-oxocamphorsulfonyl)oxaziridine has been described by Glahsl and Herrmann.[108] A simple method for the N-amination of peptide derivatives forming α-hydrazino carboxylic acids utilizes oxaziridine **14**.[109] The photochemical oxaziridine to amide rearrangement has been used by Aube in the synthesis of (−)-alloyohimbane, an alkaloid of the yohimbine and reserpine families.[110] A 4,4′-dilithium-2,2′-bipyridine was dihydroxylated in 20% yield using N-sulfonyloxaziridine **56**.[111] A key step in the enantioselective synthesis of 12(*R*)-HETE is the α-hydroxylation of a chiral oxazolidinone enolate by **56**.[112] Enolate oxidation using **56** was employed in the total synthesis of (±)-wikstromol,[113] and in the enantioselective synthesis of the $C_{1,6}$–$C_{21,16}$ segment of the antibiotics macbecins I and II.[114] A comparative study of the α-hydroxylation of a *trans*-3,4-disubstituted γ-lactone by MoOPH and by N-sulfonyloxaziridine **56** has been reported by Taschner and Aminbhavi.[115] Better selectivity was observed with MoOPH (8 : 1; *trans* : *cis*) compared to **56** (1 : 1).

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