Saturated oxygen heterocycles

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Reviewing the literature published between 1 April 1993 and 30 September 1994

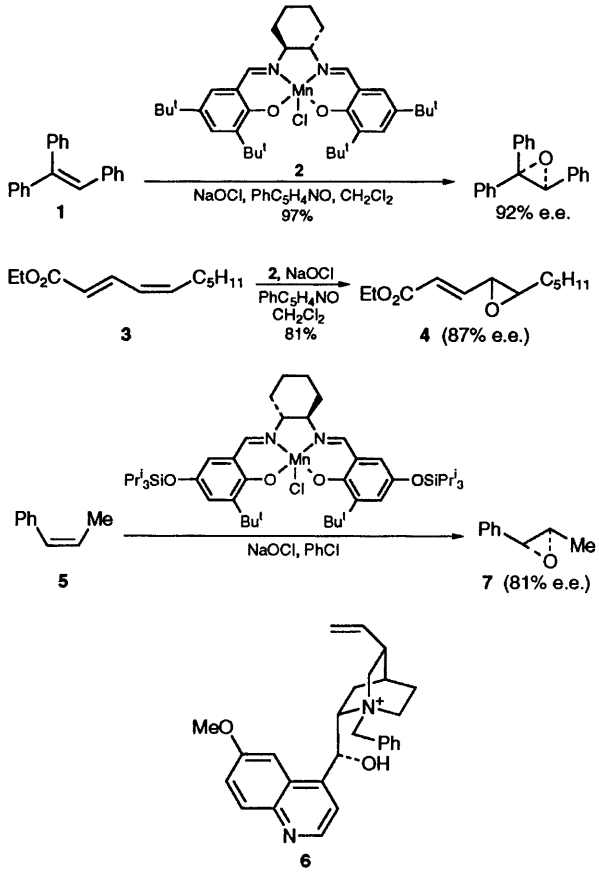
1 Introduction

This review covers the literature on small ring, *i.e.* 3→6 membered, ethers only. The literature on medium-ring ethers has recently been covered elsewhere in the journal (M. Elliott, *Contemporary Organic Synthesis*, 1994, 457), and a separate review of oxygen heterocycles accommodating additional heteroatoms will be published in a future issue of *COS*.

2 Epoxides

Studies of enantioselective epoxidations of unfunctionalized olefins continues to be an extremely active area of research. Jacobsen and his research group have shown that trisubstituted olefins such as **1** can be epoxidized in high yield and with excellent enantioselectivity using commercial bleach, the manganese complex **2**, and catalytic 4-phenylpyridine *N*-oxide.[1] Under essentially identical conditions, the *cis* double bond of conjugated *cis,trans*-dienes (such as **3**) is epoxidized with high regioselectivity, giving the *trans*-epoxide **4** in good yield and enantioselectivity.[2] Interestingly, simple *trans*-epoxides can be obtained in high optical purity from *cis*-olefins by addition of the quinine-derived salt **6** to the epoxidation reaction. For example, epoxidation of *cis*-β-methyl styrene (**5**) under these conditions furnished predominantly the *trans*-epoxide **7**.[3]

Katsuki and co-workers have also examined the use of manganese salen complexes in the epoxidations of alkenes.[4] For example, the manganese complex **9** catalyses the epoxidation of



the chromene derivative **8** with iodosylbenzene, giving the epoxide **10** in good yield and in high optical purity.[5] By analysis of the results obtained for the epoxidation of a range of *cis*-olefins using numerous manganese complexes, Katsuki *et al.* suggest that *cis*-olefins approach the manganese oxo intermediate **11** along the axis depicted in **Figure 1**.[6] The use of *N*-methyl imidazole in conjunction with a manganese complex such as **2** or **9**, allows for the use of hydrogen peroxide[7] or molecular oxygen[8] as oxidants. Dhal and co-workers have reported the use of a related polymer bound manganese salen complex **13** for the epoxidations of alkenes.[9] Use of this catalyst and iodosylbenzene as oxidant generates the epoxide **14** from indene **12** in 51% yield.

There have been a number of publications over the review period concerning the asymmetric synthesis of epoxides by biotransformation; a review containing 64 references has also been published.[10] Hager, Jacobsen, and co-workers have shown that

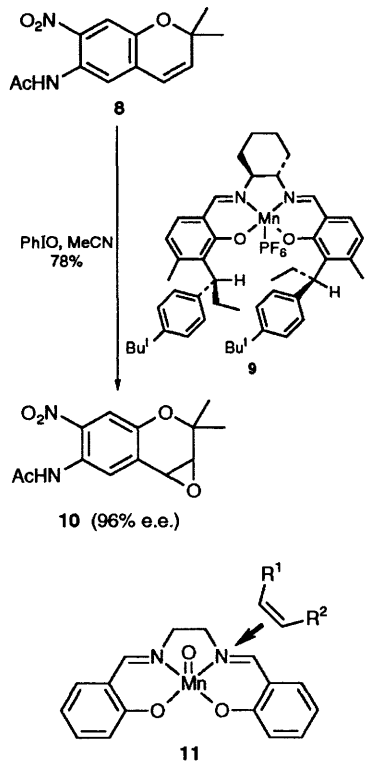
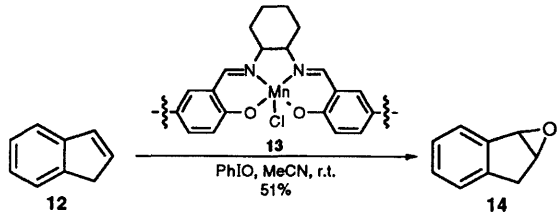
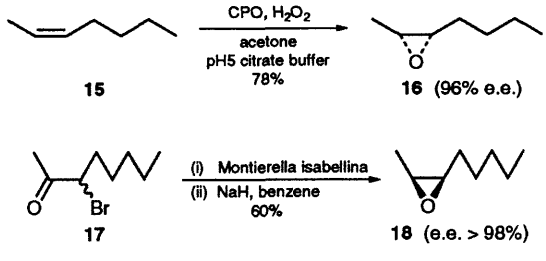


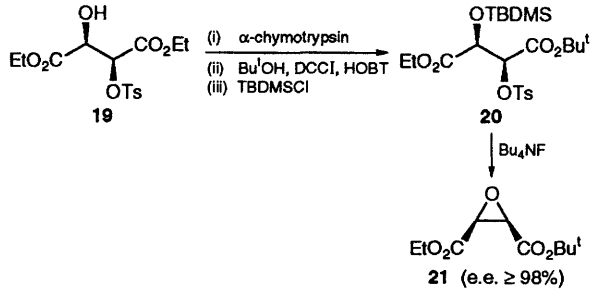
Figure 1

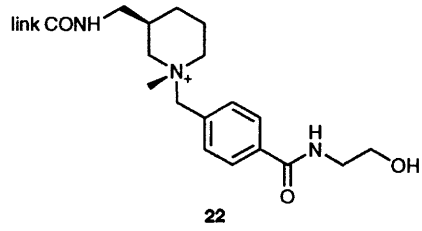


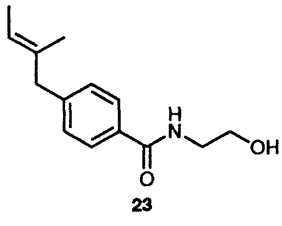
chloroperoxidase (CPO) effectively catalyses the epoxidation of aliphatic *cis*-olefins, as in the formation of the *cis*-epoxide **16** from 2-*cis*-heptene **15**.[11] Veschambre and his research group have examined a range of microbial techniques for the stereospecific reduction of halo ketones, which on treatment with base give optically pure epoxides;[12]



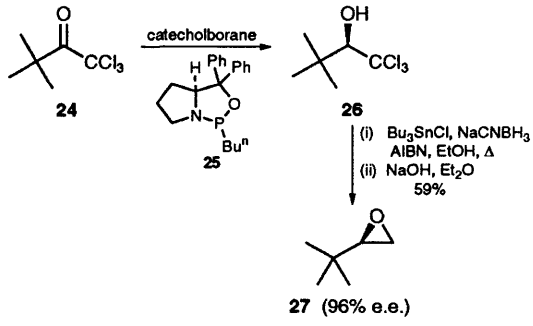
this procedure is illustrated for the synthesis of *cis*-2,3-epoxyoctane **18** from the bromohydrin **17**.[13] The differentially protected epoxy diester **21** has been prepared by Crout and his colleagues also employing an enzymatic approach.[14] Thus, selective hydrolysis of the tartrate derived diester **19** with α-chymotrypsin, followed by some functional group manipulation first afforded the silyl protected chiral diester **20** which on treatment with fluoride anion then generated the enantiomerically pure epoxide **21**. Koch, Reymond, and Lerner have raised catalytic antibodies to the hapten **22**, and have shown that one of these efficiently catalyses the epoxidation of alkenes such as **23** with hydrogen peroxide/acetonitrile as oxidant.[15] The epoxide formed has greater than 98% e.e.

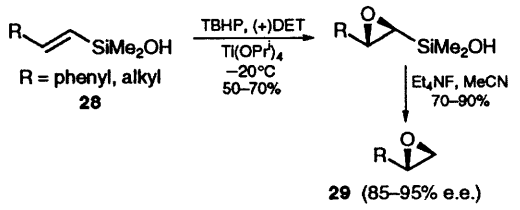




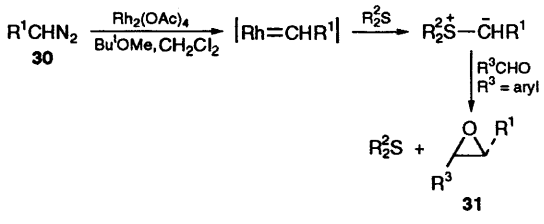


Other new methods for the synthesis of chiral epoxides include the conversion of chiral trichloromethyl carbinols into terminal epoxides.[16] Thus, reduction of the trichloromethyl ketone **24** with catecholborane in the presence of oxazaborolidine **25** first leads to the chiral carbinol **26** which, after bis-dechlorination with *in situ* generated tributyltin hydride, is subjected to base-induced ring closure producing the chiral epoxide **27** in high enantioselectivity. Chan *et al.* have demonstrated that alkenylsilanols **28** can be epoxidized enantioselectively using the Sharpless procedure, and after protodesilylation terminal epoxides **29** of high optical purity are obtained.[17]

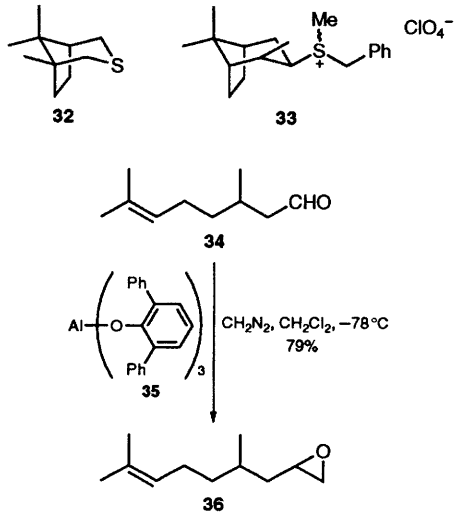




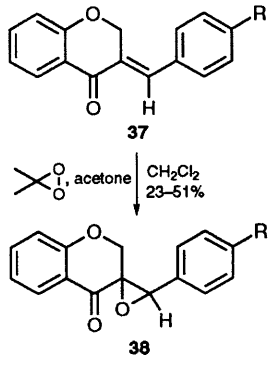
Aggarwal and his co-workers have shown that predominantly *trans*-epoxides can be obtained from the reaction of aldehydes and sulfur ylides generated by decomposition of a diazo compound in the presence of a sulfide;[18] the starting sulfide is regenerated and the process operates as a catalytic cycle. The mechanism shown in **Scheme 1** presumably operates, and use of a chiral sulfide such as **32** leads to moderate asymmetric induction. Aggarwal and his group have also shown that the reaction between aldehydes and chiral sulfur ylides (obtained from the treatment of diastereomeric sulfonium salts such as **33** with strong base) also lead to chiral epoxides, though again the e.e.'s are moderate.[19] Yamamoto and his group have shown that decomposition of diazoalkanes in the presence of an aldehyde by the bulky aluminium catalyst ATPH (**35**) is an efficient route to epoxides, as exemplified by the transformation of **34** into **36**.[20]

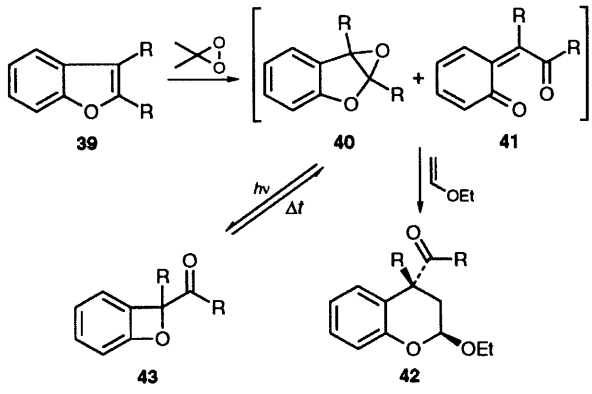


Scheme 1

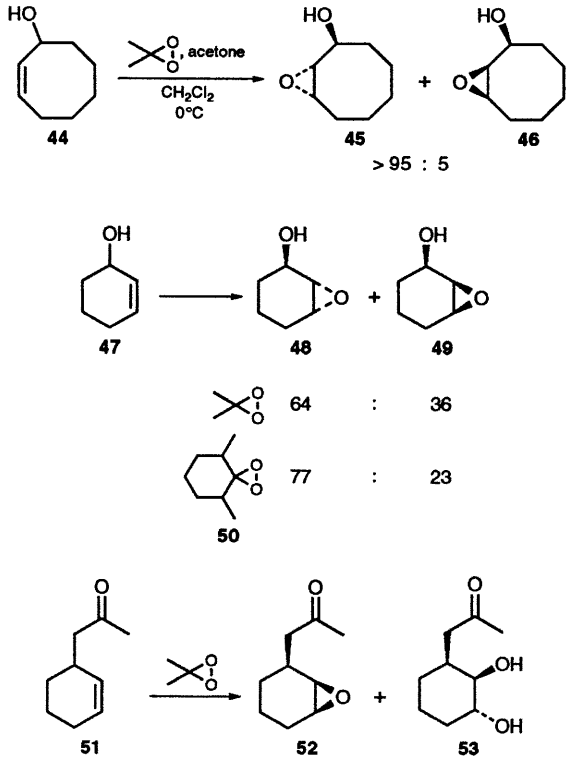


Considerable work continues to be published on novel uses of dioxiranes as epoxidizing reagents. Thus, reaction of the chromanones **37** with dimethyl dioxirane affords the interesting spiro-epoxides **38** in moderate yield,[21] while epoxidation of chalcones proceeds in excellent yield.[22] Very interesting results have been obtained with the epoxidations of benzofuran derivatives **39**, which lead to an equilibrium mixture of the epoxide **40** and quinone methide **41**,[23] which in turn can be transformed into other products, such as the benzopyran **42** by Diels–Alder reaction with ethyl vinyl ether.[24] The unstable benzoxetes **43** can also be obtained from the mixture of **40** and **41** though on warming, or over time, this reverts to the starting mixture of epoxide and quinone methide.[25]

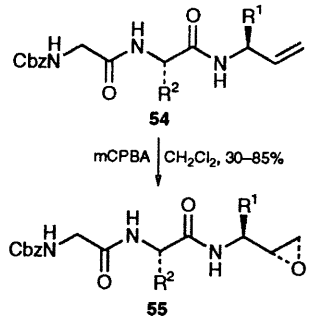




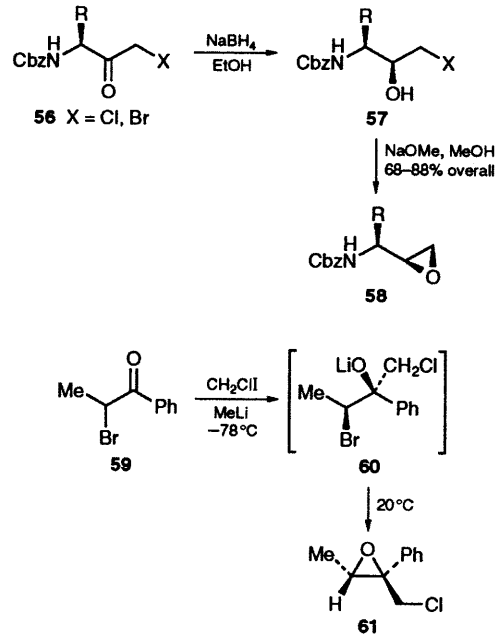
The diastereoselectivity of dioxirane epoxidations has been examined in a number of different substrates. Adam and his research group have demonstrated that epoxidations of certain allylic alcohols with dimethyl dioxirane lead preferentially to the *anti*-product, as in the epoxidation of **44** to give the epoxides **45** and **46**.[26] Substantial quantities of enone, resulting from oxidation of the alcohol moiety, can also be formed particularly if the reaction is performed at higher temperatures. Kurihara *et al.* have improved the diastereoselectivity in the epoxidation of the cyclohexenol **47** by using a more bulky dioxirane than dimethyl dioxirane (such as **50**), or alternatively by protecting the hydroxyl with a silyl ether.[27] Armstrong and co-workers have shown that the dimethyl dioxirane epoxidation of the cyclohexene ketone **51** leads to a 1:1 mixture of the *syn*-epoxide **52** and the diol **53** (presumably arising from facile ring-opening of the *anti*-epoxide), while in contrast mCPBA gives only the *syn*-epoxide **52**.[28] An oxygen labelling experiment indicates that in the latter case the diastereoselectivity arises through ketone-assisted delivery of the peracid, rather than *in situ* dioxirane formation from the ketone moiety.



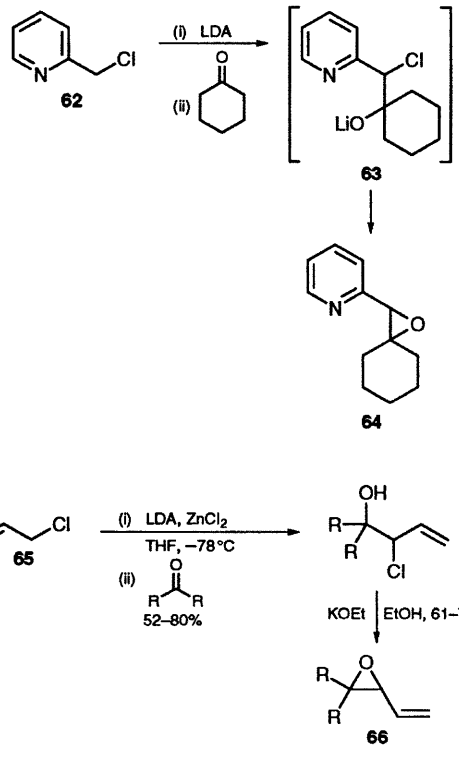
Albeck and Persky have devised an efficient route to peptide allylamines **54**, and have shown that epoxidation with mCPBA leads to predominantly the *threo*-diastereoisomer **55**.[29] Similar results have been obtained by Romeo and Rich who have also shown that the minor *erythro*-diastereomer undergoes preferential decomposition under the acidic epoxidation conditions, thereby enhancing the diastereomeric excess.[30]



The *erythro*-epoxides can be synthesized via an alternative route starting from halo ketones **56**.[31] Thus, reduction with sodium borohydride first affords the *erythro* halohydrin **57**, which on treatment with base gives the desired epoxide **58**. Similar compounds have been prepared by Barluenga and his colleagues, again using a ring-closure of preformed halohydrins.[32] A related procedure has also been used for the diastereoselective synthesis of disubstituted epichlorohydrins involving the conversion of the ketone **59**, via the lithium alkoxide **60**, into the epoxide **61**.[33]

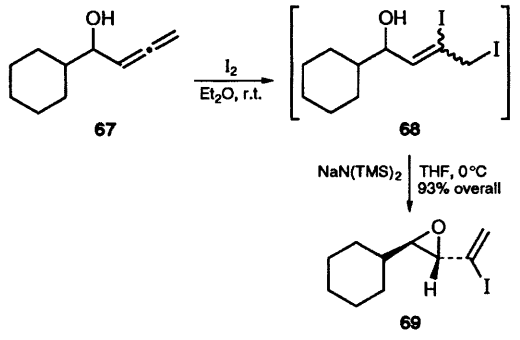


An intermediate lithium alkoxide also features in the synthesis of oxiranyl pyridines reported by Florio and Troisi.[34] In this procedure the 2-chloromethylpyridine **62** is lithiated and reacted with a ketone, such as cyclohexanone, and the intermediate alkoxide formed them undergoes cyclization to give the desired epoxide, as illustrated for the synthesis of the *spiro*-epoxide **64**. A related route to vinyl epoxides **66**, involving the addition of the allyl zinc reagent derived from allyl chloride **65** to ketones, has also been reported.[35]

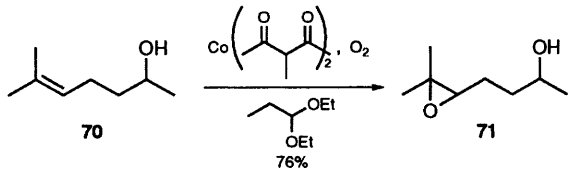


Iodovinyl epoxides have been prepared from treatment of α-allenic alcohols with iodine, followed

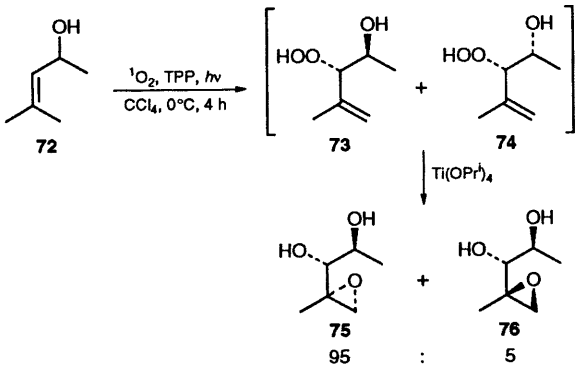
by base-induced epoxide formation.[36] For example, iodination of **67** gave the intermediate diiodide **68**, which on treatment with sodium hexamethyldisilazide then generates the epoxide **69** predominantly as the *trans*-isomer shown.

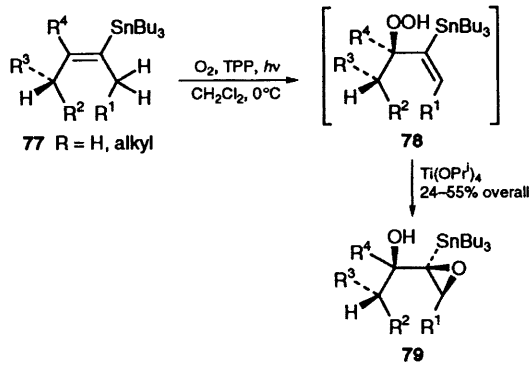


Of numerous reports detailing the use of molecular oxygen as oxidant, the work of Mukaiyama and his group is particularly noteworthy. In recent work they have demonstrated that acid-sensitive epoxides can be prepared via oxygenations of olefins in the presence of a cobalt catalyst.[37] Propionaldehyde diethyl acetal, which is also added to the reaction mixture, acting as a reductant, is converted into ethyl propionate and ethanol, the reaction therefore occurs under neutral conditions; the synthesis of the epoxide **71** from the olefin **70** is typical.



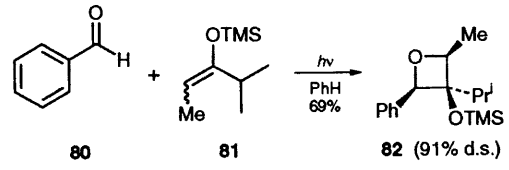
Singlet molecular oxygen has been used in the epoxy-hydroxylation of allylic alcohols catalysed by titanium tetraisopropoxide.[38] Thus, conversion of the allylic alcohol **72** into the hydroxy epoxides **75** and **76** is achieved in one-pot via the hydroperoxides **73** and **74**, and with very high diastereoselectivity.[39] A similar procedure beginning with vinyl stannanes **77** leads to the stannyl epoxides **79** through the intermediacy of the corresponding hydroperoxide **78**.[40]

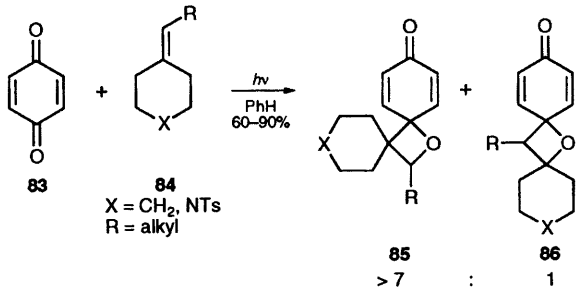




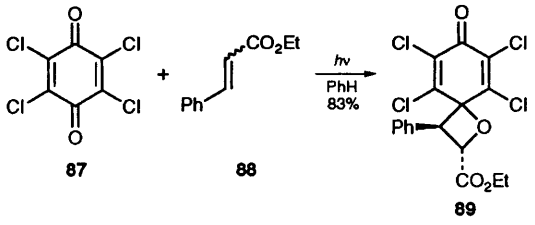
3 Oxetanes

The photocycloaddition of olefins and carbonyl compounds (Paterno–Büchi reaction) continues to be the main method of choice for the synthesis of oxetanes. Bach has demonstrated that β-alkylsubstituted silyl enol ethers undergo remarkably regio- and stereo-selective additions to aryl aldehydes, *e.g.* formation of the oxetane **82** from benzaldehyde (**80**) and the enol ether **81**.[41] Ciufolini and co-workers have examined the Paterno–Büchi reaction of benzoquinones and olefins, and have shown that alkylidenecyclohexanes **84** react with *para*-benzoquinone (**83**) in good yield to give the regioisomeric oxetanes **85** and **86** in the ratio shown.[42] Interestingly, with smaller ring alkylidenes the regioisomeric preference is reversed, whereas acyclic olefins react with little regioselectivity.[43]

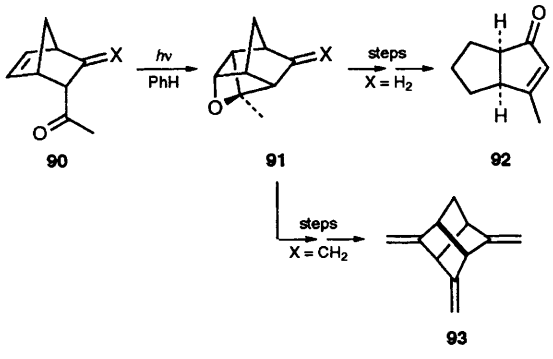




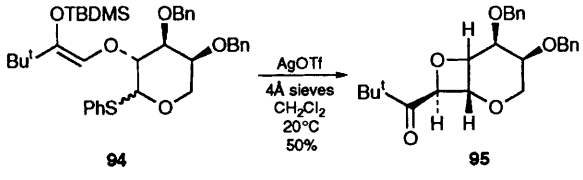
The reactions between chloranil (**87**) and α,β-unsaturated carbonyl compounds have also been investigated and proceed in good yield, generating *trans*-oxetanes.[44] For example, irradiation of a benzene solution of chloranil with ethyl cinnamate isomers **88** leads to the oxetane **89** in excellent yield.



The research groups of both Rawal[45] and Gleiter[46] have examined the use of oxetane **91**, derived from the Paterno–Büchi reaction of the norbornene **90**, in synthesis. Thus, Rawal and Dufour have transformed the simple norbornene **90** (X = H_2) into the diquinane **92** in only four steps,[45] while Gleiter and Sigwart have prepared 'stellatriene' **93** in three steps from the oxetane **91** (X = CH_2).[46]



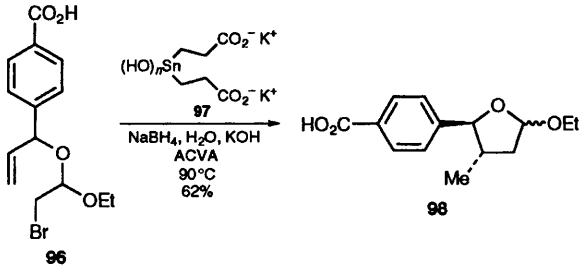
Craig and Munasinghe have synthesized keto-oxetanes via intramolecular trapping of an oxonium ion.[47] The reaction proceeds with high stereoselectivity, as shown for the synthesis of **95** from the sugar-derived silyl enol ether **94**. This work has also been extended to the synthesis of the analogous tetrahydrofurans.[48]

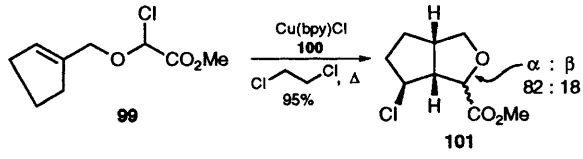


4 Five-membered rings

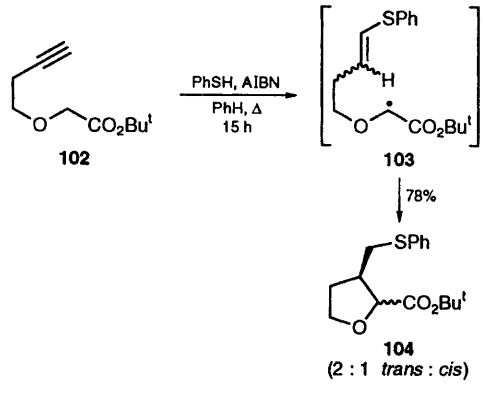
4.1 Tetrahydrofurans

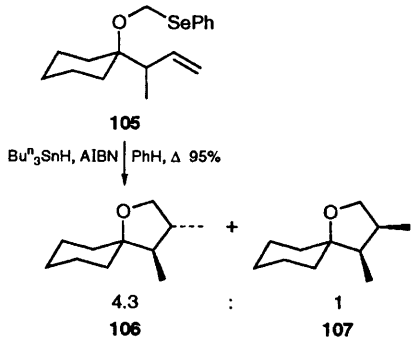
The synthesis of substituted tetrahydrofurans via free radical chemistry continues to be an active area of research. Rai and Collum have demonstrated that the radical cyclization of the ether **96** to the tetrahydrofuran **98** proceeds under aqueous conditions via *in situ* reduction of the tin species **97** with sodium borohydride in the presence of the initiator 4,4′-azobis(4-cyanovaleric acid) (ACVA).[49] Udding *et al.* have introduced the copper(I) catalyst **100** for chlorine-transfer radical cyclizations, as shown for the synthesis of the diastereomers **101** from **99**.[50] A chromium species, generated from chromium(II) acetate and various reducing agents such as $LiAlH_4$, has also been used for the generation of carbon-centred free-radicals in tetrahydrofuran synthesis.[51]





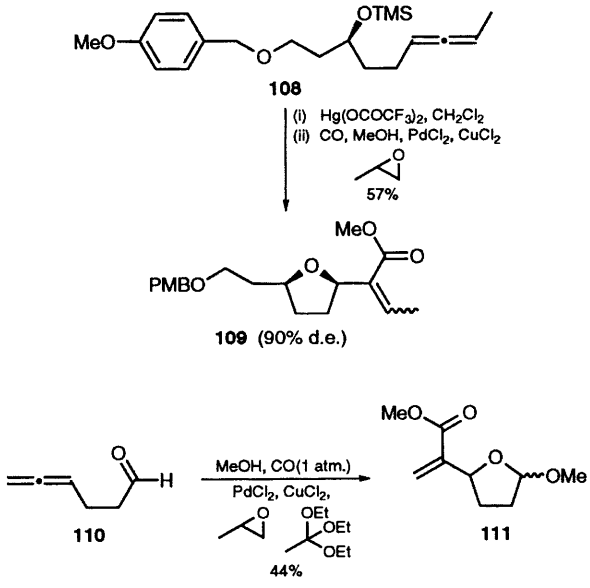
Burke and Jung have demonstrated that treatment of the alkyne **102** with thiophenol under radical conditions leads to the tetrahydrofuran diastereomers **104** presumably through the intermediacy of the alkoxymethyl radical **103**.[52] Rawal and co-workers have reported on the generation and use of simple alkoxymethyl radicals in tetrahydrofuran synthesis, *e.g.* in the synthesis of the spirocycles **106** and **107** from the selenide **105**.[53]



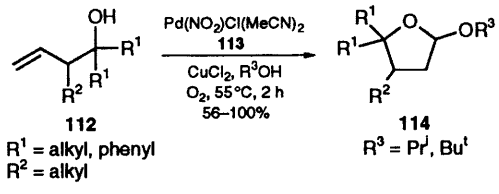


A review containing 90 references on synthetic routes to 2,5-disubstituted tetrahydrofurans has been published.[54] Walkup and Kim have prepared

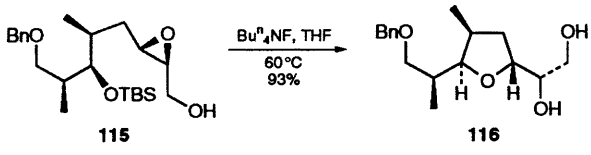
the 2,5-disubstituted tetrahydrofuran lower portion of the panamycin group of macrolides via the cyclization of γ-silyloxyallenes.[55] Thus, treatment of the chiral allene **108** with mercury(II) triflate, and subsequent carbonylation of the intermediate organomercurial gave the tetrahydrofuran **109**, predominantly as the *cis*-diastereomer shown. In a related process γ-oxoallenes have been shown to cyclize solely under the palladium-catalysis conditions of the carbonylation; for example, the formation of the furanoside **111** from the allene **110**.[56]



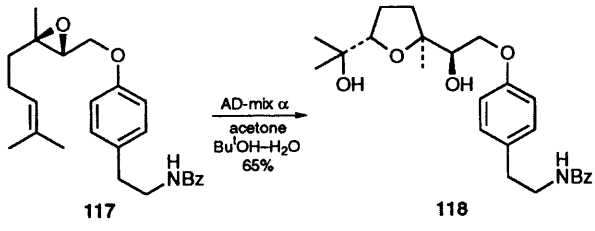
Furanosides can also be prepared by a catalytic oxidation procedure of homoallylic alcohols.[57] In this process substituted homoallylic alcohols **112** are oxidized by molecular oxygen, catalysed by the *in situ* prepared palladium complex **113**, to the products **114**.

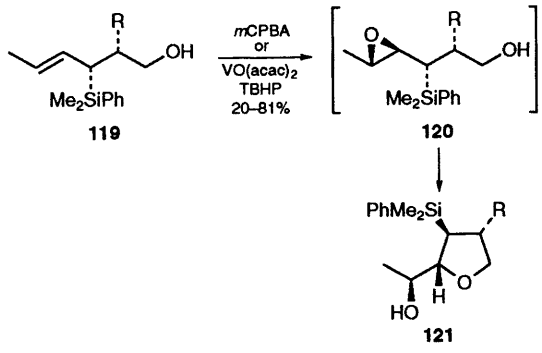


A number of research groups have reported on the synthesis of 2-hydroxymethyl substituted tetrahydrofurans via an intramolecular epoxide-ring opening process. For example, Ley and co-workers have prepared the tetrahydrofuran portion of the antibiotic tetronasin via epoxide ring-opening of the chiral epoxide **115** following desilylation of the protected secondary hydroxyl, giving the tetrahydrofuran **116** as one diastereomer in excellent yield.[58]

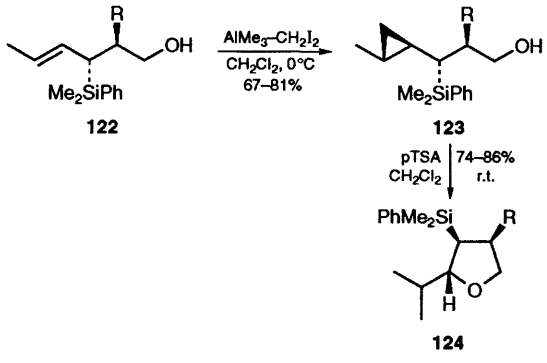


In a synthesis of (+)-tuberine, Taber *et al.* have used the intramolecular ring-opening of an epoxide to form the tetrahydrofuran portion of this natural product.[59] Thus, Sharpless asymmetric dihydroxylation of the olefin **117** afforded, in one step, the chiral tetrahydrofuran **118** in good yield. Similarly, Panek, Garbaccio, and Jain have demonstrated that epoxidations of the bis-homoallylic alcohols **119** generate the tetrahydrofurans **121** with excellent diastereoselectivity, via the intermediacy of the epoxide **120**.[60]

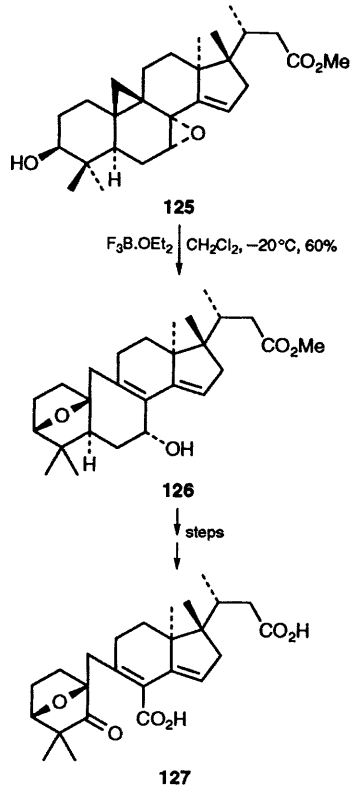




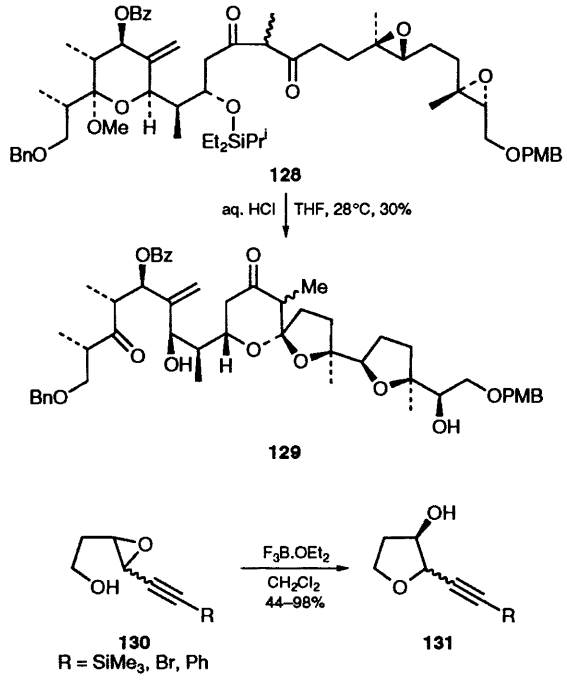
Interestingly, cyclopropanation of the isomeric alkenes **122**, followed by treatment of the derived cyclopropanes **123** with catalytic acid generates the related tetrahydrofurans **124** with excellent diastereoselectivity.[60] Corey has also used an intramolecular cyclopropane ring-opening in a biomimetic synthesis of 12-desoxy-glycinoeclepin (**127**), wherein exposure of the cyclopropane **125** to excess boron trifluoride etherate gives the bridged tetrahydrofuran **126**.[61]



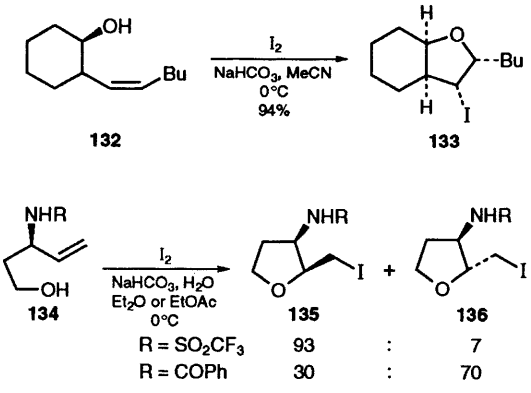
A biomimetic approach to the polyether antibiotic etheromycin has been reported by Paterson and his group, whereby an acid induced cascade reaction of the diepoxide **128** led to the bis-tetrahydrofuran **129** in moderate yield.[62] Mukai *et al.* have reported a



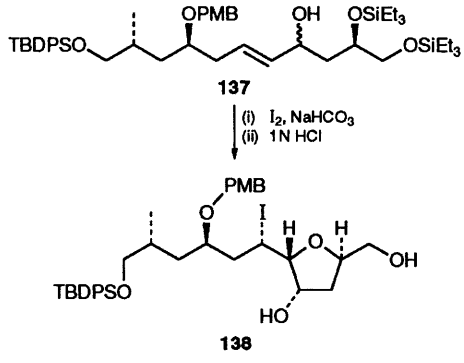
synthesis of 3-hydroxytetrahydrofurans using an epoxide ring-opening process.[63] In this reaction exposure of the epoxides **130** to catalytic boron trifluoride etherate generates the tetrahydrofurans **131** in good yield and with excellent diastereoselectivity; *cis*-epoxides are transformed into *cis*-tetrahydrofurans, while the *trans*-isomers give the *trans* products. Interestingly, complexation of the acetylene in **130** with $CO_2(CO)_8$ prior to tetrahydrofuran formation reverses the stereoselectivity.



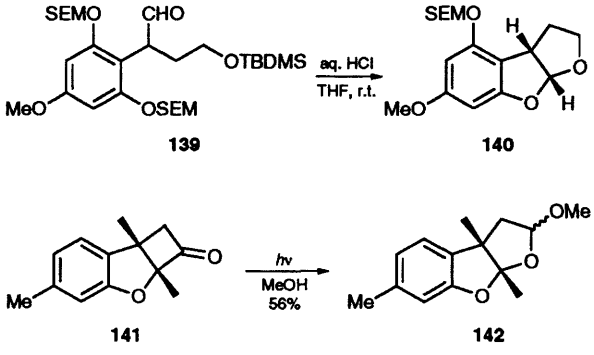
Iodocyclizations also continue to be an attractive route to functionalized tetrahydrofurans. Knight and his research group have prepared annulated tetrahydrofurans via this route, and have shown that the reaction is highly stereoselective, as shown for the synthesis of the *cis*-tetrahydrofuran **133** from the *cis*-olefin **132**.[64] Alteration of the electron-withdrawing effect of the nitrogen protecting group in the aminoalkenes **134** has a profound effect on the stereoselectivity of the iodocyclized products; the electron-withdrawing substituents force the reaction to run under electronic control giving predominantly *cis*-products **135**, as opposed to *trans*-products **136** which arise through steric control.[65]



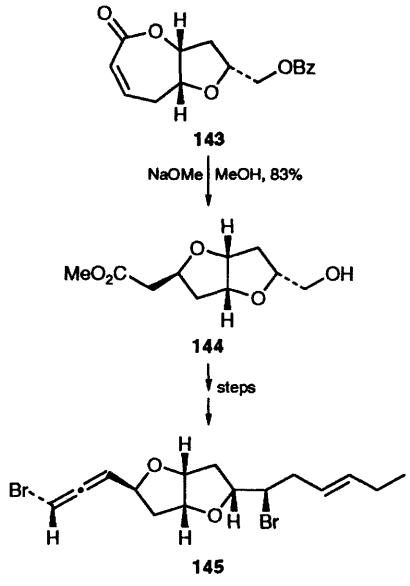
Stereoselective iodocyclizations have been used in a number of natural product syntheses over the review period, such as in the synthesis of the C_{17}–C_{22} subunit of ionomycin,[66] the synthesis of muscarine,[67] and in the synthesis of the tetrahydrofuran portion of the marine natural product halichondrin B.[68] In this latter work, the secondary triethylsilyl ether of **137** is cleaved in the cyclization reaction to give after acid treatment predominantly the tetrahydrofuran isomer **138** shown.



A number of publications concerning syntheses of annulated tetrahydrofurans have appeared recently. Thus, Koreeda and co-workers have reported a highly efficient synthesis of the tetrahydrofuran **140** from the aldehyde **139** in a formal synthesis of aflatoxin B_2.[69] Similar compounds have been prepared by a photolytic route, as shown in the preparation of the acetals **142** from the cyclobutanone **141**.[70]

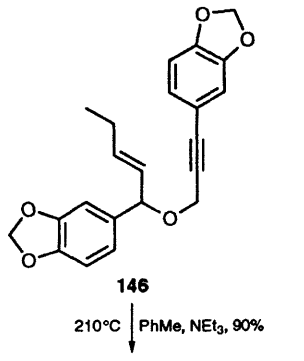


Overman and his group have prepared the annulated tetrahydrofuran **144** with high diastereoselectivity via methanolysis of the unsaturated lactone **143** in a synthesis of the marine natural product kumausallene **145**.[71]

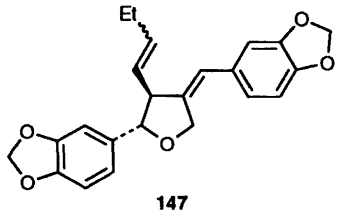


Mikami and co-workers have prepared the furofuran-containing natural product neopaulownin **148** via a stereoselective ene reaction of the ether **146** to give the *trans*-tetrahydrofuran **147**, which was then converted into the natural product **148** through regioselective olefin epoxidation, reductive double bond cleavage, and acid-catalysed epoxide ring-opening.[72] The related natural product asarinin has been prepared by Takano and co-workers.[73] In this work they found that treatment of the dioxepin **149** with a Lewis acid, followed by a reductant, gave the diastereomers **150** and **151**, the ratio being dramatically affected by the choice of reagents.

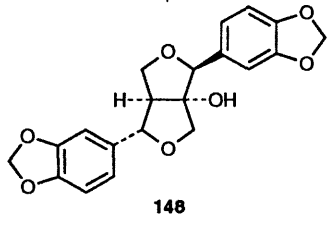
A cycloaddition approach to tetrahydrofurans has been reported by Hojo *et al.* wherein an *in situ* generated carbonyl ylide reacts with activated double bonds.[74] Thus, treatment of the trimethylsilylmethyl ether **152** with fluoride ion, in the presence of dimethyl fumarate generated the tetrahydrofurans **154** as essentially a 1:1 mixture of diastereomers at the two position, presumably through the intermediacy of the ylide **153**.

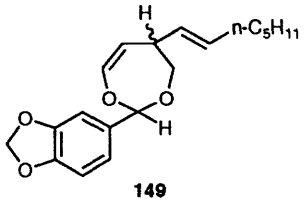


210°C | PhMe, NEt_3, 90%

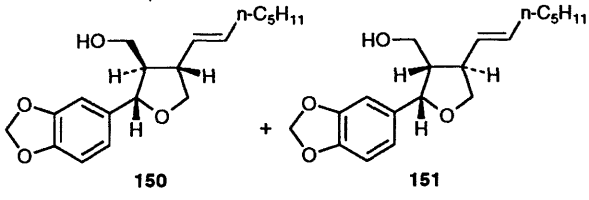


(i) mCPBA
(ii) O_3, then $NaBH_4$
(iii) pTSA, 30% overall

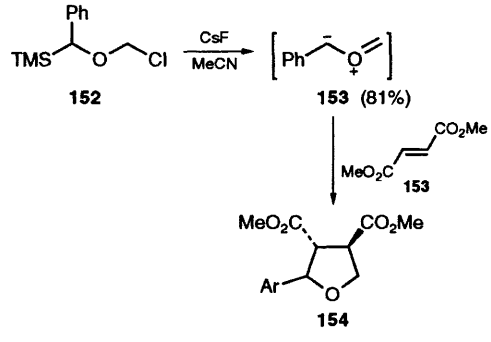




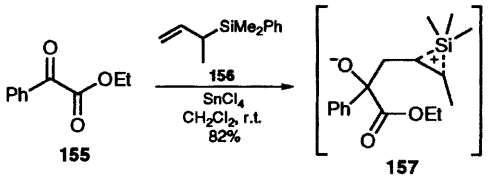
(i) Lewis acid
(ii) reductant, 27–85%

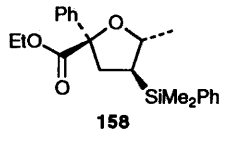


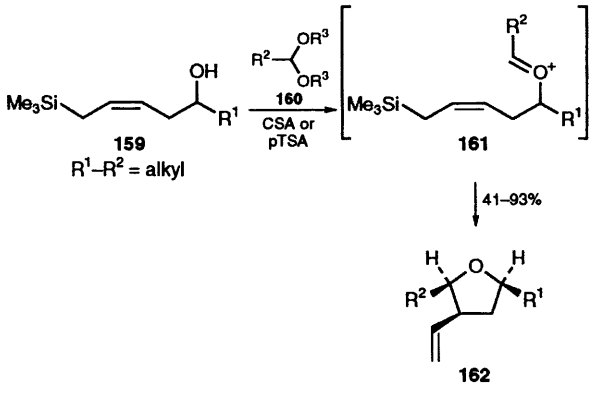
$(Pr^iO)_2TiCl_2$–$NaBH_4$	30	:	1
TBSOTf–$NaBH_4$	1	:	25



An alternative [3+2] cycloaddition approach to tetrahydrofurans has also been published.[75] In this process, tin tetrachloride promoted addition of an allyl silane such as **156** to the α-keto ester **155** gives the intermediate **157** which, after a 1,2-silicon shift, affords the tetrahydrofuran **158** in excellent yield and high diastereoselectivity. Functionalized allylsilanes have been used in an alternative synthesis of tetrahydrofurans.[76] In this work, the oxocarbenium ions **161**, formed by the reaction between the allylsilanes **159** and the acetals **160**, undergo an intramolecular Sakurai reaction to generate the all-*cis* tetrahydrofurans **162** in moderate to excellent yield.

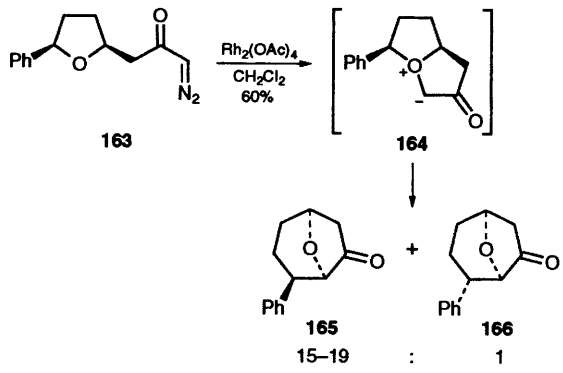


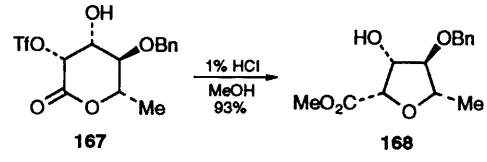




Bridged tetrahydrofurans have been prepared via the intermediacy of oxonium ylides as shown for the synthesis of the compounds **165** and **166**.[77] In this reaction, the ether oxygen adds to the rhodium carbenoid generated from the diazo compound **163** and rhodium acetate, giving the oxonium ylide **164**, which then undergoes a Stevens [1,2]-shift leading to the product tetrahydrofurans in the ratio shown.

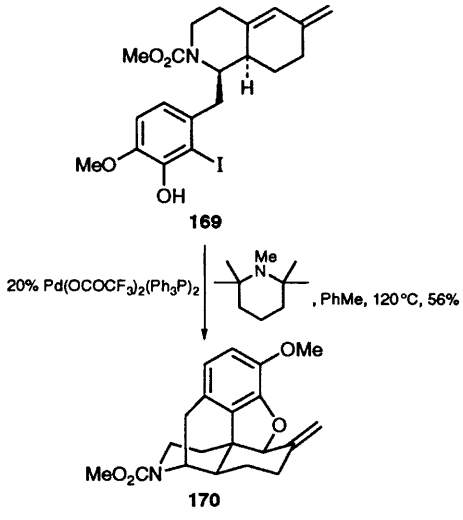
Finally, highly functionalized chiral tetrahydrofurans such as **168** can be obtained from sugar-derived γ- and δ-lactones bearing ring triflates by treatment with acidic methanol.[78] Thus, the lactone **167** was converted into the tetrahydrofuran **168** in 93% yield, with clean inversion occurring at the carbon bearing the triflate moiety. A similar base-induced rearrangement has also been reported for the synthesis of analogues of muscarine.[79]





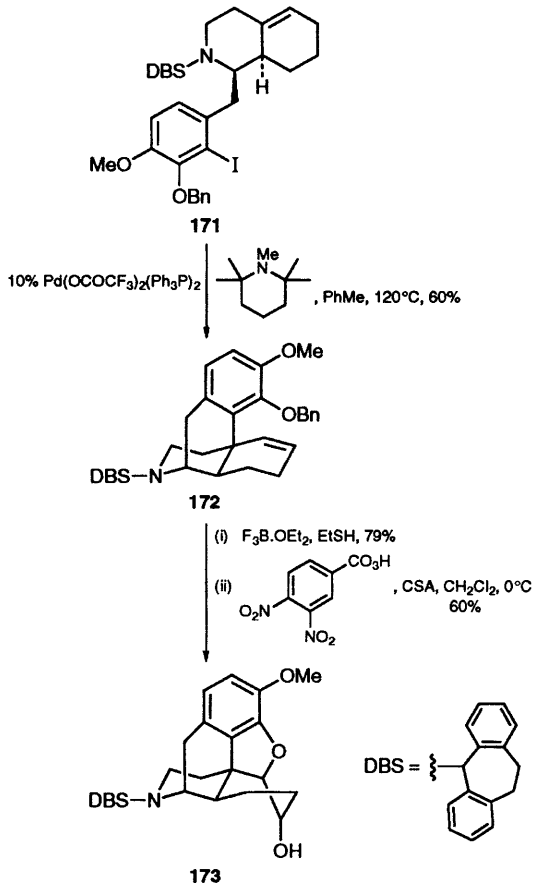
4.2 Dihydrofurans

The dihydrobenzofuran **170**, which is an intermediate in a formal synthesis of (±)-morphine, has been formed in one step from the bicycle **169** via a tandem intramolecular Heck insertion/heterocyclization reaction disclosed by Overman and Hong.[80]

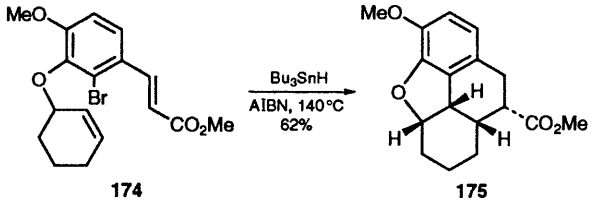


This report follows an earlier total synthesis of both antipodes of morphine by Overman's group where the dihydrofuran **173** was constructed in a separate step after Heck-cyclization of **171**, via ring-opening of an *in situ* prepared epoxide derived from **172**, as depicted in **Scheme 2**.[81] In work also directed towards the synthesis of morphine, Parker and Fokas have reported that the aryl bromide **174** undergoes free-radical cascade cyclization to produce the tetracycle **175** exclusively as the diastereomer shown.[82]

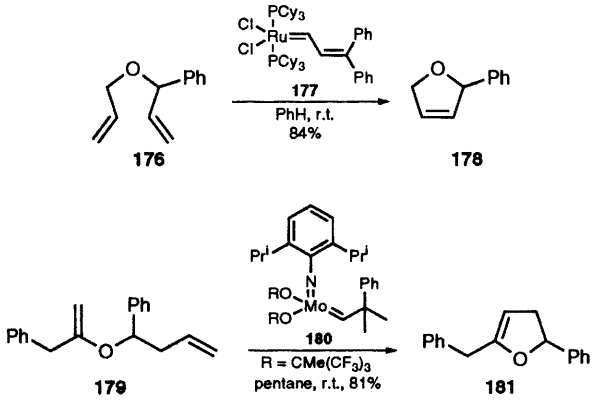
Grubbs and his research group have continued their work on the use of transition metal complexes



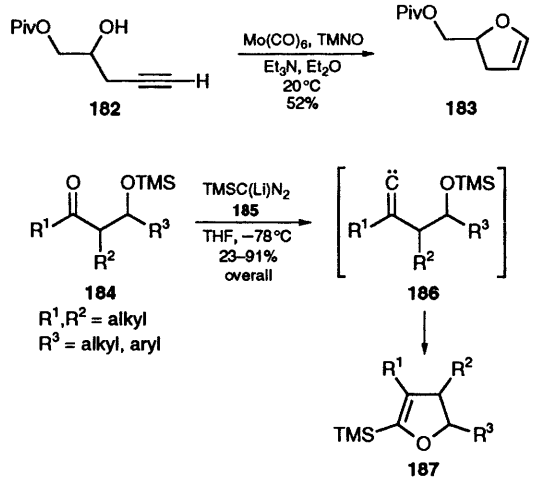
Scheme 2



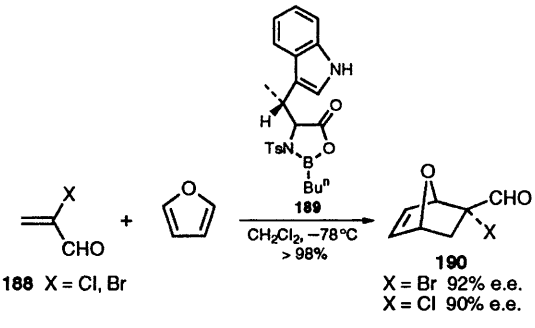
in ring-closing metathesis reactions. Thus, they report that the ruthenium carbene **177** smoothly converts the acyclic diene **176** into the dihydrofuran **178** at room temperature,[83] and that the molybdenum carbene **180** catalyses the metathesis of enol ethers such as **179**, leading to dihydrofurans such as **181**.[84]



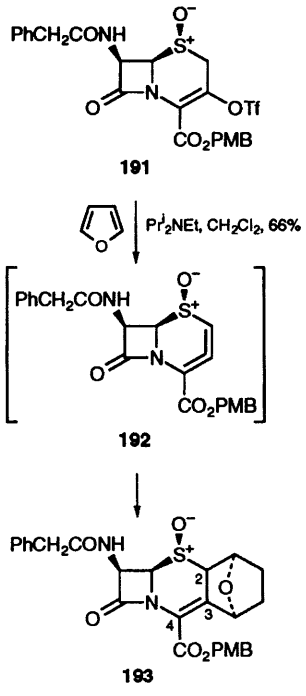
2,3-Dihydrofurans have been prepared via a different route, also through the intermediacy of carbene complexes, in a novel cyclization of homopropargylic alcohols.[85] Thus, treatment of the homopropargyllic alcohol derivative **182** with molybdenum hexacarbonyl and trimethylamine *N*-oxide (TMNO) in ether and triethylamine as solvents generates the dihydrofuran **183** in 52% yield. An *in situ* generated free-carbene has also been used in the synthesis of 2,3-dihydrofurans.[86] In this work, lithium trimethylsilyldiazomethane **185** reacts with β-trimethylsilyoxyketones **184** to generate 2,3-dihydrofurans **187**, presumably through the intermediacy of the carbene **186**.



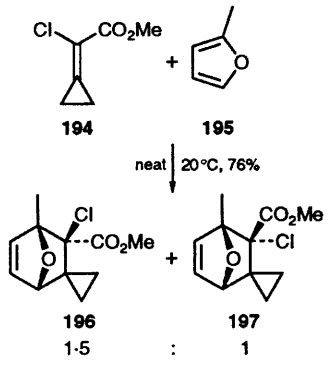
There have been numerous reports over the review period concerning the use of furan as the diene in Diels–Alder reactions, generating bridged dihydrofuran products for use in natural product synthesis. Corey and Loh report that the oxazaborolidene **189** is an effective catalyst for the enantioselective reaction of furan with 2-bromo- or 2-chloro-acrolein **188**.[87] The products **190** are formed in greater than 98% yield, with excellent stereoselectivity (*exo*/*endo* = 99/1), and high enantioselectivity.



The Diels–Alder reaction between furan and the chiral cephalosporin triflate **191** generated the bridged dihydrofuran **193**, presumably through *in situ* formation of the cyclic allene **192**.[88] Interestingly, the corresponding sulfide undergoes the Diels–Alder reaction across the 3,4 position.

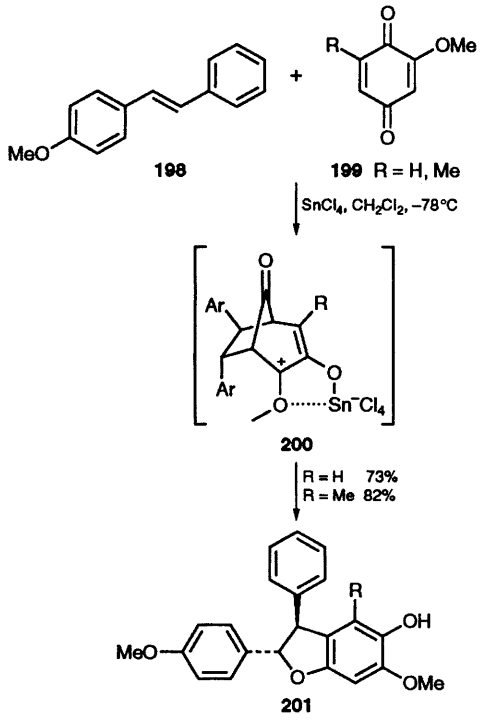


De Meijere and his group have studied the Diels–Alder reaction between substituted furans and the cyclopropylidene **194** as part of a programme directed toward the synthesis of the sesquiterpene illudin M.[89] For example, reaction of **194** with the furan **195** occurs with complete regioselectivity, to generate the *exo* and *endo* adducts **196** and **197** respectively in the ratio shown.

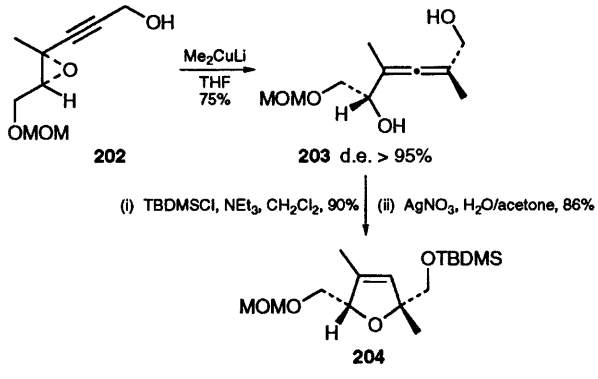


An approach to the dihydrobenzofuran natural product ε-viniferin which proceeds via a [5+2] cycloaddition has been reported by Engler *et al.*[90] In this work polarized, nucleophilic stilbenes such as **198** react with benzoquinones **199** in the presence of stannic chloride to give, via the carbocation intermediate **200**, the *trans* product **201**.

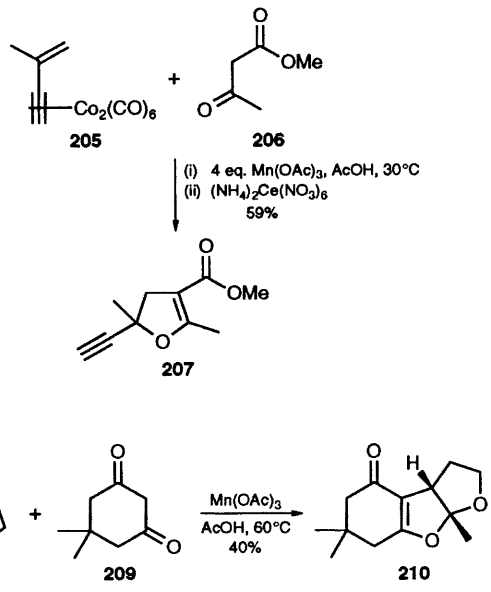
Marshall and Pinney have disclosed a stereoselective synthesis of 2,5-dihydrofurans involving cyclization of a stereoselectively formed allenyl carbinol.[91] The allenyl carbinols, such as **203**, were formed with high stereoselectivity by S_N2' addition of lithium dimethyl cuprate to chiral propargylic epoxides such as **202**, and after selective silylation underwent smooth cyclization to



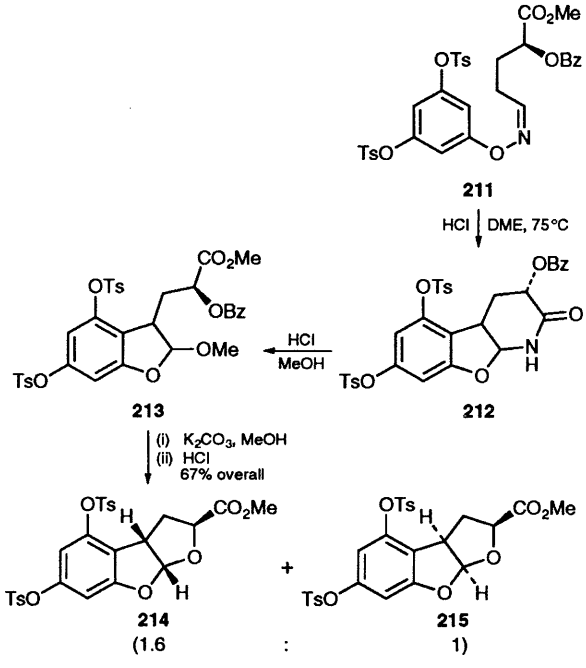
dihydrofurans, as shown for the preparation of **204**. Hydride, as opposed to cuprate addition has been used in the synthesis of the furan-containing macrocycles found in natural products of the pseudopterane family.[92]



The manganic acetate promoted addition of β-diketones to enynes usually produces a mixture of furan and dihydrofuran products depending on substitution on the enyne. Melikyan *et al.* have now shown that the triple bond of enynes can be protected with the dicobalt hexacarbonyl group, thus forcing the reaction to occur exclusively at the alkene, as depicted for the synthesis of the dihydrofuran **207** from the complexed enyne **205** and the β-ketoester **206**.[93] Mellor and Mohammed have used manganic acetate promoted additions of β-diketones to enol ethers to generate spirocyclic compounds[94] and annulated dihydrofurans.[95] In this latter work, annulated dihydrofurans related to the aflatoxins have been prepared: for example, reaction of the dihydrofuran **208** with dimedone (**209**) produces the dihydrofuran **210**.

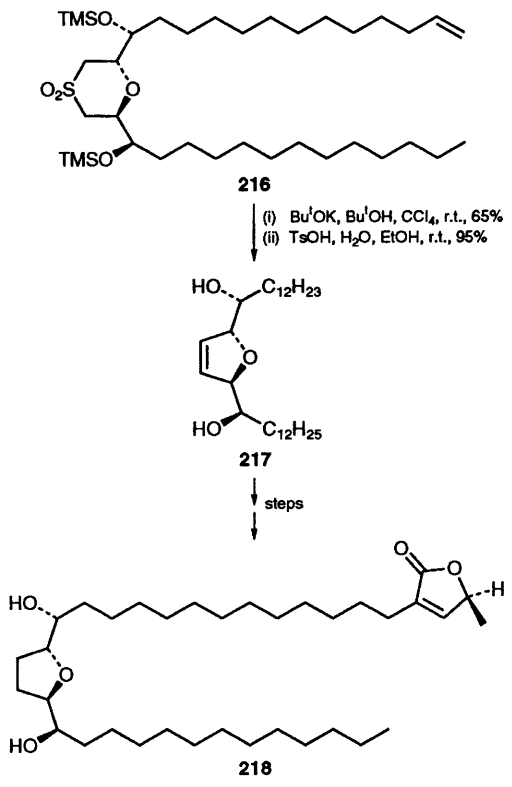


An entirely different approach to the dihydrofuran ring of annulated dihydrofurans, employing an oxaza-Cope rearrangement has been reported by Civitello and Rapoport.[96] In this work (**Scheme 3**) the chiral oxime **211** undergoes the acid-catalysed oxaza-Cope rearrangement to give the lactam **212**, which can be converted into the dihydrofuran **213** by treatment with methanolic HCl. The annulated systems **214** and **215** are obtained in the ratio shown by debenzoylation and intramolecular acetal formation.

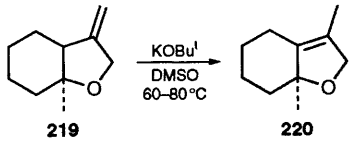


Scheme 3

Trost and Shi have reported a synthesis of the natural product solamin **218** using a Ramberg–Backlund reaction of the *in situ* generated α-chlorosulfone derived from **216** to produce the dihydrofuran **217**.[97]



Finally, a base-induced rearrangement of 3-methylenetetrahydrofurans has been shown to be an efficient method for the preparation of fused 2,5-dihydrofurans.[98] For example, treatment of the methylene tetrahydrofuran **219** with potassium t-butoxide in DMSO affords the product dihydrofuran **220** in good yield.

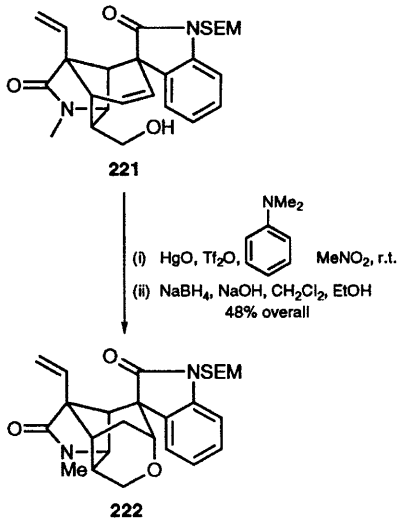


5 Six-membered rings

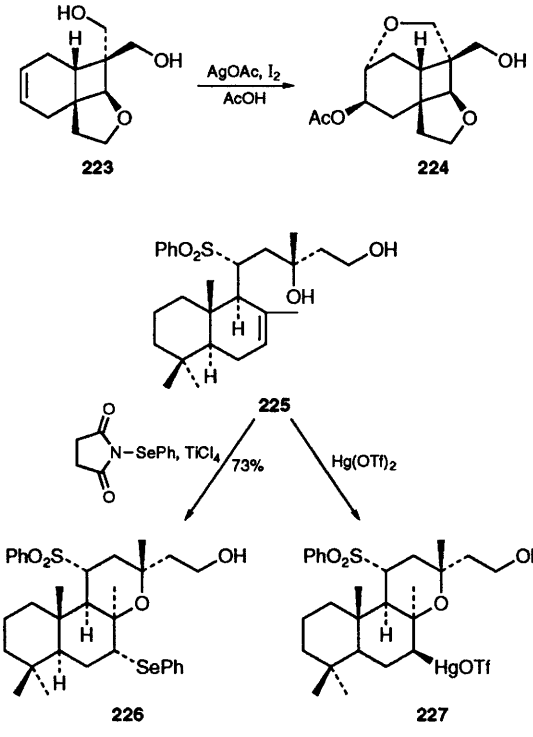
5.1 Tetrahydropyrans

Of the numerous methods available for the synthesis of tetrahydropyrans, electrophile induced ring closure processes continue to be one of the favourite routes to this ring system. For example, while cyclization of the spirocyclic oxindole derivative **221** could not be effected under iodo- or bromo-etherification conditions, recourse was made to an intramolecular oxymercuration reaction which, after organomercurial reduction, gave the complex tetrahydropyran **222**, an advanced intermediate in the synthesis of gelsemine.[99]

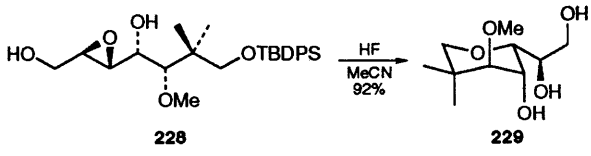
In other work directed towards the synthesis of gelsemine Johnson and co-workers have formed the tetrahydropyran derivative **224** by treatment of the tricycle **223** with silver acetate and iodine.[100] Construction of the c-ring in forskolin has been examined by Welzel and his group, who have shown that while treatment of **225** with *N*-phenylseleno-



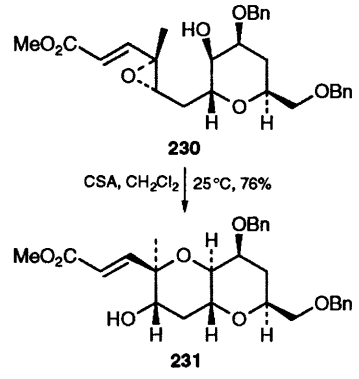
phthalimide gives the *anti*-product **226**, treatment with mercury triflate leads to **227**, the product of *syn*-addition.[101]

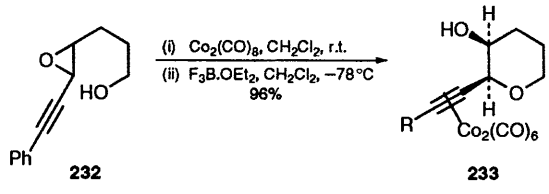


A number of research groups have used intramolecular epoxide-ring opening reactions to form complex tetrahydropyrans in the synthesis of natural products. Thus, Roush and Marron have prepared the tetrahydropyran **229** from the epoxide **228** via fluoride ion induced desilylation, as part of a programme directed toward the synthesis of the mycalamide family of antibiotics.[102]

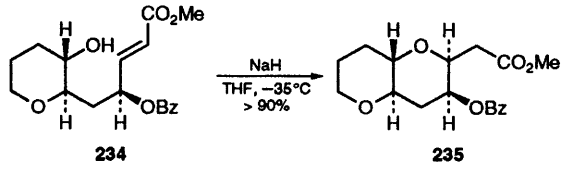


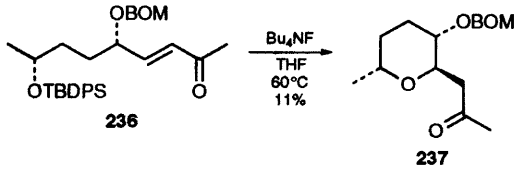
The dioxadecalin **231** has been prepared from the sugar-derived epoxide **230** via an acid-induced epoxide-ring opening, as part of the total synthesis of hemibrevetoxin B.[103] Similar approaches have been employed in the synthesis of related dioxadecalin ring systems.[104,105] 6-*endo* Ring-closure has also been shown to operate in the epoxide ring-opening of cobalt-complexed propargylic epoxides.[10] 6For example, complexation of the *trans*-propargylic epoxide **232**, followed by treatment with boron trifluoride etherate, gave almost exclusively the *cis*-tetrahydropyran **233**.





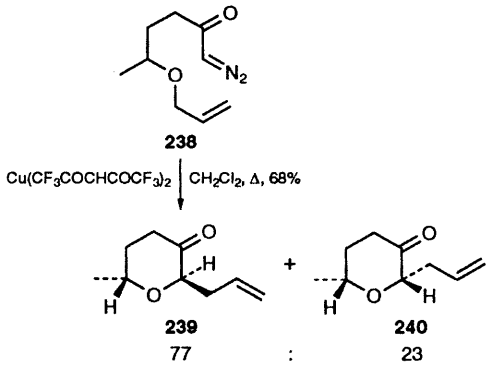
Intramolecular hetero-Michael addition has also been used for the preparation of tetrahydropyrans as shown for the preparation of the dioxadecalin **235** from the α,β-unsaturated ester **234**.[107] A fluoride ion induced Michael addition has been used as the ring-forming step in an asymmetric synthesis of the cholesterol biosynthesis inhibitor decarestrictine L, as shown in the transformation of the acyclic ketone **236** into the tetrahydropyran **237**.[108]



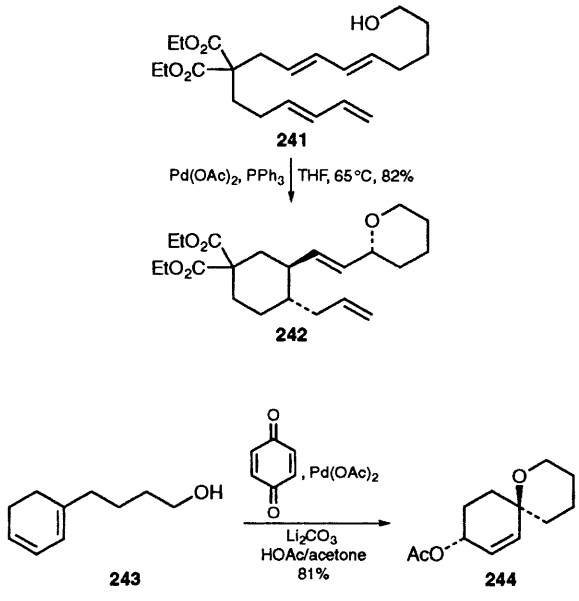


An alternative route to this ring substitution has been reported by Clark and Whitlock who have demonstrated that copper-catalysed decomposition of the diazoketone **238** affords the tetrahydropyrans **239** and **240** in the ratio shown.[109] The use of

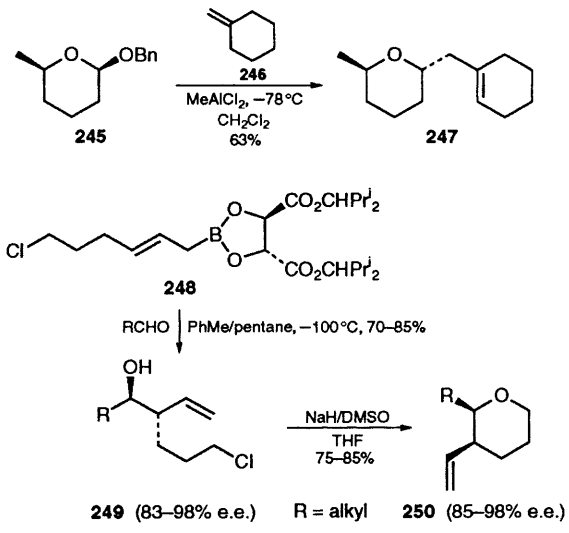
copper hexafluoroacetylacetonate in this process had been shown in previous work to promote insertion of the *in situ* formed copper carbenoid into the allyl ether oxygen in preference to CH-insertion.[110]



As part of an investigation into tetraene cyclizations, Takacs and Chandramouli have shown that treatment of the tetraene **241** with catalytic palladium(II) leads to the olefinic tetrahydropyran **242** in good yield.[111] Palladium catalysis has also been used in a highly stereoselective preparation of spirocyclic tetrahydropyrans from dienes, *e.g.* in the transformation of the diene **243** into the tetrahydropyran **244**.[112]

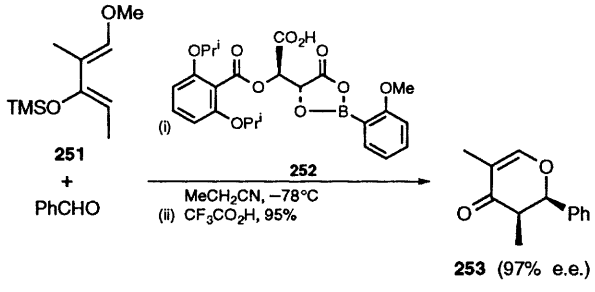


Lactols have been shown to undergo an intermolecular ene reaction generating *trans*-2,6-disubstituted tetrahydropyrans with high stereoselectivity.[113] Thus, exposure of the lactol ether **245** to methyl aluminium dichloride followed by addition of the olefin **246** gave the *trans* product **247** in good yield. *cis*-2,3-Disubstituted tetrahydropyrans **250** have been prepared in high optical purity from the chlorohydrins **249**, themselves prepared in high optical purity by the reaction between chiral allyl boronates **248** and aldehydes.[114]

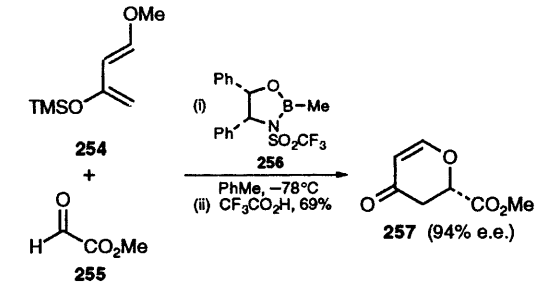


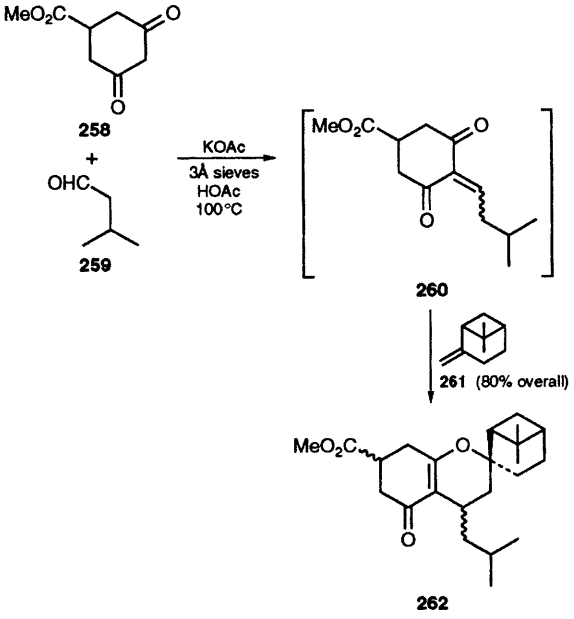
5.2 Dihydropyrans

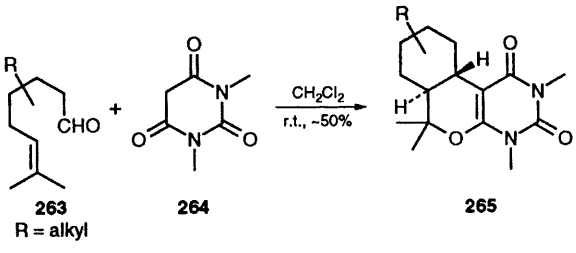
There have been numerous reports over the review period concerning the synthesis of dihydropyrans via hetero Diels–Alder reactions, and a review containing 111 references concerned with the asymmetric variant of this reaction has been published.[115] Yamamoto and his research group have shown that *in situ* prepared borane complexes derived from tartaric acid (such as **252**) catalyse the reaction of oxygenated butadienes such as **251** with benzaldehyde to give pyrones, *e.g.* **253**, in high optical purity after treatment with acid.[116] Motoyama and Mikami have demonstrated that the boron complex **256** also catalyses the Diels–Alder reaction of siloxydiene **254** and methyl glyoxylate (**255**), giving the pyrone **257**, again after acid treatment of the adduct, in good yield and in high optical purity.[117]



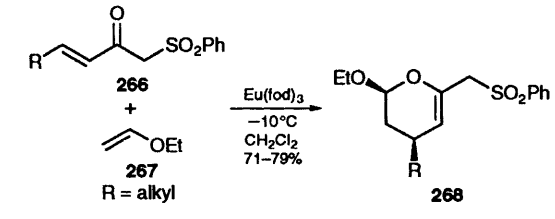
A stereoselective synthesis of precursors to the natural products robustadial A and B has been published, which employs a regioselective hetero Diels–Alder reaction.[118] Thus, Knoevenagel condensation of the 1,3-dione **258** and the aldehyde **259**, in the presence of (*S*)-β-pinene (**261**) affords the spirocyclic product **262**, presumably through the intermediate **260**. Tietze and his co-workers have used a similar approach in the synthesis of the tricycles **265** from the reaction of aldehydes **263** and the dione **264**, the *trans* products always being formed as the major isomer.[119]



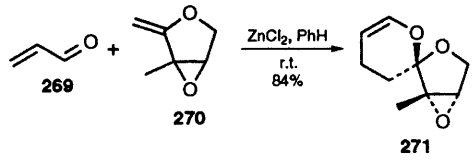




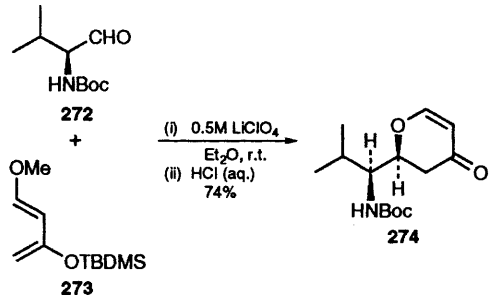
The highly stereoselective hetero Diels–Alder reactions of sulfonyl-α,β-unsaturated alkenes have been published by Wada *et al.*[120] They have shown that various Lewis acids catalyse the reaction of α,β-unsaturated alkenes **266** with ethyl vinyl ether **267**, as shown for the synthesis of **268**.

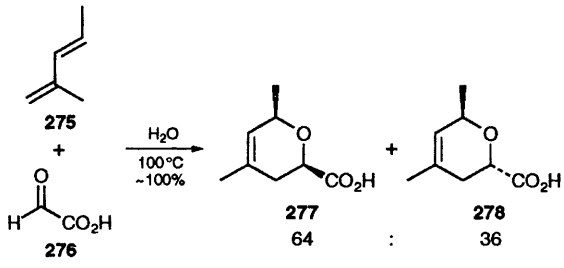


Spirocyclic dihydropyrans, such as **271**, have been formed with high stereoselectivity by the Lewis acid catalysed reaction of α,β-unsaturated aldehydes (*e.g.* acrolein, **269**) and *exo*-methylene compounds such as **270**.[121]



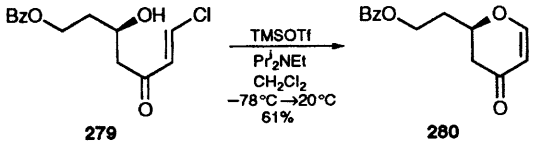
Samarium diiodide has also been shown to catalyse hetero Diels–Alder reactions,[122] and recent work by Grieco and Moher has demonstrated that lithium perchlorate in diethyl ether promotes the reaction between amino aldehydes and oxygenated dienes.[123] For example, reaction of the aldehyde **272** and the diene **273** leads to the pyrone after acid treatment, predominantly as the *threo* isomer **274** shown. Synthesis of the dihydropyrans **277** and **278** has been achieved in excellent yield by hetero Diels–Alder reaction in water between the diene **275** and glyoxylic acid **276**.[124]



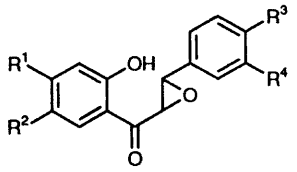


A number of significant publications concerning alternative routes to dihydropyrans and related systems have also been published recently. Paterson and Smith have prepared the chiral pyrone **280** from the alcohol **279** by a Lewis acid promoted Michael addition–elimination procedure[125] as part of a total synthesis of the marine macrolide (–)-preswinholide A.[126] An efficient synthesis of *trans*-3-hydroxyflavanones **282** from a base-promoted ring closure of the epoxides **281** has been reported, the epoxides themselves coming from dimethyl dioxirane epoxidation of the corresponding olefins.[127]

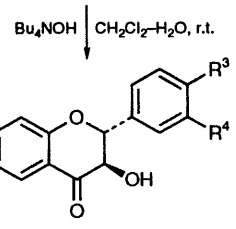
Markó and Bayston have reported on the use of the intramolecular silyl-modified Sakurai reaction in the synthesis of 3,4-dihydropyrans.[128] Thus, a trimethylsilyl triflate induced reaction between the



279 280

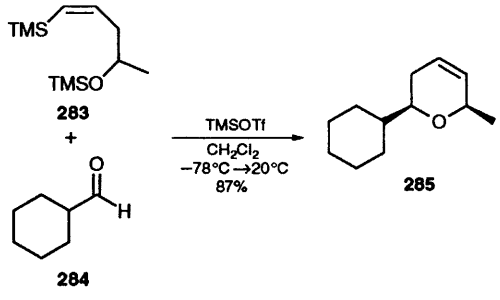


281
R = alkyl, alkoxy, chloro

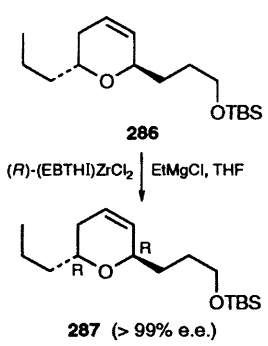


282

olefin **283** and the aldehyde **284** generates the dihydropyran **285** solely as the *cis* isomer, in excellent yield.

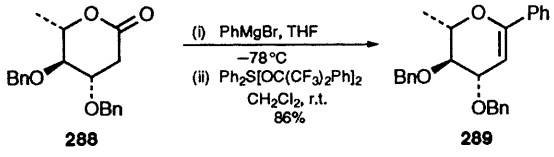


Hoveyda and co-workers have reported a very useful kinetic resolution of 3,4-dihydropyrans using a zirconium-mediated carbomagnesation process.[129] For example, when the racemic pyran **286** is treated with ethylmagnesium bromide and the chiral zirconium complex (EBTHI)$ZrCl_2$, recovered starting material of exceptionally high optical purity (**287**) is obtained when the reaction is stopped after 60% conversion.

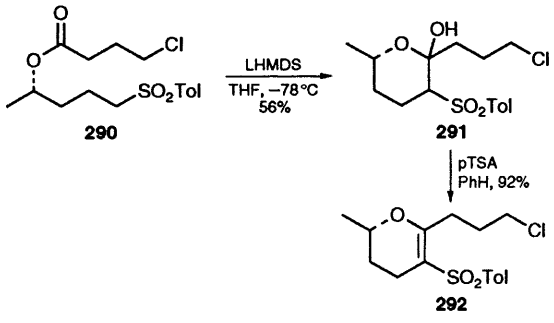


287 (> 99% e.e.)

2,3-Dihydropyrans have been prepared from sugar derived lactones via Grignard additions to the lactone carbonyl groups and subsequent dehydration of the hemiketals so formed, *e.g.* the preparation of **289** from the lactone **288**.[130] A two-step route to 6-chiral-2,3-dihydropyrans has been reported by Jacobs and Gopalan, also involving dehydration of an intermediate hemiketal.[131] For example, deprotonation of the chiral sulfone **290** generated the lactol **291** (as a mixture of diastereomers), which was then dehydrated to give the dihydropyran **292** in good yield.



288 289



290 291 292

6 References

1 B.D. Brandes and E.N. Jacobsen, *J. Org. Chem.*, 1994, **59**, 4378.
2 S. Chang, N.H. Lee, and E.N. Jacobsen, *J. Org. Chem.*, 1993, **58**, 6939.
3 S. Chang, J.M. Galvin, and E.N. Jacobsen, *J. Am. Chem. Soc.*, 1994, **116**, 6937.
4 H. Sasaki, R. Irie, and T. Katsuki, *Synlett*, 1993, 300; H. Sasaki, R. Irie, and T. Katsuki, *Synlett*, 1994, 356.
5 N. Hosoya, R. Irie, and T. Katsuki, *Synlett*, 1993, 261.
6 N. Hosoya, A. Hatayama, K. Yanai, H. Fujii, R. Irie, and T. Katsuki, *Synlett*, 1993, 641; T. Hamada, R. Irie, and T. Katsuki, *Synlett*, 1994, 479.
7 R. Irie, N. Hosoya, and T. Katsuki, *Synlett*, 1994, 255.
8 K. Imagawa, T. Nagata, T. Yamada, and T. Mukaiyama, *Chem. Lett.*, 1994, 527.
9 B.B. De, B.B. Lohray, and P.K. Dhal, *Tetrahedron Lett.*, 1993, **34**, 2371.
10 J.A.M. De Bont, *Tetrahedron: Asymmetry*, 1993, **4**, 1331.
11 E.J. Allain, L.P. Hager, L. Deng, and E.N. Jacobsen, *J. Am. Chem. Soc.*, 1993, **115**, 4415.
12 P. Besse, M.F. Renard, and H. Veschambre, *Tetrahedron: Asymmetry*, 1994, **5**, 1249.
13 P. Besse and H. Veschambre, *Tetrahedron: Asymmetry*, 1993, **4**, 1271.
14 D.H.G. Crout, V.S.B. Gaudet, and K.O. Hallinan, *J. Chem. Soc. Perkin Trans 1*, 1993, 805.
15 A. Koch, J.-L. Reymond, and R.A. Lerner, *J. Am. Chem. Soc.*, 1994, **116**, 803.

16 E.J. Corey and C.J. Helal, *Tetrahedron Lett.*, 1993, **34**, 5227.
17 T. Chan, L.M. Chen, D. Wang, and L.H. Li, *Can. J. Chem.*, 1993, **71**, 60.
18 V.K. Aggarwal, H. Abdel-Rahman, R.V.H. Jones, H.Y. Lee, and B.D. Reid, *J. Am. Chem. Soc.*, 1994, **116**, 5973.
19 V.K. Aggarwal, M. Kalomiri, and A.P. Thomas, *Tetrahedron: Asymmetry*, 1994, **5**, 723.
20 K. Maruoka, A.B. Concepcion, and H. Yamamoto, *Synlett*, 1994, 521.
21 W. Adam, J. Halász, A. Lévai, C. Nemes, T. Patonay, and G. Tóth, *Liebigs Ann. Chem.*, 1994, 795.
22 A.L. Baumstark and D.B. Harden, *J. Org. Chem.*, 1993, **58**, 7615.
23 W. Adam, G. Käb, and M. Sauter, *Chem. Ber.*, 1994, **127**, 433; W. Adam and M. Sauter, *Liebigs Ann. Chem.*, 1994, 689.
24 W. Adam, L. Hadjiarapoglou, K. Peters, and M. Sauter, *J. Am. Chem. Soc.*, 1993, **115**, 8603.
25 W. Adam, M. Sauter, and C. Zünkler, *Chem. Ber.*, 1994, **127**, 1115.
26 W. Adam, F. Prechtl, M.J. Richter, and A.K. Smerz, *Tetrahedron Lett.*, 1993, **34**, 8427.
27 M. Kurihara, S. Ito, N. Tsutsumi, and N. Miyata, *Tetrahedron Lett.*, 1994, **35**, 1577.
28 A. Armstrong, P.A. Barsanti, P.A. Clarke, and A. Wood, *Tetrahedron Lett.*, 1994, **35**, 6155.
29 A. Albeck and R. Persky, *J. Org. Chem.*, 1994, **59**, 653.
30 S. Romeo and D.H. Rich, *Tetrahedron Lett.*, 1994, **35**, 4939.
31 A. Albeck and R. Persky, *Tetrahedron*, 1994, **50**, 6333.
32 J. Barluenga, B. Baragaña, A. Alonso, and J.M. Concellón, *J. Chem. Soc., Chem. Commun.*, 1994, 969.
33 J. Barluenga, L. Llavona, P.L. Bernad, and J.M. Concellón, *Tetrahedron Lett.*, 1993, **34**, 3173.
34 S. Florio and L. Troisi, *Tetrahedron Lett.*, 1994, **35**, 3175.
35 K. Mallaiah, J. Satyanarayana, H. Ila, and H. Junjappa, *Tetrahedron Lett.*, 1993, **34**, 3145.
36 R.W. Friesen and M. Blouin, *J. Org. Chem.*, 1993, **58**, 1653.
37 K. Yorozu, T. Takai, T. Yamada, and T. Mukaiyama, *Chem. Lett.*, 1993, 1579.
38 W. Adam and B. Nestler, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 733.
39 W. Adam and B. Nestler, *J. Am. Chem. Soc.*, 1993, **115**, 7226.
40 W. Adam and P. Klug, *Chem. Ber.*, 1994, **127**, 1441.
41 T. Bach, *Tetrahedron Lett.*, 1994, **35**, 5845.
42 M.A. Ciufolini, M.A. Rivera-Fortin, and N.E. Byrne, *Tetrahedron Lett.*, 1993, **34**, 3505.
43 M.A. Ciufolini, M.A. Rivera-Fortin, V. Zuzukin, and K.H. Whitmire, *J. Am. Chem. Soc.*, 1994, **116**, 1272.
44 J.-H. Xu, L.-C. Wang, J.-W. Xu, B.-Z. Yan, H.-C. Yuan, *J. Chem. Soc., Perkin Trans 1*, 1994, 571.
45 V.H. Rawal and C. Dufour, *J. Am. Chem. Soc.*, 1994, **116**, 2613.
46 R. Gleiter and C. Sigwart, *J. Org. Chem.*, 1994, **59**, 1027.
47 D. Craig and V.R.N. Munasinghe, *J. Chem. Soc., Chem. Commun.*, 1993, 901.
48 D. Craig, M.W. Pennington, and P. Warner, *Tetrahedron Lett.*, 1993, **34**, 8539.
49 R. Rai and D.B. Collum, *Tetrahedron Lett.*, 1994, **34**, 6221.
50 J.H. Udding, C.J.M. Tuijp, M.N.A. van Zanden, H. Hiemstra, and W.N. Speckamp, *J. Org. Chem.*, 1994, **59**, 1993.
51 C. Hackmann and H.J. Schäfer, *Tetrahedron*, 1993, **49**, 4559.
52 S.D. Burke and K.W. Jung, *Tetrahedron Lett.*, 1994, **35**, 5837.
53 V.H. Rawal, S.P. Singh, C. Dufour, and C. Michoud, *J. Org. Chem.*, 1993, **58**, 7718.
54 J.-C. Harmange and B. Figadére, *Tetrahedron: Asymmetry*, 1993, **4**, 1711.
55 R.D. Walkup and S.W. Kim, *J. Org. Chem.*, 1994, **59**, 3433.
56 R.D. Walkup and M.D. Mosher, *Tetrahedron*, 1993, **49**, 9285.
57 T.M. Meulemans, N.H. Kiers, B.L. Feringa, and P.W.N.M. van Leeuwen, *Tetrahedron Lett.*, 1994, **35**, 455.
58 G.-J. Boons, D.S. Brown, J.A. Clase, I.C. Lennon, and S.V. Ley, *Tetrahedron Lett.*, 1994, **35**, 319.
59 D.F. Taber, R.S. Bhamidipati, and M.L. Thomas, *J. Org. Chem.*, 1994, **59**, 3442.
60 J.S. Panek, R.M. Garbaccio, and N.F. Jain, *Tetrahedron Lett.*, 1994, **35**, 6453.
61 E.J. Corey and B. Hong, *J. Am. Chem. Soc.*, 1994, **116**, 3149.
62 I. Paterson, R.D. Tillyer, and J.B. Smaill, *Tetrahedron Lett.*, 1993, **34**, 7137.
63 C. Mukai, Y. Sugimoto, Y. Ikeda, and M. Hanaoka, *J. Chem. Soc., Chem. Commun.*, 1994, 1161.
64 J.M. Barks, D.W. Knight, and G.G. Weingarten, *J. Chem. Soc., Chem. Commun.*, 1994, 719.
65 Y. Tamaru, H. Harayama, and T. Bando, *J. Chem. Soc., Chem. Commun.*, 1993, 1601.
66 Y. Guindon, C. Yoakim, V. Gorys, W.W. Ogilvie, D. Delorme, J. Renaud, G. Robinson, J.-F. Lavallée, A. Slassi, G. Jung, J. Rancourt, K. Durkin, and D. Liotta, *J. Org. Chem.*, 1994, **59**, 1166.
67 D.W. Knight, D. Shaw, and G. Fenton, *Synlett*, 1994, 295.
68 K. Horita, M. Nagasawa, S. Hachiya, and O. Yonemitsu, *Synlett*, 1994, 40.
69 M. Koreeda, L.A. Dixon, and J.D. Hsi, *Synlett*, 1993, 555.
70 A. Mittra, S. Biswas, and R.V. Venkateswaran, *J. Org. Chem.*, 1993, **58**, 7913.
71 T.A. Grese, K.D. Hutchinson, and L.E. Overman, *J. Org. Chem.*, 1993, **58**, 2468.
72 K. Mikami, H. Matsueda, and T. Nakai, *Synlett*, 1993, 235.
73 S. Takano, K. Samizu, and K. Ogasawara, *Synlett*, 1993, 785.
74 M. Hojo, M. Ohkuma, N. Ishibashi, and A. Hosomi, *Tetrahedron Lett.*, 1993, **34**, 5943.
75 T. Akiyama, K. Ishikawa, and S. Ozaki, *Chem. Lett.*, 1994, 627.
76 P. Mohr, *Tetrahedron Lett.*, 1993, **34**, 6251.
77 F.G. West, T.H. Eberlein, and R.W. Tester, *J. Chem. Soc., Chem. Commun.*, 1993, 2857.
78 J.R. Wheatley, C.J.F. Bichard, S.J. Mantell, J.C. Son, D.J. Hughes, G.W.J. Fleet, and D. Brown, *J. Chem. Soc., Chem. Commun.*, 1993, 1065.
79 S.J. Mantell, P.S. Ford, D.J. Watkin, G.W.J. Fleet, and D. Brown, *Tetrahedron*, 1993, **49**, 3343.
80 C.Y. Hong and L.E. Overman, *Tetrahedron Lett.*, 1994, **35**, 3453.
81 C.Y. Hong, N. Kado, and L.E. Overman, *J. Am. Chem. Soc.*, 1993, **115**, 11028.
82 K.A. Parker and D. Fokas, *J. Org. Chem.*, 1994, **59**, 3927.
83 G.C. Fu, S.T. Nguyen, and R.H. Grubbs, *J. Am. Chem. Soc.*, 1993, **115**, 9856.
84 O. Fujimura, G.C. Fu, and R.H. Grubbs, *J. Org. Chem.*, 1994, **59**, 4029.
85 F.E. McDonald, C.B. Connolly, M.M. Gleason, T.B. Towne, and K.D. Treiber, *J. Org. Chem.*, 1993, **58**, 6952.

86 K. Miwa, T. Aoyama, and T. Shiori, *Synlett*, 1994, 461.
87 E.J. Corey and T.-P. Loh, *Tetrahedron Lett.*, 1993, **34**, 3979.
88 R.L. Elliott, N.H. Nicholson, F.E. Peaker, A.K. Takle, J.W. Tyler, and J. White, *J. Org. Chem.*, 1994, **59**, 1606.
89 H. Primke, G.S. Sarin, S. Kohlstruk, G. Adiwidjaja, and A. de Meijere, *Chem. Ber.*, 1994, **127**, 1051.
90 T.A. Engler, B.W. Draney, and G.A. Gfesser, *Tetrahedron Lett.*, 1994, **35**, 1661.
91 J.A. Marshall and K.G. Pinney, *J. Org. Chem.*, 1993, **58**, 7180.
92 J.A. Marshall and B. Yu, *J. Org. Chem.*, 1994, **59**, 324.
93 G.G. Melikyan, O. Vostrowsky, W. Bauer, H.J. Bestmann, M. Khan, K.M. Nicholas, *J. Org. Chem.*, 1994, **59**, 222.
94 J.M. Mellor and S. Mohammed, *Tetrahedron*, 1993, **49**, 7547; *ibid.*, 7567.
95 J.M. Mellor and S. Mohammed, *Tetrahedron*, 1993, **49**, 7557.
96 E.R. Civitello and H. Rapoport, *J. Org. Chem.*, 1994, **59**, 3775.
97 B.M. Trost and Z. Shi, *J. Am. Chem. Soc.*, 1994, **116**, 7459.
98 J.-P. Dulcére, N. Baret, and J. Rodriguez, *J. Chem. Soc., Chem. Commun.*, 1994, 303.
99 N.J. Newcombe, F. Ya, R.J. Vijn, H. Hiemstra, and W.N. Speckamp, *J. Chem. Soc., Chem. Commun.*, 1994, 767.
100 Z. Sheikh, R. Steel, A.S. Tasker, and A.P. Johnson, *J. Chem. Soc., Chem. Commun.*, 1994, 763.
101 G. Jordine, S. Bick, U. Möller, P. Welzel, B. Daucher, and G. Maas, *Tetrahedron*, 1994, **50**, 139.
102 W.R. Roush and T.G. Marron, *Tetrahedron Lett.*, 1993, **34**, 5421.
103 K.C. Nicolau, K.R. Reddy, G. Skokotas, F. Sato, X.-Y. Xiao, and C.K. Hwang, *J. Am. Chem. Soc.*, 1993, **115**, 3558.
104 I. Kadota, Y. Matsukawa, and Y. Yamamoto, *J. Chem. Soc. Chem. Commun.*, 1993, 1638.
105 M. Sasaki, T. Nonomura, M. Murata, and K. Tachibana, *Tetrahedron Lett.*, 1994, **35**, 5023.
106 C. Mukai, Y. Ikeda, Y. Sugimoto, and M. Hanaoka, *Tetrahedron Lett.*, 1994, **35**, 2179.
107 J.M. Palazón, M.A. Soler, M.A. Mamírez, and V.S. Martin, *Tetrahedron Lett.*, 1993, **34**, 5467.
108 N. Machinaga and C. Kibayashi, *Tetrahedron Lett.*, 1993, **34**, 5739.
109 J.S. Clark and G.A. Whitlock, *Tetrahedron Lett.*, 1994, **35**, 6381.
110 J.S. Clark, S.A. Krowiak, and L. J. Street, *Tetrahedron Lett.*, 1993, **34**, 4385.
111 J.M. Takacs and S.V. Chandramouli, *J. Org. Chem.*, 1993, **58**, 7315.
112 P.G. Andersson, Y.I.M. Nilsson, and J.-E. Bäckvall, *Tetrahedron*, 1994, **50**, 559.
113 K. Mikami and H. Kishino, *J. Chem. Soc., Chem. Commun.*, 1993, 1843.
114 H.C. Brown and A.S. Phadke, *Synlett*, 1993, 927.
115 H. Waldmann, *Synthesis*, 1994, 535.
116 Q. Gao, K. Ishihara, T. Maruyama, M. Mouri, and H. Yamamoto, *Tetrahedron*, 1994, **50**, 979.
117 Y. Motoyama and K. Mikami, *J. Chem. Soc., Chem. Commun.*, 1994, 1563.
118 S. Koser, H.M.R. Hoffmann, and D.J. Williams, *J. Org. Chem.*, 1993, **58**, 6163.
119 L.F. Tietze, H. Geissler, J. Fennen, T. Brumby, S. Brand, and G. Schulz, *J. Org. Chem.*, 1994, **59**, 182.
120 E. Wada, H. Yasuoka, and S. Kanemasa, *Chem. Lett.*, 1994, 145.
121 P. Pale, J. Bouquant, J. Chuche, P.A. Carrupt, and P. Vogel, *Tetrahedron*, 1994, **50**, 8035.
122 P. Van de Weghe and J. Collin, *Tetrahedron Lett.*, 1994, **35**, 2545.
123 P.A. Grieco and E.D. Moher, *Tetrahedron Lett.*, 1993, **34**, 5567.
124 A. Lubineau, J. Augé, E. Grand, and N. Lubin, *Tetrahedron*, 1994, **50**, 10265.
125 I. Paterson and J.D. Smith, *Tetrahedron Lett.*, 1993, **34**, 5351.
126 I. Paterson, J.D. Smith, R.A. Ward, and J.G. Cumming, *J. Am. Chem. Soc.*, 1994, **116**, 2615.
127 T. Patonay, G. Tóth, and W. Adam, *Tetrahedron Lett.*, 1993, **34**, 5055.
128 I.E. Markó and D.J. Bayston, *Tetrahedron*, 1994, **50**, 7141.
129 J.P. Morken, M.T. Didiuk, M.S. Visser, and A.H. Hoveyda, *J. Am. Chem. Soc.*, 1994, **116**, 3123.
130 V.A. Boyd, B.E. Drake, and G.A. Sulikowski, *J. Org. Chem.*, 1993, **58**, 3191.
131 H.K. Jacobs and A.S. Gopalan, *J. Org. Chem.*, 1994, **59**, 2014.