Amines and amides

Michael North

Department of Chemistry, University of Wales, Bangor, Gwynedd, UK LL57 2UW.
E-mail m.north@bangor.ac.uk

Received (in Cambridge) 19th April 1999

Covering: 1998
Previous review: *J. Chem. Soc., Perkin Trans. 1*, 1998, 2959

1 Introduction, scope and coverage

This review covers the literature published during 1998, references were obtained using the online science citation index in the same way as in previous years.[1] A consequence of this is that a few papers published at the end of 1997 are included in this review, and some papers published late in 1998 may not be included, but will be included in next year's review of this area. As with last year's review, papers dealing with the solid-phase or combinatorial synthesis of amines or amides have been omitted. The initial literature search produced over 13 000 references, so this review is necessarily highly selective. The approximately 260 papers included are those which, in the opinion of the author, have general applicability or particular significance. Throughout this review, the focus has been placed on methods which create a carbon–nitrogen bond, or in which an existing carbon–nitrogen bond is critical to the subsequent chemistry.

2 Addition of nucleophiles to imines and related species

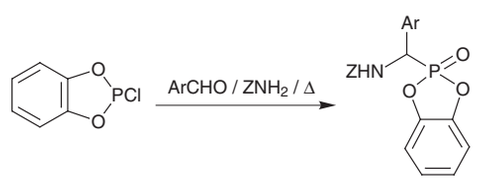
A review of modern variants of the Mannich reaction has been published,[2] and a review of the addition of organometallic reagents to compounds which contain a carbon–nitrogen double bond has appeared.[3] The stereoselective reduction of endocyclic carbon–nitrogen double bonds has also been reviewed.[4]

2.1 Methods giving achiral or racemic products

Scandium triflate has been shown to catalyse the three component condensation of aldehydes, amines and allyl triethylgermane to give homoallylamines. A feature of this reaction is the high selectivity shown by the allylgermane reagent, which adds to the intermediate imine rather than the aldehyde.[5] The same catalyst also induces the formation of homoallylic amines from aldehydes, amines and allyl tributylstannane in water in the presence of micelles formed from sodium dodecylsulfate.[6] The addition of silyl enol ethers to *N*-acyl hydrazones is also catalysed by scandium triflate, and the products can be reduced to β-amino carbonyl compounds by treatment with Raney nickel.[7]

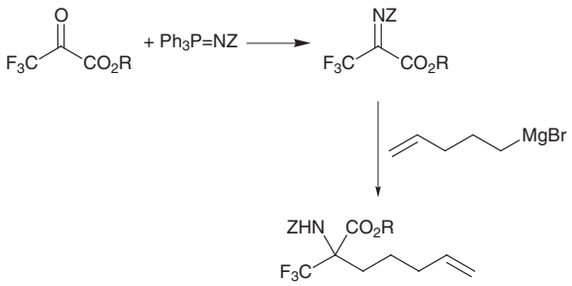
Lithium perchlorate has been found to catalyse the three component condensation between an aldehyde, an amine, and trimethylsilyl cyanide to give α-amino nitriles. If the amine used is α-methylbenzylamine, then the α-amino nitrile is formed with a diastereomeric ratio of approximately 4:1.[8] Lithium perchlorate was also used to catalyse the addition of (trimethylsilyl)diethylamine to *ortho*-trimethylsilyloxybenzaldehyde, giving an aminol which reacted with organometallic reagents to give *N*,*N*-diethyl-*ortho*-alkylaminophenols.[9] The same catalyst was used to form α-aminophosphonates from an aldehyde, an amine, and dimethylphosphinate. If a chiral amine was used, then diastereomeric ratios of between 8:2 and 9:1 were observed.[10] A lithium perchlorate induced stereoselective Mannich reaction has also been developed. Thus, reaction of an aldehyde, an *N*-trimethylsilylamine and an enamine leads to α-alkyl-β-aminoketones with a de greater than 90% in favour of the *anti*-diastereomer.[11]

In aqueous solvents, indium trichloride induces the three component condensation of aldehydes, amines and silyl enol ethers to give β-amino ketones and esters.[12] $Yb(OTf)_3$ catalyses the synthesis of α-amino phosphonates from aldehydes, primary amines, and diethyl phosphite.[13] Tetramethylguanidine also catalyses the addition of dialkyl phosphites to imines, producing α-amino phosphonates.[14] Sodium phosphites add to *N*-acyl-diaryl imines to give α,α-diaryl-α-aminophosphonates. The imines for this reaction can be prepared by the addition of an aryl Grignard reagent to benzonitrile followed by acylation.[15] A synthesis of α-amino-α-arylphosphonates which employs the catechol derivative of phosphorus trichloride has also been developed as shown in Scheme 1.[16]

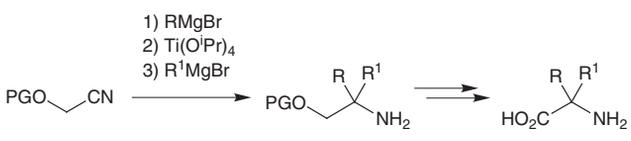


Scheme 1

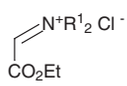
A short synthesis of an α-trifluoromethyl-α-amino acid derivative has been developed as shown in Scheme 2. Thus, trifluoropyruvate esters can be converted into the corresponding imines by treatment with $Ph_3P{=}NZ$, and the addition of pent-4-enylmagnesium bromide to the imine gives the desired amino acid derivative.[17] Reaction of iminium salts **1** with cyclohexanones gives γ-oxo-α-amino esters.[18] A synthesis of α,α-disubstituted α-amino acids has been developed starting from the protected cyanohydrin of formaldehyde (Scheme 3). Addition of a Grignard reagent to the nitrile group generates a



Scheme 2



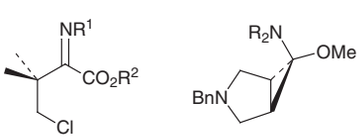
Scheme 3



1

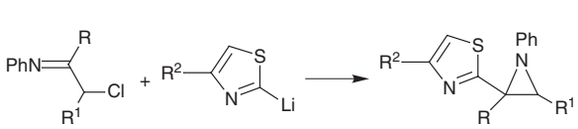
metalloimine species. The subsequent addition of a second Grignard reagent to the metalloimine was found to proceed in very poor yield unless titanium tetraisopropoxide was first added. In this way it was possible to prepare β-amino alcohols which could be oxidized to α,α-disubstituted α-amino acids.[19]

The reduction of imine **2** by sodium cyanoborohydride proceeds with concomitant cyclization to give racemic 3,3-dimethylazetidine-2-carboxylic acid derivatives.[20] Similarly, α,α-dichloro-β-methanesulfonyloxyimines react with hydride or cyanide to give 3,3-dichloroazetidines.[21] α-Chloroimines also react with thiazolium anions to give aziridinyl thiazoles (Scheme 4).[22] 2,5-Dimethoxyfuran derivatives can be ring-opened and converted into bis-oximes as shown in Scheme 5. Subsequent reduction of the oximes provides access to 1,4-diaminobutanes.[23] The use of dibutyltin chloride hydride as a chemoselective reducing agent for the reductive amination of carbonyl compounds has been described.[24] Reduction of 1-amino-1-methoxy-cyclopropane derivatives **3** with either lithium aluminium hydride or DIBAL-H gives the corresponding cyclopropylamines with retention of configuration.[25] Treatment of a ketone with methylamine and titanium tetraisopropoxide gives a titanium complexed aminol which, when treated with sodium borohydride is reduced to an *N*-methylamine.[26] Alternative methodology for reductive amination involving treatment of a ketone with molecular sieves, zinc, isopropanol (propan-2-ol), and acetic acid has been used to prepare bis[di(2-pyridyl)methyl]amine.[27]



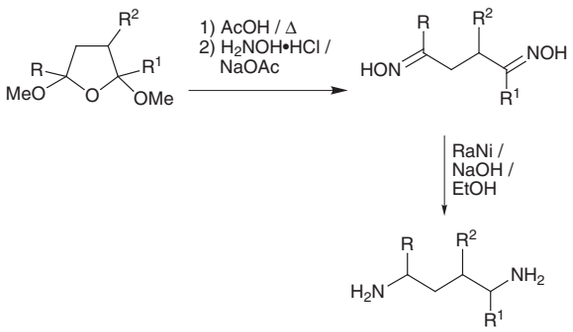
2

3

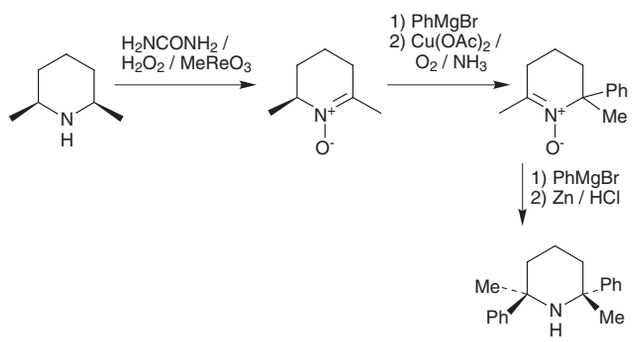


Scheme 4

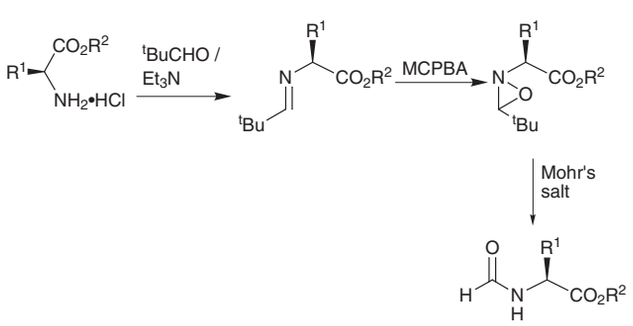
Secondary amines can be oxidized to nitrones, and this has been used as a method for the conversion of 2,6-dimethylpiperidine to *trans*-2,6-dimethyl-2,6-diphenylpiperidine as shown in Scheme 6. The initially racemic amine was subsequently resolved.[28] A novel method for the formylation of amino esters which does not employ a formylating agent has been reported. Thus, treatment of an α-amino ester with pivaldehyde gives the corresponding imine which is oxidized to an oxaziridine by MCPBA. Treatment of the oxaziridine with ammonium ferrous sulfate then gives an *N*-formyl amino ester (Scheme 7).[29]



Scheme 5

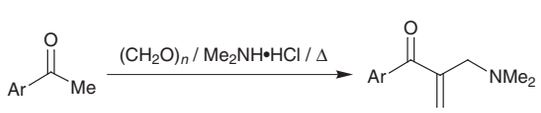


Scheme 6



Scheme 7

A combination of heat and ultrasound can be used to induce the formation of organolithium reagents from benzylic bromides and lithium in the presence of *N*-trimethylsilyl arylimines, thus providing a short synthesis of primary amines.[30] Benzaldehyde reacts with malonic acid and ammonium formate in refluxing ethanol to provide a one-pot synthesis of racemic 3-amino-3-phenylpropionic acid.[31] Treatment of an aryl methyl ketone with formaldehyde and dimethylamine gives 1-aryl-2-(dimethylaminomethyl)prop-2-en-1-ones as shown in Scheme 8.[32]

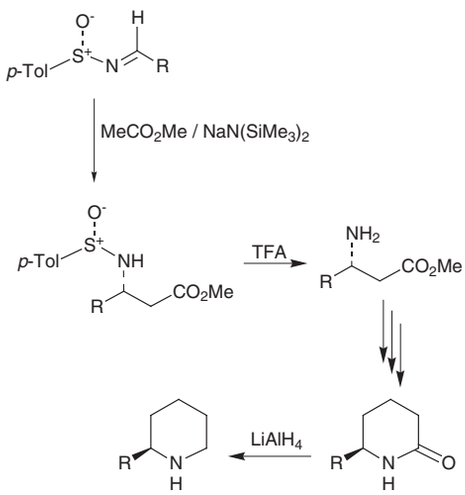


Scheme 8

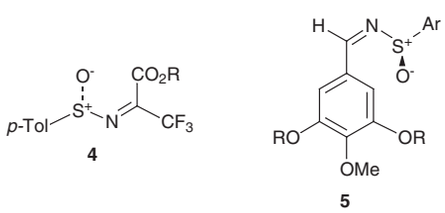
2.2 Methods utilizing a chiral imine or related species

The addition of the sodium enolate of methyl acetate to

enantiomerically pure *N*-sulfinylimines proceeds diastereoselectively as shown in Scheme 9. The *N*-sulfinyl-β-amino esters which are the initial adducts can be manipulated into β-amino esters and hence into enantiomerically pure piperidones and piperidines.[33] Similar chemistry employing the lithium enolate of methyl but-3-enoate and a Lewis acid catalyst was used to prepare α-alkylidene-β-amino esters.[34] The benzylic carbanion of *N*,*N*-diethyl-2-methyl-4-methoxybenzamide also adds diastereoselectively to *N*-sulfinylimines, and this has been used as the key step in an asymmetric synthesis of 3-substituted-1(2*H*)-isoquinolones.[35] Addition of benzyl magnesium chloride to sulfinylimines **4** occurs with 40% de and leads to a non-racemic synthesis of α-trifluoromethylphenylalanine.[36] An asymmetric Strecker reaction based upon the reaction of sulfinylimines **5** with ethyl(isopropoxy)aluminium cyanide was used to prepare (*R*)-(4-methoxy-3,5-dihydroxyphenyl)glycine.[37]

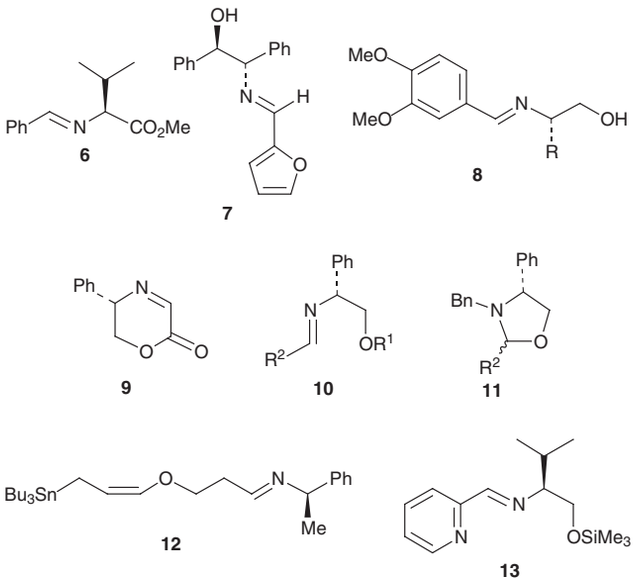


Scheme 9



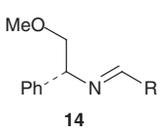
4 **5**

Samarium metal and iodine induce the diastereoselective addition of allyl bromide to imines bearing a chiral auxiliary on the nitrogen atom. A range of chiral auxiliaries were studied, and best results were obtained with the methyl ether of valinol which gave diastereomeric ratios greater than 92 : 2.[38] Lewis acids induce the addition of allylic zinc reagents to the *si*-face of imine **6**, usually with complete asymmetric induction.[39] In the presence of cerium trichloride, allylmagnesium bromide adds to the *re*-face of imine **7**. The chiral auxiliary can subsequently be cleaved by hydrogenolysis using formic acid and Pd/C without reducing the alkene.[40] Aromatic Grignard reagents were found to react preferentially on the *si*-face of β-hydroxy-imines **8**, and the adducts were converted into non-racemic 1,2,3,4-tetrahydroisoquinolin-4-ols.[41] In the presence of boron trifluoride, Grignard reagents add to the *si*-face of cyclic imine **9**. Subsequent hydrogenolysis and acidolysis gives enantiomerically pure α-amino acids.[42] The boron trifluoride induced addition of 1-TBDMS, 1-ethoxyethene to imines **10** occurs preferentially on the *si*-face of the imine. However, use of oxazolidines **11** instead of imine **10** allows the other diastereomer of the β-amino ester adduct to be obtained.[43] In the presence of Lewis acids, imine **12** was found to cyclize to a *trans*-2-vinyl-3-aminotetrahydrofuran derivative.[44] The addition of organometallic reagents to imines is not always straightforward. Thus, whilst secondary and tertiary Grignard reagents add diastereoselectively to the carbon atom of the imine of compound **13** as expected, primary Grignard reagents were found to add to the nitrogen atom of the imine.[45]

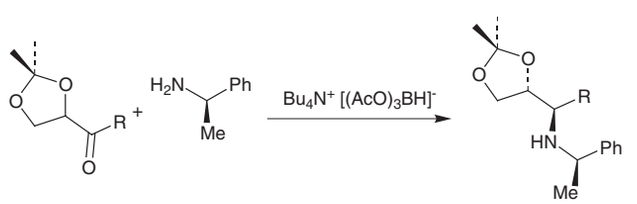


6 **7** **8** **9** **10** **11** **12** **13**

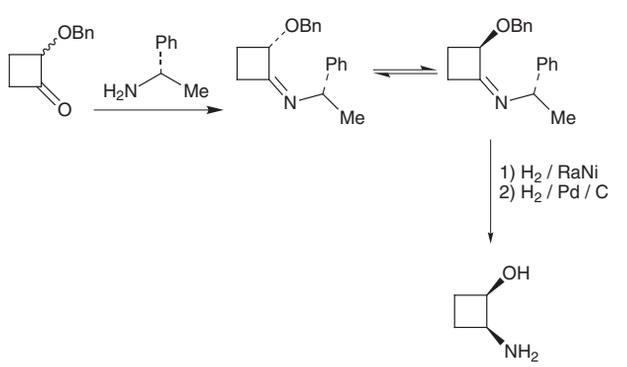
An organic syntheses procedure for the diastereoselective addition of lithium diethylphosphite to imines **14** has been published. Hydrogenation of the adducts provides an enantioselective synthesis of diethyl-α-amino phosphonates.[46] Racemic, acetonide protected, α,β-dihydroxyketones undergo a stereoselective reductive amination with *in situ* racemization of the unreacted imine when treated with α-methylbenzylamine and tetrabutylammonium triacetoxyborohydride (Scheme 10).[47] A similar stereoselective synthesis of *cis*-2-aminocyclobutanol from racemic 2-benzyloxycyclobutanone has been developed as shown in Scheme 11. Thus, condensation of the ketone with α-methylbenzylamine forms an imine and allows the stereoisomers to equilibrate. Hydrogenation and hydrogenolysis then provides enantiomerically pure *cis*-2-aminocyclobutanol.[48]



14

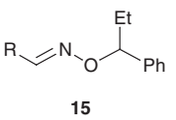


Scheme 10

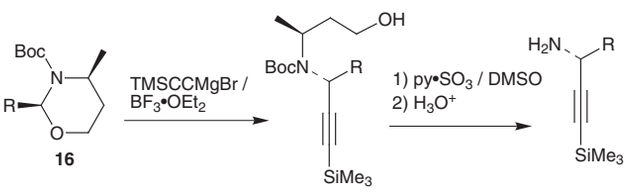


Scheme 11

The boron trifluoride induced diastereoselective addition of allylmagnesium bromide to oximes **15** has been used as the first step in a synthesis of protected β-amino acids. The β-amino acids are obtained (after subsequent manipulation of the hydroxylamine and alkene units) with ee's of 78–98%, and the direction of asymmetric induction is such that the (*R*)-enantiomer of the chiral auxiliary induces formation of the (*R*)-enantiomer of the β-amino acid derivative.[49] Boron trifluoride also induces the addition of trimethylsilylethynylmagnesium bromide to oxazine **16**, leading to enantiomerically pure propargylamines (prop-2-ynylamines) (Scheme 12).[50]



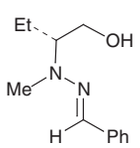
15



16

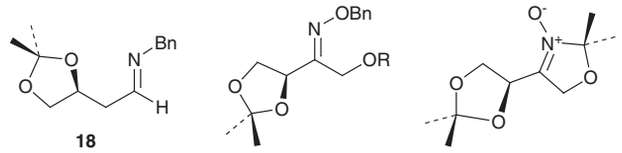
Scheme 12

The addition of Grignard reagents to enantiomerically pure hydrazone **17** occurs diastereoselectively on the *re*-face, and subsequent hydrogenolytic cleavage of the nitrogen–nitrogen bond provides chiral α-phenylalkylamines with ee's of 90–92%.[51] Enders has shown that the addition of organolithium reagents to the SAMP hydrazones derived from ferrocenecarbaldehyde or ferrocene-1,1′-dicarbaldehyde provides an asymmetric synthesis of (1-ferrocenylalkyl)amines and 1,1′-bis-(1-aminoalkyl)ferrocenes.[52] A preparation of α-amino ketones with 13–69% ee from RAMP/SAMP hydrazones has also been reported.[53] The nitrogen–nitrogen bond in hydrazines prepared from RAMP/SAMP hydrazones can be cleaved by treatment with borane·THF.[54]

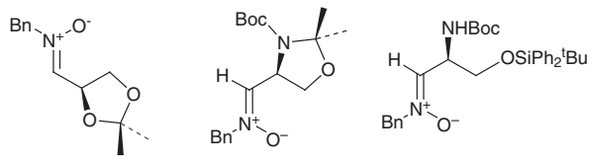


17

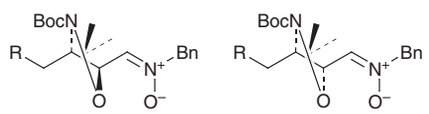
The above examples have all employed a chiral group attached to the nitrogen atom of an imine derivative. However, stereocentres located near the carbon atom of the imine can also be used to control the stereochemistry of the addition reactions of imines. Thus, aluminium trichloride induces the addition of allyltributylstanane to the *si*-face of imine **18** with a diastereoselectivity greater than 99:1. Other allylmetal reagents and Lewis acids can also be used, but with lower diastereoselectivities.[55] Organolithium reagents add selectively to the *si*-face of oximes **19**, giving products with a diastereomeric ratio greater than 95:5.[56] The same group have also investigated the addition of Grignard and organolithium reagents to cyclic nitrone **20**, and again the addition was found to occur preferentially on the *si*-face of the nitrone with diastereomeric ratios between 70:30 and greater than 95:5.[57] The stereochemistry of the addition of Grignard reagents to the closely related nitrone **21** is controlled by the choice of Lewis acid. Thus, zinc bromide favours addition to the *re*-face with a diastereoselectivity greater than 80:20, whilst diethylaluminium chloride induces addition of the Grignard reagent to the *si*-face with better than 70:30 diastereoselectivity. Both adducts could be transformed into β-amino-α-hydroxy esters.[58]



18 **19** **20**



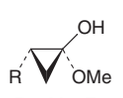
21 **22** **23**



24 **25**

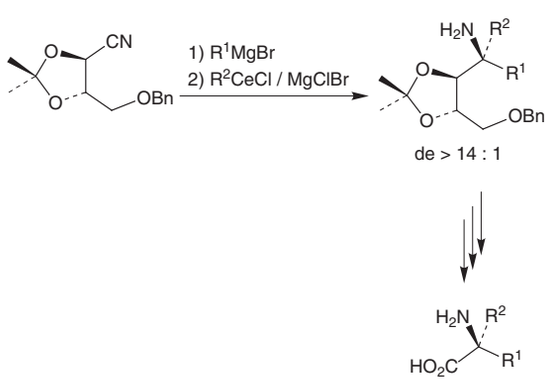
The addition of Grignard reagents and lithium trimethylsilylacetylide occurs on the *re*- and *si*-faces of α-amino nitrones **22** and **23** respectively. The adducts were transformed into α,β-diamino acids.[59] α-Hydroxyaldehydes react with amines and organoboronic acids to provide *anti*-β-amino alcohols with de's greater than 99%.[60] Dondoni *et al.* have investigated the addition of Grignard reagents to nitrones **24** and **25** as well as related compounds. Compounds **24** always reacted on the *si*-face of the nitrone, whilst the addition of Grignard reagents to nitrones **25** could be controlled to give either diastereomer of the adduct by the addition (or not) of diethylaluminium chloride to the reaction mixture. In each case, subsequent hydrogenolysis and acidolysis led to diamino alcohols.[61]

A synthesis of the enantiomerically pure, cyclopropane containing amino acids allo-norcoronamic acids and allocoronamic acids from cyclopropane hemiacetals **26** has been developed. The key step is a diastereoselective Strecker reaction between **26** (which react as synthetic equivalents to the corresponding cyclopropanone), a primary amine and sodium cyanide to give the adduct in which the cyanide is located *trans* to the R-group.[62] The addition of a Grignard reagent to a nitrile generates an iminate, to which a second organometallic reagent can be added. A stereoselective version of this reaction has been developed (Scheme 13), and used in an enantioselective synthesis of α,α-disubstituted amino acids.[63]



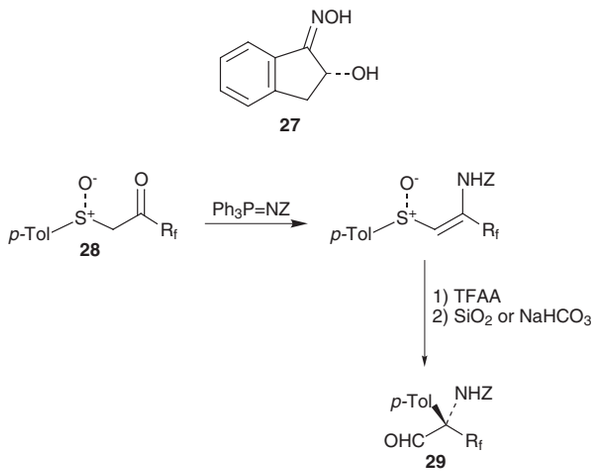
R = Me, Et

26



Scheme 13

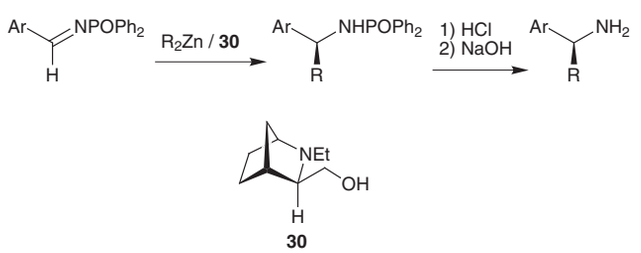
The hydrogenation of oxime **27** which can be prepared from (*S*)-phenylalanine occurs stereoselectively, and provides (1*S*,2*R*)-1-aminoindan-2-ol, a component of the HIV protease inhibitor, indinavir.[64] Enantiomerically pure fluorinated β-keto-sulfoxides **28** can be converted into the corresponding enamines and hence to aldehydes **29** with ee's up to 82% as shown in Scheme 14.[65]



Scheme 14

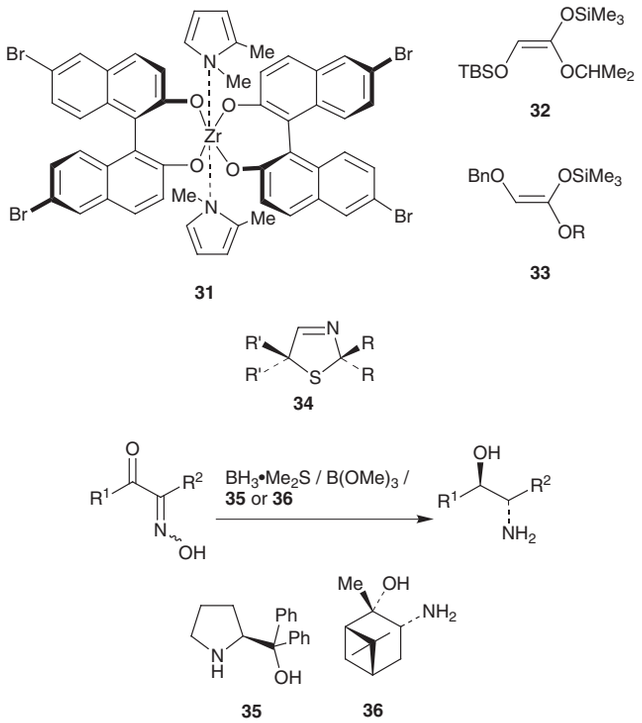
2.3 Methods utilizing a chiral catalyst, ligand, or reagent

The azanorbornane derivative **30** induces the asymmetric addition of organozinc reagents to the *si*-face of *N*-(diphenylphosphoryl)imines, giving the (*S*)-enantiomer of 1-arylalkylamines after cleavage of the nitrogen protecting group (Scheme 15). Unfortunately, it is necessary to use a stoichiometric amount of the chiral ligand to obtain good asymmetric induction.[66] In the presence of zirconium catalyst **31**, *N*-2-hydroxyphenylimines react with silyl ketene acetal **32** to give the *syn*-diastereomer of β-amino alcohols with ee's greater than 90%. The use of silyl ketene acetals **33** in contrast gives the *anti*-diastereomer of β-amino alcohols with ee's greater than 76%.[67] Similar catalysts were found to induce the enantioselective Mannich reaction between *N*-*p*-trifluoromethylbenzoyl hydrazones and silyl ketene acetals, giving β-amino esters with 79–96% ee,[68] and to induce the asymmetric addition of tributyltin cyanide to *N*-(*o*-hydroxyphenyl)imines, giving α-amino nitriles with 74–92% ee.[69] A heterobimetallic complex formed from (*R*)-binaphthol, an alkali metal and a lanthanide metal induces the asymmetric hydrophosphonylation of cyclic imines **34**, thus providing a route to α-amino-phosphonates with between 60 and 97% ee.[70] An asymmetric synthesis of *anti*-β-amino-alcohols from α-oxo-ketoximes has been developed as shown in Scheme 16. The reduction is carried out by borane in the presence of a chiral ligand which is itself a β-amino-alcohol, **35** or **36**, and gives predominantly the *anti*-diastereomer of the product with up to 98% ee.[71]



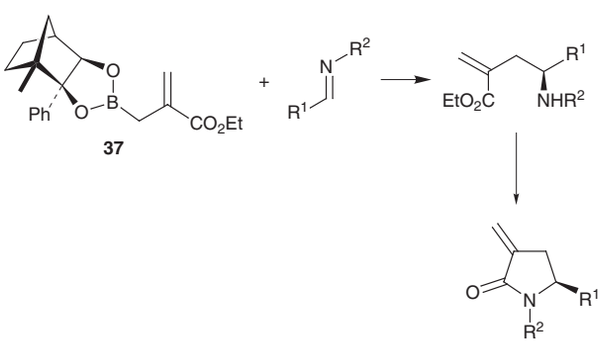
Scheme 15

The enantioselective addition of allylboronate reagent **37** to imines proceeds with greater than 94% ee as shown in Scheme 17. The initial α-methylene-γ-amino esters can be cyclized to

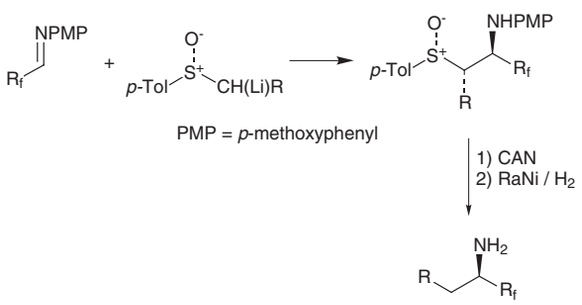


Scheme 16

α-methylene-γ-lactams.[72] The addition of lithiated, chiral sulfoxides to the *N*-*p*-methoxyphenylimines of fluorinated aldehydes occurs diastereoselectively and provides an asymmetric synthesis of α-fluoroalkylamines after cleavage of the nitrogen protecting group and the sulfoxide (Scheme 18).[73] Similar chemistry was also used to prepare enantiomerically pure aziridines by reduction of the β-amino sulfoxides to the corresponding β-amino sulfides, methylation to give β-amino sulfonium salts and base induced cyclization to form the aziridine with elimination of methyl tolyl sulfide.[74]



Scheme 17



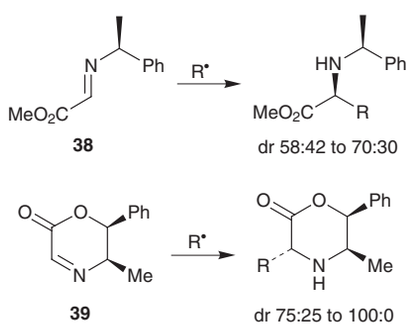
Scheme 18

3 Other syntheses of amines and amides from imines and their derivatives

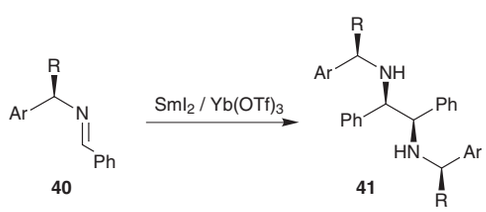
Whilst the addition of carbanions to chiral imines is a well

established process, the corresponding addition of radicals has been less well documented. However, in the presence of triethylborane and boron trifluoride, alkyl iodides react with oximes and hydrazones to give hydroxylamines and hydrazines respectively.[75] Bertrand *et al.* have shown that whilst the addition of radicals to acyclic imine **38** occurs with only low levels of asymmetric induction, the corresponding addition to cyclic imine **39** is completely stereoselective in some cases as shown in Scheme 19.[76] The diastereoselective dimerization of imines **40** to 1,2-diphenyl-1,2-diaminoethanes **41** is brought about by samarium iodide in the presence of $Yb(OTf)_3$ (Scheme 20). The reaction exhibits a preference for the formation of the *syn*-diastereomer of the coupled adduct, with the diastereoselectivity ranging from moderate (2:1) to excellent (>98:2).[77] The same reductive dimerization occurs when an imine is treated with titanium trichloride and lithium.[78] Samarium iodide has also been shown to induce the radical cyclization of ω-formyl-oxime ethers to give *trans*-β-amino-alcohol derivatives as shown in Scheme 21.[79] The cyclization of carbonyl-oxime ethers to *trans*-β-amino-alcohol derivatives can also be achieved using tributyltin hydride.[80] Another radical cyclization of imine derivatives is the reaction between an ω-unsaturated imine and thiophenol to give adducts **42** which can subsequently be converted into cyclic β-amino acids (Scheme 22). The cyclization shows *cis*-selectivity with a maximum *cis*/*trans* ratio of 4:1.[81] The intramolecular cyclization of acyl radicals onto imines takes a different pathway however, cyclization occurring onto the nitrogen atom to give lactams (Scheme 23).[82]

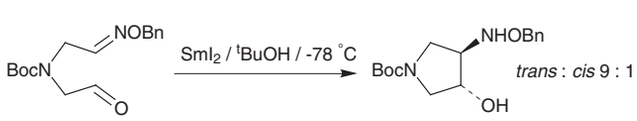
The [2+2]cycloaddition reaction between an imine and a ketene is widely used to prepare β-lactams, and it has been



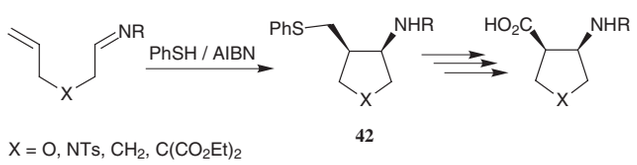
Scheme 19



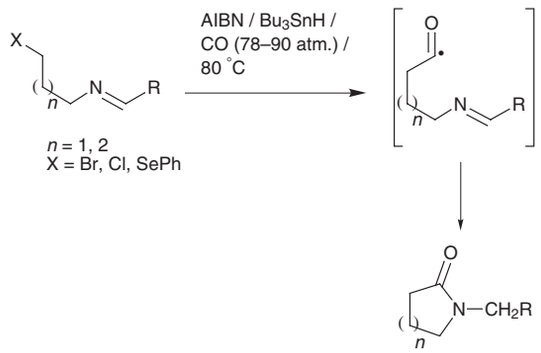
Scheme 20



Scheme 21

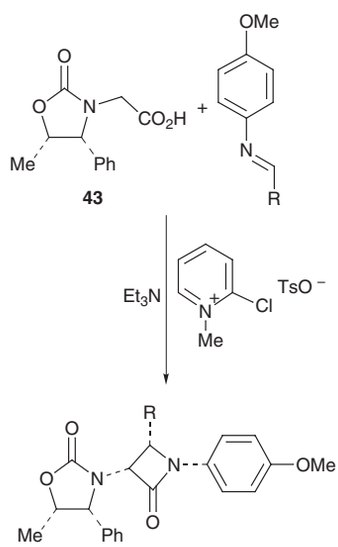


Scheme 22



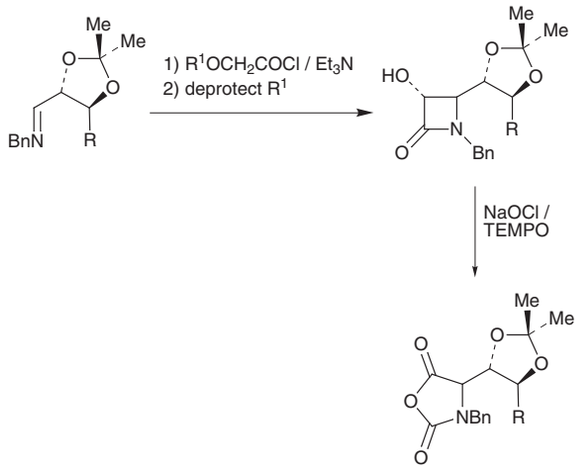
Scheme 23

demonstrated that *N*,*N*-dibenzyloxycarbonylglycidyl chloride can be used as a precursor of amino-ketene in this reaction.[83] The use of α-methyl-benzylimines of methyl glyoxylate in [2+2]cycloaddition reactions with ketenes has also been investigated. However, whilst excellent *cis*-selectivity was observed with some ketenes, only very low levels of asymmetric induction were obtained.[84] By contrast, the [2+2]cycloaddition reaction between *N*-*p*-methoxyphenylimines and the ketene derived from glycine derivative **43** was found to be highly stereoselective (Scheme 24).[85] Enantiomerically pure α-hydroxy-β-lactams can be prepared by a [2+2]cycloaddition reaction (Scheme 25), and can be oxidized to *N*-carboxy-anhydrides which can be used in peptide synthesis. The latest application of this chemistry is the synthesis of polyhydroxylated α-amino acids.[86]

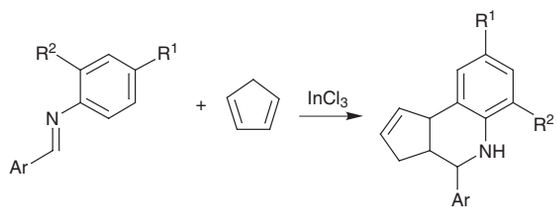


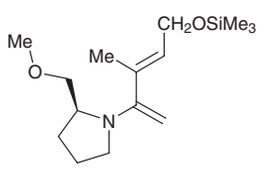
Scheme 24

Indium trichloride catalyses the imino Diels–Alder reaction between *N*-arylimines and cyclopentadiene to give adducts in which the imine has acted as the diene as shown in Scheme 26.[87] A more conventional Diels–Alder reaction occurs between *N*-trimethylsilyl(aryl)imines and diene **44**, leading to pipecolic acid derivatives with ee's greater than 95%.[88] Triphenylphosphine catalyses the [3+2]cycloaddition reaction between imines and buta-2,3-dienoates to give pyrrolidines.[89] [3+2]Cycloaddition reactions involving nitrones continue to be a popular method for the synthesis of amines, an intramolecular example from this year's literature being shown in Scheme 27. After the cycloaddition, the hydrogenolysis can be controlled to cleave either just the nitrogen–oxygen bond, or both the nitrogen–oxygen and benzylic carbon–nitrogen bonds, giving bicyclic and monocyclic amino esters respectively.[90] Another intramolecular [3+2]cycloaddition reaction of ω-unsaturated chiral nitrones has been used to prepare enantio- and diastereomerically pure



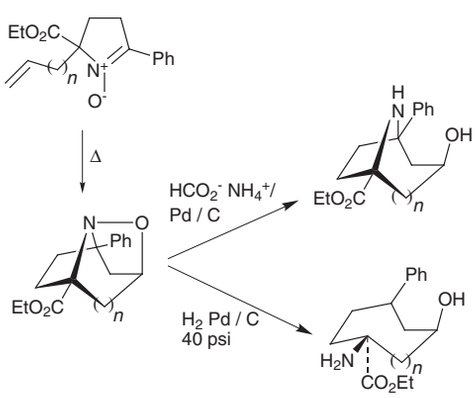
Scheme 25





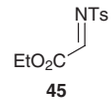
44

Scheme 26

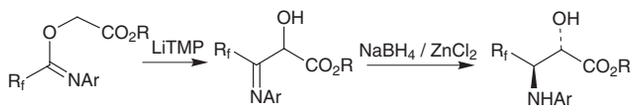


Scheme 27

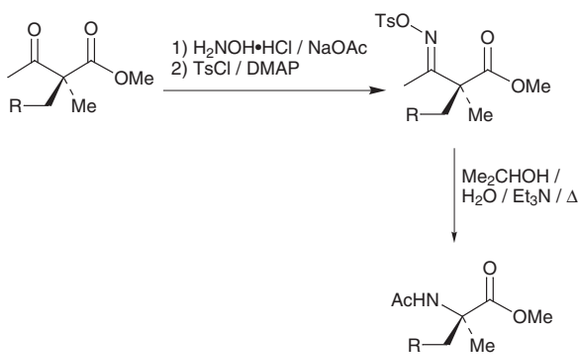
β- and γ-amino alcohols.[91] Nitro-alkenes undergo an intermolecular [4+2]cycloaddition reaction with alkenes to generate a nitrone which can subsequently undergo an intramolecular [3+2]cycloaddition with a suitably located alkene. Reductive cleavage of the nitrogen–oxygen bonds in the resulting polycyclic systems leads to highly functionalized aminocyclopentanes.[92] A catalyst derived from BINAP and copper(I) perchlorate catalyses the enantioselective ene-reaction involving imine **45**, and provides access to γ,δ-unsaturated-α-amino esters with ee's between 85 and 99%.[93] When fluorinated imino ethers are treated with a strong base, they undergo an intramolecular rearrangement to α-hydroxy-imines, and subsequent reduction of the imine leads to *anti*-β-amino-alcohols as shown in Scheme 28.[94] A synthesis of chiral, α,α-disubstituted α-amino acids from α,α-disubstituted acetoacetate derivatives in which the key step is a Beckmann rearrangement has been reported as shown in Scheme 29.[95]



45

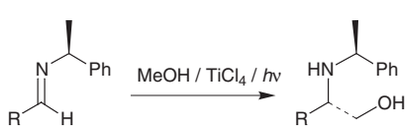


Scheme 28

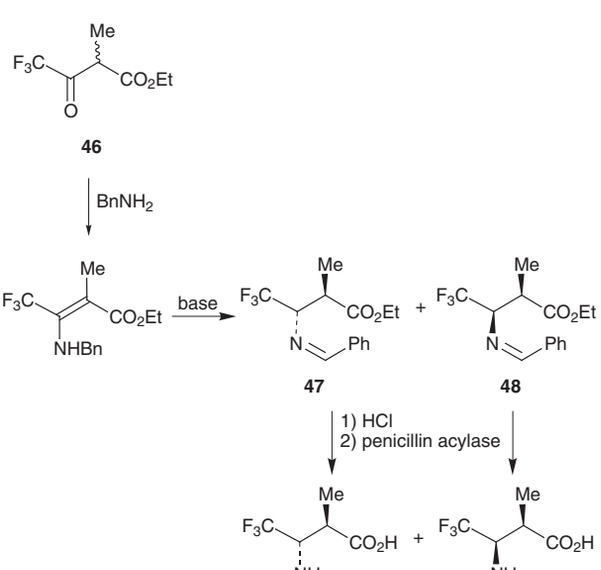


Scheme 29

Imines derived from α-methylbenzylamine react with methanol in the presence of titanium tetrachloride and light to give β-amino-alcohols as shown in Scheme 30. The products are formed with a diastereomeric ratio of between 1:1 and 4:1.[96] Treatment of β-ketoester **46** with benzylamine gives initially an enamine which can be isomerized to imine **47** or **48** by treatment with base (Scheme 31). Use of triethylamine as the base favours (70:30) formation of the *anti*-diastereomer **47**, whilst DBU leads mainly (70:30) to *syn*-diastereomer **48**. Treatment of either **47** or **48** with hydrochloric acid provides the corresponding racemic α-methyl-β-amino ester which can be resolved by penicillin acylase.[97]



Scheme 30



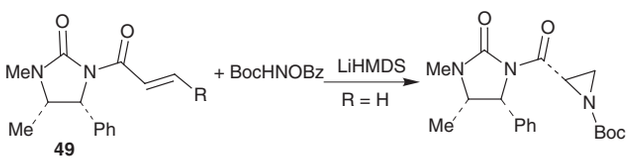
Scheme 31

4 Aziridine chemistry

4.1 Formation of aziridines

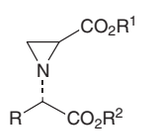
This section covers reports of new methods for the synthesis of aziridines. Papers which prepare an aziridine by established procedures and then ring-open the aziridine to give amines or amides are included in the following section. The synthesis of aziridines was also covered in a review of the synthesis of saturated nitrogen heterocycles published in 1998.[98]

The readily available chiral imide **49** (R = H) reacts diastereoselectively with *N*-Boc-*O*-benzoylhydroxylamine in the presence of lithium hexamethyldisilazide to form an aziridine carboxylic acid derivative as shown in Scheme 32.[99] Alternatively, imides **49** react with *O*-benzylhydroxylamine in the presence of a Lewis acid to give enantio- and diastereomerically pure *trans*-aziridines. The structure of the Lewis acid determines the absolute configuration of the aziridine with dimethylaluminium chloride and titanium tetrachloride giving opposite enantiomers of the product.[100] Reaction of an α-amino ester with an α-bromoacrylate leads to *N*-azirinyl esters **50**. Peptide chains can then be attached to the ester groups, or a peptide chain can be prepositioned on the α-bromoacrylate to give parallel β-sheet mimicking peptidomimetics.[101]



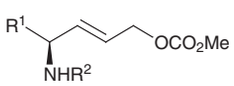
49

Scheme 32

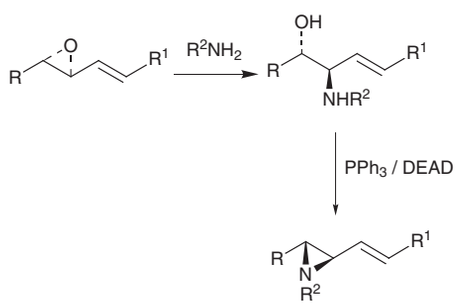


50

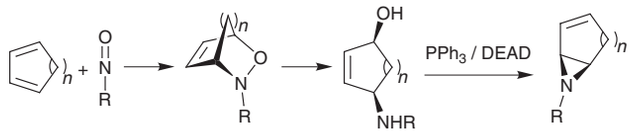
A synthesis of *cis*-2-alkyl-3-vinylaziridines by cyclization of substrates **51** in the presence of $Pd(PPh_3)_4$ has been reported.[102] Vinylaziridines can also be prepared from vinylepoxides by ring opening of the epoxide by a primary amine followed by aziridine formation under Mitsunobu conditions (Scheme 33).[103] The Diels–Alder reaction between a cyclic diene and a nitroso compound generates a six-membered heterocycle which after reductive cleavage of the nitrogen–oxygen bond gives a *cis*-4-amino-2,3-didehydrocyclic-alcohol (Scheme 34). Subsequent reaction with triphenylphosphine and diethyl azodicarboxylate forms a vinylaziridine by an S_N2' reaction.[104]



51

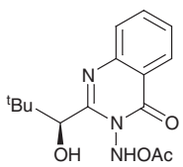


Scheme 33



Scheme 34

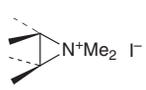
Treatment of a diazoester with an imine in the presence of a catalytic amount (10 mol%) of $Yb(OTf)_3$ results in the generation of a carbenoid and its cycloaddition with the imine to form an aziridine. It is also possible to generate the imine *in situ* from an aldehyde and an amine.[105] The combination of reagent **52** and titanium tetra-*tert*-butoxide diastereoselectively aziridinates a wide range of alkenes. In some cases (*e.g.* styrene, butadiene, and indene) complete diastereoselection is observed though some other alkenes react with a lower degree of asymmetric induction.[106]



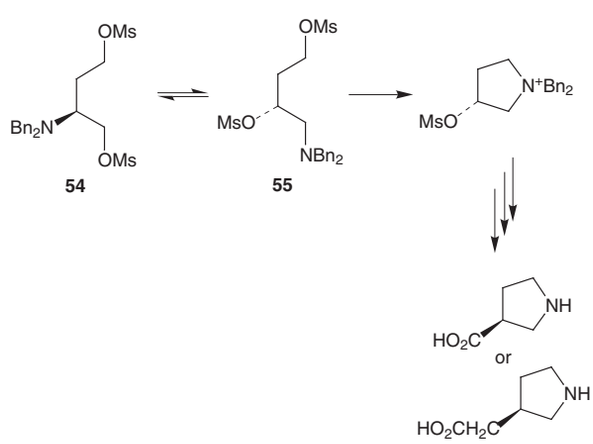
52

4.2 Formation of amines and amides by the ring opening of aziridines or aziridinium ions

The first synthesis of the highly hindered bis-tertiary amine *N*,*N*,*N*′,*N*′-tetramethyl-2,3-dimethylbutane-2,3-diamine has been achieved by reaction of aziridinium ion **53** with dimethylamine.[107] More generally, the reaction of enantiomerically pure styrene oxide with pyrrolidine gives a β-amino-alcohol which when treated with methanesulfonyl chloride and base forms an aziridinium ion with inversion of configuration at the benzylic stereocentre. Subsequent reaction of the aziridinium ion with a primary amine occurs at the benzylic position, again with inversion of configuration, and leads to chiral 1,2-diamines.[108] Bis-mesylate **54**, which can be obtained from (*S*)-aspartic acid, equilibrates *via* an aziridinium ion with the regioisomeric bis-mesylate **55**. Compound **55** cyclizes to a pyrrolidinium ion which can be manipulated to give β-proline and homo-β-proline (Scheme 35).[109]



53

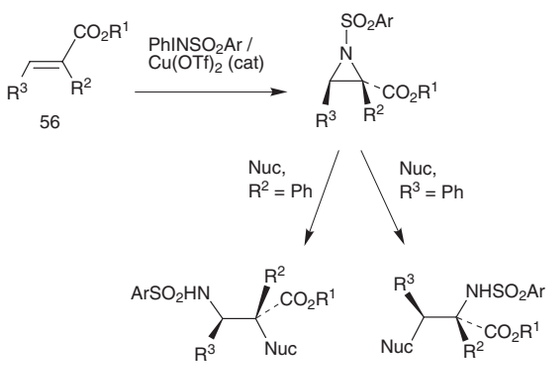


54 **55**

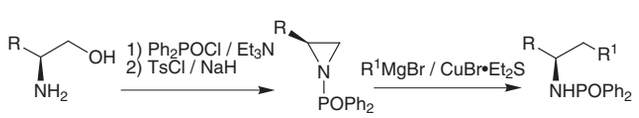
Scheme 35

Treatment of acrylate esters **56**, in which either R^2 or R^3 is a phenyl group, with $PhINSO_2Ar$ in the presence of a copper triflate catalyst results in the formation of an aziridine (Scheme

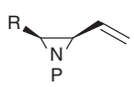
36). Reaction of the aziridine with a range of nucleophiles gives the ring-opened product resulting from cleavage of the benzylic carbon–nitrogen bond, thus allowing both α- and β-amino acids to be prepared.[110] Enantiomerically pure β-amino-alcohols can be cyclized to *N*-diphenylphosphorylaziridines which react with Grignard reagents in the presence of copper(I) bromide to give amines as shown in Scheme 37.[111] *cis*-Vinylaziridines **57** react with organocopper reagents by an S_N2' mechanism to give allylic amines.[112] Treatment of *N*-tosyl-dihydropyrrolidine with manganese salen complex **58** and trifluoroacetic anhydride forms an aziridine which can be ring opened by methanol to give a *trans*-2-methoxy-3-trifluoro-acetamidopyrrolidine as shown in Scheme 38.[113] Aziridine aldehyde **59** has been shown to be a versatile starting material for the synthesis of stereoisomerically pure amino alcohols (Scheme 39). Thus, addition of organolithium reagents to the aldehyde is stereocontrolled, and subsequent ring-opening of the aziridine ring by acetate occurs regiospecifically. If desired, a new aziridine can be formed under standard conditions and hydrogenolysis then occurs regiospecifically to give a β-amino acetate.[114] Aziridine **60** which can be prepared from (*S*)-serine is ring opened by organometallic reagents in the presence of copper salts, regiospecifically at the less hindered carbon–nitrogen bond. Subsequent deprotection and oxidation provides (*R*)-α-amino acids.[115] The hydrogenolysis or addition of organocuprates to aziridines **61** also occurs regiospecifically, giving β-amino alcohols.[116] A synthesis of pyrrolizidines by a radical cascade reaction starting from bromomethylaziridines has been developed as illustrated in Scheme 40.[117]



Scheme 36



Scheme 37

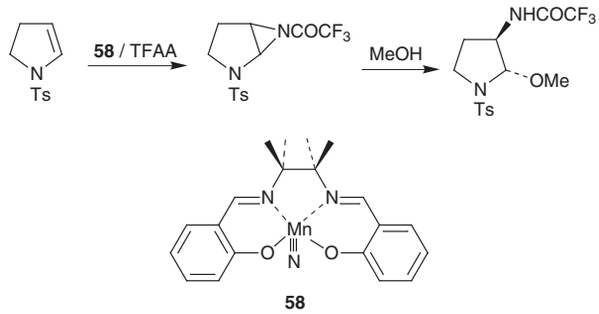


57

5 Synthesis of amines and amides by Michael additions

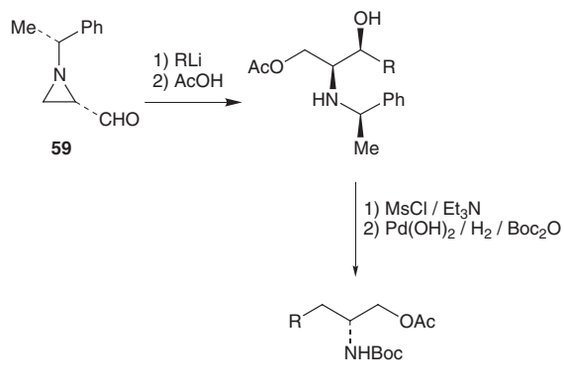
Indium trichloride has been shown to catalyse the Michael addition of amines to α,β-unsaturated carbonyl compounds in aqueous solvent systems.[118] α,β-Unsaturated esters react with phenylselenium chloride followed by a primary amine to give α-phenylseleno-β-amino esters which can subsequently be cyclized to give β-lactams.[119] Acid chlorides **62** react with primary amines to give β-lactams in which the phenyl and arenesulfonyl groups are *trans* to one another.[120]

Davies and Ichihara have continued to develop the asymmetric addition of enantiomerically pure amines to α,β-unsaturated esters as an approach to the asymmetric synthesis

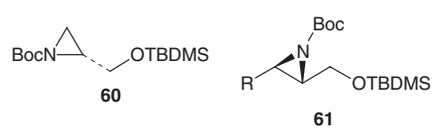


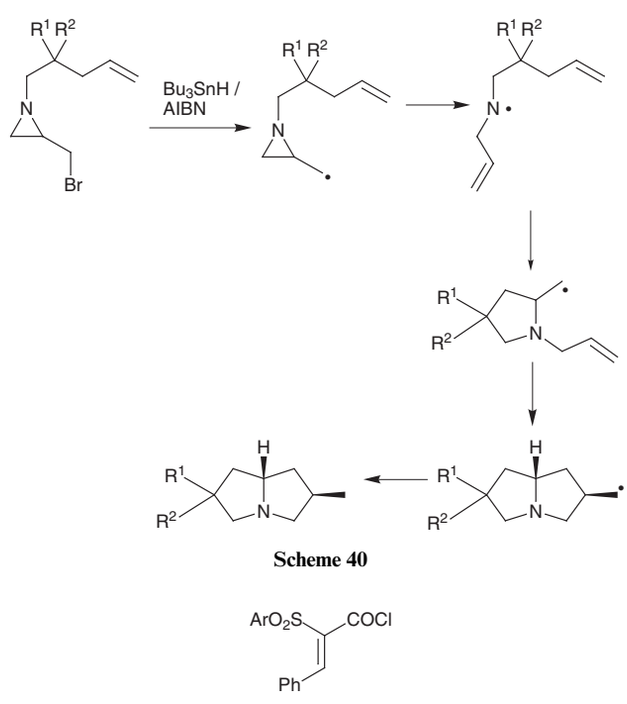
58

Scheme 38



Scheme 39

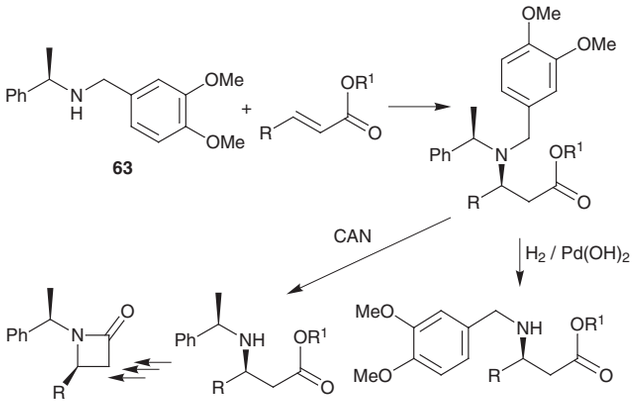




Scheme 40

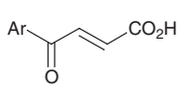
62

of β-amino acids and related compounds. Thus, the use of secondary amine **63** as the chiral amine has been reported as shown in Scheme 41. After the asymmetric Michael addition, either protecting group can be removed from the amine using ceric ammonium nitrate (to cleave the 3,4-dimethoxybenzyl group) or hydrogenolysis (to remove the α-methylbenzyl group), and in the former case the products can be cyclized to β-lactams.[121] It has been shown that in the presence of copper



Scheme 41

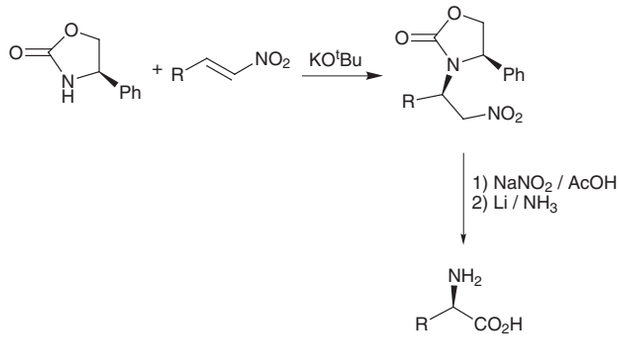
iodide, the lithium salt of α-methylbenzyl(trimethyl)silylamine can be used as the chiral amine in Michael additions to α,β-unsaturated or γ-hydroxy-α,β-unsaturated esters. The resulting enolates can be transmetallated to titanium enolates and subsequently undergo diastereoselective alkylation leading to *anti*-α-alkylated-β-amino esters.[122] The Davies methodology has also been employed in a synthesis of polyfunctional pyrrolidinones.[123] Reaction of aryl ketones **64** with (*S*)-α-methylbenzylamine leads to (*S*)-α-amino acids. The Michael addition is not very diastereoselective, but it is reversible and the (*S*,*S*)-diastereomer of the product selectively crystallizes from the reaction mixture allowing high yields of diastereomerically pure products to be obtained.[124] Warren *et al.* have shown that the lithium salt of α-methylbenzyl(benzyl)amine also undergoes diastereoselective addition to vinyl phosphine oxides, and that the resulting phosphorus stabilized carbanion can be trapped with trimethylsilyl chloride to give enantio- and diastereomerically pure α-trimethylsilyl-β-amino-phosphine oxides.[125] An alternative to the use of a chiral amine in these Michael additions has also been reported. Complexation of an achiral amine to a transition metal in the presence of chiral ligands forms chiral metal amine complexes which undergo Michael additions to achiral α,β-unsaturated imides to give adducts with up to 71% ee.[126]



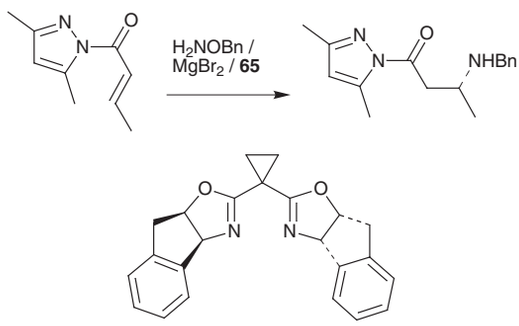
64

An asymmetric synthesis of α-amino acids involving the Michael addition of a chiral amine derivative to a nitroalkene has been developed as shown in Scheme 42. After the Michael addition, the β-amino-nitroalkane is oxidatively degraded to the corresponding α-amino acid.[127] Alternatively, the addition of achiral nitrogen anions (potassium phthalimide or potassium tosamide) to chiral α-thio-nitroalkenes bearing a camphor derived chiral auxiliary on the sulfur atom has been investigated. After oxidation of the initial adducts, thioester derivatives of α-amino acids were obtained with de's of 0 to 71%.[128] Enders *et al.* have shown that *N*-formylnorephedrine will undergo a diastereoselective (94–96% de) Michael addition to nitroalkenes. Reduction of the adducts leads to β-amino alcohols, or further manipulation can give 2-amino-1,4-diols.[129] The above processes all employ a stoichiometric amount of the chiral amine, however, the complex formed between ligand **65** and magnesium bromide catalyses the asymmetric addition of *O*-benzylhydroxylamine to an unsaturated amide with 97% ee as shown in Scheme 43.[130]

Hruby and co-workers have developed an asymmetric synthesis of β,β-disubstituted-α-amino acids based on the Michael addition of organometallic reagents to β-substituted-α,β-unsaturated chiral-imides, followed by formation of an enolate



Scheme 42

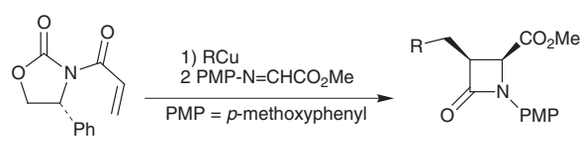


65

Scheme 43

α to the imide and trapping of this with an electrophilic nitrogen source. Full details of this chemistry have been given in previous reviews.[1] The methodology has recently been applied to the synthesis of 2-amino-3,3′-diarylpropionic acids.[131]

An asymmetric β-lactam synthesis has been developed (Scheme 44) in which an organocopper reagent undergoes a Michael addition to a chiral imide, the resulting enolate is trapped by an imine, and cyclization eliminates the chiral auxiliary. The reaction gives predominantly the *cis*-isomer of the β-lactam, with ee's greater than 94%.[132] A synthesis of enantiomerically pure, multiply substituted piperidines in which the nitrogen atom is introduced by a tandem Michael addition and iminium ion formation has been developed as illustrated in Scheme 45. If the chiral auxiliary is replaced by a methyl ester, then it is possible to first form an imine between the aldehyde and a primary amine. Subsequent reaction of the imine with trimethylsilyl cyanide forms an α-amino nitrile which undergoes an intramolecular Michael addition to give α-cyanopiperidines.[133]

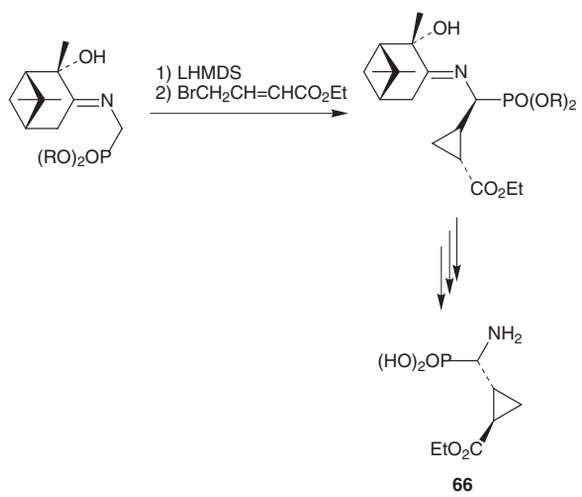


Scheme 44

Scheme 45

The Michael addition of malononitrile derivatives to *N*-Boc-didehydroalanine methyl ester has been used to prepare racemic γ-cyano-glutamates, which can be resolved with

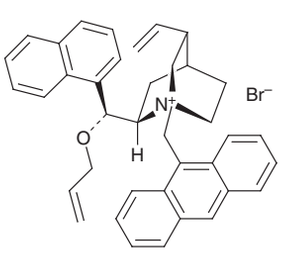
α-chymotrypsin and cyclized to γ-cyano-pyroglutamates.[134] An alternative approach to the synthesis of α-substituted, α,β-disubstituted, and α-substituted, β,γ-didehydro-pyroglutamates involves the Michael addition of an *N*-benzylidene amino ester (or nitrile) enolate onto ethyl propargylate followed by acid induced lactamization.[135] An asymmetric synthesis of the conformationally constrained phosphono-glutamic acid derivative **66** has been reported (Scheme 46). The synthesis relies upon the Michael addition of a chiral phosphonoglycine derivative to ethyl 4-bromobut-2-enoate followed by intramolecular cyclization of the resulting enolate.[136] Organozinc reagents undergo a Michael addition to di-*tert*-butyldiazodicarboxylate to give hydrazines.[137]



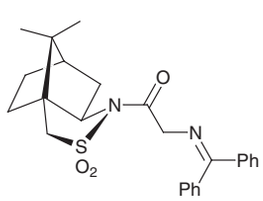
66

Scheme 46

Corey and co-workers have shown that in combination with caesium hydroxide, ammonium salt **67** functions as a chiral phase transfer catalyst for the alkylation of *tert*-butyl *N*-benzylidene glycinate. In addition to simple alkylations (which can lead to cyclic amino acids), the Michael addition of the glycine enolate onto acrylate derivatives is also catalysed, leading to functionalized amino acids with ee's in excess of 95%.[138] The same chemistry can be carried out using a chiral auxiliary to control the stereochemistry of the stereocentre formed when a glycine enolate is alkylated. Thus, reaction of glycine derivative **68** with potassium carbonate and tetrabutylammonium bromide followed by addition of an alkyl bromide or Michael acceptor results in the formation of (*S*)-amino acids after hydrolysis of the chiral auxiliary and benzylidene groups.[139]



67

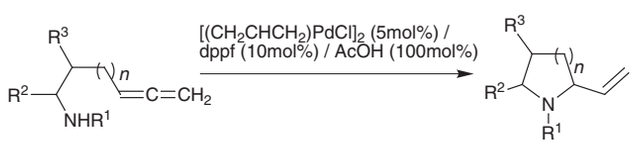


68

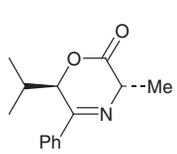
6 Transition metal mediated processes

Although allylic substitution reactions are usually carried out under palladium catalysis, nickel complexes can also catalyse this reaction. The reaction of a range of allylic esters and ethers with diethylamine to give allylic diethylamines has been investigated using a variety of nickel complexes, and the best results were obtained with Ni(dppb).[140] Nickel(0) complexes (*e.g.* the bipyridyl complex) have been shown to catalyse the amination of aryl chlorides in the presence of sodium hydride and sodium *tert*-amyloxide, providing a versatile synthesis of aromatic amines.[141] The same chemistry can be carried out using a variety of palladium(0) catalysts,[142] and has been applied to more complicated systems. Thus, reaction of di-, tri-, or tetrabrominated aromatic compounds with piperidine derivatives in the presence of Pd(0) and sodium *tert*-butoxide results in complete substitution of all of the bromine atoms present in the aromatic compound.[143] If both bromine and chlorine substituents are present on the aromatic compound, then it is possible to selectively displace the bromine atoms.[144] A synthesis of both enantiomers of hydroxyitraconazole which employed this chemistry has also been reported.[145] The amine component is not restricted to piperidine derivatives, diarylamines can be utilized to prepare triarylamines,[146] and reaction of enantiomerically pure α- or β-amino esters with aryl halides in the presence of a palladium(0) catalyst, copper iodide and potassium carbonate gives *N*-aryl-α- or β-amino esters, the latter of which can be converted into chiral 1,2,3,4-tetrahydro-4-oxo-2-alkylquinolines.[147] Whilst the palladium catalysed displacement of aryl halides by amines works well with a variety of primary and secondary amines, it fails with ammonia. However, it has been shown that mono- or di-allylamine can be used as an ammonia equivalent in these reactions.[148] The use of an alternative ammonia equivalent, the so-called 'titanium–nitrogen fixation complexes', formed from titanium tetrahalide, nitrogen, lithium and trimethylsilyl chloride has also been reported. Primary amines are the main products of the reaction, with diarylamines usually being only a very minor by-product.[149]

The palladium catalysed intramolecular hydroamination of allenes has been used to prepare substituted pyrrolidines and piperidines as shown in Scheme 47. The palladium catalyst is prepared *in situ* from bis(allylpalladium chloride) and 1,1′-diphenylphosphinoferrocene (dppf).[150] The cyclization of lactams onto allenes by a Pd(0) catalyst in the presence of iodobenzene has also been reported.[151] Larock *et al*. have shown that seven-nine membered ring nitrogen-containing heterocycles can be prepared by the palladium induced coupling of an allene and an ω-amino-vinyliodide.[152] The intermolecular aminocarbonylation of allenes is catalysed by $Pd(PPh_3)_4$ in the presence of acetic acid to give α,β-didehydroamides.[153] A combination of palladium and copper (in the form of $PdCl_2$ and $CuCl_2$ respectively) was used to catalyse the intramolecular aminocarbonylation of 5-aminocyclooctatetraene derivatives, giving [1.2.4]- or [1.3.3]bicycloamines depending upon the nature of the amine protecting group.[154]



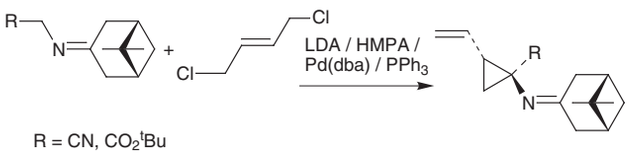
Scheme 47



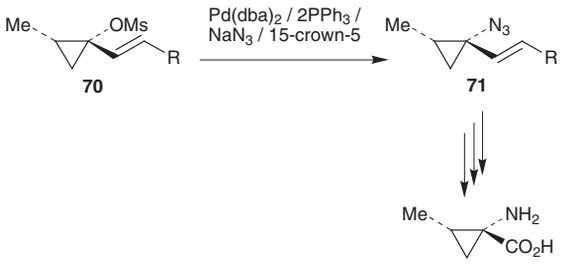
69

The chiral alanine derivative **69** can be alkylated to give α-methyl-α-amino acids under conventional basic conditions (K_2CO_3/tetrabutylammonium bromide/R–X) or by employing palladium catalysis ($Pd(OAc)_2/PPh_3/ROCO_2Et$). In both cases, the alkyl group is added to the *si*-face of compound **69**.[155] A palladium catalyst has been used to catalyse the amidocarbonylation reaction between acetamide, an aromatic aldehyde, and carbon monoxide in the presence of lithium bromide, sulfuric acid and *N*-methylpiperidine, giving racemic *N*-acylarylglycines.[156] Reaction of 2-iodoindole derivatives with primary

or secondary amines and carbon monoxide in the presence of tributylamine and a catalytic amount of $PdCl_2(PPh_3)_2$ at 115 °C results in the formation of indole-2-carboxamides.[157] Palladium catalysed processes have also been utilized in asymmetric syntheses of 1-aminocyclopropanecarboxylic acid derivatives. Thus, in the presence of a palladium(0) catalyst, chiral glycine enolate equivalents underwent both S_N2 and S_N2' reactions when treated with 1,4-dichlorobut-2-ene as shown in Scheme 48.[158] Alternatively, enantiomerically pure methanesulfonates **70** react with sodium azide in the presence of a palladium(0) catalyst to give azides **71**, no isomeric products being detected. Subsequent manipulations of the azide and alkene units led to (1*R*,2*S*)-norcoronamic acid (1-amino-2-methylcyclopropanecarboxylic acid) as shown in Scheme 49.[159]



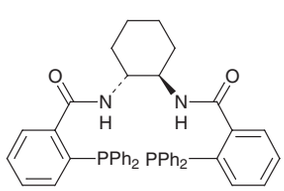
Scheme 48



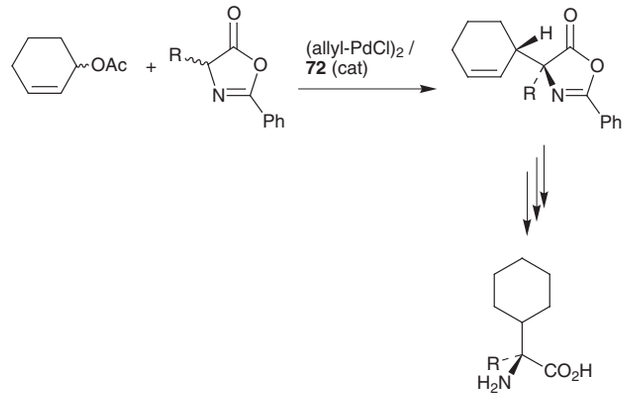
Scheme 49

Palladium catalysts are well known to induce the substitution of allylic acetates (and other leaving groups) by other nucleophiles, and Katritzky *et al.* have shown that this chemistry can be used to prepare allylic amines from *N*-allyl-benzotriazoles.[160] Trost and co-workers have shown that in the presence of ligand **72**, allylpalladium chloride and triethylamine, racemic allylic acetates react with enantiomerically pure amino esters to give *N*-alkylated amino esters with diastereomeric ratios greater than 13:1. The stereochemistry of the product is determined by the stereochemistry of ligand **72** rather than the stereochemistry of the amino ester.[161] This chemistry has been extended to allow the asymmetric synthesis of α-substituted α-amino acids. Thus, reaction of an allylic acetate with an oxazolidinone in the presence of catalytic allylpalladium chloride and ligand **72** results in enantioselective alkylation of the oxazolidinone and leads to the desired amino acids after subsequent hydrolysis, one example being shown in Scheme 50.[162] Asymmetric, palladium catalysed allylic substitution was also used to desymmetrize diacetate **73** as shown in Scheme 51. A range of chiral ligands was screened, but the best result (89% ee) was obtained with ligand **74**.[163] A palladium/BINAP catalyst was employed to induce the rearrangement of allylic sulfoximines to γ-amino-α,β-unsaturated ketones with ee's between 20 and 62% (absolute configuration unknown) as shown in Scheme 52.[164]

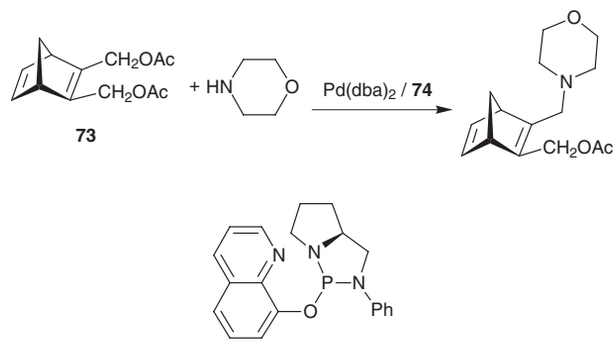
Aromatic nitro compounds undergo reduction followed by reductive carbonylative alkylation when they are treated with



72

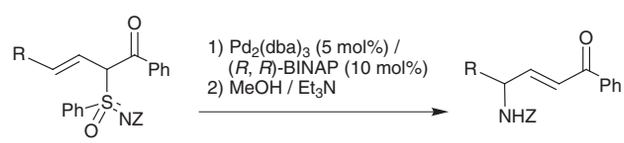


Scheme 50



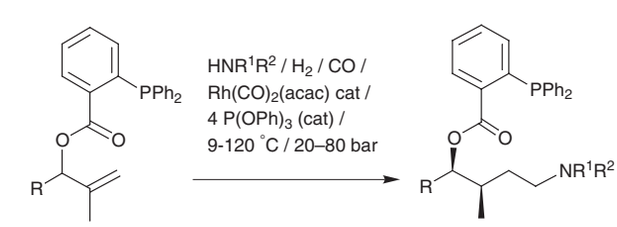
74

Scheme 51



Scheme 52

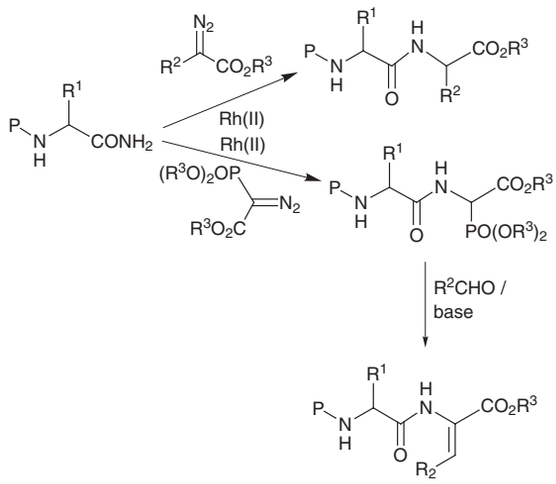
an alkene, carbon monoxide and hydrogen in the presence of $[Rh(COD)Cl]_2$ (COD = cyclooctadiene). By controlling the reaction conditions, it is possible to obtain either a secondary amine resulting from monocarbonylation and alkylation or a tertiary amine derived from dicarbonylation and alkylation of the primary amine intermediate.[165] In a closely related reaction, rhodium catalyses the hydroaminomethylation of alkenes and α,ω-dienes by secondary amines in the presence of hydrogen and carbon monoxide.[166] An unusual, diastereoselective example of this reaction has been reported (Scheme 53), in which the alkene substrate also contains a phosphine group capable of coordinating to the rhodium and thus directing the stereochemistry of the addition reaction.[167] An intramolecular, rhodium catalysed, hydroaminomethylation of alkenes has also been reported, and was used to prepare functionalized piperidines.[168]



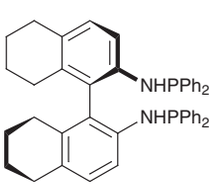
Scheme 53

In the presence of a catalytic amount of $RhH(CO)(PPh_3)_3$, amides are reduced to amines by treatment with diphenylsilane.[169] An unusual synthesis of peptides has been developed

in which a carbene generated from a diazo-compound by treatment with a rhodium salt is inserted into a pre-formed primary amide bond. The methodology can be adapted to prepare peptides containing α,β-didehydroamino acids as shown in Scheme 54.[170] An asymmetric synthesis of β-lactams in which a chiral rhodium catalyst is used to catalyse the intramolecular insertion of a diazoketone derived carbene into a C–H bond has also been developed. Ee's greater than 80% are obtained during the cyclization step.[171] The combination of rhodium and ligand **75**, generates an effective catalyst for the asymmetric hydrogenation of *N*-(1-arylethenyl)acetamide, giving *N*-(1-arylethyl)acetamides with greater than 90% ee.[172] In the presence of [Rh–(*R*,*R*)-duphos], *N*-acetyl α,β,γ,δ-tetradehydroamino esters are regio- and enantioselectively hydrogenated to γ,δ-didehydroamino acids with ee's greater than 86%.[173]

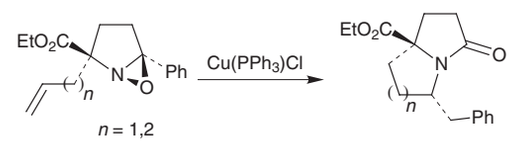


Scheme 54

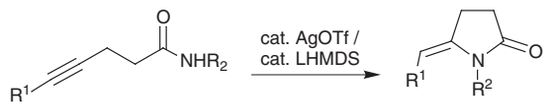


75

A copper(I) salt has been used to induce the radical rearrangement of alkenyl oxaziridines to pyrrolidines and piperidines as illustrated in Scheme 55.[174] A number of other copper catalysed reactions were discussed in the preceding section of this review. The silver benzoate induced Wolff rearrangement of *N*-tosyl-α-amino diazoketones in methanol has been reported to give a mixture of the corresponding *N*-tosyl β-lactam and *N*-tosyl-β-amino ester, a result which is in contrast to previous results with α-amino diazoketones bearing other protecting groups (Boc, Z, *etc*.). The ratio of the two products depends upon the structure of the amino acid sidechain, with glycine giving only the β-lactam and phenylalanine giving predominantly the β-amino ester. The corresponding Wolff rearrangement of *N*-tosyl-β-amino diazoketones again gave a mixture of γ-amino ester and γ-lactam products when conducted in THF, but gave only the γ-lactams when carried out in methanol.[175] As part of Seebach and co-workers' ongoing investigation of the chemistry of β-peptides, the Wolff rearrangement of diazoketones derived from the functionalized α-amino acids serine, aspartic acid and glutamic acid has been reported.[176] The Wolff rearrangement of diazoketones derived from Fmoc protected α-amino acids has also been described.[177] A catalytic amount of silver triflate and LHMDS (ratio 1:2) was found to induce the cyclization of β-alkynylpropanamides to γ-alkylidene-γ-butyrolactams



Scheme 55



Scheme 56

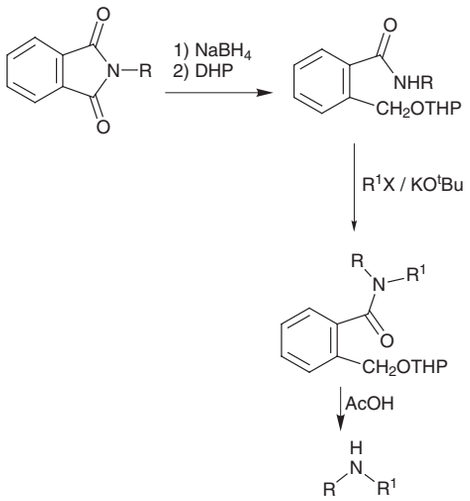
(Scheme 56). The products are formed exclusively as the *Z*-isomer.[178]

Iron(III) chloride catalyses the reduction of azides to primary amines by *N*,*N*-dimethylhydrazine.[179] The direct conversion of 2-naphthylethene to *N*-Z-(*R*)-2-naphthyl-2-aminoethanol with 91% ee has been achieved by a Sharpless asymmetric aminohydroxylation using Z–N(Cl)Na as the aminating agent. When heated, the product is converted into an oxazolidinone which can be used as a chiral auxiliary in asymmetric enolate chemistry.[180] The same chemistry has been applied to a range of arylalkenes, giving 2-aryl-2-benzyloxycarbonylaminoethanols with ee's greater than 80%. Subsequent enantiomer enrichment, oxidation and deprotection gives enantiomerically pure arylglycines.[181] The Sharpless asymmetric aminohydroxylation can also be applied to silyl enol ethers, and in this case the products are α-amino ketones which are formed with ee's of between 70 and 90%.[182]

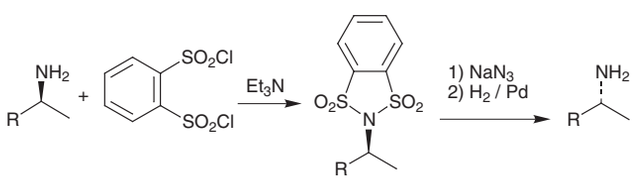
7 Derivatization of amines and amides

A review of allylic amination which includes Mitsunobu reactions, palladium catalysed chemistry and nitrene insertion reactions has been published.[183] The Gabriel synthesis is one of the classical methods for the preparation of primary amines from ammonia. The chemistry has now been modified to allow the preparation of secondary amines as well (Scheme 57). Thus, reaction of a primary amine with phthalic anhydride followed by sodium borohydride reduction, and protection of the resulting alcohol gives an amide which can be alkylated by treatment with an alkyl halide and potassium *tert*-butoxide. Subsequent acidolysis of the alcohol protecting group results in spontaneous lactonization, eliminating the secondary amine.[184] The Mitsunobu reaction is a well established method for the inversion of configuration of a chiral alcohol. A corresponding method for inverting the stereochemistry of a primary amine has been developed (Scheme 58) in which the amine is first converted into a good leaving group by reaction with 1,2-phenylenedisulfonyl chloride. Subsequent S_N2 reaction with azide and reduction furnishes a primary amine with the opposite absolute configuration to that of the starting material.[185] A synthesis of β-amino acids from the corresponding β-hydroxyacids which employs an intramolecular Mitsunobu reaction has also been reported as shown in Scheme 59.[186]

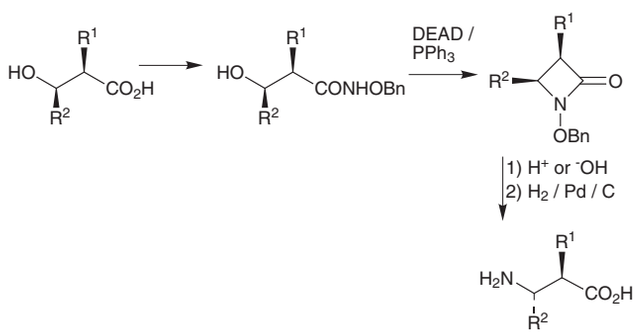
Reaction of methyl 2,4-dibromobutanoate with primary amines forms racemic azetidinecarboxylate esters which can be resolved by *Candida Antarctica* in the presence of ammonia by enantioselective conversion of the (*S*)-enantiomer to the corresponding azetidinecarboxamide.[187] Primary amines react with epichlorohydrin to give *N*-alkyl-3-hydroxyazetidines.[188] Treatment of β-bromo-amides with a base (tetrabutylammonium fluoride or sodium hydride) gives β-lactams, and this has been applied to a synthesis of the Taxol sidechain.[189] An asymmetric synthesis of (*S*)-2-cyanopiperidine has been developed, in which the key step is the reaction between (*R*)-6-bromo-(2-trifluoromethylsulfonyloxy)hexanonitrile and benzyl-



Scheme 57

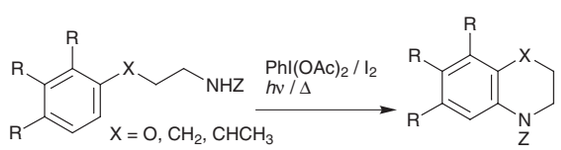


Scheme 58



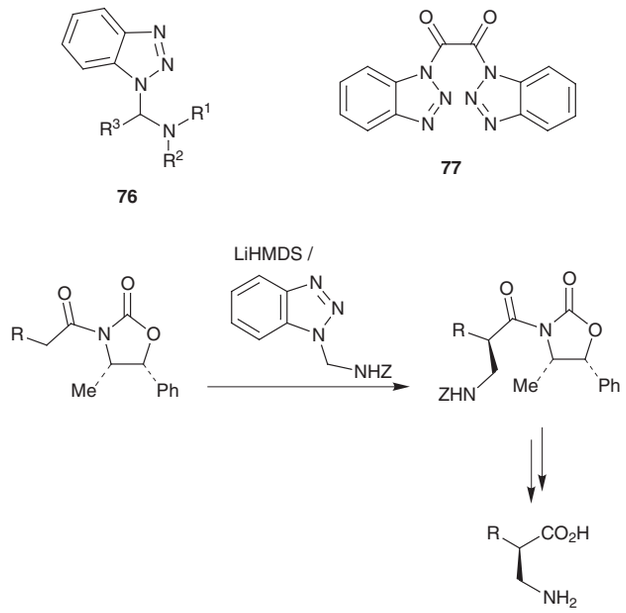
Scheme 59

amine to form the piperidine ring by a double substitution reaction with inversion of configuration at the stereocentre.[190] Reaction of an *N*-protected ω-amino-alkene with toluene-*p*-sulfonyl iodide generates an ω-amino 2-iodo-sulfone which when treated with base cyclizes to give 2-*p*-tolylsulfonylmethyl)pyrrolidines and piperidines. If the nitrogen protecting group is α-methylbenzyl, then a moderate (2.5 to 4 : 1) diastereoselectivity is observed in the cyclization step.[191] The radical cyclization of *N*-Z amines onto aromatic rings is brought about by $PhI(OAc)_2$ and iodine as illustrated in Scheme 60.[192]



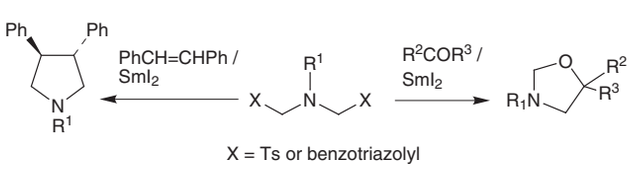
Scheme 60

The reaction of α-(benzotriazol-1-yl)amines **76** with nucleophiles results in displacement of the benzotriazole group, providing access to functionalized amines. Amongst the nucleophiles which have been used in this reaction are: organozinc reagents[193] indoles[194] and amides.[195] An enantioselective synthesis of β-amino acids in which an Evans enolate is reacted with an aminomethyl cation synthon has been developed as shown in Scheme 61.[196] Very similar chemistry but employing



Scheme 61

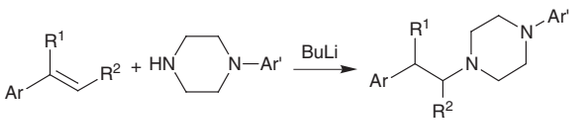
titanium tetrachloride and triethylamine to form the titanium enolate of an Evans imidate and $PhCONHCH_2Cl$ as the aminomethyl cation equivalent has also been reported.[197] α,α′-Bis(benzotriazolyl)amines and α,α′-bis(*p*-tolylsulfonyl)amines undergo [3+2]cycloaddition reactions with both alkenes and ketones in the presence of samarium iodide to give pyrrolidines and oxazolidines respectively as shown in Scheme 62.[198] 1,6-Disubstituted 1,4,5,6-tetrahydropyridazines can be prepared by the ring enlargement of 2,5-bis(benzotriazolyl)-*N*-amino-pyrrolidines.[199] Treatment of oxalyl chloride with benzotriazole gives reagent **77** which undergoes selective displacement of one benzotriazole group when treated with an amine. The second benzotriazole group can subsequently be displaced by a second amine, thus providing access to differently substituted oxamides.[200] Katritzky has reviewed the chemistry of *N*-substituted benzotriazoles, including a number of ways in which these compounds can be used as precursors of amines and amides.[201]



Scheme 62

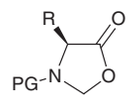
5-Bromothiophene-2-carbaldehyde reacts with secondary amines in water to give *N*,*N*-disubstituted 5-aminothiophene-2-carbaldehydes, a reaction which at least formally proceeds by a Michael addition, retro-Michael addition pathway.[202] Pyridine-2-triflates also react with primary and secondary amines to give 2-aminopyridines,[203] and pyridazolin-3-yl chlorides and triflates react with α-amino esters to give (pyridazin-3-ylamino)-α-amino acids.[204] Aryl fluorides can be coupled to anilines to give diarylamines in a reaction which is induced by potassium fluoride, alumina and 18-crown-6.[205] In the presence of butyllithium, *N*′-arylpiperazines undergo anti-Markovnikov addition to aromatic alkenes, giving *N*-β-arylethyl-*N*′-arylpiperazines as shown in Scheme 63.[206]

N-Methyl amino acids are important derivatives of amino acids in the synthesis of peptides with improved *in vivo* stability. A practical approach to the synthesis of enantiomerically pure *N*-methyl (and *N*-Boc-*N*-methyl) amino acids has been developed. The key step in the synthesis is the acid catalysed



Scheme 63

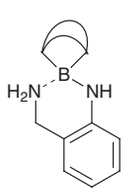
reaction between an *N*-urethane protected amino acid and formaldehyde to give an oxazolidinone **78**. Hydrogenation of the oxazolidinone results in carbon–oxygen bond cleavage, to give an *N*-methyl amino acid.[207] An alternative synthesis of *N*-methyl-α-amino acid derivatives based on the *N*-chloromethylation of hexafluorooxazolidinone protected α-amino acids followed by reduction of the carbon–chlorine bond and ring-opening of the oxazolidinone by a nucleophile has also been reported.[208]



PG = Boc or Z

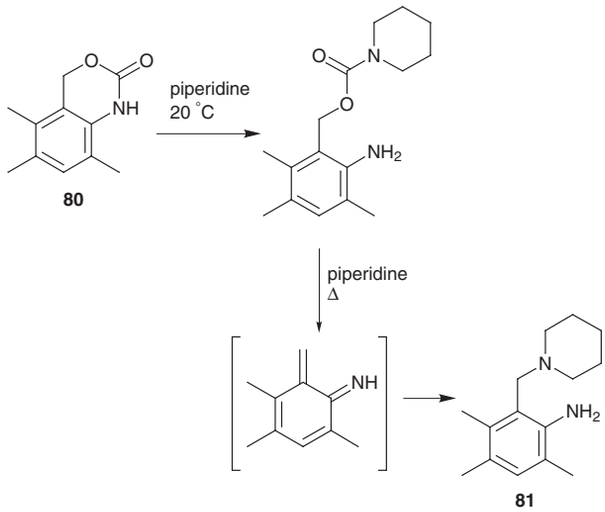
78

Complexation of a tertiary amine to borane increases the acidity of the hydrogen atoms adjacent to the amine. Simpkins and co-workers have taken advantage of this in an enantioselective synthesis of isoindoline derivatives. Thus, complexation of *N*-methylisoindoline with borane followed by deprotonation by *sec*-butyllithium in the presence of sparteine and trapping of the resulting carbanion by an electrophile gives non-racemic adducts from which the borane can be removed by treatment with ethanol.[209] A novel method for the regioselective sidechain *N*-alkylation of 2-aminobenzylamine which relies upon the complex formed between a borane and amine has been developed. Thus, reaction of 2-aminobenzylamine with 9-BBN generates chelate **79** which can be deprotonated and alkylated selectively at the benzylic nitrogen atom. Removal of the 9-BBN group then leaves the alkylated derivative.[210] Piperidine reacts with carbamate **80** to give a ring-opened piperidylcarbamate. On heating however, this extrudes carbon dioxide and forms the *o*-(1-piperidylmethyl)aniline derivative **81** as shown in Scheme 64.[211]



79

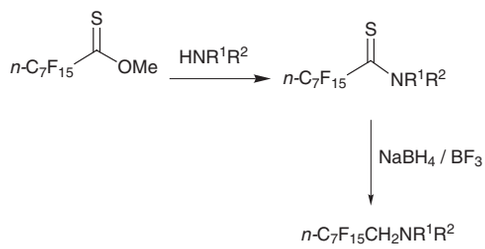
Trifluoromethylamines can be prepared by converting a secondary amine to the corresponding dithiocarbamate by treatment with butyllithium and carbon disulfide followed by methyl iodide. Subsequent oxidative desulfurization and fluorination by a combination of tetrabutylammonium hydrofluoride and a halosuccinamide gives trifluoromethylamines.[212] The synthesis of fluorinated octylamines from a fluorinated thioester has also been described (Scheme 65).[213] It is possible to reductively decyanate α-amino nitriles using alkali metals in liquid ammonia. When this chemistry is applied to *N*-protected 6-amino-3-azabicyclo[3.1.0]hexanecarbonitriles, it is possible to obtain the product corresponding to either retention or inversion of configuration at the α-amino stereocentre as shown in Scheme 66.[214] Ring-opening of α-amino acid derived heterocycles **82** by secondary amines followed by hydrolysis of the resulting β-amino sulfamic acids with boron trifluoride–diethyl ether in the presence of propanethiol and ammonium hydroxide allows the synthesis of enantiomerically



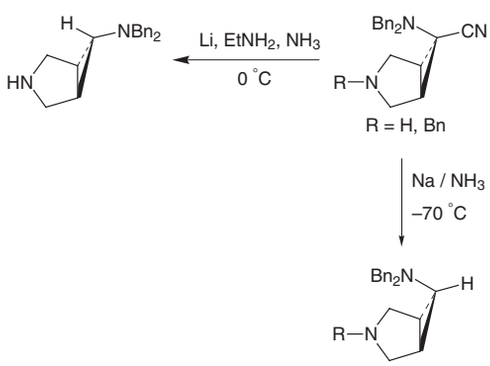
80

81

Scheme 64



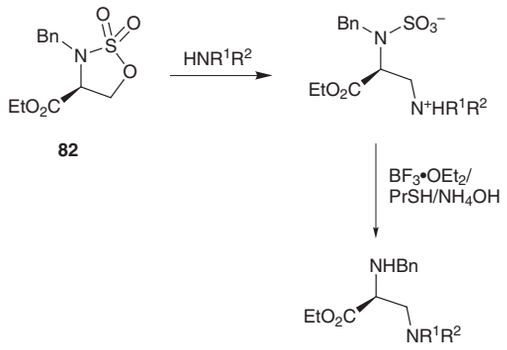
Scheme 65



Scheme 66

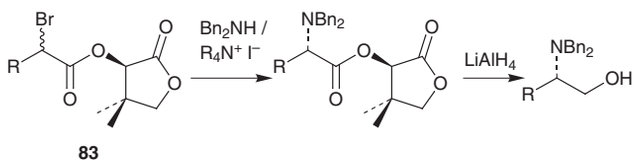
pure 2,3-diaminopropanoates (Scheme 67).[215] When they are electrolysed in the presence of lithium perchlorate and trimethylsilyl chloride, aliphatic amides undergo electroreductive coupling at a magnesium electrode to give β-amino-silyl enol ethers which on hydrolysis give α-amino ketones.[216] Treatment of epimeric bromides **83** with dibenzylamine in the presence of a tetraalkylammonium iodide results in dynamic kinetic resolution (Scheme 68) to give initially, α-amino esters with de's greater than 80%. Subsequent reduction with lithium aluminium hydride provides β-amino alcohols.[217]

The combination of dicyclohexylcarbodiimide and polystrene supported HOBt has been shown to be an effective combination for the synthesis of amides from amines and acids.[218] In the presence of AIBN and allyltributylstannane, and at 20–25 atmospheres pressure, alkyl iodides react with carbon monoxide and secondary amines to give amides.[219] A general method for the synthesis of 3,3,3-trifluoropropanamides has been developed in which the corresponding 2,2,3,3,3-pentafluoropropylamine is first formed and then converted to the corresponding 3,3,3-trifluoropropynamine by double elimination of hydrogen fluoride. Subsequent acidic hydrolysis leads to the desired 3,3,3-trifluoropropanamides (Scheme 69).[220]



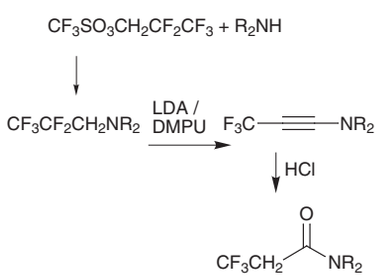
82

Scheme 67



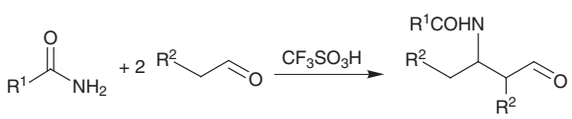
83

Scheme 68

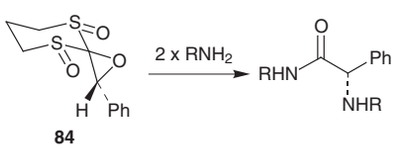


Scheme 69

Trifluoromethanesulfonic acid induces the three component condensation of a primary amide and two molecules of an aldehyde to give β-amido-aldehydes as shown in Scheme 70.[221] Amides can be labelled with ^{18}O by first forming an imino or iminium triflate by treatment with triflic anhydride, and then quenching the triflate with ^{18}O enriched water.[222] The reaction of enantiomerically pure epoxide **84** with two equivalents of a primary amine (or *trans*-cyclohexane-1,2-diamine) leads to α-amino amides with greater than 98% ee as shown in Scheme 71.[223] α,ω-Dinitriles can be regiochemically hydrolysed to ω-carboxy nitriles by treatment with a nitrilase enzyme. Hydrolysis occurs at the less hindered nitrile, and subsequent hydrogenation in the presence of a primary amine results in reductive amination and cyclization to give lactams.[224]



Scheme 70

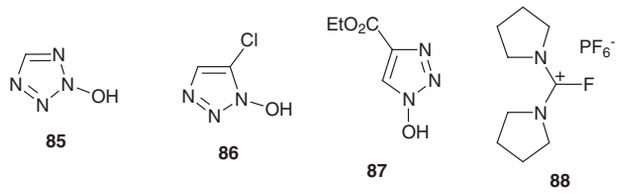


84

Scheme 71

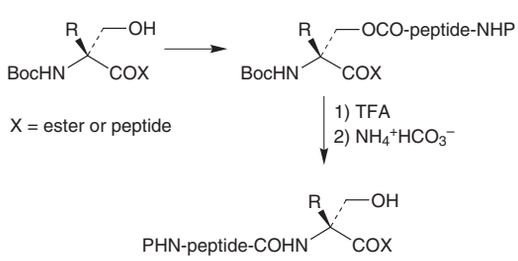
8 New methods in peptide synthesis

A study of new acylation catalysts for peptide synthesis found that 2-hydroxytetrazole **85** and 5-chloro-1-hydroxytriazole **86** had useful properties. Thus, compound **85** was found to be a more active catalyst than HOAt and to suppress racemization



85 **86** **87** **88**

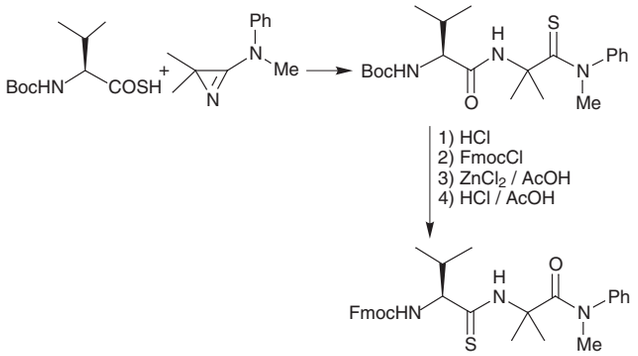
as well as HOBt. Triazole **86** was found to be an even more active catalyst, but unfortunately caused extensive racemization if used with chiral amino acids. This catalyst is however recommended for couplings between highly hindered, non-racemizable residues, for example in the synthesis of Aib–Aib units.[225] The group of Ramage recommend hydroxytriazole **87** as an active ester precursor for peptide synthesis.[226] Carpino *et al.* have also investigated the synthesis of peptides from highly hindered amino acids. They report that Fmoc-amino acid fluorides give good results for hindered couplings such as between two Aib units, but do not give satisfactory results for very hindered couplings, such as that between Aib and *N*-Me-Aib. For the latter coupling, acid chlorides are more reactive, but can only be used in conjunction with arylsulfonyl protection of the α-amino group to avoid oxazolone formation.[227] Alternatively, Fmoc–Aib acid chloride can be used to prepare peptides containing adjacent Aib residues provided that the couplings are carried out in the presence of the potassium salt of 1-hydroxybenzotriazole.[228] The use of zinc to induce peptide bond formation between Fmoc amino acid chlorides and the hydrochloride salts of amino esters in the absence of base has also been reported. The method is free of racemization, even if Fmoc–phenylglycine acid chloride is used,[229] and can also be applied to the synthesis of other amide bonds from amines and acid chlorides.[230] Bis(tetramethylene)fluoroformamidinium hexafluorophosphate **88** has been recommended as a convenient coupling agent for solid phase peptide synthesis. The reagent converts amino acids into acid fluorides *in situ*.[231] A different solution to the problem of coupling sterically hindered α-substituted-α-amino acids, at least for α-substituted serine derivatives, has been developed in which the acyl group is first introduced onto the oxygen atom of the α-substituted serine and then undergoes O–N migration as shown in Scheme 72.[232] The direct formation of dipeptides by the condensation of methyl esters of *N*-Boc-amino acids and free amino acids induced by trimethylaluminium has been reported.[233]



Scheme 72

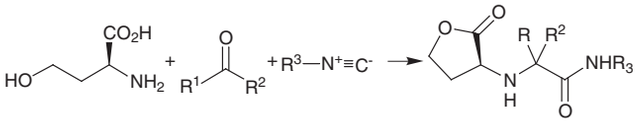
Solid-phase peptide synthesis is usually carried out from the C-terminal amino acid to the N-terminus. Alternative methodology has however, been reported in which the N-terminal amino acid is first attached to the solid support through its α-amino group. Activation of the acid group is then achieved by use of 2,4-dinitrofluorobenzene and tetrabutylammonium fluoride to form a 2,4-dinitrophenyl ester. This reacts with the lithium salt of the next amino acid to form an amide bond. The utility of the process is however limited by the fact that 18 to 100% racemization accompanies each coupling step.[234] Over recent years, Heimgartner and co-workers have developed an unusual method for the synthesis of peptides in which the amino component rather than the acid is activated for amide

formation; activation being achieved by formation of an aminoazirine. In the latest application of this procedure, it has been shown that azirines react with thioacid derivatives of amino acids to give thioamide derivatives of dipeptides (Scheme 73). The sulfur atom can subsequently migrate to the N-terminal amino acid, peptide synthesis can then be continued, allowing the synthesis of peptide analogues with *endo*-thioamide bonds.[235]



Scheme 73

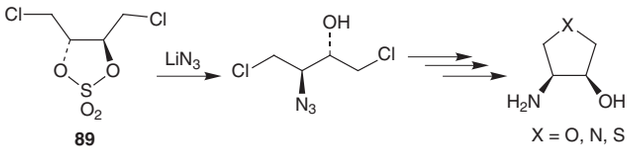
Cyclic tetrapeptides can be prepared from the methyl esters of linear tetrapeptides or from the methyl esters of two linear dipeptides by employing palladium and nickel ions as templates around which the peptide can cyclize.[236] Treatment of *N*-Boc-spirofused β-lactams with a peptide in the presence of potassium cyanide provides a way of incorporating a cyclic β,β-disubstituted-β-amino acid into a peptide.[237] Application of the Ugi synthesis to homoserine, a ketone and an isocyanide leads directly to dipeptide amides comprising homoserine lactone and an α,α-disubstituted amino acid (Scheme 74).[238] Similarly, the Ugi reaction between an *N*-Z-α-amino acid, benzophenone hydrazone and an amino ester derived isocyanide leads to tripeptides containing a central diphenylglycine residue.[239]



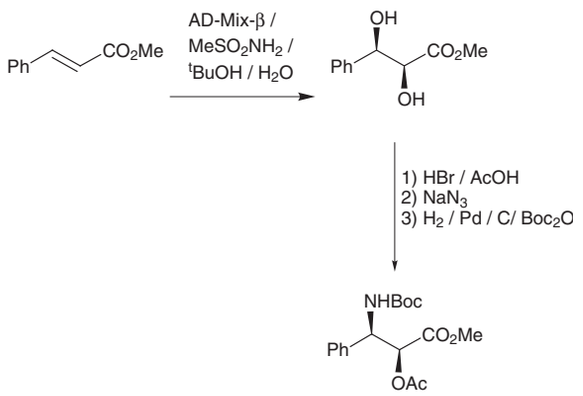
Scheme 74

9 Miscellaneous methods

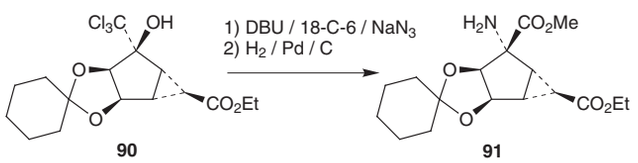
The allylic amination of an alkene with concomitant reduction of the double bond can be achieved by successive treatment of the alkene with borane at 50 °C, boron trichloride and benzyl azide.[240] Reaction of C_2 symmetric cyclic sulfonate **89** with sodium azide results in ring opening of the sulfonate, and subsequent manipulation of the adduct allows the stereocontrolled synthesis of heterocyclic β-amino alcohols as shown in Scheme 75.[241] *trans*-γ-Hydroxyproline has been converted into (2*S*,4*S*)-2,4-diaminopentanedioic acid by a series of steps, including the mesylation of the alcohol of a protected hydroxyproline derivative, substitution of the methyl sulfonate by azide and hydrogenation to give a *cis*-γ-aminoproline derivative. Subsequent oxidative ring-opening led to the desired diaminodiacid.[242] Application of the Sharpless asymmetric bis-hydroxylation protocol to methyl cinnamate provides a *syn*-diol. The benzylic alcohol can be selectively substituted by treatment with HBr followed by sodium azide, and hydrogenation then provides a *syn*-β-amino-α-hydroxy ester (Scheme 76). It is also possible to oxidize the phenyl ring of the product, giving a *syn*-β-hydroxyaspartate derivative.[243] α,α,α,-Trichloroalcohol **90** was converted into α-amino ester **91** by treatment with sodium azide followed by hydrogenolysis as shown in Scheme 77.[244] The



Scheme 75



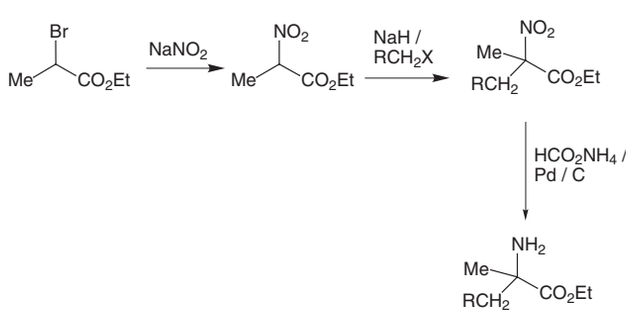
Scheme 76



Scheme 77

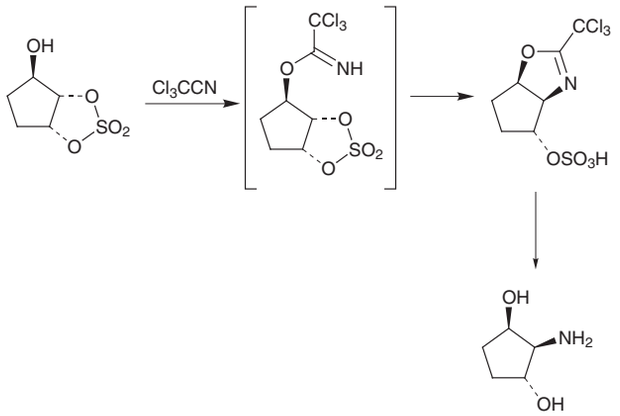
azidation of ω-bromo-carboxylic acids attached to the Evans auxiliary has been used in an asymmetric synthesis of ω-bromo-α-amino acids.[245] The Evans enolate azidation approach was also used in an asymmetric synthesis of [3,5-bis(isopropyloxy)-4-methoxyphenyl]glycine. The amino acid was also prepared by an asymmetric Strecker reaction, but the Evans approach was found to give better results.[246]

A synthesis of racemic α-methyl-α-amino acids from ethyl 2-bromopropionate has been developed as shown in Scheme 78. Thus, reaction of ethyl 2-bromopropionate with sodium nitrite gives the corresponding α-nitro ester, which can be deprotonated and alkylated to give the desired amino esters after reduction of the nitro group using ammonium formate and palladium on charcoal.[247] Similar chemistry starting from methyl nitroacetate was used to prepare α,α-disubstituted amino acids.[248]

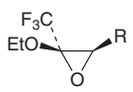


Scheme 78

A synthesis of β-amino alcohols employs the cyclization of a trichloroimidate onto a cyclic sulfonate as shown in Scheme 79.[249] A related reaction is the Overman rearrangement of allylic trichloroimidates to allylic trichloroacetamides. The reaction occurs thermally and the conditions have been optimized by the inclusion of potassium carbonate to absorb acidic by-products.[250] Epoxides **92** (as the racemate or a single



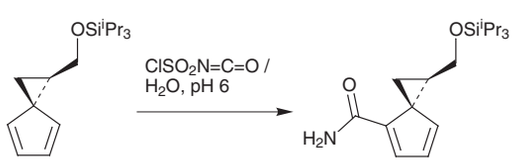
Scheme 79



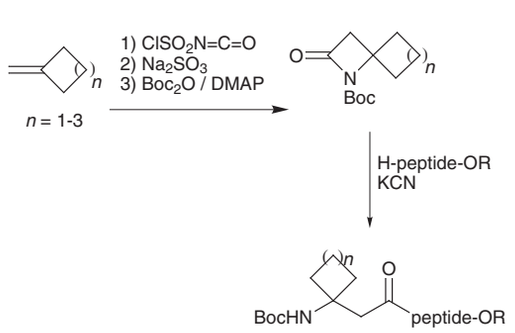
92

enantiomer) react with $Me_2AlNHBn$ followed by sodium borohydride to give β-amino-β′,β′,β′-trifluoro alcohols with a moderate (7:3) preference for formation of the *anti*-diastereomer.[251]

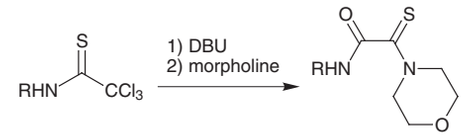
Chlorosulfonyl isocyanate can be used as a precursor to a carboxamide group as shown by the example in Scheme 80 in which the reagent reacts with an enantiomerically pure cyclopentadiene unit to produce an enantio- and diastereomerically pure amide under very mild reaction conditions.[252] The same reagent reacts with methylene cycloalkanes to give β-lactams (Scheme 81). Another unusual amide synthesis is the haloform type cleavage of trifluoromethyl ketones by lithium dialkylamides, and this has been used to prepare indole-3-carboxamide derivatives from 3-trifluoroacetylindole.[253] Treatment of trichlorothioacetamides with DBU followed by morpholine results in the formation of thiooxamides as shown in Scheme 82.[254] Reaction of β,γ-didehydro-α-hydroxy esters with *p*-toluenesulfonyl isocyanate followed by iodine results in cyclization (Scheme 83). Subsequent manipulation leads to *syn*-β-amino-α-hydroxy acids. The chemistry has been adapted to allow the synthesis of enantiomerically pure products by using a chiral ester to induce formation of a single enantiomer of the alcohol starting material.[255] Very similar chemistry has been carried out on γ-hydroxy-α,β-unsaturated sulfones, employing benzyl isocyanate to prepare β-amino alcohol derivatives.[256]



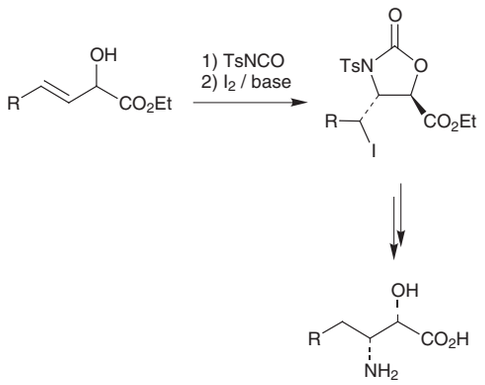
Scheme 80



Scheme 81



Scheme 82



Scheme 83

10 References

1 M. North, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 2959.
2 M. Arend, B. Westermann and N. Risch, *Angew. Chem.*, *Int. Ed.*, 1998, **37**, 1045.
3 R. Bloch, *Chem. Rev.*, 1998, **98**, 1407.
4 M. A. Yurovskaya and A. V. Karchava, *Tetrahedron: Asymmetry*, 1998, **9**, 3331.
5 T. Akiyama and J. Iwai, *Synlett*, 1998, 273.
6 S. Kobayashi, T. Busujima and S. Nagayama, *Chem. Commun.*, 1998, 19.
7 S. Kobayashi, T. Furuta, K. Sugita and H. Oyamada, *Synlett*, 1998, 1019.
8 A. Heydari, P. Fatemi and A. A. Alizadeh, *Tetrahedron Lett.*, 1998, **39**, 3049.
9 M. R. Saidi and H. R. Khalaji, *J. Chem. Res. (S)*, 1997, 340.
10 A. Heydari, A. Karimian and J. Ipaktschi, *Tetrahedron Lett.*, 1998, **39**, 6729.
11 A. Zarghi, M. R. Naimi-Jamal, S. A. Webb, S. Balalaie, M. R. Saidi and J. Ipaktschi, *Eur. J. Org. Chem.*, 1998, 197.
12 T. P. Loh and L. L. Wei, *Tetrahedron Lett.*, 1998, **39**, 245.
13 C. T. Qian and T. S. Huang, *J. Org. Chem.*, 1998, **63**, 4125.
14 D. Simoni, F. P. Invidiata, M. Manferdini, I. Lampronti, R. Rondanin, M. Roberti and G. P. Pollini, *Tetrahedron Lett.*, 1998, **39**, 7615.
15 H. J. Cristau, J. M. Lambert and J. L. Pirat, *Synthesis*, 1998, 1167.
16 Q. Dai, R. Y. Chen, C. X. Zhang and Z. Liu, *Synthesis*, 1998, 405.
17 A. Dal Pozzo, L. Muzi, M. Moroni, R. Rondanin, R. de Castiglione, P. Bravo and M. Zanda, *Tetrahedron*, 1998, **54**, 6019.
18 B. Merla, H. J. Grumbach and N. Risch, *Synthesis*, 1998, 1609.
19 A. B. Charette, A. Gagnon, M. Janes and C. Mellon, *Tetrahedron Lett.*, 1998, **39**, 5147.
20 N. De Kimpe, M. Boeykens and D. Tourwe, *Tetahedron*, 1998, **54**, 2619.
21 W. Aelterman, N. De Kimpe and J. P. Declercq, *J. Org. Chem.*, 1998, **63**, 6.
22 S. Florio, L. Troisi and V. Capriata, *Tetrahedron Lett.*, 1998, **39**, 7951.
23 B. Frydman and M. I. Ojea, *Tetrahedron Lett.*, 1998, **39**, 4765.
24 I. Shibata, T. Suwa, E. Sugiyama and A. Baba, *Synlett*, 1998, 1081.
25 E. Vilsmaier and T. Goerz, *Synthesis*, 1998, 739.
26 K. A. Neidigh, M. A. Avery, J. S. Williamson and S. Bhattacharyya, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 2527.
27 M. Renz, C. Hemmert and B. Meunier, *Eur. J. Org. Chem.*, 1998, 1271.
28 J. Einhorn, C. Einhorn, F. Ratajczak, A. Durif, M. T. Averbuch and J. L. Pierre, *Tetrahedron Lett.*, 1998, **39**, 2565.
29 T. Giard, D. Benard and J. C. Plaquevent, *Synthesis*, 1998, 297.
30 F. Gyenes, K. E. Bergmann and J. T. Welch, *J. Org. Chem.*, 1998, **63**, 2824.
31 G. Cardillo, L. Gentiliucci, A. Tolomelli and C. Tomasini, *J. Org. Chem.*, 1998, **63**, 2351.
32 U. Girreser, D. Heber and M. Schutt, *Synthesis*, 1998, 715.
33 F. A. Davis and J. M. Szewczyk, *Tetrahedron Lett.*, 1998, **39**, 5951.

34 R. L. G. Ruano, I. Fernandez, M. del P. Catalina, J. A. Hermoso, J. Sanz-Aparicio and M. Miartinez-Ripoll, *J. Org. Chem.*, 1998, **63**, 7157.
35 F. A. Davis and Y. W. Andemichael, *Tetrahedron Lett.*, 1998, **39**, 3099.
36 P. Bravo, M. Crucianelli, B. Vergani and M. Zanda, *Tetrahedron Lett.*, 1998, **39**, 7771.
37 F. A. Davis and D. L. Fanelli, *J. Org. Chem.*, 1998, **63**, 1981.
38 N. Negoro, R. Yanada, M. Okaniwa, K. Yanada and T. Fujita, *Synlett*, 1998, 835.
39 A. A. El-Shehawy, M. A. Omara, K. Ito and S. Itsuno, *Synlett*, 1998, 367.
40 L. X. Liao and W. S. Zhou, *Tetrahedron*, 1998, **54**, 12571.
41 L Carrillo, D. Badia, E. Dominguez, I. Tellitu and J. L. Vicario, *Tetrahedron: Asymmetry*, 1998, **9**, 1809.
42 L. M. Harwood, S. N. G. Tyler, A. S. Anslow, I. D. MacGilp and M. G. B. Drew, *Tetrahedron: Asymmetry*, 1997, **8**, 4007.
43 K. Higashiyama, H. Kyo and H. Takahashi, *Synlett*, 1998, 489.
44 J. Y. Park, C. H. Park, I. Kadota and Y. Yamamoto, *Tetrahedron Lett.*, 1998, **39**, 1791.
45 G. Alvaro, G. Martelli and D. Savoia, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 775.
46 A. B. Smith (III), K. M. Yager, B. W. Phillips and C. M. Taylor, *Org. Synth.*, 1998, **75**, 19.
47 P. Hutin, Y. Petit and M. Larcheveque, *Tetrahedron Lett.*, 1998, **39**, 8277.
48 P. Bisel, E. Breitling and A. W. Fraham, *Eur. J. Org. Chem.*, 1998, 729.
49 C. J. Moody and J. C. A. Hunt, *Synlett*, 1998, 733.
50 A. Rae, J. Ker, A. B. Tabor, J. L. Castro and S. Parsons, *Tetrahedron Lett.*, 1998, **39**, 6561.
51 P. Bataille, M. Paterne and E. Brown, *Tetrahedron: Asymmetry*, 1998, **9**, 2181.
52 D. Enders and R. Lochtman, *Eur. J. Org. Chem.*, 1998, 689.
53 D. Enders, C. Poiesz and R. Joseph, *Tetrahedron: Asymmetry*, 1998, **9**, 3709.
54 D. Enders, R. Lochtman, M. Meiers, S. Muller and R. Lazny, *Synlett*, 1998, 1182.
55 M. Shimizu, A. Morita and T. Fujisawa, *Chem. Lett.*, 1998, 467.
56 M. Carda, J. Murga, S. Rodriguez, F. Gonzalez, E. Castillo and J. A. Marco, *Tetrahedron: Asymmetry*, 1998, **9**, 1703.
57 J. A. Marco, M. Carda, J. Murga, R. Portoles, E. Falomir and J. Lex, *Tetrahedron Lett.*, 1998, **39**, 3237.
58 P. Merino, E. Castillo, S. Franco, F. L. Merchan and T. Tejero, *Tetrahedron*, 1998, **54**, 12301.
59 P. Merino, A. Lanaspa, F. L. Merchan and T. Tejero, *Tetrahedron: Asymmetry*, 1998, **9**, 629; P. Merino, S. Franco, F. L. Merchan and T. Tejero, *J. Org. Chem.*, 1998, **63**, 5627.
60 N. A. Petasis and I. A. Zavialov, *J. Am. Chem. Soc.*, 1998, **120**, 11798.
61 A. Dondoni, D. Perrone and M. Rinaldi, *J. Org. Chem.*, 1998, **63**, 9252.
62 A. Fadel and A. Khesrani, *Tetrahedron: Asymmetry*, 1998, **9**, 305.
63 A. B. Charette and C. Mellon, *Tetrahedron*, 1998, **54**, 10525.
64 H. Kajiro, S. Mitamura, A. Mori and T. Hiyama, *Synlett*, 1998, 51.
65 A. Volonterio, B. Vergani, M. Crucianelli, M. Zanda and P. Bravo, *J. Org. Chem.*, 1998, **63**, 7236.
66 D. Guijarro, P. Pinho and P. G. Andersson, *J. Org. Chem.*, 1998, **63**, 2530.
67 S. Kobayashi, H. Ishitani and M. Ueno, *J. Am. Chem. Soc.*, 1998, **120**, 431.
68 S. Kobayashi, Y. Hasegawa and H. Ishitani, *Chem. Lett.*, 1998, 1131.
69 H. Ishitani, S. Komiyama and S. Kobayashi, *Angew. Chem.*, *Int. Ed.*, 1998, **37**, 3186.
70 H. Groger, Y. Saida, H. Sasai, K. Yamaguchi, J. Martens and M. Shibasaki, *J. Am. Chem. Soc.*, 1998, **120**, 3089.
71 M. Masui and T. Shioiri, *Tetrahedron Lett.*, 1998, **39**, 5195.
72 I. Chataigner, F. Zammattio, J. Lebreton and J. Villiers, *Synlett*, 1998, 275.
73 P. Bravo, M. Guidetti, F. Viani, M. Zanda, A. L. Markovsky, A. E. Sorochinsky and I. V. Soloshonok, *Tetrahedron*, 1998, **54**, 12789; P. Bravo, E. Corradi, C. Pesenti, B. Vergani, F. Viani, A. Volonterio and M. Zanda, *Tetrahedron: Asymmetry*, 1998, **9**, 3731.
74 J. L. G. Ruano, A. Lorente and J. H. R. Ramos, *Tetrahedron Lett.*, 1998, **39**, 9765.
75 H. Miyabe, R. Shibata, C. Ushiro and T. Naito, *Tetrahedron Lett.*, 1998, **39**, 631; H. Miyabe, R. Shibata, M. Sangawa, C. Ushiro and T. Naito, *Tetrahedron*, 1998, **54**, 11431; H. Miyabe, N. Yoshioka, M. Ueda and T. Naito, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 3703.
76 M. P. Bertrand, L. Feray, R. Nouguier and L. Stella, *Synlett*, 1998, 780.
77 R. Annunziata, M. Benaglia, M. Cinquini, F. Cozzi and L. Raimondi, *Tetrahedron Lett.*, 1998, **39**, 3333.
78 S. Talukdar and A. Banerji, *J. Org. Chem.*, 1998, **63**, 3468.
79 H. Miyabe, S. Kanehira, K. Kume, H. Kandori and T. Naito, *Tetrahedron*, 1998, **54**, 5883.
80 J. Tormo, D. S. Hays and G. C. Fu, *J. Org. Chem.*, 1998, **63**, 201.
81 O. Miyata, K. Muroya, J. Koide and T. Naito, *Synlett*, 1998, 271.
82 I. Ryu, K. Matsu, S. Minakata and M. Komatsu, *J. Am. Chem. Soc.*, 1998, **120**, 5838.
83 G. Cainelli, P. Galletti and D. Giacomini, *Synlett*, 1998, 611.
84 M. Barreau, A. Commercon, S. Mignani, D. Mouysset, P. Perfetti and L. Stella, *Tetrahedron*, 1998, **54**, 11501.
85 S. Matsui, Y. Hashimoto and K. Saigo, *Synthesis*, 1998, 1161.
86 C. Palomo, M. Oiarbide, A. Esnal, A. Landa, J. I. Miranda and A. Linden, *J. Org. Chem.*, 1998, **63**, 5838.
87 G. Babu and P. T. Perumal, *Tetrahedron*, 1998, **54**, 1627.
88 J. Barluenga, F. Aznar, C. Valdes and C. Ribas, *J. Org. Chem.*, 1998, **63**, 3918.
89 Z. R. Xu and X. Y. Lu, *J. Org. Chem.*, 1998, **63**, 5031.
90 D. S. Black, D. C. Craig, G. L. Edwards and S. M. Laaman, *Tetrahedron Lett.*, 1998, **39**, 5849.
91 J. Marcus, J. Brussee and A. van der Gen, *Eur. J. Org. Chem.*, 1998, 2513.
92 S. E. Denmark and J. A. Dixon, *J. Org. Chem.*, 1998, **63**, 6167; S. E. Denmark and J. A. Dixon, *J. Org. Chem.*, 1998, **63**, 6178.
93 W. J. Drury, D. Ferraris, C. Cox, B. Young and T. Lectka, *J. Am. Chem. Soc.*, 1998, **120**, 11006.
94 K. Uneyama, J. A. Hao and H. Amii, *Tetrahedron Lett.*, 1998, **39**, 4079.
95 R. P. Frutos and D. M. Spero, *Tetrahedron Lett.*, 1998, **39**, 2475.
96 A. G. Griesbeck, S. Buhr and J. Lex, *Tetrahedron Lett.*, 1998, **39**, 2535.
97 V. A. Soloshonok, I. V. Soloshonok, V. P. Kukhar and V. K. Svedas, *J. Org. Chem.*, 1998, **63**, 1878.
98 A. Nadin, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 3493.
99 G. Cardillo, L. Gentilucci, I. R. Bastardas and A. Tolomelli, *Tetrahedron*, 1998, **54**, 8217.
100 A. Bongini, G. Cardillo, L. Gentilucci and C. Tomasini, *J. Org. Chem.*, 1997, **62**, 9148.
101 S. N. Filigheddu and M. Taddei, *Tetrahedron Lett.*, 1998, **39**, 3857.
102 H. Ohno, K. Ishii, A. Honda, H. Tamamura, N. Fujii, Y. Takemoto and T. Ibuka, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 3703.
103 U. M. Lindstrom and P. Somfai, *Synthesis*, 1998, 109.
104 H. F. Olivo, M. S. Hemenway, A. C. Hartwig and R. Chan, *Synlett*, 1998, 247.
105 S. Nagayama and S. Kobayashi, *Chem. Lett.*, 1998, 685.
106 R. S. Atkinson, A. P. Ayscough, W. T. Gattrell and T. M. Raynham, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 2783.
107 G. Fraenkel and J. D. Jakowski, *Tetrahedron Lett.*, 1998, **39**, 5297.
108 P. Saravanan and V. K. Singh, *Tetrahedron Lett.*, 1998, **39**, 167; S. E. de Sousa, P. O'Brien and P. Poumellec, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 1483.
109 C. Thomas, F. Orecher and P. Gmeiner, *Synthesis*, 1998, 1491.
110 P. Dauban and R. H. Dodd, *Tetrahedron Lett.*, 1998, **39**, 5739.
111 A. A. Cantrill, H. M. I. Osborn and J. Sweeney, *Tetrahedron*, 1998, **54**, 2181.
112 A. Toda, H. Aoyama, N. Mimura, H. Ohno, N. Fujii and T. Ibuka, *J. Org. Chem.*, 1998, **63**, 7053.
113 M. Sunrose, K. M. Anderson, A. G. Orpen, T. Gallagher and S. J. F. Macdonald, *Tetrahedron Lett.*, 1998, **39**, 8885.
114 J. W. Chang, J. H. Bae, S. H. Shin, C. S. Park, D. Choi and W. K. Lee, *Tetrahedron Lett.*, 1998, **39**, 9193.
115 J. M. Travins and F. A. Etzkorn, *Tetrahedron Lett.*, 1998, **39**, 9389.
116 E. Medina, A. Moyano, M. A. Pericas and A. Riera, *J. Org. Chem.*, 1998, **63**, 8574.
117 D. DeSmaele, P. Bogaert and N. DeKimpe, *Tetrahedron Lett.*, 1998, **39**, 9797.
118 T. P. Loh and L. L. Wei, *Synlett*, 1998, 975.
119 G. C. Torchiarolo, F. D'Onofrio, R. Margarita, L. Parlanti, G. Piancatelli and M. Bella, *Tetrahedron*, 1998, **54**, 15657.
120 F. Zhou, J. Rosen, J. M. Zebrowski-Young, P. M. Freihammer, M. R. Detty and R. J. Lachicotte, *J. Org. Chem.*, 1998, **63**, 5403.
121 S. G. Davies and O. Ichihara, *Tetrahedron Lett.*, 1998, **39**, 6045.
122 M. Korner, M. Findeisen and N. Sewald, *Tetrahedron Lett.*, 1998, **39**, 3463; N. Sewald, K. D. Hiller, M. Korner and M. Findeisen, *J. Org. Chem.*, 1998, **63**, 7263.
123 D. W. Ma and J. Q. Jiang, *Tetrahedron: Asymmetry*, 1998, **9**, 575.
124 M. Yamada, N. Nagashima, J. Hasegawa and S. Takahashi, *Tetrahedron Lett.*, 1998, **39**, 9019.
125 B. Bartels, C. G. Martin, A. Nelson, M. G. Russell and S. Warren, *Tetrahedron Lett.*, 1998, **39**, 1637.

126 T. Ishikawa, K. Nagai, T. Kudoh and S. Saito, *Synlett*, 1998, 1291.
127 S. Sabelle, D. Lucet, T. LeGall and C. Mioskowski, *Tetrahedron Lett.*, 1998, **39**, 2111.
128 A. G. M. Barrett, D. C. Braddock, P. W. N. Christian, D. Pilipauskas, A. J. P. White and D. J. Williams, *J. Org. Chem.*, 1998, **63**, 5818.
129 D. Enders, A. Haertwig and J. Runsink, *Eur. J. Org. Chem.*, 1998, 1771; D. Enders, A. Haertwig, G. Raabe and J. Runsink, *Eur. J. Org. Chem.*, 1998, 1793.
130 M. P. Sibi, J. J. Shay, M. Liu and C. P. Jasperse, *J. Am. Chem. Soc.*, 1998, **120**, 6615.
131 J. Lin, S. Liao and V. J. Hruby, *Tetrahedron Lett.*, 1998, **39**, 3117.
132 C. Palomo, J. M. Aizpurua, J. J. Gracenea, S. Garcia-Granda and P. Pertierra, *Eur. J. Org. Chem.*, 1998, 2201.
133 C. Borner and C. Schneider, *Synlett*, 1998, 652.
134 C. Dugave, J. Cluzeau, A. Menez, M. Gaudry and A. Marquet, *Tetrahedron Lett.*, 1998, **39**, 5775.
135 G. Guillena, B. Mancheno, C. Najera, J. Ezquerra and C. Pedregal, *Tetrahedron*, 1998, **54**, 9447.
136 S. Hannour, M.-L. Roumestant, P. Viallefont, C. Riche, J. Martinez, A. El Hallaoui and F. Ouazzani, *Tetrahedron: Asymmetry*, 1998, **9**, 2329.
137 R. Velarde-Ortiz, A. Guijarro and R. D. Rieke, *Tetrahedron Lett.*, 1998, **39**, 9157.
138 E. J. Corey, M. C. Noe and F. Xu, *Tetrahedron Lett.*, 1998, **39**, 5347.
139 A. Lopez and R. Pleixats, *Tetrahedron: Asymmetry*, 1998, **9**, 1967.
140 H. Bricout, J. F. Carpentier and A. Mortreux, *Tetrahedron*, 1998, **54**, 1073.
141 E. Brenner and Y. Fort, *Tetrahedron Lett.*, 1998, **39**, 5359.
142 M. Nishiyama, T. Yamamoto and Y. Koie, *Tetrahedron Lett.*, 1998, **39**, 617; F. Kerrigan, C. Martin and G. H. Thomas, *Tetrahedron Lett.*, 1998, **39**, 2219.
143 B. Witulski, S. Senft and A. Thum, *Synlett*, 1998, 504.
144 S. Morita, K. Kitano, J. Matsubara, T. Ohtani, Y. Kawano, K. Otsubo and M. Uchida, *Tetrahedron*, 1998, **54**, 4811.
145 G. J. Tanoury, C. H. Senanayake, R. Hett, A. M. Kuhn, D. W. Kessler and S. A. Wald, *Tetrahedron Lett.*, 1998, **39**, 6845.
146 T. Yamamoto, M. Nishiyama and Y. Koie, *Tetrahedron Lett.*, 1998, **39**, 2367.
147 D. W. Ma and J. Q. Jiang, *Tetrahedron: Asymmetry*, 1998, **9**, 1137; D. W. Ma, Y. D. Zhang, J. C. Yao, S. H. Wu and F. G. Tao, *J. Am. Chem. Soc.*, 1998, **120**, 12459.
148 S. Jaime-Figueroa, Y. Z. Liu, J. M. Muchowski and D. G. Putman, *Tetrahedron Lett.*, 1998, **39**, 1313.
149 K. Hori and M. Mori, *J. Am. Chem. Soc.*, 1998, **120**, 7651.
150 M. Meguro and Y. Yamamoto, *Tetrahedron Lett.*, 1998, **39**, 5421.
151 W. F. J. Karstens, M. Stol, F. P. J. T. Rutjes and H. Hiemstra, *Synlett*, 1998, 1126.
152 R. C. Larock, C. Tu and P. Pace, *J. Org. Chem.*, 1998, **63**, 6859.
153 R. Grigg, M. Monteith, V. Sridharan and C. Terrier, *Tetrahedron*, 1998, **54**, 3885.
154 C. Y. Oh, K. S. Kim and W. H. Ham, *Tetrahedron Lett.*, 1998, **39**, 2133.
155 T. Abellan, C. Najera and J. M. Sansano, *Tetrahedron: Asymmetry*, 1998, **9**, 2211.
156 M. Beller, M. Eckert and E. W. Holla, *J. Org. Chem.*, 1998, **63**, 5658.
157 J. M. Herbert and A. H. McNeill, *Tetrahedron Lett.*, 1998, **39**, 2421.
158 P. Dorizon, G. F. Su, G. Ludvig, L. Nikitina, J. Ollivier and J. Salaun, *Synlett*, 1998, 483.
159 V. Atlan, S. Racouchot, M. Rubin, C. Bremer, J. Ollivier, A. de Meijere and J. Salaun, *Tetrahedron: Asymmetry*, 1998, **9**, 1131.
160 A. R. Katritzky, J. C. Yao and M. Qi, *J. Org. Chem.*, 1998, **63**, 5232.
161 B. M. Trost, T. L. Calkins, C. Oertelt and J. Zambrano, *Tetrahedron Lett.*, 1998, **39**, 1713.
162 B. M. Trost and X. Ariza, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2635.
163 G. Muchow, J. M. Brunel, M. Maffei, O. Pardigon and G. Buono, *Tetrahedron*, 1998, **54**, 10435.
164 S. G. Pyne, D. M. David and Z. M. Dong, *Tetrahedron Lett.*, 1998, **39**, 8499.
165 T. Rische and P. Eilbracht, *Tetrahedron*, 1998, **54**, 8441.
166 T. Rische, B. Kitsos-Rzychon and P. Eilbracht, *Tetrahedron*, 1998, **54**, 2723; C. L. Kranemann and P. Eilbracht, *Synthesis*, 1998, 71.
167 B. Breit, *Tetrahedron Lett.*, 1998, **39**, 5163.
168 I. Ojima, D. M. Iula and M. Tzamarioudaki, *Tetrahedron Lett.*, 1998, **39**, 4599.
169 R. Kuwano, M. Takahashi and Y. Ito, *Tetrahedron Lett.*, 1998, **39**, 1017.
170 C. J. Moody, L. Ferris, D. Haigh and E. Swann, *Chem. Commun.*, 1997, 2391.
171 M. Anada, N. Watanabe and S. Hashimoto, *Chem. Commun.*, 1998, 1517.
172 F. Y. Zhang, C. C. Pai and A. S. C. Chan, *J. Am. Chem. Soc.*, 1998, **120**, 5808.
173 M. J. Burk, J. G. Allen and W. F. Kiesman, *J. Am. Chem. Soc.*, 1998, **120**, 657.
174 D. S. Black, G. L. Edwards and S. M. Laaman, *Tetrahedron Lett.*, 1998, **39**, 5853.
175 J. B. Wang and Y. H. Hoe, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1919.
176 J. L. Matthews, K. Gademann, B. Jaun and D. Seebach, *J. Chem. Soc., Perkin Trans. 1*, 1998, 3331.
177 A. Muller, C. Vogt and N. Sewald, *Synthesis*, 1998, 837.
178 Y. Koseki, S. Kusano and T. Nagasaka, *Tetrahedron Lett.*, 1998, **39**, 3517.
179 A. Kamal and B. S. N. Reddy, *Chem. Lett.*, 1998, 593.
180 G. G. Li, R. Lennington, S. Willis and S. H. Kim, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1753.
181 K. L. Reddy and K. B. Sharpless, *J. Am. Chem. Soc.*, 1998, **120**, 1207.
182 P. Phukan and A. Sudalai, *Tetrahedron: Asymmetry*, 1998, **9**, 1001.
183 M. Johannsen and K. A. Jorgensen, *Chem. Rev.*, 1998, **98**, 1689.
184 T. Fichert and U. Massing, *Tetrahedron Lett.*, 1998, **39**, 5017.
185 K. Sorbye, C. Tautermann, P. Carlsen and A. Fiksdahl, *Tetrahedron: Asymmetry*, 1998, **9**, 681.
186 Y. H. Jin and D. H. Kim, *Synlett*, 1998, 1189.
187 W. A. J. Starmans, R. G. Doppen, L. Thijs and B. Zwanenburg, *Tetrahedron: Asymmetry*, 1998, **9**, 429.
188 T. Constantieux, S. Grelier and J. P. Picard, *Synlett*, 1998, 510.
189 C. E. Song, S. W. Lee, E. J. Roh, S. G. Lee and W. K. Lee, *Tetrahedron: Asymmetry*, 1998, **9**, 983.
190 S. Nazabadioko, R. J. Perez, R. Brieva and V. Gotor, *Tetrahedron: Asymmetry*, 1998, **9**, 1597.
191 D. C. Craig, G. L. Edwards and C. A. Muldoon, *Synlett*, 1997, 1441.
192 H. Togo, Y. Hoshina, T. Muraki, H. Nakayama and M. Yokoyama, *J. Org. Chem.*, 1998, **63**, 5193.
193 A. R. Katritzky, D. A. Nichols and M. Qi, *Tetrahedron Lett.*, 1998, **39**, 7063; A. R. Katritzky, S. Strah and S. A. Belyakov, *Tetrahedron*, 1998, **54**, 7167.
194 B. E. Love and B. T. Nguyen, *Synlett*, 1998, 1123.
195 A. R. Katritzky, C. N. Fali, W. L. Bao and M. Qi, *Synthesis*, 1998, 1421.
196 E. Arvanitis, H. Ernst, A. A. Ludwig, A. J. Robinson and P. B. Wyatt, *J. Chem. Soc., Perkin Trans. 1*, 1998, 521.
197 D. Seebach, S. Abele, K. Gademann, G. Guichard, T. Hintermann, B. Jaun, J. L. Matthews and J. V. Schreiber, *Helv. Chim. Acta*, 1998, **81**, 932.
198 A. R. Katritzky, D. M. Feng and M. Qi, *Tetrahedron Lett.*, 1998, **39**, 6835.
199 A. R. Katritzky, D. P. M. Pleynet, B. Z. Yang and J. C. Yao, *Synthesis*, 1998, 1627.
200 A. R. Katritzky, J. R. Levell and D. P. M. Pleynet, *Synthesis*, 1998, 153.
201 A. R. Katritzky, X. F. Lan, J. Z. Yang and O. V. Denisko, *Chem. Rev.*, 1998, **98**, 409.
202 D. Prim, G. Kirsch and J. F. Nicoud, *Synlett*, 1998, 383.
203 S. Cacchi, A. Carangio, G. Fabrizi, L. Moro and P. Pace, *Synlett*, 1997, 1400.
204 S. Chayer, E. M. Essassi and J. J. Bourguignon, *Tetrahedron Lett.*, 1998, **39**, 841.
205 J. S. Sawyer, E. A. Schmittling, J. A. Palkowitz and W. J. Smith, *J. Org. Chem.*, 1998, **63**, 6338.
206 M. Beller and C. Breindl, *Tetrahedron*, 1998, **54**, 6359.
207 G. V. Reddy, G. V. Rao and D. S. Iyengar, *Tetrahedron Lett.*, 1998, **39**, 1985.
208 J. Spengler and K. Burger, *Synthesis*, 1998, 67.
209 A. J. Blake, M. R. Ebden, D. N. A. Fox, W. S. Li and N. S. Simpkins, *Synlett*, 1998, 189.
210 G. Bar-Haim and M. Kol, *Tetrahedron Lett.*, 1998, **39**, 2643.
211 S. S. Nikam, P. W. Yuen, B. E. Kornberg, B. Tobias and M. F. Rafferty, *J. Org. Chem.*, 1997, **62**, 9331.
212 K. Kanie, K. Mizuno, M. Kuroboshi and T. Hiyama, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 1973.
213 L. E. Kiss, J. Rabai, L. Varga and I. Kovesdi, *Synlett*, 1998, 1243.
214 E. Vilsmaier, G. Milch and U. Bergstrasser, *Tetrahedron*, 1998, **54**, 6403.
215 B. M. Kim and S. M. So, *Tetrahedron Lett.*, 1998, **39**, 5381.
216 S. Kashimura, M. Ishifune, Y. Murai, H. Murase, M. Shimomura and T. Shono, *Tetrahedron Lett.*, 1998, **39**, 6199.

217 J. A. O'Meara, N. Gardee, M. Jung, R. N. Ben and T. Durst, *J. Org. Chem.*, 1998, **63**, 3117.
218 K. Dendrinos, J. Jeong, W. Huang and A. G. Kalivretenos, *Chem. Commun.*, 1998, 499.
219 I. Ryu, K. Nagahara, N. Kambe, N. Sonoda, S. Kreimerman and M. Komatsu, *Chem. Commun.*, 1998, 1953.
220 H. Yamanaka, T. Mantani, K. Shiomi and T. Ishihara, *Chem. Lett.*, 1998, 615.
221 C. M. Marson and A. Fallah, *Chem. Commun.*, 1998, 83.
222 A. B. Charette and P. Chua, *Tetrahedron Lett.*, 1998, **39**, 245.
223 V. K. Aggarwal, J. K. Barrell, J. M. Worrall and R. Alexander, *J. Org. Chem.*, 1998, **63**, 7128.
224 J. E. Gavagan, S. K. Fager, R. D. Fallon, P. W. Folsom, F. E. Herkes, A. Eisenberg, E. C. Hann and R. DiCosimo, *J. Org. Chem.*, 1998, **63**, 4792.
225 J. C. Spetzler, M. Meldal, J. Felding, P. Vedso and M. Begtrup, *J. Chem. Soc.*, *Perkin Trans. 1*, 1998, 1727.
226 L. Jiang, A. Davison, G. Tennant and R. Ramage, *Tetrahedron*, 1998, **54**, 14233.
227 L. A. Carpino, D. Ionescu and A. El-Faham, *Tetrahedron Lett.*, 1998, **39**, 241.
228 V. V. S. Babu and H. N. Gopi, *Tetrahedron Lett.*, 1998, **39**, 1049.
229 H. N. Gopi and V. S. Babu, *Tetrahedron Lett.*, 1998, **39**, 9769.
230 H. M. Meshram, G. S. Reddy, M. M. Reddy and J. S. Yadav, *Tetrahedron Lett.*, 1998, **39**, 4103.
231 A. El-Faham, *Chem. Lett.*, 1998, 671.
232 M. Horikawa, T. Nakajima and Y. Ohfune, *Synlett*, 1998, 609.
233 S. F. Martin, M. P. Dwyer and C. L. Lynch, *Tetrahedron Lett.*, 1998, **39**, 1517.
234 R. Leger, R. Yen, M. W. She, V. J. Lee and S. J. Hecker, *Tetrahedron Lett.*, 1998, **39**, 4171.
235 J. Lehmann, A. Linden and H. Heimgartner, *Tetrahedron*, 1998, **54**, 8721.
236 K. Haas, W. Ponikwar, H. Noth and W. Beck, *Angew. Chem.*, *Int. Ed.*, 1998, **37**, 1086.
237 C. Palomo, M. Oiarbide and S. Bindi, *J. Org. Chem.*, 1998, **63**, 2469.
238 S. J. Park, G. Keum, S. B. Kang, H. Y. Koh and Y. Kim, *Tetrahedron Lett.*, 1998, **39**, 7109.
239 T. Yamada, Y. Omote, Y. Yamanaka, T. Miyazawa and S. Kuwata, *Synthesis*, 1998, 991.
240 F. Lhermitte and P. Knochel, *Angew. Chem.*, *Int. Ed.*, 1998, **37**, 2460.
241 B. M. Kim, S. J. Bae and G. Seomoon, *Tetrahedron Lett.*, 1998, **39**, 6921.
242 K. Tanaka and H. Sawanishi, *Tetrahedron: Asymmetry*, 1998, **9**, 71.
243 J. G. Deng, Y. Hamada and T. Shiori, *Synthesis*, 1998, 627.
244 C. Dominguez, J. Ezquerra, S. R. Baker, S. Borrelly, L. Prieto, M. Espada and C. Pedregal, *Tetrahedron Lett.*, 1998, **39**, 9305.
245 J. T. Lundquist and T. A. Dix, *Tetrahedron Lett.*, 1998, **39**, 775.
246 C. Vergne, J. P. Bouillon, J. Chastanet, M. Bois-Choussy and J. P. Zhu, *Tetrahedron: Asymmetry*, 1998, **9**, 3095.
247 V. Beraud, P. Perfetti, C. Pfister, M. Kaafarni, P. VAnelle and M. P. Crozet, *Tetrahedron*, 1998, **54**, 4923.
248 R. S. Fornicola, E. Oblinger and J. Montgomery, *J. Org. Chem.*, 1998, **63**, 3528.
249 V. W. F. Tai and B. Imperiali, *Tetrahedron Lett.*, 1998, **39**, 7215.
250 T. Nishikawa, M. Asai, N. Ohyabu and M. Isobe, *J. Org. Chem.*, 1998, **63**, 188.
251 A. Abouabdellah, J.-P. Beghu, D. Bonnet-Delpon, A. Kornilov, I. Rodrigues and C. Richard, *J. Org. Chem.*, 1998, **63**, 6529.
252 J. T. Starr, A. Baudat and E. M. Carreira, *Tetrahedron Lett.*, 1998, **39**, 5675.
253 H. L. Hassinger, R. M. Soll and G. W. Gribble, *Tetrahedron Lett.*, 1998, **39**, 3095.
254 S. Braverman, M. Cherkinsky and L. Kedrova, *Tetrahedron Lett.*, 1998, **39**, 9259.
255 H. Sugimura, M. Miura and N. Yamada, *Tetrahedron: Asymmetry*, 1997, **8**, 4089.
256 A. G. H. Wee and F. X. Tang, *Can. J. Chem.*, 1998, **76**, 1070.

Review 9/03369F