Allylic Amination

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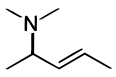
Contents

1. Introduction

Allylamines, **1**, are fundamental building blocks in organic chemistry and their synthesis is an important industrial and synthetic goal. The allylamine fragment can be encountered in natural products, but often the allylamine is transformed to a range of products by functionalization, reduction, or oxidation of the double bond. Thus allylamines have been used as starting materials for the synthesis of numerous compounds such as α- and β-amino acids,[1−4] different alkaloids[5,6] and carbohydrate derivatives.[7]



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The synthesis of allylamines can in principle be divided into three groups of reactions of which two are outlined in Scheme 1. The first type (*i*) constitutes allylamines synthesized by nucleophilic allylic substitution and the second (*ii*) is the direct allylic amination of simple alkenes.

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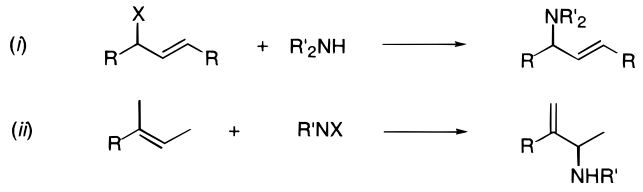
The third type is a variety of more or less indirect approaches to obtain allylamines. However, these reactions are beyond the scope of this review. Some of these methods include reduction of α,β-unsatur-

Scheme 1



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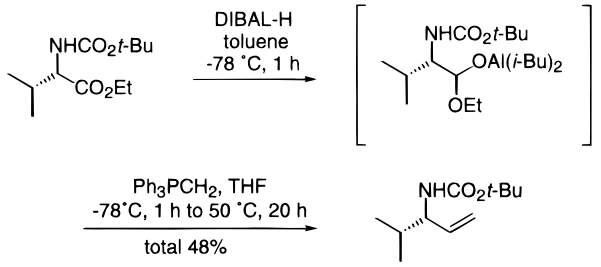
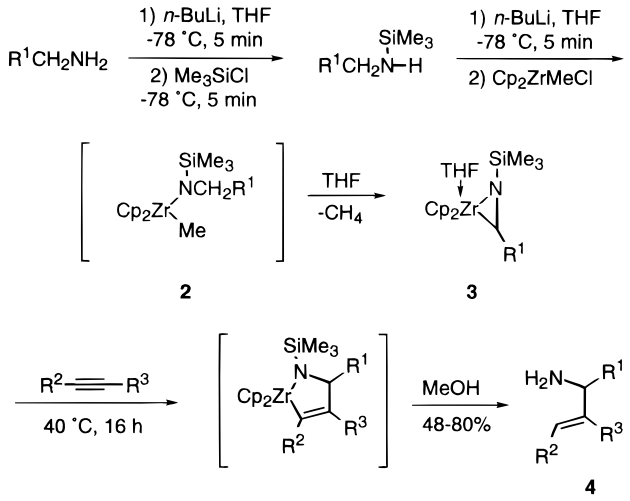
Scheme 2



Scheme 3



ated imines and oximes, rearrangement of aziridines and elimination of water from vicinal amino alcohols and were reviewed in 1983.[8] A few examples of the indirect approaches will be mentioned here (Schemes 2 and 3), otherwise these and related methods will not be discussed any further. Instead we refer to the review and some of the papers which have appeared since then.[9−19]

One way to obtain chiral allylamines is by transformation of compounds from the chiral pool and a recent example is the degradation of α-amino acids as shown in Scheme 2.[20] Through reduction and concomitant Wittig reaction, optically active allylamines could be obtained in 48−78% yield depending on the structure of the starting amino acid.

The use of organo-transition metal chemistry in preparative organic synthesis is still a relatively unexplored research area. An elegant example by Buchwald et al. leading to allylamines is presented in Scheme 3. This reaction sequence involves the formation of a zirconocene−imine complex **3** by a formal *β*-elimination followed by reductive elimination of methane from a zirconium amine complex **2**. Insertion of an alkyne and final protonolysis with methanol yields the allylamine **4**.[21] The procedure is generally high yielding and gives stereochemically pure products with the substituents R^2 and R^3 in a *cis* arrangement. The stereoselectivity of the reaction is unique; however, the stoichiometric use of the transition metal is a drawback for the practical use. Buchwald et al. have also examined the enantioselection obtained with chiral *ansa*-zirconocenes. The results were encouraging with the ee often exceeding 90%.[22] A related example using titanium complexes has also appeared.[10]

The present review on allylic amination will be restricted mainly to an overview of the major developments for the transformation of allylic compounds into allylamines by the two reaction types *i* and *ii* in Scheme 1. Examples of the use of these transformations for total synthesis will also be presented briefly. The two types of allylic amination reactions in Scheme 1 reflect different approaches to the reaction, and to a certain extent also a "traditional" and a "modern" way of thinking in chemistry. The allylic amination in *i* takes its starting point from a substrate which has an allylic C−X (X = heteroatom, halide) bond, whereas the second approach (*ii*) is a direct allylic amination of an alkene, involving a cleavage of a C−H bond, of which the latter imposes some challenges/problems due to the bond strength of the carbon−hydrogen bond.

2. Amination of Functionalized Alkenes (Nucleophilic Amination)

The amination of alkenes functionalized by an allylic C−X (X = heteroatom, halide) outlined in eq 1 has been developed to be one of the most simple and direct ways of synthesizing an allylamine, since very efficient methods for the selective allylic functionalization of alkenes exist.

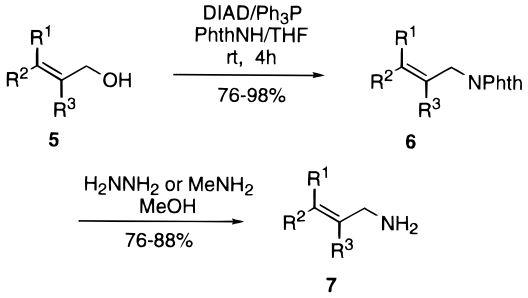
(1)

2.1. Amination of Allyl Alcohols (Mitsunobu Reaction, Etc.)

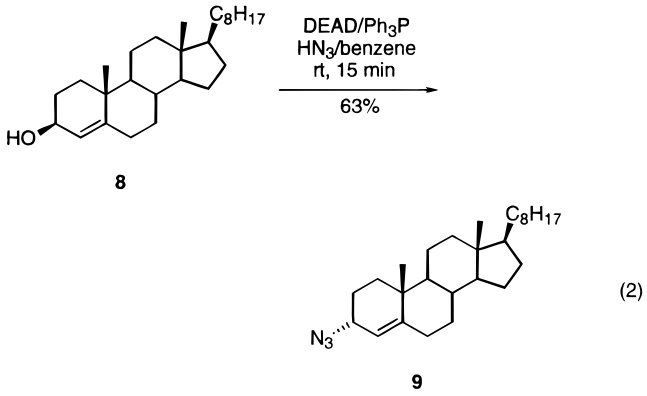
The ready availability of allylic alcohols have made them into the precursors of choice for the synthesis of allylamines. Several methods for their preparation are available. One very mild procedure to obtain allylic alcohols from alkenes is to oxidize them in the α-position by the addition of a stoichiometric amount of selenium dioxide. The mechanism is thought to involve a selenium-oxo-ene reaction followed by a [2,3]-sigmatropic rearrangement, in analogy to the selenium−imido amination procedure (vide infra). The allylic alcohol obtained can be converted to the corresponding amine by various procedures.

The Mitsunobu reaction offers one of the most attractive ways to transform the alcohol into the amine as the reaction can be carried out under very mild conditions with a variety of amine nucleophiles.[23] The procedure has recently been used to synthesize geometrically pure isoprenoide amines by treatment of the allyl alcohol **5** with diisopropyl azodicarboxylate (DIAD) and triphenylphosphine, followed by phthalimide as the ammonia synthon giving **6** Scheme 4). Treatment of **6** with hydrazine or methylamine liberates the primary allylamine **7**. The almost complete conservation of alkene geometry, not only under the Mitsunobu coupling conditions but also after deprotection of the phthaloyl group, is clearly an advantage of this reaction sequence.[24] This is of great value, as analogous coupling reactions using metal azide salts as the nitrogen nucleophile donor give mixtures of trans and cis products (see also eq 7).

Scheme 4



Hydrazoic acid (azide nucleophile) has been used under Mitsunobu reaction conditions with cyclic allyl alcohols, such as the steroid **8** as the substrate, with the formation of the corresponding azide **9** (eq 2).[25]



(2)

The reaction is regioselective (no S_N2' substitution) with inversion of the configuration. The azide **9** can selectively be reduced to the primary allylamine by standard procedures (e.g., H_2/Lindlar cat.).[8]

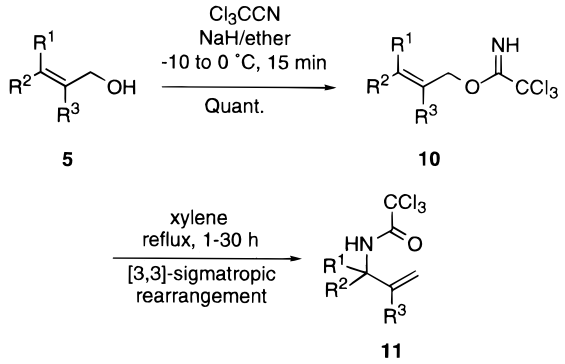
Generally, the Mitsunobu reaction is regioselective, i.e. there is no allylic rearrangement during the reaction. However, a thorough investigation performed by Mulzer et al. revealed that in some cases there can be partial rearrangement under standard conditions for the allylic amination.[26]

N,*N*,*N*′,*N*′-Tetramethylazodicarboxamide[27] and *N*-alkyl- and *N*-acyl sulfonamides[28] have also been used for the synthesis of allylamines under Mitsunobu reaction conditions.

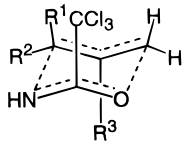
Another elegant amination procedure for the formation of allylamines from allylic alcohols involves the thermal [3,3]-sigmatropic rearrangement of allylic trichloroacetimidates **10** to allylic amides **11**, which then can be hydrolyzed to the desired amines—the Overman rearrangement (Scheme 5).[29,30] The yields are generally good for reactions giving primary and secondary amides, but low for products where the amide nitrogen is bound to a tertiary carbon atom (10−40%). The hydrolysis of the amides is quite slow, as stirring for 30 h in 3 N sodium hydroxide water/ethanol solution is necessary.

On the basis of investigations of the reaction mechanism a cyclic six-membered transition state **12** was proposed.[29] The stereoselectivity observed in the formation of substituted alkenes is similar to that observed for other [3,3]-sigmatropic rearrangements and, furthermore, the preferred formation of the

Scheme 5



trans isomer of the di- and trisubstituted alkenes is consistent with transition state **12**. The activation

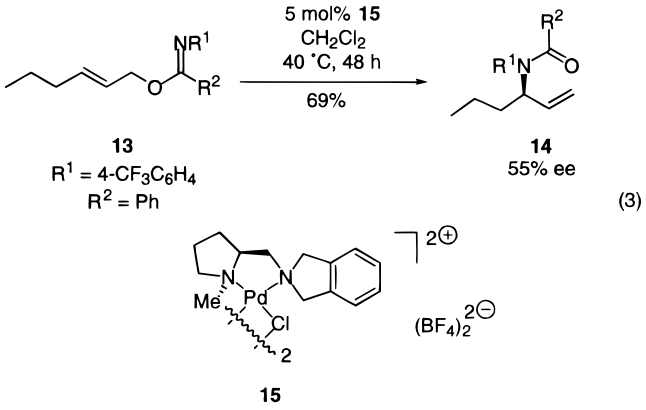


parameters for the rearrangement ($\Delta H^{\ddagger} = 24$ kcal/mol and $\Delta S^{\ddagger} = -19$ eu) are also typical for other [3,3]-sigmatropic rearrangements. However, on the basis of the small increase in rate found by changing the solvent from xylene to nitrobenzene and by the attachment of carbocation stabilizing groups to the imidate-bearing carbon atom indicate that there is some charge separation in the transition state.

The rearrangement has also been carried out at ambient temperatures by adding a catalytic amount of mercury(II) trifluoroacetate.[29,30] The yields and selectivities were comparable to the thermal reactions above. A two-step mechanism for the mercury-(II)-catalyzed rearrangement was proposed,[29] the first step being a mercuric electrophilic addition to the double bond forming a mercurinium ion (or its equivalent) which then is captured intramolecularly by the nucleophilic imino nitrogen atom.

Because of the relatively high basicity of the imidates, only a few metals should be able to catalyze the rearrangement.[31] Apart from the mercury salt, soluble palladium(II) complexes have emerged as relatively good catalysts. The possible ligand variety is reduced by the fact that phosphines inhibit the reaction.[32,33] The reason is presumably that they are too electron donating, thereby diminishing the Lewis acid character of the catalyst.

In an attempt to perform an enantioselective rearrangement, a cationic palladium catalyst with a chiral nitrogen ligand was used. The inventors this way succeeded in making the first enantioselective version of the Overman rearrangement (eq 3). The rearrangement of **13** catalyzed by **15** proceeds to give **14** in 69% yield and up to 55% ee. The enantioselectivity of the reaction was also investigated in various solvents; in nitromethane 55% ee was obtained, whereas only 35% ee was found in DMF. Other palladium(II) complexes were also tested, but moderate to poor yields and low enantioselectivities were observed.[33]

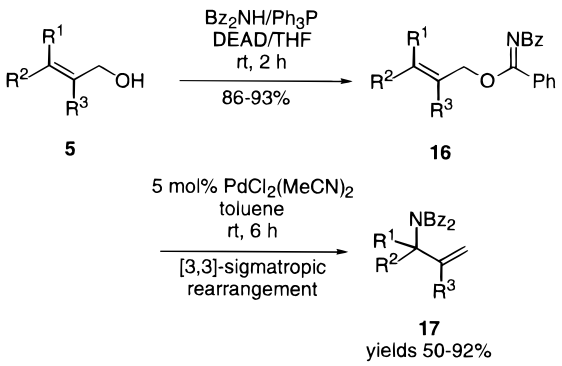


Even though quite successful in the enantioselective reaction (eq 3), the authors state the ongoing problems with the basicity of the imidates. In light of this, Overman, 23 years after his first paper on the reaction, introduced the rearrangement of the less basic allylic *N*-benzoylbenzimidates **16** catalyzed by palladium(II) chloride (Scheme 6).[31] The yields, selectivities, and rates for the formation of the allylamines **17** are better than those observed by the first procedure and even the rearrangement, giving a tertiary amide, proceeds well. It is notable that for substrates where no allylic dibenzamide can be detected under the thermal reaction conditions up to 91% of the product is formed in the presence of the palladium(II) catalyst. This is promising for the future development of an asymmetric version of the reaction,[33] and for increasing the substrate tolerance.[34] Hopefully, it will be possible to apply not only nitrogen, but also phosphine ligands, and thereby open up an extensive screening of the variety of chiral phosphine ligands available.

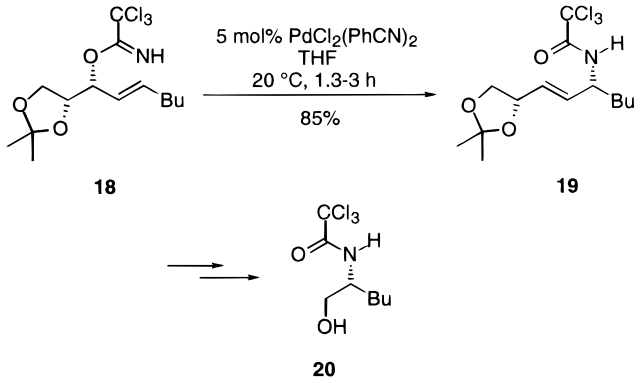
The palladium(II)-catalyzed rearrangement of allyl imidates for the formation of allylamines has also been studied by Metz et al.[32] The rearrangement proceeds well for allyl *N*-phenylimidates and was applied to the chiral imidate **18** which in the presence of palladium(II) rearranges to **19**, a precursor for the synthesis of (*R*)-*N*-(trichloracetyl)norleucinol **20** as outlined in Scheme 7.

The Overman rearrangement has also been applied to many other substrates and some examples are given in the references.[35−41] An elegant application of this reaction has been published by Danishefsky et al. for the synthesis of (±)-pancratistatin **23** (Scheme 8).[42] The Overman rearrangement of compound **21** to **22** proceeds in 56% yield.

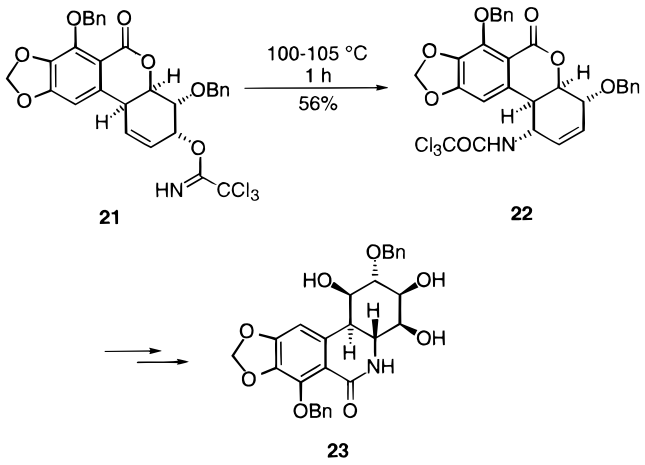
Scheme 6



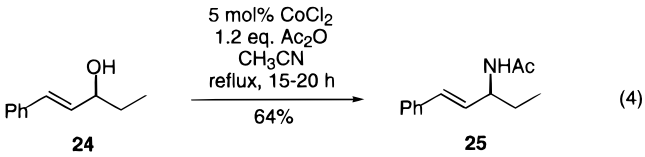
Scheme 7



Scheme 8



The last conversion of alcohols to allylamines which shall be discussed here is the Ritter reaction. A newly published improvement makes it possible to run this, originally perchloric acid catalyzed, reaction under practically neutral conditions, by adding a catalytic amount of cobalt(II) chloride and acetic anhydride (eq 4).[43,44] An example is given in eq 4 in



which the aromatic allyl alcohol **24** reacts to give the allyl acetamide **25**. However, about 10% of the corresponding allyl acetate is also isolated. This points to a common intermediate with the allylic substitution catalyzed by transition metals proceeding by π-allyl complexes (vide infra).

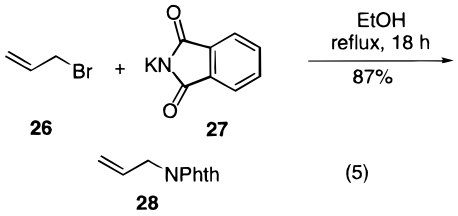
The attractivity of the reaction is in the simple procedure, and maybe the future might bring even milder and more selective variants arising from tuning of the catalyst and reaction conditions. A drawback for the reaction is the lack of regio- and diastereoselectivity (cis/trans isomerization), as mixtures of products mainly arising from S_N2 and S_N2' attack with scrambled double bonds are isolated.[43,44] A regioselective allylic amination of allyl alcohols can also be performed using a catalytic amount of palladium(II), a stoichiometric amount of tin(II) chloride,

and an amine nucleophile.[45] This reaction probably also proceeds by a π-allyl complex intermediate (vide infra).

2.2. Amination of Allyl Halides, Acetates, Etc. (Gabriel Synthesis, Etc.)

Despite the high activity of allylic halides in S_N2 reactions, the direct coupling of allyl halides with nitrogen nucleophiles has met with limited success,[24] mainly because di- and trialkylated byproducts often predominate.

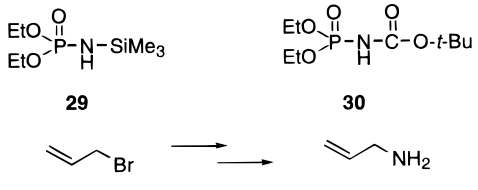
A traditional way to overcome the problem of polyalkylation of amines is to apply the Gabriel synthesis, which uses a stabilized (phthalimide) anion as nucleophile (eq 5).[46] This method has been



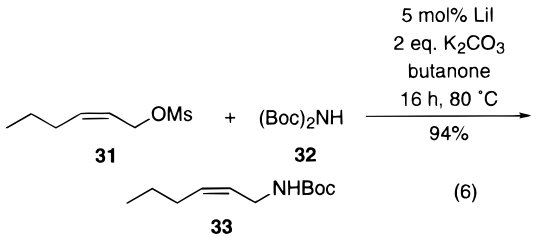
used to prepare primary allylamines from alkyl halides **26** and potassium phthalimide **27**. However, the reaction often suffers from problems in removing the phthaloyl group from the product **28**.[47,48]

There has also been focus on the development of reagents with a more labile protecting group than the phthalimide. Among the reagents investigated are compounds **29** and **30** shown below in Scheme 9, in which the substituents at the nitrogen atom can easily be removed with gaseous hydrogen chloride after alkylation.[49−51] With these reagents better yields of some primary allylamines have been obtained, compared to the traditional method using the phthalimide. Unfortunately, the substrate tolerance is rather low and the reagents are quite exotic.

Scheme 9



More promising is the amination with the stabilized anion of di-*tert*-butyl iminocarbonate ($(Boc)_2NH$) **32**. Under very mild conditions, this reagent reacts with a variety of primary and secondary halides and mesylates, giving the allylamines in excellent yields. For example, the reaction of the mesylate **31** with **32** gives the allylamine **33** in high yield (eq 6).[52] The procedure has one great advantage compared to the palladium-catalyzed amination with the same reagent (vide infra). *cis*-Alkenes react without scrambling of the double bond, an important aspect considering the isomerization sometimes observed using palladium-catalyzed substitution (compare eq 6 with eq 7).



2.3. Amination of Allyl Halides, Acetates, Etc. Catalyzed by Transition Metal Complexes

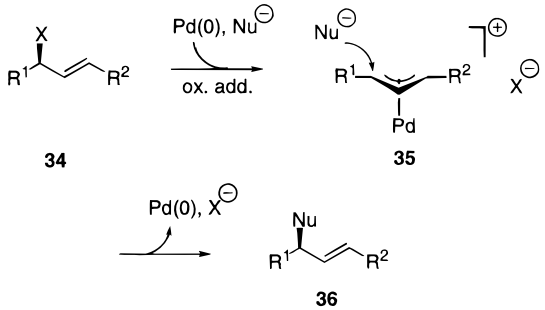
An attractive way to expand the scope of the allylic amination reactions mentioned above is to add a catalytic or in some cases stoichiometric amount of a transition metal salt. Since the discovery of the palladium-catalyzed allylic alkylation by Tsuji et al. in 1965,[53] an intense research has been carried out in this field, and even though complexes of nickel, platinum, rhodium, iron, ruthenium, molybdenum, cobalt, and tungsten have been found to catalyze the alkylation, palladium complexes have by far received the greatest attention.[54−57] Today, very efficient palladium catalysts for carrying out the allylic alkylation exist. As a spin off, not only the alkylation, but also the allylic amination can now be performed with a high degree of efficiency and selectivity, and the palladium-catalyzed allylic amination has become quite established in organic synthesis.[6,54]

The mechanism for the palladium-catalyzed allylic amination is generally accepted to proceed via a neutral or cationic palladium π-allyl complex **35** (Scheme 10), which is formed by nucleophilic attack on **34** by palladium. In the second step, the nucleophile (the amine) attacks directly at the allylic ligand, in analogy with the reaction mechanism for soft carbon nucleophiles. The net result of this mechanism is a substitution with retention of configuration in the product **36**.[57] For a more thorough discussion of the reaction mechanism see also Hayashi.[56]

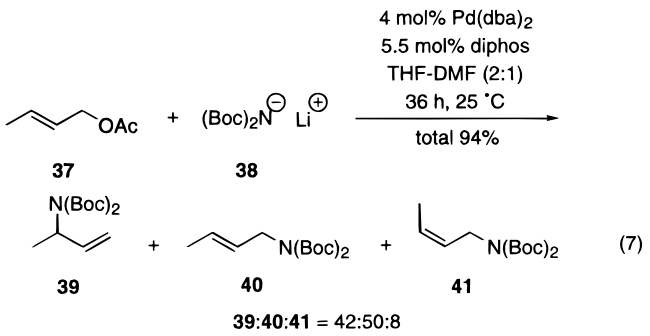
While primary and secondary amines can be used as nucleophiles, ammonia does not react. As a consequence, many ammonia synthons have been developed, and protected primary allylamines are now readily available through the use of azide, sulfonamide, phthalimide, di-*tert*-butyl iminocarbonate ($(Boc)_2NNa$), and dialkyl *N*-(*tert*-butoxycarbonyl)-phosphoramide anions as nucleophiles.[2,58] The substrates are normally allyl acetates, carbonates, phosphates, and in some cases even the reactive chlorides have been used.[59,60]

In general, unsymmetrical allyl systems (e.g., $R^2 \neq R^1 = H$ in Scheme 10) are attacked by the

Scheme 10

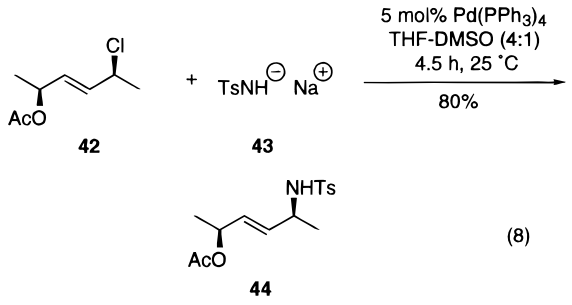


nucleophile at the less substituted carbon atom, although there have been observations of reactions on nonsymmetrical substrates with low (no) regioselectivity as shown in eq 7. The reaction of **37** with di-*tert*-butyl iminocarbonate **38** gives a mixture of the products **39**−**41**.[61]



Even though the reaction rate with amine nucleophiles is somewhat lower than the rates observed with stabilized carbon nucleophiles, very good yields can normally be obtained after prolonged reaction times (>24 h, >90%) (eq 7).

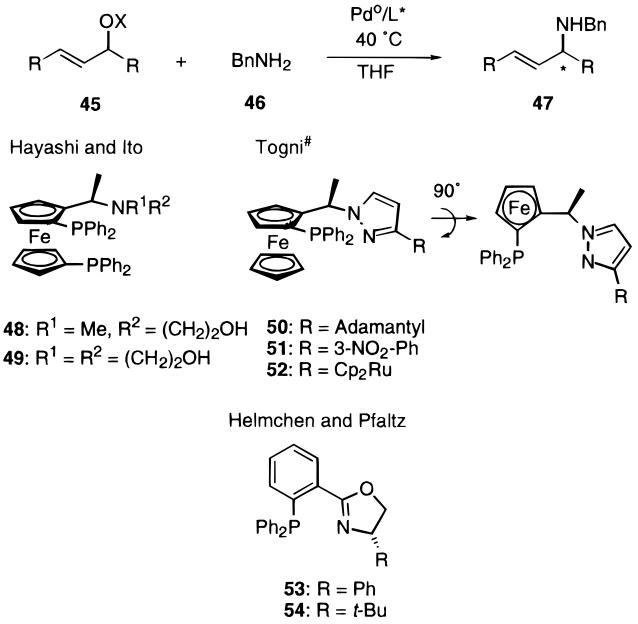
The stereochemistry of *trans*-alkenes is normally preserved through the reaction, whereas the use of *cis*-alkenes has been limited. Even chloride in the presence of an acetate group can be substituted selectively. The reaction of compound **42** with the tosyl amide nucleophile **43** leads to **44** as the sole product in good yield (eq 8).[59] Sometimes substitution of the chloride takes place even in the absence of a catalyst. As this can be a disadvantage, the somewhat less reactive acetates are normally used in the catalytic reactions.



The allylic amination can, as previously described, be carried out with a high degree of regio- and diastereoselectivity. During the past decade(s), the focus mainly has been on the development of efficient chiral catalysts, which can induce high enantioselectivity in allylic alkylation reactions.[57] The application of some of these complexes in allylic amination reactions has been quite successful. The best results for the reaction of **45** with benzylamine **46** catalyzed by palladium(0) in the presence of the three major types chiral ligands used, **48**−**54** are given in Table 1.[1,3,60,62,63]

The allylpalladium complexes involved in these substitution reactions have been thoroughly investigated. They are often relatively easy to crystallize and since palladium(II) is diamagnetic, the complexes can be analyzed by standard NMR techniques.[1,62−66]

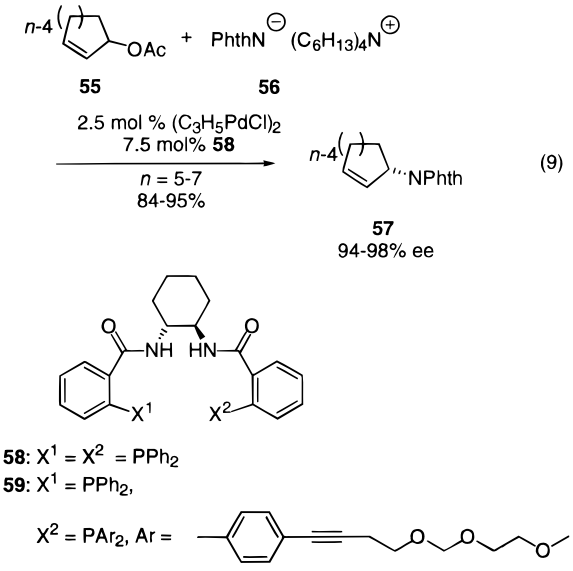
Table 1. Enantioselective Allylic Amination of 1,3-Diphenyl- and 1,3-Dimethyl-2-propenyl Acetates 45 with Benzylamine 46 Catalyzed by Palladium(0) in the Presence of Various Chiral Ligands 48−54[1,3,60,62,63]



#The enantiomer of the Togni ligand has been drawn to facilitate comparison with the two other ligand types.

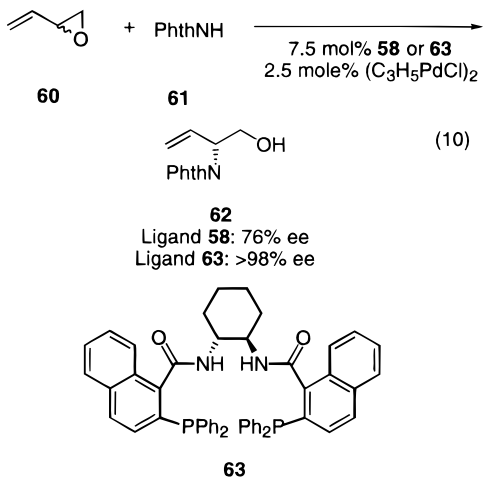
R	ligand L* (mol%)	Pd (mol %)	X	reaction time (h)	**47** yield (%)	ee (%)	ref
Ph	**48** (2.6)	2.5	CO_2Et	31	80	79	1
Ph	**49** (2.6)	2.5	CO_2Et	37	93	97	1
Ph	**50** (4.5)	3.0	CO_2Et	12	90−95	99	63
Ph	**51** (4.5)	3.0	CO_2Et	12	90−95	97	63
Ph	**52** (4.5)	3.0	CO_2Et	12	90	99	64
Ph	**53** (3.0)	3.0	CO_2Me	1	98	94	61
Ph	**54** (3.0)	3.0	CO_2Me	2	93	88	61
Me	**53** (10.0)	3.0	CO_2Me	15	93	30	61
Me	**54** (10.0)	3.0	CO_2Me	96	87	57	61
Me	**49** (2.0)	1.0	$P(O)Ph_2$	13	84	73	1

In asymmetric palladium-catalyzed allylic amination reactions there is a great difference between cyclic and acyclic substrates. Usually many of the ligands developed for acyclic substrates are largely inefficient on cyclic substrates. Recently Trost et al. have developed a ligand type which is very efficient for both acyclic and cyclic substrate types.[67] The ligand is based upon 2-(diphenylphosphino)benzoic acid (DPPBA) and a chiral C_2-symmetric diamine or diol. Two examples of ligands **58** and **59** derived from a vicinal diamine are depicted in eq 9. The palladium-catalyzed reaction of racemic five- to seven-membered rings **55** with the anion of the phthalimide **56** as nucleophile in the presence of **58** as the chiral ligand gave the corresponding allylamine **57** in good yield (84−95%) and high ee (94−98%) (eq 9). Standard removal (NH_2NH_2, C_2H_5OH, and HCl) of the phthalic acid moiety gave the corresponding allylamine with (*S*) configuration.[67] The use of a bulky ammonium cation in combination with the relatively unpolar dichloromethane as solvent is essential to obtain a high enantioselectivity. The authors suggest a tight ion pair to be involved and the effect of the bulky ammonium ion to be more pronounced in the less polar dichloromethane solvents. In THF, lower selectivity is observed and a less tight ion pair



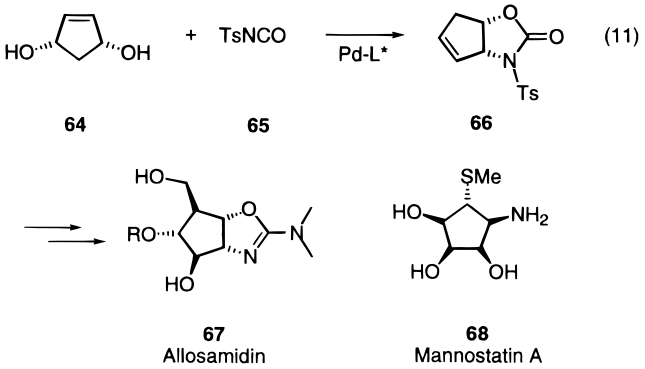
probably is present. Using derivative **59** with a cationic binding site leads to a reaction which could be performed with as little as 0.25 mol % of the catalyst giving 91% yield of **57** ($n = 6$) with an ee of 98%.[68]

Other very successful applications of this ligand type include the regioselective opening of vinyl epoxides and the dissymmetrization of allylic diols with tosyl isocyanate.[7,57,69] The palladium-catalyzed reaction of vinyl epoxide **60** with phthalimide **61** in the presence of **58** as the chiral ligand gave **62** as the major regioisomer (9:1) in 76% ee (eq 10). The ee and



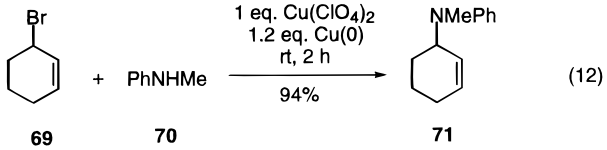
the regioselectivity in eq 10 could be improved to >98% and >75:1, respectively, by the application of **63** as a chiral ligand which has a restricted rotational freedom of the carboxamide group.

The dissymmetrization of allylic diols such as **64** with tosyl isocyanate **65** in the presence of chiral palladium complexes (eq 11) has been developed and used in total synthesis by Trost et al. and has recently been described in detail in this Journal.[57] The general reaction is presented in eq 11 along with two natural products allosamidin **67** and mannostatin A **68** synthesized from **66**.[7] Recently palladium-catalyzed reactions have also been used for total synthesis of (−)-mesembrane and (−)-medembrine.[70]



The use of the palladium-catalyzed approach for the formation of allylamines has also been pursued briefly by others and further details can be obtained in the review by Trost.[57]

It is interesting to note that the number of reports on allylic amination promoted by metals other than palladium is very sparse. The effect of adding a mixture of copper(II) perchlorate and metallic copper was recently investigated by Samuelson et al. Substrates such as 3-bromocyclohexene **69** react with *N*-methylaniline **70** to give the allylic aminated product **71** in high yield (eq 12).[71] The yields using

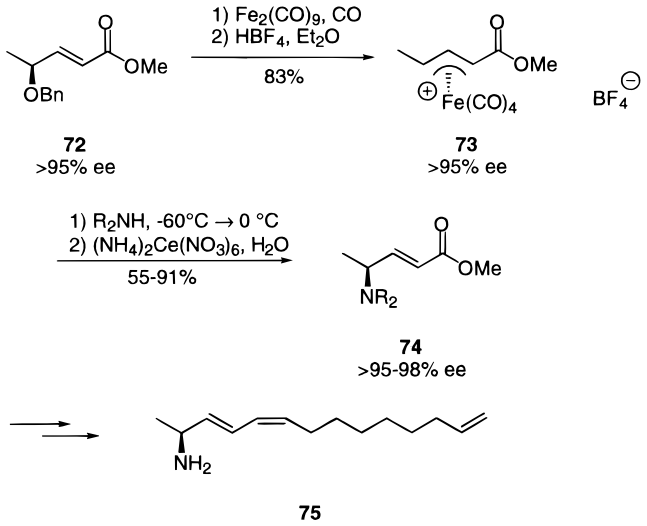


secondary amines as nucleophiles are generally high, and a somewhat different regioselectivity compared with the palladium-catalyzed substitutions has been observed as the nucleophile has a tendency to attack at the highest substituted carbon termini.

Iron complexes have also been used to promote allylic amination.[72−74] The nucleophilic addition of various acyclic and cyclic amines to the highly enantiomerically enriched 1-methoxycarbonyl-3-methyl-(η^3-allyl)-tetracarbonyliron cation **73**, formed in 83% yield from **72**, followed by oxidative removal of the iron tetracarbonyl moiety group by reaction with cerium(IV) gives **74** with high optical purity and retention of the stereochemistry from **72** (Scheme 11).[72] The reaction proceeds well for the different amines and was used for the synthesis of **75** which shows cytotoxic activity against diverse cell lines.[73]

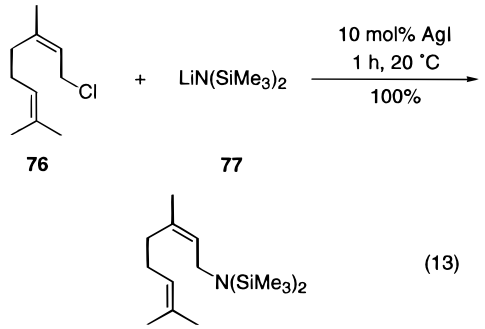
Allylic amination of allyl halides can also be achieved using lithium and potassium bis(trimethylsilyl)amides[75,76] and potassium 1,1,3,3-tetramethyldisilazide[77] as the nucleophiles. For the reaction of alkyl-substituted allylic chlorides using lithium bis(trimethylsilyl)amides **77** as the nucleophile the allylic amination proceeds smoothly in S_N2 fashion to give *N*,*N*-disilylamines in high yields when silver(I) iodide was used as an additive. The reaction of neryl chloride **76** with **77** takes place with retention of configuration of the carbon−carbon double bond to give only one isomer, **78**, in high yield (eq 13).[75] In the absence of silver(I) iodide only traces of **78** are formed. The reaction of crotyl chloride with **77** is facilitated by addition of only 2 mol % of silver(I)

Scheme 11



72 >95% ee **73** >95% ee **74** >95-98% ee **75**

iodide. Other metal complexes such as copper(I) iodide and other silver(I) salts could also be used as additives for the reaction. On the basis of NMR investigations it was proposed that lithium amide complexes such as $(Me_3Si)_2NAg^ILi$ and $[(Me_3Si)_2N]_2Ag^ILi_2$ are formed in the reaction mixture and the reactivity of **77** is controlled by forming these species.

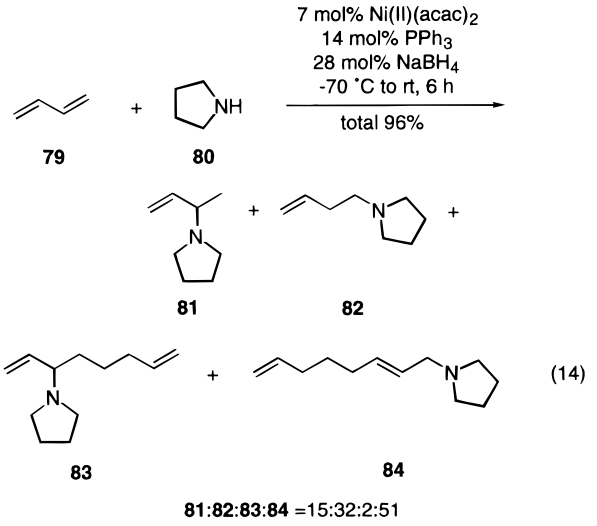


76 **77** **78** (13)

2.4. Direct Amination of Dienes and Allenes

The direct hydroamination of dienes and allenes is a very attractive reaction to obtain allylamines, although the selectivity of especially the reaction of allenes is very hard to control.[12,78−80] The reaction catalyzed by transition metals has been studied in some detail, and is generally thought to involve π-allyl intermediates similar to what has been observed in the allylic substitution reaction (vide supra).

The nickel-catalyzed coupling of 1,3-butadiene **79** with various amines such as pyrrolidine **80** (eq 14) was studied by Baker et al.[78] and Kiji et al.[81] Apart from the two monoaddition products **81** and **82**, the telomeric products **83** and **84** are also observed. The two latter arise through an oxidative coupling of two dienes in the coordination sphere of a nickel complex forming a bis-π-allyl nickel metallacycle intermediate, which subsequently reacts with one amine molecule.[78] Other metals such as rhodium, cobalt, and iridium can also catalyze the reaction. The ratio of the products **81**−**84** is dependent on the metals,

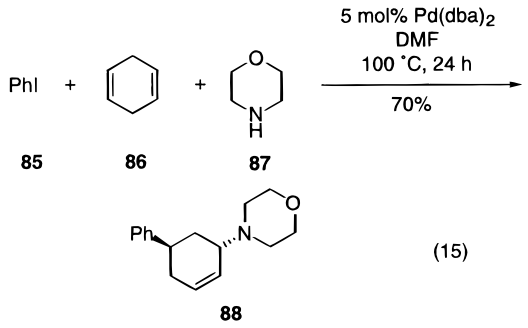


79 **80** **81** **82** **83** **84** (14)

81:**82**:**83**:**84** =15:32:2:51

as well as other factors.[78] More recently ammonia has also been reacted with **79** under two-phase catalysis giving mainly telomeric products.[82]

The three-component coupling of an aryl iodide **85**, a nonconjugated diene **86**, and an amine **87** is a very elegant reaction (eq 15).[83] The yields of the reaction



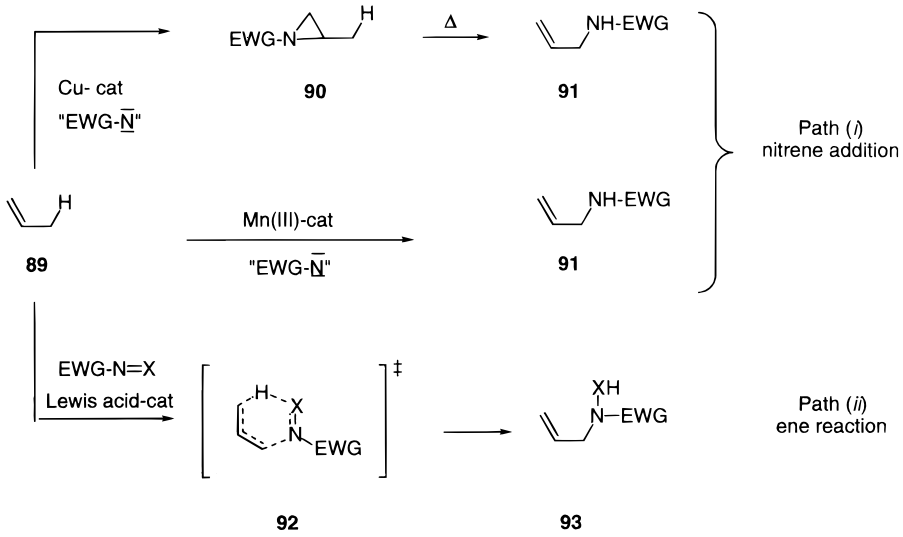
85 **86** **87** **88** (15)

are generally quite good; however, the selectivity is difficult to control. In the example outlined, only one product is observed (**88**) with the two substituents being trans to each other. The mechanism is thought to involve oxidative addition of the aryl iodide to palladium, insertion of the alkene into the palladium aryl bond, followed by palladium migration through repetitive palladium hydride β-eliminations and readditions to form a π-allyl complex. The product is finally obtained by nucleophilic displacement of palladium by the amine nucleophile.[83] At present, the reaction demands rather high temperatures to proceed (100 °C). This might turn out to be an obstacle for the development of (enantio-)selective variants, but does on the other hand not exclude this. Larock et al. have also used this approach for the three component coupling of vinyl halides, alkenes, and amines, giving allylamines in good yields.[84]

3. Amination of Nonfunctionalized Alkenes (Electrophilic Amination)

The direct electrophilic amination of alkenes is an attractive way for the synthesis of allylamines. The single step procedures allow an easy and fast allylic functionalization, which probably is the most important part of this amination chemistry. The perfor-

Scheme 12

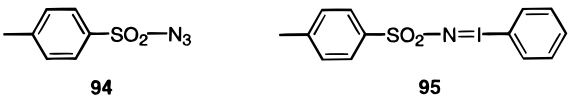


mance of the different catalytic systems is, however, still not competitive with e.g. the palladium-catalyzed substitution reaction.

The majority of direct electrophilic aminating reagents for alkenes can be divided into two subgroups (path *i* and *ii*, Scheme 12). The first group consists of the nitrene precursors, which on treatment with a metal catalyst, such as copper and manganese, transfers the nitrene fragment to the alkene **89**. The addition is either direct to the alkene **89**, forming an aziridine **90**, or by insertion in the allylic C−H bond forming the allylamine **91**. The aziridine **90** can undergo a thermal or metal-catalyzed rearrangement to **91** (Scheme 12, path *i*). The second group of electrophilic amination reagents are aza compounds which undergo the ene reaction forming the (homo) allylamine **93** directly via an ene transition state **92** (path *ii*).[85−90]

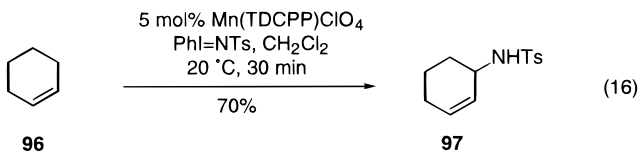
3.1. Amination with Nitrene Complexes

It has been known for quite a long time that nitrenes or nitrenoids (nitrene complexes) can add to an alkene, forming an aziridine, or insert into the allylic C−H bond, forming an allylamine. As nitrene precursors a variety of N derivatives have been used, with tosyl azide **94** and *N*-tosyliminophenyliodinane (PhI=NTs) **95** maybe being among the most widely applied.[86−88,91−98]



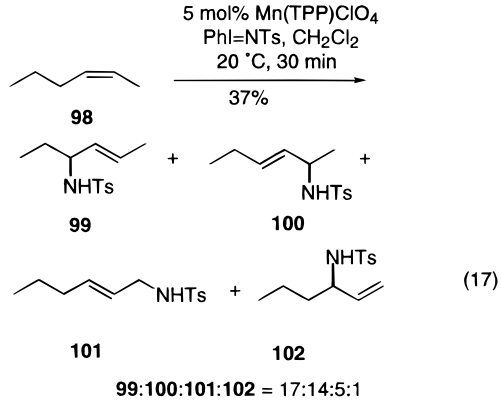
94 **95**

It has been stated by Mansuy et al. that by proper choice of the metal catalyst, the chemoselective addition of **95** to either the alkene or the allylic C−H bond can be controlled (eq 16).[86] This observation was later confirmed by Evans et al.[87] Generally, manganese catalysts tend to give the allylic amination product, whereas copper catalysts gives the aziridine as the main product. Despite the fact that the aziridination reaction recently has been developed in detail, and quite efficient systems now are available for the enantioselective addition of the tosyl nitrenoid species to alkenes,[87,93,94,99] the selective insertion of nitrenoids into the allylic C−H bond has been explored to a very low extent. This leaves the attractive possibility to develop the insertion reaction into a practical and selective one open!



96 **97** (16)

In the insertion reaction (eq 16) with cyclohexene **96**, an acceptable yield of 70% of allylamine **97** is isolated.[86,88] The analogous reactions with other cyclic systems do not proceed quite as well, since the yields do not exceed 44% in these cases.[88,100] In a related example with *cis*-2-hexene **98**, a range of isomeric insertion products **99**−**102** arise (eq 17). Unfortunately the total yield is also quite low (37%) and it is notable that only the trans products **99**−**101** are formed, although a *cis*-alkene (**98**) was used as the substrate.

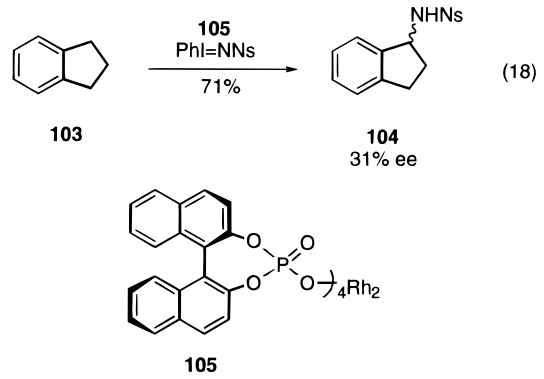


98 **99** **100** **101** **102** (17)

99:**100**:**101**:**102** = 17:14:5:1

To our knowledge, only one report exists on the asymmetric nitrene insertion reaction catalyzed by a chiral transition metal complex. The reaction which uses the more soluble nosyl-imine derivative as nitrene donor and Pirrung's catalyst **105** gives in

the reaction with indan **103** the insertion product **104** in good yield and fair ee (eq 18).[100−102]

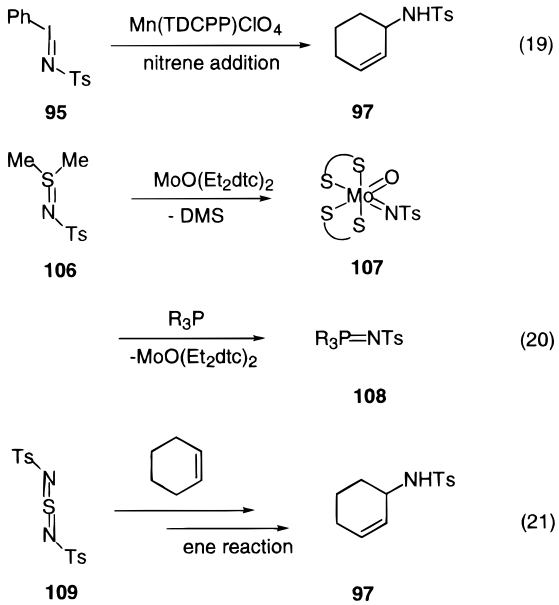


3.2. Amination Based on Ene Reaction Like Processes

The difference between nitrene donor reagents (vide supra) and nitrogen functionalities (enophiles) which undergo ene reactions can in some instances be very subtle (Scheme 13). Apart from the *N*-tosyliminophenyliodinane reagent **95** (Scheme 13, eq 19), the dialkyl sulfimine **106** also is reported to transfer the tosyl nitrogen fragment to a molybdenum complex, forming a molybdenum nitrene complex **107**, which can form aminated phosphines **108** (Scheme 13, eq 20).[95] On the other hand, the analogous sulfur reagent **109** is known for its facile nitrogen transfer to alkenes through an ene reaction−sigmatropic rearrangement process (Scheme 13, eq 21).[103] These borderline cases are worth keeping in mind, to keep track of the (by-)products formed during an electrophilic amination reaction.

The ene reactions are in general all normal electron demand ene reactions, i.e., the enophile reacts as the electrophilic partner, which means that the lower the LUMO energy of the enophile, the higher the reactivity is. Since the orbitals of the more electronegative heteroatoms such as oxygen and nitrogen are lower in energy compared to carbon, the LUMO energy of

Scheme 13



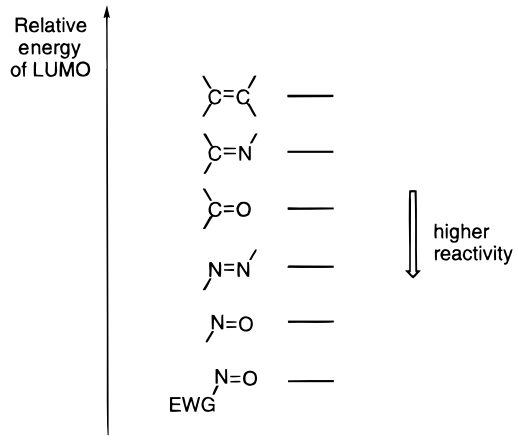


Figure 1. A schematic presentation of the relative LUMO energies for a series of enophiles.

the enophile is also lower in energy than the LUMO energy of an alkene. This, by virtue, makes them more reactive in normal electron demand ene, as well as, Diels−Alder reactions.

For the same reason substitution at either end of the enophile with an electron withdrawing group enhances the reactivity even further. A schematic diagram of the relative LUMO energies of some enophiles is presented in Figure 1. Note that some of the enophiles might change position with each other depending on their substitution pattern.

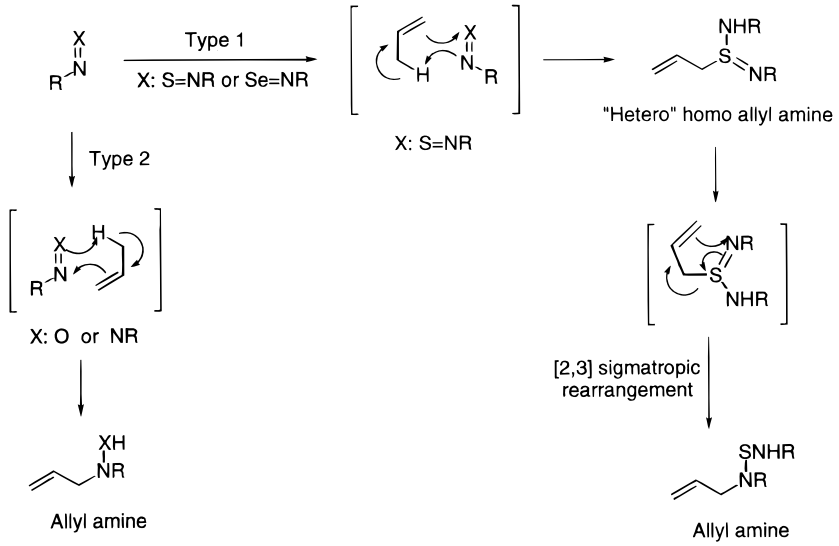
Depending on the nature of the enophile, the regioselectivity can vary (type 1 and 2, Scheme 14). As a rule of thumb, the nucleophilic attack by the allylic system takes place at the end of the enophile where the least electronegative atom is positioned. Thus only nitroso and azo compounds should be attacked at the nitrogen atom (type 2). This directly gives rise to the allylamine through the ene reaction depicted.

When selenium or sulfur imido compounds are applied in the ene synthesis, the regioselectivity is reversed, and a "hetero" homo allylamine is formed (type 1). This designation is used to emphasize that a homo allylamine is formed, but that this also contains a heteroatom (selenium or sulfur). The initially formed homo allylamine undergoes a second pericyclic [2,3]-sigmatropic in situ rearrangement to give the desired allylamine product.

3.2.1. Ene Reaction Followed by [2,3]-Sigmatropic Rearrangement (Type 1 Reaction)

As outlined in Scheme 14, selenium and sulfur diimido compounds (type 1 reaction) can undergo a two-step reaction sequence when treated with an allyl alkene to form allylamines. The two steps are analogous to those observed in the selenium dioxide promoted allylic oxidation. The amination reactions were independently discovered by Kresze et al. in 1975[104] (sulfur imido amination) and by Sharpless et al. in 1976[103,105] (sulfur and selenium imido amination). Both of them are highly attractive as they proceed under very mild reaction conditions and are quite selective, the biggest problem being the final deprotection (vide infra). The cleavage of the nitrogen−selenium or sulfur bond can easily be carried

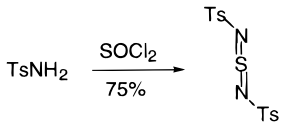
Scheme 14



Scheme 15

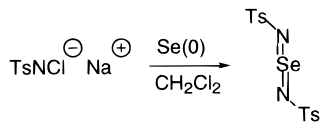
Original *N*-Tosyl reagents:

Kresze (1975), Sharpless (1976)



109

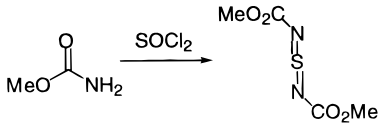
Sharpless (1976)



Chloramine T **110**

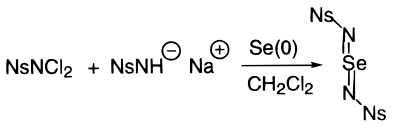
Improved reagents:

Kresze (1983), Katz (1994)



111

Sharpless (1996)



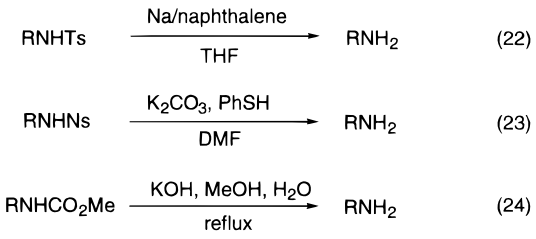
112

out. This either occurs in situ (in case of selenium) or by alkaline hydrolysis at room temperature (in case of sulfur). However, removal of the *N*-tosylate group imposes some difficulties (R = Ts in Scheme 14).[8,106,107] For the same reason, both of the amination procedures have recently been improved and today, alternatives for the original reagents exist which can be deprotected easily (Scheme 15).[106−108]

The development in selenium and sulfur diimido reagents is presented in Scheme 15, and any allylic amination should be carried out using these slightly modified reagents.

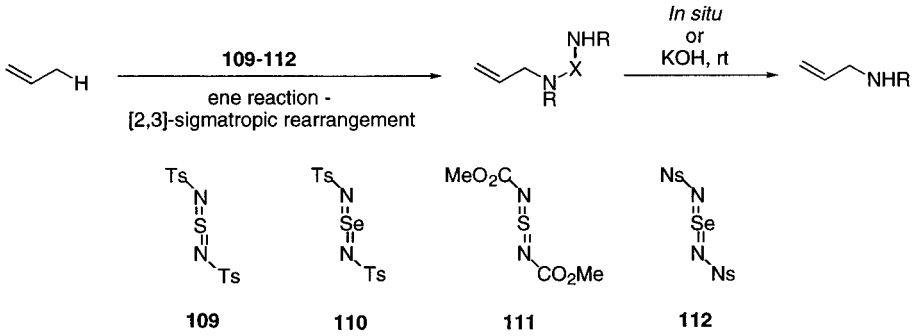
The detosylation of amines normally requires reductive conditions such as Na/naphthalene to proceed (eq 22, Scheme 16). A milder version has been developed but requires 3−4 additional steps.[8,109] The substitution of the tosylate with the *o*-nitrobenzenesulfonyl (nosyl or Ns) is a major improvement as this group can be removed under almost neutral conditions using a method developed by Fukuyama et al. (eq 23, Scheme 16).[110] The carbamate group can, in contrast to the tosylate group, be removed by simple alkaline hydrolysis (eq 24, Scheme 16).[107]

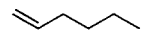
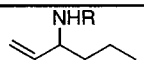
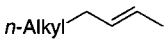
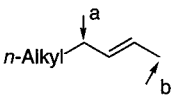
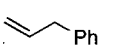
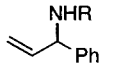
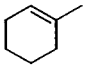
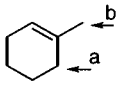
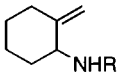
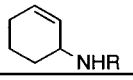
Scheme 16



In general, the sulfur compound **109** (Scheme 15) gives the most clean and highly yielding reactions of the four reagents with the different propene derivatives (Table 2).[103] The selenium reagents **110** and **112** (Scheme 15) are attractive, mainly because of the very simple one-pot procedure for amination, but the mild and easy deprotection strategy for the nosyl derivatives recently developed increases the synthetic value for the latter even further. The amination with

Table 2. Allylic Amination of Different Alkenes Using the Various Diimido Compounds 109−112 (Scheme 15)[103−108]



Entry	Alkene	Protected amine	109	110	111	112
			% yield	% yield	% yield	% yield
1			45	-	54	51
2			a/b	a	a/b	-
			56/3	53	51/11	
3			56	58	40	-
4			a/b	-	a/b	-
			38/33		35/20	
5			84	-	74	64
6			70	51	45	-

the alkoxycarbonyl sulfur diimido compound **111** (Scheme 15) also proceeds well, although this reagent is not quite so reactive as the sulfonate compounds and often prolonged reaction times are necessary (up to 120 h).[107] The deprotection of the amine products from **111** (Scheme 15) is quite easy, and a recent report states that this reagent also can be prepared in situ using methyl carbamate, thionyl chloride, and a base.[108]

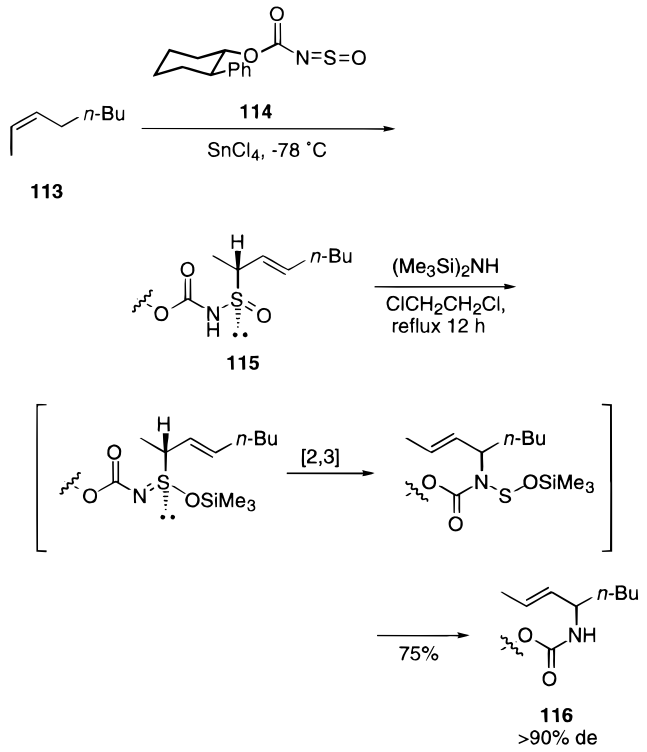
Table 2 presents a comparison of the various diimido compounds **109**−**112** for the allylic amination of a series of alkenes.

As shown in Table 2 the yields of allylamines are moderate to good, depending on the substrate and the aminating agent used. The aminations normally give *trans*-alkenes, regardless of the configuration of the starting alkene (no example of this is shown in the table) and when disubstituted dienes are employed, the ease of allylic amination is normally CH_2 > CH_3 > CH (see entries 2 and 4).

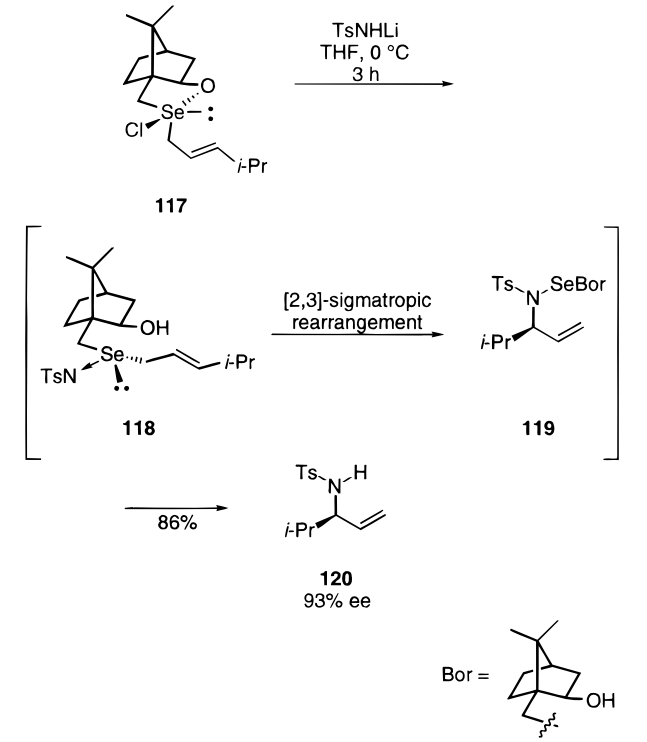
Finally, it should be mentioned that at least two attempts have been made to perform the reaction diastereoselectively.[111,112] Tsushima et al. prepared both enantiomers of *N*,*N*′-bis[*N*-(*p*-tolylsulfonyl)benzenesulfonimidoyl]selenium diimide and used these for diastereoselective allylic amination of alkenes.[111] Asymmetric allylic amination of different alkenes such as methylene cyclohexane, cyclohexene, 1-heptene, and cyclooctene with the chiral selenium diimide reagent gave the allylic amides with 42%, 34%, 32%, and 20% de, respectively. It was found that the (*S*)-configurated diimido selenium reagent gave an (*S*) configuration in the allylic amination product. The method published by Whitesell et al. uses the well-known *trans*-2-phenylcyclohexanol as the chiral auxiliary and gives the most promising asymmetric induction (Scheme 17).[112] The reaction proceeds well for a series of cyclic and acyclic alkenes, such as **113** which reacts with the *N*-sulfinylcarbamate **114** of *trans*-2-phenylcyclohexanol in the presence of $SnCl_4$, giving the allylic product **115** in reasonable yields and absolute stereocontrol at both the carbon and sulfur stereocenter. The [2,3]-sigmatropic rearrangement is promoted by silylation of the intermediary ene product, giving the allylamine **116** in 75% yield and with a de >90%.

Even though the following [2,3]-sigmatropic rearrangements are not direct allylic aminations of nonfunctionalized alkenes, they deserve to be presented here, as they in principle represent the last reaction step in type 1 reactions in Scheme 14. A great deal of work has been devoted to the development of diastereoselective rearrangement of allylic sulfimides, selenimides and tellurimides.[113−119] Koizume et al. have prepared the borneol derived allylic selenide **117**, which by reaction with tosylamide gave the chiral allylic selenimide **118**.[114] Compound **118** undergoes an in situ [2,3]-sigmatropic rearrangement

Scheme 17



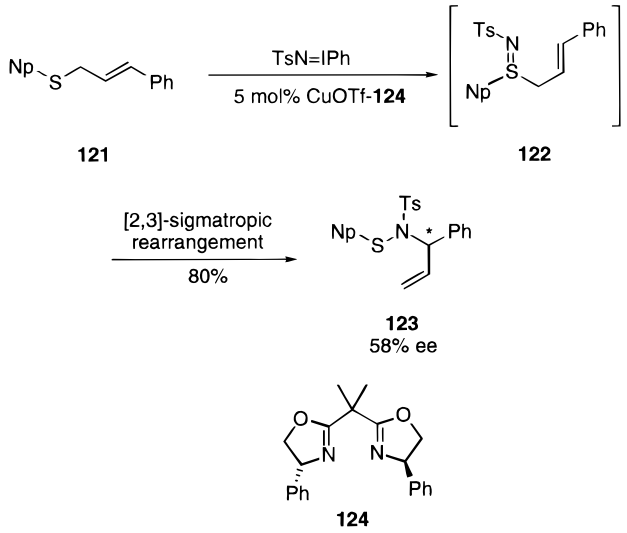
Scheme 18



via an endo transition state to the chiral *N*-derived allylamine **119** which instantly gives allylimine **120** with 93% ee (Scheme 18).[114]

Asymmetric catalysis has also been used for the synthesis of optically active sulfimines.[113] Uemura and Taylor et al. have used the protocol for aziridination developed by Evans et al. By application of 5 mol % of the optically active complex formed from copper(I) triflate and the bisoxazoline ligand **124** the sulfide **121** is oxidized catalytically to **122** which

Scheme 19

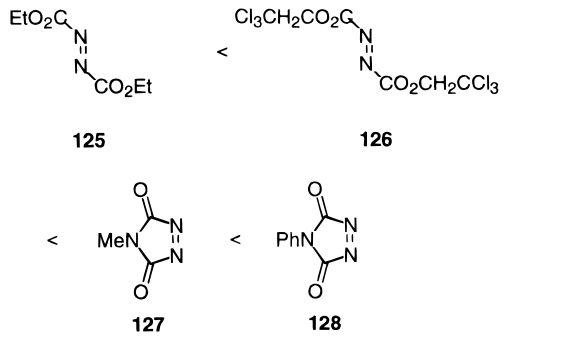


undergoes a [2,3]-sigmatropic rearrangement, giving the allylamine **123** in 80% yield and with 58% ee (Scheme 19). Other alkenes was found to give lower ee.

3.2.2. Ene Reaction (Type 2 Reaction)

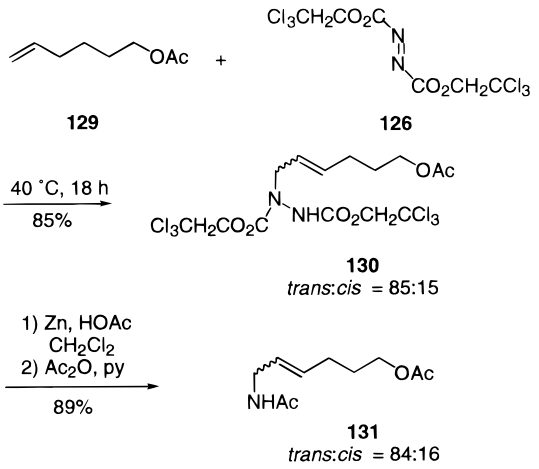
The ability of the two enophiles of type 2 (Scheme 14), the azo and the nitroso compounds, to undergo the ene reaction was recognized in 1943 and around 1965, respectively.[120−122] Despite this, and the fact that they belong to some of the most reactive dienophiles, their ene reaction chemistry has only been exploited to a very limited extent. This might be incidental, but also due to problems related with their chemistry (vide infra).

The most frequently used compounds in the azo series are shown below (**125**−**128**), listed according to their reactivity. Compounds **127** and **128** are found to be very reactive, probably caused by the extra ring tension in these compounds.[123−129]

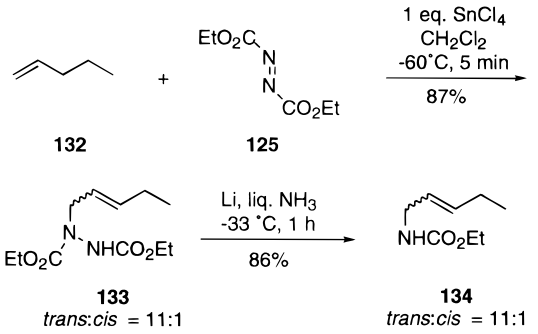


To illustrate the use of azo compounds in allylic amination reactions, two recent examples shall be emphasized. The first example is taken from an investigation performed by Leblanc et al. who used a more reactive trichloro derivative **126** of diethyl azodicarboxylate (DEAD) **125**. With compound **126** they were able to perform ene reactions at various temperatures, without any Lewis acid catalyst present, for both cyclic and acyclic alkenes to give allylamines in good yields. The reaction between the acyclic alkene **129** with **126** gives the allylic amination

Scheme 20



Scheme 21



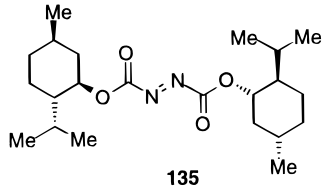
product **130** in 85% yield in a trans:cis ratio of 85:15. (Scheme 20).[128] The cleavage of the hydrazine ene product **130** was successful when a suspension of zinc powder in an acetic acid/dichloromethane solution was used.

Yields and selectivities comparable to the above-mentioned thermal reaction were obtained in an analogues Lewis acid promoted reaction between different alkenes and DEAD **125** (Scheme 21).[129] Many standard Lewis acids were tested and failed before $SnCl_4$ was successfully applied in this reaction. Use of $SnCl_4$ in a stoichiometric amount makes the ene reaction with both acyclic and cyclic alkenes run smoothly even at −60 °C in less than 5 min. The reaction of 1-pentene **132** with **125** gives the ene adduct **133** in 87% yield in a trans:cis ratio of 11:1 (Scheme 21). To preserve the alkene functionality in the hydrazine adducts **133** the N−N bond cleavage was effected by lithium in liquid ammonia.

The azo-ene allylic amination reaction has also been promoted by a 5 mol lithium perchlorate solution in ether, which gave large rate enhancements compared to the noncatalyzed reaction.[123,124]

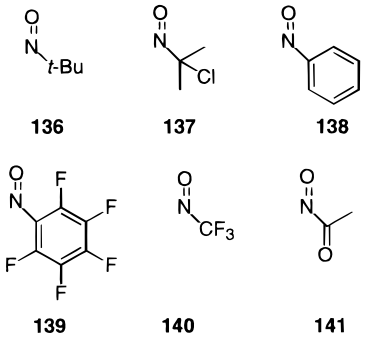
To our knowledge only one attempt to perform a diastereoselective azo-ene reaction has been reported.[130] The chiral di-(+)-menthyl diazenedicarboxylate **135** was found to react with various alkenes in the presence of 2 equiv of $SnCl_4$. The corresponding allylic aminated product was obtained with de up to 42%. However, removal of the chiral menthyl ester auxiliary was found to be difficult.

The nitroso compounds are by virtue some of the best electrophiles known (see Figure 1), and even



135

nonactivated aliphatic nitroso compounds have been reported to undergo the ene reaction at room temperature.[131] Some nitroso compounds applied in ene reactions are shown in **136**−**141**.[122,131−138] The "super



136 **137** **138**

139 **140** **141**

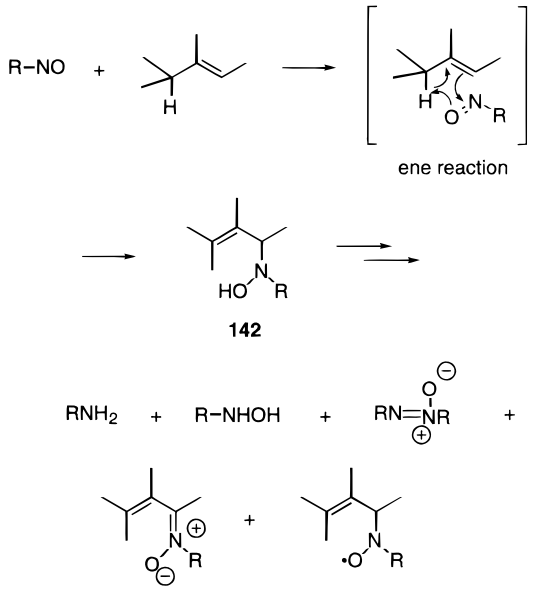
dienophile" **141** is normally made in situ because of the extremely high reactivity, but the other nitroso compounds can be synthesized and handled without too many precautions taken. Some of them have a tendency to form dimers, however, these reactions are reversible. Normally, they are susceptible to oxidation by air though, and should therefore not be exposed to intense light and air.

In the literature, a great number of papers, as well as reviews on the symmetric and diastereoselective Diels−Alder reaction between nitroso compounds and dienes, have appeared.[137,139−142] These can be considered as a fundament for the understanding of the reactivity and selectivity of nitroso compounds, not only in Diels−Alder reactions, but also in the ene reactions (Scheme 14), since the two are highly similar. However, the products obtained by the two routes are quite different; where the Diels−Alder products are quite stable, many ene products tend to undergo further in situ transformations. Among them are oxidations, decompositions, disproportionations, and other reactions of the intermediate hydroxylamine **142** formed to give nitroxides, nitrones, hydroxylamines, azoxy compounds, and amines, respectively (Scheme 22). All types of products can be observed in a typical ene reaction with e.g. nitroso benzene (R = Ph). The exact mechanism for the different transformations are unknown, but many of them might involve radicals.[122,137]

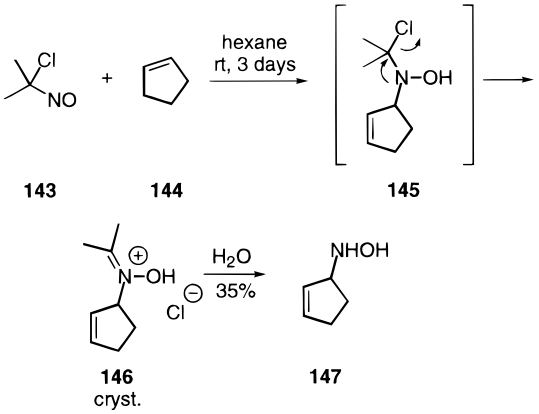
The many transformations that the hydroxylamine **142** can undergo might explain some of the problems encountered in this kind of chemistry. It can be very difficult to isolate the hydroxylamine, and often the nitroxide, or in some cases the nitrone or the azoxy compound are among the main products obtained.[122,131,143−145]

It is worth noticing that ene products derived from nitroso compounds with electron-withdrawing groups on the α-carbon are relatively stable. The main reason is probably that they are not oxidized as easily

Scheme 22



Scheme 23



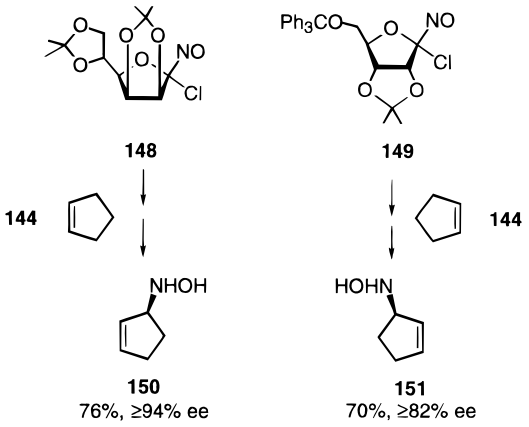
to nitroxides, as the ene products from nitrosobenzene.[136−138,146,147]

An ingenious way to overcome the problems by in situ oxidation of the ene product was presented by Schenk et al. They used α-chloro nitroso compounds, such as **143**, for the reaction with cyclopentene **144**, which after ene reaction, giving **145**, rearranges to the stable nitrone hydrochloride salt **146**. This salt can then easily be hydrolyzed to the hydroxylamine **147** (Scheme 23).[134,135]

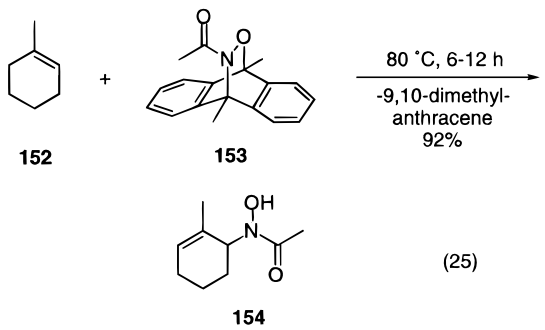
The same methodology was later used by Kresse et al. in the diastereoselective ene reaction between sugar derivatives and various alkenes. One example is the highly diastereoselective reaction between cyclopentene **144** and the two pseudo enantiomeric nitroso sugar compounds, **148** and **149**, respectively. After removal of the sugar moiety, the two hydoxylamines **150** and **151** were obtained in good yield and with high ee (Scheme 24). The ene reactions with other alkenes were in general high yielding, and as an alternative to the hydrolytic workup in situ reduction was also carried out and the stable allylamines isolated.[133,135]

The allylic amidation reaction between nitroso compounds with carbonyl groups attached to the nitrogen atom and alkenes has been studied by Keck

Scheme 24



et al., and it works equally well.[147−149] In this way the problems with decomposition of the products have been partly overcome, as the products are quite stable. At the same time these substituents increase the reactivity of the aminating reagent. The reaction of e.g. 1-methyl-cyclohexene **152** with the nitrosocarbonylmethane equivalent **153** gives the allylic aminated product **154** in 92% yield (eq 25). Generally

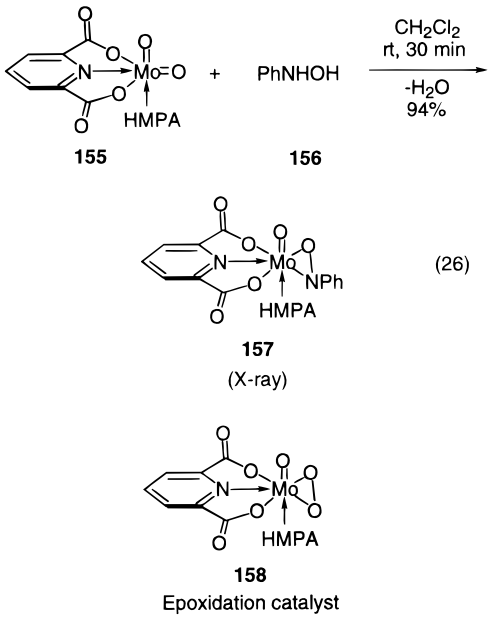


reactions with **153** and other alkenes are regioselective and highly yielding. According to our knowledge, no publications on the diastereoselective ene reaction have appeared, which is surprising if one takes the many publications on highly diastereoselective hetero-Diels−Alder reactions with chiral nitroso carbonyl derivatives into account.[141,150] It should be mentioned that it is generally accepted that the reaction rates are so high that a Lewis acid catalysis is practically impossible, and therefore probably also also chiral Lewis acids.

3.3. Allylic Amination with Ar–NX and a Metal Catalyst

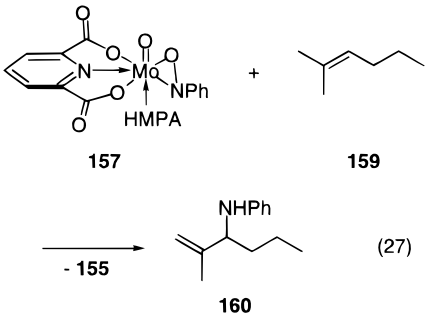
In 1978 Sharpless et al. and Muccigrosso et al. synthesized the molybdenaoxaziridine **157** from a molybdenum dioxo complex **155** and phenyl hydroxylamine **156** (eq 26).[151,152] In relation to the discussion of the chemistry of **157** it should be mentioned that molybdenum peroxides, such as **158**, are known to transfer a peroxide oxygen atom to alkenes leading to epoxides.[153]

On the basis of earlier success with developing new N-transfer reagents by permutations of oxygen with nitrogen in a variety of oxidants such as SeO_2 and OsO_4, Sharpless et al. hoped that **157**, which was characterized by X-ray diffraction and IR spectros-



(26)

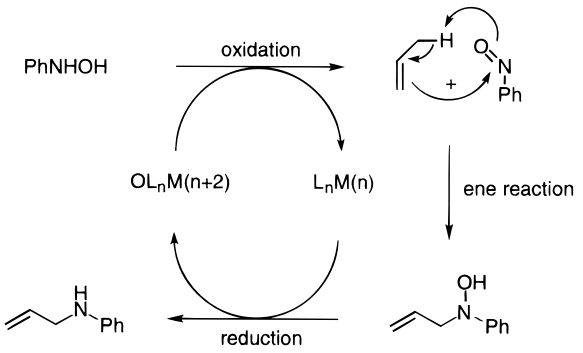
copy, would be a new and useful nitrogen transfer reagent.[151] Heating a solution of **157** with 2-methyl-2-hexene **159** indeed gave an aminated product (eq 27). However, allylamine **160** rather than the anticipated aziridine was isolated (57% yield) together with high yields of the parent molybdenum dioxo complex **155**. The formation of **160** involves a shift of the double bond from its original position, but Sharpless et al. did not draw any further conclusions on the mechanism.



(27)

The allylic amination reaction (eq 27) was later developed into a catalytic reaction by Nicholas et al.,[154] using a catalytic amount of the molybdenum dioxo complex **155** (10 mol %) and phenyl hydroxylamine **156** as the nitrogen fragment donor. Reaction of various alkenes with **156** in the presence of **155** as the catalyst gave the corresponding allylamines in 4−52% yield together with various amounts of phenyl hydroxylamine derived byproducts. The allylic amination reaction catalyzed by the molybdenum dioxo complex **155** using **156** as a nitrogen donor has also been studied from a mechanistic point of view using kinetics, trapping experiments, and model reactions.[155] On the basis of the mechanistic investigation it was suggested that the reaction is an *off*-metal process, which means that the metal is not involved in the amination step, and it was postulated that the molybdenum catalyst serves as a molybdenum(VI)/molybdenum(V)/molybdenum(IV) redox

Scheme 25



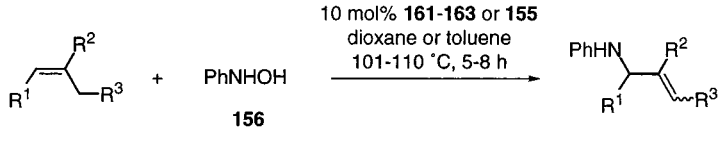
shuttle. The mechanism is outlined in Scheme 25. The first step is proposed to be an oxidation of the hydroxylamine to the corresponding nitroso compound with a concomitant reduction of the metal complex. The next step is an ene reaction leading to the hydroxylamine, which is reduced to the allylamine giving the metal complex in an oxidated state. The function of the metal is then solely being a redox catalyst and the molybdenumoxaziridine **157** to liberate the aromatic nitroso compound.[156]

Various metal complexes have been screened as catalysts for allylic amination using phenyl hydroxylamine **156** as the nitrogen fragment donor and it was found that iron complexes and salts have superior redox capacity compared to molybdenum.[157−160] With the former higher yields and a lower amount of hydroxylamine derived byproducts are obtained. These byproducts constitute one of the larger problems encountered in this reaction, as their formation is hard to suppress and they by virtue diminish the amount of allylamine product one possibly can obtain.

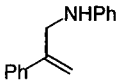
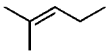
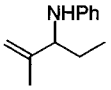
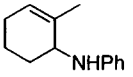
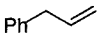
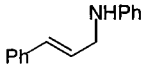
Table 3 presents a summary of the allylic amination of various alkenes with phenyl hydroxylamine **156** catalyzed by the iron and molybdenum complexes, **161**−**163**, and **155**, respectively.[157−159,161]

It appears from Table 3 that the allylic amination of alkenes with phenyl hydroxylamine **156** as nitrogen fragment donor and the metal catalysts **161**−**163** and **155** share some characteristics. All of the reactions proceed with an ene-like transposition of the double bond. Higher substituted alkenes tend to give the best yields and unsymmetrical alkenes (trisubstituted) react with virtually complete regioselectivity, as only one isomer is detected. Moreover, the concomitant byproducts are primarily azoxybenzene and aniline derived from condensation of nitrosobenzene with **156** and reduction of **156**, respectively. The mechanism for iron phthalocyanine (**161**) catalyzed reaction is probably similar to one previously outlined in Scheme 25.[162] Every single step of the cycle in Scheme 25 was shown to be feasible, and in particular the oxidation and reduction of the hydroxylamines. It has been proposed that the allylic amination catalyzed by **161** is an *off*-metal process, but an *on*-metal transfer was not excluded.[162] The latter aspect has recently been investigated in detail for the iron(II) and iron(III) chloride catalyzed reactions by Nicholas et al.,[158−160] They found strong evidence for an *on*-metal transfer, i.e. that the nitroso moiety and/or alkene is coordinated to the metal

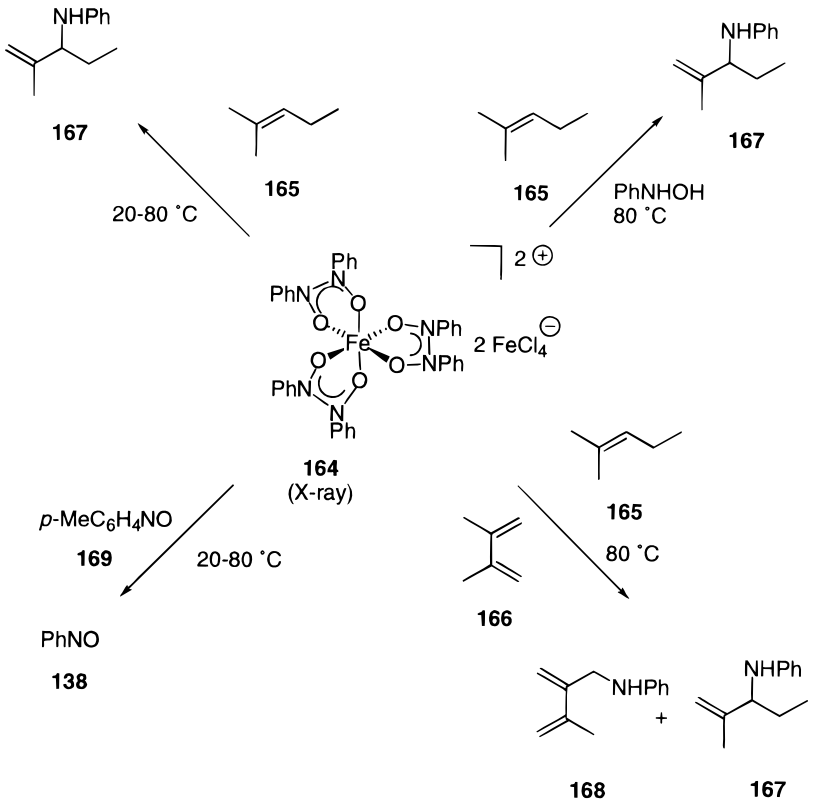
Table 3. Comparison of the Allylic Amination of Various Alkenes by Phenyl Hydroxylamine 156 Catalyzed by the Iron and Molybdenum Complexes 161−163 and 155[154,157−160]



161 162 163 155

Entry	Alkene	Allyl amine	161 % yield	162 % yield	163 % yield	155 % yield
1			76	41	-	42
2			-	72	88	52
3			22	13	-	-
4			30	22	-	11

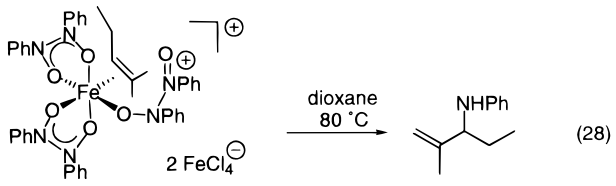
Scheme 26



during the ene reaction. The strongest argument for an *on*-metal reaction was the isolation of the catalyst intermediate **164**, which after recrystallization gave crystals suitable for X-ray analysis.[159,160] The structure of **164** revealed the first example of a metal complex having an azodioxide ligand, and more

importantly, the species was active as an amination catalyst (Scheme 26, see also Table 3).

Of special interest to the allylic amination mechanism are the experiments outlined in Scheme 26.[159,160] First, the complex **164** aminates 2-methyl-2-pentene **165** by simple stirring at room temperature (83% yield of **167** after 8 h). Second, **164** acts as a catalyst when added to a solution of phenyl hydroxylamine and **165** in substoichiometric amounts. In a competition experiment between the allylic amination of **165** and 2,3-dimethyl-1,3-butadiene **166** and hetero-Diels−Alder reaction of **166** using **164** no hetero-Diels−Alder product was observed, but **167** and **168**, in a ratio of 7:3. It should be noted that reaction of nitrosobenzene with **166** gives the hetero-Diels−Alder product. Finally, treatment of the **164** with *p*-methylnitrosobenzene **169** liberates nitroso benzene **138**. Further evidence for the involvement of **164** in the amination reaction comes from the isolation of the related alkene complex **170** which by heating in dioxane solution gives allylamine **167** (eq 28). The latter results for the iron chlorides indicate an *on*-metal process with the ene reaction taking place in the sphere of the iron center with both the nitroso and alkene compound coordinated more or less directly to the metal.



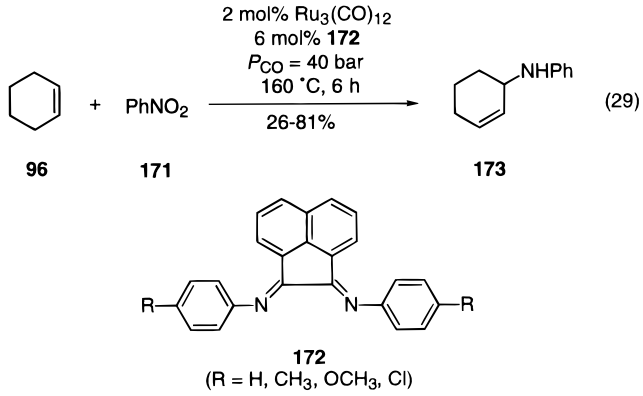
170
Postulated structure
(IR, NMR and UV-vis)

167 (28)

Recently, two new approaches have been developed to aminate alkenes. First, Nicholas et al. showed that the allylic amination with aniline in an oxidative environment, instead of phenyl hydroxylamine, is possible using *t*-BuOOH as terminal oxidant.[161] The procedure is analogues to the in situ hetero-Diels−Alder reaction of nitroso compounds developed earlier by others.[163]

Second, the allylic amination reaction now also can be carried out with nitro benzene **171** as N-donor under reductive conditions using a ruthenium complex derived from **172** and $Ru_3(CO)_{12}$ as catalyst and carbon monoxide as reductant (eq 29).[164] At 40 bar pressure of CO at 160 °C, the allylamine **173** derived from the cyclohexene (**96**) solvent was detected in up to 81% yield.[164]

According to the authors the reaction also works for α-methyl styrene, cyclopentene, and cyclooctene. However, 1-hexene gives only poor yields of a mixture of isomeric adducts.[164] Although the information on this latter amination procedure with nitro benzene is quite sparse, the amination reactions with different N-phenyl donors (aniline, phenyl hydroxylamine, nitroso benzene, and nitro benzene) seem quite similar, and it will be interesting to see how many parallels can, and will, be drawn between them in the future. It can be mentioned that at present an X-ray structure has been made of a π-bound nitroso



172
(R = H, CH_3, OCH_3, Cl) (29)

arene ruthenium complex, which was formed during the reaction of a nitro arene with a ruthenium carbonyl complex at room temperature.[165]

4. Final Remarks

The allylic amination reactions covered in this review represent important reactions for the preparation of allylamines. Allylic amination reactions starting from compounds having an allylic C−X (heteroatom, halide) bond have been developed so far as to include enantioselective reactions leading to allylamines with high enantiomeric excess. These "traditional" reactions are now "corner stone" reactions and are widely used in organic chemistry. The "modern" approach to allylamines using alkenes having allylic C−H bonds as the substrate is a relatively new field, and the majority of the work done in this field has been devoted to the development of the reactions. One important future aspect for chemistry is the preperation of optically active compounds and the challenge for the latter type of reactions is probably to develop reactions where alkenes react with "simple" nitrogen fragment donors in the presence a chiral catalyst leading to nonracemic allylamines.

5. Abbreviations

Ac	acetyl
acac	acetyl acetonate
Bn	benzyl
cat	catalyst
Cp	cyclopentadiene
dba	*trans,trans*-dibenzylideneacetone
de	diastereometic excess
DEAD	diethyl azodicarboxylate
DIAD	diisopropyl azodicarboxylate
DIBAL	diisobutyl aluminum hydride
DPPBA	2-(diphenylphosphino)benzoic acid
ee	enantiomeric excess
EWG	electron-withdrawing group
LUMO	lowest unoccupied molecular orbital
Ns	nosyl, *o*-nitrobenzenesulfonyl
PhthNH	phthalimide
rt	room temperature
Ts	tosyl
TPP	*meso*-tetraphenylporphyrin dianion
TDCPP	*meso*-tetra-2,6-dichlorophenylporphyrin dianion

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References

(1) Hayashi, T.; Yamamoto, A.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301.
(2) Jumnah, R.; Williams, J. M. J.; Williams, A. C. *Tetrahedron Lett.* **1993**, *34*, 6619.
(3) Bower, J. F.; Jumnah, R.; Williams, A. C.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1411.
(4) Burgess, K.; Liu, L. T.; Pal, B. *J. Org. Chem.* **1993**, *58*, 4758.
(5) Magnus, P.; Lacour, J.; Coldham, I.; Mugrage, B.; Bauta, W. B. *Tetrahedron* **1995**, *51*, 11087.
(6) Trost, B. M. *Angew. Chem.* **1989**, *101*, 1199.
(7) Trost, B. M.; Van Vranken, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 444.
(8) Cheikh, R. B.; Chaabouni, R.; Laurent, A.; Mison, P.; Nafti, A. *Synthesis* **1983**, 685.
(9) Petasis, N. A.; Akritopoulou, I. *Tetrahedron Lett.* **1993**, *34*, 583.
(10) Gao, Y.; Harada, K.; Sato, F. *Tetrahedron Lett.* **1995**, *36*, 5913.
(11) Kurose, N.; Takahashi, T.; Koizumi, T. *J. Org. Chem.* **1996**, *61*, 2932.
(12) Besson, L.; Goré, J.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 3857.
(13) Ofial, A. R.; Mayr, H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 143.
(14) Merino, P.; Anoro, S.; Merchan, F.; Castillo, E.; Tejero, T. *Tetrahedron: Asymmetry* **1996**, *7*, 1887.
(15) Dieter, R. K.; Dieter, J. W.; Alexander, C. W.; Bhinderwala, N. S. *J. Org. Chem.* **1996**, *61*, 2930.
(16) Kocovsky, P. *Synlett* **1990**, 677.
(17) Kimpe, N. D.; Stanoeva, E.; Verhé, R.; Schamp, N. *Synthesis* **1988**, 587.
(18) Enders, D.; Schankat, J. *Helv. Chim. Acta* **1995**, *78*, 970.
(19) Kündig, E. P.; Xu, L. H.; Schnell, B. *Synlett* **1994**, 413.
(20) Wei, Z.-Y.; Knaus, E. E. *Synthesis* **1994**, 1463.
(21) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486.
(22) Grossman, R. B.; Davis, W. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 2321.
(23) Mitsunobu, O. *Synthesis* **1981**, 1.
(24) Sen, S. E.; Roach, S. L. *Synthesis* **1995**, 756.
(25) Loibner, H.; Zbiral, E. *Helv. Chim. Acta* **1976**, *59*, 2100.
(26) Mulzer, J.; Funk, G. *Synthesis* **1995**, 101.
(27) Tsunoda, T.; Otsuka, J.; Yamamiya, Y.; Itô, S. *Chem. Lett.* **1994**, 539.
(28) Henry, J. R.; Marcin, L. R.; McIntosh, M. C.; Scola, P. M.; Harris, G. D. J.; Weinreb, S. M. *Tetrahedron Lett.* **1989**, *30*, 5709.
(29) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901.
(30) Clizbe, L. A.; Overman, L. E. *Org. Synth.* **1978**, *58*, 4.
(31) Overman, L. E.; Zipp, G. G. *J. Org. Chem.* **1997**, *62*, 2288.
(32) Metz, P.; Mues, C.; Schoop, A. *Tetrahedron* **1992**, *48*, 1071.
(33) Calter, M.; Hollis, T. K.; Overman, L. E.; Ziller, J.; Zipp, G. G. *J. Org. Chem.* **1997**, *62*, 1449.
(34) Felix, C.; Laurent, A.; Lebideau, F.; Mison, P. *J. Chem. Res.* **1993**, 389.
(35) Imogaï, H.; Petit, Y.; Larchevêque, M. *Tetrahedron Lett.* **1996**, *37*, 2573.
(36) Doherty, A. M.; Kornberg, B. E.; Reily, M. D. *J. Org. Chem.* **1993**, *58*, 795.
(37) Mehmandoust, M.; Petit, Y.; Larchevêque, M. *Tetrahedron Lett.* **1992**, *33*, 4313.
(38) Eguchi, T.; Koudate, T.; Kakinuma, K. *Tetrahedron* **1993**, *49*, 4527.
(39) Chida, N.; Takeoka, J.; Tsutsumi, N.; Ogawa, S. *J. Chem. Soc., Chem. Commun.* **1995**, 793.
(40) Isobe, M.; Fukuda, Y.; Nishikawa, T.; Chabert, P.; Kawai, T.; Goto, T. *Tetrahedron Lett.* **1990**, *31*, 3327.
(41) Campbell, M. M.; Floyd, A. J.; Lewis, T.; Mahon, M. F.; Ogilvie, R. J. *Tetrahedron Lett.* **1989**, *30*, 1993.
(42) Danishefsky, S.; Lee, J. Y. *J. Am. Chem. Soc.* **1989**, *111*, 4829.
(43) Nayyar, N. K.; Reddy, M. M.; Iqbal, J. *Tetrahedron Lett.* **1991**, *32*, 6965.
(44) Mukhopadhyay, M.; Reddy, M. M.; Maikap, G. C.; Iqbal, J. *J. Org. Chem.* **1995**, *60*, 2670.
(45) Masuyama, Y.; Kagawa, M.; Kurusu, Y. *Chem. Lett.* **1995**, 1121.
(46) Gibson, M. S.; Bradshaw, R. W. *Angew. Chem.* **1968**, *80*, 986.
(47) Osby, J. O.; Martin, M. G.; Ganem, B. *Tetrahedron Lett.* **1984**, *25*, 2093.
(48) Sasaki, T.; Minamoto, K.; Itoh, H. *J. Org. Chem.* **1978**, *43*, 2320.
(49) Koziara, A.; Zwierzak, A. *Tetrahedron* **1976**, *32*, 1649.
(50) Zwierzak, A. *Synthesis* **1982**, 920.
(51) Zwierzak, A.; Pilichowska, S. *Synthesis* **1982**, 922.
(52) van Benthem, R. A. T. M.; Michels, J. J.; Hiemstra, H.; Speckamp, W. N. *Synlett* **1994**, 368.
(53) Morikawa, M.; Takahashi, J.; Tsuji, J. *Tetrahedron Lett.* **1965**, *6*, 4387.
(54) Godleski, S. A. In *Comprehensive Organic Synthesis*; 1st ed.; Semmelhack, M. F., Ed.; Pergamon Press: New York, 1991; Vol. 4; p 585.
(55) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; 2nd ed.; University Science Books: Mill Valley, 1987.
(56) Hayashi, T. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH Verlagsgesellschaft mbH: Weinheim, 1993; p 325.
(57) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395.
(58) Hutchins, R. O.; Wei, J.; Rao, S. J. *J. Org. Chem.* **1994**, *59*, 4007.
(59) Byström, S. E.; Aslanian, R.; Bäckvall, J.-E. *Tetrahedron Lett.* **1985**, *26*, 1749.
(60) von Matt, P.; Loiseleur, O.; Koch, G.; Pfaltz, A.; Lefeber, C.; Feucht, T.; Helmchen, G. *Tetrahedron: Asymmetry* **1994**, *5*, 573.
(61) Connell, R. D.; Rein, T.; Åkermark, B.; Helquist, P. *J. Org. Chem.* **1988**, *53*, 3845.
(62) Togni, A.; Burckhardt, U.; Gramlich, V.; Pregosin, P. S.; Salzmann, R. *J. Am. Chem. Soc.* **1996**, *118*, 1031.
(63) Burckhardt, U.; Baumann, M.; Trabesinger, G.; Gramlich, V.; Togni, A. *Organometallics* **1997**, *16*, 5252.
(64) Blöchl, P. E.; Togni, A. *Organometallics* **1996**, *15*, 4125.
(65) Sprinz, J.; Kiefer, M.; Helmchen, G.; Reggelin, M.; Huttner, G.; Walter, O.; Zsolnai, L. *Tetrahedron Lett.* **1994**, *35*, 1523.
(66) Steinhagen, H.; Reggelin, M.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2108.
(67) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 4089.
(68) Trost, B. M.; Radinov, R. *J. Am. Chem. Soc.* **1997**, *119*, 5962.
(69) Trost, B. M.; Bunt, R. C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 99.
(70) Mori, M.; Kuroda, S.; Zhang, C.-S.; Sato, Y. *J. Org. Chem.* **1997**, *62*, 3263.
(71) Baruah, J. B.; Samuelson, A. G. *Tetrahedron* **1991**, *47*, 9449.
(72) Enders, D.; Finkam, M. *Synlett* **1993**, 401.
(73) Enders, D.; Jandeleit, B.; von Berg, S. *Synlett* **1997**, 421.
(74) Silverman, G. S.; Strickland, S.; Nicholas, K. M. *Organometallics* **1986**, *5*, 2117.
(75) Murai, T.; Yamamoto, M.; Kondo, S.; Kato, S. *J. Org. Chem.* **1993**, *58*, 7440.
(76) Brüning, J. *Tetrahedron Lett.* **1997**, *38*, 3187.
(77) Itsuno, S.; Koizumi, T.; Okumura, C.; Ito, K. *Synthesis* **1995**, 150.
(78) Baker, R.; Onions, A.; Popplestone, R. J.; Smith, T. N. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1133.
(79) Grigg, R.; Sridharan, V.; Xu, L.-H. *J. Chem. Soc., Chem. Commun.* **1995**, 1903.
(80) Gasc, M. B.; Lattes, A.; Perie, J. J. *Tetrahedron* **1983**, *39*, 703.
(81) Kiji, J.; Sasakawa, E.; Yamamoto, K.; Furukawa, J. *J. Organomet. Chem.* **1974**, *77*, 125.
(82) Prinz, T.; Keim, W.; Driessen-Hölscher, B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1708.
(83) Larock, R. C.; Wang, Y.; Lu, Y.; Russell, C. E. *J. Org. Chem.* **1994**, *59*, 8107.
(84) Larock, R. C.; Tu, C. *Tetrahedron* **1995**, *51*, 6635.
(85) Borzilleri, R. M.; Weinreb, S. M. *Synthesis* **1995**, 347.
(86) Mansuy, D. *Pure Appl. Chem.* **1990**, *62*, 741.
(87) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 2742.
(88) Mahy, J. P.; Bedi, G.; Battioni, P.; Mansuy, D. *Tetrahedron Lett.* **1988**, *29*, 1927.
(89) Laurent, A.; Mison, P.; Nafti, A.; Cheikh, R. B.; Chaabouni, R. *J. Chem. Res.* **1984**, 354.
(90) Barton, D. H. R.; Hay-Motherwell, R. S.; Motherwell, W. B. *J. Chem. Soc., Perkin Trans. 1* **1983**, 445.
(91) Aggarwal, V. K.; Anderson, E.; Giles, R.; Zaparucha, A. *Tetrahedron: Asymmetry* **1995**, *6*, 1301.
(92) Kobayashi, S.; Murakami, M.; Harada, T.; Mukaiyama, T. *Chem. Lett.* **1991**, 1341.
(93) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889.
(94) Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326.
(95) Harlan, E. W.; Holm, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 186.
(96) Emig, N.; Réau, R.; Krautscheid, H.; Fenske, D.; Bertrand, G. *J. Am. Chem. Soc.* **1996**, *118*, 5822.
(97) Braun, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 519.
(98) Lai, T.-S.; Kwong, H.-L.; Che, C.-M.; Peng, S.-M. *J. Chem. Soc., Chem. Commun.* **1997**, 2373.
(99) Evans, D. A.; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993**, *115*, 5328.
(100) Müller, P.; Baud, C.; Jacquier, Y.; Moran, M.; Nägeli, I. *J. Phys. Org. Chem.* **1996**, *9*, 341.
(101) Pirrung, M. C.; Zhang, J. *Tetrahedron Lett.* **1992**, *33*, 5987.
(102) Nägeli, I.; Baud, C.; Bernardinelli, G.; Jacquier, Y.; Moran, M.; Müller, P. *Helv. Chim. Acta* **1997**, *80*, 1087.
(103) Sharpless, K. B.; Hori, T. *J. Org. Chem.* **1976**, *41*, 176.
(104) Schönberger, N.; Kresze, G. *Liebigs Ann. Chem.* **1975**, 1725.
(105) Sharpless, K. B.; Hori, T.; Truesdale, L. K.; Dietrich, C. O. *J. Am. Chem. Soc.* **1976**, *98*, 269.

(106) Bruncko, M.; Khuong, T.-A. V.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 454.
(107) Kresze, G.; Münsterer, H. *J. Org. Chem.* **1983**, *48*, 3561.
(108) Katz, T. J.; Shi, S. *J. Org. Chem.* **1994**, *59*, 8297.
(109) Singer, S. P.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 1448.
(110) Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373.
(111) Tsushima, S.; Yamada, Y.; Onami, T.; Oshima, K.; Chaney, M. O.; Jones, N. D.; Swartzendruber, J. K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1167.
(112) Whitesell, J. K.; Yaser, H. K. *J. Am. Chem. Soc.* **1991**, *113*, 3526.
(113) Takada, H.; Nishibayashi, Y.; Ohe, K.; Uemura, S.; Baird, C. P.; Sparey, T. J.; Taylor, P. C. *J. Org. Chem.* **1997**, *62*, 6512.
(114) Kurose, N.; Takahashi, T.; Koizumi, T. *J. Org. Chem.* **1996**, *61*, 2932.
(115) Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *Tetrahedron Lett.* **1988**, *29*, 4949.
(116) Nishibayashi, Y.; Srivastava, S. K.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **1995**, *36*, 6725.
(117) Takada, H.; Nishibayashi, Y.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1996**, 931.
(118) Nishibayashi, Y.; Chiba, T.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, 1243.
(119) Shea, R. G.; Fitzner, J. N.; Fankhauser, J. E.; Spaltenstein, A.; Carpino, P. A.; Peevey, R. M.; Pratt, D. V.; Tenge, B. J.; Hopkins, P. B. *J. Org. Chem.* **1986**, *51*, 5243.
(120) Alder, K.; Pascher, F.; Schmitz, A. *Chem. Ber.* **1943**, *76*, 27.
(121) Diels, O.; Alder, K. *Liebigs Ann. Chem.* **1926**, *450*, 237.
(122) Knight, G. T.; Pepper, B. *Tetrahedron* **1971**, *27*, 6201.
(123) Kinart, W. J. *J. Chem. Res.* **1994**, 486.
(124) Davies, A. G.; Kinart, W. J. *J. Chem. Soc., Perkin Trans. 2* **1993**, 2281.
(125) Huisgen, R.; Pohl, H. *Chem. Ber.* **1960**, *93*, 527.
(126) Hoye, T. R.; Bottorff, K. J.; Caruso, A. J.; Dellaria, J. F. *J. Org. Chem.* **1980**, *45*, 4287.
(127) Thaler, W. A.; Franzus, B. *J. Org. Chem.* **1964**, *29*, 2226.
(128) Leblanc, Y.; Zamboni, R.; Bernstein, M. A. *J. Org. Chem.* **1991**, *56*, 1971.
(129) Brimble, M. A.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 5261.
(130) Brimble, M. A.; Heathcock, C. H.; Nobin, G. N. *Tetrahedron: Asymmetry* **1996**, *7*, 2007.
(131) Motherwell, W. B.; Roberts, J. S. *J. Chem. Soc., Chem. Commun.* **1972**, 329.
(132) Seymour, C. A.; Greene, F. D. *J. Org. Chem.* **1982**, *47*, 5226.
(133) Braun, H.; Felber, H.; Kresse, G.; Ritter, A.; Schmidtchen, F. P.; Schneider, A. *Tetrahedron* **1991**, *47*, 3313.
(134) Schenk, C.; de Boer, T. J. *Tetrahedron* **1979**, *35*, 147.
(135) Kresse, G.; Vasella, A.; Felber, H.; Ritter, A.; Ascherl, B. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 295.
(136) Barlow, M. G.; Haszeldine, R. N.; Murray, K. W. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1960.
(137) Zuman, P.; Shah, B. *Chem. Rev.* **1994**, *94*, 1621.
(138) Abramovitch, R. A.; Challand, S. R.; Yamada, Y. *J. Org. Chem.* **1975**, *40*, 1541.
(139) Kresze, G.; Firl, J. *Fortschr. Chem. Forsch.* **1969**, *11*, 245.
(140) Hamer, J.; Ahmad, M. In *1,4 Cycloaddition Reactions*; Hamer, J., Ed.; Academic Press: New York, 1967; p 419.
(141) Waldmann, H. *Synthesis* **1994**, 535.
(142) Streith, J.; Defoin, A. *Synlett* **1996**, 189.
(143) Knight, G. T.; Pepper, B. *J. Chem. Soc., Chem. Commun.* **1971**, 1507.
(144) Sullivan, A. B. *J. Org. Chem.* **1966**, *31*, 2811.
(145) Cain, M. E.; Knight, G. T.; Lewis, P. M.; Saville, B. *Rubber J.* **1968**, *150*, 10−22, 57.
(146) Knight, G. T. *J. Chem. Soc., Chem. Commun.* **1970**, 1016.
(147) Keck, G. E.; Webb, R. R.; Yates, J. B. *Tetrahedron* **1981**, *37*, 4007.
(148) Keck, G. E.; Yates, J. B. *Tetrahedron Lett.* **1979**, *20*, 4627.
(149) Keck, G. E.; Webb, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 3173.
(150) Gouverneur, V.; Dive, G.; Ghosez, L. *Tetrahedron: Asymmetry* **1991**, *2*, 1173.
(151) Liebeskind, L. S.; Sharpless, K. B.; Wilson, R. D.; Ibers, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 7061.
(152) Muccigrosso, D. A.; Jacobsen, S. E.; Apgar, P. A.; Mares, F. *J. Am. Chem. Soc.* **1978**, *100*, 7063.
(153) Jørgensen, K. A. *Chem. Rev.* **1989**, *89*, 431.
(154) Srivastava, S.; Ma, Y.; Pankayatselvan, R.; Dinges, W.; Nicholas, K. M. *J. Chem. Soc., Chem. Commun.* **1992**, 853.
(155) Srivastava, R. S.; Nicholas, K. M. *J. Org. Chem.* **1994**, *59*, 5365.
(156) Møller, E. R.; Jørgensen, K. A. *J. Am. Chem. Soc.* **1993**, *115*, 11814.
(157) Johannsen, M.; Jørgensen, K. A. *J. Org. Chem.* **1994**, *59*, 214.
(158) Srivastava, R. S.; Nicholas, K. M. *Tetrahedron Lett.* **1994**, *35*, 8739.
(159) Srivastava, R. S.; Nicholas, K. M. *J. Am. Chem. Soc.* **1997**, *119*, 3302.
(160) Srivastava, R. S.; Khan, M. A.; Nicholas, K. M. *J. Am. Chem. Soc.* **1996**, *118*, 3311.
(161) Srivastava, R. S.; Nicholas, K. M. *J. Chem. Soc., Chem. Commun.* **1996**, 2335.
(162) Johannsen, M.; Jørgensen, K. A. *J. Org. Chem.* **1995**, *60*, 5979.
(163) Møller, E. R.; Jørgensen, K. A. *J. Org. Chem.* **1996**, *61*, 5770.
(164) Cenini, S.; Ragaini, F.; Tollari, S.; Paone, D. *J. Am. Chem. Soc.* **1996**, *118*, 11964.
(165) Skoog, S. J.; Campbell, J. P.; Gladfelter, W. L. *Organometallics* **1994**, *13*, 4137.

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