

Asymmetric Silver-Catalyzed Reactions

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Asymmetric Silver-Catalyzed Reactions

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1. Introduction

In the last few decades, the use of transition metals in organic synthesis has become commonplace.¹ A distinct group of late transition metals, the so-called coinage metals, are widely used for various organic transformations; these include copper, silver, and gold. While copper chemistry has been studied extensively for decades, utilization of silver and gold in organic chemistry has begun only in the past several years.

Silver has been known since ancient times; it has been valued as a precious metal and used for ornaments and jewelry. Slightly softer than gold, this coinage metal is still used mainly as a precious metal, despite its outstanding electrical conductivity and unique redox chemistry. In the past century, use of silver(I) was broadened to application in photography and in dentistry for fittings due to its low toxicity.

The use of silver in organic chemistry today can be classified into two well-defined areas: heterogeneous oxidation processes and homogeneous silver-mediated and catalyzed reactions. Silver-promoted oxidation of ethylene to ethylene oxide, a process first discovered in 1933, has been used on preparative and industrial scales for decades.² Due to the increased demand for ethylene glycol, this method has recently seen great improvements. One of the crucial

advancements includes extension of its application to substrates such as butadiene.³ In addition to oxidation of olefins and alcohols, other examples of silver-based heterogeneous processes include catalytic oxidation of CO to CO₂⁴ and reduction of NO_x.⁵

Similar silver-promoted oxidation reactions used in research laboratories are some of the first examples of the use of silver in organic synthesis.^{2a,6} With a reduction potential of 0.8 eV, silver(I) is considered to be a mild oxidizing agent, suitable for efficient oxidation of primary and secondary alcohols to aldehydes and ketones. Owing to such properties, Ag₂CO₃ and AgNO₃ (the complex of AgNO₃ with ammonia is well-known as Tollens' reagent) are commonly used for the preparation of carbonyls from the corresponding alcohols under mild conditions.⁶ It should be noted that these reactions employ stoichiometric amounts of silver (I) salts and proceed via a radical pathway.

Homogenous silver-mediated reactions, under either stoichiometric or catalytic conditions, have been known for some time, but a significant number of these accounts are dated within the past 2 decades and newer and more unique reactions within the last 5 years.^{21–23} Much like gold, silver has been neglected in the arena of organic synthesis for a long time. This is probably due to its moderate Lewis acidity. Complexes of Ag(I) with π -donors (such as alkenes and aromatics) and n -donors (ethers and amines) are well documented.⁷ Accounts of Ag(I)-mediated nucleophilic addition reactions that involve silver cation activation of olefin, propargyl, and allenyl substrates strongly support the aforementioned carbophilic nature of Ag(I). These reactions include cyclization of alkyl alcohols, acids, amines, and imines,⁸ cyclization of allenyl ketones and aldehydes,⁹ and nucleophilic cyclization of allenes.¹⁰ In addition to these reactions, nucleophilic intermolecular addition to alkynes¹¹ and nucleophilic additions of hydroxyl and carboxylic groups to unactivated alkenes¹² have been reported recently.

The oxophilic character of Ag(I) has been a somewhat less investigated property but is nevertheless known.¹³ Early accounts of catalytic Ag(I)-promoted reactions where the oxophilic Lewis acid character has been ascribed to the Ag(I) cation¹⁴ are inspired by analogous gold(I)-catalyzed reactions.¹⁵ More specifically, the report by Hayashi et al. of asymmetric ferrocenylgold(I)-catalyzed aldol reactions of isocyanoacetate¹⁵ led to the development of the ferrocenyl-silver(I)-catalyzed asymmetric aldol reaction of tosylmethyl isocyanides^{14a} and isocyanoacetate^{14b} with aldehydes. In 1984, Sims and colleagues reported a different mode of reactivity of the Ag(fod) catalyst compared to Eu(fod)₃ and Yb(fod)₃ in the hetero-Diels–Alder reaction of 1,3-dimethoxy-1-((trimethylsilyl)oxy)butadiene and cinnamaldehyde.¹⁶ Even though some speculations were made, a clear understanding of the exact role of Ag(fod) has yet to be defined.

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Marina Naodovic was born and raised in Novi Sad, Serbia. She obtained her bachelor's degree from the University of Novi Sad in Serbia. During her undergraduate studies, her primary research focused on the total synthesis of biologically active molecules. In 2005, she joined Yamamoto's group at The University of Chicago and is pursuing her Ph.D. in organic synthesis. Her current research involves application of chiral tethered bis(8-quinolinato) (TBOxH) ligands for Lewis acid mediated asymmetric organic transformations and silver-catalyzed reactions.



Hisashi Yamamoto was born in Kobe, Japan, in 1943. He received his Bachelor's degree from Kyoto University in 1967, where he got his start in a research group headed by Prof. H. Nozaki. Professor Yamamoto received his Ph.D. from Harvard University under the mentorship of Professor E. J. Corey. Yamamoto returned to Japan in 1971 to join Toray-Industries, Inc., for one year under Professor J. Tsuji. His first academic position was as an Assistant Professor of Chemistry at the University of Hawaii. In 1980 he moved to Nagoya University, where he became Professor in 1983. In 2002, he decided to move to the United States and from July 1st has held the title of Arthur Holly Compton Distinguished Professor at The University of Chicago. Professor Yamamoto's research laid the foundation for modern designer Lewis acid chemistry. He established chiral Lewis acid catalysts for asymmetric carbon-carbon bond formation processes, which have rapidly become a universal synthetic tool. More recently, he introduced the concept of combined Lewis/Bronsted acid catalysts. His recent achievements in nitroso-aldol synthesis are also noteworthy. To date, Professor Yamamoto has co-authored over 400 publications and 100 reviews and has delivered over 80 invited, keynote, and plenary lectures at the international conferences of chemistry.

Since these early reports, two silver-based catalytic systems with more general reactivity profiles have been reported. In 1996 Yamamoto and Yanagisawa developed the BINAP-Ag(I) system and demonstrated its excellent reactivity for the enantioselective allylation reaction of aldehydes with allylic stannanes¹⁷ and great efficiency for the Mukaiyama-aldol reaction of tributyltin enolates and aldehydes.¹⁸ In 2004, Hoveyda's and Snapper's groups introduced an amino acid derived phosphine-Ag(I) catalyst for the asymmetric cycloaddition reaction of Danishefsky's diene with arylimines.¹⁹

Since then, examples of other asymmetric reactions using the same catalytic systems have been reported.²⁰

The oxo- and azaphilic character of silver(I) salts has been exploited in reactions such as: various cycloaddition reactions, allylation of carbonyls, aldol-type reactions, Michael and Mannich reactions, and others.

Conceptually different silver chemistry has been actively pursued over the past several years. He and colleagues have synthesized a unique disilver(I) complex that efficiently catalyzes the aziridation of olefins and intramolecular amidation, reactions that involve the intermediacy of nitrene species.²¹ In addition to the nitrene-transfer reaction, silver catalysts have been successfully used in silylene-transfer reactions²² and carbene-transfer reactions.²³

For some of the aforementioned reactions other catalytic systems have been developed. In some instances, using different metals and chiral ligands, better reactivity and/or selectivity is observed. However, there are certain advantages of silver catalysts that make them a very appealing alternative. Shorter reaction times, increased stability toward exposure to air or moisture, and ease of preparation and storage of the catalyst are some of the highly beneficial properties of silver catalysts. A good example is an amino acid derived phosphine-Ag(I) catalyst that efficiently promotes reactions regardless of the quality of the solvent or exposure of the reaction mixture to air.²⁰ Furthermore, the BINAP-Ag(I) system exhibits the ability to promote asymmetric Michael addition in water.²⁴

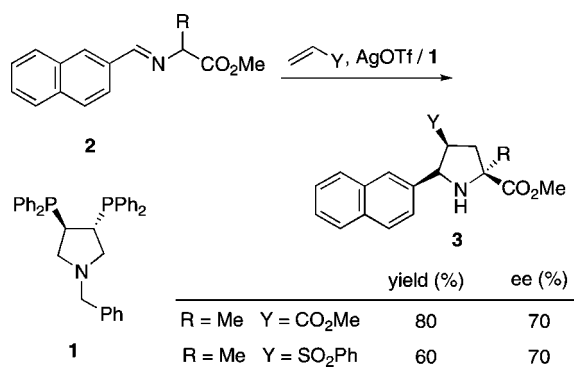
This review will cover asymmetric silver-promoted reactions reported since 2000. Most of these reactions utilize the Lewis acid character of the Ag(I) cation toward O and N atoms. To illustrate this point, examples of cycloaddition reactions, allylation of carbonyls, and aldol and Mannich reactions will be discussed. Attempts will also be made to cover conceptually different "group-transfer" stereoselective reactions that include carbene, nitrene, and silylene transfers. Even though these reactions are generally not asymmetric, there are examples of stereoselective transformations that show promise of advancing to truly asymmetric reactions. Yamamoto and Yanagisawa's BINAP-Ag(I) and Hoveyda and Snapper's amino acid derived phosphine-Ag(I) system will be described separately in more detail, owing to their more general reactivity. The section dedicated to the BINAP-Ag(I) catalyst also serves as an account of the research conducted in our group. Other asymmetric reactions are classified into several major areas where silver catalysts have shown remarkable reactivity. We also wish to bring to the reader's attention reviews and accounts closely related to silver catalysis in organic synthesis published prior to this review.²⁵

2. Asymmetric Reactions

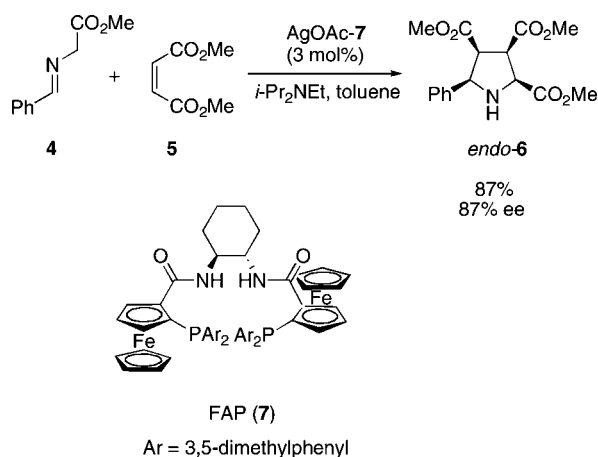
2.1. Cycloaddition Reactions

Cycloaddition reactions of various types have a long-held reputation as one of the most efficient transformations in organic synthesis.²⁶ These reactions furnish functionally and stereochemically complex carbo- and heterocyclic structures present as the key architectural feature of many biologically important molecules. As early as 1973, silver(I) compounds were recognized as suitable promoters of 1,4-cycloadditions.²⁷ It was shown that in the presence of Ag(I) a 1,3-dipole is generated from 2-methoxyallyl halides that undergo cycloaddition with conjugated dienes. Soon thereafter, several

Scheme 1



Scheme 2



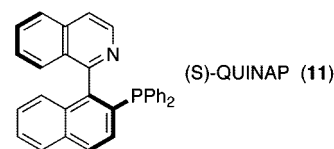
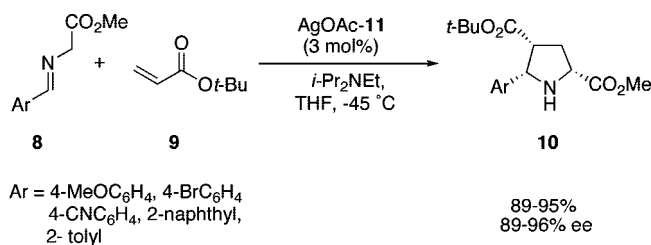
other examples of silver-based cycloaddition reactions were reported.²⁸ Those older accounts will not be further discussed here, but we direct readers to an earlier review for detailed discussion.^{25a,d}

2.1.1. [3 + 2] Cycloaddition

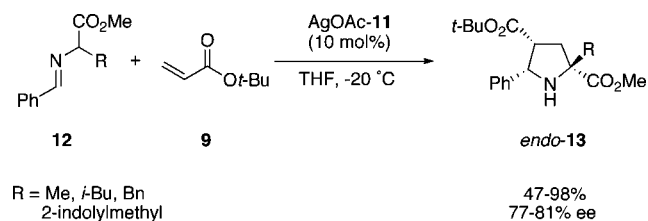
Recent reports of transition-metal-catalyzed 1,3-dipolar cycloaddition reactions of imines with various dipolarophiles clearly indicate that copper(I)²⁹ and silver(I)³⁰ compounds are highly superior promoters of these reactions. Ag(I)-promoted asymmetric [3 + 2] cycloadditions of imines were pioneered by Grigg's group in 1995.^{30a} The combination of stoichiometric amounts of AgOTf and the chiral ligand **1** yields proline derivatives of different olefins with similar ee's (Scheme 1). Although the transformation requires a stoichiometric amount of AgOTf, it was demonstrated that the diphosphine–Ag(I) system affords products with excellent regioselectivity and good enantioselectivity.

One of the first truly catalytic reactions carried out in the presence of Ag(I) was reported by Zhang and colleagues.^{30b} Using 1 mol % of AgOAc with 2 mol % of PPh₃, the endo cycloadduct of imine **4** and dimethyl maleate was obtained exclusively as the only diastereomer (Scheme 2). When PPh₃ was replaced with a chiral, nonracemic bis-ferrocenyl amide phosphine ligand (FAP, **7**), endo products with ee's as high as 97% were obtained for various azomethine ylides (generated from α -imino esters **4**) and dipolarophiles (Scheme 2). Alkyl imino esters exhibited somewhat lower reactivity that required prolonged reaction times; however, excellent diastereoselectivity and satisfactory yields and ee's were observed. It was postulated that the imino ester coordinates to the chiral complex Ag(I)-**7** and is then deprotonated to

Scheme 3



Scheme 4



generate an azomethine ylide that undergoes cycloaddition. The chiral complex Ag(I)-**7** accommodates the imine so as to effectively block one of its enantiotopic faces and furnish **6** exclusively (Scheme 2).

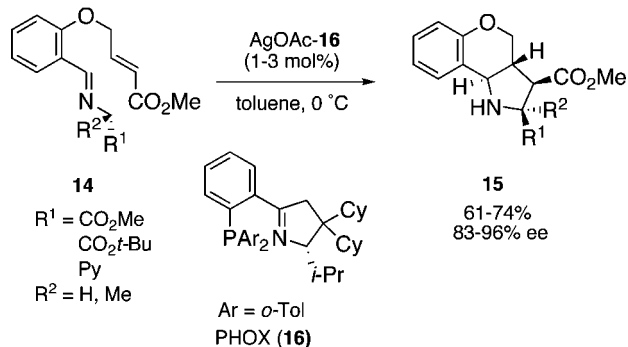
The examples of asymmetric 1,3-dipolar cycloaddition discussed so far use diphosphine chiral ligands for the induction of stereoselectivity. A report by Schreiber's group^{30c} describes a new catalyst system for 1,3-dipolar cycloaddition (Scheme 3) that enables the extension of the substrate scope, improves the selectivity, and is compatible with reagents used in a one-bead/one-stock technology for diversity-oriented synthesis.³¹ The QUINAP–AgOAc system provides either diastereomer with high enantioselectivity. Moreover, it enables installment of a quaternary stereocenter in the pyrrolidine product **13** (Scheme 4). It was further demonstrated that (S)-QUINAP–Ag(I)-catalyzed cycloaddition can be efficiently performed on polystyrene beads, yielding pyrrolidine products in 79% yield (overall for three steps), with >20:1 dr and 90% ee.³¹

Several examples of highly diastereo- and enantioselective azomethine ylide cycloadditions present in the literature involve the use of different N,P-based chiral ligands to afford cycloadducts in a highly efficient manner, as the described phosphine-based systems do. For instance, Pfaltz's PHOX(**16**)–AgOAc system provides access to a single diastereomer of tricyclic cycloadduct **15** with 96% ee and 74% yield (Scheme 5).³⁰ Another case in point is the ligand Pinap (**19**), designed by Carreira's group. Among several asymmetric reactions screened, catalytic cycloaddition was successfully carried out with ligand **19** and AgOAc (Scheme 6).^{30d}

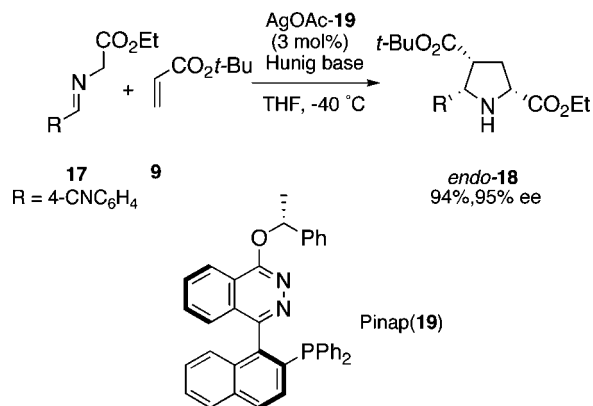
The generally accepted mechanism of the Ag(I)-catalyzed cycloaddition of azomethine ylides involves the coordination of an imino ester to the chiral Ag(I) complex followed by intermolecular deprotonation by a base to furnish the azomethine ylide, which undergoes cycloaddition with dipolarophiles.^{29a,30b}

Early models of silver-promoted cycloadditions of azomethine ylides were based on the intermolecular deprotonation

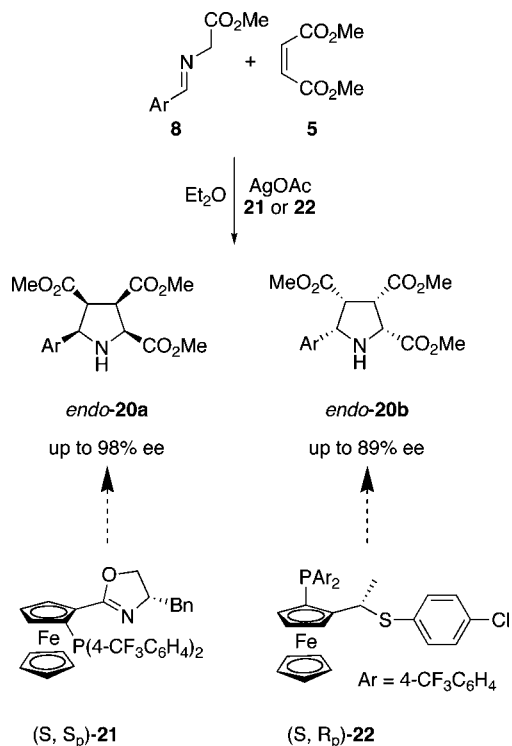
Scheme 5



Scheme 6

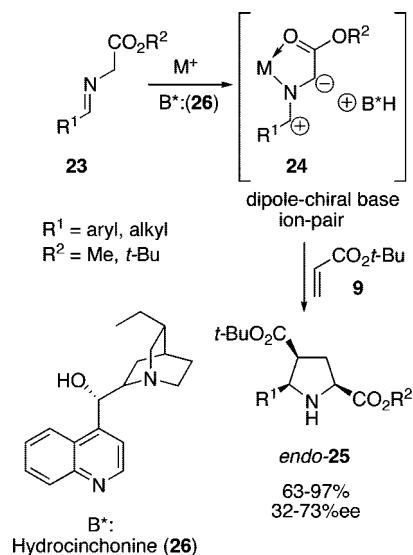


Scheme 7



of the imine substrate to generate reactive species in situ. Zhou et al. have demonstrated that the ferrocenyloxazoline N,P-based ligand–AgOAc system **21** can operate as a bifunctional catalyst that incorporates Ag(I) as a Lewis acid and its counteranion (OAc^-) as a base (Scheme 7).^{30f} In this way, pyrrolidine derivatives **20a** were obtained as a single diastereomer with high ee's and excellent yields under milder

Scheme 8



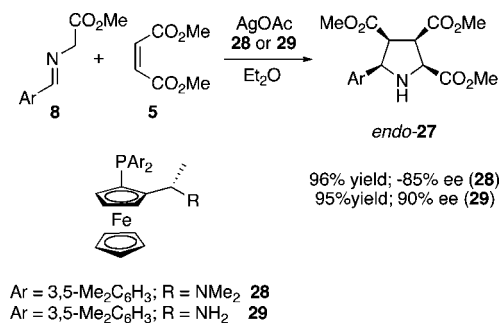
conditions without the use of external amine bases. The same group reported a new type of P,S-heterodonor ferrocenyl ligand, **22**, which effectively catalyzes cycloaddition of the azomethine ylides with only 3 mol % of AgOAc. It was observed, in the case of Ag(I)–**22**, that the planar chirality of the ligand has a significant influence on the stereochemical outcome of the product **20**. More specifically, when a similar ligand with the same central chirality but opposite planar chirality of the ligand **21** is used, products were obtained with opposite absolute configuration and higher enantioselectivity. The difference in ee's observed most likely arises from the mismatched nature of the planar chirality with the central chirality of the ligand.

A novel and highly efficient methodology for azomethine ylide cyclization using a conceptually different strategy was reported by Jørgensen's group (Scheme 8).^{30g} Their approach was based on the use of Ag(I) and chiral base, both in catalytic amounts (Scheme 8).

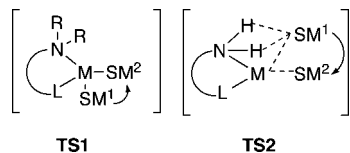
For this purpose, several chiral bases, mostly from the cinchona alkaloid family, were investigated and hydrocinchonine (**26**) exhibited the highest induction of chirality. It was observed that the use of *tert*-butyl acrylates gives higher enantioselectivities compared to methyl acrylates. The advantage of this feature is generation of pyrrolidines with two different orthogonally protected ester groups, which enables independent manipulation during further synthetic elaboration.

In the examples described so far, asymmetric transformation was achieved through either the use of a chiral ligand coordinated to the Ag(I) cation or the use of a chiral base to obtain predominantly one enantiomer. Access to its antipode would require the use of a ligand or base with opposite chirality. In contrast to this approach, Li and Zhou's group have developed a methodology that relies on the use of hydrogen bonding to reverse the enantioselectivity (Scheme 9).³⁰ⁱ The difference in the catalysts **28** and **29** is the presence/absence of substituents on the N atom of the ligand (R group, Scheme 9). Both ligands yield **endo-27** product exclusively as the only diastereomer but opposite enantiomers (ee values for products **27** are almost the same). This observation can be attributed only to the structural difference of the ligands, since other reaction parameters remain unaltered. Although catalysis by hydrogen bonding is a well-

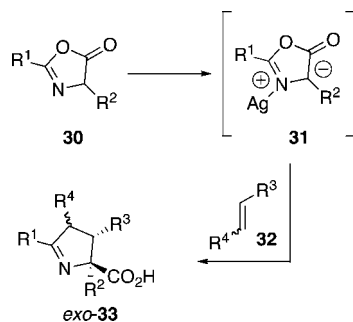
Scheme 9



Scheme 10



Scheme 11

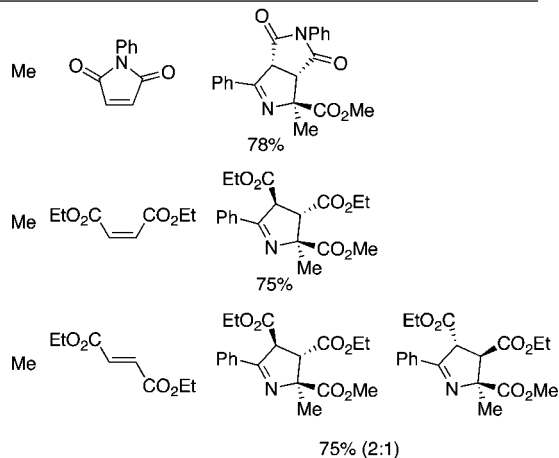


known concept,³² this is a rare example of reversal of selectivity induced by hydrogen bonding.³³ The rationale for the observance of this phenomenon was ascribed to a switch in the transition states occurring during the reaction. As shown in Scheme 10, in the absence of an H-bond donor, both substrates (SM¹ and SM²) would coordinate to the metal (M) as in **TS1**. If, however, one substrate could interact with the ligand through the H-bond (**TS2**, Scheme 10) different enantiofacial attack leading to the opposite enantiomer is possible.

Judging from the number of reports available to date, azomethine ylides are superior substrates for Ag(I)-catalyzed 1,3-dipolar cycloadditions. Tepe and co-workers have expanded the scope of silver-catalyzed cycloaddition reactions using azalactone **30** to generate the Δ^1 -pyrrolines **33** with high *exo/endo* diastereoselectivity (Scheme 11).^{30k} The reaction proceeds well with electron-deficient alkenes at room temperature to furnish the highly substituted Δ^1 -pyrrolines **33**.

Except for *trans*-diethyl fumarate as substrate **32**, other alkenes give products with excellent *exo* selectivity (Scheme 12), which is in contrast to the *endo* preference observed in the reaction with acyclic azomethine ylides. One reason for such selectivity is the locked anti configuration of münchnones **31** in comparison to the acyclic azomethine ylides, which preferentially adopt a *syn* orientation.^{30k} The benefits of this protocol are extensive, considering that it provides highly substituted Δ^1 -pyrroline-5-carboxylic acid scaffolds with up to three contiguous stereocenters. It is worth mentioning that further isomerization or decarboxylation of

Scheme 12



Δ^1 products does not occur and high diastereocontrol over three stereogenic centers is maintained for a series of substrates.

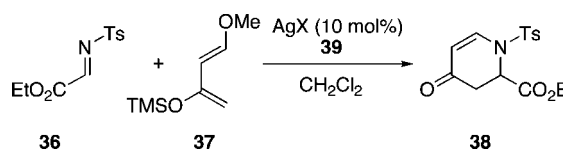
2.1.2. Hetero-Diels–Alder Reaction

The hetero-Diels–Alder reaction is one of the most powerful reactions for the construction of polyfunctional heterocyclic molecules in a single step.^{26,34} The aza-Diels–Alder reaction, a subclass of hetero-Diels–Alder reactions, is among the most efficient strategies for the construction of nitrogen-containing compounds such as piperidine and tetrahydroquinolidine derivatives.³⁵ Despite the fact that Ag(I) salts act as very proficient activators of imines and catalysts for 1,3-dipolar cycloadditions involving imines, only a few accounts of silver-catalyzed aza-Diels–Alder reactions have been reported so far.^{19,24d,36} Among those reported, only a few represent truly stereoselective catalytic reactions, and it is those that will be discussed in this section in more detail. Interesting points of other reports will be briefly mentioned.

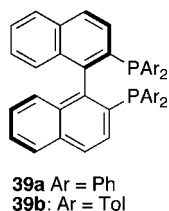
Jørgensen's group began investigating catalytic aza-Diels–Alder reactions in the late 1990s. One of their first results indicated that AgSbF₆, AgOTf, and AgClO₄ possessed sufficient catalytic activity, yielding cycloadduct **38** with low selectivity but good yields (Scheme 13).^{36a} Weller and colleagues have tested silver–carborane catalysts ([Ag(PPh₃)(CB₁₁H₁₂)], [Ag(PPh₃)₂(CB₁₁H₁₂)], [Ag(PPh₃)(CB₁₁H₆Br₆)], [Ag(PPh₃)₂(CB₁₁H₆Br₆)]) for the aza cycloaddition between *N*-benzylideneaniline and Danishefsky's diene **37**.^{36c}

Using only 1 mol % of the catalysts, products were obtained in 85–99% yield, within just 1 h at room temperature. Catalyst loading could be decreased to 0.1 mol % without a loss of reactivity. The authors have shown, through a competition experiment between the aldehyde and imine, an exclusive preference for an imine, since the aldehyde-derived adduct was isolated in less than 5% yield. Another example of an aza-Diels–Alder reaction is the report by Kobayashi's group of AgOTf-catalyzed cycloaddition of

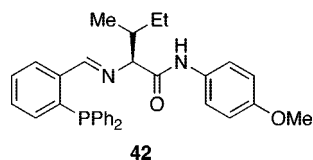
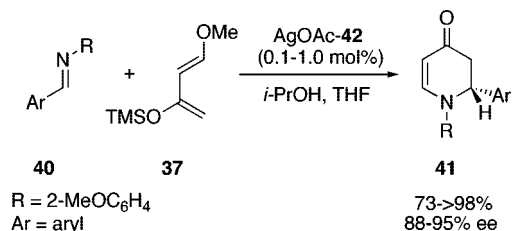
Scheme 13



AgX	39	yield(%)	ee(%)
AgSbF ₆	39a	75	33
AgOTf	39b	85	30
AgSbF ₆	39b	90	34



Scheme 14

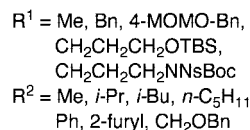
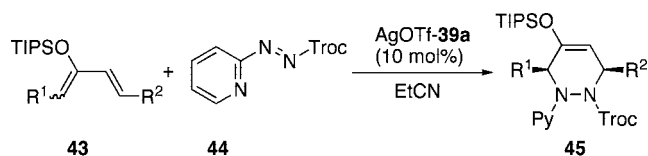


imines with Danishefsky's diene in aqueous media.^{24d} Alternatively, the same reaction can be carried out as a three-component reaction with the imine being generated in situ. Although the products obtained are racemic, this method has great importance from the standpoint of economic, environmental, and safety issues.

Until the present day, there have only been two highly effective silver-based aza-Diels–Alder protocols available for implementation in a large-scale enantioselective synthesis. One of those protocols, developed by the Hoveyda and Snapper groups, entails the Ag(I) amino acid derived phosphine system **42** (Scheme 14).¹⁹ Using AgOAc-**42**, adducts of arylamines with Danishefsky's diene were produced with excellent yields and enantioselectivities under mild conditions.

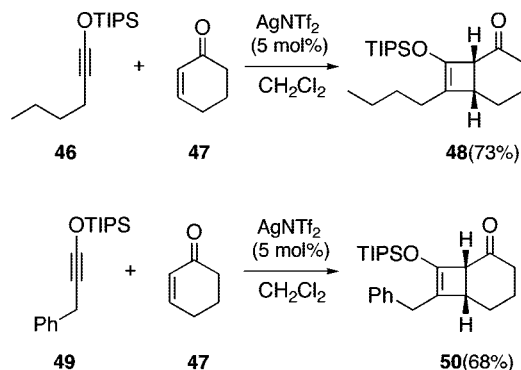
Considering that products **41** can be further modified to other enantioenriched N-heterocycles, this transformation is highly beneficial. The importance of this method can also be illustrated with the following details. (i) The chiral ligand **42** used in this reaction was easily prepared from inexpensive amino acid derivatives and other commercially available materials. (ii) The reactions with various arylimines were effected in the presence of ≤ 1 mol % catalyst without a significant loss of reactivity or selectivity. (iii) Catalytic reactions can be carried out in the presence of air and with undistilled solvent without diminished reactivity or selectivity. However, the reaction requires 1 equiv of *i*-PrOH (other sources of proton such as MeOH, *t*-BuOH, and H₂O are equally efficient) for high conversion and satisfactory enantioselectivity. The necessity of the proton source might be to facilitate the shuttle of the TMS group from O to N (or vice versa) or simply to free the Ag(I) from its complex with the product. The authors have demonstrated that this method

Scheme 15



65-87%
55->99% ee

Scheme 16



can be extended to high-throughput synthesis using a Wang-resin-supported ligand (products are obtained in 86% yield and 96% ee).

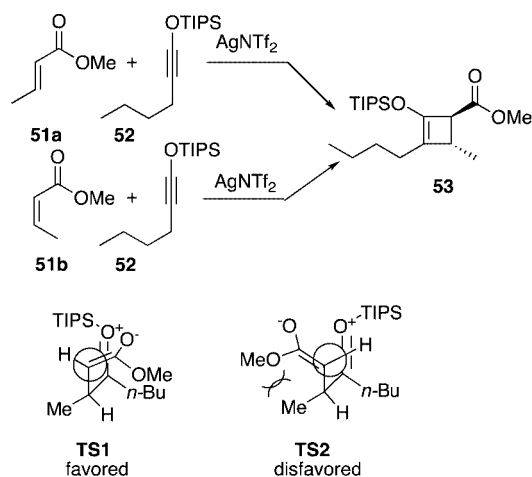
Another example of a highly effective silver catalyst for the hetero-Diels–Alder reaction is the BINAP–Ag(I) complex developed by Yamamoto's group.^{36d} The 2-diazopyridine **44** underwent facile cycloaddition with the siloxydiene **43** to furnish the densely substituted cyclic diamine **45** with high ee's (Scheme 15).^{36d} Even though alternative approaches to stereoselective aza-Diels–Alder reaction of this type are known,³⁷ this is one of the rare examples of a truly enantioselective reaction.

High reactivity and selectivity are general trends not only for various simple dialkyl dienes but also for substrates with Lewis basic groups. The conditions developed for the facile conversion of products **45** to chiral 1,4-diamine alcohols render this technique highly useful.

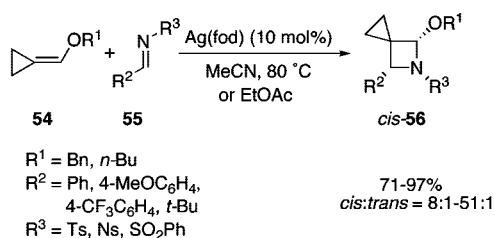
2.1.3. [2 + 2] Cycloaddition

[2 + 2] Cycloaddition of olefins and alkynes is a versatile method for the preparation of cyclobutane derivatives. Typically, these cycloadditions are achieved through thermal reactions,³⁸ photoreactions,³⁹ or transition-metal-catalyzed reactions.⁴⁰ While the first two pathways of [2 + 2] cycloadditions can be tedious procedures involving radical intermediates, the development of alternative metal-catalyzed procedures presents an advantageous solution. In this aspect, Kozmin et al.'s report of the cycloaddition of siloxyalkynes and unsaturated carbonyls (Scheme 16) is a significant contribution to this area.⁴¹ Their methodology establishes a novel mode of reactivity of silyl ynol ethers⁴² and provides direct access to complex siloxy cyclobutenes. An interesting feature of this reaction is that *trans* adducts are the exclusive products, regardless of the double-bond configuration of the substrates (Scheme 17). This observation indicates that the reaction proceeds by a stepwise mechanism. The observed

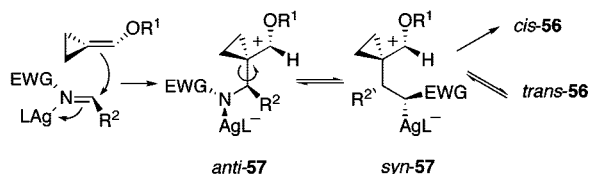
Scheme 17



Scheme 18



Mechanism of the silver-catalyzed [2+2] cycloaddition:



diastereoselectivity is most likely caused by minimization of the allylic strain in the transition state **TS2** (Scheme 17).

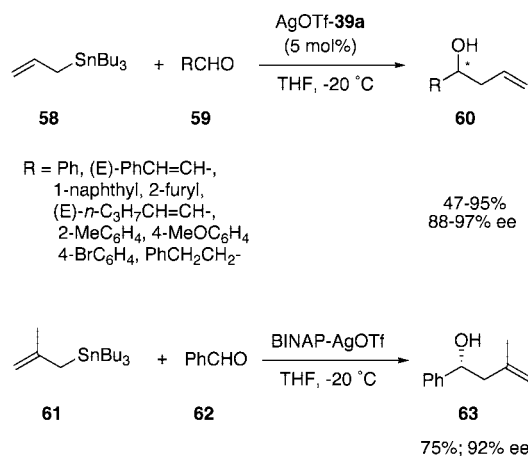
With regard to the mechanistic scenario, the authors propose Ag(I) activation of the alkyne, 1,4-addition, and subsequent trapping of the ketenium ion intermediate.⁴¹

Silver-promoted [2 + 2] cycloaddition can be successfully extended to substrates such as imines and (alkoxymethylene)cyclopropanes, as was demonstrated by Nakamura's group in 2006.⁴³ Due to the ease of their preparation and their ring strain, (alkoxymethylene)cyclopropanes are very appealing substrates for various types of cycloaddition reactions.⁴⁴ Products of [2 + 2] cycloaddition with imines are highly functionalized azetidines (Scheme 18) which are useful building blocks for the synthesis of α -cyclopropanated β -amino acids.⁴³ Investigations conducted by Nakamura's group have shown that the reaction does proceed by thermal activation, albeit sluggishly. On the other hand, in the presence of 10 mol % of Ag(fod) catalyst the reaction is complete within hours at room temperature. The *cis* diastereoselectivity observed in this reaction is strongly favored over *trans*. Apparently, ring closure of intermediate **57** to furnish either *cis*-**56** or *trans*-**56** is reversible and *cis*-**56** is thermodynamically more stable (Scheme 18).⁴³

2.2. BINAP–Ag(I) Catalytic System

In 1996 Yamamoto's group introduced the BINAP–AgF catalytic system for the asymmetric allylation of aldehydes.⁴⁵

Scheme 19



Since then, major improvements have been achieved for the allylation reaction⁴⁶ and the application of this catalytic system has been extended to other types of asymmetric reactions. Currently, BINAP–Ag(I) is successfully used for (i) allylation reactions,^{45,46} (ii) Mukaiyama-aldol reactions,⁴⁷ (iii) nitroso-aldol reactions,⁴⁸ (iv) protonation of enolates,⁴⁹ and (v) hetero-Diels–Alder reactions.^{36d}

2.2.1. Allylation Reaction

The asymmetric addition of allylic units to aldehydes and ketones to generate homoallylic alcohols is one of the most effective pathways to β -hydroxy carbonyls and various other chiral molecules.⁵⁰

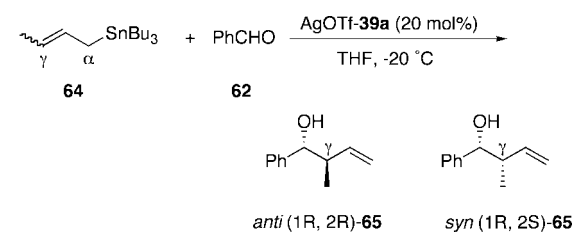
Early accounts of allylation reactions utilizing chiral silver(I) complexes focused on the use of allyltributyltin as the allylating agent.⁴⁵ These results are summarized in Scheme 19.

The reaction proceeds well for aromatic aldehydes, while aliphatic aldehydes give slightly lower yields and selectivities. It is noteworthy that in the case of α,β -unsaturated aldehydes only the products of 1,2-addition are observed. It was also demonstrated that methallylstannane **61** adds to benzaldehyde to furnish the corresponding homoallylic alcohol in good yield and excellent enantioselectivity.

The advantages of this system are obvious when the more challenging task of addition of γ -substituted allylic units is considered. Condensation of γ -substituted allylmetals with aldehydes is a fascinating subject with regard to the regioselectivity (α vs γ) and stereoselectivities (*E* vs *Z* or *anti* vs *syn*).⁵¹ When benzaldehyde is treated with (*E*)- or (*Z*)-2-butenyltributylstannane the *anti* product **65** is predominantly formed, regardless of the configuration of the double bond in the starting stannane (Scheme 20).^{46b} Similarly, in the reaction of tributylpentadienylstannane and benzaldehyde, the products of γ -allylation were observed exclusively.

Generally, synthetically highly valuable molecules are obtained in high yields and excellent diastereo- and enantioselectivity. The only drawback is the use of toxic trialkyltin compounds as the source of the allylic moiety. To avoid the use of such reagents, trimethoxysilane was introduced as an alternative to tin compounds.^{46a} Allylic trialkoxysilanes are commonly used as allylating agents, owing to their capability of forming highly reactive pentacoordinated silicates with nucleophiles.⁵² To achieve better results, the use of trimethoxysilanes required switching to the (*R*)-*p*-Tol-BINAP(**39b**)–AgF system. This new catalyst gives yields

Scheme 20



E/Z-64 ratio	yield	65 anti (ee%)/syn (ee%)
95/5	56	85 (94)/15 (64)
2/98	72	85 (91)/15 (50)
95/5	45	85 (94)/15 (57)

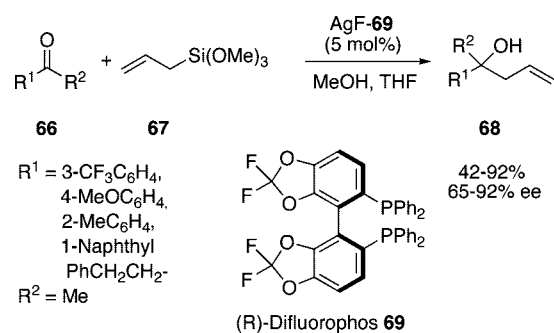
and ee's as high as those previously obtained with BINAP–AgOTf for a series of aromatic aldehydes (70–93% yields and 78–94% ee's). Anti diastereoselectivity and γ -allylation preferences were operative in this system as well. The newly developed protocol requires the use of alcohol solvents to achieve high conversion. The main reason for low conversion in THF (which was used in previous reactions) is the extremely low solubility of metal fluorides in THF. Among the alcohols tested, MeOH provides the highest yields and good enantioselectivities.^{46a} Although MeOH is an excellent solvent for some reactions, in some instances it causes the undesired protonation of less reactive species. The use of alcohol solvents can be avoided by the use of the more general bifunctional catalytic system KF/BINAP(39a)/AgOTf/18-crown-6.^{46c}

In the examples discussed so far, addition of allyl organometallic reagents was focused primarily on addition to aldehydes. Allylation of ketones represents a more daunting task and, if achieved effectively in an asymmetric manner, structurally attractive tertiary homoallylic alcohols would be readily available. Yamamoto's group established a highly effective protocol for catalytic asymmetric Sakurai–Hosomi allylation of ketones in the presence of BINAP(39a)-AgF.^{46d} Representative results and a plausible mechanism are shown in Scheme 21. The reaction proceeds smoothly and cleanly for a variety of ketones, while substrates with electron-withdrawing groups give slightly higher enantioselectivities. Remarkably, cyclic ketones produce alcohols with more than 90% ee. The 1,2-addition pattern observed previously (Scheme 19) is present in this case as well, with both cyclic and acyclic enones. Crotyltrimethoxysilane gives branched syn products with high enantioselectivities (93 and 95% ee).

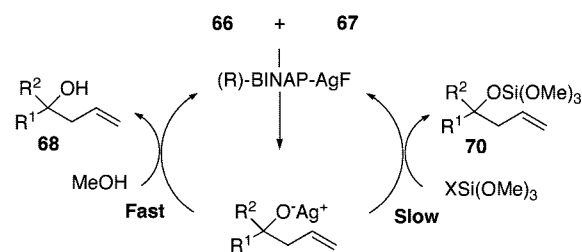
Interestingly, with racemic allylsilanes as starting materials, optically pure products were obtained almost exclusively. In contrast to previous accounts of the SE'-allylation using a combination of chiral allylsilanes and Lewis acid,⁵¹ this catalyst provides high diastereo- and enantioselectivities, regardless of the chirality of the starting material.⁴⁶ During the investigation into the asymmetric Sakurai–Hosomi reaction, it was observed that the product generated is the tertiary alcohol **68** and not its silyl derivative **70**. The yields of the products strongly reflected the amount of MeOH present in the reaction vessel. These observations indicated that proton transfer from MeOH was much faster than silyl transfer (Scheme 21).^{46d}

As discussed so far, the BINAP–Ag(I) system used for asymmetric allylation produces homoallyl alcohols in a

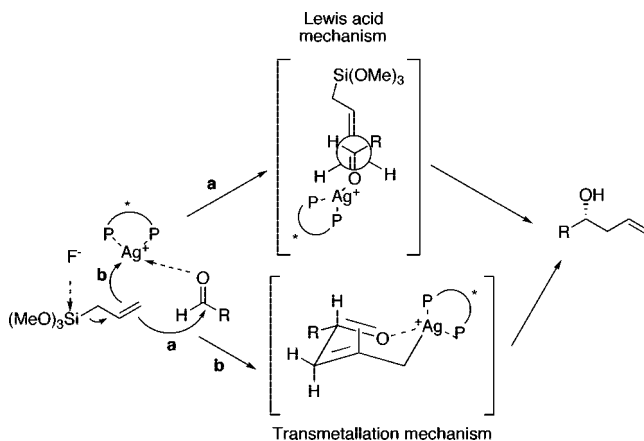
Scheme 21



Proposed Catalytic Cycle:



Scheme 22



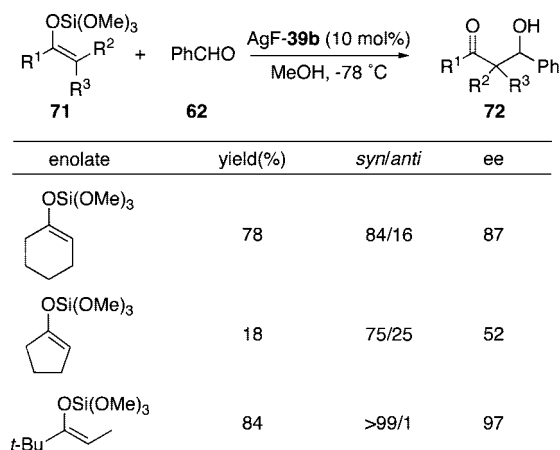
highly diastereo- and enantioselective manner, regardless of the chirality of the starting allylsilanes. Although the detailed stereochemical profile of the mechanism is not fully understood, two scenarios are conceivable for the explanation of the observed phenomena (Scheme 22).

One mechanistic pathway (a, Scheme 22) entails Lewis acid activation of the carbonyl group and proceeds via an acyclic antiperiplanar transition state.⁵³ The second possible mechanism (b, Scheme 22) involves transmetalation of allylsilane and Ag(I) to generate an organosilver intermediate that adds to the carbonyl group. It is possible to obtain an anti product starting from either (*E*)- or (*Z*)-crotylsilane if one considers the option of fast isomerization of the generated crotyl silver species.

2.2.2. Mukaiyama–Aldol Reaction

The diphosphine–Ag(I) catalyst introduced by Yamamoto's group was shown to effectively promote asymmetric aldol-type reactions.⁴⁷ Although several reports of the catalytic asymmetric Mukaiyama reactions using chiral Lewis acid are present in the current literature, examples of the utility of tin enolates are scarce. Early accounts by Yamamoto et al. described the procedure for enantioselective aldol reactions of trialkyltin enolates catalyzed by the BINAP–Ag(I)

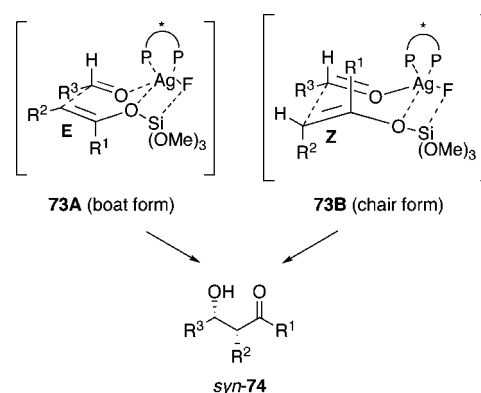
Scheme 23



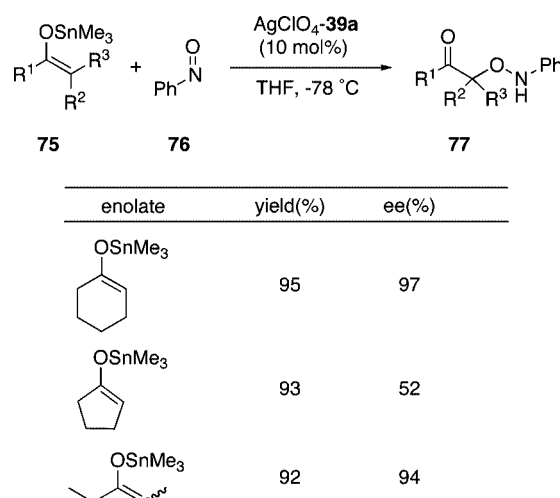
system.^{47a} The tributyltin enolate is generated from the corresponding enol acetate and tributyltin methoxide in the absence of solvent.⁵⁴ Tin enolates prepared in this manner exist in both O–Sn and C–Sn forms, and either can be used for the reaction with aldehydes. Characteristic features of this reaction are as follows: (i) the reactions yield aldol products in moderate to good yields without the formation of dehydrated aldol adducts; (ii) 1,2-addition occurs exclusively with α,β -unsaturated aldehydes; (iii) sterically demanding tin enolates yield products with higher ee's; (iv) anti diastereoselectivity is the general mode of stereoselectivity, in contrast to the syn selectivity typical for the majority of other Lewis acid catalyzed processes.⁵⁵ The main disadvantage was the use of stoichiometric amounts of toxic tin compounds; hence, improved conditions were reported soon thereafter.^{47b} The optimized procedure involves the use of catalytic amounts of tin enolates generated in situ from trichloroacetoxy enolates. Although only catalytic amounts of tin compounds were required for high conversion, the use of toxic materials was still needed. The *p*-Tol-BINAP–AgF system that was successfully implemented for asymmetric allylation reactions of allyltrimethoxysilanes could be equally effectively used for the asymmetric aldol reaction of trimethoxysilyl enol ethers.^{47c} Representative results are depicted in Scheme 23.

Reactions were effected with only 0.1 mol % of diphosphine–Ag(I) catalyst to produce aldol products enantioselectively with high syn diastereoselectivity for a series of different aldehydes. 1,2-Addition to α,β -unsaturated aldehydes was the only reactivity mode observed. Aliphatic aldehydes and ketones were insufficiently reactive for the aldol reaction, yielding less than 1% of the product, even at room temperature. The use of MeOH was necessary for conversion with high selectivity, since AgF shows low solubility in other organic solvents. However, in this solvent the undesired hydrolysis of the silyl enol ether occurs even at low temperatures. Interestingly, 1:1 mixtures of MeOH with acetone, THF, or *i*-PrOH not only were suitable solvents for high yields but also could increase the selectivity. To obtain more detailed information regarding the syn selectivity observed, NMR experiments were carried out. ¹H NMR studies that were conducted showed the disappearance of signals due to the silyl enol ether of cyclohexanone in the presence of BINAP–AgF catalyst. Furthermore, the disappearance of those signals was accompanied by the appearance of signals assignable to a 1-cyclohexenyl group. During the reaction, no signals due to (MeO)₃SiF or cyclohexanone were

Scheme 24



Scheme 25



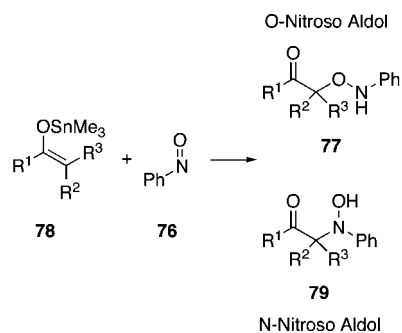
seen. In accordance with these results, the mechanism depicted in Scheme 24 was proposed as a rationale for the stereochemical outcome of the reaction. Cyclic transition states **73A** and **73B** (Scheme 24) can be considered as possible models for aldol reaction. In these assemblies, the BINAP–AgF complex acts as a chiral Lewis acid and coordinates to both an aldehyde and a silyl enol ether to form a six-membered cyclic structure, which is further stabilized by the adjacent AgF–Si(OMe)₃ ring.⁵⁶ An (*E*)-enol ether trapped in a boatlike structure can give the same syn diastereomer as a (*Z*)-enol ether trapped in a chairlike cyclic structure. It should be noted here that this mechanism is different from that proposed for allylation of aldehydes with allyltrimethoxysilanes.

2.2.3. Nitroso-Aldol Reaction

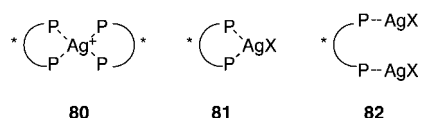
After the early studies of nitroso-aldol synthesis,⁵⁷ it was demonstrated by Yamamoto's group that the BINAP–silver complex effectively catalyzes the *O*-nitroso-aldol reaction of tin enolates.^{48b} Illustrated in Scheme 25 are some of the results of silver-catalyzed nitroso-aldol reactions. The *O* regioselectivity and enantioselectivity were both maintained for a range of different tin enolates. Among the tin enolates investigated, tributyltin enolates provided slightly higher *N* selectivity.

Further investigation of silver-catalyzed nitroso-aldol reactions indicated an intriguing relationship between the structure of the active catalytic complex and the regio- and enantioselectivity profile of the reaction.^{48a} Three forms of diphosphine–Ag(I) complexes were generated when silver

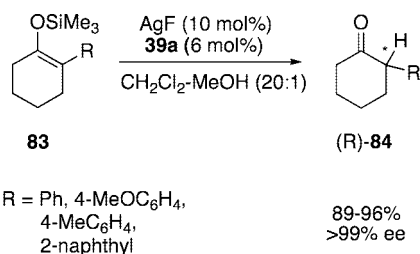
Scheme 26



Complexes of Ag(I) and diphosphine ligands:



Scheme 27



salts and chiral ligands were combined (Scheme 26). It was found that the ratio of these complexes depends strongly on (i) the stoichiometry of the silver salt and diphosphine used and (ii) the nature of the counteranion. Complex **81** (X = OCOCF₃) was exceptionally active for *O*-nitroso aldol reactions, giving products with high yields and ee's. On the other hand, complexes **80** and **82** were significantly less effective, displaying low enantioselectivity/regioselectivity profiles.

The conditions for improved N selectivity have also been explored. Both **80** (X = OTf) and **81** (X = OAc) yielded *N*-nitroso-aldol products predominantly, albeit with low enantioselectivity. A dramatic increase in the regioselectivity and enantioselectivity occurred when **82** (X = OTf) was used (the N adduct is formed with 96% regioselectivity and 87% enantioselectivity). From these findings, a protocol for the enantioselective synthesis of α -hydroxyamino ketones was devised. Typical features of these reactions are excellent regioselectivities favoring the N-adduct (N:O >99:1) and high enantioselectivities (77–98% ee's).

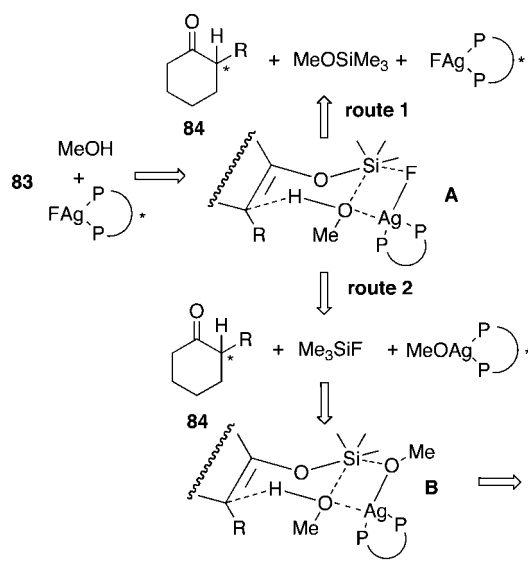
2.2.4. Protonation of Silyl Enolates

As described earlier, the BINAP–AgF catalyst shows excellent reactivity with allylsilanes and silyl enol ethers. Its reactivity relies strongly on the enhanced activation of the silyl moiety by fluoride anion. For the same reason the AgF catalyst acts as a proficient promoter of the enantioselective protonation of prochiral silyl enolates.⁴⁹

The reactions proceed with high enantioselectivities and good yields for a series of substrates derived from 2-aryl-cyclohexanone (Scheme 27).

Among the different alcohols screened, MeOH was shown to give products with the highest ee's. ¹H NMR studies

Scheme 28



revealed the appropriate ratio of AgF and (*R*)-BINAP to be 1.0:0.6 for the formation of a 1:1 (BINAP:AgF) complex, since a 1:1 mixture affords significant amounts of the unreactive 2:1 (BINAP:AgF) complex.

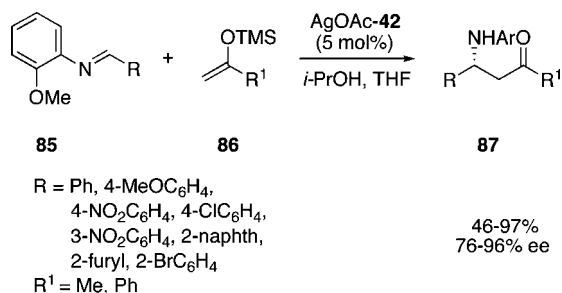
Even though a detailed mechanism is still not fully clear, two mechanistic scenarios can be postulated (Scheme 28). The authors propose **A** to be the initial transition state that is formed upon mixing of **83**, MeOH, and the catalyst. Along the line of route 1 in this scheme, product **84** is released together with the formation of methoxytrimethylsilane. Route 2 considers the possibility of transmetalation, where fluoro-silane and BINAP–AgOMe are generated. In the following transition state **B**, BINAP–AgOMe acts as the catalyst and is recovered thereafter.⁴⁹

2.3. Amino Acid Derived Phosphine–Ag(I) Catalyst

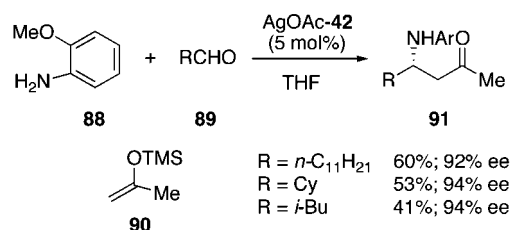
The amino acid derived phosphine ligand **42** (Scheme 14), introduced by the Hoveyda and Snapper groups, was initially used for hetero-Diels–Alder reactions of imines and Danishefsky's diene.¹⁹ Prior to this report, several protocols for asymmetric catalytic versions of this reaction were published.⁵⁸ Those methodologies require relatively high catalyst loadings (20–40 mol %) and afford moderate selectivities (often <90% ee). The Hoveyda–Snapper catalyst, on the other hand, provides access to cycloadducts in >77% yield and >89% ee (Scheme 14).¹⁹

Further improvements extended the application of this catalyst to several Mannich reactions^{20a,b,d} and enantioselective addition of silyl enol ethers to α -keto esters.^{20c} The main advantages of the amino acid derived phosphine–Ag(I) system are (i) the system is easy to prepare from inexpensive commercial materials, (ii) catalytic reactions generally proceed smoothly for a wide range of substrates with good yields and selectivities, (iii) yields and selectivities remain practically unaltered when Ag salts and solvents are used without prior purification or when the catalytic reactions are carried out in air. Owing to these characteristics, this catalyst would most likely be a primary choice for the aforementioned reactions.

Scheme 29



Three-Component Ag-Catalyzed Mannich Reaction:



2.3.1. Mannich Reaction

β -Amino carbonyls and their derivatives represent an increasingly important group of organic molecules, since they are present in a large number of biologically significant molecules.⁵⁹ Hence, the development of asymmetric, catalytic protocols for the Mannich reaction, which is the most straightforward pathway to this class of molecules, would be very beneficial. The catalytic system described in this section facilitates Mannich reactions of various imines with silyl ketene acetals^{20b} and enol ethers.^{20a} Highly efficient vinylogous Mannich reactions^{20d} and enantioselective additions of silyl enol ethers to α -keto esters^{20c} have also been reported for the same catalyst.

One of the first catalytic enantioselective synthesis of β -alkynyl- β -amino esters reported by the Hoveyda and Snapper groups was achieved by using the *iso*-Leu-derived phosphine ligand **42** (Scheme 14) in combination with AgOAc.^{20b} This method presents a further extension of the methodology devised for Mannich reactions of various aryl imines with enol ethers.^{20a} Representative results for these reactions are depicted in Schemes 29 and 30.

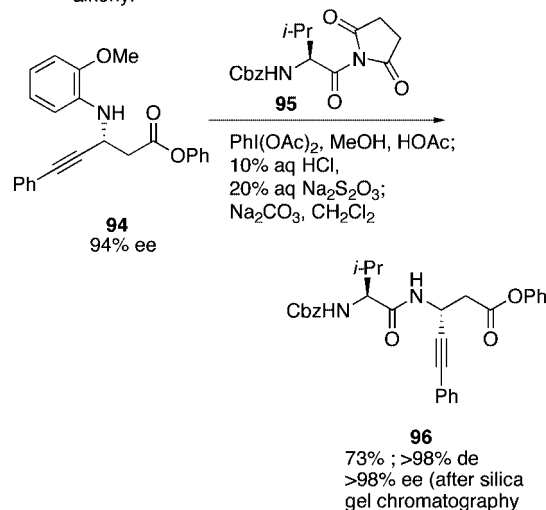
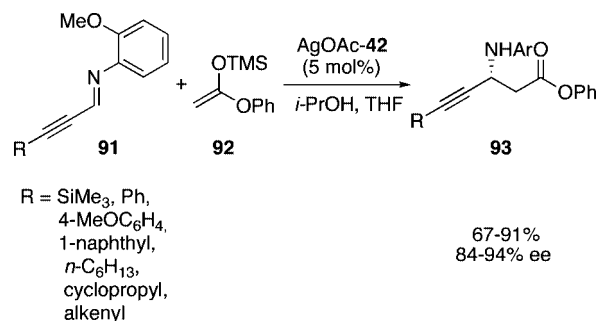
High conversions and enantioselectivities could be achieved for the series of aromatic imines **85**. Electron-poor imines were more reactive, allowing the reaction to proceed at lower temperatures with higher ee's. Heterocyclic imines undergo transformation smoothly to furnish products **87** with excellent enantioselectivities (86 and 90% ee).

The substrate scope could be extended to unsaturated imines that showed similarly high selectivities, albeit with lower yields.

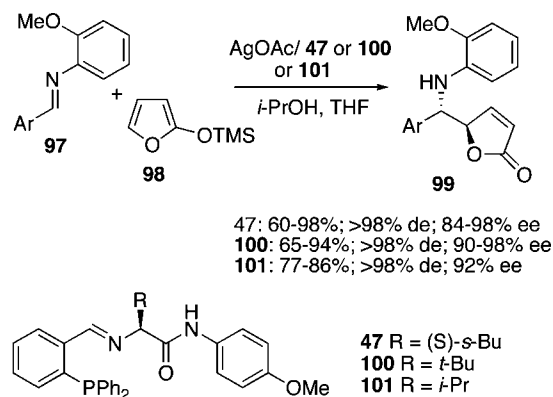
A similar reactivity pattern was observed for aliphatic imines that can undergo three-component condensation (Scheme 29). It is important to mention that the reaction required 1 equiv of *i*-PrOH for high conversion. The efficiency of this protocol was further displayed by a brief total synthesis of (-)-sedamine.^{20a}

Various alkynyl imines screened for silver-catalyzed reactions showed good selectivities and provided products in synthetically useful yields.^{20b} β -Amino esters obtained in this way can be further synthetically elaborated through oxidative removal of the activating group attached at the N atom followed by the introduction of an amide group (**96**,

Scheme 30



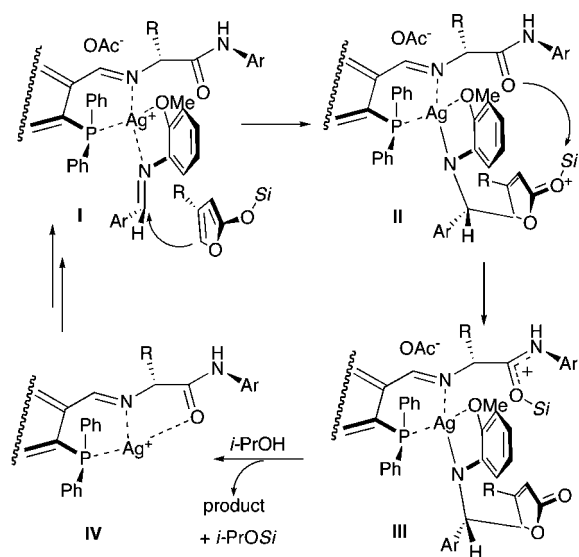
Scheme 31



Scheme 30). Remarkably, all these concomitant transformations were carried out without significant loss of optical purity.^{20b}

Phosphine ligands bearing different amino acid residues were used in combination with AgOAc in an asymmetric vinylogous Mannich reaction with siloxyfurans.^{20d} Products obtained in this manner are highly complex, enantioenriched γ -butenolide units which serve as useful chiral building blocks. The presence of two contiguous stereogenic centers in these assemblies makes these molecules extremely appealing chiral precursors. The Hoveyda and Snapper groups have demonstrated that siloxyfuran undergoes addition to imines in a highly diastereo- and enantioselective fashion.^{20d} Three chiral ligands used in the initial investigation exhibited similar efficiencies for asymmetric induction as well as comparable reactivities (Scheme 31). For the reaction of substrate **98**, bearing methyl group at the 3-position, a ligand bearing a Thr(*O-t*-Bu) residue was identified as the most

Scheme 32



efficient. Interestingly, in this case complete reversal of diastereoselectivity in favor of the syn product was observed.

The mechanistic model proposed (Scheme 32) offers a rationale for the stereochemical outcome of the reaction. The authors suggest that Ag^+ operates as a Lewis acid through coordination with the N atom of the imine (**I**, Scheme 32). To minimize undesired steric interactions, the imine coordinates anti to the residue R of the ligand. The siloxyfuran reacts with the complex **I** in an endo fashion, and intermediate **II** is formed.

Desilylation occurs intramolecularly by the participation of the amide moiety. Finally, in the presence of *i*-PrOH, the product is released and the catalyst is recovered in its original form (**IV**, Scheme 32).

Some of the benefits of the phosphine ligand described are its relatively simple preparation and the structural modification of its backbone to fine-tune the steric and electronic properties of the catalytic complex. The complex $\text{Ag}(\text{II})$ -**105**, obtained by substitution of the phosphine moiety with a pyridyl unit, effectively promotes the addition of enolsilanes to α -keto esters (Scheme 33).^{20c} The protocol for addition of enolsilanes to keto esters is especially useful for sterically hindered substrates **102** ($G = i\text{-Pr}$, Cy; Scheme 33), where 88–96% ee's and >90% yields were obtained.

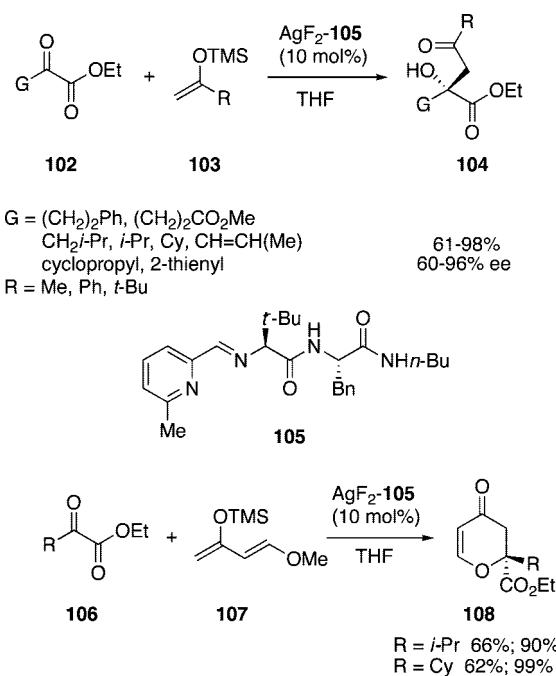
For α,β -unsaturated substrates only traces (<2%) of the conjugate addition products were observed. It was also demonstrated that AgF_2 -**105** promotes hetero-Diels–Alder cycloadditions of Danishefsky's diene with excellent enantioselectivity (Scheme 33).

2.4. Group-Transfer Reactions

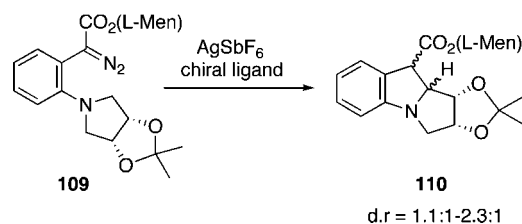
Reactions discussed in the previous sections were primarily concerned with Ag-catalyzed reactions where $\text{Ag}(\text{I})$ operates as a Lewis acid and predominantly as an oxo- or azaphilic reagent. It should be noted that a fair amount of reports describe reactions where $\text{Ag}(\text{I})$ functions in a carbophilic manner, activating C–C multiple bonds (those accounts are briefly mentioned in the Introduction). In some instances, the exact mode of activation is still ambiguous, leaving equal opportunity for oxophilic and carbophilic mechanisms.^{41,60}

In the following section, reactions that include different reactivity modes of silver catalysts will be summarized.

Scheme 33



Scheme 34



Those reactions include stereoselective silver-catalyzed carbene-, nitrene-, and silylene-transfer reactions.

2.4.1. Carbene-Transfer Reactions

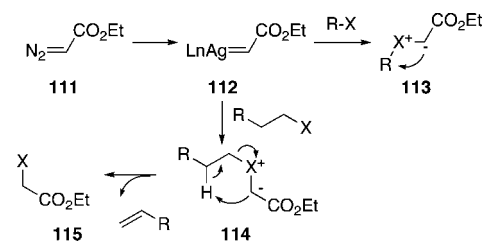
Carbene-transfer reactions that involve the use of diazo compounds are well-known processes.⁶¹ The use of silver salts with diazo compounds is also well-documented, especially for the Wolff rearrangement reaction.⁶² In addition to the Wolff rearrangement reaction, silver compounds were used in conjunction with diazo compounds for C–H activation,^{23a,d,f} N–H activation,^{23c} aziridation,^{23b} and cyclopropanation^{23g} of olefins.

It was first recognized by Burgess and co-workers that AgSbF_6 possesses the ability to catalyze the intramolecular insertion of carbene (Scheme 34).^{23a} Using high-throughput catalyst screening techniques, a series of catalytic systems were tested for the carbene insertion reaction. Product **110** was obtained with a rather low diastereoselectivity and in some cases low yields (<5%). At that point, no speculations were made regarding the mechanism of the reaction.

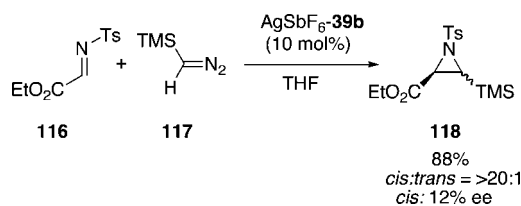
Years later, the mechanism of silver-catalyzed C–X activation was proposed and the intermediacy of the silver carbene species **112** was suggested (Scheme 35).^{23c} The authors have also indicated that this novel metal-mediated process is specific for silver and tris(pyrazolyl)borate ligands ($[\text{BH}(3,5\text{-}(\text{CF}_3)_2\text{Pz}_3)]^-$).^{23e}

In 1999, Jørgensen et al. reported the diastereoselective synthesis of aziridines starting from imines and (trimethylsilyl)diazomethane in the presence of Tol-BINAP– $\text{Ag}(\text{I})$

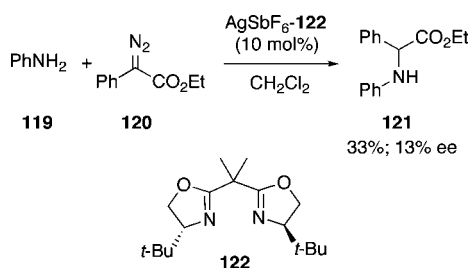
Scheme 35



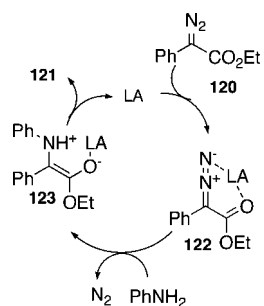
Scheme 36



Scheme 37

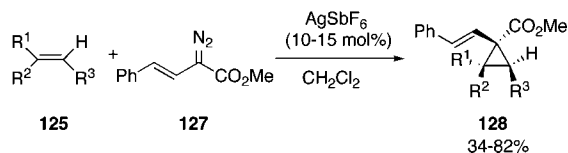
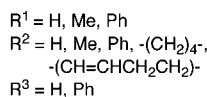
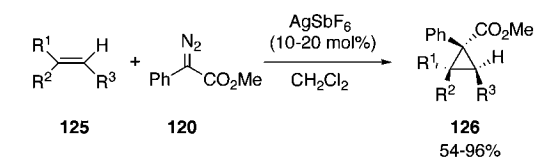


Scheme 38



catalyst (Scheme 36).^{23b} Products were obtained in good yields (~88%) and moderate diastereoselectivity (>20:1), albeit with low enantioselectivities (12% ee). A comparison of the reactivities of Ag(I) and Cu(I) suggests that the reaction with silver proceeds via Lewis acid activation, while in the case of copper, a metallocarbene intermediate is formed. A similar comparative study of Cu(I) and Ag(I) catalysts for asymmetric catalytic N–H activation reactions was reported by the same group in 2004.^{23c} Copper exhibited slightly better reactivity, affording products **121** with higher yields than for silver (Scheme 37). However, both metals provided products with low enantioselectivities (usually not exceeding 30% ee). For the N–H activation reaction (Scheme 37) Lewis acid character was again ascribed to Ag(I) and a plausible mechanism in accordance with its Lewis acid properties proposed (Scheme 38). Although the Lewis acid mechanism was suggested as being the most likely, participation of metallocarbene cannot be completely excluded. The authors have observed traces of olefinic products from the elimination of **120**, which indicates that either reduction of Ag(I) to Ag(0) occurs or silver hydrides possibly participate in the reaction.^{23c}

Scheme 39



One of the most successful organic stereoselective transformations involving silver carbenoid species is intermolecular cyclopropanation using aryl diazoacetates.^{23g} This methodology, developed by Davies and colleagues, utilizes carbenoids with both acceptor and donor groups in conjunction with AgSbF_6 to furnish cyclopropane derivatives in excellent yields and diastereoselectivities (Scheme 39). A comparative study of the reactivity of silver and rhodium, which is traditionally used for these types of reactions, shows a superior reactivity of AgSbF_6 over Rh catalyst. The silver catalyst yields cyclopropane derivatives in excellent yields and diastereoselectivities (Scheme 39). A comparative study of the reactivity of silver and rhodium, which is traditionally used for these types of reactions, shows a superior reactivity of AgSbF_6 over Rh catalyst. The silver catalyst yields cyclopropane derivatives in excellent yields and diastereoselectivities (Scheme 39). A comparative study of the reactivity of silver and rhodium, which is traditionally used for these types of reactions, shows a superior reactivity of AgSbF_6 over Rh catalyst. The silver catalyst yields cyclopropane derivatives in excellent yields and diastereoselectivities (Scheme 39).

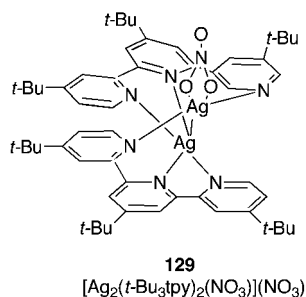
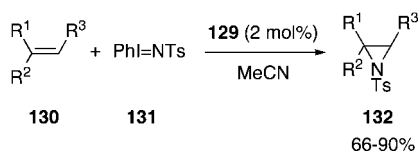
The reaction proceeds smoothly with various alkenes in the presence of 10–20 mol % of AgSbF_6 , and only one diastereomer was observed. Remarkably, good yields and selectivities were preserved for highly substituted alkenes **125** and the styrene-derived diazo compound **127**. Under the same conditions, Rh(I)-promoted reactions afforded products of C–H insertion or carbene dimerization predominantly.

2.4.2. Nitrene-Transfer Reaction

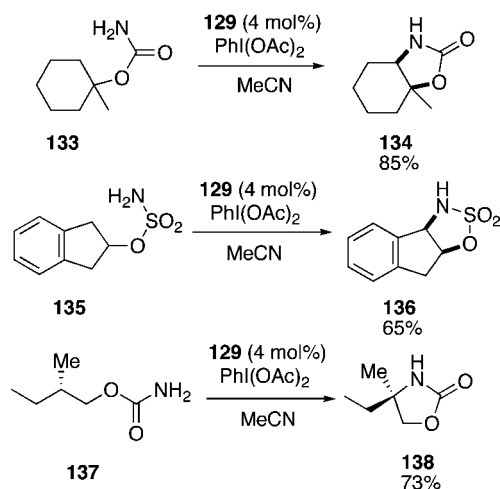
In 2003, He's group reported one of the major breakthroughs in the oxidation chemistry of high-valent silver. They introduced the unique disilver(I) complex **129** (Scheme 40) for catalytic aziridation of alkenes.^{21a} A dinuclear complex is prepared from the tridentate ligand (*t*Bu₃tpy) and AgNO_3 that displays unique architectural features responsible for its reactivity. More specifically, it features Ag(I) and Ag(II) centers, stabilized by N atoms present in the ligand, that are both pentacoordinated when the Ag–Ag interaction is taken into account. Although the mechanistic details have not yet been fully disclosed, a plausible mechanism involves the intermediacy of $\text{Ag}=\text{NTs}$ species. Since the reaction is highly specific for complex **129**, it can be envisioned that electronic relay between the two Ag centers facilitates formation of such nitrene species.^{21a,b} Complex **129** also catalyzes intramolecular amidation^{21b} and intermolecular amination^{21c} of sp^3 C–H bonds.

The amidation reaction was shown to be stereospecific (Scheme 41). To obtain detailed information about the mechanism, the chiral compound **137** was subjected to the standard reaction conditions to cleanly yield **138** (Scheme 41). Comparison of the optical rotation values of **138** and

Scheme 40



Scheme 41



137 indicated that **138** was formed with retention of the configuration, which unambiguously proves the reaction to be stereospecific. On the basis of this observation, a radical mechanism can be excluded, since it would produce **138** as a racemic mixture. The intermediacy of a silver nitrene species and its insertion into a C–H bond represents a more plausible mechanistic scenario. From a mechanistic standpoint, the silver-based dinuclear complex **129** presents an important achievement in oxidative homogeneous silver catalysis that does not involve a radical mechanism.

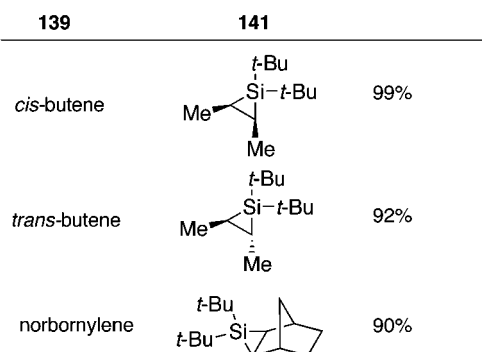
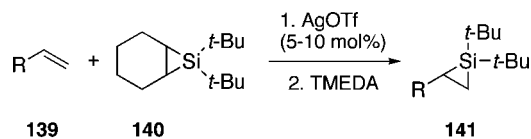
2.4.3. Silylene-Transfer Reaction

As described so far, silver efficiently participates in the transfers of carbenes and nitrenes to alkenes or their insertion into otherwise inert bonds and valuable aziridine and cyclopropane precursors are generated. Pioneered by Woerpel's group, silacyclopropanation has been recently added to this family of very powerful organic transformations.^{22a}

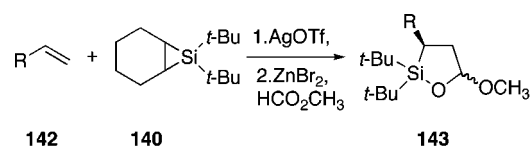
Silver-promoted silacyclopropanation of olefins circumvents the otherwise harsh conditions generally required for the preparation of silylene intermediates (R_2Si). Woerpel's group reported the stereospecific and diastereoselective *tert*-butylsilylene transfer to alkenes in the presence of catalytic amounts of AgOTf (Scheme 42).^{22a}

The reactions are generally carried out at low temperatures ($-30\text{ }^\circ\text{C}$) and require short reaction times. Aryl, benzyl, and silyl ether moieties present in the olefin substrates remained intact, indicating increased functional group tolerance. The

Scheme 42



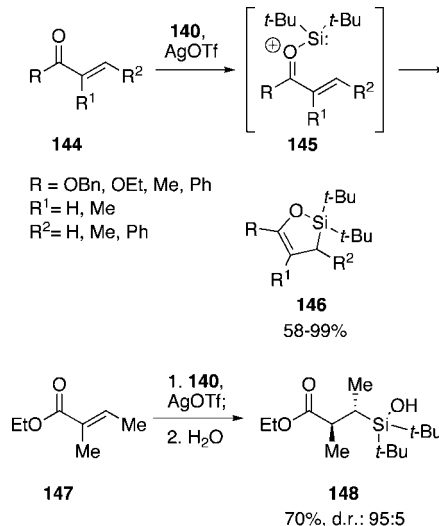
Scheme 43



R = Bu, *t*-Pr, *t*-Bu
 CH₂Ph,
 CH₂CH₂OTIPS

61-92%
 regioselectivity: 97:3→99:1
 d.r.: 70:30-91:9

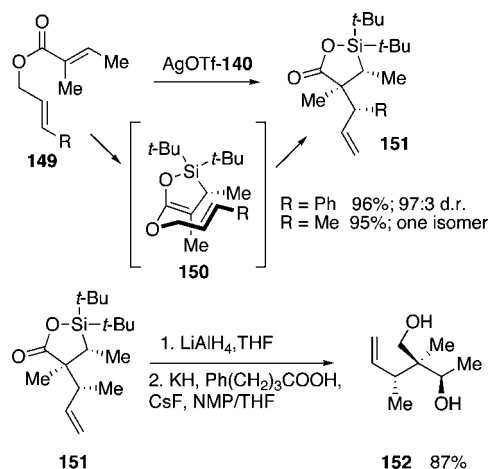
Scheme 44



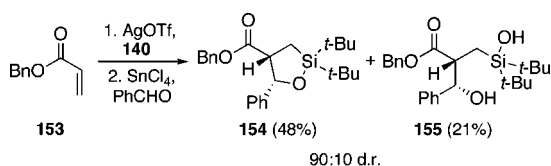
methodology was further extended to a diastereoselective synthesis of oxasilacyclopentanes when the silylene-transfer process is coupled with ZnBr₂-catalyzed methyl formate insertion (Scheme 43).^{22a} Both silacyclopropanes⁶³ **141** and oxasilacyclopentanes^{63,64} **143** are highly useful compounds that can be further modified in a stereoselective fashion to furnish enantioenriched polyol compounds.^{63,64} α,β -Unsaturated carbonyls undergo the silylene-transfer reaction under mild conditions to afford oxasilacyclopentenes **146** in good yields (Scheme 44).^{22c}

In this case, the carbonyl group exhibits increased reactivity over the alkene moiety, which is consistent with the electrophilic nature of the silver silylene species.^{22b} As suggested by the authors, the intermediacy of silacarbonyl

Scheme 45



Scheme 46



ylide **145** generated by nucleophilic attack of carbonyl group at the silver silylenoid intermediate is the most likely mechanism.^{22c} Due to their instability, oxasilacyclopentenes were not isolated but were hydrolyzed to the corresponding β -silyl ester products with high diastereoselectivity.

Oxacyclopentene **146** possesses an embedded silyl ketene acetal unit; hence, this transformation can serve as a facile approach to tetrasubstituted silyl ketene acetals. When ester **149** was subjected to the standard reaction conditions, silylene transfer occurred at the α,β -unsaturated ester moiety instead of at the terminal alkene (Scheme 45).

Oxasilacyclopentene intermediate **150** can achieve suitable geometry for Ireland–Claisen rearrangement to produce rearranged products with high diastereoselectivities. It is noteworthy that this transformation leads to the formation of three contiguous stereocenters, one being a quaternary stereocenter. Products of the rearrangement can be reduced and subjected to oxidative cleavage of the C–Si bond to produce 1,3-diols (**152**, Scheme 45).

A silyl ketene acetal functionality embedded in the cyclic product **146** (Scheme 44) can efficiently participate in Lewis acid catalyzed Mukaiyama–aldol reactions with remarkable diastereoselectivity (Scheme 46).

3. Conclusion

Although silver catalysts have been largely neglected by organic chemists until recently, the efficiency that they exhibit in various areas of organic synthesis is undeniable. Owing to their mild Lewis acidity and favorable redox potential, Ag-based catalysts will most likely be the first choice of reagent for many organic reactions. This review, hopefully, details the superiority of silver catalysts for various asymmetric transformations. Generally, short reaction times and mild conditions are required for highly efficient conversions. Other attractive features of the silver catalysts are experimentally simple procedures and the fact that intricate catalyst manipulating techniques are not needed.

The newly developed silver-catalyzed group-transfer reactions complement an array of transition-metal-promoted C–H

and C–C bond activation reactions that represent a state-of-the-art strategy for functionalization of otherwise unactivated molecules. Even though Ag-promoted group transfer reactions are generally not asymmetric, it was shown that they are stereoselective. Considering the potential of these reactions, endeavors to perform these transformations in a truly asymmetric manner will spur new developments in silver chemistry.

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