

1.1 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 catalytic reactions for fine chemicals. An organic chemist looking at properties of silver would perhaps be interested in parameters enlisted in chart 1.

Chart 1. Properties of Silver of Interest to an Organic Chemist

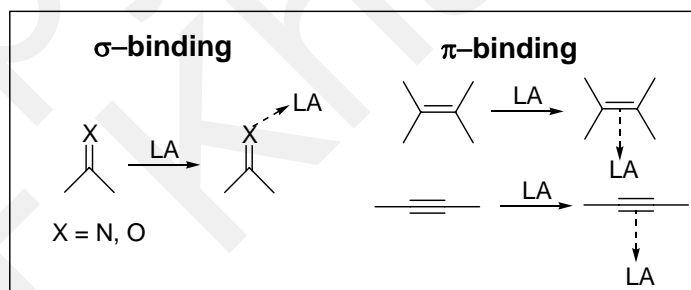
Oxidation State	I, II, III	Electronic Configuration	[Kr]4d ¹⁰ 5s ¹
Electronegativity	1.93 (Pauling Scale)	Hardness	2.5 Moh
Ionization Potential	1 st : 731.0 KJmol ⁻¹ 2 nd : 2070 KJmol ⁻¹ 3 rd : 3361 KJmol ⁻¹	Atomic Radius	144 pm

Silver exists as two isotopes, ¹⁰⁷Ag and ¹⁰⁹Ag, occurring in nearly equal natural abundance. It exhibits three formal oxidation states: Ag(I), Ag(II), and Ag(III). Recent research has recognized the highly reactive nature of the silver ion and its ability to form numerous inorganic and organic complexes (halide, sulfide, nitrate, oxide, and acetylide compounds, cyano-derivatives, olefin complexes, etc). Ag(II) complexes are less stable than those of Ag(I) and Ag(III). Ag(II) compounds are also brightly colored red or blue. Silver ion binds readily to proteins in the human body (including albumins and metallothioneins) and interacts with trace metals in metabolic pathways.

1.2 Ability of Ag(I) to bind σ and π center

Coinage metals are at the borderline between main group elements and transition metals due to their d^{10} electronic configuration. Distinct Lewis acid character of transition metals usually depends on their position in the Periodic Table. In the coinage metal series, silver and gold exhibit special properties due to the availability of the f orbitals and relativistic contraction of their electron cloud. As a result, both of them show marked Lewis acid character.² Metal mediated organic transformations are often preceded by substrate binding via σ - or π - mode. Relative ability of Lewis Acids to form σ - and π -complexes depends on the nature of metal. In general main group metal halide such as BCl_3 , $AlCl_3$, etc., are known to make strong σ -complexes with organic functionalities that make them versatile catalysts in Friedel-Crafts, Diels-Alder, and other electrophilic reactions. On the other hand, the transition metals salts can operate as bifunctional Lewis acids activating either (or both) carbon carbon multiple bonds via π -binding or (and) make the σ -complexes with heteroatom in the same fashion as the conventional Lewis acids (Scheme 1).³ Silver salts are also able to act as σ -Lewis acid and/or π -Lewis acid. There are suggestions from theoretical studies that σ -coordination of Ag(I) is slightly preferred over π -coordination and that this preference is higher for nitrogen than for oxygen Lewis bases.³

Scheme 1

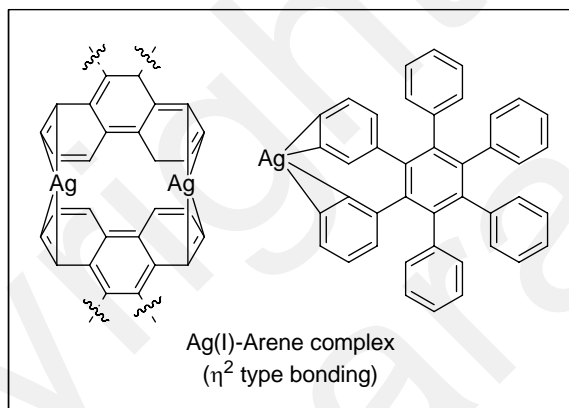


Silver has a single s -electron outside the completed d -shell resulting in weak crystal field and directional effects. Therefore, silver(I) ions can be regarded as extremely soft acids, favoring co-ordination to soft bases. The coordination complexes of silver with soft ligands show an interesting array of geometries and stereochemistry. Activation of functional groups, such as carbonyls, imines via σ -coordination with Lewis acids is a useful and important method to facilitate many different types of organic coupling

reaction.⁴ In recent years, alkene or alkyne activation with silver complexes has attracted keen interest of a number of organic chemists because the activation brings about important transformations, such as cyclization, cycloisomerization, cycloaddition.⁵

Cation- π interaction between metal and polycyclic hydrocarbon provide a powerful tool for building novel molecular architectures and allow the introduction of a wide variety of electrical and electrochemical properties.⁶ Due to the overall planarity of the molecules and the extended delocalized π -system, many polycyclic unsaturated hydrocarbons have been selected as potential donor molecules to design donor-acceptor materials both in the solid state and in solution. In general, for such type of complexes bearing Ag(I), the binding mode is η^2 -type (Scheme 2).⁷

Scheme 2



1.3 Silver NMR: Salient Feature

All naturally occurring silver is found in two isotopic forms: ^{107}Ag or ^{109}Ag , which are magnetically active. Relevant data for the NMR spectroscopist are found in Table 1.1. It is important to note that although the two isotopes have nearly equal natural abundances the receptivity of ^{109}Ag is about 1.4 times that of ^{107}Ag . Therefore, the former isotope is preferred in NMR experiments. Note that, with all other factors being constant the relative NMR receptivity of two spin-1/2 nuclei will depend on $A\gamma^3$, where A is the abundance of the isotope and γ is the gyromagnetic ratio for the isotope.⁸ The two most serious difficulties encountered when performing silver NMR experiments in solution or in the solid state are poor sensitivity and extremely long spin-lattice relaxation times. Both of these stem from the very low gyromagnetic ratios γ for ^{107}Ag and ^{109}Ag . Unless otherwise noted, all references to Ag-NMR made here are that of ^{109}Ag isotope.

Table 1.1 NMR Properties of the Magnetic Isotopes of Silver

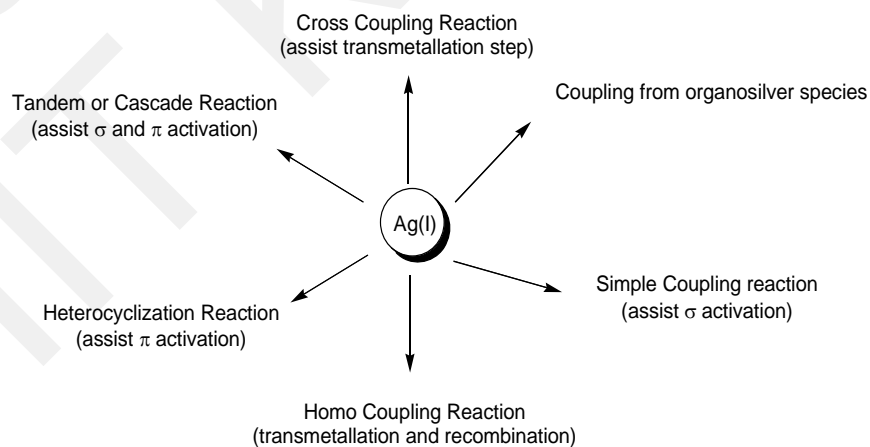
Isotope	Spin (I)	Natural Abundance (A)/%	Gyromagnetic Moment (γ)/radT ⁻¹ S ⁻¹	Frequency (ν_0) at 11.75 T/MHz	Relative Receptivity ^a
¹⁰⁷ Ag	1/2	51.82	-1.087x10 ⁷	20.24	0.197
¹⁰⁹ Ag	1/2	48.18	-1.250x10 ⁷	23.27	0.279

^aThe receptivity (unitless) given by $\gamma^3 AI(I + 1)$ relative to ¹³C

Reports of early silver NMR experiments are few and far between. This was primarily due to various limitations such as poor signal strength at low fields and long relaxation times. The introduction of polarization transfer techniques, which increase the silver NMR signal significantly and are limited only by the shorter T1 of the abundant nucleus, brought about more popularity of Ag-NMR in studying phenomenon in solutions. ¹⁰⁹Ag solid state NMR also gained popularity in recent years. This is due to the availability of spectrometers with high magnetic fields and ability to enable cross-polarization.

1.4 Organic Reactivity of Ag(I)

In organic chemistry the reactivity of Ag(I) arises due to its capability (i) to activate both σ - and π - center (ii) to abstract halide from organometallic intermediates, rendering the metal more electropositive and creating a vacant site in the coordination sphere (iii) to generate organosilver species *in situ* which can either act as a nucleophile or participate in transmetallation step. Various types of reactions assisted by Ag(I) are shown in chart 2.

Chart 2

In cross-coupling reactions, silver salts abstract halides from organometallic intermediates, rendering the metal more electropositive and opening a vacant site in the coordination sphere enabling subsequent steps. With starting materials such as alkynes, silver salts produce organosilver species. These species alone can show nucleophilic reactivity, for example in the reaction with activated carbonyl and iminium group.⁹ They can also participate in transmetallation for example towards the generation of organopalladium intermediates.¹⁰ Silver-catalyzed alkyl-alkyl homocoupling proceeds through a transmetallation followed by recombination steps.¹¹ Simple coupling reactions are controlled by σ -activation of the starting material. Silver-catalyzed intra- or intermolecular heterocyclizations and tandem or cascade reaction provide efficient access to a variety of *O*- and *N*-heterocycles.¹²

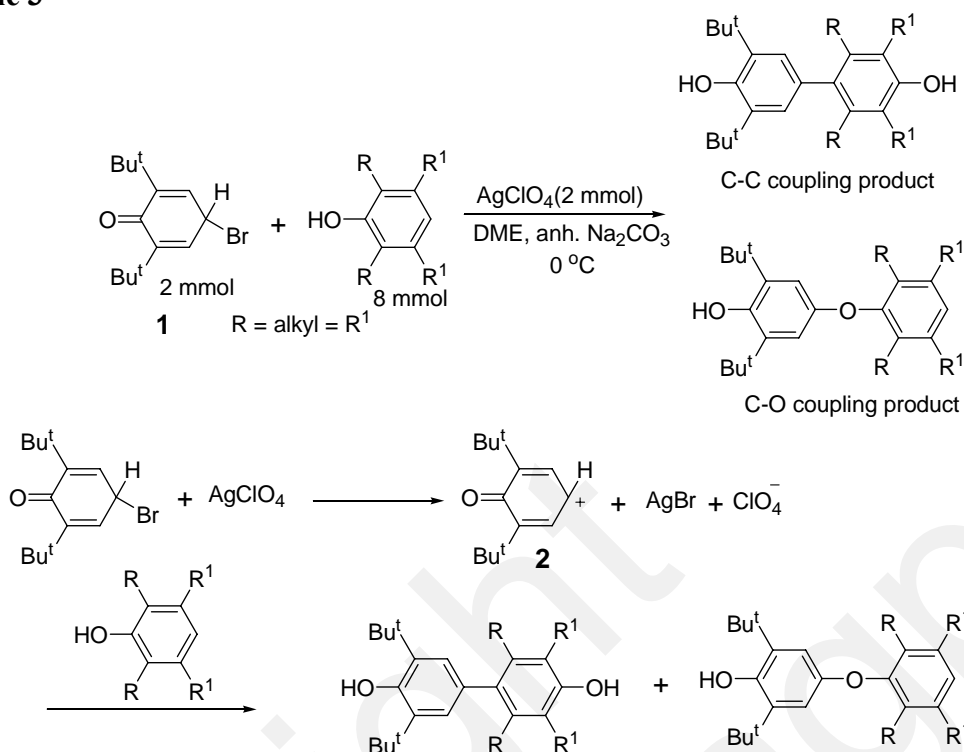
1.5 Coupling Reactions via Ag(I)

In organic chemistry, a large variety of metal mediated C-C bond forming reactions belong to the class of formal nucleophilic substitution.¹³ Among the metals, palladium has proven to be highly versatile.¹⁴ In the coinage metal series, silver has shown to be effective as a catalyst or co-catalyst in various cross coupling reaction. In literature C-C bond formation via transmetallation involving silver and Pd, Au, Rh, Ru etc is well discussed.¹⁵ In this section we will limit our discussion to only silver catalyzed coupling reactions.

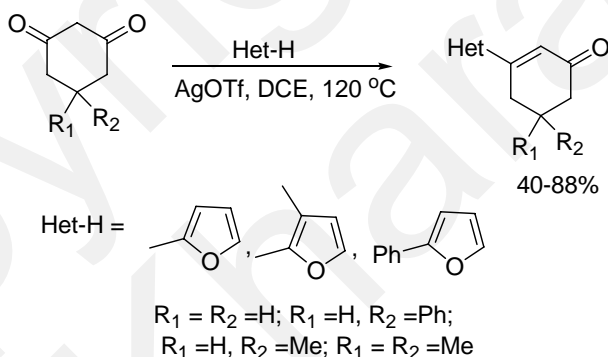
Omura showed that silver ion promotes the nucleophilic substitution of 4-bromo-2,6-di-*tert*-butylcyclohexa-2,5-dienone **1** with phenolic nucleophiles.¹⁶ Thus compound **1** react with substituted phenols in presence of AgClO₄ (1 molar equiv.) at 0 °C to afford both C-C and C-O coupling product (Scheme 3). The phenolic nucleophiles chosen were mainly alkyl-substituted ones. The reaction proceeds through carbocation **2**.

Silver-catalyzed reaction of 2-substituted furan with cyclic 1,3-diketones provides convenient access to 2-alkenyl furans (Scheme 4).¹⁷ It is reasonable to assume that activation of the carbonyl group by silver ion, follows a Friedel-Crafts-type reaction leading to the formation of the product.

Scheme 3



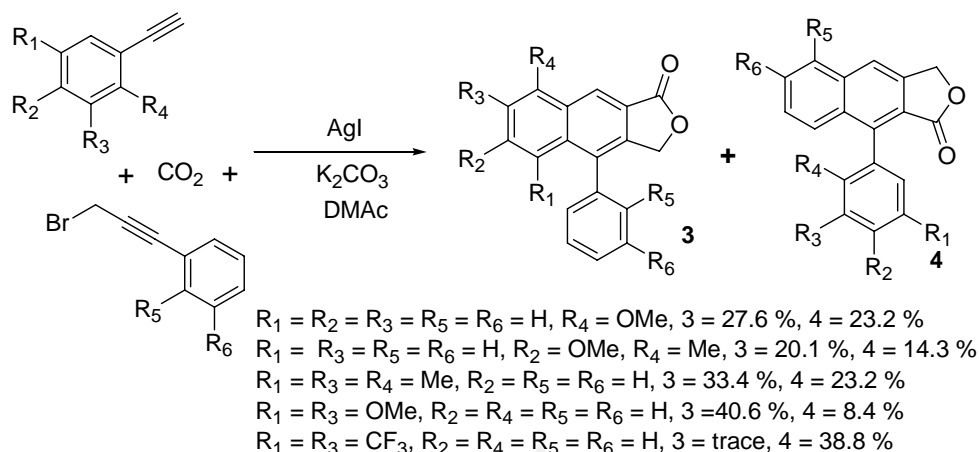
Scheme 4



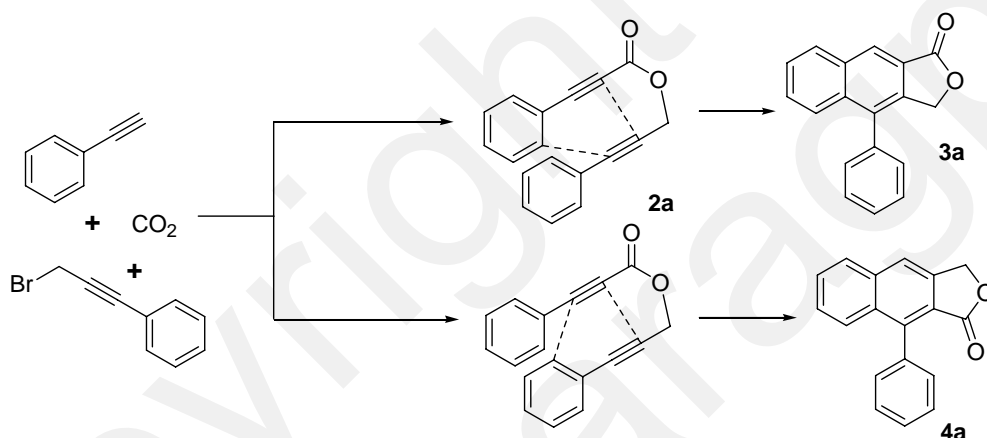
1.5.1 Multicomponent Coupling

Arylnaphthalene lignan lactones are valuable natural products with promising anticancer and antiviral properties, and are synthesized in a one-pot multicomponent coupling reaction involving substituted phenylacetylene, carbon dioxide, and 3-bromo-1-phenyl-1-propyne (Scheme 5).¹⁸ The reaction proceeds via the intermediacy of 1,6-diyne **2a** that cyclizes to naphthalene core **3a** and **4a** through a [2+2+2] cycloaddition (Scheme 6).

Scheme 5



Scheme 6

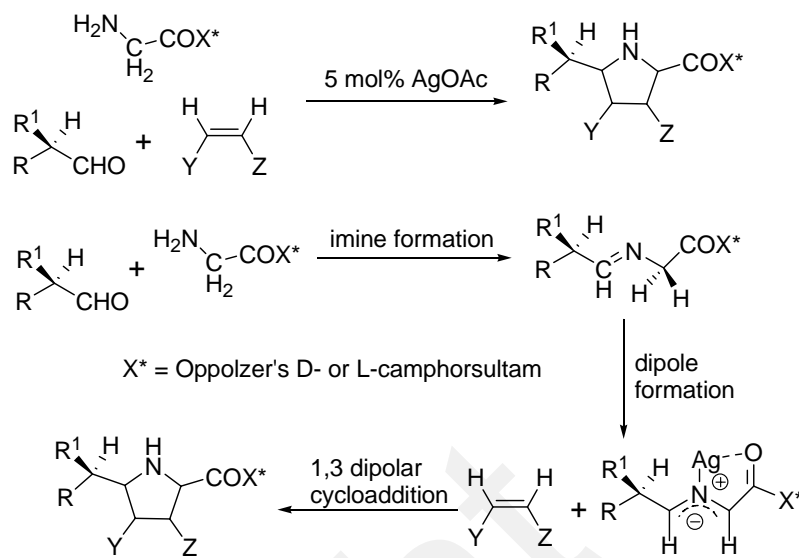


Highly functionalized pyrrolidines are obtained in a single step via an efficient and selective Ag(I)-catalyzed asymmetric [C+NC+CC] coupling process. The reaction follows a three-component cascade involving imine \rightarrow azomethine ylide \rightarrow 1,3-dipolar cycloaddition sequence (Scheme 7).¹⁹

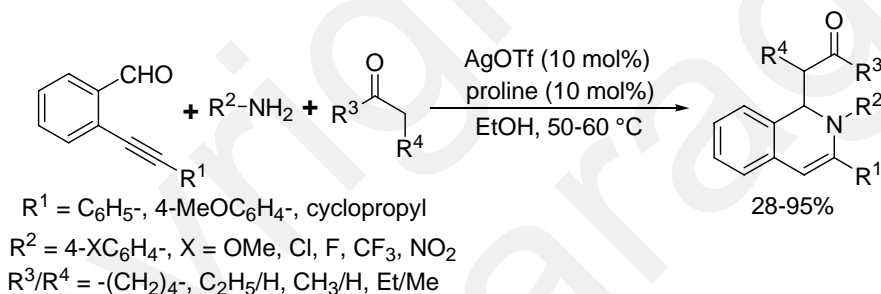
A novel and highly effective one-pot combination of AgOTf and proline catalysis was reported for the synthesis of 1,2-dihydroisoquinoline derivatives via multicomponent reaction of 2-alkynylbenzaldehyde, amine, and ketone (Scheme 8).²⁰ The optimized reaction condition requires AgOTf (10 mol %), proline (10 mol %) in EtOH at 50-60 °C.

The multicomponent reaction between amine, aldehyde, and isocyanide bearing an acidic α -proton gives easy access to a diverse range of highly substituted 2-imidazolines (Scheme 9).²¹

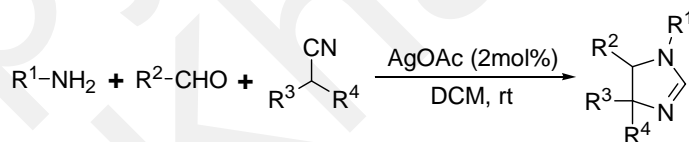
Scheme 7



Scheme 8



Scheme 9

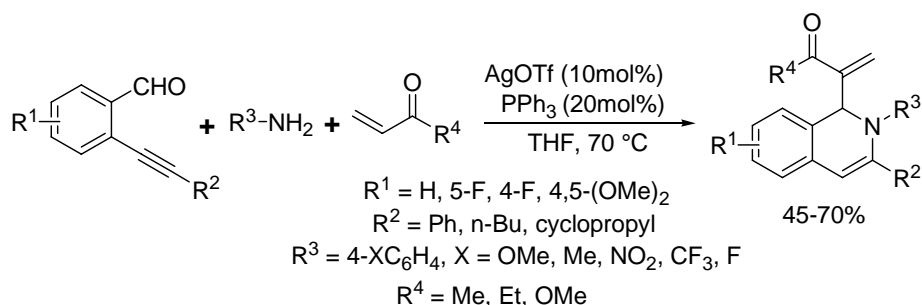


A two-component activation system combining catalytic AgOTf and PPh₃ has been employed in the three-component reaction involving 2-alkynylbenzaldehyde, amine, and α,β -unsaturated ketone (Scheme 10).²² The reaction involves mild conditions leading to the functionalized 1,2-dihydroisoquinolines in moderate to good yields.

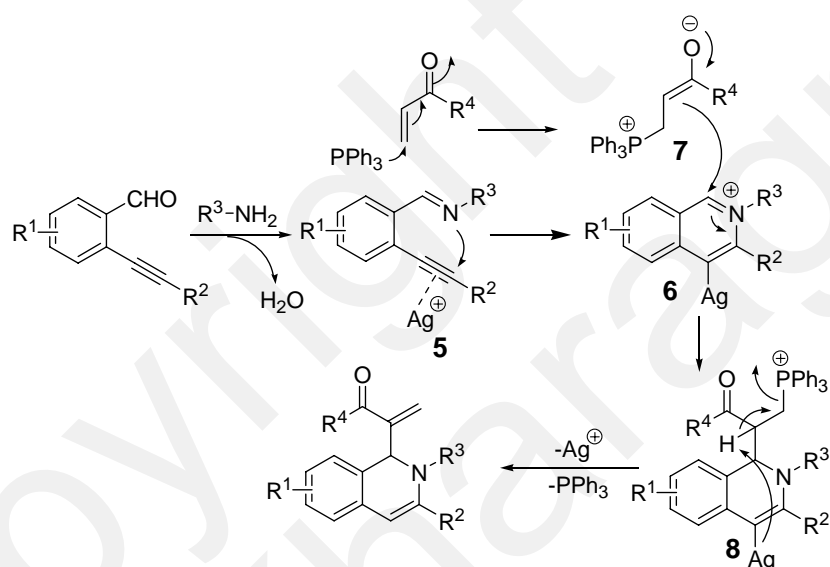
The reaction course proposed by the author involves prior activation of the triple bond by AgOTf. Thereafter the nitrogen atom of imine **5** could attack the triple bond leading to 6-*endo*-cyclization affording the isoquinolinium intermediate **6**. An activation of α,β -unsaturated ketone by triphenylphosphine is envisaged leading to the enolate **7**. The latter can intermolecularly attack the isoquinolinium intermediate **6** to generate

phosphonium **8**. Finally, elimination of phosphine leads to the desired product (Scheme 11).

Scheme 10



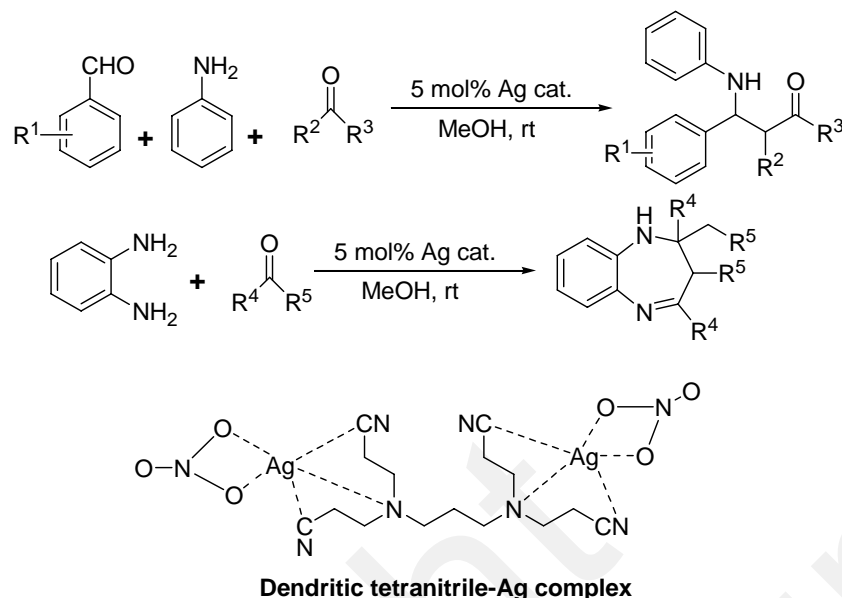
Scheme 11



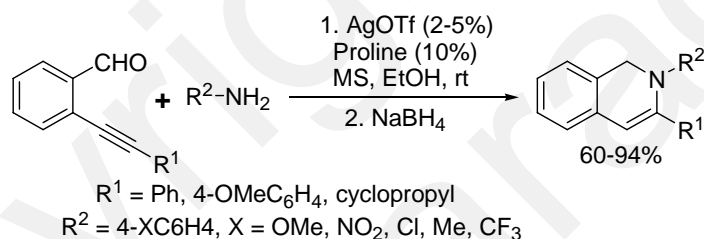
A dendritic tetranitrile-Ag complex was used as a homogeneous catalyst for (i) one-pot three component Mannich reaction between aromatic aldehyde, aniline and ketone, (ii) the synthesis benzodiazepine derivatives from *o*-phenylene diamine and various ketones (Scheme 12).²³

Under the catalytic influence of AgOTf, one-pot reaction of 2-alkynylbenzaldehyde, amine, and sodium borohydride provides 1,2-dihydroisoquinoline derivatives (Scheme 13).²⁴ The reaction proceeds smoothly with a set of substrates using AgOTf (2–5 mol %), proline (10 mol %), and 4A° MS in ethanol as solvent.

Scheme 12



Scheme 13

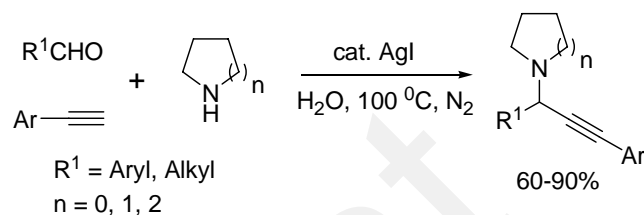


1.5.2 Coupling through Silver Acetylide Intermediate

Silver acetylides, or alkynyl silvers are among the early examples of organometallic compounds. For example 3-ethoxy-prop-1-ynyl silver and phenylethyne silver were reported as early as 1865 and 1870 respectively.^{25,26} However these organometallics were only sparingly applied to organic chemistry. The reaction of isolated silver acetylides with nucleophiles have been hardly developed.²⁷ One example of such silver catalysis is the Mannich-type three-component coupling of aldehydes, amines, and terminal alkynes, leading to propargyl amines.²⁸ Because of the importance of the resulting propargyl amine derivatives, catalytic aldehyde-alkyne-amine couplings (A³-couplings) have been extensively studied recently, and efficient methods have been developed using catalysts based on transition-metal elements including Cu, Ru-Cu, Ir, and Au.²⁹

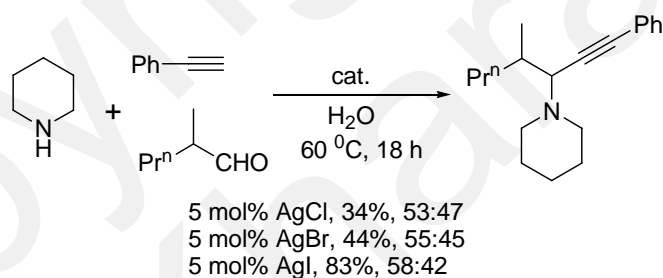
In 2003, Li and co-workers reported the first silver-catalyzed A³-coupling (Scheme 14).³⁰ While AgNO₃, Ag₂O, AgOAc, Ag₂SO₄, AgOTf, and AgBF₄ showed low conversion (25-45%) together with the formation of some carboxylic acid, however, AgCl, AgBr, and AgI showed good results, and AgI was found to be the most effective catalyst. No other additive was needed for this reaction. Noticeably, either in absence of AgI or in presence of oxygen, the reaction fails.

Scheme 14



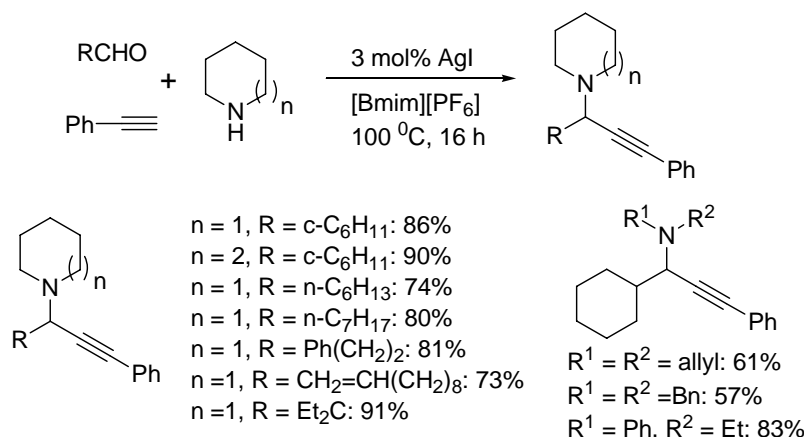
The Ag(I)-catalyzed three-component coupling of α -alkylaldehyde, alkyne, and amine was investigated in water. AgI showed high efficiency and propargylamines are obtained in good yields with low diastereoselectivity (Scheme 15).³¹

Scheme 15



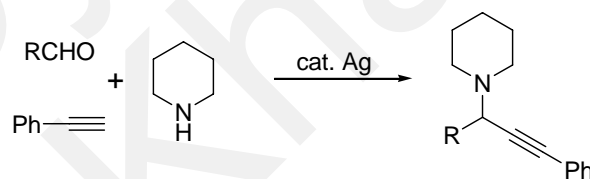
Li and coworkers also executed A³-coupling in ionic liquids. The reactions with aliphatic aldehydes gave promising results in [Bmim][PF₆] or [Bmim][BF₄] (Scheme 16),³² whereas aromatic aldehydes led to a complex mixture. In addition to cyclic secondary amines, acyclic derivatives were able to undergo A³-coupling to give coupling products albeit in lower yields. Facile coupling of cyclohexyl carboxaldehyde, piperidine, and triethylsilylacetylene indicated the superiority of ionic liquid over water as solvent. Other dialkyl or alkyl aryl amines also reacted smoothly.

Scheme 16



Since the first report by Li et al., A^3 -coupling has been examined with other silver promoters such as $[\text{Ag}(\text{MeCN})_4][\text{B}(\text{C}_6\text{F}_5)_4]$,^{33a} Ag-NaY zeolite,^{33b} Ag nanoparticles in PEG (400 Da),^{33c} Ag-salt of 12-tungstophosphoric acid (AgTPA),^{33d} and AgNO_3 under microwave irradiation (MWI).^{33e} Scheme 17 summarizes the results obtained for the typical A^3 -coupling reactions. Heterogeneous catalysts, Ag-NaY zeolite, Ag nanoparticles in PEG, and AgTPA could be recycled at least three times. The reactions employing Ag-NaY zeolite and AgNO_3 under MWI were carried out without the solvent. In the latter case, both significant increase in the yield and shorter reaction time were realized as compared to the conventional heating.

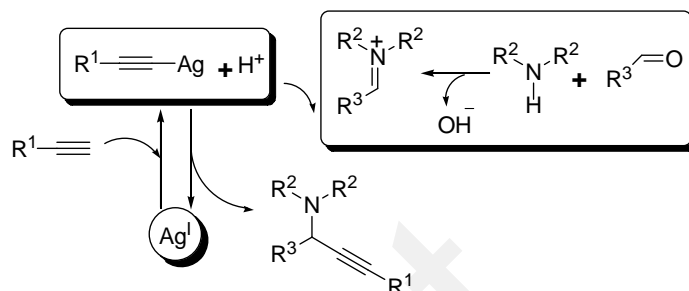
Scheme 17



Catalyst System (%)	Conditions	Yields (%)	Reference
$[\text{Ag}(\text{MeCN})_4][\text{B}(\text{C}_6\text{F}_5)_4]$ (3 %)	PhMe, 75 °C R = Ph, R = Cyclohexyl	96, 98	33a
Ag-NaY zeolite (5 %)	100 °C, 15 h R = Ph, R = n-hexyl	81, 71	33b
Ag nanoparticles, PEG (2 %)	100 °C, 20 h, R = Ph R = Cyclohexyl, 10 h	77, 95	33c
AgTPA	MeCN, 80 °C R = Ph, 6 h; R = cyclohexyl, 3 h	98, 93	33d
AgNO_3 (5 %)	105 °C, MWI, 10 min, R = Ph	90	33e

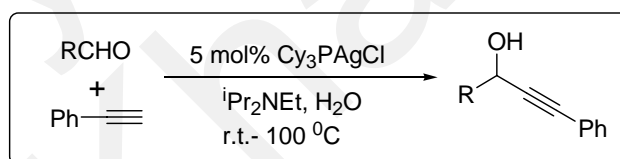
A mechanism of A^3 -coupling was proposed involving the exchange of H of the C-H bond of alkyne by a Ag(I) species. The silver acetylide intermediate reacts with the iminium ion (generated in situ from aldehyde and amine) to give the corresponding propargylamine and regenerating the Ag(I) catalyst (Scheme 18).

Scheme 18

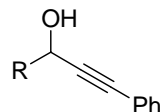
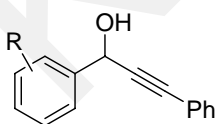


Silver acetylides are long known to form insoluble coordination polymers in which each alkyne moiety is σ -bonded to one silver atom and π -bonded to the other.³⁴ The polymeric nature reduces their reactivity toward electrophiles. It is postulated that the addition of tertiary phosphines enables depolymerization of silver acetylides leading to soluble monomeric species.³⁵ Yao and Li showed that the addition of phenyl acetylene to aldehydes proceeded smoothly when tricyclohexylphosphine is used as ligand to the silver salt (Scheme 19).³⁶

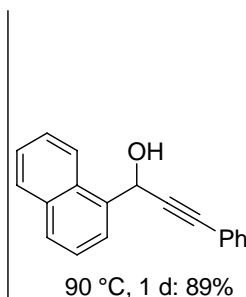
Scheme 19



R = H, 70 °C, 1 d: 69%
 α -Cl, 60 °C, 12 h: 98%
 m -Cl, 60 °C, 12 h: 86%
 p -Cl, 80 °C, 12 h: 85%
 α -F, 100 °C, 12 h: 87%; p -F, 100 °C, 6 h: 79%
 α -Br, 60 °C, 12 h: 90%; p -Br, 90 °C, 12 h: 82%
 α -CF₃, 80 °C, 6 h: 93%; p -CF₃, r.t., 2 d: 64%
 α, m -(OMe)₂, 90 °C, 12 h: 82%; α -Me, 90 °C, 1 d: 80%
 α -OMe, 90 °C, 1 d: 87%; p -OHCH₂, 80 °C, 1.5 d: 73%



R = H, 60 °C, 12 h: 74%
ⁿBu, 100 °C, 12 h: 63%
 c -C₆H₁₁, 70 °C, 2 d: 81%
 E -PhCH=CH, 70 °C, 1 d: 35%



The following conclusions are noteworthy: (a) by changing the counter anion on Ag(I) from chloride or fluoride lowers the yield, while noncoordinating anion (such as -OTf) inhibits the reaction; (b) electron donating P-ligands favors the reaction, and the combination of Cy₃PAgCl with 0.2 equiv of *i*-Pr₂NEt in water gave the best result; (c) aromatic aldehydes are more suited for the reaction than aliphatic aldehyde. A few of the control experiments to show the necessity of phosphine as ligand, water as solvent, and amine as additive in the reaction is highlighted in Scheme 20, Table 1.2.

Scheme 20

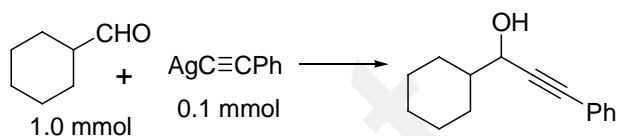


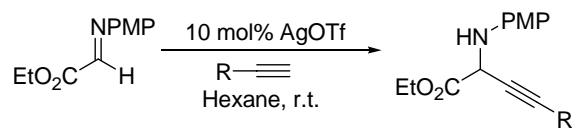
Table 1.2

Entry	Condition	Product ^a
1	Water, 95°C, overnight	No reaction
2	Toluene, 95°C, overnight	No reaction
3	0.11 mmol Pcy ₃ , water, 35°C, overnight	68%
4	0.11 mmol Pcy ₃ , toluene, 35°C, overnight	Trace
5	0.11 mmol Pcy ₃ , 1.5 mmol phenyl acetylene, 2 mL H ₂ O, 95°C, overnight	86%
6	0.11 mmol Pcy ₃ , 1.5 mmol phenyl acetylene, 0.2 mmol <i>i</i> -Pr ₂ NEt, 2 mL H ₂ O, 95°C, overnight	32%

^aYield with respect to silver acetylide

Chan and co-workers synthesized β,γ-alkynyl-α-amino acid derivatives by direct addition of terminal alkynes to α-imino esters in the presence of catalytic Ag(I) salt under mild conditions (Scheme 21).³⁷ In the presence of 10 mol% AgOTf, several terminal alkynes were added to 4-methoxyphenyl-protected α-iminoester at room temperature, resulting in the formation of alkynylglycinates in good yields.

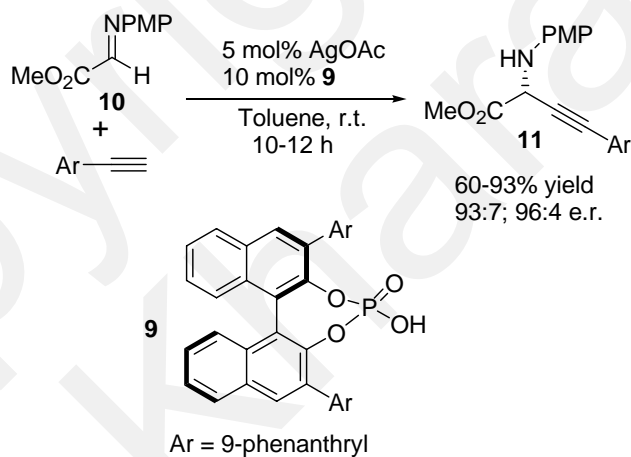
Scheme 21



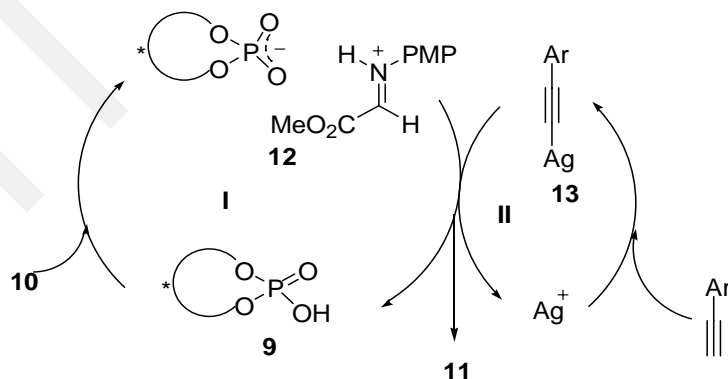
R = Ph, 0.5 h: 93%; PhCH₂CH₂, 0.5 h: 87%;
ⁿBu, 0.5 h: 84%; ⁿC₆H₁₃, 0.5 h: 91%; TMSCH₂, 1 h: 79%

The method was extended to an asymmetric version by Rueping and co-workers (Scheme 22).³⁸ They used chiral Brønsted acid **9** together with a silver salt, AgOAc, to realize the nonracemic synthesis of base-labile alkynylglycinates **11** with excellent enantioselectivity (*ee* 92-94%). The mechanism proposed invokes two catalytic cycles operating in tandem (cycle I and II) in which the activation of the electrophile **10** by a chiral Brønsted acid catalyst **6** and the activation of the alkyne by silver (I) proceed simultaneously (Scheme 23). The above sequence leads to the formation of an intermediary chiral ion pair **12** and an achiral metal complex **13**, which give the desired amino acid **11** and regenerates the catalysts.

Scheme 22

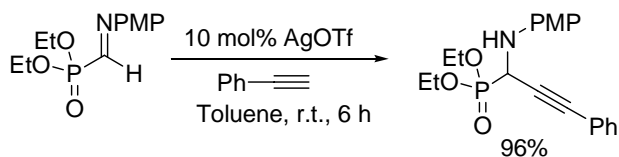


Scheme 23



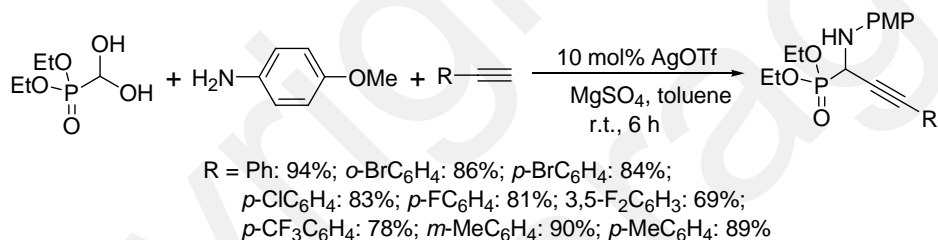
Similarly, AgOTf catalyzed addition of phenyl acetylene to (*R*)-iminophosphonate in toluene at room temperature gives α -amino propargyl phosphonate in 96% yield (Scheme 24). Note that α -amino phosphonate is a mimic of the corresponding glycinate.

Scheme 24



Dodda and Zhao further developed the three component coupling of α -formyl phosphonatehydrate, 4-anisidine, and terminal alkynes as shown in Scheme 25.³⁹ The reaction effectively proceeds under ambient condition with aromatic and aliphatic alkynes and in the presence of silver(I) catalyst and MgSO₄ (to quench water), giving rise to the desired α -aminopropargyl phosphonates in 55-94% yields.

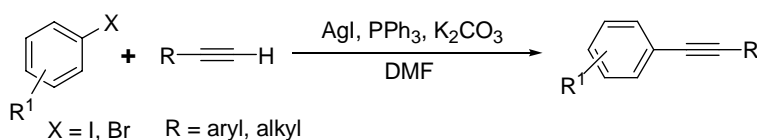
Scheme 25



In 2006 Wang et al. demonstrated the silver(I) catalyzed Sonogashira coupling (Scheme 26).⁴⁰ The protocol uses silver iodide (10 mol %), triphenylphosphine and potassium carbonate, and the cross-coupling products are obtained in good to excellent yields. Studies on the influence of ligands in the catalysis confirmed the superiority of phosphorous over nitrogen ligands. Amongst all ligands, PPh₃ gave the better response.

Krische et al. reported Ag(I)-catalyzed formal alkyne-carbonyl metathesis. Under the influence of 10 mol% AgSbF₆, alkynes and aldehydes undergo intra- and intermolecular alkyne-carbonyl coupling to provide tri substituted enones (Scheme 27).⁴¹ The reaction accommodates aliphatic and aromatic aldehyde and substituted alkynes.

Scheme 26



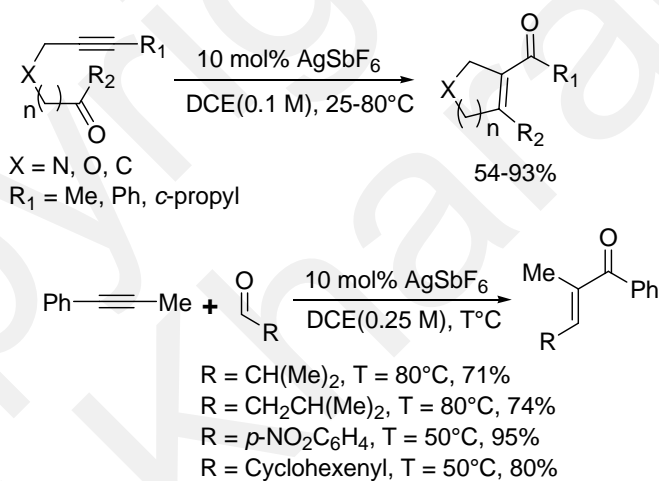
X = I

R = Ph, R ¹ = <i>p</i> -OMe, 92%	R = Ph, R ¹ = <i>m</i> -CN, 91%
R = Ph, R ¹ = <i>p</i> -Me, 93%	R = <i>p</i> -MeC ₆ H ₄ , R ¹ = Ph, 96%
R = Ph, R ¹ = H, 95%	R = <i>p</i> -C ₆ H ₅ C ₆ H ₄ , R ¹ = Ph, 94%
R = Ph, R ¹ = <i>p</i> -NO ₂ , 99%	R = <i>p</i> -FC ₆ H ₄ , R ¹ = Ph, 98%
R = Ph, R ¹ = <i>p</i> -COMe, 94%	R = <i>p</i> -BrC ₆ H ₄ , R ¹ = Ph, 95%
R = Ph, R ¹ = <i>p</i> -CF ₃ , 99%	R = <i>n</i> -C ₈ H ₁₇ , R ¹ = Ph, 80%
R = Ph, R ¹ = <i>m</i> -NO ₂ , 80%	R = <i>n</i> -C ₆ H ₁₃ , R ¹ = Ph, 83%
R = Ph, R ¹ = <i>o</i> -CF ₃ , 73%	

X = Br

R = Ph, R ¹ = <i>p</i> -CNC ₆ H ₄ , 92%
R = Ph, R ¹ = <i>p</i> -NO ₂ C ₆ H ₄ , 95%
R = Ph, R ¹ = <i>p</i> -COMeC ₆ H ₄ , 85%
R = Ph, R ¹ = <i>p</i> -MeC ₆ H ₄ , 62%

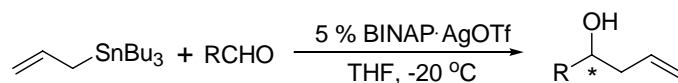
Scheme 27



1.5.3 Enantioselective Coupling Reaction

Enantioselective allylation of carbonyl compounds continues to be important in organic synthesis. Yamamoto and co-workers employed chiral phosphine-silver(I) complexes for asymmetric allylation of aldehydes with allylstannanes (Scheme 28).⁴² The reaction yields good to excellent enantioselectivity.

Scheme 28



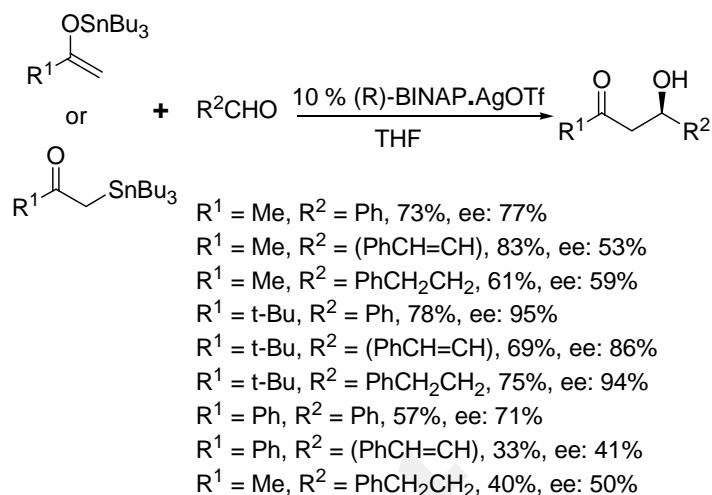
R = Ph: 88%, ee: 96%(S)
 (E)-PhCH=CH: 83%, ee:88%
 1-naphthyl: 89%, ee: 97%
 2-furan: 94% ee: 93%
 (E)-n-C₃H₇CH=CH: 72%, ee: 93%
 o-C₆H₄Me: 85%, ee: 97%
 p-C₆H₄OMe: 59%, ee: 97%
 p-C₆H₄Br: 95%, ee:96%

It is proposed that the BINAP-Ag(I) complex possibly acts as a chiral Lewis acid in the present reaction. The following observations are suggestive of this view. (*S*)-BINAP-AgOTf complex was treated with an equimolar amount of allyltributyltin in THF at 20 °C, and one half of the reaction mixture was quenched with brine (case-A); while the other half of the mixture was reacted with 1 equiv of benzaldehyde at -20 °C for 8 h followed by work-up (case-B). Noticeably in case-A, 98% of the allyltributyltin remained unreacted. On the other hand in case-B, the allylation proceeded leading to the corresponding (*S*)-homoallylic alcohol in 35% yield with >99% ee. This result shows that the allylation does not proceed via a transmetalation pathway.

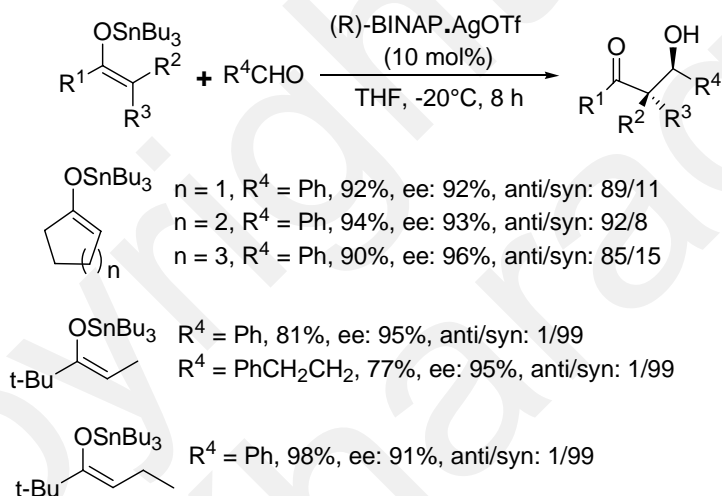
The BINAP-AgOTf complex is proved to be a good catalyst in enantioselective aldol addition of tributyltin enolates to aldehydes (Scheme 29).⁴³ The tributyltin enolate is easily prepared from the corresponding enol acetate and tributyltin methoxide in the absence of solvent. The tin enolate thus obtained exists in O-Sn form and/or C-Sn form; however, both species can be used for the aldol reaction in the present system. The reaction accommodates aromatic, α,β -unsaturated, and aliphatic aldehydes. The chiral silver(I) catalyst also promotes excellent diastereoselectivity in the aldol reaction (Scheme 30).⁴⁴

Cyclic transition state **A** and **B** (Scheme 31) are invoked to explain the diastereoselection. Thus, from the (*E*)-enolate the *anti*-aldol product can be obtained via the transition state **A**, while transition state **B** connects the (*Z*)-enolate to the *syn*- product.

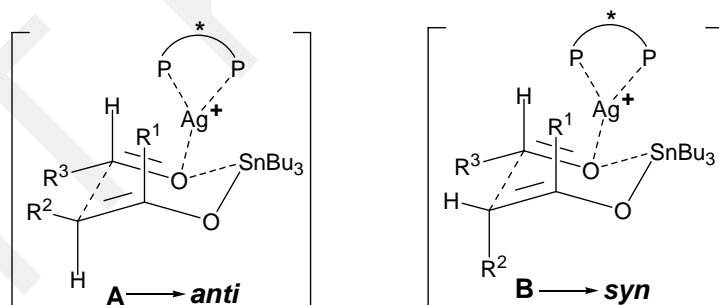
Scheme 29



Scheme 30



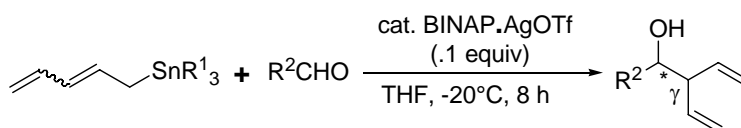
Scheme 31



The chiral BINAP-AgOTf catalyst has been found to be equally successful in mediating the coupling of (*E*)-2,4-pentadienyltributyltins and trimethyltins with various

aromatic and aliphatic aldehyde to afford the corresponding γ -pentadienylated alcohols with high enantioselectivity (Scheme 32).⁴⁵

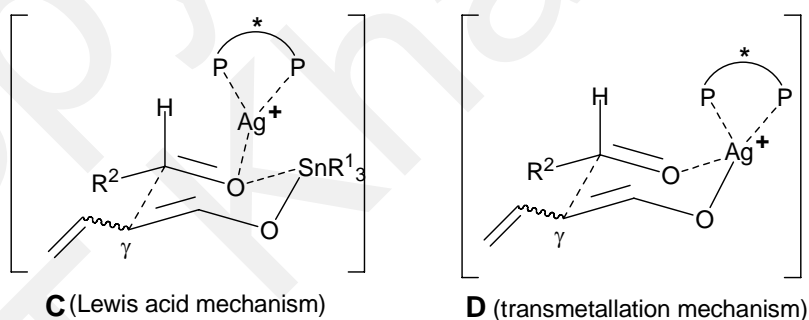
Scheme 32



- R¹ = Bu, R² = Ph, 61%, ee: 90%
- R¹ = Me, R² = Ph, 68%, ee: 89%
- R¹ = Me, R² = *o*-Me-C₆H₄, 57%, ee: 90%
- R¹ = Me, R² = *p*-Me-C₆H₄, 41%, ee: 87%
- R¹ = Me, R² = 2-furyl, 62%, ee: 89%
- R¹ = Bu, R² = (E)-PhCH=CH, 73%, ee: 58%
- R¹ = Me, R² = (E)-PhCH=CH, 68%, ee: 58%
- R¹ = Me, R² = (E)-MeCH=CH, 65%, ee: 62%
- R¹ = Bu, R² = 1-cyclohexenyl, 13%, ee: 90%
- R¹ = Bu, R² = PhCH₂CH₂, 52%, ee: 71%
- R¹ = Bu, R² = PhCOCH₃, 1%,

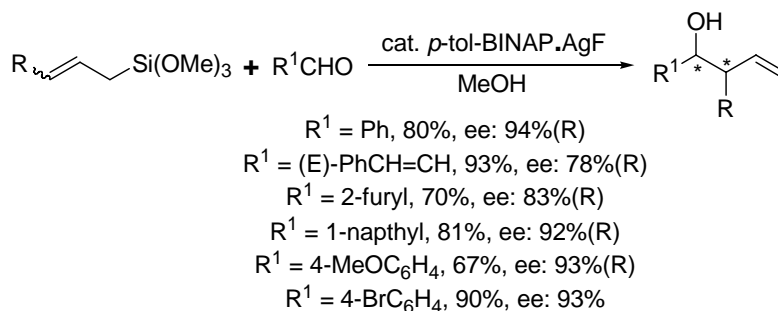
Author proposed a cyclic transition state for γ -adduct. Two plausible models are shown in Scheme 33. If the BINAP-Ag complex acts as Lewis acid, the reaction should go through a six membered cyclic model **C**. In contrast, a similar cyclic transition state model **D** containing a BINAP coordinated silver atom instead of trialkylstannyl group is a probable alternative when the transmetalation to pentadienylsilver occurs rapidly.

Scheme 33



Enantioselective addition of allyltrimethoxy silane to aldehyde is catalyzed by *p*-tolyl-BINAP-AgF complex (Scheme 34).⁴⁶ The general experimental condition is as follows: allyltrimethoxysilane (1.5 equiv), aldehyde (1 equiv), (*R*)-*p*-tol-BINAP (6 mol %) and AgF (10 mol %) in MeOH at -20°C, 4 h. The homoallylic alcohols are obtained in good yield and in high enantioselectivity.

Scheme 34



Chiral (*S*)-BINAP.AgPF₆ promotes asymmetric Mukaiyama Aldol reaction in polar solvents leading to fairly high enantioselectivity in the aldol product (Scheme 35).⁴⁷ It has been observed that using the same chiral ligand, but varying the counter anion one can reverse the absolute configuration in the end product. For example, the absolute configuration of the product in case of (*S*)-BINAP.AgPF₆ as catalyst is opposite to that of the product obtained using (*S*)-BINAP.AgOAc as the catalyst. The differences in reactivity between the two catalysts are summarized in Table 1.3 and 1.4.

Scheme 35

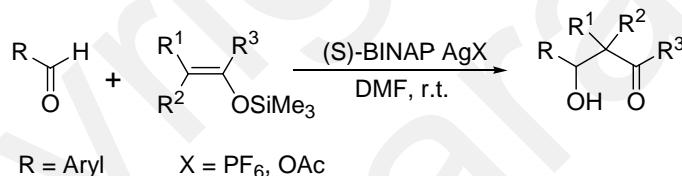
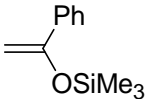
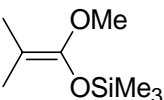


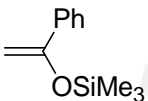
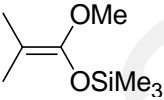
Table 1.3 Mukaiyama Aldol Reaction with (*S*)-BINAP.AgPF₆ Catalyst^a (Here S/C/Nu ratio is Substrate/Catalyst/Nucleophile)

Entry	Aldehydes	Nucleophiles	Time (h)	Yield (%)	e.e (%)
1	PhCHO		2	100	69 (<i>S</i>)
2 ^b	„	„	96	36	80 (<i>S</i>)
3	1-NpCHO	„	2	82	54 (–)
4	2-NpCHO	„	2	100	58 (–)
5	CyCHO	„	24	83	47 (–)

6	PhCHO		24	0
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^asolvent, DMF; temperature, 25°C;
S/C/Nu = 50/1/100. ^bThe reaction performed at -30°C.

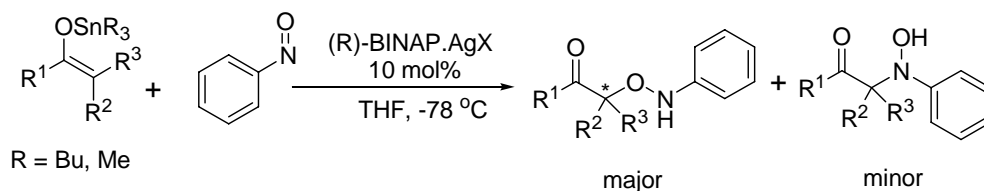
Table 1.4 Mukaiyama aldol reaction with (*S*)-BINAP.AgOAc catalyst^a

Entry	Aldehydes	Nucleophiles	Time	Yield (%)	e.e (%)
1	PhCHO		5 min	100	11(R)
2 ^b	„	„	72 h	100	11(R)
3	1-NpCHO	„	5 min	100	17 (+)
4	2-NpCHO	„	5 min	83	15 (+)
5	2-NpCHO	„	1 h	100	15 (+)
6	CyCHO	„	4 h	100	6 (+)
7	PhCHO		5 min	100	0

^asolvent, DMF; temperature, 25°C;
S/C/Nu = 50/1/100. ^bThe reaction performed at -30°C.

Chiral Ag(I)-BINAP complex also catalyzes the introduction of an oxy group at the α -position of ketone enolates using nitrosobenzene (Scheme 36).⁴⁸ Reaction of nitrosobenzene and tin enolate provided amino oxyketone as the major product with hydroxyl aminoketone in trace. Amidst various silver salts (*R*)-BINAP.AgOTf furnished the amino oxyketone in high enantiometric excess and with high *O*-selectivity.

Scheme 36



AgOTf, 88%, 19/20: 99/1, ee: 99%(19)
 AgClO₄, 95%, 19/20: 99/1, ee: 95%(19)
 AgBF₄, 64%, 19/20: 99/1, ee: 54%(19)
 AgNTf₂, 78%, 19/20: 88/12, ee: 63%(19)
 AgSbF₆, 85%, 19/20: 81/19, ee: 87%(19)
 AgPF₆, 86%, 19/20: 80/10, ee: 76%(19)
 AgOAc, 82% 19/20: 72/28, ee: 87%(19), 23%(20)

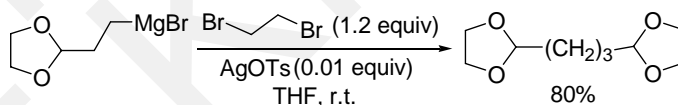
1.5.4 Homo Coupling Reaction

The earliest coupling reactions involving silver salts could be traced back to the studies of Wurtz-type coupling of Grignard reagents in the presence of various metal salts.⁴⁹ These studies revealed that silver salts are capable of catalyzing alkyl-alkyl homocoupling of Grignard reagents, and that they do so by transmetalation and then recombination (Scheme 37). An example of the synthesis of 1,3-dioxolane derivatives via AgOTs catalyzed homocoupling of Grignard reagent with 1,2-dibromoethane as a reoxidant is shown in Scheme 38.⁵⁰

Scheme 37

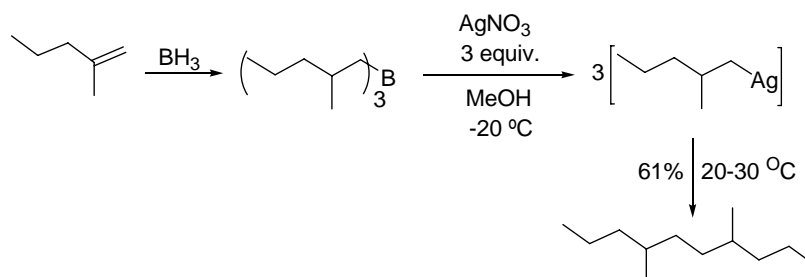


Scheme 38



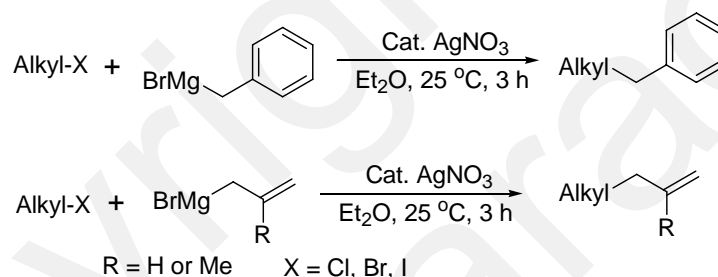
In related studies, Brown et al. showed that alkylboranes, obtained from hydroboration of the corresponding alkenes, could be transmetalated to silver salts provided that hydroxide was added. The so-formed alkyl silver seemed to be stable at low temperature, but at room temperature they gave the homocoupling product (Scheme 39).⁵¹

Scheme 39



Recently Oshima et al. reported that treatment of alkyl halides, including tertiary alkyl bromides, with benzylic or allylic magnesium reagent in the presence of a catalytic amount of silver nitrate (1-2.5 mol %) affords the corresponding cross-coupling products in high yields. The coupling reactions of tertiary alkyl halides provide efficient access to quaternary carbon centers (Scheme 40).⁵²

Scheme 40



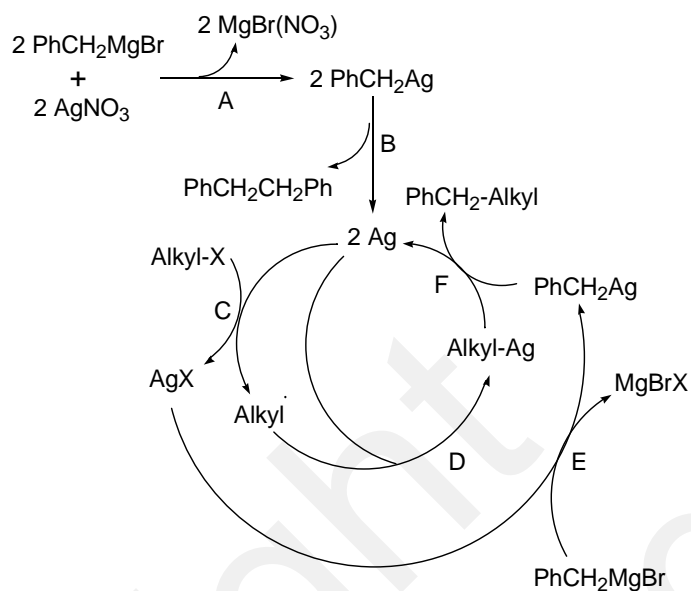
The mechanistic proposal for alkyl-benzyl coupling is outlined in Scheme 41. The proposal invokes a series of steps involving among others transmetalation from magnesium to silver, homocoupling of benzylsilver(I) to generate reactive $\text{Ag}(0)$, halide abstraction from alkyl halide to generate alkylsilver(I), and finally heterocoupling between benzylsilver(I) and alkylsilver(I) to give the final product.

Silver(I) also catalyzes the cross coupling of alkyl bromide with alkyl or aryl Grignard reagents; best results are obtained using 10 mol% AgBr/KF for alkylmagnesium and 10 mol% AgBr/P(OPh)_3 for arylmagnesium. (Scheme 42).⁵³

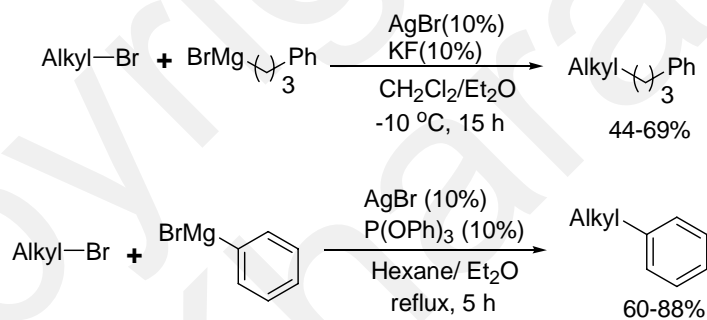
Williams et al. reported the coupling between silver(I) acetylides with adamantyl halide leading to C-C bond formation at the bridgehead position of adamantane (Scheme 43).⁵⁴ The reaction require strongly coordinating aprotic solvents DMSO, HMPA or NMM. Aliphatic and silylated silver(I) acetylides also react with adamantyl iodide under

these conditions but at higher temperatures, and the yields of the coupling product are lower as compared to the aryl-adamantyl coupling.

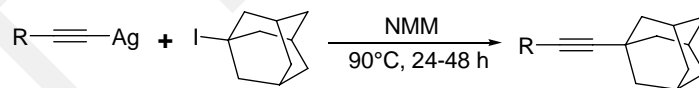
Scheme 41



Scheme 42



Scheme 43

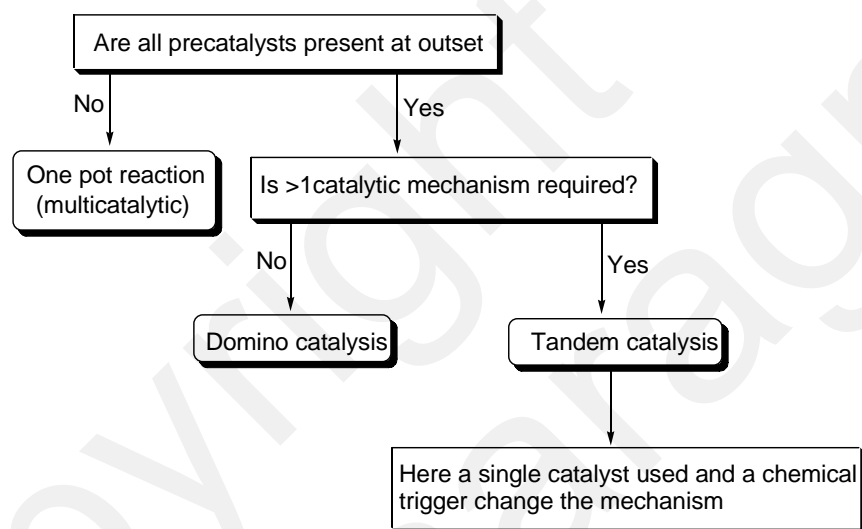


- R = Ph, 68%
- R = *p*-MeC₆H₄, 44%
- R = Me(CH₂)₄C₆H₄, 57%
- R = *p*-BrC₆H₄, 20%
- R = *o*-ClC₆H₄, 62%
- R = *p*-OMe, 51%
- R = Me(CH₂)₃, 29%
- R = CMe₃, 42%
- R = 1-cyclohexenyl, 25%
- R = Trimethylsilyl, 25%

1.6 Cascade or Tandem Reaction

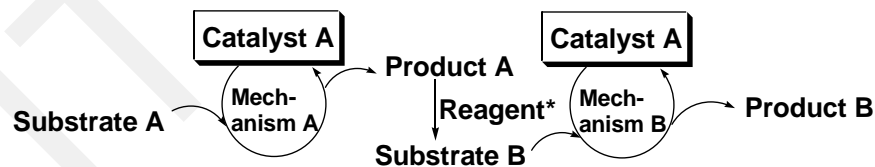
Devising methodologies for elaboration of simple precursors into complex molecular targets is the underlying theme in much of synthetic organic chemistry. With recent focus on green processes, much interest has been attached to “one-pot” multiple catalytic transformations followed by a single workup stage. The variations to one-pot procedures include domino, cascade, and tandem reactions. Fogg and Dos Santos presented a useful flowchart for classification of one-pot processes involving sequential elaboration of an organic substrate via multiple catalytic transformations (Chart 3).⁵⁵

Chart 3 Classification of One Pot process Multiple Catalytic Reaction



A tandem reaction often involves two or more bond-forming transformations in which sequential transformation of the substrate occurs via two (or more) mechanistically distinct processes (Scheme 44). Three categories have been distinguished: orthogonal, assisted, and auto-tandem catalysis.⁵⁵

Scheme 44

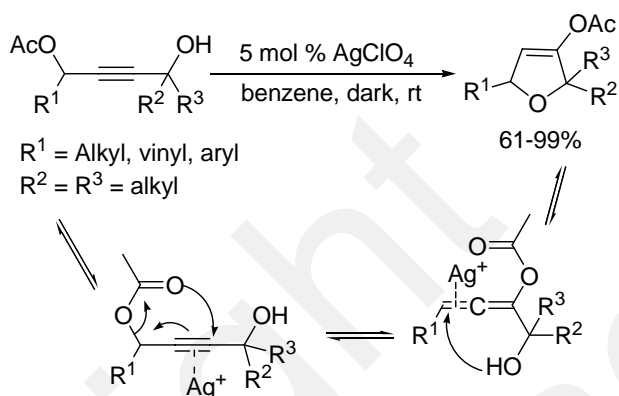


Cyclization reactions in general exhibit high interest in organic synthesis. Cyclization from alkynes or allenes are of significant importance since the cyclization products retain an olefin which can be further manipulated, leading to a wide variety of end products having diverse applications. An extensive survey of the literature shows few examples of

Ag(I)-catalyzed cascade/tandem reaction leading to cyclization. A brief highlight of these reactions is presented in this section.

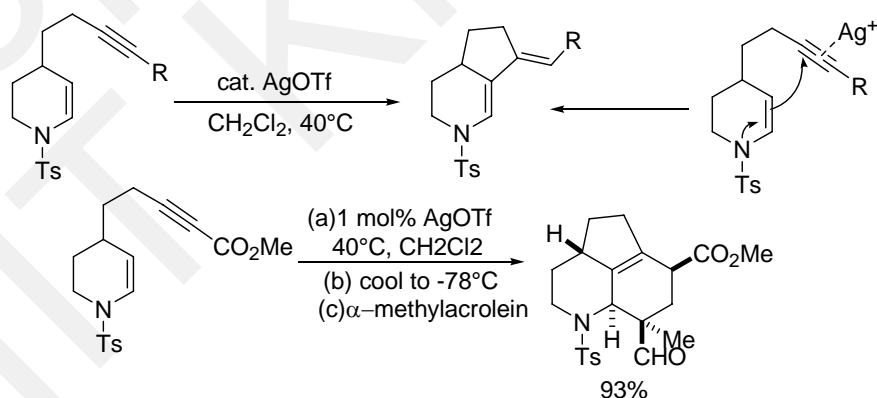
Treatment of monoacetyled butynediols in presence of 5 mol% AgClO₄ in refluxing benzene in the dark gives rise to the substituted 2,5-dihydro pyrans in good yield (Scheme 45).⁵⁶ The transformation can be explained by Ag(I)-catalyzed isomerizations of the monoacetate to an allenyl acetate followed by Ag(I)-assisted allenol cyclization.

Scheme 45



Silver(I) can promote the tandem cycloisomerization-cycloaddition reactions in one pot to generate functionalized 1-azadecalin ring systems in a highly stereo controlled manner (Scheme 46).⁵⁷ Treatment of substituted alkynes with catalytic amount of AgOTf leads to the corresponding cyclization product. The cyclized alkene derivative 2-azahydridans can be reacted further using Diels-Alder reaction through silver catalysis. Ester functionality makes the alkene more reactive for cycloaddition reaction.

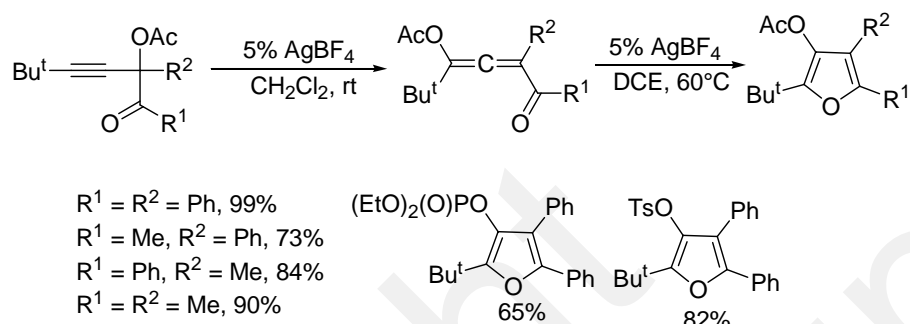
Scheme 46



Schwier et al. demonstrated an attractive possibility to access tetra substituted furans by the sequential cascade transformation involving propargyl esters containing acyloxy,

phosphatyloxy, and tosyloxy groups (Scheme 47).⁵⁸ The one pot sequential reaction takes place in the presence of 5% AgBF₄ in DCE as the solvent. In the first step the propargyl ester undergoes a thermal [3,3] alkoxy shift leading to an allene intermediate. In the second step the allene intermediate undergoes 1,2-migration/cycloisomerization in cascade to afford the furan derivative.

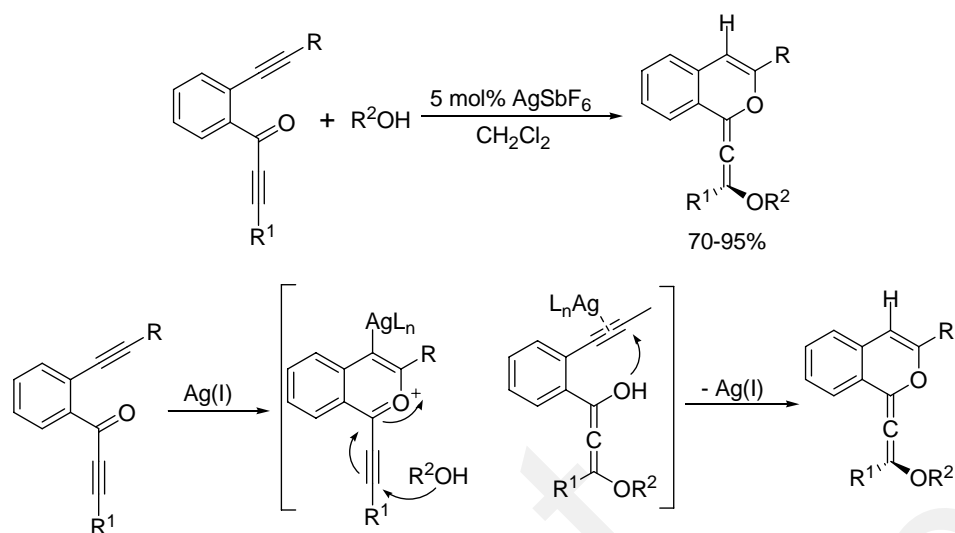
Scheme 47



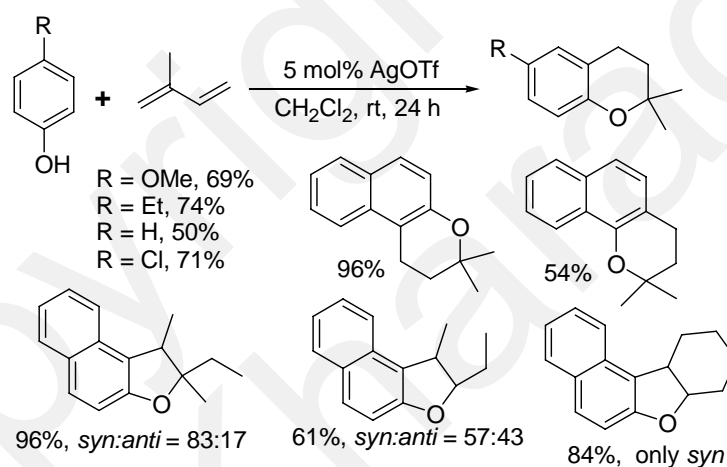
The silver(I)-catalyzed reaction of alkynones with alcohols offers a general route for the synthesis of 1-allenyl isochromenes (Scheme 48).⁵⁹ The mechanism likely involves the formation of benzopyrylium cation or allenyl intermediate, which subsequently undergoes nucleophilic attack of an alcohol or cyclizes to give the annulation product. The mild reaction conditions, simple procedure, easily available starting materials, and reasonable yields make the method attractive. The presence of the allenyl moiety in the end product makes it attractive towards further functionalization leading to highly substituted heterocycles.

Silver(I)-catalyzed sequential C-C/C-O bond formation between a phenol and a diene is a versatile route⁶⁰ for the construction of dihydrobenzopyran and dihydrobenzofuran ring systems (Scheme 49). Both the heterocycles are important motifs in naturally occurring and biologically active compounds. A plausible mechanistic proposal is shown in Scheme 50. Accordingly, activation of the diene via coordination to Ag(I) is followed by intermolecular nucleophilic attack by the arene. The resulting Ag-C bond is protonated to give the 2-allylphenol intermediate. Subsequent intramolecular cyclization results in the end-product.

Scheme 48

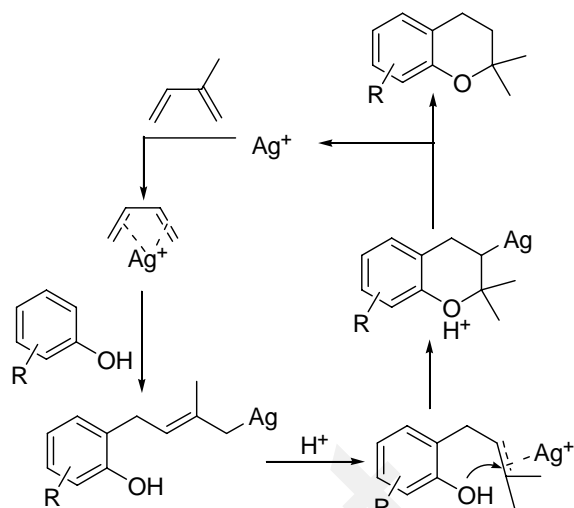


Scheme 49

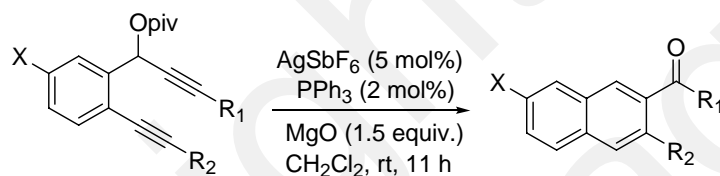


Toste et al. developed a $Ag(I)$ -catalyzed tandem [3,3]-sigmatropic rearrangement/formal Myers-Saito cyclization of propargyl esters to generate aromatic ketones (Scheme 51).⁶¹ Both terminal and internal alkynes show promising reactivity in this $Ag(I)$ -catalyzed tandem cyclization, allowing the preparation of 2-substituted naphthyl ketones and aldehydes. Remarkably, the reaction also accommodates substrates containing a cyclopropyl ring and an additional alkynyl group.

Scheme 50



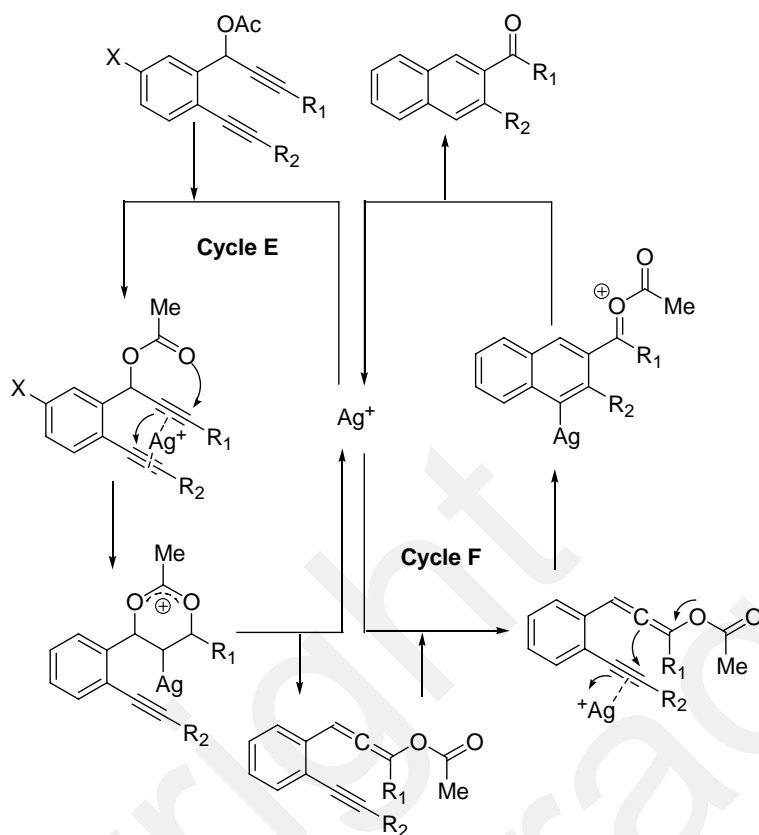
Scheme 51



- R₁ = Me, R₂ = H, X = H, 82%
- R₁ = Me, R₂ = Bu, X = H, 64%
- R₁ = Me, R₂ = Bu, X = CF₃, 94%
- R₁ = Me, R₂ = Bu, X = Cl, 53%
- R₁ = Me, R₂ = Bu, X = OMe, 64%
- R₁ = Me, R₂ = Ph, X = H, 62%
- R₁ = Me, R₂ = cyclopropyl, X = H, 60%
- R₁ = H, R₂ = H, X = H, 63%
- R₁ = Bu, R₂ = H, X = H, 83%

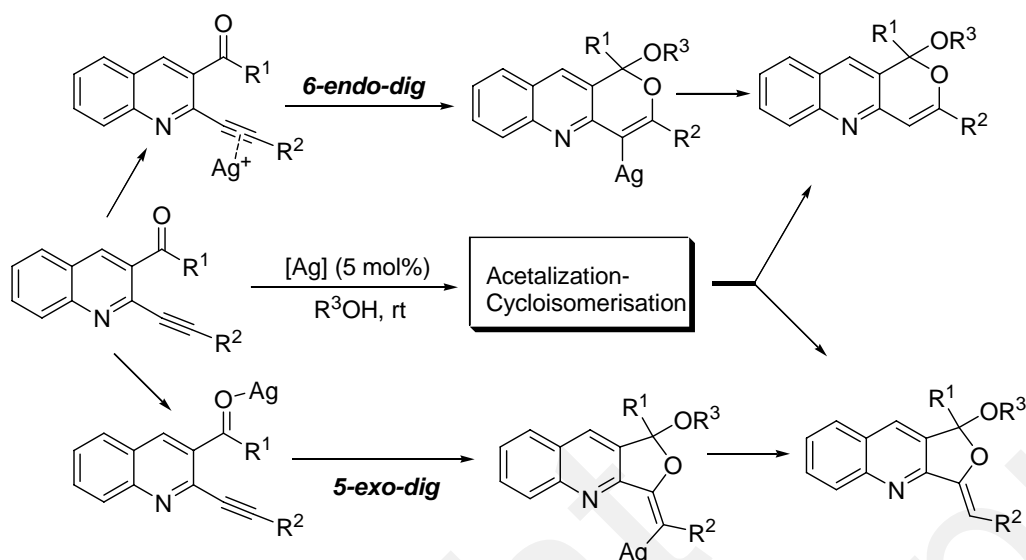
The proposed mechanism involves initial activation of alkyne followed by sequential rearrangement steps (Scheme 52). In the first step, coordination of the metal to the propargyl ester produces enyne allene through a [3,3]-sigmatropic rearrangement (Cycle E). Activation of the remaining alkyne induces 6-*endo-dig* addition of the allenyl acetate (Cycle F).

Scheme 52



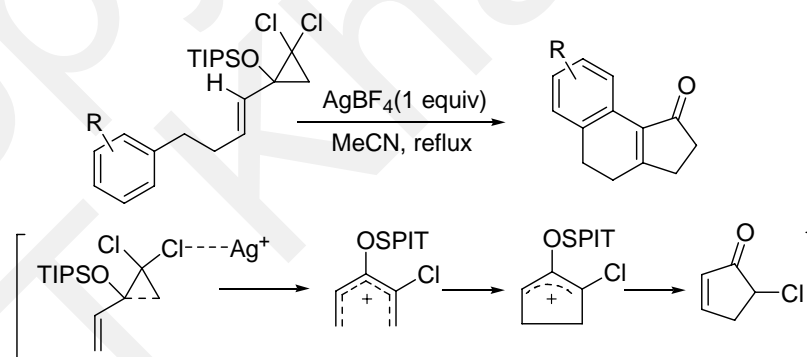
An efficient and versatile tandem process involving acetalization and cycloisomerization of 1-alkynyl-2-carbonylquinoline substrates has been developed (Scheme 53).⁶² Various silver salts promote the transformation of quinoline derivative to the *6-endo-dig* product pyranoquinolines and *5-exo-dig* product furoquinolines. Two different pathways have been proposed for this tandem reaction. In first case the silver salt coordinates to the triple-bond of quinoline substrate, which is followed by nucleophilic attack of the carbonyl oxygen atom and solvent MeOH to form *6-endo-dig* product. The second pathway proposed invokes a direct coordination of aldehyde oxygen atom to Ag(I) and nucleophilic attack of MeOH to form an acetate intermediate, which is then cyclized to give the *5-exo-dig* product.

Scheme 53



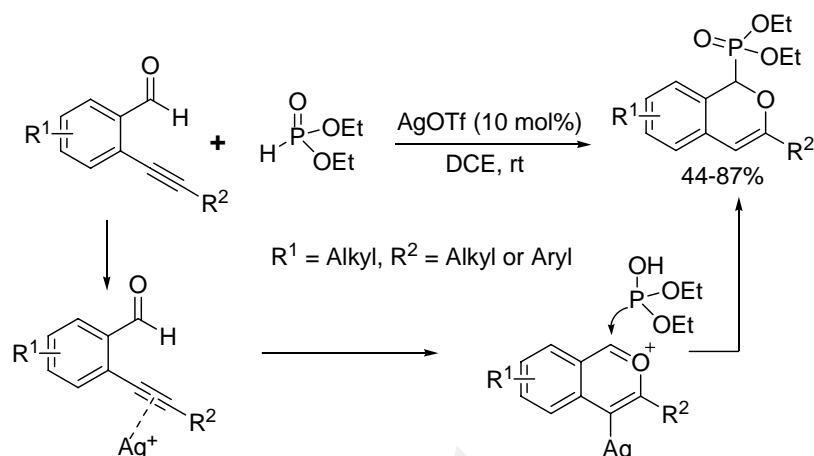
Stoichiometric silver (I) salts have been shown to activate siloxydienes with a variety of pendent aryl groups and are converted to fused products via a two-step sequence (Scheme 54).⁶³ The proposed mechanism involves silver-assisted opening of the dichlorocyclopropane and 4π -electrocyclization of the resulting pentadienyl cation. Once the cyclopentenyl cation is formed, electrophilic aromatic substitution and rearomatization can proceed to give the cyclization product chlorocyclopentenones. Subsequent elimination of HCl generates the cyclopentenone.

Scheme 54



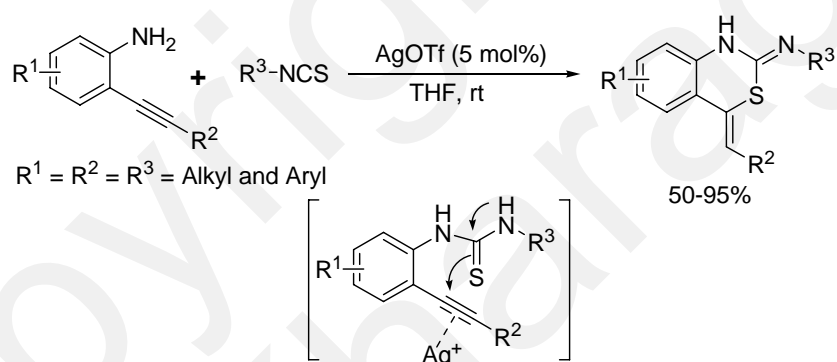
Silver(I) is shown to promote tandem cyclization–addition reaction involving 2-alkynylbenzaldehyde and diethylphosphite giving rise to 1H-isochromen-1-ylphosphonates in moderate to good yields (Scheme 55).⁶⁴

Scheme 55



Silver(I) triflate also promotes tandem addition-cyclization of 2-alkynylbenzenamines with isothiocyanates leading to an efficient synthesis of 2,4-dihydro-1H benzo[d][1,3]thiazines (Scheme 56).⁶⁵

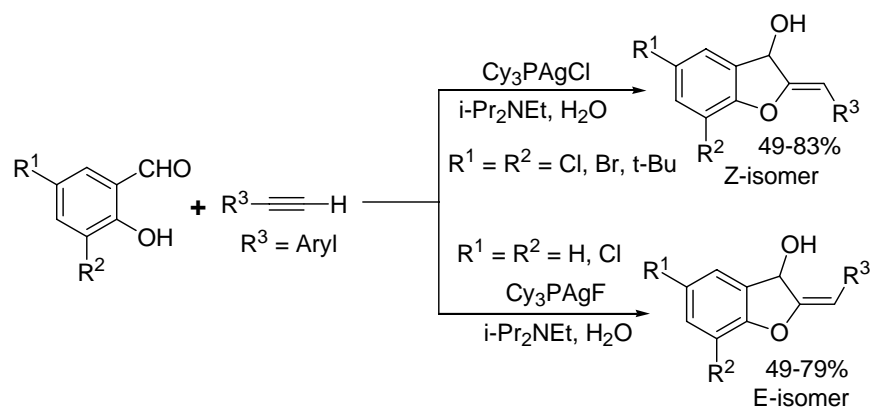
Scheme 56



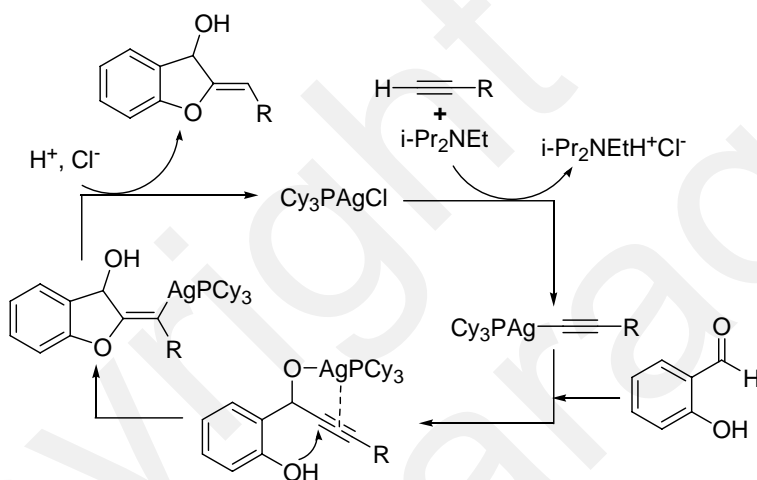
The silver(I)-phosphine complex namely $\text{Cy}_3\text{P}\cdot\text{AgX}$ catalyzes the cascade alkynylation-cyclization of terminal alkynes with salicylaldehyde and analogues leading to substituted 2,3-dihydrobenzofuran-3-ol derivatives (Scheme 57).⁶⁶ The reaction occurs in water as solvent. Counter anions in the silver complex affects the (*E*)/(*Z*) stereoselectivity in the reaction.

A tentative mechanism for the silver(I)-catalyzed cascade alkynylation/cyclization of salicylaldehydes is described in Scheme 58. Reaction of terminal alkynes with Cy_3AgCl in the presence of a weak base generates the silver(I) acetylide. The latter reacts with aldehyde to give propargylic alcohol intermediate, in the presence of water. This is followed by a silver(I)-promoted attack of phenol to the triple bond to give the vinyl silver intermediate which is converted to the product by protodemetalation.

Scheme 57

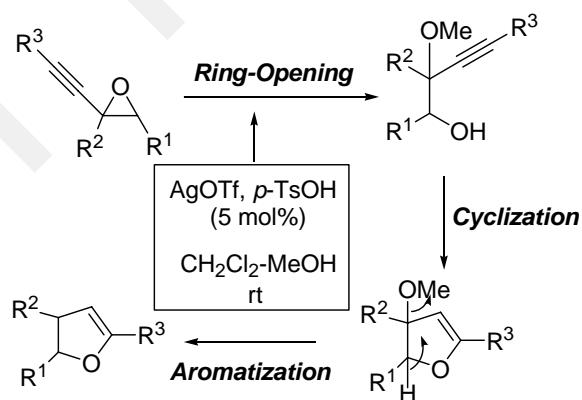


Scheme 58



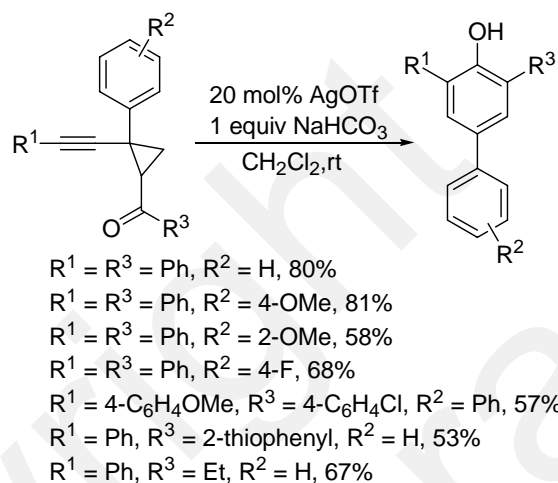
Blanc et al. executed an Ag(I)-catalyzed cascade reaction of (*R*)-alkynyl oxiranes leading to functionalized furans via ring-opening, cyclization and aromatization sequence (Scheme 59).⁶⁷

Scheme 59

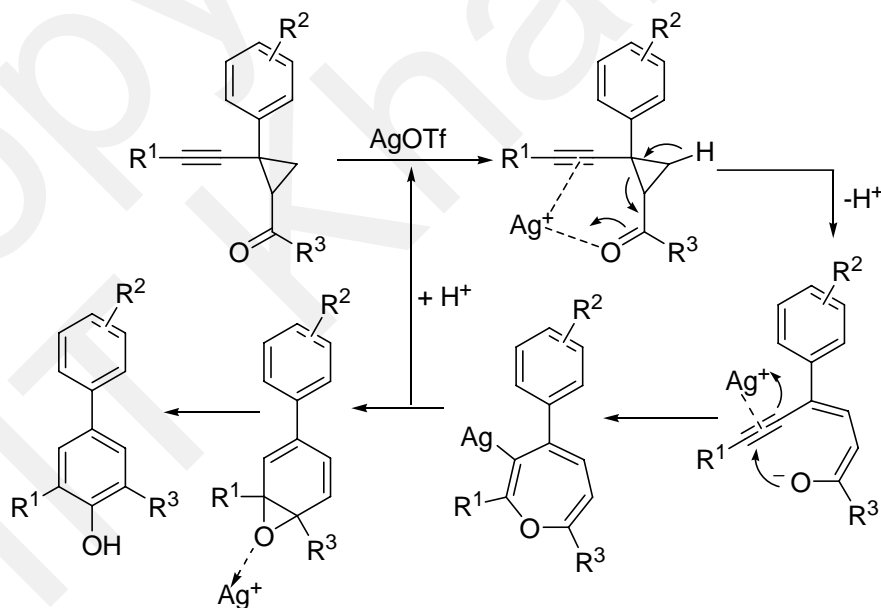


2,4,6-Trisubstituted phenols are easily accessed by tandem cyclization/ isomerisation reaction of substituted cyclopropanol via silver(I) catalysis (Scheme 60).⁶⁸ The proposed mechanism involves initial coordination of AgOTf to both the triple bond and the carbonyl oxygen, followed by the cleavage of the cyclopropane to give an ene-yne intermediate. The latter undergoes cyclization to deliver oxepin, which transforms into arene oxide. Being a Lewis acid, AgOTf activates the arene oxide, leading to ring opening and migration of one substituent on oxide yielding the end product (Scheme 61).

Scheme 60



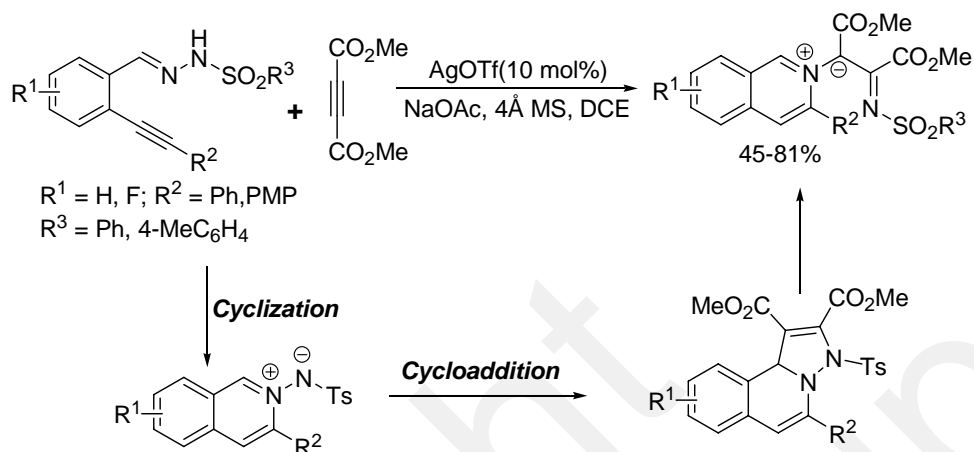
Scheme 61



Chen et al. demonstrated an efficient Ag(I)-catalyzed tandem cyclization/[3+2] cycloaddition reaction of *N*-(2-alkynylbenzylidene) hydrazides with dimethyl

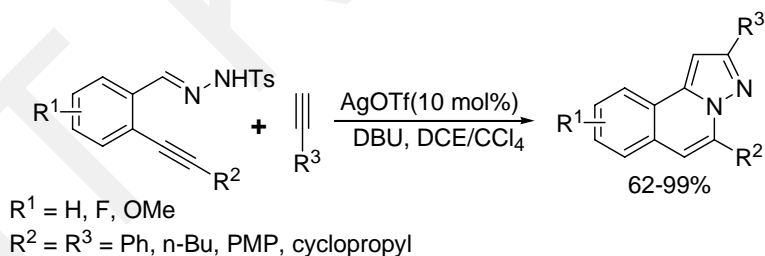
acetylenedicarboxylate (Scheme 62).⁶⁹ Various Lewis acids were screened and silver triflate (10 mol %) was shown to be the best choice when this reaction was performed at 70 °C in dichloroethane as solvent.

Scheme 62

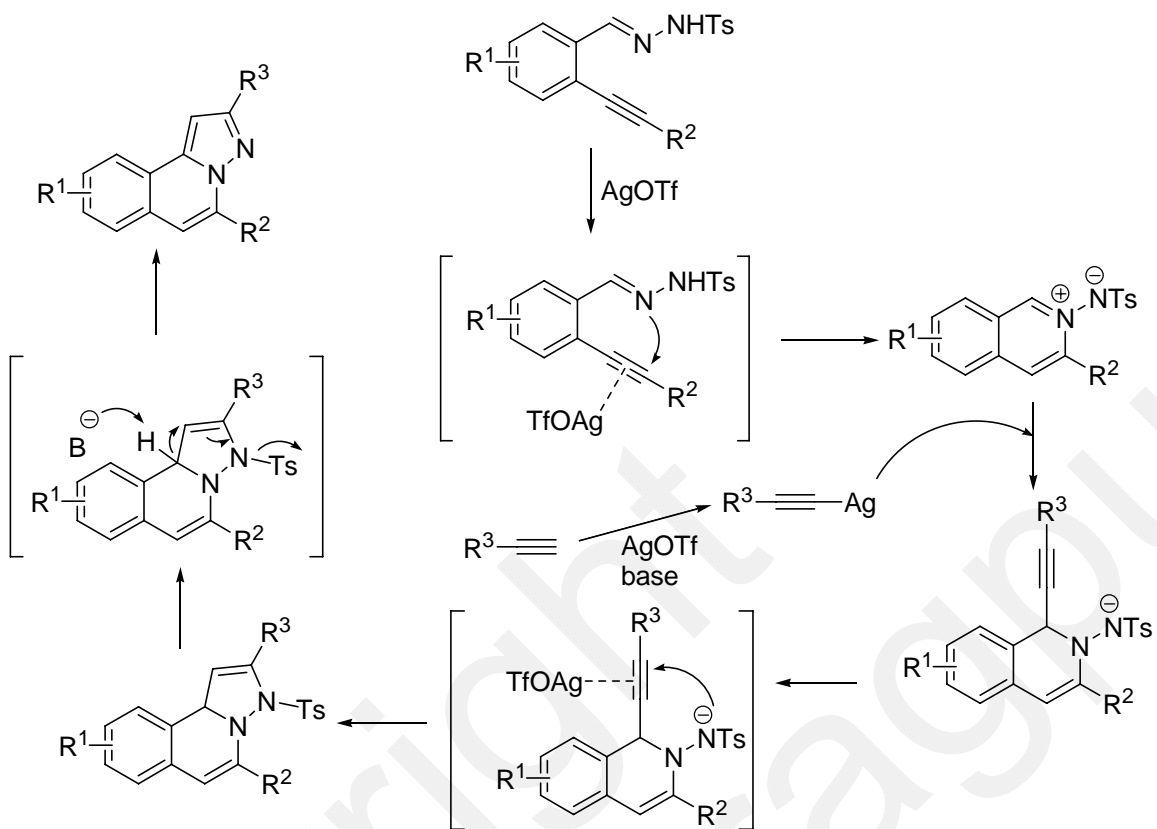


Wu et al. described an efficient tandem reaction of *N*-(2-alkynylbenzylidene) hydrazide with alkynes catalyzed by silver triflate (Scheme 63).⁷⁰ The reaction proceeds smoothly for both aromatic and aliphatic substituted terminal alkynes. It is suggested that the cascade reaction occurs (Scheme 64) through initial coordination of the triple bond to the silver(I). Subsequently the nitrogen atom of *N*-(2-alkynylbenzylidene) hydrazide attacks on the triple bond triggering *6-endo*-cyclization and affording isoquinolinium intermediate. Finally nucleophilic addition of alkyne to the isoquinolinium intermediate affords the corresponding product, which undergoes intramolecular *5-endo* cyclization and then aromatization leading to 1,2-dihydroisoquinoline.

Scheme 63



Scheme 64



1.7 Scope of the Present Work

The discussion in this chapter highlighted the silver(I) catalysis pertaining to coupling and cyclization which involves activation of both σ - and π - center across Ag(I). It may be noted that in the past several years, significant progress has been made in exploring silver(I)-based heterocyclizations and coupling. Silver(I) complexes have been shown to efficiently catalyze the intra or inter molecular addition of oxygen and nitrogen nucleophiles to alkynes, allenes, and olefins to generate oxygen and nitrogen heterocycles. Silver catalyzed asymmetric reactions are also well described. Most of these reactions utilize the Lewis acidic character of the Ag(I) cation and preferential bind toward O and N donor atoms. Complexes of Ag(I) with π -donors (such as alkenes and aromatics) and σ -donors (alcohols and amines) are well documented. Accounts of Ag(I)-mediated nucleophilic addition reactions that involve silver cation activation of olefin, propargyl, and allenyl substrates strongly support the carbophilic nature of Ag(I).

Keeping the above perspective in mind, we endeavored to develop new synthetic protocols based on silver(I) mediated activation of both σ - and π - center for carbon-carbon and carbon-heteroatom bond formation. The results presented in chapter 2 to 4 describe our success in utilizing this strategy for the activation of aziridines, azetidines, arenes, alkynes, alcohols, amines and thiols.

1.8 References

1. Hegedus, L. S. Transition metals in the synthesis of complex organic molecules; University science book: Sausalito, CA, 1999.
2. Pyykkö, P. Theoretical chemistry of gold. *Angew. Chem., Int. Ed.* **2004**, *43*, 4412.
3. Yamamoto, Y. From σ - to π - electrophilic lewis acids. Application to selective organic transformations. *J. Org. Chem.* **2007**, *72*, 7817.
4. (a) Weibel, J-M.; Blanc, A.; Pale, P. Ag-mediated reaction: Coupling and heterocyclization reactions. *Chem. Rev.* **2008**, *108*, 3149; (b) Dias, H. V. R.; Lovely, C. J. Carbonyl and olefin adducts of coin age metals supported by poly (pyrazolyl)borate and poly(pyrazolyl)alkane ligands and silver mediated atom transfer reaction. *Chem. Rev.* **2008**, *108*, 3223.
5. Miriam, A-C.; Manuel, M-D.; Ignacio, R-G. Silver-mediated synthesis of heterocycles. *Chem. Rev.* **2008**, *108*, 3174.
6. (a) Rodesiler, P. F.; Griffith, E. A. H.; Amma, B. L. Metal ion-aromatic complexes. XIII. Trigonal planar silver(I) in structure of indene silver perchlorate. *J. Am. Chem. Soc.* **1972**, *94*, 761; (b) Griffith, E. A. H.; Amma, B. L. Metal ion-aromatic complexes. XVIII. Preparation and molecular structure of naphthalenetetrakis(silver perchlorate)tetrahydrate. *J. Am. Chem. Soc.* **1974**, *96*, 743; (c) Griffith, E. A. H.; Amma, B. L. Metal ion-aromatic complexes. XVIII. Preparation and molecular structure of anthracenetetrakis(silver perchlorate)monohydrate. *J. Am. Chem. Soc.* **1974**, *96*, 5407.
7. Munakata, M.; Wu, L. P.; Ning, G. L. A new type of multilayer system-silver(I) complexes of polycyclic aromatic compounds. *Coord. Chem. Rev.* **2000**, *198*, 171.
8. Penner, G. H.; Liu, X. Silver NMR spectroscopy. *Progress in Nuclear Magnetic Resonance Spectroscopy.* **2006**, *49*, 151.
9. (a) Davis, R. B.; Scheiber, D. H. The preparation of acetylenic ketones using soluble silver acetylides. *J. Am. Chem. Soc.* **1956**, *78*, 1675; (b) Naka, T.; Koide, K. A novel and simple method to prepare γ -hydroxy- α , β -(E)-alkenoic esters from γ -keto-alkynoic esters. *Tetrahedron Lett.* **2003**, *44*, 443.
10. (a) Halber, U.; Bertus, P.; Pale, P. The first direct coupling of 1-trialkylsilyl-1-alkenes with vinyl triflates: A new access to enynes. *Tetrahedron Lett.* **2001**, *42*, 8641; (b)

Halber-Letinois, U.; Vasiliev, A.; Pale, P. Regio- and chemoselective coupling of polyalkynes: A convenient access to polyaryl acetylenes and polyenes. *Eur. J. Org. Chem.* **2001**, 2828.

11. Bickley, E. A.; Gardner, J.H. The action of Grignard reagents on heavy metal salts. IV. The mechanism of the reaction with silver bromide. *J. Org. Chem.* **1940**, *5*, 126.

12. Weibel, J-M.; Blanc, A.; Pale, P. Ag-mediated reaction: Coupling and heterocyclization reactions. *Chem. Rev.* **2008**, *108*, 3149.

13. Smith, M. B.; March, J. *Advance Organic Chemistry*, 5th Ed.; Wiley: New York, 2001; P 534.

14. (a) Negishi, E-I.; De Meijere, A. *Handbook of organopalladium chemistry for organic synthesis*; Wiley: New York, 2002; (b) Tsuji, J. *Palladium reagents and catalysts*; Wiley: New York, 2004.

15. (a) Weibel, J-M.; Blanc, A.; Pale, P. Ag-mediated reaction: Coupling and heterocyclization reactions. *Chem. Rev.* **2008**, *108*, 3149; (b) Yamamoto, Y. Silver-catalyzed C_{sp}-H and C_{sp}-Si bond transformation and related process. *Chem. Rev.* **2008**, *108*, 3199.

16. Omura, K. Silver ion-mediated coupling of 4-bromo-2,6-di-tert-butylcyclohexa-2,5-dienone with phenols. *J. Org. Chem.* **1998**, *63*, 10031.

17. Arcadi, A.; Alfonsi, M.; Marinelli, F. Silver-catalyzed direct couplings of 2-substituted furans with cyclic 1,3-dicarbonyls. *J. Organomet. Chem.* **2007**, *692*, 5322.

18. Eghbali, N.; Eddy, J.; Anastas, P. T. Silver-catalyzed one pot synthesis of aryl naphthalene lactones. *J. Org. Chem.* **2008**, *73*, 6932.

19. Garner, P.; Kaniskan, H. U.; Hu, J.; Youngs, W. J.; Panzner, M. Asymmetric multicomponent [C + NC + CC] synthesis of highly functionalized pyrrolidines catalyzed by silver(I). *Org. Lett.* **2006**, *8*, 3647.

20. Ding, Q.; Wu, J. Lewis acid- and organocatalyst- cocatalyzed multicomponent reactions of 2-alkenylbenzaldehydes, amines and ketones. *Org. Lett.* **2007**, *9*, 4959.

21. Bon, R. S.; Vliet, B. V.; Sprenkels, N. E.; Schmitz, R. F.; De Kanter, F. J. J.; Stevens, C. V.; Swart, M.; Bickelhaupt, F. M.; Groen, M. B.; Orru, R. V. A. Multicomponent synthesis of 2-imidazolines. *J. Org. Chem.* **2005**, *70*, 3542.

22. Ye, S.; Wu, J. Silver triflate and triphenyl phosphine co-catalyzed reactions of 2-alkenylbenzaldehyde, amine and α,β -unsaturated ketones. *Tetrahedron Lett.* **2009**, 50, 6273.
23. Krishnan, G. R.; Sreerexha, R.; Sreekumar, K. Three component Mannich reaction and 1,5-benzodiazepine synthesis catalyzed by a tetranitrile silver complex. *Lett. Org. Chem.* **2009**, 6, 17.
24. Ding, Q.; Yu, X.; Wu, J. AgOTf-catalyzed one-pot reaction of 2-alkenylbenzaldehyde, amine, and sodium borohydride. *Tetrahedron Lett.* **2008**, 49, 2752.
25. (a) Berend, M.; Liebermann, C. *Justus Liebigs Ann. Chem.*, **1865**, 135, 259; (b) Glaser, C. *Justus Liebigs Ann. Chem.*, **1870**, 154, 157.
26. (a) Noltes, J. G.; Van Coten, G. *Comprehensive organometallic chemistry I*, Ed. Wilkinson, G.; Abel, E. W.; Stone, F. G. A. Pergamon, Oxford, **1982**, vol 2, p 709; (b) Van Coten, G.; James, S. L.; Jastrzebski, J. T. B. H. *Comprehensive organometallic chemistry II*, Ed. Wilkinson, G.; Abel, E. W.; Stone, F. G. A. Pergamon, Oxford, **1995**, vol 3, p 57.
27. Ulla, H-L.; Weibel, J-M.; Pale, P. The organic chemistry of silver acetylides. *Chem. Soc. Rev.* **2007**, 36, 759.
28. Tramontini, M.; Angiolini, L. Further advances in the chemistry of Mannich bases. *Tetrahedron.* **1990**, 46, 1791.
29. Wei, C.; Li, Z.; Li, C-J. The development of A^3 -coupling (aldehyde-alkyne-amine) and AA^3 -coupling (asymmetric aldehyde-alkyne-amine). *Synlett.* **2004**, 1472.
30. Wei, C.; Li, Z.; Li, C-J. The first silver-catalyzed three-component coupling of aldehyde, alkyne, and amine. *Org. Lett.* **2003**, 5, 4473.
31. Huang, B.; Yao, X.; Li, C-J. Diastereoselective synthesis of α -oxyamines via gold-, silver-, and copper-catalyzed, three component couplings of α -oxyaldehydes, alkynes, and amines in water. *Adv. Synth. Catal.* **2006**, 348, 1528.
32. Li, Z.; Wei, C.; Chen, L.; Varma, R. S.; Li, C-J. Three-component coupling of aldehyde, alkyne, and amine catalyzed by silver in ionic liquid. *Tetrahedron Lett.* **2004**, 45, 2443.
33. (a) Zhang, Y.; Santos, A. M.; Herdtweck, E.; Mink, J.; Kühn, F. E. Organonitrile ligated silver complexes with perfluorinated weakly coordinating anions and their

- catalytic application for coupling reaction. *New J. Chem.* **2005**, *29*, 366; (b) Maggi, R.; Bello, A.; Oro, C.; Sartori, G.; Soldi, L. AgY zeolite as catalyst for the effective three component synthesis of propargylamines. *Tetrahedron* **2008**, *64*, 1435; (c) Yan, W.; Wang, R.; Xu, Z.; Xu, J.; Lin, L.; Shen, Z.; Zhou, Y. A novel, practical and green synthesis of Ag nanoparticles catalysts and its applications in three component coupling of aldehyde, alkyne, and amine. *J. Mol. Catal. A* **2006**, *255*, 81; (d) Reddy, K. M.; Babu, N. S.; Suryanarayana, I.; Prasad, P. S. S.; Lingaiah, N. The silver salt of 12-tunstophosphoric acid: An efficient catalyst for the three-component coupling of an aldehyde, an alkyne, and amine. *Tetrahedron Lett.* **2006**, *47*, 7563; (e) He, T.; Zha, Z.; Pan, C.; Wang, Z. Microwave-promoted, solvent-free, three-component coupling of aldehyde, alkyne, and amine catalyzed by AgNO₃. *Synth. Commun.* **2007**, *37*, 849.
34. Davis, R. B.; Scheiber, D. H. The preparation of acetylenic ketones using soluble silver acetylides. *J. Am. Chem. Soc.* **1956**, *78*, 1675.
35. Royer, E. C.; Barral, M. C. Interaction of copper and silver alkynylides with tertiary phosphines. *Inorg. Chim. Acta* **1984**, *90*, L47.
36. Yao, X.; Li, C-J. Phosphine-triggered complete chemo switch: From efficient aldehyde-alkyne-amine coupling to efficient aldehyde-alkyne coupling in water. *Org. Lett.* **2005**, *7*, 4395.
37. Ji, J-X.; Terry, T. -L.; Yeung, A.; Wu, J.; Yip, C. W.; Chan, A. S. C. Efficient synthesis of β,γ -alkenyl α -amino acid derivatives by Ag(I)-catalyzed alkynylation of α -imino esters. *Adv. Synth. Catal.* **2004**, *346*, 42.
38. Rueping, M.; Antonchick, A. P.; Brinkmann, C. Dual catalysis: A combined enantioselective bronsted acid and metal-catalyzed reaction-metal catalysis with chiral counteranions. *Angew. Chem., Int. Ed.* **2007**, *46*, 6903.
39. Dodda, R.; Zhao, C-G. Silver(I) triflate catalyzed direct synthesis of N-PMP protected α -aminopropargylphosphonates from terminal alkynes. *Org. Lett.* **2007**, *9*, 165.
40. Li, P.; Lei, W. A novel silver iodide catalyzed sonogashira coupling reaction. *Synlett.* **2006**, 2261.
41. Rhee, U. J.; Krische, M. J. Alkynes as synthetic equivalents to stabilized Wittig reagents: Intra- and intermolecular carbonyl olefinations catalyzed by Ag(I), BF₃, and HBF₄. *Org. Lett.* **2005**, *7*, 2493.

42. Yanagisawa, A.; Nakashima, H.; Ishiba, A.; Yamamoto, H. Catalytic asymmetric allylation of aldehyde using achiral silver(I) complex. *J. Am. Chem. Soc.* **1996**, *118*, 4713.
43. Yanagisawa, A.; Matsumoto, Y.; Nakashima, H.; Asakawa, K.; Yamamoto, H. Enantioselective aldol reaction of tin enolates with aldehydes catalyzed by BINAP-silver(I) complex. *J. Am. Chem. Soc.* **1997**, *119*, 9319.
44. See reference 43.
45. Yamagisawa, A.; Nakatsuka, Y.; Nakashima, H.; Yamamoto, Y. Asymmetric γ -selective pentadienylation of aldehydes catalyzed by BINAP-Ag(I) complex. *Synlett.* **1997**, 933.
46. Yanagisawa, A.; Kageyama, H.; Nakatsuka, Y.; Asakawa, K.; Matsumoto, Y.; Yamamoto, Y. Enantioselective addition of allylic trimethoxysilanes to aldehydes catalyzed by p-tol-BINAP-AgF. *Angew. Chem., Int. Ed.* **1999**, *38*, 3701.
47. Ohkouchi, M.; Masui, D.; Yamaguchi, M.; Yamagishi, T. Mechanism of silver(I)-catalyzed Mukaiyama aldol reaction: Active species in solution in AgPF₆-(S)-BINAP versus AgOAc-(S)-BINAP systems. *J. Mol. Catal. A: Chemical*, **2001**, *170*, 1.
48. Momiyama, N.; Yamamoto, H. Catalytic enantioselective synthesis of α -aminooxy and α -hydroxy ketone using nitrosobenzene. *J. Am. Chem. Soc.* **2003**, *125*, 6038.
49. Kochi, J. K.; Tamura, M. Mechanism of the silver-catalyzed reaction of Grignard reagents with alkyl halide. *J. Am. Chem. Soc.* **1971**, *93*, 1483.
50. Nagano, T.; Hayashi, T. Silver-catalyzed alkyl-alkyl homo-coupling of Grignard reagents. *Chem. Lett.* **2005**, *34*, 1152.
51. Brown, H. C.; Verbrugge, C.; Snyder, C. H. The reaction of mixed trialkylboranes with alkaline silver nitrate-hydroboration as a convenient route for the synthesis of carbon structures. *J. Am. Chem. Soc.* **1961**, *83*, 1002.
52. Someya, H.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. Silver-catalyzed benzylation and allylation reaction of tertiary and secondary alkyl halides with Grignard reagents. *Org. Lett.* **2008**, *10*, 969.
53. Someya, H.; Yorimitsu, H.; Oshima, K. Silver-catalyzed cross-coupling reactions of alkyl bromides with alkyl or aryl Grignard reagents. *Tetrahedron Lett.* **2009**, *50*, 3270.

54. Pouwer, R. H.; Harper, J. B.; Vyakaranam, K.; Michl, J.; Williams, C. M.; Jessen, C. H.; Bernhardt, P. V. Investigating direct alkynylation at the bridge head of bicyclic cages using silver(I)-acetylides. *Eur. J. Org. Chem.* **2007**, 241.
55. Fogg, D. E.; Dos Santos, E. N. Tandem catalysis: a taxonomy and illustrative review. *Coord. Chem. Rev.* **2004**, 248, 2365.
56. Saimoto, H.; Hiyama, T.; Nozaki, H. Regiocontrolled hydration of 2-butyne-1,4-diol derivatives to give 4,5-dihydro-3(2H)-furanones, practical synthesis of bullatenone and geiparvarin. *J. Am. Chem. Soc.* **1981**, 103, 4975.
57. Harrison, T. J.; Dake G.R. Pt(II) or Ag(I) salt catalyzed cycloisomerizations and tandem cycloadditions forming functionalized azacyclic arrays. *Org. Lett.* **2004**, 6, 5023.
58. Schwier, T.; Sromek, A. W.; Yap, D. M. L.; Chernyak, D.; Gevorgyan, V. Mechanistically diverse copper-, silver-, and gold-catalyzed acyloxy and phosphatyloxy migrations: Efficient synthesis of heterocycles via cascade migration/cycloisomerization approach. *J. Am. Chem. Soc.* **2007**, 129, 9868.
59. Patil, N. T.; Pahadi, N. K.; Yamamoto, Y. Silver(I)-catalyzed novel cascade cyclization reactions: Incorporation of allenes into the isochromenes. *J. Org. Chem.* **2005**, 70, 10096.
60. Youn, S. W.; Im Eom, J. Ag(I)-catalyzed sequential C-C and C-O bond formations between phenols and dienes with atom economy. *J. Org. Chem.* **2006**, 71, 6705.
61. Zhao, J.; Hughes, C. O.; Toste, F. D. Synthesis of aromatic ketones by a transition metal-catalyzed tandem sequence. *J. Am. Chem. Soc.* **2006**, 128, 7436.
62. Godet, T.; Vaxelaire, C.; Michel, C.; Milet, A.; Belmont, P. Silver versus gold catalysis in tandem reactions of carbonyl functions onto alkynes: A versatile access to furoquinoline and pyranoquinoline cores. *Chem. Eur. J.* **2007**, 13, 5632.
63. Grant, T. N.; West, F. G. Interrupted Nazarov reactions using dichlorocyclopropanes: A novel mode of arene trapping. *Org. Lett.* **2007**, 9, 3789.
64. Yu, X.; Ding, Q.; Wanga, W.; Wu, J. Synthesis of 1H-isochromen-1-ylphosphonates via AgOTf-catalyzed reaction of 2-alkynylbenzaldehyde with diethyl phosphate. *Tetrahedron Lett.* **2008**, 49, 4390.
65. Ding, Q.; Wu, J. A facile route to 2,4-dihydro-1H-benzo[d][1,3]thiazines via silver-catalyzed tandem addition-cyclization reactions. *J. Comb. Chem.* **2008**, 10, 541.

66. Yu, M.; Skouta, R.; Zhou, L.; Jiang, H-F.; Yao, X.; Li, C-J. Water-triggered, counter-anion-controlled, and silver-phosphines complex-catalyzed stereoselective cascade alkynylation/cyclization of terminal alkynes with salicylaldehydes. *J. Org. Chem.* **2009**, *74*, 3378.
67. Blanc, A.; Tenbrink, K.; Weibel, J-M.; Pale, P. Silver(I)-catalyzed cascade: Direct access to furans from alkynyloxiranes. *J. Org. Chem.* **2009**, *74*, 4360.
68. Zhang, X-M.; Tu, Y-Q.; Jiang, Y-J.; Zhang, Y-Q.; Fan, C-A.; Zhang, F-M. Tandem reactions of cis-2-acyl-1-alkynyl-1-aryl cyclopropanes tuned by gold(I) and silver(I) catalysts: efficient synthesis of pyran-fused indene cores and 2,4,6-trisubstituted phenols. *Chem. Commun.* **2009**, 4726.
69. Chen, Z.; Ding, Q.; Yu, X.; Wu, J. Silver triflate-catalyzed or electrophile-mediated tandem reaction of N'-(2-Alkynylbenzylidene)hydrazides with dimethyl acetylenedicarboxylate. *Adv. Synth. Catal.* **2009**, *351*, 1692.
70. Chen, Z.; Yang, X.; Wu, J. AgOTf-catalyzed tandem reaction of N-(2-alkynylbenzylidene)hydrazide with alkyne. *Chem. Commun.* **2009**, 3469.