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Ligand Effects in Homogeneous Au Catalysis

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1. Introduction

1.1. Context and Meta-Review

Despite the ubiquity of metallic gold (Au) in popular culture, its deployment in homogeneous catalysis has only recently undergone widespread investigation. In the past decade, and especially since 2004, great progress has been made in developing efficient and selective Au-catalyzed transformations, as evidenced by the prodigious number of reviews available on various aspects of this growing field. Hashmi has written a series of comprehensive reviews outlining the progression of Au-catalyzed reaction development,[1] and a number of more focused reviews provide further insight into particular aspects of Au catalysis. A brief meta-review of the available range of perspectives published on Au catalysis helps to put this *Chemical Reviews* article in context.

The vast majority of reactions developed with homogeneous Au catalysts have exploited the propensity of Au to activate carbon-carbon π-bonds as electrophiles. Gold has come to be regarded as an exceedingly mild, relatively carbophilic Lewis acid, and the broad array of newly developed reactions proceeding by activation of unsaturated carbon-carbon bonds has been expertly reviewed.[2]

Further reviews and highlights on Au catalysis focus on particular classes of synthetic reactions. An excellent comprehensive review of Au-catalyzed enyne cycloisomerizations is available.[3] Even more focused highlights on hydroarylation of alkynes,[4] hydroamination of C-C multiple bonds,[5] and reactions of oxo-alkynes[6] and propargylic esters[7] provide valuable perspectives on progress and future directions in the development of homogeneous Au catalysis.

Most of the reviews on Au catalysis emphasize broad or specific advances in synthetic utility. Recently, we have invoked relativistic effects to provide a framework for understanding the observed reactivity of Au catalysts, in order to complement empirical advancements.[8] In this *Chemical Reviews* article, we attempt to enumerate the ways in which selectivity can be controlled in homogeneous Au catalysis. It is our hope that lessons to guide catalyst selection and the design of new catalysts may be distilled from a thorough evaluation of ligand, counterion, and oxidation state effects as they influence chemo-, regio-, and stereoselectivity in homogeneous Au catalysis.

1.2. Scope and Structure of This Review

This review will address ligand effects in homogeneous catalysis through December 2007. Obvious differences in reactivity and selectivity arising from changing neutral or anionic ligands will be comprehensively addressed, with special emphasis on ligands and complexes enabling enantioselective catalysis. Instances where catalyst choice, including ligand,

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counterion, or oxidation state of Au, enables control over reaction pathways will be comprehensively reviewed, including influence over diastereoselectivity, regioselectivity, and chemoselectivity. There are many instances where catalyst choice provides slight improvement in reaction yields or efficiencies; extensive, but not comprehensive, discussion of this phenomenon is included herein.

The review is organized primarily by reactivity pattern, so that privileged ligands and catalysts for a given class of reactions are highlighted. Further divisions within the broad section headings are organized by substrate class. We begin by addressing the Hayashi/Ito asymmetric aldol reaction, which remains the quintessential and seminal example of ligand effects in homogeneous Au catalysis, and preceded the current surge of interest in the field by over a decade. The review then proceeds according to our perception of the most broadly studied subfields of homogeneous Au catalysis, with substantial weight given to advances within the past year. Due to the ever accelerating rate of publications on Au catalysis, great strides in the field have been made even since the last comprehensive review in 2007.[1c]

2. Carbonyl Activation

2.1. Asymmetric Catalysis

In 1986, long before the current surge in interest in homogeneous Au catalysis, Ito, Sawamura, and Hayashi reported the asymmetric reaction of various aldehydes (i.e., **1**) with isocyanoacetate **2**, catalyzed by $[Au(CNCy)_2]BF_4$ and chiral ferrocenylphosphine ligand **4** (Scheme 1).[9] High diastereo- and enantioselectivities were observed for a series of aliphatic and aromatic aldehydes. The amine group of the ligand was essential for achieving high enantioselectivity in the reaction, and it was proposed that the pendant Lewis base enforced an organized transition state structure *via* cyanoacetate deprotonation.[10] Spectroscopic studies, particularly by NMR, suggested that both phosphines of the ligand might associate to Au.[11] Thus, in contrast to the vast majority of Au-catalyzed reactions that were subsequently developed, the asymmetric Aldol is proposed to proceed via a four-coordinate (bisphosphine) Au(I) intermediate.[12]

For reasons that remain unclear, the findings of Ito, Sawamura, and Hayashi did not result in the large-scale deployment of chiral Au-complexes as catalysts for the activation of polar functionality. Recently, Toste disclosed the enantioselective 1,3-dipolar cycloaddition of Münchnones with electron-deficient alkenes, which is proposed to proceed via activation of a cyclic azlactone **5** by cationic Au(I) to generate the reactive Münchnone species (Table 1).[13] The planer chiral skeleton Segphos (**8**) provided superior enantioselectivity compared to Binap (**7**) (entries 1 and 2).[14] Varying the other substituents on the phosphine provided striking results; no clear trend emerged with increasing steric bulk, and DTBM-Segphos (**10**) and Cy-Segphos (**11**) provided similar ee, suggesting that more electron-rich ligands imparted increased selectivity (entries 4 and 5). Changing the solvent to fluorobenzene with catalytic Cy-Segphos $(AuOBz)_2$ provided optimal enantioselectivities (76% yield, 95% ee for **6**).

For this and most of the other enantioselective Au-catalyzed reactions discovered thus far, bisphosphine digold(I) complexes were used; the phosphorus:gold stoichiometry for Au(I) complexes derived from ligands **7**-**11** is 1:1, rather than 2:1 as in the **4**-ligated Au(I) catalyst used by Hayashi. Consequently, most Au(I) catalysts to date fit the general observation that Au(I) prefers a two-coordinate, linear coordination geometry.[15] Stable, isolable chiral phosphinegold(I) benzoate complexes were initially developed by Toste for allene hydroamination,[16] and generally are less reactive catalysts than cationic Au(I) species with relatively noncoordinating counterions.

2.2. With Achiral Catalysts

Lewis acidic activation of polar functionality in a racemic sense has also been relatively undeveloped with Au catalysts. Liu reported a remarkable example of catalyst-dependent selectivity in the Au-catalyzed Prins reaction of *cis*-2,4-dien-1-als and external nucleophiles (Table 2).[17] In the reaction of **12** with allyltrimethylsilane, $Ph_3PAuCl/AgSbF_6$ provided the double-addition product **13** in high yield (entry 4). Other Au sources, as well as other Lewis and Brønsted acids, provided significant or even exclusive quantities of elimination product **14**, which was formed as a mixture of olefin regioisomers (entries 1-3). The reaction presumably proceeds via cyclization and initial formation of a Au alkoxide, and given the observed products, the rate of proton elimination from this intermediate is retarded relative to that of intermolecular trapping when Au(I) is the catalyst.

Gold catalysts also have potential applications in polymerization chemistry. Recently, Ghosh applied *N*-heterocyclic carbene (NHC) Au(I) complexes to the polymerization of lactide.[18]

2.3. Carbonylation

Souma and Xu reported the carbonylation of olefins by a catalyst formed from Au_2O_3 and H_2SO_4 to produce carboxylic acids.[19] On the basis of spectroscopic studies, the authors proposed that $Au(CO)^+$ and $Au(CO)_2^+$ were present *in situ* and that $Au(CO)_2^+$ was a catalytically active species. In 2001, Deng investigated amines as nucleophiles in place of olefins and reported the Au-catalyzed carbonylation of amines to synthesize carbamates.[20] A variety of complexes were competent catalysts for the carbonylation of **15** to **16**, but the most efficient and selective catalysts were those formed with greater than 1:1 stoichiometry of phosphine:gold (Table 3, entries 3 and 5). Inferior selectivity was observed with a Au(III) precatalyst (entry 1). Given the harsh reaction conditions, the nature of the active catalyst remains an open question.

3. Addition of Nucleophiles to Carbon π-Electrophiles

This section includes reactions that proceed via addition of a nucleophile to a *π*-electrophile with subsequent proton transfer to close the catalytic cycle. Reactions proceeding by more complex mechanisms where the initially formed cation induces further bond scission and/or formation are covered in sections 4 and 5.

3.1. To Alkynes

3.1.1. Oxygen Nucleophiles to Alkynes—Fukuda and Utimoto first reported the addition of water and methanol to alkynes catalyzed by sodium tetrachloroaurate.[21] In a seminal contribution, Teles reported the intermolecular addition of alcohol nucleophiles to internal and terminal alkynes catalyzed by cationic phosphinegold(I) complexes on kilogram scale.[22] Ligand effects on the reactivity of the Au catalyst were examined for the addition of methanol to **17**, which provided the Markovnikov addition product **18** (Table 4). Catalyst activity inversely correlated with the Lewis basicity of the ligand, consistent with the hypothesis that increased electrophilicity of the Au catalyst confers greater reactivity. The comparison of PPh_3 with $P(OPh)_3$ indicates that higher reactivity comes at the expense of catalyst stability (entries 3 and 6). Several of Teles' observations later became the basis for further catalyst design and employment: an *N*-heterocyclic carbene (NHC) ligand catalyzed the hydroalkoxylation, while trinuclear Au complex $[(Ph_3PAu)_3O]BF_4$ was not sufficiently reactive. Teles also examined multiple methods for generating the cationic Au(I) catalysts, including protonation of the corresponding methyl complexes and halide or nitrate abstraction with silver salts or $BF_3 \cdot Et_2O$, respectively.

Teles' studies focused predominately on the addition of alcohol nucleophiles to alkynes, and hydration was only briefly mentioned in a patent filed contemporaneously.[22b] Tanaka later showed that phosphine-stabilized Au(I) complexes were efficient catalysts for addition of water to alkynes.[23] Methyl(triphenylphosphine)Au(I), in concert with sulfuric acid, provided an active catalyst for hydration of terminal and internal alkynes. High yields of the Markovnikov addition product were obtained with unsymmetrical alkynes, typically with low catalyst loading. Furthermore, the reaction showed promising chemoselectivity, as nitrile hydration was not observed.

When the amount of catalyst was brought below 0.1 mol% relative to **19**, poor conversion to **20** resulted, and a metallic precipitate was observed in the reaction mixture (Table 5, entry 1). Interestingly, the addition of electron-withdrawing ligands returned high activity (TON > 9000), and abolished precipitate formation (entries 2 and 3). The additive was proposed to exert a stabilizing effect on the Au complex, which enhanced catalyst lifetime without adversely impacting reactivity. Ligand basicity was an important parameter to consider, as additional triphenylphosphine completely inhibited the catalytic reaction (entry 4).

Schmidbaur examined isolable phosphinegold(I) carboxylates as catalysts for the hydration of 3-hexyne (Table 6).[24] It was necessary to add $BF_3 \cdot Et_2O$ to generate a cationic catalyst, demonstrating the relatively low reactivity of Au carboxylate complexes. Ligand effects were examined, though uniformly lower catalyst efficiencies were observed relative to those previously disclosed.

Although Teles mentioned in a footnote that nucleophilic carbenes are suitable ligands on Au for the hydration of alkynes, a more extensive study of this ligand type was deferred for several years. In 2003, Herrmann applied a Au(I) acetate complex bearing NHC ligand **23** to the hydration of **21** (Scheme 2).[25] The (NHC)Au(I) carboxylate was synthesized from the corresponding chloride complex.

Laguna employed sulfonated phosphine ligands to produce water-soluble phosphinegold(I) σ-acetylide complexes, such as **24**, which were examined as catalysts for alkyne hydration in H_2O (Figure 1).[26] Protic acid was required to generate an active catalyst, presumably via protonation of the acetylide ligand. High TOFs (>1000 h^{-1}) were obtained in some cases, and the feasibility of catalyst recycling was demonstrated by extraction of the product with organic solvent and reusing the Au-containing aqueous layer with new substrate.

Water-soluble Au(II) complex **25** with cocatalytic acid was also a viable catalyst for the hydroalkoxylation of phenylacetylene.[27] Although the TOF and TON compare poorly with other identified catalysts, this class of Au compounds has only been sparingly investigated in catalytic transformations. NHC-ligated Au(III) complexes have also been tested for the hydration of phenylacetylene, and TONs of ~10 were achieved.[28] Organometallic Au(III) complexes were similarly investigated, with TONs of up to 200 obtained.[29]

Nolan has investigated the formation of α,β-unsaturated carbonyl compounds from propargyl esters with cationic NHC-supported Au catalysts (Scheme 3).[30] Mechanistic work suggests that the transformation of **26** to **28** does not proceed via initial [3,3]-rearrangement of the propargyl ester, but rather by an S_N2'-type addition of water to the alkyne with displacement of the ester to form intermediate **27**. Sterically bulky NHC ligands were far superior to less encumbered ligands (I-*t*-Bu vs ITM). Zhang used phosphinegold(I) complexes for the same transformation.[31]

Unsurprisingly, the intramolecular addition of oxygen nucleophiles to alkynes is also readily catalyzed by Au complexes. Pale employed catalytic $AuCl/K_2CO_3$ in the cyclization of acetylenic alcohols and carboxylates to form oxacycles, a rare demonstration of a catalyst

mixture including Au and inorganic base.[32] An effective catalyst system could also be formed using Ph_3PAuCl/K_2CO_3, while Ph_3PAuCl alone did not catalyze the reaction.

3.1.2. Nitrogen Nucleophiles to Alkynes—The Au-catalyzed intramolecular addition of amine nucleophiles to carbon π-electrophiles dates to the work of Utimoto in 1987.[33] In 2003, Tanaka applied the Teles system for intermolecular hydroalkoxylation/hydration of alkynes to imine synthesis; he found that polyoxometalates are equal or superior to organic acids for the generation of an active Au catalyst from Ph $PAuCH_3$[34]. A tandem intramolecular hydroamination/intermolecular hydroamination sequence was developed by Li for the synthesis of *N*-vinyl indoles from *o*-alkynyl anilines.[35] Gold(III) complexes were among several viable catalysts tested, although the combination of $AuCl_3$/AgOTf permitted the lowest reaction temperature of all the catalysts.

A strong counterion effect was observed by Shin in the intramolecular cyclization of propargyl trichloroacetimidates (Scheme 4).[36] While treatment of **29** with Ph_3PAuCl and AgOTf resulted in only trace formation of **30**, use of $Ph_3PAuNTf_2$ or $Ph_3PAuCl/AgBF_4$ produced **30** in moderate yield. Although the different reaction times and lack of data on the mass balance of the reaction preclude a rigorous comparison, these results suggest that counterion effects may confound reaction optimization efforts. In this case, it is possible that Brønsted acid generated in situ from the Ag or Au salts mediates decomposition of the starting material, product, or both.

3.1.3. Carbon Nucleophiles to Alkynes

3.1.3.1. Hydroarylation: In an early example of carbon-carbon bond formation using alkynes and catalyzed by cationic Au(I), Reetz investigated the intermolecular hydroarylation of alkynes.[37] The differing regioselectivities observed for addition of mesitylene (**31**) to electron-rich alkynes such as **32** versus electron-poor alkynes such as **34** may be attributed to substrate control. Notably, different Au sources proved optimal for each type of substrate: $AuCl_3$/$AgSbF_6$ for addition to phenyl acetylene (**32**) (Scheme 5) and cationic phosphinegold(I) complexes for addition to methylacetylene carboxylate (**34**) (Table 7).

A closer examination of the optimization experiments for the hydroarylation of **32** with **31** to produce **33** illustrates that cocatalytic $AgSbF_6$ enhances the reaction. Strikingly, the use of $AgClO_4$ with $AuCl_3$ provides an inferior catalyst to $AuCl_3$ alone. Neither cationic Au(I) nor $AgSbF_6$ catalyze this reaction.

For the hydroarylation of ynoate **34**, the reaction proceeds with high regioselectivity to **35** in similar yield regardless of the oxidation state of the precatalyst. The diastereomeric ratio of the olefin isomers formed does vary with the catalyst, and cationic Au(I) catalysts were pursued owing to the superior diastereomeric ratios obtained (Table 7, entries 2-4). It is unclear whether the lower dr observed with $AuCl_3$ results from a kinetic or thermodynamic process (entry 1). A number of methods to generate the catalyst were successfully tested, including the use of $AgBF_4$ and $BF_3 \cdot Et_2O$ for chloride abstraction from phosphinegold(I)chloride (entries 2 and 3) and *in situ* mixing of AuCl, **36**, and a halide abstraction agent (entry 4).

Echavarren examined the intramolecular hydroarylation of alkynes with indoles, observing that the regioselectivity (formal 7-*exo*-dig vs 8-*endo*-dig) of the cyclization is highly dependent upon the catalytic Au source (Table 8).[38] In the cyclization of **37**,$Ph_3PAuCl/AgSbF_6$ resulted in little discrimination between the pathways leading to **38** and **39** (entry 4). Remarkably, AuCl and $AuCl_3$ overwhelmingly provided the eight-membered ring product **39** (entries 2 and 3). Diametrically, isolable complex **40** featuring a Buchwald-type ligand[39] provided exclusively the seven-membered ring product **38** (entry 1). Such cationic Au acetonitrile complexes

provide an additional isolable, stable alternative to the *in situ* generation of cationic Au complexes from phosphinegold(I) chloride and silver salts.[40]

3.1.3.2. Enol Nucleophiles: In 2004, Toste reported the 5-*exo*-dig addition of *β*-ketoesters to alkynes catalyzed by triphenylphosphinegold(I) chloride and silver triflate.[41] Au(III) chloride led to complete consumption of the starting material, but furnished only 30% of the desired product. The cationic Au source initially used by Hayashi/Ito, $[(CyNC)_2Au]PF_6$, provided no catalytic activity. Yang demonstrated that thiourea-supported Au(I) chloride complexes also catalyzed the cyclization reaction upon treatment with AgOTf, albeit far more slowly.[42]

Sawamura observed remarkable rate accelerations when triethynylphosphine-ligated Au(I) catalysts were used for 6-*exo*-dig *β*-ketoester additions, as in the cyclization of **41** to **42** (Table 9, entries 5 and 6).[43] It was proposed that a decrease in the entropy of activation, enforced by the "holey catalytic environment" of the ligand, was the source of increased catalytic activity in the cyclization. The triflimide (NTf_2) anion employed by Sawamura was initially used in Au catalysis by Gagosz, and generally behaves similarly to other weakly or noncoordinating counterions.[44] One key difference is that phosphinegold(I) triflimide salts are isolable and bench stable, in contrast to other cationic Au salts (i.e., SbF_6^-, BF_4^-, OTf^-), providing a preparative advantage. An analogous cationic Au(I)-catalyzed reaction using electron-rich alkenes, rather than 1,3-dicarbonyls, as the nucleophiles to produce similar products was studied by Echavarren, who found that an array of phosphine ligands were suitable.[45]

A striking dimerization reaction was observed by Hashmi while examining the reactivity of *o*-alkynyl benzyl alcohol **43** with Au catalysts (Scheme 6).[46] Generally, $AuCl_3$ led to higher selectivity for the dimerization product **49**, while the use of chloride-bridged cationic Au(I) complex $[(Mes_3\text{-}PAu)_2)Cl]BF_4$ provided larger quantities of the expected isochromene. The authors proposed that the reaction proceeds via transient formation of an α-carbene Au-carbenoid **45** from coordination of Au to the alkyne of **44**, which subsequently undergoes C-H insertion to form **46**. A mechanism proceeding through formation of enol tautomer **47** followed by Au-catalyzed addition to the alkyne, in analogy to the cyclizations discussed above, is also possible.[47] Protonation of **48** followed by olefin isomerization would provide **49**.

3.1.3.3. Cyclocarbinol Nucleophiles: The ring expansion of strained alkynyl cyclocarbinols was investigated by Toste.[48] The efficiency of the reaction was dependent upon ligand; $(4\text{-}CF_3\text{-}Ph)_3PAuCl/AgSbF_6$ provided exomethylene cyclobutane **51** from alkynyl cyclopropanol **50** in optimal yield and rate (Table 10). Triarylphosphines were generally superior to other examined ligands. A variety of propargyl cyclopropanols and cyclobutanols readily isomerized. In all cases, a single olefin isomer was obtained; the authors found this to be a kinetic process, and, with additional supporting evidence, proposed a mechanism proceeding by activation of the alkyne followed by Pinacol-type ring expansion.

3.1.4. Fluoride Nucleophiles to Alkynes—Sadighi investigated the nucleophilic addition of fluoride to alkynes catalyzed by Au(I) complexes, which resulted in *trans*-hydrofluorination products.[49] Although triphenylphosphine and sterically unencumbered NHC ligands on Au resulted in low yields, bulkier NHC ligands efficiently provided vinyl fluorides. In the course of these investigations, two stable (NHC)Au(I) complexes were isolated, including an η^2-alkyne complex and a complex with a *tert*-butoxide counterion. The (NHC)Au(*tert*-butoxide) was a competent catalyst for the reaction as compared with the analogous catalysts derived from (NHC)AuCl and $AgBF_4$.

3.2. To Allenes

3.2.1. Oxygen Nucleophiles to Allenes

3.2.1.1. Hydroalkoxylation: Krause noted significant differences in reactivity for the Au-catalyzed cyclization of *β*-hydroxy allenes to dihydropyrans upon screening multiple catalytic Au sources and additives (Table 11).[50] Either the rate or yield of the $AuCl_3$-catalyzed transformation of **52** to **53** could be improved upon addition of pyridine or 2,2-bipyridine, respectively (entries 2 and 3). The highest reaction rates were observed with cationic Au(I) catalysts, even at decreased temperature (entries 4 and 5).

Krause's investigation of chirality transfer in the cyclization of diastereomerically enriched allenyl alcohols is illustrative of the possibility that optimization of the Au catalyst may impact not only the desired transformation, but also other pathways available to the substrate (Table 12).[51] In this case, epimerization of both allene **54** and dihydrofuran **55** may be catalyzed by various Au or other Lewis acidic species formed *in situ* (entries 1 and 2).[47c] The addition of bipyridine as an additive permitted the isolation of highly diastereoenriched dihydrofurans (entries 3 and 4); the authors propose that the bipyridine acts as a ligand to attenuate the Lewis acidity of the catalyst, slowing epimerization. It is also possible that addition of a base helps to buffer small amounts of Brønsted acid generated under the reaction conditions. Notably, lowering the reaction temperature without additive provided the same benefit as adding bipyridine (entry 5).

In 2006, Widenhoefer reported the Au-catalyzed intramolecular hydroalkoxylation of allenes.[52] Choice of counterion in the cocatalytic silver salt was crucial to optimizing the regioselectivity of the nucleophilic addition in reactions where 5-*exo*-trig- and 6-*exo*-dig-derived products were competitively formed. For example, treatment of **56** with 5% (*o*-biphenyl)(*t*-Bu)$_2$PAuCl/AgOTf provided a 1.3:1 mixture of **57** and **58** (Table 13, entry 1), while use of the same Au complex with AgOTs provided exclusively the 5-*exo* product **57** in 96% yield (entry 2). This selectivity contrasts nicely with that observed for a previously employed Pt(II) complex (entry 3).[53]

3.2.1.2. Asymmetric Hydroalkoxylation and Hydrocarboxylation: In 2007, Widenhoefer described the asymmetric intramolecular hydroalkoxylation of allenes, as exemplified by the transformation of **59** to **60** (Scheme 7).[54] Hydroalkoxylation to afford tetrahydrofuran and tetrahydropyran architectures was investigated. Of the chiral ligands examined on Au(I), Biphep derivative **62**[55] provided optimal enantioselectivities in conjunction with AgOTs as the halide abstraction reagent. Catalyst control of the sense of asymmetric induction was absolute, overriding any bias that might arise due to the chirality of the allene. Chiral allenes reacted to afford products in the same enantiomeric series, which differed only in olefin geometry, as demonstrated by the hydrogenation of **60**, a mixture of *E*/*Z* olefin isomers, to form **61** in the expected ee.

In a paradigm shift for enantioselective Au catalysis, Toste then reported that the use of chiral counterions, rather than chiral neutral ligands, could provide high enantioselectivity in additions of oxygen nucleophiles to allenes.[56] In the hydroalkoxylation of *γ*-hydroxy allenes, neither noncoordinating (BF_4) nor more coordinating (OPNB) counterions associated with dicationic chiral bisphosphine(digold) species induced significant enantioselectivity in the cyclization of **63** to **64** (Table 14, entries 1-3). Chiral counterions with nonchiral phosphines were then investigated, and high ee was obtained. Chiral Binol-derived phosphoric acid **65** in conjunction with the dppm ([bis(diphenyl)phosphino]methane) ligand proved optimal (entry 4).[57,58] Consistent with a mechanism involving intimate ion pairing, changing the solvent to benzene from methylene chloride provided tetrahydrofuran **64** from **63** in 90% yield and 97%

ee. Some dependence of the ee on the nonchiral phosphine was observed, as Ph_3PAuCl provided lower ee compared to the dppm complex.

When attempting to extend the chiral counterion strategy to carboxylate nucleophiles, Toste found that neither chiral phosphine ligands nor chiral organophosphate counterions provided high levels of enantioselectivity (Table 15, entries 1 and 2). Crucially, use of both chiral components together synergistically provided higher enantioselectivity in the cyclization of **66** to γ-lactone **67**. Both the mismatched (entry 3) and matched (entry 4) cases were identified, indicating that the transition state for the enantio-determining step is influenced by both the ligand on Au and the counterion, and providing another promising avenue for rendering catalytic reactions asymmetric in the future.

3.2.1.3. Isomerization of Allenyl Ketones: In 2005, while studying the cyclization of haloallenyl ketone **68**, Gevorgyan reported divergent product distributions favoring either **71** or **75** depending upon the oxidation state of the Au precatalyst (Scheme 8).[59] The divergent product selectivity was proposed to be a consequence of the increased oxophilicity of Au(III) relative to Au(I). In the Au(III)-catalyzed reaction, activation of the carbonyl induces bromonium ion formation. Intermediate **70** then cyclizes to 3-bromo-furan **71**. With Au(I), activation of the allene by the catalyst produces **73**/**74**, which undergoes [1,2]-H-shift to liberate 2-bromo-furan **75**. Higher selectivity for the formation of **75** was observed with Et_3PAuCl than with Ph_3PAuCl. Since no mention of a cocatalytic halide abstraction agent is made, this appears to be a rare example of π-acidic activation by a neutral phosphinegold(I) halide.

Che applied Au(III)porphyrin complexes to the cycloisomerization of allenones to furans.[60] The porphyrin precatalysts offered superior yields compared to other Au complexes under the reaction conditions, and, importantly, showed little evidence of decomposition, in contrast to the instability generally observed with $AuCl_3$. The catalyst was subjected to ten cycles of reaction, isolation, and resubjection to substrate, demonstrating over 800 turnovers per reaction and a total TON of 8300.

3.2.2. Nitrogen Nucleophiles to Allenes—The Au-catalyzed intramolecular hydroamination of allenes has been extensively investigated by Krause.[61] The intermolecular hydroamination of allenes was disclosed by Yamamoto in 2006.[62] Initially, the addition of anilines to allenes was found to be optimally catalyzed by $AuBr_3$. Further studies to develop conditions for the use of morpholine (**77**) as the nucleophile with allene **76** demonstrated the need for an alternative catalyst; halide salts such as $AuBr_3$ were not suitable (Scheme 9).[63] Instead, cationic phosphinegold(I) catalysts were successfully employed in the synthesis of **78**. The authors noted that optimal yields were obtained with ortho-substituted triaryl phosphine ligands, and suggested that a steric, rather than electronic effect, was responsible for improving the reaction efficiency.

Intramolecular hydroamination of allenes has recently emerged as a proving ground for the potential of modulating both the ligand and counterion of phosphinegold(I) catalysts to achieve high enantioselectivities. Initially, Toste subjected **79** to an *in situ* generated catalyst formed from 3% (*R*)-xylyl-Binap$(AuCl)_2$ and 6% $AgBF_4$, which produced the expected pyrrolidine **80** in high yield but dismal ee (Table 16, entry 1).[16] Varying the stoichiometry of the silver salt relative to Au revealed marked differences in selectivity: use of 3% $AgBF_4$ with 3% (*R*)-xylyl-Binap$(AuCl)_2$ produced **80** in 51% ee (entry 2).

Given the unexpected influence of the counterion stoichiometry on enantioselectivity, other, more coordinating counterions were screened in the hydroamination. This represented the first use of such counterions in asymmetric catalysis with Au, and contrasted previous investigations of Au(I) carboxylates, which generally were precatalysts that required further activation by

Lewis acids (see section 3.1.1). Although the benzoate anion provided superb enantioselectivity, catalyst reactivity was depressed (entry 3). Further screening of substituted benzoates demonstrated that 4-nitro-benzoate struck an ideal balance between reactivity and selectivity (entry 4), presumably due to attenuated Lewis basicity imparted by the electron-withdrawing group. Thus, phosphinegold(I) 4-nitrobenzoate catalysts, which could be isolated and stored, provided high yields and enantioselectivities for a variety of pyrrolidine and piperidine products (14 examples, 81-99% ee) (entry 5).

Later, while examining the potential of chiral counterions in asymmetric Au catalysis, Toste revisited the allene hydroamination.[56] With dppm as the ligand on Au(I) and a chiral phosphoric acid counterion, **65**, high ee's could be obtained, demonstrating a second strategy for the highly enantioselective synthesis of azacycles.

Widenhoefer reported the analogous reaction with Cbz-protected amines as the nucleophiles. Dicationic chiral bisphosphine digold complexes were used with ClO_4 as the counterion.[64] High enantioselectivities (>80% ee) were obtained in four cases using DTBM-OMe-Biphep (**62**)as the ligand. Furthermore, the reaction was demonstrated to proceed with a substrate scope complementary to that reported by Toste, since the protecting group on nitrogen differs (Cbz vs Ts). Additionally, the DTBM-OMe-Biphep- $(AuCl)_2/AgClO_4$-catalyzed reaction was optimized for terminally unsubstituted allenes, which were not previously reported. Some dependence of the enantioselectivity on the counterion was observed, but neither coordinating nor chiral counterions were investigated, rendering a direct comparison to the Toste systems impossible.

Widenhoefer subsequently applied his catalyst system to the dynamic kinetic resolution of trisubstituted γ-amino allenes (Scheme 10). This investigation is a striking exploitation of the Au-catalyzed allene racemization previously observed by Toste[47c] and Krause,[51] which enables the dynamic resolution. As in previous work, Widenhoefer employed DTBM-OMe-Biphep (**62**) as the chiral ligand. Overall, high diastereoselectivities and moderate rate differences in the reaction of each enantiomer of the starting allene were observed.[65] Based on the absolute configurations of the cyclic products, the stereochemical outcome of the cyclization appears to be under catalyst control. Regardless of the stereochemistry of the allene **81**, products in the same enantiomeric series are obtained ((*R*,*E*)-**82** and (*R*,*Z*)-**82** as shown).

3.2.3. Carbon Nucleophiles to Allenes—The Au-catalyzed intramolecular hydroarylation of *N*-arylallenamines was investigated by Fujii and Ohno.[66] Cationic phosphinegold(I) complexes were highly active catalysts for the transformation. The parent $Ph_3PAuCl/AgOTf$ catalyst provided the dihydroquinoline product in 57% yield; marked improvement (98% yield) was observed with (*o*-biphenyl)(t-Bu)$_2$P as the ligand.

En route to an enantioselective synthesis of (-)-Rhazinilam, Nelson subjected diastereomerically enriched allene **83** to Au-catalysis in order to achieve intramolecular hydroarylation (Table 17). The desired tetrahydroindolizine **84** could be isolated in good yield.[67] High regioselectivity was observed for all of the catalysts tested, but reactivity and chirality transfer were sensitive to the precise catalyst. Although $AuCl_3$ provided the product in high d.r., only low yield was obtained (entry 2). Use of $AuCl_3/AgOTf$ as the catalyst mixture dramatically improved reactivity (entry 3), and $Ph_3PAuCl/AgOTf$ provided even higher yield and fidelity in the chirality transfer (92% yield, 97:3 d.r.) (entry 4).

Widenhoefer reported the enantioselective addition of indoles to pendant allenes with dicationic, axially chiral digold bisphosphine complexes.[68] A significant effect of the counterion on enantioselectivity was observed in the cyclization of **85** to **86** for the weakly coordinating counterions screened (Table 18). Optimization of the ligand revealed that bulky

aryl substituents on the phosphine were crucial to achieving high enantioselectivity regardless of the axially chiral structural motif used (Binap or Biphep). Further optimization of the solvent and temperature in the reaction catalyzed by 2.5% DTBM-OMe-Biphep$(AuCl)_2$/5% $AgBF_4$ permitted **86** to be obtained in 88% yield and 92% ee.

3.3. To Alkenes

3.3.1. Heteroatomic Nucleophiles to Alkenes—Reports on the intermolecular addition of phenols, carboxylic acids, and amines to olefins with catalytic amounts of Au emerged in 2005.[69] A similar mode of reactivity was observed by Li in the annulation of phenols and dienes with $AuCl_3$/AgOTf.[70] Subsequently, investigations by Hartwig and He suggested that some of these additions may be catalyzed by Brønsted acid formed under the reaction conditions.[71]

In early 2006, Widenhoefer reported the intramolecular cyclization of alkenyl carbamates, such as **88**, catalyzed by Au(I).[72] The nature of the phosphine ligand in this process had a dramatic effect on conversion, with (*o*-biphenyl)(*t*-Bu)$_2$P emerging as the most advantageous (Table 19, entry 5). The poor yield of **89** obtained from cyclization of **88** with dimethylphenylphosphine relative to that with the biphenyl phosphine ligand implies that steric protection of the metal center enhances reaction efficiency (entry 4). Comparison of the yields of **89** obtained with triaryl phosphines bearing electron-donating (entry 2) and electron-withdrawing (entry 3) substituents further suggests that more electron-rich phosphines provide superior catalysts, a surprising notion considering the increased Lewis acidity that electron-deficient ligands should confer on the metal center.

Application of this catalyst system to the cyclization of alkenyl carboxamides further demonstrated the importance of the ligand, as a variety of *N*-acyl substrates could be cyclized in high yield, representing the first transition metal-catalyzed hydroamination with such nucleophiles.[73] Control experiments demonstrated that no conversion of the starting material occurred in the presence of TfOH.

The use of biphenyl based ligands on Au(I) allowed the hydroamination reaction to be conducted at 60 °C - 80 °C for the majority of substrates examined. In order to further reduce the required temperature, Widenhoefer sought a more active catalyst system through steric and electronic adjustment of the supporting ligand. This ultimately led to the employment of NHC ligands on Au(I).[74] The benefits of this ligand modification are readily apparent in the cyclization of urea **90** with IPrAuCl/AgOTf, which occurred at room temperature as opposed to at 80 °C with the phosphine-supported catalyst. The isolated yield of pyrrolidine **91** was also slightly higher with the (IPr)Au(I) catalyst (Scheme 11).

3.3.2. Carbon Nucleophiles to Alkenes—In 2004, Li reported the intermolecular addition of 1,3-diketones to styrenes in the presence of catalytic $AuCl_3$ and a silver salt.[75] The reaction yield is dependent upon the silver salt used, and very low reactivity was exhibited by $AuCl_3$ in the absence of Ag. The authors propose a mechanism proceeding by formal insertion of Au into the methylene C-H bond of the nucleophile; activation of the olefin as an electrophile by Brønsted acid formed *in situ* also seems possible.

Che reported the intramolecular cyclization of alkene-tethered *β*-ketoamide compounds catalyzed by Au(I) complexes.[76] A variety of *γ*- and *δ*-lactams could successfully be accessed. Optimal yields were obtained with Au[P(*t*-Bu)$_2$(*o*-biphenyl)]Cl/AgOTf at 50 °C.

4. Cascade Reactions Initiated by Carbon Nucleophiles with π-Electrophiles

4.1. Hashmi Phenol Synthesis

In 2000, Hashmi reported the intramolecular cyclization of alkynyl furans to phenols with Au (III) chloride.[77] In the ensuing years, his group has dedicated immense effort to the understanding and extension of this Au-catalyzed arene synthesis. Despite the reaction's many successes, catalyst stability was a persistent concern, and likely a consequence of the ligand-free system.[78] To address this obstacle, Au(III) complexes **92**, **93**, **94**, and **95** bearing pyridine-derived ligands were tested for catalytic activity in the cyclization reaction (Figure 2).[79]

Turnover numbers approaching 1200, as opposed to between 20 and 50 for the chloride salt, were observed in the isomerization of furan **96** to phenol **97** (Scheme 12). Of the three carboxylate-containing ligands, acceptor-substituted species **94** provided the most reactive Au catalyst, consistent with the anticipated increase in electrophilicity of the metal center (Scheme 12).

Although an arene oxide had long been suspected as a key intermediate in the phenol synthesis, such a species was never observed in the $AuCl_3$-catalyzed reaction. Interestingly, when a catalytic quantity of pyridine alkoxide complex **98** was used, up to 80% of an equilibrium mixture of **99** and **100** was obtained (Scheme 13).[80] Precisely why changing the nature of the catalyst allows for the detection of these sensitive intermediates is unclear; the ligated Au(III) complex somehow alters the reaction coordinate such that breakdown of compounds **99**/**100** is slow relative to their formation.

Though complexes in the plus three oxidation state were remarkably active catalysts for the intramolecular phenol synthesis, none were capable of promoting the intermolecular variant. When readdressing the activity of Au(I) complexes in 2006, Hashmi noted a significant effect of precatalyst structure on reactivity in the intermolecular reaction of **32** with **101**.[81] Typical mononuclear precatalysts, including $(Et_3P)AuCl$, $(Ph_3P)AuCl$, and (tht)AuCl (tht = tetrahydrothiophene), in combination with $AgBF_4$ failed to provide acceptable results. Dinuclear bisphosphine complexes, such as $(dppm)(AuCl)_2$, also resulted in inefficient cyclization. However, dinuclear catalysts containing a bridging chloride ligand were remarkably effective in promoting the formation of **102**, albeit with competitive formation of **103** (Scheme 14). It was suggested that employing a dinuclear catalyst precursor provided a stable resting state, which allowed reversible entry into the catalytic cycle.

4.2. 1,5 Enynes

In 2004, Fürstner and Toste independently reported the cationic Au(I)-catalyzed cycloisomerization of 1,5-enynes to [3.1.0] bicyclic products.[82] Toste observed that $AuCl_3$ was less reactive than $Ph_3PAuCl/AgOTf$; attempts to generate a more active Au(III) catalyst by addition of a silver salt resulted in the formation of significant decomposition products. In the course of investigating a related cycloisomerization of 6-siloxy-1,5-enynes to form cyclohexadienes, Kozmin determined that AuCl could also catalyze the formation of [3.1.0] bicycles from 1,5-enynes.[83]

In his initial investigation, Toste observed that MeOH could serve as an external nucleophile to trap the proposed intermediate **109** and provide alkoxy-cyclization product **105**. Kozmin subsequently investigated the analogous intramolecular trapping by using substrates with tethered nucleophiles (i.e., **104**, $R_2 = CH_2OH$) to form compounds such as **106**.[84] Shin recently extended this strategy to include intramolecular trapping by a carbonate (**104**, $R_3 = OBoc$).[85] In the carbonate cyclization, Buchwald-type ligands provided superior catalyst reactivity compared to Ph_3P.

Gagosz observed yet another class of cycloisomerization/nucleophilic addition products. When 1,1-disubstituted 1,5-enynes were subjected to cationic Au(I), alkoxy cyclization products such as **108** were formed, presumably via a change in the regioselectivity for intermolecular trapping of **109** (Scheme 15).[86] The change in regioselectivity was apparently substrate-controlled; the site best able to stabilize carbocationic character was attacked by the nucleophile. A further element of control was provided by the ligand. Gagosz observed that the use of $Ph_3PAuNTf_2$ provided a mixture of the desired alkoxy-cyclization product and products arising from direct alkoxylation of the alkyne, while sterically encumbered Buchwald ligand **107** provided the desired product in high yield and selectivity.

Kirsch investigated the reaction of 3-siloxy-1,5-enyes with Au catalysts, finding that the cationic intermediate generated via initial cyclization of the olefin onto the alkyne may be trapped by intramolecular Pinacol shift.[87] The active catalyst was generated, as usual, by halide abstraction from Ph_3PAuCl with $AgSbF_6$. In testament to the mild reaction conditions proffered by cationic Au(I) catalysts, excess Au was needed to ensure that no soluble Ag species remained in the reaction solution; both the starting material and products were decomposed in the presence of Ag^+.

A number of 1,5-enynes containing heteroatoms have been investigated with Au catalysts. Substrates bearing an oxygen tether at the 4-position underwent a formal [3,3] isomerization.[88] This propargyl Claisen rearrangement, as reported by Toste, demonstrated two separate selectivities that needed optimization: discriminating between [1,3] and [3,3] isomerization of **110** and maintaining chiral information during the [3,3] rearrangement of enantioenriched **110** (Table 20). Trinuclear complex $[(Ph_3PAu)_3O]BF_4$ provided **111** in high yield and with excellent conservation of stereochemical information (entry 3). Further experiments demonstrated that Au-catalyzed racemization of the product allene was likely responsible for the poor chirality transfer observed with mononuclear phosphinegold(I) catalysts (entries 1 and 2). The precise nature of the active catalytic species remains unclear, but precatalytic assemblies such as the trinuclear complex employed may offer further potential for tuning the properties of Au catalysts. A similar system employing modified substrates was later investigated by Kirsch in a tandem propargyl Claisen/allenone cycloisomerization to produce furans.[89]

1,5-enynes bearing silicon tethers have also been studied. The cationic Au(I)-catalyzed cycloisomerization/alkoxylation of allyl vinyl silanes was investigated independently by Lee and Toste.[90] Depending on the external nucleophile, different regioselectivity for trapping was observed; methanol trapped at the carbocation generated from 6-*endo*-dig cyclization of the olefin onto the alkyne, while phenol trapped at the silyl cation generated subsequent to β-silyl fragmentation. A substantial rate acceleration was attained through use of $(t\text{-Bu})_3PAuCl$ rather than Ph_3PAuCl as the precatalyst.

4.3. 1,6 Enynes

In 2004, Echavarren reported the cycloisomerization and methoxycyclization of 1,6-enynes catalyzed by phosphinegold(I) complexes (Scheme 16).[91] Depending on the reaction conditions, either skeletally rearranged product **114** or methanol-trapped product **115** could be isolated in high yield from the reaction of **113**. Tricyclohexylphosphine could be used as an additive in the alkoxycyclization without an adverse effect on the reactivity, as exemplified in the conversion of enyne **116** to cyclopentane **117** (Scheme 17). Conversely, addition of triphenylphosphine or bisphosphines such as dppm greatly retarded the reaction rate, presumably due to catalyst inhibition. A staggering diversity of Au-catalyzed skeletal rearrangements have subsequently been discovered for variously substituted and tethered 1,6 enynes, with the product distribution generally being substrate, rather than catalyst, dependent.

In 2005 Echavarren reported on the benefits of biphenyl based ligands in the Au(I)-catalyzed methoxycyclization of enynes.[92] Good yields of **115** could be obtained from **113** with a variety of triaryl phosphine ligands (Table 21). Tri(*o*-tolyl)phosphine provided higher yield than Ph_3P (entry 2). Buchwald-type ligand (*o*-biphenyl)$(Cy)_2P$ provided nearly quantitative yield of **115** in significantly shortened reaction time (entry 4).

Yoshifuji reported that phosphaalkeneAu(I) chloride complexes **118**, **119**, and **120** catalyze the 1,6-enyne cycloisomerization even in the absence of a halide abstraction agent (Scheme 18).[93] The complexes could be recovered and reused. The authors speculate that the low-lying LUMO of the phosphorus-carbon double bond may increase the electrophilicity of the formally neutral Au center, presumably via increased backbonding from Au into the ligand.

Subsequently, 1,6-enynes have been extensively studied as model substrates for demonstrating alternative modes of reactivity available in Au-catalyzed reaction manifolds. Thus, compound **121** was prepared in order to provide pendant functionality for the trapping of proposed intermediate **122** (Scheme 19). Cationic acetonitrile complexes, including the parent triphenylphosphine complex, were ultimately utilized as catalysts for a biscyclopropanation process initiated by 1,6-enyne cyclization.[94] Such acetonitrile complexes may be isolated and stored as salts with noncoordinating anions (i.e., BF_4), thereby obviating the need for a silver cocatalyst and *in situ* catalyst generation.[40] Replacing the tethered olefin with a carbonyl moiety or a 1-cyclopropan-2-ol group resulted in Prins or Pinacol-type trapping, respectively.[95]

Intermolecular trapping of the proposed cyclopropyl carbenoid intermediate (i.e., **122**) with olefins has also been investigated. Echavarren found that PPh_3 (Table 22, entry 1) and a biphenyl phosphine (entry 2) exhibited only modest selectivity in differentiating between skeletal rearrangement and intermolecular cyclopropanation pathways. A phosphite ligand was similarly unselective, providing 40% yield of **125** and 52% yield of rearrangement products **126** and **127** from **124** (entry 3). In contrast, intermolecular cyclopropanation with norbornylene was the dominant pathway when NHC ligand IMes was used (entry 4).[96] Although the selectivity observed with IMes might suggest that steric effects are responsible for the product ratio, similarly high selectivity for **125** was also observed with “ligandless” AuCl (entry 5).

Subsequently, Toste explored the oxidation of Au carbenoid intermediates, and reported that 1,6-enynes readily participated in cycloisomerization/oxidation in the presence of diphenylsulfoxide, as exemplified by the transformation of **124** to **128** (Scheme 20).[97] As noted by Echavarren in the above cyclopropanation experiments, the highest selectivities for trapping with sulfoxide rather than skeletal rearrangement were obtained with bulky NHC ligands.

Further intermolecular trapping studies on 1,6-enynes were carried out with indoles as nucleophiles.[98] In the case of **129**, regioisomeric products arising from trapping of the proposed metallocarbenoid were observed (Scheme 21). Rather than observing ligand-dependent competition between the nucleophilic addition and skeletally rearranged products, Echavarren instead saw the competitive formation of constitutionally isomeric trapping products. Phosphine- and phosphite-based catalysts provided **131** from addition by indole to the metallocarbenoid in intermediate **130**, in analogy to a 1,2-addition, while the IMes ligand demonstrated increased selectivity for **132**, presumably formed from trapping remote to the carbenoid in **130**, in analogy to a 1,4-addition.

Michelet and Genêt previously reported the 1,4-trapping of 1,6-enyne-derived metallocarbenoids with a variety of electron-rich arenes using $Ph_3PAuCl/AgSbF_6$[99]. For substrates examined by both Michelet/Genêt with $Ph_3PAuCl/AgSbF_6$ and Echavarren with

((2,4-(*t*-Bu)$_2$-Ph)O)$_3$PAuCl/AgSbF$_6$, significant differences in product yield or selectivity are not evident, although the Echavarren system used much lower temperature (-50 °C vs 40 °C).

Helmchen similarly applied the Ph$_3$PAuCl/AgSbF$_6$ catalyst system to the intermolecular trapping of metallocarbenoid reaction intermediates with carbonyl compounds.[100] The substitution patterns on the substrates were crucial to successful trapping; only primary alkenes, such as in substrate **133**, were tolerated, in contrast to those tested in the indole trapping experiments described above (Scheme 22). The carbonyl insertion reaction to provide **141** is particularly remarkable considering that, in the absence of benzaldehyde, **136** is the major product, which presumably arises via *endo* cyclization of **133** to intermediate **134**. In contrast, compound **141** presumably forms via *exo* cyclization of **133** to cyclopropyl carbenoid **137**, indicating that there is an additive effect on the regioisomeric outcome of the cyclization. Whether this effect arises due to a reversible initial cyclization of **133** or due to a reversal in the kinetic preference for formation of **134** or **137** remains unclear. Echavarren previously observed cyclopropanation of metallocarbenoid **138**, suggesting that trapping of this intermediate is not additive-specific.[96]

In 2005, Echavarren published an asymmetric variant of the methoxy cyclization of 1,6-enynes, representing the first reported Au-catalyzed enantioselective reaction since the seminal work of Hayashi/Ito 20 years prior.[101] Despite synthesizing a variety of Au-complexes, with various supporting ligands (eleven were discussed in the report), Echavarren found a general asymmetric reaction to be elusive. Ultimately, tol-Binap was selected as the optimal ligand, although ferrocenyl ligands Josiphos and Walphos also provided promising levels of enantioselectivity (42% ee and 38% ee, respectively). Under optimized conditions, enyne **142** was converted to cyclopentane **143** with an impressive 94% ee, but the five additional examples did not proceed in greater than 55% ee (Scheme 23).

4.4. 1,*n*-Allenynes

In 2006, Aubert, Fensterbank, and Malacria jointly reported their studies on the cycloisomerization of 1,7-allenynes with electrophilic late transition metal catalysts.[102] Halide-containing complexes, including PtCl$_4$, NaAuCl$_4$, and AuCl, catalyzed the formation of fused [4.3.0] bicyclic product **145** from **144** (Scheme 24). Alternatively, conjugated triene product **146** was obtained as a mixture of olefin regioisomers upon reaction of **144** with cationic Au and Pt complexes lacking halides.

The authors proposed that the divergent product selectivities arise due to the viability of a mechanistic pathway proceeding by transient formation of HCl with chloride-containing catalysts. It should be noted that cationic phosphinegold(I) catalysts such as Ph$_3$PAuSbF$_6$ were generated from the corresponding gold chloride complex and AgSbF$_6$. Thus, if the presence or absence of halides is indeed responsible for the product distribution, this serves as a testament to the insolubility/spectator status of AgCl under the reaction conditions.

1,6-Allenynes have also been investigated as substrates for Au-catalyzed cycloisomerization. Liu found that AuCl and AuCl$_3$ were unreactive, while cationic phosphinegold(I) complexes readily catalyzed a skeletal rearrangement.[103]

4.5. 1,*n*-Allenenes

Toste reported the cationic Au(I)-catalyzed synthesis of cyclopentadienes from vinyl allenes.[104] Although Ph$_3$PAuCl/AgSbF$_6$ was an efficient catalyst system for most of the substrates examined, higher yields could be obtained in certain cases using (*t*-Bu)$_3$PAuCl/AgSbF$_6$. The alternate conditions were especially useful for substrates bearing protected alcohol and amine functionality.

Zhang investigated the cycloisomerization of 3,4-dihydroxyl-1,5-allenenes bearing different protecting groups on the alcohols (Scheme 25).[105] The product selectivity was under substrate-control, and products of type **148** or **149** were formed depending upon the alcohol protecting groups employed. Use of 2-pyridine carboxylate as a ligand on Au(III) afforded higher yields of the desired products than $AuCl_3$, although those obtained with AuCl were comparable. Cationic phosphinegold(I) complexes were poor catalysts in these cases.

Enantioselective cycloisomerizations of 1,7-allenenes have recently been developed by Gagne and Toste (Scheme 26). Although the two groups investigated differently substituted allenenes leading to two different classes of products, similar catalyst systems were employed. The divergent behavior may be ascribed to the substitution patterns of the substrates, which determine the regioselectivity of the initial addition of the alkene to the allene by preferentially stabilizing one possible cationic reaction intermediate over another. Bulky aryl substituents on the phosphines within chiral biaryl-based bisphosphine digold complexes provided the maximum ee's.

Gagne investigated allenes of type **150** possessing 1,1-disubstituted olefins ($R_1 \neq H$,) and terminally unsubstituted allenes ($R_3 = H$), which isomerized to cyclohexenes such as **151/152**.[106] These products were isolated as mixtures of olefin isomers. Using 3% (*R*)-xylyl-Binap$(AuCl)_2$/6% AgOTf as the catalyst, **150** could be converted to **151/152** in 77% ee as a 3.5:1 mixture. A general enantioselective reaction proved elusive; all of the other substrates examined provided lower ee's. Notably, the regioisomeric mixture obtained was somewhat dependent upon catalyst. Ratios ranging from 3.5:1 to 1:3 could be obtained depending upon the chiral phosphine employed.

Toste investigated allenes of type **150** possessing 1,2-disubstituted olefins ($R_1 = H$, R_2 = aryl) and terminally substituted allenes ($R_3 \neq H$).[107] These substrates underwent formal [2 + 2] cycloadditions[108] to form diastereomerically pure fused [3.2.0] bicycles. The reaction was rendered enantioselective through the employment of 3% (DTBM-Segphos)$(AuCl)_2$/6% $AgBF_4$. Product **153** could be obtained in 92% yield and 95% ee; other substrates bearing geminal diesters in the allenene backbone cyclized with similarly high enantioselectivities (6 examples, 92-97% ee). For reasons yet undetermined, replacing the diester with a sulfonamide linker resulted in sharply decreased ee.

4.6. 1,6-Diynes

Liu observed dramatic effects on reactivity and product selectivity in the [3 + 2] or [4 + 2] annulation of aryl-substituted 1,6-diynes depending on the catalyst (Table 23).[109] The SbF_6^- counterion proved most effective in attaining high yield of a single product, **155**, from **154** (entry 1). Conversely, experiments with other counterions (i.e., OTf^-) and gold sources (AuCl, $AuCl_3$) resulted in the erosion or even reversal of product selectivity (entries 2-4).

5. Cascade Reactions Initiated by Heteroatom Nucleophiles with π-Electrophiles

In the cycloisomerization reactions reviewed above, the carbocation generated upon nucleophilic addition of one π-bond (alkene or allene) to another (alkene, allene, or alkyne) may be stabilized by backbonding from Au to form carbenoid intermediates or be quenched by other bond rearrangement processes. The following section covers transformations that are initiated by addition of a heteroatomic nucleophile to a Au-activated electrophile. The resulting cationic intermediates are proposed to undergo further rearrangements, rather than simple proton transfer as exemplified by the reactions covered earlier in this review (section 3). The subdivisions of this section are organized according to the fate of the initially formed cation.

5.1. Bond Scission

5.1.1. Carbocationic Leaving Groups

5.1.1.1. Carbonyl Nucleophiles: Gagosz investigated the cyclization of propargyl *tert*-butyl carbonates to 4-alkylidene-1,3-dioxolan-2-ones using phosphinegoldtriflimide complexes.[110] The cation intially formed by cyclization of the carbonate onto the alkyne is quenched by loss of *tert*-butyl cation. Although $Ph_3PAuNTf_2$ smoothly catalyzed the cyclization of several substrates, propargyl esters containing electron-rich internal alkynes, such as **157**, were inert under the initially developed conditions (Scheme 27). The use of an electron-withdrawing ligand provided a more reactive catalyst, $(4\text{-}CF_3\text{-}Ph)_3PAuNTf_2$, for the cyclization of these problem substrates, presumably due to the increased Lewis acidity of the metal center. For these substrates, the expected cyclization product was not obtained; instead, a further rearrangement occurred, as exemplified by the transformation of **157** to **158**.

An analogous 6-*exo*-dig cyclization of homopropargyl carbonates catalyzed by cationic Au(I) was reported by Shin.[111] Carretero, Gagosz, and Shin changed the heteroatom linker, using *N*-Boc propargyl amines rather than carbonates, and found cationic Au(I) complexes to be superior to simple Au salts.[112]

Bäckvall studied the intramolecular hydrocarboxylation of allenes, finding that methyl esters may serve as nucleophiles in such transformations (Scheme 28).[113] The yield of **160** obtained from **159** with catalytic $AuCl_3$ could be augmented by the addition of AgOTf as an additive, and similar yield could be obtained with AuCl/AgOTf without the need for superstoichiometric silver relative to Au.

Shin studied additive effects in the Au(III)-catalyzed cyclization of allenyl *tert*-butyl carbonates.[114] While addition of Ph_3P completely shut down the catalytic activity of $AuCl_3$, perfluorinated phosphine $P(C_6F_5)_3$ or triethoxyphosphite were tolerated in cocatalytic quantities. Although the role of the phosphine is unclear, this is a notable rare example of a Au (III)/phosphine catalyst system.

5.1.1.2. *o*-Alkynyl Benzylic Ethers: In 2006, Toste reported the intramolecular carboalkoxylation of alkynes to form indenyl ethers, which proceeds by cyclization of the ether onto the alkyne, C-O bond scission to generate a benzylic carbocation, and finally trapping of the cation by the vinyl Au moiety (Scheme 29).[115] The reaction is stereospecific; enantioenriched benzylic ethers transfer stereochemical information to the newly formed tertiary carbon stereocenter. The reactivity was highly dependent upon both the counterion and ligand present; an electron-deficient phosphine in conjunction with $AgBF_4$ proved optimal. Highest yields of the methyl enol ether **162** were obtained from **161** upon addition of molecular sieves, which were proposed to inhibit hydrolytic deprotection of the methyl enol ether and formation of **163**.

5.1.1.3. Allyl transfer: Recently, Gagosz reported a pyrrole synthesis that proceeds by initial intramolecular cyclization of a trisubstituted nitrogen to generate a reactive ammonium species.[116] In this chemistry, upon cyclization of the allyl substituted amine onto the pendant alkyne in **164**, the resulting 1,5-diene **165** undergoes an aza-Claisen rearrangement en route to the corresponding 2-substituted pyrrole **167** (Scheme 30). Regiospecific crotyl transfer and lack of crossover between double-labeled substrates were observed, consistent with intramolecular shift of the allyl-substituent via a concerted [3,3]-rearrangement. Relative to Au(I) complexes with PPh_3 and Buchwald-type ligands, $(4\text{-}CF_3\text{-}C_6H_4)_3PAuCl$ provided superior reactivity and selectivity. A similar furan synthesis was recently disclosed.[117]

5.1.2. Cationic Heteroatomic Leaving Groups

5.1.2.1. Homopropargyl Azides: An early investigation into the potential for Au(I) species to serve as a "pull-push" catalyst, to first activate an electrophile by withdrawing electron density and then stabilize the resulting cation by backbonding, was based on the hypothesis shown in Scheme 31, wherein a nucleophile tethered to a leaving group would add to Au-activated alkyne **168**. Loss of the leaving group from **169** would generate Au-stabilized cationic intermediate **170**.

The acetylenic Schmidt reaction was reported by Toste in 2005.[118] In order to execute this process in an efficient manner, a dinuclear Au bisphosphine catalyst was required (Table 24). Bisphosphine digold catalysts provided optimal yield of pyrrole **172** from homopropargyl azide **171**, apparently due to increased turn-over numbers (entries 4 and 5). The origin of this benefit remains obscure; it may be due to longer catalyst lifetime owing to stabilizing aurophilic interactions.[119]

The proposed carbenoid intermediate formed after loss of N_2 could be trapped with diphenylsulfoxide.[97a] Substrates bearing hydrogen substituents at the propargyl position rapidly formed the pyrrole products even in the presence of sulfoxide. In order to slow the rate of pyrrole formation, gem-dimethyl substituted substrate **173** was synthesized, since the [1,2] alkyl shift to form **176** should be slower than [1,2] hydrogen shift (Scheme 32). Even so, it was necessary to optimize the catalyst to slow the rate of alkyl shift relative to oxidation. With a bulky NHC ligand, the desired pyrrolone **175** was the predominant product.

5.1.2.2. Alkyne-Tethered Sulfoxides: In early 2007, Toste demonstrated that homopropargyl sulfoxides undergo a series of Au-catalyzed cycloisomerization reactions, which afforded benzothiepinones or benzothiopines depending on the alkyne substituent.[120] As was observed in certain enyne cycloisomerization reactions, *N*-heterocyclic carbene ligands provided superior catalysts relative to phosphine-stabilized systems for the isomerization of **177** to **179** (Scheme 33). Zhang studied the same reaction and found that dichloro-(pyridine-2-carboxylato)Au(III) also catalyzed the annulation in good yield.[121] Zhang extended the methodology to replace the final annulation step with a Pinacol-type ring-expansion to trap the Au-carbenoid intermediate, again finding that (NHC)Au(I) complexes were optimal catalysts.

Toste similarly investigated propargyl sulfoxides, and divergent product selectivity was observed depending on the catalytic Au source used (Scheme 34). While cationic Au(I) catalysts yielded complex product mixtures from **180**, (DMS)AuCl (DMS = dimethylsulfide) provided **181** in high yield. Alternatively, catalytic AuCl provided the dimerization product **182** in high yield along with the corresponding disulfide. The reason for the diametric selectivity remains unclear; Malacria has previously proposed that the active catalysts formed *in situ* from AuCl are actually Au(III) species, and perhaps these demonstrate different activity than Au(I) catalysts.[102] The drastically different reaction concentrations also cannot be ignored.

5.2. Addition of Nucleophiles

5.2.1. Addition of Nucleophiles to o-Alkynyl Benzaldehydes—*o*-Alkynyl benzaldehydes have been extensively investigated for their reactivity with Au catalysts, as the formation of benzopyrylium species by intramolecular addition of the aldehyde to the alkyne provides a highly reactive intermediate for subsequent intra- or intermolecular trapping. In 2002, Yamamoto and Asao reported the Au(III)-catalyzed intermolecular [4 + 2] annulation of *o*-alkynyl benzaldehydes and alkynes (Scheme 35).[122] Substituted naphthalenes were synthesized in good yield with $AuCl_3$ and $AuBr_3$, although the authors reported slightly improved yields and faster reaction times with $AuBr_3$, as observed in the conversion of **183** to

184.[123] By tethering an alkyne to *o*-alkynyl benzaldehyde, Oh developed an intramolecular variant on this reaction that undergoes [3 + 2] rather than [4 + 2] annulation. The authors propose that strain in the transition state of the cycloaddition dictates the product selectivity. In this case, $AuBr_3$ again was found to more efficiently catalyze the reaction than $AuCl_3$.

In 2006, Li reported the synthesis of 1-alkynyl-1H-isochromenes by reaction of *o*-alkynyl benzaldehydes with terminal alkynes (Table 25).[124] The reaction was carried out in H_2O/toluene with catalytic phosphinegold(I) chloride catalysts, without need to abstract the chloride with a cocatalyst. Notably, the same substrates (**183** and **32**) that underwent Yamamoto's formal [4 + 2] cycloaddition, as described above, were diverted down an alternative reaction pathway to **185** by Li's conditions.

Iwasawa reversed the connectivity on the aldehyde moiety, using *N*-(2-alkynyl-phenyl)-aldimines as precursors for azomethine ylides and subsequent cycloadditions with electron-rich alkenes.[125] $AuBr_3$ was a superior catalyst relative to Au(I) complexes. Li investigated the annulation of salicylaldehyde **186** and **32** to produce isoflavanone **187**, and found catalytic $AuCN/PBu_3$ in toluene at 150 °C to be the optimal reaction conditions (Scheme 36).[126] The regioisomer of the product obtained is opposite to that expected for a process initiated by intermolecular hydroalkoxylation of **32** by **186**, leading the authors to propose an unusual Au-mediated activation of the aldehydic C-H bond. Mechanistic alternatives include an unanticipated reversal in the regioselectivity of the hydroalkoxylation for the particular substrates/conditions examined or a reaction proceeding via initial nucleophilic addition of the aldehyde to the alkyne, oxa-6-π electrocyclization, and isomerization to **187**.

5.2.2. Addition of Nucleophiles to Other Oxocarbenium Species—Kirsch incorporated an alkyl [1,2]-Pinacol-type shift into a tandem process involving cyclization/migration to synthesize 3-(2H)-furanones (Scheme 37).[127] Carbocycles and simple alkyl substituents readily underwent the [1,2]-shift. Both Au(I) and Au(III) sources were examined as possible catalysts, and $AuCl_3$ readily catalyzed the reaction of **188** to **189**, via proposed intermediate **190**, in high yield. Alternatively, only decomposition products were observed in the reaction of **188** with catalytic $Ph_3PAuCl/AgBF_4$. A similar strategy relying upon strain-release ring-expansion rather than the Pinacol shift to trap the oxonium intermediate was disclosed by Schmalz, who found that cationic Au(I) catalysts actually offered superior reaction rates and yields compared with those of neutral Au halides.[128]

Shi investigated the reactivity of epoxides tethered to alkynes, and products arising from initial attack of the epoxide oxygen onto the alkyne followed by intermolecular epoxide ring-opening with oxygen nucleophiles were obtained.[129] For a model substrate, the yield of the reaction showed a pronounced counterion effect; $Ph_3PAuCl/AgOTf$ provided 25% yield of the desired product while switching to $AgSbF_6$ raised the yield to 68%.

5.3. Migration of Propargyl (and Other) Esters

5.3.1. [2,3]-Migration of Propargyl Esters—In 1984, Rautenstrauch first demonstrated the generation and intramolecular trapping of intermediates with carbenelike behavior from propargyl esters using a palladium(II) catalyst.[130] In 2005, Toste reported a Au(I)-catalyzed version of the Rautenstrauch rearrangement.[131] Stereochemical information from enantioenriched 3-acetoxy-1,4-enynes was conserved in the resulting cyclopentenones, an observation inconsistent with formation of a full metallocarbenoid intermediate.[132] It was necessary to optimize the counterion and temperature to obtain high fidelity in the chirality transfer reaction. Although AgOTf with Au(I) efficiently catalyzed the cycloisomerization of racemic substrates in high yield, $AgSbF_6$ was superior for the synthesis of enantioenriched substituted cyclopentenones.

Fürstner had previously studied the cycloisomerization of 5-acetoxy-1,6-enynes, as opposed to the 3-acetoxy-1,4-enynes studied by Rautenstrauch and Toste, with Au and Pt halides.[133] He also reported a single example of the cycloisomerization of a 4-acetoxy-1,5-enyne catalyzed by $Ph_3PAuCl/AgSbF_6$.[82a] In 2006, Nolan investigated similar substrates with cationic Au(I) complexes bearing NHC and phosphine ligands.[134] By tethering two alkenes within substrate **191**, Nolan studied the intramolecular competition between [3.1.0] and [4.1.0] bicycle formation (Table 26).

Surprisingly, two regioisomeric [3.1.0] products, **193** and **194**, were observed with (IPr)AuCl/$AgBF_4$ (entry 2). Although products similar to **193** had been previously observed by Fürstner, **194** was the major product in this case. The product distribution varied depending on the ligand employed; triphenylphosphine provided the [4.1.0] bicycle **192** somewhat selectively (entry 1). When AgOTf, rather than $AgBF_4$, was used as the halide abstraction reagent with (IPr)AuCl, the selectivity inverted, and the [4.1.0] pathway dominated (entry 4). In all of the cycloisomerizations of acetoxy-enynes, it is difficult to differentiate between mechanisms initiated by carbocyclization as opposed to those initiated by propargyl ester migration.

Ohe and Uemura reported that metallocarbenoids generated from [2,3]-rearrangement of propargyl esters undergo intermolecular cyclopropanation with olefins.[135] Ruthenium complexes were optimal catalysts, though Au(III) chloride was also examined. In November of 2005, Toste reported a Au(I)-catalyzed variant of the Ohe-Uemura cyclopropanation in which ligand effects were manifest in the diastereoselectivity of the transformation of **195** to **196** (Scheme 38).[136] Given the high steric bulk of $(t\text{-Bu})_3P$ and the observation that phenyl propargyl pivaloate **197** provided the product *cis*-**200** as a single olefin isomer, a stereochemical model accounting for the observed diastereoselectivity was proposed. Cyclopropanation is proposed to occur via the less sterically encumbered Au carbenoid **198** to provide the *Z*-olefin isomer, while the transition state *cis*-**199** is favored over *trans*-**199** due to steric clash between the ligand on Au and the substituent on the incoming olefin (Scheme 39).

The diastereoselective cyclopropanation was extended to an asymmetric variant using chiral phosphine ligands on Au. Bisphosphine digold catalysts afforded the desired product with good enantioselectivity, while MOPAuCl, a mononuclear monophosphine complex bearing a similar axially chiral backbone, resulted in very low enantioselectivity. Ultimately, bulky aryl substituents on the phosphines were found to induce greater ee, with the catalyst formed from (*R*)-DTBM-Segphos$(AuCl)_2$ and $AgSbF_6$ proving optimal (Scheme 40). Enantioselectivities ranging from 76% to 94% for a series of eight cyclopropanes of type **201** were obtained.

Further investigations into the intermediate formed by [2,3]-rearrangement of propargyl esters with Au were carried out by Toste in 2007.[97a] It was found that the proposed metallocarbenoid could be trapped by nucleophilic oxidants, specifically diphenyl sulfoxide. When pivaloate ester **197** was treated with cationic Au(I), diastereomeric ratios of complex **202** between 3:1 for the triphenylphosphine complex and 99:1 for the IPr complex were observed (Scheme 41). The *E*:*Z* ratio for the resulting olefin appears to be under kinetic control, based on the observed failure of the *Z* isomer to isomerize under the reaction conditions.

Echavarren explored the trapping of the proposed metallocarbenoid intermediate **198** with carbon nucleophiles.[137] When 1,3-diphenyl-1,3-propanedione was reacted with phenyl propargyl acetate, a catalyst-dependent mixture of the carbenoid-trapping product and the propargyl substitution product was obtained.[138] Consistant with the hypothesis that bulky ligands inhibit intramolecular bond reorganization relative to intermolecular trapping, NHC-supported catalyst $IMesAuCl/AgSbF_6$ provided a mixture of products. In contrast, AuCl or phosphine-ligated complexes provided exclusively the desired product arising from trapping subsequent to the [2,3]-rearrangement.

In 2006, Toste investigated carbenoid intermediates derived from 1-acetoxy-2,4-pentadiynyl substrates.[139] Notably, although two regioisomeric metallocarbenoids could conceivably be formed, only a single cyclopropanation product was obtained in all cases examined. A tandem cyclopropanation/hydroarylation process leading to benzonorcaradiene products was described. Although the initial cyclopropanation could be catalyzed by Au(I) and Au(III) complexes, only cationic phosphinegold(I) complexes efficiently catalyzed the one-pot tandem process.

5.3.2. [3,3]-Migration of Propargyl Esters—Ligand effects on olefin geometry were observed by Zhang in the reaction of **203** to **204** (Table 27). The reaction mechanism is proposed to be initiated by [3,3]-rearrangement of **203**.[140] Use of 2-pyridinecarboxylate as the ligand on Au(III) resulted in significant enrichment of the *E* olefin isomer, in contrast to $AuCl_3$. Further studies on other substrates showed the *E*:*Z* ratio was not constant throughout the reaction, making it unclear whether the ligand effect results from increased kinetic preference for formation of one olefin isomer, or a change in the rate of olefin isomerization to form a thermodynamic product mixture.

In 2006, Nolan reported the Au-catalyzed formation of indenes from aryl propargyl esters.[141] When bulky (NH-C)Au(I) complexes were used in the reaction of **205**, a tandem process involving [3,3]-rearrangement/hydroarylation to produce **206** was preferred over direct hydroarylation to **207** (Table 28, entries 3 and 4). This contrasts the low selectivity observed when $Ph_3PAuCl/AgBF_4$ was employed as the catalyst (entry 1). Toste reported the synthesis of naphthyl ketones via a tandem [3,3]/Myers-Saito sequence from similar substrates bearing 2-alkynyl substitution on the aryl ring catalyzed by $(t\text{-Bu})_3PAuCl/AgSbF_6$[142].

Alkene nucleophiles can also be used to engage the allene intermediates stemming from [3,3]-rearrangement of propargyl acetates. Gagosz found that, in analogy to 1,5-enynes, *in situ* generated 1,5-allenenes underwent a cycloisomerization reaction to afford bicyclo[3.1.0] hexenes (Table 29).[143] A bulky Buchwald-type ligand provided greater reactivity compared with other electron-rich or electron-deficient phosphines, and nearly quantitative conversion of **208** to **210** occurred for the tandem process. With the other catalysts, significant quantitites of **209** were isolated. Gagosz also developed a tandem [3,3]/allenol cyclization strategy to produce dihydrofurans.[144]

A similar strategy of generating allene functionality *in situ* was investigated by Shin for a tandem [3,3]/ring expansion reaction of *O*-acetylated propargyl cycloalkanols.[145] Shin found that the ligand employed on the cationic Au(I) catalyst influenced the relative rates of [3,3]-isomerization vs direct ring expansion[48] and of allene hydroalkoxylation vs ring expansion.

Building upon the tandem [3,3]-rearrangement/Nazarov cyclization of 5-acetoxy-1-penten-3-ynes reported by Zhang,[146] Malacria reported that, in the reaction of **211**, the proposed metallocarbenoid intermediate **214** could be intercepted by a tethered alkene to provide cyclopropanation product **215** (Scheme 42).[147] Cationic Au(I) complexes were more active catalysts for the reaction compared to $AuCl_3$, and use of PPh_3 as the ligand provided superior selectivity for **215** compared to a Buchwald-type ligand, which produced a substantial quantity of **216**. The choice of ligand apparently influences the rate of intramolecular cyclopropanation relative to [1,2]-H-shift.

5.3.3. Other Ester Migrations

5.3.3.1. Homopropargyl Acetates: As discussed so far in this section, the Au-induced rearrangement of propargyl acetates provides access to a diverse array of reaction pathways. An alternate pathway to the [3,3]- and [2,3]-migrations discussed so far was exploited by Zhang for the synthesis 1,4-cyclohexadienes by cycloisomerization of 3-acetoxy-1,5-enynes (Scheme

43).[148] The reaction of **217** to **220** is initiated by 6-*exo*-dig cyclization of the ester onto the alkyne to produce intermediate **218**, rather than the typical 6-*endo*-dig addition. This is one of few examples where a vinyl Au intermediate (**219**) is proposed to react as a nucleophilic carbanion.[149] Dichloro(pyridine-2-carboxylato)Au optimally catalyzed the reaction, which did not proceed in the presence of cationic Au(I) complexes.

5.3.3.2. Allenyl Acetates: The [3,3]-rearrangement of allenyl acetates has been investigated by Gagosz for the synthesis of 2-acetoxy-1,3-dienes (Table 30).[150] High selectivity for the *E*-olefin isomer was obtained, which was rationalized as a kinetic phenomenon. Gold(III) bromide was insufficiently reactive and did not catalyze the transformation (entry 1). The parent $Ph_3PAuNTf_2$ catalyst provided only 15% conversion of **221** to **222** in 24 h (entry 2), while use of a bulky biphenyl phosphine ligand resulted in full conversion to **222** after only 3 h (entry 3).

5.3.3.3. Allylic Acetates: Allylic acetates have also been investigated as substrates in a Au-catalyzed hetero-Claisen rearrangement.[151] Nolan reported the [3,3]-rearrangement of *O*-acetylated benzyl-allyl-alcohols to the corresponding styrenyl acetates with cationic NHC-ligated Au catalysts. The use of bulky NHC ligands was crucial in mitigating oligomerization and other decomposition pathways.

6. Oxidation Reactions

In contrast to the rich oxidation chemistry catalyzed by heterogeneous Au species,[1b,c] oxidative transformations catalyzed by homogeneous Au catalysts have only been sparingly investigated. Initial work in this area dates to 1983, when Gasparrini reported the oxidation of sulfides to sulfoxides in the presence of catalytic Au(III) salts.[152]

Recent advancements in catalytic oxidation chemistry were presaged by Cinellu, who found that bipyridine-ligated Au(III)-oxo complex **223** stoichiometrically reacted with norbornene to afford alkene complex **224**, auraoxacyclobutane **225**, and various oxidized organic products (Scheme 44).[153] Although stoichiometric, this work foreshadowed the utility of nitrogen donor ligands for catalytic homogeneous oxidation, and suggested that alkene oxidation might be possible.

6.1. Oxidation of Alcohols

In late 2005, Shi and co-workers reported the Au(I)-catalyzed oxidation of primary and secondary alcohols, using molecular oxygen as the terminal oxidant (Scheme 45).[154] Striking success was attained when Au(I) chloride was used along with anionic 1,3-diimine ligand **228**, affording 96% isolated yield of benzaldehyde (**227**) from benzyl alcohol (**226**) after 24 h. Data for the reaction catalyzed by other ligand-Au complexes were not reported, so it is not possible to draw any conclusion on the role of the ligand.

6.2. Oxidative Cleavage of Olefins

In early 2006, Shi reported the Au(I)-catalyzed oxidative cleavage of alkenes, using *tert*-butyl hydrogen peroxide as the stoichiometric oxidant.[155] As with the oxidation of alcohols discussed earlier, nitrogen donor ligands were used in the optimal reaction conditions (Table 31). The choice of ligand drastically influenced reactivity, with the highest reaction rate and conversion to **230** obtained with a neocuproine ligand (entry 5). In this reaction, as in the oxidation of **226**, the precise mechanism and role of Au remain uncertain.

Despite the success of nitrogen donor ligands in recent reports of homogeneous Au-catalyzed oxidation, they are not required for oxidative behavior. Shortly after Shi reported the oxidative

cleavage of alkenes, Liu described a tandem hydroalkoxylation/oxidative cleavage reaction of alkynols (Scheme 46).[156] The oxidative cleavage of **232** occurred in the presence of the familiar (Ph_3P)AuCl/AgOTf catalyst system to provide **233**, illustrating that such reactivity is also accessible with phosphine-ligated Au complexes. Additionally, Toste has reported the oxidation of Au-carbenoid intermediates with sulfoxides in the presence of phosphine- and NHC-supported catalysts.[97a] Further details on the oxidation of various intermediates can be found elsewhere in this review (sections 4.3, 5.1.2.1, 5.3.1).

7. Reductive and Dehydrogenative Reactions

7.1. Hydroboration/Diboration

As with oxidative transformations, Au(I)-catalyzed reductive and dehydrogenative reactions remain rare. In 1995, Baker and Westcott described a series of three-coordinate Au(I) phosphine complexes and their application as catalysts for imine hydroboration.[157] A less sterically encumbered polymeric catalyst containing the diphenylphosphinoferrocene ligand demonstrated enhanced reaction rate, by at least a factor of 2, over the other catalysts examined for the reaction of **234** to **236** (Table 32).

Very shortly after their report on imine hydroboration, Baker and Westcott described the diboration of vinylarenes catalyzed by an *in situ* generated three-coordinate Au(I) phosphine complex.[158] Neither triethylphosphine- nor triphenylphosphine-ligated Au catalysts affected the desired diboration reaction, but when dcpe (ethane-1,2-bis-diylbis-(dicyclohexylphosphine)) was added to a solution of triethylphosphinegold(I) chloride, an active catalyst mixture was obtained.

7.2. Silylation

Approximately 5 years after the original Baker/Westcott report, Hosomi reported a Au(I)-catalyzed hydrosilylation of aldehydes and ketones.[159] When a colorless DMF solution of benzaldehyde and triphenylphosphinegold(I) chloride was treated with dimethylphenylsilane, a rapid darkening of the reaction mixture to deep purple occurred, and a metallic precipitate was formed. Under these conditions, no carbonyl hydrosilylation product was obtained. Strikingly, when tributylphosphine was used as an additive, clean formation of the desired silyl ether was observed by ^{1}H NMR spectroscopy, and the solution remained colorless and homogeneous throughout the reaction (Scheme 47). This additive effect is reminiscent of that described in the diboration system in section 7.1. The reduction of **227** to **226** is particularly intriguing considering that the reverse reaction can also be catalyzed by Au under different conditions, as described in section 6.1. Stradiotto observed similar additive effects in studies on the hydrosilylation activity of Au catalysts supported by indenyl-phosphine ligands in the same reaction.[160] Low conversions were observed when 3% (3-*i*-Pr_2P-indene)Au(I) chloride was employed, but addition of substoichiometric quantities of the ligand as an additive permitted full conversion of benzaldehyde to the hydrosilylation product.

Horvath applied fluorous phase-soluble, recyclable Au(I) catalysts to the hydrosilylation reaction and suggested that the excess phosphine might serve as an organocatalyst to generate an electrophilic intermediate from the carbonyl substrate.[161] Corma extended this mode of reactivity with Au-catalysts to include the hydrosilylation of styrenes with Au(I) and Au(III) precatalysts.[162] In the absence of excess phosphine, Ph_3PAuCl was inactive as a catalyst, but replacing the phosphine with a more labile ligand (tetrahydrothiophene) restored reactivity. No information on the regioselectivity of the hydrosilylation (linear vs branched products) was provided.

An alternative use of silanes as reductants was developed by Ito and Sawamura, who reported the hydrogenative coupling of silanes and alcohols catalyzed by Au(I) (Table 33). [163] When a

three-coordinate (Xantphos)Au(I) chloride complex was employed, quantitative conversion to the desired silyl ether **238** from **237** was observed (entries 5 and 6). The source of the superior catalytic activity of Xantphos is unclear, but its unique reactivity suggests that geometrically constrained coordination environments might provide a means to tuning the activity and selectivity of Au catalysts.

7.3. Hydrogenation

In the spring of 2005, Corma and co-workers reported the first example of Au-catalyzed asymmetric carbon-hydrogen bond formation using a Duphos-ligated complex (Scheme 48).[164] Despite containing data on only four substrates, with the enantioselectivities ranging from 20% to 95%, this paper stands out as a rare example of π-bond reduction using a purportedly homogeneous Au catalyst.[165]

8. Group Transfer Reactions

8.1. Diazo-Derived Carbene Transfer

The catalytic decomposition of α-diazoesters to metal-carbenes has a storied history with the group 11 elements.[166] Up to 2004, however, homogeneous Au-catalyzed carbene transfer reactions of diazoesters were unknown. Nolan, Díaz-Requejo, and Pérez reported the first such process in the summer of 2005, using *N*-heterocyclic carbenes as stabilizing ligands.[167] The ligand choice, in this instance, served to compare the Au-catalyzed transformation with a copper-catalyzed version reported one year earlier.[168] As was observed in the copper system, diazo coupling was completely suppressed. Surprisingly, both cyclopropanation (**242**) and C-H insertion (**243**) products were observed in the reaction of **241** with styrene, as opposed to only cyclopropanation products as obtained from the Cu-catalyzed reaction (Scheme 49).

As carbene insertion into aryl carbon-hydrogen bonds rarely competes with alkene cyclopropanation in metal-catalyzed reactions of diazoesters, further investigation of the Au-catalyzed system was warranted. Removing the cyclopropanation pathway by employing benzene rather than styrene as the reactant, Nolan et al. observed a 3-to-1 mixture of C-H and C-C insertion products. Notably, the product selectivity using the IPr complex differed markedly to that observed with a terpyridine ligated Au catalyst, as reported by He (Scheme 50).[169] The suppression of diazo-coupling with IPr was not observed with the *N*-donor ligand. Temptingas it is to attribute these results to a ligand-controlled phenomenon, the change in counterion and temperature cannot be ignored.

A clearer example of the ability to influence product selectivity through ligand modification was uncovered when the Nolan-Díaz-Requejo-Pérez catalyst system was applied to insertion of **241** into alkane C-H bonds (Table 34).[170] Dramatic differences in product selectivity in the formation of **248** and **249** were observed when a series of (NHC)Au(I) complexes were tested. With IPr, predominant functionalization of 1° C-H bonds was observed, while a diametric product distribution was exhibited by the IMes-supported catalyst.

8.2. Nitrene Transfer

In addition to carbene transfer, Au-catalyzed nitrene transfer has also received attention. In 2006, He described the reaction of styrenes with an *in situ* generated iodinane.[169] This process utilized a Au(I) catalyst and terpyridine supporting ligand. The Au(III)-mediated functionalization of benzylic C-H groups with nitrenes was recently reported by He.[171]

9. Activation of Terminal Alkynes

9.1. With Carbonyl Electrophiles

Following up on an earlier report on Mannich-type three-component couplings,[172] Li found that α-oxyaldehydes, amines, and terminal alkynes react to produce propargyl amines in the presence of catalytic amounts of Au(I) complexes.[173] The reactions were run in water, and AuI was a more reactive catalyst than AuCl.

Che studied the three-component Mannich-type reaction of aldehydes, amines, and terminal alkynes.[174] Salen Au(III) complexes were successfully employed as catalysts for the reaction, which could be run in aqueous medium. A Au(III)porphyrin complex was not a suitable catalyst. An enantioenriched analogue of artemisinin was synthesized through use of a proline-derived amine, which permitted the subsequent diastereoselective alkynylation of the *in situ* formed imine to provide stereodefined products. Che furthermore used the intermolecular hydroamination of alkynes with anilines as the basis for a tandem process leading to dihydroquinolines and quinolines, wherein the enamine formed from the initial intermolecular hydroamination tautomerizes to form an iminium electrophile, which is trapped by a second equivalent of alkyne en route to the products.[175]

9.2. In Cross-Coupling Reactions

While attempting to better understand the heterogeneous Au-catalyzed cross-coupling of iodoarenes and terminal alkynes (Sonagashira-type reaction), Corma investigated the reactivity of Schiff-base Au(I) and Au(III) complexes[176] Intriguingly, the results were highly dependent upon the oxidation state of the homogeneous precatalyst employed. While the Au(I) complex **250** effectively catalyzed the formation of alkynyl benzenes, Au(III) complex **251** does not provide the same product, instead mediating alkyne homocoupling (Figure 3).[177] The Sonagashira-type hetero-coupling of iodoarenes and alkynes could also be catalyzed by Ph_3PAuCl.

In 2007, Bertrand reported a Au-catalyzed variant of the Crabbe homologation, where enamines serve as carbene donors and react with terminal alkynes to provide allene cross-coupling products (Scheme 51).[178] Remarkably, only the cationic complex formed via chloride abstraction from a Au complex ligated by cyclic (alkyl)(amino)carbene ligand **256** provided the allene product **254** from **32** and **252**. Other typical Au(I) catalysts overwhelmingly provided propargyl amine **255**, likely via addition of a Au-acetylide to a transiently generated iminium species. Mechanistic experiments suggested that **254** did not form via the propargyl amine **255**. The proposed mechanism for formation of **254** involves several steps and organometallic intermediates rarely invoked in Au catalysis, including oxidative addition of a Au-acetylide to a **252**-derived iminium species, α-elimination to liberate **253** and generate a Au(carbene)(vinylidene) intermediate, and finally reductive elimination to form **254**.

10. Conclusions

Although a great deal of empirical information is now available on means to control selectivity in homogeneous Au catalysis, the development of new catalysts and reactions continues to rely upon trial and error. Nonetheless, certain ligand classes have emerged as privileged structures for Au-mediated reactions. Some loose guidelines may be distilled from the available data:

a. For carbophilic activation with Au(I), the reactivity and selectivity of cationic Au(I) complexes may be tuned by switching the ligand. Biphenyl-substituted phosphines and NHC ligands have repeatedly been observed to induce greater reactivity and modulate selectivity among competing reaction pathways.

b. The stability of Au(III) catalysts may be greatly improved with *N*-donor ligands. In some cases, the reactivity of the Au(III) center may be attenuated. Such ligands have also been successfully employed with Au(I) precatalysts in oxidation and group transfer reactions.

c. Axially chiral, biaryl-based bisphosphine ligands with a 1:1 P:Au stoichiometry have been successfully employed in the development of new catalytic, asymmetric reactions. Chiral phosphoric acids are capable of inducing high levels of enantioselectivity in additions of nucleophiles to allenes.

d. Three-coordinate bisphosphine Au(I) chloride complexes are particularly effective for reduction and hydrogen atom transfer.

As Au-catalyzed reactions continue to emerge from laboratories worldwide, undoubtedly the area of ligand-controlled selectivity will be of paramount interest. Further understanding of active catalysts should allow for the development of models to predict and understand reaction outcomes, perhaps even leading to the rational design of new ligands.

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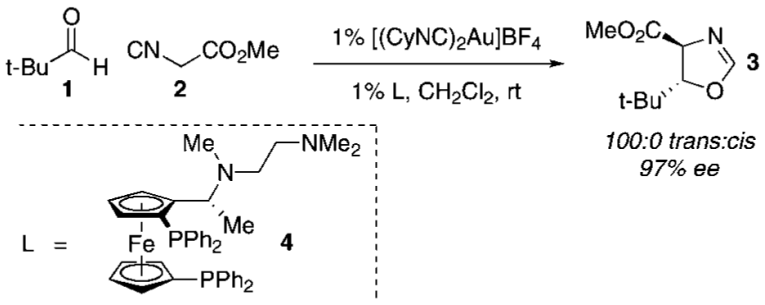
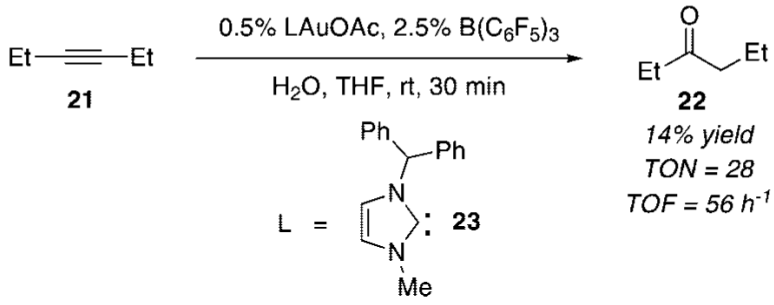
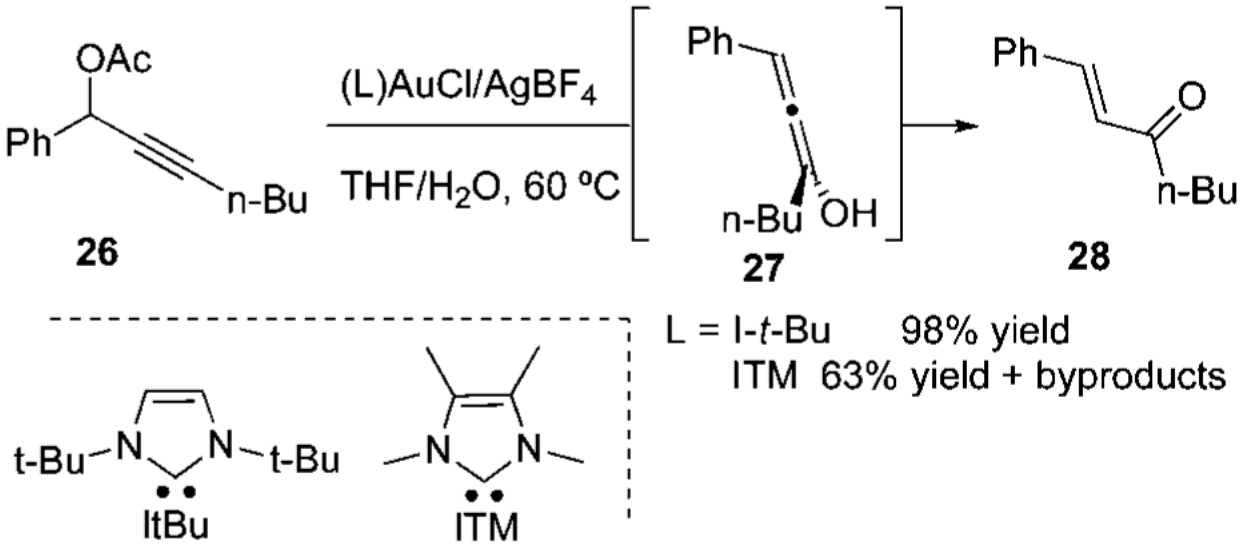


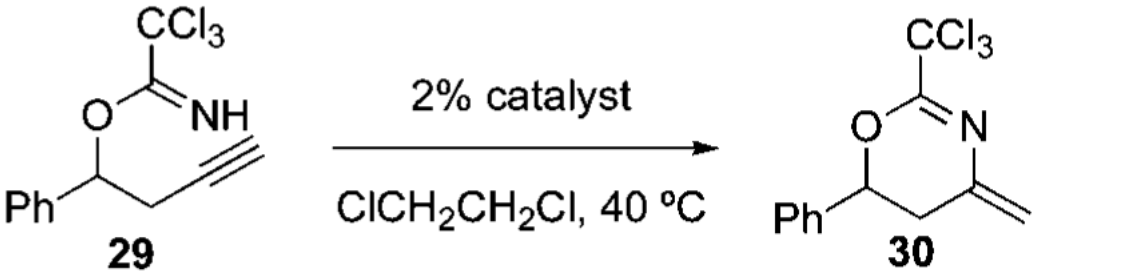
Scheme 1.



Scheme 2.

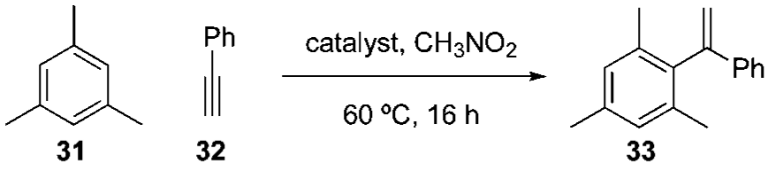


Scheme 3.



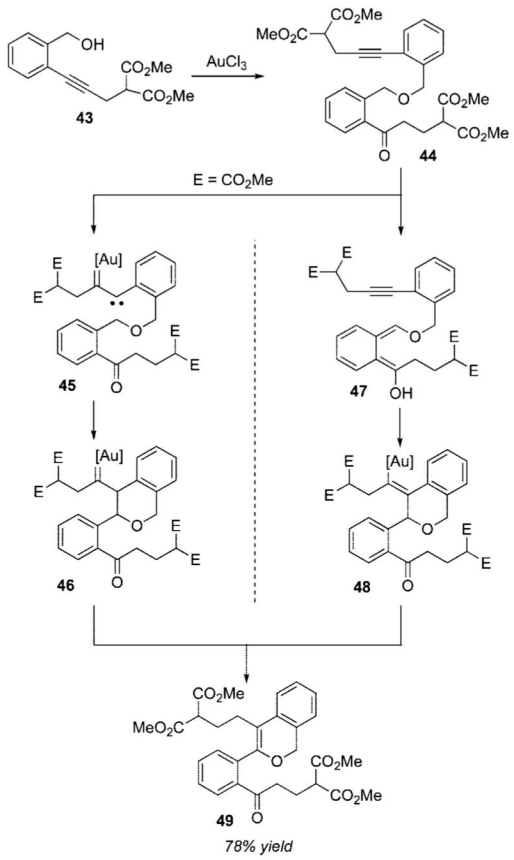
catalyst	time	yield
$Ph_3PAuNTf_2$	4 h	49%
$Ph_3PAuCl/AgOTf$	30 min	7%
$Ph_3PAuCl/AgBF_4$	10 min	57%

Scheme 4.

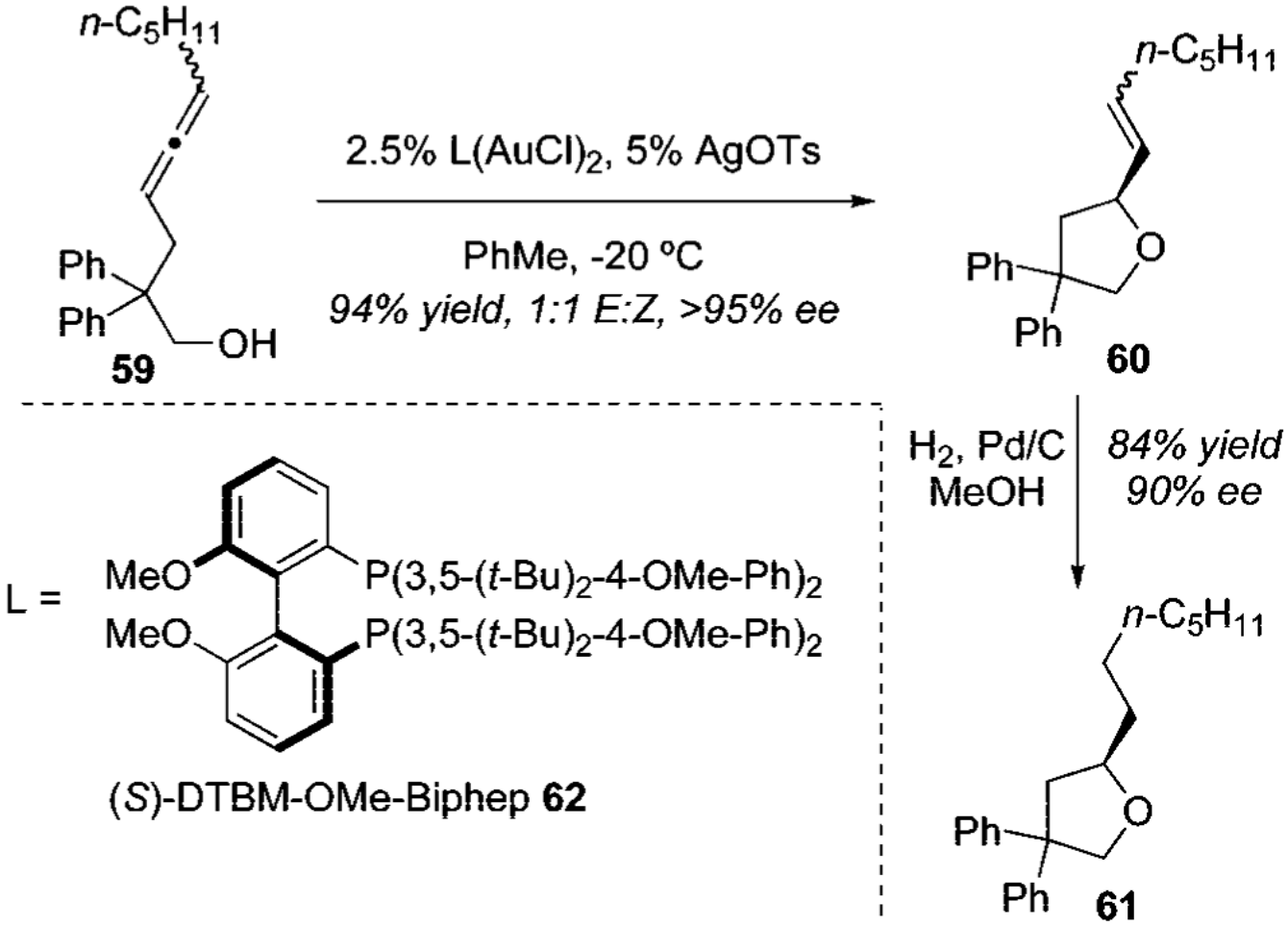


catalyst	yield
5% $AuCl_3$	20%
5% $AuCl_3$/15% $AgSbF_6$	85%
5% $AuCl_3$/15% $AgClO_4$	5%
$AgSbF_6$	nr
$Ph_3PAuCl/AgSbF_6$	nr

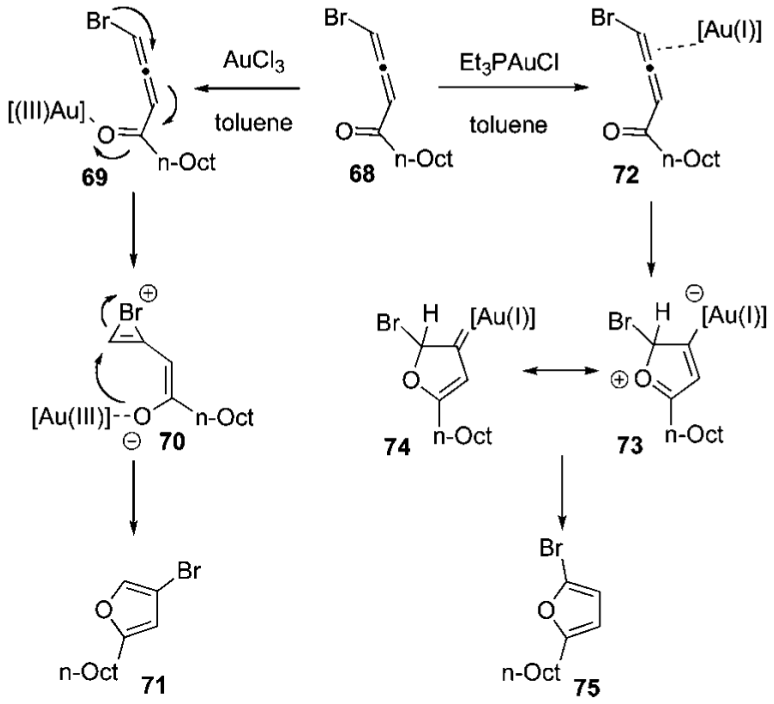
Scheme 5.



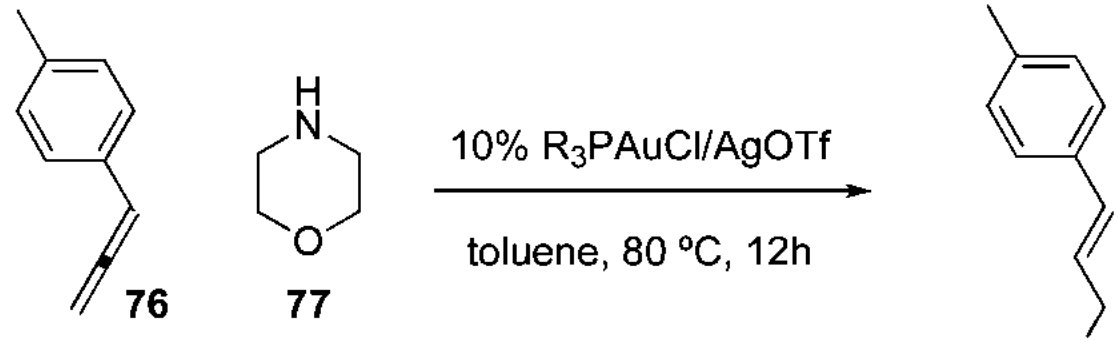
Scheme 6.



Scheme 7.



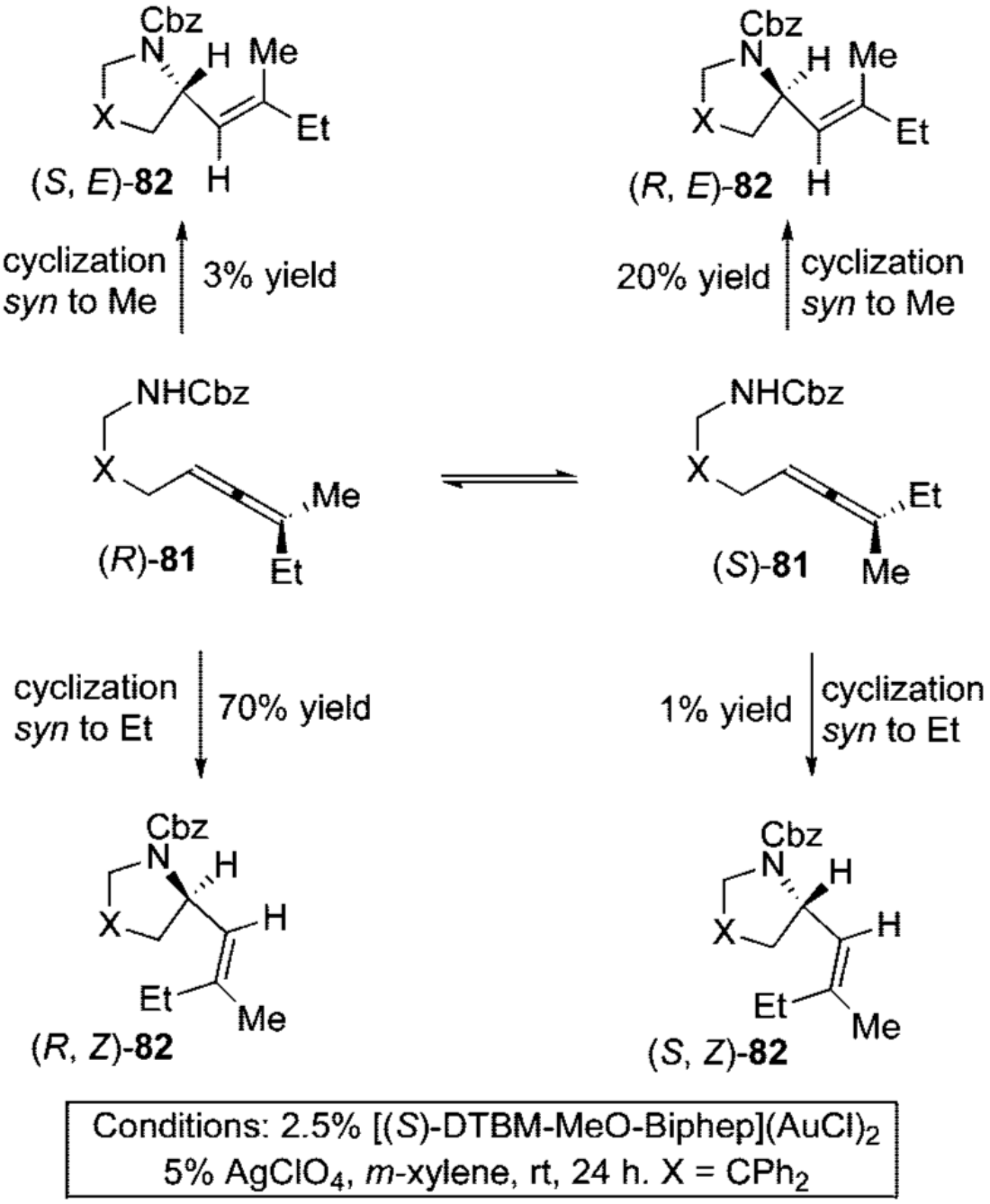
Scheme 8.



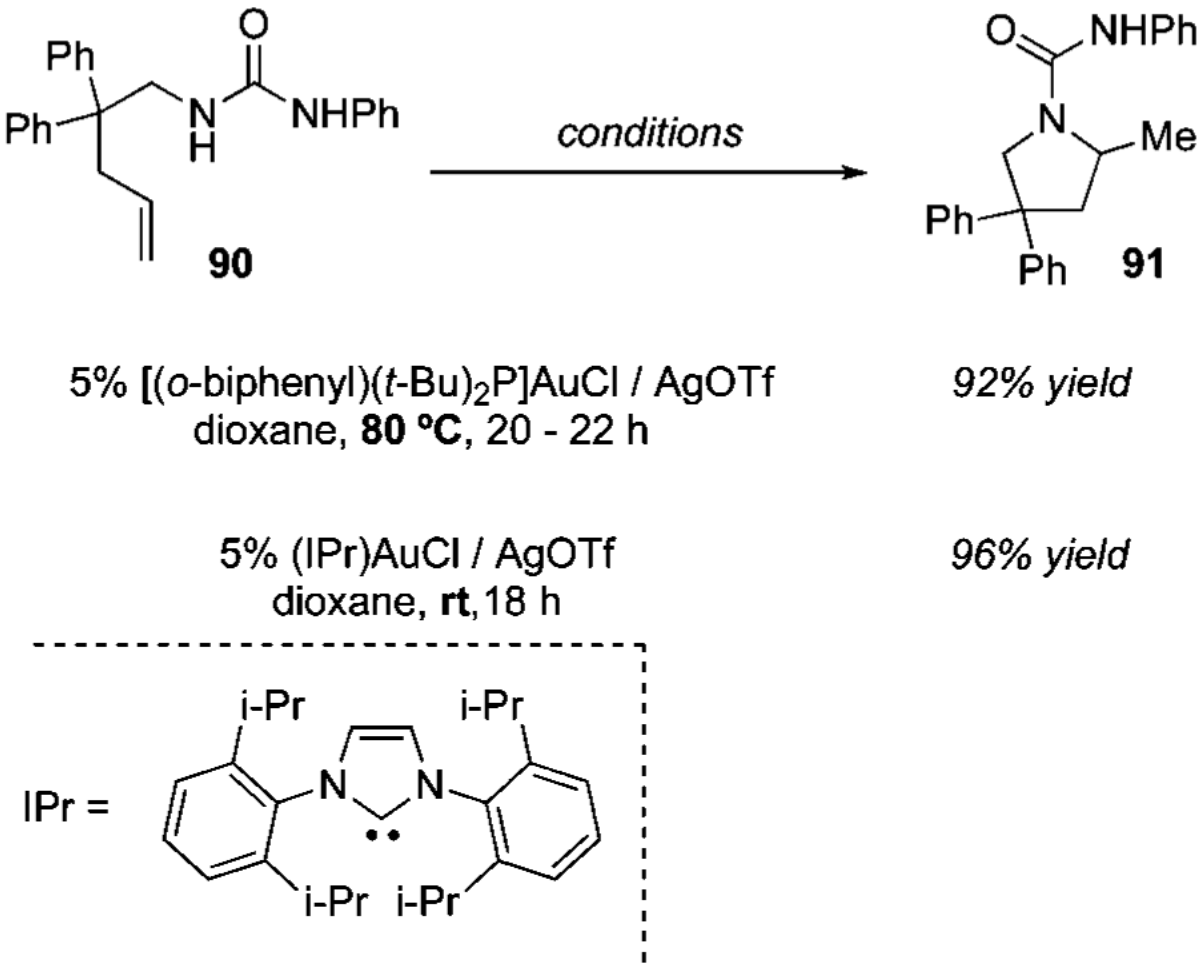
76 **77** **78**

R_3P	yield
Ph_3P	64%
$P(t\text{-}Bu)_2$(o-biphenyl)	51%
PPh_2(o-anisyl)	63%
PPh_2(p-CF_3-C_6H_4)	63%
PPh_2(o-tolyl)	83%

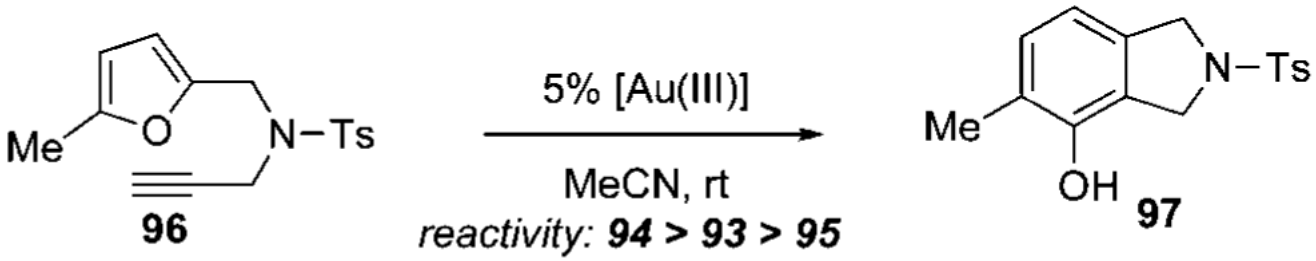
Scheme 9.



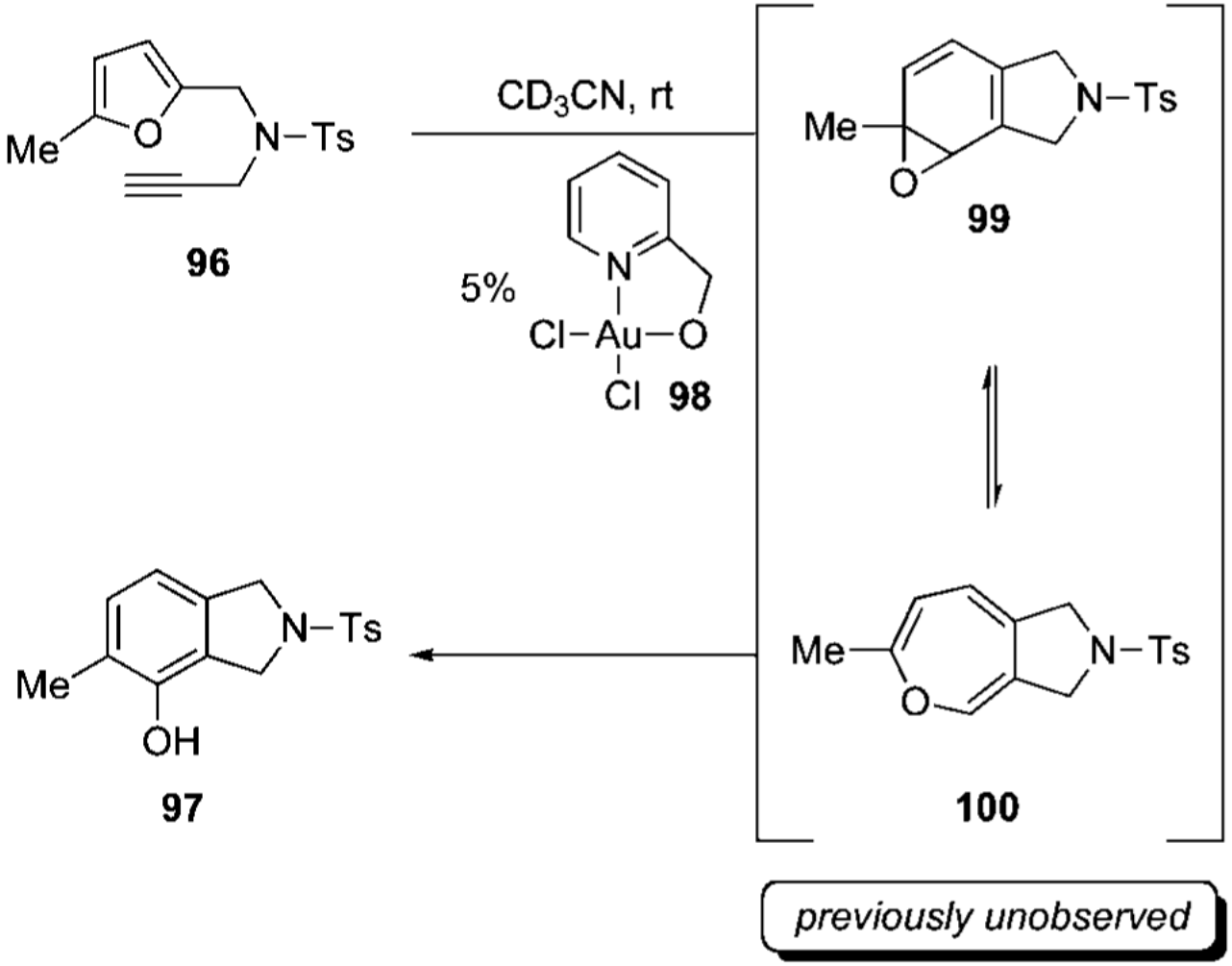
Scheme 10.



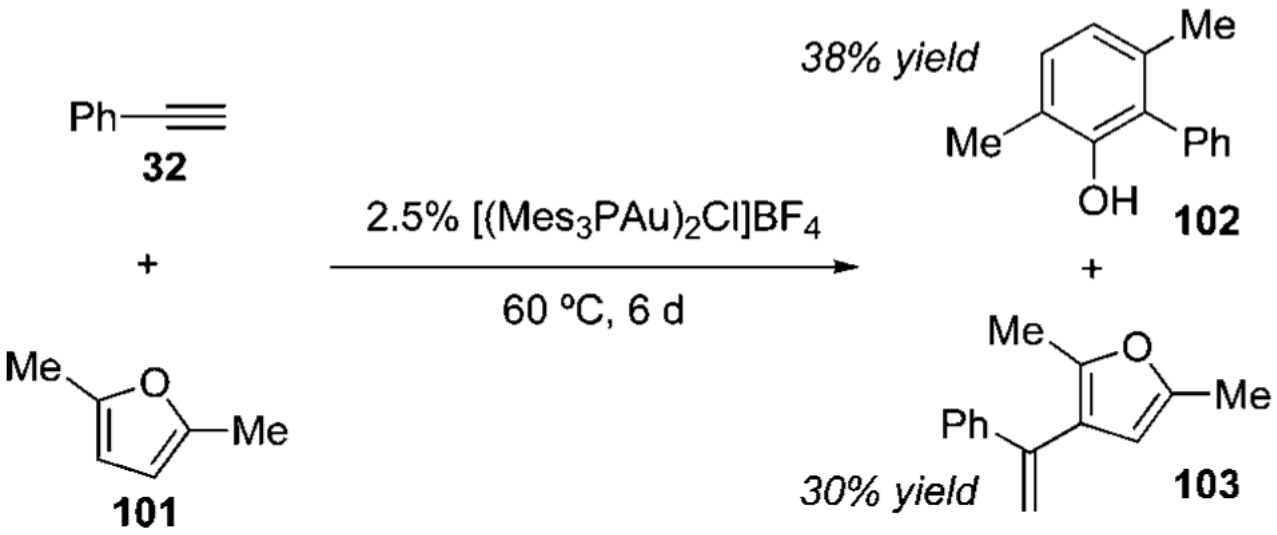
Scheme 11.



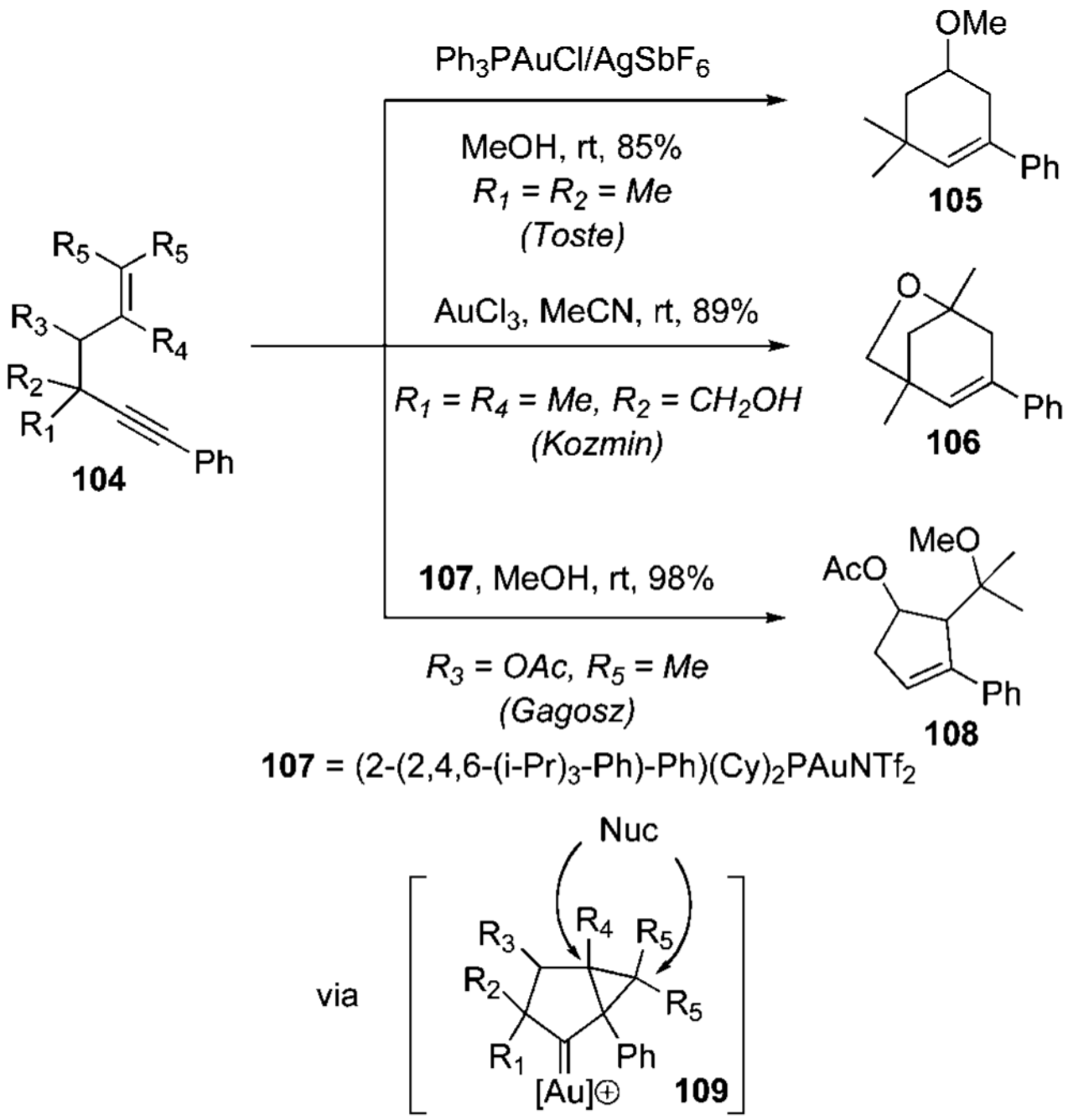
Scheme 12.



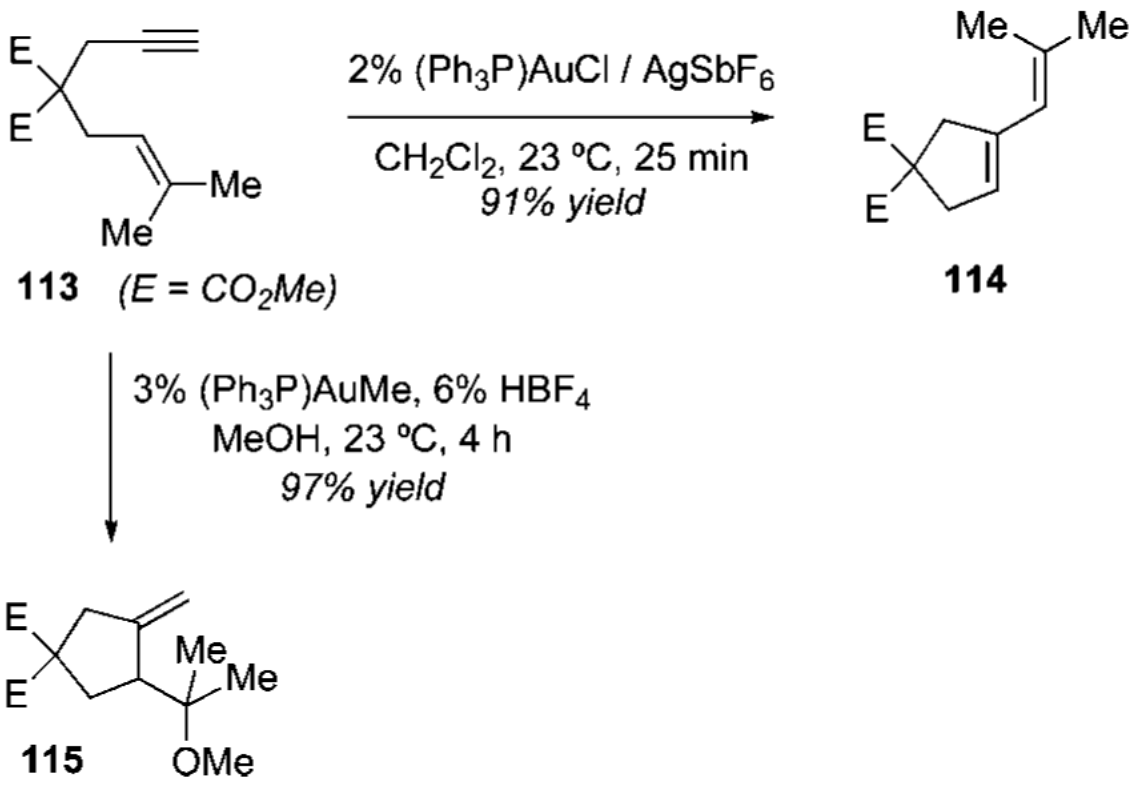
Scheme 13.



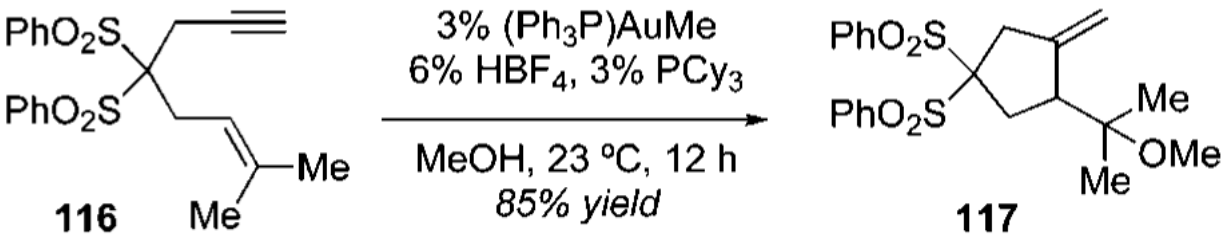
Scheme 14.



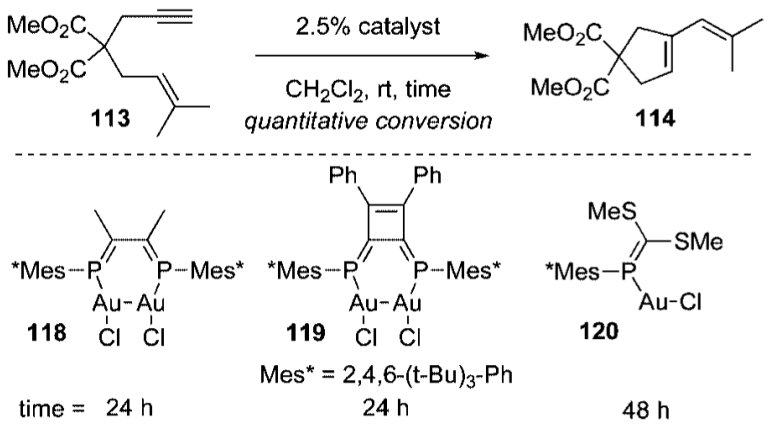
Scheme 15.



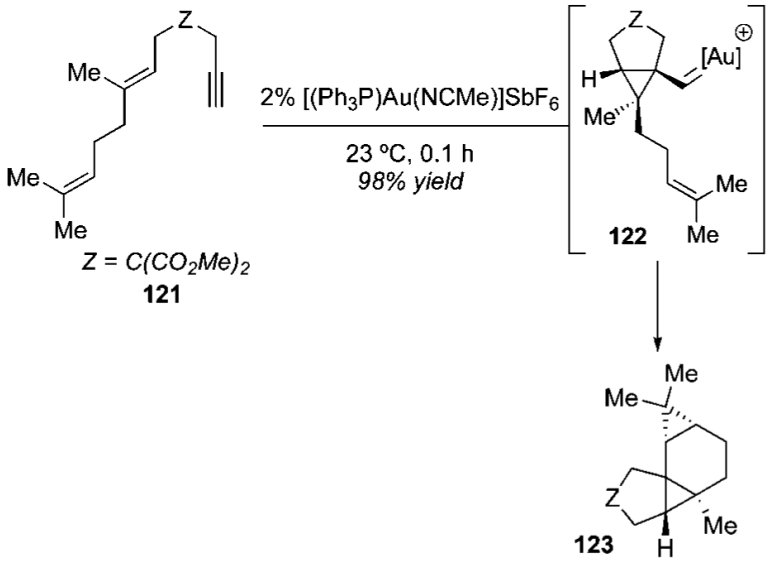
Scheme 16.



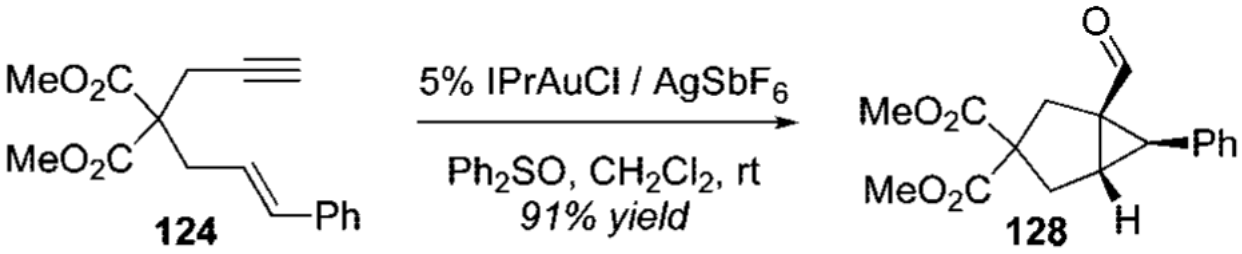
Scheme 17.



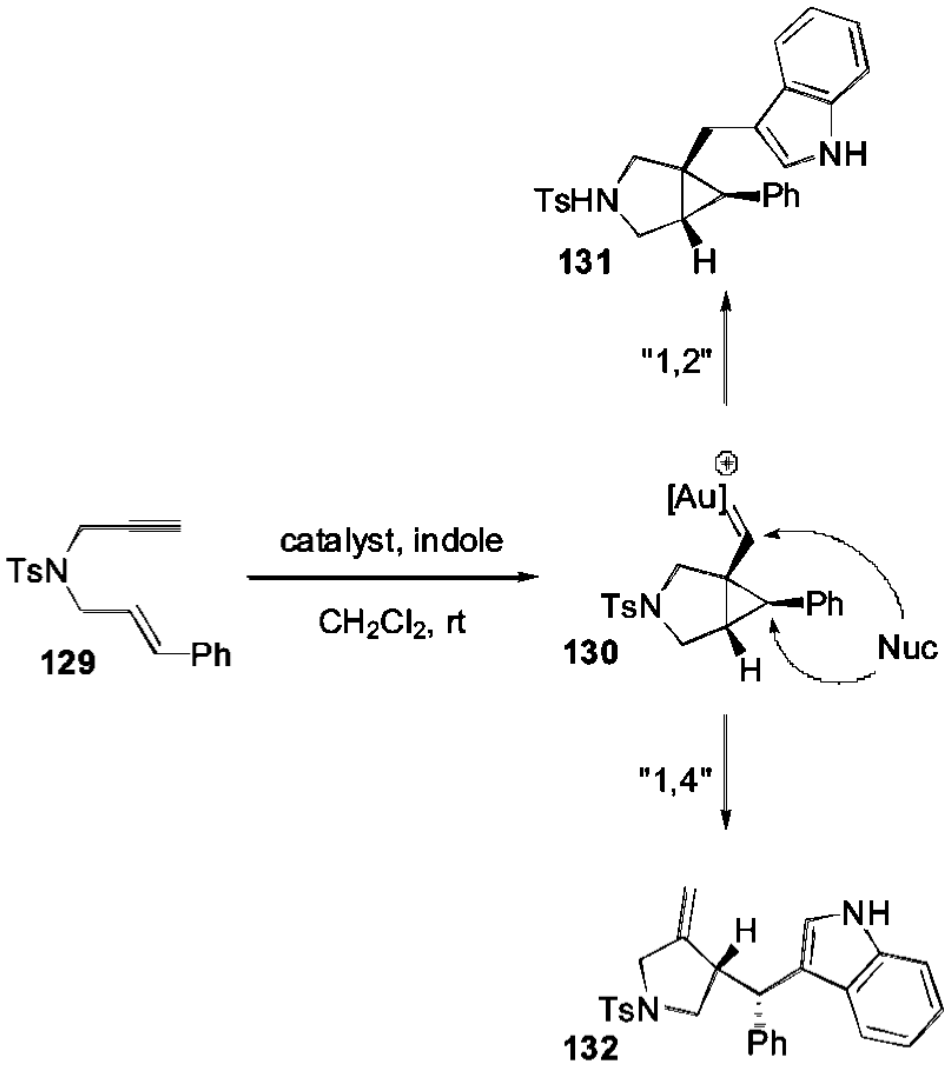
Scheme 18.



Scheme 19.

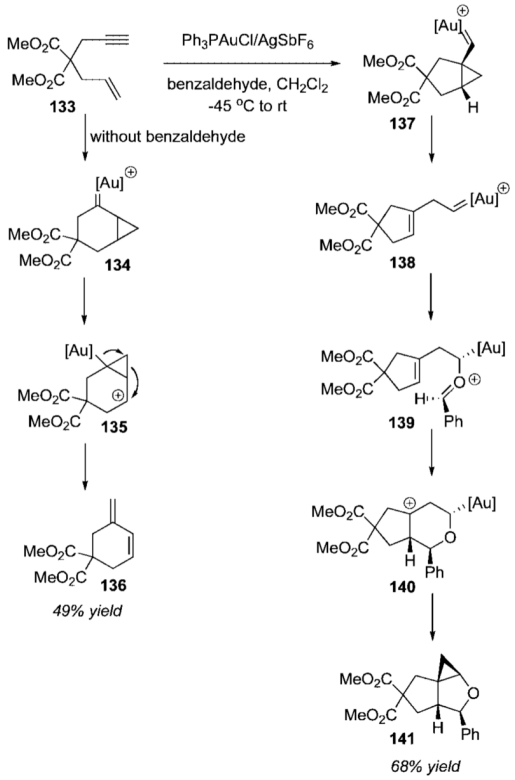


Scheme 20.

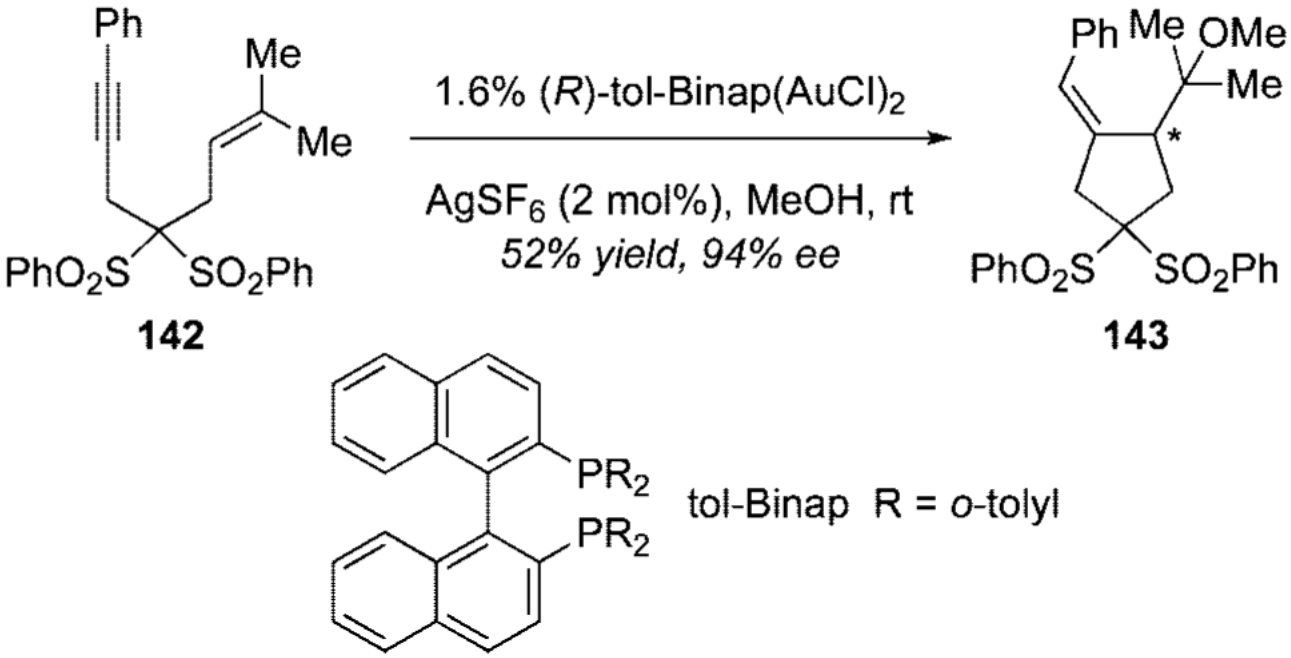


catalyst	132:131
[(o-biphenyl)(t-Bu)$_2$PAu(NCMe)]SbF$_6$	4:1
((2,4-(t-Bu)$_2$-Ph)O)$_3$PAuCl/AgSbF$_6$	10:1
(IMes)AuCl/AgSbF$_6$	0.8:1

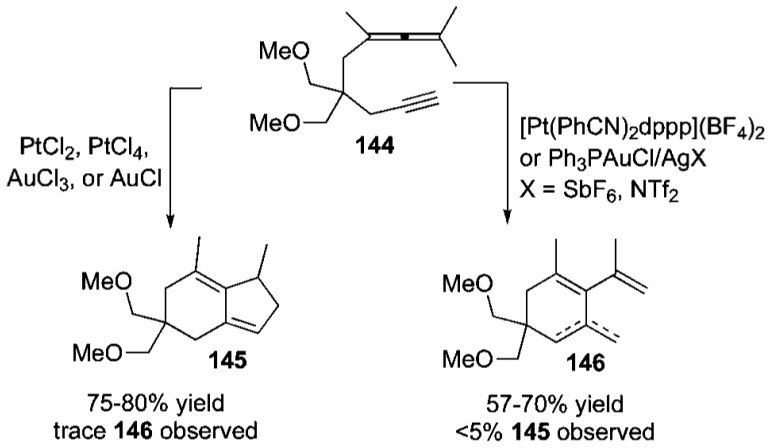
Scheme 21.



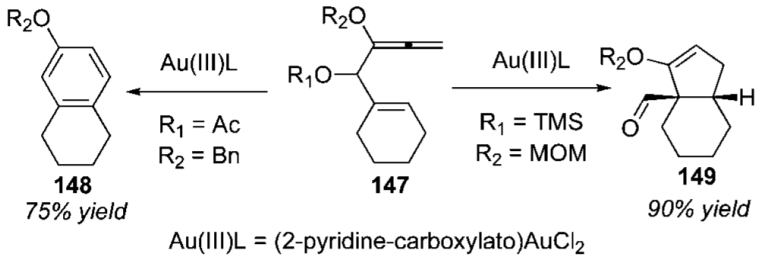
Scheme 22.



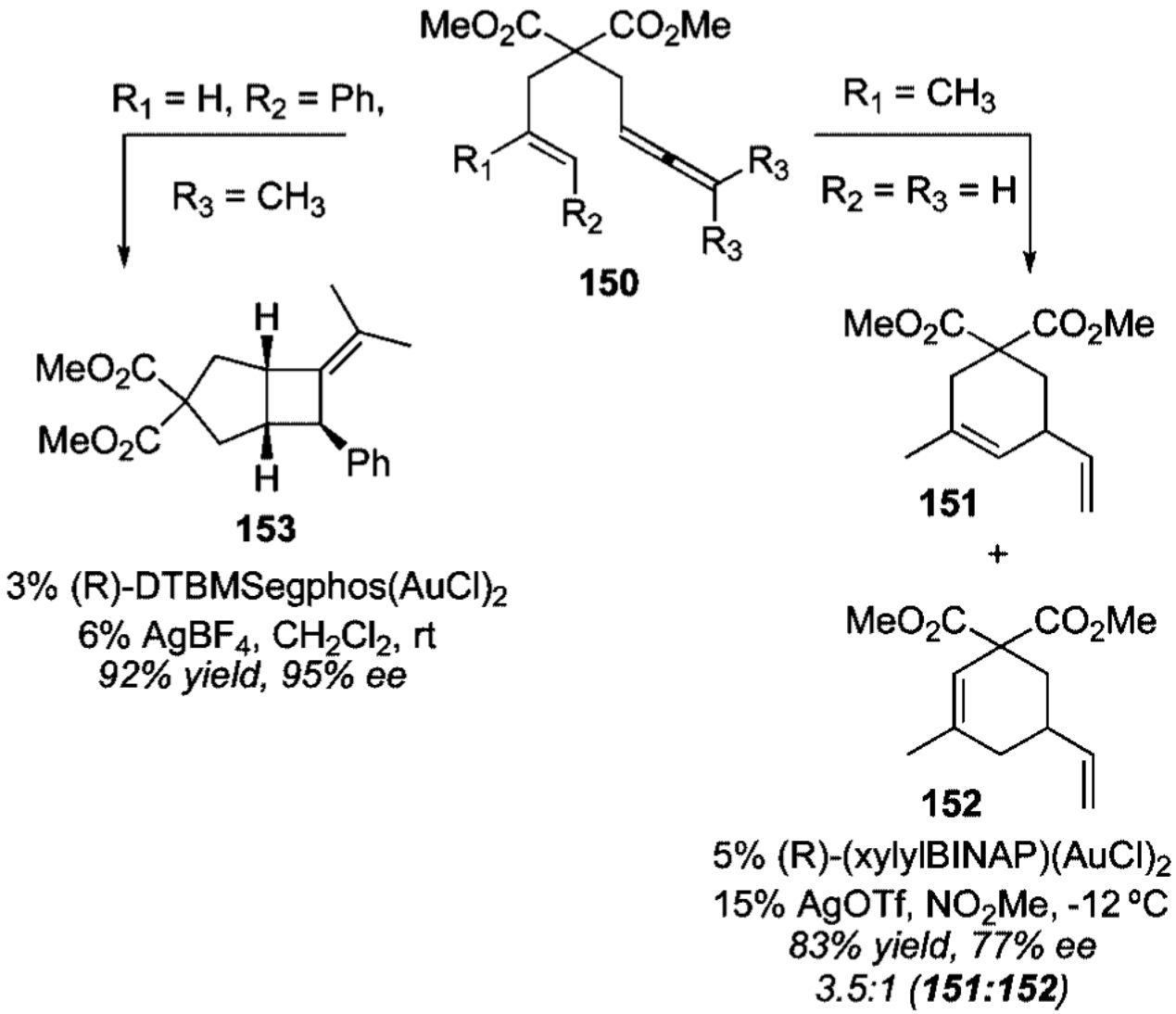
Scheme 23.



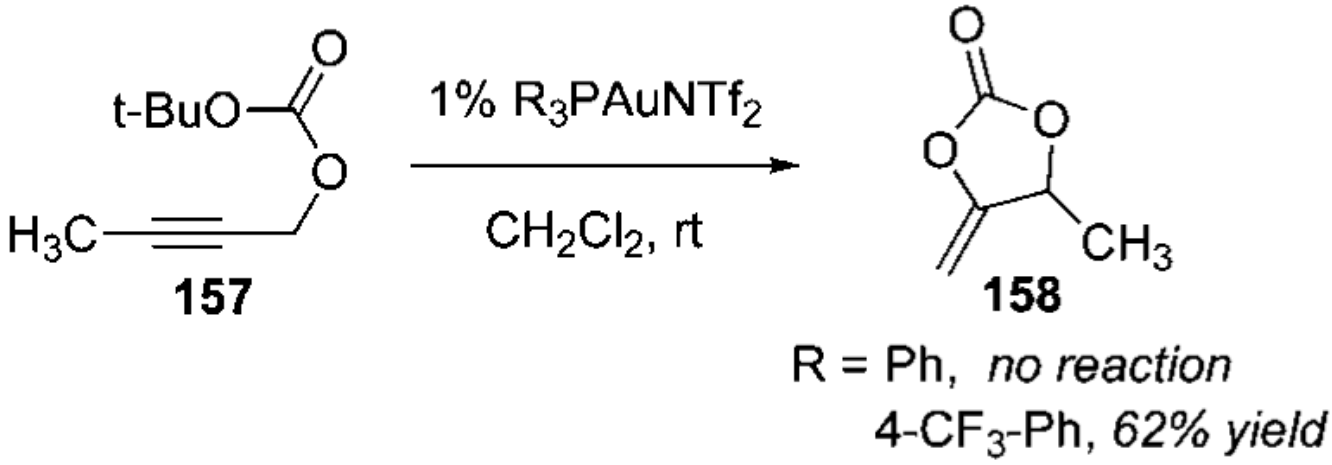
Scheme 24.



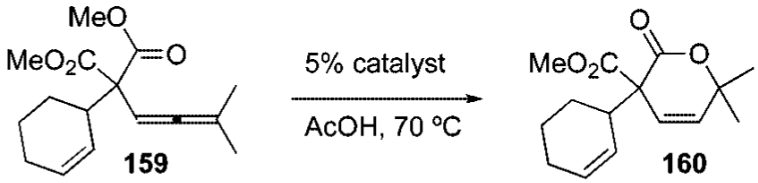
Scheme 25.



Scheme 26.

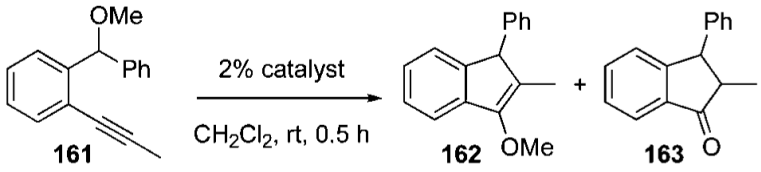


Scheme 27.



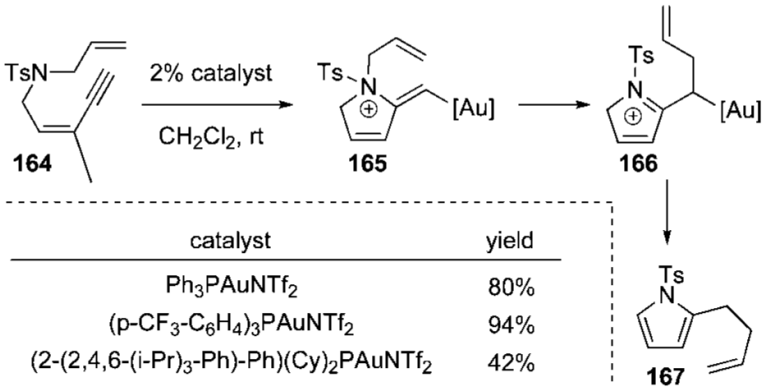
catalyst	yield
$AuCl_3$	46%
$AuCl_3$/15% AgOTf	75%
AuCl/AgOTf	70%
Ph_3PAuCl/AgOTf	53%

Scheme 28.

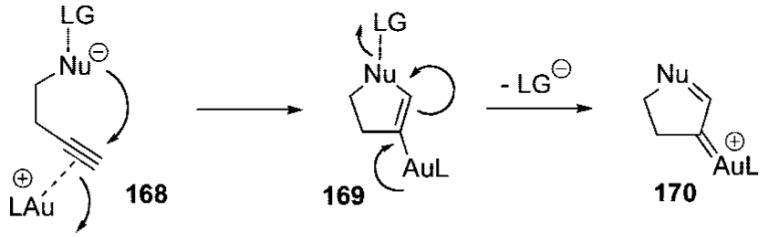


catalyst	yield
$Ph_3PAuNTf_2$	0%
$Ph_3PAuCl/AgBF_4$	32%
$(p\text{-}CF_3\text{-}C_6H_4)_3PAuCl/AgBF_4$	70%
$(p\text{-}CF_3\text{-}C_6H_4)_3PAuCl/AgSbF_6$	25%
$AuCl_3$	0%

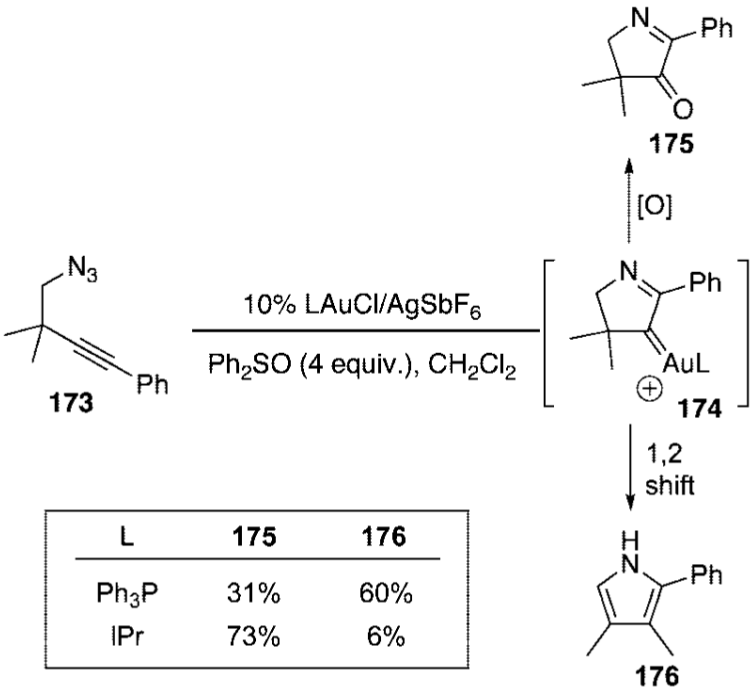
Scheme 29.



Scheme 30.

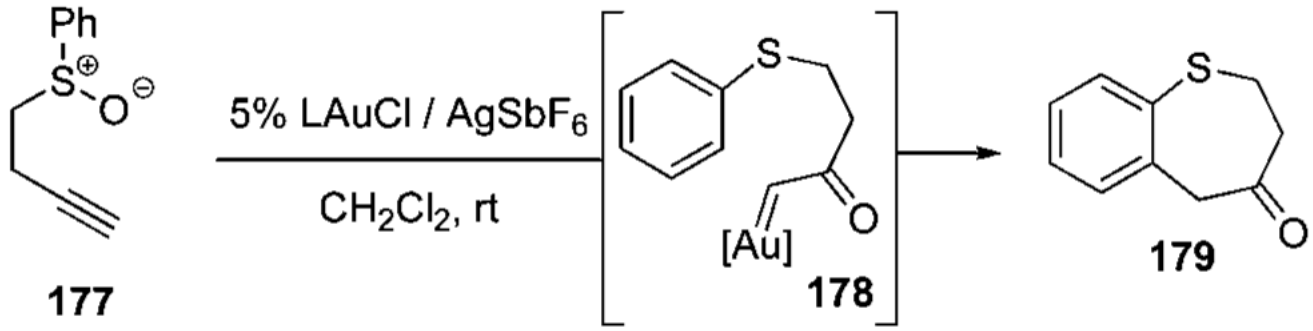


Scheme 31.



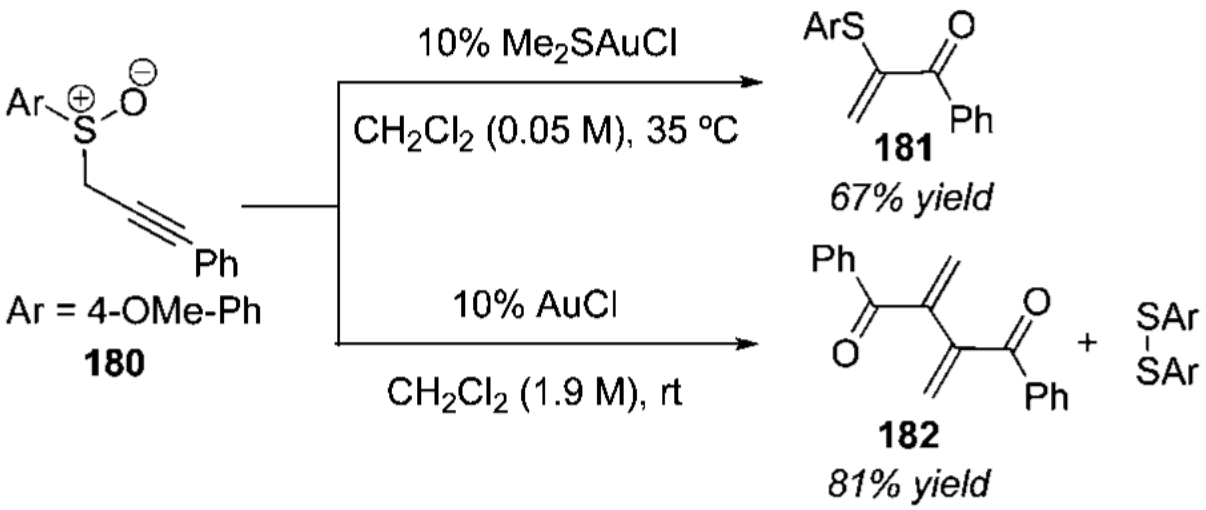
L	175	176
Ph_3P	31%	60%
IPr	73%	6%

Scheme 32.

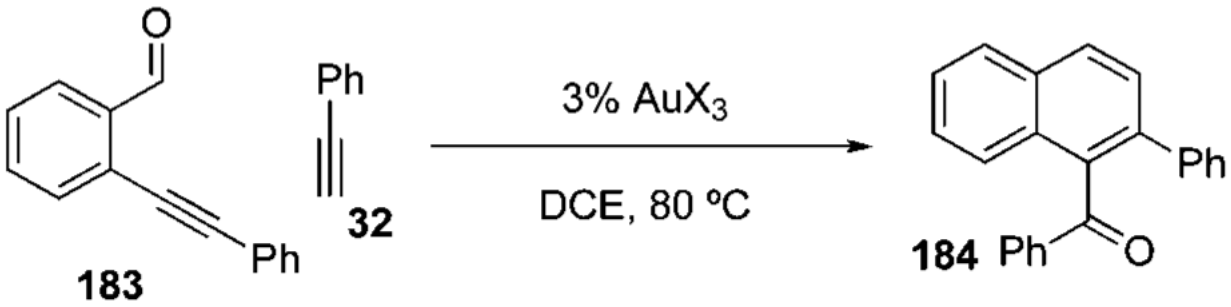


ligand	yield
PPh_3	34%
$P(4\text{-}CF_3\text{-}Ph)_3$	25%
IMes	94%

Scheme 33.

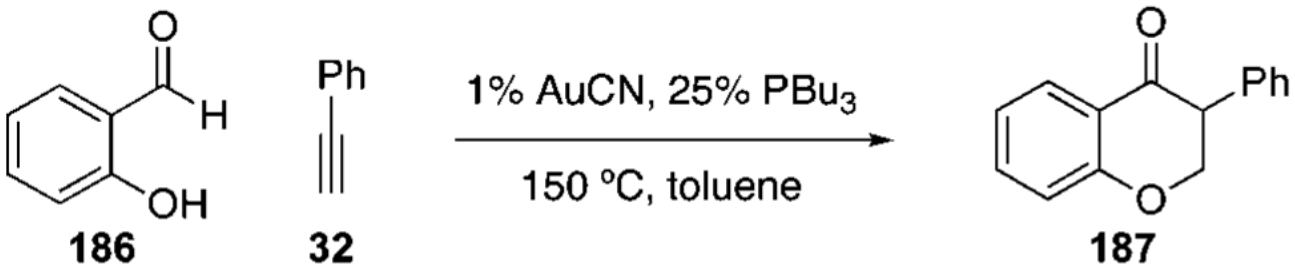


Scheme 34.

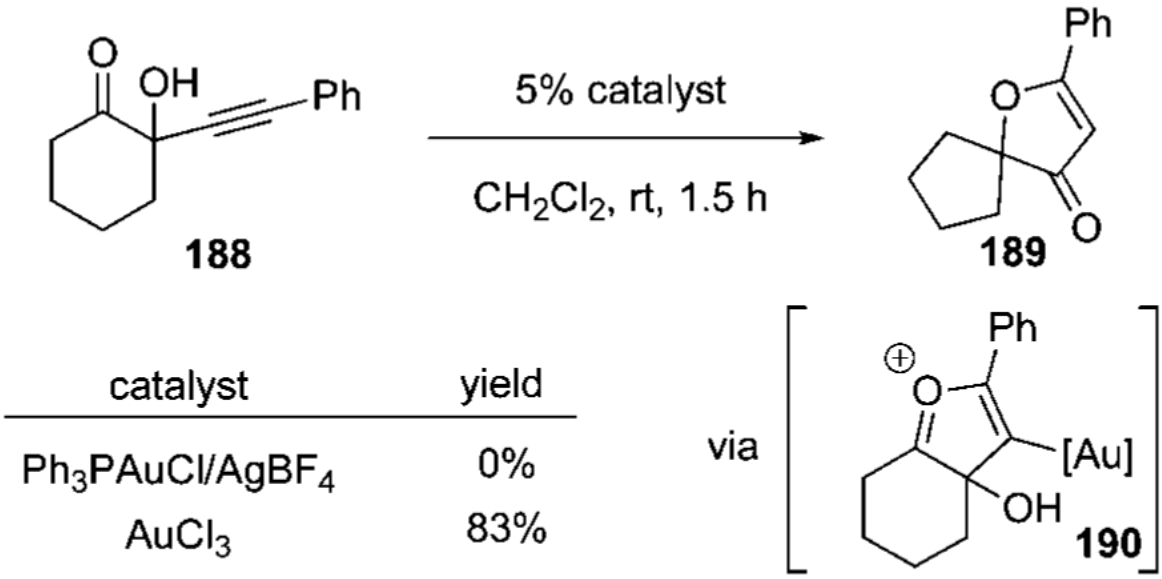


X	time	yield
Cl	2.5 h	96%
Br	0.7 h	100%

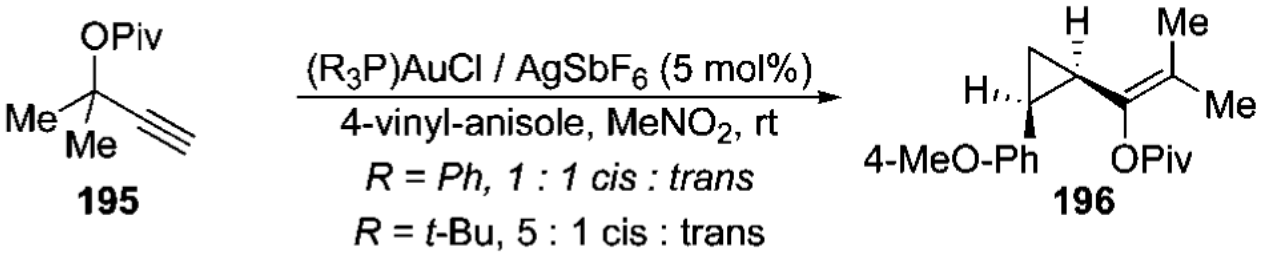
Scheme 35.



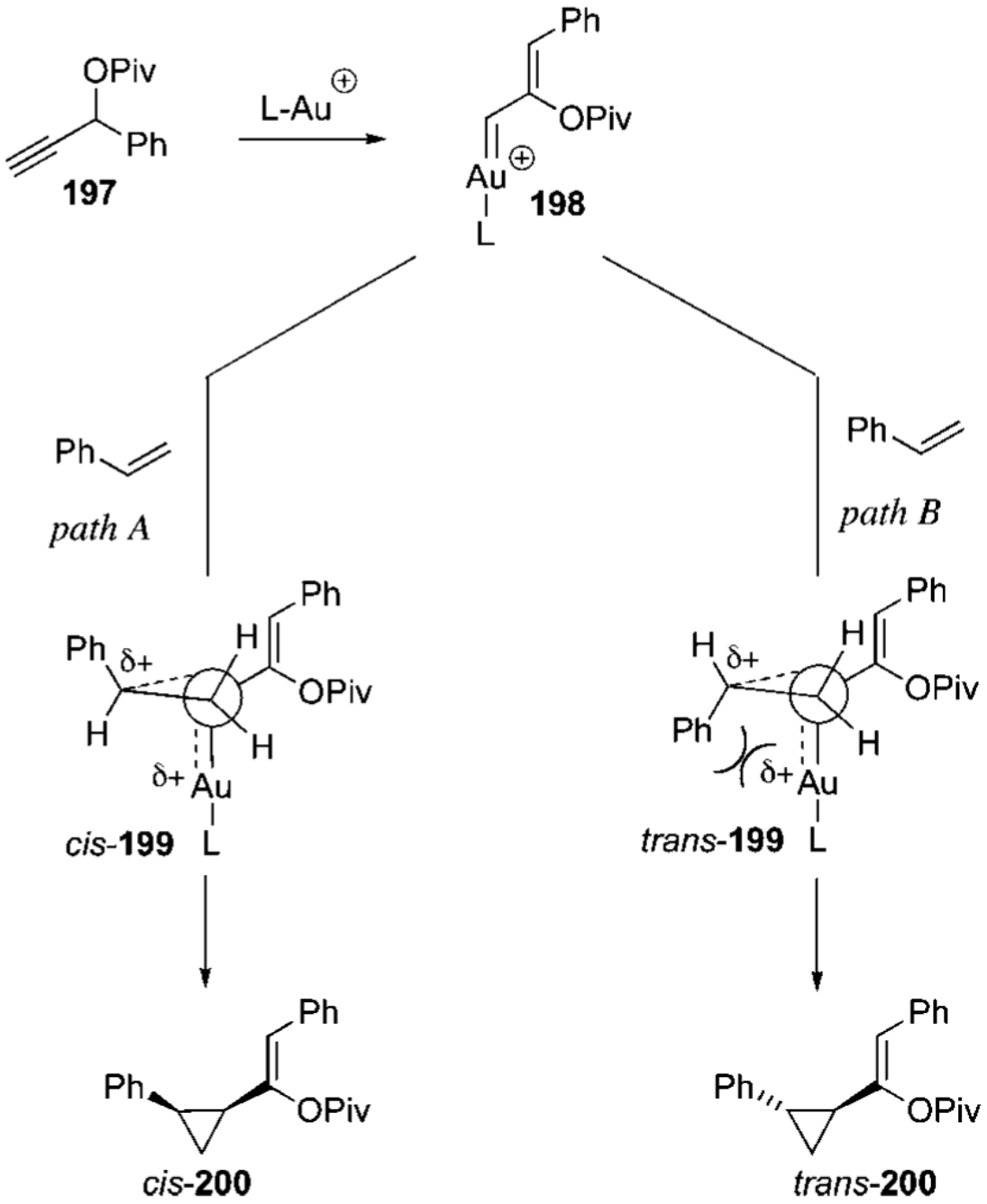
Scheme 36.



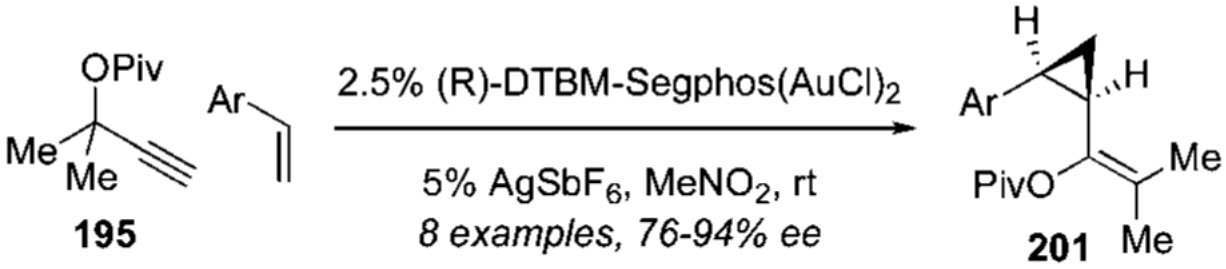
Scheme 37.



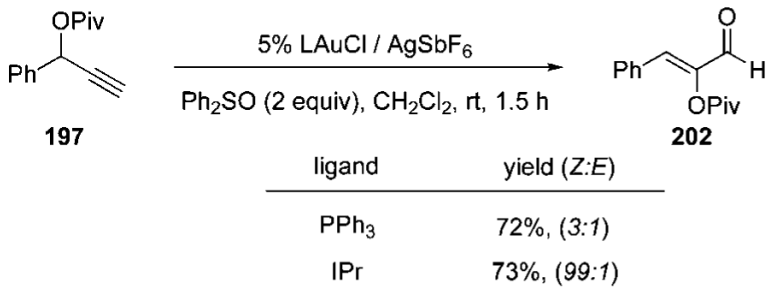
Scheme 38.



Scheme 39.

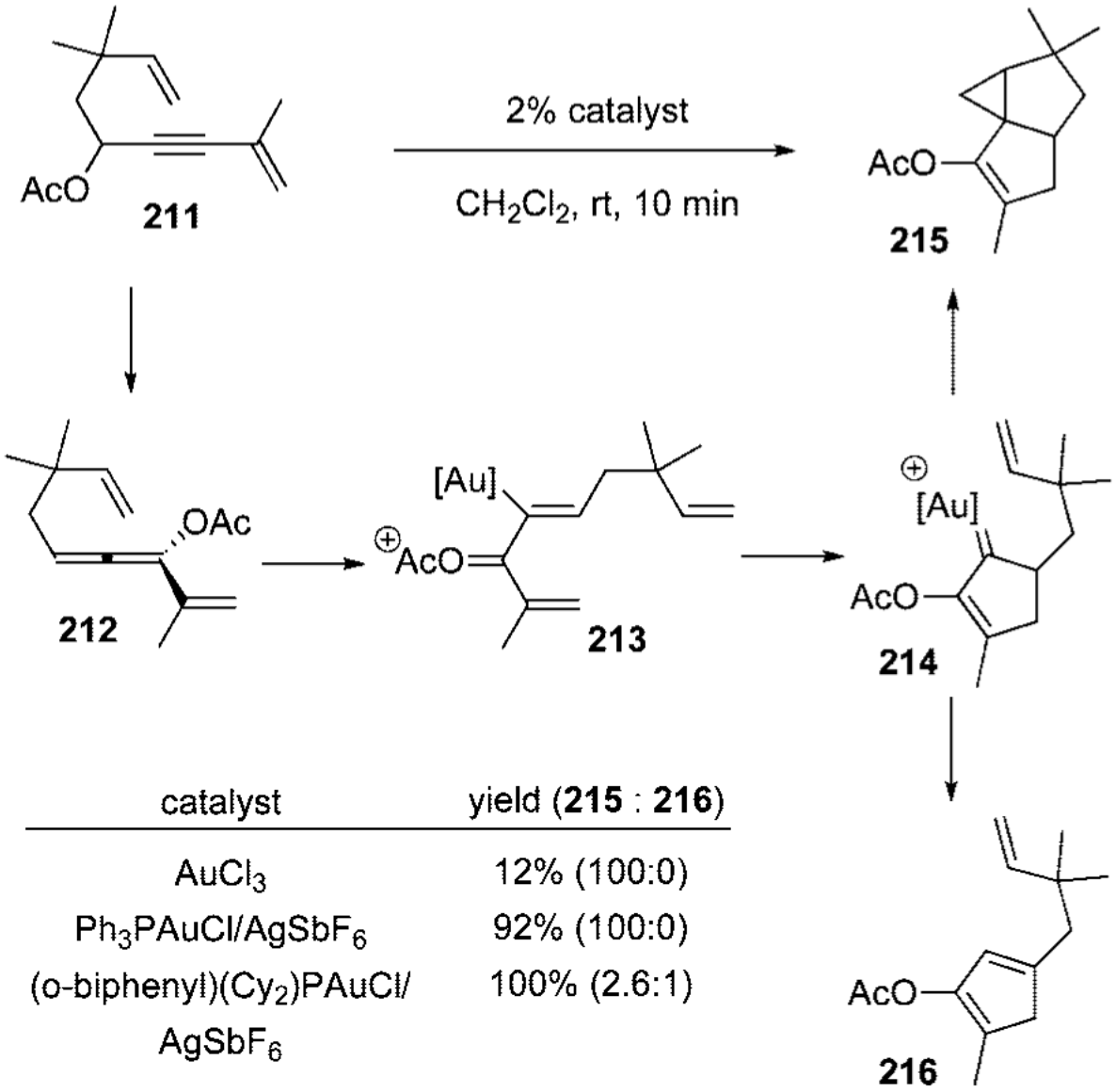


Scheme 40.



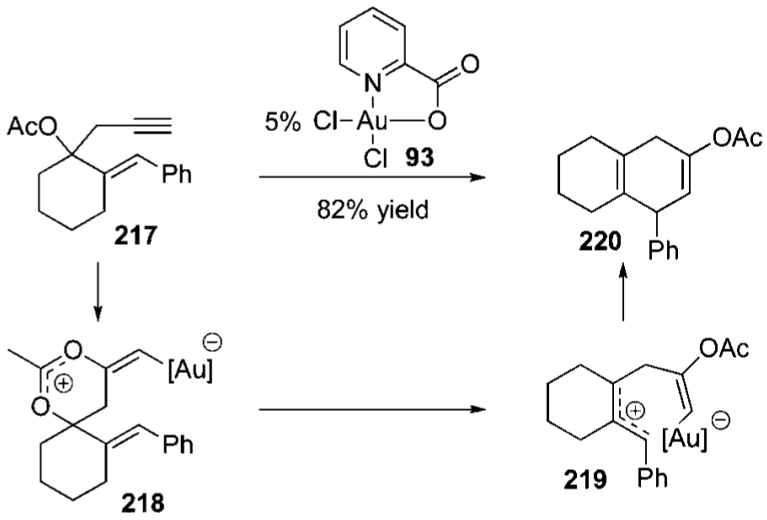
ligand	yield (*Z:E*)
PPh_3	72%, (*3:1*)
IPr	73%, (*99:1*)

Scheme 41.

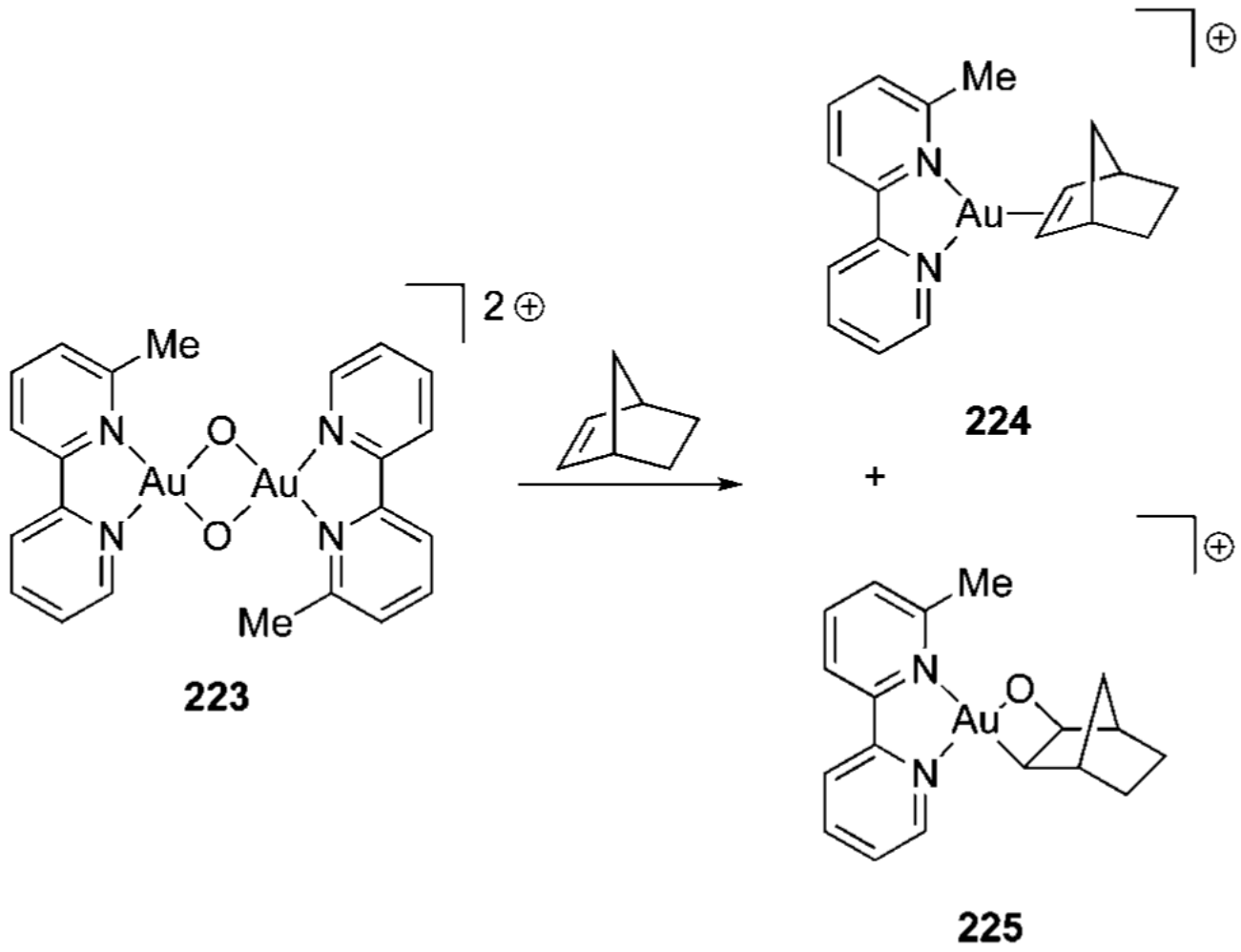


catalyst	yield (**215** : **216**)
$AuCl_3$	12% (100:0)
$Ph_3PAuCl/AgSbF_6$	92% (100:0)
(o-biphenyl)(Cy_2)PAuCl/ $AgSbF_6$	100% (2.6:1)

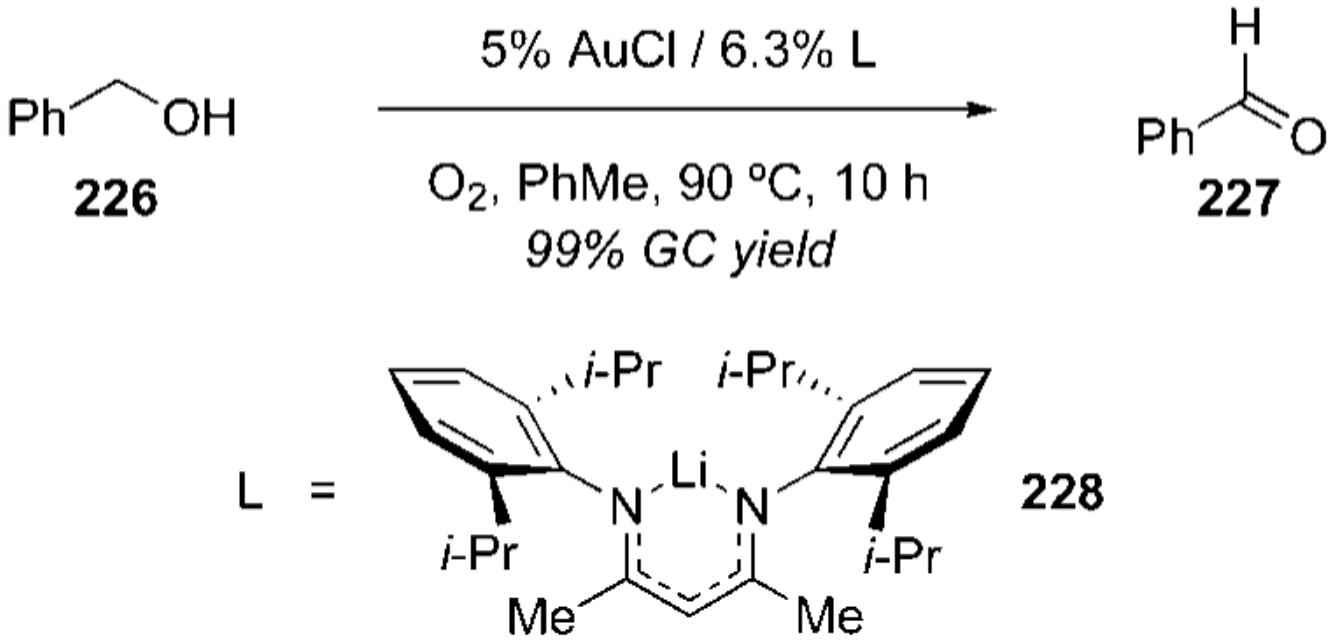
Scheme 42.



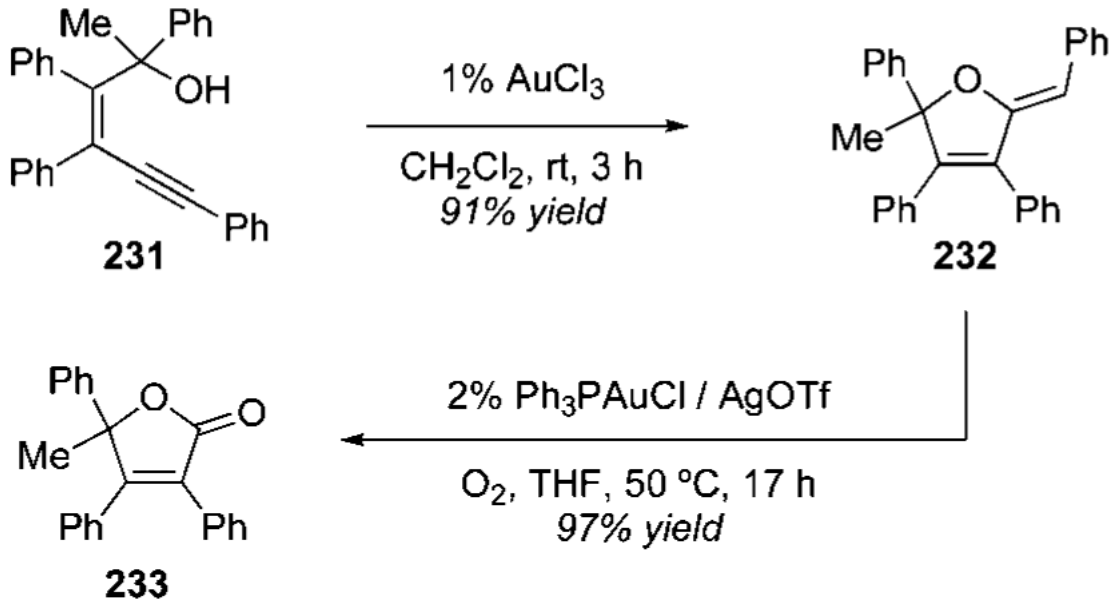
Scheme 43.



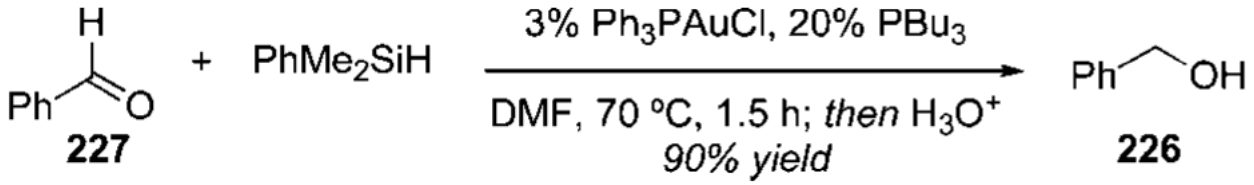
Scheme 44.



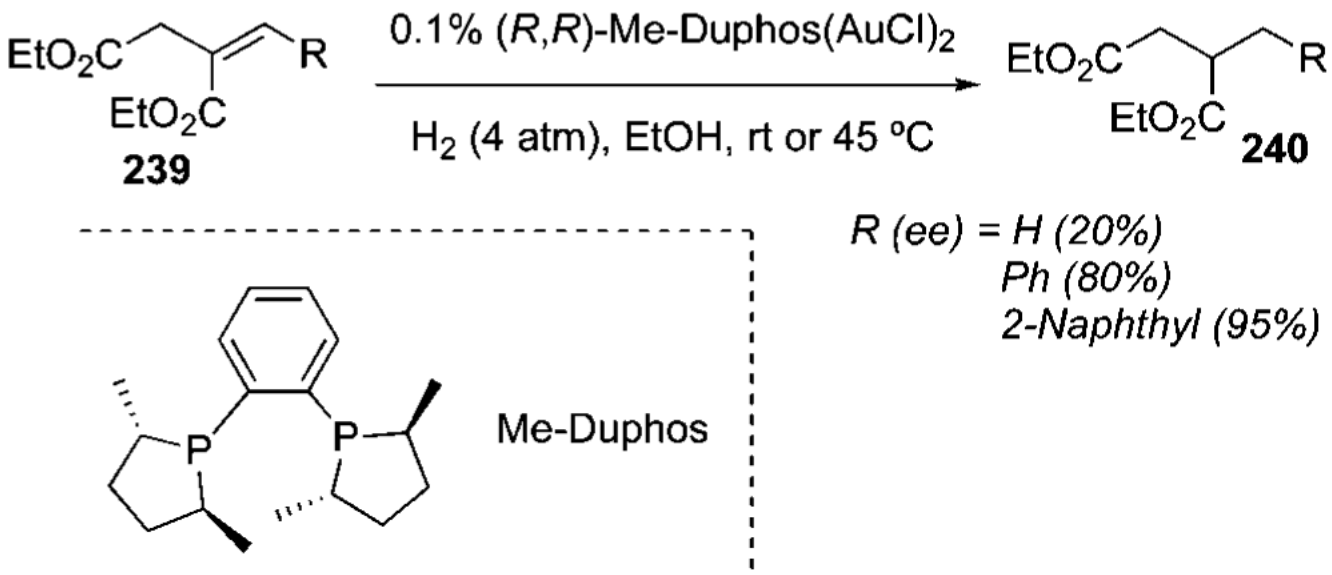
Scheme 45.



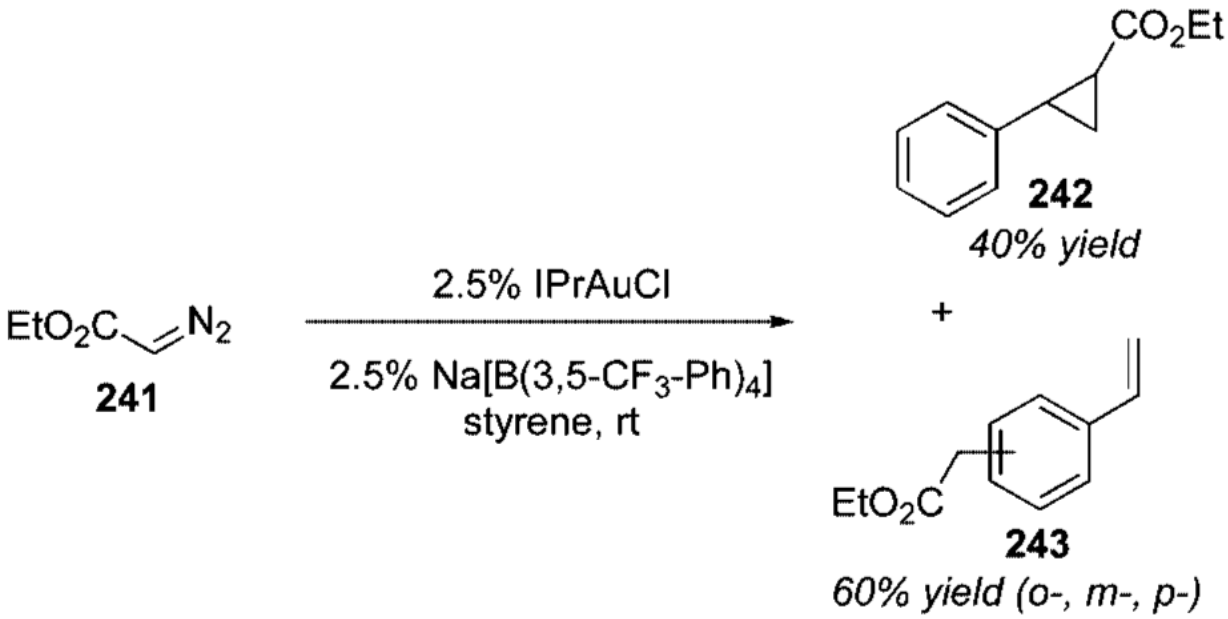
Scheme 46.



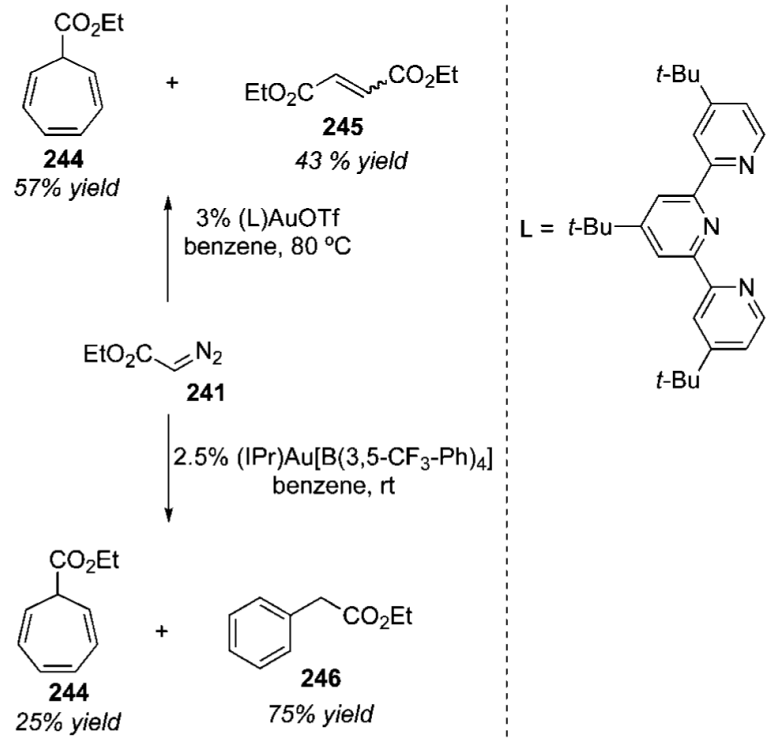
Scheme 47.



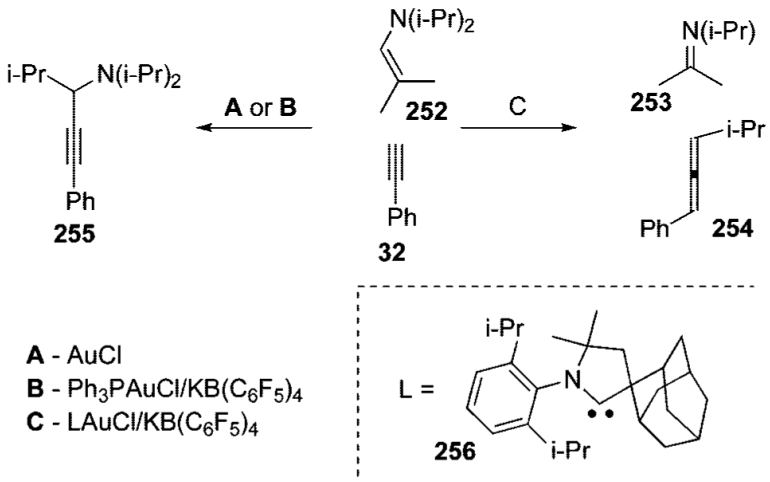
Scheme 48.



Scheme 49.



Scheme 50.



Scheme 51.

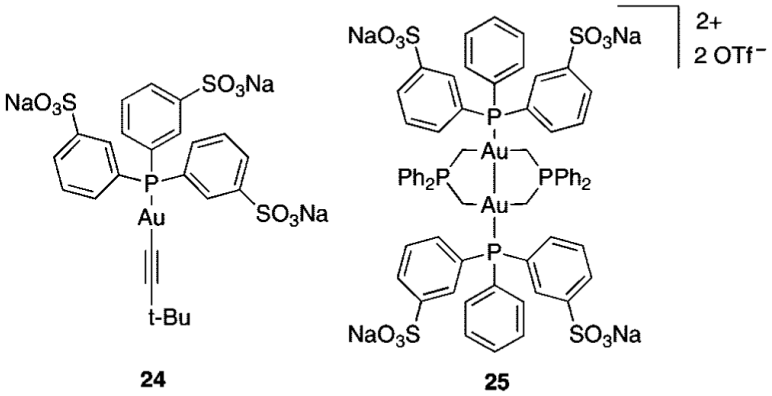


Figure 1.

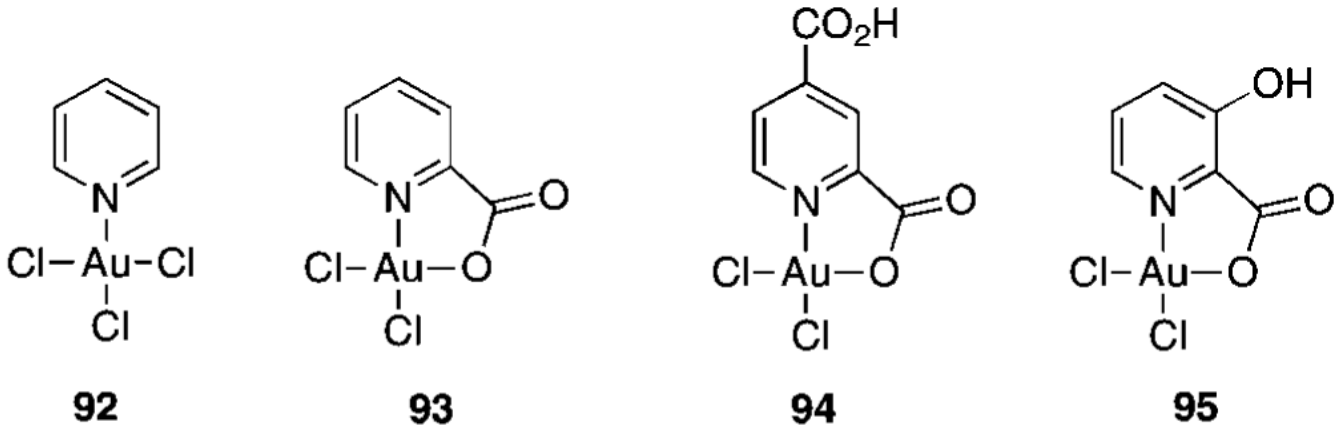


Figure 2.

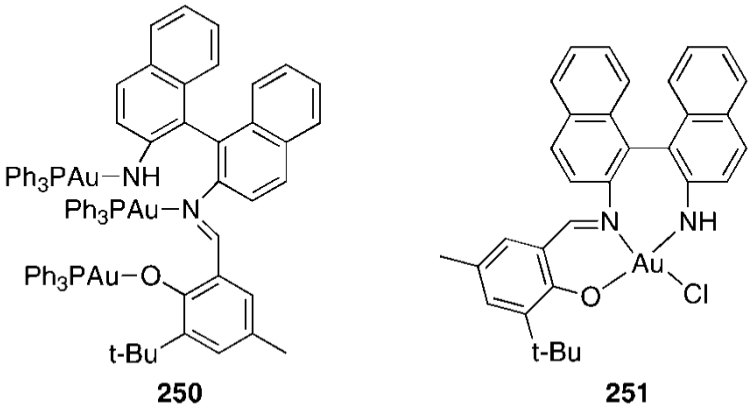
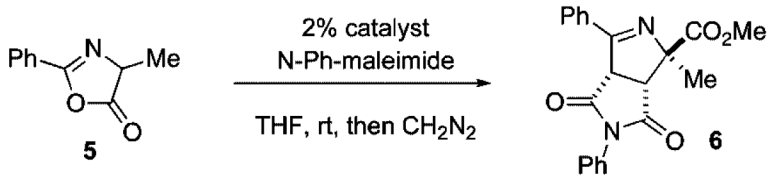


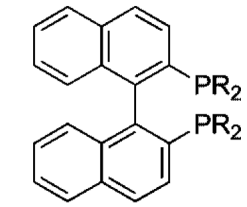
Figure 3.

Table 1

Enantioselective [3 + 2] Dipolar Cycloadition

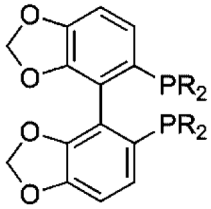


entry	catalyst	yield	ee
1	(*R*)-Binap(AuOBz)$_2$	78%	8%
2	(*R*)-Segphos(AuOBz)$_2$	81%	40%
3	(*R*)-xylyl-Binap(AuOBz)$_2$	63%	24%
4	(*R*)-DTBM-Segphos(AuOBz)$_2$	81%	83%
5	(*S*)-Cy-Segphos(AuOBz)$_2$	70%	-88%



Binap, R = Ph **7**

xylyl-Binap,
R = 3,5-$(CH_3)_2$-Ph **9**



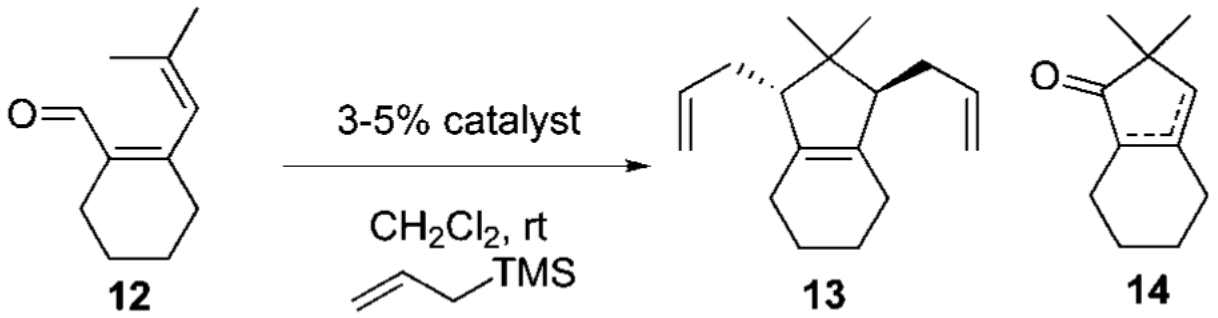
Segphos, R = Ph **8**

DTBM-Segphos,
R = (3,5-(*t*-Bu)$_2$-4-OMe)-Ph **10**

Cy-Segphos, R = cyclohexyl **11**

Table 2

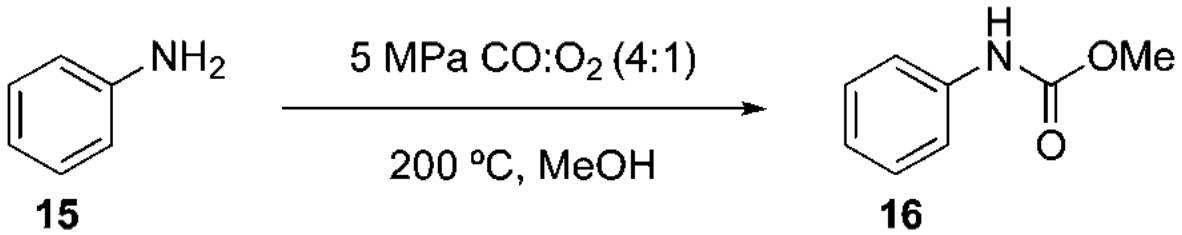
Tandem Allylation of Dienal 12



entry	catalyst	13 (yield, %)	14 (yield, %)
1	HOTf	0	65
2	$BF_3 \cdot E_2O$	16	38
3	$AuCl_3$	36	27
4	$Ph_3PAuCl/AgSbF_6$	78	0

Table 3

Carbonylation of Aniline



15 **16**

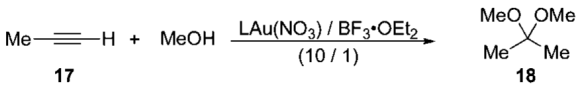
entry	precatalyst	TOF[a]	selectivity[b] (%)
1	$HAuCl_4$	11	37
2	Ph_3PAuCl	14	70
3	$(Ph_3P)_2AuCl$	23	60
4	Ph_3PAuNO_3	16	43
5	$Ph_3PAuCl + PPh_3$	36	89

[a] Moles of substrate converted per moles of Au per hour.

[b] % **16**/% conversion of **15**.

Table 4

Hydroalkoxylation of Propyne

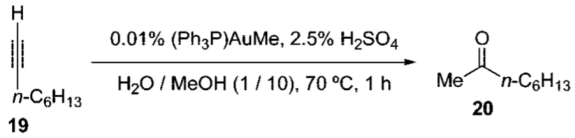


17 18

entry	ligand	initial TOF (h^{-1})	TON
1	$AsPh_3$	430	-
2	PEt_3	550	-
3	PPh_3	610	>5000
4	$P(4\text{-}F\text{-}Ph)_3$	640	-
5	$P(4\text{-}OMe\text{-}Ph)_3$	1200	-
6	$P(OPh)_3$	1500	2500

Table 5

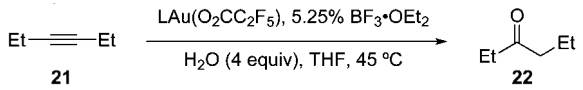
Hydration of 1-Octyne



entry	additive	GC yield (%)
1	-	35
2	CO (1 atm)	99
3	$P(OPh)_3$ (0.02 mol%)	90
4	PPh_3	*noreaction*

Table 6

Hydration of 3-Hexyne with Au(I) Carboxylate Precatalysts

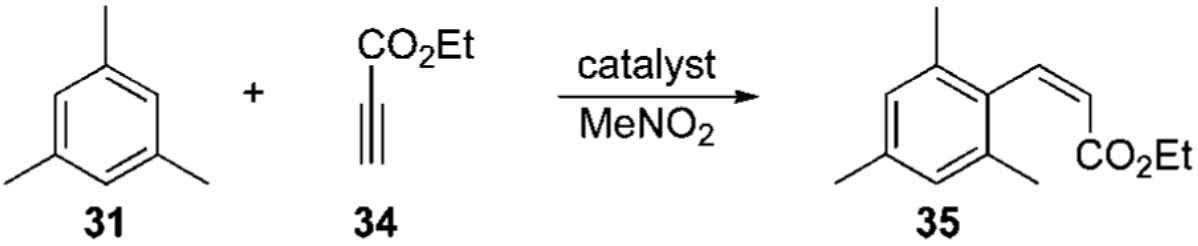


entry	cat. mol %	ligand	time (h)	GC yield (%)	TOF (h^{-1})
1	0.134	PPh_3	1.8	51.2	213
2	0.137	$P(p\text{-tol})_3$	2	43.2	163
3[a]	0.095	PMe_3	2	18.8	99

[a]Decomposition to metallic gold was observed within minutes.

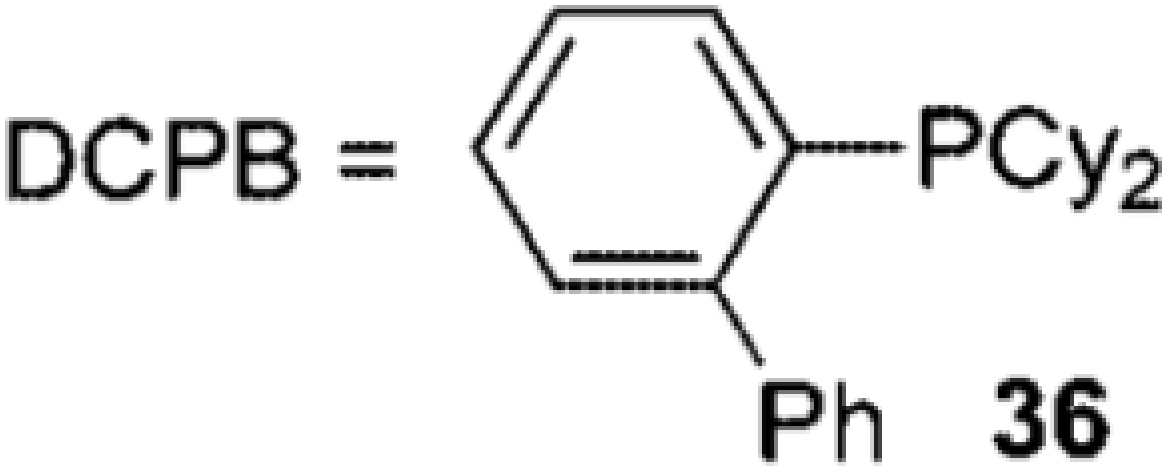
Table 7

Hydroarylation of Ynoate 34



31 34 35

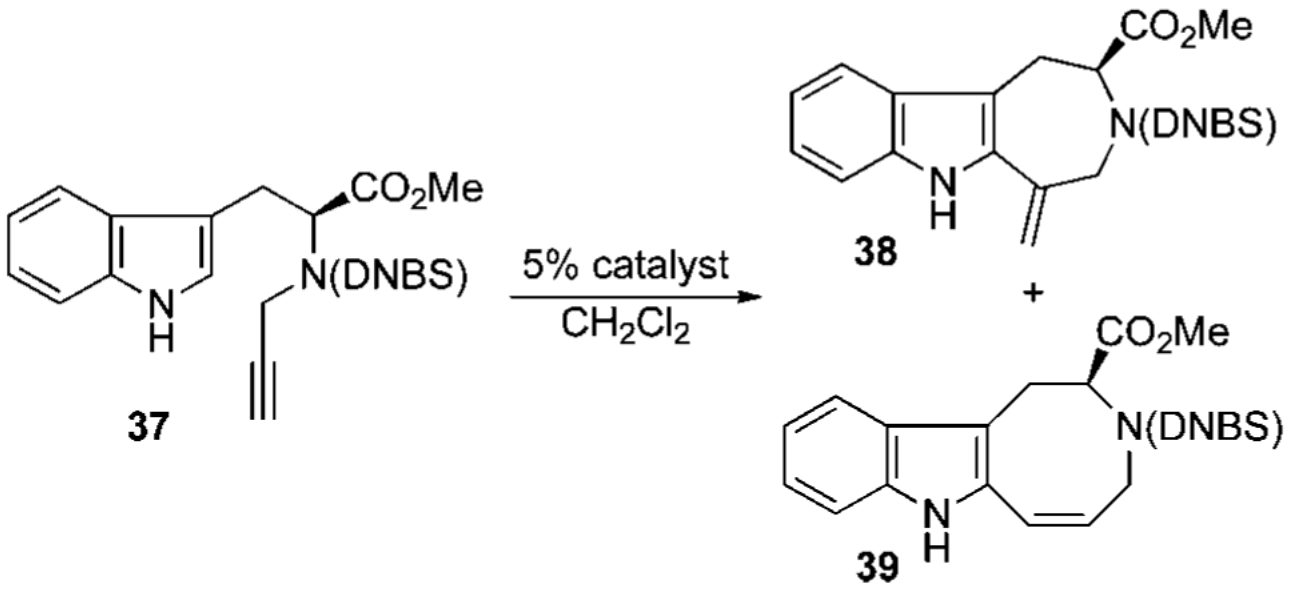
entry	catalyst	*T* (°C)	% yield (*Z*:*E*)
1	5% $AuCl_3$/15% $AgBF_4$	60	60 (78:22)
2	5% $Ph_3PAuCl/AgBF_4$	60	57 (100:1)
3	3% $Ph_3PAuCl/BF_3 \cdot Et_2O$	50	62 (100:1)
4	3% AuCl/DCPB/$BF_3 \cdot Et_2O$	50	71 (100:1)



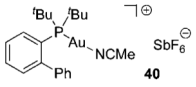
36

Table 8

7-*exo*-dig vs 8-*endo*-dig Hydroarylation



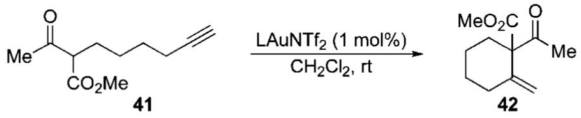
entry	catalyst	yield (%)	38:39
1	**40**	82	100:0
2	$AuCl_3$	75	0:100
3	AuCl	70	0:100
4	$Ph_3PAuCl/AgSbF_6$	80	1.3:1



40

Table 9

Rate Acceleration with Tri(ethynyl)phosphine Ligands



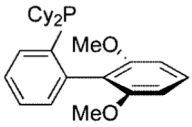
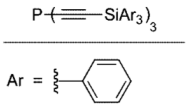
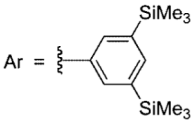
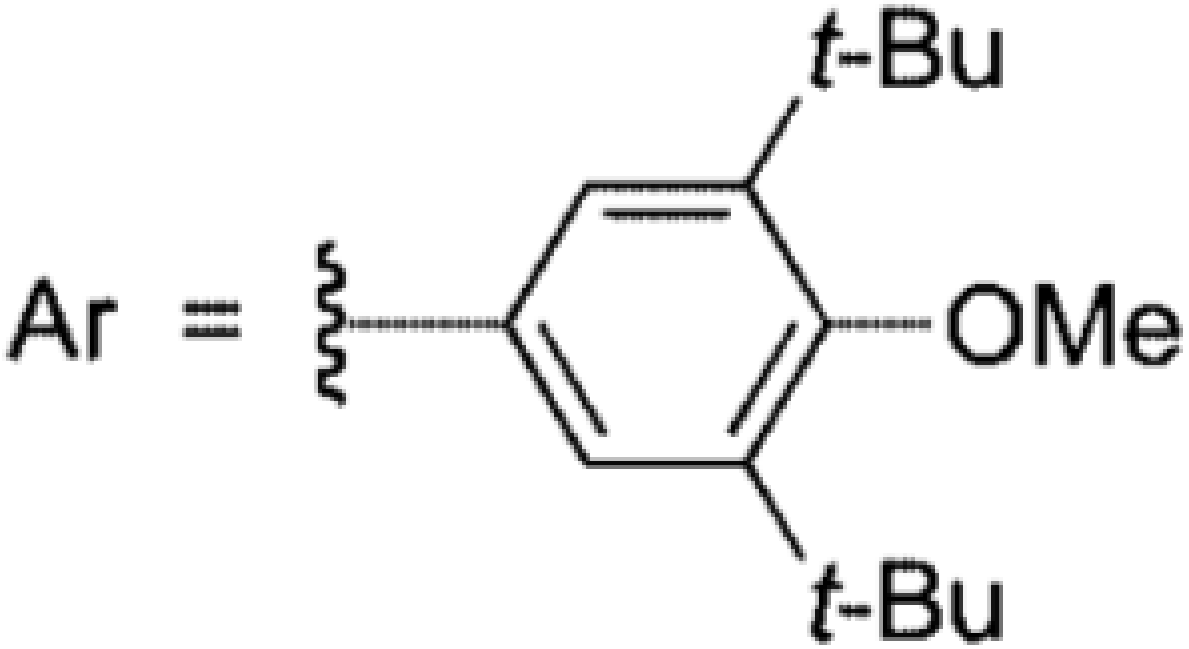
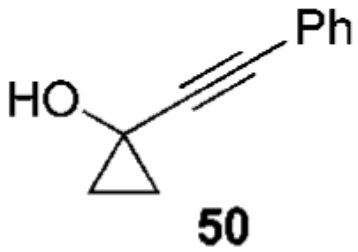
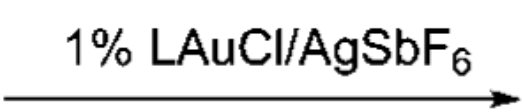
entry	ligand	time
1	PPh_3	1.5 h
2		1.5 h
3	$(P(OPh)_3$	6 h
4		2.5 h
5		5 h
6		1.5h

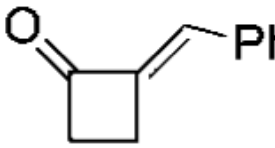
Table 10

Ring Expansion of Propargyl Cyclopropanol 50

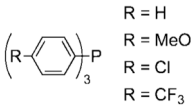


50





51

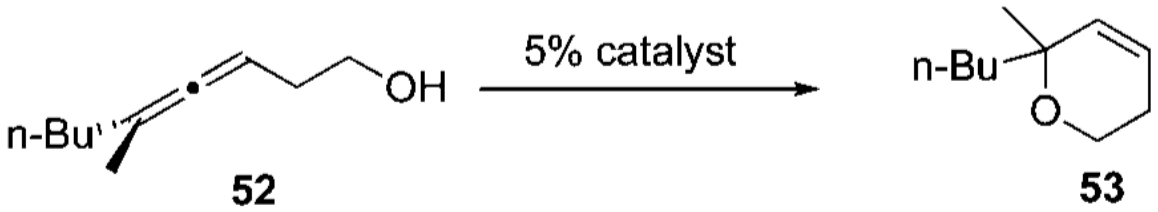
entry	ligand(L)	tim
1	 R = H	115 m
2	R = MeO	160 m
3	R = Cl	85 m
4	$R = CF_3$	25 m
5	*t*-Bu_3P	24
6		24

[a] Time to 99% conversion of SM.

[b] Determined by ^{1}H NMR.

Table 11

Cyclization of *γ*-Allenyl Alcohols

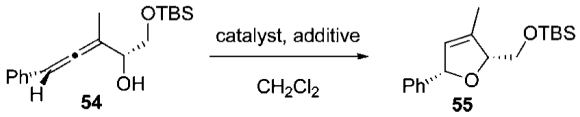


52 53

entry	catalyst	solvent, (*T*)	time	yield (%)
1	$AuCl_3$[a]	CH_2Cl_2 (rt)	6 d	58
2	$AuCl_3$/pyridine	CH_2Cl_2 (rt)	4.5 h	64
3	$AuCl_3$/2,2′-bipyridine	CH_2Cl_2 (rt)	5 d	86
4	$Ph_3PAuCl/AgBF_4$	CH_2Cl_2 (rt)	1.5 h	60
5	$Ph_3PAuCl/AgBF_4$	toluene (0 °C)	1.25 h	66

[a] 0.195 M solution in CH_3CN.

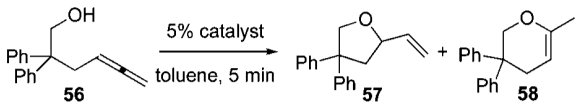
Table 12
Chirality Transfer From Stereodefined Allenyl Alcohols



entry	catalyst (%)	additive (%)	*T*	% yield (cis:trans)
1	$AuCl_3$ (2%)	-	rt	81 (75:25)
2	AuCl (2%)	-	rt	85 (60:40)
3	$AuCl_3$ (2.5%)	2,2-bipyridine (5%)	rt	70 (>97:3)
4	AuCl (2.5%)	2,2-bipyridine (3.8%)	rt	96 (95:5)
5	$AuCl_3$ (1%)	-	-30 °C	92 (97:3)

Table 13

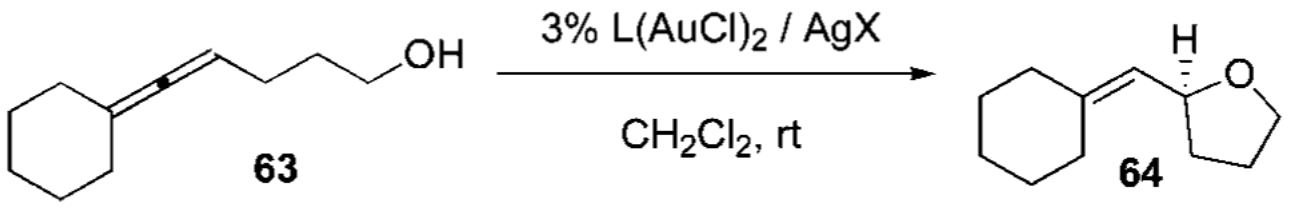
5-*exo*-trig vs 6-*exo*-dig Cyclization



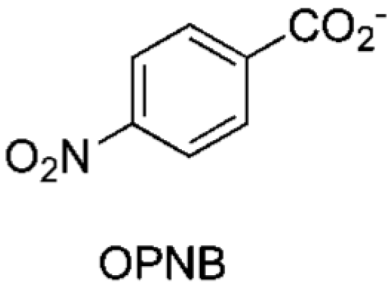
entry	catalyst	57:58	yield (%)
1	(*o*-biphenyl)(*t*-Bu)$_2$PAuCl/AgOTf	56:44	85
2	(*o*-biphenyl)(t-Bu)$_2$PAuCl/AgOTs	99:1	96
3	[PtCl(ethylene)$_2$]$_2$/(*p*-CF_3-C_6H_4)$_3$P	0:100	49

Table 14

Chiral Counterion Effects in a Tetrahydrofuran Synthesis



entry	ligand (L)	X	yield (%)	ee (%)
1	(*R*)-3,5-xylyl-BINAP	BF_4	68	0
2	(*R*)-3,5-xylyl-BINAP	OPNB	89	8
3	(*R*)-DTBMSegphos	BF_4	79	2
4	dppm	**65**	76	65



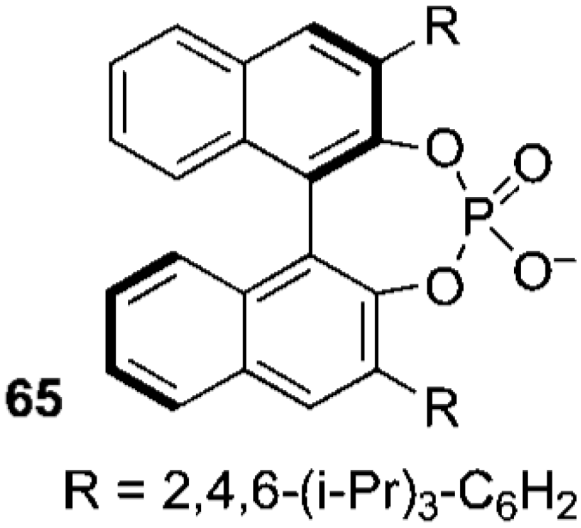
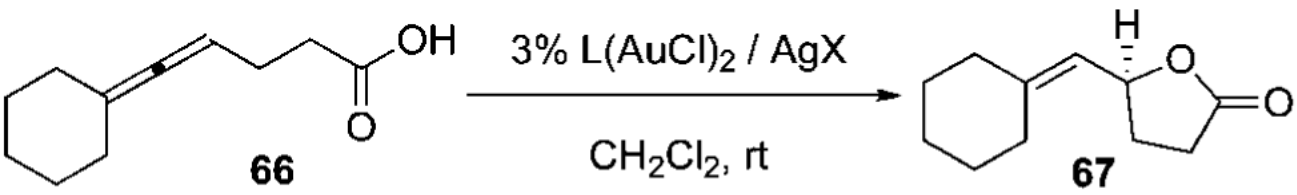


Table 15

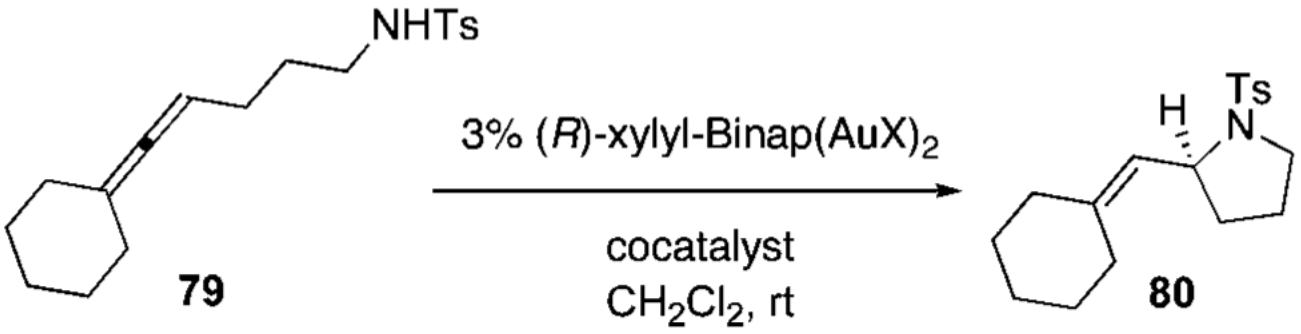
Enantioselective Cyclization of Allenyl Carboxylate 66



entry	L	X	yield (%)	ee (%)
1	(*R*)-Binap	OPNB	80	38 (*R*)
2	dppm	(*R*)-65	89	12 (*S*)
3	(*R*)-Binap	(*R*)-65	91	3 (*R*)
4	(*S*)-Binap	(*R*)-65	88	82 (*S*)

Table 16

Counterion Effects in Enantioselective Allene Hydroamination



entry	X	% cocatalyst	yield (%)	ee (%)
1	Cl	6 $AgBF_4$	82	1
2	Cl	3 $AgBF_4$	81	51
3	Cl	6 AgOBz	27	98
4	Cl	6 AgOPNB	76	98
5	OPNB	none	88	98

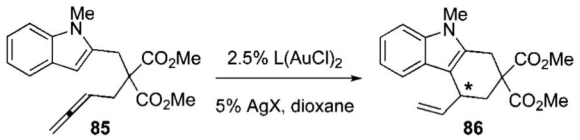
Table 17

Au-Catalyzed Hydroarylation Toward (-)-Rhazinilam

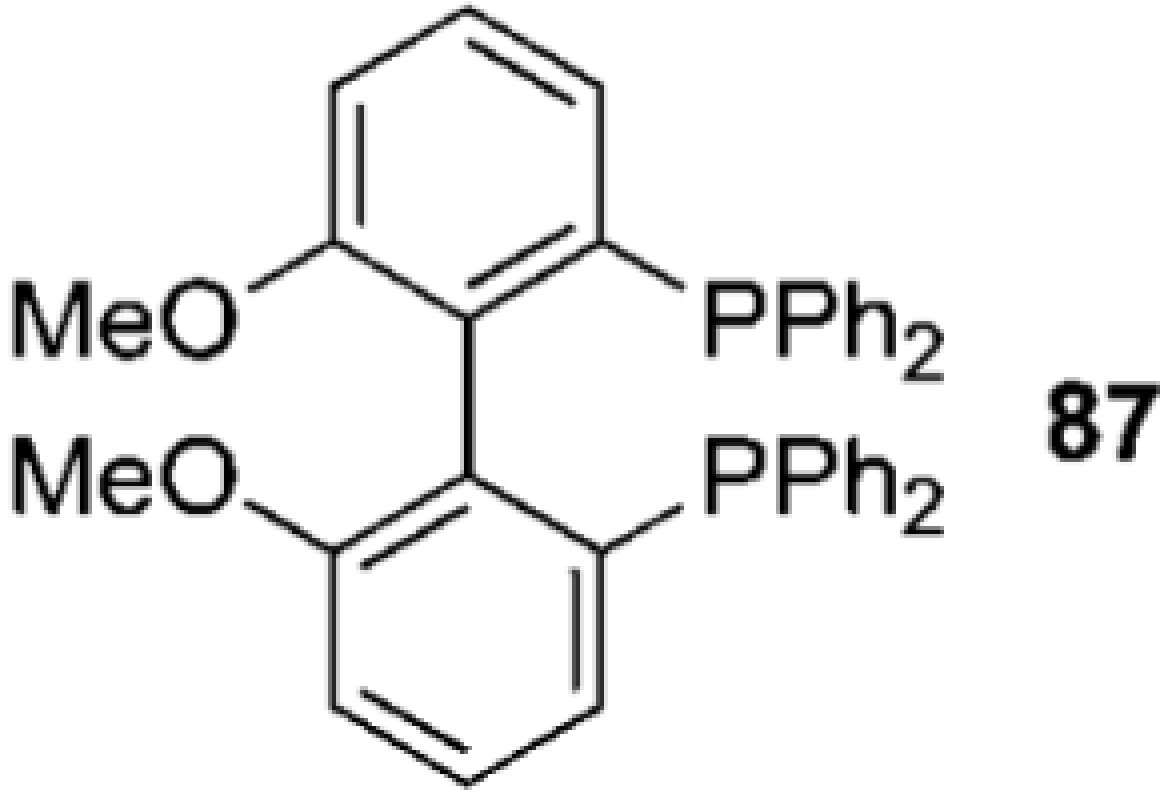
entry	% catalyst	dr	yield (%)
1	30 $(MeCN)_2PdCl_2$	67:33	83
2	10 $AuCl_3$	92:8	27
3	5 $AuCl_3$, 20 AgOTf	92:8	82
4	5 Ph_3PAuCl, 5 AgOTf	97:3	92

Table 18

Asymmetric Hydroarylation of Allenes



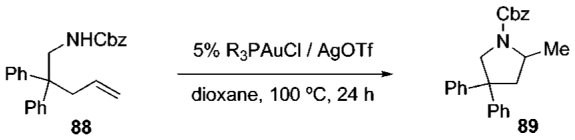
entry	ligand (L)	X	ee (%)
1	(*S*)-Binap (**7**)	OTf	32
2	(*S*)-xylyl-Binap (**9**)	OTf	42
3	(*S*)-MeO-Biphep (**87**)	OTf	48
4	(*S*)-MeO-Biphep (**87**)	BF_4	55
5	(*S*)-DTBM-MeO-Biphep (**62**)	BF_4	76



87

Table 19

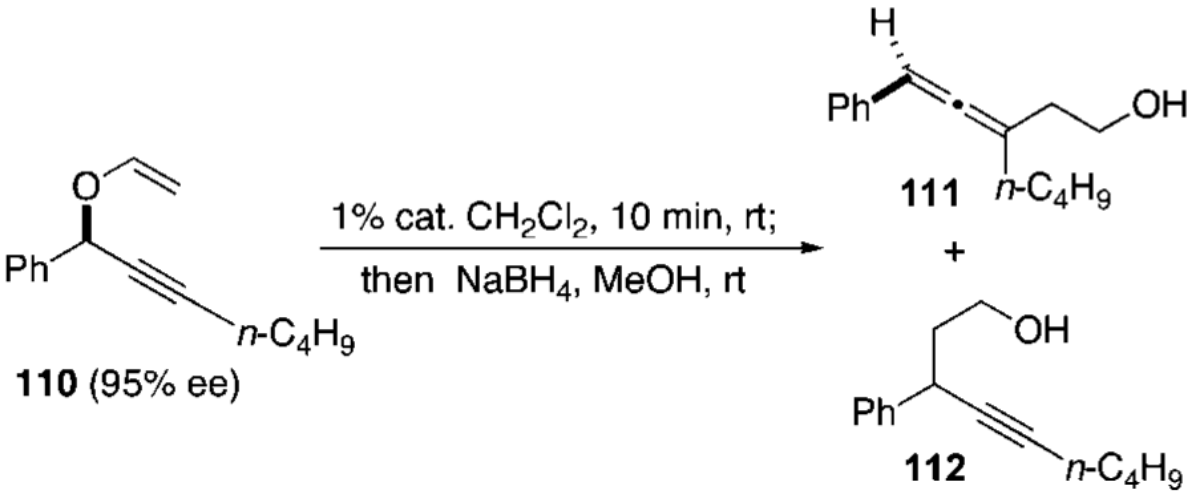
Gold(I)-Catalyzed Alkene Hydroamination



entry	PR_3	^{1}H NMR yield (%)
1	PPh_3	75
2	P(4-OMe-Ph)$_3$	70
3	P(4-CF_3-Ph)$_3$	23
4	PMe_2Ph	7
5	P(*t*-Bu)$_2$(*o*-biphenyl)	98

Table 20

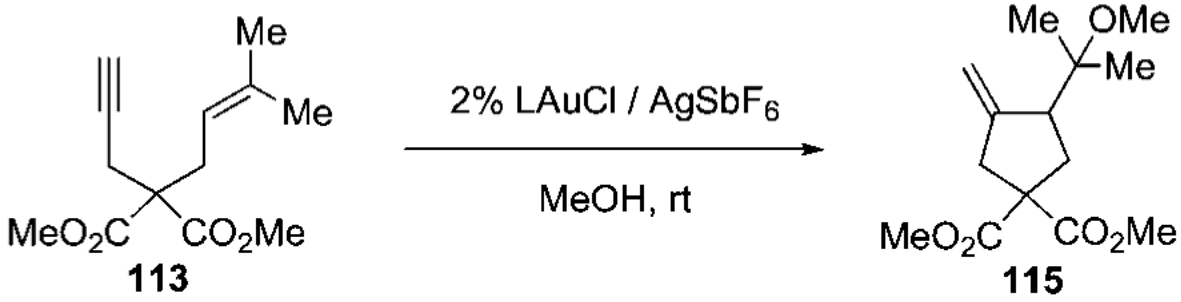
Au-Catalyzed Propargyl Claisen Reaction



entry	catalyst	111:112	ee (111) (%)	yield (111) (%)
1	$Ph_3PAuCl/AgOTf$	1.7:1	82	44
2	$Ph_3PAuCl/AgBF_4$	20:1	4	85
3	$[(Ph_3PAu)_3O]BF_4$	20:1	90	91

Table 21

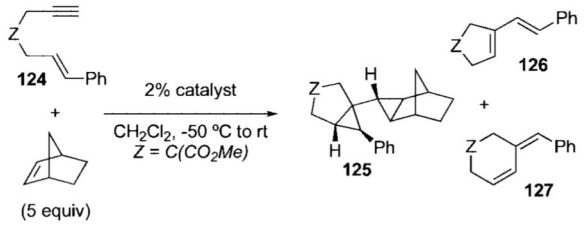
Biphenyl Phosphine Ligands in the Reaction of 113



entry	ligand (L)	time (h)	yield (%)
1	PPh_3	3	84
2	P(*o*-tol)$_3$	24	90
3	P(1-naphthyl)$_3$	18	76
4	P(Cy)$_2$(*o*-biphenyl)	0.5	97

Table 22

Intermolecular Cyclopropanation of 1,6-Enynes



entry	gold catalyst	125	126 + 127
1	$[(Ph_3P)Au(NCMe)]SbF_6$	66%	29% (1:1.2)[a]
2	$[((t\text{-}Bu)_2(o\text{-biphenyl})P)Au(NCMe)]SbF_6$	34%	62% (1.1:1)
3	$(ArO)_3PAuCl$ / $AgSbF_6$[b]	40%	52% (1:1.6)
4	(IMes)AuCl / $AgSbF_6$	93%	3% (>10:1)
5	AuCl	94%	0%

a) 126 : 127

b) Ar = (2,4-(t-Bu)$_2$-Ph)

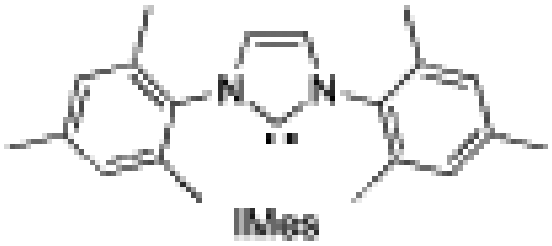
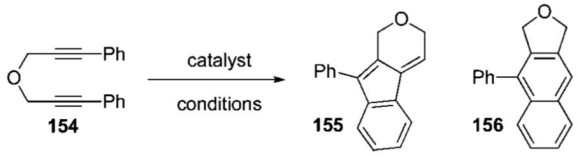


Table 23

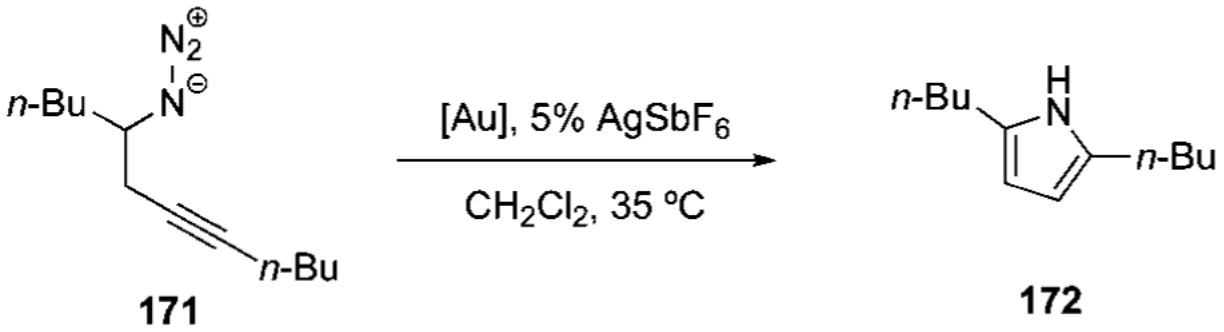
Isomerization of 1,6-Diyne 154



entry	catalyst	conditions	yield (%) (155:156)
1	2% $Ph_3PAuCl/AgSbF_6$	CH_2Cl_2, 23 °C	93 (100:0)
2	5% $Ph_3PAuCl/AgOTf$	DCE, 50 °C	20 (90:10)
3	5% AuCl	toluene, 100 °C	17 (18:82)
4	5% $AuCl_3$	toluene, 100 °C	29 (48:52)

Table 24

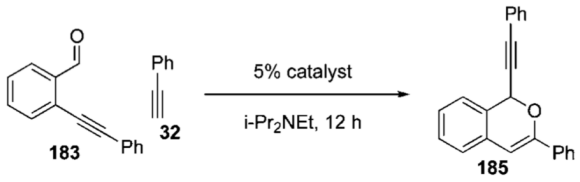
Acetylenic Schmidt Reaction



entry	gold catalyst (mol%)	yield 171 (%)	yield 172 (%)
1	$(Ph_3P)AuCl$ (5)	9	72
2	$[(4\text{-}OMe\text{-}Ph)_3P]AuCl$ (5)	23	58
3	$[(4\text{-}CF_3\text{-}Ph)_3P]AuCl$ (5)	42	51
4	$(dppm)(AuCl)_2$ (2.5)	0	93
5	$(dppp)(AuCl)_2$ (2.5)	0	86

Table 25

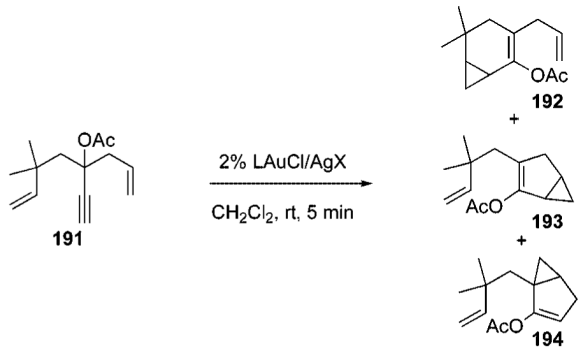
Au-Catalyzed Isochromene Synthesis



entry	catalyst	conditions	yield (%)
1	$Cy_3PAuCl/AgOTf$	H_2O, 80 °C	trace
2	Cy_3PAuCl	H_2O, 80 °C	0
3	Ph_3PAuCl	H_2O, 80 °C	11
4	Me_3PAuCl	H_2O, 80 °C	44
5	Me_3PAuCl	toluene, 70 °C	nr
6	Me_3PAuCl	H_2O/toluene (1:1), 70 °C	87

Table 26

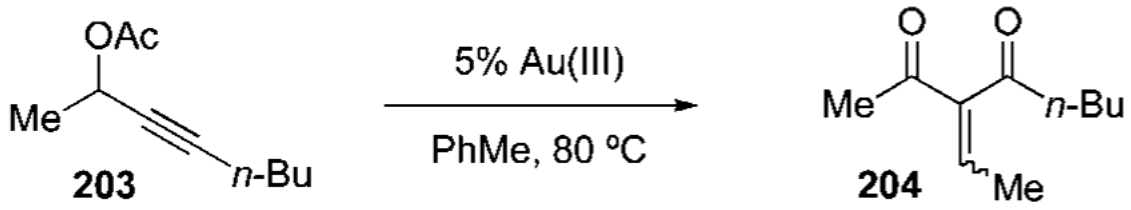
Cycloisomerization of Acetoxy 1,n-Enynes



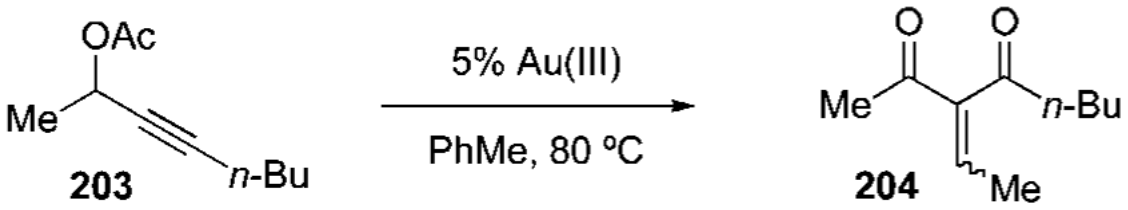
entry	L	X	192 (yield %)	193 (yield %)	194 (yield %)
1	Ph_3P	BF_4	50	2	12
2	IMes	BF_4	26	12	40
3	IPr	BF_4	30	12	42
4	IPr	OTf	63	13	0

Table 27

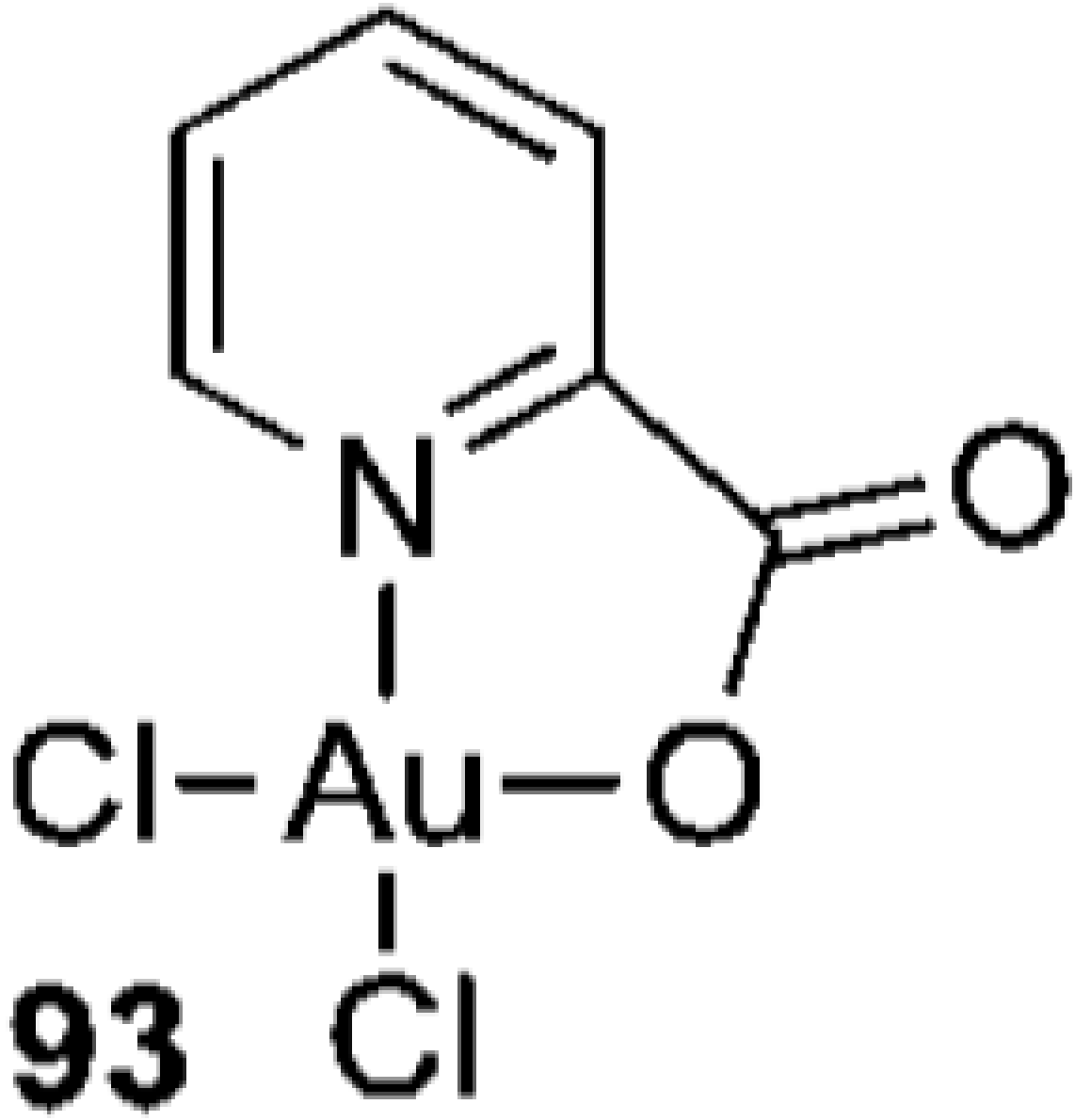
Au-Catalyzed Enedione Synthesis



entry	catalyst	time
1	$AuCl_3$	0.25h
2	$(py)AuCl_3$	12 h



203 204

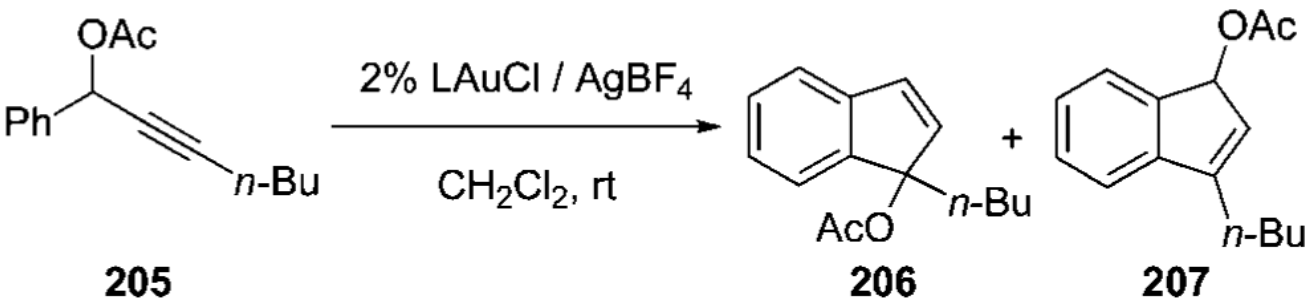
entry	catalyst	time
3		1.5h

93

[a] Isolated Yield.

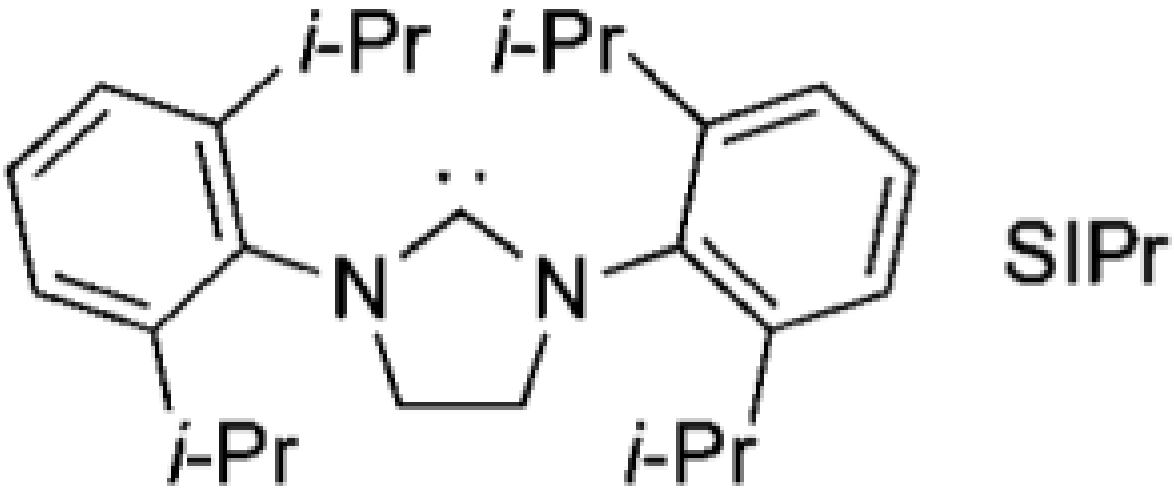
Table 28

Au-Catalyzed Indene Synthesis



205 **206** **207**

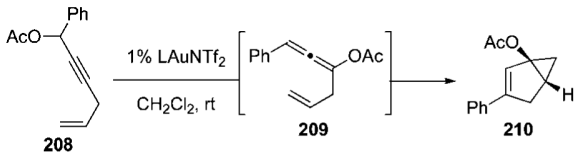
entry	ligand	time (min)	206 (%)	207 (%)
1	PPh_3	5	51	32
2	ITM	5	54	23
3	SIPr	5	88	5
4	IPr	5	92	0



SIPr

Table 29

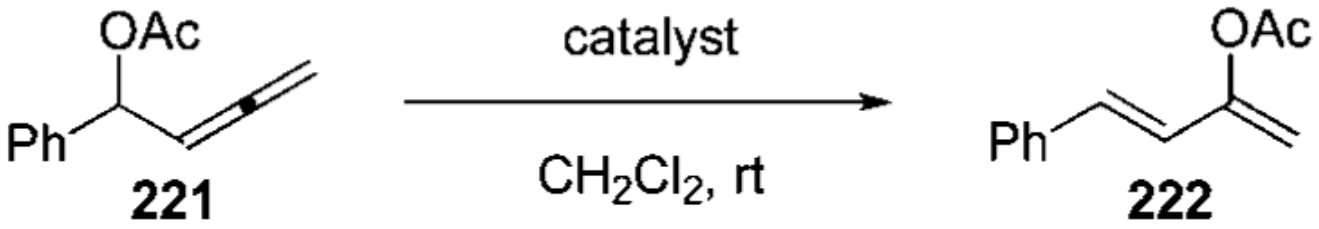
Tandem [3,3]/Allenene Cycloisomerization



entry	ligand	time (h)	209 (%)/210 (%)
1	PPh_3	6	41/49
2	$P(4\text{-}CF_3\text{-}Ph)_3$	6	53/32
3	$P(n\text{-}Bu)(Ad)_2$	6	21/78
4	$P(t\text{-}Bu)_2(o\text{-biphenyl})$	1	0/98

Table 30

[3,3] Rearrangement of Allenyl Acetates

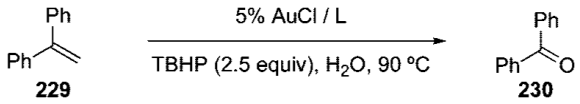


entry	catalyst	conversion (%)	yield (%)
1	2% $AuBr_3$	<5	0
2	1% $Ph_3PAuNTf_2$	15	6
3	1% (2-(Ar)-Ph)$(Cy)_2PAuNTf_2$ [a]	100	98

[a] Ar = 2,4,6-(*i*-Pr)3-Ph

Table 31

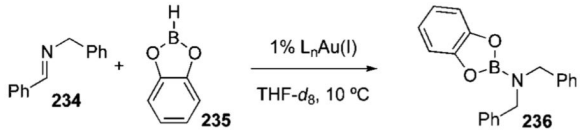
Au-Catalyzed Oxidative Cleavage



entry	ligand	time (h)	yield (%)
1	-	24	<10
2	pyridine	10	41
3	bipyridine	10	23
4	phenanthroline	10	16
5	neocuproine	2	93

Table 32

Imine Hydroboration



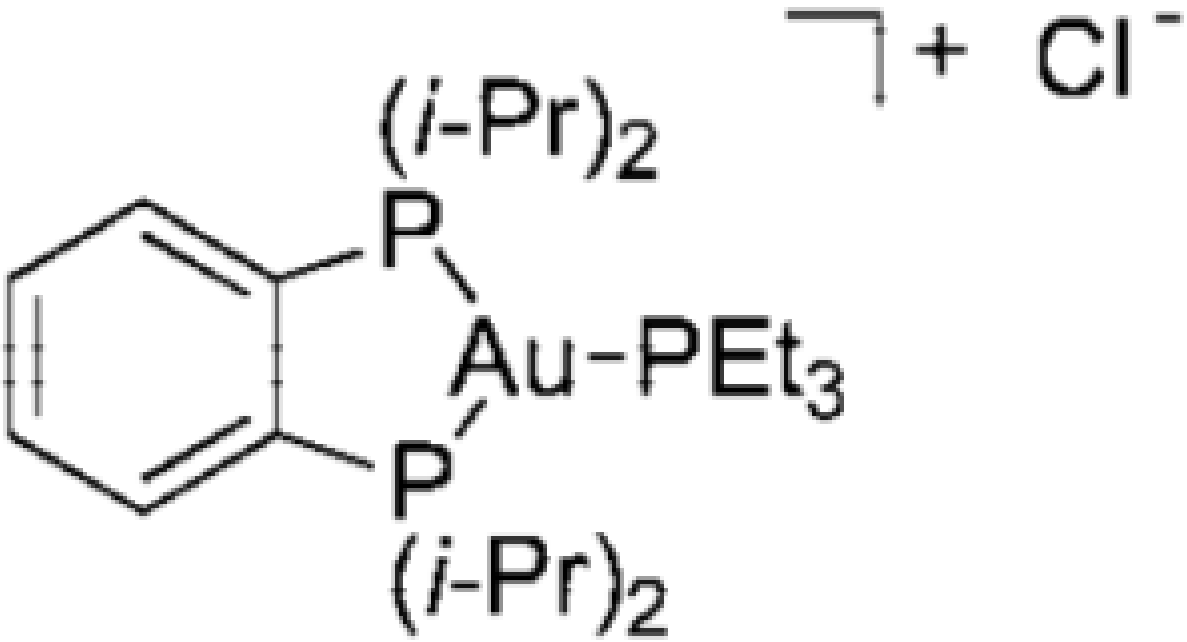
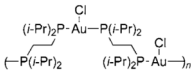
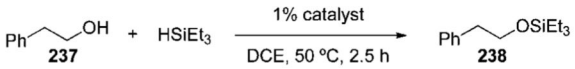
entry	catalyst	relati
1	*none*	
2	$(Et_3P)AuCl$	
3		
4		1
5	$[AuCl(\mu\text{-DPPF})]_n$	>

Table 33

Reductive Silylation of 237



entry	catalyst	GC yield (%)
1	$(Me_2S)AuCl$	11
2	dppe/$(Me_2S)AuCl$	0
3	dppf/$(Me_2S)AuCl$	11
4	$(Ph_3P)AuCl$	2
5	Xantphos/$(Me_2S)AuCl$	94
6	(Xantphos)AuCl	100

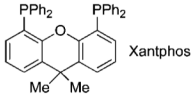
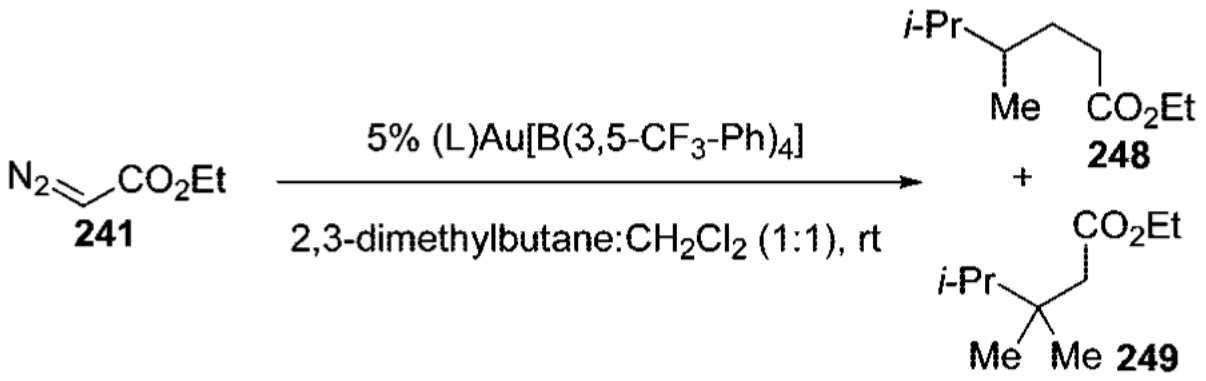


Table 34

Alkane C-H Insertion



entry	L	yield (%) (248:249)
1	IPr	85 (83:17)
2	IAd	74 (60:40)
3	I-*t*-Bu	61 (53:47)
4	IMes	25 (32:68)