Published in final edited form as:

Chem Rev. 2021 July 28; 121(14): 8979–9038. doi:10.1021/acs.chemrev.0c00774.

Homogeneous Gold-Catalyzed Oxidation Reactions

Zhitong Zheng[†],
Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Xu Ma[†],
Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Xinpeng Cheng,
Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Ke Zhao,
Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Kaylaa Gutman,
Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Tianyou Li,
Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Liming Zhang
Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States

Abstract

Homogeneous gold catalysis has experienced extraordinary development since the dawn of this millennium. Oxidative gold catalysis is a vibrant and fertile subfield and has over the years delivered a diverse array of versatile synthetic methods of exceptional value to synthetic practices. This review aims to cover this topic in a comprehensive manner. The discussions are organized by the mechanistic aspects of the metal oxidation states and further by the types of oxidants or oxidizing functional groups. Synthetic applications of oxidative gold catalysis are also discussed

Graphical Abstract

Corresponding Author Liming Zhang – *Department of Chemistry and Biochemistry, University of California, Santa Barbara, California 93106, United States*; zhang@chem.ucsb.edu.
[†]Author Contributions
Z.Z. and X.M. contributed equally. The manuscript was written through contributions of all authors.

The authors declare no competing financial interest.

1. INTRODUCTION

Since the beginning of this millennium, homogeneous gold catalysis has experienced explosive development. With increasing efforts from many laboratories around the world, this research field has contributed a diverse array of versatile synthetic methods and remains vibrant. One highly rewarding area of gold chemistry is oxidative gold catalysis[1–11] employing an internal or external oxidant. The high redox potentials of gold metal offer the advantage of oxidation state stability in the presence of mild oxidants. As a result, many versatile oxidative methodologies have been developed using Au(I) or Au(III) catalysis wherein the metal oxidation state does not change; these methods are covered in Section 2. The related reactions involving α-imino gold carbene intermediates are also formally oxidative and have recently been reviewed;[12] they will not be covered here. In the presence of strong oxidants, Au(I) complexes can be oxidized to Au(III) species, which can subsequently undergo reductive elimination. Section 3 discusses the manifestations of this mechanistic pathway.[1] The related cross-coupling reactions using aryldiazonium salts do not result in substrate oxidation despite the nature of Au(I)/Au(III) catalysis. Hence, they are not covered here, but they have been recently reviewed.[13–15] Also not covered are reactions where the oxidation step apparently does not involve gold. Oxidative gold catalysis methods with little mechanistic insights or under-standing are discussed in Section 4.

Though many reviews on gold catalysis have been published, few focus solely on oxidative gold catalysis.[1–7,10,11] This review aims to provide comprehensive coverage of the topic and is organized by the mechanistic aspects of metal oxidation state and furthermore by the external oxidants or oxidizing functional groups employed in the reactions.

2. REACTIONS WITHOUT METAL OXIDATION STATECHANGE

2.1. Activated Alkynes or Allenes Attacked by Nucleophilic Oxidants or Oxidizing Groups

Au salts/complexes and especially cationic Au(I) in the form of LAu^+X^- (L = ligand; X^- = weakly coordinating or non-coordinating anion) are potent π-acids and can effectively activate unsaturated systems, particularly alkynes and allenes, toward nucleophilic attack. As the nucleophile is an oxidant, this attack would lead to eventual substrate oxidation. Scheme 1 outlines the two pathways of this type of gold-catalyzed oxidation. Initially, the C–C triple bond is activated by a π-acidic cationic Au(I) complex or a Au(III) salt, thereby making it susceptible toward attack by a nucleophile. In this particular case, an O-nucleophilic oxidant featuring a weak O–Z bond attacks the alkyne to deliver alkenylgold intermediate **A**. Subsequent heterolytic fragmentation of its weak O–Z bond constitutes alkyne oxidation and is the driving force for diverse subsequent transformations. One outcome is the formation of the highly electrophilic α-oxo gold carbene **B**. Although α-diazo carbonyl compounds could in principle be employed to access the same carbene species,[16,17] these substrates are hazardous and potentially explosive. Moreover, preparation of the diazo substrates often uses hazardous/energetic reagents and requires multiple steps. As alkynes are in general benign and readily accessible, this carbene pathway of oxidative gold catalysis can offer much-improved operational safety and synthetic efficiency relative to the diazo approach.[18] On the other hand, the initial adduct **A** might bypass the carbene intermediate **B** if an alternative lower-energy pathway is available and directly undergo transformations to afford the same oxidized functional products. It is often the case (*vide infra*) that density functional theory (DFT) calculations and/or experimental mechanistic studies are required to elucidate whether the α-oxo gold carbene **B** is formed. Literature reports of this nature will be discussed accordingly. Because **A**, when bypassing **B**, exhibits carbene-like reactivity en route to the anticipated carbene pathway product, we term this alternative reaction path as the carbenoid pathway.[19]

2.1.1. Sulfoxides as Oxidants.—Sulfoxides, though they are mild oxidants, were the first class of nucleophilic oxidants employed in this type of oxidative gold catalysis. Toste[20] and L. Zhang[21] reported separately in 2007 that the tethered sulfoxide of (but-3-yn-1-ylsulfinyl)benzene (i.e., **1**) can oxidize its terminal C–C triple bond in the presence of a cationic Au(I) catalyst or a Au(III) salt, affording the 2,3-dihydrobenzo[*b*]-thiepin-4(5*H*)-one (i.e., **2**) in >90% yield in both cases (Scheme 2A). The reaction mechanism initially proposed by both research groups is shown in the scheme and entails intramolecular nucleophilic attack at the gold-activated C–C triple bond by the sulfoxide oxygen of **1** in a 5-*exo*-*dig* cyclization, subsequent formation of 1,2-oxathiolan-2-ium-containing alkenylgold intermediate **C**, heterolytic fragmentation of the weak S–O bond to form the anticipated α-oxo gold carbene **D**, and finally Friedel–Crafts-type cyclization by the carbene center to form the product. What is surprising is the high efficiency in the formation of the seven-membered ring under this mechanistic scenario. When a substrate possessing an internal alkyne was employed, the alternative 6-*endo*-*dig* cyclization occurred, leading to a thiochromane product such as **4.**

DFT studies by Fang[22] on the formation of 3 and its corresponding *endo*-attack product (related to **4**) under the Toste conditions lend support to the proposed carbene pathway mechanism. However, the theoretical work did not consider alternative reaction pathways and in particular an alternative carbenoid pathway. Apparent issues with the carbene mechanism are the exceptionally high yield of the seven-membered ring and, more concerningly, the absence of the likely facile formation of five-membered sulfonium salt **E** due to attack at the electrophilic gold carbene by sulfur. Later DFT studies and experimental works by Y. Li and L Zhang[23] concluded that an alternative 3,3-sigmatropic rearrangement of C resulting in one-step construction of the seven-membered ring of intermediate **F** is more likely and readily addresses the issues associated with the carbene pathway. This carbenoid pathway is also likely responsible for the formation of **4**. This reaction was extended to the formation of eight- and nine-membered sulfur-containing cyclic ketones.[23]

However, this mechanistic complexity does not necessarily invalidate this oxidative approach to reactive α-oxo gold carbene intermediates. In L. Zhang's study,[21] the intended gold carbene formation is coupled with a semipinacol rearrangement, which leads to the formation of 1,3-dicarbonyl compounds **5** (Scheme 2B). The use of 2-chlorophenyl apparently slows the 3,3-sigmatropic rearrangement process. Consequently, the formation of α-oxo gold carbene intermediate **G** is kinetically viable, although an alternative carbenoid pathway entailing concerted R^1 migration and S–O bond fragmentation of the initial cyclized intermediate could not be ruled out.

Perhaps a more definitive demonstration of the carbene pathway is the work reported by Davies.[24] As shown in Scheme 3, the proposed mechanism involves trapping of the gold carbene moiety of **H** by sulfur to generate sulfonium salt **I** and subsequently sulfur ylide **J** upon gold dissociation, which can then undergo a 2,3-sigmatropic rearrangement (the Doyle–Kirmse reaction) to afford the observed product. It appears that there was no readily available carbenoid alternative for this transformation. Notably, $PtCl_2$ is able to promote this reaction as well, albeit less effectively than the Au(III) catalyst.

External sulfoxides, in the form of aryl sulfoxides (see Scheme 4, compounds **6** and **7**), can also oxidize alkynes under gold catalysis. Ujaque and Asensio reported a gold-catalyzed intermolecular oxoarylation of terminal alkynes in 2009 (Scheme 4A).[25] The exclusive functionalization at the *ortho*-position of sulfoxide **6** is consistent with a 3,3-sigmatropic rearrangement of the initial adduct **K** and does not support a Friedel–Crafts reaction by an α-oxo gold carbene. This conclusion is further supported by DFT studies and inspired subsequent mechanistic work on the intramolecular variants by L. Zhang (see Scheme 2A).[23] A related study was later reported by Davies and Grainger by using dibenzo[*b,d*]thiophene 5-oxide as the oxidant (Scheme 4B).[26]

In 2010, R.-S. Liu realized another gold-catalyzed intermolecular oxidation of alkynes with sulfoxides, in which cyclopropyl alkynes are converted to cyclobutenyl ketone products (e.g., **8**) in moderate to excellent yields (Scheme 5).[27] High temperature (100 °C) and a large excess of diphenyl sulfoxide (5 equiv) were necessary to achieve reasonable yields and full substrate conversions. Although the intermediacy of an α-oxo gold carbene in the reaction was initially considered, subsequent mechanistic studies all suggested a carbenoid pathway

in which the ring expansion is concurrent with the expulsion of diphenyl sulfide, as outlined in the structures of **L** and **M**. Additionally, the authors were able to synthesize a series of *2H*-pyrans **9,** which was facilitated by ring cleavage of the dimethylcyclopropyl moiety.

After the initial gold-catalyzed nucleophilic addition, the alkyne–sulfoxide adduct (e.g., **N**) could undergo further oxidation in the presence of additional sulfoxide oxidants, giving benzils as the product. C.-Y. Li reported such a transformation on aryl alkynes and ynamides with diphenyl sulfoxide as the oxidant (Scheme 6).[28] Attempts to trap the gold carbene intermediate with a large excess of styrene failed to give any cyclopropanation product, which suggests that the reaction might follow a carbenoid pathway. A series of substituted benzils and 2-oxo-2-phenylacetamides were prepared with high efficiency.

The synthesis of 2-acyl-1-naphthols by gold-catalyzed oxidative cyclization of 2-alkenylphenyl alkynyl ketones was reported by Matsuda (Scheme 7).[29] Two distinct mechanistic pathways were proposed. In path A, the starting material **10** undergoes a 6-*exo*-*dig* cycloisomerization to give gold carbene intermediate **O**, followed by sulfoxide oxidation of the gold carbene center to furnish the final product **11** (see Section 2.2 for related works on sulfoxide oxidation of gold carbenes). In path B, the gold-facilitated sulfoxide oxidation of the C–C triple bond occurs first, and α-oxo gold carbene **P** undergoes electrophilic cyclization to the C–C double bond to give the final product. Although the authors did not attempt to intercept any reactive intermediates to further elucidate the actual mechanism, a comparative experiment was run with compound **12,** a structural isomer of the methyl homologue of the original substrate **10.** Interestingly, the original conditions using diphenyl sulfoxide as the oxidant did not lead to substrate oxidation and furnished only the alkenylation product **14**, while employing pyridine *N*-oxide as the oxidant led to the desired oxidation and the expected 2-acyl-1-naphthol **13**.

2.1.2. *N*-Oxides as Oxidants.—In comparison to sulfoxides, *N*-oxides are in general stronger nucleophiles, which can be correlated with their stronger Brønsted basicity, and can be stronger oxidants. Their employment as nucleophilic oxidants has greatly enriched the field of oxidative gold catalysis and has evolved into the prime strategy for accessing gold-catalyzed alkyne oxidation. Among the *N*-oxides, aniline- or tertiary-amine-derived ones are only employed intramolecularly. Their participation in oxidative gold catalysis, as discussed in Sections 2.1.2.4 and 2.1.2.8, most likely follows carbenoid mechanistic pathways. On the other hand, *N*-oxides of *N*-heteroarenes, in particular pyridines and quinolines, are the overwhelming choices for nucleophilic oxidants. Of high synthetic significance is the fact that they readily participate in intermolecular alkyne oxidations, which conceptually and in many instances practically achieve the replacement of hazardous diazo carbonyl compounds with benign and easily accessible alkynes.

A list of *N*-heteroarene *N*-oxides that have been successfully employed as external oxidants with their frequencies of occurrence is shown in Figure 1. The frequencies were derived by counting the number of publications in which they were employed in the reaction scope studies. From the figure, it is apparent that 8-alkylquinoline *N*-oxides, with 41 combined occurrences out of a total of 110, are versatile and preferred nucleophilic oxidants. Of pyridine *N*-oxides, ones that are electron-deficient and/or sterically hindered are preferred.

In early studies using sterically unhindered pyridine *N*-oxides, stoichiometric amounts of an acid additive (typically MsOH) were added to reactions in order to neutralize pyridine byproducts, which are basic and can impede or inhibit gold catalysis via metal binding. With sterically hindered 8-alkylquinoline *N*-oxides (in orange color) and 2-substituted or 2,6-disubstituted pyridine *N*-oxides (in azure color), no acid additives are needed since the *N*-arene byproducts are too sterically hindered to bind to gold effectively. Notably, nitrones can be effective internal oxidants and in some cases serve as valuable external oxidants that deliver an *in situ*-generated imine that can be subsequently trapped. Hashmi recently conducted kinetic studies of several oxidative gold catalysis reactions using an extensive collection of *N*-heteroarene *N*-oxides. That work revealed that 2,5-dibromopyridine *N*-oxide and 2-trifluorome-thylpyridine *N*-oxide are highly effective nucleophilic oxidants and confirmed that 8-methylquinoline *N*-oxide is among the best oxidants.[30] They recommended that these three oxidants should be screened in condition optimizations.

2.1.2.1. Reactions of Carbene/Carbenoid Intermediates with Oxygen-Based Nucleophiles.: The first examples of intermolecular generation of proposed *α*-oxo gold carbenes were reported by L. Zhang in 2010,[31] where 3,5-dichloropyridine *N*-oxide was the optimized oxidant. An example is shown in Scheme 8A, where a cyclohexane-fused homoproparyglic alcohol is converted into strained *trans*-fused dihydrofuranone **15** in 88% yield. The proposed mechanism entails the oxidative generation of *α*-oxo gold carbene **Q** followed by an intramolecular carbene O–H insertion. Because of the highly electrophilic nature of the gold carbene center, it is likely, as demonstrated later,[32] that the insertion is not concerted and may involve the gold *C*-enolate **R** and/or gold *O*-enolate **S** intermediate prior to protodeauration, which furnishes the final product. Various dihydrofuran-3-ones can be accessed in moderate to excellent yields. Of note is that in this early work stoichiometric amounts of MsOH were used in order to neutralize the 3,5-dichloropyridine generated during the reaction. This pyridine byproduct apparently traps the cationic gold catalyst and therefore halts the reaction in the absence of an acid additive, as later confirmed by Hashmi's study.[30]

Soon after, L. Zhang applied this strategy in the synthesis of more challenging oxetan-3-ones.[33] As shown in Scheme 8B, secondary propargylic alcohols or tertiary propargylic alcohols with an electron-withdrawing carboxylate group terminating the C–C triple bond react well under different optimized conditions. Because of the strong acidity of Tf_2NH employed to neutralize the pyridine byproducts, the ester group in the cases of tertiary propargylic alcohol substrates is essential to avoid propargylic cation formation. This method provides a straightforward synthesis of enantiomerically enriched oxetan-3-one products from chiral propargylic alcohol substrates. For example, propargylic alcohol **16** with 80% ee is converted to cyclobutanone **17** (81% ee) without detectable configuration erosion. While a carbenoid pathway for the formation of the five-membered-ring product in Scheme 8A could not be ruled out, this one-step construction of strained four-membered rings most likely involves an *α*-oxo gold carbene intermediate.

In 2019, Hu and X. Xu reported that *O*-enolate **S** could be trapped in preference to protodeauration in the form of aldol interception by isatin (Scheme 8C).[34] The high diastereoselectivity of this step is explained by the assembly shown in **T** that involves

hydrogen bonding between the isatin oxygens and the oxonium proton. In this case, a pyridine *N*-oxide is used, and an acid additive (i.e., trifluoroacetic acid) is needed.

By the use of homopropargylic ethers as substrates, oxonium intermediates of the type **R/S** in which the proton is replaced by an alkyl group would be generated. In 2012, C. Li reported a study of the reactivity of these substrates.[35] As shown in Scheme 9, a homopropargylic methyl/benzyl ether is oxidatively converted into either enone **18**, cyclobutanone **19**, or both. There is a clear trend in product distribution: when R^1 is alkyl, phenyl, or electron-withdrawing group (EWG)-substituted phenyl, only **18** is formed, and when R^1 is an electron-rich aryl group such as 4-methoxyphenyl or 2-furyl, **19** is formed as the major or exclusive product. In the proposed mechanism, oxonium **U** would in most cases undergo E2-type elimination followed by protodeauration to afford enone **18**, but when R^1 can accommodate the positive charge effectively, **U** undergoes C–O bond fragmentation to form carbocation **V**, which can then undergo cyclization to deliver the cyclobutanone product **19**. The one-step conversion of **U** to **19** in a [1,2]-shift, as outlined by the purple arrows, is less likely.

A related trapping strategy was applied by L.-W. Ye for the synthesis of versatile 3-coumaranones (Scheme 10A).[36] In this case, oxonium intermediate **X** undergoes demethylation. DFT studies of the reaction revealed that the initial adduct, formed by attack at the gold-activated C–C triple bond by 8-isopropylquinoline *N*-oxide, does not undergo fragmentation to form the α-oxo gold carbene **W**. Instead, a carbenoid pathway is more likely and entails concerted MeO cyclization and N–O bond cleavage. This development suggests that the alcohol trapping in Scheme 8A en route to dihydrofuranones might follow a carbenoid pathway.

Bis(homopropargylic) ethers can be converted to isochroman-4-ones and 2*H*-pyran-3(6*H*)-ones in a related manner, as shown by Gagosz in 2019 (Scheme 10B).[37] The bulky phosphonite **L1** is used as the ligand. The reaction mechanism may follow the carbene or carbenoid pathway.

Combining the trapping of the α-oxo gold carbene by an allyl ether with a subsequent allyl migration was first reported by Z. Yang and Y. Tang in 2013 (Scheme 11A).[38] This strategy can be applied to a variety of substrates. Three pathways were proposed for the further transformation of the allyl oxonium intermediate **Y** on the basis of the observed reaction intermediates and initial mechanistic studies. For the substrates with R^2 = H, alkyl, or a fused alkyl ring, since transposition of the allyl moiety in a deuterium-labeling experiment was observed and no vinyl allylic ether intermediate **Z** was detected, path A involving a concerted 2,3-sigmatropic rearrangement should be in operation. It should be noted that at almost the same time, J. Tae discovered a related reaction with a substrate scope similar to that reported by Z. Yang and Y. Tang with path A and proposed a similar mechanism.[39] For aromatic-ring-fused substrates, benzofuryl allylic ether **Z** was detected in the reaction mixture. Hence, the likely pathway (i.e., path B) entails sequential tautomerization of **Y**, 1,4-allyl migration to form **Z**, and Claisen rearrangement. Alternatively, a [1,2] rearrangement (i.e., path C) might occur in some cases. For example, product **20a** may have resulted from

this pathway. J. Tae and co-workers demonstrated the synthetic utility of this chemistry in the total synthesis of (±)-kumausallene from product **21a**.[39]

In 2012, K. Ohe reported a gold-catalyzed cycloisomerization reaction for the synthesis of 9-acyloxyindolizinones. This is a rare case of the use of internal pyridine *N*-oxides as oxidants (Scheme 12).[40] In the proposed mechanism, α-oxo gold carbene **AA**, generated upon intramolecular alkyne oxidation by the tethered pyridine *N*-oxide, undergoes [2,3]-acyloxy migration to generate (*E*)-**22**. This compound is subsequently converted to the observed indolizinone product **23** upon cyclization and benzoyl migration. In 2013, L. Zhang reported a gold-catalyzed regioselective oxidation of propargylic carboxylates that features [2,3]-acetoxy migration of the gold carbene intermediate.[41] Unlike the work reported by K. Ohe, the gold carbene intermediate is generated using an external oxidant, i.e., 8-methylquinoline *N*-oxide. This intermolecular oxidation is highly regioselective, as enone **26** was barely detected. Excellent ratios of structure-isomeric enones **25** and **24** were reported, reflecting high levels of preference for the 2,3-acetoxy migration over the 1,2-C–H insertion of the carbene intermediate. This was achieved by using the bidentate *P,S*-bidentate ligand **L2** or the *P,N*-bidentate ligand Mor-DalPhos, which leads to attenuated electrophilicity of the carbene center.[42] In 2014, Y. Liu applied a related strategy involving 1,2-carbonate migration to access α-functionalized-α,β-unsaturated ketones.[43]

Despite advances in intramolecular trapping, the intermolecular trapping of α-oxo gold carbenes remained challenging and had only been previously achieved by employing the trapping agent as the solvent or in large excess.[44,45] By using *P,N*-bidentate ligands, L. Zhang demonstrated in 2012 for the first time that stoichiometric amounts of trapping agents could be used.[42] The highly electrophilic nature of α-oxo gold carbenes is evident in the work shown in Scheme 21 [45] (*vide infra*) and often leads to the formation of intractable reaction mixtures. The work detailed the Au(I)-catalyzed synthesis of 2,4-disubstituted oxazoles via a dehydrative [3 + 2] annulation between the α-oxo gold carbene moiety and a primary carboxamide (Scheme 13A). The annulation entails intermolecular attack at the carbene center by the amide carbonyl oxygen, yielding protonated imidate **AC**. Subsequent protodeauration and dehydrative cyclization afford the oxazole products. While various conventional ligands were shown to be completely ineffective in this chemistry, *P,N*-bidentate ligands such as Mor-DalPhos and Me-DalPhos are capable of enabling this reaction with moderate to excellent efficiency. To account for this, the authors proposed the formation of a tris-coordinated gold carbene intermediate (i.e., **AB**) that possesses increased electron density at the gold center in comparison with the bis-coordinated counterpart. As a result, the carbene center is less electron-deficient because of enhanced back-donation from the metal center and hence exhibits attenuated electrophilicity. Consequently, the gold carbene reacts selectively with the amide in this reaction. Further evidence was provided by DFT calculations, which revealed that the tris-coordinated structure **AB** is 5.4 kcal/mol more stable than the bis-coordinated form.

The synthesis of 4-acyloxazoles was reported by Hashmi in 2019 (Scheme 13B).[46] Although α-oxo gold carbene intermediate **AD** is proposed in their reaction design, considering its acceptor–acceptor nature and hence likely exceptional electrophilicity, a carbenoid pathway to reach intermediate **AE** could not be ruled out.

In 2013, L. Zhang revealed another intermolecular trapping of the α-oxo gold carbene with more challenging carboxylic acids, which are weaker nucleophiles relative to carboxamides and used only in slight excess (i.e., 1.2 equiv; Scheme 14A).[47] Again, this reaction is enabled by a *P,N*-bidentate ligand. The ligand optimization revealed that 3,5-dimethylpiperidine-based ligand **L3** is substantially more effective than Mor-DalPhos, which possesses a pendent morpholine ring. This phenomenon was rationalized by the greater shielding of the metal carbene center by the ligand, thereby minimizing side reactions. This reasoning is supported by the positive correlation between the reaction yield and the effective ligand bulk imposed on the carbene center. With 1.3 equiv of the terminal alkyne, the reaction is highly efficient and exhibits a broad scope. It should be noted that W. He and J. Xiang reported a similar trapping at around the same time using PCy_3 as the ligand.[48] However, carboxylic acids are mostly used as the solvent in the reaction, the addition of stoichiometric MsOH is required, and the reaction yields tend to be lower.

In 2013, W. He and J. Xiang employed MsOH to trap the α-oxo carbene intermediates to afford α-mesyloxy ketones (Scheme 14B).[49] Notably, the reaction was run in PhCl, and MsOH was used only in slight excess. In 2014, L. Zhang reported a generally more efficient synthesis of the same products using Mor-DalPhos as the ligand and mesylate as the gold catalyst counteranion.[50] Furthermore, they combined this reaction with a subsequent condensation with a thioamide to achieve the one-pot synthesis of 2,4-disubstituted thiazoles.

This oxidative approach to methanesulfonyloxymethyl ketones was employed by T. Luo in 2016 as a critical step in the total synthesis of (±)-vinblastine.[51] As shown in Scheme 14C, quaternary ammonium salt **29** was obtained in 73% yield from tertiary amine alkyne **27** upon oxidative gold catalysis and subsequent *N*-alkylation. The formation of methanesulfonyloxymethyl ketone intermediate **29** was supported by LC–MS analysis.

Substituted glyoxals can be prepared via gold-catalyzed double oxidation of terminal alkynes. Hashmi reported such a study in 2013 using 6-methoxyquinoline *N*-oxide as the oxidant. The glyoxal products can be converted to quinoxalines in this one-pot strategy (Scheme 15A).[52] To probe the mechanism, 10 equivalent of styrene was introduced to the reaction under the optimized conditions to capture the anticipated α-oxo gold carbene, but no cyclopropanation product was observed. Consequently, the carbenoid pathway is preferred, where the initial adduct **AF** is attacked by another molecule of the oxidant to deliver the *C*-gold enolate, which can then eliminate 6-methoxyquinoline by breaking the N–O bond heterolytically to deliver the double-oxidized product.

In 2019, Dubovtsev and Kukushkin developed several conditions to expand the scope of this type of double oxidation to various terminal and internal alkynes[53–55] and further demonstrated the synthetic utilities of the glyoxal products. They can be converted into several types of heterocycles using one-pot transformations (Scheme 15B).[54] 1,2,3-Tricarbonyl compounds can also be obtained using the same strategy.[56] K. Severin reported that the C–C triple bond of alkynyl triazenes can be similarly double-oxidized under gold catalysis as long as the carbene 1,2-C–H insertion pathway is not available.[57]

In 2011, L. Zhang extended this type of oxidative gold catalysis to terminal allene substrates.[58] As shown in Scheme 16, the reaction results in the formation of α-methanesulfonyloxy methyl ketone **31**. This product differs from those in Scheme 14B by having the α-MsO group attached at the non-methyl side of the ketone. The proposed mechanism begins with regioselective attack at the terminal double bond by 3,5-dichloropyridine *N*-oxide. The resulting allylgold intermediate **AG** then undergoes protonation to form intermediate **AH**, which can undergo S_N2'-type substitution by mesylate to afford the product **31**. This last step is facilitated by the annihilation of the charges and the cleavage of the weak N–O bond.

2.1.2.2. Reactions of Carbene/Carbenoid Intermediates with Nitrogen-Based Nucleophiles.: In 2011, L. Zhang described the first intermolecular trapping of α-oxo gold carbene intermediates by employing the trapping nucleophiles, i.e., nitriles, as the solvent. This chemistry offers rapid access to 2,5-disubstituted oxazoles (Scheme 17A).[44] In the cases of expensive liquid nitriles, 3 equiv was used under neat conditions to achieve moderate yields. The use of 8-methylquinoline *N*-oxide permits the avoidance of any acid addition, as initially demonstrated by L. Zhang in the oxidation of alkynes to give enones (see Scheme 40). Mechanistically, the nitrilium intermediate **AI** generated upon trapping undergoes cyclization and deaurative aromatization to yield the final product. The use of excess nitrile and the avoidance of using other solvents are due to the high electrophilicity of the gold carbene intermediates and hence the need for efficient trapping. The overall reaction is a [2 + 2 + 1] annulation between the alkyne, the nitrile, and the *N*-oxide oxygen. This chemistry was applied to the two-step synthesis of pimprinaphine from Boc-protected 3-trimethylsilylethynylindole. In 2012, W. He and J. Xiang expanded the scope of this chemistry with indole substrates.[59] The scope of nitriles was expanded to include cyanamides by Rassadin and Kukushkin in 2015, which resulted in the formation of 2-aminooxazoles 32 (Scheme 17B).[60] In this chemistry, the use of PhCl as the solvent allows the amount of cyanamide to be decreased from 5 equiv to 3 equiv with little impact on the reaction yield. The use of 2-picoline *N*-oxide necessitates the use of MsOH in order to prevent catalyst inhibition by 2-picoline. Later, ynoates were shown by Dubovtsev and Kukushkin to be suitable alkyne substrates in this annulation chemistry (Scheme 17C).[53] The reaction provides access to a range of fully substituted oxazole-4-carboxylates **33**. Hashmi demonstrated in 2020 that alkynylamides are also suitable alkynes in this chemistry.[61]

In 2014, R.-S. Liu reported an intramolecular variant of carbene trapping by nitriles that allows rapid access to *N*-(pyridine-2-yl)-ε-lactams (Scheme 18).[62] The proposed mechanism entails the formation of seven-membered nitrilium intermediate **AJ** upon trapping and subsequent nucleophilic addition at its nitrilium carbon by another molecule of pyridine *N*-oxide to form intermediate **AK**, which then undergoes cyclization to generate tricyclic dihydropyridine intermediate **AL**. This species undergoes eliminative rearomatization of the pyridine ring and protodeauration to produce the final product. This reaction is applicable for arylacetylenes as well as cycloalkenylacetylenes.

In 2011, L. Zhang reported the one-step synthesis of azetidin3-ones from propargylic sulfonamides (Scheme 19A).[63] This reaction is related to the oxetan-3-one chemistry

shown in Scheme 8B but differs by the internal trapping nucleophile, which is a much bulkier sulfonamide. The optimized conditions employ 2,6-dibromopyridine *N*-oxide as the nucleophilic oxidant and BrettPhos as the optimal ligand. As a result of the steric bulk of both, no acid additive is required in this chemistry. With chiral propargylic sulfonamides readily accessible from the chiral *tert*-butylsulfinamide chemistry,[64] this reaction provides expedient access to chiral azetidin-3-ones with excellent enantioselectivities. Linear carboxamide substrates are not permitted in this chemistry because of the competing amide 5-*exo*-*dig* cyclization, but the lactam substrates circumvent this problem and react readily to form bicyclic azetidin-3-ones such as **34**. In 2014, employing the same strategy but different optimized conditions, L.-W. Ye described the synthesis of chiral pyrrolidine-3-ones **35** and indolin-3-ones **36**.[65,66]

In 2013, R.-S. Liu reported that the α-oxo gold carbene intermediate generated from a terminal dienyne (i.e., **AM**) could be trapped by the quinoline byproduct to initiate a [3 + 2] cycloaddition between the remote electron-deficient alkene and the quinolinium ylide to deliver a tetracyclic dihydroquinoline product (Scheme 20).[67] Interestingly, sterics were demonstrated not to influence the reaction outcome, as the R^3 group in the oxidant and the added quinoline can be H or a sterically hindered isopropyl group. Though the quinoline is generated as the byproduct of the reaction, its inclusion as a reactant understandably increases the reaction yield. In 2014, Toste reported the synthesis of imidazo[1,2-*a*]pyridine from 2-aminopyridine *N*-oxides and terminal alkynes (Scheme 20B).[68] The α-oxo gold carbene generated in the reaction is trapped by the pyridine byproduct to form the pyridinium species **AN**, which is followed by cyclization, dehydration, and deaurative aromatization to deliver the observed product. The fact that no additional 2-aminopyridine was added suggests that the trapping might occur in a solvent cage. This reaction tolerates a range of functional groups including *N*-Boc, phenol, alcohol, and carboxylic acid.

2.1.2.3. Reactions of Carbene/Carbenoid Intermediates with Other Heteroatom-Containing Nucleophiles.: In 2012, J. Xiang and L. Zhang reported that α-oxo gold carbenes generated from terminal alkynes are highly electrophilic and capable of abstracting halogen from halogenated solvents such as 1,2-dichloroethane and 1,2-dibromoethane (Scheme 21).[45] By the use of 8-methylquinoline *N*-oxide as the oxidant and PPh_3AuNTf_2 as the catalyst, α-halogen ketones can be formed in moderate yields. In the proposed mechanism with 1,2-dichloroethane as the solvent, the α-oxo gold carbene is trapped by the alkyl halide to form chloronium species **AO**. Subsequent loss of ethylene chloronium and protodeauration afford the product **37**. In addition to being a convenient means to access to α-chloro ketones, this chemistry sheds light on the difficulty of trapping α-oxo gold carbene intermediates with stoichiometric nucleophiles because of their high electrophilicity. Furthermore, it offered important experimental evidence for carbene intermediacy during the early days of oxidative gold catalysis.

In 2014, L. Zhang[69] and Davies[70] simultaneously reported that the α-oxo gold carbene intermediate could be trapped by an external allyl sulfide to generate the sulfonium salt **AP** and then likely the sulfur ylide **AQ** (Scheme 22A). Subsequent 2,3-sigmatropic rearrangement of either of these intermediates affords an α-thio-γ,δ-unsaturated ketone as the product. L. Zhang discovered that the use of a bidentate ligand such as Mor-DalPhos

or the *P,S*-bidentate phosphine ligand in gold precatalyst **38** led to good reaction yields, while conventional ligands such as Ph_3P and BrettPhos resulted in ≤5% yield. Notably, this chemistry accommodates a broad scope of terminal alkyne substrates, with Y being an alkyl, alkenyl, or aryl group. Various substituents at the allyl sulfide are also tolerated. Davies found that the α-oxo gold carbenes generated from aryl-terminated ynamides can likewise be trapped by allylic sulfides to afford imide-bearing sulfur-substituted quaternary carbons in mostly moderate yields. IPr was employed as the ligand. The fact that a *P,N*-bidentate ligand is not compulsory for this trapping could be attributed to the less reactive nature of the imide gold carbene intermediate in comparison with the ketone gold carbene generated in L. Zhang's work. In 2019, Davies[71] developed the synthesis of α-aryl-α-allylthiomorpholine-3-ones **40** from ynamides **39** bearing a tethered thioether via intramolecular carbene trapping.[54] Notably, when benzyl sulfide was employed, a 1,2-benzyl migration occurs, affording **41** in 50% yield.

In 2019, R.-S. Liu reported a 1,2-arylthio migration in the oxidation of thioalkyne substrates (Scheme 23).[72] Arylthioketenes **AS** are generated and subsequently trapped by alcohols to afford the corresponding α-arylthio esters **42.** Various arylthio groups are allowed, and the electronic properties of the aryl group were shown to not significantly influence the reaction outcome. In addition to terminal thioalkynes, thiolated propiolates and even thiolated alkyl alkynes are allowed. DFT calculations excludes the formation of an α-oxo gold carbene intermediate and favored a carbenoid pathway, where the initial adduct **AR** undergoes a direct 1,2-migration of the arylthio group to generate **AS**. In the case of alkyl alkyne substrates, some enone side products are formed in minor quantities, suggesting a competing carbene pathway. When the R^1 group is an oxime ether, the thioketene intermediates undergo further cyclo-isomerization to deliver azirines **43** in good yields.

Also in 2019, R.-S. Liu reported the gold-catalyzed oxidation of propargyl aryl sulfides **44** by 8-alkylquinoline *N*-oxides (Scheme 24).[73] One quinoline molecule is incorporated into the final product, which exhibits two conformers that are stabilized by different hydrogen-bonding interactions. The proposed mechanism entails trapping of the gold carbene by the tethered sulfide to form four-membered sulfonium **AT**, its subsequent ring opening by residual water to arrive at gold enolate **AS**, and finally the reaction of the gold *O*-enolate with another molecule of the oxidant. Various substituents at the 8-position of the oxidant quinoline ring are allowed, including methyl, ethyl, isopropyl, and benzyl.

In 2016, B. Xu reported that α-oxo gold carbene **AV** generated via oxidative gold catalysis can react with pyridine-HF to afford the α-fluoroketone product (Scheme 25A).[74] The proposed mechanism includes insertion of HF into the α-oxo gold carbene, although a carbenoid pathway might be more likely considering the likely high electrophilicity of **AV**. Compared with conventional electrophilic fluorination, this oxidative gold catalysis occurs under milder conditions. Various functional groups are tolerated, including electron-rich aryl and alkenyl groups. In 2017, the same lab reported that ynoates could be used as the substrates in the same reaction to afford α-fluorinated β-keto esters in good yields (Scheme 25B).[75] It was found that in this chemistry 2,6-dibromopyridine *N*-oxide is significantly more efficient than the previously used 8-methylquinoline *N*-oxide.

In 2018, Zhu and Zhou reported that the in situ generated α-oxo gold carbene could insert into the B–H bond of trimethylamine–borane (Scheme 26).[76] Sterically bulky Me_4ᵗBuXPhos was found to be the optimal ligand that slows the detrimental reduction of gold(I) by the borane complex. Aryl, alkenyl, and alkyl acetylenes are suitable substrates. The insertion into the B–H bond is believed to be a concerted process. Kinetic isotope effect (KIE) studies indicated that the insertion step is facile, and the expulsion of 8-isopropylquinoline should be the rate-determining step in the catalytic cycle.

2.1.2.4. Friedel–Crafts Reactions of Carbene/Carbenoid Intermediates with Arenes.: The earliest gold-catalyzed alkyne oxidation using an *N*-oxide as the oxidant and leading to electrophilic arene alkylation (i.e., Friedel–Crafts alkylation) was reported by L. Zhang in 2009, where tetrahydrobenz[*b*]-azepin-4-ones were prepared in one pot from tertiary aniline substrates (Scheme 27).[77] This two-step, one-pot synthesis commences with *m*-CPBA oxidation of the aniline nitrogen to the corresponding *N*-oxide, which functions as the tethered oxidant for subsequent gold-catalyzed alkyne oxidation. The initially proposed mechanism for the oxidation evokes the formation of an α-oxo gold carbene intermediate, which could subsequently cyclize to the aromatic ring and afford the benzene-fused hetereocycle, as illustrated in Scheme 27 path A. However, in light of the related sulfoxide chemistry and its revised mechanism (see Scheme 2A), it is most likely that this chemistry follows a similar 3,3-sigmatropic rearrangement (i.e., Scheme 27 path B, a carbenoid pathway). Interestingly, if the substrate features an EWG-terminated alkyne, this reaction proceeds in the absence of any gold catalyst. These results are consistent with path B, where no gold carbene is involved. This chemistry provides rapid access to benzene-fused azepinones.

With the advent of substituted pyridine/quinoline *N*-oxides being effective external oxidants in oxidative gold catalysis, the need for a tertiary amine moiety in the substrate, as shown in Scheme 27, is effectively eliminated. Thus, a variety of gold-catalyzed oxidative Friedel–Crafts alkylation reactions are allowed. In 2012, L. Zhang reported the synthesis of chroman3-ones through electrophilic cyclization of the α-oxo gold carbenes generated from propargyl aryl ethers (Scheme 28A).[78] The observed reactivity trend is consistent with Friedel–Crafts reactions, with electron-deficient aryl groups giving generally lower yields and vice versa.

Shortly thereafter, Gagosz reported the synthesis of indan-2-ones using 3-arylpropynes as substrates (Scheme 28B).[79] It was found that the Au(I) complex derived from the electron-poor biarylphosphonite ligand **L4** exhibits higher catalytic activity relative to the more electron-donating ᵗBuXPhos. Electron-rich arenes are mostly employed, and the reaction exhibits fair to good yields. On the basis of the observed preference for less electron-donating ligands, the reaction is thought to not involve the formation of the α-oxo gold carbene; conversely, a carbenoid pathway via an S_N2' process is also unlikely since 5-*endo*-*trig* cyclization is disfavored according to Baldwin's rules. Thus, a mechanism between the carbene and carbenoid pathways is proposed.

In 2017, K. Ji reported the related synthesis of dihydronaphthalen-2(1*H*)-ones or phenanthrenols from 1-phenyl-3-butyne or 1-phenyl-3-butyn-1-ene derivatives (Scheme

28C).[80] Even though the aryl ring is generally less electron-rich, the reaction gave typically better yields than those in L. Zhang's work[78] with a similar catalytic system. In 2018, T. Li reported the conversion of *N*-propargylindoles to 1*H*-pyrrolo[1,2-*a*]indol-2(3*H*)-ones (Scheme 28D). This approach is related to that by Gagosz, although the bulky and electron-rich $Me_4{}^tBuXPhos$ was determined to be the optimal ligand.[81]

Ynamides, being a versatile functional group in organic synthesis and featuring an electronically activated alkyne, have seen frequent usage in oxidative gold catalysis. Resonance stabilization of the amidyl moiety largely dictates the regioselectivity during the gold-catalyzed addition of *N*-oxides, and the gold carbene is exclusively formed on the alkyne carbon distal to the amidyl group (see compound **AW**). In 2013, C.-Y. Li achieved the synthesis of oxindoles via the intramolecular Friedel–Crafts reaction of α-oxo gold carbenes **AW** generated from terminal *N*-arylynamides (Scheme 29A).[82] In 2018, Davies reported an expansion of the substrate scope to include internal *N*-arylynamides.[83] Both methods provide facile access to a series of fused γ-lactams. Similarly, L.-W. Ye discovered that synthetically useful fluorene-9-carboxamides could be obtained from N-arylynamide-functionalized biaryl compounds **45** through the intramolecular Friedel–Crafts reaction of oxidatively generated gold carbenes **AX** (Scheme 29B).[84]

L.-W. Ye also demonstrated the generation of α-oxo gold carbenes from ynamides in water and their subsequent intermolecular trapping. This method enables access to synthetically valuable functionalized indoles (Scheme 30).[85] It was reported that the use of aqueous media appreciably mitigates undesired overoxidation at the carbene center, an issue that is often associated with the trapping of α-oxo gold carbenes with external nucleophiles. In this chemistry, indoles are used as the trapping reagent. The reaction exhibits a large scope, furnishing the desired products in moderate to excellent yields.

The chemistry was further developed in a subsequent publication by the same lab that described the use of *o*-alkynyl anilines instead of indoles as one of the reaction partners (Scheme 30).[86] The gold catalyst serves a dual catalytic role in the preparation of the indole from the aniline and the alkyne oxidation.

Electron-deficient C–C triple bonds bearing a carbonyl substituent (e.g., ynones and propiolamides) have also been successfully employed in this oxidative gold catalysis. The gold carbene intermediates (e.g., **AY** and **AZ**) are acceptor/acceptor-type carbenes and hence are expected to be highly reactive. J. Zhang first reported the generation of such species from *N*-phenylpropiolamides and their subsequent Friedel–Crafts cyclization to afford 3-acyloxindoles (Scheme 31A).[87] The scope of the reaction was generally broad, although substrates with an additional electron-withdrawing group on the amide nitrogen did not undergo the desired transformation. K. Ji reported a similar reaction in which an aryl enynone or naphthyl ynone was used as the α-oxo gold carbene precursor (Scheme 31B).[88] In that reaction, the intermediacy of 1,3-diketo-2-gold carbene **AZ** was corroborated by the observed cyclopropanation of a tethered alkene.

The cationic gold-containing intermediates generated during the intramolecular Friedel–Crafts cyclization of an α-oxo gold carbene (e.g., intermediates **BA** and **BB**/**BB′**) could be

trapped internally or by external nucleophiles, leading to polycyclic structures. In 2018, X. Huang reported the gold-catalyzed oxidative cyclization of tryptamine-derived enynamides to form tetracyclic spiroindolines (Scheme 32A).[89] Notably, tetracyclic spiroindoline **47** bearing two contiguous tetrasubstituted stereocenters is formed as a single diastereomer. The mechanism is thought to involve an α-oxo gold carbene intermediate that undergoes a stepwise cyclization, as outlined in Scheme 32A path A. It is postulated that an additional pathway exists wherein the α-oxo gold carbene intermediate undergoes intramolecular cyclopropanation followed by ring expansion to furnish the product, as shown in path B. The substituents on the indole benzene ring were found to have no appreciable effect on the reaction outcome.

In 2019, R.-S. Liu reported the synthesis of 4-alkylidenechroman-2-ones and 3-alkylidenebenzofuran-2-ones from homopropargylic and propargylic phenyl ethers, respectively, via oxidative gold catalysis (Scheme 32B).[90] The mechanism is believed to involve the interception of the Friedel–Crafts intermediate BB′ by a second equivalent of the quinoline *N*-oxide. The reaction scope is generally broad with good functional group tolerance. The desired products are furnished in moderate to good yields.

X. Huang reported the synthesis of fused furopyridine scaffolds from easily accessible 1,3-diynamides (Scheme 33A).[91] This chemistry was also found to be applicable in the synthesis of fused tetracyclic compounds from *N*-indolemethyl-1,3-diynamides. The scope of R^2 is broad, though the arene ring must be electron-rich (e.g., anisole or indole). The mechanism is thought to involve the generation of an α-oxo gold carbene intermediate (i.e., **BC**) and its subsequent Friedel–Crafts reaction with the tethered aryl group. The resulting lactam could then cyclize to the remaining C–C triple bond in the presence of the gold catalyst to furnish the heteroaromatic product upon elimination of one molecule of sulfinic acid.

In 2019, K. Ji explored the reaction of phenyl propargylic ethers containing an acyl group at the alkyne terminus (Scheme 33B).[92] This chemistry furnishes 4-(1-hydroxyalkylidene)-chroman-3-ones **48** and is related to the work by L. Zhang (Scheme 33A), although the Au(III) salt (i.e., $PicAuCl_2$) is used as the catalyst. When diynones were used as substrates (R^2 = alkynyl), further gold-catalyzed cyclizations could occur to afford the tricyclic ketones **49**. During mechanistic studies, it was found that diazo compound **50** was not converted to the desired product under the optimal reaction conditions, even after prolonged heating at 120 °C. Consequently, it was reasoned that the key Friedel–Crafts cyclization does not involve a gold carbene but rather gold allenolate intermediate **BD**.

2.1.2.5. Reaction of Carbene/Carbenoid Intermediates with Alkenes: Cyclopropanation and Beyond.: Gold-catalyzed cycloisomerizations of 1,5-enynes[93] lay the early foundation of homogeneous gold catalysis. In these transformations, a cyclopropyl gold carbene intermediate (e.g., **BE**) is generated (Scheme 34A). In the context of oxidative gold catalysis, particularly in the presence of a nucleophilic oxidant, this intermediate could be oxidized to deliver cyclopropyl ketone product 51 (path A). However, with the advancement of gold-catalyzed facile intermolecular alkyne oxidation, alternative pathways,

i.e., the carbene pathway (path B) and the carbenoid pathway (path C), where alkyne oxidation proceeds cyclo-propanation, have been proposed in the literature.

In 2011, R.-S. Liu reported the first examples of oxidative cycloisomerization of 1,5-enynes.[94] As shown in Scheme 34B, 1,5-enynes or 1,3,5-dienynes **52** were converted into bicyclo[3.1.0]hex-3-en-2-ones **53**. The reaction tolerates a range of benzene ring substituents, R^1/R^2 can be alkyl, aryl, or in one case electron-withdrawing CO_2Et, and R^4 can be methyl or H in the form of a terminal alkyne. When R^1/R^2 = ester, no reaction occurs in the absence of 8-methylquinoline *N*-oxide. Moreover, with $R^1 = R^2$ = Me and $R^3 = R^4$ = H on a benzenefused substrate, the absence of oxidant led to a complex mixture. On the basis of these results and additional mechanistic considerations, the authors proposed that the reaction follows path B. However, the tolerance of an internal alkyne substrate (i.e., R^4 = Me) suggests that path C might also be plausible, as α-oxo gold carbene intermediates possessing α'-hydrogens can undergo facile 1,2-C–H insertions, leading to enone products (see Section 2.1.2.7). In 2015, L. Zhang published an enantioselective approach to this chemistry that employs terminal alkyne substrates tethered mostly to electron-deficient alkenes (R^4 = H, R^2 is mostly EWG in **52**; Scheme 34C).[95] They designed a series of chiral P,*N*-bidentate ligands in which the protected (3R,5R)-3,5-dihydroxypiperidine imposes a C_2-symmetric chiral environment for the cyclopropanation step, as illustrated in **BF** in the presence of the optimal ligand. The reaction exhibits >85% ee with substrates featuring electron-withdrawing alkene substituents, including ethoxycarbonyl, acetyl, and benzoyl, but moderate to good ee with electron-rich C–C double bonds.

In 2013, C.-Y. Li reported another oxidative 1,5-enyne cycloisomerization that uses substrates featuring an electronically activated ynamide moiety (Scheme 34D).[96] With 1.2 equiv of MsOH as the pyridine scavenger, the parent pyridine *N*-oxide can be employed as the oxidant. The inferior results from the corresponding diazo substrates rule out a carbene pathway (i.e., path B), and the reaction mechanism was believed to either follow path A or the carbenoid pathway (i.e., path C), though the latter is thought to be more probable. This reaction works with ynamides terminated by H, Me, an electron-neutral or moderately electron-deficient phenyl group, acyl, or alkoxyacyl and tolerates methyl or Ph substitution on the C–C double bond. Notably, with the ynamide terminated by an even slightly electron-rich phenyl group, i.e., 4-methylphenyl, the reaction yield was lowered to 26%, and the major side product was an α-keto amide, the result of double oxidation.

By using readily accessible TBS-protected 1,5-enyn-3-ol substrates, L. Zhang realized an efficient oxidative cyclopropanation using gold catalysis in 2014 (Scheme 34E).[97] 8-Methylquinoline *N*-oxide was found to be the optimal oxidant. Ligand screening revealed that **L3**, a *P*,*N*-bidentate ligand modified from Mor-DalPhos, performed substantially better than Mor-DalPhos and other conventional phosphine and *N*-heterocyclic carbene (NHC) ligands (e.g., 92% vs <35% yield). It was also reported that no product was formed when the oxidant was changed to diphenyl sulfoxide. These observations support a mechanism following path B over path A. When this reaction was applied to cycloalkene substrates, angularly fused tricyclic cyclopropanes (e.g., **54**) were formed in moderate to excellent yields. Around the same time, Nakada reported a similar oxidative approach to fused tricyclic cyclopropane products such as **55** (Scheme 34F).[98] In that chemistry, the enyne

substrates possess an ester-terminated C–C triple bond and a 1,4-cyclohexadiene moiety as the alkene component. CyJohnPhos was found to be the optimal ligand, although the reaction yields are mostly moderate.

For 1,5-enyne substrates with a simple aliphatic linkage and an electron-deficient C–C triple bond, the reaction likely follows path B or C to the final cyclopropane products. Nakada reported such a case to furnish **56**.[98] In 2017, Davies and Grainger employed a sulfoxide-terminated alkyne substrate to deliver cyclopropane sulfoxide products (e.g., **57**).[99]

In 2018, Oishi and Ohno published the construction of tropone-fused furan scaffolds from symmetric 1,4-diyn-3-one substrates containing 1,5-enyne moieties (Scheme 35).[100] In this gold-catalyzed oxidative cascade cyclization, one of the proposed mechanisms entails initial generation of β-diketone-α-gold carbene **BG**, intramolecular cyclopropanation, subsequent ring opening, and cyclization/ring fragmentation. The troponefused furan products **58** can undergo further cyclization to yield the pentacyclic product **59**.

When a C–C double bond is too close to the gold carbene center for cyclopropanation to occur, the reaction could proceed through a cationic pathway. For example, in the work published by R.-S. Liu in 2011 (Scheme 36A),[94] the gold carbene is generated regioselectively because of the electronically activated and hence biased nature of the ynamide C–C triple bond. Thus, it is γ to the C–C double bond and cannot cyclopropanate the π-systems because of the difficulty in forming the highly strained bicyclo[2.1.0]pentene system. Consequently, the carbene center cyclizes to the C–C double bond as an electrophile to generate carbocation **BH**, which can then undergo hydride migration and deauration to afford indenecarboxamide **60**. R.-S. Liu also reported a related study in which the C–C π-systems were 1,1-disubstituted on a cyclopropane ring (Scheme 36B).[101] In that chemistry, the carbene cyclization is followed by migration of a carbon-based group. Interestingly, it was found that only the migration of the *cis*-substituent (i.e., R^2) was detected. This was rationalized, with the help of DFT calculations, by the idea that gold in carbocation **BI** facilitates the migration of its neighboring *anti*-substituent R^2 via hyperconjugation.

In contrast to the oxidation of 1,5-enynes, which yields only 5-*endo* carbonyl products, oxidative gold catalysis of 1,6-enynes could lead to either 6-*endo* carbonyl products **61**, 5-*exo* carbonyl products **62**, or both (Scheme 37A). The reported examples of this chemistry achieve selective product formation by controlling the regiochemistry of the initial alkyne oxidation and hence allowing selective access to either gold carbene **BJ** or **BK** or, in the event of a carbenoid pathway, one of the carbenoid regioisomers. The regioselectivities are dictated by the electronic and steric biases of the C–C triple bond.

In 2011, J. Zhang reported the conversion of an enynone or enynamide (i.e., **65**) to bicyclic cyclopropanone **66** under oxidative gold catalysis (Scheme 37B).[102] In that study, a combination of 4-acetylpyridine *N*-oxide and MsOH was initially employed. It was later found that 8-methylquinoline *N*-oxide in the absence of any acid additives leads to faster reactions at ambient temperature and in some cases better yields. The reaction works with an amide or a ketone linkage between the two π-systems, but not with an ester counterpart. Notably, various protecting groups on the amide nitrogen and different types of substituents

at the alkyne terminus (i.e., R^3 in **65**) are allowed. This chemistry was also applied successfully to an amide-linked 1,7-enyne substrate ($n = 2$ in **66**). The regiochemistry of the oxidation is dictated by the electron-withdrawing carbonyl group. The proposed mechanism follows the carbene pathway via the intermediacy of **BK**.

In 2014, the same group developed an asymmetric version of this reaction (Scheme 37C).[103] With the chiral binol phosphoramidite (*S,S,S*)-**L5** as the ligand, the reaction exhibits good to excellent enantioselectivities. Mechanistic studies indicate that the α-oxo gold carbene species **BL** is likely not involved in this reaction and that the reaction follows a carbenoid pathway, as outlined by **BM**. The scope study mostly employed ketone substrates. The one amide (X = NMe, R^3 = PMP, and $R^1 = R^2$ = H) resulted in 84% ee.

In 2017, Davies and Grainger employed 1,6-enyn-5-sulfoxides as substrates for oxidative cyclopropanation (Scheme 37D).[99] This reaction exhibits moderate to good diastereoselectivity. Additionally, individual cases of oxidative cyclopropanation of 1,6-enynes have been documented, e.g., **63**[94] and **64**[98] (Scheme 37E).

The oxidatively generated α-oxo gold carbene can also cyclopropanate a tethered benzene ring, thereby providing access to the Buchner reaction manifold by the use of alkynes as the substrate. In 2018, K. Ji and L. Zhang reported such a reaction en route to dihydropyranone-fused cycloheptatrienes (Scheme 38).[104] Mechanistically, norcaradiene intermediate **BN** is formed via benzene cyclopropanation by the expected α-oxo gold carbene. Subsequent treatment of the reaction mixture with triethylamine drives the equilibrium between **BN** and the ring-opened heptatriene structure **BO** toward the observed product by isomerization of the C–C double bonds of the latter. The reaction works well with propargyl ether substrates. When a substrate featuring an all-carbon backbone was tested, a mixture of the Buchner product and the Friedel–Crafts product was isolated.

2.1.2.6. Reaction of Carbene/Carbenoid Intermediates with C–C Triple Bonds.: Substrates of this type of reaction are typically 1,5-diynes or 1,6-diynes. Three mechanistic scenarios upon initial α-oxo gold carbene generation have been proposed and are summarized in Scheme 39A: in path A, carbene metathesis with the pendent C–C triple bond would directly deliver vinyl carbene intermediate **BP**; alternatively, **BP** could be generated via ring opening of cyclopropene intermediate **BQ** (path B); in path C, nucleophilic attack at the carbene center by the tethered alkyne would generate reactive β-gold vinyl cation intermediate **BR.**

From 2013 to 2019, Hashmi described several gold(I)-catalyzed oxidative transformations of 1,2-dialkynylbenzenes (Scheme 39B). It is proposed that alkenyl carbene **BS** is generated through either path A or path B and can undergo different subsequent transformations depending on substrate functionalities and reaction parameters. For example, with a ^{t}butyl substituent at the carbene center, methyl migration affords indenone **67** as the final product (X = halide, R^2 = Me).[105] When X = H and the substituent is a trityl group (i.e., R^2 = Ph), indenone **67** tends to decompose and undergo autoxidation. As a result, it is converted in one pot into benzo[*a*]fluorenone 68 via photocyclization and oxidation.[106] When the X group of **BP** is a carbonyl group as in carbene **BT**, it can undergo carbonyl cyclization to

form indenofuranone **69** as the product.[107] It is noteworthy that the author indicated that the vinyl cation pathway (i.e., path C) is also possible. Furthermore, carbene **BU** can be trapped by acetonitrile to afford oxazole product **70** via an [2 + 2 + 1] annulation similar to that described in Section 2.1.2.2.[108]

It is noteworthy that these studies all involve the exocyclic vinyl carbene intermediate **BP**. In 2019, L.-W. Ye proposed that the endocyclic vinyl carbene intermediate **BV** might be generated from 1,2-diethynylbenzenes en route to naphthoquinone product **71.**[109]

In 2015, K. Ji described the first examples of gold(I)-catalyzed oxidative cyclizations of 1,6-diynes and proposed vinyl cations of type **BR** as the key reaction intermediates (i.e., path C).[110] When R^2 = Bn, the *β*-gold vinyl cation intermediate **BW** generated in the reaction can undergo Friedel–Crafts cyclization to form chromen-3(4*H*)-ones **72** (Scheme 39C). When $R^2 \neq$ Bn, another molecule of the *N*-oxide can oxidize vinyl cation intermediate **BY** to give 2*H*-pyran-3(6*H*)-ones **74** through the intermediacy of the adduct **BZ**. In 2018, K. Ji reported that vinyl cation intermediate **BX**, which was generated from a 1,6-diynone using gold(III) catalysis, could readily be trapped by the pendent carbonyl group to afford fused furan product **73**.[76] Notably, gold(I) catalysts were found to be inefficient in this transformation. In 2015, L. Zhang reported that the related vinyl cation intermediate **CA** would undergo a concerted C–H insertion process, leading to the formation of tricyclic 2*H*-pyran-3(6*H*)-ones **75**.[111] The observed reaction diastereoselectivities are consistent with the vinyl cation pathway (i.e., path C).

2.1.2.7. 1,2-Insertions of Carbene/Carbenoid Intermediates into C(sp^3)–C, C(sp^3)–H, and Other Bonds.: One of the valuable transformations of metal carbenes is 1,2-insertion, which entails the 1,2-migration of an *α*-group to the carbene center followed by metal elimination. Because *α*-oxo gold carbenes are highly electrophilic, this type of insertion is the main carbene decomposition pathway when an *α*-C(sp^3)–C and/or *α*-C(sp^3)–H bond is present, leading to the formation of conjugated enones. The 1,2-C–H insertion is particularly facile, and the absence of the enone products is often a mechanistic indication against the formation of a discrete *α*-oxo gold carbene species, although the observation of such products does not rule out a carbenoid pathway.

In 2010, L. Zhang[112] reported the oxidation of internal alkynes to give conjugated enones (Scheme 40A). For the first time, 8-alkylquinoline *N*-oxides were shown to be highly effective external oxidants, and moreover, the oxidation reactions do not require stoichiometric acid additives. Similarly, 2-bromopyridine *N*-oxide was found to be a suitable oxidant without an acid additive. The regioselectivity challenge associated with electronically unbiased dialkylacetylenes was largely overcome by using bulky 8-isopropylquinoline *N*-oxide as the oxidant, IPr as the ligand and by running the reaction at −20 °C. For example, with R^1 = Me and R^2 = *n*-hexyl, this oxidation achieves a selectivity of 11:1 favoring the delivery of the oxidant at the less hindered alkyne end. Likewise, an *n*Bu group is favored over cyclohexyl by a ratio of 13:1 and methyl over cyclohexyl by 50:1.

For electronically biased internal alkynes, including aryl alkynes, enynes, and ynamides, an acidic and bulky phosphite ligand was employed to maximize such a bias. As a result, the

selectivity is routinely above 10:1, and the major α,β-unsaturated carbonyl products have the carbonyl group α to the conjugated π-systems or the amide moiety.

This enone synthesis has been successfully employed in the total synthesis of citrinadin alkaloids. Martin[113] and Wood[114] separately reported the conversion of **76** into **77** in the presence of an array of other functional groups (Scheme 40B). Notably, 1.1 equiv of $Ph_3PAuNTf_2$ was used in both instances because of the binding and deactivation of the gold catalyst by the substrate basic tertiary amine moiety.

This transformation of internal alkynes into α,β-unsaturated carbonyl compounds has been further explored with functionalized substrates. In 2011, Davies[115] reported the reactions of a variety of ynamides and one case of ynol ethers (Scheme 41A). In this reaction, because of the electron-rich nature of the C–C triple bond and hence the ease of alkyne activation, simple and economical pyridine *N*-oxide can be used as the nucleophilic oxidant. The reactions are generally efficient, albeit exhibiting moderate *E/Z* selectivity. In 2014, L. Zhang reported that the reaction of propargylic ethers can be highly regioselective, which was attributed to the inductive effect of the alkoxy group (Scheme 41B).[116] With linear substrates, Ph_3P was shown to be a suitable ligand, but for secondary propargylic ethers, the shown *P,N*-bidentate ligand is preferred because the competitive alkyl migration is minimized. In 2017, Prandi reported the use of enynes as substrates, leading to the formation of dialkenyl ketones (Scheme 41C).[117] Good regioselectivity was achieved in all cases, and the general preference was in accordance with the previous study by L. Zhang (see Scheme 40A).[112,116] Interestingly, the authors found that the DFT-calculated enthalpy values of the two regioisomeric gold carbenes were not always in agreement with the reaction outcome, suggesting the presence of an entropic influence in the reaction. The dialkenyl ketone products were successfully subjected to a one-pot Nazarov cyclization. In 2019, Severin employed 1-alkynyl triazenes as substrates in this type of oxidative gold catalysis to deliver unsaturated acyl triazenes (Scheme 41D).[57]

1,2-C–C insertions by α-oxo gold carbenes are often assisted by the release of ring strain and/or the generation of a carbocation stabilized by a heteroatom substituent. Under these circumstances, the transformation is likely stepwise via 1,2-alkyl/alkenyl/aryl migration followed by E1-type elimination of the gold catalyst (e.g., see Scheme 42A). When the migrating group is α to a hydroxyl group, the transformation resembles the semipinacol rearrangement.

In 2012, Hashmi reported the gold-catalyzed oxidation of tertiary propargyl alcohols **78**, affording the 1,3-diketone products **79** (Scheme 42A).[118] The regioselectivity of the oxidation, i.e., oxygen delivered distal to the hydroxyl group, is due to its inductive effect, as is evident in Scheme 41B, and augmented by steric hindrance at the proximal C(sp). For the substrate with R^1 = Me and R^2 = Ph, the migration aptitude of the Ph group is >3 times that of the methyl group.

S. Li and Y. Liu reported a related work using propargylic tertiary alcohols prepared from quinones (Scheme 42B).[119] The 1,2-migration of the alkenyl group to the carbene center enables a facile synthesis of various functionalized tropones and their analogues. Another

study published by Z. Zhang[120] described the selective 1,2-migration of electron-rich furan, pyrrole, and thiophene rings to generate 2-heteroaryl-1,3-diketone products **80**, which can be trapped in one pot by phenylhydrazine or hydroxylamine to furnish trisubstituted pyrazoles or isoxazoles.

In 2013, Y. Liu reported the synthesis of dihydro-γ-carbolines via oxidative gold catalysis (Scheme 43A).[121] The reaction exhibits generally good yields and is compatible with a series of aryl and alkyl substituents on the alkyne and the imine. The α-oxo gold carbene intermediate **CC** was thought to be generated during the reaction. In 2019, DFT studies by Ariafard[122] found that the proposed gold carbene **CC** could not be located as an energetic minimum. Instead, a carbenoid reaction route involving a facile 1,2-aryls migration of alkyne/*N*-oxide adduct **CB** occurs to afford β-keto aldehyde enol tautomer **CD**, which is then trapped by an imine in a stepwise [4 + 2] annulation to furnish the final product. It was also found in this study that the *N*-oxide served as the best "proton shuttle" among numerous basic species in the reaction mixture.

In 2014, Hashmi reported the gold-catalyzed oxidation of 1,1-dialkynyl carbinols and their tosylamide counterparts (Scheme 43B).[123–125] The proposed mechanism entails 1,2-alkynyl migration of the α-oxo gold carbene intermediate followed by cyclization. The method provides rapid access to 2,5-disubstituted 3-formylfurans and 3-formylpyrroles **82**. Interestingly, no sign of 1,2-hydride migration was observed, despite the facile nature of such a transformation, which was demonstrated in several previous studies.[112,115,116] It was later found by DFT calculations that the transition state for a 1,2-hydride migration is significantly higher in energy than that of the corresponding 1,2-alkynyl migration, with a difference of as much as 5.4 kcal/mol. With the addition of *N*-iodosuccinimide (NIS), *in situ* iodination of furylgold(I) intermediate **81** occurs.

The azepine ring is a medium-sized *N*-heterocycle and can be found as a key structural motif in many bioactive natural products. Y. Liu and Y. Li reported the synthesis of functionalized azepines via ring expansion of 1,2-dihydropyridines triggered by alkyne oxidation (Scheme 44).[126] The reaction tolerates alkyl, ferrocenyl, cyclopropyl, and phenyl groups with various electronic characteristics as R^2 and permits R^3 to be a fused benzene ring or an alkyl, halogen, or CF_3 group. The reaction yields are mostly >80%. Three possible reaction pathways based on the results of deuterium labeling experiments were proposed: via 1,2-alkenyl migration of the discrete α-oxo gold carbene **CE** (path A), via direct intramolecular attack at the vinylgold moiety of the initial adduct by the dihydropyridine double bond followed by subsequent ring opening of intermediate **CF** (path B), via formation of intermediate **CF** by intramolecular nucleophilic attack in α-oxo gold carbene **CE** (path C). DFT studies concluded that the bicyclic intermediate **CF** is the most probable intermediate and that the attack by the electron-rich dihydropyridine double bond and the expulsion of pyridine occur in a concerted manner. Consequently, it was concluded that path B, a carbenoid pathway, is most likely.

A later study by Y. Liu employed TBS propargylic ethers as substrates (Scheme 45).[127] In that work, the regioselective formation of an α-oxo gold carbene causes an enynyl or o-alkynylaryl migration to give 1,3-keto aldehyde intermediate CG. Subsequent gold(I)-

catalyzed cyclization delivers the functionalized 1*H*-isochromene product **83**. The proposed reaction mechanism was consistent with the isotopic labeling experiments.

Steric and/or electronic biases have been extensively exploited in the regioselective generation of α-oxo gold carbenes from internal alkyne substrates. However, this approach could not selectively access the disfavored α-oxo gold carbene regioisomer (i.e., **CH**). To address this challenge, L. Zhang developed a desulfonylative 1,2-migration method that uses alkynyl sulfone 84 as the substrate (Scheme 46).[128] As a result of the strong electronic bias of the C–C triple bond of 84, α-oxo gold carbene **CI** was generated with high regioselectivity. Subsequent stepwise desulfonylative 1,2-aryl migration gives the desired carbene **CH**. It is noteworthy that this aryl migration does not lead to the formation of a double bond as in all other cases. Carbene CH can be further oxidized or undergo cyclopropanation reactions. Comparative experiments with diazo compounds as precursors to carbene **CI** led to a similar outcome, thereby supporting the intermediacy of acceptor-acceptor-type carbene **CI**.

The 1,2-insertion into a carbon–heteroatom bond by the α-oxo gold carbene or its carbenoid precursor was reported by Y. Liu in 2015 (Scheme 47).[129] It results in the formation of the six-membered heterocyclic product **85** from a five-membered heterocycle precursor. Three possible reaction pathways were proposed, two of which involve gold carbene/carbenoid intermediates generated in different manners (**CL** and **CM**). However, as no trace of 1,2-C–H insertion side products was detected in the reaction mixture, any participation of carbene intermediates was deemed unlikely. Therefore, it was suggested that path A, a carbenoid pathway that involves direct attack at the vinylgold intermediate by the migrating heteroatom (i.e., from **CJ** to **CK**) is more likely.

In 2019, X. Xu and L. Zhang reported the Wolff rearrangement of α-oxo gold carbene **CN** (Scheme 48).[130] Such an alkyne oxidation/Wolff rearrangement cascade has seldom been reported as a synthetically useful transformation in the realm of oxidative gold catalysis. With TBS-terminated alkynes as the substrates, a series of silylketenes (i.e., **86**) were synthesized and then trapped by thiophenol in one pot. This strategy of silylketene generation is advantageous over the previously reported method featuring a rhodium-catalyzed Wolff rearrangement of diazo ketones,[131] as it requires fewer reaction steps and avoids the hazards associated with diazo compounds.

2.1.2.8. Remote C(sp^3)–H Insertion/Functionalization by Carbene/Carbenoid Intermediates.: Functionalization of remote C(sp^3)–H bonds by oxidatively generated gold carbenes has been a topic of interest since the early stage of the oxidative gold catalysis field. In 2009, L. Zhang reported intramolecular alkyne oxidation by one-pot-generated amine *N*-oxide.[132] As shown in Scheme 49A, the design was to generate an α-oxo gold carbene intermediate that could undergo remote abstraction of a hydride α to the amine nitrogen and subsequent cyclization to deliver a piperidin-4-one as the product. In combination with the preparation of the substrate from a secondary amine and a but-3-yn-1-yl tosylate, the overall two-step process constitutes a [4 + 2] annulation for the synthesis of the piperidine ring. One year later, this chemistry was extended to the synthesis of azepan-4-ones in a two-step [5 + 2] annulation.[133] When the secondary amine has two different alkyl

substituents, the apparent hydride abstraction occurs selectively at the smaller group, as shown by the indicated regioselectivities. Moreover, substantially higher regioselectivities were observed in the case of the [5 + 2] annulation than in the [4 + 2] counterpart. This phenomenon is inconsistent with the mechanism of carbene hydride abstraction, where the more substituted group should be favored. In 2011, a revised mechanism was proposed on the basis of DFT calculations.[134] As shown in Scheme 49A, intermediate **CO** might not undergo fragmentation to generate the proposed *α*-oxo gold carbene intermediate. Instead, the reaction proceeds by an energetically favored hetero-retro-ene pathway, as outlined by the transition states **CP** and **CQ.** Subsequent cyclization of the iminium gold enolate would furnish the product and regenerate the cationic gold catalyst. In the hetero-retro-ene transition states, the calculations reveal the preference for **CP**, which places the smaller group (i.e., the Me group) in the (pseudo)axial position of the *N,O*-containing ring. This is consistent with the observation that smaller groups on the nitrogen are preferred in this type of remote C–H functionalization. This calculated mechanism is supported by the failure of the same reaction when the corresponding diazo ketone is used as the substrate.

The synthetic utility of the [4 + 2] annulation was demonstrated in the synthesis of (+)-lentiginosine from L-(+)-tartaric acid[135] and the highly diastereoselective synthesis of (±)-cermizine C from simple 4-methylpiperidine in five steps[132] by L. Zhang. In 2012, this chemistry was employed as a key step in the total synthesis of lasubine II and (±)-decinine by Y. Yang, J. Chen, and Z. Yang (Scheme 49B).[136]

In 2012, R.-S. Liu reported the gold-catalyzed oxidation of *ortho*-substituted phenylacetylenes to form indan-1-ones (Scheme 50).[137] The reaction involves an apparent 1,5-C–H insertion. The chemistry was also applied to the related 1,3-enyne substrates, furnishing cyclopentenone products. Mechanistic studies, including a comparison to the experimental outcomes using the corresponding *α*-diazo ketone substrates, support a carbenoid pathway in which the initial adduct **CR** undergoes the sequence of a 1,5-hydride shift and fragmentative cyclization.

In 2015, L. Zhang revealed the first examples of insertion of *α*oxo gold carbenes into unactivated C(sp^3)–H bonds (Scheme 51).[138] With bulky ^{t}BuBrettPhosAuNTf$_2$ as the catalyst, the C–H insertion exhibits poor regioselectivity, delivering a cyclopentanone and two cyclobutanones as the products in similar yields. Selective 1,5-C–H insertion was realized when the previously reported *P,N*-bidentate ligand **L3** was used.[47] In addition to the monocyclic cyclopentanone products, spiro, fused, and bridged bicyclic cyclopentanones were formed in good yields. L. Zhang later optimized the C(sp^3)–H insertion chemistry toward the selective formation of cyclobutanones.[139] A bulky phosphine ligand such as BrettPhos or ^{t}BuBrettPhos is essential for the desired regioselectivity, which is supported by DFT studies. One common feature of these cases is the presence of a quaternary carbon center in the substrate backbone in order to harness the rate-enhancing Thorpe–Ingold effect. In its absence, the reaction yield in one case was <50%. Mechanistically, an acceptor/acceptor-type gold carbene is the proposed reactive intermediate, which is supported by the observation of a similar product distribution when the corresponding *α*-diazo *β*-diketone substrate was treated with ^{t}BuBrettPhosAuNTf$_2$.

2.1.2.9. Reaction of N-Alkenoxy-N-heteroarenes.: In 2016, L. Zhang described the enolate umpolung reactivity of an *N*-alkenoxy-N-heteroarene intermediate (i.e., **88**; Scheme 52A).[140] This intermediate is generated upon the gold(I)-catalyzed nucleophilic addition of a protonated pyridine *N*-oxide to the terminal alkyne and is stable on column chromatography. Intermediate **88** can react as a surrogate or precursor to acylcarbenium ion **CS** to furnish the oxidized ketone product **89**. In this initial study,[140] an intramolecular Friedel–Crafts reaction of *N*-alkenoxypyridinium **90** was carried out in hexafluoroisopropanol at 80 °C, offering an efficient one-pot, two-step synthetic route to valuable benzene-fused seven- and eightmembered cyclic ketones **91** (Scheme 52B). In 2017, Z. Xu and L. Zhang reported that alcohols and thiols can also act as nucleophiles in intermolecular variants of this chemistry, affording α-alkoxymethyl/α-thiomethyl ketones **92** in moderate to high yields.[141] In 2018, Z. Xu reported the synthesis of linear α-aryl/α-heteroaryl ketones **93** via intermolecular Friedel–Crafts alkylation of **88**.[142] Interestingly, DFT calculations and KIE studies in that work suggested that the Friedel–Crafts reaction occurs via an acylcarbenium intermediate of type **CS**, which is formed upon the decomposition of **88**, rather than the alternative S_N2' process.

2.1.2.10. Miscellaneous Reactions.: In 2012, R.-S. Liu reported the gold-catalyzed oxidation of 3-en-1-ynamide **94** to furnish 2-aminofuran **95** (Scheme 53).[143] Mechanistically, the α-oxo gold carbene generated undergoes oxo-Nazarov cyclization followed by migratory protodeauration. The overall transformation constitutes a [4 + 1] cycloaddition between the enyne moiety and the *N*-oxide oxygen. In most cases, R^1 is a methyl group. When R^1 = H, the overoxidation product (e.g., α-keto amide 96) is formed.

2.1.3. Other Oxygen-Based Oxidants or Oxidizing Groups.

2.1.3.1. Tethered Nitro Groups.: The nitro group can serve as an intramolecular oxidant in oxidative gold catalysis. In 2003, N. Asao and Y. Yamamoto reported an oxidative cyclization of *o*-nitrophenylalkynes to access anthranils **97** and isatogens **98** (Scheme 54).[144] The proposed mechanism includes two diverging pathways upon hydrative oxidation of the C–C triple bond by the nitro group and generation of nitrosobenzene intermediate **CT**: the nitroso group could be attacked by the enediol double bond (path A) or its oxygen (path B). When R is an aryl group, both products are formed (e.g., **97a** and **98a**). In contrast, when R is an alkyl group, only the anthranil product **97** is obtained (e.g., **97b** and **97c**). Notably, no gold carbene is invoked as a reaction intermediate.

In 2011, R.-S. Liu reported cycloaddition reactions with *o*-nitrophenylacetylene substrates (Scheme 55).[145] The proposed mechanism involves gold carbene intermediate **CU**, the formation of which is supported by its successful trapping by styrene. Subsequent cyclization of the nitroso group on the carbene center generates gold *C*-enolate **CV**. The tautomerized *O*-enolate form **CW** would then undergo concerted 1,3-dipolar cycloaddition to furnish the polycyclic product with excellent *exo*-selectivity. Various electron-rich alkenes can participate in this reaction in moderate to good yields. It is noteworthy that with the help of the chiral ligand (*R*)-DM-Segphos, the product **99** was obtained with 73.1% ee, which provides evidence of gold participation in the cycloaddition step.

2.1.3.2. Nitrones.: Nitrones are the *N*-oxides of imines and can be used as either internal or external oxidants in oxidative gold catalysis. In both cases, the imine, generated as the reaction byproduct, often further participates in the reaction. Therefore, this approach does not offer the same synthetic flexibility as those using *N*-heteroarene *N*-oxides, but it can be fully atom-economical and deliver products with enhanced structural complexity.

In 2008, S. Shin reported the first case using a tethered nitrone as the oxidant (Scheme 56A).[146] The reaction begins with 6-*exo*-*dig* cyclization of the nitrone oxygen of **100** to the $AuCl_3$-activated C–C triple bond, followed by fragmentation of the *N*–O bond and hence the generation of gold carbene **CX**. The imine nitrogen subsequently cyclizes to the carbene center to form gold *C*-enolate intermediate **CY**. Its *O*-enolate tautomer then undergoes intramolecular [3 + 2] cycloaddition to furnish the azabicyclo[3.2.1]octane product **101** mostly as a single diastereomer. In 2011, the same group reported an asymmetric version of this reaction by introducing a chiral auxiliary on the nitrone moiety (Scheme 56B).[147] Various auxiliaries were tested, but most suffered from low yields and poor diastereoselectivities, with the exception of (S)-1-(4-nitrophenyl)ethyl. Generally, for the substrate scope, diastereomeric ratios are high (e.g., >20:1) for intramolecular cycloaddition but moderate in intermolecular cases, as shown in the selected examples in Scheme 56. The stereochemistry can be explained by a Felkin–Anh-type model, as shown in **CZ**, in which the C–Ar bond is aligned perpendicular to the azomethine ylide and avoids the possible 1,3-allylic interaction between the auxiliary methyl group and the alkynyl substituent R.

In 2009, S. Shin reported a cascade cyclization to access isoindoles from oxime or nitrone substrates (Scheme 57A).[148] The proposed mechanism entails a 7-*endo*-*dig* cyclization to give transient intermediate **DA**, subsequent carbene generation, and its intramolecular trapping by the imine moiety to deliver isoindoles **102**. The contrast between the initial cyclizations in this reaction and that in Scheme 56A can be mainly attributed to the gold catalysts used, as during the condition optimization of the reaction shown in Scheme 56A JohnPhosAuOTf led to 7-*endo*-*dig* cyclization selectively while $AuCl_3$ resulted in 6-*exo*-*dig* cyclization. In 2011, A. Jia and X. Li discovered unusual alternative reactivities by changing the substituent of the nitrone nitrogen from benzyl to bulky *t*-butyl (Scheme 57B).[149] With a terminal alkyne substrate, the imine generated during the carbene formation could not attack the carbene center because of steric hindrance. Instead, it was proposed that migration of a hydride to the carbene moiety occurs, generating a nucleophilic gold enolate tethered to an electrophilic nitrilium. Attack of the enolate O atom at the nitrilium and demetalation afford cyclic imidate **103**. For internal alkynes, again, the imine attack does not occur. Rather, the gold carbene intermediate undergoes 1,2-C–H insertion to furnish the aldehyde–enone product **104** upon imine hydrolysis.

In 2010, S. Shin extended the nitrone reaction to the synthesis of 1-aminoindanes and 5,6-fused azabicycles (Scheme 58A).[150] In the proposed mechanism, the gold carbene intermediate undergoes a semipinacol-type rearrangement to deliver either **DB** or **DC** for the subsequent Mannich reaction, which forms the product **105**. When R^2 is a vinyl group, an additional Michael cyclization results in the formation of azabicycles **106**. As shown in the selected examples, various spiro or bicyclic structures can be obtained in most cases with good to excellent diastereoselectivity. An asymmetric version of this reaction was developed

by J. Zhang in 2013 (Scheme 58B).[151] The key step for the enantioselectivity is shown as **DB***. With the help of a chiral phosphoric acid that activates the imine moiety, spirocyclic diketones were accessed in high yields with good to excellent enantioselectivities.

In 2011, R.-S. Liu's group reported the 1,2-difunctionalization of ynamides using external nitrones as the oxidant (Scheme 59).[152] The proposed mechanism for the formation of 2-aminoamides **107** involves inner-sphere trapping of the gold carbene by the imine byproduct. The propensity for inner-sphere trapping might be attributed to strong dipole–dipole interactions between the electron-deficient carbene center and the imine, as shown in **DE**. Hydrolysis furnishes the final product. When a nitrosobenzene is used as the reacting partner, nitrone carbene intermediate **DF** undergoes intramolecular cyclization to generate a four-membered-ring intermediate, followed by ring opening and demetalation. This alkyne/nitroso metathesis gives access to the α-oxoamidine products **108** in moderate to good yields. It is noteworthy that 1,2-amino alcohols with opposite regioselectivities (i.e., **110** vs **109**) are selectively accessed upon $NaBH_4$ reduction in these two reactions.

In 2018, R.-S. Liu further reported a gold-catalyzed oxidation–Mannich cascade (Scheme 60).[153] With 2-ethynylphenols or 4-hydroxy-1-ynes **111** as the substrates, amino-dihydrofuran-3(2*H*)-ones **112** or **113** can be accessed with *syn*-selectivity. In the proposed mechanism, the Mannich reaction between the oxonium-type gold enolate intermediate of type **DH** and the imine byproduct generated from nitrone reduction is facilitated by a key hydrogen-bonding interaction. This is the first report revealing that the gold enolate intermediate generated upon nucleophilic attack could be trapped by nonprotic electrophiles in preference to protodeauration, which is often considered facile. This oxidation–Mannich strategy was extended to phenoxyethynes for the synthesis of alkylidenebenzofuranones (i.e., **114**). In that chemistry, a different downstream reaction of the gold enolate generated upon electrophilic carbene cyclization to the benzene ring is postulated to engage another molecule of the nitrone as the electrophile, as shown in **DI**.

Later in the same year, W. Hu and X. Xu[32] reported the asymmetric synthesis of **113** by the addition of a chiral phosphoric acid cocatalyst. The reaction exhibits excellent enantioselectivity. The assembly **DG** is proposed to account for the observed enantioselectivity.

In 2019, R.-S. Liu revealed that using a combination of a more acidic gold catalyst (i.e., in situ-generated PPh_3AuNTf_2 vs JohnPhosAuNTf_2) and a nonpolar solvent (i.e., toluene) completely impedes the reaction of 3-butyn-1-ol shown in Scheme 60A.[154] Instead, the reaction leads to the formation of dihydropyran-fused indole **115** (Scheme 61A). In the proposed mechanism, vinylgold intermediate **DJ** is formed initially upon gold-promoted addition and undergoes a 3,3-sigmatropic rearrangement to form **DK**, which upon rearomatization, deauration, hydrolysis of the imine group, and condensation affords indole **DL** bearing a tertiary alcohol moiety. It is then further proposed that LAu^+ would promote the ionization of the pendent tertiary alcohol to generate tertiary carbocation **DM**. A stepwise Prins-type cyclization furnishes the final product 115 in moderate to excellent yields. When 2-propyn-1-ols are used as substrates, tetrahydro[1,2]oxazino[5,4-*b*]indoles are produced by a formal [3 + 3] annulation between the related indolic allyl cation and

the nitrone oxidant (Scheme 61B). In the case of styryl nitrones (Scheme 61C), ketone intermediate **DN** is similarly formed, which is followed by two cyclizations to ultimately afford dihydrooxazolo[3,4-*a*]indole **116** in moderate to good yields. A range of ring-fused indoles can be accessed in synthetically useful yields via these impressive cascade reactions.

2.1.3.3. Oximes.: In 2009, Shin described a geometry-dependent intramolecular redox reaction using *o*-alkynylaryl ketoximes 117 as the substrates to access isoquinolines **118**, isoindoles **119**, or isoquinoline *N*-oxides (Scheme 62).[148] When subjected to the reaction conditions, (*Z*)-**117** undergoes direct *O*-6-*exo*-*dig* cyclization to generate intermediate **DO**, which is followed by a redox process to generate gold carbene intermediate **DP**. The isoquinoline product **118** is then formed via nucleophilic attack at the gold carbene by the tethered imine and subsequent protodeauration. This reaction occurs only when R^2 = aryl, which stabilizes gold carbene **DP**. Without such a cation-stabilizing group, an alternative 7-*endo*-*dig* cyclization dominates, affording isoindole **119**. When (*E*)-**117** is used, *N*-cyclization leads to isoquinoline *N*-oxide products without incurring redox chemistry.

2.1.3.4. Tethered Epoxides.: Epoxides are not known as oxidants but have been shown to act as internal nucleophilic oxidants in oxidative gold catalysis. The epoxide oxygen of **120** is delivered to the neighboring C–C triple bond in a two-step sequence that entails initial cyclization, opening of the strained three-membered ring, and heterolytic fragmentation of the other epoxide C–O bond (Scheme 63A). The *α*-oxo gold carbene **DQ** thus generated can then undergo Nazarov-type cyclization, proton migration, and deauration to furnish a 3-acylindene as the product. This chemistry was reported in 2008 by Hashmi[155] and R.-S. Liu[156,157] separately. Interestingly, in his studies,[156,157] R.-S. Liu noticed a shift in regioselectivity during the initial epoxide attack when non-aromatic epoxides (e.g., **121**) are used as substrates (Scheme 63B). In that case, a different gold carbene (e.g., **DR**) is generated and then undergoes a different Nazarov-type cyclization to yield the polycyclic product (e.g., **122**).

R.-S. Liu later reported the gold-catalyzed synthesis of 2-hydroxyindanones from *o*-alkynylaryl epoxides (Scheme 64).[158] The primary difference from the studies in Scheme 63 is the addition of diphenyl sulfoxide in the reaction, which apparently oxidizes the gold carbene center to a carbonyl group. As a result, 1,2-diketone **DS** is formed as the intermediate, which is proposed to undergo an intramolecular ene reaction to deliver the product. Notably, excellent diastereoselectivities were observed in most cases.

2.1.3.5. Hydroxyamine-Based Oxidants.: Hydroxylamines can also serve as nucleophilic oxidants in oxidative gold catalysis, delivering the oxygen atom through cleavage of the N–O bond. In 2011, Shin published the first examples of this transformation with *N*-sulfonylhydroxylamine-functionalized terminal alkyne substrates (Scheme 65).[159] It was surmised that the N-sulfonyl group facilitates the N–O bond cleavage and hence the generation of *α*-oxo gold carbene intermediate **DT**. The carbene would then be trapped intramolecularly by the negatively charged sulfonamide to furnish *N*-sulfonyl-3-pyrrolidinone **123** as the product. Mostly moderate yields were reported, and a limited range of substituents are tolerated.

An indirect way to generate *α*-oxo gold carbenes with *N*-arylhydroxylamine-type oxidants was reported in 2016 by R.-S. Liu (Scheme 66).[160] Rather than directly attacking the gold-activated terminal alkyne, the *N*-arylhydroxylamine attacks the oxocarbenium center of intermediate **DU**, which is formed through gold-promoted cyclization of the ketone carbonyl oxygen to the C–C triple bond. The cleavage of the N–O bond occurs afterward and generates *α*-oxo gold carbene **DV**, which is trapped by the free aniline formed from the original hydroxylamine. The subsequent intramolecular aldol condensation furnishes the 2-aminoindenone product **126**. The R^1 group in **124** cannot be alkyl, as nitrone **125** would be generated preferentially and eventually form an isoindole (see Scheme 62). An additional gold-catalyzed cyclization could occur in one pot if R^1 is alkynyl, affording polycyclic pyrrole **127.**

In addition to being oxidants for the generation of gold carbenes, hydroxylamines participate in gold-catalyzed cascade reactions as nucleophiles and apparent oxidants. In 2011, L. Zhang published a study of this nature that achieved the synthesis of 2-alkylindoles from N-arylhydroxylamines and terminal alkynes (Scheme 67).[161] The key step in this chemistry is the 3,3-sigmatropic rearrangement of *N*-aryl-*O*-alkenylhydroxylamine intermediate **DW**, which is generated by *O*-nucleophilic addition of hydroxylamine **128** to a gold-activated alkyne. One feature of this indole synthesis is its mild reaction conditions (even a tetrahydropyran group is tolerated) in comparison with the related Fischer indole synthesis, which often requires strong acids and/or elevated reaction temperatures. In a later study in 2013, L. Zhang further improved this indole synthesis by employing the more stable *N*-arylhydroxamic acid as the substrate and $Zn(OTf)_2$ as the cocatalyst.[162] The role of this Lewis acid is to enhance the nucleophilicity of the hydroxamic acid by forming a chelated metal hydroxamate (DX). In comparison with the 2011 study, this system dramatically expands the scope of the alkynes with the inclusion of enynes and internal alkynes, reduces the reaction time significantly, and improves the overall reaction efficiency.

A slightly different approach to the 3,3-sigmatropic rearrangement/dehydrative cyclization cascade was reported in 2010 by Camp (Scheme 68A).[163] This reaction utilizes gold-catalyzed addition of a ketoxime to an electron-deficient C–C triple bond to generate *N,O*-dialkenylhydroxylamine **DY** upon tautomerization, which undergoes the cascade to furnish tetrasubstituted pyrroles **129**. Notably, the reaction requires a rather high reaction temperature. L. Zhang later reported a related two-step approach in which the first step is the formation of the *N*-alkenylhydroxylamine through the condensation between an alkyne-tethered hydroxylamine and a 1,3-diketone and subsequent tautomerization, and the second step is the gold-catalyzed cyclization and subsequent 3,3-sigmatropic rearrangement/dehydrative cyclization cascade. This reaction delivers 1,2-fused pyrroles **130** as the products (Scheme 68B).[164]

2.2. Non-oxidatively Generated Carbenes or Related Intermediates Oxidized by Nucleophilic Oxidants

In addition to the direct oxidation of alkynes/allenes, nucleophilic oxidants can facilitate oxidative gold catalysis by oxidizing electrophilic intermediates generated in nonoxidative

manners during gold catalysis. These intermediates are often gold carbenes or related species.

2.2.1. Sulfoxides.—In 2007, Toste reported a series of gold(I)-catalyzed oxidative reactions in which the *in situ*-generated gold carbene intermediates are oxidized by diphenyl sulfoxide to furnish the corresponding carbonyl products in good to excellent yields (Scheme 69A).[165] For example, the gold carbene **DZ** generated upon gold-promoted cyclization of 1,6-enyne **131** can be intercepted by the sulfoxide to produce sulfonium species **EA**, which is followed by deaurative elimination to afford aldehyde **132** as the product. This direct oxidation of a gold carbene into a carbonyl group was further investigated with gold carbenes generated *in situ* in various other manners. For example, *α*-diazo ketone **133** is converted into 1,2-diketone **134** in 88% yield. Diazo ketone **135** undergoes gold-promoted 5-*exo*-*dig* cyclization followed by loss of nitrogen to generate a gold carbene intermediate, which is then oxidized to furnish 1,4-enedione **136** as the product. The vinylgold carbene intermediate generated upon 1,2-pivaloxy migration of propargyl ester **137** is oxidized to afford aldehyde **138** in 70% yield. Homopropargyl azide **139** is converted into pyrrolone **140** in 73% yield, and triazene **141** can be transformed into aldehyde **142** in 66% yield. Similarly, in 2013 Shin reported that *N*-allylpropiolamide **143** is oxidized under gold catalysis to give bicyclic aldehyde/ketone **144** (Scheme 69B).[166]

In 2016, Echavarren described an efficient access to barbaralones through gold(I)-catalyzed oxidative cyclization (Scheme 69C).[167] 7-Ethynyl-1,3,5-cycloheptatriene **145** undergoes 6-*endo*-*dig* cyclization to generate cyclopropyl carbene intermediate **EB**, which is then oxidized by either a sulfoxide or an *N*-oxide to produce barbaralone **146** in moderate to excellent yield. However, when 7-propargyl-1,3,5-cycloheptatriene is employed as the substrate, it undergoes 6-*exo*-*dig* cyclization to generate carbene intermediate **EC**, which can then be oxidized to afford 1-formylbarbaralane in 92% yield.

In 2019, Hashmi developed a gold-catalyzed oxidative cyclization of amide diynes **147** that uses diphenyl sulfoxide as the oxidant, leading to the formation of inden-1-one-3-carboxamides 148 in good to excellent yields (Scheme 69D).[168] The reaction is initiated by gold-promoted 5-*endo*-*dig* cyclization of the amide diyne to afford keteniminium intermediate ED, which is then trapped by the sulfoxide to deliver intermediate **EE**. Expulsion of diphenyl sulfide gives access to gold carbene intermediate **EF**, which is further oxidized by the sulfoxide to produce the observed product.

2.2.2. *N*-Oxides.—It is not surprising that *N*-oxides can behave as oxidants in gold carbene oxidation in the same manner as diphenyl sulfoxide. In 2013, Metz reported that the gold-catalyzed cascade cyclization of enyne carbonyl compound **149** generates gold carbene **EG** (Scheme 70A).[169] Its subsequent oxidation by 3,5-dichloropyridine *N*-oxide affords tetracyclic keto ether **150**. In addition, it was shown that R^1 could also accommodate a tethered alkene for an alternative [3 + 2] cycloaddition. In 2015, Echavarren succeeded in applying oxidative gold catalysis in the total synthesis of (–)-nardoaristolone B (Scheme 70B).[170] In this key step, 1,5-enyne **151** is converted to tricyclic cyclopropyl ketone **152**, along with a significant amount of tricyclic diene **153**. A mechanism following Scheme 34A

path A (i.e., oxidation of cyclopropylgold carbene **EI** by 3,5-dichloropyridine *N*-oxide) is suggested and can readily rationalize the observation of **153**, but the alternative reaction pathway via *α*-oxo gold carbene **EH** cannot be ruled out.

In 2013, R.-S. Liu discovered that when 3,5-dichloropyridine *N*-oxide is employed instead of 8-methylquinoline *N*-oxide in the reaction of dienyne **154**, oxidative gold catalysis different from that shown in Scheme 34B occurs (Scheme 71).[171] Because of the decreased nucleophilicity of 3,5-dichloropyridine oxide, gold-promoted cyclization occurs instead of alkyne oxidation. As a result, cyclopentadienylgold carbene **EJ** is generated and then oxidized to afford the aldehyde product **155**. It was also shown that a 3,5-dichloro-*N*-iminopyridium ylide could deliver a tosylnitrene moiety to the gold carbene center to furnish cyclopentadienyl imines **156** in moderate yields.

2.2.3. Other Oxygen-Based Oxidants.—In 2013, R.-S. Liu reported that nitrosobenzene can oxidize a gold carbene to a carbonyl group (Scheme 72).[172] In this reaction, the gold-promoted cyclization of 2-alkenylphenylalkyne **157** generates cyclopropyl gold carbenes **EK** and **EK′**, which are in equilibrium. It is proposed that a [3 + 2] cycloaddition occurs selectively between nitrosobenzene and **EK** to form gold carbene **EL**, which is then oxidized by another molecule of nitrosobenzene to afford the product **158**.

Hydrogen peroxide is a mild and clean oxidant that possesses a weak oxygen–oxygen single bond. A few examples of the use of hydrogen peroxide to oxidize gold carbenes to carbonyl groups have been reported. In 2007, R.-S. Liu revealed that gold carbene **EM** generated upon cyclization and elimination is oxidized by H_2O_2 to afford a naphthyl aldehyde/ketone (Scheme 73A).[173] Notably, a chloride scavenger such as AgOTf is not required in this reaction, which could be attributed to the elevated reaction temperature, the use of electron-rich triethylphosphine as the ligand, and the facile nature of the cyclization. In addition to terminal alkynes, internal alkynes with R^2 = aryl or alkyl are allowed. In the latter case, minor amounts of 1,2-C–H insertion products (i.e., 2-alkenylnaphthalenes) were observed. Interestingly, when $PtCl_2$ is applied as the catalyst under a CO atmosphere, the yield of ketone **159** decreases dramatically while the 1,2-C–H insertion product becomes the major product.

In 2010, J. Zhang succeeded in the conversion of 3-(1-alkynyl)-2-alken-1-ones **160** to 2,4-diacylfurans using $AuCl_3$ as the catalyst and H_2O_2 as the oxidant (Scheme 73B).[174] In the reaction, gold carbene intermediate **EN** is generated upon gold-promoted carbonyl cyclization. When R^1 is an alkyl group, 10 equiv of hydrogen peroxide is required to overcome the competitive 1,2-C–H insertion reaction. It was also reported that the alkenylgold carbenes generated from propargylic pivalates can be oxidized by H_2O_2 to deliver the enal products **138**.

In 2015, H. Cao reported one example of the oxidation of a gold carbene by air (Scheme 74).[175] Gold-catalyzed cyclization of the condensation product of propiolaldehyde **161** and pyridine-2-amine **162** affords imidazo[1,2-*a*]pyridine-substituted gold carbene **EO**, which is then oxidized to the corresponding ketone product. When $H_2{}^{18}O$ was added to the reaction,

no ^{18}O-labeled **163** was detected. Consequently, dioxygen in the air instead of a trace amount of water is believed to be the oxygen source.

2.3. Reactions of Non-carbene/Non-carbenoid Intermediates with Electrophilic Oxidants

During gold catalysis, various gold-functionalized catalytic intermediates are generated, many of which feature a C–Au bond in the form of alkenylgold, arylgold, alkynylgold, or to a lesser extent alkylgold. Reactions of these organogold intermediates with electrophilic oxidants that do not involve metal oxidation state changes are discussed in this section. Because of uncertainties with reaction mechanisms, some of the reactions included in this section are chosen on the basis of the likely mechanisms, despite the fact that related mechanisms involving a Au(I)/Au(III) catalytic cycle may not be ruled out.

2.3.1. With Eletrophilic Halide (Excluding Fluoride).—

As the reactions of organogold species with electrophilic fluorides are frequently proposed to involve a Au(I)/Au(III) catalytic cycle, they will be discussed in Section 3.

In 2006, Gagosz reported that in the gold-catalyzed cyclizations of propargylic tert-butyl carbonates, a vinylgold intermediate reacts with NIS to deliver a vinyl iodide product with retention of the double-bond geometry.[176] In 2007, L. Zhang reported the synthesis of α-iodoenones **165** from propargylic acetates 164 using NIS as the oxidant (Scheme 75A).[177] It was found that a small amount of water in acetone can increase the stereoselectivity dramatically without compromising the reaction yield. When both R^1 and R^2 are alkyl groups, good *Z* selectivities are achieved. Notably, β,β-disubstituted α-iodoenones **165′** are accessible under the same conditions in good to excellent yields. To rationalize the formation of both the *Z* and *E* products, two competing mechanistic pathways are proposed. After the gold-catalyzed acetoxy 3,3-rearrangement, allenyl ester **EP** reacts with NIS from the less hindered side to afford (*E*)-**165** upon hydrolysis. In the other pathway, allenyl ester **EP** is activated by the same gold catalyst to form oxocarbenium species **EQ** with the *Z* configuration. Subsequent stereospecific iodination of this species and hydrolysis then afford (*Z*)-**165**, which can also be generated with the hydrolysis preceding the iodination. The observed product *Z*-selectivity suggests that the reaction of **EP** with Ph_3PAu^+ outcompetes direct iodination. In 2010, X. Shi reported an *E*-selective version of this chemistry that uses benzotriazole-coordinated Ph_3PAu^+ as the catalyst (Scheme 75B).[178] This could be rationalized by the mildly basic benzotriazole, which tempers the reactivity of the cationic gold(I). Consequently the reaction favors the direct iodination of **EP**, leading to the *E* isomer as the major product. Interestingly, it was established that (*E*)-**165** is the kinetic isomer and can be isomerized into the *Z* counterpart nearly completely in two reported cases.

In 2009, L. Zhang further developed a protocol for the synthesis of α-haloenones (Scheme 75C).[179] In that chemistry, the oxomolybdenum cocatalyst functions as a surrogate of the acetyl group of **164** in a reversible and catalytic fashion. As a result, propargylic alcohols are directly converted into α-haloenones in moderate to excellent yields. The catalytic amount of triphenylphosphine oxide improves the *Z*/*E*-selectivity and yield, which could be attributed to the formation of a dinuclear molybdenum complex. Notably, in comparison

with the reactions using propargylic acetates, the *Z*/*E*-selectivities were significantly improved.

In 2008, Gouverneur reported the halogenation of the alkenylgold species generated from the gold(I)-catalyzed cyclization of **166** (Scheme 76A).[180] Iodination, bromination, and chlorination lead to moderate to good yields, but fluorination is less efficient because of the competing protodeauration process. Mechanistic investigation indicated that the electrophilic halogen reagents should react with alkenylgold **ER** rather than its protodeaurated form, which is attributed to the inductive deactivation by the *gem*-difluoro substituents.

In 2011, a study published by R.-S. Liu employed *N*-chlorosuccinimide (NCS) as the electrophilic oxidant in the gold(III)-catalyzed reaction of alkynycyclopropyl epoxides **167** (Scheme 76B).[181] The reaction involves initial gold-promoted cyclization followed by cyclopropane ring expansion to form gold-functionalized cyclobutane cation **ES**. Upon its hydration, the expected chlorinated product **169** with X = Cl was not detected. Instead, the eight-membered-ring product **168** was formed in moderate to good yields. It is proposed that the gold moiety in **ET** activates the proximal alcohol toward electrophilic attack of NCS to open the four-membered ring. It was also found that adding triphenylphosphine oxide slows protodeauration and significantly improves the reaction yields. When $AuCl_3$ was used as the catalyst and NIS or *N*-bromosuccinimide (NBS) as the oxidant, the iodinated or brominated products **169** were formed in moderate yields via direct halogenation of the alkenylgold moiety in **ET** because of the more reactive nature of the electrophilic halogen reagents.

In 2014, Sheppard reported the synthesis of α,α-diiodo-β-hydroxy ketones from propargylic alcohols **170** (Scheme 76C). This was achieved using NIS as the oxidant and $Ph_3PAuNTf_2$ as the catalyst.[182] Mechanistically, it is proposed that the gold(I) catalyst is oxidized by NIS to form a gold(III) species, which then activates the C–C triple bond toward attack by acetonitrile. This attack generates intermediate **EU**, which undergoes cyclization, reductive elimination, further iodination, and hydrolysis to furnish α,α-diiodo-β-hydroxy ketones **171**. However, it is also possible that the first iodination may not occur via a Au(I)/Au(III) catalytic cycle, as NIS is unlikely to be a strong enough oxidant to oxidize cationic Ph_3PAu^+ to a Au(III) species. Instead, **EV** with X = AuL should be formed via the sequence of Au(I)-promoted nitrile addition to the C–C triple bond and rapid alcohol cyclization to the nitrilium moiety. This intermediate then undergoes direct Au–C bond halogenation. We place this chemistry here under this consideration.

Notably, when trichloroisocyanuric acid (TCICA) was applied as the electrophilic halide source, α,α-dichloro-β-hydroxy ketones were formed in the absence of a gold catalyst. The author proposed that the electrophilic chlorine in TCICA can activate the alkyne in a similar way as gold.

In 2010, J. Wang reported the gold(III)-catalyzed bromination of benzene and naphthalene (Scheme 77).[183] During the reaction, $AuCl_3$ forms arylgold(III) complex **EW**, likely via a Friedel–Crafts mechanism; meanwhile, the reactivity of NBS is also enhanced by the same catalyst. With such dual activation, the bromination occurs readily at room temperature to 80 °C. The regioselectivity is consistent with the electrophilic aromatic substitution mechanism,

and the participation of gold is reflected by the observed good to excellent *para* to *ortho* ratios (e.g., only *para* in the case of anisole). The catalyst loading can be decreased to 0.01 mol % for several aromatic compounds without significant yield loss. Notably, moderately strong electron-withdrawing groups are tolerated. Moreover, for all of the starting materials tested, only monobrominated products were reported.

In 2016, L. Zhang[184] reported a gold-catalyzed C–H insertion reaction via a reactive gold vinylidene intermediate[185] (i.e., **EY**; Scheme 78). In the proposed mechanism, silyated *α*-alkynone **172** is first converted to an alkynylgold complex, which is activated by *in situ*-generated TMS^+ to form gold complex **EX**, which is in resonance with gold allenylidene complex **EX′**. The reaction of **EX′** with *N*-bromoacetamide or its Lewis acidactivated form would generate gold vinylidene **EY**, which undergoes intramolecular C–H insertion to furnish *α*-bromocyclopentenone **173** as the product. The reaction exhibits moderate to excellent yields, accommodates a range of $C(sp^3)$–H bonds including the challenging methine C–H bond, and displays synthetically valuable regio- and diastereoselectivities. Moreover, the C–H insertion does not require kinetic facilitation of the Thorpe–Ingold effect and is effective with a cyclobutane ring.

2.3.2. With Oxygen/Nitrogen-Based Oxidants.—In 2015, N. Jiao and X. Shi reported a synergistic Au/Fe catalysis in which an alkenylgold intermediate undergoes Fe-catalyzed oxidation by O_2 to deliver oxazole-/indole-/benzofurancarbaldehydes (Scheme 79).[186] Their mechanistic studies support the crucial role of cyclization intermediate **EZ** in the subsequent oxidation, including much slower oxidation of the corresponding protodeaurated alkene in the presence of only Fe/O_2. It was proposed that an iron-associated peroxy radical adds to the vinylgold intermediate, which is more electron-rich than its protonated alkene counterpart and consequently is more reactive. Interestingly, substituted indoles and benzofurans can also be prepared from propargylic substrates via this method in moderate to high yields, although slightly different reaction conditions are employed. Notably, internal alkynes are not suitable for this reaction.

Another gold-catalyzed oxidative transformation of propargylic amide substrates was reported by Song in 2017 (Scheme 80).[187] The reaction leads to the formation of 5-cyanooxazoles **174** with $Cu(OAc)_2$ as the cocatalyst or oxazole-5-carboxamides **175** with $Ni(acac)_2$ as the cocatalyst. Interestingly, it was shown that neither alkenylgold intermediate **FA** nor its corresponding protodeaurated alkene could lead to the formation of **174** in the absence of $Ph_3PAuNTf_2$. Therefore, it was proposed that **FB**, a structurally undefined intermediate formed upon the interaction of $Ph_3PAuNTf_2$ and **FA**, reacts with the *in situ*-generated NO radical to form radical **FC** featuring a newly constructed C–N bond. Subsequent hydrogen atom transfer from **FC**, isomerization, and deauration afford aldoxime **FD**, which is selectively converted into either of the isolated products under nickel or copper catalysis. Both reactions work well with R being various aryl/heteroaryl groups but exhibit fair to moderate yields when R is an alkyl group. In the case of **174a**, no product was formed.

In 2016, Guo reported a dehydrogenative coupling reaction between phenols and symmetric diarylacetylenes using oxygen as the oxidant (Scheme 81).[188] The proposed mechanism

involves initial *syn* addition of Ph_3PAu^+ and phenol to the alkyne C–C triple bond followed by dehydrogenative coupling to deliver the benzofuran product. However, no mechanistic studies were performed to support this proposal. The reported cases exhibit good yields, but the scope is limited to symmetric diarylacetylene substrates.

3. OXIDATIONS INVOLVING A AU(I)/AU(III) CATALYTIC CYCLE

In the early stages of homogeneous gold catalysis (i.e., before 2008), the gold center, either Au(I) or Au(III), mostly did not undergo redox change during catalysis, or at least was not proposed to do so. Often reduction of the metal center results in gold precipitates and signals catalyst decomposition. It was a curiosity at that time as to whether Au(I) could be oxidized to Au(III) in a catalytic setting because of the perceived challenge of such an oxidation. Theoretically, however, oxidative Au(I)/Au(III) catalysis could be readily envisioned. As shown in Scheme 82, the reaction would commence with a Au(I) complex (i.e., **FE**). It would react with a substrate to arrive at an organogold(I) intermediate, which because of the increased electron density at the metal center would be oxidized to a gold(III) complex. This gold species would then undergo either direct reductive elimination or some additional transformations before the final step in the catalytic cycle. We refer to this as catalytic path A (i.e., **CP-A**). Alternatively, **FB** could be oxidized first to a gold(III) salt (i.e., **FF**), which then reacts with substrates and eventually closes the catalytic cycle by reductive elimination. It is conceivable that this latter catalytic pathway, i.e., catalytic path B (**CP-B**), can commence with a gold(III) catalyst. When a cationic gold(I) complex is employed, **CP-A** is more likely since its oxidation to gold(III) could be challenging. However, in the case of a neutral gold(I) complex, the initial oxidation to a gold(III) species and hence the catalytic pathway B is plausible.

This oxidative Au(I)/Au(III) catalysis permits oxidative functionalization of Au–C bonds, which would otherwise be typically replaced by a C–H bond upon protodeauration. Thus, it substantially enriches gold chemistry. The most commonly used oxidants are Selectfluor and hypervalent iodine reagents such as phenyl iodide diacetate (PIDA). Again, reactions involving a Au(I)/Au(III) catalytic cycle that do not employ external oxidants are considered redox-neutral and are not covered here.

3.1. Selectfluor and Other Electrophilic Fluorine Reagents as Oxidants

Electrophilic fluorine reagents, especially Selectfluor, can readily oxidize Au(I) to Au(III) and hence enable oxidative Au(I)/Au(III) catalysis (Schemes 83–91). In several cases, they play a dual role as the oxidant as well as the fluorine source in fluorination chemistry (see Schemes 92 and 93).

In 2009, L. Zhang reported the first examples of the use of Selectfluor as the oxidant in oxidative gold catalysis.[189,190] As shown in Scheme 83, the reactions employ a propargylic acetate as the substrate and can yield either homoenone dimer **177**[189] or the cross-coupling product, α-arylenone **178**.[190] In the proposed mechanism, which follows catalytic path A (see Scheme 82), oxocarbenium intermediate **FG** is first generated by gold-catalyzed tandem 3,3-rearrangement of the propargylic acetate and further gold activation. Its subsequent hydrolysis leads to the formation of α-auroenone **FH**, which is then oxidized by Selectfluor

to generate a Au(III) species, possibly as **FI**. In the absence of an external organometallic reagent, transmetalation between **FG** or **FH** and **FI** would arrive at Au(III) complex **FJ** with two identical enonyl ligands, which would then undergo reductive elimination to furnish the enone dimer. Alternatively, when excess arylboronic acid is present, the transfer of its aryl group to FI outcompetes the formation of **FJ**, which eventually results in the formation of the cross-coupled product **178**. This is the first instance where Au(I)/Au(III) catalysis was employed in synthetically versatile cross-coupling reactions. It is noteworthy that the homodimerization chemistry employs CyJohnPhosAuNTf$_2$ as the catalyst, which is capable of catalyzing the conversion of **176** to **FG** because of its cationic nature but in the cross-coupling reaction, neutral Ph$_3$PAuCl is employed as the gold source and cannot promote the formation of **FG**. It is likely that in the latter case, Ph$_3$PAuCl is oxidized at the beginning by Selectfluor to form either a gold(III) species, thereby following the catalytic path B (see Scheme 82), or a gold(I) species with its phosphine ligand lost as a result of its oxidation to phosphine oxide. In 2013, Faza and co-workers performed a computational study of these two reactions starting from **FH**/**FI** and offered in-depth understanding of the transmetalation and reductive elimination steps.[191] It was found that fluoride plays an important role in assisting both transmetalation and reductive elimination.

It is noteworthy that acetonitrile is a preferred solvent over chlorinated ones, as it can dissolve Selectfluor. In the cross-coupling reaction, the addition of a small amount of water in the system enhances boronic acid transmetalation while keeping the protodeauration of **FI** at an acceptable level. The homodimerization chemistry offers access to highly hindered products such as **177a**, and the cross-coupling reaction can accommodate phenylboronic acids containing electron-withdrawing or slightly donating groups at the *meta*- or *para*-position.

In the same year, L. Zhang reported another oxidative gold catalysis using Selectfluor as the oxidant (Scheme 84A).[192] Various 1-benzoxyvinyl ketones were obtained in moderate to good yields. In the proposed mechanism, gold oxocarbenium intermediate **FK** is oxidized to give gold(III) intermediate **FL**. Subsequent cyclization of its carboxy group to the cationic gold(III) center forms cyclic complex **FM**. This intermediate then undergoes hydrolysis and reductive elimination to afford the observed product. However, in 2014, R. Zhu and C. Liu performed a detailed computational study of this chemistry (Scheme 84B).[193] The findings suggested that an electrophilic fluorination pathway is favored over all of the other pathways, including the originally proposed one. In this mechanism, the benzoxyallene intermediate generated upon gold-catalyzed 3,3-sigmatropic rearrangement undergoes an alternative 5-*exo*-*dig* cyclization to arrive at **FN**, which reacts with Selectfluor to generate fluorinated cyclic oxocarbenium **FO**. Hydration of this species is followed by ring opening and expulsion of HF to furnish the final product.

In 2010, L. Zhang demonstrated the first example of gold-catalyzed oxidative carboheterofunctionalization of alkenes using Ph$_3$PAuCl as the source of catalytic gold (Scheme 85A).[194] Various *N*- or *O*-heterocycles were accessed in moderate to high yields. A concurrent study detailing similar aminoarylation of alkenes was reported by Toste later in the year (Scheme 85B).[195] In Toste's study, a bisgold complex, i.e., dppm(AuBr)$_2$, was used as the catalyst, and the reaction was run at ambient temperature. Several mechanisms

were proposed in order to rationalize the relative stereochemistry of the deuterium-labeled product **180a**. In one of the pathways proposed by L. Zhang, the Au(I) catalyst is first oxidized, which is followed by transmetalation to generate the Au(III) species **FQ**. This acidic complex then activates the C–C double bond to promote an antiheteroauration of the π-system to generate the alkylgold intermediate **FR**, which then undergoes reductive elimination to furnish the pyrrolidine product **180a** with the correct relative stereochemical outcome. A different mechanism was proposed by Toste, wherein the alkylgold(III) **FS** is generated through a syn-heteroauration of **179**. A subsequent S_N2-like delivery of the aryl group of the arylboronic acid at the carbon center in a five-centered transition-state shown in **FT** leads to the final product with correct stereochemistry. The synheteroauration and the backside delivery via a five-membered transition state in this latter mechanism are conceptually surprising and were later revised. In 2011, Goddard and Toste[196] offered a third mechanism based on DFT studies, wherein an antiheteroauration occurs via a dual Au(III) species (i.e., FU) and a bimolecular reductive elimination shown in FV proceeds with the retention of stereochemistry. Cyclic voltammetry data of the reaction is consistent with the formation of the bisgold(III) complex FU, which is detected regardless of whether the monodentate PPh_3 or the bidentate ligand dppm was used.

The intermolecular gold-catalyzed oxidative oxyarylation of monosubstituted alkenes was reported by Toste in 2010 under similar reaction conditions (Scheme 86).[197] The alcohol or H_2O is used in large excess. Later in the same year, Lloyd-Jones and Russell[198] as well as Toste[199] reported similar oxyarylations using arylsilanes as the aryl source. As shown in the selected examples, these reactions achieve three-component coupling and deliver ether or alcohol products. In cases where a benzoate *ortho*-substituted by a $B(OH)_2$ or TMS group and H_2O are used for the reaction, the formed alcohol product undergoes spontaneous lactonization.

In contrast to the 5-*exo* products observed in the studies by L. Zhang and Toste (see Scheme 85), Nevado reported in 2011 that in the absence of an arylboronic acid, the 6-*endo* cyclization product **182** with solvent or acetate from PIDA as the nucleophile is formed selectively over the corresponding 5-*exo* product **183** (Scheme 87A).[200] For monosubstituted alkenes, piperidine products 3- or 5-substituted by MeO, AcNH, or acetoxy were obtained as the major products. For internal alkene sulfonamide substrates with R^1 = Ph, the tricyclic product **181** was formed via 5-*exo* cyclization followed by intramolecular Friedel–Crafts alkylation. In this case, PhI(Phth) was used as the oxidant. Mechanistic experiments revealed that starting from the isolated 5-*exo* cyclization alkylgold intermediate **FW**, the six-membered product **182** was obtained. On that basis, two reaction pathways were proposed for the formation of 182: In path A, the gold catalyst would cause 6-*endo* attack to generate alkylgold(I) complex **FX**, which would then be oxidized and substituted by a suitable nucleophile such as water, alcohol, or acetonitrile and finally undergo reductive elimination. When $PhI(OAc)_2$ is used as the oxidant, direct reductive elimination would deliver the aminoacetoxylation products (e.g., 182a). Alternatively, in path B, intermediate **FW** would be generated via 5-*exo* cyclization. Its subsequent oxidation would afford gold(III) intermediate **FY**, which could either deliver the minor pyrrolidine product **183** or form aziridinium intermediate **FZ** via intramolecular nucleophilic attack

by the sulfonamide nitrogen with concomitant reductive metal departure. The strained ring of **FZ** is opened by a nucleophile to afford the final product. In 2018, a similar study using DMF as the nucleophile in the presence of water led to the formate product (Scheme 87B).[201] Notably, in that study, in addition to Selectfluor, several PIDA variants containing different carboxylates were also employed as oxidants, which led to the formation of aminoesterification products featuring an ester group rather than formate.

In 2010, Gouverneur reported an intramolecular oxidative cross-coupling reaction using allene substrates (Scheme 88A).[202] In the proposed mechanism, benzyl-substituted *tert*-butyl allenoate **184** first undergoes cyclization and *tert*-butyl fragmentation, and the resulting gold(I) complex **GA** is then oxidized to gold(III) complex **GB**. Both of its benzyl groups could undergo intramolecular Friedel–Crafts-type substitution by the cationic Au(III) center, resulting in the formation of either of the two cyclic Au(III) complexes, which upon reductive elimination would afford one of the two tricyclic products. Complete axis-to-center chirality transfer was demonstrated in the conversion of **185** to **186**. It is noteworthy that because of the intramolecular nature of this chemistry, the unfunctionalized benzene ring is delivered to the Au(III) center as a nucleophile. In 2012, Y.-K. Liu reported a different outcome of this oxidative reaction when the ^{t}Bu ester substrate was replaced by an ethyl or other nontertiary ester.[203] In that work, further fluorination, lactone opening, and alcohol oxidation led to the formation of the fluorinated indene product (Scheme 88B).

In 2011, L. Zhang reported a formal intramolecular [3 + 2] annulation approach for the construction of tricyclic indolines (Scheme 88C).[204] The reaction exhibited moderate to good yields. The reaction mechanism is thought to entail gold(I)-activated anti-cyclization to generate alkylgold complex **GC**, oxidation by Selectfluor, Friedel–Crafts cyclization, and finally reductive elimination. The final two steps are similar to those of Gouverneur's mechanism. The results of the deuterium labeling study are consistent with initial urea cyclization in an *anti*-fashion and stereoretentive reductive elimination.

To further explore their work using allenoate substrates, Gouverneur employed terminal alkynes as the external nucleophile in the cyclization/oxidative cross-coupling cascade discussed in Scheme 88A.[205] In that reaction (Scheme 89A), either the alkyne or the aurated form (i.e., **GD**) is transferred to gold(III) complex **GF** to form **GG** for subsequent reductive elimination (path A). An alternative pathway, path B, was also proposed for the reaction, where **GD** is oxidized to give alkynylgold(III) complex **GE**, which can then promote the allenoate cyclization to arrive at the same Au(III) species **GG**. The reaction yields a β-alkynylbutenolide as the product. The yields are in general good to excellent with arylacetylenes but poor with aliphatic terminal alkynes. In some cases, the Glaser–Hay products, i.e., 1,3-diynes, were observed. In 2013, M. Shi reported a similar reaction using arylboronic acids as the nucleophile and coupling partner (Scheme 89B).[206] In most of the reported cases, bisbutenolides, the result of homocoupling, are formed as side products.

The Glaser–Hay reaction initially reported by Gouverneur[205] was examined in a detailed mechanistic study by Corma in 2011 (Scheme 90A).[207] On the basis of experimental results from cyclic voltammetry and kinetic studies, a mechanism was proposed. In the first step, a π-coordinated alkyne–gold adduct is formed and then converted to σ-acetylide gold(I)

complex **GH**, which is subsequently oxidized by Selectfluor to give gold(III) complex **GI**. This Au(III) species then reacts with another molecule of **GH** to furnish the diyne product and two different gold(I)–phosphine complexes. The presence of two different gold complexes was confirmed by cyclic voltammetry. In this reaction, hard cations such as Na^+ allow for better removal of the fluoride from the catalytic cycle, thus leading to a better outcome. In 2014, J. You reported another type of gold-catalyzed oxidative cross-coupling reaction leading to the formation of aryl–aryl bonds (Scheme 90B).[208] In their proposed mechanism, the pyridine nitrogen in 2-(2-methylphenyl)pyridine directs *ortho*-auration by $AuBr_3$ to form Au(III) complex **GJ**. Notably, NFSI was the fluorine-based oxidant used in this reaction.

In addition to alkenes and allenes, alkynes were subjected to difunctionalization under oxidative gold catalysis. In 2016, Patil reported the synthesis of ionic pyridinium–oxazoles in moderate to high yields, which were shown to be useful in cell imaging (Scheme 91).[209] In the proposed mechanism, the gold(I) catalyst is first oxidized by Selectfluor to give a cationic gold(III) species, which is followed by *anti* or *syn* attack by the ring nitrogen at the gold-activated alkyne to generate geometrically isomeric **GK** or **GL**, respectively. From **GK**, loss of isobutylene followed by intramolecular S_N2-type nucleophilic displacement furnishes the product **189**. This is consistent with the observation that electron-deficient gold catalysts such as $(C_6F_5)_3PAuCl$ showed higher catalytic efficiency. Alternatively, from **GL**, exclusion of an isobutene molecule followed by attack at the gold(III) center by the amide oxygen furnishes the same product upon reductive elimination. It is noteworthy that R must be an aryl group. This reaction constitutes an alkyne 1,2-amino-oxygenation.

In addition to oxidizing Au(I) to Au(III), these electrophilic fluorine reagents can also deliver fluorinated products either through direct fluorination or via reductive elimination of an R–Au(III)–F intermediate. In 2010, Hammond and B. Xu reported a hydrative fluorination/arylation of alkynes to afford α-fluoro-α-aryl ketones (Scheme 92A).[210] In the proposed mechanism, the gold(I) catalyst is first oxidized to a cationic gold(III) species, which promotes addition of H_2O to the C–C triple bond to generate gold(III) enol intermediate **GM**, which then undergoes sequential transmetalation with a boronic acid, reductive elimination, and electrophilic fluorination to yield the product. An alternative pathway entails switching the order of the reductive elimination and the reaction with Selectfluor. This chemistry is applicable to internal alkynes and results in complete functionalization of the C–C triple bond in the process; however, in most cases mixtures of regioisomers are obtained. Later in the same year, Nevado performed a similar reaction using methanol instead of water as the nucleophile. In this way, α-fluoro ketals or ketones can be synthesized from alkynes (Scheme 92B).[211] Notably, terminal alkynes are suitable substrates. The proposed mechanism entails Ph_3PAu^+-catalyzed/promoted double MeOH addition to the π-system to form alkylgold intermediate **GN**, which undergoes oxidation by Selectfluor followed by reductive elimination. Alternative direct electrophilic fluorination of an enol ether without the involvement of gold is possible and was demonstrated experimentally but resulted in lower yields.

Interestingly, when IPr is used as the ligand, propargylic acetates undergo direct reductive elimination of fluorinated Au(III) complex **GO** (Scheme 93A) to furnish α-fluoro ketones

as the products, as reported by Nevado in 2010.[212] This chemistry is related to the homocoupling reaction shown in Scheme 83, in which CyJohnPhos is the metal ligand. In 2014, Ryu showed in another study that a C(sp^2)–F bond can be installed from a C(sp^2)–Au bond, which is generated upon gold-promoted cyclization of an oxime to an alkyne, via a sequence of oxidation and reductive elimination (Scheme 93B).[213] This chemistry provides access to 4-fluoroisoxazoles.

Y.-K. Liu reported in 2013 that the C–C triple bond of an *o*-alkynylbenzoate could be doubly oxidized to afford a 1,2-diketone product (Scheme 93C).[214] The mechanistic studies revealed that the neighboring ester group is essential for this dual oxidation, and *α,α*-difluoroketone **190** is proposed as a reaction intermediate, although it was not isolated from the reaction. At least one of the fluorination steps is proposed to occur via reductive elimination. Michelet documented another type of difluorination gold chemistry, although the product could be formed via double fluorination of an indole intermediate generated upon gold-catalyzed cyclization (Scheme 93D).[215]

3.2. Iodine-Based Reagents as Oxidants

While I_2 is known to oxidize the organogold(I) complex (NHC)AuR to its gold(III) counterpart (NHC)AuI_2R,[156,216] hypervalent iodine reagents have been almost exclusively employed as iodine-based oxidants in Au(I)/Au(III) catalysis. These reagents are a group of iodine-containing compounds in which the iodine atom breaks the “octet rule” and formally contains more than eight electrons in its valence shell. Among these relatively strong oxidants, PIDA sees the most usage in oxidative gold catalysis. On the other hand, the λ^3-iodane compounds that deliver a nominal positively charged carbon center (e.g., the Togni reagent) have also been extensively used in gold-catalyzed cross-coupling reactions. Since they are often considered “preoxidized” building blocks for an overall redox-neutral process, the applications of those λ^3-iodane compounds, including triisopropylsilylethynyl-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX) developed by Waser,[217,218] in gold catalysis are not discussed in this review.

The first report of gold-catalyzed homocoupling of arenes was reported by Tse in 2008 using PIDA as the oxidant (Scheme 94A).[219] One year later, the same authors presented a more detailed study of the same chemistry as well as some extension of the reaction scope.[220] A large excess of the arene was employed in both studies. They also explored oxidative cross-coupling between benzene and 4-haloanisoles under the homocoupling conditions (Scheme 94B).[220] Interestingly, it was found that the ratios of biphenyl and the cross-coupling product **191** are in agreement with the ratios of anisole and benzene, suggesting that benzene is activated first by the gold catalyst and then trapped by either arene in the reaction mixture.

One inherent challenge for gold-catalyzed dehydrogenative cross-couplings of arenes is discrimination of the two distinct arene coupling partners. In an ideal scenario, the arene activated first would be selectively trapped by the other arene partner, thereby minimizing homocoupling side products. It is known in the literature that gold(I) salts can activate the C–H bonds of electron-poor arenes under mild conditions to give arylgold(I) intermediates.[221,222] In 2013, Larrosa reasoned that with a suitable oxidant in the reaction mixture, EWG-substituted arylgold(I) intermediate **GP** would be oxidized

to the corresponding arylgold(III) intermediate **GQ** (Scheme 95A). In contrast to Au(I), Au(III) is known to activate electron-rich arenes to give the corresponding arylgold(III) intermediates.[223–226] It was expected that **GQ** would behave accordingly in the reaction to generate biaryl gold(III) complex **GR**. Its subsequent reductive elimination would afford the biaryl final product while regenerating the gold(I) catalyst. Uncertain about the selectivity of the initial gold(I) activation step, Larrosa started with pregenerated arylgold(I) species, treated them with electron-rich arenes and [hydroxy(tosyloxy)iodo]benzene (Koser's reagent), and successfully obtained a series of crosscoupled biaryl products in good yields (Scheme 95B).[227]

Encouraged by the results, the authors achieved cross-couplings of different combinations of electron-rich and electron-poor arenes in a catalytic setting in 2015 (Scheme 95C).[228] In this chemistry, PBX was the preferred oxidant. Additionally, in most cases the selectivity toward cross-coupling products is almost exclusive, even when the two coupling arenes are used in near-stoichiometric amounts. Interestingly, an excess amount of the silver salt was found to be essential for reaction efficiency, and the silver salt alone gave 21% conversion. These observations strongly indicate that the silver salt functions as more than just a halogen scavenger in this reaction.

In 2019, the role of the silver salt was revealed by J. Xie, S. Li, and C. Zhu in their gold-catalyzed dehydrogenative cross-coupling of fluorinated arenes and pyrazoles (Scheme 96).[229] They investigated a proposed catalytic cycle similar to that in Larrosa's work.[227,228] It was determined experimentally and via DFT studies that silver(I) is mainly responsible for activating the C–H bond of electron-poor arenes. The arylsilver(I) species **GS** formed after C–H activation undergoes transmetalation to give arylgold(I) species **GT**. Subsequent oxidation of Au(I) to Au(III), C–H activation of the electron-rich arene, and reductive elimination furnish the biaryl product. The high selectivities observed in this study and in Larrosa's work[227,228] originate from the orthogonal C–H activation by silver(I) and gold(III) on arenes of contrasting electronic properties: the silver(I) catalyst favors the most acidic C–H bond on the electron-poor arene via a concerted metalation–deprotonation process, while the gold(III) catalyst selectively aurates the most electron-rich C–H bond of the electron-rich arene via an electrophilic aromatic substitution (S_EAr) mechanism. With the new understanding of the mechanism, the authors explored the reaction scope of this Au/Ag dual catalysis and successfully synthesized a series of polyfluorinated biaryl compounds from fluorinated benzenes and pyrazoles.

In addition to the dehydrogenative coupling of two arenes, an alternative approach to the synthesis of nonsymmetrical biaryl compounds is the oxidative cross-coupling between an arene and an aryl organometallic compound. This approach largely circumvents the challenge of discriminating between two different arenes and was first implemented by Lloyd-Jones and Russell in 2012. Arylsilanes were employed as the "organometallic" reagents, and electron-rich arenes were employed as the coupling partners (Scheme 97).[230] The reaction leads to the formation of biaryl compounds featuring various functional groups in mostly good yields. In a follow-up work, they performed detailed studies of the reaction mechanism.[231] The authors first noted the formation of phosphine oxide during the induction period of the reaction, suggesting the formation of a Au(III) species via oxidation

of the Au(I) catalyst. Indeed, several Au(III) salts were found to show excellent catalytic activity with a minimal induction period. As expected, the first auration from **GU** to **GV** occurs selectively on the arylsilane via *ipso*-substitution of the silyl group. Through DFT studies and experiments, it was determined that the associative arene substitution step (i.e., from **GW** to **GX)** is the rate-limiting step, in which the electron-rich arene is preferred over the arylsilane because of steric effects. The authors observed erosion of the chemoselectivity when more π-basic arylsilanes or less π-basic arenes were used, supporting their rationale for the observed chemoselectivity.

Additional studies of this type of oxidative cross-coupling reaction led to expanded reaction scopes. In 2015, Segawa and Itami reported the use of various heteroarenes as the coupling partner by employing a highly electron-rich nonclassical carbene “PyC” as the ligand (Scheme 98A).[232] This strong electron-donating carbene ligand facilitates the oxidation of Au(I) to Au(III), but unlike phosphine ligands, it survives the process and helps stabilize the catalytically active Au(III) species. The authors achieved cross-coupling between electron-poor arylsilanes and a series of substituted isoxazoles, indoles, and benzothiophenes. Soon after, Lloyd-Jones optimized the original coupling reaction and improved the scope of electron-rich arenes to include various nitrogen-, oxygen-, and sulfur-containing heteroarenes (Scheme 98B).[233] On the basis of their prior mechanistic studies,[231] the authors employed a Au(III) catalyst to minimize the reaction induction period. One major cause of low yields with these electron-rich heteroarenes is their propensity for oxidative decomposition, which was suppressed by employing a more sterically hindered variant of PIDA, i.e., $(AcO)_2IAr$ (Ar = 2,4,6-$^{i}Pr_3C_6H_2$). Additionally, the tethered–OH group on the silyl moiety eliminates the need for methanol as a cosolvent, thereby avoiding catalyst inhibition by methanol.[231] In 2018, Lloyd-Jones further investigated the negative and even inhibiting effect of *ortho*-substitution of the arylsilane on the cross-coupling reaction and revealed that it is due to steric hindrance of the subsequent C–H auration step.[234]

Other organometallic compounds have also been successfully utilized in gold-catalyzed oxidative cross-coupling with arenes. In 2016, Nevado reported an oxidative cross-coupling between electron-rich arenes and arylboronates (Scheme 99).[235] In that study, acetate was found to be the most efficient counterion for the Au(I) catalyst. The reaction features a broad scope and generally exhibits good yields, but it requires heating at 110 °C. Recently, Schoenebeck reported the use of arylgermanium compounds as the organometallic reactant in this type of gold catalysis.[236] Despite being commonly considered to have low reactivity in homogeneous catalysis, arylgermanes were found to be much more potent than their silane and boronate counterparts in this reaction. It was also discovered that auration of the C–Ge bond would happen with both Au(I) and Au(III) species, and the reaction shows no induction period, unlike the reactions with arylsilanes. Finally, a computational study suggested that the high reactivity of arylgermanes can primarily be attributed to the relatively low C–Ge bond dissociation energy, thereby lowering the overall energy barrier to reach the key transition state for C–Ge bond activation.

In 2019, J. Xie reported the first gold-catalyzed oxidative coupling of two aryl organometallic compounds using a bisgold complex (Scheme 100).[237] Previous studies

had shown that arylsilanes undergo C–Si bond activation only with Au(III) species,[230,231] while arylboronates are known to undergo transmetalation with either Au(I) or Au(III) species.[194,238–244] The authors proposed that the binuclear Au(I)/Au(III) complex would take advantage of such a difference in reactivity and achieve consecutive transmetalation with arylboronates and arylsilanes on the Au(I) and Au(III) centers, respectively. Subsequent facile reductive elimination would furnish the desired cross-coupled biaryl product with minimal homocoupling counterparts. With a suitable binuclear gold complex, optimized coupling partners, and proper reaction conditions, the authors achieved the proposed transformation in good yields with a broad scope. Interestingly, *in situ* NMR studies suggested that a binuclear Au(II)/Au(II) intermediate is the active catalytic species after initial oxidation of the Au(I)/Au(I) complex by PIDA. Experimental evidence also revealed that the arylboronate undergoes transmetalation with the said Au(II)/Au(II) species before the reaction with the arylsilane occurs.

Dehydrogenative coupling between an electron-rich arene and a terminal alkyne allows for the direct functionalization of an aromatic ring with a C–C triple bond. In 2010, Nevado reported the first examples of this approach using Ph_3PAuCl as the catalyst and PIDA as the oxidant (Scheme 101A).[245] A series of electron-rich arenes, including a few heteroarenes, were successfully coupled with EWG-activated terminal alkynes. In 2019, the same lab reported in-depth mechanistic studies of this chemistry via DFT calculations and stoichiometric experiments on tentative reaction intermediates.[246] It was revealed that the $Ph_3PAuOAc$ generated upon anion exchange between Ph_3PAuCl and PIDA is crucial for the formation of alkynylgold(I) complex **GY**, which is then oxidized to Au(III) species **GZ** by PhI(OAc)Cl, the intermediate of the aforementioned anion exchange. Friedel–Crafts arylation by **GZ** followed by reductive elimination affords the observed arylalkyne product (Scheme 101B).

While gold-catalyzed dehydrogenative homocoupling of terminal alkynes (i.e., the Glaser–Hay coupling) was realized with Selectfluor as the oxidant (see Scheme 90A), X. Shi reported the first examples of cross-coupling of two different terminal alkynes by using PIDA as the oxidant, a bisgold complex as the catalyst, and phenanthroline as a critical additive (Scheme 102A).[247] This reaction achieves excellent selectivity for cross-coupling between an arylacetylene and an alkylacetylene over the competing homocouplings, exhibits a rather broad scope, and tolerates various functional groups. It was found that the acetate anion generated from the reduction of PIDA plays an essential role in this reaction. In 2018, the same lab extended this intermolecular diyne formation to intramolecular reactions (Scheme 102B).[248] This chemistry permits the synthesis of a series of macrocyclic 1,3-diynes, which are otherwise difficult to access.[231,249,250] A comparable method utilizing dual Au/Cu catalysis was reported at around the same time by Mohapatra (Scheme 102B).[251] The synthetic utility of their method was demonstrated in the total synthesis of the natural product ivorenolide B, a 17-membered macrolide bearing a 1,3-diyne moiety.

In 2011, Michelet[252] and J. Wang[253] independently reported their studies on the gold-catalyzed oxidative acyloxylation of arenes with PIDA serving as the oxidant (Scheme 103A). Though different gold catalysts were used in those two studies, a Au(III) salt is believed to undergo electrophilic arene auration in both studies. Michelet proposed that

the product is formed upon subsequent reductive elimination. Conversely, Wang suggested that direct Au(III)–aryl bond acetoxylation occurs. With an external carboxylic acid as the solvent, Michelet showed that the corresponding acyloxy moiety instead of the acetoxy group from PIDA could be introduced to the arene ring, therefore offering more synthetic flexibility.[252] Shortly thereafter, Michelet reported arene polyacyloxylation under the same reaction conditions with the exception of an increased amount of PIDA.[254] In comparison with the monoacyloxylation,[252] this reaction exhibits low or moderate yields.

In 2015, DeBoef reported the gold-catalyzed direct phthalimidation of arenes promoted by a Au(I) catalyst and a large excess of PIDA (8 equivalents in two portions; Scheme 103B).[255] The observed regioselectivity of the reaction is dictated by electronic and steric effects. Additionally, electron-poor arenes served as viable substrates, albeit generally in low yields. The reaction mechanism is likely analogous to that of the acetoxylation chemistry.

Finally, the alkylgold intermediate generated upon gold-catalyzed nucleophilic addition to an alkene can also be oxidized by hypervalent iodine, which permits alkene difunctionalization. In 2009, Muñiz reported the first examples of this chemistry using bishomoallylic ureas as substrates (Scheme 104A).[256] With PIDA as the oxidant, the reaction yields a double amination product. Mechanistic studies suggested that the Au(I) catalyst promotes the initial intramolecular attack by the urea N atom at the C–C double bond. After the formation of alkylgold intermediate **HA**, PIDA oxidizes the Au(I) center to a Au(III) center in **HB**, which then undergoes cyclization to afford bicyclic urea product **192**. This second cyclization entails the reduction of Au(III) to Au(I) and is likely an S_N2 process at the gold-substituted carbon. In 2017, Bower and Russell extended the intermolecular oxidative oxyarylation of alkenes (see Scheme 86) to the use of ethylene as the substrate (Scheme 104B).[257] The key step of the reaction, i.e., from **HC** to **HD**, is proposed to be nucleophilic addition of an alcohol to Au(III)-activated ethylene. The hypervalent iodine employed is IBA-OTf, and the arylsilane is the source of the aryl group and can accommodate various substituents, except strongly electron-donating ones.

3.3. Other Oxidants

Oxidants other than electrophilic fluorine and hypervalent iodine reagents have seldom been reported in oxidative Au(I)/Au(III) catalysis. In 1993, Gasparrini reported the use of nitric acid as the oxidant.[258] This oxidative gold catalysis converts a terminal alkyne to an isoxazole (Scheme 105). Tetrabutylammonium tetrachloroaurate was used to facilitate the biphasic reaction, and nitric acid is also the source of the nitrogen atom. According to the proposed mechanism, gold(III)-promoted nucleophilic attack of nitrite at the terminal alkyne is followed by a redox rearrangement that generates nitrile oxide **HE** and reduces Au(III) to Au(I) in the form of $AuCl_2^-$. The 1,3-dipolar cycloaddition between **HE** and another molecule of the terminal alkyne gives the final isoxazole product. To close the catalytic cycle, $AuCl_2^-$ is oxidized to $AuCl_3$ by nitric acid, which is simultaneously reduced to nitrite.

In 2008, Wegner reported a gold-catalyzed oxidative cyclization/dimerization with *tert*-butyl hydroperoxide (TBHP) as the oxidant (Scheme 106).[259] The reaction employs $HAuCl_4$ as the catalyst. In the proposed mechanism, this Au(III) salt promotes the cyclization of the phenyl alkynoate substrate twice to generate intermediate **HF**. This dialkenylgold(III)

complex then undergoes reductive elimination to afford the biscoumarin product and a Au(I) complex, which is oxidized back to the catalytically active Au(III) complex by TBHP. A series of symmetric biscoumarins were generated, albeit only in moderate yields. The coumarin side products formed upon competitive protodeauration were also detected.

4. MISCELLANEOUS GOLD-CATALYZED OXIDATIONS

4.1. Oxidation of Alcohols to Carbonyl Compounds

In 2005, Z. Shi reported aerobic oxidation of alcohols via gold catalysis (Scheme 107).[260] The *β*-diketiminate anion **L6**, which can be easily accessed from acetylacetone, was used as the ligand to stabilize AuCl. This oxidation is performed under an O_2 atmosphere to furnish aldehydes or ketones in moderate to excellent yields. Primary and secondary alcohols are suitable substrates for the reaction. Notably, overoxidation of primary alcohols to carboxylic acids was not detected. Two years later, Z. Shi described another gold-catalyzed oxidation of secondary alcohols into ketones in aqueous media using neocuproine (i.e., **L7**) as the ligand (Scheme 107).[261] This reaction requires higher O_2 pressure, and the scope is limited to benzylic and allylic alcohols. In 2014, M. Lu reported a similar aerobic oxidation of alcohols using the combination of $AuCl_3$ and ionic-liquid-immobilized TEMPO in catalytic amounts.[262]

4.2. Oxidation of Alkane C–H Bonds

In 2008, Z. Shi reported the gold-catalyzed oxidation of benzylic C(sp^3)–H bonds using TBHP as the oxidant (Scheme 108).[263] The corresponding carbonyl compounds were formed in moderate to excellent yields. $KAuCl_4$ serves as the catalyst and pyridine as the solvent as well as the ligand to presumably stabilize the gold catalyst. In 2004, Perianas reported a gold-catalyzed selective oxidation of methane to methanol in H_2SO_4 at 180 °C.[264]

4.3. Oxidative Cleavage of C–C Double Bonds

Several examples of gold-catalyzed oxidative cleavage of C–C double bonds have been documented. The first study on this topic was reported by Z. Shi in 2006 (Scheme 109A),[265] where the catalyst generated *in situ* from AuCl and neocuproine (i.e., L7) promotes in-water alkene oxidation with TBHP as the oxidant. The reaction results in the formation of a pair of carbonyl compounds, though the product with the lower molecular weight (e.g., formaldehyde) was detected but not isolated. The reaction mechanism likely involves radical intermediates. In 2014, Y. Huang reported examples of gold-catalyzed cleavage of enamine C–C double bonds (Scheme 109B).[266] The combination of an aldehyde, pyrrolidine, and TIPS-EBX (i.e., **HG**) affords ynenamine intermediate **HH**, which then undergoes gold-catalyzed aerobic C–C double bond oxidation to give the TIPS-terminated ynone product along with pyrrolidine-1-carbaldehyde. This reaction exhibits generally good yields and offers an alternative approach to synthetically valuable ynones.

Oxidative C–C double bond cleavage is also observed with alkene reaction intermediates formed during gold catalysis. Y. Liu reported a gold-catalyzed (*Z*)-enynol cyclization/oxidative C–C bond cleavage cascade (Scheme 110A).[267,268] O_2 was used as the oxidant in that chemistry. It was proposed that dihydrofuran intermediate HI is initially formed

upon gold-catalyzed cyclization, followed by oxidative C–C bond cleavage to deliver the butenolide product. In 2009, R.-S. Liu reported the oxidative cleavage of aryl-substituted propargyl ethers **192** to yield arylcarboxylates (Scheme 110B).[269] In this reaction, 10% O_2 is used as the oxidant. The proposed mechanism involves consecutive oxidative C–C double bond cleavages in vinylgold species **HJ** and **HK**. In 2014, Han and Shin reported an oxidative C–C double cleavage diverging from the gold(I)-catalyzed 1,6-enyne cycloisomerization reaction (Scheme 110C).[270] Cleavage of the C–C double bond occurred readily at room temperature in open-vial reactions with 2,2,2-trifluoroethanol as the solvent. The authors proposed a mechanism involving the formation of gold-bound metalloradical **HL** via reaction between triplet dioxygen and the gold intermediate of the 1,6-enyne cycloisomerization.

4.4. Catalyzed or One-Pot Oxidative Aromatization

Several gold-catalyzed reactions are accompanied by oxidative aromatization to deliver aromatic products. The stoichiometric oxidant is atmospheric oxygen. Because of the lack of mechanistic studies, it is not clear whether this typically terminal oxidation step involves gold catalysis. Nevertheless, these reactions are covered briefly here.

In 2009, Z. Xu reported the oxidative aromatization of 1,3,5-trisubstituted pyrazolines to give the corresponding pyrazoles using catalytic tetrachloroauric acid under an O_2 atmosphere (Scheme 111A).[271] AuCl was found to be a less effective catalyst. The substituents on the pyrazoline ring are limited to aromatic groups, which can accommodate substituents of differing electronic characteristics. In 2012, B. Ji reported the gold-catalyzed synthesis of 2-trifluoromethylquinolines **194** from trifluoromethylated propargylamines **193** (Scheme 111B).[272] The proposed mechanism entails gold-catalyzed 6-*endo*-*dig* cyclization followed by air oxidation to produce the observed product. In 2017, G. Verniest reported a synthetic route to dihydrodibenzoquinolizinium salt **196** from 1-alkylcinoline **195** (Scheme 111C).[273] The reaction is catalyzed by *in situ*-generated $Ph_3PAuNTf_2$ at ambient temperature, requires stoichiometric MsOH, and works with either an aromatic or alkyl substituent at the alkyne terminus. Interestingly, quinolinium intermediate **HM** is isolable and can undergo protodeauration in the presence of trifluoracetic acid to afford the final product. On the basis of these observations, the author proposed a mechanism that entails gold-catalyzed 6-*endo*-*dig* cyclization, subsequent oxidative aromatization by atmospheric oxygen, and finally protodeauration.

4.5. Oxidation of Sulfides and Other Functional Groups

One of the earliest studies of oxidative gold catalysis was reported in 1983 by Gasparrini (Scheme 112A).[274] In that work, a series of sulfides were successfully oxidized to sulfoxides under phase-transfer conditions. Aqueous nitric acid was used as the stoichiometric oxidant, and $^{n}Bu_4NAuCl_4$ was used as the catalyst. This oxidation is remarkably chemoselective, as tertiary amines, alcohols, and diols are tolerated. Moreover, for bissulfides, only monosulfoxides are formed. Interestingly, cyclic thioketals were readily hydrolyzed under the reaction conditions to afford the corresponding ketones in almost quantitative yield. In 2007, a similar sulfide oxidation was reported by Y. Yuan using hydrogen peroxide as the stoichiometric oxidant (Scheme 112B).[275] The ratio of sulfoxide to sulfone products was

higher than 97 to 3 in all of the reported cases except for a ratio of 91 to 9 in the case of electron-rich *p*-methoxyphenyl methyl sulfide. Notably, the gold catalyst can be recovered and reused for six cycles without significant loss of activity.

In 2001, Y. Deng reported the synthesis of carbamates via gold-catalyzed oxidative carbonylation of amines (Scheme 113A).[276] The addition of extra catalytic triphenylphosphine was found to significantly improve the conversion and turnover frequency (TOF). Excellent conversions were achieved for anilines. However, when aliphatic amines were employed, the reactions were contaminated by competing formamide and urea formation.

In 2017, B. Feng reported the Au(III)-complex-catalyzed dehydrogenation–Povorov oxidation cascade between *N*-arylglycinates and styrenes (Scheme 113B).[277] For the reported reaction scope, the R^1 group at the *para*-position can be Me, MeO, Cl, and Br, but interestingly, *o*- or *m*-Me is not allowed. 4-Methylphenylacetylene can replace 4-methylstyrene in this reaction to afford the same product, albeit in a slightly lower yield. Their control experiments revealed that imine **HN** can be generated under the dioxygen atmosphere in the absence of the gold(III) complex. Thus, mechanistically, **197** is oxidized to **HN** first without involving gold, followed by a gold-catalyzed [4 + 2] cycloaddition to afford tetrahydroquinoline **HO**. Its further oxidative aromatization affords the quinoline product **198**.

5. CONCLUSION AND OUTLOOK

Oxidative gold catalysis is an integral component of the rapidly developing field of homogeneous gold chemistry. The majority of the developments in this area have occurred in the past dozen years and were achieved by competing and synergistic efforts of many researchers around the world. A broad array of versatile synthetic methods have been developed, and various new reactivities have been unearthed. Among a plethora of enabling strategies in oxidative gold catalysis, the oxidation of alkynes by nucleophilic oxidants and oxidative Au(I)/Au(III) catalysis stand out and constitute the two main thrusts propelling the rapid advance of this field. It is anticipated that further applications of these two strategies toward the construction of new structural motifs and/or in the development of more efficient accesses to valuable structures will continue to augment the field of synthetic chemistry. The emergence of new oxidative strategies or the evolution of less-researched strategies will offer new opportunities for reactivity discovery and method development.

This field would improve remarkably with regard to practicality and sustainability if the following issues were to be adequately addressed: (a) the low atom economy of the nucleophilic oxidants–most of the external nucleophilic oxidants contribute only a single oxygen atom to the eventual product, and the bulk part of them (i.e., *N*-arene or sulfide) is generated as waste; (b) the requirement of strong oxidants in Au(I)/Au(III) catalysis–this diminishes functional group compatibility and impacts the environment adversely; and (c) relatively high gold catalyst loadings (typically 5 mol %)–the development of catalysts with ultralow loadings would further enhance the appeal of this oxidative strategy in scaled-up syntheses.

ACKNOWLEDGMENTS

The authors thank NIH (R01GM123342) and NSF (CHE 1800525) for financial support.

Biography

Zhitong Zheng received his Bachelor of Science in Chemistry at Peking University in Beijing, China, in 2012 and his Ph.D. in Organic Synthesis at the University of California, Santa Barbara in 2017. Under the mentorship of Prof. Liming Zhang, he developed a series of novel synthetic methodologies based on oxidative gold catalysis. He briefly stayed in the Zhang Lab as a postdoctoral fellow studying stereoselective construction of glycosidic bonds and is currently a postdoctoral fellow in Professor Yoshito Kishi's lab at Harvard University.

Xu Ma received his Bachelor of Science in Chemistry from Wuhan University in China in 2015. He is currently a Ph.D. candidate in organic chemistry at the University of California, Santa Barbara under the supervision of Prof. Liming Zhang. His research interests lie broadly in homogeneous gold-catalyzed cascade reactions and stereoselective glycosylation.

Xinpeng Cheng received his Bachelor of Science in Chemistry from Zhejiang University in Zhejiang, China, in 2016. He is currently a Ph.D. candidate in organic chemistry at the University of California, Santa Barbara under the supervision of Prof. Liming Zhang. His current research focuses on the development of chiral bifunctional ligands for novel transformations in gold and copper catalysis.

Ke Zhao received his Bachelor of Science in Chemistry from Lanzhou University in 2017. He is currently a third-year graduate student in the research group of Prof. Liming Zhang. His research focuses on the application of bifunctional ligands in asymmetric catalysis.

Kaylaa Gutman received her Bachelor of Science in Chemistry from the University of Idaho in 2019, where she worked under the guidance of Professor Kristopher Waynant on the development and characterization of redox-active ligands. She is currently a graduate student the University of California, Santa Barbara working under Professor Liming Zhang, where she primarily researches the use of gold catalysis in isomerization reactions and in the synthesis of functionalized butenolides.

Tianyou Li received his Bachelor of Science in Chemistry from Xiamen University in 2019, where he conducted his undergraduate research with Professor Long-Wu Ye. In the same year, he began his graduate study in the University of California, Santa Barbara in the laboratory of Professor Liming Zhang.

Liming Zhang received his Bachelor of Science in Chemistry from Nanchang University in 1993, his first Master's degree in Organometallic Chemistry from Nankai University in 1996 with Professor Zhengzhi Zhang, and his second Master's degree in Organic Chemistry from the University of Alabama in 1998 with Professor Michael P. Cava. He obtained his Ph.D. with Professor Masato Koreeda from the medicinal chemistry program at the University of Michigan in 2003 and then carried out a postdoctoral study with Professor Sergey A. Kozmin at the University of Chicago. He started his independent academic career as an Assistant Professor at the Department of Chemistry at the University of Nevada, Reno in

July 2005 and continued at the University of California, Santa Barbara in July 2009. He is currently a Professor of Organic Chemistry. His research interests include late transition metal-catalyzed reactions, natural product synthesis, and medicinal chemistry.

REFERENCES

(1). Hopkinson MN; Gee AD; Gouverneur V AuI/AuIII Catalysis: An Alternative Approach for C–C Oxidative Coupling. Chem. - Eur. J. 2011, 17, 8248–8262. [PubMed: 21678513]

(2). Pina CD; Falletta E; Rossi M Update on Selective Oxidation Using Gold. Chem. Soc. Rev. 2012, 41, 350–369. [PubMed: 21727977]

(3). Nunes dos Santos Comprido L; Hashmi ASK Catalytic Oxidative Cyclisation Reactions of 1,6-Enynes: A Critical Comparison between Gold and Palladium. Isr. J. Chem. 2013, 53, 883–891.

(4). Yeom H-S; Shin S Catalytic Access to α-Oxo Gold Carbenes by N–O Bond Oxidants. Acc. Chem. Res. 2014, 47, 966–977. [PubMed: 24517590]

(5). Zhang L A Non-Diazo Approach to α-Oxo Gold Carbenes via Gold-Catalyzed Alkyne Oxidation. Acc. Chem. Res. 2014, 47, 877–888. [PubMed: 24428596]

(6). Zheng Z; Wang Z; Wang Y; Zhang L Au-Catalysed Oxidative Cyclisation. Chem. Soc. Rev. 2016, 45, 4448–4458. [PubMed: 26781300]

(7). Huple DB; Ghorpade S; Liu R-S Recent Advances in Gold-Catalyzed N- and O-Functionalizations of Alkynes with Nitrones, Nitroso, Nitro and Nitroxy Species. Adv. Synth. Catal. 2016, 358, 1348–1367.

(8). Yuan L-Z; Hamze A; Alami M; Provot O Synthesis of Substituted Benzils from Diarylalkyne Oxidation. Synthesis 2017, 49, 504–525.

(9). Lin J; Song R-J; Hu M; Li J-H Recent Advances in the Intermolecular Oxidative Difunctionalization of Alkenes. Chem. Rec. 2019, 19, 440–451. [PubMed: 30033609]

(10). Bhunia S; Ghosh P; Patra SR Gold-Catalyzed Oxidative Alkyne Functionalization by N–O/S–O/C–O Bond Oxidants. Adv. Synth. Catal. 2020, 362, 3664–3708.

(11). Shen W-B; Tang X-T Recent Advances in Catalytic Asymmetric Intermolecular Oxidation of Alkynes. Org. Biomol. Chem. 2019, 17, 7106–7113. [PubMed: 31290899]

(12). Aguilar E; Santamaría J Gold-Catalyzed Heterocyclic Syntheses through α-Imino Gold Carbene Complexes as Intermediates. Org. Chem. Front. 2019, 6, 1513–1540.

(13). Hopkinson MN; Tlahuext-Aca A; Glorius F Merging Visible Light Photoredox and Gold Catalysis. Acc. Chem. Res. 2016, 49, 2261–2272. [PubMed: 27610939]

(14). Akram MO; Banerjee S; Saswade SS; Bedi V; Patil NT Oxidant-Free Oxidative Gold Catalysis: The New Paradigm in Cross-Coupling Reactions. Chem. Commun. 2018, 54, 11069–11083.

(15). Nijamudheen A; Datta A Gold-Catalyzed Cross-Coupling Reactions: An Overview of Design Strategies, Mechanistic Studies, and Applications. Chem. -Eur. J 2020, 26, 1442–1487. [PubMed: 31657487]

(16). Prieto A; Fructos MR; Mar Díaz-Requejo M; Pérez PJ; Pérez-Galan P; Delpont N; Echavarren AM Gold-Catalyzed Olefin Cyclopropanation. Tetrahedron 2009, 65, 1790–1793.

(17). Pawar SK; Wang C-D; Bhunia S; Jadhav AM; Liu R-S Gold-Catalyzed Formal Cycloaddition of 2-Ethynylbenzyl Ethers with Organic Oxides and α-Diazoesters. Angew. Chem., Int. Ed. 2013, 52, 7559–7563.

(18). Doyle MP; McKervey MA; Ye T Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides; Wiley: New York, 1998.

(19). Wang Y; Muratore ME; Echavarren AM Gold Carbene or Carbenoid: Is There a Difference? Chem. - Eur. J 2015, 21, 7332–7339. [PubMed: 25786384]

(20). Shapiro ND; Toste FD Rearrangement of Alkynyl Sulfoxides Catalyzed by Gold(I) Complexes. J. Am. Chem. Soc. 2007, 129, 4160–4161. [PubMed: 17371031]

(21). Li G; Zhang L Gold-Catalyzed Intramolecular Redox Reaction of Sulfinyl Alkynes: Efficient Generation of α-Oxo Gold Carbenoids and Application in Insertion into R–Co Bonds. Angew. Chem., Int. Ed. 2007, 46, 5156–5159.

(22). Fang R; Yang L Mechanism of the Gold(I)-Catalyzed Rearrangement of Alkynyl Sulfoxides: A DFT Study. Organometallics 2012, 31, 3043–3055.

(23). Lu B; Li Y; Wang Y; Aue DH; Luo Y; Zhang L [3,3]-Sigmatropic Rearrangement versus Carbene Formation in Gold-Catalyzed Transformations of Alkynyl Aryl Sulfoxides: Mechanistic Studies and Expanded Reaction Scope. J. Am. Chem. Soc. 2013, 135, 8512–8524. [PubMed: 23731178]

(24). Davies PW; Albrecht SJC Gold- or Platinum-Catalyzed Synthesis of Sulfur Heterocycles: Access to Sulfur Ylides without Using Sacrificial Functionality. Angew. Chem., Int. Ed. 2009, 48, 8372–8375.

(25). Cuenca AB; Montserrat S; Hossain KM; Mancha G; Lledós A; Medio-Simón M; Ujaque G; Asensio G Gold(I)-Catalyzed Intermolecular Oxyarylation of Alkynes: Unexpected Regiochemistry in the Alkylation of Arenes. Org. Lett. 2009, 11, 4906–4909. [PubMed: 19785397]

(26). Barrett MJ; Davies PW; Grainger RS Regioselective Functionalisation of Dibenzothiophenes through Gold-Catalysed Intermolecular Alkyne Oxyarylation. Org. Biomol. Chem. 2015, 13, 8676–8686. [PubMed: 26177794]

(27). Li C-W; Pati K; Lin G-Y; Sohel SMA; Hung H-H; Liu R-S Gold-Catalyzed Oxidative Ring Expansions and Ring Cleavages of Alkynylcyclopropanes by Intermolecular Reactions Oxidized by Diphenylsulfoxide. Angew. Chem., Int. Ed. 2010, 49, 9891–9894.

(28). Xu C-F; Xu M; Jia Y-X; Li C-Y Gold-Catalyzed Synthesis of Benzil Derivatives and α-Keto Imides via Oxidation of Alkynes. Org. Lett. 2011, 13, 1556–1559. [PubMed: 21332143]

(29). Matsuda T; Nishida Y; Yamanaka K; Sakurai Y Synthesis of 2-Acyl-1-naphthols by Gold-Catalyzed Oxidative Cyclization of 2-Alkenylphenyl Alkynyl Ketones. Tetrahedron 2015, 71, 869–874.

(30). Schießl J; Stein PM; Stirn J; Emler K; Rudolph M; Rominger F; Hashmi ASK Strategic Approach on *N*-Oxides in Gold Catalysis – a Case Study. Adv. Synth. Catal. 2019, 361, 725–738.

(31). Ye L; Cui L; Zhang G; Zhang L Alkynes as Equivalents of α-Diazo Ketones in Generating α-Oxo Metal Carbenes: A Gold-Catalyzed Expedient Synthesis of Dihydrofuran-3-ones. J. Am. Chem. Soc. 2010, 132, 3258–3259. [PubMed: 20166668]

(32). Wei H; Bao M; Dong K; Qiu L; Wu B; Hu W; Xu X Enantioselective Oxidative Cyclization/Mannich Addition Enabled by Gold(I)/Chiral Phosphoric Acid Cooperative Catalysis. Angew. Chem., Int. Ed. 2018, 57, 17200–17204.

(33). Ye L; He W; Zhang L Gold-Catalyzed One-Step Practical Synthesis of Oxetan-3-ones from Readily Available Propargylic Alcohols. J. Am. Chem. Soc. 2010, 132, 8550–8551. [PubMed: 20521793]

(34). Cai J; Wang X; Qian Y; Qiu L; Hu W; Xu X Gold-Catalyzed Oxidative Cyclization/Aldol Addition of Homopropargyl Alcohols with Isatins. Org. Lett. 2019, 21, 369–372. [PubMed: 30596509]

(35). Xu M; Ren T-T; Li C-Y Gold-Catalyzed Oxidative Rearrangement of Homopropargylic Ether via Oxonium Ylide. Org. Lett. 2012, 14, 4902–4905. [PubMed: 22954390]

(36). Shu C; Liu R; Liu S; Li J-Q; Yu Y-F; He Q; Lu X; Ye L-W Practical, Modular, and General Synthesis of 3-Coumaranones through Gold-Catalyzed Intermolecular Alkyne Oxidation Strategy. Chem. - Asian J. 2015, 10, 91–95. [PubMed: 25287758]

(37). Zhao Q; Henrion G; Gagosz F Synthesis of Isochroman-4-ones and 2H-Pyran-3(6H)-ones by Gold-Catalyzed Oxidative Cycloalkoxylation of Alkynes. Bioorg. Med. Chem. 2019, 27, 2616–2620. [PubMed: 30952389]

(38). Fu J; Shang H; Wang Z; Chang L; Shao W; Yang Z; Tang Y Gold-Catalyzed Rearrangement of Allylic Oxonium Ylides: Efficient Synthesis of Highly Functionalized Dihydrofuran-3-ones. Angew. Chem., Int. Ed. 2013, 52, 4198–4202.

(39). Han M; Bae J; Choi J; Tae J Synthesis of 2,5-Disubstituted Dihydrofuran-3(2H)-ones via [2,3]-Sigmatropic Rearrangement of Oxonium Ylides Generated from α-Oxo Gold Carbenes. Synlett 2013, 24, 2077–2080.

(40). Murai M; Kitabata S; Okamoto K; Ohe K Gold-Catalysed Cycloisomerisation Reactions of 2-(2-Propynyl)pyridine N-Oxides Leading to Indolizinones. Chem. Commun. 2012, 48, 7622–7624.

(41). Ji K; Nelson J; Zhang L Gold-Catalyzed Regioselective Oxidation of Propargylic Carboxylates: A Reliable Access to α-Carboxy-α,β-Unsaturated Ketones/Aldehydes. Beilstein J. Org. Chem. 2013, 9, 1925–1930. [PubMed: 24204402]

(42). Luo Y; Ji K; Li Y; Zhang L Tempering the Reactivities of Postulated α-Oxo Gold Carbenes Using Bidentate Ligands: Implication of Tricoordinated Gold Intermediates and the Development of an Expedient Bimolecular Assembly of 2,4-Disubstituted Oxazoles. J. Am. Chem. Soc. 2012, 134, 17412–17415. [PubMed: 23039251]

(43). Sun N; Chen M; Liu Y Gold-Catalyzed Oxidative Reactions of Propargylic Carbonates Involving 1,2-Carbonate Migration: Stereoselective Synthesis of Functionalized Alkenes. J. Org. Chem. 2014, 79, 4055–4067. [PubMed: 24731195]

(44). He W; Li C; Zhang L An Efficient [2 + 2 + 1] Synthesis of 2,5-Disubstituted Oxazoles via Gold-Catalyzed Intermolecular Alkyne Oxidation. J. Am. Chem. Soc. 2011, 133, 8482–8485. [PubMed: 21563762]

(45). He W; Xie L; Xu Y; Xiang J; Zhang L Electrophilicity of α-Oxo Gold Carbene Intermediates: Halogen Abstractions from Halogenated Solvents Leading to the Formation of Chloro/Bromomethyl Ketones. Org. Biomol. Chem. 2012, 10, 3168–3171. [PubMed: 22419033]

(46). Xu Y; Wang Q; Wu Y; Zeng Z; Rudolph M; Hashmi ASK Gold-Catalyzed Synthesis of 2,5-Disubstituted Oxazoles from Carboxamides and Propynals. Adv. Synth. Catal. 2019, 361, 2309–2314.

(47). Ji K; Zhao Y; Zhang L Optimizing P,N-Bidentate Ligands for Oxidative Gold Catalysis: Efficient Intermolecular Trapping of α-Oxo Gold Carbenes by Carboxylic Acids. Angew. Chem., Int. Ed. 2013, 52, 6508–6512.

(48). Wu C; Liang Z; Yan D; He W; Xiang J Straightforward and Highly Efficient Synthesis of α-Acetoxy Ketones through Gold-Catalyzed Intermolecular Oxidation of Terminal Alkynes. Synthesis 2013, 45, 2605–2611.

(49). Xie L; Liang Z; Yan D; He W; Xiang J Gold-Catalyzed Intermolecular Oxidation of Terminal Alkynes: Simple and Efficient Synthesis of α-Mesyloxy Ketones. Synlett 2013, 24, 1809–1812.

(50). Wu G; Zheng R; Nelson J; Zhang L One-Step Synthesis of Methanesulfonyloxymethyl Ketones via Gold-Catalyzed Oxidation of Terminal Alkynes: A Combination of Ligand and Counter Anion Enables High Efficiency and a One-Pot Synthesis of 2,4-Disubstituted Thiazoles. Adv. Synth. Catal. 2014, 356, 1229–1234.

(51). Zhang Y; Xue Y; Li G; Yuan H; Luo T Enantioselective Synthesis of Iboga Alkaloids and Vinblastine via Rearrangements of Quaternary Ammoniums. Chem. Sci. 2016, 7, 5530–5536. [PubMed: 30034694]

(52). Shi S; Wang T; Yang W; Rudolph M; Hashmi ASK Gold-Catalyzed Synthesis of Glyoxals by Oxidation of Terminal Alkynes: One-Pot Synthesis of Quinoxalines. Chem. - Eur. J 2013, 19, 6576–6580. [PubMed: 23576273]

(53). Dubovtsev AY; Dar'in DV; Kukushkin VY Three-Component [2 + 2 + 1] Gold(I)-Catalyzed Oxidative Generation of Fully Substituted 1,3-Oxazoles Involving Internal Alkynes. Adv. Synth. Catal. 2019, 361, 2926–2935.

(54). Dubovtsev AY; Dar'in DV; Krasavin M; Kukushkin VY Gold-Catalyzed Oxidation of Internal Alkynes into Benzils and Its Application for One-Pot Synthesis of Five-, Six-, and Seven-Membered Azaheterocycles. Eur. J. Org. Chem. 2019, 2019, 1856–1864.

(55). Dubovtsev AY; Shcherbakov NV; Dar'in DV; Kukushkin VY Nature of the Nucleophilic Oxygenation Reagent Is Key to Acid-Free Gold-Catalyzed Conversion of Terminal and Internal Alkynes to 1,2-Dicarbonyls. J. Org. Chem. 2020, 85, 745–757. [PubMed: 31849233]

(56). Dubovtsev AY; Dar'in DV; Kukushkin VY Gold(I)-Catalyzed Oxidation of Acyl Acetylenes to Vicinal Tricarbonyls. Org. Lett. 2019, 21, 4116–4119. [PubMed: 31090426]

(57). Landman IR; Acuña-Bolomey E; Scopelliti R; Fadaei-Tirani F; Severin K Synthesis and Properties of 1-Acyl Triazenes. Org. Lett. 2019, 21, 6408–6412. [PubMed: 31361494]

(58). Luo Y; Zhang G; Hwang ES; Wilcoxon TA; Zhang L Gold-Catalyzed Regioselective Oxidation of Terminal Allenes: Formation of α-Methanesulfonyloxy Methyl Ketones. Beilstein J. Org. Chem. 2011, 7, 596–600. [PubMed: 21647259]

(59). Wu Y; Peng S; Ouyang Y; Qian P; He W; Xiang J Total Synthesis of 5-(3-Indolyl) Oxazole Natural Product via Gold-Catalyzed Intermolecular Alkyne Oxidation. Acta Chim. Sin. 2012, 70, 1367–1370.

(60). Rassadin VA; Boyarskiy VP; Kukushkin VY Facile Gold-Catalyzed Heterocyclization of Terminal Alkynes and Cyanamides Leading to Substituted 2-Amino-1,3-oxazoles. Org. Lett. 2015, 17, 3502–3505. [PubMed: 26135038]

(61). Wang Q; Hoffmann S; Schießl J; Rudolph M; Rominger F; Hashmi ASK A Gold-Catalyzed Acid-Assisted Regioselective Cyclization for the Synthesis of Polysubstituted Oxazoles. Eur. J. Org. Chem. 2020, 2020, 2384–2388.

(62). Karad SN; Liu R-S Gold-Catalyzed 1,2-Oxoarylations of Nitriles with Pyridine-Derived Oxides. Angew. Chem., Int. Ed. 2014, 53, 5444–5448.

(63). Ye L; He W; Zhang L A Flexible and Stereoselective Synthesis of Azetidin-3-ones through Gold-Catalyzed Intermolecular Oxidation of Alkynes. Angew. Chem., Int. Ed. 2011, 50, 3236–3239.

(64). Jin J; Zhao Y; Sze EML; Kothandaraman P; Chan PWH Chiral Bronsted Acid and Gold Catalyzed Enantioselective Synthesis of 1,8-Dihydroindeno[2,1-b]Pyrroles. Adv. Synth. Catal. 2018, 360, 4744–4753.

(65). Shu C; Li L; Xiao X-Y; Yu Y-F; Ping Y-F; Zhou J-M; Ye L-W Flexible and Practical Synthesis of 3-Oxyindoles through Gold-Catalyzed Intermolecular Oxidation of O-Ethynylanilines. Chem. Commun. 2014, 50, 8689–8692.

(66). Shu C; Li L; Yu Y-F; Jiang S; Ye L-W Gold-Catalyzed Intermolecular Oxidation of Chiral Homopropargyl Sulfonamides: A Reliable Access to Enantioenriched Pyrrolidin-3-ones. Chem. Commun. 2014, 50, 2522–2525.

(67). Huple DB; Ghorpade S; Liu R-S Gold-Catalyzed Oxidative Cycloadditions to Activate a Quinoline Framework. Chem. - Eur. J 2013, 19, 12965–12969. [PubMed: 24038347]

(68). Talbot EPA; Richardson M; McKenna JM; Toste FD Gold Catalysed Redox Synthesis of Imidazo[1,2-a]pyridine Using Pyridine *N*-Oxide and Alkynes. Adv. Synth. Catal. 2014, 356, 687–691. [PubMed: 24839436]

(69). Li J; Ji K; Zheng R; Nelson J; Zhang L Expanding the Horizon of Intermolecular Trapping of in Situ Generated α-Oxo Gold Carbenes: Efficient Oxidative Union of Allylic Sulfides and Terminal Alkynes via C–C Bond Formation. Chem. Commun. 2014, 50, 4130–4133.

(70). Santos MD; Davies PW A Gold-Catalysed Fully Intermolecular Oxidation and Sulfur-Ylide Formation Sequence on Ynamides. Chem. Commun. 2014, 50, 6001–6004.

(71). Baker T; Davies PW Synthesis of Thiomorpholin-3-ones by a Gold-Catalysed Oxidative Cyclisation–Rearrangement Cascade from Ynamides. Eur. J. Org. Chem. 2019, 2019, 5201–5204.

(72). Sharma P; Singh RR; Giri SS; Chen L-Y; Cheng M-J; Liu R-S Gold-Catalyzed Oxidation of Thioalkynes to Form Phenylthio Ketene Derivatives via a Noncarbene Route. Org. Lett. 2019, 21, 5475–5479. [PubMed: 31274331]

(73). Wagh SB; Singh RR; Sahani RL; Liu R-S Gold-Catalyzed Oxidative Hydrative Alkenylations of Propargyl Aryl Thioethers with Quinoline *N*-Oxides Involving a 1,3-Sulfur Migration. Org. Lett. 2019, 21, 2755–2758. [PubMed: 30957496]

(74). Zeng X; Liu S; Shi Z; Liu G; Xu B Synthesis of α-Fluoroketones by Insertion of HF into a Gold Carbene. Angew. Chem., Int. Ed. 2016, 55, 10032–10036.

(75). Zeng X; Lu Z; Liu S; Hammond GB; Xu B Gold-Catalyzed Fluorination of Alkynyl Esters and Ketones: Efficient Access to Fluorinated 1,3-Dicarbonyl Compounds. Adv. Synth. Catal. 2017, 359, 4062–4066. [PubMed: 29483850]

(76). Yang J-M; Zhao Y-T; Li Z-Q; Gu X-S; Zhu S-F; Zhou Q-L Gold-Catalyzed Oxidative Coupling of Terminal Alkynes and Borane Adducts: Efficient Synthesis of α-Boryl Ketones. ACS Catal. 2018, 8, 7351–7355.

(77). Cui L; Zhang G; Peng Y; Zhang L Gold or No Gold: One-Pot Synthesis of Tetrahydrobenz[*b*]azepin-4-ones from Tertiary N-(But-3-ynyl)anilines. Org. Lett. 2009, 11, 1225–1228. [PubMed: 19220014]

(78). Wang Y; Ji K; Lan S; Zhang L Rapid Access to Chroman-3-ones through Gold-Catalyzed Oxidation of Propargyl Aryl Ethers. Angew. Chem., Int. Ed. 2012, 51, 1915–1918.

(79). Henrion G; Chavas TEJ; Le Goff X; Gagosz F Biarylphosphonite Gold(I) Complexes as Superior Catalysts for Oxidative Cyclization of Propynyl Arenes into Indan-2-ones. Angew. Chem., Int. Ed. 2013, 52, 6277–6282.

(80). Ling H-B; Chen Z-S; Yang F; Xu B; Gao J-M; Ji K Gold-Catalyzed Oxidation Terminal Alkyne: An Approach to Synthesize Substituted Dihydronaphthalen-2(1H)-ones and Phenanthrenols. J. Org. Chem. 2017, 82, 7070–7076. [PubMed: 28618784]

(81). Li T; Yang P Au(I)-Catalyzed Access to 1H-Pyrrolo[1,2-a]indol-2(3-H)-ones via Oxidation of Terminal Alkynes. J. Org. Chem. 2018, 83, 14751–14757. [PubMed: 30441899]

(82). Yang L-Q; Wang K-B; Li C-Y Synthesis of Oxindoles through the Gold-Catalyzed Oxidation of N-Arylynamides. Eur. J. Org. Chem. 2013, 2013, 2775–2779.

(83). Sánchez-Cantalejo F; Priest JD; Davies PW A Gold Carbene Manifold to Prepare Fused γ-Lactams by Oxidative Cyclisation of Ynamides. Chem. - Eur. J 2018, 24, 17215–17219. [PubMed: 30248205]

(84). Pan F; Liu S; Shu C; Lin R-K; Yu Y-F; Zhou J-M; Ye L-W Gold-Catalyzed Intermolecular Oxidation of *O*-Alkynylbiaryls: An Easy and Practical Access to Functionalized Fluorenes. Chem. Commun. 2014, 50, 10726–10729.

(85). Li L; Shu C; Zhou B; Yu Y-F; Xiao X-Y; Ye L-W Generation of Gold Carbenes in Water: Efficient Intermolecular Trapping of the α-Oxo Gold Carbenoids by Indoles and Anilines. Chem. Sci 2014, 5, 4057–4064.

(86). Shen C-H; Li L; Zhang W; Liu S; Shu C; Xie Y-E; Yu Y-F; Ye L-W Gold-Catalyzed Tandem Cycloisomerization/Functionalization of in Situ Generated α-Oxo Gold Carbenes in Water. J. Org. Chem. 2014, 79, 9313–9318. [PubMed: 25229883]

(87). Qian D; Zhang J Catalytic Oxidation/C–H Functionalization of N-Arylpropiolamides by Means of Gold Carbenoids: Concise Route to 3-Acyloxindoles. Chem. Commun. 2012, 48, 7082–7084.

(88). Ji K; Yang F; Gao S; Tang J; Gao J Gold-Catalyzed Oxidation/C–H Functionalization of Ynones: Efficient and Rapid Access to Functionalized Polycyclic Salicyl Ketones. Chem. - Eur. J. 2016, 22, 10225–10229. [PubMed: 27276524]

(89). Lin M; Zhu L; Xia J; Yu Y; Chen J; Mao Z; Huang X Gold-Catalyzed Oxidative Cyclization of Tryptamine Derived Enynamides: A Stereoselective Approach to Tetracyclic Spiroindolines. Adv. Synth. Catal. 2018, 360, 2280–2284.

(90). Wagh SB; Sharma P; Patil MD; Liu R-S Gold-Catalyzed Oxidative Cycloalkenations of Alkynes with Quinoline N-Oxides. Org. Chem. Front. 2019, 6, 226–230.

(91). Liu J; Zhu L; Wan W; Huang X Gold-Catalyzed Oxidative Cascade Cyclization of 1,3-Diynamides: Polycyclic *N*-Heterocycle Synthesis via Construction of a Furopyridinyl Core. Org. Lett. 2020, 22, 3279–3285. [PubMed: 32242410]

(92). Li J; Yang F; Ma Y-T; Ji K Gold(III)-Catalyzed Intermolecular Oxidation-Cyclization of Ynones: Access to 4-Substituted Chroman-3-ones. Adv. Synth. Catal. 2019, 361, 2148–2153.

(93). Jiménez-Nùñez E; Echavarren AM Gold-Catalyzed Cycloisomerizations of Enynes: A Mechanistic Perspective. Chem. Rev. 2008, 108, 3326–3350. [PubMed: 18636778]

(94). Vasu D; Hung H-H; Bhunia S; Gawade SA; Das A; Liu R-S Gold-Catalyzed Oxidative Cyclization of 1,5-Enynes Using External Oxidants. Angew. Chem., Int. Ed. 2011, 50, 6911–6914.

(95). Ji K; Zheng Z; Wang Z; Zhang L Enantioselective Oxidative Gold Catalysis Enabled by a Designed Chiral P,N-Bidentate Ligand. Angew. Chem., Int. Ed. 2015, 54, 1245–1249.

(96). Wang K-B; Ran R-Q; Xiu S-D; Li C-Y Synthesis of 3-Azabicyclo[3.1.0]hexan-2-one Derivatives via Gold-Catalyzed Oxidative Cyclopropanation of N-Allylynamides. Org. Lett. 2013, 15, 2374–2377. [PubMed: 23651134]

(97). Ji K; Zhang L A Non-Diazo Strategy to Cyclopropanation via Oxidatively Generated Gold Carbene: The Benefit of a Conformationally Rigid P,N-Bidentate Ligand. Org. Chem. Front. 2014, 1, 34–38. [PubMed: 25431658]

(98). Uetake Y; Niwa T; Nakada M Synthesis of Cycloalkanone-Fused Cyclopropanes by Au(I)-Catalyzed Oxidative Ene–Yne Cyclizations. Tetrahedron Lett. 2014, 55, 6847–6850.

(99). Barrett MJ; Khan GF; Davies PW; Grainger RS Alkynyl Sulfoxides as α-Sulfinyl Carbene Equivalents: Gold-Catalysed Oxidative Cyclopropanation. Chem. Commun. 2017, 53, 5733–5736.

(100). Hamada N; Yamaguchi A; Inuki S; Oishi S; Ohno H Gold(I)-Catalyzed Oxidative Cascade Cyclization of 1,4-Diyn-3-ones for the Construction of Tropone-Fused Furan Scaffolds. Org. Lett. 2018, 20, 4401–4405. [PubMed: 30036068]

(101). Ghorpade S; Su M-D; Liu R-S Gold-Catalyzed Oxidative Cyclizations on 1,4-Enynes: Evidence for a γ-Substituent Effect on Wagner–Meerwein Rearrangements. Angew. Chem., Int. Ed. 2013, 52, 4229–4234.

(102). Qian D; Zhang J A Gold(I)-Catalyzed Intramolecular Oxidation–Cyclopropanation Sequence of 1,6-Enynes: A Convenient Access to [N.1.0]Bicycloalkanes. Chem. Commun. 2011, 47, 11152–11154.

(103). Qian D; Hu H; Liu F; Tang B; Ye W; Wang Y; Zhang J Gold(I)-Catalyzed Highly Diastereo- and Enantioselective Alkyne Oxidation/Cyclopropanation of 1,6-Enynes. Angew. Chem., Int. Ed. 2014, 53, 13751–13755.

(104). Ji K; Zhang L Cyclopropanation of Benzene Rings by Oxidatively Generated α-Oxo Gold Carbene: One-Pot Access to Tetrahydropyranone-Fused Cycloheptatrienes from Propargyl Benzyl Ethers. Adv. Synth. Catal. 2018, 360, 647–651. [PubMed: 31814809]

(105). Nösel P; dos Santos Comprido LN; Lauterbach T; Rudolph M; Rominger F; Hashmi ASK 1,6-Carbene Transfer: Gold-Catalyzed Oxidative Diyne Cyclizations. J. Am. Chem. Soc. 2013, 135, 15662–15666. [PubMed: 24050384]

(106). Nösel P; Moghimi S; Hendrich C; Haupt M; Rudolph M; Rominger F; Hashmi ASK Oxidative Gold Catalysis Meets Photochemistry – Synthesis of Benzo[a]fluorenones from Diynes. Adv. Synth. Catal. 2014, 356, 3755–3760.

(107). Rode N; Marinelli F; Arcadi A; Adak T; Rudolph M; Rominger F; Hashmi ASK Sequential Gold-Catalyzed Carbene Transfer/Ring Closure: Oxidative Cyclization of β-(2-Alkynylphenyl)-α,β-Ynones to Indenofuranones. Adv. Synth. Catal. 2018, 360, 4790–4794.

(108). Wang Q; Rudolph M; Rominger F; Hashmi ASK Gold-Catalyzed Intermolecular Oxidative Diyne Cyclizations via 1,6-Carbene Transfer. Adv. Synth. Catal. 2020, 362, 755–759.

(109). Shu C; Shi C-Y; Sun Q; Zhou B; Li T-Y; He Q; Lu X; Liu R-S; Ye L-W Generation of Endocyclic Vinyl Carbene Complexes via Gold-Catalyzed Oxidative Cyclization of Terminal Diynes: Toward Naphthoquinones and Carbazolequinones. ACS Catal. 2019, 9, 1019–1025.

(110). Ji K; Liu X; Du B; Yang F; Gao J Gold-Catalyzed Selective Oxidation of 4-Oxahepta-1,6-Diynes to 2H-Pyran-3(6H)-ones and Chromen-3(4H)-ones via β-Gold Vinyl Cation Intermediates. Chem. Commun. 2015, 51, 10318–10321.

(111). Zheng Z; Zhang L C–H Insertions in Oxidative Gold Catalysis: Synthesis of Polycyclic 2H-Pyran-3(6H)-ones via a Relay Strategy. Org. Chem. Front. 2015, 2, 1556–1560.

(112). Lu B; Li C; Zhang L Gold-Catalyzed Highly Regioselective Oxidation of C–C Triple Bonds without Acid Additives: Propargyl Moieties as Masked α,β-Unsaturated Carbonyls. J. Am. Chem. Soc. 2010, 132, 14070–14072. [PubMed: 20853846]

(113). Bian Z; Marvin CC; Martin SF Enantioselective Total Synthesis of (–)-Citrinadin a and Revision of Its Stereochemical Structure. J. Am. Chem. Soc. 2013, 135, 10886–10889. [PubMed: 23837457]

(114). Kong K; Enquist JA; McCallum ME; Smith GM; Matsumaru T; Menhaji-Klotz E; Wood JL An Enantioselective Total Synthesis and Stereochemical Revision of (+)-Citrinadin B. J. Am. Chem. Soc. 2013, 135, 10890–10893. [PubMed: 23837485]

(115). Davies PW; Cremonesi A; Martin N Site-Specific Introduction of Gold-Carbenoids by Intermolecular Oxidation of Ynamides or Ynol Ethers. Chem. Commun. 2011, 47, 379–381.

(116). Ji K; D'Souza B; Nelson J; Zhang L Gold-Catalyzed Oxidation of Propargylic Ethers with Internal C–C Triple Bonds: Impressive Regioselectivity Enabled by Inductive Effect. J. Organomet. Chem. 2014, 770, 142–145. [PubMed: 25284890]

(117). Nejrotti S; Prina Cerai G; Oppedisano A; Maranzana A; Occhiato EG; Scarpi D; Deagostino A; Prandi C A Gold(I)-Catalyzed Oxidative Rearrangement of Heterocycle-Derived 1,3-Enynes

Provides an Efficient and Selective Route to Divinyl Ketones. Eur. J. Org. Chem. 2017, 2017, 6228–6238.

(118). Hashmi ASK; Wang T; Shi S; Rudolph M Regioselectivity Switch: Gold(I)-Catalyzed Oxidative Rearrangement of Propargyl Alcohols to 1,3-Diketones. J. Org. Chem. 2012, 77, 7761–7767. [PubMed: 22877083]

(119). Zhao J; Liu J; Xie X; Li S; Liu Y Gold-Catalyzed Synthesis of Tropone and Its Analogues via Oxidative Ring Expansion of Alkynyl Quinols. Org. Lett. 2015, 17, 5926–5929. [PubMed: 26596136]

(120). Yao X; Wang T; Zhang X; Wang P; Zhang B; Wei J; Zhang Z One-Pot Synthesis of 4-Heteroaryl-Substituted Pyrazoles: A Gold-Catalyzed Oxidation/1,2-Heteroaryl Migration Cascade Constitutes the Key Step. Adv. Synth. Catal. 2016, 358, 1534–1539.

(121). Wang L; Xie X; Liu Y Gold-Csatalyzed Oxidative Rearrangement Involving 1,2-Acyl Migration: Efficient Synthesis of Functionalized Dihydro-γ-carbolines from α-(2-Indolyl) Propargylic Alcohols and Imines. Angew. Chem., Int. Ed. 2013, 52, 13302–13306.

(122). Zarkoob F; Ariafard A Mechanistic Elucidation of Gold(I)-Catalyzed Oxidation of a Propargylic Alcohol by a *N*-Oxide in the Presence of an Imine Using DFT Calculations. Organometallics 2019, 38, 489–497.

(123). Wang T; Huang L; Shi S; Rudolph M; Hashmi ASK Synthesis of Highly Substituted N-(Furan-3-ylmethylene)benzenesulfonamides by a Gold(I)-Catalyzed Oxidation/1,2-Alkynyl Migration/Cyclization Cascade. Chem. - Eur. J 2014, 20, 14868–14871. [PubMed: 25236914]

(124). Wang T; Shi S; Hansmann MM; Rettenmeier E; Rudolph M; Hashmi ASK Synthesis of Highly Substituted 3-Formylfurans by a Gold(I)-Catalyzed Oxidation/1,2-Alkynyl Migration/Cyclization Cascade. Angew. Chem., Int. Ed. 2014, 53, 3715–3719.

(125). Wang T; Shi S; Rudolph M; Hashmi ASK Synthesis of Fully Substituted 3-Formyl-4-Iodofurans via a Gold(I)-Catalyzed Oxidation/1,2-Alkynyl Migration/Cyclization/Iodination Cascade. Adv. Synth. Catal. 2014, 356, 2337–2342.

(126). Chen M; Chen Y; Sun N; Zhao J; Liu Y; Li Y Gold-Catalyzed Oxidative Ring Expansion of 2-Alkynyl-1,2-Dihydropyridines or -Quinolines: Highly Efficient Synthesis of Functionalized Azepine or Benzazepine Scaffolds. Angew. Chem., Int. Ed. 2015, 54, 1200–1204.

(127). Zhao J; Xu W; Xie X; Sun N; Li X; Liu Y Gold-Catalyzed Oxidative Cyclizations of {O-(Alkynyl)phenyl Propargyl} Silyl Ether Derivatives Involving 1,2-Enynyl Migration: Synthesis of Functionalized 1H-Isochromenes and 2H-Pyrans. Org. Lett. 2018, 20, 5461–5465. [PubMed: 30102048]

(128). Chen H; Zhang L A Desulfonylative Approach in Oxidative Gold Catalysis: Regiospecific Access to Donor-Substituted Acyl Gold Carbenes. Angew. Chem., Int. Ed. 2015, 54, 11775–11779.

(129). Chen M; Sun N; Xu W; Zhao J; Wang G; Liu Y Gold-Catalyzed Ring Expansion of Alkynyl Heterocycles through 1,2-Migration of an Endocyclic Carbon–Heteroatom Bond. Chem. - Eur. J 2015, 21, 18571–18575. [PubMed: 26490371]

(130). Zheng Y; Zhang J; Cheng X; Xu X; Zhang L Wolff Rearrangement of Oxidatively Generated α-Oxo Gold Carbenes: An Effective Approach to Silylketenes. Angew. Chem., Int. Ed. 2019, 58, 5241–5245.

(131). Marsden SP; Pang W-K Efficient, General Synthesis of Silylketenes via an Unusual Rhodium Mediated Wolff Rearrangement. Chem. Commun. 1999, 1199–1200.

(132). Cui L; Peng Y; Zhang L A Two-Step, Formal [4 + 2] Approach toward Piperidin-4-ones via Au Catalysis. J. Am. Chem. Soc. 2009, 131, 8394–8395. [PubMed: 19492799]

(133). Cui L; Ye L; Zhang L Gold-Catalyzed Efficient Synthesis of Azepan-4-ones via a Two-Step [5 + 2] Annulation. Chem. Commun. 2010, 46, 3351–3353.

(134). Noey EL; Luo Y; Zhang L; Houk KN Mechanism of Gold(I)-Catalyzed Rearrangements of Acetylenic Amine-N-oxides: Computational Investigations Lead to a New Mechanism Confirmed by Experiment. J. Am. Chem. Soc. 2012, 134, 1078–1084. [PubMed: 22191473]

(135). Cui L; Zhang L Total Synthesis of (+)-Lentiginosine via a Key Au Catalysis. Sci. China: Chem. 2010, 53, 113–118.

(136). Shan Z-H; Liu J; Xu L-M; Tang Y-F; Chen J-H; Yang Z Total Synthesis of (±)-Decinine via an Oxidative Biaryl Coupling with Defined Axial Chirality. Org. Lett. 2012, 14, 3712–3715. [PubMed: 22746388]

(137). Bhunia S; Ghorpade S; Huple DB; Liu R-S Gold-Catalyzed Oxidative Cyclizations of cis-3-En-1-ynes to Form Cyclo-pentenone Derivatives. Angew. Chem., Int. Ed. 2012, 51, 2939–2942.

(138). Wang Y; Zheng Z; Zhang L Intramolecular Insertions into Unactivated C(sp3)–H Bonds by Oxidatively Generated β-Diketone-α-Gold Carbenes: Synthesis of Cyclopentanones. J. Am. Chem. Soc. 2015, 137, 5316–5319. [PubMed: 25835372]

(139). Zheng Z; Wang Y; Ma X; Li Y; Zhang L Non-Diazo C–H Insertion Approach to Cyclobutanones via Oxidative Gold Catalysis. Angew. Chem., Int. Ed. 2020, 59, 17398–17402.

(140). Xu Z; Chen H; Wang Z; Ying A; Zhang L One-Pot Synthesis of Benzene-Fused Medium-Ring Ketones: Gold Catalysis-Enabled Enolate Umpolung Reactivity. J. Am. Chem. Soc. 2016, 138, 5515–5518. [PubMed: 27082456]

(141). Xu Z; Zhai R; Liang T; Zhang L Efficient One-Pot Multifunctionalization of Alkynes en Route to α-Alkoxyketones, α-Thioketones, and α-Thio Thioketals by Using an Umpolung Strategy. Chem. - Eur. J. 2017, 23, 14133–14137. [PubMed: 28683191]

(142). Zhai RL; Xue YS; Liang T; Mi JJ; Xu Z Regioselective Arene and Heteroarene Functionalization: N-Alkenoxypyridinium Salts as Electrophilic Alkylating Agents for the Synthesis of α-Aryl/α-Heteroaryl Ketones. J. Org. Chem. 2018, 83, 10051–10059. [PubMed: 30019900]

(143). Dateer RB; Pati K; Liu R-S Gold-Catalyzed Synthesis of Substituted 2-Aminofurans via Formal [4 + 1]-Cycloadditions on 3-En1-ynamides. Chem. Commun. 2012, 48, 7200.

(144). Asao N; Sato K; Yamamoto Y AuBr3-Catalyzed Cyclization of O-(Alkynyl)nitrobenzenes. Efficient Synthesis of Isatogens and Anthranils. Tetrahedron Lett. 2003, 44, 5675–5677.

(145). Jadhav AM; Bhunia S; Liao H-Y; Liu R-S Gold-Catalyzed Stereoselective Synthesis of Azacyclic Compounds through a Redox/[2 + 2 + 1] Cycloaddition Cascade of Nitroalkyne Substrates. J. Am. Chem. Soc. 2011, 133, 1769–1771. [PubMed: 21244004]

(146). Yeom H-S; Lee J-E; Shin S Gold-Catalyzed Waste-Free Generation and Reaction of Azomethine Ylides: Internal Redox/Dipolar Cycloaddition Cascade. Angew. Chem., Int. Ed. 2008, 47, 7040–7043.

(147). Jeong J; Yeom H-S; Kwon O; Shin S Auxiliary-Controlled Asymmetric [3 + 2]-Dipolar Cycloaddition of Azomethine Ylides Generated from Au-Catalyzed Intramolecular Redox Reaction of Nitronyl Alkynes. Chem. - Asian J. 2011, 6, 1977–1981. [PubMed: 21710683]

(148). Yeom H-S; Lee Y; Lee J-E; Shin S Geometry-Dependent Divergence in the Gold-Catalyzed Redox Cascade Cyclization of *O*-Alkynylaryl Ketoximes and Nitrones Leading to Isoindoles. Org. Biomol. Chem. 2009, 7, 4744–4752. [PubMed: 19865712]

(149). Chen D; Song G; Jia A; Li X Gold- and Iodine-Mediated Internal Oxygen Transfer of Nitrone- and Sulfoxide-Functionalized Alkynes. J. Org. Chem. 2011, 76, 8488–8494. [PubMed: 21902170]

(150). Yeom H-S; Lee Y; Jeong J; So E; Hwang S; Lee J-E; Lee SS; Shin S Stereoselective One-Pot Synthesis of 1-Aminoindanes and 5,6-Fused Azacycles Using a Gold-Catalyzed Redox-Pinacol-Mannich-Michael Cascade. Angew. Chem., Int. Ed. 2010, 49, 1611–1614.

(151). Qian D; Zhang J Gold/Brønsted Acid Relay Catalysis for Enantioselective Construction of Spirocyclic Diketones. Chem. - Eur. J 2013, 19, 6984–6988. [PubMed: 23609995]

(152). Mukherjee A; Dateer RB; Chaudhuri R; Bhunia S; Karad SN; Liu R-S Gold-Catalyzed 1,2-Difunctionalizations of Amino-alkynes Using Only N- and O-Containing Oxidants. J. Am. Chem. Soc. 2011, 133, 15372–15375. [PubMed: 21905664]

(153). Sahani RL; Patil MD; Wagh SB; Liu R-S Catalytic Transformations of Alkynes into Either α-Alkoxy or α-Aryl Enolates: Mannich Reactions by Cooperative Catalysis and Evidence for Nucleophile-Directed Chemoselectivity. Angew. Chem., Int. Ed. 2018, 57, 14878–14882.

(154). Sahani RL; Liu R-S Gold-Catalyzed Oxidative Arylations of 3-Butyn-1-ols and 2-Propyn-1-ols with Nitrones to Yield Distinct Fused Indoles Bearing a Heterocyclic Ring. ACS Catal. 2019, 9, 5890–5896.

(155). Hashmi AS; Bührle M; Salathé R; Bats J Gold Catalysis: Synthesis of 3-Acylindenes from 2-Alkynylaryl Epoxides. Adv. Synth. Catal. 2008, 350, 2059–2064.

(156). Scott VJ; Labinger JA; Bercaw JE Mechanism of Reductive Elimination of Methyl Iodide from a Novel Gold-(III)–Monomethyl Complex. Organometallics 2010, 29, 4090–4096.

(157). Chaudhuri R; Liu R-S Gold-Catalyzed Oxidative Cyclizations of 2-Oxiranyl-1-alkynylbenzenes for Diastereoselective Synthesis of Highly Substituted 2-Hydroxyindanones. Adv. Synth. Catal. 2011, 353, 2589–2592.

(158). Chaudhuri R; Liu R-S Gold-Catalyzed Oxidative Cyclizations of 2-Oxiranyl-1-alkynylbenzenes for Diastereoselective Synthesis of Highly Substituted 2-Hydroxyindanones. Adv. Synth. Catal. 2011, 353, 2589–2592.

(159). Yeom H-S; So E; Shin S Gold-Catalyzed Synthesis of 3-Pyrrolidinones and Nitrones from N-Sulfonyl Hydroxylamines via Oxygen-Transfer Redox and 1,3-Sulfonyl Migration. Chem. - Eur. J 2011, 17, 1764–1767. [PubMed: 21274923]

(160). Mokar BD; Huple DB; Liu R-S Gold-Catalyzed Intermolecular Oxidations of 2-Ketonyl-1-ethynyl Benzenes with *N*-Hydroxyanilines to Yield 2-Aminoindenones via Gold Carbene Intermediates. Angew. Chem., Int. Ed. 2016, 55, 11892–11896.

(161). Wang Y; Ye L; Zhang L Au-Catalyzed Synthesis of 2-Alkylindoles from N-Arylhydroxylamines and Terminal Alkynes. Chem. Commun. 2011, 47, 7815–7817.

(162). Wang Y; Liu L; Zhang L Combining Zn Ion Catalysis with Homogeneous Gold Catalysis: An Efficient Annulation Approach to N-Protected Indoles. Chem. Sci. 2013, 4, 739–746.

(163). Ngwerume S; Camp JE Gold-Catalysed Rearrangement of O-Vinyl Oximes for the Synthesis of Highly Substituted Pyrroles. Chem. Commun. 2011, 47, 1857–1859.

(164). Zheng Z; Tu H; Zhang L One-Pot Synthesis of Fused Pyrroles through a Key Gold-Catalysis-Triggered Cascade. Chem. - Eur. J 2014, 20, 2445–2448. [PubMed: 24482098]

(165). Witham CA; Mauleón P; Shapiro ND; Sherry BD; Toste FD Gold(I)-Catalyzed Oxidative Rearrangements. J. Am. Chem. Soc. 2007, 129, 5838–5839. [PubMed: 17432862]

(166). Yeom H-S; Shin S Au(I)-Catalyzed Intramolecular Oxidative Cyclopropanation of 1,6-Enynes Derived from Propiolamides with Diphenyl Sulfoxide. Org. Biomol. Chem. 2013, 11, 1089. [PubMed: 23321793]

(167). Ferrer S; Echavarren AM Synthesis of Barbaralones and Bullvalenes Made Easy by Gold Catalysis. Angew. Chem., Int. Ed. 2016, 55, 11178–11182.

(168). Claus V; Molinari L; Büllmann S; Thusek J; Rudolph M; Rominger F; Hashmi ASK Gold-Catalyzed Cyclisation by 1,4-Dioxidation. Chem. - Eur. J. 2019, 25, 9385–9389. [PubMed: 30829424]

(169). Groß T; Metz P An Efficient Gold-Catalyzed Domino Process for the Construction of Tetracyclic Ketoethers. Chem. - Eur. J. 2013, 19, 14787–14790. [PubMed: 24114853]

(170). Homs A; Muratore ME; Echavarren AM Enantioselective Total Synthesis of (–)-Nardoaristolone B via a Gold(I)-Catalyzed Oxidative Cyclization. Org. Lett. 2015, 17, 461–463. [PubMed: 25563976]

(171). Hung H-H; Liao Y-C; Liu R-S Oxidant-Dependent Chemoselectivity in the Gold-Catalyzed Oxidative Cyclizations of 3,4,6,6-Tetrasubstituted 3,5-Dien-1-ynes. J. Org. Chem. 2013, 78, 7970–7976. [PubMed: 23875583]

(172). Chen C-H; Tsai Y-C; Liu R-S Gold-Catalyzed Cyclization/Oxidative [3 + 2] Cycloadditions of 1,5-Enynes with Nitrosobenzenes without Additional Oxidants. Angew. Chem., Int. Ed. 2013, 52, 4599–4603.

(173). Taduri BP; Sohel SMA; Cheng H-M; Lin G-Y; Liu RS Pt- and Au-Catalyzed Oxidative Cyclization of 2-Ethenyl-1-(prop-2′-yn-1′-ol)benzenes to Naphthyl Aldehydes and Ketones: Catalytic Oxidation of Metal–Alkylidene Intermediates Using H2O and H2O2. Chem. Commun. 2007, 2530–2532.

(174). Wang T; Zhang J Synthesis of 2-Acylfurans from 3-(1-Alkynyl)-2-alken-1-ones via the Oxidation of Gold–Carbene Intermediates by H2O2. Dalton Trans. 2010, 39, 4270–4273. [PubMed: 20379602]

(175). Zhan H; Zhao L; Liao J; Li N; Chen Q; Qiu S; Cao H Gold-Catalyzed Synthesis of 3-Acylimidazo[1,2-a]pyridines via Carbene Oxidation. Adv. Synth. Catal. 2015, 357, 46–50.

(176). Buzas A; Gagosz F Gold(I)-Catalyzed Formation of 4-Alkylidene-1,3-dioxolan-2-ones from Propargylic Tert-Butyl Carbonates. Org. Lett. 2006, 8, 515–518. [PubMed: 16435873]

(177). Yu M; Zhang G; Zhang L Gold-Catalyzed Efficient Preparation of Linear α-Iodoenones from Propargylic Acetates. Org. Lett. 2007, 9, 2147–2150. [PubMed: 17465561]

(178). Wang D; Ye X; Shi X Efficient Synthesis of E-α-Haloenones through Chemoselective Alkyne Activation over Allene with Triazole– Au Catalysts. Org. Lett. 2010, 12, 2088–2091. [PubMed: 20384312]

(179). Ye L; Zhang L Practical Synthesis of Linear α-Iodo/Bromo-α,β-unsaturated Aldehydes/Ketones from Propargylic Alcohols via Au/Mo Bimetallic Catalysis. Org. Lett. 2009, 11, 3646–3649. [PubMed: 19637857]

(180). Schuler M; Silva F; Bobbio C; Tessier A; Gouverneur V Gold(I)-Catalyzed Alkoxyhalogenation of β-Hydroxy-α,α-difluoroynones. Angew. Chem. 2008, 120, 8045–8048.

(181). Liao H-H; Liu R-S Effects of Haloniums on Gold-Catalyzed Ring Expansion of 1-Oxiranyl-1-alkynylcyclopropanes. Chem. Commun. 2011, 47, 1339–1341.

(182). D'Oyley JM; Aliev AE; Sheppard TD Regioselective Dihalohydration Reactions of Propargylic Alcohols: Gold-Catalyzed and Noncatalyzed Reactions. Angew. Chem., Int. Ed. 2014, 53, 10747–10750.

(183). Mo F; Yan JM; Qiu D; Li F; Zhang Y; Wang J Gold-Catalyzed Halogenation of Aromatics by N-Halosuccinimides. Angew. Chem., Int. Ed. 2010, 49, 2028–2032.

(184). Wang Y; Zarca M; Gong L-Z; Zhang L A C–H Insertion Approach to Functionalized Cyclopentenones. J. Am. Chem. Soc. 2016, 138, 7516–7519. [PubMed: 27276014]

(185). Gagosz F Gold Vinylidenes as Useful Intermediates in Synthetic Organic Chemistry. Synthesis 2019, 51, 1087–1099.

(186). Peng H; Akhmedov NG; Liang Y-F; Jiao N; Shi X Synergistic Gold and Iron Dual Catalysis: Preferred Radical Addition toward Vinyl–Gold Intermediate over Alkene. J. Am. Chem. Soc. 2015, 137, 8912–8915. [PubMed: 26136160]

(187). Mai S; Rao C; Chen M; Su J; Du J; Song Q Merging Gold Catalysis, Organocatalytic Oxidation, and Lewis Acid Catalysis for Chemodivergent Synthesis of Functionalized Oxazoles from *N*-Propargylamides. Chem. Commun. 2017, 53, 10366–10369.

(188). Liao J; Guo P; Chen Q Au-Catalyzed Synthesis of Benzofurans from Phenols and Alkynes Using Molecular Oxygen. Catal. Commun. 2016, 77, 22–25.

(189). Cui L; Zhang G; Zhang L Homogeneous Gold-Catalyzed Efficient Oxidative Dimerization of Propargylic Acetates. Bioorg. Med. Chem. Lett. 2009, 19, 3884–3887. [PubMed: 19362834]

(190). Zhang G; Peng Y; Cui L; Zhang L Gold-Catalyzed Homogeneous Oxidative Cross-Coupling Reactions. Angew. Chem., Int. Ed. 2009, 48, 3112–3115.

(191). Faza ON; López CS Computational Study of Gold-Catalyzed Homo- and Cross-Coupling Reactions. J. Org. Chem. 2013, 78, 4929–4939. [PubMed: 23597253]

(192). Peng Y; Cui L; Zhang G; Zhang L Gold-Catalyzed Homogeneous Oxidative C–O Bond Formation: Efficient Synthesis of 1-Benzoxyvinyl Ketones. J. Am. Chem. Soc. 2009, 131, 5062–5063. [PubMed: 19301899]

(193). Geng C; Zhu R; Li M; Lu T; Wheeler SE; Liu C Revised Role of Selectfluor in Homogeneous Au-Catalyzed Oxidative C–O Bond Formations. Chem. - Eur. J. 2014, 20, 15833–15839. [PubMed: 25293670]

(194). Zhang G; Cui L; Wang Y; Zhang L Homogeneous Gold-Catalyzed Oxidative Carboheterofunctionalization of Alkenes. J. Am. Chem. Soc. 2010, 132, 1474–1475. [PubMed: 20050647]

(195). Brenzovich WE Jr.; Benitez D; Lackner AD; Shunatona HP; Tkatchouk E; Goddard WA III; Toste FD Gold-Catalyzed Intramolecular Aminoarylation of Alkenes: C–C Bond Formation through Bimolecular Reductive Elimination. Angew. Chem., Int. Ed. 2010, 49, 5519–5522.

(196). Tkatchouk E; Mankad NP; Benitez D; Goddard WA; Toste FD Two metals are better than one in the gold catalyzed oxidative heteroarylation of alkenes. J. Am. Chem. Soc. 2011, 133, 14293–14300. [PubMed: 21861448]

(197). Melhado AD; Brenzovich WE; Lackner AD; Toste FD Gold-Catalyzed Three-Component Coupling: Oxidative Oxyarylation of Alkenes. J. Am. Chem. Soc. 2010, 132, 8885–8887 [PubMed: 20557048]

(198). Ball LT; Green M; Lloyd-Jones GC; Russell CA Arylsilanes: Application to Gold-Catalyzed Oxyarylation of Alkenes. Org. Lett. 2010, 12, 4724–4727. [PubMed: 20879724]

(199). Brenzovich WE; Brazeau J-F; Toste FD Gold-Catalyzed Oxidative Coupling Reactions with Aryltrimethylsilanes. Org. Lett. 2010, 12, 4728–4731. [PubMed: 21028911]

(200). de Haro T; Nevado C Flexible Gold-Catalyzed Regioselective Oxidative Difunctionalization of Unactivated Alkenes. Angew. Chem., Int. Ed. 2011, 50, 906–910.

(201). Feige P; de Haro T; Rusconi G; Merino E; Nevado C Gold-Catalyzed Oxidative Aminoesterification of Unactivated Alkenes. Monatsh. Chem. 2018, 149, 749–754.

(202). Hopkinson MN; Tessier A; Salisbury A; Giuffredi GT; Combettes LE; Gee AD; Gouverneur V Gold-Catalyzed Intramolecular Oxidative Cross-Coupling of Nonactivated Arenes. Chem. - Eur. J 2010, 16, 4739–4743. [PubMed: 20340120]

(203). Liu Y; Zhu J; Qian J; Xu Z Gold-Catalyzed Simultaneous Formation of C–C, C=O, and C–F Bonds in the Presence of Selectfluor: A Synthesis of Fluoroindenes from Allene Esters. J. Org. Chem. 2012, 77, 5411–5417. [PubMed: 22646995]

(204). Zhang G; Luo Y; Wang Y; Zhang L Combining Gold(I)/Gold(III) Catalysis and C–H Functionalization: A Formal Intramolecular [3 + 2] Annulation Towards Tricyclic Indolines and Mechanistic Studies. Angew. Chem., Int. Ed. 2011, 50, 4450–4454.

(205). Hopkinson MN; Ross JE; Giuffredi GT; Gee AD; Gouverneur V Gold-Catalyzed Cascade Cyclization–Oxidative Alkynylation of Allenoates. Org. Lett. 2010, 12, 4904–4907. [PubMed: 20936849]

(206). Zhang R; Xu Q; Chen K; Gu P; Shi M Gold-Catalyzed Cascade Oxidative Cyclization and Arylation of Allenoates. Eur. J. Org. Chem. 2013, 2013, 7366–7371.

(207). Leyva-Pérez A; Doménech A; Al-Resayes SI; Corma A Gold Redox Catalytic Cycles for the Oxidative Coupling of Alkynes. ACS Catal. 2012, 2, 121–126.

(208). Wu Q; Du C; Huang Y; Liu X; Long Z; Song F; You J Stoichiometric to Catalytic Reactivity of the Aryl Cycloaurated Species with Arylboronic Acids: Insight into the Mechanism of Gold-Catalyzed Oxidative C(sp2)–H Arylation. Chem. Sci. 2015, 6, 288–293. [PubMed: 28626549]

(209). Shaikh AC; Ranade DS; Rajamohanan PR; Kulkarni PP; Patil NT Oxidative Intramolecular 1,2-Amino-oxygenation of Alkynes under Au^{I}/Au^{III} Catalysis: Discovery of a Pyridinium–Oxazole Dyad as an Ionic Fluorophore. Angew. Chem., Int. Ed. 2017, 56, 757–761.

(210). Wang W; Jasinski J; Hammond GB; Xu B Fluorine-Enabled Cationic Gold Catalysis: Functionalized Hydration of Alkynes. Angew. Chem., Int. Ed. 2010, 49, 7247–7252.

(211). de Haro T; Nevado C Gold-Catalyzed Synthesis of α-Fluoro Acetals and α-Fluoro Ketones from Alkynes. Adv. Synth. Catal. 2010, 352, 2767–2772.

(212). de Haro T; Nevado C Domino Gold-Catalyzed Rearrangement and Fluorination of Propargyl Acetates. Chem. Commun. 2011, 47, 248–249.

(213). Jeong Y; Kim B-I; Lee JK; Ryu J-S Direct Synthesis of 4-Fluoroisoxazoles through Gold-Catalyzed Cascade Cyclization–Fluorination of 2-Alkynone O-Methyl Oximes. J. Org. Chem. 2014, 79, 6444–6455. [PubMed: 24979530]

(214). Liu Y; Chen X; Zhang J; Xu Z Gold(I)-Catalyzed Diketonization of Alkynes and Its Application for the One-Pot Synthesis of Quinoxaline Derivatives. Synlett 2013, 24, 1371–1376.

(215). Arcadi A; Pietropaolo E; Alvino A; Michelet V Amino-fluorination of 2-Alkynylanilines: A Au-Catalyzed Entry to Fluorinated Indoles. Beilstein J. Org. Chem. 2014, 10, 449–458.

(216). Mankad NP; Toste FD C(sp3)–F Reductive Elimination from Alkylgold(III) Fluoride Complexes. Chem. Sci. 2012, 3, 72–76. [PubMed: 23087810]

(217). Brand JP; Charpentier J; Waser J Direct Alkynylation of Indole and Pyrrole Heterocycles. Angew. Chem., Int. Ed. 2009, 48, 9346–9349.

(218). Brand JP; Waser J Direct Alkynylation of Thiophenes: Cooperative Activation of TIPS–EBX with Gold and Brønsted Acids. Angew. Chem., Int. Ed. 2010, 49, 7304–7307.

(219). Kar A; Mangu N; Kaiser HM; Beller M; Tse MK A General Gold-Catalyzed Direct Oxidative Coupling of Non-Activated Arenes. Chem. Commun. 2008, 386–388.

(220). Kar A; Mangu N; Kaiser HM; Tse MK Gold-Catalyzed Direct Oxidative Coupling Reactions of Non-Activated Arenes. J. Organomet. Chem. 2009, 694, 524–537.

(221). Gaillard S; Slawin AMZ; Nolan SP A N-Heterocyclic Carbene Gold Hydroxide Complex: A Golden Synthon. Chem. Commun. 2010, 46, 2742–2744.

(222). Lu P; Boorman TC; Slawin AMZ; Larrosa I Gold(I)-Mediated C–H Activation of Arenes. J. Am. Chem. Soc. 2010, 132, 5580–5581. [PubMed: 20364835]

(223). Bott RW; Eaborn C; Jackson PM Organosilicon Compounds XXXIX. Effects of Varying R on the Rate of Acid Cleavage of P-$MeOC_6H_4SiR_3$ Compounds. J. Organomet. Chem. 1967, 7, 79–83.

(224). de Haro T; Nevado C On Gold-Mediated C–H Activation Processes. Synthesis 2011, 2011, 2530–2539.

(225). Wegner HA; Auzias M Gold for C–C Coupling Reactions: A Swiss-Army-Knife Catalyst? Angew. Chem., Int. Ed. 2011, 50, 8236–8247.

(226). Gaillard S; Cazin CSJ; Nolan SP N-Heterocyclic Carbene Gold(I) and Copper(I) Complexes in C–H Bond Activation. Acc. Chem. Res. 2012, 45, 778–787. [PubMed: 22166092]

(227). Cambeiro XC; Boorman TC; Lu P; Larrosa I Redox-Controlled Selectivity of C–H Activation in the Oxidative Cross-Coupling of Arenes. Angew. Chem., Int. Ed. 2013, 52, 1781–1784.

(228). Cambeiro XC; Ahlsten N; Larrosa I Au-Catalyzed Cross-Coupling of Arenes via Double C–H Activation. J. Am. Chem. Soc. 2015, 137, 15636–15639. [PubMed: 26645996]

(229). Li W; Yuan D; Wang G; Zhao Y; Xie J; Li S; Zhu C Cooperative Au/Ag Dual-Catalyzed Cross-Dehydrogenative Biaryl Coupling: Reaction Development and Mechanistic Insight. J. Am. Chem. Soc. 2019, 141, 3187–3197. [PubMed: 30681846]

(230). Ball LT; Lloyd-Jones GC; Russell CA Gold-Catalyzed Direct Arylation. Science 2012, 337, 1644. [PubMed: 23019647]

(231). Ball LT; Lloyd-Jones GC; Russell CA Gold-Catalyzed Oxidative Coupling of Arylsilanes and Arenes: Origin of Selectivity and Improved Precatalyst. J. Am. Chem. Soc. 2014, 136, 254–264. [PubMed: 24367895]

(232). Hata K; Ito H; Segawa Y; Itami K Pyridylidene Ligand Facilitates Gold-Catalyzed Oxidative C–H Arylation of Heterocycles. Beilstein J. Org. Chem. 2015, 11, 2737–2746.

(233). Cresswell AJ; Lloyd-Jones GC Room-Temperature Gold-Catalysed Arylation of Heteroarenes: Complementarity to Palladium Catalysis. Chem. - Eur. J. 2016, 22, 12641–12645. [PubMed: 27325239]

(234). Robinson MP; Lloyd-Jones GC Au-Catalyzed Oxidative Arylation: Chelation-Induced Turnover of Ortho-Substituted Arylsilanes. ACS Catal. 2018, 8, 7484–7488.

(235). Hofer M; Genoux A; Kumar R; Nevado C Gold-Catalyzed Direct Oxidative Arylation with Boron Coupling Partners. Angew. Chem., Int. Ed. 2017, 56, 1021–1025.

(236). Fricke C; Dahiya A; Reid WB; Schoenebeck F Gold-Catalyzed C–H Functionalization with Aryl Germanes. ACS Catal. 2019, 9, 9231–9236. [PubMed: 31608162]

(237). Liu K; Li N; Ning Y; Zhu C; Xie J Gold-Catalyzed Oxidative Biaryl Cross-Coupling of Organometallics. Chem. 2019, 5, 2718–2730.

(238). Partyka DV; Zeller M; Hunter AD; Gray TG Relativistic Functional Groups: Aryl Carbon–Gold Bond Formation by Selective Transmetalation of Boronic Acids. Angew. Chem., Int. Ed. 2006, 45, 8188–8191.

(239). Hashmi ASK; Ramamurthi TD; Rominger F Synthesis, Structure and Reactivity of Organogold Compounds of Relevance to Homogeneous Gold Catalysis. J. Organomet. Chem. 2009, 694, 592–597.

(240). Rosca D-A; Smith DA; Bochmann M Cyclometallated Gold(III) Hydroxides as Versatile Synthons for Au–N, Au–C Complexes and Luminescent Compounds. Chem. Commun. 2012, 48, 7247–7249.

(241). Levin MD; Toste FD Gold-Catalyzed Allylation of Aryl Boronic Acids: Accessing Cross-Coupling Reactivity with Gold. Angew. Chem., Int. Ed. 2014, 53, 6211–6215.

(242). Gauchot V; Lee A-L Dual Gold Photoredox C(sp2)–C(sp2) Cross Couplings – Development and Mechanistic Studies. Chem. Commun. 2016, 52, 10163–10166.

(243). Kumar R; Linden A; Nevado C Evidence for Direct Transmetalation of Au^{III}–F with Boronic Acids. J. Am. Chem. Soc. 2016, 138, 13790–13793. [PubMed: 27685011]

(244). Witzel S; Xie J; Rudolph M; Hashmi ASK Photo-sensitizer-Free, Gold-Catalyzed C–C Cross-Coupling of Boronic Acids and Diazonium Salts Enabled by Visible Light. Adv. Synth. Catal. 2017, 359, 1522–1528.

(245). de Haro T; Nevado C Gold-Catalyzed Ethynylation of Arenes. J. Am. Chem. Soc. 2010, 132, 1512–1513. [PubMed: 20088525]

(246). Hofer M; de Haro T; Gómez-Bengoa E; Genoux A; Nevado C Oxidant Speciation and Anionic Ligand Effects in the Gold-Catalyzed Oxidative Coupling of Arenes and Alkynes. Chem. Sci. 2019, 10, 8411–8420. [PubMed: 31803420]

(247). Peng H; Xi Y; Ronaghi N; Dong B; Akhmedov NG; Shi X Gold-Catalyzed Oxidative Cross-Coupling of Terminal Alkynes: Selective Synthesis of Unsymmetrical 1,3-Diynes. J. Am. Chem. Soc. 2014, 136, 13174–13177. [PubMed: 25184690]

(248). Ye X; Peng H; Wei C; Yuan T; Wojtas L; Shi X Gold-Catalyzed Oxidative Coupling of Alkynes toward the Synthesis of Cyclic Conjugated Diynes. Chem 2018, 4, 1983–1993. [PubMed: 30911697]

(249). Bédard A-C; Collins SK Phase Separation as a Strategy toward Controlling Dilution Effects in Macrocyclic Glaser-Hay Couplings. J. Am. Chem. Soc. 2011, 133, 19976–19981. [PubMed: 22029394]

(250). Godin É; Bédard A-C; Raymond M; Collins SK Phase Separation Macrocyclization in a Complex Pharmaceutical Setting: Application toward the Synthesis of Vaniprevir. J. Org. Chem. 2017, 82, 7576–7582. [PubMed: 28677966]

(251). Rangaraju SK; Gonela UM; Kavita A; Yadav JS; Mohapatra DK Synergistic Gold and Copper Dual Catalysis for Intramolecular Glaser–Hay Coupling: Rapid Total Synthesis of Ivorenolide B. Eur. J. Org. Chem. 2018, 2018, 4376–4380.

(252). Pradal A; Toullec PY; Michelet V Gold-Catalyzed Oxidative Acyloxylation of Arenes. Org. Lett. 2011, 13, 6086–6089. [PubMed: 22032339]

(253). Qiu D; Zheng Z; Mo F; Xiao Q; Tian Y; Zhang Y; Wang J Gold(III)-Catalyzed Direct Acetoxylation of Arenes with Iodobenzene Diacetate. Org. Lett. 2011, 13, 4988–4991. [PubMed: 21882855]

(254). Pradal A; Faudot dit Bel P; Toullec PY; Michelet V Gold-Catalyzed C–H Oxidative Polyacyloxylation Reaction of Hindered Arenes. Synthesis 2012, 44, 2463–2468.

(255). Marchetti L; Kantak A; Davis R; DeBoef B Regioselective Gold-Catalyzed Oxidative C–N Bond Formation. Org. Lett. 2015, 17, 358–361. [PubMed: 25539392]

(256). Iglesias A; Muñiz K Oxidative Interception of the Hydroamination Pathway: A Gold-Catalyzed Diamination of Alkenes. Chem. - Eur. J. 2009, 15, 10563–10569. [PubMed: 19746362]

(257). Harper MJ; Emmett EJ; Bower JF; Russell CA Oxidative 1,2-Difunctionalization of Ethylene via Gold-Catalyzed Oxyarylation. J. Am. Chem. Soc. 2017, 139, 12386–12389. [PubMed: 28829593]

(258). Gasparrini F; Giovannoli M; Misiti D; Natile G; Palmieri G; Maresca L Gold(III)-Catalyzed One-Pot Synthesis of Isoxazoles from Terminal Alkynes and Nitric Acid. J. Am. Chem. Soc. 1993, 115, 4401–4402.

(259). Wegner HA; Ahles S; Neuburger M A New Gold-Catalyzed Domino Cyclization and Oxidative Coupling Reaction. Chem. - Eur. J. 2008, 14, 11310–11313. [PubMed: 19006147]

(260). Guan B; Xing D; Cai G; Wan X; Yu N; Fang Z; Yang L; Shi Z Highly Selective Aerobic Oxidation of Alcohol Catalyzed by a Gold(I) Complex with an Anionic Ligand. J. Am. Chem. Soc. 2005, 127, 18004–18005. [PubMed: 16366542]

(261). Li H; Guan B; Wang W; Xing D; Fang Z; Wan X; Yang L; Shi Z Aerobic Oxidation of Alcohol in Aqueous Solution Catalyzed by Gold. Tetrahedron 2007, 63, 8430–8434.

(262). Wang Z.-g.; Xu K; Shen M.-n.; Lu M A Facile and Efficient Catalytic System for the Oxidation of Alcohols With gold(III) and Ionic Liquid Immobilized Tempo under Solvent-Free Conditions. Synlett 2014, 25, 2459–2462.

(263). Li H; Li Z; Shi Z Gold-Catalyzed Benzylic Oxidation to Carbonyl Compounds. Tetrahedron 2009, 65, 1856–1858.

(264). Jones CJ; Taube D; Ziatdinov VR; Periana RA; Nielsen RJ; Oxgaard J; Goddard WA III. Selective Oxidation of Methane to Methanol Catalyzed, with C–H Activation, by Homogeneous, Cationic Gold. Angew. Chem., Int. Ed. 2004, 43, 4626–4629.

(265). Xing D; Guan B; Cai G; Fang Z; Yang L; Shi Z Gold(I)-Catalyzed Oxidative Cleavage of a C–C Double Bond in Water. Org. Lett. 2006, 8, 693–696. [PubMed: 16468744]

(266). Wang Z; Li L; Huang Y A General Synthesis of Ynones from Aldehydes via Oxidative C–C Bond Cleavage under Aerobic Conditions. J. Am. Chem. Soc. 2014, 136, 12233–12236. [PubMed: 25133731]

(267). Liu Y; Song F; Guo S Cleavage of a Carbon–Carbon Triple Bond via Gold-Catalyzed Cascade Cyclization/Oxidative Cleavage Reactions of (Z)-Enynols with Molecular Oxygen. J. Am. Chem. Soc. 2006, 128, 11332–11333. [PubMed: 16939238]

(268). Song F; Liu Y A Facile Approach to Spirocyclic Butenolides through Cascade Cyclization/ Oxidative Cleavage Reactions of (Z)-Enynols Catalyzed by Gold under Dioxygen Atmosphere. J. Organomet. Chem. 2009, 694, 502–509.

(269). Das A; Chaudhuri R; Liu R-S Gold-Catalyzed Oxidative Cleavage of Aryl-Substituted Alkynyl Ethers Using Molecular Oxygen. Simultaneous Degradation of C–H and Single and Triple Carbon– Carbon Bonds under Ambient Conditions. Chem. Commun. 2009, 4046–4048.

(270). Patil DV; Park H-S; Koo J; Han JW; Shin S Aerobic Oxygenative Cleavage of Electron Deficient C–C Triple Bonds in the Gold-Catalyzed Cyclization of 1,6-Enynes. Chem. Commun. 2014, 50, 12722–12725.

(271). Liu Y; Mao D; Lou S; Qian J; Xu Z-Y Oxidative Aromatization of 1,3,5-Trisubstituted Pyrazolines Using Hydrogen Tetrachloroaurate as Catalyst under an Oxygen Atmosphere. Org. Prep. Proced. Int. 2009, 41, 237–242.

(272). Zhu M; Fu W; Zou G; Xun C; Deng D; Ji B An Efficient Synthesis of 2-Trifluoromethyl Quinolines via Gold-Catalyzed Cyclization of Trifluoromethylated Propargylamines. J. Fluorine Chem. 2012, 135, 195–199.

(273). Marien N; Verniest G Gold(I)-Catalyzed Synthesis of Dihydrodibenzoquinolizinium Salts. Adv. Synth. Catal. 2017, 359, 1996–2000.

(274). Gasparrini F; Giovannoli M; Misiti D; Natile G; Palmieri G Gold(III) Catalyzed Oxidation of Sulfides to Sulfoxides by Nitric Acid under Phase-Transfer Conditions: A New Synthesis of Sulfoxides. Tetrahedron 1983, 39, 3181–3184.

(275). Yuan Y; Bian Y Gold(III) Catalyzed Oxidation of Sulfides to Sulfoxides with Hydrogen Peroxide. Tetrahedron Lett. 2007, 48, 8518–8520.

(276). Shi F; Deng Y First Gold(I) Complex-Catalyzed Oxidative Carbonylation of Amines for the Syntheses of Carbamates. Chem. Commun. 2001, 443–444.

(277). Ni M; Zhang Y; Gong T; Feng B Gold-Oxazoline Complex-Catalyzed Cross-Dehydrogenative Coupling of Glycine Derivatives and Alkenes. Adv. Synth. Catal. 2017, 359, 824–831.

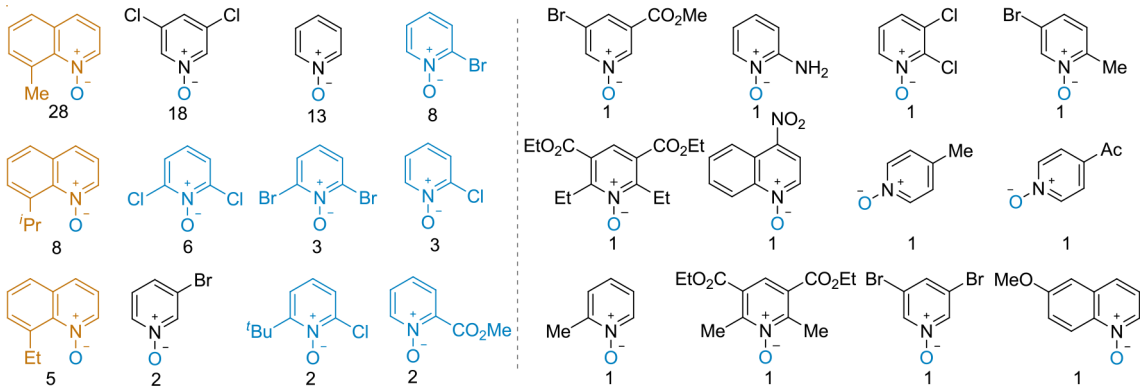
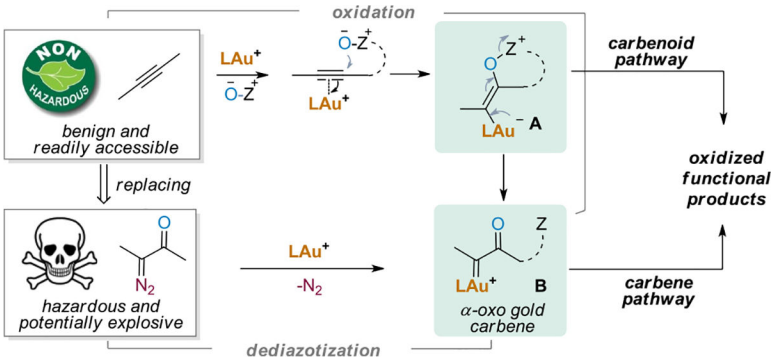


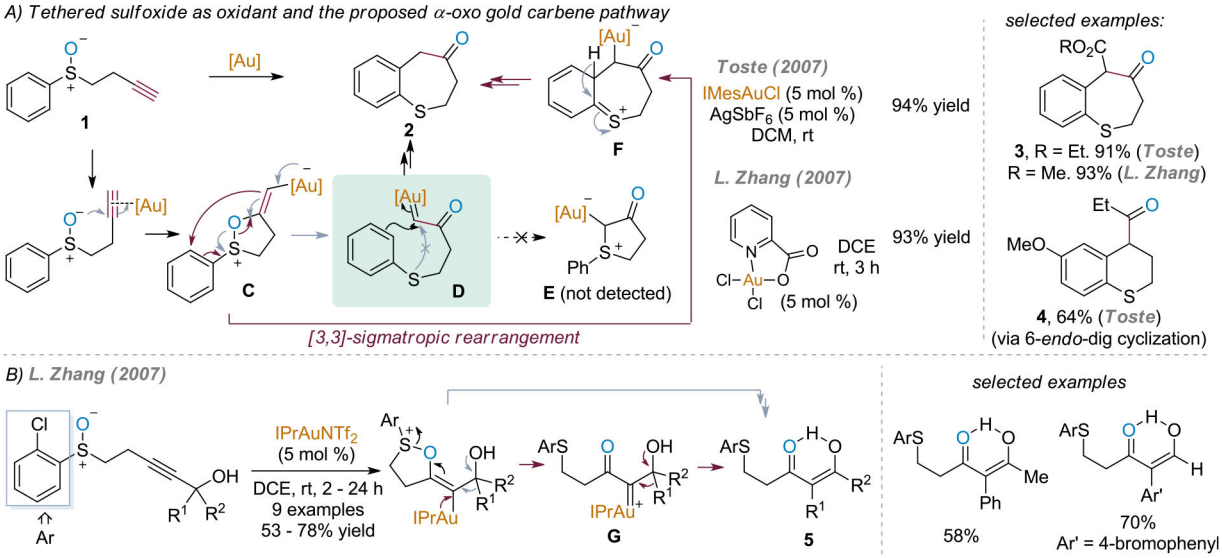
Figure 1.

Commonly employed *N*-heteroarene *N*-oxides and their frequencies of occurrence in scope studies in reported oxidative gold catalyses (110 occurrences out of 102 papers).



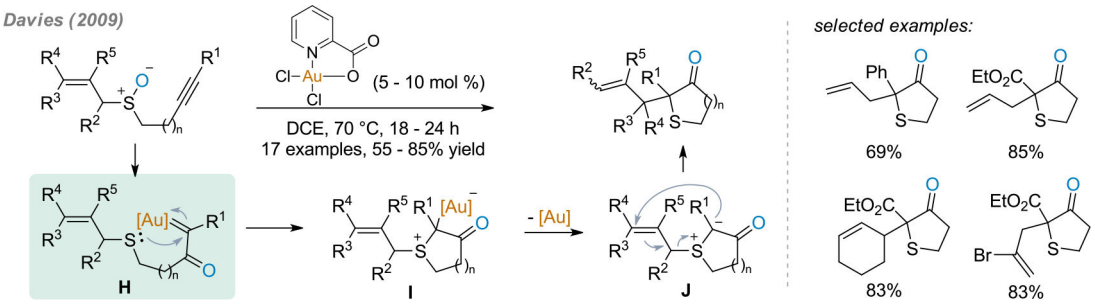
Scheme 1.

Au-Catalyzed Oxidation of Alkynes by Nucleophilic Oxidants: General Reactivity and Comparison to Dediazotization



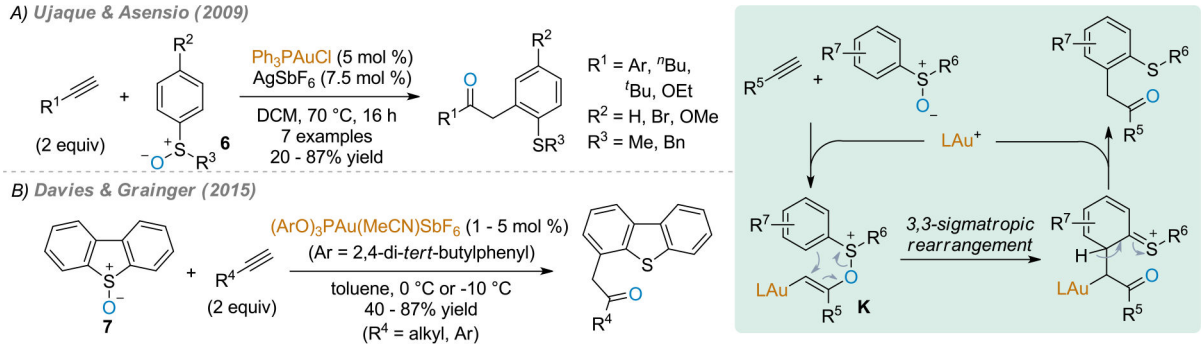
Scheme 2.

Sulfoxides as Oxidants: Early Studies and Mechanistic Investigations



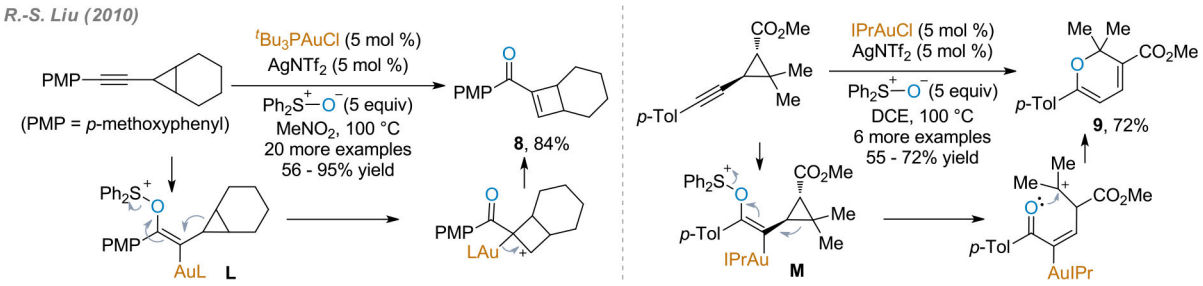
Scheme 3.

Generation of Sulfur Ylides through Gold-Catalyzed Oxidation of Alkynes by a Tethered Sulfoxide



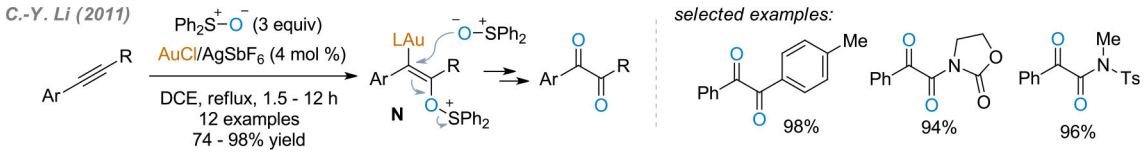
Scheme 4.

Gold-Catalyzed Intermolecular Oxyarylation of Alkynes by Sulfoxides



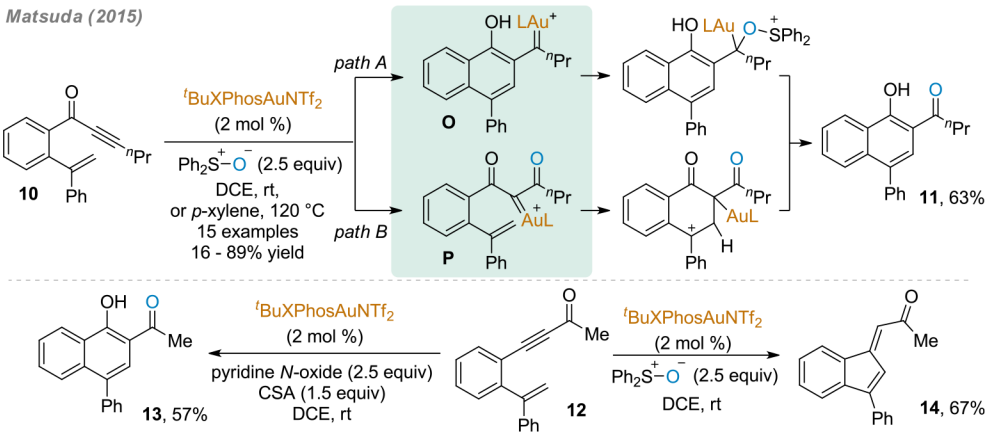
Scheme 5.

Carbenoid Pathways of the Sulfoxide–Alkyne Adduct Involving Ring Expansion/Opening



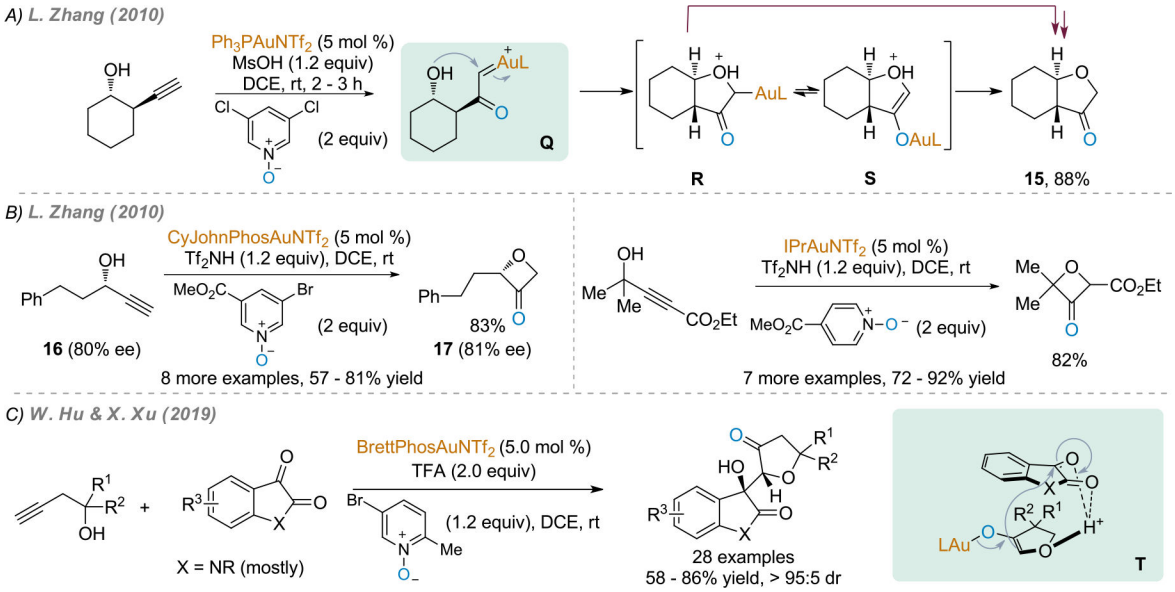
Scheme 6.

Synthesis of Benzil Derivatives via Double Oxidation of Alkynes and Ynamides



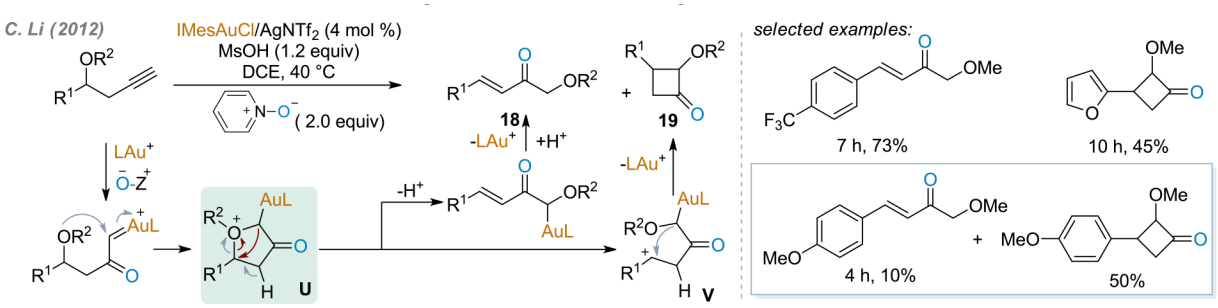
Scheme 7.

Synthesis of 2-Acyl-1-naphthols via Gold-Catalyzed Oxidative Cyclization of 2-Alkenylphenyl Alkynyl Ketones

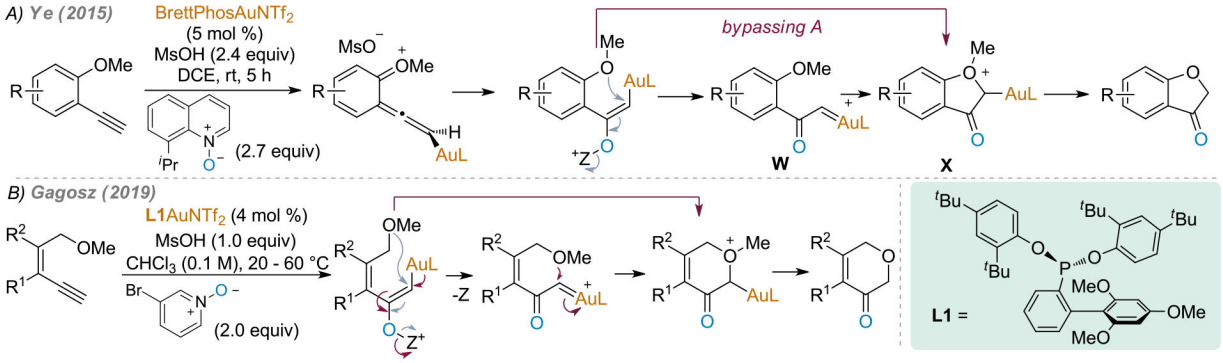


Scheme 8.

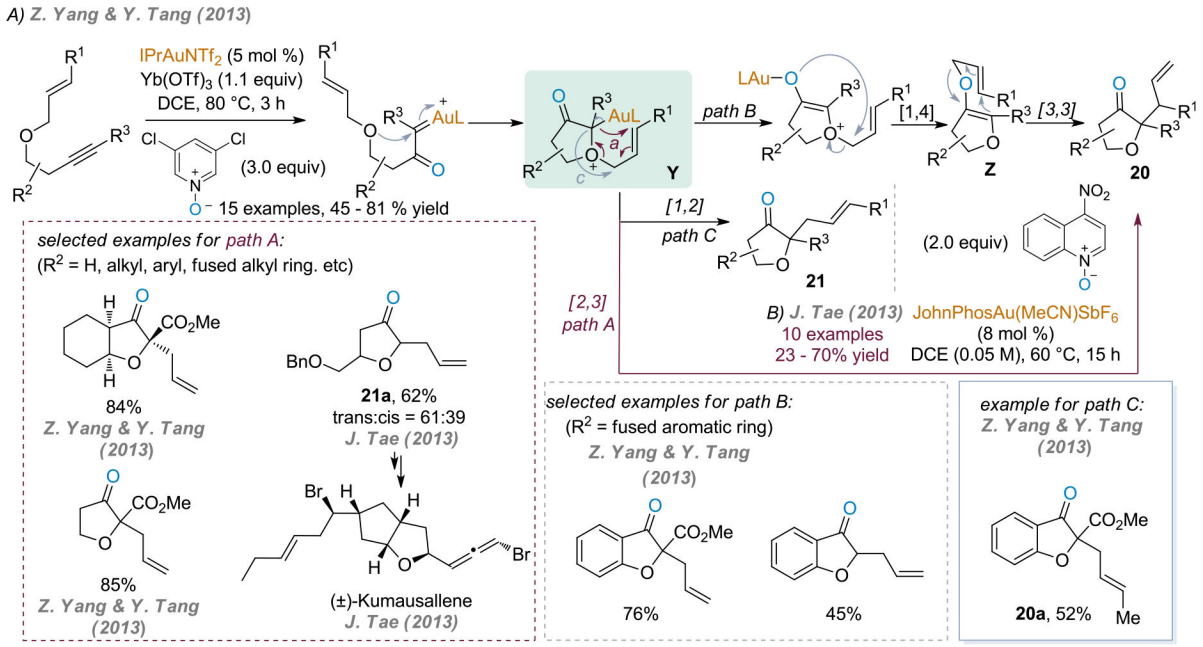
Intramolecular O–H Insertion of α-Oxo Gold Carbenes



Scheme 9.
Gold-Catalyzed Oxidative Rearrangement of Homopropargylic Ethers

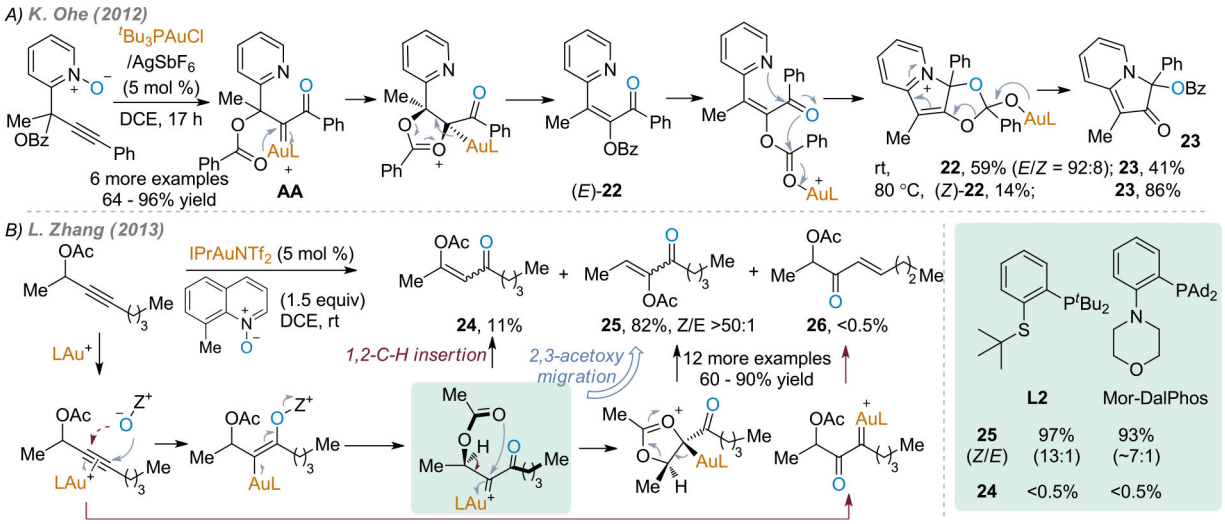


Scheme 10.
Gold-Catalyzed Oxidative Demethylative Cyclization



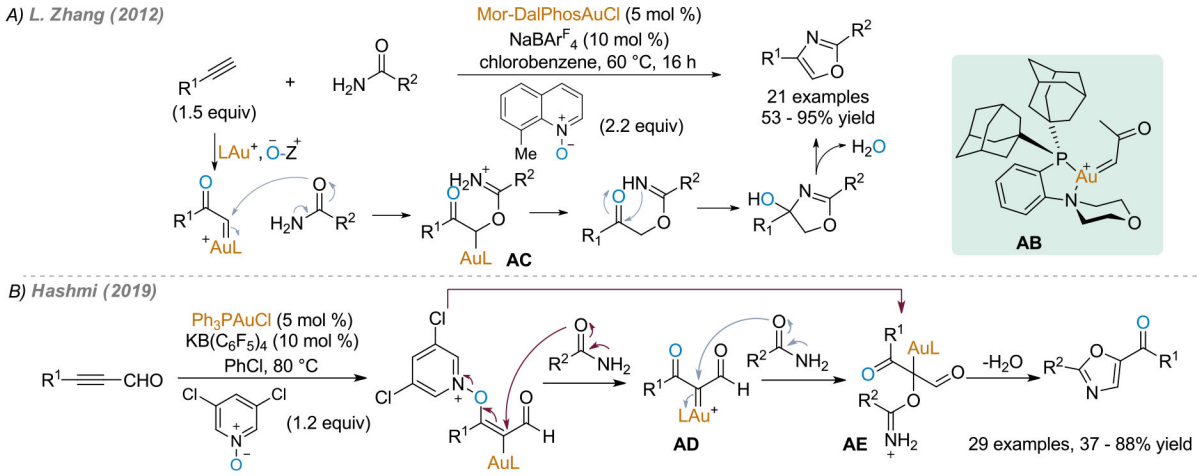
Scheme 11.

Rearrangements of Oxidatively Generated Allyl Oxonium Ions



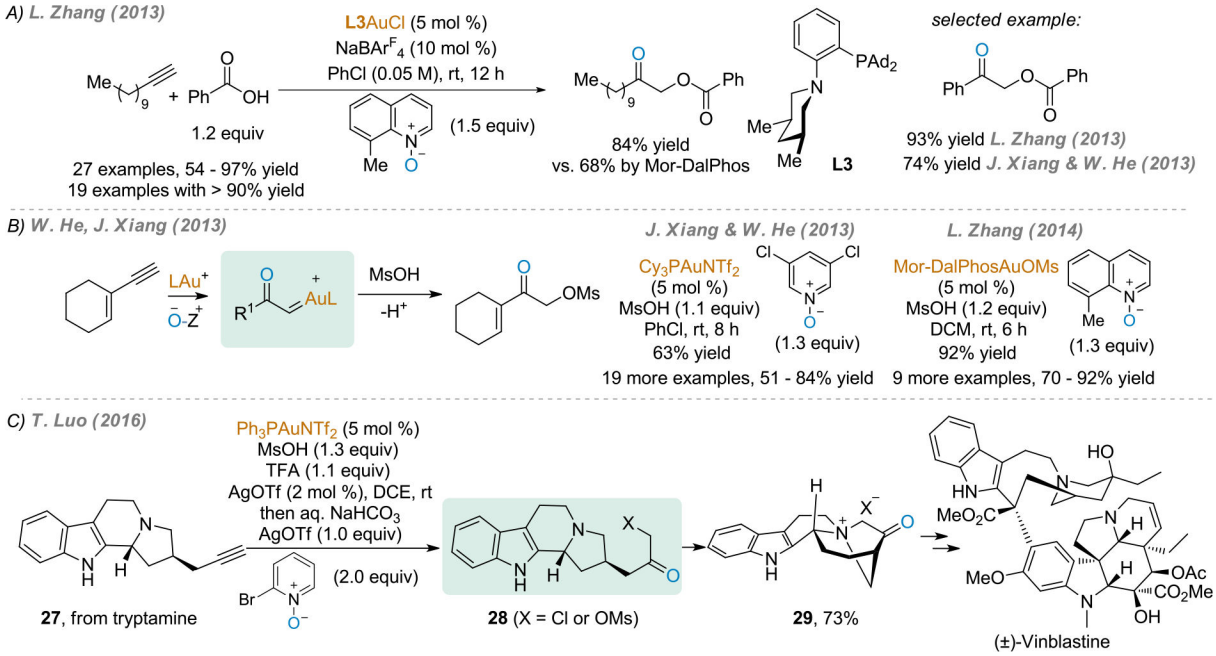
Scheme 12.

Intramolecular Trapping by Carbonyl Group en Route to [2,3]-Acyloxy Migration



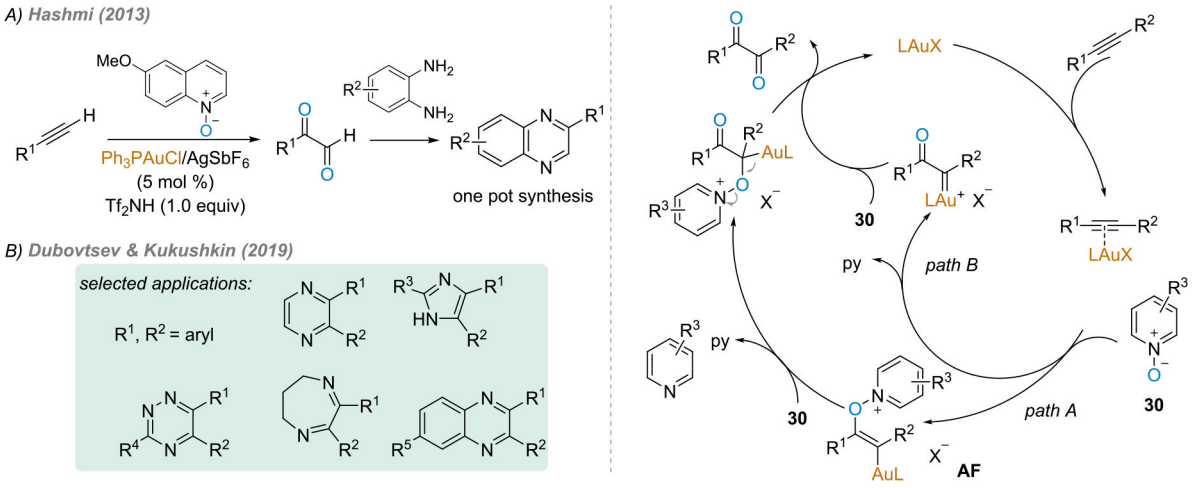
Scheme 13.

Intermolecular Trapping of the α-Oxo Gold Carbene Intermediate with Amides

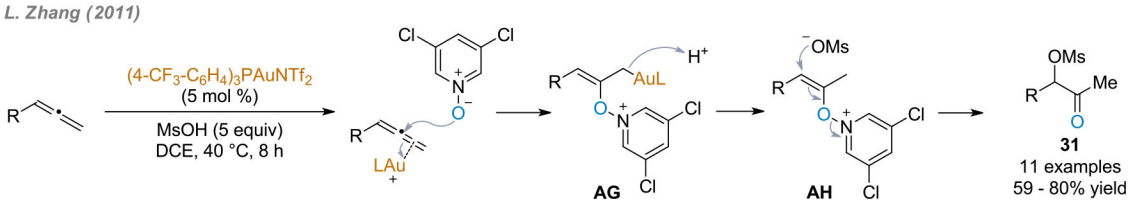


Scheme 14.

Intermolecular Trapping of the α-Oxo Gold Carbene Intermediate with Acid

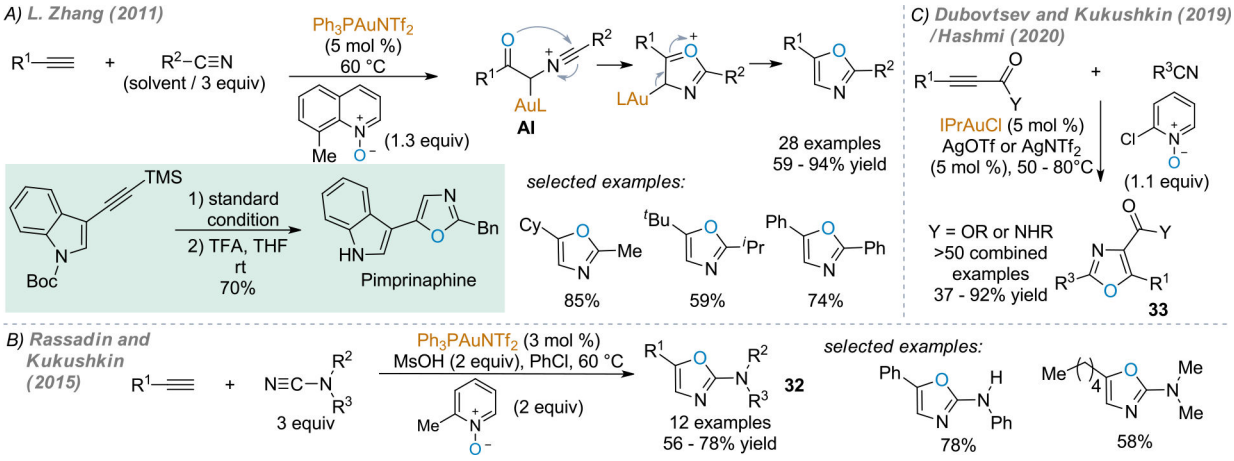


Scheme 15.
Gold-Catalyzed Double Oxidation of Alkynes



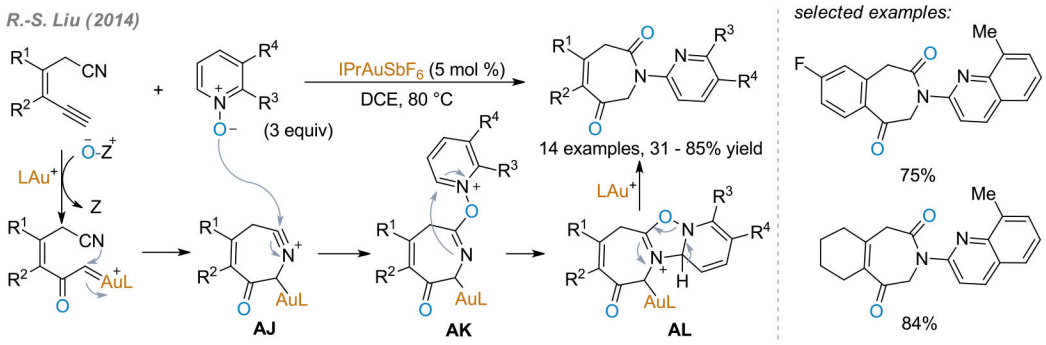
Scheme 16.

Gold-Catalyzed Regioselective Oxidation of Allenes: Formation of α-Methanesulfonyloxy Methyl Ketones



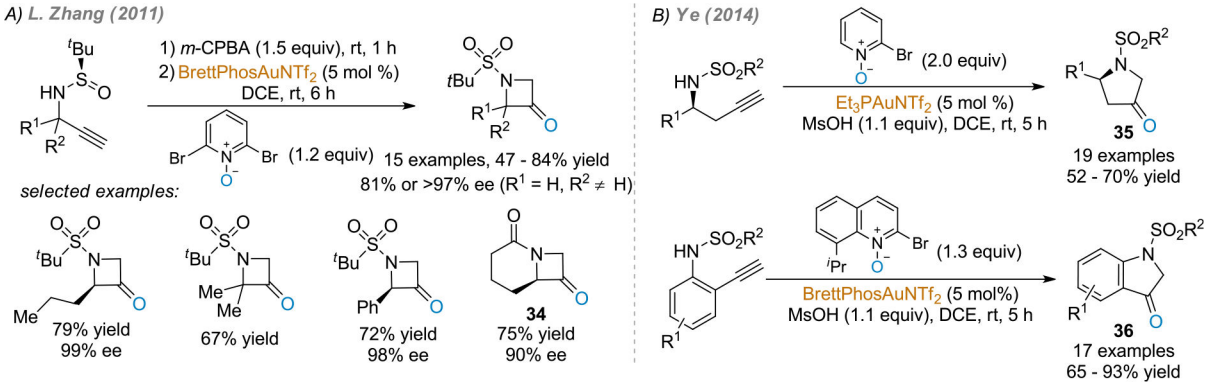
Scheme 17.

Intermolecular Reaction of α-Oxo Gold Carbenes with Nitriles



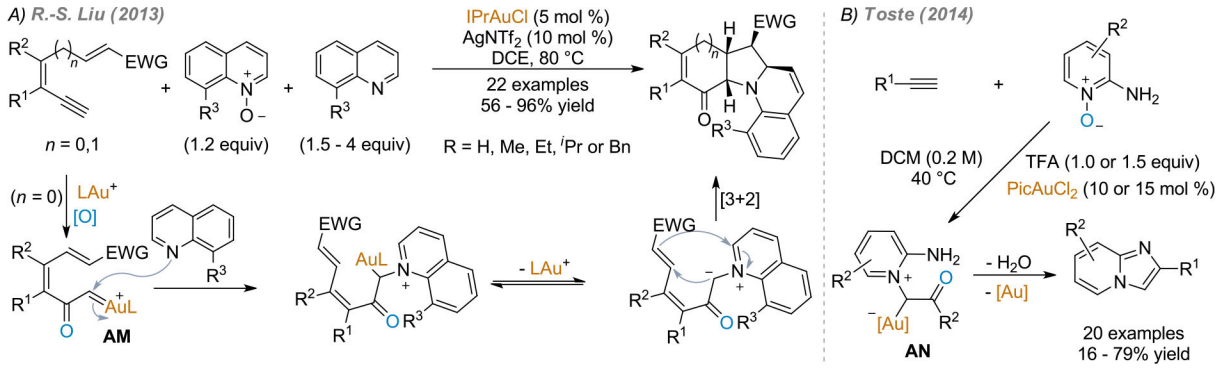
Scheme 18.

Intramolecular Trapping of α-Oxo Gold Carbenes by Nitriles



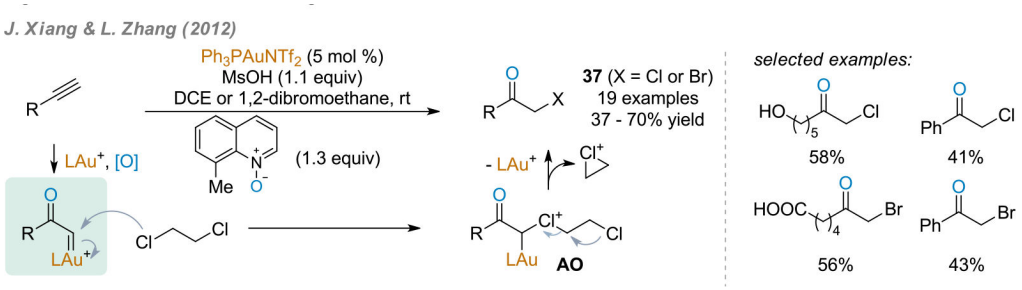
Scheme 19.

Intramolecular Trapping of α-Oxo Gold Carbene by Sulfonamide



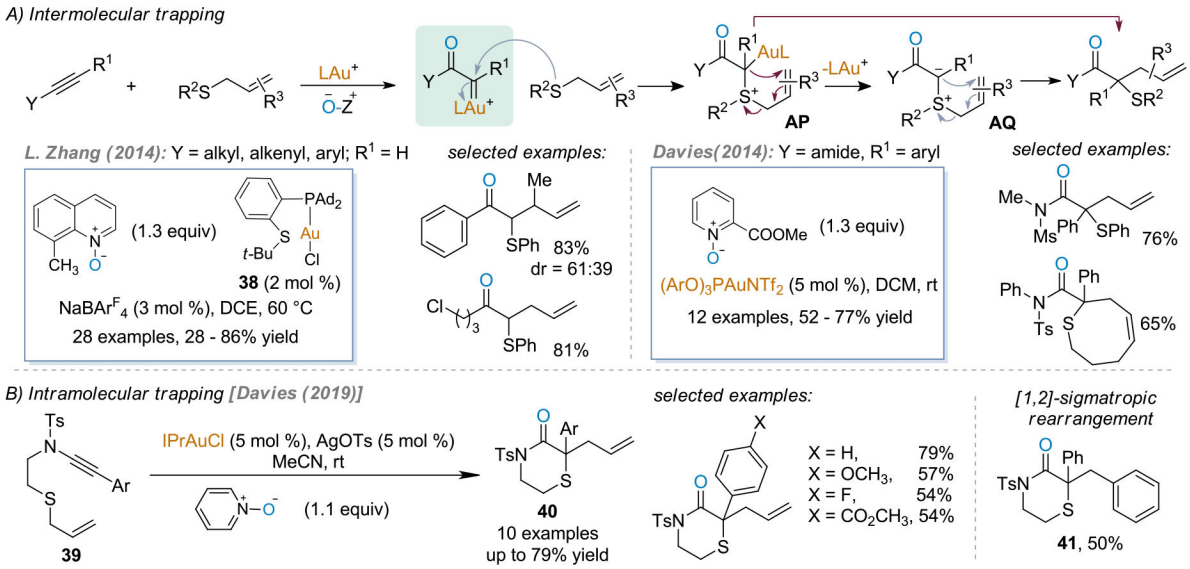
Scheme 20.

Intramolecular Reaction of the α-Oxo Gold Carbenoid with the Pyridine/Quinoline Byproduct



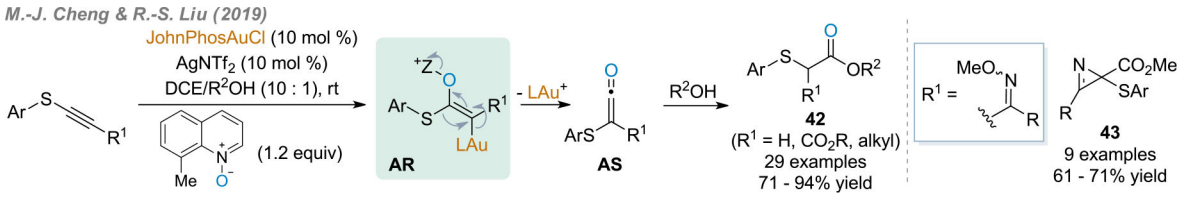
Scheme 21.

Halogen Abstraction from Halogenated Solvents by an α-Oxo Gold Carbene Intermediate



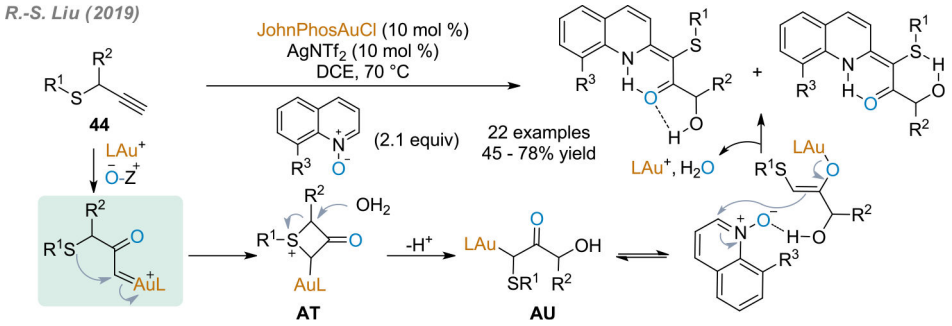
Scheme 22.

Reaction of α-Oxo Gold Carbenes with Allylic Sulfides and Subsequent Sigmatropic Rearrangement

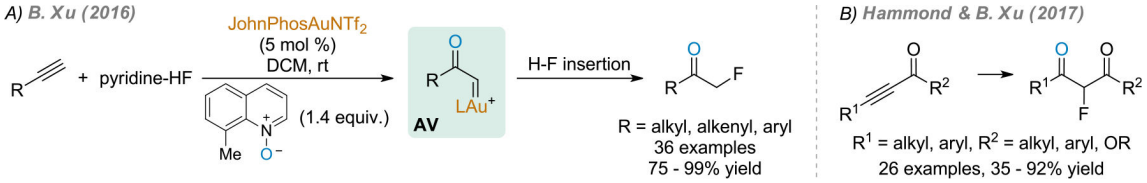


Scheme 23.

Gold-Catalyzed Oxidation of Thioalkynes to Form Arylthio Ketenes

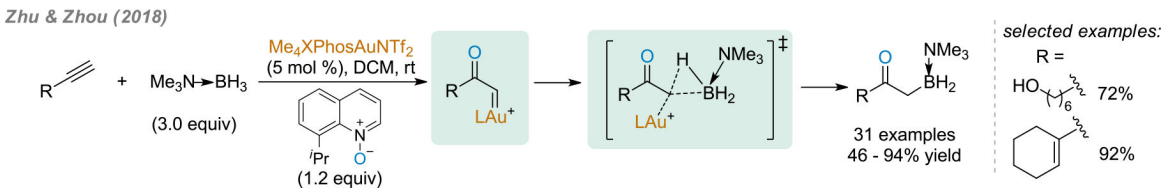


Scheme 24.
Gold-Catalyzed Oxidation of Propargyl Aryl Sulfides

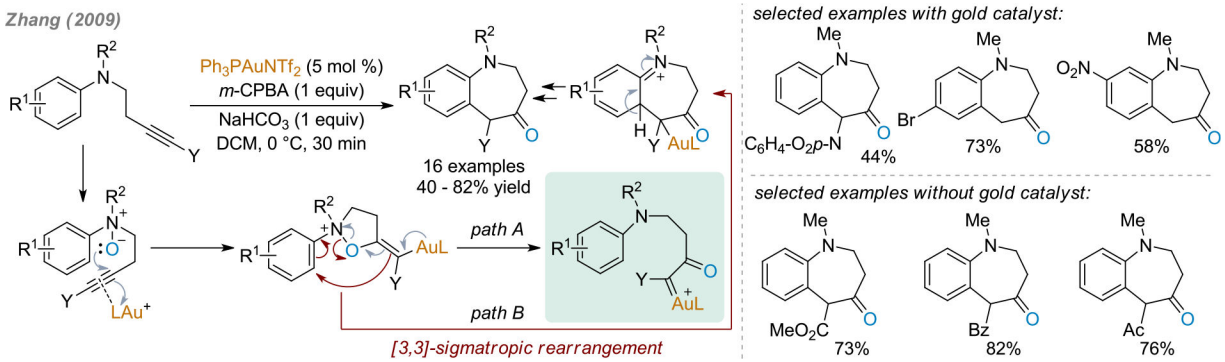


Scheme 25.

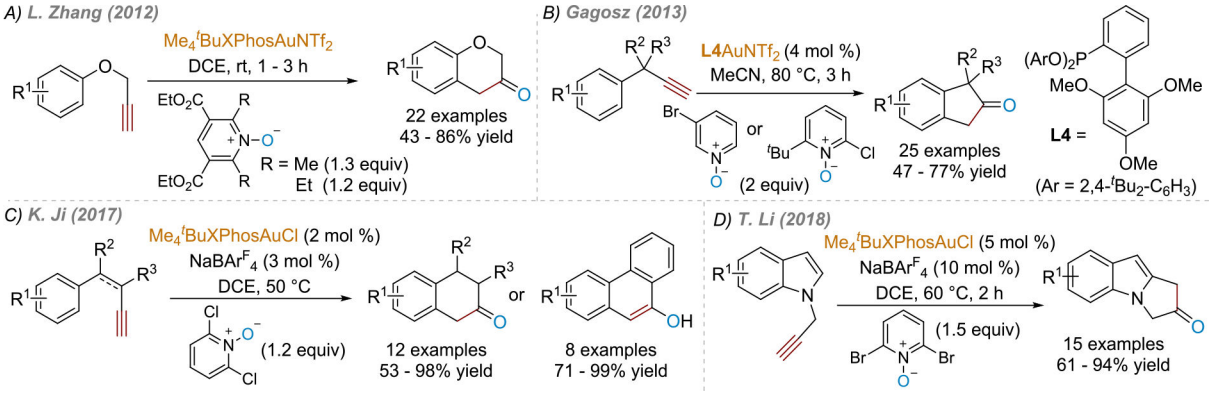
H–F Insertion into α-Oxo Gold Carbenes



Scheme 26.
B–H Insertion into α-Oxo Gold Carbenes

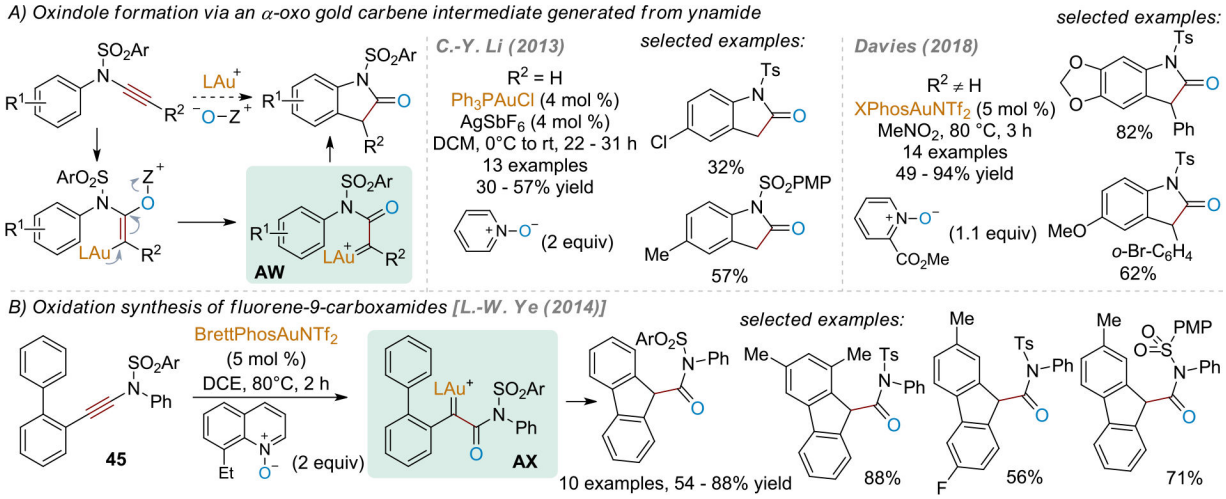


Scheme 27.
Gold-Catalyzed Cycloisomerization of Alkynylaniline *N*-Oxide



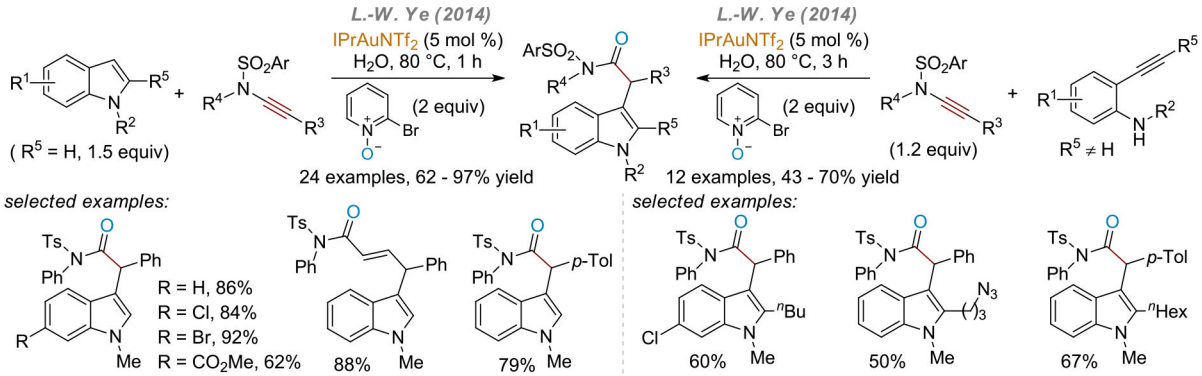
Scheme 28.

Friedel–Crafts Reaction of α-Oxo Gold Carbenes Generated from Terminal Alkynes



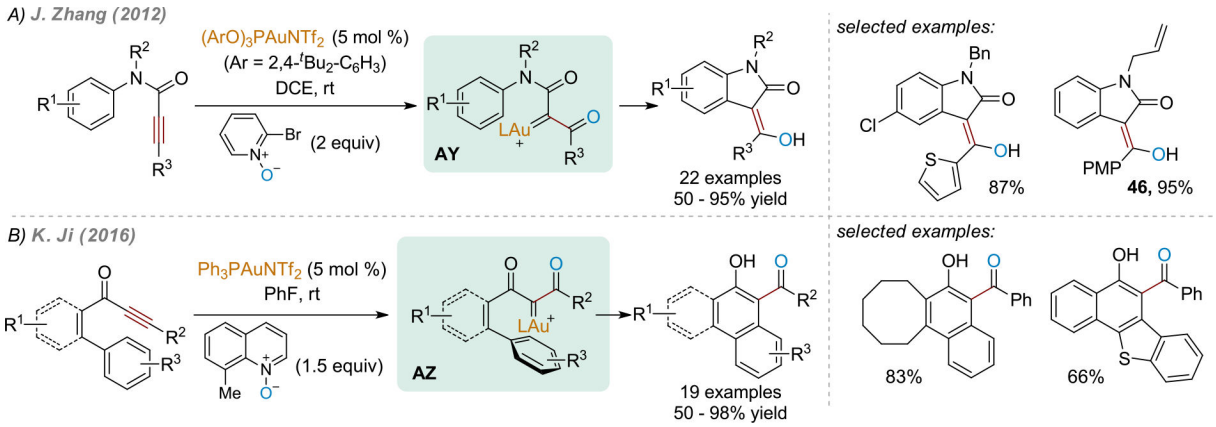
Scheme 29.

Intramolecular Friedel–Crafts Reaction of α-Oxo Gold Carbenes Generated from Ynamides

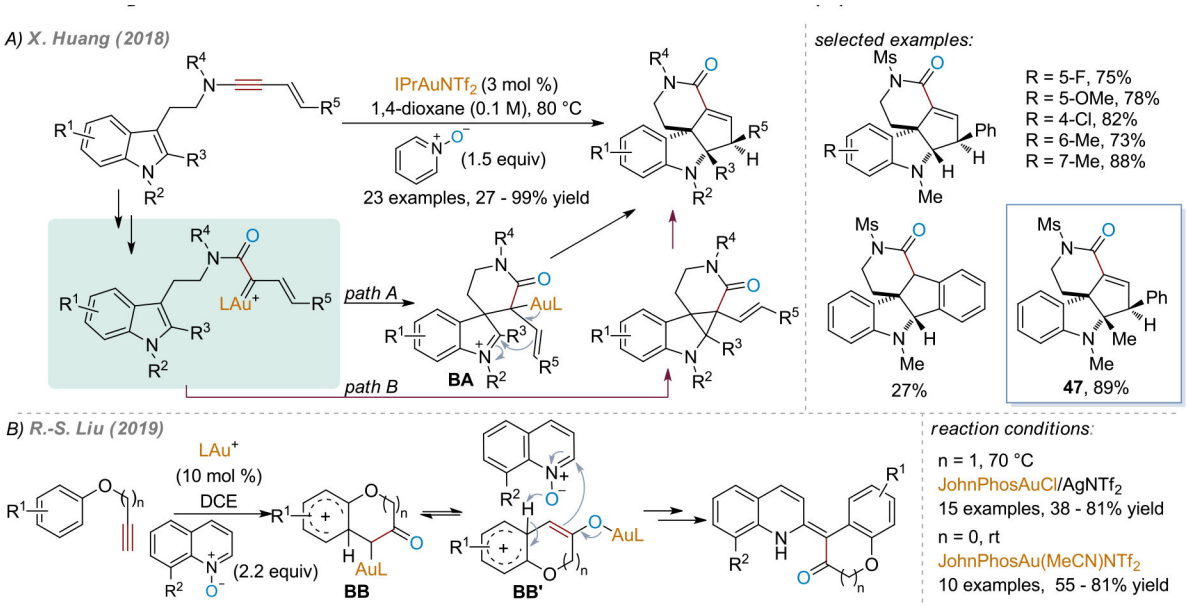


Scheme 30.

In-Water Generation of α-Oxo Gold Carbenes and Their Intermolecular Friedel–Crafts Reaction with Indoles

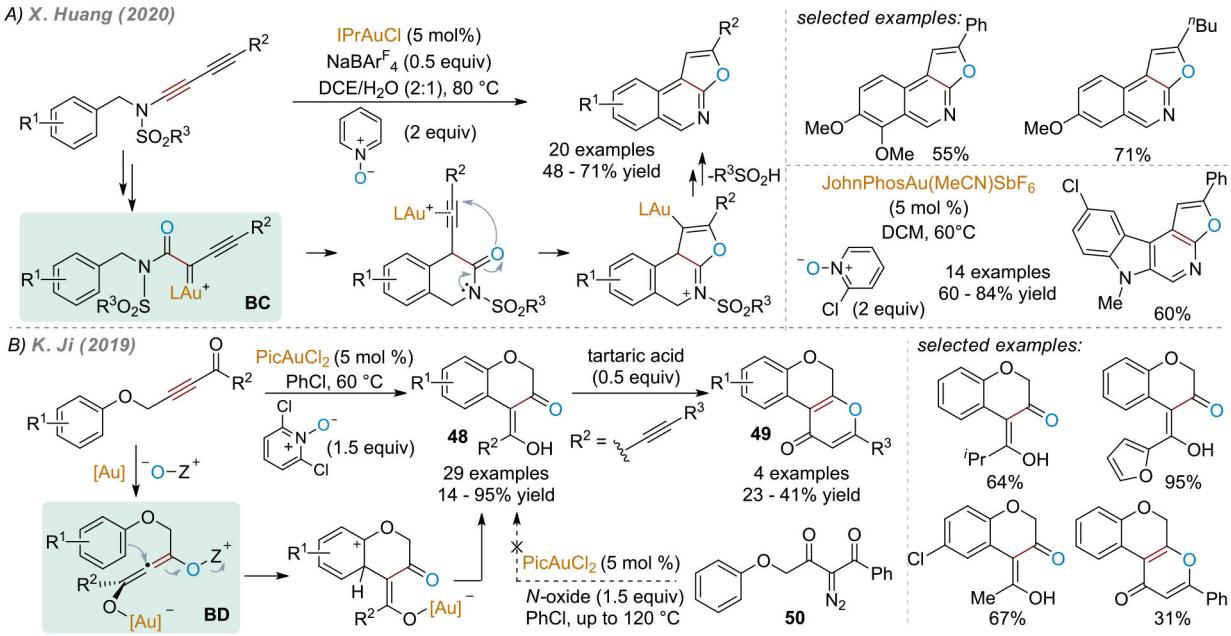


Scheme 31.
Friedel–Crafts Reaction of 1,3-Dioxo-2-gold Carbenes



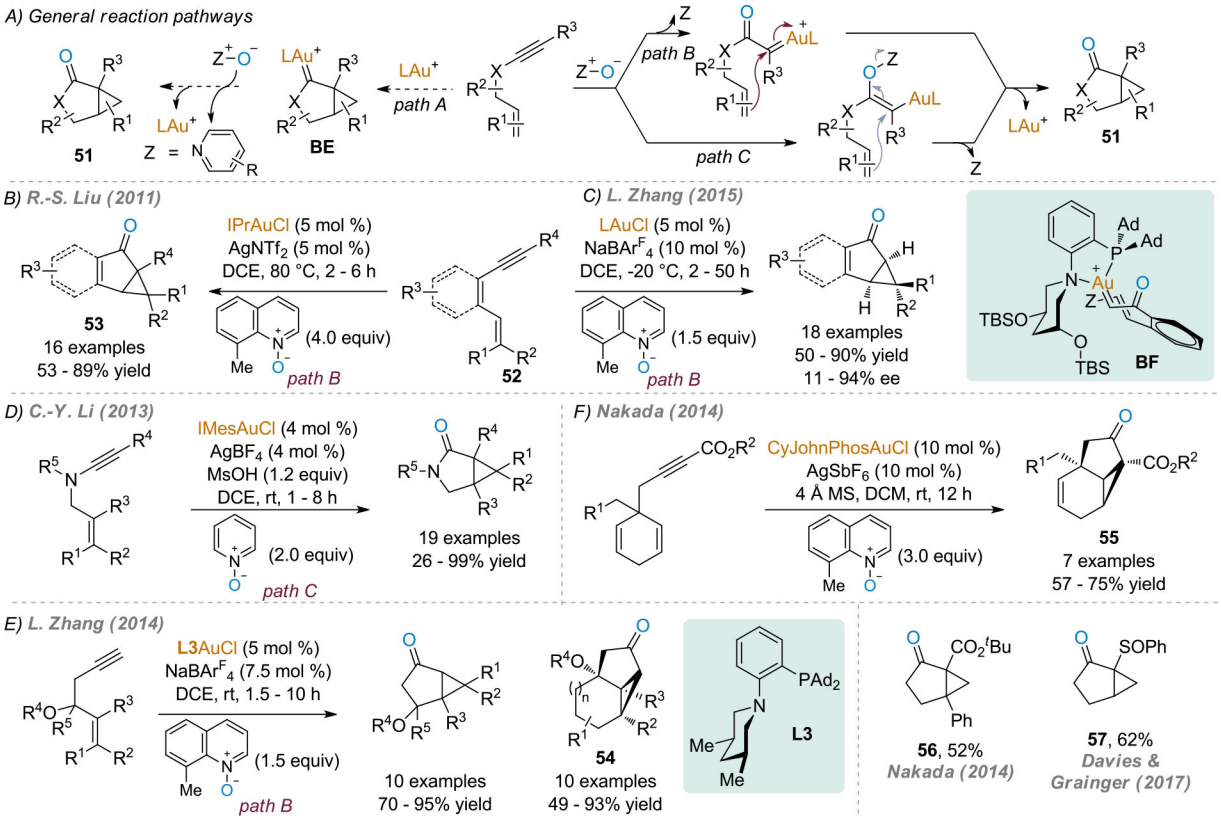
Scheme 32.

Interception of the Friedel–Crafts Reaction Intermediate to Access Polycyclic Structures



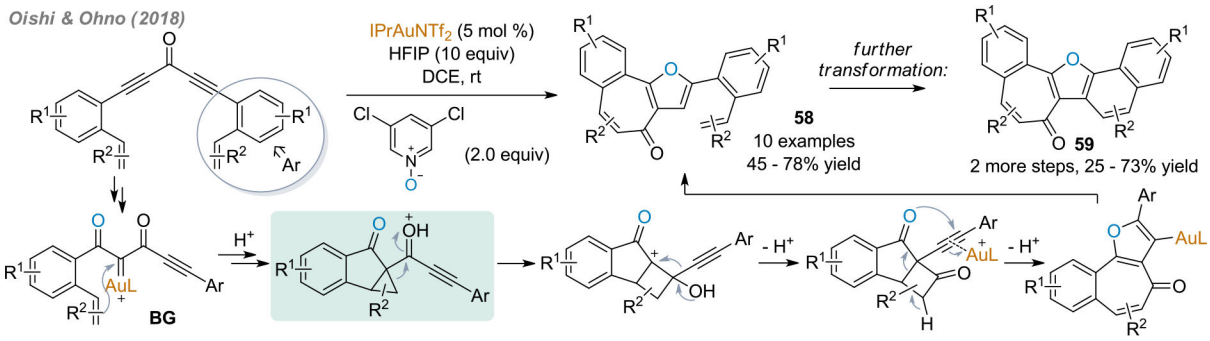
Scheme 33.

One-Pot Cascade Reaction Involving the Friedel–Crafts Reaction of α-Oxo Gold Carbenes



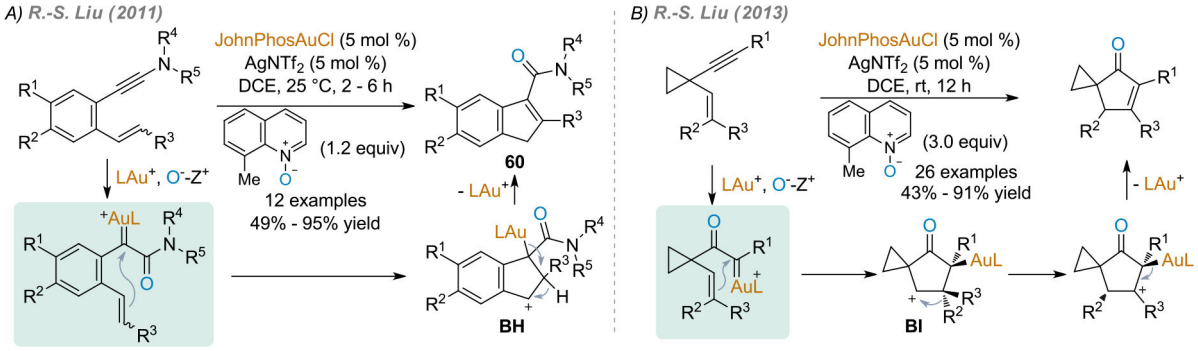
Scheme 34.

Oxidative Cyclopropanation of 1,5-Enynes

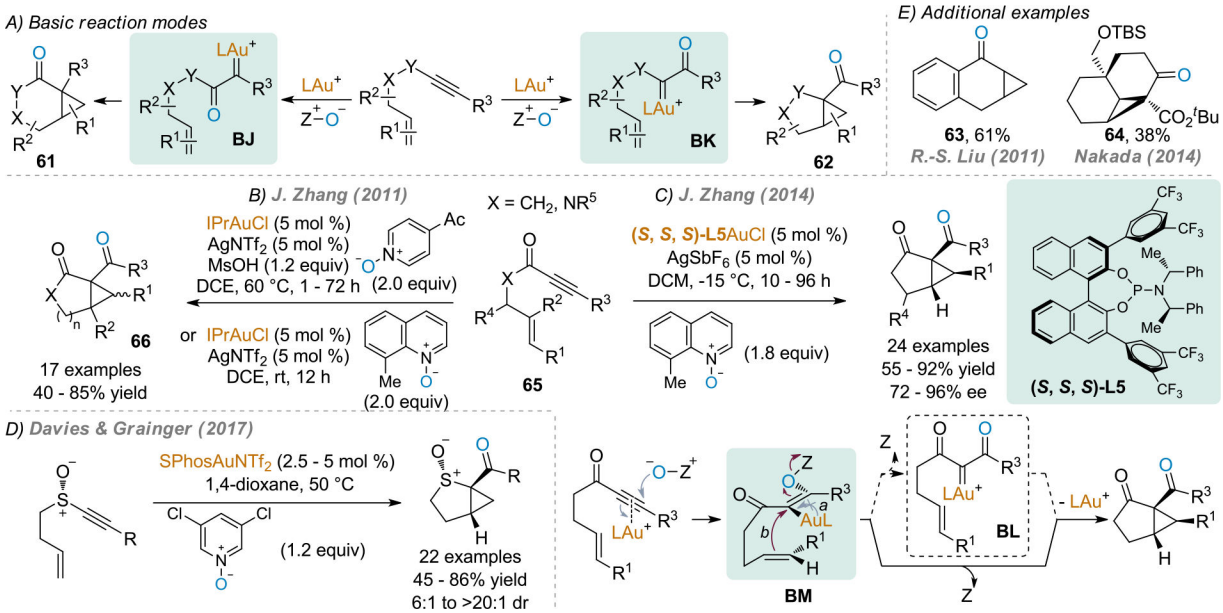


Scheme 35.

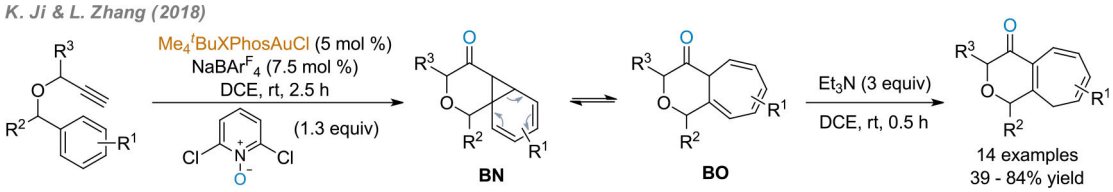
Formation of Tropone-Fused Furans via Gold-Catalyzed Oxidative Cascade Cyclization



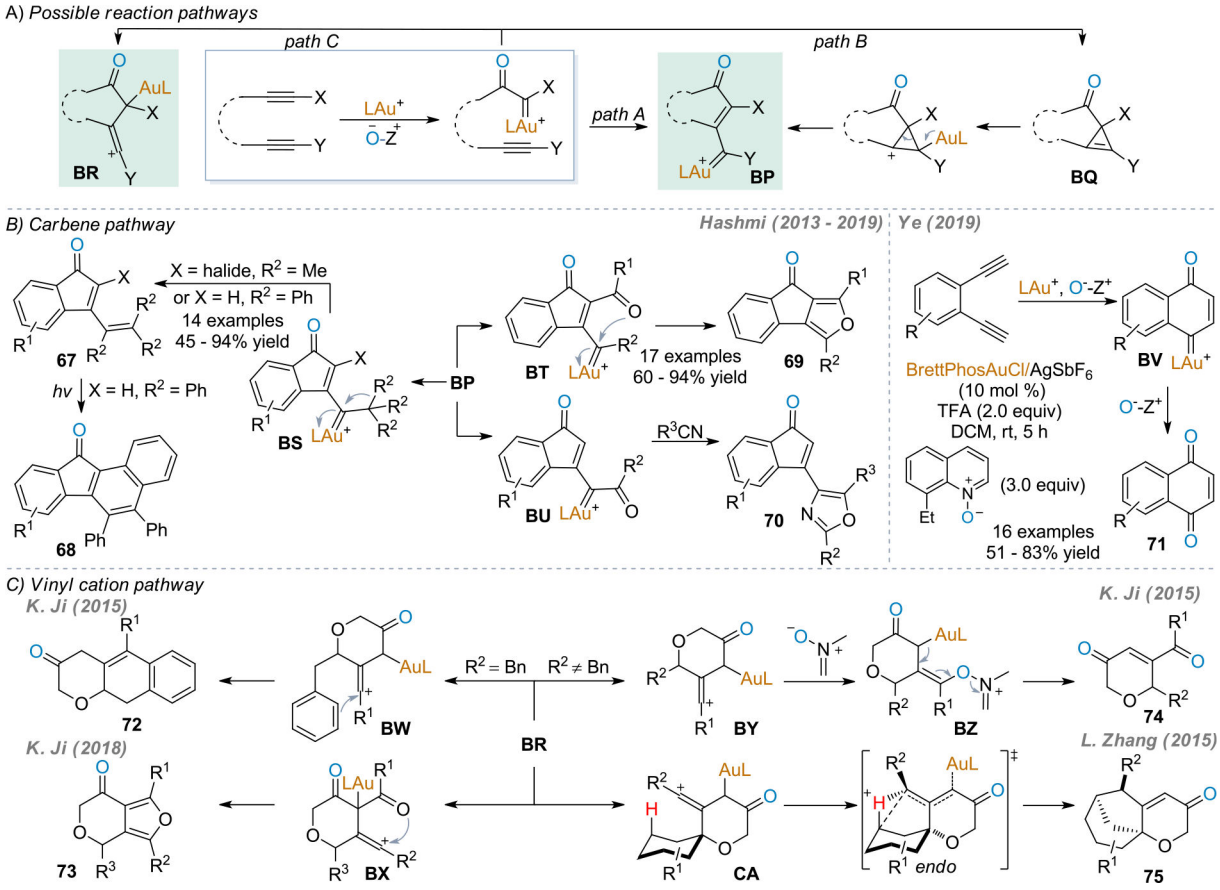
Scheme 36.
Gold-Catalyzed Oxidative Cyclization of Enynes



Scheme 37.
Cyclopropanation of 1,6-Enynes

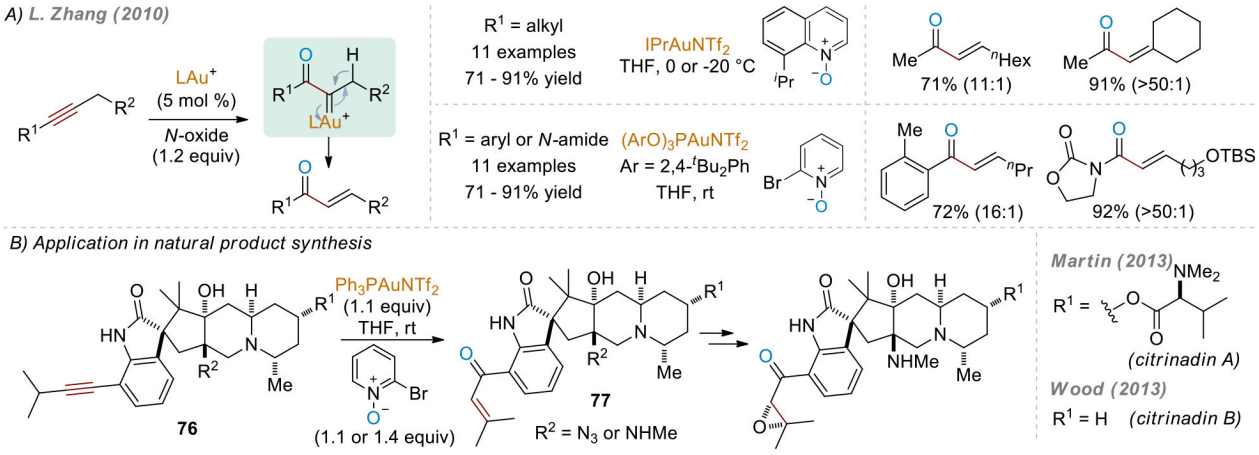


Scheme 38.
Oxidative Gold(I)-Catalyzed Cyclopropanation of Benzene Ring



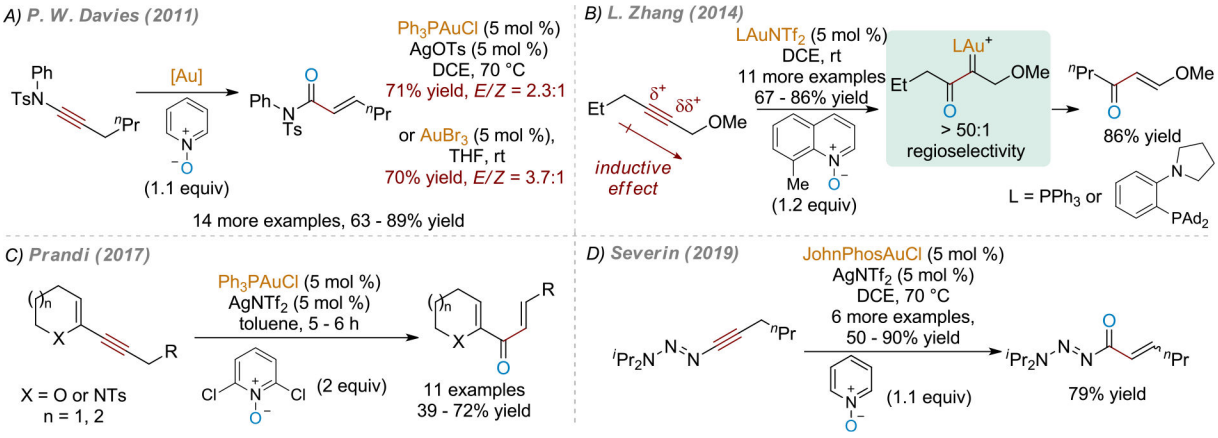
Scheme 39.

Reaction of Carbene/Carbenoid Intermediates with Tethered C–C Triple Bonds



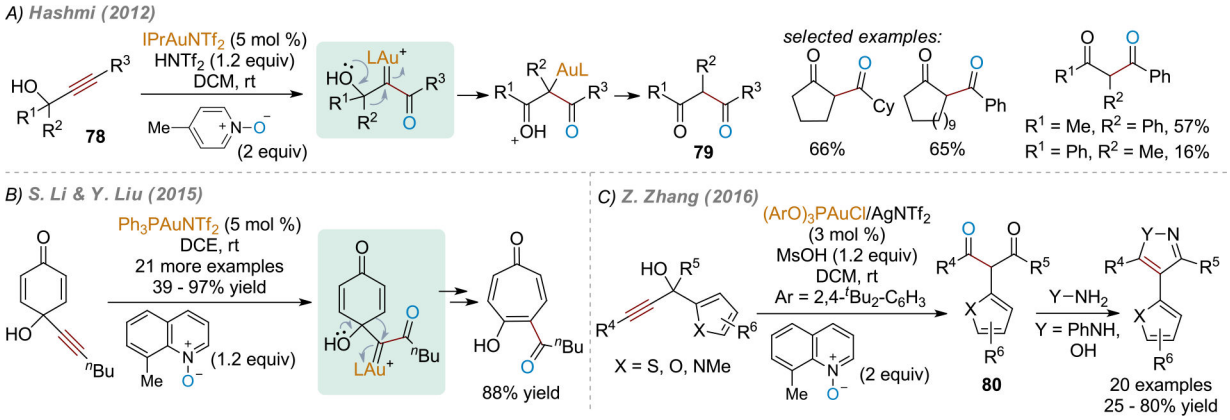
Scheme 40.

1,2-C–H Insertion by Oxidatively-Generated Gold Carbenes: Early Study and Application in Total Synthesis



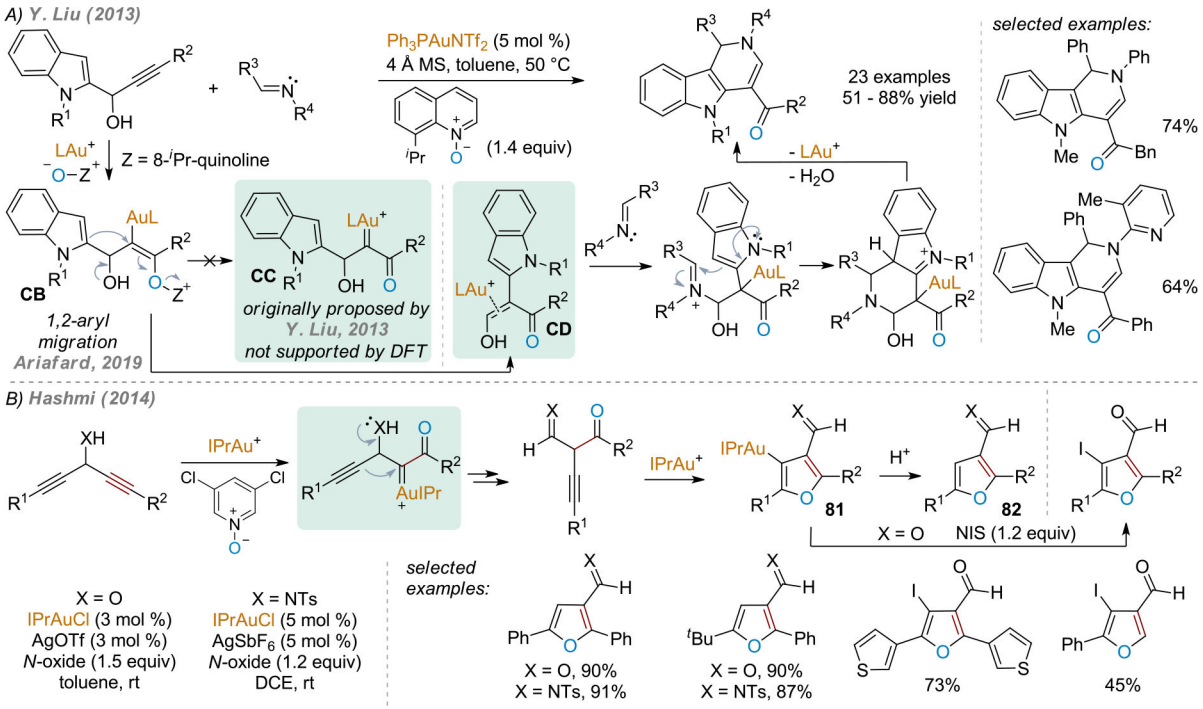
Scheme 41.

Further Studies of 1,2-C–H Insertion in Oxidative Gold Catalysis



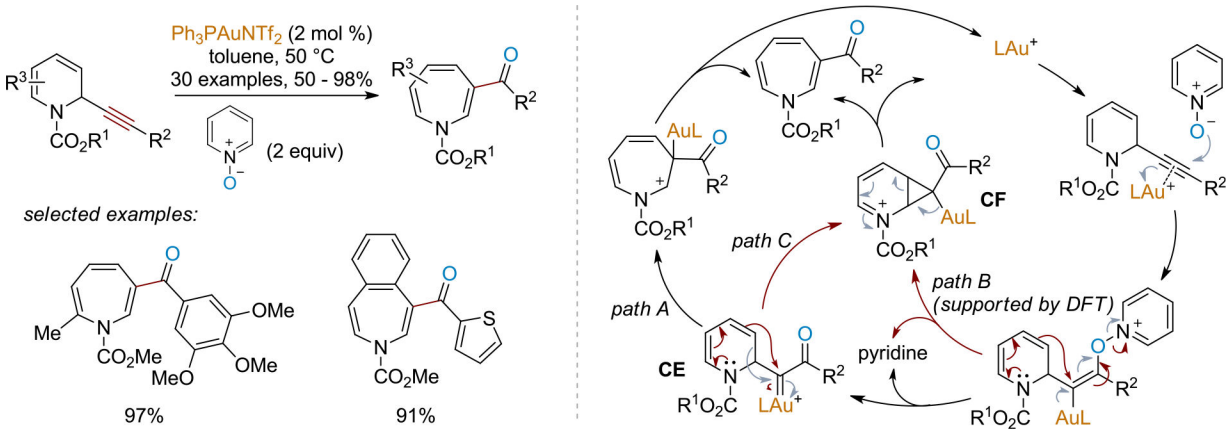
Scheme 42.

Gold-Catalyzed Oxidation of Tertiary Propargylic Alcohols Involving Semi-Pinacol-Type Rearrangement



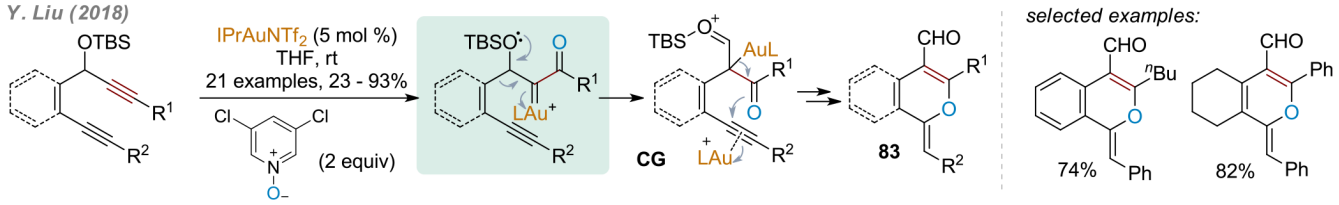
Scheme 43.

More Studies of Gold-Catalyzed Oxidative 1,2-C–C Insertion Reactions



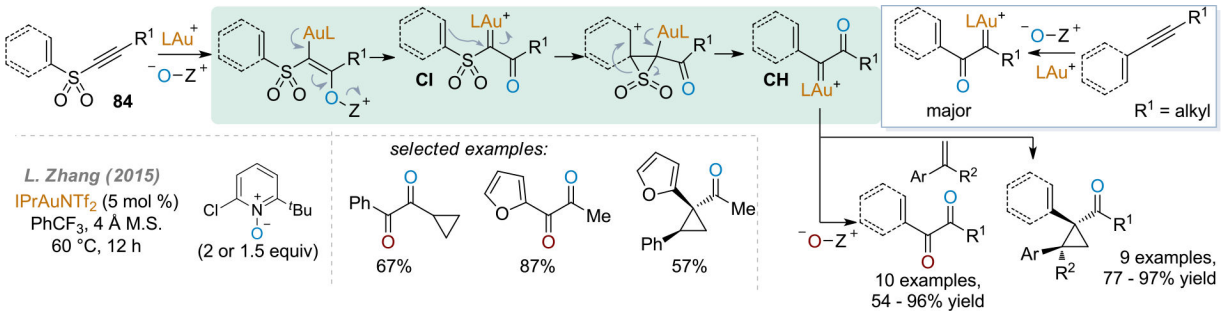
Scheme 44.

Ring Expansion of 1,2-Dihydropyridines to Access Functionalized Azepine Scaffolds



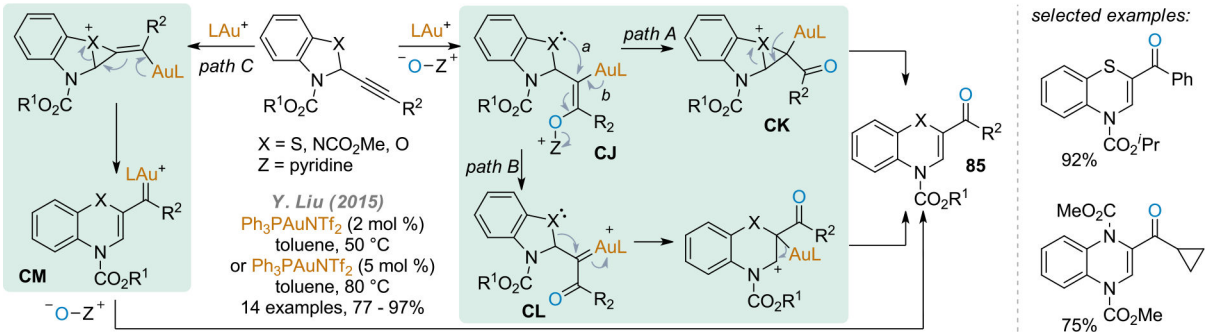
Scheme 45.

1,2-Enynyl/*o*-Alkynylaryl Migration in Gold-Catalyzed Oxidation of Propargylic Silyl Ethers



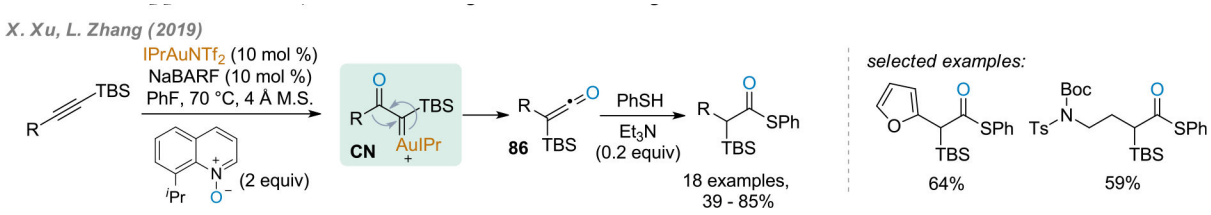
Scheme 46.

Desulfonylative 1,2-Aryl Migration to Access Regiochemically Disfavored α-Oxo Gold Carbenes



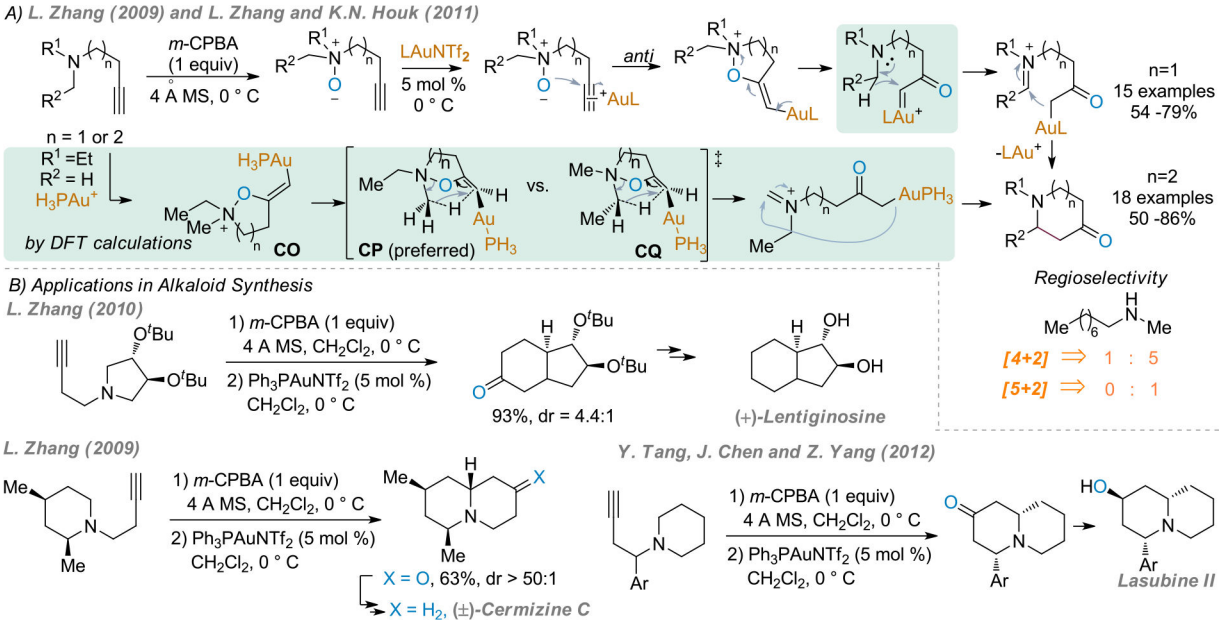
Scheme 47.

Ring Expansion of Alkynyl Heterocycles through 1,2-Insertion into a Carbon–Heteroatom Bond by Gold Carbene



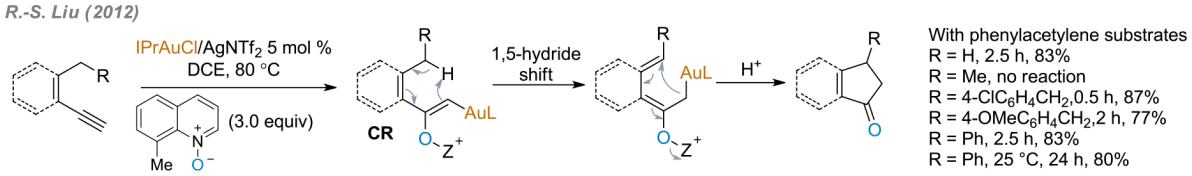
Scheme 48.

Facile Approach to Silylketenes through Wolff Rearrangement of Gold Carbenes



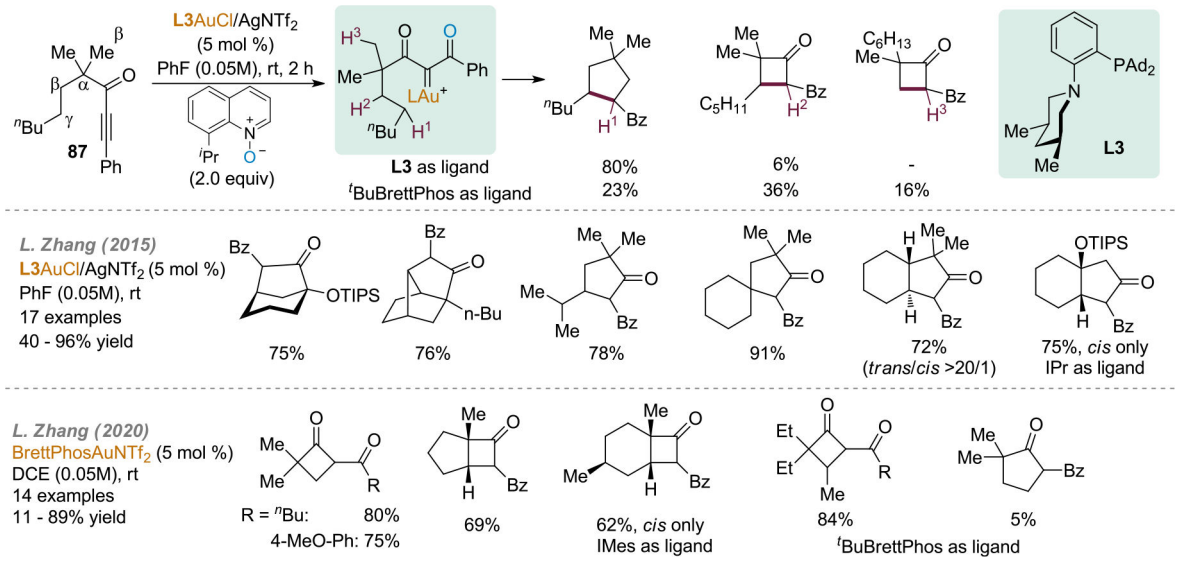
Scheme 49.

Intramolecular Oxidative Cyclization and Remote C–H Functionalization and Mechanistic Studies



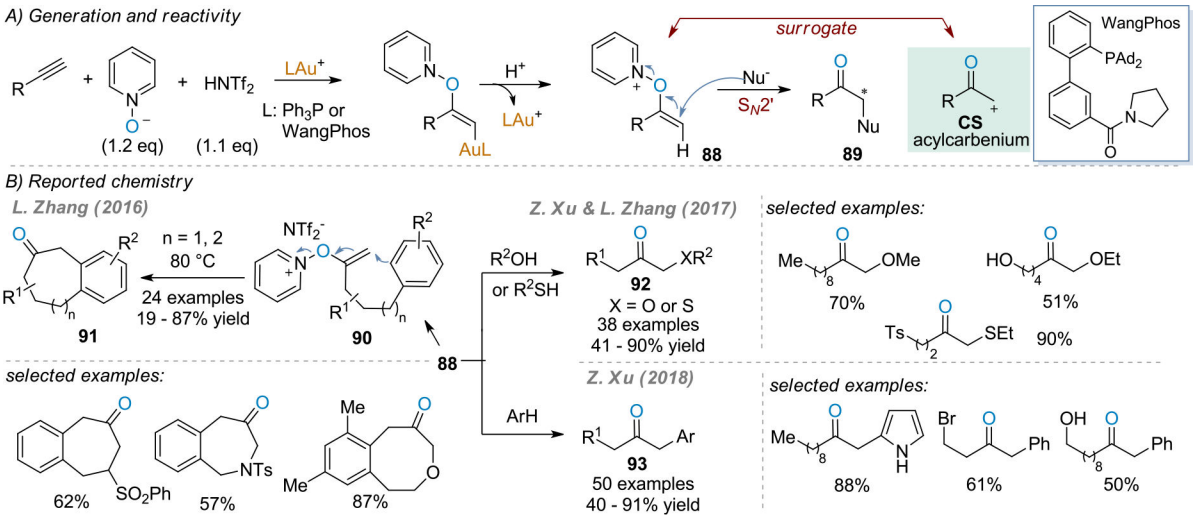
Scheme 50.

Gold-Catalyzed Oxidative Cyclizations of *cis*-3-En-1-ynes or *o*-Alkylphenylacetylenes



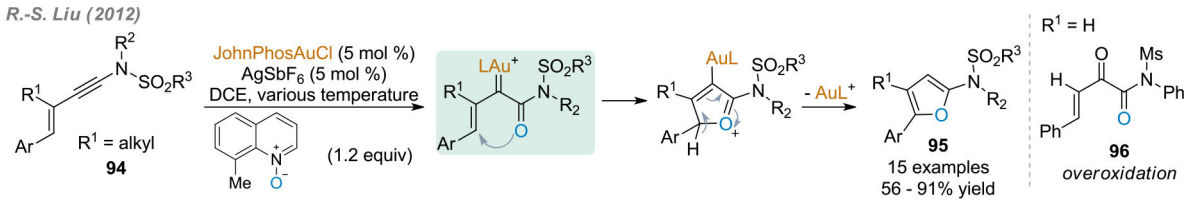
Scheme 51.

Intramolecular Gold Carbene Insertions into Inactivated C(sp^3)–H Bonds

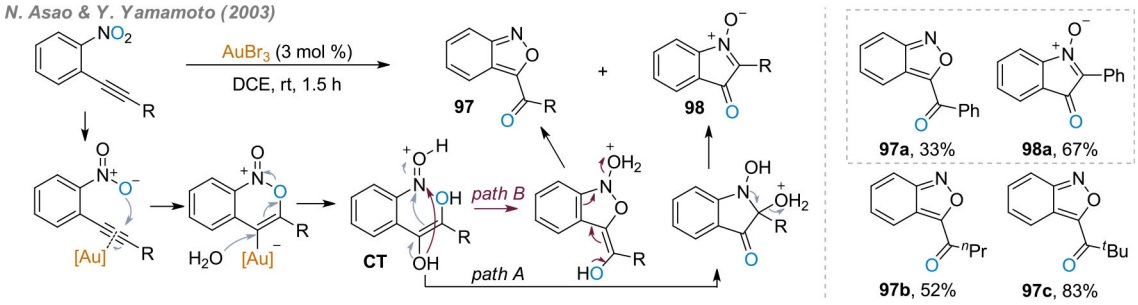


Scheme 52.

Reaction of *N*-Alkenoxy-N-heteroarenes Generated via Gold(I) Catalysis

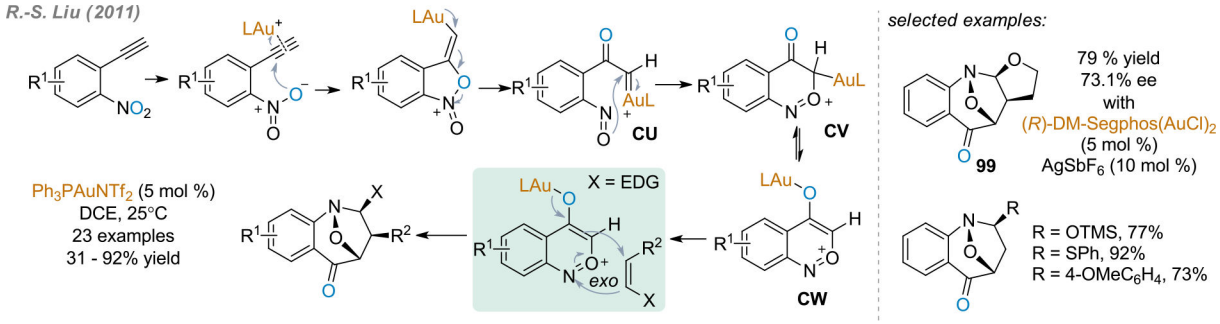


Scheme 53.
Gold(I)-Catalyzed Formal [4 + 1] Cycloadditions



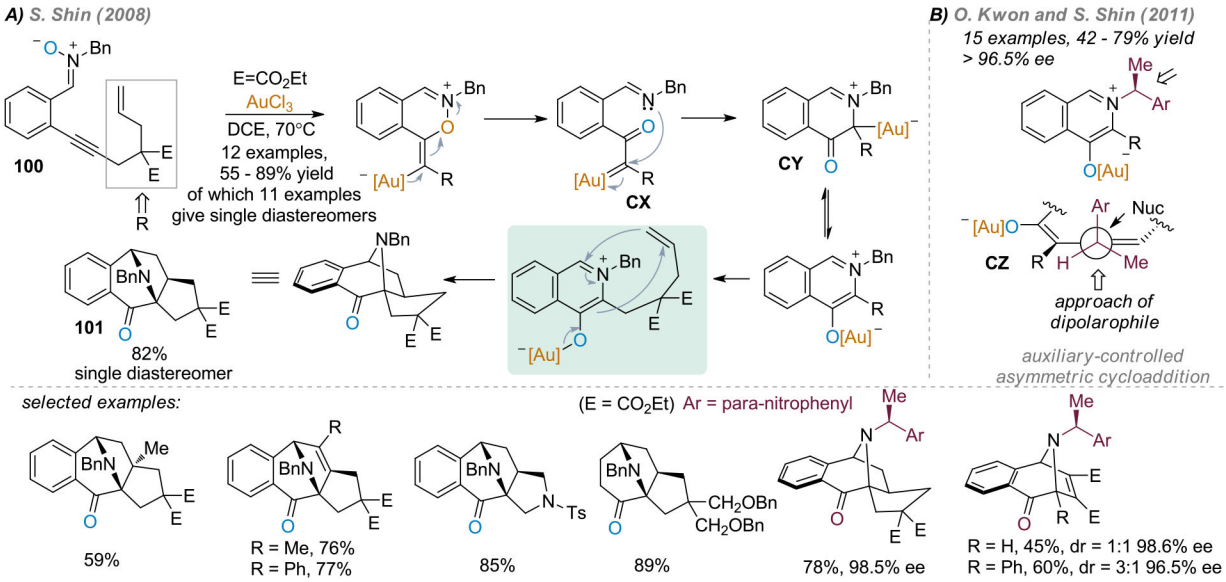
Scheme 54.

AuBr3-Catalyzed Oxidative Cyclization of *o*-Nitrophenylalkynes



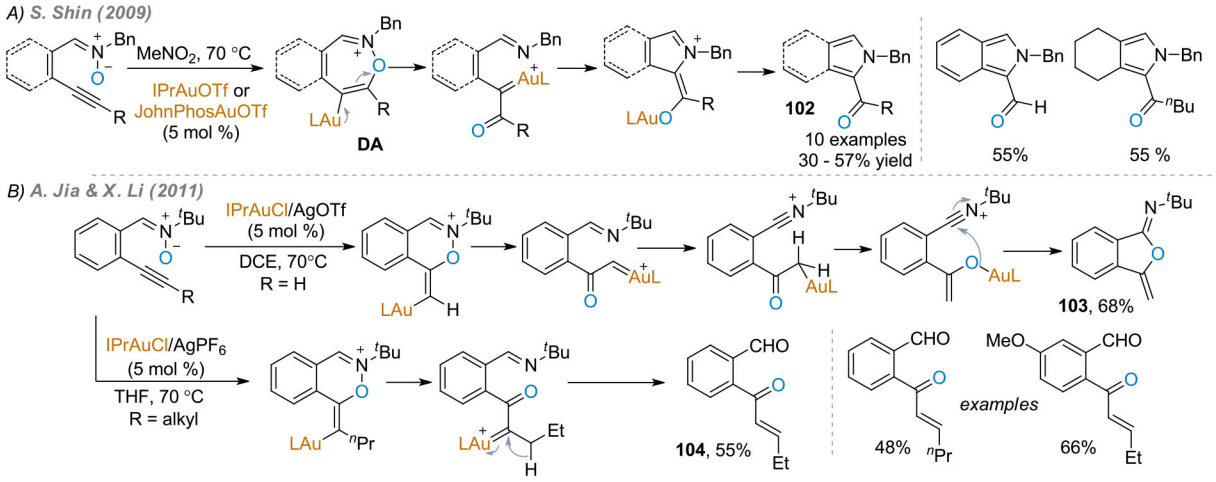
Scheme 55.

Gold-Catalyzed Oxidative Cycloaddition Cascade of *o*-Nitrophenylacetylenes



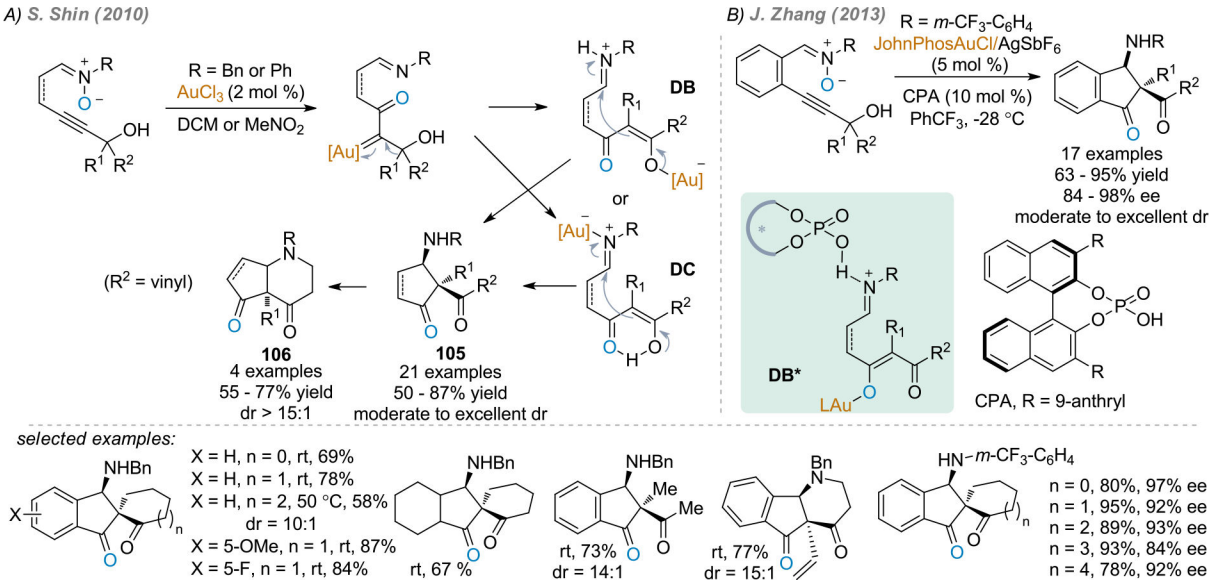
Scheme 56.

Generation of Azomethine Ylides from *o*-Alkynylphenyl Nitrones and Their Cycloaddition Reactions



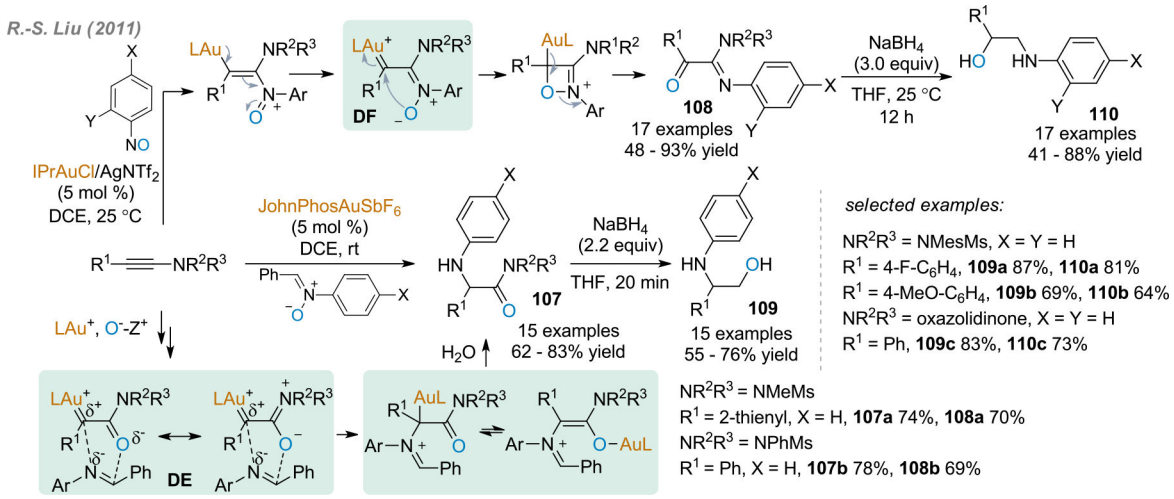
Scheme 57.

Additional Gold-Catalyzed Reactions of *o*-Alkynylphenyl Nitrones and Their Alkene Counterparts



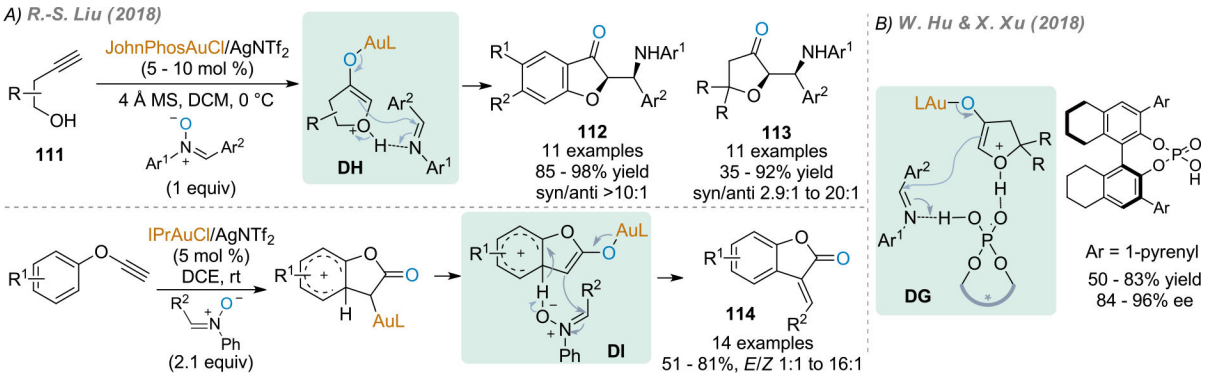
Scheme 58.

Gold-Catalyzed Intramolecular Redox−Pinacol−Mannich−Michael Cascade



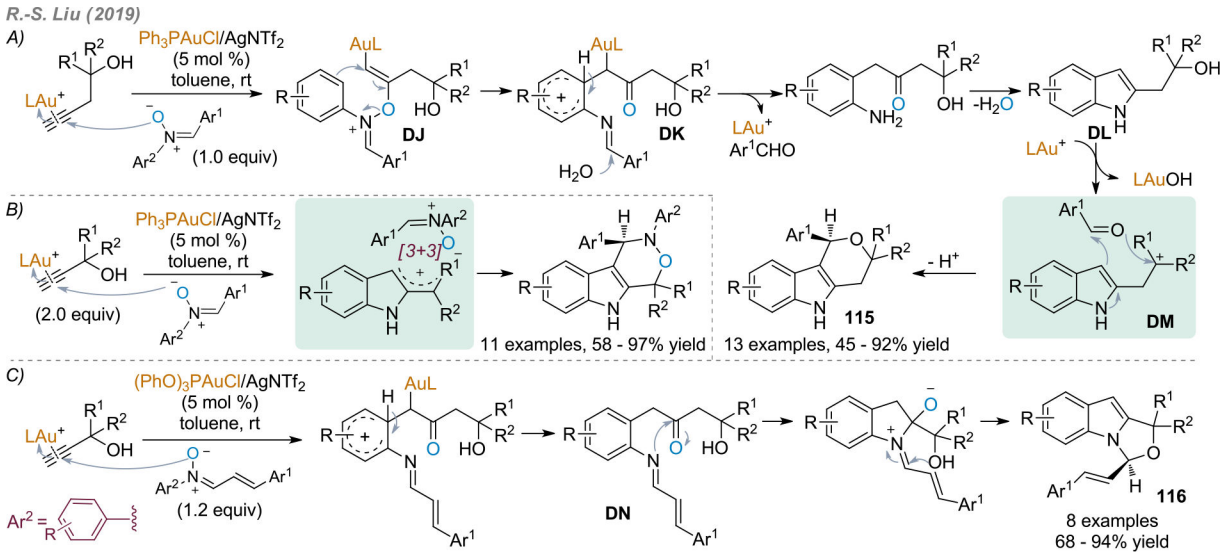
Scheme 59.

Gold-Catalyzed Oxidative 1,2-Difunctionalization of Ynamides by External Nitrones and Nitrosoarenes



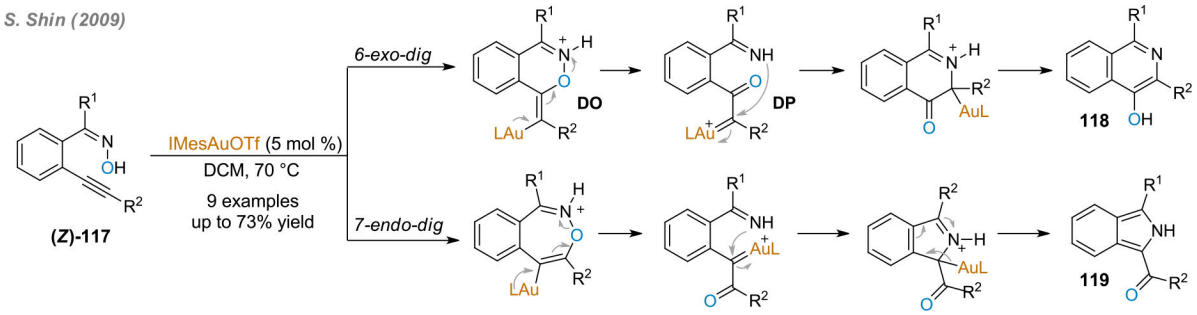
Scheme 60.

Gold-Catalyzed Alkyne Oxidation by Nitrones Terminated by the Mannich Reaction

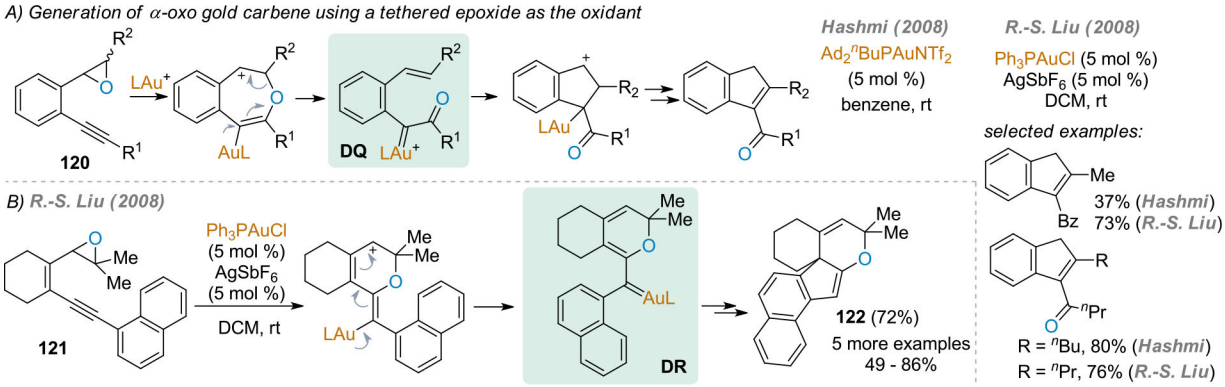


Scheme 61.

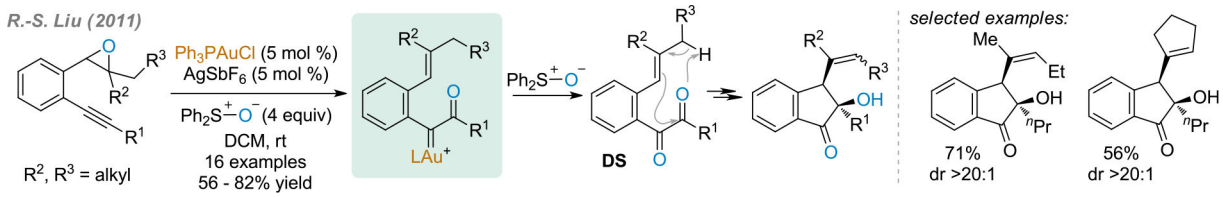
Use of Nitrone as an External Oxidant: Formation of Fused Indoles



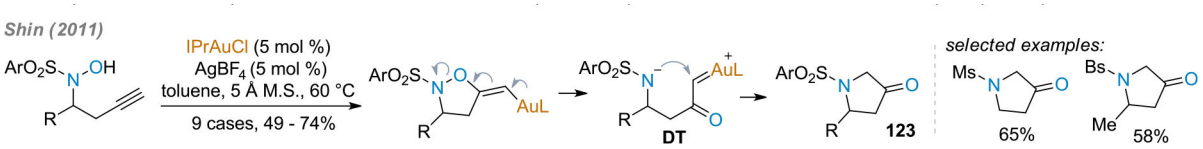
Scheme 62.
Gold-Catalyzed Cascade Cyclization of *o*-Alkynylaryl Ketoximes



Scheme 63.
Studies of Isomerization of *o*-Alkynylaryl Epoxides

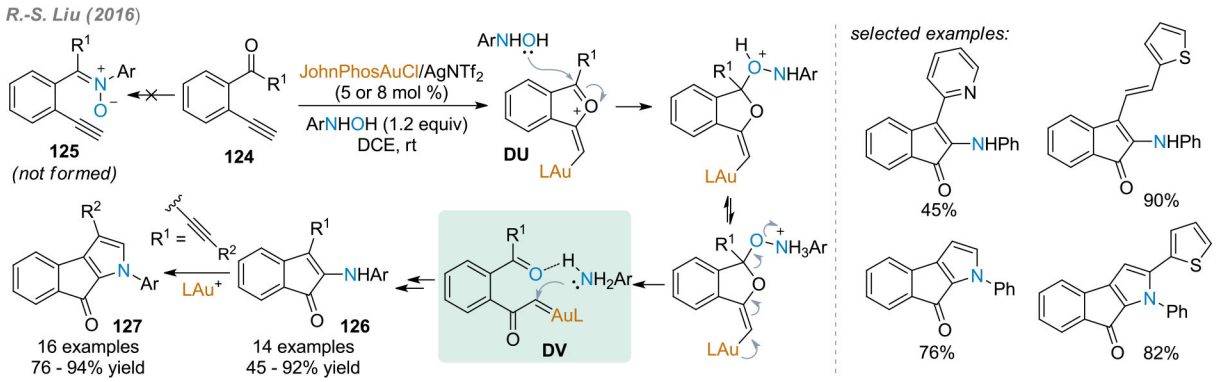


Scheme 64.
Stereoselective Synthesis of 2-Hydroxyindanones



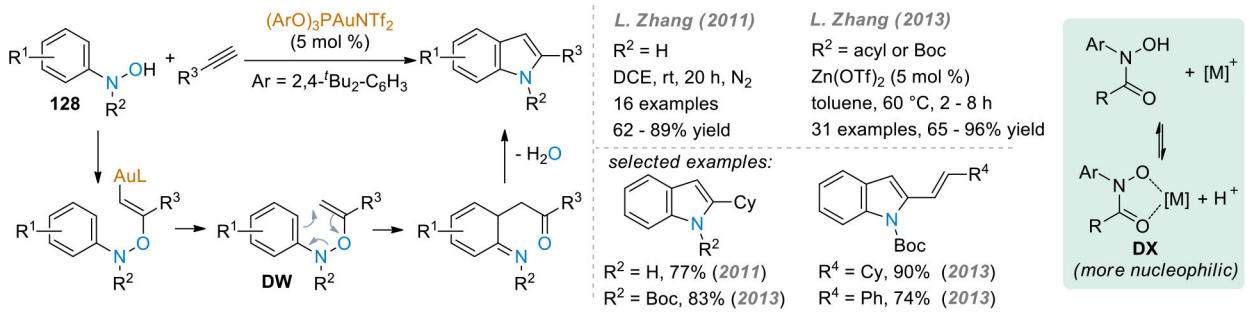
Scheme 65.

Synthesis of 3-Pyrrolidinones via Gold-Catalyzed Alkyne Oxidation with *N*-Sulfonyl Hydroxylamines



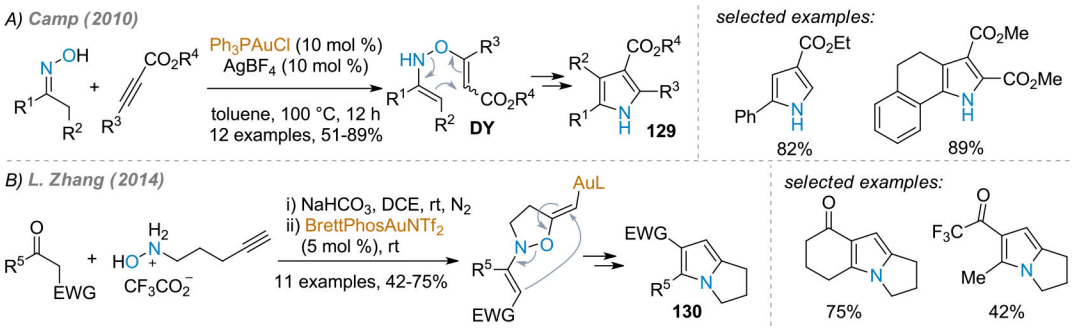
Scheme 66.

Indirect Method for *α*-Oxo Gold Carbene Generation with *N*-Arylhydroxylamines and 2-Alkynylphenyl Ketones



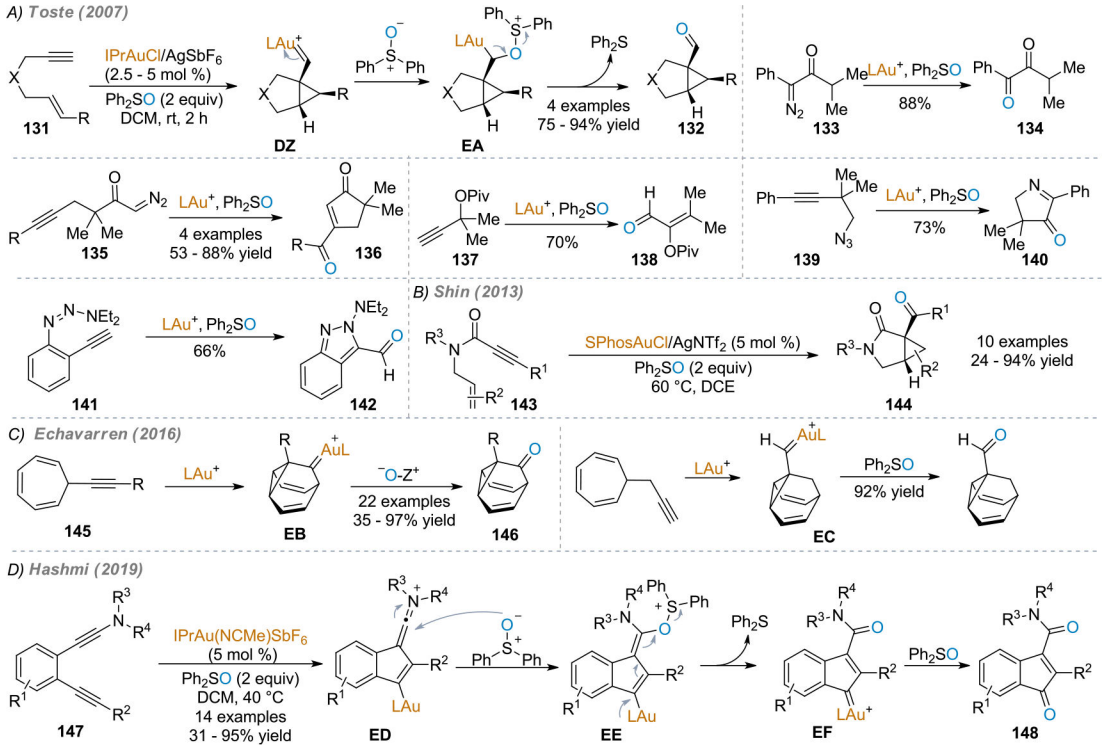
Scheme 67.

Synthesis of 2-Alkylindoles from *N*-Arylhydroxylamines and Terminal Alkynes

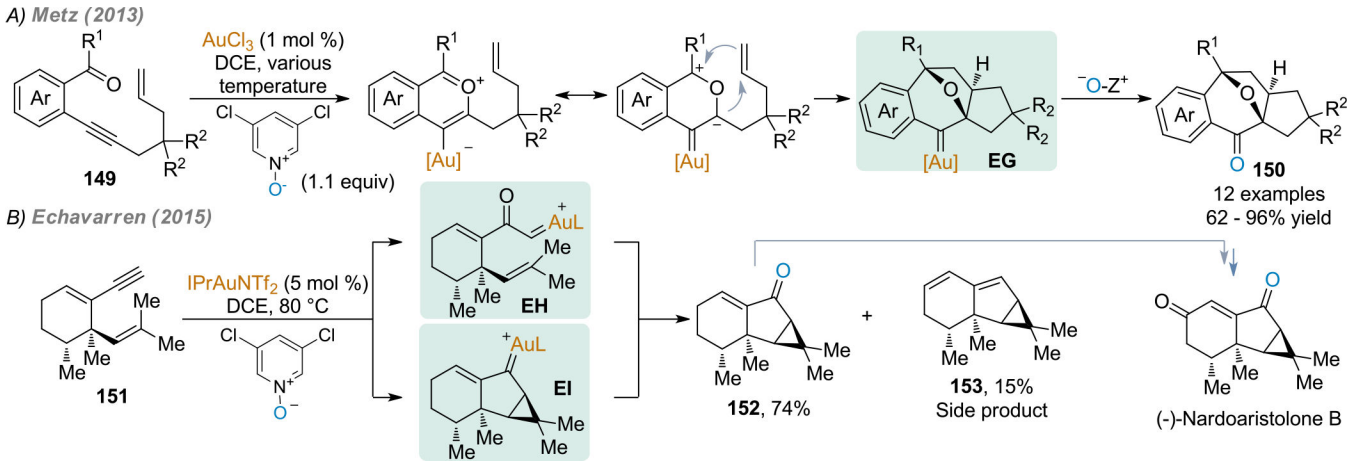


Scheme 68.

Pyrrole Synthesis Employing 3,3-Sigmatropic Rearrangement of the Adduct Formed from Hydroxylamine

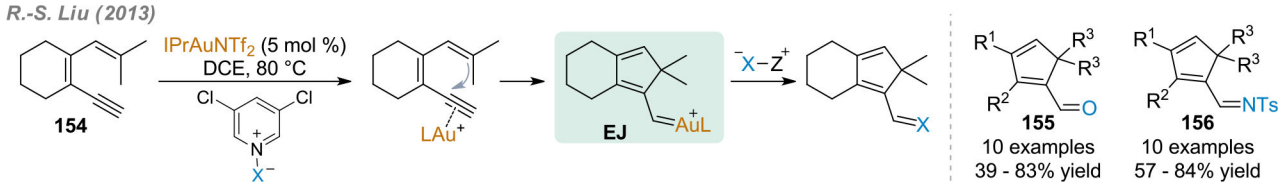


Scheme 69.
Oxidation of Gold Carbene by Sulfoxides

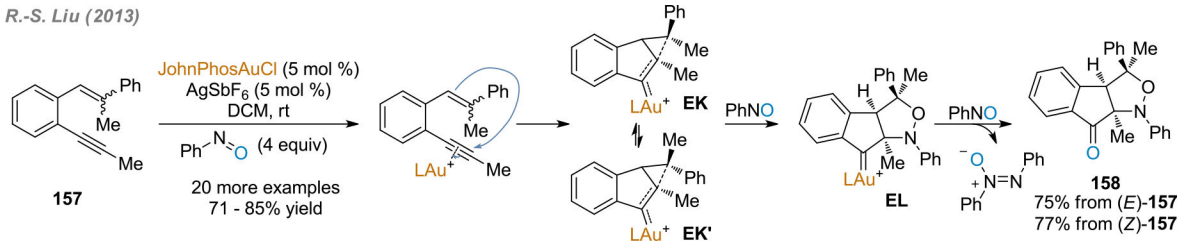


Scheme 70.

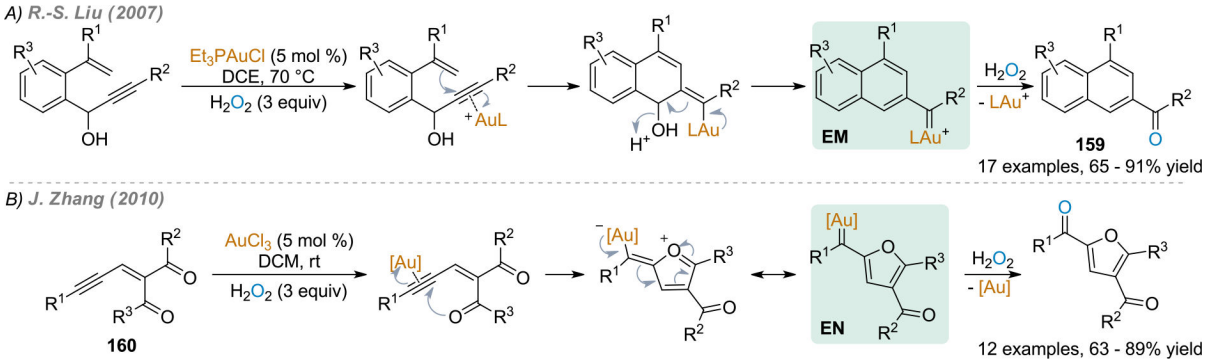
N-Oxide Oxidation of Gold Carbenes Generated Non-oxidatively



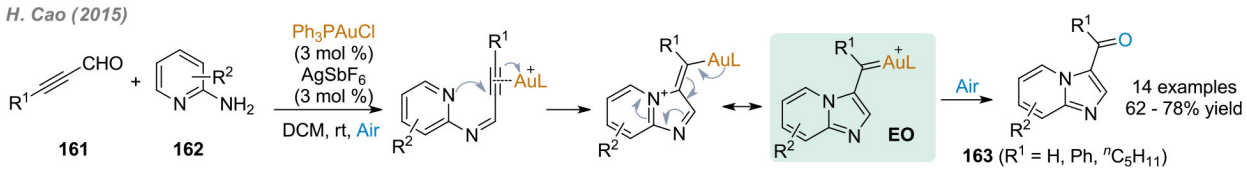
Scheme 71.
Oxidation of Gold Carbene by *N*-Oxide



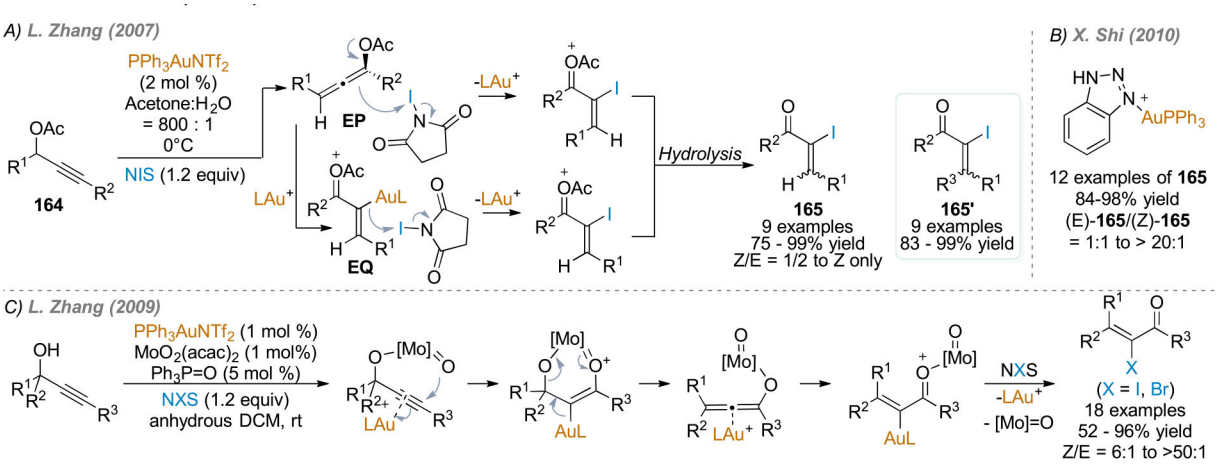
Scheme 72.
Gold(I)-Catalyzed Oxidative Cycloaddition with Nitrosobenzene



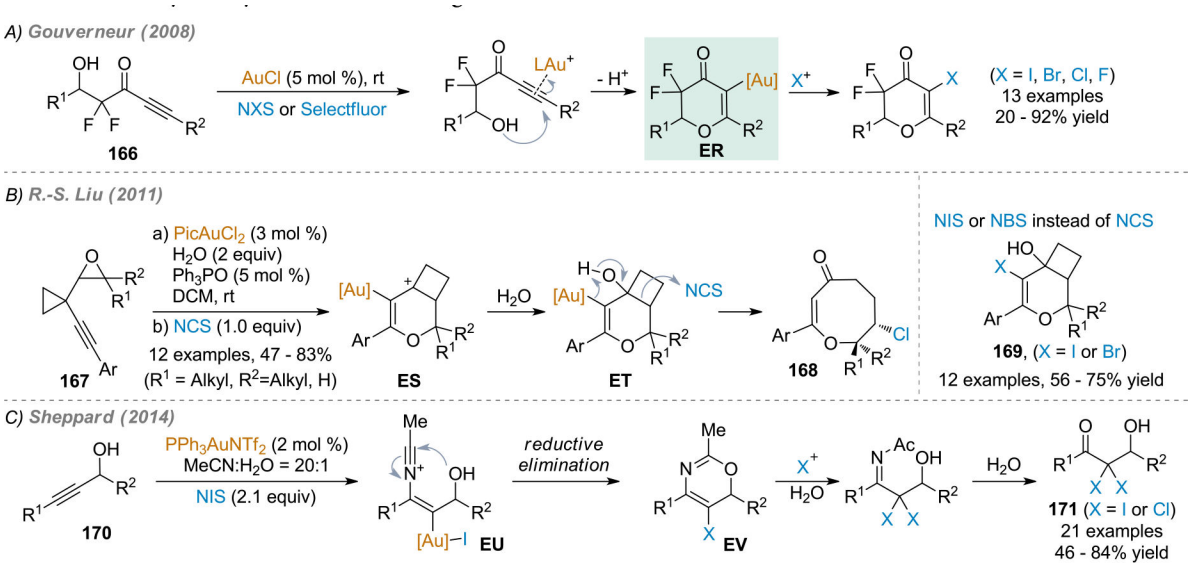
Scheme 73.
Oxidation of Gold Carbenes by H_2O_2



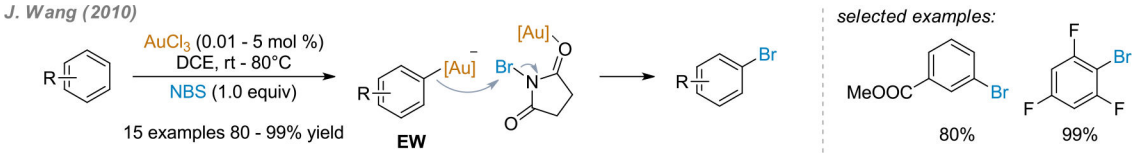
Scheme 74.
Oxidation of Gold Carbene by Atmospheric Oxygen



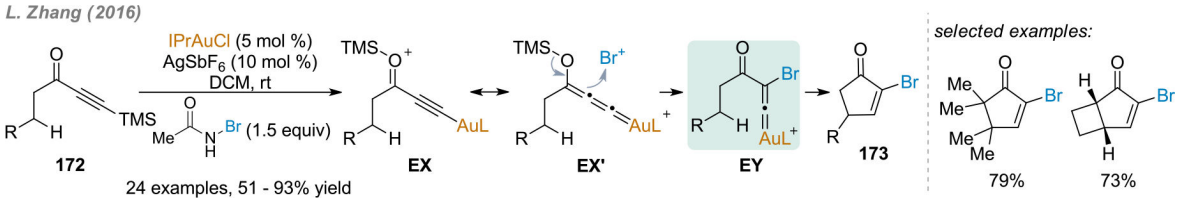
Scheme 75.
Gold-Catalyzed Synthesis of α-Iodoenones



Scheme 76.
Gold-Catalyzed Cyclization and Halogenation

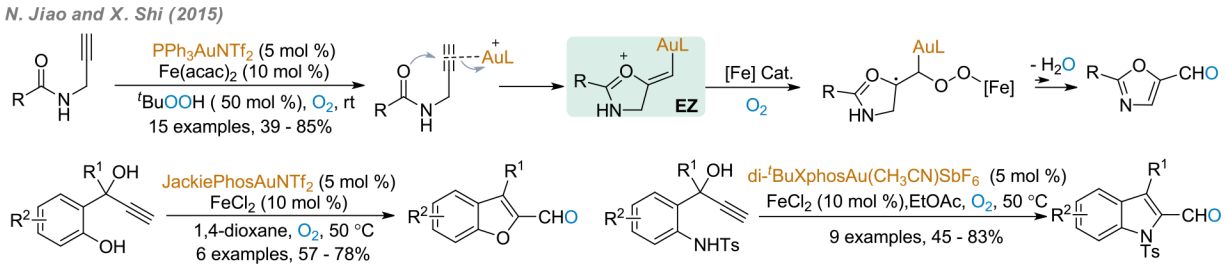


Scheme 77.
Gold-Catalyzed Bromination of Aromatic Rings



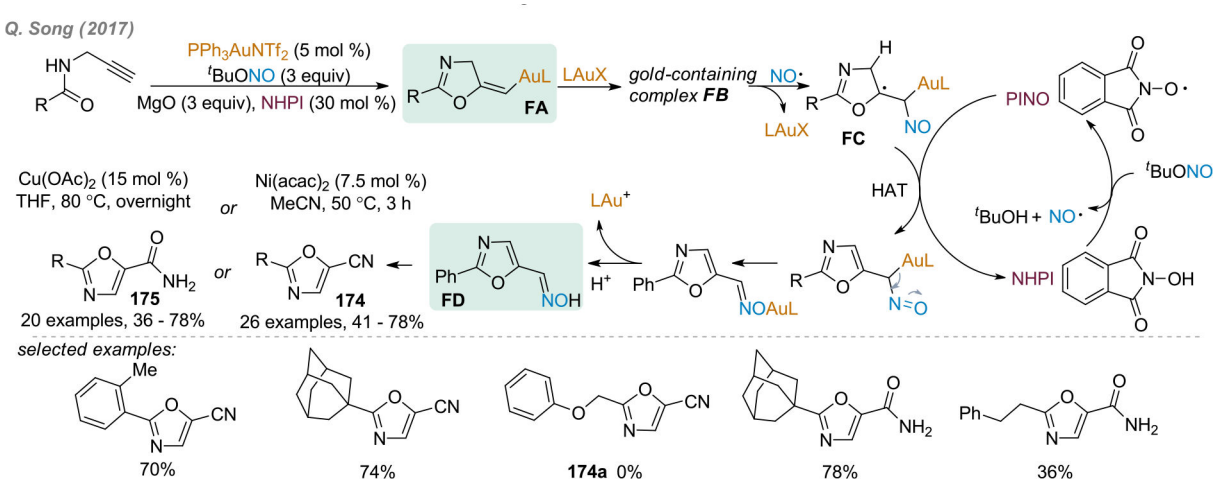
Scheme 78.

Gold(I)-Catalyzed C–H Insertion Reaction by *In Situ*-Generated Gold Vinylidenes



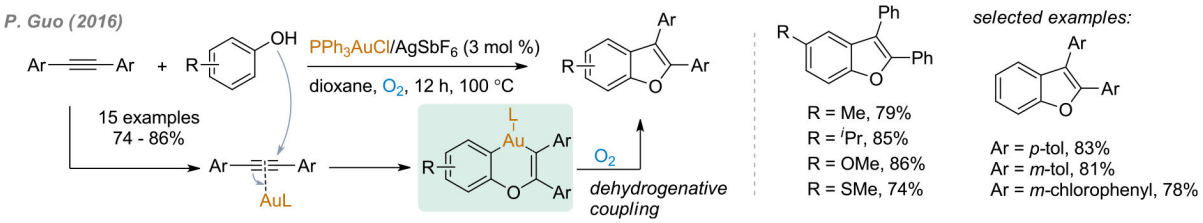
Scheme 79.

Synthesis of Functionalized Oxazoles via Synergistic Au/Fe Catalysis Using O_2 as the Oxidant

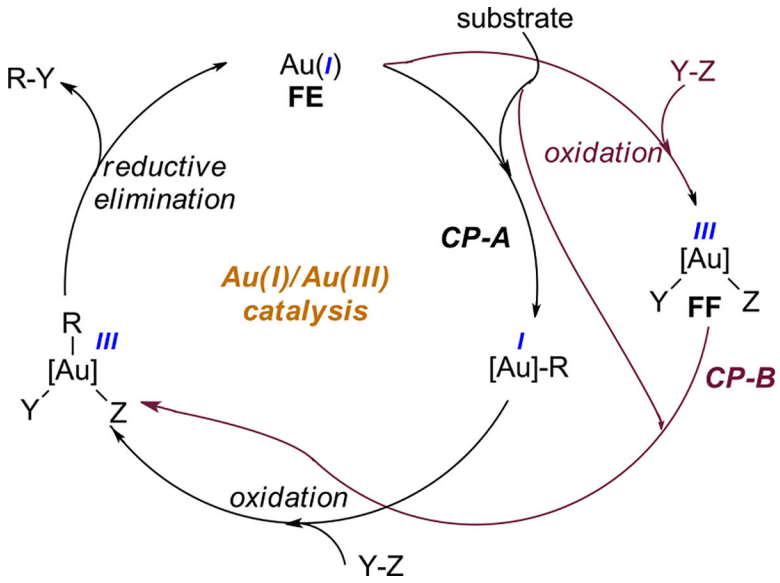


Scheme 80.

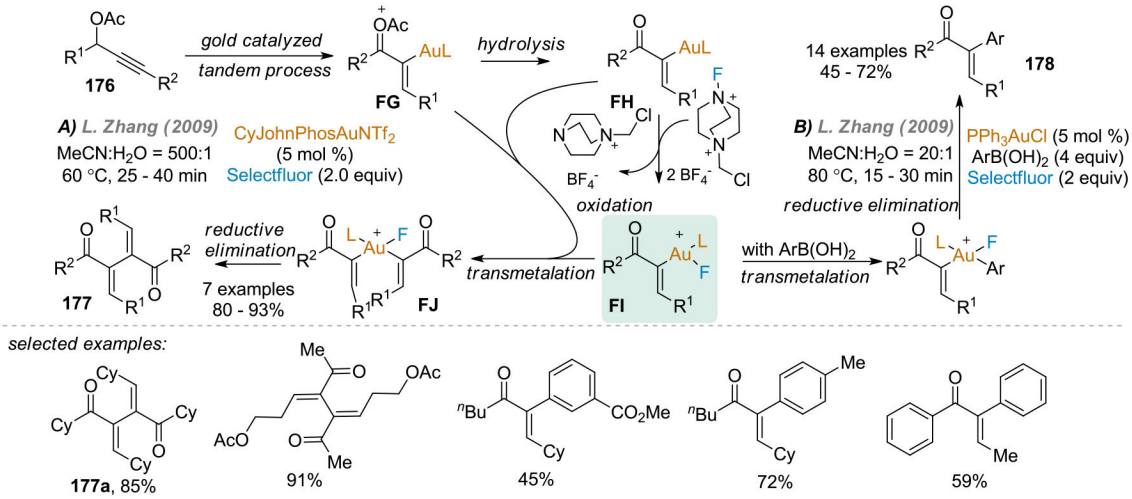
Synthesis of Functionalized Oxazoles Using *tert*-Butyl Nitrite as the Oxidant



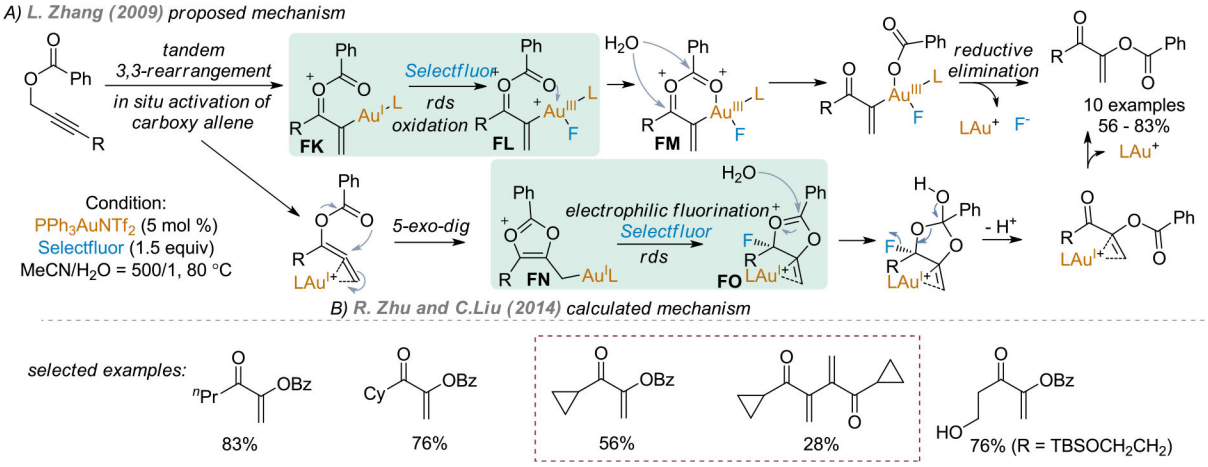
Scheme 81.
Gold-Catalyzed Dehydrogenative Synthesis of Benzofurans



Scheme 82.
Oxidative Au(I)/Au(III) Catalysis: Mechanistic Considerations

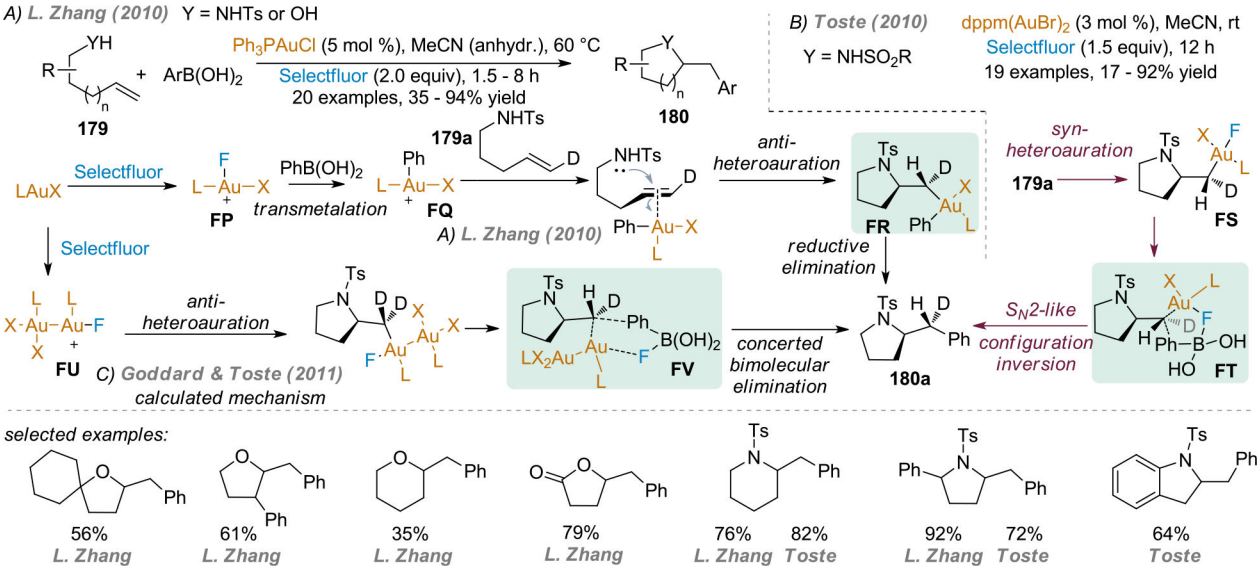


Scheme 83.
Oxidative Homo- and Cross-Coupling of Propargylic Acetates



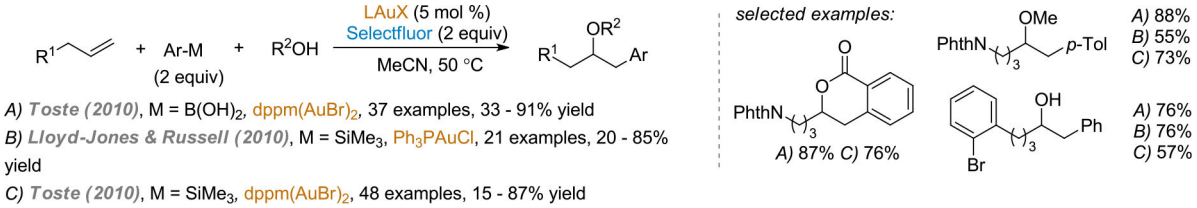
Scheme 84.

Homogeneous Au-Catalyzed Oxidative C–O Bond Formations and Mechanistic Studies



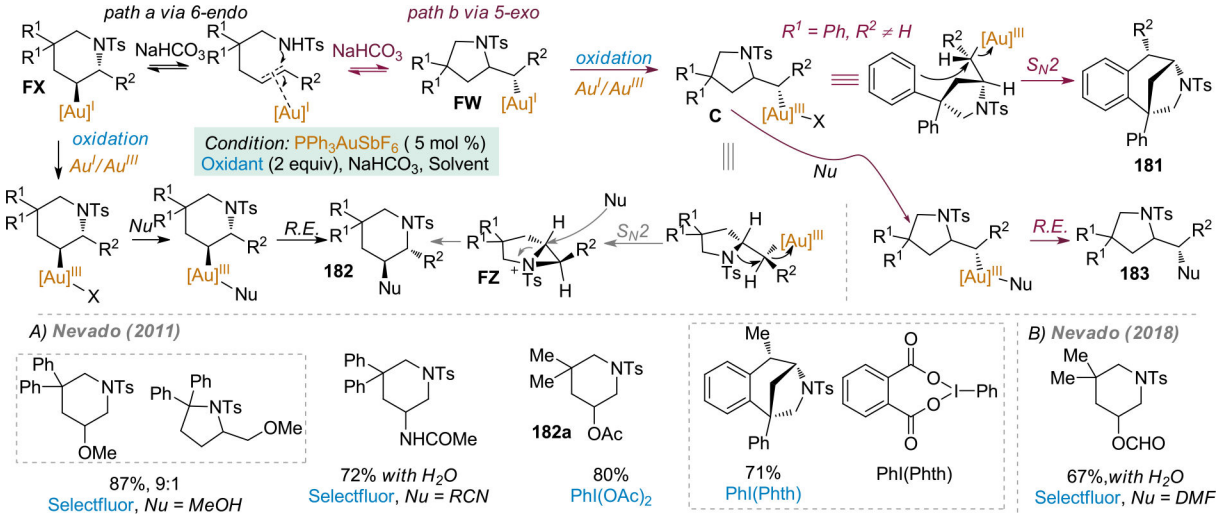
Scheme 85.

Gold-Catalyzed Oxidative Carboheterofunctionalization of Alkenes



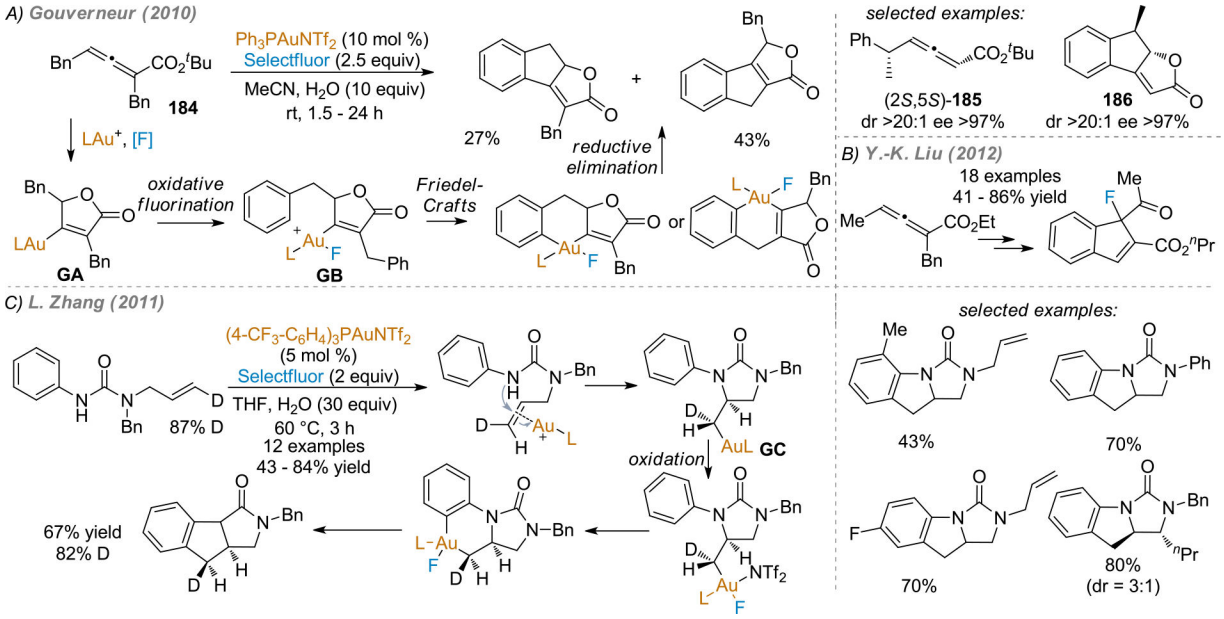
Scheme 86.

Gold-Catalyzed Intermolecular Oxidative Oxyarylation of Alkenes



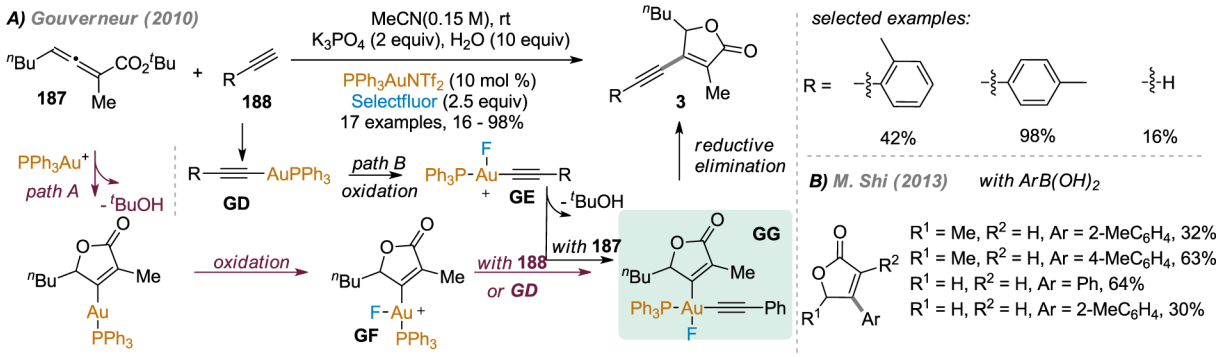
Scheme 87.

Oxidative Alkene Dual Functionalization Leading to 6-*endo* Products

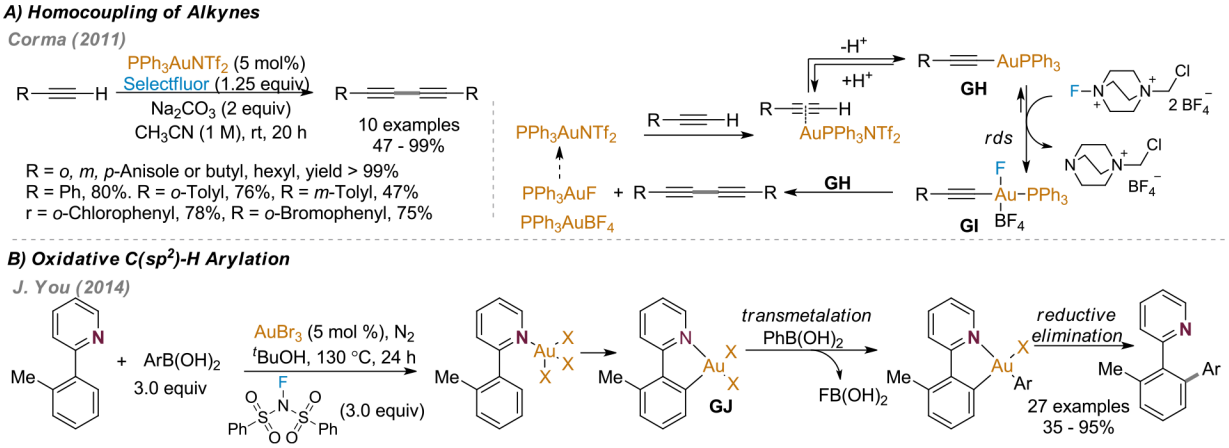


Scheme 88.

Gold-Catalyzed Intramolecular Oxidative Cross-Coupling Reactions

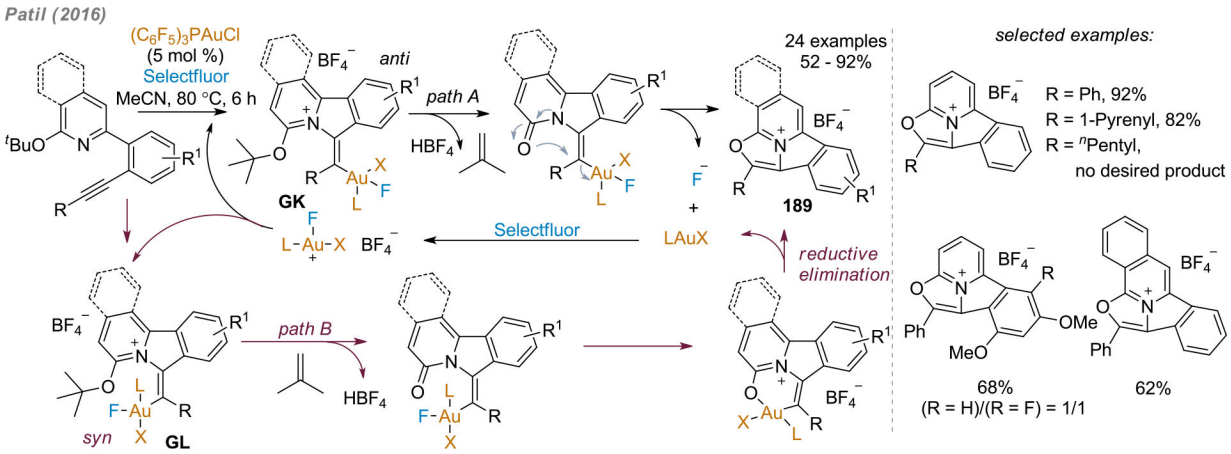


Scheme 89.
Gold-Catalyzed Cyclization Followed by Oxidative Coupling Reactions

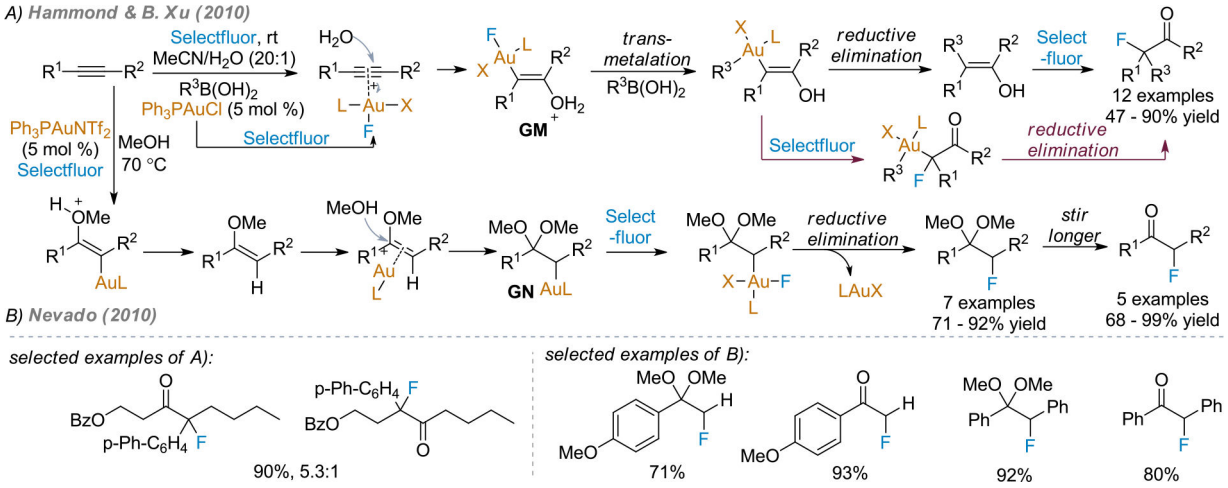


Scheme 90.

Gold-Catalyzed Oxidative Homocoupling of Alkynes and Cross-Coupling between Aryl Compounds

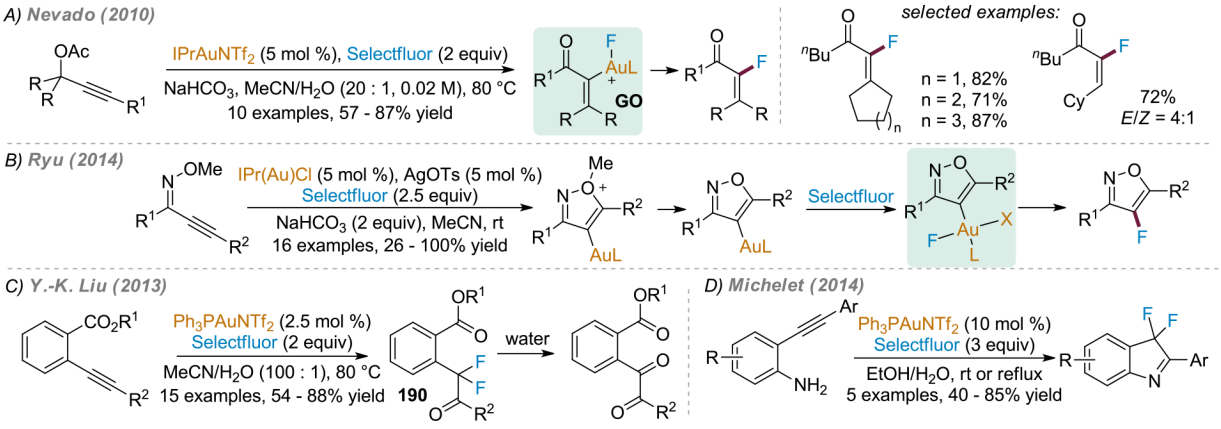


Scheme 91.
Gold-Catalyzed 1,2-Amino-oxygenation of Alkynes



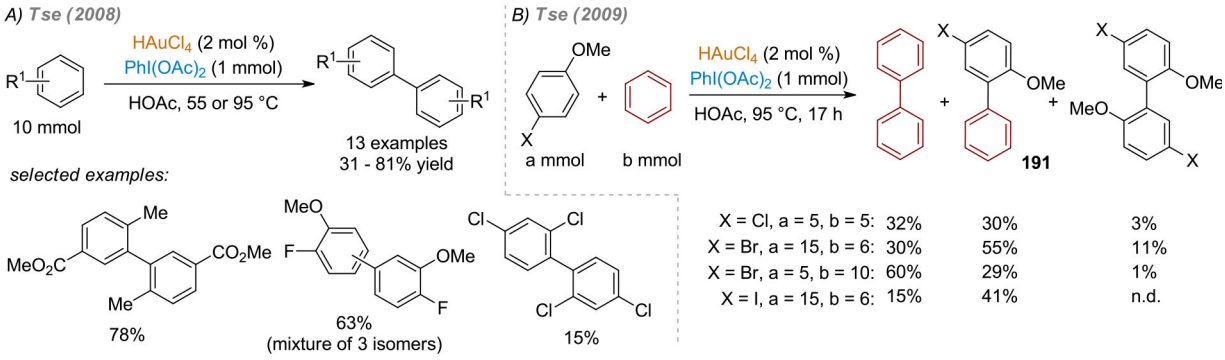
Scheme 92.

Synthesis of α-Fluoro Ketones from Simple Alkynes



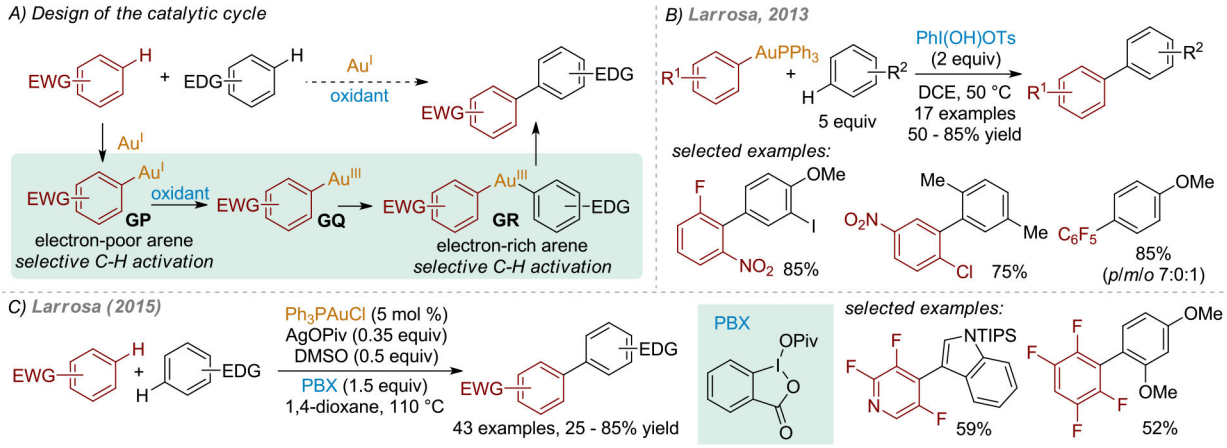
Scheme 93.

Other Oxidative Gold Catalysis Leading to C–F Bond Formation

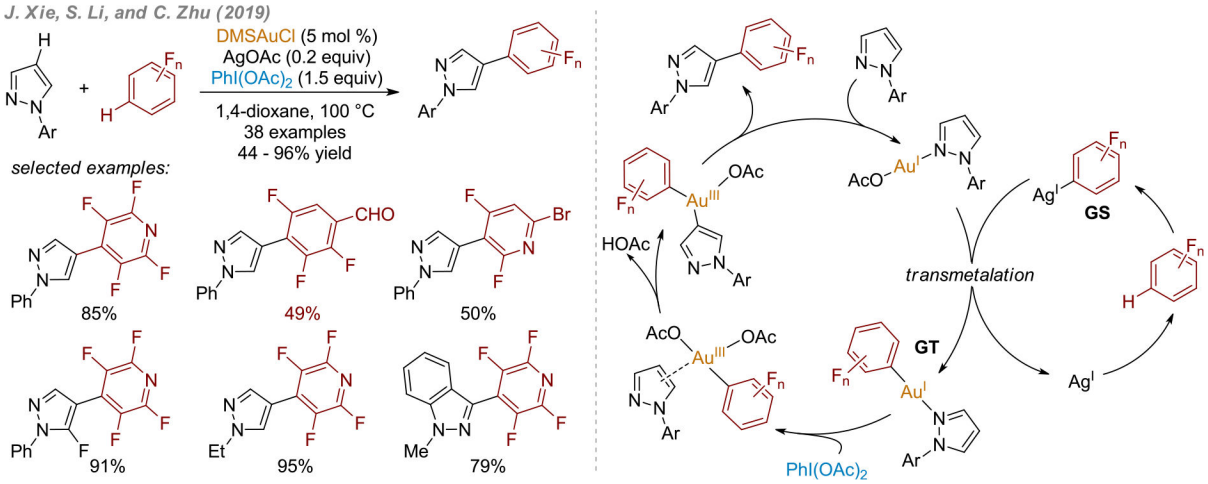


Scheme 94.

Gold-Catalyzed Dehydrogenative Coupling of Arenes: Early Works with Hypervalent Iodine as the Oxidant

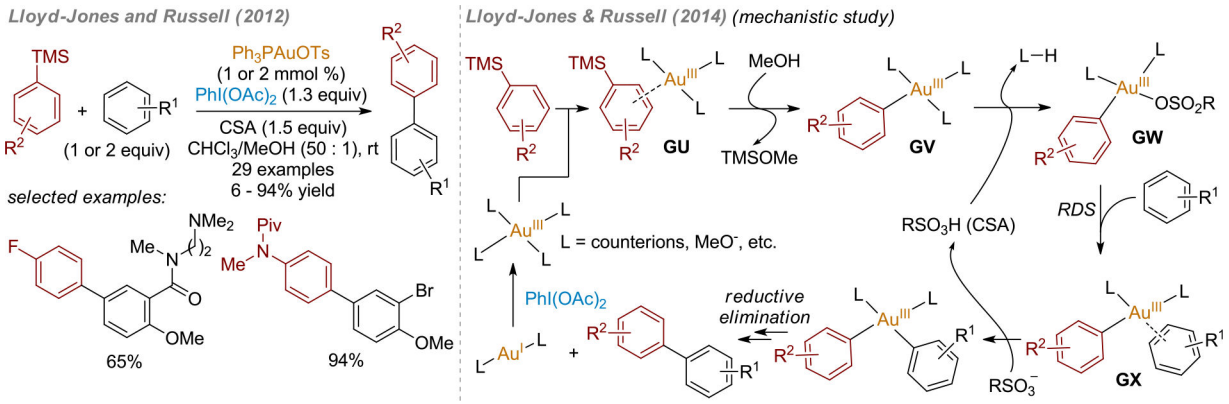


Scheme 95.
Dehydrogenative Arene Cross-Couplings



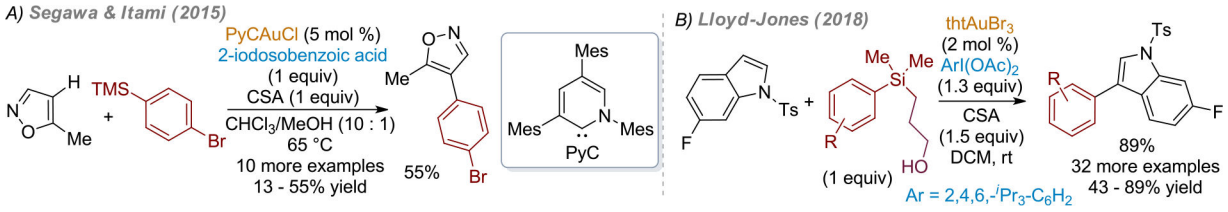
Scheme 96.

Role of the Silver Salt in the Gold-Catalyzed Dehydrogenative Arene Cross-Coupling Reaction



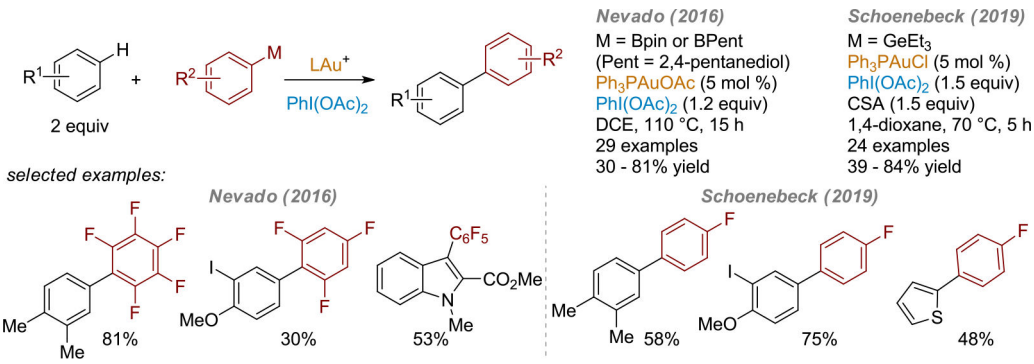
Scheme 97.

Gold-Catalyzed Oxidative Cross-Coupling of Arenes and Arylsilanes



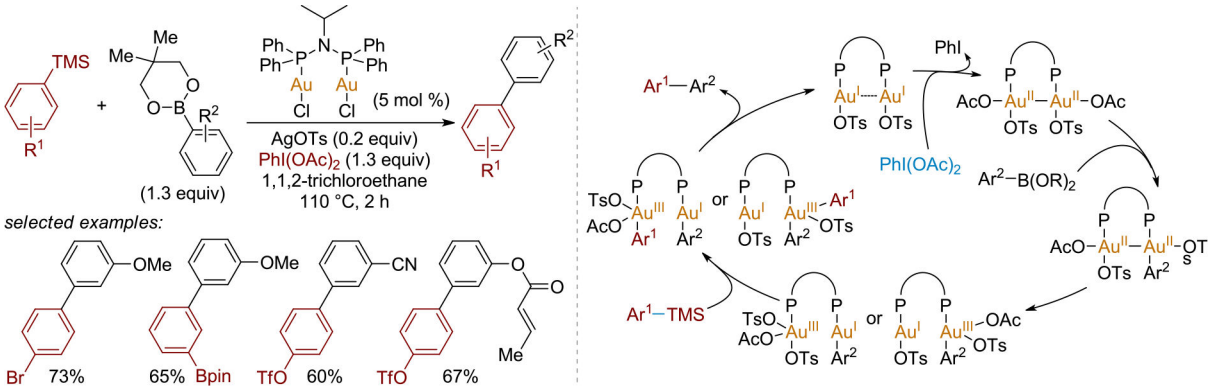
Scheme 98.

Optimization of the Gold-Catalyzed Oxidative Cross-Coupling of Arenes and Arylsilanes



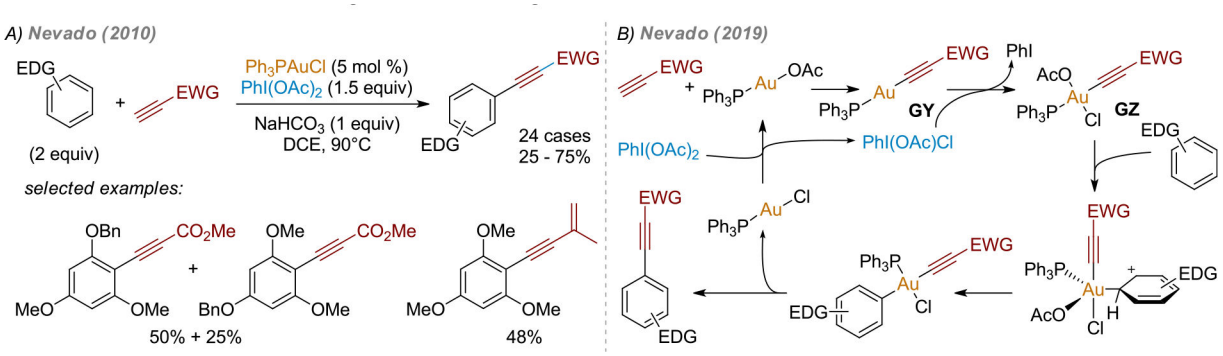
Scheme 99.

Gold-Catalyzed Oxidative Cross-Coupling between Arenes and Other Aryl Organometallics



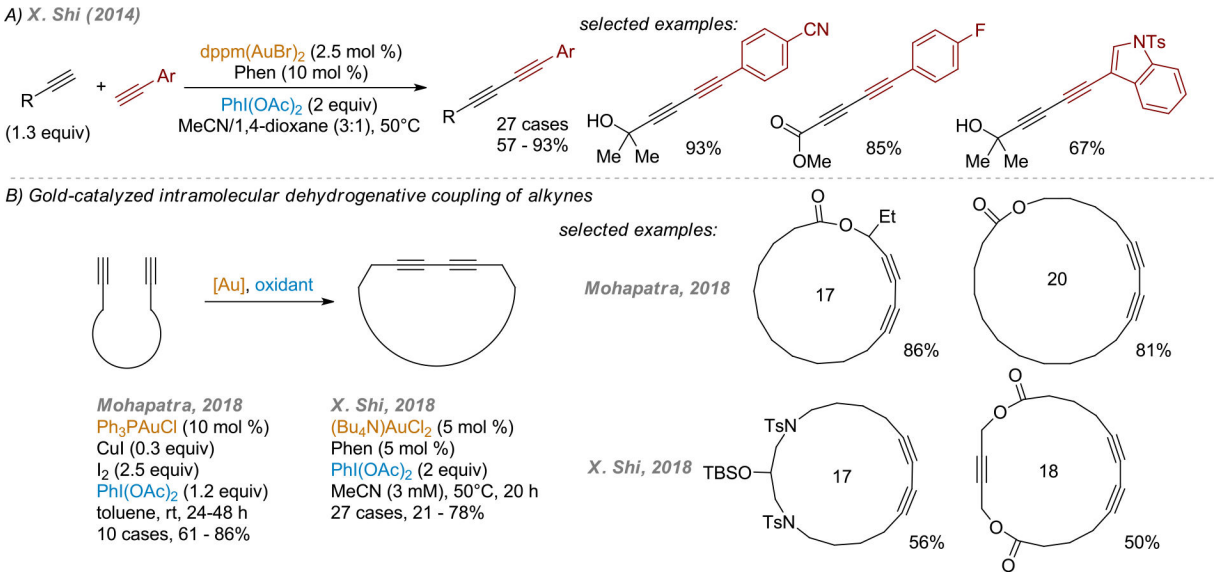
Scheme 100.

Gold-Catalyzed Oxidative Coupling between Aryl Organometallics



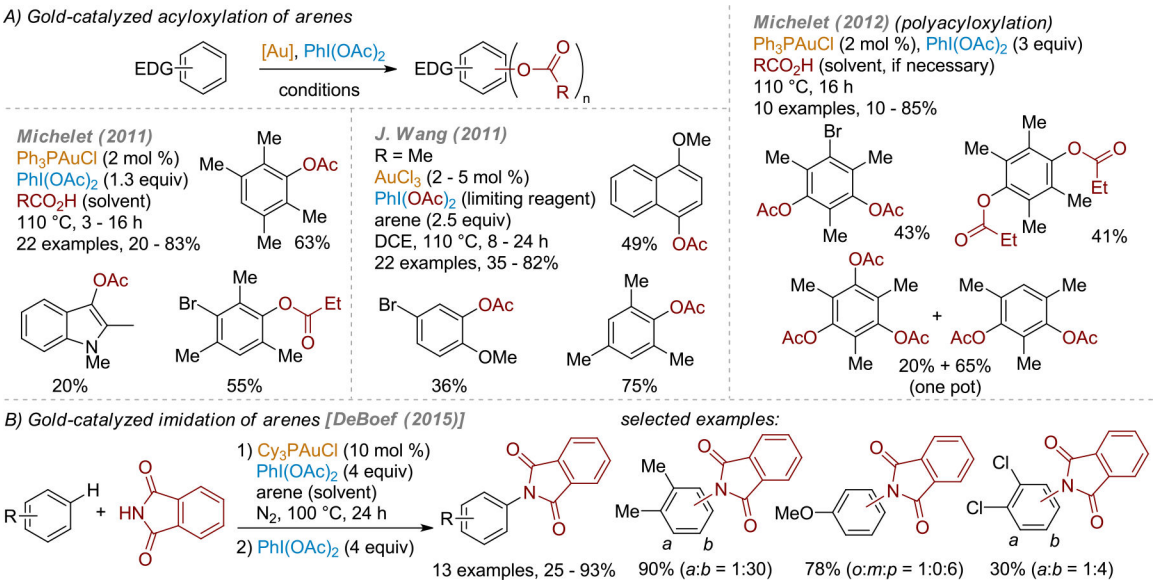
Scheme 101.

Gold-Catalyzed Dehydrogenative Coupling of Arenes and Terminal Alkynes



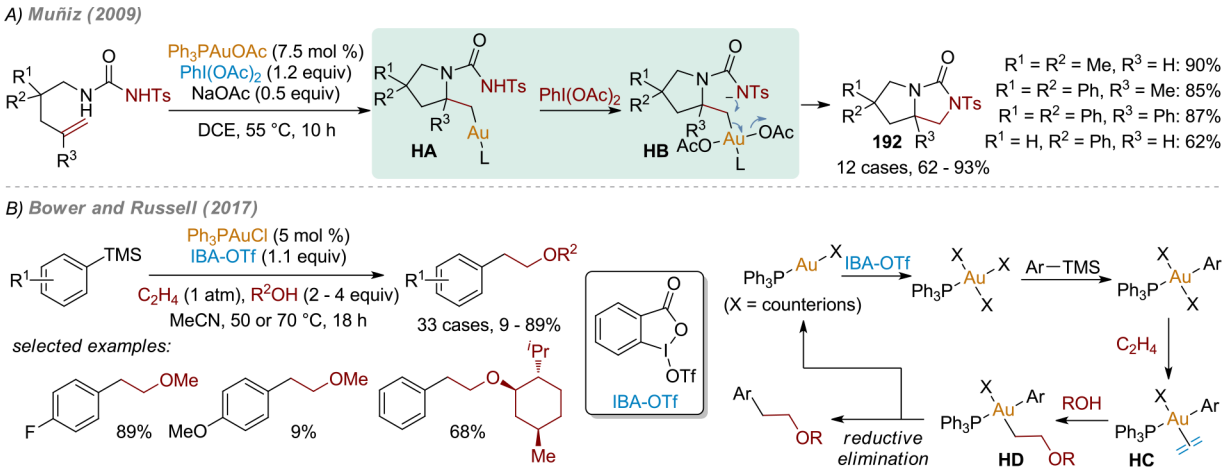
Scheme 102.

Gold-Catalyzed Dehydrogenative Cross-Coupling of Terminal Alkynes



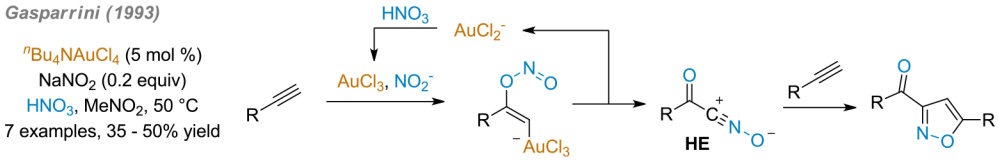
Scheme 103.

Gold-Catalyzed Oxidative C(sp^2)−Heteroatom Bond Formation Reactions



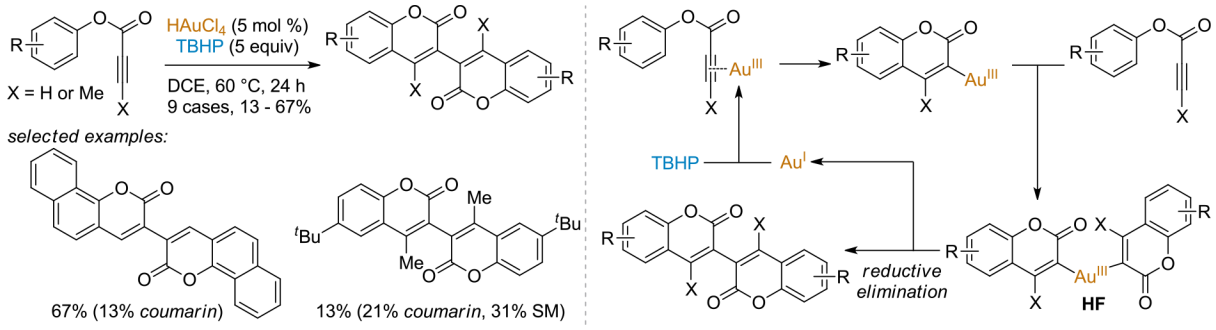
Scheme 104.

Hypervalent Iodine Reagent in Gold-Catalyzed Alkene Activation



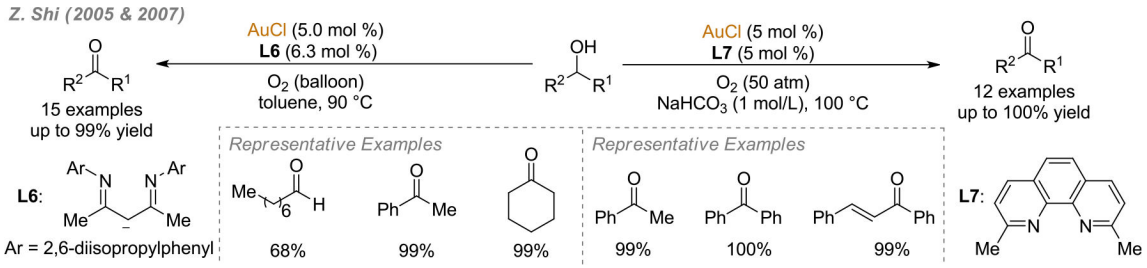
Scheme 105.

Gold-Catalyzed One-Pot Synthesis of Isoxazoles from Terminal Alkynes and Nitric Acid



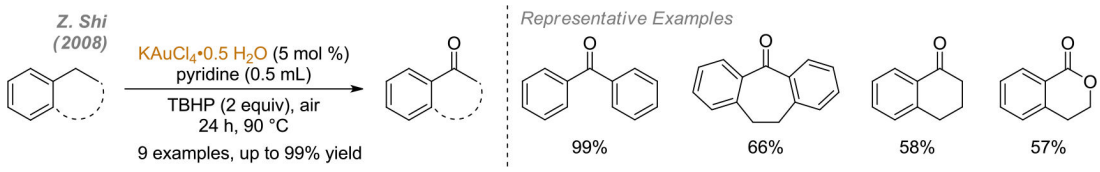
Scheme 106.

Gold-Catalyzed Domino Cyclization and Oxidative Coupling Reaction

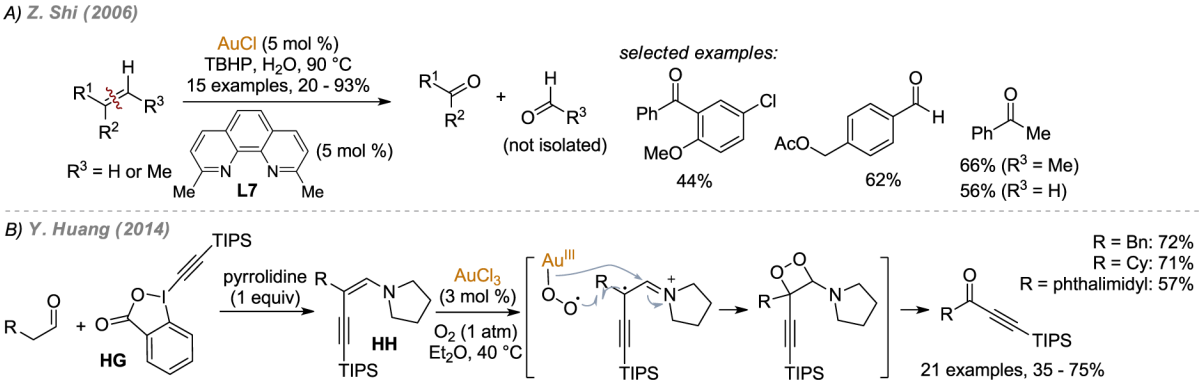


Scheme 107.

Gold-Catalyzed Oxidation of Alcohols into Ketones

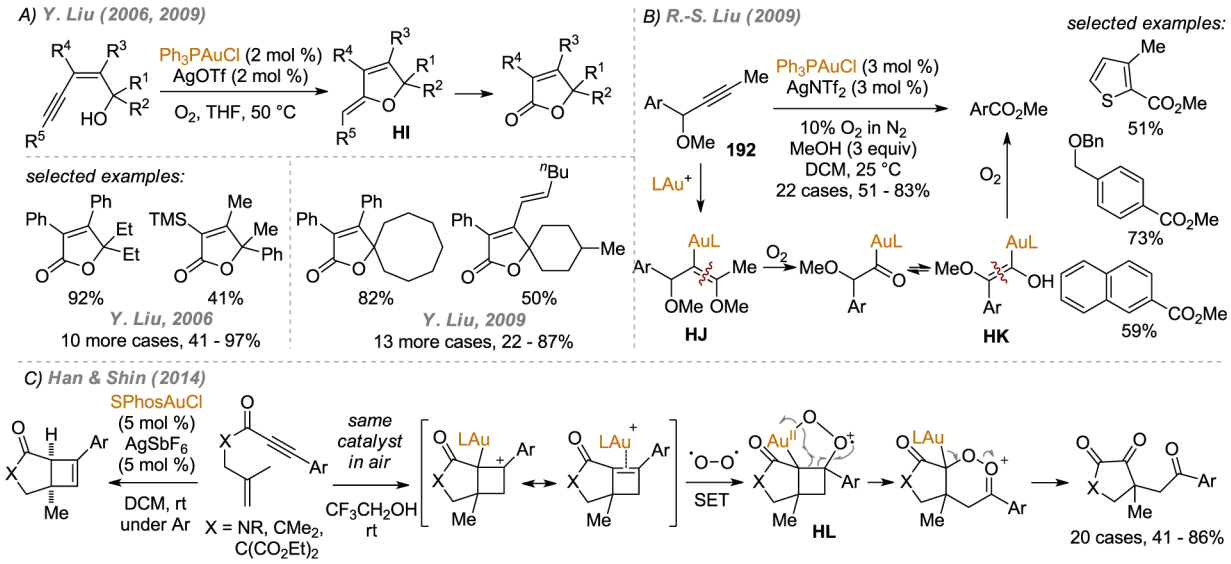


Scheme 108.
Gold-Catalyzed Benzylic Oxidation



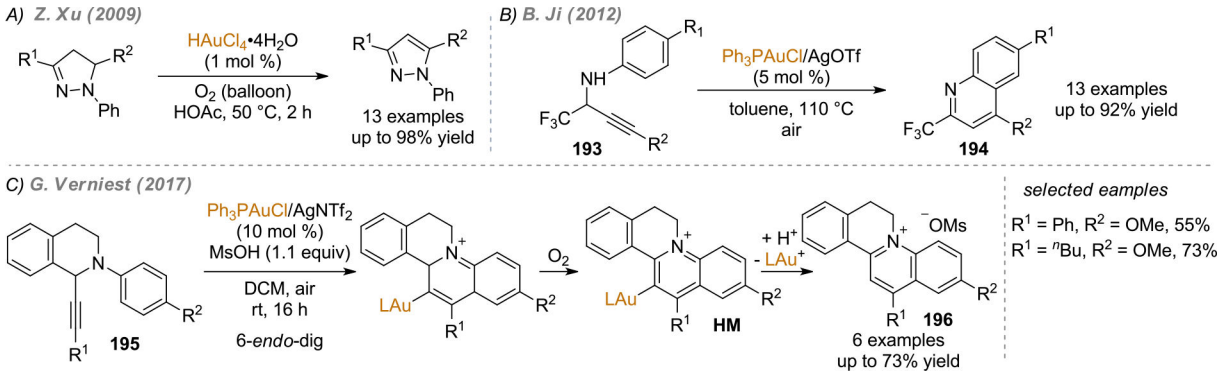
Scheme 109.

Gold-Catalyzed Direct Oxidative Cleavage of C–C Double Bonds

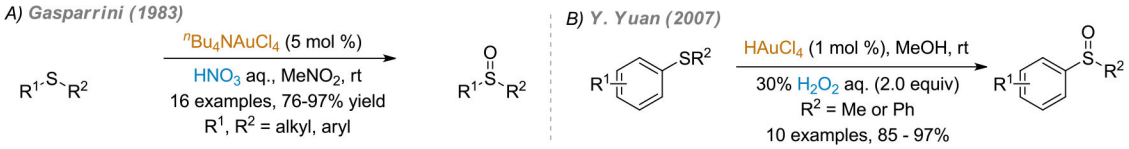


Scheme 110.

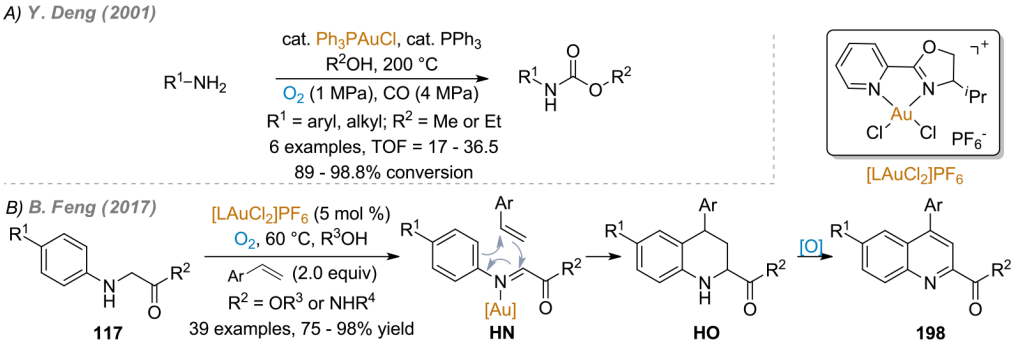
Oxidative Cleavage of C–C Double Bonds Formed via Gold Catalysis



Scheme 111.
Oxidative Aromatization of 1,3,5-Trisubstituted Pyrazolines



Scheme 112.
Gold-Catalyzed Oxidation of Sulfides to Sulfoxides



Scheme 113.

Other Oxidations in the Presence of Gold Catalysts