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Review

Ag–NHC Complexes in π-Activation of Alkynes

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Abstract: Silver–NHC (NHC = N-heterocyclic carbene) complexes play a special role in the field of transition-metal-complexes due to (1) their prominent biological activity, and (2) their critical role as transfer reagents for the synthesis of metal-NHC complexes by transmetalation. However, the application of silver–NHCs in catalysis is underdeveloped, in particular, when compared to their group 11 counterparts, gold–NHCs (Au–NHC) and copper–NHCs (Cu–NHC). In this Special Issue on *Featured Reviews in Organometallic Chemistry*, we present a comprehensive overview of the application of silver–NHC complexes in π-activation of alkynes. Functionalization of alkynes is one of the most important processes in chemistry that is at the bedrock of organic synthesis. The recent studies on silver–NHC complexes show significant promise as unique and highly selective catalysts in this class of reactions. The review covers π-activation reactions catalyzed by Ag–NHCs since 2005 (the first example of π-activation in catalysis by Ag–NHCs) through December 2022. The review focuses on the structure of NHC ligands and π-functionalization methods, covering the following broadly defined topics: (1) intramolecular cyclizations; (2) CO_2 fixation; (3) hydrofunctionalization reactions. By discussing the role of Ag–NHC complexes in π-functionalization of alkynes, the Reader is provided with an overview of this important area of research and the role of Ag–NHCs to promote reactions that are beyond other group 11 metal–NHC complexes.

Keywords: silver; Ag; N-heterocyclic carbenes; NHCs; alkynes; π-functionalization; π-activation; Ag–NHCs, group 11 metals, gold–NHCs, copper–NHCs

1. Introduction

After the first synthesis of a silver–NHC complex in 1993 by Arduengo [1], the breakthrough was achieved in 1998 by Lin and co-workers who found that Ag(I)–NHCs serve as efficient transfer reagents for the synthesis of other NHC–metal complexes [2]. Owing to the ease of synthesis of Ag–NHCs, their stability, and avoidance of free-carbenes, this reaction now represents one of the most straightforward approaches to the synthesis metal–NHCs that has enormously contributed to the widespread application of metal–NHC complexes in catalysis and biology [3,4].

Simultaneously, another major direction in the area of Ag–NHCs was their investigation as potential antimicrobial and anticancer agents, where Ag–NHC complexes have been proposed to serve as slow releasing agents [5]. The area of silver–NHCs in medicinal chemistry is a vibrant area of research with numerous reviews published in the last years [5,6].

Electronically, silver is a [Kr] $4d^{10}5^{1}$ coinage metal [7] with the current market price [8] significantly lower than gold (Ag, $24.00, 1 oz vs. Au, $1,815, 1 oz), but higher than copper (Cu, $3.73, 1 oz), which is mirrored by the relative abundance of group 11 metals in the Earth's crust (Ag, 0.07 ppm; Cu, 50 ppm; Au, 0.0011 ppm) [9]. Complexation of strongly σ-donating NHC ligands to silver enhances stability of silver, which can be exploited in catalysis [4,10]. Studies have found that compared with other group 11 metals, Ag–NHC bond is longer (e.g., IPr–AgCl, 2.056 Å, Ag–Cl, 2.313 Å; IPr–AuCl, 1.941 Å, Au–Cl, 2.270 Å; IPr–CuCl, 1.881 Å, Cu–Cl, 2.106 Å) owing to the weaker π-donation of silver [11]. Furthermore, studies on π-activation of alkynes [12] established that π to σ metal donation as well as metal to π* back-bonding is in the order of Au > Cu > Ag [13]. Overall, these

mechanistic studies highlight that (1) silver–NHC complexes are well-suited as transmetalating reagents, and (2) silver–NHC complexes are suitable for electrophilic activation of alkynes by π-coordination of cationic silver(I)–NHC to alkynes with electronic features complementary to other coinage metals.

In this Special Issue on *Featured Reviews in Organometallic Chemistry*, we present a comprehensive overview of the application of silver–NHC complexes in π-activation of alkynes. Several excellent reviews on silver and silver–NHC complexes have been published [10]. These reviews have addressed general aspects and applications of silver in organic synthesis [6,10]. A review addressing specifically π-functionalization of alkynes by silver–NHC complexes has not been published thus far. π-Functionalization of alkynes [12] is one of the most important processes in chemistry that is used for the synthesis of a wide range of compounds in the areas ranging from drug discovery, through agrochemistry, biochemistry and natural product synthesis to materials science [14]. The recent studies on silver–NHC complexes show significant promise as unique and highly selective catalysts in this class of reactions. The present review covers π-activation reactions catalyzed by Ag–NHCs since 2005 (the first example of π-activation in catalysis by Ag–NHCs) through December 2022. The review focuses on the structure of NHC ligands and π-functionalization methods. The review is divided into the following sections: (1) intramolecular cyclizations; (2) CO_2 fixation; (3) hydrofunctionalization reactions. Where relevant π-functionalization of olefins by silver–NHCs is also discussed for comparison purposes or to introduce the topic from a historical perspective. We hope that by discussing the role of Ag–NHC complexes in π-functionalization of alkynes, the Reader will be provided with an overview of this important area of research and the role of Ag–NHC to promote reactions that are beyond other group 11 metal–NHC complexes [7].

Structures of the most common Ag–NHC complexes used in π-functionalization of alkynes are presented in Figure 1. Relevant bond lengths are presented in Table 1. For studies on electronic and steric properties of NHC ligands, the Reader is encouraged to consult the following reviews [3,4].

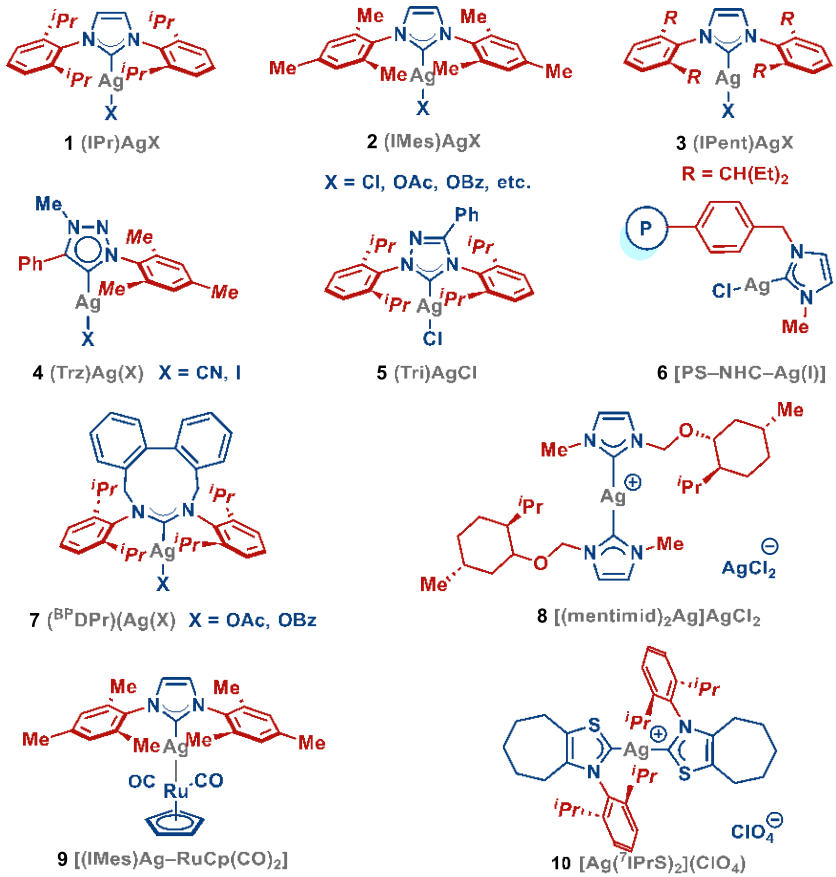


Figure 1. Structures of the most common Ag–NHC complexes used in π-functionalization of alkynes.

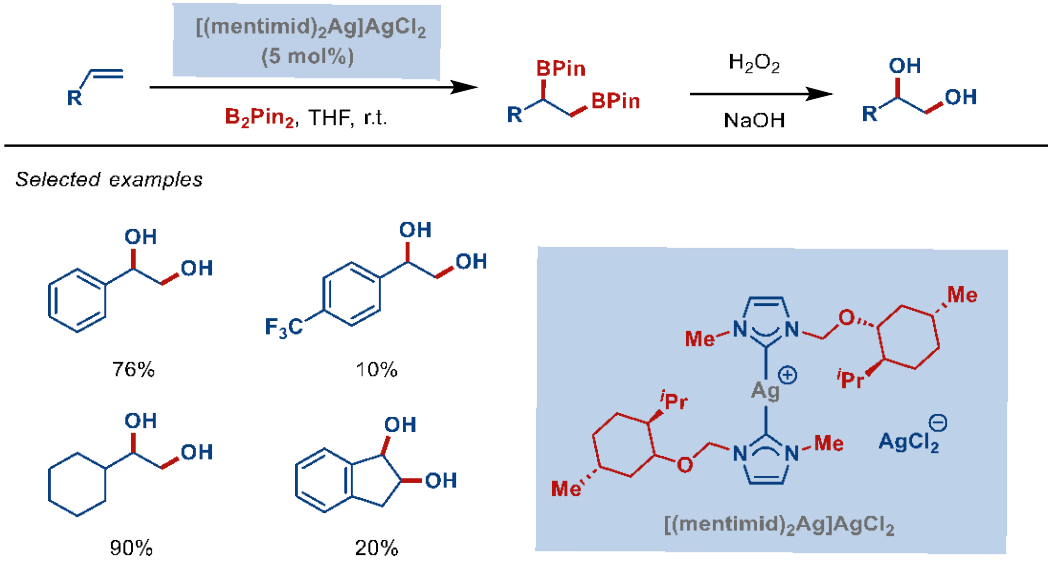
Table 1. Ag–$C_{(carbene)}$ bond lengths of the most common Ag–NHC complexes used in π-functionalization of alkynes. Ag–X bond lengths are shown for comparison.

Entry	Complex No.	[(NHC)Ag(X)]	Ag–C bond length (Å)	Ag–X bond length (Å)	Reference
1	**1**	[(IPr)Ag(Cl)]	2.056	2.313 (X = Cl)	11d
2	**2**	[(IMes)Ag(Cl)]	2.056	2.314 (X = Cl)	11e
3	**3a**	[(IPent)Ag(OAc)]	2.067	2.111 (X = OAc)	17
4	**3b**	[(IPent)Ag(OBz)]	2.059	2.100 (X = OBz)	17
5	**3c**	[(IPent)Ag(4-ClOBz)]	2.064	2.100 (X = 4-ClOBz)	17
6	**4a**	[(Trz)Ag(CN)]	2.087	2.073 (X = CN)	24
7	**4b**	[(Trz)Ag(I)]	2.091	2.636 (X = I)	24
8	**7a**	[(^{BP}DPr)Ag(OAc)]	2.089	2.112 (X = OAc)	28
9	**7b**	[(^{BP}DPr)Ag(OBz)]	2.089	2.122 (X = OBz)	28
10	**8**	[(mentimid)$_2$Ag($AgCl_2$)]	2.102	2.952 (X = $AgCl_2$)	15
11	**9**	[(IMes)Ag($RuCp(CO)_2$)]	2.111	2.617 (X = $RuCp(CO)_2$)	32
12	**10**	[Ag(^{7}IPrS)$_2$]$^+$[ClO_4]$^-$	2.081	-	19

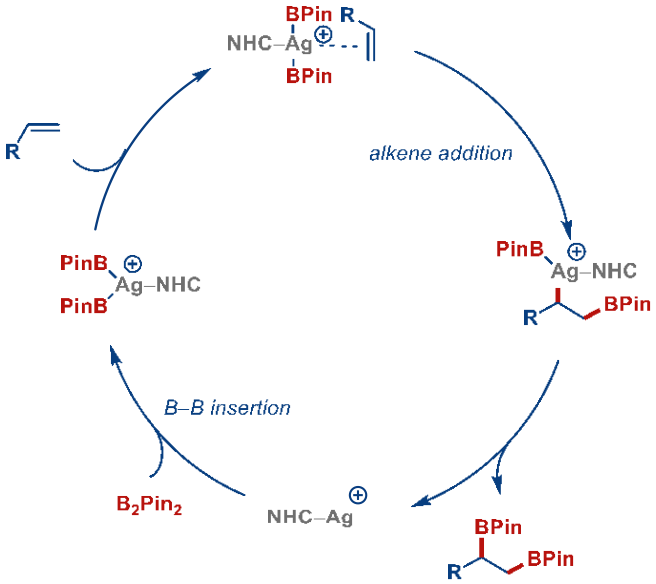
It should be noted that Ag–$C_{(carbene)}$ distances of the complexes shown in Figure 1 range between 2.056-2.091 Å for monomeric complexes and between 2.102-2.111 Å for bimetallic complexes. As expected, there is a much greater variation in the Ag–X bond lengths, with values ranging from 2.073-2.636 Å for monomeric complexes and 2.617-2.952 Å for bimetallic complexes. These distances in the most common NHC–Ag complexes used in π-activation of alkynes are consistent with the major role of the counterion on their reactivity. Likewise, it should be noted that the three orbital contributions to the Ag–NHC bond involve σ-donor, d→π* (Ag to NHC π*-backdonation) and π→d (NHC to Ag π-donation). All three contributions should be considered in understanding the properties of Ag–NHC complexes in catalysis, which depend on the nature of the NHC scaffolds. The most effective Ag–NHC complexes discovered to date in π-activation of alkynes are sterically-hindered IPent, half-umbrella shaped thiazol-2-ylidene ^{7}IPrS and heteroatom-substituted 1,2,4-triazolylidene Tri NHC ligands. Future studies should carefully address the role of orbital contributions in elucidating the reactivity of Ag–NHCs in catalysis.

2. Intramolecular Cyclizations

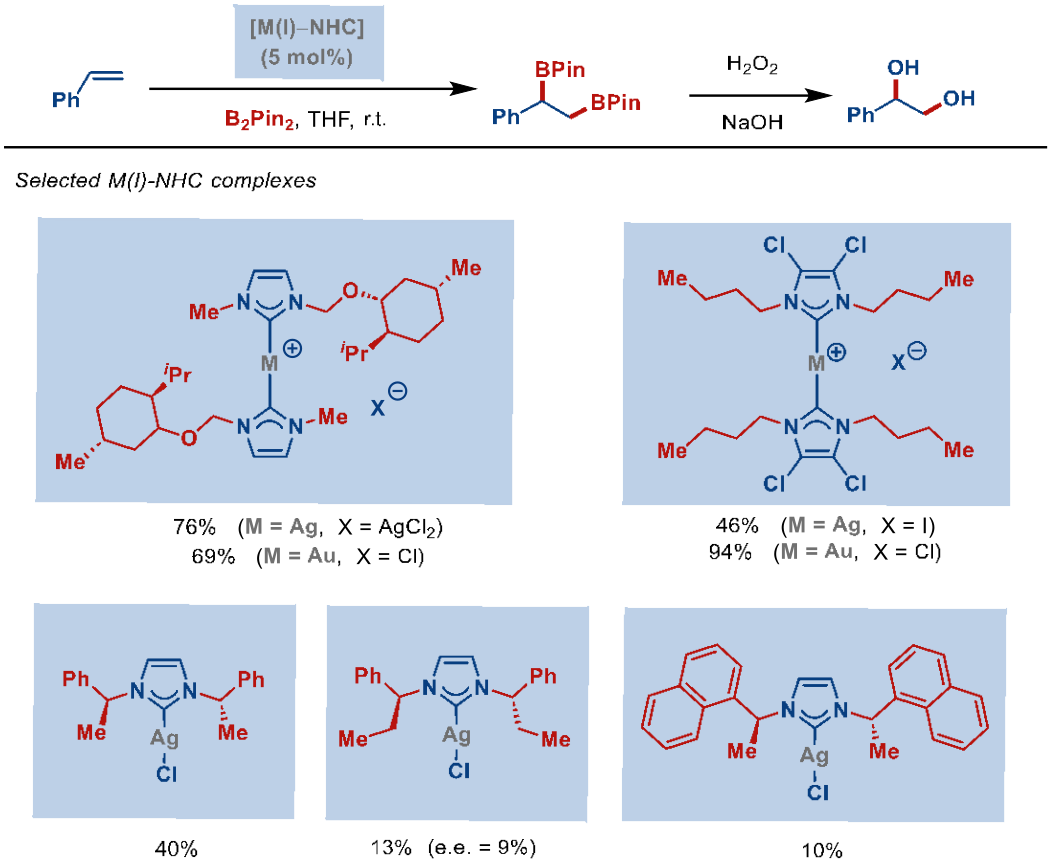
The first application of silver–NHC complexes in catalysis was reported by Fernandez and Peris in 2005 in catalytic diboration of alkenes (Scheme 1) [15]. The authors developed a menthol-based bis-metallic Ag(I)–NHC complex, [(mentimid)$_2$Ag]$AgCl_2$, which provided relatively high reactivity in diboration of terminal and activated internal alkenes using B_2Pin_2. Although no asymmetric induction was observed, the authors demonstrated the beneficia effect of Ag(I)–NHC in that the analogous Ag(I)-phosphine and cationic Ag^+ salts were completely unreactive. The high reactivity was ascribed to the combination of strong σ-donation allowing to break the B–B bond and low propensity of Ag(I)–NHC in β-hydride elimination of alkyl–boryl intermediate due to low π-back-bonding from Ag(I)–NHC. The proposed catalytic cycle is presented in Scheme 2. The key step involves insertion of the Ag–NHC complexes into the B–B bond to afford diboryl species, which undergoes alkene diborylation. An improved Ag(I)–NHC catalyst system was subsequently reported by the same authors (Scheme 3) [16]. This 2005 study set the stage for the exploration of Ag(I)–NHCs as efficient catalysts for electrophilic activation of alkynes.



Scheme 1. Ag(I)−NHC-Catalyzed Diboration of Terminal and Activated Internal Alkenes Using B_2Pin_2 Reported by Fernandez and Peris.

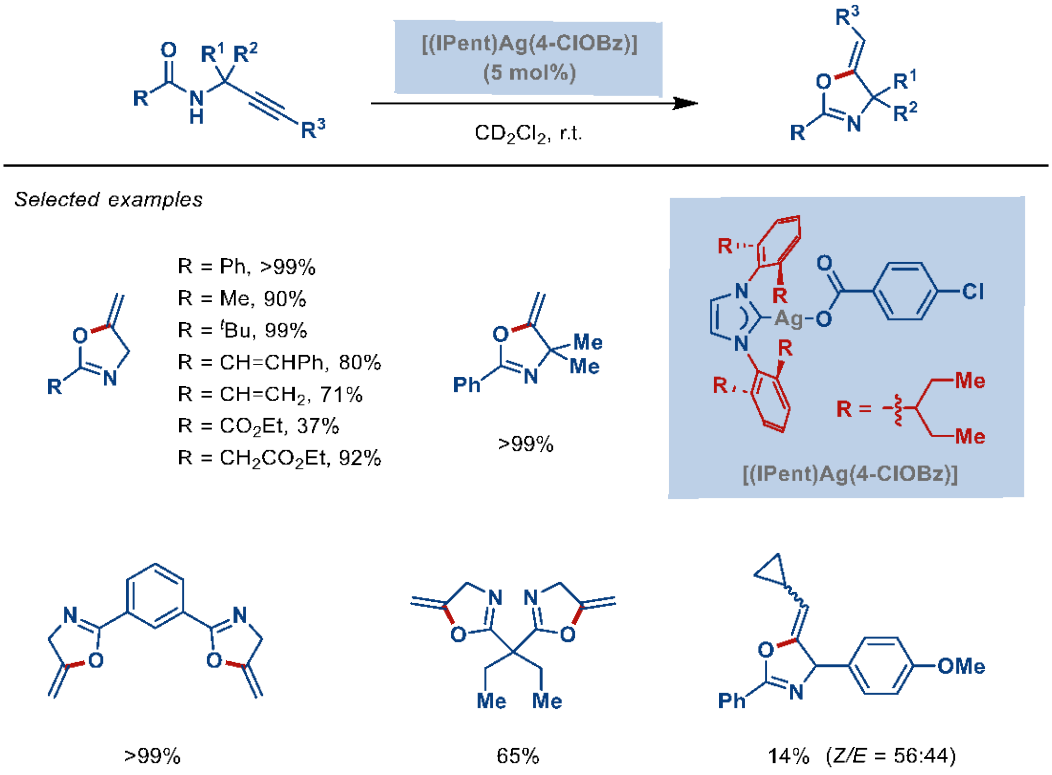


Scheme 2. The Catalytic Cycle of Ag(I)−NHC-Catalyzed Diborylation of Alkenes Reported by Fernandez and Peris.



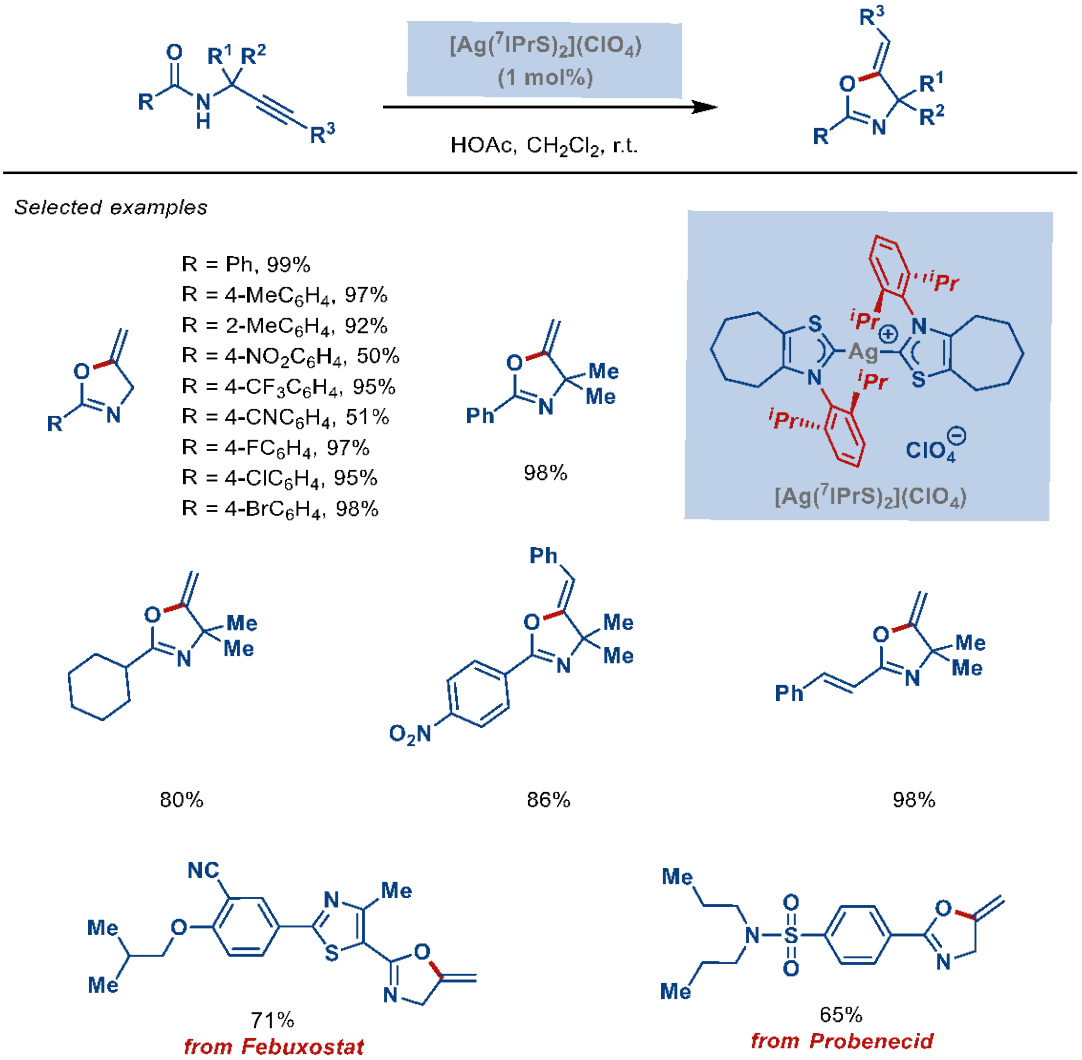
Scheme 3. Metal–NHC-Catalyzed Diboration of Internal Alkenes Using B_2Pin_2 Reported by Fernandez and Peris.

In 2016, Hii, Nolan and co-workers reported an impressive study on the effect of Ag(I)–NHC carboxylates, [(NHC)Ag(O_2CR)], in intramolecular cyclization of propargylic amides to afford oxazolidines (Scheme 4) [17]. The authors synthesized a series of [(NHC)Ag(O_2CR)] complexes with the goal of tuning electronic and steric properties of Ag(I)–NHC complexes by the NHC ligand, and their stability by the carboxylate ligand. The balance between the stability and activity of Ag(I)–NHCs is a major consideration in catalysis. The authors identified [(IPent)Ag(4-ClOBz)] bearing a bulky IPent ligand and electron-deficient 4-Cl-OBz throw-away ligand as the most effective combination for catalysis. A range of propargylic amides was cyclized to oxazolidines under very mild room temperature conditions at 5 mol% catalyst loading. The substrate scope of this intramolecular cyclization was found to be complementary to Au–NHC catalysis [18], showcasing the synthetic utility of Ag(I)–NHC complexes in catalysis. An important finding of this study is the capacity to independently tune sterics of the NHC ligand together with stability of the Ag(I)–NHC complex by carboxylate ancillary ligand.



Scheme 4. Ag(I)−NHC-Catalyzed Intramolecular Cyclization of Propargylic Amides to Afford Oxazolidines Reported by Hii, Nolan and co-workers.

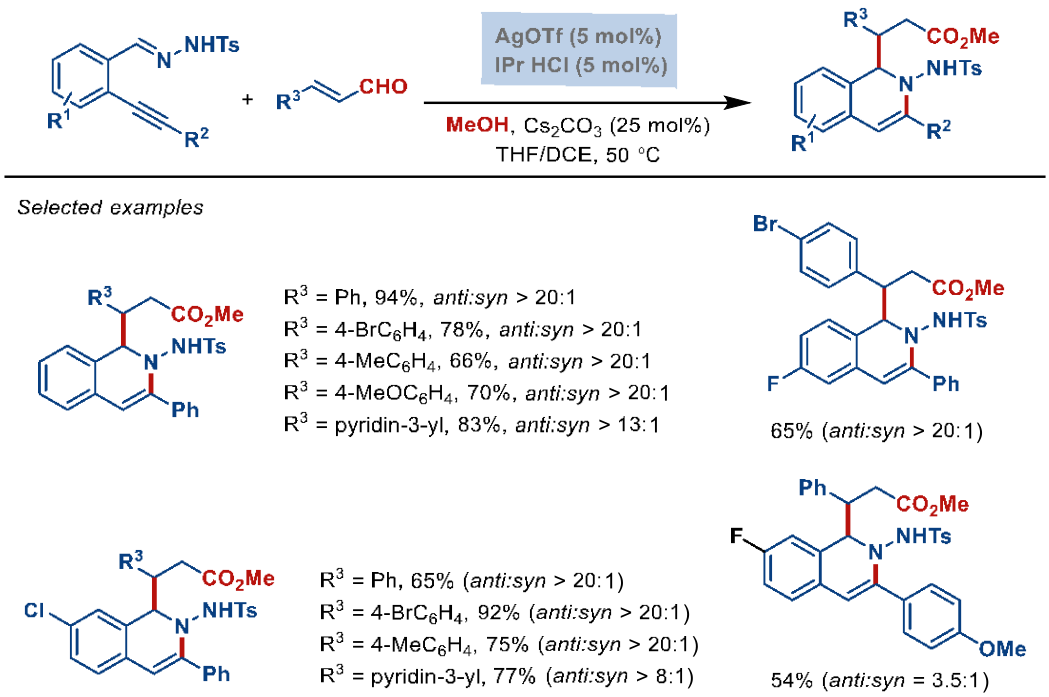
In 2022, we reported Ag(I)–thiazol-2-ylidene complexes and their application in the intramolecular cyclization to afford oxazolidines (Scheme 5) [19]. The non-classical framework of thiazol-2-ylidene offers new opportunities in catalysis due to differentiated half-umbrella-shaped ligand structure and enhanced π-electrophilicity [20]. We found that these Ag(I)–thiazol-2-ylidene complexes are highly active in the electrophilic cyclization of propargylic amides. These reactions proceeded in excellent yields at room temperature in the presence of 1 mol% of the bis-NHC–Ag(I) complex. The most reactive was [Ag(^{7}IPrS)$_2$](ClO$_4$) bearing a cycloheptyl thiazol-2-ylidene and perchlorate anion. The reaction was applied to late-stage functionalization of pharmaceuticals, showcasing the mild reaction conditions and potential applications in medicinal chemistry.



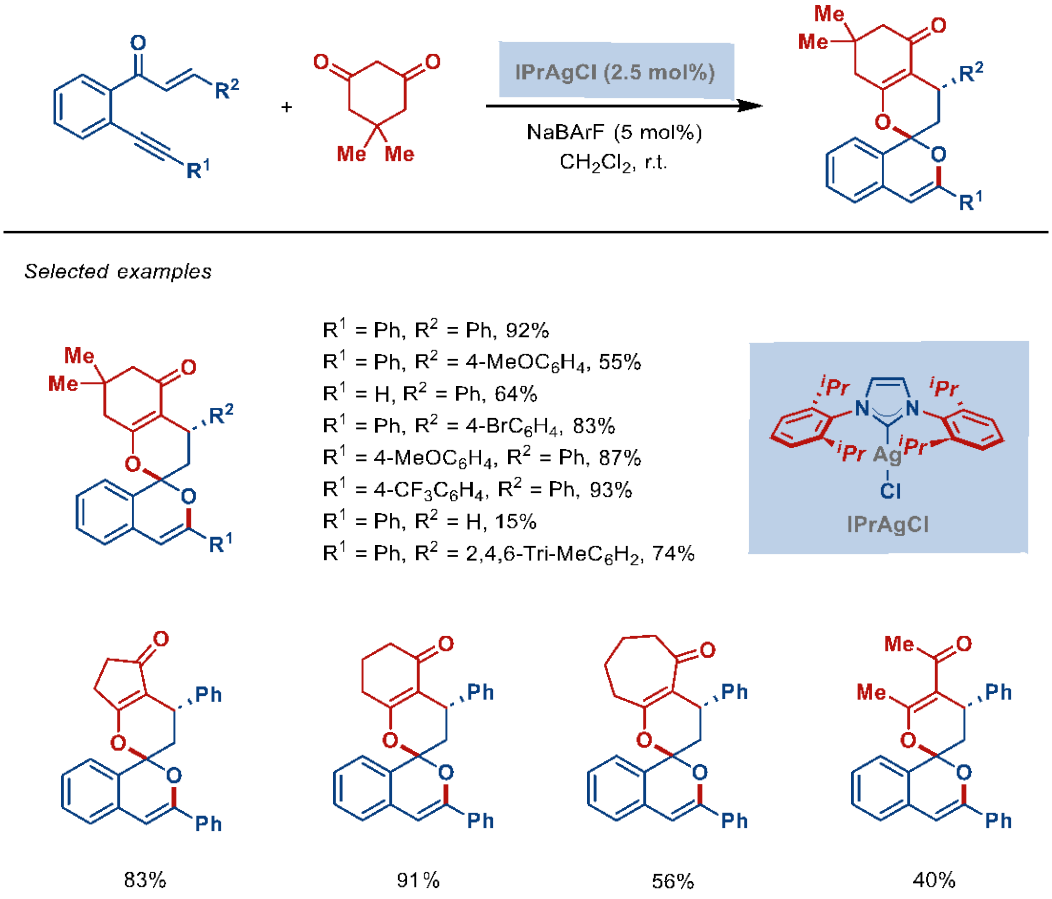
Scheme 5. Ag(I)–NHC-Catalyzed Intramolecular Cyclization of Propargylic Amides to Afford Oxazolidines Reported by Zhang, Fang, Szostak and co-workers.

Another intramolecular cyclization involving Ag(I)–NHCs was reported by Wu and co-workers in 2010 (Scheme 6) [21]. In this work, the authors found that the combination of AgOTf and IPrHCl in the presence of Cs_2CO_3 as a base enabled a tandem tricomponent cyclization of N′-(2-alkynylbenzylidene)-hydrazides with α,β-unsaturated aldehydes and methanol to afford functionalized 1,2-dihydroisoquinolines. The reaction proceeds via intramolecular cyclization of hydrazide onto the π-activated alkyne, followed by nucleophilic addition of homoenolate and methanol. The scope of the synthesis of the 2-amino-1,2-dihydroisoquinoline products is significant, permitting for the synthesis of medicinally-relevant heterocycles.

In 2019, Hashmi and co-workers reported a related approach based on Ag(I)–NHC-catalyzed intramolecular 6-*endo-dig* cyclization to form 6-membered benzofused spirocycles (Scheme 7) [22].



Scheme 6. Ag(I)–NHC-Catalyzed Tandem Tricomponent Cyclization to Afford 2-Amino-1,2-Dihydroisoquinolines Reported by Wu and co-workers.



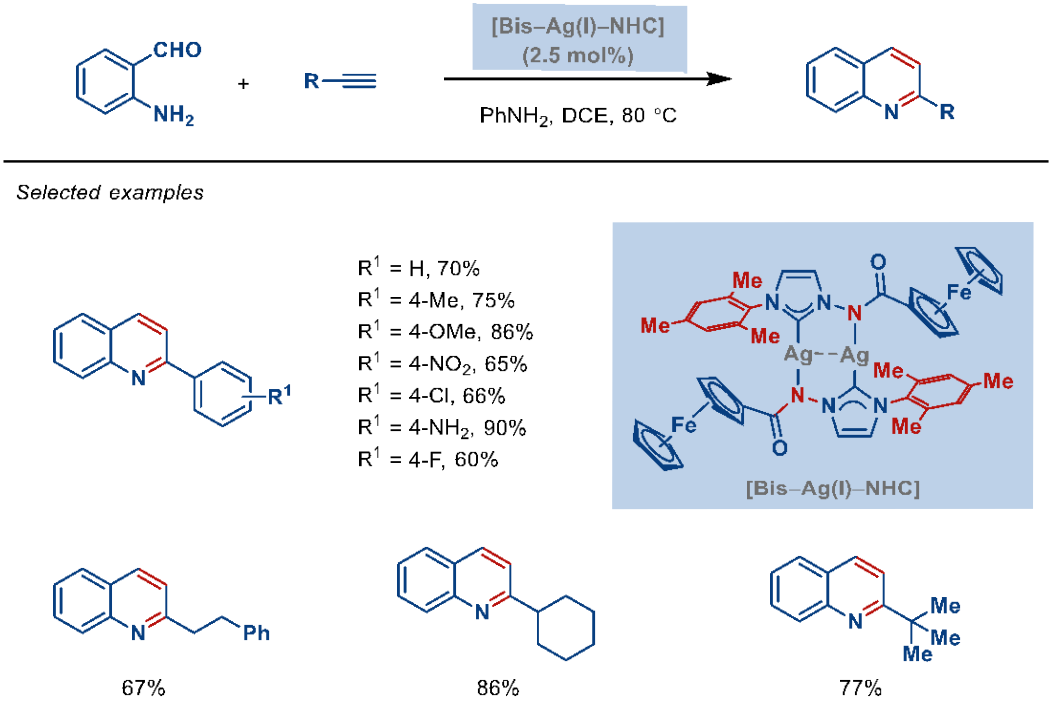
Scheme 7. Ag(I)–NHC-Catalyzed Intramolecular 6-*endo-dig* Cyclization to Form 6-Membered Benzofused Spirocycles Reported by Hashmi and co-workers.

Mechanistically, the key step involves intramolecular cyclization of the carbonyl group onto π-activated alkyne, followed by intermolecular Michael addition and spirocyclization. The role of Ag–

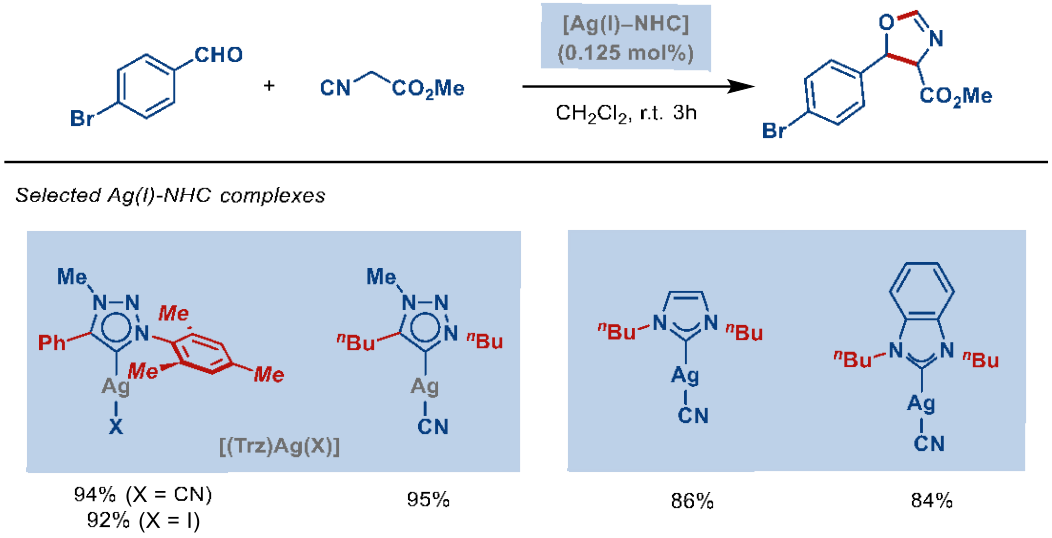
NHC is two-fold: as an alkyne and enol π-activator to facilitate intramolecular cyclizations. The authors screened various group 11 metal catalysts for this intriguing spriocyclization and found that [(IPr)AgCl]/$NaBAr^F$ is the most effective catalyst. This system outperformed simple Ag salts, such as $AgNTf_2$, $AgBF_4$ or AgOTf as well as various Au and Cu catalysts, such as $AuBr_3$, [(IPr)$AuCl_3$] or [(IPr)CuCl]/$NaBAr^F$. The methodology is particularly notable for broad substrate scope and rapid, convergent approach to biologically privileged 6,6-spiroketals, highlighting the utility of Ag(I)–NHCs catalysis in the synthesis of *O*-heterocycles.

In 2013, Bera and co-workers reported an interesting synthetic approach to quinolines by Ag(I)–NHC catalysis (Scheme 8) [23]. In contrast to the approaches described in Schemes 3-6, this reaction involves Ag(I)–NHC-catalyzed alkyne hydroamination, followed by condensation with 2-aminobenzaldehyde. The catalyst used in this case is a bimetallic Ag(I)–NHC bridged by two anionic N-Mes/N-ferrocenoyl amide ligands. Although no information was provided on the comparative activity of other complexes, the scope of the method appears to be quite broad. The reaction delivers important 2-funtionalized quinoline heterocycles in high yields by a three-component coupling.

In light of the reactions described above, it is important to mention Ag(I)–NHC-catalyzed synthesis of oxazolines from benzaldehydes and isocyanates reported by Albrecht in 2015 (Scheme 9) [24]. This reaction features non-classical silver triazolylidene complexes prepared readily by the Lin method from Ag_2O and the corresponding triazolium salts. In the complex synthesis, the use of CH_3CN as a solvent resulted in C–C bond activation and the formation of [(trz)Ag(CN)] complexes, while [(trz)Ag(X)] complexes were formed in CH_2Cl_2. These Ag(I)–trz complexes showed slightly higher reactivity than the analogous imidazol-2-ylidene Ag(I) complexes in the synthesis of oxazolines. The reaction was highly effective even at 0.10 mol% catalyst loading, showcasing the powerful role of Ag(I)–NHC in promoting intramolecular cyclizations.



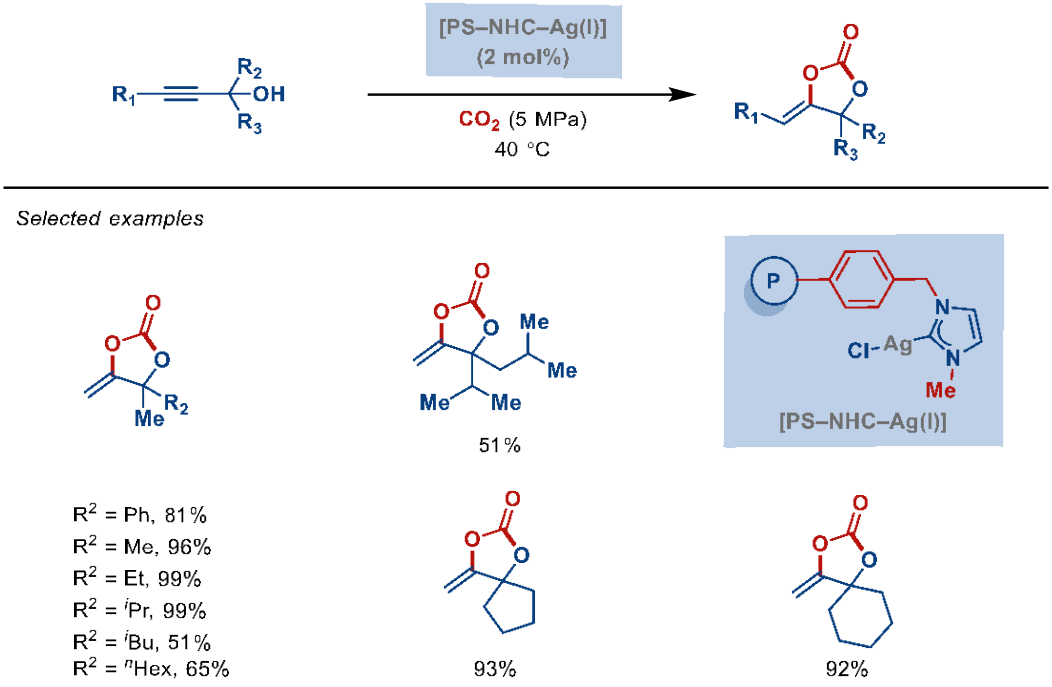
Scheme 8. Bimetallic Ag(I)–NHC-Catalyzed Tandem Tricomponent Cyclization to Afford 2-Funtionalized Quinolines Reported by Bera and co-workers.



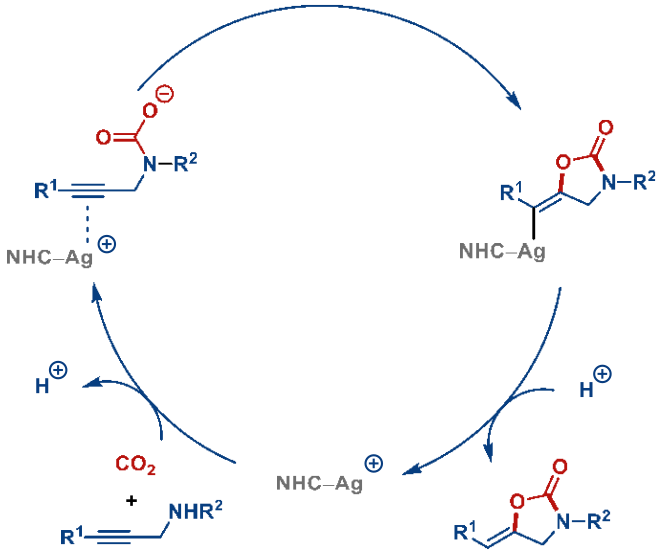
Scheme 9. Ag(I)–NHC-Catalyzed Synthesis of Oxazolines from Benzaldehydes and Isocyanates Reported by Albrecht and co-workers.

3. CO_2 Fixation

The ability to incorporate CO_2 in carbon–carbon bond forming reactions as a renewable C1 synthon is of great interest in organic synthesis [25]. In 2013, Jiang and co-workers reported polystyrene supported Ag(I)–NHC complexes, [PS–NHC–Ag(I)], for CO_2 fixation into propargylic alcohols (Scheme 10) [26]. The [PS–NHC–Ag(I)] complexes were readily prepared by the reaction of appropriately substituted N-alkyl-imidazoles with polystyrene-supported benzyl chloride. The most active was N-Me substituted complex. Interestingly, analogous Cu–NHC complex, [PS–NHC–Cu(I)], showed no activity under the reaction conditions. These [PS–NHC–Ag(I)] complexes promoted the carboxylative cyclization of a range of propargylic alcohols to terminal alkylidene cyclic carbonates in generally excellent yields under 5 MPa pressure of CO_2 at 40 °C. This approach by Jiang and co-workers has several benefits, including high catalytic activity, ease of catalyst separation and catalyst recyclability.



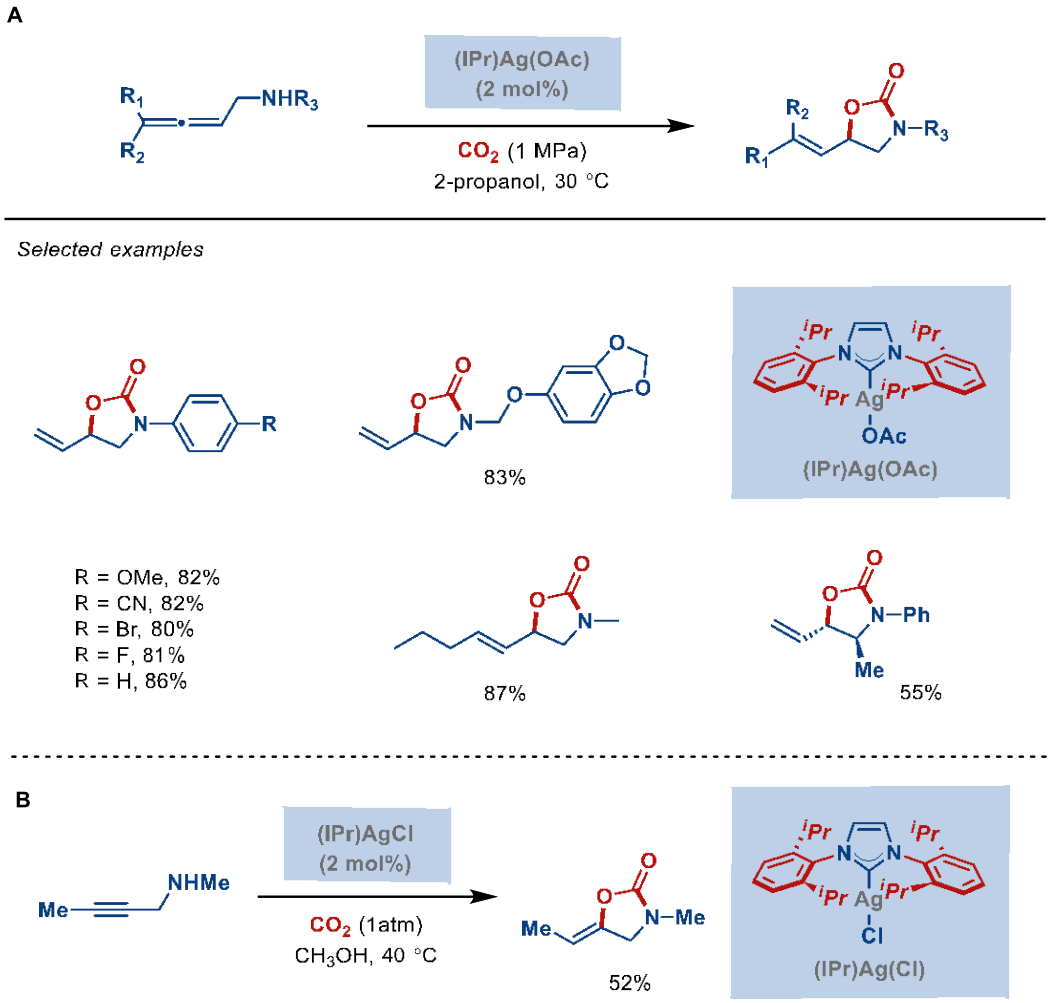
Scheme 10. Polystyrene Supported Ag(I)–NHC-Catalyzed CO_2 Fixation into Propargylic Alcohols Reported by Jiang and co-workers.



Scheme 11. The General Catalytic Cycle of Ag(I)–NHC-Catalyzed CO_2 Fixation to Propargylamines.

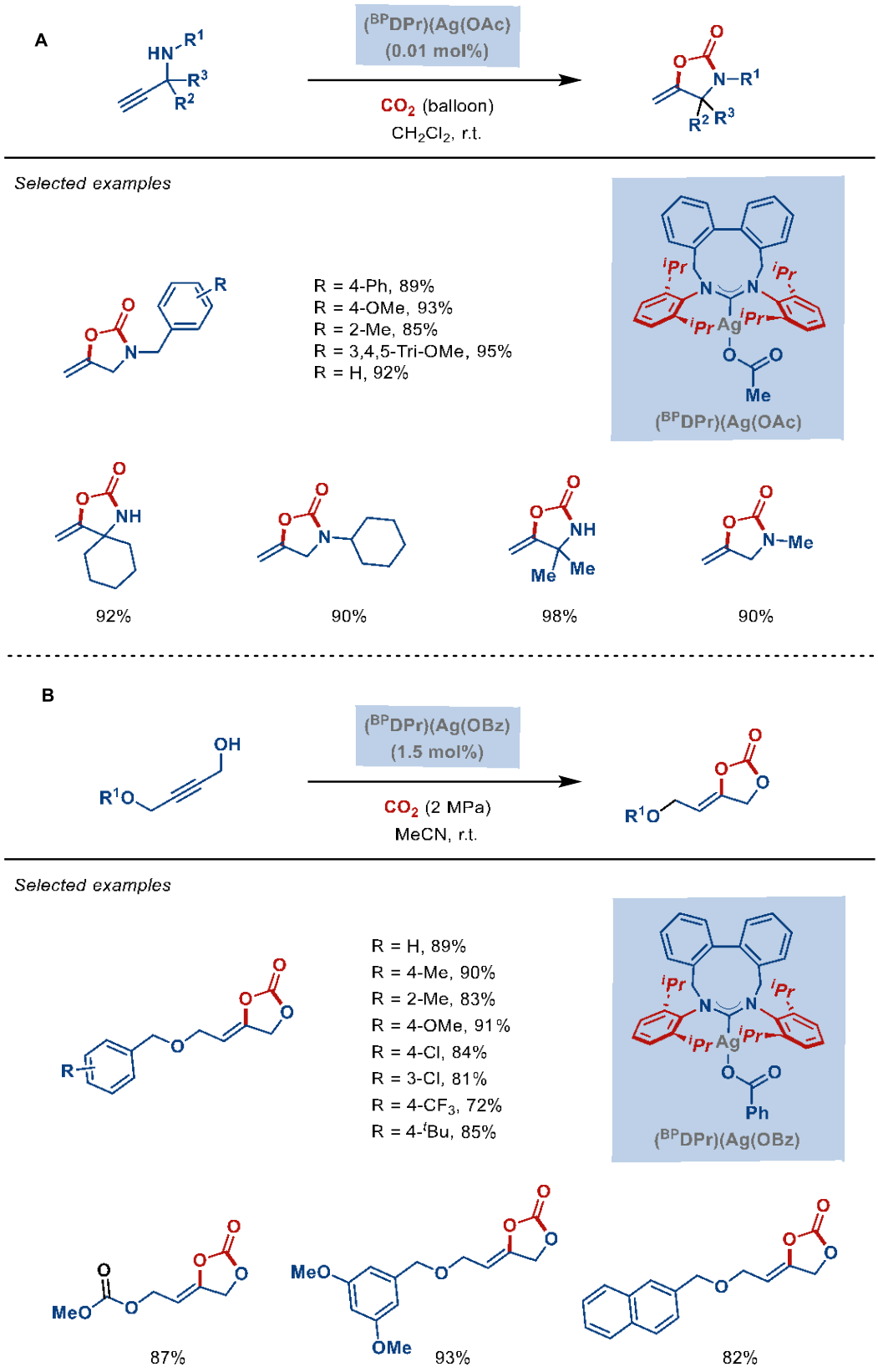
The proposed catalytic cycle is presented in Scheme 11. The reaction invovles π-activation of the alkyne by cationic Ag–NHC species, followed by nucleophilic attack of the carbamate anion. Protonolysis regenerates the active Ag–NHC species. This represents a general mechanism for cyclization reactions mediated by Ag–NHC complexes.

In 2015, Ikariya and co-workers reported Ag(I)–NHC-catalyzed fixation of CO_2 into allenylmethylamines (Scheme 12A) [27]. The authors identified [(IPr)Ag(OAc)] as the most effective catalyst to afford alkenyl-1,3-oxazolidin-2-ones. The choice of metal, ancillary ligand and counterion was critical for this process. The analogous Au and Cu complexes, [(IPr)Au(OAc)] and [(IPr)Cu(OAc)], were completely ineffective, while [(IPr)Ag(Cl)] showed minimal activity (<10%). The reaction showed good scope of allenylmethylamines at atmospheric pressure of CO_2 at 30 °C. Mechanistically, two competing pathways were proposed, carboxylative cyclization leading to alkenyl-1,3-oxazolidin-2-ones and intramolecular hydroamination resulting in 2,-5-dihydropyrroles, initiated by π-coordination to the internal or external allene double bond. Interestingly, the same group reported intramolecular carboxylative cyclization of propargylamines to alkylidene-1,3-oxazolidin-2-ones mediated by [(IPr)AgCl] in modest yield (Scheme 12B).



Scheme 12. Ag(I)–NHC-Catalyzed CO_2 Fixation into Allenylmethylamines Reported by Ikariya and co-workers.

In 2021, an important breakthrough was reported by Cervantes-Reyes, Hashmi and co-workers in identifying ring expanded Ag(I)–NHC complexes as efficient catalysts for carboxylative cyclization of propargylic alcohols and amines (Scheme 13) [28]. The most active complexes were [(^{BP}DPr)(Ag(OAc)] and [(^{BP}DPr)(Ag(OBz)] featuring a nine-membered, bulky NHC ligand (^{BP}DPr = 1,3-bis(2,6-diisopropylphenyl)-1,3-diazonine-2-ylidene) and carboxylate counterions. These complexes are characterized by some of the largest buried volumes reported for [(NHC)AgX] complexes to date, ([(^{BP}DPr)(Ag(OAc)]: $\%V_{bur}$ = 52.9%; [(^{BP}DPr)(Ag(OBz)]: $\%V_{bur}$ = 54.5%). The scope of the carboxylative cyclization mediated by these ring-expanded NHCs is particularly broad, which has been ascribed to the steric distribution of the ligand on the metal center. The highlight is the ability to promote carboxylative cyclization of unsubstituted propargylic alcohols and amines to afford terminal and internal unsubstituted oxazolidinones and cyclic α-methylene carbonates in excellent yields.

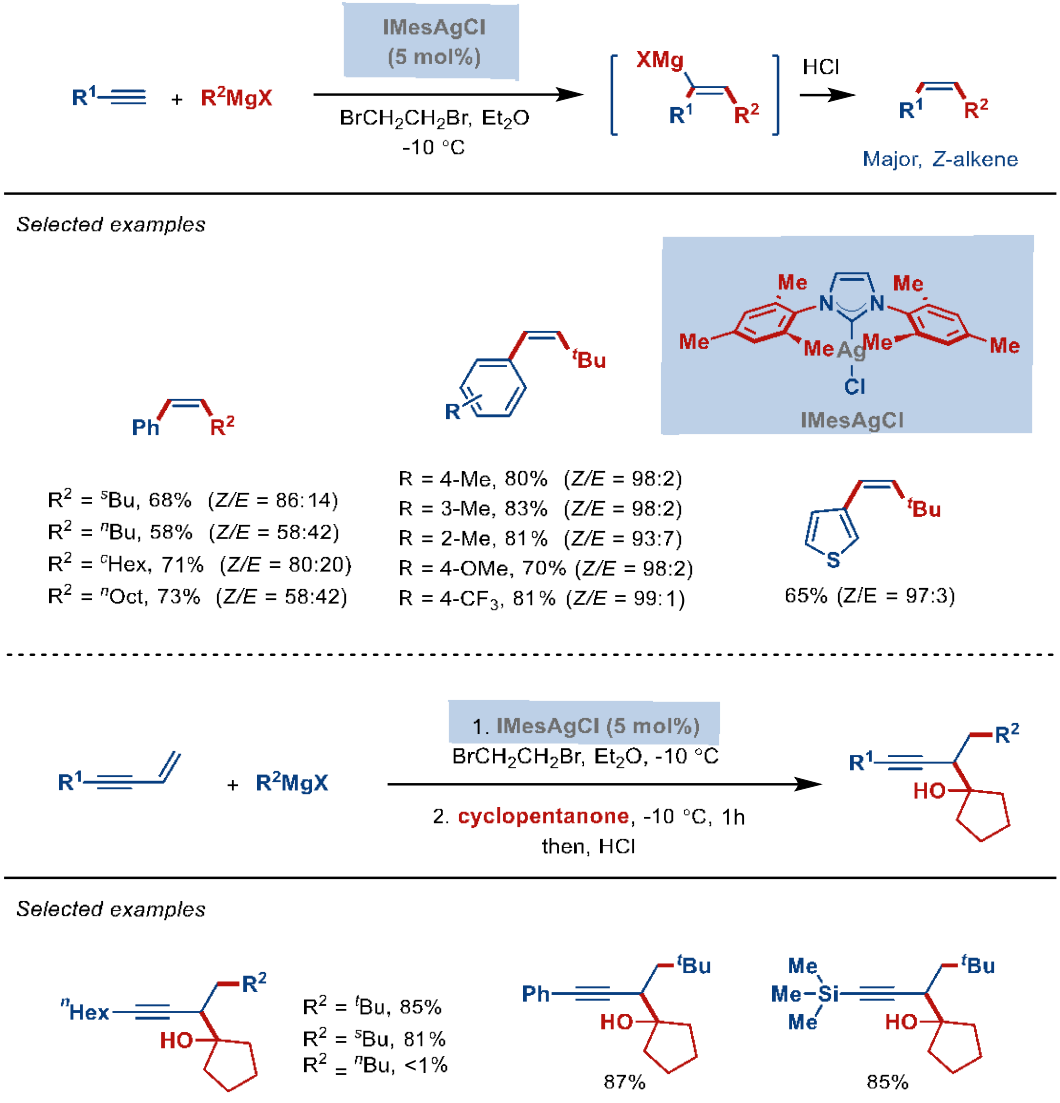


Scheme 13. Ag(I)–NHC-Catalyzed Carboxylative Cyclization of Propargylic Alcohols and Amines Reported by Cervantes-Reyes, Hashmi and co-workers.

4. Hydrofunctionalization Reactions

The catalytic hydrofunctionalization of alkynes is among the most useful transformations in organic synthesis. [29] In 2009, Kambe and co-workers reported carbomagnesiation of alkynes

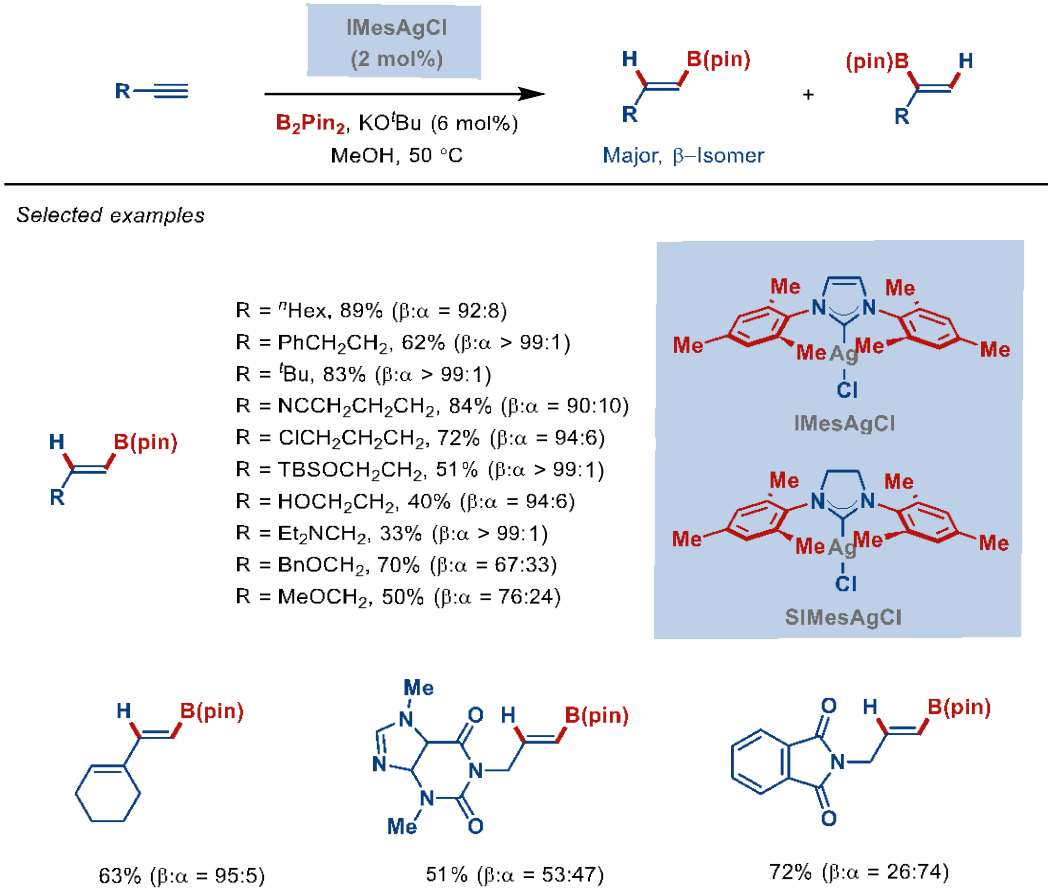
catalyzed by Ag(I)–NHC complexes (Scheme 14) [30]. This reaction proceeds in the presence of [(IMes)AgCl] as a catalyst, alkyl Grignard reagent as a nucleophile and $BrCH_2CH_2Br$ as a stoichiometric additive. Ag–NHCs are the preferred catalyst over simple silver salts, such as AgOTs, and Ag–phosphine systems, such as AgOTs/PPh_3, affording higher yields and *Z*:*E* selectivity up to 99:1. Mechanistically, the reaction involves the formation of an alkyl silver complex, followed by *anti*-alkyne insertion and transmetalation. The scope of this process is broad with respect to aryl alkynes using *t*-BuMgCl as a nucleophile. However, lower selectivity was observed with less sterically-hindered Grignard reagents. The authors extended the utility of this process to carbofunctionalization of enynes and trapping with carbonyl electrophiles.



Scheme 14. Ag(I)–NHC-Catalyzed Carbomagnesiation of Alkynes Reported by Kambe and co-workers.

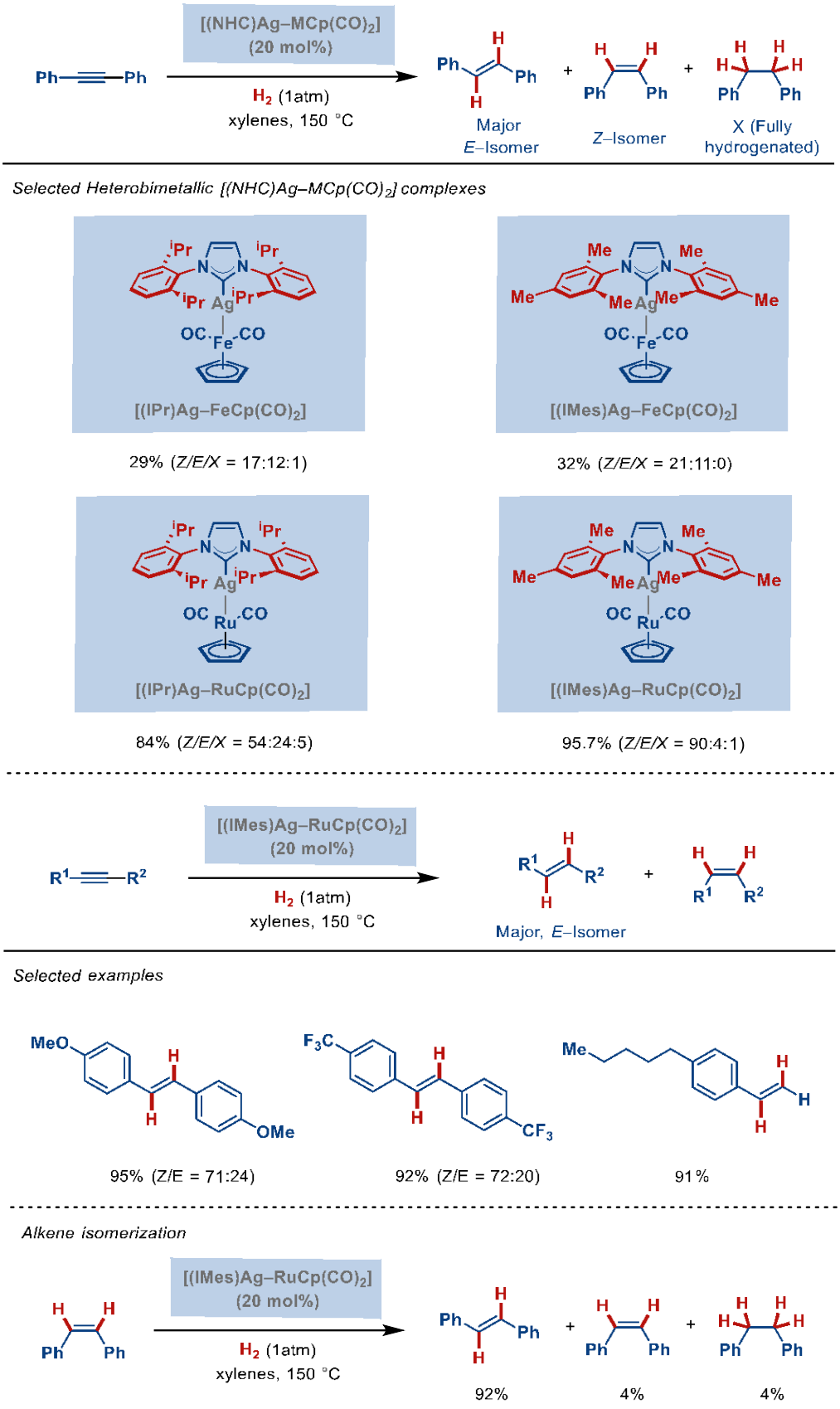
In 2014, a significant method for hydroboration of alkynes catalyzed by Ag(I)–NHC complexes was reported by Yoshida and co-workers (Scheme 15) [31]. [(IMes)AgCl] in the presence of catalytic KO*t*Bu and B_2Pin_2 (1 equiv) in MeOH at 50 °C was identified as the optimal system for this transformation. Interestingly, the imidazolin-2-ylidene analogue, [(SIMes)AgCl], showed almost identical reactivity, while the imidazol-2-ylidene counterpart, [(IPr)AgCl], was completely unreactive under the tested conditions. The scope of the reaction is very broad and involves terminal aliphatic alkynes and internal aromatic alkynes. The yields and selectivity for the formation of β-hydroboration products are generally high to excellent. Mechanistically, the key step is the formation

of [(IMes)Ag–BPin] species by σ-metathesis between [(IMes)Ag–O*t*Bu] and B_2Pin_2. This [(IMes)Ag–BPin] species adds across the alkyne bond to generate β-boryl–organosilver, which undergoes protonolysis.

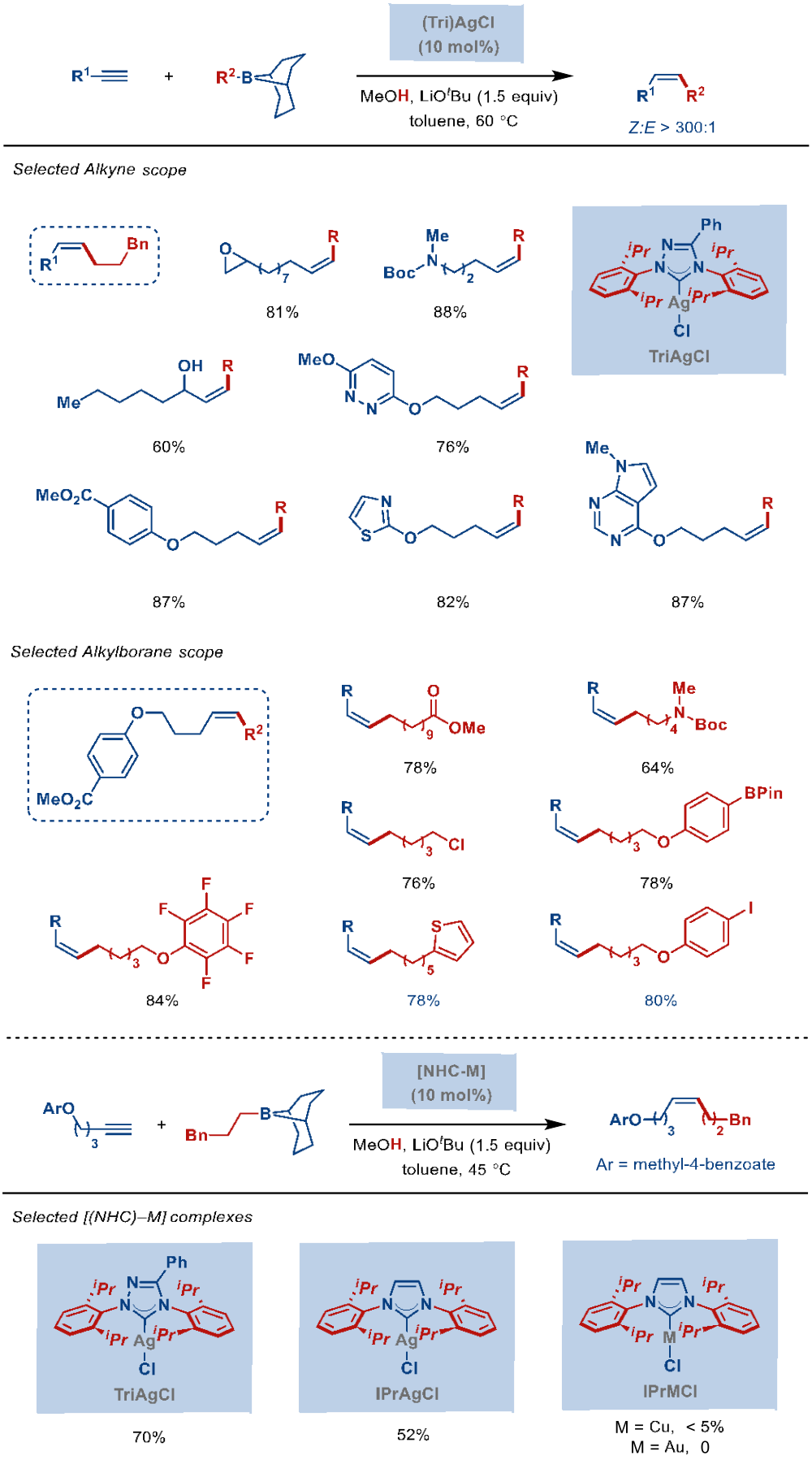


Scheme 15. Ag(I)–NHC-Catalyzed Hydroboration of Alkynes Reported by Yoshida and co-workers.

In 2014, Mankad and co-workers reported an intriguing *E*-selective hydrogenation of alkynes by [Ag–Ru] bimetallic catalysis (Scheme 16) [32]. The most effective catalyst system is [(IMes)Ag–$RuCp(CO)_2$] under atmospheric pressure of H_2 in xylenes at 150 °C. The bimetallic cooperation is critical to this process as no reaction is observed by each of the catalyst systems alone. IPr and Cu as well as $FeCp(CO)_2$ can be used, however, the yields and selectivity are lower than with [(IMes)Ag–$RuCp(CO)_2$] complex. Mechanistically, bimetallic H_2 activation is followed by *syn*-alkyne insertion into [(IMes)–Ag–H] to afford α-alkenyl–Ag(NHC) intermediate and protonolysis by [$RuCp(CO_2)$–H]. The authors demonstrated that *Z*/*E* alkene isomerization takes place under the reaction conditions. The functional group tolerance of this method is broad as demonstrated by the Glorius robustness test, where only aldehydes were found to inhibit the reaction rate. This study demonstrates the potential of Ag–NHCs as an effective class of ligands in the emerging area of bimetallic catalysis [33]. In 2019, Lalic group reported hydroalkylation of alkynes catalyzed by Ag(I)–NHC complexes (Scheme 17) [34]. The most intriguing feature of this report is the use of 1,2,4-triazolylidene NHC, [(Tri)AgCl] (Tri = 1-phenyl-2,4-Dipp-1,2,4-triazolylidene) as the more effective ligand than the classical imidazol-2-ylidene, [(IPr)AgCl]. Furthermore, the analogous Cu complex, [(IPr)CuCl] was completely unreactive. 1,2,4-Triazol-5-ylidenes are significantly less basic than imidazol-2-ylidenes (pK_a = 16.1 vs. 21.5, calculated values, DMSO) [35], which may contribute to the higher reactivity of [(Tri)AgCl] vs. [(IPr)AgCl]. The reaction yields *Z*-alkenes with full stereoselectivity and excellent functional group tolerance.

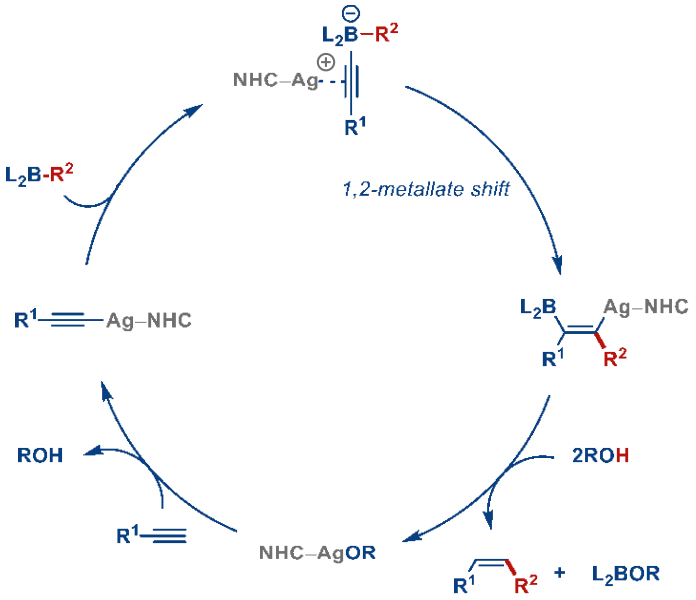


Scheme 16. Bimetallic [Ru-Ag(I)–NHC]-Catalyzed *E*-Selective Hydrogenation of Alkynes Reported by Mankad and co-workers.



Scheme 17. Ag(I)–NHC-Catalyzed Hydroalkylation of Alkynes Reported by Lalic and co-workers.

Mechanistically, the reaction involves the combination of σ- and π-activation of alkynes, which may further explain better reactivity of Ag–NHCs vs. Cu–NHCs. The authors proposed that silver acetylide reacts with alkyl borane, followed by 1,2-metalate shift after π-activation. The catalytic cycle is completed by protodemetalation and protodeboronation (Scheme 18). This report provides a clear example of the advantages of using Ag(I)–NHCs in catalysis by combining two activation modes inherently favored by silver.



Scheme 18. The Catalytic Cycle of Ag(I)–NHC-Catalyzed Hydroalkylation of Alkynes Reported by Lalic and co-workers.

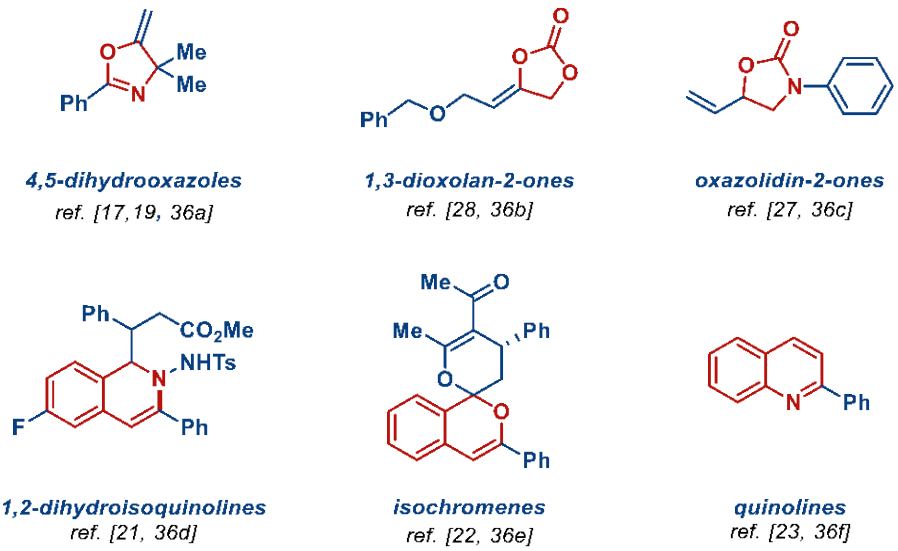


Figure 2. Heterocyclic Scaffolds Synthesized by Ag(I)–NHC Complexes.

5. Conclusions and Outlook

In summary, in the past 15 years significant advances have been made in using Ag–NHC complexes for the synthetically important functionalization of alkynes. Among the major advantages of Ag–NHCs is the enhanced stability of silver rendered possible by strongly σ-donating NHC ligands, ligand amplified reactivity in several general classes of reactions, and the improved reactivity over other group 11 metals. In particular, progress has been considerable in the following generic classes of reactions: intramolecular cyclizations, CO_2 fixation, and hydrofunctionalization

reactions. These reactions provide heterocyclic products important for medicinal chemistry research and functionalized building blocks for organic synthesis. Among the reported reactions, the most noteworthy are processes that specifically demonstrate the beneficial role of Ag–NHCs, such as electrophilic cyclization of propargylic amides, CO_2 fixation, bimetallic Ag–Ru hydrogenation of alkynes, and hydroalkylation of alkynes.

An interesting consideration is the fact that Ag–NHC complexes appear to be particularly well-suited for the synthesis of heterocycles that are part of potential therapeutic agents (Figure 2) [36]. This reactivity of Ag–NHCs in π-activation of alkynes bodes well for the broad practical application of this class of M–NHCs in medicinal chemistry research.

Despite significant progress, there are several areas that should be addressed in the future to render this Ag–NHC manifold even of more general utility in organic synthesis: (1) mechanistic studies are urgently needed to elucidate the role of Ag–NHCs in comparison with other group 11 metal–NHC complexes; (2) the role of NHC ligands has been rarely explored in Ag–NHC catalysis, with majority of reactions limited to testing only IPr and IMes ligands; (3) although the mechanistic basis for several alkyne functionalization manifolds using Ag–NHCs has been established, few reactions have been explored using this catalysis manifold; (4) the role of counterion has not been fully elucidated, with simple carboxylate anions typically preferred for activation of alkynes; (5) the development of asymmetric processes using chiral Ag–NHCs has not been accomplished.

In the group of coinage metals, silver has several major advantages over Au and Cu, including low price and availability (vs. Au), capacity to promote various activation modes, ease of transmetallation, complementary electronic properties, such as π to σ metal donation and metal to π* back-bonding. The reported studies clearly demonstrate that researchers using group 11 metal–NHC complexes should always consider Ag(I)–NHCs in the development of catalytic processes.

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References:

1. Arduengo, A. J., III; Dias, H. R.; Calabrese, J. C.; Davidson, F. Homoleptic Carbene-Silver (I) and Carbene-Copper (I) Complexes. *Organometallics* **1993**, *12*, 3405−3409.
2. Wang, H. M.; Lin, I. J. Facile Synthesis of Silver (I)−Carbene Complexes. Useful Carbene Transfer Agents. *Organometallics* **1998**, *17*, 972−975.
3. For representative books and chapters on NHCs, see: (a) Nolan, S. P. *N-Heterocyclic Carbenes in Synthesis*, 1st ed.; Wiley: New York, **2006**. (b) Glorius, F. *N-Heterocyclic Carbenes in Transition Metal Catalysis*, 1st ed.; Springer: Berlin, **2007**. (c) Nolan, S. P. *N-Heterocyclic Carbenes: Effective Tools for Organometallic Synthesis*. 1st ed.; Ed.; Wiley: Weinheim, **2014**. (d) Díez-Gonzalez, S. *N-Heterocyclic Carbenes: From Laboratory to Curiosities to Efficient Synthetic Tools*, 2nd ed.; Royal Society of Chemistry: London, **2016**. (e) Nolan, S.; Cazin, C. N-Heterocyclic Carbenes in Catalytic Organic Synthesis, 1st ed.; Thieme: Stuttgart, **2017**. (f) Huynh, H. V. *The Organometallic Chemistry of N-Heterocyclic Carbenes*, Wiley: Hoboken, **2017**.
4. For selected reviews on metal-NHCs, see: (a) Fortman, G. C.; Nolan, S. P. N-Heterocyclic carbene (NHC) ligands and palladium in homogeneous cross-coupling catalysis: a perfect union. *Chem. Soc. Rev.* **2011**, 40, 5151-5169. (b) Velazquez, H. D.; Verpoort, F. N-Heterocyclic Carbene Transition Metal Complexes for Catalysis in Aqueous Media. *Chem. Soc. Rev.* **2012**, *41*, 7032−7060. (c) Liu, W. K.; Gust, R. Metal N-Heterocyclic Carbene Complexes as Potential Antitumor Metallodrugs. *Chem. Soc. Rev.* **2013**, *42*, 755− 773. (d) Hopkinson, M. N.; Richter, C.; Schedler, M.; Glorius, F. An Overview of N-Heterocyclic Carbenes. *Nature* **2014**, *510*, 485. (d) Visbal, R.; Gimeno, M. C. N-Heterocyclic Carbene Metal Complexes: Photoluminescence and Applications. *Chem. Soc. Rev.* **2014**, *43*, 3551−3574. (e) Peris, E. Smart N-Heterocyclic Carbene Ligands in Catalysis. *Chem. Rev.* **2018**, *118*, 9988−10031. (f) Huynh, H. V. Electronic Properties of *N*-Heterocyclic Carbenes and Their Experimental Determination. *Chem. Rev.* **2018**, *118*, 9457-9492. (g) Shi, S.; Nolan, S. P.; Szostak, M. Well-Defined Palladium(II)-NHC (NHC = *N*-Heterocyclic Carbene) Precatalysts for Cross-Coupling Reactions of Amides and Esters by Selective Acyl CO–X (X = N, O) Cleavage. *Acc. Chem.*

Res. **2018**, *51*, 2589-2599. (h) Zhao, Q.; Meng, G.; Nolan, S. P.; Szostak, M. N-Heterocyclic Carbene Complexes in C–H Activation Reactions. *Chem. Rev.* **2020**, 120, 1981-2048. (i) Chen, C.; Liu, F. S.; Szostak, M. BIAN-NHC Ligands in Transition-Metal-Catalysis: A Perfect Union of Sterically Encumbered, Electronically Tunable N-Heterocyclic Carbenes? *Chem. Eur. J.* **2021**, *27*, 4478-4499.

5. Melaiye, A., Simons, R. S., Milsted, A., Pingitore, F., Wesdemiotis, C., Tessier, C. A., and Youngs, W. J. Formation of water-soluble pincer silver(I)-carbene complexes: a novel antimicrobial agent. *J. Med. Chem.* **2004.** *47*, 973–977.
6. For recent reviews on biological activity of silver-NHCs, see: (a) Garrison, J. C.; Youngs, W. J. Ag(I) N-Heterocyclic Carbene Complexes: Synthesis, Structure, and Application. *Chem. Rev.* **2005**, *105*, 3978– 4008. (b) Ray, S.; Mohan, R.; Singh, J. K.; Samantaray, M. K.; Shaikh, M. M.; Panda, D.; Ghosh, P. Anticancer and Antimicrobial Metallopharmaceutical Agents Based on Palladium, Gold, and Silver N-Heterocyclic Carbene Complexes. *J. Am. Chem. Soc.* **2007**, *129*, 15042– 15053. (c) Johnson, N. A.; Southerland, M. R.; Youngs, W. J. Recent Developments in the Medicinal Applications of Silver-NHC Complexes and Imidazolium Salts. *Molecules* **2017**, *22*, 1263. (d) Liang, X.; Luan, S.; Yin, Z.; He, M.; He, C.; Yin, L.; Zou, Y.; Yuan, Z.; Li, L.; Song, X.; Lv, C.; Zhang, W. Recent advances in the medical use of silver complex. *Eur. J. Med. Chem.* **2018**, *157*, 62–80. (e) Hussaini, S. Y.; Haque, R. A.; Razali, M. R. Recent Progress in Silver(I)-, Gold(I)/(III)- and Palladium(II)-N-Heterocyclic Carbene Complexes: A Review Towards Biological Perspectives. *J. Organomet. Chem.* **2019**, *882*, 96–111.
7. For selected reviews on coinage metals, see: (a) Lipshutz, B. H.; Yamamoto, Y. Introduction: Coinage metals in organic synthesis. *Chem. Rev.* **2008**, *108*, 2793–2795. (b) Patil, N. T.; Yamamoto, Y. Coinage metal-assisted synthesis of heterocycles. *Chem. Rev.* **2008**, *108*, 3395–3442. (c) Lin, J. C. Y.; Huang, R. T. W.; Lee, C. S.; Bhattacharyya, A.; Hwang, W. S.; Lin, I. J. B. Coinage Metal–*N*-Heterocyclic Carbene Complexes. *Chem. Rev.* **2009**, *109*, 3561– 3598. (d) Jazzar, R.; Soleilhavoup, M.; Bertrand, G. Cyclic (Alkyl)- and (Aryl)-(Amino)Carbene Coinage Metal Complexes and Their Applications. *Chem. Rev.* **2020**, *120*, 4141– 4168.
8. Metal Prices: Gold, Silver, Copper and More. https://thestockmarketwatch.com/metal/prices.aspx accessed on Dec, 30, 2022.
9. Haynes, W. M. *Handbook of Chemistry and Physics*, 96th ed., Haynes, W. M.; Bruno, T. J.; Lide, D. R., Eds.; CRC Press: Boca Raton, FL, **2015**.
10. For selected reviews on silver and silver–NHCs in catalysis, see: (a) Weibel, J.-M.; Blanc, A.; Pale, P. Ag-Mediated Reactions: Coupling and Heterocyclization Reactions. *Chem. Rev.* **2008**, 108, 3149-3173. (b) Muñoz, M. P. Silver and Platinum-Catalysed Addition of O-H and N-H Bonds to Allenes. *Chem. Soc. Rev.* **2014**, *43*, 3164– 3183. (c) Fang, G.; Bi, X. Silver-Catalyzed Reactions of Alkynes: Recent Advances. *Chem. Soc. Rev.* **2015**, *44*, 8124– 8173. (d) Zheng, Q.-Z.; Jiao, N. Ag-Catalyzed C–H/C–C Bond Functionalization *Chem. Soc. Rev.* **2016**, 45, 4590– 4627. (e) Zheng, Q.-Z.; Jiao, N. Ag-Catalyzed C–H/C–C Bond Functionalization *Chem. Soc. Rev.* **2016**, 45, 4590–4627. (f) Pellissier, H. Enantioselective silver-catalyzed transformations. *Chem. Rev.* **2016**, *116*, 14868–14917. (g) Sekine, K.; Yamada, T. Silver-catalyzed carboxylation. *Chem. Soc. Rev.* **2016**, *45*, 4524– 4532. (h) Wang, Z.; Tzouras, N. V.; Nolan, S. P.; Bi, X. Silver N-Heterocyclic Carbenes: Emerging Powerful Catalysts. *Trends Chem* **2021**, *3*, 674– 685.
11. For relevant studies, see: (a) Wanniarachchi, Y. A.; Khan, M. A.; Slaughter, L. G. M. An Unusually Static, Sterically Hindered Silver Bis(N-heterocyclic carbene) Complex and Its Use in Transmetalation. *Organometallics* **2004**, *23*, 5881– 5884. (b) Green, S. P.; Jones, C.; Mills, D. P.; Stasch, A. Group 9 and 11 Metal(I) Gallyl Complexes Stabilized by N-Heterocyclic Carbene Coordination: First Structural Characterization of Ga–M (M = Cu or Ag) Bonds. *Organometallics* **2007**, *26* (14), 3424– 3430. (c) Gaillard, S.; Bantreil, X.; Slawin, A. W.; Nolan, S. P. Synthesis and Characterization IPrMe-containing Silver(I), Gold(I) and Gold(III) Complexes Dalton Trans. **2009**, 6967– 6971. (d) de Frémont, P.; Scott, N. M.; Stevens, E. D.; Ramnial, T.; Lightbody, O. C.; Macdonald, C. L. B.; Clyburne, J. A. C.; Abernethy, C. D.; Nolan, S. P. Synthesis of Well-Defined *N*-Heterocyclic Carbene Silver(I) Complexes. *Organometallics* **2005**, *24*, 6301– 6309. (e) Ramnial, T.; Abernethy, C. D.; Spicer, M. D.; McKenzie, I. D.; Gay, I. D.; Clyburne, J. A. C. A monomeric imidazol-2-ylidene–silver(I) chloride complex: Synthesis, structure, and solid-state ^{109}Ag and ^{13}C CP/MAS NMR characterization Inorg. Chem. **2003**, 42, 1391-1393.
12. For representative reviews on π-functionalization of alkynes, see: (a) Gorin, D. J.; Toste, F. D. Relativistic Effects in Homogeneous Gold Catalysis. *Nature* **2007**, *446*, 395– 403. (b) Fürstner, A.; Davies, P. W. Catalytic Carbophilic Activation: Catalysis by Platinum and Gold π-Acids. *Angew. Chem., Int.*

Ed. **2007**, *46*, 3410– 3449. (c) Meldal, M.; Tornøe, C. W. Cu-Catalyzed Azide–Alkyne Cycloaddition. *Chem. Rev.* **2008**, *108*, 2952– 3015. (d) Chinchilla, R.; Nájera, C. Recent Advances in Sonogashira Reactions *Chem. Soc. Rev.* **2011**, 40, 5084– 5121. (e) Chinchilla, R.; Nájera, C. Chemicals from Alkynes with Palladium Catalysts. *Chem. Rev.* **2014**, *114*, 1783– 1826. (f) Yamamoto, Y. Synthesis of Heterocycles *via* Transition-Metal Catalyzed Hydroarylation of Alkynes. *Chem. Soc. Rev.* **2014**, *43*, 1575– 1600. (g) Kumar, R. K.; Bi, X. Catalytic σ-Activation of Carbon–Carbon Triple Bonds: Reactions of Propargylic Alcohols and Alkynes. *Chem. Commun.* **2016**, *52*, 853– 868. (h) Trost, B. M.; Masters, J. T. Transition Metal-Catalyzed Couplings of Alkynes to 1,3-Enynes: Modern Methods and Synthetic Applications. *Chem. Soc. Rev.* **2016**, *45*, 2212– 2238. (i) Boyarskiy, V. P.; Ryabukhin, D. S.; Bokach, N. A.; Vasilyev, A. V. Alkenylation of Arenes and Heteroarenes with Alkynes. *Chem. Rev.* **2016**, *116*, 5894– 5986.

13. For relevant studies, see: (a) Nechaev, M. S.; Rayon, V. M.; Frenking, G. Energy Partitioning Analysis of the Bonding in Ethylene and Acetylene Complexes of Group 6, 8, and 11 Metals: $(CO)_5TM–C_2H_x$ and $Cl_4TM–C_2H_x$ (TM = Cr, Mo, W), $(CO)_4TM–C_2H_x$ (TM = Fe, Ru, Os), and $TM^+–C_2H_x$ (TM = Cu, Ag, Au). *J. Phys. Chem. A* **2004**, *108*, 3134-3142. (b) Shapiro, N. D.; Toste, F. D. Synthesis and Structural Characterization of Isolable Phosphine Coinage Metal π-Complexes *Proc. Natl. Acad. Sci.* U.S.A. **2008**, *105*, 2779– 2782.

14. For representative reviews on applications of alkynes functionalization, see: (a) Fournier, D.; Hoogenboom, R.; Schubert, U. S. Clicking polymers: a straightforward approach to novel macromolecular architectures. *Chem. Soc. Rev.* **2007**, 36, 1369– 1380. (b) Lutz, J. F.; Zarafshani, Z. Efficient Construction of Therapeutics, Bioconjugates, Biomaterials and Bioactive Surfaces using Azide-Alkyne "Click" Chemistry. *Adv. Drug Delivery Rev.* **2008**, *60*, 958– 970. (c) Debets, M. F.; van Berkel, S. S.; Dommerholt, J.; Dirks, A. J.; Rutjes, F. P. J. T.; van Delft, F. L. Bioconjugation with Strained Alkenes and Alkynes. *Acc. Chem. Res.* **2011**, *44*, 805– 815. (d) Godoi, B.; Schumacher, R. F.; Zeni, G. Synthesis of Heterocycles *via* Electrophilic Cyclization of Alkynes Containing Heteroatom. *Chem. Rev.* **2011**, *111*, 2937– 2980. (e) Dorel, R.; Echavarren, A. M. Gold(I)-Catalyzed Activation of Alkynes for the Construction of Molecular Complexity. *Chem. Rev.* **2015**, *115*, 9028– 9072.

15. Ramírez, J.; Corberán, R.; Sanaú, M.; Peris, E.; Fernandez, E. Unprecedented Use of Silver (I) *N*-Heterocyclic Carbene Complexes for the Catalytic Preparation of 1,2-Bis (Boronate) Esters. *Chem. Commun.* **2005**, 3056– 3058.

16. Corberan, R.; Ramírez, J.; Poyatos, M.; Peris, E.; Fernández, E. Coinage Metal Complexes with N-Heterocyclic Carbene Ligands as Selective Catalysts in Diboration Reaction Tetrahedron: Asymmetry **2006**, *17*, 1759– 1762.

17. Wong, V. H. L.; Vummaleti, S. V. C.; Cavallo, L.; White, A. J. P.; Nolan, S. P.; Hii, K. K. Synthesis, Structure and Catalytic Activity of NHC-Ag-I Carboxylate Complexes. *Chem. - Eur. J.* **2016**, *22*, 13320– 13327.

18. (a) Weyrauch, J. P.; Hashmi, A. S. K.; Schuster, A.; Hengst, T.; Schetter, S.; Littmann, A.; Rudolph, M.; Hamzic, M.; Visus, J.; Rominger, F.; Frey, W.; Jan, W. B. Cyclization of propargylic amides: mild access to oxazole derivatives *Chem. - Eur. J.* **2010**, *16*, 956– 963. (b) Hashmi, A. S. K.; Schuster, A. M.; Gaillard, S.; Cavallo, L.; Poater, A.; Nolan, S. P. Selectivity Switch in the Synthesis of Vinylgold(I) Intermediates. *Organometallics* **2011**, *30*, 6328-6337. (c) Hashmi, A. S. K.; Schuster, A. M.; Schmuck, M.; Rominger, F. Gold-catalyzed cyclization of nonterminal propargylic amides to substituted alkylideneoxazolines and -oxazines Eur. J. Org. Chem. **2011**, *2011*, 4595– 4602.

19. Zhang, J.; Li, T.; Li, X.; Lv, A.; Li, X.; Wang, Z.; Wang, R.; Ma, Y.; Fang, R.; Szostak, R.; Szostak, M. Thiazol-2-ylidenes as N-Heterocyclic carbene ligands with enhanced electrophilicity for transition metal catalysis. *Commun Chem.* **2022**, *5*, no. 60.

20. Zhang, J.; Li, X.; Li, T.; Zhang, G.; Wan, K.; Ma, Y.; Fang, S.; Szostak, R.; Szostak, M. Copper(I)–Thiazol-2-ylidenes: Highly Reactive N-Heterocyclic Carbenes for the Hydroboration of Terminal and Internal Alkynes. Ligand Development, Synthetic Utility, and Mechanistic Studies. *ACS Catal.* **2022**, *12*, 15323– 15333.

21. Chen, Z.; Yu, X.; Wu, J. Silver Triflate and N-Heterocyclic Carbene Co-Catalyzed Reaction of N′-(2-Alkynylbenzylidene)Hydrazide, Methanol with α,β- Unsaturated Aldehyde. *Chem. Commun.* **2010**, *46*, 6356– 6358.

22. Ahrens, A.; Heinrich, N. F.; Kohl, S. R.; Hokamp, M.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. A Silver-Catalyzed Modular Intermolecular Access to 6,6-Spiroketals. *Adv. Synth. Catal.* **2019**, *361*, 5605– 5615.

23. Sarbajna, A.; Sadhukhan, N.; Saha, S.; Bera, J. K. Ferrocene-appended anionic N-heterocyclic carbene and its complex with silver (I): Synthesis, structure and catalytic evaluation. *Indian J. Chem*. **2013**, *52*, 1072-1077.
24. Heath, R.; Muller-Bunz, H.; Albrecht, M. Silver(I) NHC Mediated C-C Bond Activation of Alkyl Nitriles and Catalytic Efficiency in Oxazoline Synthesis. *Chem. Commun.* **2015**, *51*, 8699– 8701.
25. (a) Tortajada, A.; Juliá-Hernández, F.; Börjesson, M.; Moragas, T.; Martin, R. Transition-Metal-Catalyzed Carboxylation Reactions with Carbon Dioxide. *Angew. Chem., Int. Ed.* **2018**, *57*, 15948– 15982. (b) Dabral, S.; Schauba, T. The Use of Carbon Dioxide (CO_2) as a Building Block in Organic Synthesis from an Industrial Perspective. *Adv. Synth. Catal.* **2019**, *361*, 223– 246.
26. Tang, X.; Qi, C.; He, H.; Jiang, H.; Ren, Y.; Yuan, G. Polystyrene-Supported N-Heterocyclic Carbene-Silver Complexes as Robust and Efficient Catalysts for the Reaction of Carbon Dioxide and Propargylic Alcohols. *Adv. Synth. Catal.* **2013**, *355*, 2019– 2028.
27. Yamashita, K.; Hase, S.; Kayaki, Y.; Ikariya, K. Highly selective carboxylative cyclization of allenylmethylamines with carbon dioxide Using *N*-heterocyclic carbene-silver(I) catalysts. *Org. Lett.* **2015**, *17*, 2334– 2337.
28. Cervantes-Reyes, A.; Saxl, T.; Stein, P. M.; Rudolph, M.; Rominger, F.; Asiri, A. M.; Hashmi, A. S. K. Expanded Ring NHC Silver Carboxylate Complexes as Efficient and Reusable Catalysts for Carboxylative Cyclization of Unsubstituted Propargylic Derivatives. *ChemSusChem* **2021**, *14*, 2367-2374.
29. Whyte, A.; Torelli, A.; Mirabi, B.; Zhang, A.; Lautens, M. Copper-Catalyzed Borylative Difunctionalization of π-Systems. *ACS Catal.* **2020**, *10*, 11578– 11622. (b) Cheng, Z.; Guo, J.; Lu, Z. Recent advances in metal-catalysed asymmetric sequential double hydrofunctionalization of alkynes. *Chem. Commun.* **2020**, *56*, 2229– 2239 (c) Guo, J.; Cheng, Z.; Chen, J.; Chen, X.; Lu, Z. Iron- and Cobalt-Catalyzed Asymmetric Hydrofunctionalization of Alkenes and Alkynes. *Acc. Chem. Res.* **2021**, *54*, 2701– 2716.
30. Fujii, Y.; Terao, J.; Kambe, N. Silver-Catalyzed Carbomagnesiation of Terminal Aryl and Silyl Alkynes and Enynes in the Presence of 1,2-Dibromoethane Chem. Commun. **2009**, 1115– 1117.
31. Yoshida, H.; Kageyuki, I.; Takaki, K. Silver-Catalyzed Highly Regioselective Formal Hydroboration of Alkynes. *Org. Lett.* **2014**, *16*, 3512– 3515.
32. Karunananda, M. K.; Mankad, N. P. E-Selective Semi-Hydrogenation of Alkynes by Heterobimetallic Catalysis. *J. Am. Chem. Soc.* **2015**, *137*, 14598– 14601.
33. Farley, C. M.; Uyeda, C. Organic Reactions Enabled by Catalytically Active Metal-Metal Bonds. *Trends Chem.* **2019**, *1*, 497– 509.
34. Lee, M. T.; Goodstein, M. B.; Lalic, G. Synthesis of Isomerically Pure (*Z*)-Alkenes from Terminal Alkynes and Terminal Alkenes: Silver-Catalyzed Hydroalkylation of Alkynes. *J. Am. Chem. Soc.* **2019**, *141*, 17086– 17091.
35. Wang, Z.; Xue, X.-S.; Fu, Y.; Ji, P. Comprehensive Basicity Scales for N-Heterocyclic Carbenes in DMSO: Implications on the Stabilities of N-Heterocyclic Carbene and CO_2 Adducts. *Chem. - Asian J.* **2020**, *15*, 169– 181.
36. (a) Pandey, A. K.; Sharma, S.; Pandey, M.; Alam, M. M.; Shaquiquzzaman, M.; Akhter, M. 4, 5-Dihydrooxazole-pyrazoline hybrids: Synthesis and their evaluation as potential antimalarial agents *Eur. J. Med. Chem.* **2016**, *123*, 476-486. (b) Chen, J. J.; Lin, W. J.; Liao, C. H.; Shieh, P. C. Anti-inflammatory benzenoids from *Antrodia camphorata J. Nat. Prod.* **2007**, *70*, 989– 992. (c) Jandu, K. S.; Barrett, V.; Brockwell, M.; Cambridge, D.; Farrant, D. R.; Foster, C.; Giles, H.; Glen, R. C.; Hill, A. P.; Hobbs, H.; Honey, A.; Martin, G. R.; Salmon, J.; Smith, D.; Woollard, P.; Selwood, D. L. Discovery of 4-[3-(*trans*-3-Dimethylaminocyclobutyl)-1*H*-indol-5-ylmethyl]- (4*S*)-oxazolidin-2-one (4991W93), a $5HT_{1B/1D}$ Receptor Partial Agonist and a Potent Inhibitor of Electrically Induced Plasma Extravasation. J. Med. Chem. **2001**, 44, 681– 693. (d) Matada, B. S.; Pattanashettar, R.; Yernale, N. G. Comprehensive Review on the Biological Interest of Quinoline and Its Derivatives. *Bioorg. Med. Chem.* **2021**, *32*, 115973. (e) Bodor, N.; Farag, H. H.; Barros, M. D. C.; Wu, W.-M.; Buchwald, P. In Vitro and In Vivo Evaluations of Dihydroquinoline- and Dihydroisoquinoline-based Targetor Moieties for Brain-specific Chemical Delivery Systems. *J. Drug Target.* **2002**, *10*, 63– 71. (f) Wang, W.; Li, T.; Milburn, R.; Yates, J.; Hinnant, E.; Luzzio, M. J.; Noble, S. A.; Attardo, G. Novel 1,3-disubstituted-5,10-dihydro-5,10-dioxo-1*H*-mbenzo[*g*]isochromene-3-carboxamides as potent antitumor agents. Bioorg. Med. Chem. Lett. **1998**, 8, 1579-1584.