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Alkynes as Electrophilic or Nucleophilic Allylmetal Precursors in Transition Metal Catalysis

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Abstract

Diverse late transition metal catalysts convert terminal or internal alkynes to transient allylmetal species that display electrophilic or nucleophilic properties. Whereas classical methods for the generation of allylmetal species often mandate formation of stoichiometric byproducts, recent use of alkynes as allylmetal precursors enables completely atom-efficient catalytic processes, including enantioselective transformations.

MINIREVIEW

Keywords

allylation; nucleophilic; electrophilic; alkynes; catalysis

1. Introduction

As exemplified by the Tsuji-Trost reaction^[1] and carbonyl allylation,^[2] allylmetal species may display electrophilic or nucleophilic properties,^[3,4] respectively. Consequently, allylmetal complexes are found to mediate an especially diverse range of catalytic or stoichiometric transformations.^[3] Classical methods for the generation of discrete or transient allylmetal species often exploit precursors that mandate generation of

stoichiometric byproducts, for example, allylic carboxylates.^[1–3] It has been shown that allenes^[5,6] or dienes^[7,8] provide completely atom-efficient access to allylmetal intermediates. Although the stoichiometric conversion of alkynes to allenes^[9] and π -allylmetal complexes^[10] has been documented, the use of alkynes as allylmetal precursors is far less developed. However, the use of alkynes as precursors to both electrophilic or nucleophilic allylmetal species recently has witnessed enormous progress. In the context of electrophilic allylation, that is, alkyne-mediated Tsuji-Trost reactions, catalysts based on palladium^[11–15] and rhodium^[16–19] have been developed. Even more recently, alkyne-mediated nucleophilic allylations of carbonyl compounds under the conditions of iridium^[20] or ruthenium^[21] catalysis have been reported. In both electrophilic or nucleophilic modes, completely atom-efficient catalytic processes are enabled, and in several cases enantioselective transformations have been achieved.^[11–21] Many of these processes represent examples of “tandem catalysis,” as a single metal complex will catalyze the isomerization of an alkyne to an allene and, in a separate catalytic process, transform the allene to a product of electrophilic or nucleophilic allylation. In this mini-review, we offer an exhaustive account of this emerging area of research.

2. Alkynes as Electrophilic π -Allyl Precursors

Allylic substitution and oxidation reactions to generate linear or branched adducts is an important research topic in modern organic chemistry, especially due to the versatility of the allyl moiety in terms of further functionalization. However, from the perspective of modern chemical synthesis, one can recognize that a major drawback of these methods is the requirement of preinstalled leaving groups and consequent generation of stoichiometric byproducts, which diminish atom-economy^[22] and synthetic efficiency^[23] (Scheme 1). Hence, the byproduct-free addition of pronucleophiles to allenes and alkynes is an attractive alternative.

2.1. C-O Bond-Forming Reactions

Trost and co-workers were the first to demonstrate the concept of “tandem catalysis” embodied by alkyne-mediated allylic substitutions. In 1992, under the conditions of palladium catalysis using carboxylic acid pronucleophiles, propargyl acetates were isomerized to the corresponding allenes. Allene hydropalladation forms a π -allylpalladium intermediate, which upon addition of acetate delivers the indicated *gem*-diacetates (Scheme 2).^[11a,12] A variety of propargyl acetates were converted to the corresponding *gem*-diacetates in good yields with exclusive olefin (*E*)-stereoselectivity. Beyond intermolecular additions of acetic acid, macrocycle formation also occurs in excellent yield with good olefin (*E,Z*)-stereoselectivity and good diastereocontrol.

In 2001, Yamamoto and co-workers reported the first in a series of studies involving the use of internal alkynes as π -allyl precursors. Using a palladium catalyst in combination with substoichiometric benzoic acid, aryl propynes react with alcohols to form linear products of hydroalkoxylation as single regioisomers (Scheme 3).^[11b] Application of these conditions to acetylenic alcohols, enabled formation of tetrahydrofurans and tetrahydropyrans, albeit in modest yields.

The proposed mechanism for this transformation, which encompasses the tandem action of two discrete catalytic cycles, is shown in Scheme 4. In the first cycle, the palladium-hydride (**A**), generated from benzoic acid, hydropalladates the alkyne to form the vinyl-palladium species (**B**), which upon β -hydride elimination releases the allene (**C**). Then, in a second catalytic cycle, allene hydropalladation delivers a π -allylpalladium species, which upon regioselective alcohol addition releases the linear allylic ether along with palladium(0).^[5]

An alternative class of oxygen pro-nucleophiles, carboxylic acids, were found to be suitable reaction partners in alkyne-mediated Tsuji-Trost reactions, as reported independently by Zhang^[11c] and Yamamoto.^[11d] Using a palladium catalyst, a range of different aromatic and aliphatic carboxylic acids are converted to the linear allylic esters with complete alkene (*E*)-stereoselectivity (Scheme 3). Later in 2006, Yamamoto reported an enantioselective variant of his previously described cyclization of acetylenic alcohols.^[11e] Using a chiral palladium catalyst modified by (*R,R*)-renorphos, tetrahydrofurans, tetrahydropyrans and isochromanes were generated with modest levels of enantiomeric enrichment (Scheme 5). This reaction is limited to internal aryl-substituted alkynes. One year later, a related palladium catalyzed cyclization of acetylenic carboxylic acid to form racemic γ - and δ -lactones was achieved (Scheme 5).^[11f]

In 1987, Werner described the stoichiometric reaction of the indicated rhodium-2-butyne complex with Brønsted acids possessing non-coordinating counterions to form the π -allyl rhodium complex **A** (Scheme 6).^[10b] This transformation was postulated to involve initial rhodium hydride formation, alkyne hydrometalation and subsequent β -hydride elimination to deliver the allene complex **B**, which could be detected by NMR spectroscopy. Upon warming, allene complex **B** isomerizes to form π -allyl complex **A**. This observation suggested the feasibility of utilizing rhodium complexes as catalysts for alkyne-based Tsuji-Trost reactions.

In 2011, Breit reported the first alkyne-based Tsuji-Trost reaction catalyzed by rhodium (Scheme 7).^[16a] A broad range of alkyl-substituted terminal alkynes react efficiently with various aliphatic, aromatic and α,β -unsaturated carboxylic acids to form the branched allylic esters as single regioisomers. Such branched regioselectivity, which also is evident in conventional rhodium-catalyzed allylic substitutions^[24] and related allene hydrofunctionalizations,^[5] complements the linear regioselectivity observed in corresponding palladium catalyzed reactions. This transformation proved very sensitive to the nature of the ligand. Whereas rhodium-DPEPhos provides the branched allylic esters, the P/N-ligand DPPMP provides the (*Z*)-enol esters as the major product in good yields and selectivities (Scheme 7).^[16b,c]

An intramolecular variant of this process enabled an atom economic macrolactone synthesis (Scheme 8).^[16d] Remarkably, the macrolactonization does not require high dilution or syringe pump addition to avoid the formation of diolides or higher oligomers. The synthesis of γ - and δ -lactones was possible, although attempted formation of medium-sized lactones resulted in diolide generation. In 2017, Breit applied this method as a key step in the total synthesis of the 16-membered macrolactone epothilone D (Scheme 8).^[16e] The rhodium-catalyzed macrolactonization proceeded in a diastereoselective fashion, albeit in moderate

yield with high catalyst loading. This synthesis also utilizes several other methods developed in the Breit laboratory, including the stereospecific zinc-catalyzed cross-coupling of α -hydroxy ester triflates with Grignard reagents^[25] and hydroboration-magnesium exchange.^[26]

Mechanistic studies involving both experimental and computational methods corroborate the indicated catalytic cycle for the rhodium catalyzed alkyne-based Tsuji-Trost reaction (Scheme 9).^[16f] The rhodium chloride dimer modified by DPEphos dissociates to form a monomer, which in the presence of the terminal alkyne forms the η^2 -alkyne complex **C**. The carboxylic acid binds to the rhodium center, forming a rather stable hydrogen-bond to the terminal sp-carbon. Complete proton transfer to this carbon delivers the vinylrhodium carboxylate **E**. Reductive elimination from this species accounts for the formation of enol-ester side-products. β -Hydride elimination from **E** leads to the hydridorhodium allene complex **F**. Isotopic labeling experiments corroborate fast and reversible interconversion of **E** and **F**. Allene hydrometalation furnishes the π -allyl complex **G**, which is in equilibrium with the thermodynamically more stable σ -allyl complex. As established by *in situ* IR, NMR and MS studies, the σ -allyl complex is the resting state of the catalytic cycle. Indeed, the σ -allyl complex **H** could be isolated and was characterized by X-ray diffraction analysis. DFT calculations indicate a reisomerization from **H** to the π -allyl **G** followed by an inner sphere reductive elimination process to form the allylic C-O bond.

Catalytic enantioselective formation of branched allylic esters from alkynes was achieved by Breit in 2015 using chiral rhodium catalysts modified by DIOP-family phosphine ligands (Scheme 10).^[16g] Although the reaction products are themselves potential π -allyl precursors, erosion of enantiomeric enrichment was not observed. This methodology enabled protecting group-free syntheses of *trans*-whiskey and cognac lactones. In 2016, Breit reported that aliphatic alcohols participate in enantioselective alkyne-based Tsuji-Trost allylation using chiral rhodium catalysts modified by (*R,R*)-DTBM-Garphos (Scheme 10).^[16h] The use of diphenylphosphate as Brønsted acid cocatalyst was essential in terms of promoting alkyne-to-allene isomerization.

2.2. C-S Bond-Forming Reactions

Despite their significance in medicinal chemistry,^[27] *S*-nucleophiles are not frequently employed in metal catalyzed C-S bond formation, perhaps due to catalyst poisoning.^[28] In 2014, Breit reported the use of sulfonyl hydrazides as precursors to sulfinic anions in rhodium catalyzed alkyne-based Tsuji-Trost allylations (Scheme 11).^[17] Although a Brønsted acid cocatalyst, benzoic acid, is required to promote alkyne-to-allene isomerization, the more reactive *S*-nucleophile captures the resulting π -allyl. The allylic sulfones are formed in good yield with complete branched regioselectivity. Later, in 2016, Lu and Jin developed a related palladium catalyzed process that delivers the linear regioisomers (Scheme 11).^[13]

2.3. C-N Bond-Forming Reactions

Nitrogen-containing compounds are ubiquitous in medicinal and agricultural chemistry.^[29] As over 25 of the 150 top-selling small-molecule drugs incorporate stereogenic C-N

bonds,^[30] atom-efficient methods that convert π -unsaturated feedstocks to amines, enamines or imines remain in high demand.^[22,31,32] Under the conditions of palladium catalysis, Yamamoto developed alkyne-based Tsuji-Trost aminations of aliphatic secondary amines or aniline-derivatives (Scheme 12).^[14a,b] In both cases, benzoic acid serves as a co-catalyst and the allylic amines are generated with complete alkene (*E*)-stereoselectivity. Use of aliphatic primary amines led to significant quantities of *N,N*-diallylated product.

Intramolecular variants of this reaction deliver pyrrolidines, piperidines, tetrahydroisoquinolines and tetrahydroquinolines (Scheme 13).^[14c-f] Although rather high catalyst loadings are required, chiral palladium catalysts modified by (*R,R*)-renorphos provide access to enantiomerically enriched heterocycles. To highlight the utility of this chemistry, Yamamoto applied the palladium-catalyzed alkyne hydroamination reaction as a key step for the construction of indolizidine alkaloid (–)-209D (**10**) (Scheme 13).^[14g] The hydroamination precursor **9** was prepared in five steps from the (*L*)-proline derived aldehyde **8**. Highly diastereoselective palladium catalyzed alkyne hydroamination followed by alkene hydrogenation delivered indolizidine (–)-209D (**10**). Furthermore, *N*-Tosyl amides also participate in cyclization reactions to furnish racemic δ -lactams.^[14h]

In 2015, Dong reported the rhodium catalyzed hydroamination of internal aromatic alkynes with indolines (Scheme 14).^[18a] Remarkably, upon variation of the acidic additive, the formation of either linear or branched regioisomers could be achieved. Using the chiral rhodium catalyst modified by (*S,S*)-bdpp in combination with xylylic acid, enantiomerically enriched branched adducts were formed with moderate to good selectivities and yields. Conversely, using an achiral rhodium catalyst with phthalic acid, linear adducts are formed.

In a contemporaneous independent study, Breit showed that the chiral rhodium catalyst modified by JoSPOphos converts internal methyl-substituted or terminal alkynes to branched *N*-allylated pyrazoles (Scheme 15).^[18b] Using pyridinium *p*-toluene sulfonic acid (PPTS) as cocatalyst, good yields were accompanied by excellent regioselectivity and good to excellent levels of enantioselectivity. Notably, nonsymmetric pyrazoles engage in highly position-selective *N*-functionalization.

2.2. C-C Bond-Forming Reactions

The first examples of *C*-nucleophiles in alkyne-based Tsuji-Trost reactions were reported by Yamamoto in 1998 and 2004 (Scheme 16).^[15a,b] Using a palladium catalyst and benzoic acid as cocatalyst, internal alkynes react with malonitrile and malonic ester derivatives to form linear adducts in good to excellent yield. Using α -branched or cyclic β -dicarbonyl pronucleophiles, racemic all-carbon quaternary stereocenters were formed in an efficient manner (Scheme 16).^[15c] Improvements to these conditions were subsequently disclosed. Using DavePhos as ligand, these transformations could be conducted at significantly lower temperatures (50°C).^[15d] A solvent free, microwave assisted version decreased reaction time to only a few minutes.^[15e] Additionally, intramolecular variants^[11e] and the use of activated aldehyde pronucleophiles were reported.^[14b]

Based on this work, in 2016 Lin developed a cooperative palladium/proline-catalyzed process wherein unactivated ketones or aldehydes are coupled to aryl propynes to form

racemic γ,δ -unsaturated ketones and aldehydes in moderate to good yields (Scheme 17).^[15f] The structure of the amino acid cocatalyst was decisive. Only (*L*)-proline enforced high levels of efficiency, which was rationalized by postulating intervention of the indicated 7-membered palladacycle. In a concurrent study, Lin and Yao reported the dearomatizing allylic alkylation of indoles with aryl propynes to furnish indolines bearing C3-quaternary stereocenters. Again, carboxylic acid cocatalysts were required as additives (Scheme 17).^[15g]

The first rhodium-catalyzed addition of *C*-pronucleophiles to alkynes was reported by Breit in 2016 (Scheme 18).^[19a] A diverse range of 1,3-dicarbonyl partners couple efficiently with terminal alkynes with complete levels of branch-regioselectivity. Again, the Brønsted acid cocatalyst played a critical role. Electron poor carboxylic acids were required to obtain the resulting γ,δ -unsaturated diketones in good to excellent yields. To demonstrate the utility of this methodology, the allylated adducts were converted to high-value building blocks. For example, treatment with ethanolic potassium hydroxide promotes retro-Claisen condensation to form the γ,δ -unsaturated ketones or trisubstituted dihydropyrans. Related reactions of internal alkynes were subsequently developed and applied to the synthesis of heterocycles (Scheme 18).^[19b] In 2016, the laboratories of Dong and Breit simultaneously demonstrated that direct access to γ,δ -unsaturated ketones may be achieved in decarboxylative couplings of alkynes with β -keto acids (Scheme 19).^[19c,19d]

More recently in 2017, Dong employed two chiral co-catalysts to promote diastereo- and enantioselective alkyne-based allylations of α -aryl aldehydes (Scheme 20).^[19e] A chiral amine is used to generate a transient enamine from the aldehyde pronucleophile, and an (*R*)-BINAP-modified rhodium-catalyst is used to generate a chiral allylrhodium intermediate. Depending on the choice of chiral amine two of the four stereoisomers of the product can be obtained selectively.

3. Alkynes as Nucleophilic π -Allyl Precursors

Unlike related alkyne-based Tsuji-Trost allylations, the use of alkynes as nucleophilic π -allyl precursors is far less developed. To date, this mode of reactivity has only been observed in hydrogen transfer-mediated carbonyl allylations of alcohol proelectrophiles.^[2j,33] In 2009, following reports by Krische on related allylative processes involving allenes,^[6] dienes^[8] and allylic carboxylates,^[34] Obora and Ishii reported the first examples of alkyne-alcohol C-C coupling to form products of carbonyl allylation.^[20a,b] Specifically, using the iridium catalyst derived from $[\text{Ir}(\text{OH})(\text{cod})]_2$ and $\text{P}(n\text{Oct})_3$ primary alcohols react with aryl propynes to provide racemic products of (α -aryl)allylation with complete levels of *anti*-diastereoselectivity. Although mechanistic studies were not undertaken, previously reported alcohol-allene C-C couplings deliver products of carbonyl allylation,^[6] suggesting a catalytic cycle involving alkyne-to-allene isomerization is operative (Scheme 21).

In ruthenium catalyzed alkyne-alcohol C-C couplings developed by Krische, subtle changes in reaction conditions can result in widely different outcomes (Scheme 22). For example, using the cationic ruthenium catalyst generated through the acid-base reaction of $[\text{H}_2\text{Ru}(\text{CO})(\text{PPh}_3)_3]$ and 2,4,6-(2-Pr)₃PhSO₃H, alkynes isomerize to form transient allenes. The cationic

ruthenium complex exists in equilibrium with a ruthenium(0) species that promotes allene-aldehyde oxidative coupling to form an oxaruthenacycle, which upon primary alcohol-mediated transfer hydrogenolysis delivers the (*Z*)-homoallylic alcohols.^[21a] Oxidative coupling pathways are suppressed upon introduction of iodide ion and a chelating phosphine ligand, Josiphos SL-J009-1, yet alkyne-to-allene isomerization pathways are maintained. Under these conditions, alcohol dehydrogenation triggers allene hydrometalation to form chiral allylruthenium-aldehyde pairs that deliver enantiomerically enriched branched homoallylic alcohols as single diastereomers.^[21b] For both reaction types, an extensive series of deuterium labelling studies were undertaken to corroborate the proposed mechanisms (Scheme 22).

Krische reports that a third distinct mechanism for alkyne-alcohol C-C coupling is operative when the preceding conditions (Scheme 22)^[21b] are applied to the propargyl ether, TIPSOCH₂C≡CMe (TIPS = triisopropylsilyl). The n-σ* interaction between the silyl ether oxygen atom and the propargylic C-H bond promotes a 1,2-hydride shift that converts the metal-bound alkyne to a vinyl carbene, which upon protonation forms the indicated siloxy-π-allylruthenium nucleophile. Carbonyl addition occurs from the σ-allylruthenium haptomer where ruthenium resides at the oxygen-bearing carbon, presumably due to the negative inductive effect of oxygen. Using a Josiphos (SL-J009-1) modified ruthenium(II) catalyst, the resulting products of siloxy-crotylation form as single regioisomers with complete levels of *anti*-diastereoselectivity and high levels of enantioselectivity.^[21c] Although mixtures of enol geometrical isomers are produced, the (*E/Z*)-selectivity is inconsequential as fluoride assisted cleavage of the enol in the presence of NaBH₄ converts both isomers to the same 1,4-diol (Scheme 23).

This pathway for hydride shift enabled π-allyl formation is general and transferrable to other metal catalysts. Using the chiral iridium complex formed *in situ* from [Ir(cod)Cl]₂ and (*R*)-H₈-BINAP, Krische reports the direct enantioselective C-C coupling of the simple propargyl ether, TIPSOCH₂C≡CH, with primary alcohols to form products of (*Z*)-siloxyallylation. Uniformly high levels of enantioselectivity are accompanied by complete alkene (*Z*)-stereoselectivity (Scheme 24).^[20c]

4. Summary and Outlook

New reactivity is the foremost basis for methodological innovation in the field of chemical synthesis. The recent ability of metal catalysts to transform alkynes into π-allylmatal species streamlines methods for electrophilic or nucleophilic allylation. In alkyne-based Tsuji-Trost reactions, one circumvents generation of stoichiometric byproducts associated with the use of allylic carboxylates, the traditional electrophilic π-allyl precursors. Similarly, in alkyne-based nucleophilic allylations via hydrogen auto-transfer, one bypasses the requirement of discrete allylmatal reagents, enabling completely atom-efficient carbonyl addition. In both polarity modes, highly enantioselective processes have been established and hitherto inaccessible extensions in scope have been achieved. It is the authors hope that the present review of this burgeoning area will accelerate further progress toward allylative transformations of alkynes.

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Biographies

Alexander M. Haydl obtained a Diploma in chemistry from Albert-Ludwigs-University Freiburg in 2012, where he conducted research on electrophilic allylation in the laboratory of Professor Bernhard Breit and earlier as a research scholar on nucleophilic allylation at the University of Texas at Austin in the group of Professor Michael J. Krische. He received his Ph.D. in Organic Chemistry from the Albert-Ludwigs-Universität Freiburg with Professor Bernhard Breit. In 2016, he began his postdoctoral studies at the University of California at Berkeley in the laboratory of Professor John F. Hartwig.

Professor Bernhard Breit is a graduate of the University of Kaiserslautern (Diploma, Dr. rer. nat.). After postdoctoral studies at Stanford University he joined the faculty at the University of Marburg for his habilitation and was appointed Professor of Organic Chemistry at the University of Heidelberg. He is presently a Professor of Organic Chemistry at the Albert-Ludwigs-Universität in Freiburg. Professor Breit's research in organic synthesis and catalysis encompasses pioneering studies on supramolecular concepts in homogeneous catalysis and the development of atom-economic bond forming reactions

Tao Liang obtained a B.S. degree in chemistry from Shanghai Jiao Tong University in 2008, where he conducted undergraduate research in the laboratory of Professor Zhaoguo Zhang. He received his Ph.D. in organic chemistry from University of South Florida with Professor Jon C. Antilla where he studies chiral Brønsted acid catalysis. In 2014, he began postdoctoral studies at the University of Texas at Austin in the laboratory of Professor Michael J. Krische.

Professor Michael J. Krische is a graduate of the University of California at Berkeley (BS) and Stanford University (Ph.D.). After postdoctoral studies at Université Louis Pasteur, he joined the faculty at the University of Texas at Austin, where he was promoted directly to the rank of a full professor and appointed the Robert A. Welch Chair in Science. Professor Krische has developed a new class of C-C bond formations that merge the characteristics of carbonyl addition and catalytic hydrogenation. His research has been recognized by numerous awards, including the Mukaiyama Award (2010), the ACS Cope Scholar Award (2012) and the RSC Pedlar Award (2015).

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Allylic substitution and oxidation reactions

Transition metal catalyzed hydrofunctionlization reactions

Scheme 1.

Classic allylic substitution and C-H oxidation chemistry and alternative entries for Tsuji-Trost-type allylation chemistry by allenes and alkynes.

Trost, 1992:

Scheme 2.

Pd-catalyzed addition of carboxylic acids to internal alkynes. TBDPS = *tert*-butyldiphenylsilyl.

Zhang, 2002 and Yamamoto, 2005:

Scheme 4.

Proposed mechanism for the Pd-catalyzed hydroalkoxylation of alkynes.

Yamamoto, 2006:

Yamamoto, 2007:

Scheme 5.

Pd-catalyzed intramolecular addition of alcohols and carboxylic acids to internal alkynes.

Werner, 1987:

Scheme 6.

Initial study of the stoichiometric rhodium-mediated conversion of alkynes to π -allyl species.

Scheme 7.

Chemoselective rhodium-catalyzed hydrofunctionalization reactions of terminal alkynes

Breit, 2012:

Breit, 2017: Total Synthesis of Epothilone D

Scheme 8.

Rh-catalyzed macrolactonization with ω -alkynyl substituted carboxylic acids and application to the total synthesis of epothilone D.

Scheme 9.

Mechanism for the Rh-catalyzed coupling of carboxylic acids with terminal alkynes to form branched allylic esters.

Breit, 2015:

Breit, 2016:

Scheme 10.

Rh-catalyzed branched-selective addition of alcohols and carboxylic acids to alkynes.

Breit, 2014:

Lu and Jin, 2016:

Scheme 11.

Rh- and Pd-catalyzed regiodivergent hydrofunctionalization reactions to allylic sulfones.

Yamamoto, 1999:

Yamamoto, 2004:

Secondary aliphatic amines:

Primary aliphatic amines:

Secondary aromatic amines:

Primary aromatic amines:

Scheme 12.*In situ* alkyne isomerization followed by catalytic hydroamination.

Dong, 2015:

Scheme 14.

Intermolecular enantioselective Rh-catalyzed hydroamination of alkynes with indolines.

Yamamoto, 1998 and 2004:

Yamamoto, 2004:

Scheme 16.

Pd-catalyzed addition of active methylene precursors to internal alkynes.

Lin, 2016:

Lin and Yao, 2016:

Scheme 17.

Pd-catalyzed addition of ketones, aldehydes and indole precursors to internal alkynes.

Breit, 2016:

Breit, 2016:

Scheme 18.

Rh-catalyzed addition of β -keto esters, β -keto amides and 1,3-diketones to terminal and internal alkynes and deacetylation through retro-Claisen condensation.

Breit, 2016:

Dong, 2016:

Scheme 19. Rh-catalyzed decarboxylative addition of β -keto acids to alkynes.

Dong, 2017:

Scheme 20.

Rh-catalyzed stereodivergent coupling of aldehydes to alkynes.

Obora and Ishii, 2009 and 2013:

Scheme 21.

Ir-catalyzed coupling of aryl propynes and primary alcohols to form racemic products of carbonyl *anti*-(α -aryl)allylation.

Scheme 22.

Alkynes as latent allenes in Ru-catalyzed alkyne-alcohol C-C coupling: oxidative coupling *versus* hydrometalative pathways.

Krische, 2015:

Scheme 23.

Ru-catalyzed enantioselective carbonyl siloxycrotylation via hydride shift enabled π -allyl formation.