

Metal Catalysis in Thiolation and Selenation Reactions of Alkynes Leading to Chalcogen-Substituted Alkenes and Dienes

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This review covers recent achievements in metal-catalyzed Z–H and Z–Z (Z=S, Se) bond addition to the triple bonds of alkynes—a convenient and atom-efficient way to carbon-element bond formation. Various catalytic systems (both homogeneous and heterogeneous) developed to date to obtain mono- and bis-chalcogen-substituted alkenes or dienes, as well as carbonyl compounds or heterocycles, starting from simple and available alkynes and chalcogenols or dichalcogenides are described. The right choice of metal and ligands allows us to perform these transformations with high selectivities under mild

reaction conditions, thus tolerating unprotected functional groups in substrates and broadening ways of further modification of the products. The main aim of the review is to show the potential of the catalytic methods developed in synthetic organic chemistry. Thus, emphasis is made on the scope of reactions, types of products that can be selectively formed, convenience, and scalability of the catalytic procedures. A brief mechanistic description is also given to introduce new readers to the topic.

1 Introduction

Organic sulfides and selenides represent an important class of compounds finding wide application in chemistry, biology, medicine, and materials sciences.^[1] Numerous efficient approaches for their synthesis have been developed over the previous decades.^[2] Nevertheless, current needs of both industry and academia require new synthetic methods to be elaborated which will allow to perform the chemical transformations in a highly selective manner with minimal production of waste. Metal-catalyzed transformations have become a powerful tool in modern organic synthesis to construct new bonds with high selectivity under mild reaction conditions. The latter is essentially important when natural compounds containing sensitive functionalities are involved.^[3] Despite the fact that efficient metal-based catalytic systems for selective formation of C–C, C–O, C–N, C–Si, C–P, C–B, and C–Sn bonds have been being developing since 1970s,^[4] sulfur and selenium species were excluded from this rapidly growing area for a long time as they were considered catalyst poisons.^[5] Only in the beginning of the 1990s was this problem solved, thus allowing C–Z (Z=S, Se) bond formation in an efficient manner with good atom economy via selective Z–H and Z–Z bond addition to alkynes using transition-metal catalysts.

The scope of this review is to describe achievements made in utilization of transition- and main-group metal catalysts in Z–H and Z–Z (Z=S, Se) bond addition to alkynes as an 100% atom-efficient method of C–S and C–Se bond formation which is advantageous compared to substitution reactions, in terms of green chemistry, because all atoms of the starting compounds are incorporated into the products. The main emphasis is placed on the diversity of catalytic systems developed, comparison of their efficiency, and the types of products which can be selectively obtained, as well as alternation of the selectivity of product formation depending on the catalytic system used.^[6] At first, metal-catalyzed additions of Z–H (Z=S, Se) bonds to alkynes leading to either Markovnikov (M) or *E*- or *Z*-anti-Markovnikov (a-M) vinyl chalcogenides are reviewed (Scheme 1, A). After that catalytic systems for Z–Z (Z=S, Se) bond addition to alkynes leading to bis-chalcogen-substituted alkenes or dienes are considered (Scheme 1, B and C). Finally, multicomponent transition-metal-catalyzed reactions including CO incorporation are covered (Scheme 1, D). The detailed experimental and theoretical mechanistic investigations are out of the scope of the present review and can be found in several excellent recent publications on the topic.^[7]

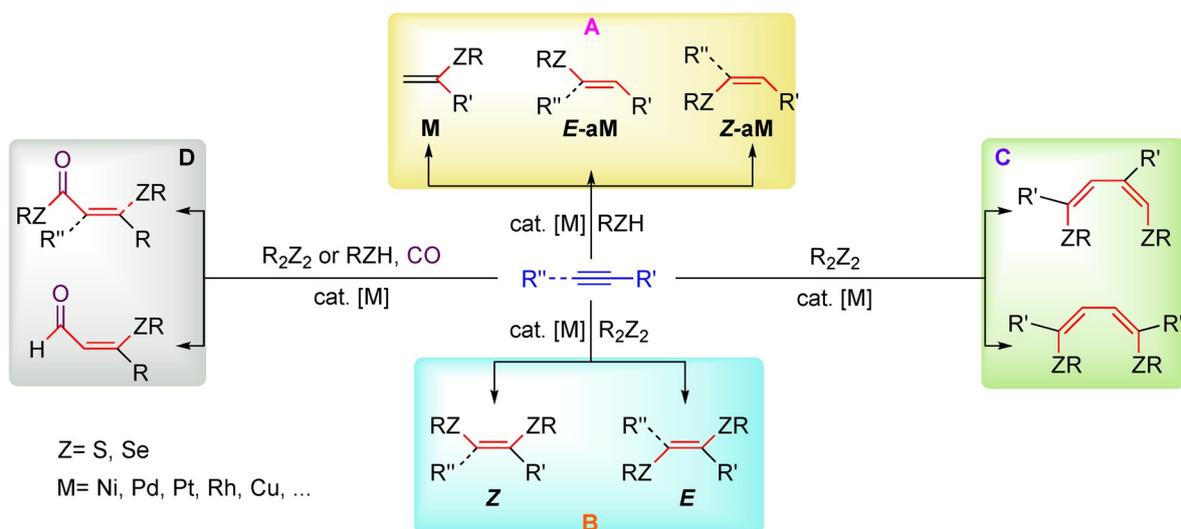
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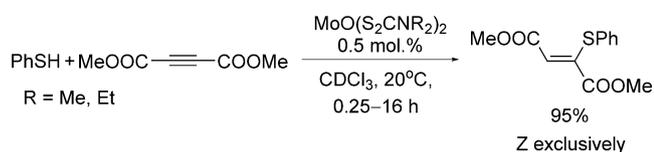
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2 Formation of Monofunctionalized Alkenes (Vinyl Chalcogenides)

The first known transition-metal-catalyzed addition of a thiol to an alkyne to form vinyl sulfide was reported by the group of Newton in 1976.^[8] Several molybdenum and iridium complexes were found to catalyze stereoselective thiophenol addition to dimethyl acetylenedicarboxylate at room temperature with the formation of vinyl sulfide of *Z*-configuration



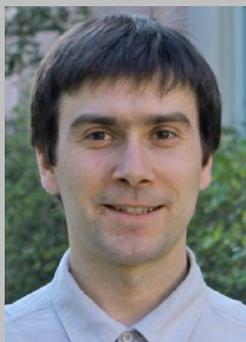
Scheme 1. Overview of the transition-metal catalyzed reactions of Z–H and Z–Z (Z=S, Se) bonds with alkynes discussed in the review.



Scheme 2. First example of metal-catalyzed selective thiol addition to alkynes.

(Scheme 2). As little as 0.5 mol.% of the metal complex was enough to run the reaction. Despite this promising result, no further success in the development of efficient and general catalytic systems has been achieved in the following years, and sulfur as well as selenium compounds have been considered as catalyst poisons for a long time.

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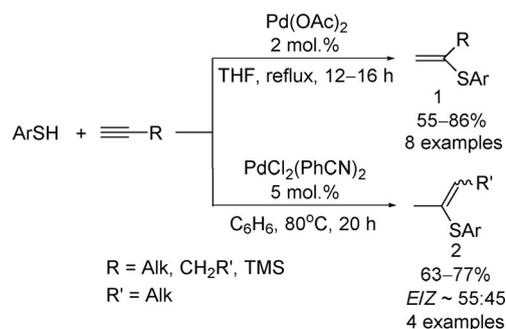


2.1 Catalytic systems leading to Markovnikov-type (branched) vinyl chalcogenides

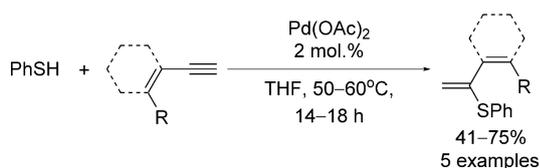
A real breakthrough in this field was made in 1992 when the group of Ogawa and Sonoda et al. revealed that different transition-metal complexes (Pd, Pt, Rh, Ni) could catalyze the addition of various aryl thiols to terminal alkynes with the formation of vinyl sulfides.^[9] The selectivity of the process depended much on the type of the metal (Scheme 3).^[10] Pd(OAc)₂ led to Markovnikov-type vinyl sulfides **1** as major products. However, PdCl₂(PhCN)₂, Pt(PPh₃)₄, and NiCl₂(PPh₃)₂ caused double-bond isomerization in initially formed products **1** to furnish internal thiosubstituted alkenes **2** as a mixture of *E* and *Z* isomers (though Pt and Ni complexes were less active and selective in this transformation).

The main advantages of the catalytic systems developed were mild reaction conditions, high tolerance to functional groups in alkynes and thiols, and, most importantly, formation of Markovnikov-type products which were unreachable in the case of addition reactions under nucleophilic or radical conditions.

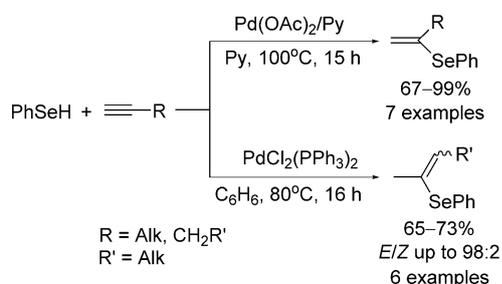
Soon after, the scope of alkynes was extended to conjugated enynes.^[11] Use of 2–10 mol.% of Pd(OAc)₂ resulted in exclu-



Scheme 3. First general catalytic system based on Pd salts for selective Z–H (Z=S) bond addition to terminal alkynes.



Scheme 4. Pd-catalyzed selective addition of thiols to the triple bonds of enynes.

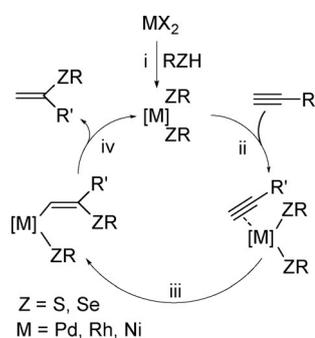


Scheme 5. Pd-based catalytic systems for selective benzeneselenol addition to alkynes.

sive addition of PhSH to triple carbon–carbon bonds with excellent regioselectivity to obtain a series of 2-thiosubstituted 1,3-dienes in 41–75% yield (Scheme 4).

In the case of PhSeH addition to terminal alkynes, high regioselectivity of the Pd-catalyzed reaction was achieved using pyridine as a solvent (Scheme 5).^[12] As a result Markovnikov-type products were obtained in 67–98% yields. Even arylacetylene, which is prone to formation of noncatalytic anti-Markovnikov products, gave the target vinyl sulfide as the major product (M 56%, Z-a-M 38%). The authors assumed that pyridine could act as a ligand thus improving catalyst stability and selectivity. Quite similar to aryl thiols, sequential addition/double-bond isomerization in the presence of 2 mol.% of PdCl₂(PPh₃)₂ was realized for benzeneselenol.^[13] The products were obtained in good yields 61–73% as a mixture of *E*- and *Z*-isomers resulting from the isomerization step. Nevertheless, in the case of alkynes bearing Cl and CN substituents, *E*-alkenes were formed almost exclusively.

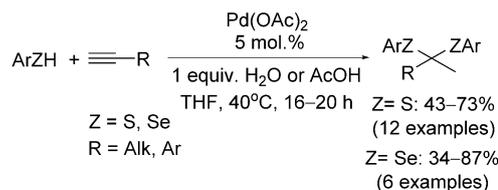
The proposed mechanistic pathway depicted in Scheme 6 included initial ligand exchange upon interaction of Pd(OAc)₂ with chalcogenol (i) followed by alkyne coordination to metal



Scheme 6. Mechanism of Markovnikov-type vinyl chalcogenide formation via metal-catalyzed addition of Z–H (Z=S, Se) bond to terminal alkynes.

center (ii), and insertion into metal–chalcogen bond (iii). Finally, protonolysis of metal–carbon bond by another thiol or selenol molecule (iv) released the target vinyl chalcogenide and regenerated the catalytically active metal species. This mechanism was found to be operative not only for Pd-based catalysts but Ni, Rh, Zr, lanthanides, and actinides as well.^[7a,b,h] However, in the case of Rh complexes, an alternative pathway can be realized depending on the ligands at the metal center (see below).

When a twofold excess of PhSH or PhSeH was used, Pd-catalyzed selective addition of two Z–H (Z=S, Se) bonds to terminal alkynes occurred, leading to dithio- and diselenoacetals, respectively (Scheme 7).^[14] It was revealed that water or acetic

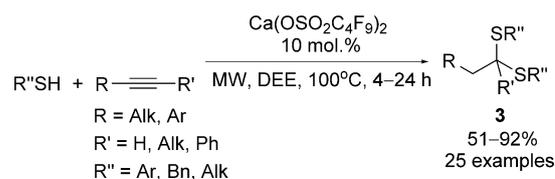


Scheme 7. Pd-catalyzed formation of dithio- and diselenoacetals as a result of selective double Z–H (Z=S, Se) bond addition to terminal alkynes.

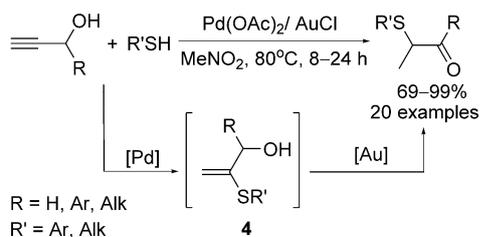
acid additives substantially accelerated the reactions, most likely facilitating formation of vinyl chalcogenide without any influence on overall selectivity. Benzeneselenol and aromatic thiols bearing electron-withdrawing substituents were the most active substrates in the reaction providing the target products in up to 87% yield, while less nucleophilic aromatic and aliphatic thiols were much less reactive.

Lewis-acidic Ca complex Ca(OSO₂C₄F₉)₂ allowed the opposite selectivity of bis-hydrothiolation furnishing anti-Markovnikov dithioacetals.^[15] Use of microwave heating significantly decreased the reaction time. Under optimized conditions, both aliphatic and aromatic thiols and alkynes reacted well in 1,2-diethoxyethane (DEE) leading to clean formation of dithioacetals **3** in up to 92% yield (Scheme 8). Both terminal and internal alkynes reacted smoothly with dithiols resulting in 1,3-dithianes or 1,3-dithiolanes in high yields. This was the first example of Ca catalysis in S–H bond addition to alkynes.

In a recent excellent work of Samec et al., Pd catalysis was successfully combined with Au catalysis to obtain α -sulfenylated aldehydes and ketones from propargylic alcohols and thiols.^[16] In this transformation, Pd(OAc)₂ catalyzed selective formation of branched vinyl sulfide **4** at the first step, while AuCl promoted subsequent rearrangement via a 1,2-hydride shift (Scheme 9). The reaction had broad substrate scope: both



Scheme 8. Ca-catalyzed selective double S–H bond addition to terminal and internal alkynes.

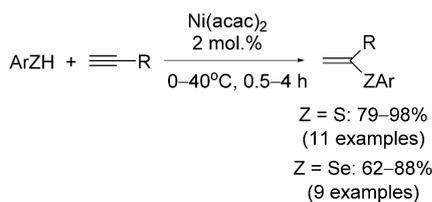


Scheme 9. Dual Pd/Au catalysis to obtain thiosubstituted carbonyl compounds.

aromatic and aliphatic thiols were successfully involved, resulting in up to 99% yields. Challenging propargylic alcohols having aryl ring in the α -position reacted smoothly under the developed conditions of dual Pd/Au catalysis; no substitution of hydroxyl group was observed. AuCl alone was found to catalyze both steps of the sequence as well; however, in this case, good selectivity was achieved only for interaction of aromatic thiols with internal alkynes.^[17] Thorough experimental and theoretical mechanistic investigations have been performed to shed light on Au-catalyzed reaction sequence.^[18]

Ni complexes were found to be very promising in Z-H (Z=S, Se) bond addition to alkynes to obtain Markovnikov-type products. In the first report on Ni catalysis, it was shown that Ni(PPh₂Me)₄ allowed to perform addition of PhSH to 1-octyne under very mild reaction conditions leading to a high yield (92%) and excellent selectivity (>91%) of the branched product in a short time (3 h versus 16–20 h in the case of Pd).^[19] In the further studies of group of Ananikov and Beletskaya, very efficient heterogeneous catalysts generated in situ from cheap Ni^{II} precursors were introduced,²⁰ with Ni(acac)₂ being found the most active catalyst for Z-H (Z=S, Se) bond addition to alkynes. Using this cheap and available salt, an efficient and convenient preparative method of aryl thiol and aryl selenol addition to terminal and internal alkynes in a highly selective manner (M/a-M up to 98:2) was developed resulting in up to 50 g of the highly pure vinyl chalcogenides (Scheme 10).^[21] In addition to terminal alkynes leading to branched products with excellent selectivity and high yields (up to 99%), internal alkynes successfully reacted as well with excellent stereoselectivity and moderate regioselectivity.^[21b]

Special investigations have revealed that activity of the catalysts depended much on the size and morphology of heterogeneous particles [M(ZR)₂]_n (M=Ni, Pd, Z=S, Se) formed in situ upon interaction with Ni or Pd precursor. Ni(acac)₂ led to the

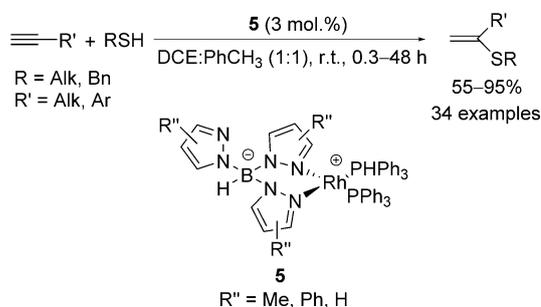


Scheme 10. Ni-based catalytic system for selective Markovnikov-type addition of thiols and selenols to terminal alkynes.

most uniform and fine catalyst structure and thus resulted in the highest activity under very mild reaction conditions.^[22] This study demonstrated a rare example of heterogeneous catalysts to surpass homogeneous ones in activity and selectivity.^[23]

Thus, Ni- and Pd-based catalytic systems developed disproved the poisonousness of thiols and selenols for transition-metal catalysis and introduced efficient methods for highly selective synthesis of vinyl chalcogenides. However, despite all these achievements, alkyl thiols still have remained a challenge.

This problem was successfully solved using Rh catalysts thoroughly investigated by Love et al. They envisioned that highly electron-rich metal complexes could be able to activate less nucleophilic alkyl thiols thus increasing their reactivity with alkynes. Indeed, rhodium pyrazolylborate complexes **5** were found to catalyze regioselective addition of various alkyl, cycloalkyl, and benzyl thiols to terminal aromatic and aliphatic alkynes under very mild reaction conditions (Scheme 11).^[24] Sur-



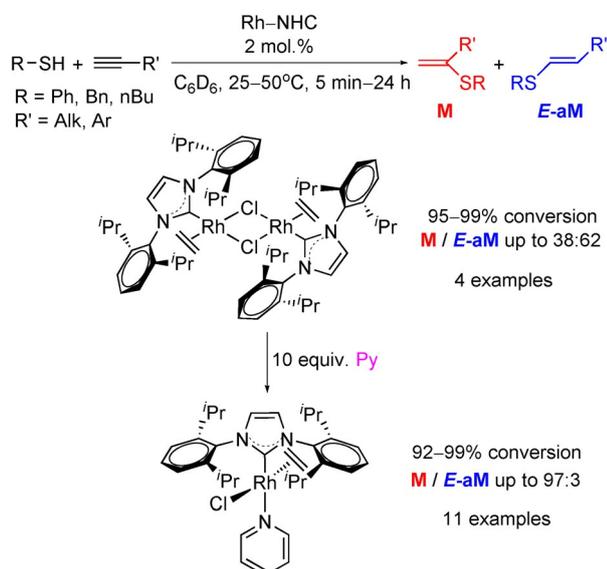
Scheme 11. Rh-based catalytic system for selective addition of alkyl thiols to terminal alkynes.

prisingly, only moderate selectivity was observed in ArSH addition to terminal alkynes using these type of complexes, which however could be improved much by replacing phosphine ligands at rhodium by acetonitrile and cyclooctene.^[25] The products of Rh-catalyzed propanethiol addition to alkynes were shown to participate in a Ni-catalyzed cross-coupling reaction in a one-pot manner thus leading to 1,1-disubstituted alkenes with moderate yields.^[26] The rhodium catalysts were readily synthesized from Wilkinson's complex^[27] and had high tolerance to functional groups in thiols and alkynes. The catalytic activity and selectivity of the complexes depended much on the substituents at pyrazolyl ring with 3,5-disubstituted ones being found the most active in a series. The only drawback of the developed catalysts was high air-sensitivity which required manipulations in a glove box.

It is important to mention that this study has shown the high potential of rhodium complexes to switch regioselectivity of an addition reaction depending on the ligands used. Complexes **5** led exclusively to branched vinyl sulfides, while Wilkinson's complex (PPh₃)₃RhCl is a well-known catalyst to obtain linear vinyl sulfides of *E*-configuration (see below).

High potential of such ligand control has been demonstrated recently in the excellent work of Castarlenas and Oro et al.

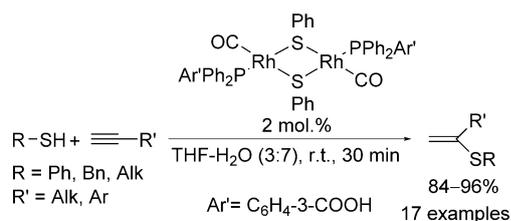
who have found rhodium complexes with N-heterocyclic carbene (NHC) ligands to possess high efficiency in alkyl thiol addition to alkynes.^[28] Depending on the type of the rhodium complexes, which could be switched in situ by addition of pyridine, the reaction could be directed towards linear or branched products (Scheme 12). Pyridine played an important



Scheme 12. Pyridine-induced switch of selectivity in Rh–NHC catalyzed thiol addition to terminal alkynes.

role, blocking vacant coordination site *trans* to NHC ligand, thus favouring formation of the branched product with excellent selectivity via alkyne insertion into the Rh–S bond. Diminished selectivity in the absence of pyridine was accounted for by competitive processes of alkyne insertion into Rh–S and Rh–H bonds. The experimental findings were confirmed by theoretical calculations.

Water-soluble dinuclear Rh complexes with hydrophilic phosphines have been developed to perform Markovnikov-type addition of a wide range of thiols to aryl- and alkylacetylenes at room temperature with high yields and excellent regioselectivity (Scheme 13).^[29] Use of a THF–H₂O solvent system allowed catalyst recyclization up to five times without any significant loss of activity and selectivity. The authors assumed

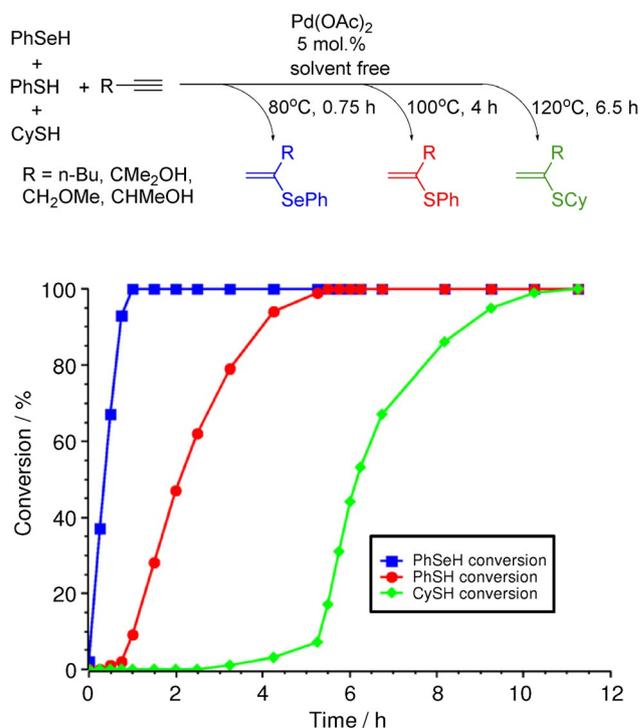


Scheme 13. Rh-based recyclable catalytic system for Markovnikov-type thiol addition to terminal alkynes.

the active form of the catalyst to be dimeric, with one metal center being involved in the catalytic transformation.

Palladium nanosalts [Pd(SR)₂]_n formed in situ from a Pd(OAc)₂ precursor were found to catalyze selective addition of aliphatic thiols to terminal alkynes as well, though much more harsh conditions were required compared with Rh-based systems to achieve high yields of Markovnikov-type vinyl sulfides.^[30] Nevertheless the products were formed with excellent selectivity (M/aM up to 99:1), and various functional groups tolerated the reaction conditions.

Recently such a Pd-based catalytic system was found to be very efficient in the capture of thiols and selenols from the mixture by alkynes in a highly chemo- and regioselective manner.^[31] Under the conditions employed, the active form of the catalyst performed subsequent addition of Z–H (Z=S, Se) bonds to alkynes, thus leading to exclusive formation of only one product at every instant (Scheme 14). The next Z–H (Z=S, Se) bond species started to react only after the previous ones

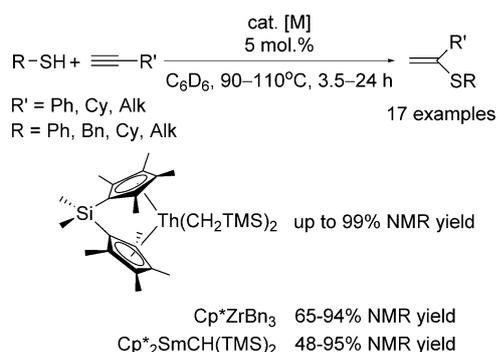


Scheme 14. Pd-based catalytic system for chemo- and regioselective capture of thiols and selenols from the mixture by terminal alkynes and NMR monitoring of the reaction.

were completely consumed. Based on the mechanistic investigations performed, this was rationalized by quick adaptive tuning of the catalyst which could smartly recognize and differentiate Z–H (Z=S, Se) species according to their activity. Certainly, the developed catalytic system will be greatly benefited by flow-chemistry conditions.

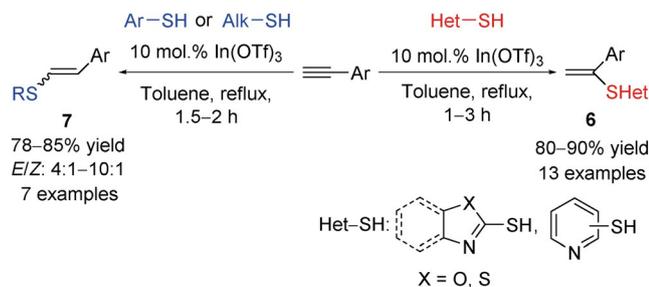
In addition to Pd, Ni, and Rh, complexes of lanthanides (Sm, La, Lu) and actinides (U, Th),^[32] as well as zirconium,^[33] were also found to possess catalytic activity in aromatic and aliphatic thiol addition to terminal alkynes. Yields and selectivity of

Markovnikov-type product formation depended much on the structure of the alkyne and thiol; the catalysts were found to be highly efficient in selective addition of linear alkyl thiols to various aliphatic and aromatic alkynes (up to 99% of branched product), as well as propargyl amine. Quite harsh reaction conditions (90–120 °C, 3.5–24 h) didn't influence selectivity and yields (Scheme 15). The Zr-catalyzed reaction was shown to be easily scaled up to 1 g of the product in 99% selectivity and 72% yield.



Scheme 15. Lanthanide-, actinide-, and Zr-based catalysts for regioselective Markovnikov-type addition of thiols to terminal alkynes.

Another example of regioselectivity control has been recently shown using catalytic amounts of In(OTf)₃.^[34] Addition of heteroaromatic thiols to arylacetylenes proceeded in a Markovnikov-type fashion leading to vinyl sulfides **6** in good yields 80–90% (Scheme 16), while aliphatic and aromatic thiols

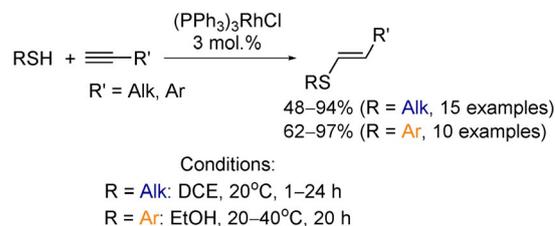


Scheme 16. Substrate-induced switch of selectivity in thiol addition to aryl acetylenes catalyzed by In(OTf)₃.

formed linear products **7** (*E/Z* > 5:1). Though no mechanistic investigations have been performed in this communication, it was assumed that depending on the thiol nucleophilicity, In(OTf)₃ may interact either with an alkyne to form acetylenide or with a thiol to form sulfide, thus leading to linear or branched products.

2.2 Catalytic systems leading to anti-Markovnikov-type (linear) vinyl chalcogenides of *E*-configuration

Wilkinson's catalyst—(PPh₃)₃RhCl—was found to be the first one that possessed opposite regioselectivity (compared to Pd- and Ni-based catalysts) in thiol addition to alkynes, leading to selective formation of *E*-vinyl chalcogenides. Both aromatic^[10] and aliphatic^[35] thiols reacted smoothly (Scheme 17); however,

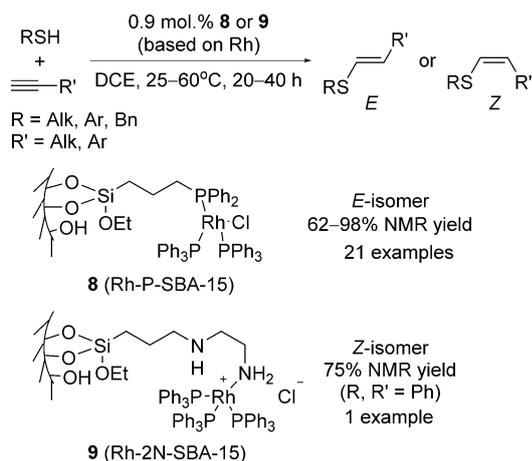


Scheme 17. Rh(PPh₃)₃Cl as a catalyst for selective formation of linear *E*-vinyl sulfides.

it was shown that the solvent had a crucial effect on selectivity and yields of the target products. Ethanol was a solvent of choice for aryl thiols, while 1,2-dichloroethane (DCE) was more preferable in the case of alkyl thiols. Such dependence was attributed to better solubility of (PPh₃)₃RhCl in DCE and probable specific interactions between the chlorine-containing solvent and metal complex.^[35]

Some other catalytic systems introduced later were mentioned in a previous section; however, they had limited substrate scope like In(OTf)₃ (Scheme 16) or moderate selectivity like Rh–NHC complexes (Scheme 12). Thus, further studies in this field were concentrated on the development of immobilized recyclable catalysts.

In recent years, several types of efficient immobilized Rh and Au catalysts have been described which allowed high yields and selectivity combined with easy catalyst recovery and recycling. MCM-41-supported Wilkinson's catalyst afforded an easily recycled catalytic system to obtain linear *E*-vinyl sulfides from aryl thiols and terminal aromatic and aliphatic alkynes under mild reaction conditions (EtOH, 40 °C, 24 h). The catalyst could be separated by simple filtration and was still highly active even after 10 cycles leading to the products in 63–97% yields.^[36] In another work, Yang and Rioux found that depending on the functional groups linked to the polymer support, stereoselectivity of the Rh-catalyzed reaction can be switched from *E* to *Z*.^[37] Under optimized conditions using Rh-P-SBA-15 **8** as a catalyst, a wide range of alkynes and thiols interacted with excellent *E*-stereoselectivity and high yields (Scheme 18). Both electron-rich and electron-poor aromatic alkynes and thiols reacted smoothly; however, in the case of aliphatic alkynes or thiols, prolonged heating at elevated temperature was required to reach high conversions of alkynes. Though stereoselectivity was excellent for all types of substrates, in the case of alkyl thiols, 10–30% of branched product was also formed. When Rh complex was immobilized to the support using amino-functionality, presumably charged complex **9** was

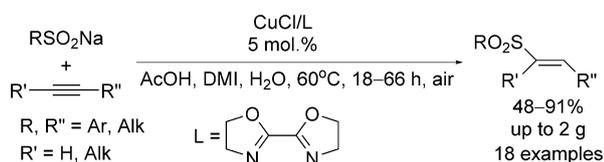


Scheme 18. Influence of linkage functionality in immobilized Rh complexes on stereoselectivity of thiol addition to terminal alkynes.

formed which reversed stereoselectivity from *E* to *Z*. The catalyst **8** could be easily recovered by filtration, and no significant loss of activity and selectivity was observed after 4 runs.

Opposite to Au^I (see above), homogeneous and heterogeneous Au^I and Au^{III} complexes with NHC ligands led to linear *E*-vinyl sulfides exclusively in 89–94% yields. Both homogeneous and heterogeneous systems possessed similar catalytic activity, though the latter allowed catalyst recycling up to three times without loss of selectivity and yield.^[38]

Recently Taniguchi has shown that sodium sulfinates can be efficiently involved in the reaction with alkynes under copper catalysis to form *E*-alkenyl sulfones (Scheme 19).^[39] The trans-



Scheme 19. First example of selective sulfinate addition to the triple bond of alkynes catalyzed by Cu salt.

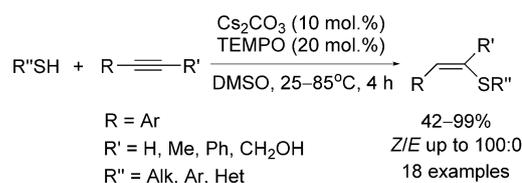
formation involves a broad range of aromatic and aliphatic alkynes (the latter gave lower yields). Internal alkynes reacted smoothly giving single regio- and stereoisomers. The catalytic procedure was shown to be easily scaled up to several grams of the products.

The presence of air was found crucial for the reaction to proceed. It was assumed that oxygen either promotes generation of RSO₂ radicals or oxidation of Cu^I into Cu^{II}.

Based on the results of Markovnikov-type vinyl chalcogenide formation (see Section 2.1), catalytic systems developed for anti-Markovnikov thiol addition to alkynes should be suitable for selenols as well. However, surprisingly, there are still no reports about metal-catalyzed addition of Se–H bond to alkynes which lead to linear vinyl selenides of *E*- or *Z*-configuration.

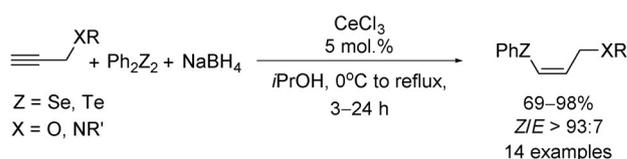
2.3 Catalytic systems leading to anti-Markovnikov-type (linear) vinyl chalcogenides of *Z*-configuration

Despite obvious success in the development of selective catalytic systems to obtain branched or linear *E*-vinyl chalcogenides, metal-catalyzed formation of linear *Z*-isomers has been a challenge for a long time. Only in 2005 was the first catalytic system based on Cs₂CO₃ developed to allow thiol addition to terminal arylacetylenes with good to excellent *Z*-stereoselectivity in the presence of the radical inhibitor (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO, Scheme 20).^[40] Excellent selectivities were achieved with alkyl thiols, while aromatic thiols were much less reactive. Cheap K₂CO₃ was found to catalyze the reaction as well, though selectivity and yields were slightly lower.



Scheme 20. First example of Cs-catalyzed linear *Z*-vinyl sulfide formation.

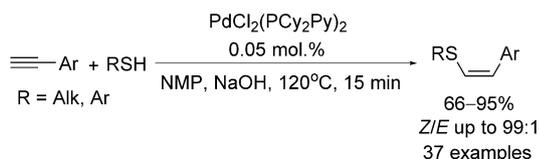
Later Silveira et al. found CeCl₃ to be an efficient catalyst for selective addition of in-situ-formed selenolates and tellurolates to propargylic alcohols and amines resulting in linear products of *Z*-configuration (Scheme 21).^[41] The solvent had a crucial effect on regioselectivity of the reaction, with the best results being achieved in *i*PrOH. To date, this is the only example of vinyl telluride formation via addition to the triple bond of alkynes.



Scheme 21. Ce-based catalytic system for selective synthesis of aryl vinyl selenides and tellurides.

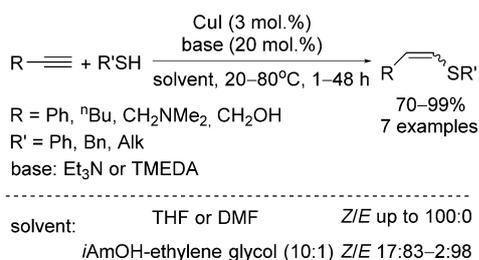
Recently, Gerber and Frech have developed the first generally applicable, highly active Pd-based catalytic system to obtain linear *Z*-vinyl sulfides with excellent regioselectivity using a wide range of aromatic alkynes and aromatic and aliphatic thiols as substrates (Scheme 22).^[42] The reaction was complete within several minutes in *N,N*-dimethylpyrrolidone (NMP) as a solvent using as few as 0.05 mol.% of Pd complex leading to high yields of the target products of *Z*-configuration. However, in the case of aliphatic alkynes, Markovnikov-type vinyl sulfides were obtained as the major products, accounting for the alteration of the reaction pathway.

Copper complexes were found to be highly promising to achieve *Z*-vinyl sulfides. Beletskaya and Trostyanskaya discov-



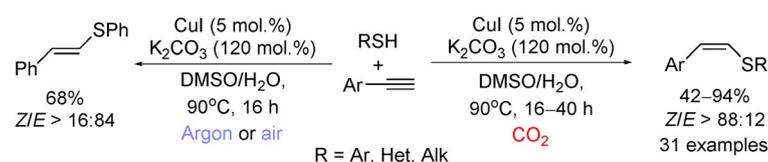
Scheme 22. Generally applicable Pd-based catalytic system for selective formation of linear Z-vinyl sulfides.

ered that CuI efficiently catalyzed the addition of aromatic and aliphatic thiols to terminal alkynes.^[43] In some cases, addition of Et₃N or tetramethylethylenediamine (TMEDA) improved the selectivity of the reaction. Changing solvent from tetrahydrofuran (THF) or dimethylformamide (DMF) to isoamyl alcohol resulted in a selectivity switch to E-isomer as the major product (Scheme 23). This was, most likely, due to isomerization of initially formed Z-isomer promoted by the protic solvent and Cu salt. The catalytic system could be implemented to symmetrical and nonsymmetrical internal alkynes, as well leading to highly selective formation of Z-isomers.



Scheme 23. Solvent-dependent stereoselectivity control in Cu-catalyzed addition of thiols to terminal alkynes.

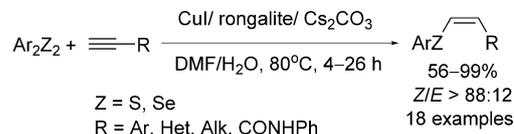
In another study with CuI as a catalyst, it was found that Z-stereoselectivity of alkyl and aryl thiol addition to terminal aryl acetylenes can be achieved under a CO₂ atmosphere (Scheme 24).^[44] Unlike many catalytic systems which are very moisture-sensitive, water as a source of protons was crucial to accelerate the reaction. According to the proposed mechanism, reversible generation of propiolic acid upon interaction of CO₂ with alkyne activated the triple bond and governed selectivity via formation of a carboxylate–copper complex. This mechanistic assumption is strongly supported by an earlier work in which Z-vinyl sulfides resulted from CuI-catalyzed addition of thiols to arylpropionic acids.^[45] K₂CO₃ as an additive greatly improved the selectivity. Aliphatic, benzylic, and aro-



Scheme 24. CO₂-induced alternation of stereoselectivity in Cu-catalyzed thiol addition to aryl acetylenes.

matic thiols were equally efficient under the optimized reaction conditions leading to the products in high yields (up to 94%) and selectivities (Z/E > 88:12).

Combination of CuI with rongalite and Cs₂CO₃ led to Z-vinyl chalcogenides as major products starting from dichalcogenides and alkynes (Scheme 25).^[46] The catalytic system tolerated



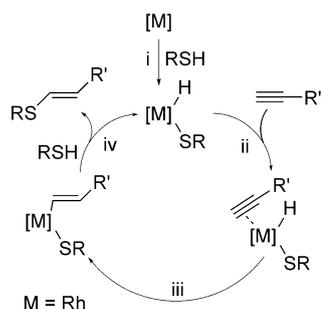
Scheme 25. Z-Stereoselective addition of in-situ-formed ArZ (Z=S, Se) species to terminal alkynes catalyzed by CuI.

a wide range of functional groups well, including methoxy, amino, nitro, amide, hydroxyl, and halogene, both in the alkyne and dichalcogenide moieties. The speculative mechanism suggested includes initial formation of radicals from Ar₂Z₂ (Z=S, Se) which then converted into anions; the latter reacted with alkynes to furnish the products upon protonolysis by water.

Immobilization of Cu–NHC complex on mesoporous silica SBA-15 led to a heterogeneous catalyst whose activity and selectivity in addition of thiols to terminal alkynes surpassed those of the homogeneous analog.^[47] This accounted for higher stability of the bound complex under the reaction conditions (homogeneous Cu–NHC was found to decompose into metallic Cu particles thus losing catalytic activity). The heterogeneous catalytic system developed was equally efficient for aromatic and aliphatic terminal alkynes and aryl thiols leading to highly stereoselective formation of Z-vinyl sulfides (Z/E > 87:13). Yields of the products depended on electronic properties of substituents in alkynes and thiols with a decrease in the case of electron-withdrawing groups. Aliphatic thiols were successfully involved in the reaction as well, though lower selectivity was observed and higher temperature and longer time were required to achieve satisfactory yields. The catalytic system was shown to be easily scaled up to 2 g of the product and the catalyst could be recycled up to six times without significant loss of activity and selectivity.

External nucleophilic attack on the metal-activated triple bond is assumed to explain formation of linear vinyl chalcogenides under Cu or Cs, as well as recent examples of Pd catalysis,^[7g] while Rh complexes introduced are shown to catalyze the reaction via insertion pathway (Scheme 26).^[7a,b,h] The catalytic cycle in this case starts from thiol oxidative addition to the metal center (i) followed by alkyne coordination (ii) and insertion into the metal–hydrogen bond (iii) which is more favorable compared with a metal–chalcogen one. Finally, thiol-assisted reductive elimination takes place (iv) leading to the product and regenerating the catalyst.

Thus, to date, there are several efficient homogeneous and heterogeneous catalytic systems developed based on Pd, Ni, Rh, Au, Zr, Cu, and Cs to



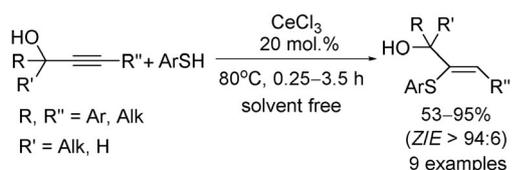
Scheme 26. Mechanism of anti-Markovnikov-type vinyl chalcogenides formation via rhodium-catalyzed addition of Z–H (Z=S, Se) bond to terminal alkynes.

obtain various types of vinyl chalcogenides (branched and linear *E* or *Z*) with excellent regio- and stereoselectivity starting from various terminal alkynes and thiols (both aromatic and aliphatic).^[71, 10, 20a, 29, 38, 41, 44] Large substrate scope and functional group tolerance, as well as the possibility to scale up the reactions and recycle the catalyst, make them highly useful and efficient tools for synthetic applications.

The majority of the catalytic systems described above can be applied to both terminal and internal alkynes. For the latter, an important question arises to control regioselectivity in the case of Z–H (Z=S, Se) bond addition to nonsymmetrical alkynes. Usually it is a steric factor of substituents at the triple bond that governs the addition: RZ moiety (Z=S, Se) adds to less sterically hindered carbon. Besides, there are some examples in which coordination of a catalyst to functional groups of alkyne is possible thus directing thiol addition. Nevertheless, development of a regioselective catalyst efficiently applicable to a wide range of alkynes (especially those which don't contain functional groups or bulky substituents adjacent to the triple bond) still remains a challenge.

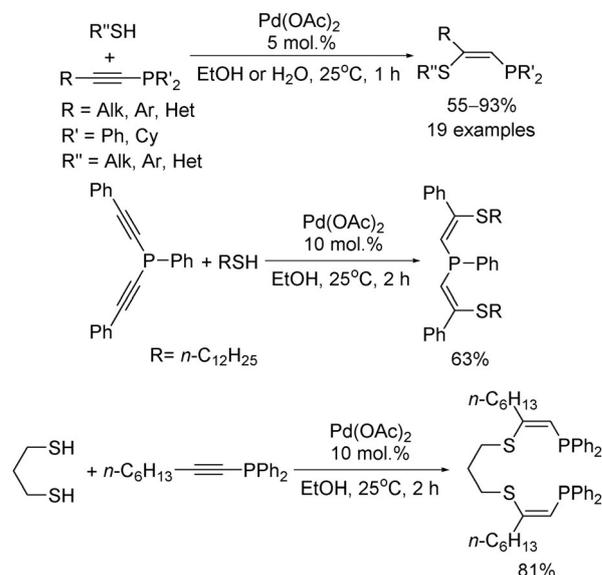
Recently CeCl₃ was found to be highly efficient in aromatic thiol addition to internal alkynes bearing an OH-group adjacent to the C≡C bond (Scheme 27). *Z*-vinyl sulfides were obtained under solvent-free conditions with excellent stereo- and regioselectivity (*Z/E* > 94:6).^[48] The only drawback was the quite high loading of the anhydrous catalyst (20 mol.%).

Similar selectivity was observed in a Pd(OAc)₂-catalyzed addition of aliphatic, aromatic, and heteroaromatic thiols and dithiols to 1-alkynylphosphines.^[49] Reaction could be performed in both nonpolar and polar solvents, including water and ethanol, and was complete in 1 h at room temperature, resulting in *Z*-1-phosphino-2-thio-alkenes in 55–93% yield. Multiple addi-



Scheme 27. Ce-catalyzed highly regioselective substrate-directed addition of aryl thiols to internal alkynes.

tions to diynes and dialkynyl phosphines were also possible thus providing promising objects with multicoordination sites for supramolecular chemistry (Scheme 28).



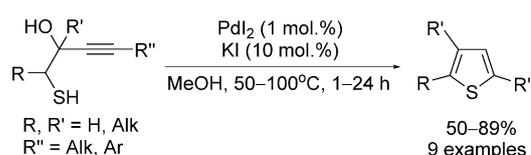
Scheme 28. Pd-based catalytic system for regioselective thiol addition to internal 1-alkynylphosphines.

In both cases, metal salts acted as Lewis acids coordinating to oxygen and phosphorous, respectively, thus, providing stereo- and regioselectivity.

The (PPh₃)₃RhCl–Ph₂P(O)H catalytic system was found to be efficient for regio- and stereoselective addition of PhSeH to internal alkynes bearing electron-withdrawing substituents (COOMe, CPh, COMe, P(O)Ph₂). As a result, vinyl selenides of *E*-configuration were obtained in 45–95% yield.^[50] The role of Ph₂P(O)H was revealed to suppress side reactions.

All the work described above concerns intermolecular addition of Z–H (Z=S, Se) bonds to alkynes; on contrary, transition-metal-catalyzed intramolecular variants of such reactions are rare. To date, only one general catalytic system—PdI₂/KI—is known which leads to substituted thiophenes in moderate to good yields (Scheme 29).^[51] When [bmim][BF₄] was used as a solvent instead of methanol in this work, catalyst recyclization could be performed up to six times without noticeable loss of activity.

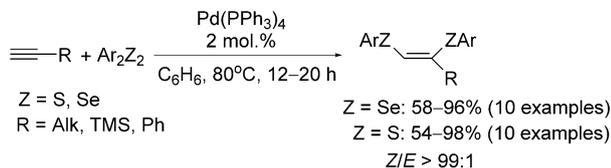
In addition, a single example of Au-catalyzed thiophene formation has been recently reported.^[52]



Scheme 29. PdI₂/KI catalysis to obtain trisubstituted thiophenes via intramolecular S–H bond addition to the triple bond of internal alkynes.

3 Formation of Bisfunctionalized Alkenes

When diaryl disulfides and diselenides were used as substrates in the Pd-catalyzed reaction with terminal alkynes, 1,2-disubstituted alkenes of *Z* configuration were selectively obtained (Scheme 30). It should be emphasized that while bis(thio)- or



Scheme 30. First example of stereoselective diaryl dichalcogenide addition to terminal alkynes catalyzed by Pd complexes.

bis(seleno)-substituted alkenes of *E*-configuration can be easily obtained under nucleophilic conditions, selective formation of *Z*-isomers has been a challenge for a long time. The key to success was in utilization of palladium complexes with phosphine ligands which promoted oxidative cleavage of Z–Z (Z=S, Se) bond.^[53] The catalytic system developed tolerated different functional groups (amino, hydroxyl, trimethylsilyl) and didn't affect double bonds in enynes. In all cases the products were obtained with high yields (up to 98%) and excellent *Z*-stereoselectivity (*Z/E* > 99:1).

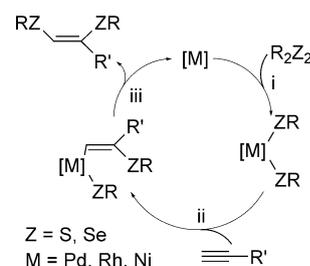
Though various diaryl dichalcogenides reacted smoothly under the catalytic conditions developed, dialkyl analogues gave products with only moderate yields. Reaction of diaryl dichalcogenides with internal alkynes also led to trace amounts of the desired products.

The initially proposed mechanism was confirmed and defined more exactly in numerous further investigations^[71, 53, 54, 59] and included the following steps: oxidative addition of the Z–Z (Z=S, Se) bond to the metal center (i); coordination and insertion of alkyne into the M–Z (Z=S, Se) bond (ii), and finally, reductive elimination of the product (iii) (Scheme 31). It should be noted that this mechanism is related to transition metals only, while main group metal catalysis (see below), most likely, is based on nucleophilic additions to activated triple bonds of alkynes.

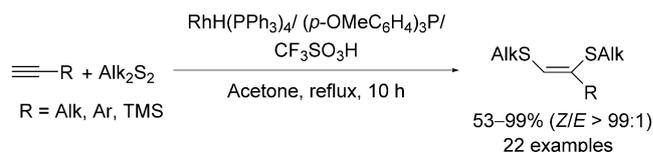
Further thorough mechanistic investigations resulted in improved catalyst stability,^[54] utilization of cheaper palladium catalyst precursors, and simplification of the isolation procedure.^[55]

When Pd(PPh₃)₄-catalyzed addition of diaryl dichalcogenides to terminal alkynes was performed in ionic liquid [bmim][PF₆], both reaction time and temperature could be decreased without affecting high yields of the products. In addition, the catalyst could be reused a minimum of four times, keeping high activity and selectivity.^[56]

After several efforts, low activity of dialkyl dichalcogenides in the reaction with alkynes was overcome, and the first efficient catalytic system based on rhodium complex was introduced in 2001 by Yamaguchi (Scheme 32).^[57]

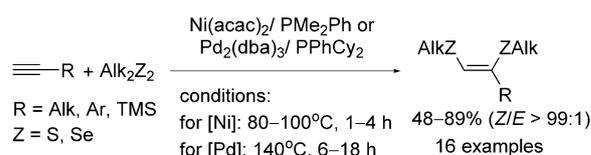


Scheme 31. Mechanism of transition-metal-catalyzed Z–Z (Z=S, Se) bond addition to terminal alkynes leading to *Z*-1,2-bis(chalcogen)-substituted alkenes.



Scheme 32. Rh-catalyzed addition of dialkyl disulfides to terminal alkynes.

Later Ananikov, Beletskaya et al. showed that this transformation can be successfully performed using palladium or nickel complexes bearing phosphine ligands.^[58] Upon comparison of bond strength in diaryl and dialkyl dichalcogenides, they envisaged that in the former case, the Z–Z (Z=S, Se) bond is weaker than the Z–C bond, while the opposite relationship is observed for the latter substrates. Thus, it was concluded that the right choice of the phosphine ligand was the key to generate highly active catalysts capable of selectively cleaving stronger Z–Z (Z=S, Se) bonds in dialkyl dichalcogenides while leaving untouched weaker Z–C bonds. As a result of thorough ligand screening, phosphines with donor substituents were found to perform well in the reaction, and two efficient catalytic systems Ni(acac)₂/PPhMe₂ and Pd₂(dba)₃/PPhCy₂ were developed (Scheme 33). The catalytic systems were tolerant to various functional groups in alkynes leading to the products with high yields (48–89%) and excellent stereoselectivity (*Z/E* > 99:1) and could be easily scaled to gram quantities of the products with the similar efficiency. The nickel-based catalytic system was found to be superior in catalytic activity and reagents scope (both disulfides and diselenides were successfully involved in the reaction while palladium-based system was applicable to disulfides only). The only drawback of the nickel catalyst was causing side reactions with alkynes containing hydroxy groups and product decomposition after

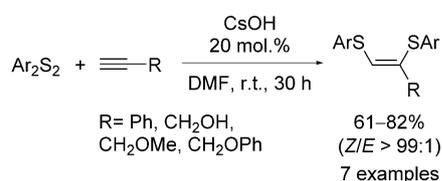


Scheme 33. Ni- and Pd-based catalytic system for stereoselective addition of dialkyl dichalcogenides to terminal alkynes.

prolonged heating. Thus, the palladium-based catalytic system, which didn't suffer from such disadvantages, is complementary to the nickel one.

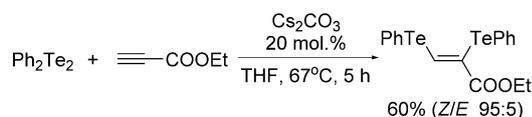
These catalytic systems were found to be efficient in addition of cyclic dichalcogenides to terminal alkynes as well.^[59] The Ni-based catalyst provided the desired vinyl chalcogenides of *Z*-configuration in 50–91% yield. The Pd-based solvent-free catalytic system was less efficient from synthetic point of view because it required more harsh reaction conditions; however, it was found highly valuable in mechanistic investigations to study processes of catalyst leaching and to rationalize role of excess of phosphine ligand in maintaining the high activity of the catalytic species.

Among other catalytic systems developed so far, cheap CsOH was introduced recently for stereoselective S–S bond addition to alkynes. In this case, functionalized aliphatic and aromatic terminal alkynes reacted well with diaryl disulfides under very mild reaction conditions leading exclusively to *Z*-isomers in 61–82% yields (Scheme 34).^[60]



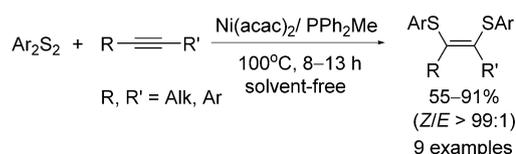
Scheme 34. Cs-catalyzed formation of *Z*-1,2-bis(thio)-substituted alkenes.

Nishiyama et al. investigated the addition of diaryl dichalcogenides to activated alkynes under CsF or Cs₂CO₃ catalysis.^[61] Though stereoselectivities in the case of disulfides and diselenides were modest, they succeeded for the first time with highly stereoselective Ph₂Te₂ addition to an activated alkyne (Scheme 35). To date, this is the single example of a challenging problem to involve ditellurides in this type of metal-catalyzed reactions.



Scheme 35. First example of stereoselective ditelluride addition to terminal alkyne catalyzed by Cs salt.

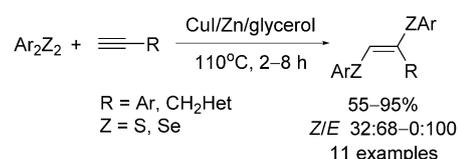
Another challenging problem—development of an efficient catalytic system for *Z*–*Z* (*Z*=S, Se) bond addition to internal alkynes—has been successfully solved in 2010 when Ananikov and Beletskaya et al. found a nickel-based catalyst with PPh₂Me ligand to be highly active in this transformation.^[62] The choice of phosphine ligand was found to be the crucial factor to run the reaction. Initial screening of various mono- and bidentate phosphines has shown almost all of them to be completely inactive. Surprisingly, PPh₂Me led to complete conver-



Scheme 36. First example of Ni-based catalytic system for stereoselective addition of diaryl disulfides to internal alkynes.

sion of model 3-hexyne and exclusive formation of *Z*-1,2-bis(thio)-substituted alkene (Scheme 36). Under optimized conditions, various diaryl disulfides smoothly reacted with internal alkynes, furnishing the target products in 55–91% yields. Such dramatic difference in ligand effect was explained based on the theoretical calculations. A new reaction pathway was proposed for internal alkynes which includes 5-coordinated intermediate nickel complex, while generally accepted 4-coordinated nickel complex, which requires preliminary ligand dissociation, seems to be a resting state in this case.

While all the catalytic systems described above resulted in selective formation of *Z*-1,2-bis(thio)- or *Z*-1,2-bis(seleno)-substituted alkenes, *E* isomers still could be obtained only via addition under nucleophilic conditions using stoichiometric amounts of reagents. Only recently, a recyclable CuI/Zn/glycerol catalytic system has been developed to perform *Z*–*Z* (*Z*=S, Se) bond addition to alkynes with *E* selectivity for the first time (Scheme 37).^[63] The best selectivities of *E*-isomer formation (*E/*



Scheme 37. Stereoselective formation of *E*-1,2-bis(chalcogen)-substituted alkenes performed by recyclable CuI/Zn/glycerol catalytic system.

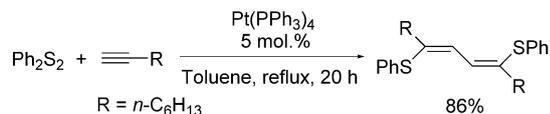
Z > 90:10) were achieved for diaryl diselenides containing electron-donating groups, while diselenides with electron-withdrawing groups and diaryl disulfides resulted in a mixture of *E* and *Z* products. Several propynyl pyrazoles were involved in the reaction; though the yields were high, the stereoselectivity depended much on the substituents at the pyrazole ring. The catalytic system could be easily separated by filtration and recycled at least five times without a noticeable loss of activity.

4 Formation of Substituted Dienes

It has been shown that even more complex products can be obtained in a one-pot transition-metal-catalyzed interaction of alkynes with *Z*–*Z* or *Z*–H (*Z*=S, Se) bonds.

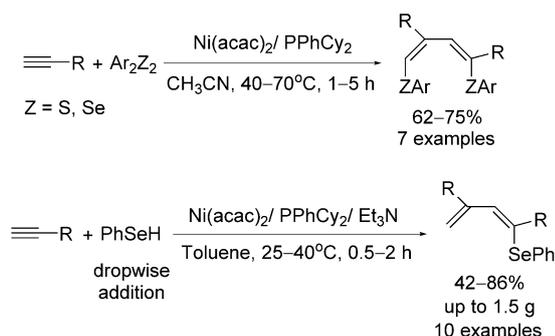
In 2001, a Pt-based catalytic system was reported to furnish formation of symmetrical bis(thio)-substituted dienes with excellent selectivity starting from diaryl disulfide and terminal alkynes.^[64] Pt-catalyzed subsequent formation of S–C and C–C bonds resulted in an easy way to build valuable diene skele-

tons in an atom-efficient manner. Only one type of possible regio- and stereoisomers was formed (Scheme 38) thus emphasizing advantages of transition-metal catalysts.



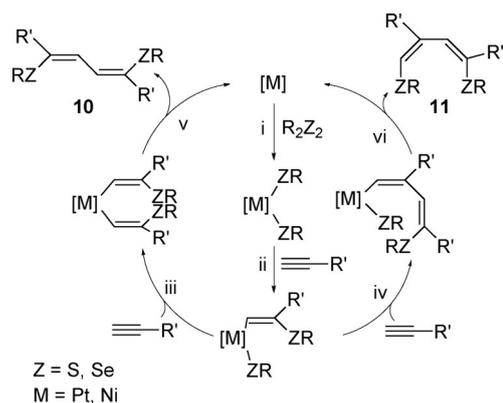
Scheme 38. Pt-catalyzed stereo- and regioselective 1,4-thiosubstituted diene formation starting from diphenyl disulfide and terminal alkyne.

Recently, this type of reactivity was extended by Ananikov, Beletskaya et al., and a Ni-based catalytic system for synthesis of previously unknown type of chalcogen-substituted dienes has been developed.^[65] The right choice of the phosphine ligand with bulky cyclohexyl substituents resulted in formation of unsymmetrical bisubstituted dienes as major products (Scheme 39). Both disulfides and diselenides were successfully involved in the reaction, providing the products with high yields (62–75% after column chromatography).



Scheme 39. Ni-based catalytic systems for selective formation of unsymmetrical bis- and mono-chalcogen-substituted dienes starting from alkynes.

These reactions were possible due to the propensity of platinum and nickel complexes for insertion of several alkyne molecules within a catalytic cycle (Scheme 40). In both cases, reactions started from oxidative addition of dichalcogenide to the metal center (i) followed by coordination and insertion of first alkyne molecule into metal-chalcogen bond (ii) similar to the mechanism of bis-substituted alkene formation described in the previous section. However, another alkyne insertion (iii or iv) takes place in this case prior to reductive elimination, thus leading to formation of the diene skeleton. Selectivity of this step depends much on the metal catalyst used: platinum complexes undergo alkyne insertion into the metal-chalcogen bond exclusively (iii) thus resulting in symmetrical dienes **10** after reductive elimination step (v). On the other hand, nickel complexes are able to insert the second alkyne molecule both into the metal-chalcogen (iii) and metal-carbon (iv) bonds. In the latter case, dienes of unsymmetrical type **11** are formed upon reductive elimination (vi). The selectivity of second



Scheme 40. Mechanism of formation of symmetric and unsymmetric bis-(chalcogen)-substituted dienes starting from alkynes and dichalcogenides.

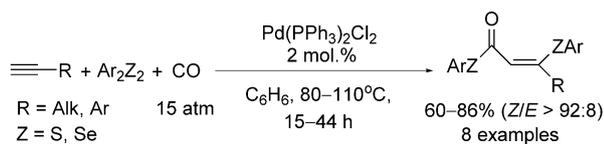
alkyne insertion is determined by the choice of ligands at the nickel center.^[65a]

When PhSeH was used instead of dichalcogenides, monoselective dienes were obtained using a similar Ni-based catalytic system. The reaction proceeded smoothly under very mild conditions and resulted in the target products with exclusive chemoselectivity in 42–86% yield (Scheme 39).^[65b] Dropwise addition of PhSeH was found to be crucial to improve selectivity of the diene formation. Use of cheap nickel precursors and quick in situ formation of the active form of the catalyst allowed easy scaling of the catalytic reactions to gram quantities of the desired products. A unique property of unsymmetrical mono- and bis(chalcogen)-substituted dienes was revealed based on X-ray and NMR data: both types of dienes preferred *gauche*-conformation in solid state and solution which is not common for diene skeletons usually having thermodynamically a more stable *s-trans* conformation. Such a twist was rationalized based on theoretical calculations which revealed stabilization of the nickel-dienyl complex by additional π -bonding.^[65a]

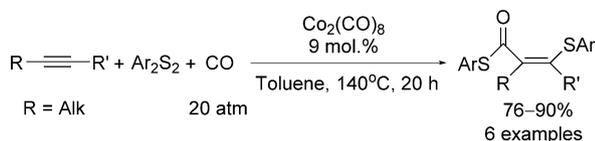
5 Miscellaneous Reactions

In 1991 Ogawa and Sonoda et al. found that Pd-catalyzed interaction of Ar_2Z_2 ($\text{Z}=\text{S}, \text{Se}$) with terminal alkynes under CO atmosphere led to the formation of carbonylated products in 56–89% yield (Scheme 41).^[53] This resulted from CO insertion into the Pd–C bond prior to final reductive elimination step (similar to insertion of the second alkyne molecule in Scheme 40). Increase of CO pressure or replacement of $\text{Pd}(\text{PPh}_3)_4$ by $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ resulted in almost complete suppression of 1,2-bis(chalcogen)-substituted alkene formation. In addition to excellent stereoselectivity ($Z/E > 92:8$) reaction was found to be highly chemoselective: the carbonyl group was introduced exclusively at the terminal carbon of the alkyne.

Internal alkynes could be involved in the reaction under $\text{Co}_2(\text{CO})_8$ catalysis (Scheme 42).^[66] Using various aromatic disulfides, products of thiolative carbonylation were formed with excellent *Z*-stereoselectivity and high yields (up to 90%). When unsymmetrical internal alkynes were employed, a mixture of regioisomers was obtained. Aliphatic disulfides failed to react.

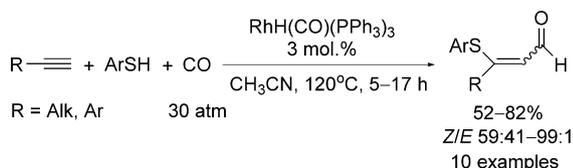


Scheme 41. Pd-catalyzed selective carbonylative bis-addition of diaryl dichalcogenides to terminal alkynes.



Scheme 42. Co-based catalytic system for bis-thiolative carbonylation of internal alkynes.

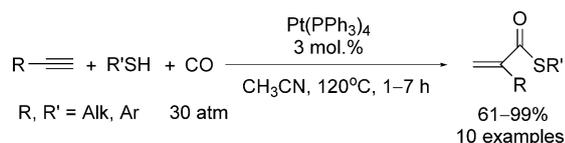
The same group revealed Rh complexes to be active in selective thioformylation of terminal acetylenes using PhSH under CO atmosphere (Scheme 43).^[67] The target products



Scheme 43. Regioselective thioformylation of terminal alkynes catalyzed by Rh complexes.

were obtained in moderate to good yields (52–82%) and excellent regioselectivity (CO and phenylthio groups were introduced into the terminal and internal positions of alkynes, respectively), however stereoselectivity was from moderate to good. It was revealed that initially formed kinetic product of *Z*-configuration isomerized into *E*-alkene under prolonged heating thus diminishing the stereoselectivity. Alkyl thiol (dodecanethiol) was shown to react under the optimized reaction conditions, but the product yield was low (27%) and thioester was formed as a by-product (23%).

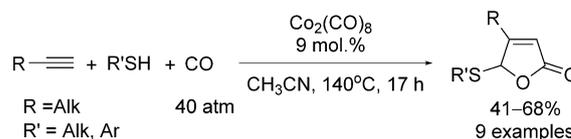
Use of $\text{Pt}(\text{PPh}_3)_4$ in the reaction resulted in inversion of regioselectivity compared with Rh catalysis thus leading to the exclusive formation of hydrothiocarboxylation products— α,β -unsaturated thioesters (Scheme 44).^[68] Even aliphatic thiols reacted easily leading to the target products in up to 99% yield. In the case of aromatic thiols, excess of alkyne was essential to prevent thiol addition to the double bond while with less



Scheme 44. Selective formation of thioesters under $\text{Pt}(\text{PPh}_3)_4$ catalysis.

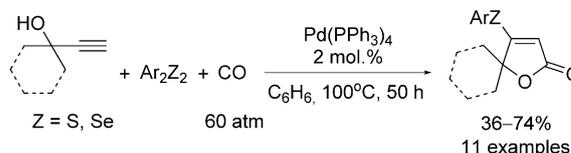
acidic aliphatic thiols alkynes could be used in equimolar amounts.

$\text{Co}_2(\text{CO})_8$ as a catalyst allowed to obtain thiolactones as a result of double CO insertion into the triple bond of terminal alkynes.^[69] Aliphatic thiols were found to react smoothly leading to desired products in excellent selectivity and 41–68% yields (Scheme 45). On the contrary, aryl thiols showed poor selectivity in the reaction, and thiolative monocarbonylation by-products were formed in considerable amounts.



Scheme 45. Co-catalyzed formation of thiolactones via carbonylative thiols addition to terminal alkynes.

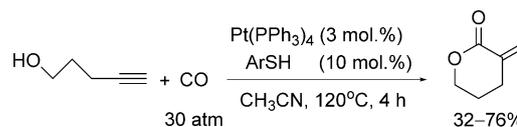
Similar thiolactone and selenolactone products could be obtained in a one-pot lactonization under $\text{Pd}(\text{PPh}_3)_4$ -catalyzed interaction of diaryl dichalcogenides with terminal alkynes containing a hydroxy group in the aliphatic chain (Scheme 46).^[70] The yields of the target products (five and six-membered lactones as well as spirocyclic lactones, depending on the alkyne used) were from moderate to good, in some cases chalcogenoesters were formed as the major products.



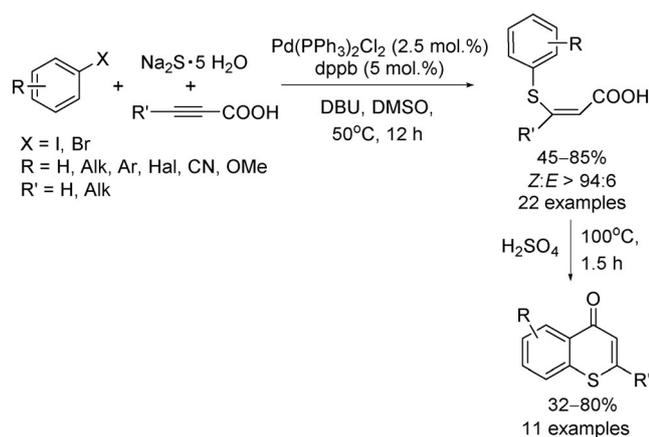
Scheme 46. Pd-based catalytic system for preparation of thio- and selenolactones via carbonylative monoaddition of diaryl dichalcogenides to terminal alkynes.

A similar reaction using aryl thiols and $\text{Pt}(\text{PPh}_3)_4$ catalyst resulted in the formation of lactones without a chalcogen moiety (Scheme 47).^[71] Based on the mechanistic investigations performed, it was revealed that the thiol could be used in catalytic amounts as it was regenerated at the lactonization step of the catalytic cycle.

Another interesting example of a three-component reaction mixture was recently described by Lee, Song et al.^[72] Using aryl halides, Na_2S and propionic acids under Pd catalysis, they ob-



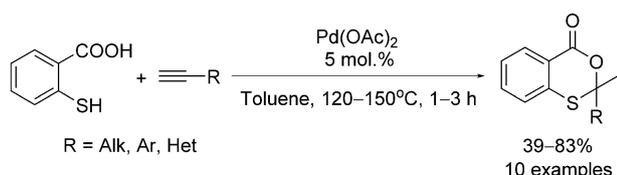
Scheme 47. $\text{Pt}(\text{PPh}_3)_4/\text{ArSH}$ -catalyzed formation of lactones from terminal alkynes and CO.



Scheme 48. Simple way to thiochromenones using Pd-catalyzed selective formation of Z-vinyl sulfides.

tained Z-vinyl sulfides with excellent stereoselectivity (Z/E > 94:6) and from moderate to good yields (Scheme 48). The products formed could be selectively transformed into thiochromenones in a one-pot manner. Based on mechanistic investigations performed, the reaction pathway including initial Pd-catalyzed formation of ArSNa upon interaction of ArX with Na₂S followed by thiophenolate attack on triple bond of alkyne was proposed. It should be mentioned that the authors don't claim the necessity of an inert atmosphere which is a great advantage of the catalytic system developed.

When Pd(OAc)₂ was used to catalyze regioselective S–H bond addition of thiosalicylic acids to terminal alkynes in a Markovnikov-type fashion followed by intramolecular cyclization, 3,1-benzoxathiines were selectively obtained in a one-pot reaction (Scheme 49).^[73] Various terminal alkynes with alkyl and aryl



Scheme 49. One-pot protocol to obtain 3,1-benzoxathiines via Pd-catalyzed S–H bond addition/intramolecular cyclization.

substituents reacted smoothly; activated alkynes (R=Ac, COOEt, COOPh) furnished the target products even without the catalyst. Mechanistic investigations performed have revealed intramolecular hydrooxycarbonylation of the initially formed vinyl sulfide, most likely, to proceed via a radical pathway.

6 Conclusion

Over the past 25 years, compounds containing Z–H or Z–Z (Z=S, Se) bonds have turned from catalytic outcasts and terrifying

catalyst poisons to welcome substrates in metal catalysis. To date, numerous catalytic systems both homogeneous and heterogeneous (including nanostructured) have been developed to perform selective and atom-efficient Z–H and Z–Z (Z=S, Se) bond additions to the triple bonds of alkynes under mild reaction conditions. The right choice of metal and ligands gives an opportunity to control regio- and stereoselectivity in the formation of various mono- and bis(chalcogen)-substituted alkenes and alkanes, as well as dienes and carbonyl derivatives. One of the main recent trends in this chemistry is the replacement of noble metals (Pt, Pd, Rh) by cheaper nickel, copper, and cesium which not only makes synthesis less expensive and thus allows easy scale up, but introduces new reactivity leading to unexpected highly functionalized products. Another rapidly growing and challenging area of investigations is the development of switchable catalysts capable of producing different types of products with high selectivity depending on reaction conditions (solvent or additives). Currently, only the first steps in this direction have been taken; nevertheless, the road promises to be exciting and full of new discoveries. Finally, use of flow chemistry still remains unexplored for the metal-catalyzed interactions of thio- and selenium-containing compounds with alkynes.

Future progress in this area promises not only the development of new compounds with even more complex structures but will also contribute much to a better understanding of the general principles of metal catalysis itself.

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