Review

Recent Advances in the Addition of Amide/Sulfonamide Bonds to Alkynes

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Abstract: The addition of amide/sulfonamide bonds to alkynes is not only one of the most important strategies for the direct functionalization of carbon–carbon triple bonds, but also a powerful tool for the downstream transformations of amides/sulfonamides. The present review provides a comprehensive summary of amide/sulfonamide bond addition to alkynes, including direct and metal-free aminoacylation, based-promoted aminoacylation, transition-metal-catalyzed aminoacylation, organocatalytic aminoacylation and transition-metal-catalyzed aminosulfonylation of alkynes up to December 2018. The reaction conditions, regio- and stereoselectivities, and mechanisms are discussed and summarized in detail.

Keywords: amide bond; sulfonamide bond; alkynes; addition reaction; aminoacylation; aminosulfonylation

1. Introduction

The addition of atom–atom bonds to alkynes has become an important strategy for the functionalization of carbon–carbon triple bonds [1–16]. These intermolecular and intramolecular addition reactions provide a facile and efficient access to highly functionalized alkenes and cyclic compounds, respectively, in a high atom- and step-economic manner. Considering the large occurrence of amide/sulfonamide motifs in natural products and pharmaceutical agents, the addition of amide/sulfonamide bonds to alkynes, namely aminoacylation/aminosulfonylation of alkynes, is particularly important. Because they allow the direct downstream transformations of amides/sulfonamides by the insertion of carbon–carbon triple bonds into the amide/sulfonamide bonds, they thus produce more complex and skeletally different addition molecules (Scheme 1). In addition, the aminoacylation/aminosulfonylation of alkynes also constitutes a tool for the structural modification of compounds carrying amide/sulfonamide bonds, especially for peptides, which are an important class of drugs used in the clinic [17–19]. Besides, amide/sulfonamide bond addition to alkynes, which constructs one C–C/S and one C–N bond in a single step featuring high atom- and step-economy, is in accordance with the concept of “green and sustainable chemistry”.

It should be noted that the addition of amide/sulfonamide bonds to alkynes has not been reviewed before. Moreover, amide/sulfonamide bond addition to alkynes has achieved many important developments in recent decades, especially in transition-metal-catalyzed and organocatalytic processes. Therefore, a review focused on the aminoacylation/aminosulfonylation of alkynes
would enrich the knowledge of synthetic chemists who are interested in amide/sulfonamide bond activation. The aim of the present review is to provide a systematical and comprehensive summary on the addition of amide/sulfonamide bonds to alkynes, including direct and catalyst-free aminoacylation, based-promoted aminoacylation, transition-metal-catalyzed aminoacylation, organocatalytic aminoacylation, and transition-metal-catalyzed aminosulfonylation of alkynes up to December 2018. We hope this review will serve as a handy reference for chemists interested in the addition of amide/sulfonamide bonds to alkynes, and will encourage further developments in this field in overcoming the remaining challenges.

![Scheme 1](image)

**Scheme 1.** The addition of amide/sulfonamide bonds to alkynes.

### 2. Addition of Amide Bonds to Alkynes

#### 2.1. Direct Addition of Amide Bonds to Alkynes without Catalysts and Additives

The first example of amide bond addition to alkynes was a catalyst- and additive-free process as reported by Ege’s group in 1976 [20]. They found the treatment of active 2-phenylpyrazolidin-3-ones 4 with dimethyl acetylenedicarboxylate 5 in CH$_3$CN under reflux led to the formation of the interesting ring expansion products 1,2-diazepin-5-ones 6, albeit with unsatisfactory selectivities and yields (Scheme 2). The main byproducts of this reaction were the cis- and trans- Michael-type addition products. Besides, this transformation was strongly influenced by the solvent used. Polar but nonprotic solvents such as acetone and acetonitrile gave the best results while few products were obtained in protic solvents such as ethanol. Similar results were also observed in Stvete and Stanovnik’s research on the addition reactions between 5,5-dimethyl-2-(1H-indenyl)-3-pyrazolidinones 7 and acetylenedicarboxylates 8 (Scheme 3) [21]. A plausible reaction mechanism was outlined in Scheme 4.

![Scheme 2](image)

**Scheme 2.** Insertion of 2-phenylpyrazolidin-3-ones into amide bonds.
Scheme 3. Catalyst- and additive-free amide bond addition to alkynes.

Scheme 4. Proposed mechanism for the insertion of 2-phenylpyrazolidin-3-ones into amide bonds.

In contrast, Hanack’s group developed a more general and practical addition of amide bonds to carbon–carbon triple bonds without any catalysts and additives in 1989 [22]. Amides 15 were directly added to alkynyl trifluoromethyl sulfones 14 to afford the cis-adducts 16 with excellent regioselectivity and good yields, despite the fact that a long reaction time was required (Scheme 5). This protocol showed advantages such as simple operation, broad substrate scope, and the avoidance of metals and additives. A plausible mechanism was proposed in Scheme 6. The Michael reaction of nitrogen atom of the amides to alkynyl trifluoromethyl sulfones yields a zwitterion 17, which undergoes cyclization to form intermediate 18. The subsequent rupture of the carbon–nitrogen bond of 18 gives the products 16. The regio- and stereoselectivity observed in this reaction could be well explained by this mechanism.

Scheme 5. Direct aminoacylation of alkynyl trifluoromethyl sulfones.
What seems particularly interesting is the addition of 1,1′-carbonyldiimidazole (CDI) 19 to alkynoic acids 20 with the release of CO₂, as reported by Knölker and co-workers in 1993 (Scheme 7) [23]. This reaction proceeded well under mild conditions to provide the E-adducts 23 in moderate yields. The reaction of CDI 19 with alkynoic acids 20 generated intermediate 21 and imidazole 22 with the release of CO₂, and the subsequent addition of the imidazole 22 to the electron deficient alkyne 21 stereoselectively produced the products 23.

![Scheme 6. Proposed mechanism for the direct aminoacylation of alkynyl trifluoromethyl sulfones.](image)

![Scheme 7. Direct addition of 1,1′-carbonyldiimidazole to alkynes.](image)

2.2. Base-Promoted Addition of Amide Bonds to Alkynes

In 1987, Suzuki and Tsuchihashi disclosed a sequential process for the preparation of enaminoles 27 through the insertion of lithium (triphenylsilyl)acetylide into amides (Scheme 8) [24]. Acyclic amides reacted smoothly to give the E-enaminoles in high yields, while lower yields of the desired ring expansion products were obtained when cyclic amides were used as the substrates. It is worth noting that the triphenyl group on silicon was essential for the transformation as other silylacetylides failed to give the enaminole products. The possible reaction pathway may involve the initial formation of the silylalkynone, the subsequent Michael addition of in situ-formed lithium amide and the final protodesilylation.

![Scheme 8. The insertion of lithium (triphenylsilyl)acetylide into amides.](image)

Subsequently, Jeong et al. successfully realized the addition of Weinreb amides 29 to the carbon–carbon triple bond of trifluoropropynyl lithium 30 in a one-pot two-step pathway [25–27].
Weinreb amides completely. The reaction temperature had a decisive impact on the outcome of the reaction (Scheme 10a) [28]. The selectivity of the 1,2-addition product propynoate 35 yields (Scheme 11) [29].

Saturated NH

N of the extruded substitution of the lithiated acetylides with Weinreb amides, and a following Michael reaction suggesting the 1,2-addition reactions proceeded in a highly trans-selective manner. In addition, the stabilizing the key intermediate 31, which was formed from the addition of trifluoropropynyl lithium with Weinreb amides. Then 31 was quenched by H2O to give the ynone intermediate 32, which rapidly reacted with N-methoxy-N-methylamine 33 generated from the reaction to give the products 34. The N-methoxy group in Weinreb amides was essential because the oxygen could coordinate with the lithium cation to stabilize the key intermediate 31. Particularly, the fact that trapping 31 with trimethylsilyl chloride afforded the corresponding siloxane derivative in a high yield further demonstrated the mechanism.

It should be noticed that an excessive amount of trifluoropropynyl lithium was required to consume methylbenzamide under optimal conditions did not provide the desired product at all, only the recovery of starting material. This indicated that the N-methoxy group in Weinreb amides but gave recovery of Weinreb amides. Besides, the use of N,N-dimethylbenzamide instead of N-methoxy-N-methylanilide under optimal conditions did not provide the desired product.

Soon afterwards, the group of Nielsen reported the insertion of sodium acetylide of ethyl propynoate 35 into Weinreb amides 29 to produce the 1,2-addition products 37 as the major products (Scheme 10a) [28]. The selectivity of the 1,2-addition products 37 over 1,1-addition products 38 depended on the R group of the Weinreb amides. Substrates with bigger R substituents showed higher selectivity than those with smaller ones. For example, substituents such as phenyl showed excellent selectivity, providing the 1,2-addition adduct as the single product in high yield. However, substrates carrying bulky substituents such as tert-butyl or 2,4-dimethoxyphenyl did not undergo this transformation. Notably, the tertiary enaminoones 37 preferentially adopted E-geometry in all cases, suggesting the 1,2-addition reactions proceeded in a highly trans-selective manner. In addition, the β-enamino keteesters 37 were employed by the authors to react with hydrazines 39 under microwave irradiation to construct pyrazoles 40 through a regioselective cyclocondensation (Scheme 10b). Similarly, Choudhury’s group reported a one-pot sequential process consisting of nucleophilic substitution of the lithiated acetylides with Weinreb amides, and a following Michael reaction of the extruded N-methoxy-N-methylamine to a carbon–carbon triple bond after quenching with saturated NH4Cl, producing the E-β-enamino ketones 43 as the single geometrical isomer in high yields (Scheme 11) [29].
intermediate 50 undergoes a Michael-type addition to the alkynones 45. This transformation suffered from unsatisfactory stereoselectivities, excellent regioselectivities were observed. The reaction proceeded smoothly with the addition of a base such as K₂CO₃ at -78 °C, affording the corresponding tetra-substituted enamides in good yields. Although this transformation suffered from unsatisfactory stereoselectivities, excellent regioselectivities were observed. The acyl group and amide group were dominantly located at the α-position and β-position of the carbonyl, respectively. Interestingly, in the reactions of alkynones 47 bearing an ortho-bromo-substituted aryl ring, highly functional chromones 48 were selectively formed in good to high yields via the O-cyclization pathway (Scheme 13). Control experiments showed that the base played an important role. It could deprotonate the imides 45 to form a nitrogen anion, which undergoes a Michael-type addition to the alkynones 49 to produce the anion intermediate 50. Then intermediate 50 undergoes an intramolecular nucleophilic addition/ring-opening sequence to provide intermediate 52. Hydrolysis of intermediate 52 generates enamides 46 (X = H), or imine–enamine.

Scheme 10. (a) Insertion of sodium acetylide of ethyl propynoate into Weinreb amides. (b) Synthesis of pyrazoles employing β-enaminoketoesters.

Scheme 11. One-pot sequential transformation of Weinreb amides to enamino ketones.

Very recently, Li and co-workers reported the addition of the amide bond of imides 45 to the carbon–carbon triple bond of alkynones 44 under basic conditions (Scheme 12) [30]. This addition reaction proceeded smoothly with the addition of a base such as K₂CO₃ in DMSO at high temperature, affording the corresponding tetra-substituted enamides 46 in good yields. Although this transformation suffered from unsatisfactory stereoselectivities, excellent regioselectivities were observed. The acyl group and amide group were dominantly located at the α-position and β-position of the carbonyl, respectively. Interestingly, in the reactions of alkynones 47 bearing an ortho-bromo-substituted aryl ring, highly functional chromones 48 were selectively formed in good to high yields via the O-cyclization pathway (Scheme 13). Control experiments showed that the base played an important role. It could deprotonate the imides 45 to form a nitrogen anion, which undergoes a Michael-type addition to the alkynones 49 to produce the anion intermediate 50. Then intermediate 50 undergoes an intramolecular nucleophilic addition/ring-opening sequence to provide intermediate 52. Hydrolysis of intermediate 52 generates enamides 46 (X = H), or imine–enamine.
tautomerization of intermediate 52 followed by nucleophilic aromatic substitution (S_NAr) to give the chromones 48 (X = Br) (Scheme 14).

Scheme 12. Addition of imides to alkynones promoted by K_2CO_3 to synthesize enamides.

Scheme 13. Addition of imides to alkynones promoted by K_2CO_3 to synthesize chromones.

Scheme 14. Proposed catalytic cycle for the addition of imides to alkynones promoted by K_2CO_3.

Soon afterwards, Li and co-workers presented the insertion of alkynones 53 into the amide bond of amide 54 promoted by Cs_2CO_3 (Scheme 15), providing the functionalized enamines 55 with high
stereoselectivity and excellent regioselectivity [31]. It should be noted that the combination of Cs$_2$CO$_3$ and 1,10-phenanthroline hydrate (Phen·H$_2$O) is essential to obtain good yields in a short reaction time. The authors hypothesized that 1,10-phenanthroline hydrate may act as a metal ion chelator, which increased the basicity of Cs$_2$CO$_3$ to accelerate the reaction. Similarly, 3-carbonyl-4-quinolinones 58 were selectively formed via a subsequent N-cyclization pathway in the cases of alkynes 56 bearing an ortho-bromo-substituted aryl ring (Scheme 16). The proposed reaction mechanism is outlined in Scheme 17. The Michael-type addition of amides 57 to alkynes 59 under basic conditions yields an allenol intermediate 60. The subsequent intramolecular nucleophilic addition gives a highly reactive cyclobutenol intermediate 61, which undergoes ring opening to produce a formal alkyne insertion intermediate 62. Then intermediate 62 undergoes imine-enamine tautomerization to provide intermediate 63, which undergoes a nucleophilic aromatic substitution (SNAr) to afford the quinolinone products 64 (Y = Br). In contrast, the protonation of intermediate 62 or 63 leads to the formation of the enamino products 65 (Y = H).

Scheme 15. Insertion of alkynes into amides to synthesize enaminoones promoted by Cs$_2$CO$_3$.

Scheme 16. Insertion of alkynes into amides to synthesize quinolinones promoted by Cs$_2$CO$_3$. 
Scheme 17. Proposed reaction mechanism for the insertion of alkynones into amides promoted by Cs$_2$CO$_3$.

2.3. Transition-Metal-Catalyzed Addition of Amide Bonds to Alkynes

In 2004, Yamamoto’s group reported the platinum catalyzed synthesis of highly functional indoles through an intramolecular amide C–N bond addition to alkynes with the [1,3]-migration of acyl groups (Scheme 18) [32]. PtCl$_2$ showed the highest catalytic activity compared with other platinum catalysts such as PtCl$_2$(CH$_3$CN)$_2$, PtBr$_2$, and Pt(PPh$_3$)$_4$. Various ortho-alkynylanilides 66 bearing diverse alkyl or aryl groups at $R_1$ could be converted into the corresponding indole products 67 with good to high yields with PtCl$_2$. Notably, a variety of acyl groups could undergo intramolecular [1,3]-migration to give 3-acyl-indoles 67. The main drawback of this method is that the desired products 67 are together with deacylated byproducts 68 in most cases. Based on the results of deuterium-labeling experiments and crossover experiments, the authors proposed a catalytic cycle of this intramolecular aminocyclation of alkynes. As shown in Scheme 19, coordination of alkyn moiety to PtCl$_2$ yields the $\pi$-complex 69, followed by nucleophilic attack of nitrogen to the alkyne, affording the zwitterionic intermediate 70. An intramolecular [1,3]-migration of the acyl group then gives intermediate 71, which affords the product and regenerates the catalyst. The 3-deacylated byproducts 68 may attribute to the deacylation which takes place through the protonolysis of the C–Pt bond of intermediate 70.
The reactions of ortho carbamates proceeded successfully under the catalysis of PtI4, providing an efficient method to synthesize indole-3-carboxylates in good yields along with the 3-protonated byproducts. Interestingly, ortho-carbamoyl carbamates could be converted into the corresponding indole-3-carboxylates in good yields without the generation of 3-protonated byproducts. The authors proposed a similar mechanism to that of Yamamoto’s group. They assumed the generation of the 3-protonated byproducts in the reactions of ortho-carbamoylureas may be attributed to protodemetalation of intermediate by a proton from the methyl moiety of intermediate, which was extruded in the reaction (Scheme 21). Notably, this work proved that amide and ester groups could be used as the migrating groups, thus
providing an efficient method to synthesize indole-3-carbamides/carboxylates which could not be prepared via Friedel–Crafts electrophilic substitution into the C3-position of the indole ring.

Scheme 20. Platinum-catalyzed intramolecular carboamination.

Scheme 21. Proposed pathway for the generation of 3-protonated byproducts.

In 2007, Nakamura’s group revealed that PdBr₂ could also catalyze the intramolecular amide C–N bond addition to alkynes (Scheme 22), affording the indole adduct 82 from ortho-alkynylanilide 81 in 52% yield [34]. Encouraged by the catalytic performance of PdBr₂ towards the intramolecular aminoclylation of alkynes, Liu’s group further screened a series of palladium complexes. They found that PdCl₂(CH₃CN)₂ showed excellent catalytic activity (Scheme 23) [35]. Substrates 83 with alkyl/aryl groups at R₁ furnished the corresponding products 84 in good to excellent yields. The protocol was also compatible with substrates 83 bearing electron-donating substituents, halides, and electron-withdrawing substituents at R₂, which produced the corresponding products 84 in high yields. In addition, the reactions of substrates 83 with different alkyl substituents at R₃ also took place smoothly, providing the desired products 84 in high yields. More importantly, various acyl and amide groups could migrate smoothly and be conveniently introduced at the C3-position of indoles.

Scheme 22. PdBr₂-catalyzed intramolecular aminoacylation of alkynes.
were used as migrating groups for the first time. Compared with previously reported protocols, mechanism which is similar to that proposed by Yamamoto’s group [32].

Interestingly, a 3-diketoindole dimer was synthesized in a high yield when substrate was subjected to the optimal reaction conditions (Scheme 25). Finally, the authors proposed a reaction mechanism which is similar to that proposed by Yamamoto’s group [32].

Subsequently, Liu and coworkers further extended their palladium catalytic system to the synthesis of 3-diketoindoles 86 from ortho-alkynyl-N-α-ketoacylanilines 85 via the intramolecular amide bond addition to alkynes (Scheme 24) [36]. Notably, this addition reaction proceeded smoothly to give the high functional 3-diketoindoles with the [1,3]-migration of α-ketoacyl groups, which were used as migrating groups for the first time. Compared with previously reported protocols such as Friedel–Crafts acylation [37], Glyoxylation/Stephens–Castro coupling sequence [38], and the oxidative cross-coupling of indoles [39–41], which achieved the synthesis of 3-diketoindoles through the modification of the indole ring, but suffered from poor selectivity, operational complexity, the requirement of strict exclusion of moisture, limited substrate scope and low atom economy, this new method successfully prepared 3-diketoindoles via the construction of an indole ring with valuable features such as operational simplicity, high atom economy, broad substrate scope and high yields. Interestingly, a 3-diketoindole dimer 88 was synthesized in a high yield when substrate 87 was subjected to the optimal reaction conditions (Scheme 25). Finally, the authors proposed a reaction mechanism which is similar to that proposed by Yamamoto’s group [32].
were observed in all examples. However, the main shortcoming of this method is that unsatisfactory products and regenerate the catalyst (Scheme 27).

Based on the mechanistic study results with deuterium-labeling experiments, the authors hypothesized that the reaction mechanism may involve the complexation of substrates with ruthenium catalyst, the subsequent oxidative addition of ruthenium catalyst across the amide bond, the following addition to alkynes, as was reported by Li’s group in 2012 (Scheme 26) [42]. Their study showed that [RuCl₂(p-cym)]₂ could undergo intramolecular annulation through amide bond addition to the alkyne moiety to synthesize highly functional indoles 84. A variety of substrates 83 carrying diverse functional groups such as olefin, ester, aldehyde were well tolerated and could be converted into the corresponding indole products 84 in moderate to high yields. Despite the fact that a longer reaction time was required compared with platinum or palladium catalytic systems, it is worth noting that no 3-deacylated indoles were observed in all examples. However, the main shortcoming of this method is that unsatisfactory yields were obtained when bigger acyl groups such as acetyl were employed as the migrating groups. Based on the mechanistic study results with deuterium-labeling experiments, the authors hypothesized that the reaction mechanism may involve the complexation of substrates with ruthenium catalyst, the subsequent oxidative addition of ruthenium catalyst across the amide bond, the following addition of the N–Ru bond to carbon–carbon triple bonds, and the final reductive elimination to produce the products and regenerate the catalyst (Scheme 27).
2.4. Addition of Amide Bonds to Alkynes through Organocatalysis

In addition to the metal-catalyzed processes, methods utilizing organocatalysis, which feature advantages such as low cost, environmental economy, and the avoidance of metal contamination, have also been developed in recent years. What seems particularly interesting is the insertion of an electron-deficient alkyne 5 into the amide bond of an acyl-onio salt 92 (Scheme 28), as reported by Weiss and Huber [43]. This reaction could be achieved in the presence of a catalytic amount of small organic molecules such as PPh₃ or DMAP, providing the desired β-oniovinylation products 93 in good yields. The stereochemistry of this process depends on the reaction conditions, preferentially E- or Z-stereochemistry was observed, and the Z-isomer is the thermodynamically more stable isomer. More importantly, the onio substituent in the products 93 could be selectively replaced by a number of nucleophiles, such as anilines, phenols, and thiophenols, to prepare Michael systems with donor
functions in the β-position, which could be further converted into quinolones, thiochromones, and pyrazoles by intramolecular cyclization. The authors proposed a catalytic cycle for this organocatalytic process. Taking the transformation catalyzed by PPh₃ as the example (Scheme 29), the conjugate addition of PPh₃ to alkyne 5 produces the zwitterionic intermediate 94, which attacks the electrophilic carbonyl center of 92 to provide intermediate 95 with liberation of 4-dimethylaminopyridine (DMAP). Then intermediate 95 reacts with the liberated DMAP to give the products 93 and regenerates the catalyst.

![Scheme 28](image)

Scheme 28. The addition of amide bonds of acyl-onio salts to alkynes through PPh₃ or 4-dimethylaminopyridine (DMAP) organocatalysis.

![Scheme 29](image)

Scheme 29. Proposed catalytic cycle for the addition of amide bond of acyl-onio salts to alkynes.

Recently, Doi’s group reported an example of amide addition to alkynes through tertiary amine organocatalysis (Scheme 30) [44]. They found that α-alkynylaniline derivatives 96 could undergo intramolecular aminoaclylation of the carbon–carbon triple bonds successfully under the catalysis of 9-azajulolidine (9-AJ) to afford the 3-acyl-4-quinolinones 97 in moderate to good yields with excellent regioselectivity. Notably, a variety of acyl groups including ester groups could act as migrating groups to be transferred to the C3-position of the quinolinones. Particularly, the synthesis of pyrrolyl 4-quinolone alkaloid, quinolactacide, and its analogues were successfully achieved by the authors employing this organocatalytic process. Finally, a plausible reaction mechanism was outlined in
Scheme 31. 1,4-addition of 9-AJ to substrates 96 takes place at first, and the subsequent nucleophilic attack of the resulting anion to the acyl group provides intermediate 98, which could be converted into the intermediate 99. Then the acyl group in allenolate 99 could be transferred to the C3-position, thus leading to the formation of enone 100, which undergoes 6-endo cyclization to provide the products 97 with the regeneration of 9-AJ.

Scheme 30. The 9-azajulolidine-catalyzed intramolecular amide addition to alkynes.

Scheme 31. Proposed mechanism for the 9-azajulolidine-catalyzed intramolecular amide addition to alkynes.

3. Transition-Metal-Catalyzed Addition of Sulfonamide Bonds to Alkynes

The group of Nakamura reported the first example of the addition of sulfonamides to alkynes in 2007. As shown in Scheme 32, ortho-alkynyl-N-sulfonylanilines 101 could undergo the intramolecular aminosulfonylation of carbon–carbon triple bonds successfully under the catalysis of AuBr3 to give the 3-sulfonylindoles 102 in good to high yields [45,46]. Although small amounts of 4- and 6-sulfonylindoles were obtained as the byproducts in some examples, this process provides a facile and efficient method for the synthesis of 3-sulfonylindoles, which cannot be synthesized directly from the corresponding unsubstituted indoles by electrophilic substitution because the electrophilicity of the...
sulfonil groups is much lower than that of the acyl groups and halogens [47,48]. Interestingly, when 2-alkynyl-6-methoxy-N-sulfonylanilines 105 were employed as the substrates, this transformation could also occur under the catalysis of InBr3. However, the intramolecular aminosulfonylation products 106 were obtained as minor products, whereas 6-sulfonylindoles 107 were observed as the major products (Scheme 33). The reaction mechanism of this process may involve the initial coordination of the catalyst to the alkyne moiety, subsequent nucleophilic attack of the nitrogen atom to the carbon–carbon triple bond, the following migration of the sulfonyl group to the C3-position of the indole skeleton, and the final generation of the products with elimination of the catalyst (Scheme 34).

Scheme 32. AuBr3-catalyzed intramolecular aminosulfonylation of alkynes.

Scheme 33. InBr3-catalyzed intramolecular aminosulfonylation of alkynes.

Scheme 34. Proposed mechanism for AuBr3/InBr3-catalyzed intramolecular aminosulfonylation of alkynes.
Subsequently, Chan’s group presented a gold-catalyzed domino aminocyclization/1,3-sulfonyl migration of N-substituted N-sulfonyl-aminobut-3-yn-2-ols 111 to synthesize highly functional pyrroles 112 (Scheme 35) [49]. A screening of gold catalysts disclosed that the NHC (N-heterocyclic carbene)-gold(I) complex 113 was found to be the most effective catalyst for this intramolecular aminosulfonylation of alkynes. It could catalyze the conversion of various substrates 111 carrying electron-withdrawing, electron-donating, and sterically demanding groups to the corresponding pyrroles 112 in moderate to high yields. It is worth noting that this method provides an efficient and convenient tool to prepare penta-substituted highly functional pyrroles. The mechanism of this transformation is outlined in Scheme 36. The coordination of gold cation to the alkyne moiety of the substrates gives intermediate 114, which undergoes a nucleophilic attack of the nitrogen atom to the alkynes to produce intermediate 115. At this juncture, dehydration of intermediate 115 yields cationic pyrrole–gold adduct 116, subsequent 1,3-sulfonyl migration of intermediate 116 then results in deauration with the regeneration of the gold catalyst and delivery of the products 112. Alternatively, intermediate 115 could undergo the deaurative 1,3-sulfonyl migration first to afford intermediate 117, which undergoes dehydrative aromatization to produce the products 112.

Scheme 35. Gold-catalyzed intramolecular aminosulfonylation of N-substituted N-sulfonyl-aminobut-3-yn-2-ols.

Scheme 36. Possible reaction mechanism for gold-catalyzed intramolecular aminosulfonylation of N-substituted N-sulfonyl-aminobut-3-yn-2-ols.
Soon afterwards, Liu’s group reported a more general and efficient intramolecular aminosulfonylation of alkynes to synthesize 3-sulfonylindoles 119 through palladium catalysis (Scheme 37) [35,50]. The reactions took place smoothly with PdCl₂(CH₃CN)₂ in CH₃CN at 90 °C to afford 3-sulfonylindoles 119 as the single products without the generation of 4- and 6-sulfonylindole regioisomers, which were obtained as the byproducts in the gold- and indium-catalyzed process. In addition, this protocol features broad substrate scope, good functional group tolerance, and moderate to high yields, thus providing a practical access to functional 3-sulfonylindoles. A plausible mechanism, which is similar to gold- or indium-catalyzed aminosulfonylation of alkynes [45,46], was also proposed by the authors.

Scheme 37. PdCl₂(CH₃CN)₂-catalyzed intramolecular aminosulfonylation of alkynes.

4. Conclusions and Perspectives

In this review, we presented a summary of the addition of amide/sulfonamide bonds to alkynes, which has emerged as a highly important tool to functionalize carbon–carbon triple bonds. The aminocylation/aminosulfonylation of alkynes, which is characterized by high atom- and step-economy in an environmentally-friendly manner, has also become a remarkable method for the downstream transformations of amide/sulfonamides compounds. Notably, the intramolecular aminocylation/aminosulfonylation of alkynes has provided a facile and efficient protocol for the synthesis of valuable heterocycles such as chromones, quinolinones, indoles, and pyrroles. Despite the remarkable achievements made, there are at least three areas where some critical advances are necessary to make the aminocylation/aminosulfonylation of alkynes more general and powerful: (a) the intermolecular addition of unactivated amide/sulfonamide bonds to alkynes is still in high demand; (b) as the reported metal-catalyzed process employed expensive metals, the development of cheap metal catalysis as well as organocatalysis, will be a good direction to take; (c) the exploration of tandem reactions involving aminocylation/aminosulfonylation of alkynes will continue to drive this field considering their efficiency and step-economy in constructing complex heterocyclic compounds.

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