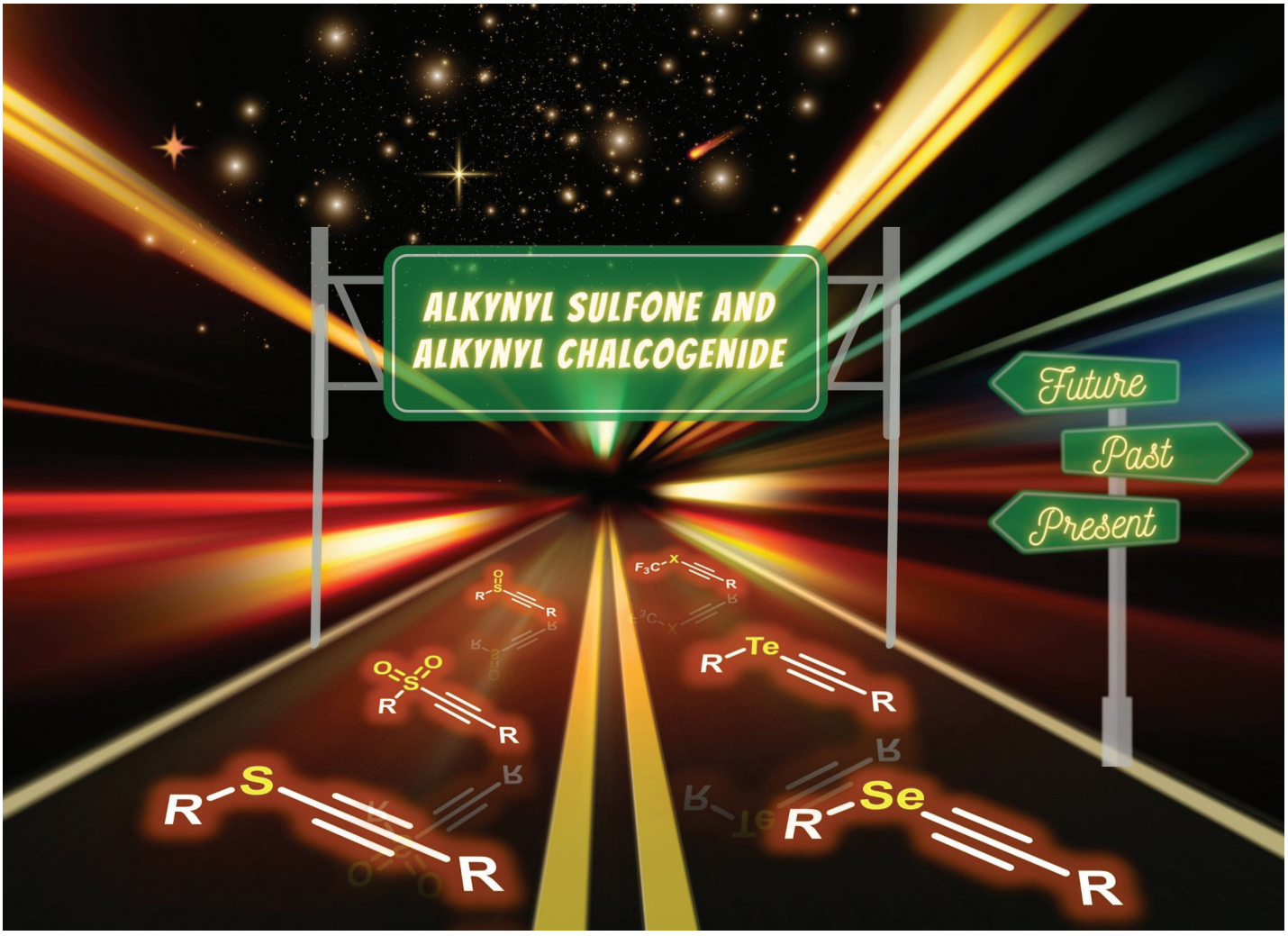


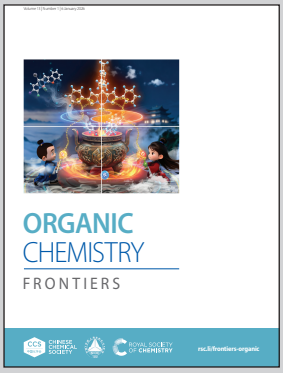
Showcasing research from the laboratories of Gabriel Pereira da Costa and Alex F.C. Flores (Center for Structural Study and Synthesis of Heterocycles – NEESH) and Angelita M. Barcellos (Research in Sustainable Organic Synthesis – PSOS), Federal University of Rio Grande – FURG, Rio Grande – RS, Brazil.

A decade of advances in alkynyl sulfone and alkynyl chalcogenide synthesis

This review summarizes the major advances in the past decade on the synthesis of alkynyl sulfones and chalcogen derivatives, highlighting sustainable catalytic methods, improved selectivity, functional-group tolerance, and the expanding synthetic utility of sulfur-, selenium-, and tellurium-substituted alkynes.

Image reproduced by permission of Gabriel P. da Costa from *Org. Chem. Front.*, 2026, **13**, 258.

As featured in:



See Angelita M. Barcellos, Alex F. C. Flores, Gabriel P. da Costa *et al.*, *Org. Chem. Front.*, 2026, **13**, 258.

CCS 中国化学会 CHINESE CHEMICAL SOCIETY
SIOC 1950
ROYAL SOCIETY OF CHEMISTRY
rsc.li/frontiers-organic

ORGANIC CHEMISTRY FRONTIERS

REVIEW

View Article Online
View Journal | View Issue

Cite this: *Org. Chem. Front.*, 2026, **13**, 258

A decade of advances in alkynyl sulfone and alkynyl chalcogenide synthesis

Douglas de C. Vieira,[a] Luiz H. Dapper,[b] Rafael C. Brinkerhoff,[a] Angelita M. Barcellos, *[a] Alex F. C. Flores *[b] and Gabriel P. da Costa *[b]

Received 25th September 2025,
Accepted 14th November 2025

DOI: 10.1039/d5qo01359c

rsc.li/frontiers-organic

Over the past decade, the synthesis of alkynyl sulfones and alkynyl chalcogen derivatives has witnessed significant advances. Modern methodologies have increasingly focused on sustainable protocols, catalytic efficiency, milder reaction conditions, and atom-economical processes. Traditional approaches relying on harsh reagents or stoichiometric activators have increasingly been replaced by transition-metal-catalyzed couplings, photoredox transformations, electrochemical processes, and metal-free oxidative strategies. These innovations have enabled access to structurally diverse alkynyl sulfones, sulfides, selenides, tellurides, and their trifluoromethylated counterparts. This review highlights the progress made during the last ten years, emphasizing mechanistic innovations, improvements in selectivity and functional group tolerance, and the expanding chemical space accessible through chalcogen-substituted alkynes.

1 Introduction

Organochalcogens (selenides, tellurides, sulfides, sulfoxides and sulfones) are of great interest across multiple fields; they represent an attractive molecular class in synthetic chemistry, materials science, and medicinal chemistry.[1] Among them, organosulfur and organoselenium compounds have garnered considerable attention in recent years due to their unique reactivity and diverse applications.[2] In this context, compounds containing C–S bonds are found in various sources, such as natural products, and are key structural components of many commercial drugs, including the antibiotics nelfinavir, esomeprazole, and cephalosporins. Sulfur-containing compounds exhibit a broad spectrum of biological activities, including antibacterial, antiviral, antitumor, and anti-inflammatory effects. Notably, organosulfur derivatives represent nearly 20%

[a]*Pesquisa em Síntese Orgânica Sustentável – PSOS, Universidade Federal do Rio Grande – FURG, Escola de Química e Alimentos – EQA, Itália Ave., km 8, no number – Campus Carreiros, 96.203-900-Rio Grande, RS, Brazil*
[b]*Núcleo de Estudo Estrutural e Síntese de Heterociclos – NEESH, Universidade Federal do Rio Grande – FURG, Escola de Química e Alimentos – EQA, Itália Ave., km 8, no number – Campus Carreiros, 96.203-900-Rio Grande, RS, Brazil.*
E-mail: gabrielpdacosta@furg.br

Douglas de C. Vieira

Douglas de Castro Vieira, born in 1997 in Rio Grande, RS, Brazil, earned his Bachelor's degree in Chemistry in 2024. He is currently pursuing a Master's degree in Chemistry under the supervision of Professor Angelita Manke Barcellos. His research focuses on the synthesis of organochalcogen compounds and heterocycles, with a particular interest in developing bioactive molecules as potential drug candidates.

Luiz H. Dapper

Luiz Henrique Dapper was born in 1998 in Novo Hamburgo, RS, Brazil. He received his B.S. degree (2020) and Ph.D. degree (2024) from the Federal University of Pelotas (UFPel, Brazil), under the supervision of Prof. Eder J. Lenardão. He is currently a postdoctoral researcher at the Federal University of Rio Grande (FURG, Brazil), under the supervision of Prof. Alex F. C. Flores. His present research interests focus on the development of organochalcogen and heterocyclic compounds through clean synthetic transformations.

of FDA-approved drugs, underscoring their central role in drug discovery and development.[3] Moreover, sulfur-based functional groups are consistently among the most frequently encountered motifs in bioactive molecules, further highlighting their importance in medicinal chemistry.[4]

In parallel, organoselenium compounds have also advanced significantly in both chemistry and biochemistry.[5] Recent studies have demonstrated that selenium derivatives have therapeutic properties, with potential as anticancer, antiviral, and anti-Alzheimer's agents, among others.[2,6] Beyond biomedicine, organoselenium compounds find wide applications as fluorescent probes,[7] catalysts in organic synthesis,[8] and functional components of advanced materials.[9]

On the other hand, tellurium (Te), a rare chalcogen (~0.027 ppm), is less studied than sulfur and selenium due to its scarcity and limited biological roles.[10] Its large size, low electronegativity, and high polarizability endow organotellurium compounds with unique reactivity and broad applications.[11] Although their pharmacological and toxicological profiles are not yet fully understood, several organotellurium derivatives have demonstrated promising bioactivities.[12] From a synthetic perspective, their utility has expanded considerably in recent decades, as the weak C–Te and Te–Te bonds facilitate radical pathways and enable efficient carbon–carbon bond formation as well as functional group interconversions.[10a] Furthermore, tellurium-centered radicals and Te's propensity to engage in σ-hole-induced chalcogen bonds highlight their emerging role in noncovalent catalysis,[13] and this class of organotellurium compounds has also been shown to promote oxidation reactions.[14]

Consequently, the efficient and selective formation of C–S, C–Se and C–Te bonds has been a longstanding focus of methodological research, driving innovative advances in the art of synthetic organic chemistry. In particular, transition-metal catalysis continues to offer valuable tools for the construction of C–S, C–Se, and C–Te bonds under milder conditions, and remains one of the most established approaches for their formation.[15] In addition, radical chemistry is opening avenues for highly targeted functionalization, providing direct and atom-economical routes to the synthesis of chalcogen compounds.[16] Furthermore, metal-free methods are being developed to meet the demand for accessible and environmentally friendly synthetic protocols.[17]

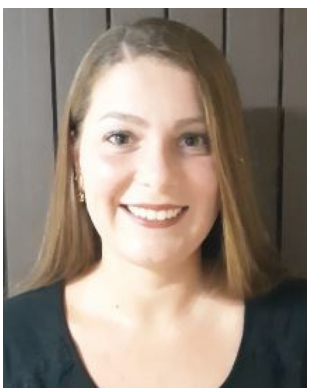
Within this context, chalcogen-substituted alkynes have emerged as a particularly intriguing class of compounds. The incorporation of sulfur, selenium, or tellurium atoms directly onto an alkyne is crucial, as these compounds have proven to be versatile building blocks for constructing complex molecular architectures and high-value structures.[18] Sustainable protocols, photoredox strategies, and electrochemical methods have profoundly transformed the preparation of organochalcogen compounds, replacing traditional harsh conditions with greener and more selective alternatives. These advances not only enable access to increasingly complex molecular architectures but also respond to pressing global demands for environmentally responsible and efficient synthetic chemistry.

While several reviews have addressed specific aspects of organosulfur or organoselenium chemistry, and others have focused on photoredox or electrochemical bond-forming strategies, no comprehensive account has yet covered the full scope of synthetic advances in chalcogen-substituted alkynes. The distinctive contribution of the present review lies in its integrated analysis of sulfones, sulfides, selenides, tellurides, and their trifluoromethylated analogues, examined across all major synthetic paradigms—including metal-catalyzed, radical, photochemical, electrochemical, and metal-free methodologies (Fig. 1). This broad and unified perspective makes the review both timely and unique in its coverage.

This review provides a comprehensive overview of the substantial progress achieved over the past decade in the synthesis of chalcogen-containing alkynes. The discussion is organized as follows: we first examine the development of (i) alkynyl sul-

Rafael C. Brinkerhoff

Rafael C. Brinkerhoff obtained his B.S. in Chemistry from the Federal University of Rio Grande (FURG, Brazil) in 2011, followed by an M.Sc. (2014) and Ph.D. (2018) in organic synthesis under the supervision of Prof. Marcelo G. D'Oca (FURG). In 2018, he completed a one-year postdoctoral fellowship at the Leibniz Institute of Plant Biochemistry (IPB), Germany, under the guidance of Prof. Ludger Wessjohann. Since 2014, he has been a chemistry technician at FURG.



Angelita M. Barcellos

Angelita Manke Barcellos was born in 1989 in Pelotas-RS, Brazil. She studied chemistry at the Federal University of Pelotas (UFPel, Brazil) and received her BS in 2011 and MSc degrees in 2014, focusing on organic synthesis under the supervision of Prof Eder J. Lenardão. In 2018, she completed her doctoral studies in organic chemistry at UFPel, under the supervision of Prof Gelson Perin. Since 2022, she has been a professor of Organic and General Chemistry at the FURG, Brazil. Her research interests lie in the development of new organochalcogen compounds through clean synthetic transformations.

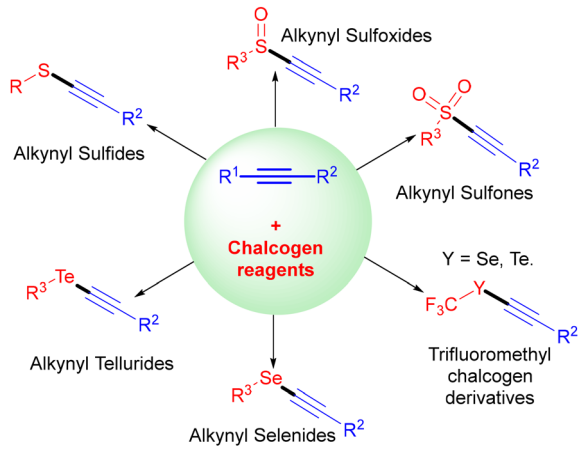


Fig. 1 A general diagram of alkynyl sulfone and alkynyl chalcogenide synthesis.

fones, which are considered synthetic workhorses and crucial precursors, and therefore receive special attention; (ii) next, highlight the applications of alkynyl sulfides, which play vital roles ranging from medicine to materials science; (iii) we subsequently discuss alkynyl selenides and tellurides, offering insights into this comparatively less explored field; and (iv) finally, we analyze the scarce yet intriguing class of trifluoromethyl-substituted alkynyl sulfides and selenides. Specifically, the articles were classified according to their chemical class and organized in chronological order, allowing readers to clearly follow the evolution of methodologies over time. This systematic classification facilitates direct comparison between methodologies and highlights the main advances achieved in each category. Our goal is to connect synthetic progress with potential applications, thereby providing a pathway to stimulate further exploration into this dynamic and impactful area of synthetic chemistry.

2 Advances in the preparation of alkynyl sulfones

In this section, we focus on the reports concerning the synthesis of alkynyl sulfones. These compounds have emerged as valuable building blocks in organic chemistry, owing to the unique combination of the sulfone moiety with alkyne functionality. Their structural features confer remarkable stability while maintaining a high degree of reactivity, enabling their use as versatile intermediates in a wide range of synthetic transformations, including cross-coupling reactions, radical processes, and cyclizations. Over the years, a variety of strategies have been developed for their preparation, ranging from classical approaches involving sulfonylation of alkynes to more recent methods that emphasize catalytic efficiency, atom economy, and sustainability.[19] The following section highlights the main advances and methodologies reported in the last 10 years for the synthesis of alkynyl sulfones, with particular attention to both traditional and modern catalytic protocols.

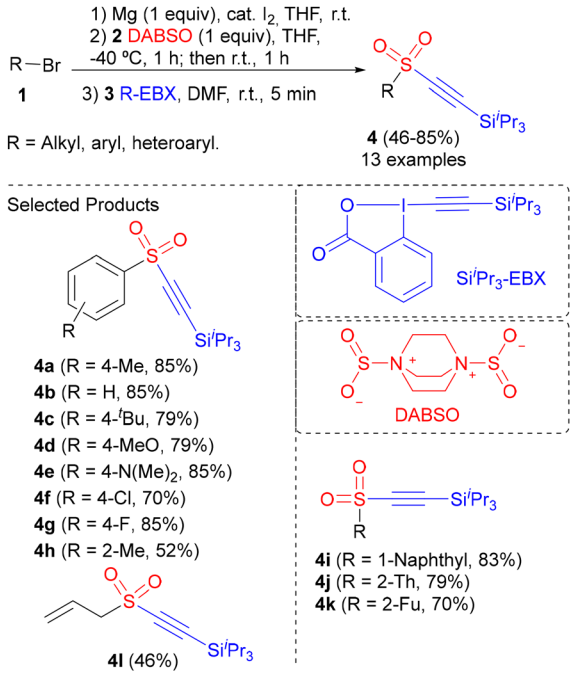
In 2015, Chen and Waser[20] reported an elegant approach for the synthesis of organyl alkynyl sulfones **4** through two distinct pathways. The first pathway involves a three-component reaction of an alkyl bromide **1**, 1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) (DABSO) **2** as the sulfone source, and ethynyl-1,2-benziodoxol-3(1*H*)-one (EBX) **3** as the alkynylating reagent (Scheme 1). The process proceeds *via* the *in situ* generation of an organomagnesium intermediate, using magnesium (1 equiv.) in the presence of iodine as a catalyst in tetrahydrofuran (THF) at room temperature. Subsequently, DABSO (1 equiv.) was added to the reaction medium at −40 °C and the mixture was stirred for 1 h, followed by the addition of EBX in dimethylformamide (DMF) at room temperature for 5 min. This protocol affords 13 examples of alkynyl sulfones **4**, in yields ranging from moderate to good (52%–85%). The

Alex F. C. Flores

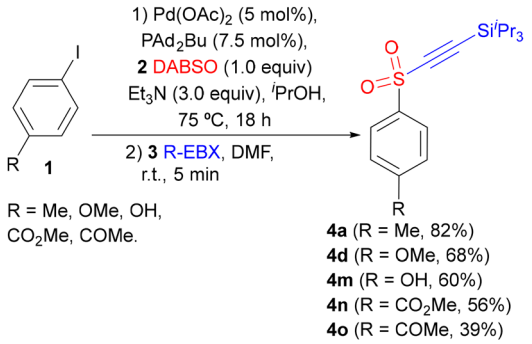
Alex Fabiani Claro Flores, received his B.S. (1989), Master (1994), and PhD (1997) degrees from the Federal University of Santa Maria (Brazil) under the supervision of Prof. Marcos Antônio Pinto Martins. He worked as a research professor at the UFSM until 2013. He is currently an associate professor at the Federal University of Rio Grande and a researcher/advisor in the PPGQTA-FURG. He has experience in Organic Synthesis, working mainly with heterocycles, NMR spectroscopy, organic synthesis, structural analysis, and organic analysis.

Gabriel P. da Costa

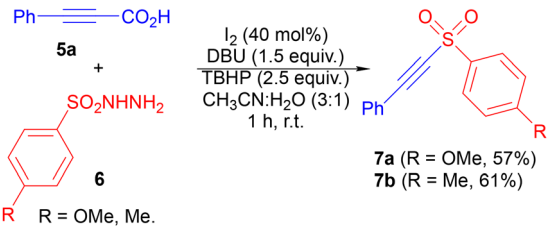
Gabriel Pereira da Costa was born in 1993 in Santa Vitória do Palmar-RS, Brazil. He received his B.S. (2016), Master (2017), and PhD (2021) degrees from the Federal University of Pelotas (UFPel-Brazil) under the supervision of Prof. Diego Alves. In 2022, he worked as a researcher at Pontifícia Universidade Católica do Rio Grande do Sul (PUC-RS), as well as a postdoctoral student at the Federal University of Rio Grande (FURG) under the supervision of Prof. Alex Flores. Currently, he is a chemistry technician and researcher at FURG. His current scientific interest lies in the development of new organochalcogen, and heterocycle compounds.



Scheme 1 Synthesis of alkynyl sulfonyl compounds **4** described by Chen and Waser in 2015.[20]



Scheme 2 Another pathway for the synthesis of aryl alkynyl sulfones **4** described by Chen and Waser in 2015.[20]



Scheme 3 Descarboxylative synthesis of organyl alkynyl sulfones **7a–b** described by Singh and co-workers in 2015.[21]

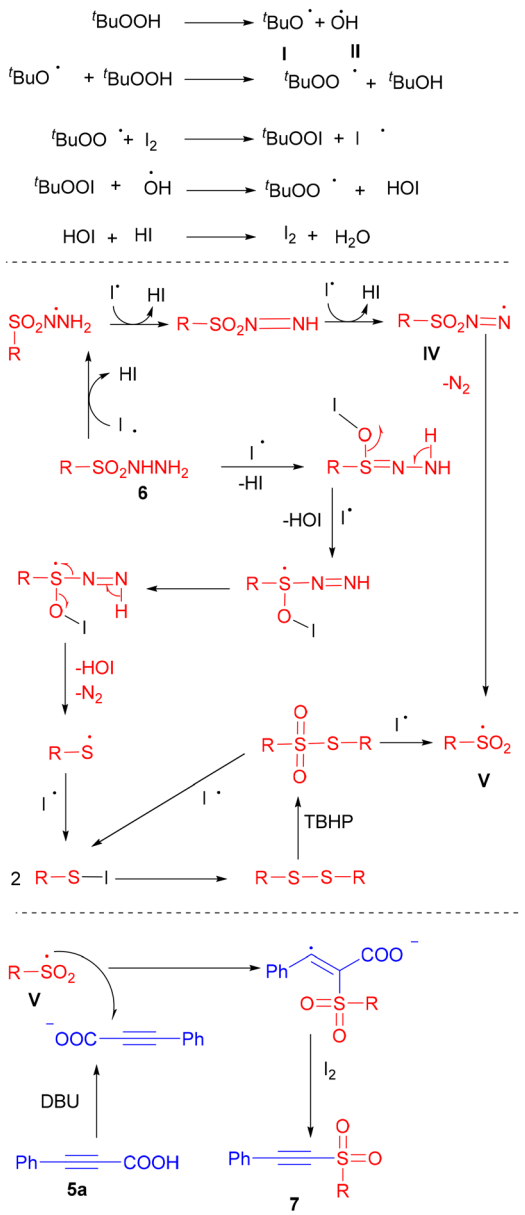
approach was efficiently extended to aryl bromides substituted with electron-donating (EDG) and electron-withdrawing groups (EWG) on the aromatic ring, as well as alkyl (allyl) and heteroaryl (1-naphthyl, 2-Th and 2-Fu) bromide, which afforded the target compounds **4l**, **4i**, **4j** and **4k** in yields of 46%, 83%, 79% and 70%, respectively (Scheme 1).

In another pathway, the author describes the use of palladium acetate (Pd II), di(adamantyl)(*n*butyl)phosphine (PAd_2Bu), DABSO **2** as a sulfone source and EBX as alkynyl donator, under basic conditions. In this methodology, aryl iodides **1** were first combined with palladium acetate (5 mol%), PAd_2Bu (7.5 mol%) and DABSO **2** (1 equiv.) in the presence of Et_3N (3 equiv.) in ^{i}PrOH at 75 °C for 18 h. In the next step EBX in DMF was added at room temperature and after 5 min, the desired products **4a,d, m–o** were obtained, affording 5 examples in yields ranging from 39% to 82% (Scheme 2).

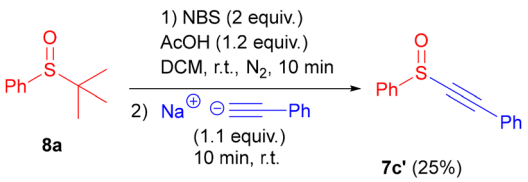
In 2015, Singh and co-workers[21] reported a metal-free decarboxylative methodology for the synthesis of organyl alkynyl sulfones **7** from 3-phenylpropiolic acid **5a** and arylsulfonyl hydrazines **6**. In this procedure, 3-phenylpropiolic acid **5a** was reacted with arylsulfonyl hydrazine **6** (1 equiv.) in the presence of iodine (I_2, 40 mol%) under catalyst. The reaction was performed under basic conditions using 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU, 1.5 equiv.) and ^{t}butyl hydroperoxide (TBHP, 2.5 equiv.) as a radical initiator, with acetonitrile/water (in a ratio of 3 : 1) as the solvent mixture at room temperature for 1 h. Using this methodology, two alkynyl sulfones **7a** and **7b** were obtained in yields of 57% and 61%, respectively (Scheme 3). In the same year, Wu and co-workers[22] employed the same starting materials under copper-catalyzed conditions [CuI (10 mol%), 2,2′-bipyridine (10 mol%), DMF at 100 °C, air, 18 h], leading exclusively to the formation of vinyl sulfones *via* a direct decarboxylative hydrosulfonylation reaction.

The authors proposed a mechanism for the described reaction, in which a key step involves the formation of a radical intermediate **I** and **II** *via* homolytic cleavage of the O–OH bond of TBHP. The resulting ^{t}butoxyl radical **I** activates iodine, generating an iodine-centered radical **III**. This radical **III** abstracts a hydrogen atom from the hydrazine **6** moiety, producing hydroiodic acid (HI) and forming a diazo intermediate **IV**, which rapidly releases N_2 as an excellent leaving group to generate the sulfonyl radical **V**. The sulfonyl radical **V** subsequently reacts with 3-phenylpropiolic acid **5a** under basic conditions in the presence of DBU, affording the desired alkynyl sulfone **7** (Scheme 4).

In 2015, Wei and Sun[23] developed a metal-free method under mild conditions for the synthesis of organyl alkynyl sulfoxide (**7c′**). The reaction employed ^{t}butyl sulfoxide (**8a**) as the sulfinyl source and sodium phenylethynyl as the nucleophile, with *N*-bromosuccinimide (NBS) and acetic acid as reagents, to afford phenylethynyl sulfone (**7c′**). The procedure involved mixing ^{t}butyl sulfoxide (**8a**) with NBS (2 equiv.) in acetic acid (1.2 equiv.) and dichloromethane (DCM) for 10 min under a nitrogen atmosphere at room temperature. Subsequently, the nucleophilic salt, sodium phenylethynyl (1.1 equiv.), was added, and the reaction mixture was stirred for an additional 10 min at the same temperature. The target product **7c′** was obtained in 25% yield upon completion of the reaction (Scheme 5).



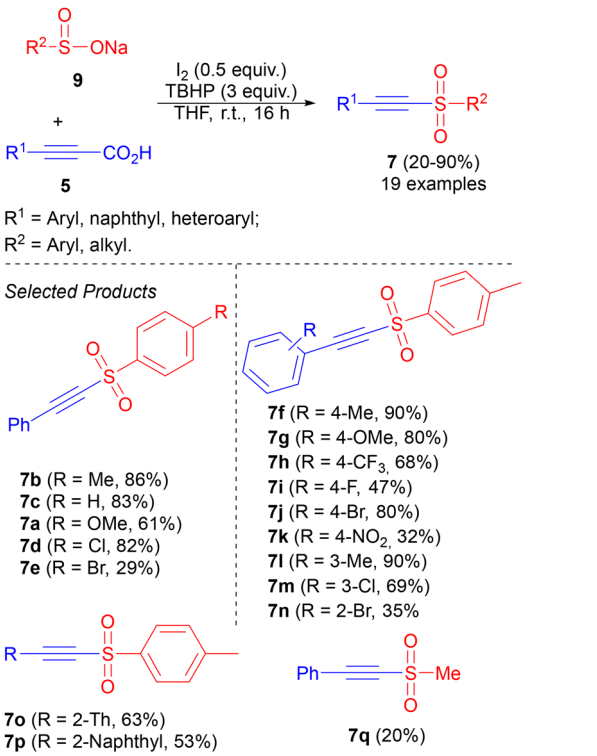
Scheme 4 Proposed mechanism for the I_2/TBHP-promoted decarboxylative coupling of alkynyl carboxylic acids **5**.[21]



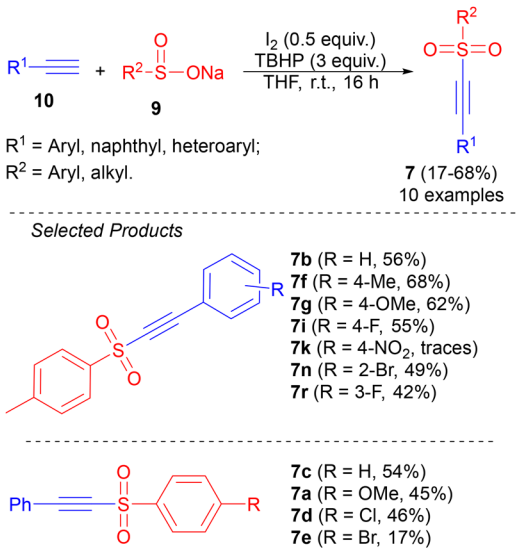
Scheme 5 Synthesis of aryl alkynyl sulfoxide **7c'** described by Wei and Sun in 2015.[23]

In 2016, Kuhakarn and co-workers[24] reported an iodine-catalyzed metal-free protocol for the synthesis of organyl alkynyl sulfones **7** derivatives from acetylenic acids **5** and sodium sulfinates **9**. This methodology features simple and readily available reagents, broad functional group tolerance, and efficient access to a wide range of acetylenic sulfones (organyl alkynyl sulfones). As shown in Scheme 6, a total of 19 examples of **7** were obtained, bearing diverse substituents: aryl, alkyl, and heteroaryl groups on the acetylenic acid fragment, and aryl or alkyl groups on the sulfone moiety. The optimized reaction conditions consisted of acetylenic acid **5**, sodium sulfinate **9** (2 equiv.), iodine as the catalyst (0.5 equiv.), and ^{t}butyl hydroperoxide (TBHP, 3 equiv.) in THF at room temperature for 16 h, affording the desired products **7** in yields of 20–90% (Scheme 6).

Subsequently, the protocol was also extended to terminal alkynes, as shown in Scheme 7, in this case, 10 examples of alkynyl sulfones **7** were synthesised employing various substituents attached to the terminal alkynes **10**, including aryl, naphthyl, and heteroaryl groups, while the sulfone moiety bore the same substituents as those described in Scheme 7. The reactions were carried out using terminal alkynes **10**, sodium sulfinates **9** (2 equiv.), iodine as the catalyst (0.5 equiv.), and ^{t}butyl hydroperoxide (TBHP, 3 equiv.) in THF at room temperature for 16 h. Under these conditions, several alkynyl sulfones **7** were synthesised in yields ranging from low to good (17–68%) (Scheme 7). The protocol was efficient for electron-donating groups (EDG) and electron-withdrawing groups (EWG) attached in both starting materials, with the exception that when 1-ethynyl-4-nitrobenzene was used under



Scheme 6 Synthesis of alkynyl sulfones **7** under I_2/TBHP oxidative conditions described by Kuhakarn and co-workers in 2016.[24]

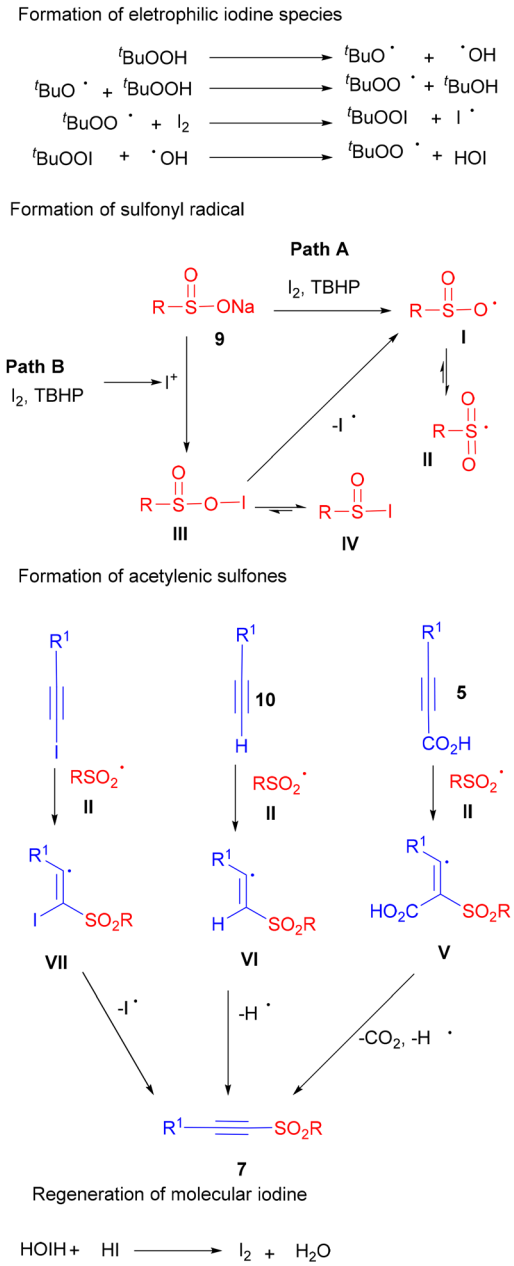


Scheme 7 Synthesis of alkynyl sulfones **7** under I_2/TBHP oxidative conditions using terminal alkynes **10**, described by Kuhakarn and co-workers in 2016.[24]

standard conditions, the desired product **7k** was not formed (Scheme 7).

The authors proposed a plausible mechanism for this transformation. Initially, TBHP undergoes homolytic cleavage, generating radical intermediates that subsequently react with iodine. The resulting ^{t}butoxyl radical can oxidize sodium sulfinate **9**, affording the corresponding sulfonyl radical (**I**). This radical then adds to arylacetylenic acid **5**, generating a vinyl radical intermediate **V**, which undergoes decarboxylation to form the desired alkynyl sulfone **7**, by abstraction of a hydrogen atom by an iodine-derived radical (Scheme 8). Similar pathways occur when the terminal alkynes **10** are used as starting materials, in this case, the intermediate **VI** is formed.

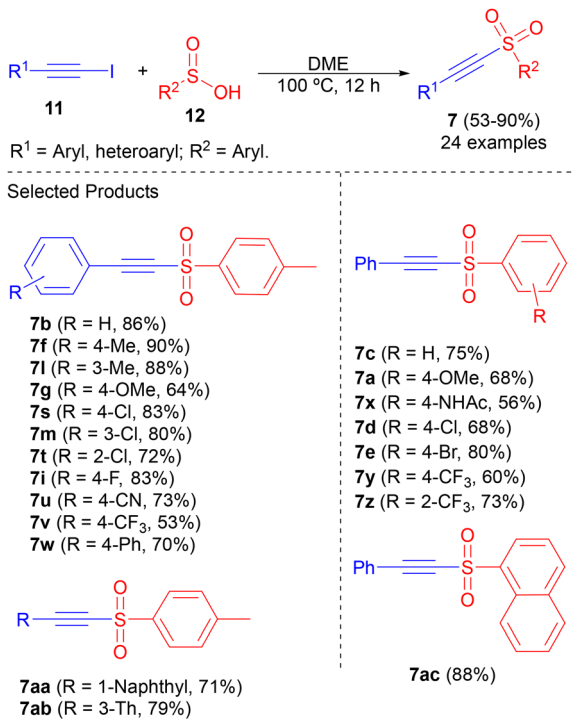
In 2017, Wang and co-workers[25] reported a one-pot, catalyst-free, and additive-free approach for the synthesis of alkynyl sulfones **7** through the direct cross-coupling of aryl or heteroaryl alkynyl iodides **11** with aryl sulfinic acids **12**. The reaction, performed in dimethoxyethane (DME) at 100 °C for 12 h, furnished 24 examples of alkynyl sulfones **7** in yields ranging from 53% to 90% (Scheme 9). The method is distinguished by readily available starting materials, simple operation, and the absence of catalysts or additives, making it operationally simple and eco-friendly. Substrate scope analysis revealed broad functional group tolerance, though yields varied with the electronic and steric nature of the substituents. For instance, a 4-Me group on the aryl iodide delivered the highest yield (**7f**, 90%), whereas other electron-donating substituents such as 4-OMe or 4-NHAc gave only moderate yields (**7g**, 64% and **7x**, 56%, respectively). Electron-withdrawing groups showed similarly variable outcomes, with 4-CF_3 affording 60% (**7y**) and 2-CF_3 giving a higher yield (**7z**, 73%). The method also demonstrated compatibility with polycyclic and heteroaryl systems, such as 1-naphthyl (**7aa**, 71%) and 3-thienyl (**7ab**,



Scheme 8 Proposed mechanism for the synthesis of alkynyl sulfones **7**.[24]

79%). Thus, in general this protocol offers a practical route to alkynyl sulfones under mild conditions, with good functional group tolerance.

Based on their experimental observations, the authors proposed that the reaction proceeds through a radical pathway initiated by the generation of a sulfonyl radical **II** from sulfinic acid **12** in the presence of iodine radicals. These iodine radicals are formed *in situ via* homocoupling of alkynyl iodide **11**. The sulfonyl radical **II** then undergoes selective addition to the alkynyl iodide **III**, producing an alkenyl radical intermediate **IV**. This species subsequently undergoes β-fragmentation to release an iodine radical, which in turn abstracts a hydrogen

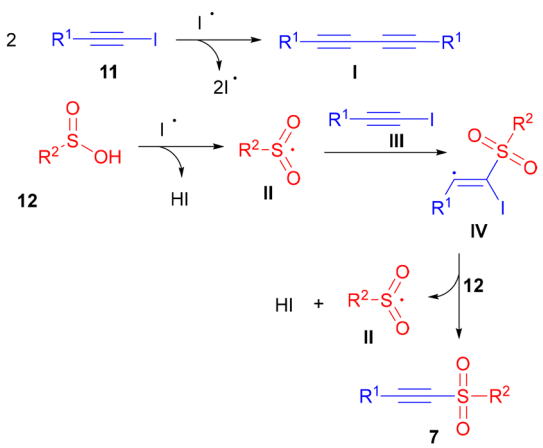


Scheme 9 Synthesis of alkynyl sulfones **7** from sulfinic acids **12** described by Wang and co-workers in 2017.[25]

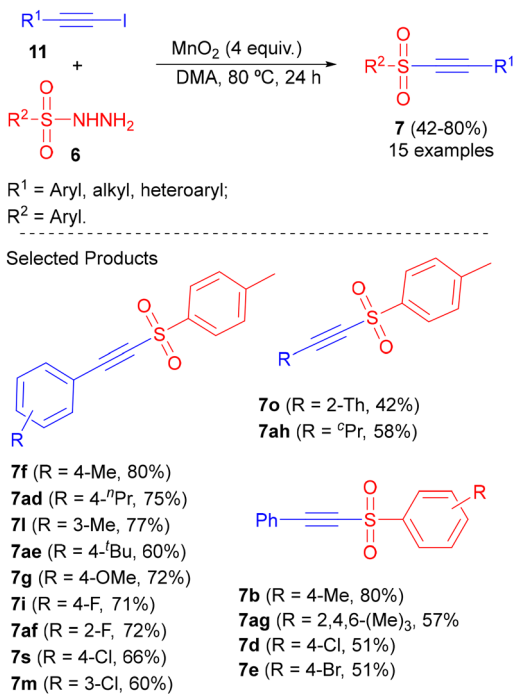
atom from another molecule of sulfinic acid **12**, thereby propagating the radical chain and producing the alkynyl sulfone product **7**. An alternative pathway, involving the coupling of the sulfonyl radical with an alkyne-derived radical generated *in situ* from the alkynyl iodide, may also contribute to the overall transformation (Scheme 10).

In 2017, Jiang and co-workers[26] described a new method for the synthesis of alkynyl sulfones **7** *via* a catalyst-free oxidative radical sulfonylation of haloalkynes **11** with various sulfonyl hydrazides **6**, representing the first example of C(sp)–S bond formation using sulfonyl radicals derived from sulfonyl hydrazides **6**. A total of 15 examples **7** were synthesized in moderate to good yields (42–80%) using 4 equiv. of MnO_2 in dimethylacetamide (DMA) at 80 °C for 24 h (Scheme 11). Importantly, the use of MnO_2 under these optimized conditions, in addition to enabling C(sp)–S bond formation, also effectively suppressed the competing self-coupling of haloalkynes *via* C(sp)–C(sp) bond formation. This study highlights the potential of catalyst-free oxidative radical sulfonylation as a practical strategy for constructing C(sp)–S bonds from readily available starting materials. The reaction displayed a broad substrate scope, tolerating both electron-donating and electron-withdrawing substituents on the aromatic rings of either coupling partner. In general, products were obtained in good yields, independent of the electronic nature or position of the substituents. The method was also applicable to heteroaryl (**7o**, 42%) and alkyl alkyne (**7ah**, 58%) derivatives, further underscoring its versatility across different structural frameworks.

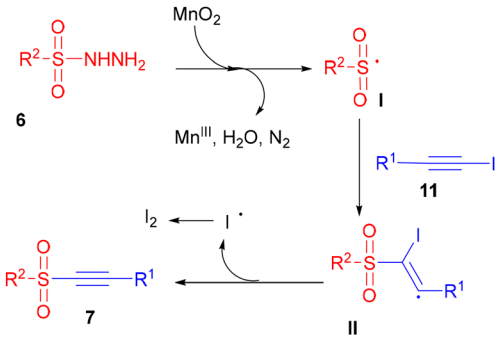
In the proposed reaction mechanism, the authors suggested that the sulfonyl radical **I** is generated from the corresponding sulfonyl hydrazide **6** under oxidative conditions. This radical then undergoes intermolecular addition to the iodoalkyne **11**, affording a vinyl radical intermediate **II**, which is subsequently converted into the final alkynyl sulfone product **7** with the concomitant release of an iodo radical (Scheme 12). In addition, the authors observed that the purple coloration of the reaction mixture indicated the formation of I_2 in the reaction medium.



Scheme 10 Proposed mechanism for the sulfinic acid-mediated synthesis of alkynyl sulfones **7**.[25]

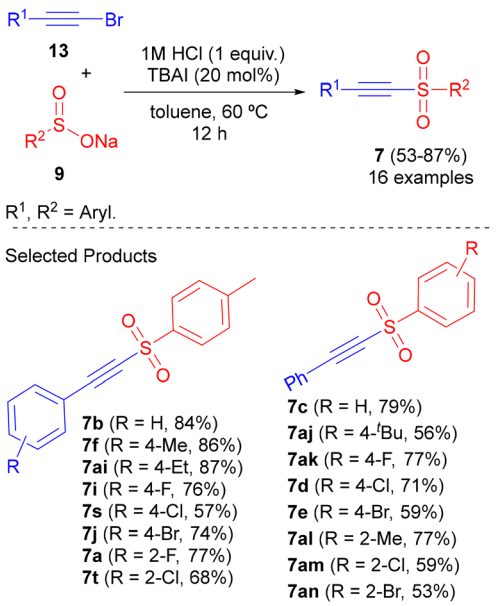


Scheme 11 Synthesis of alkynyl sulfones **7** described by Jiang and co-workers in 2017.[26]



Scheme 12 Proposed mechanism for the synthesis of alkynyl sulfones **7**.[26]

In 2017, Tang and co-workers[27] reported a methodology for the synthesis of 16 examples of alkynyl sulfones **7**, obtained in moderate to very good yields (53–87%) through the reaction of arylethynyl bromides **13** with sodium arylsulfinates **9**. The transformation was acid-mediated, employing 1 equivalent of 1 M HCl and 20 mol% tetrabutylammonium iodide (TBAI) as a phase-transfer catalyst in toluene at 60 °C for 12 h (Scheme 13). Importantly, the choice of solvent strongly influenced the product outcome: while toluene led to alkynyl sulfones, the use of dimethylsulfoxide (DMSO) produced (*E*)-1,2-bis(arylsulfonyl)ethylenes instead (16 examples were also obtained). More specially, for the synthesis of the alkynyl sulfones **7**, the method proved to be versatile, tolerating a broad range of substituents on both the arylethynyl bromide **13** and sodium arylsulfinate components **9**, including EDG and EWG. In general, electron-rich arylethynyl bromides **9**, such as those bearing methyl or ethyl substituents, delivered products in



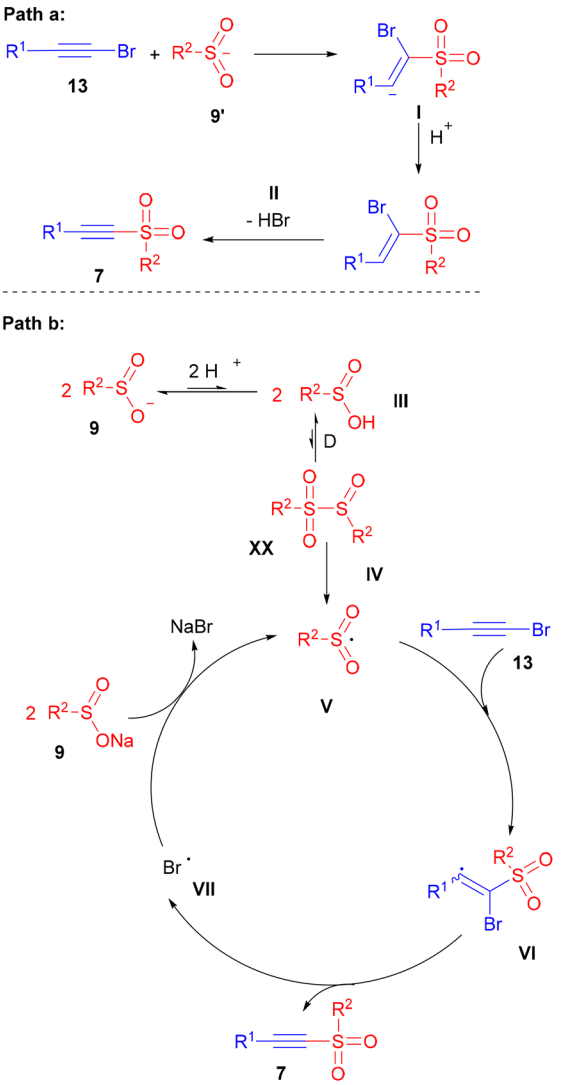
Scheme 13 Synthesis of alkynyl sulfones **7** described by Tang and co-workers in 2017 using TBAI/HCl.[27]

higher yields (**7f**, 86% and **7ai**, 87% respectively), while sterically hindered or certain halogenated derivatives showed diminished efficiency, for example 2-Br (**7an**, 53%), 4-Br (**7e**, 59%), and 4-^{t}Bu (**7aj**, 56%). Overall, the combination of mild conditions, functional group tolerance, high selectivity, and the avoidance of metal catalysts or strong oxidants makes this protocol an efficient tool for the synthesis of alkynyl sulfones.

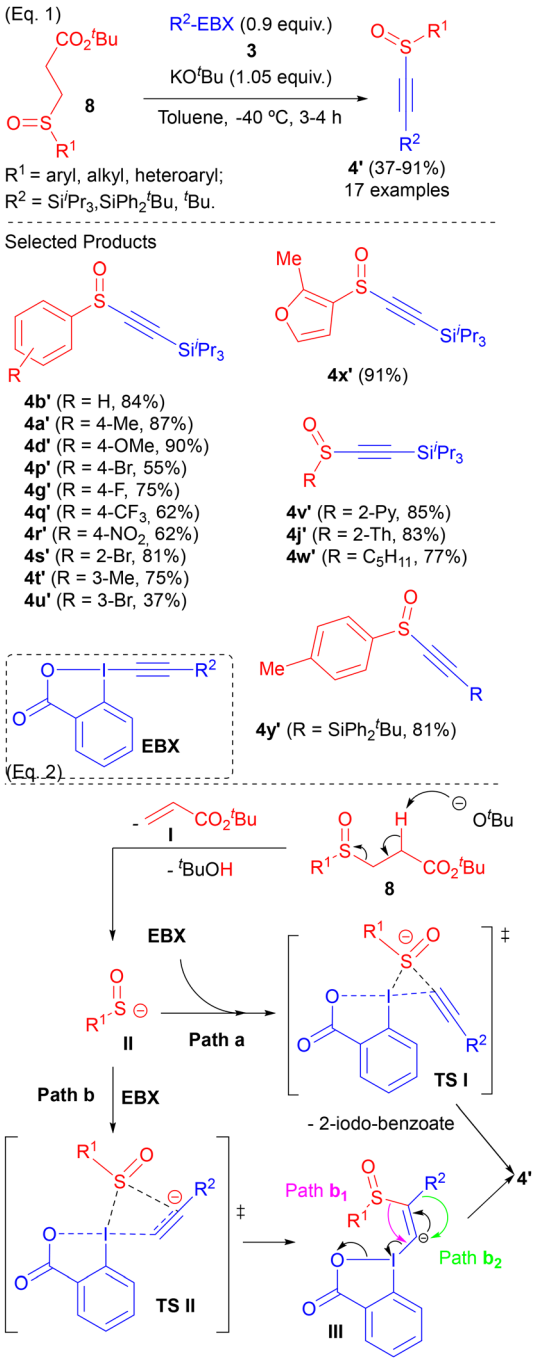
The mechanism proposed by the authors suggests two possible pathways for the formation of the desired alkynyl sulfones **7**. In the first pathway (path a), a nucleophilic addition/elimination sequence is proposed. The sulfinate anion **9** initially attacks the arylethynyl bromide **13**, generating the intermediate **I**, which undergoes protonation to give **II**. This intermediate **II** then eliminates hydrogen bromide to afford the final product **7**. The alternative pathway (path b) involves a radical process, initiated by the acid-promoted generation of the arylsulfonyl radical **V** from sodium arylsulfinate **9**. This radical adds to the alkyne **13** to form the bromovinyl radical **VI**, which subsequently eliminates a bromine radical to deliver the product **7**. The liberated bromine radical **VII** oxidizes another molecule of sodium arylsulfinate **9**, regenerating radical **V** and completing the catalytic cycle (Scheme 14). It is important to note that the polarity of the solvent plays a crucial role in determining which pathway predominates and, consequently, the final product.

In 2019, Waser and co-workers[28] developed an efficient method for the synthesis of alkynyl sulfoxides **4′** through the reaction of β-alkynyl carboxylates **8** with hypervalent iodine reagents of the EBX type **3**. The transformation, performed in toluene at −40 °C for 3–4 h in the presence of 1.05 equiv. of KO^{t}Bu and 0.9 equiv. of EBX **3**, proceeded under mild and metal-free conditions and tolerated a wide variety of aryl, alkyl, and heteroaryl substrates, affording 17 examples of **4′** in yields ranging from 37% to 91% (Scheme 15, eqn (1)). This strategy relies on an inverse-polarity alkynylation, in which sulfenate anions are generated *in situ via* retro-Michael elimination and then efficiently captured by the EBX **3** reagent, serving as a soft electrophilic alkynyl source. As a result, electron-neutral and mildly electron-rich aryl substrates delivered some of the best yields (R = H, **4b′**, 84%; R = 4-Me, **4a′**, 87%, and R = 4-OMe, **4d′**, 90%), while strongly electron-withdrawing substituent like 4-CF_3 tended to reduce the yields (62% of **4q′**). Overall, the method's simplicity, along with the use of accessible materials, and its broad substrate scope, make it a versatile route to alkynyl sulfoxides with valuable applications in different areas.

The authors proposed a plausible mechanism for the synthesis of the target alkynyl sulfoxides **4′**, which likely begins with a base-promoted retro-Michael fragmentation, affording the unstable sulfenate anion **II** (Scheme 15, eqn (2)). Subsequently, two mechanistic alternatives may operate. In the first scenario (path a), a direct, concerted attack through a three-membered transition state (**TSI**) provides sulfoxide **4′**. Alternatively (path b), anion **II** can undergo a conjugate addition *via* a four-centered transition state (**TSII**), generating the vinyl benziodoxolone intermediate **III**. This intermediate



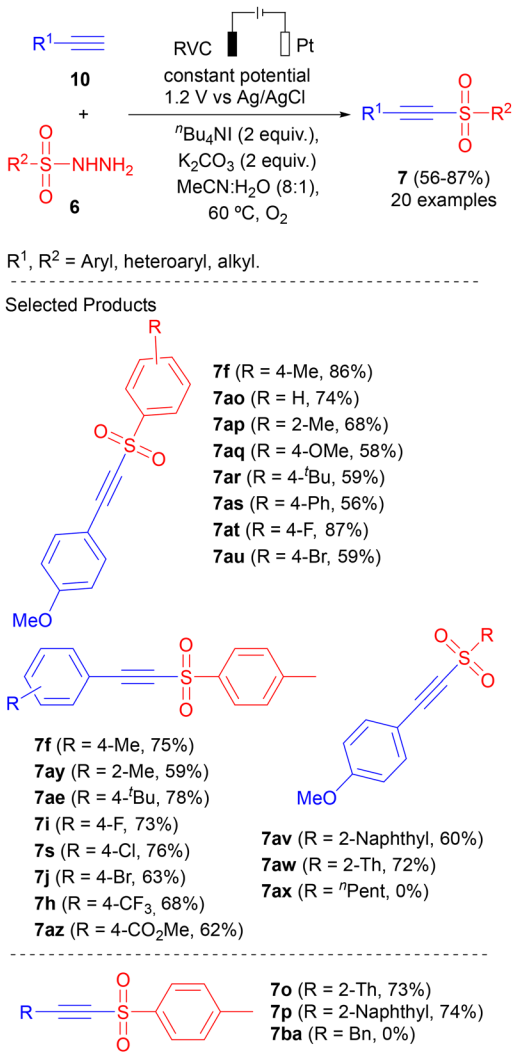
Scheme 14 Proposed mechanism for the TBAI/HCl-mediated synthesis of alkynyl sulfones **7**.[27]



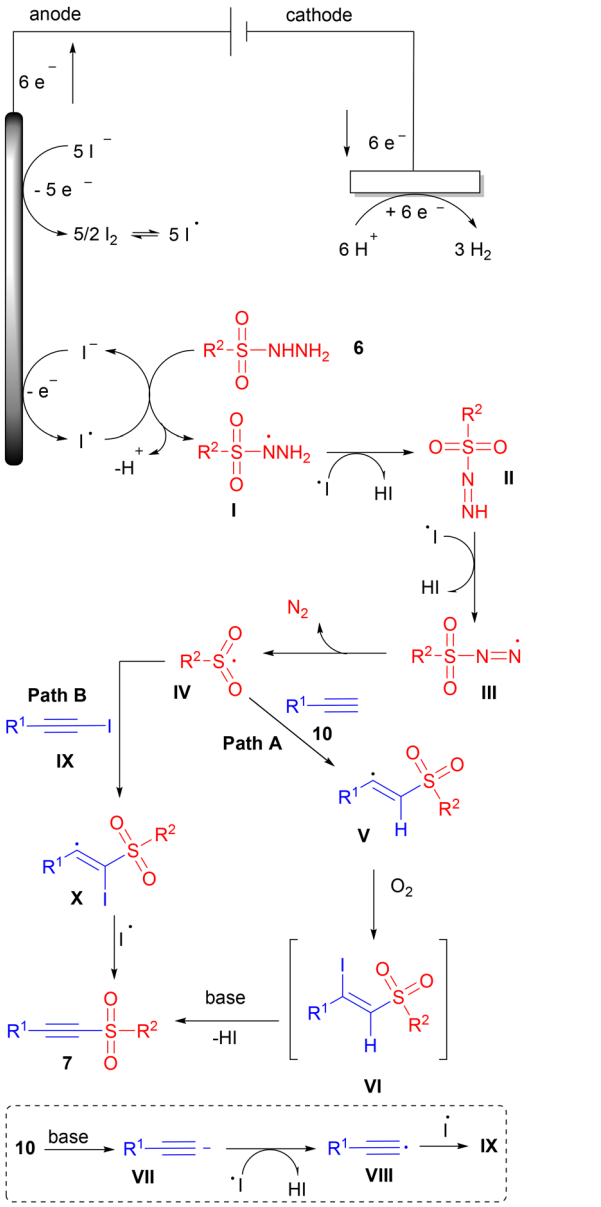
Scheme 15 Synthesis of alkynyl sulfoxides **4'** described by Waser and co-workers in 2019, along with the proposed reaction mechanism.[28]

III can then evolve through a 1,2-migration—either of the sulfoxide fragment (path b_1) or of the R^2 substituent (path b_2)—concomitant with α-elimination of iodine, ultimately yielding sulfoxide **4′**. This transformation may proceed in a fully concerted manner or, if α-elimination occurs first, through a carbene-like species. The dominant route is expected to depend strongly on the electronic and steric nature of the R^2 substituent attached to the alkyne (Scheme 15, eqn (2)).

In 2020, Tang and co-workers[29] reported an electrochemical oxidative cross-coupling method for the synthesis of alkynyl sulfones **7** from terminal alkynes **10** and sulfonyl hydrazides **6** under constant potential electrolysis (1.2 V *vs.* Ag/AgCl) in an RVC/Pt cell. The reaction was conducted in MeCN/H_2O (8 : 1) at 60 °C under an O_2 atmosphere, using 2 equiv. of *n*-Bu_4NI as both the supporting electrolyte and redox mediator, and 2 equiv. of K_2CO_3 as the base, affording 20 examples in yields of 56–87% (Scheme 16). The protocol requires no prefunctionalization of the alkyne, generates only H_2 and N_2 as byproducts, and operates under transition-metal-free and oxidant-free conditions with high atom economy. In addition, the protocol exhibited broad functional group tolerance, accommodating aryl, heteroaryl, and alkyl sulfone partners, with electron-rich and electron-deficient aryl alkynes reacting efficiently. On the other hand, aliphatic sulfonyl groups lacking conjugative stabilization, such as benzyl **7ba** and pentyl, **7ax** failed, both giving 0% yield. Beyond its synthetic utility, this method is note-



Scheme 16 Electrochemical synthesis of alkynyl sulfones **7** described by Tang and co-workers in 2020.[29]



Scheme 17 Proposed mechanism for the electrochemical synthesis of alkynyl sulfones **7**.[29]

worthy for the biological potential of its products, since most compounds exhibited significant inhibitory activity against tumor cell lines, and one derivative, **7az**, was shown to inhibit cell migration, increase reactive oxygen species levels, and induce apoptosis in HeLa cells. Thus, in general this electrochemical strategy offers a sustainable, efficient, and biologically relevant route for the synthesis of alkynyl sulfones.

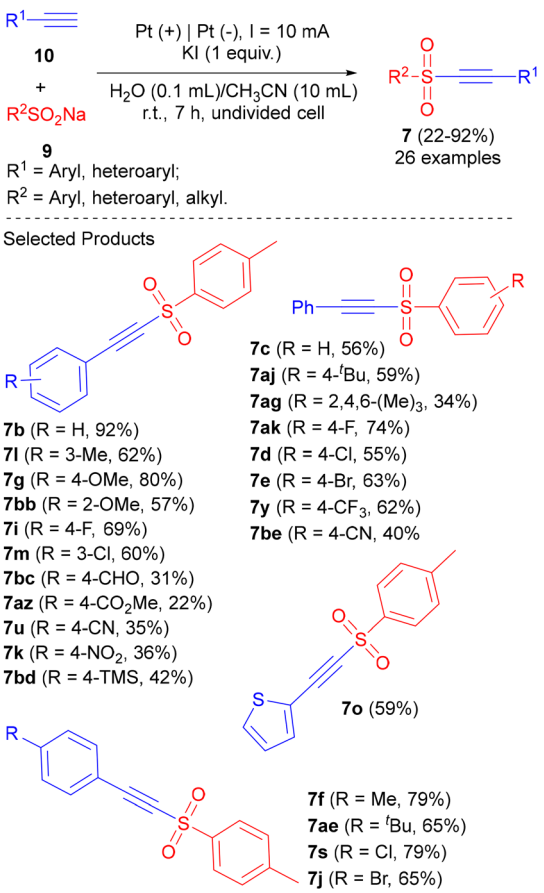
The authors proposed two plausible pathways for this electrochemical transformation, as illustrated in Scheme 17. In path A, iodide ions undergo anodic oxidation to generate iodine radicals. Simultaneously, sulfonyl hydrazide **6** is oxidized at the anode, first forming radical intermediate **I**, which is further oxidized in the presence of iodine radicals to give radical **III**. This species releases nitrogen to produce sulfonyl radical **IV**, which adds to the terminal alkyne **10** along with an iodine radical, affording vinyl radical **V**. Subsequently, rapid conversion of **V** leads to intermediate **VI**, which, upon base-assisted elimination of HI, yields the alkynyl sulfone product **7**. The oxygen present in the reaction medium can also accelerate the transformation of **V** into the final product **7**. In path B, the terminal alkyne **10** is deprotonated by the base to form acetylide anion **VII**, which is then oxidized by an iodine radical to generate alkyne radical **VIII**. Thus, the combination with another iodine radical generates iodoalkyne **IX**, which subsequently couples with sulfonyl radical **IV** to give radical intermediate **X**. Finally, elimination of an iodine radical from **X** produces the desired product **7**. At the cathode, proton reduction produces hydrogen gas, completing the electrochemical cycle.

In 2020, Huang and co-workers[30] reported a transition-metal-free, external oxidant-free, and base-free protocol to synthesize alkynyl sulfones **7** for the first time at room tempera-

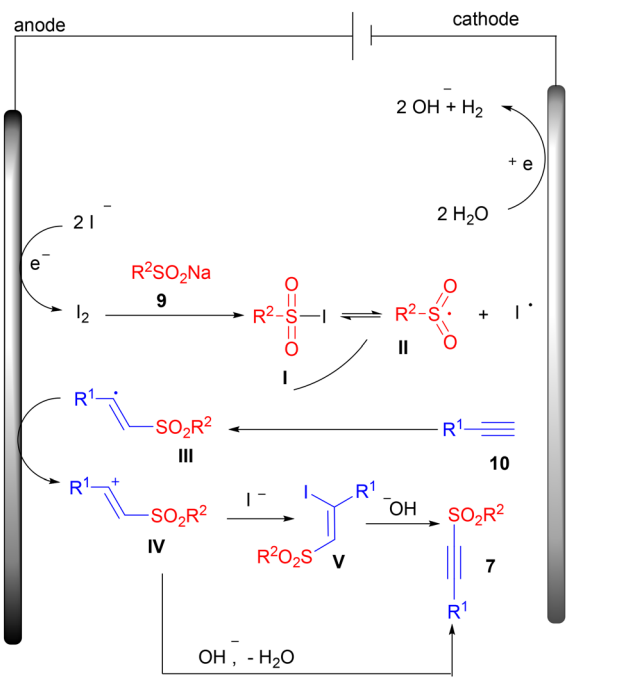
ture through the reaction of sodium sulfinates **9** and terminal alkynes **10** in an electrochemical process (Scheme 18). This direct sulfonylation of terminal alkynes **10** occurs in the presence of an undivided cell equipped with platinum electrodes (both the anode and cathode) by platinum electrodes Pt(+)|Pt (−), 1 equiv. of KI, and a solvent mixture of H_2O/MeCN (1 : 100 v/v) at room temperature (r.t.) for 7 h. The reactions were carried out under electrolysis at a constant current of 10 mA (*I*) (Scheme 18). Under these conditions, several alkynyl sulfones **7** (26 examples) were synthesized in yields ranging from low to excellent (22–92%). This protocol was sensitive to the electronic nature of the substituents; electron-donating groups (EDGs) on the aromatic ring of terminal alkynes afforded target products in better yields (compound **7g**, R = 4-OMe, 80%) compared with EWG, which gave the desired compounds in poor yields, such as the compounds **7az** (R = 4-CO_2Me, 22%), **7u** (R = CN, 35%) and **7k** (R = NO_2, 36%) (Scheme 18). A similar result was observed for the steric effect, as *ortho*-substituted alkynes afforded the target compounds in poor yields compared to the *para*-substituted. Additionally, heteroaryl terminal alkyne and substituted aryl sulfinates were also efficiently tolerated. This approach offers the advantage of employing sodium sulfinates-commercially available, benchstable, and easy to handle-as a sustainable sulfonyl source for the direct coupling reaction (Scheme 18).

The authors proposed a plausible mechanism for the synthesis of alkynyl sulfones **7**, which starts with the reaction of iodide at the anode to afford molecular iodine through an oxidation step. Next, the sodium sulfinate **9** reacts with the previously formed molecular iodine to yield a sulfur-centered radical **II** through homolytic bond cleavage. Subsequently, addition of radical **II** to alkyne **10** generates the vinyl sulfonyl radical **III**, which, after oxidation, affords the vinyl cation intermediate **IV**. Finally, the target product **7** can be formed by two different pathways. In the first pathway, iodine adds to the vinyl cation **IV**, followed by deprotonation of this intermediate **V** and an elimination step. In the second pathway, the target product **7** is formed directly by deprotonation of the vinyl cation intermediate **IV**. In both cases, H_2O is formed, which, after cathodic reduction, produces hydrogen gas and a hydroxide ion (Scheme 19).

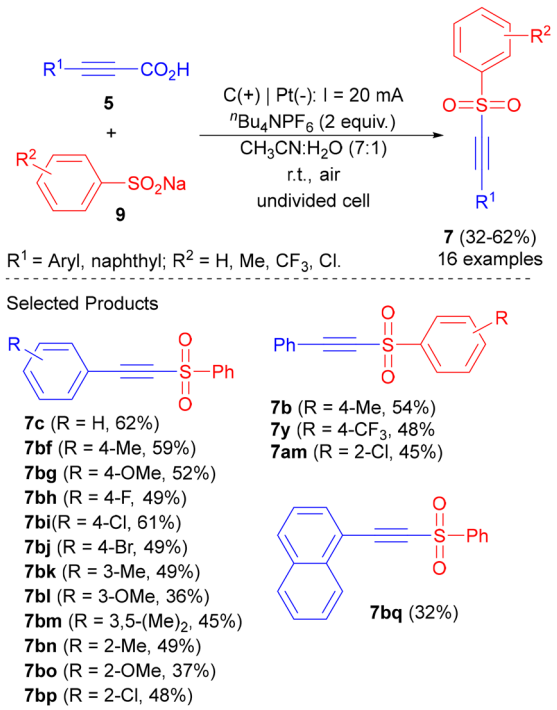
In 2020, Chen and co-workers[31] reported a metal-free and external oxidant-free electro-oxidative protocol the synthesis of alkynyl sulfones **7** from the reaction of arylacetylenic acids **5** with sodium arylsulfinates **9** using a simple, efficient, and environmentally friendly decarboxylative method (Scheme 20). Several substrates were reacted in the presence of 2 equiv. of $^nBu_4PF_6$ in a solvent mixture CH_3CN/H_2O (7 : 1 v/v) in an undivided cell [C(+)|Pt(−)], with a graphite rod as the anode and a platinum plate (10 × 10 mm) as the cathode. At room temperature, the reaction mixture was electrolyzed at a constant current of 20 mA (*I*). After 2 h, a wide range of alkynyl sulfones **7** (16 examples) were synthesized in yields ranging from



Scheme 18 Synthesis of alkynyl sulfones **7** described by Huang and co-workers in 2020 under electrochemical conditions.[30]



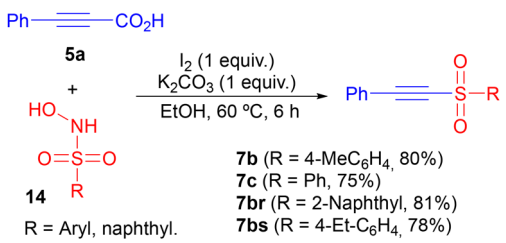
Scheme 19 Proposed mechanism for the KI-assisted electrochemical oxidative coupling.[30]



Scheme 20 Electrochemical synthesis of alkynyl sulfones **7** using sulfonate salts **9** described by Chen and co-workers in 2020.[31]

32–62% (Scheme 20). In this protocol, only aryl-substituted starting materials **5** and **9** were evaluated, and the method was not sensitive to the electronic effects of both EDG and EWG substituents attached in the aromatic ring. When 1-naphthyl substituted acetylenic acid was used, a lower yield was obtained for the compound **7bq**, which was isolated in only 32% (Scheme 20).

In 2021, Raghuvanshi and Verma[32] developed a new protocol using the I_2/K_2CO_3 system for the regio- and stereoselective sulfonylation of thiophenols and aromatic alkynes through reaction with *N*-hydroxy sulfonamides. In this study, the authors also applied the system in the reaction of 3-phenylpropiolic acid **5a** with *N*-hydroxy sulfonamide **14**, where the decarboxylative sulfonylation of acetylenic acid **5a** was performed in the presence of 1 equiv. of I_2, 1 equiv. of K_2CO_3, and EtOH as solvent at 60 °C for 6 h (Scheme 21). Under these conditions, 4 examples of alkynyl sulfones **7** were obtained in good yields

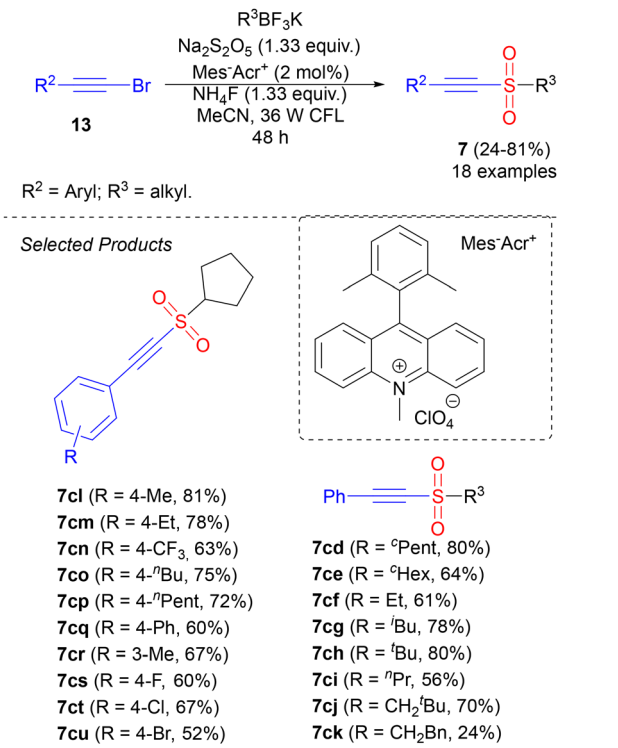


Scheme 21 Synthesis of alkynyl sulfones **7** from sulfinic acids and alkynoic acids described by Raghuvanshi and Verma in 2021.[32]

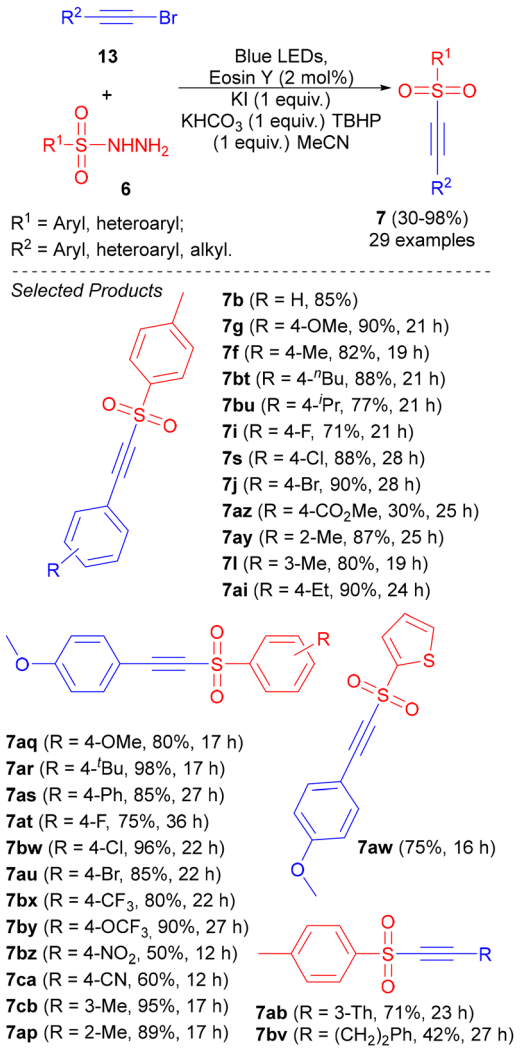
(75–80%). Only *N*-hydroxy sulfonamide **14** aryl-substituted with EDG were evaluated, the presence of phenyl, 4-MeC_6H_4 and 4-Et-C_6H_4 groups in this starting material afforded the target products **7c**, **7b** and **7bs** in 75%, 80% and 78%, respectively. In addition, the *N*-hydroxynaphthalene-2-sulfonamide **14** was efficiently applied under standard conditions, which gave the desired alkynyl sulfone **7br** in good yield (81%) (Scheme 21).

In 2020, Wu and co-workers[33] reported the synthesis of alkylalkynyl sulfones **7** through a photoinduced three-component reaction of potassium alkyltrifluoroborates, sodium metabisulfite, and alkynyl bromides **13**. Sodium metabisulfite served as a sulfur dioxide source. The optimized reaction conditions involved Mes-Acr$^+$ (2 mol%) as the photocatalyst, NH_4F (1.33 equiv.) as an additive, and MeCN as the solvent under irradiation with a 36 W compact fluorescent lamp (CFL) for 48 h. Under these conditions, the desired alkylalkynyl sulfones **7** were obtained in yields ranging from low to good (24–81%) across 18 examples (Scheme 22).

Fan and co-workers in 2023,[34] developed a new and efficient protocol to obtain alkynyl sulfones **7** by photocatalytic reaction using Light Emitting Diode (LEDs) as an alternative energy source, through the reaction of benzenesulfonyl hydrazides **6** with bromoacetylene **13** (Scheme 23). In this approach, several benzenesulfonyl hydrazides **6** were reacted with a wide range of bromoacetylene **13** in the presence of 2 mol% of Eosin Y as a photocatalyst, 1 equiv. of KI, 1 equiv. of $KHCO_3$, 1 equiv. of TBHP in MeCN as solvent using blue LEDs as energy



Scheme 22 Visible-light mediated synthesis of alkynyl sulfones **7** reported by Wu and co-workers in 2020.[33]

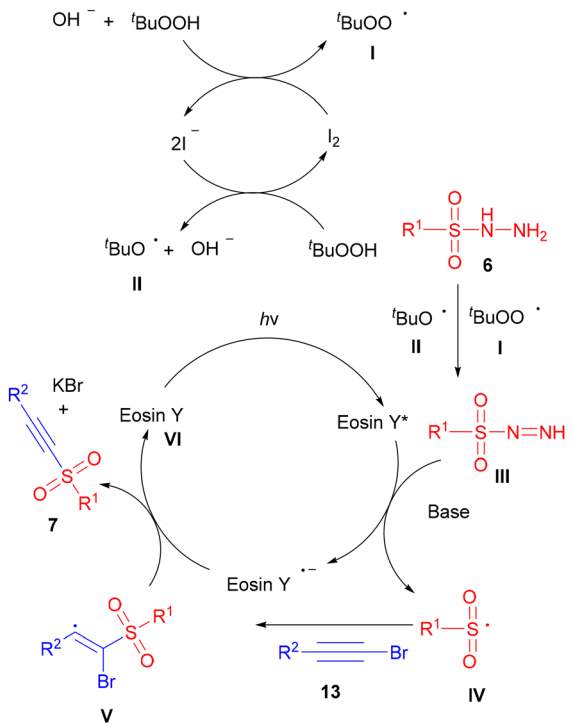


Scheme 23 Visible-light mediated synthesis of alkynyl sulfones **7** reported by Fan and co-workers in 2023.[34]

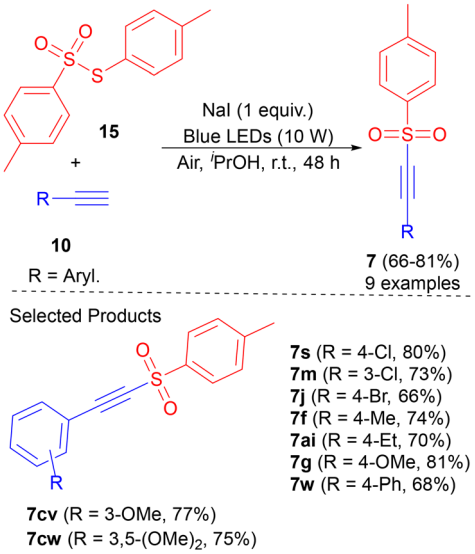
source. Under these conditions, 29 examples of alkynyl sulfones **7** were synthesized in yields ranging from low to excellent (30–98%) after reaction times of 12–36 h (Scheme 23). The protocol was slightly sensitive to the electronic effect when starting materials containing inductive EDG and EWG on the aromatic ring of bromo acetylenes were evaluated. In these cases, starting materials **6** and **13** containing EDG afforded the target products in yields slightly larger than EWG ones. However, the same effect was not observed when starting materials containing mesomeric EDG and EWG were tested, the presence of EDG (such as R = OMe) attached to the aromatic ring of bromoacetylenes **13** afforded the target alkynyl sulfone **7** in excellent yields. On the other hand, the presence of EWG (R = CO_2Me), gave the desired compound **7az** in poor yield (30%). The same effect was observed for EWG and EDG attached to the aromatic ring of benzenesulfonyl hydrazide **6**, such as to the compounds **7aq** (R = 4-OMe), which was synthesized in better yield (80%) compared to the compounds **7bz** (R = NO_2) and **7ca** (R = CN), which were formed in significantly lower yields, 50% and 60%, respectively. Additionally, this approach was efficiently extended to heteroaryl group (*e.g.* Th) attached in both starting materials (sulfonyl hydrazides and bromoalkynes), which gave the target compounds **7aw** and **7ab** in good yields 75% and 71%, respectively. Finally, an alkyl bromoacetylene was also evaluated, affording the target product **7bv** in moderate yield (42%) (Scheme 23).

The plausible mechanism for the formation of alkynyl sulfones **7** from the photocatalytic process begins with the iodide anion-promoted decomposition of TBHP, generating intermediates **I** and **II**. These *tert*-butoxyl **II** and *tert*-butylperoxy radical **I** species react with benzenesulfonyl hydrazide **6** in an oxidation step to form the sulfonylimide intermediate **III** (Scheme 24). This intermediate **III** reacts with the photoexcited catalyst to form the benzenesulfonyl radical **IV**, which subsequently reacts with alkynyl bromide **13**. Subsequently, the vinyl radical **V** undergoes a single-electron transfer (SET) with the excited photocatalyst, producing the vinyl anion, which then eliminates bromide to afford the target alkynyl sulfone **7** and generating Eosin Y **VI** to a new catalytic cycle (Scheme 24).

In 2024, Li and co-workers[35] promoted the preparation of alkynyl sulfones **7** through a method that uses mild conditions, metal- and photocatalyst-free, promoted by visible-light irradiation (Scheme 25). The best conditions were achieved when terminal alkynes **10** were reacted with *S*-(*p*-tolyl) 4-methylbenzenesulfonothioate **15** in the presence of 1 equiv. of sodium iodide, ^{i}PrOH as a solvent, using visible light irradiation as an alternative energy source under an air atmo-



Scheme 24 Proposed mechanism for the visible-light promoted synthesis of alkynyl sulfones **7**.[34]

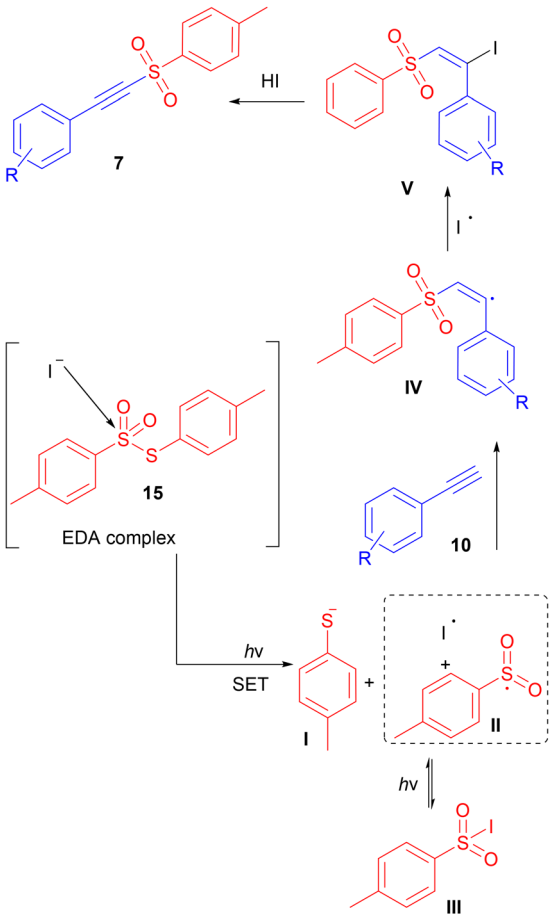


Scheme 25 Blue LEDs mediated synthesis of alkynyl sulfones **7** developed by Li and co-workers in 2024.[35]

sphere at room temperature for 48 h. Under these conditions, different alkynyl sulfones **7** were synthesized in yields ranging from moderate to good (66–81%) (Scheme 25). The reaction was not sensitive to the electronic nature of substituents (EWGs or EDGs) on the aromatic ring of terminal alkynes **10**. This approach tolerates several substituents on the aromatic ring of the substrate **10**, including Me, Et, OMe, Ph, affording the target alkynyl sulfones **7** generally in good yields. When halogen atoms were attached to this substrate, a slight decrease in yield was observed. For instance, the *para*-bromo-substituted substrate **10** formed the product **7j** in poor lower yield (66%) compared to the *para*-chloro analogue (compound **7s**, 80%) (Scheme 25).

The mechanism proposed by the authors indicates the formation of an EDA complex between *S*-(*p*-tolyl) 4-methylbenzenesulfonothioate **15** and sodium iodide, which undergoes a single electron transfer (SET), to generate the sulfonyl radical **II**, and sulfur anion PhS^- **I** along with the iodine radical. The previously formed sulfonyl radical **II** reacts with terminal alkyne **10**, forming the vinyl radical **IV**, which undergoes coupling with the iodine radical to generate species **V**. Finally, this intermediate undergoes an elimination step, releasing HI and forming the target alkynyl sulfone **7** (Scheme 26).

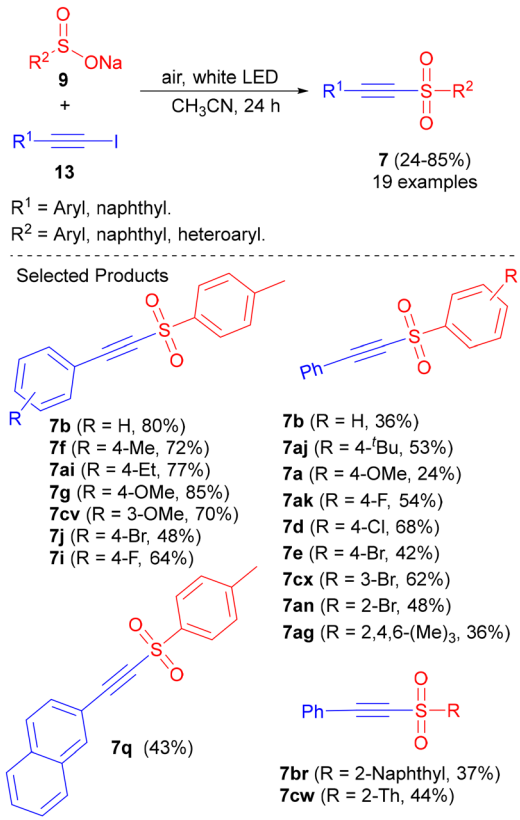
In 2024, Jia and co-workers[36] reported an efficient synthesis of organyl alkynyl sulfones **7** *via* a coupling reaction between alkynyl iodides **13** and sodium sulfinates **9** under white-light irradiation and in the presence of air. The reaction was performed in an open flask using acetonitrile as solvent, where alkynyl iodides **13** and sodium sulfinates **9** (2 equiv.) were stirred under white LED illumination for 24 hours. Under these mild and metal-free conditions, nineteen examples of organyl alkynyl sulfones **7** were obtained in yields ranging from 24% to 85% (Scheme 27).



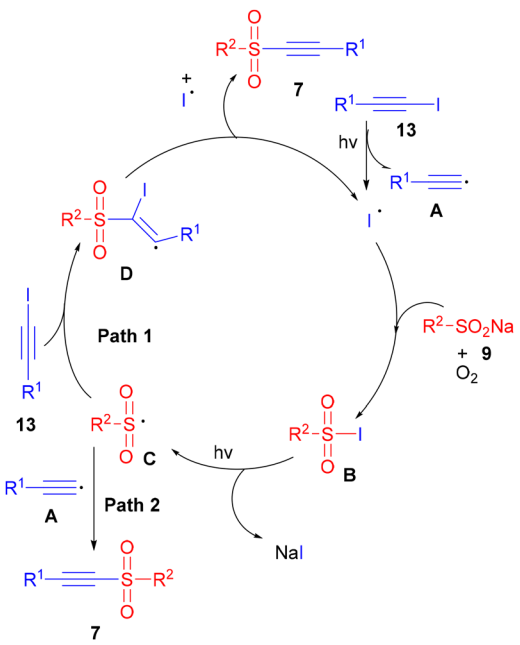
Scheme 26 Proposed mechanism for the NaI/blue LED promoted synthesis of alkynyl sulfones **7**.[35]

This study demonstrated a practical and environmentally benign methodology for the synthesis of alkynyl sulfones under light and air conditions. The reaction efficiency was strongly influenced by the electronic nature of the substituents on the alkynyl iodides **13**. Substrates bearing electron-donating groups (EDGs) afforded higher yields, while no significant electronic effect was observed for the sulfonyl reagents **9**. These observations are consistent with a radical pathway, where the alkynyl iodide serves as a key precursor for radical generation. Electron-donating substituents stabilize the resulting radical intermediates, thereby enhancing the reaction efficiency. The proposed radical mechanism is illustrated in Scheme 28.

The authors[36] proposed a plausible mechanism for this transformation (Scheme 28). Initially, the phenyl alkynyl iodide **13** undergoes homolytic cleavage under white-light irradiation, generating the alkynyl radical **A** and an iodine radical. The iodine radical subsequently oxidizes sodium *p*-toluenesulfinate **9** to form the corresponding sulfonyl iodide **B**. Upon further irradiation, sulfonyl iodide **B** undergoes a second homolytic cleavage, affording the sulfonyl radical **C**. From this point, two possible reaction pathways were



Scheme 27 Synthesis of alkynyl sulfones **7** reported by Jia and co-workers in 2024.[36]



Scheme 28 Proposed mechanism for the synthesis of alkynyl sulfones **7**.[36]

suggested. In path 1, the sulfonyl radical **C** reacts with another molecule of alkynyl iodide **13** to form the intermediate radical **D**. The intermediate **D** then undergoes homolytic cleavage of the C–I bond, followed by C–C bond formation and re-establishment of the triple bond, ultimately yielding the desired product **7**. Alternatively, in path 2, the sulfonyl radical **C** directly couples with the alkynyl radical **A** to produce the target sulfonyl alkyne **7**.

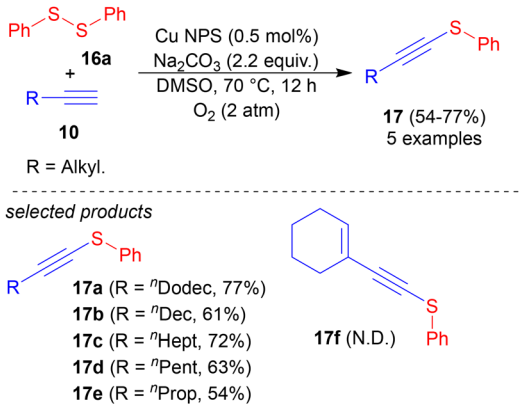
The construction of C(sp)–C bonds from alkynyl sulfones has been extensively reported, particularly through SOMOphilic alkynylation reactions, which employ acetylenic sulfones as versatile functional reagents. This strategy enables the incorporation of alkynyl units into surrogate C-centered radical.[37] Alkynyl sulfones have been employed as starting materials for the synthesis of ynones *via* reaction with carboxylic acids under visible light-induced photoredox conditions, as reported by Wan and co-workers.[38]

3 Advances in the preparation of alkynyl sulfides

In this section, we focus our attention on describing the reports concerning the synthesis of alkynyl sulfides. The incorporation of a sulfide group into an alkyne framework provides compounds of high synthetic value, as the C–S bond offers both stability and functional versatility. Alkynyl sulfides serve as useful precursors in diverse transformations, including transition-metal-catalyzed cross-couplings, heterocycle construction, and radical-based processes. Classical strategies typically involve nucleophilic substitution or thiolation reactions, whereas more recent approaches highlight catalytic methods, oxidative couplings, and sustainable protocols that expand the structural diversity and applicability of these sulfur-containing building blocks. The following section outlines the main methodologies reported for their synthesis, ranging from traditional routes to modern catalytic advances.

In 2015, Park and co-workers[39] reported the use of copper nanoparticles as an efficient catalyst for the synthesis of alkynyl sulfides **17** by a cross coupling reaction (Scheme 29). In this protocol, the authors treated diphenyl disulfide **16a** with several terminal alkynes **10** in the presence of a small amount of Cu NPS catalyst (0.5 mol%), and 2.2 equiv. of Na_2CO_3 as the base, using DMSO as the solvent. The starting materials were heated at 70 °C for 12 h under O_2 (2 atm) atmosphere to afford the target alkynyl sulfides **17** (5 examples) in moderate yields (54–77%). This new catalytic route uses oxygen as a green oxidant and promotes the dual activation of S–S and C–H bonds under ligand-free conditions leading to the desired products by a new S–C_{sp} bond formation. In this approach, the authors employed only alkyl terminal alkynes **10** as starting materials. On the other hand, the protocol was not efficient when the 1-ethynylcyclohex-1-ene was used as a starting material; in this case, the desired product **17** was not detected. Additionally, the synthesis of alkynyl selenide and telluride was also reported by the authors, as described in section 4, Scheme 63.

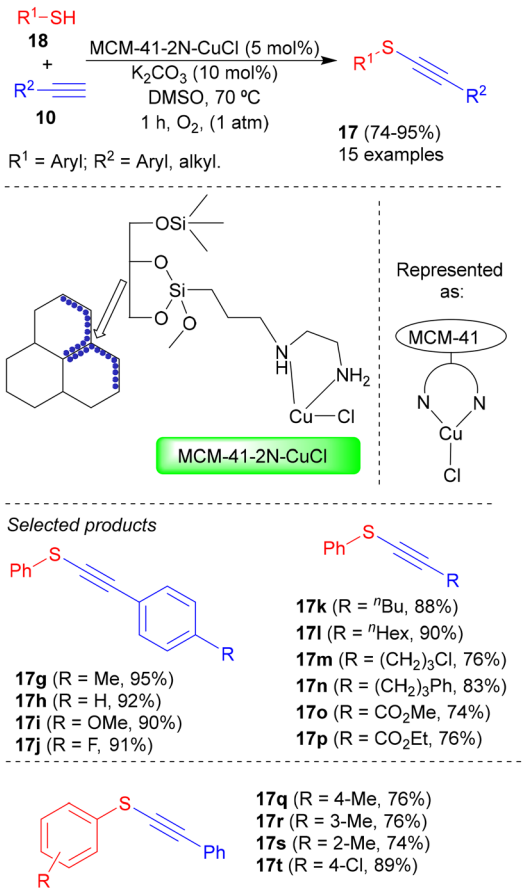
In 2015, Zhao and co-workers[40] described the synthesis of a range of alkynyl sulfides through cross-dehydrogenative coup-



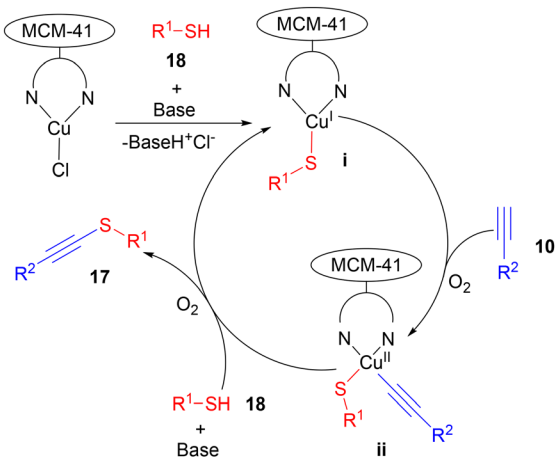
Scheme 29 Synthesis of alkynyl sulfides **17** from diphenyl disulfide **16a** and alkynes **10** described by Park and co-workers in 2015.[39]

ling of terminal alkynes **10** with thiols **18**. The method employs 5 mol% of a copper-based recyclable catalyst, the MCM-41-supported bidentate nitrogen copper(I) complex [MCM-41-2N-CuCl] (Scheme 30). This heterogeneous catalyst can be prepared from inexpensive and commercially available reagents and was developed based on the mesoporous material MCM-41, known for its high surface area, uniform pores, and modifiable silanol groups. It allows for the stable anchoring of bidentate nitrogen ligands and copper salts, resulting in a solid-supported complex that is both efficient and recyclable. In addition, the methodology uses 10 mol% of K_2CO_3 as the base in DMSO at 70 °C under an oxygen atmosphere. In only 1 h, a series of alkynyl sulfides **17** were obtained in good to excellent yields (74–95%). A wide range of substituents was explored on both the thiol **18** and alkyne components **10**, including alkyl, aryl, halogen and ester groups (Scheme 30). This structural diversity highlights the versatility of the system, which consistently afforded high and uniform yields across different substrates. These results suggest that the MCM-41-2N-CuCl catalyst performs effectively under various electronic and steric environments, reinforcing its potential for broader synthetic applications. Moreover, the catalyst could be easily recovered by simple filtration and reused up to ten times without any significant loss of catalytic activity, further demonstrating its practicality (Scheme 30).

The authors proposed a mechanistic pathway to explain the course of this heterogeneous copper-catalyzed oxidative cross-dehydrogenative coupling process, under aerobic conditions. Initially, the MCM-41-2N-CuCl complex interacts with the thiol **18** in the presence of base, generating a copper(I) thiolate species anchored on the MCM-41 support **I** (Scheme 31). This species is then thought to undergo a transmetalation process with the terminal alkyne **10**, likely facilitated by molecular oxygen, leading to the formation of a copper(II) intermediate **II** (Scheme 31). Subsequent reductive elimination from this intermediate **II**, in the presence of an excess of thiol, yields the desired alkynyl sulfide **17** while regenerating the copper(I) thiolate species **I**. Additionally, in this reaction sequence, molecular oxygen is considered crucial for promoting the oxidation



Scheme 30 Synthesis of alkynyl sulfides **17** using MCM-41-2N-CuCl heterogeneous catalyst developed by Zhao and co-workers in 2015.[40]

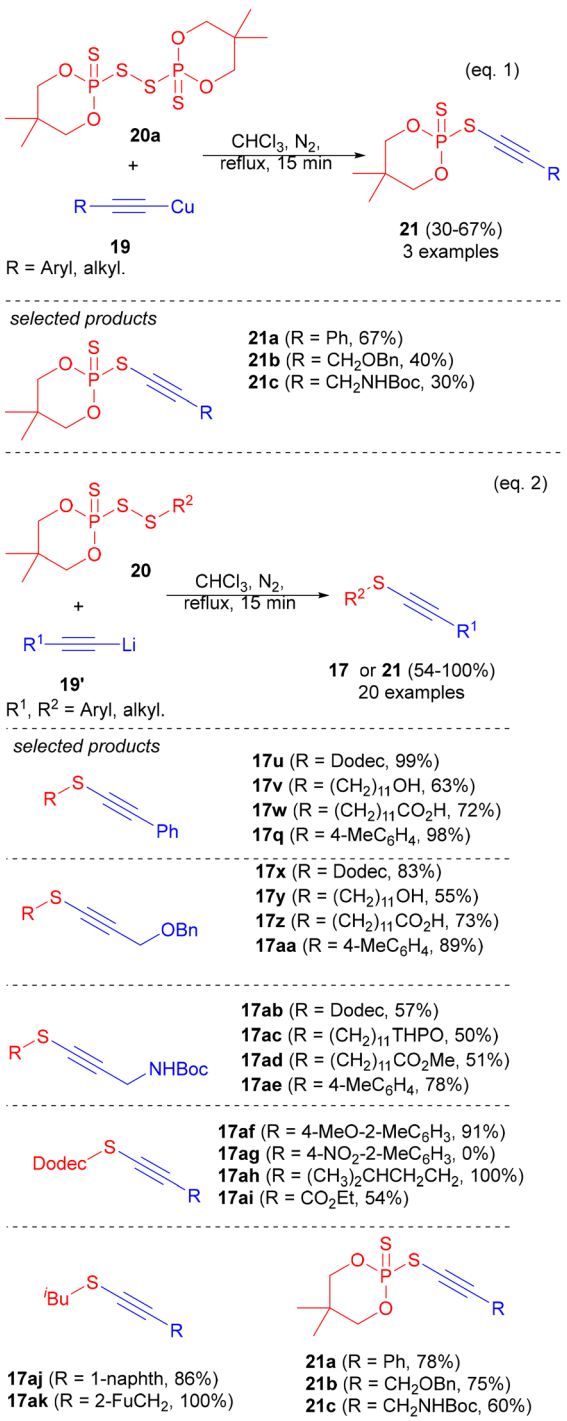


Scheme 31 Proposed mechanism for the MCM-41-2N-CuCl catalysed synthesis of alkynyl sulfides **17**.[40]

of the copper center and facilitating the activation of the terminal alkyne's C–H bond (Scheme 31).

In 2016, Witt and co-workers[41] developed a protocol to obtain unsymmetrical alkynyl sulfides **17** and **21** through the reaction of 5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphorinan-2-

disulfanyl **20a** derivatives with copper or lithium acetylides **20a** or **19′**. In this protocol, mild conditions were employed to synthesize unsymmetrical alkynyl sulfides **17** and **21** with a broad tolerance for functional groups, using $CHCl_3$ as the solvent under N_2 atmosphere at reflux temperature for 15 minutes (Scheme 32). The authors carried out the reaction of phosphorodithioic acid disulfane **20a** with copper acetylides **19** under

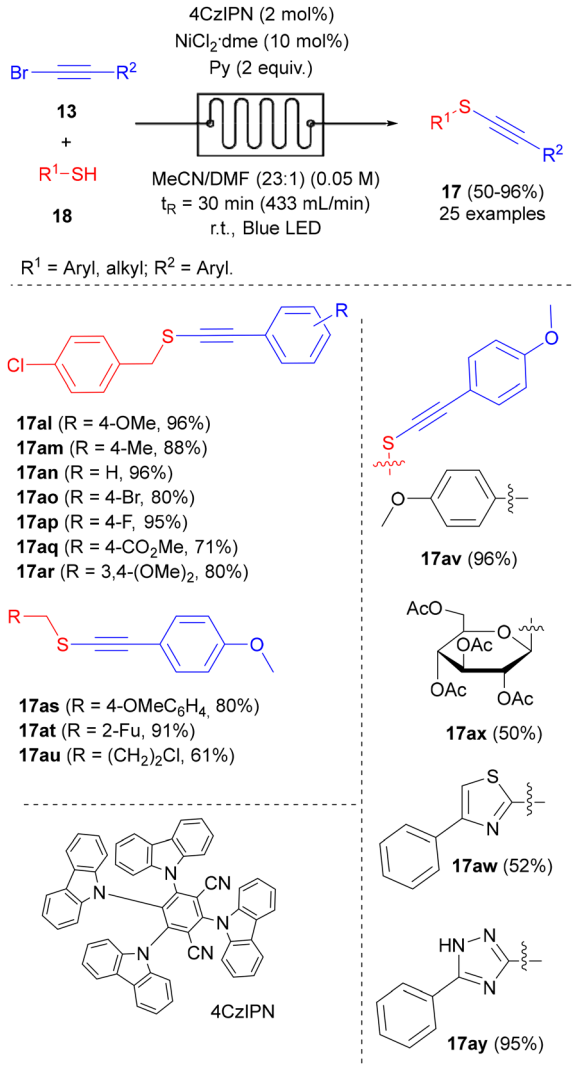


Scheme 32 Synthesis of alkynyl sulfides **21** reported by Witt and coworkers in 2016.[41]

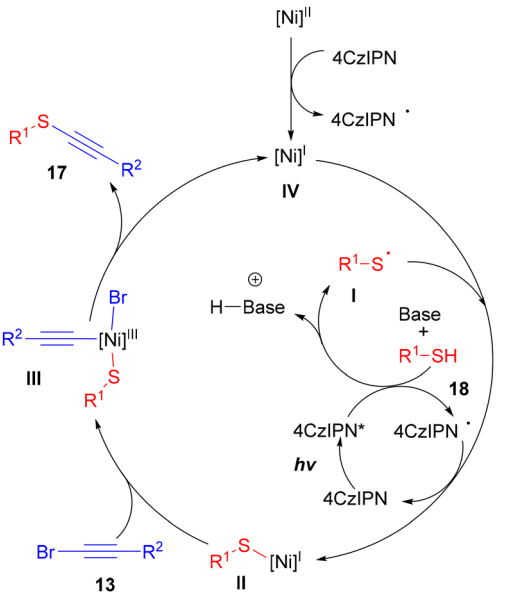
these conditions, obtaining the target alkynyl sulfides **21a**, **21b** and **21c** in 67%, 40% and 30%, respectively. Additionally, the same reaction conditions were applied to lithium acetylides **19′** and non-symmetrical disulfanes **20** as organosulfur sources (Scheme 32). This protocol tolerates aryl and alkyl groups attached to both starting materials **19′** and **20**, affording a wide range (20 examples) of target alkynyl sulfides **17** and **21** in yields ranging from moderate to quantitative (54–100%), containing several functional groups, such as hydroxyl, carboxyl, or amino ones (Scheme 32).

In 2017, Collins and co-workers[42] reported a novel method for the synthesis of alkynyl sulfides **17** *via* flow photochemistry. In their protocol, a variety of thiols **18** were reacted with differently substituted alkynyl bromides **13** using 2 mol% of 4CzIPN, a carbazole-based organic photoredox catalyst, along with 10 mol% of $NiCl_2$·dme and 2 equivalents of pyridine in a MeCN/DMF (23 : 1) mixture (Scheme 33). The reaction was carried out at room temperature under blue light irradiation, with a residence time of 30 minutes. Under these conditions, a total of 25 alkynyl sulfides **17** were synthesized in yields ranging from moderate (50%) to excellent (96%) (Scheme 33). The method showed broad functional group tolerance for both the thiol and aryl the halide components. Thiols bearing electron-donating groups, such as methoxy and methyl substituents, gave high yields (up to 96%), likely due to the increased nucleophilicity of the corresponding thiolate. Halogenated thiols (F, Cl, Br) were also well tolerated. On the aryl alkynyl bromide side, electron-withdrawing groups like 2-fluoro provided excellent yields (**17ap**, 95%), probably due to their increased reactivity toward oxidative addition. In contrast, substrates with aliphatic chains and more structurally complex substituents, such as $(CH_2)_2Cl$, showed reduced efficiency (**17au**, 61%). Furthermore, a thioglucose derivative was successfully coupled, affording the desired product **17ax** in 50% yield, the lowest among the examples tested, yet still demonstrating the method's remarkable tolerance to functional group diversity. In general, the method proved to be versatile, working well with a wide variety of starting materials and functional groups. Additionally, the protocol exhibited high reproducibility on the gram scale and was successfully applied to macrocyclization, representing the first example of incorporating an alkynyl sulfide unit into a macrocyclic scaffold *via* dual photoredox/nickel dual catalysis (Scheme 33).

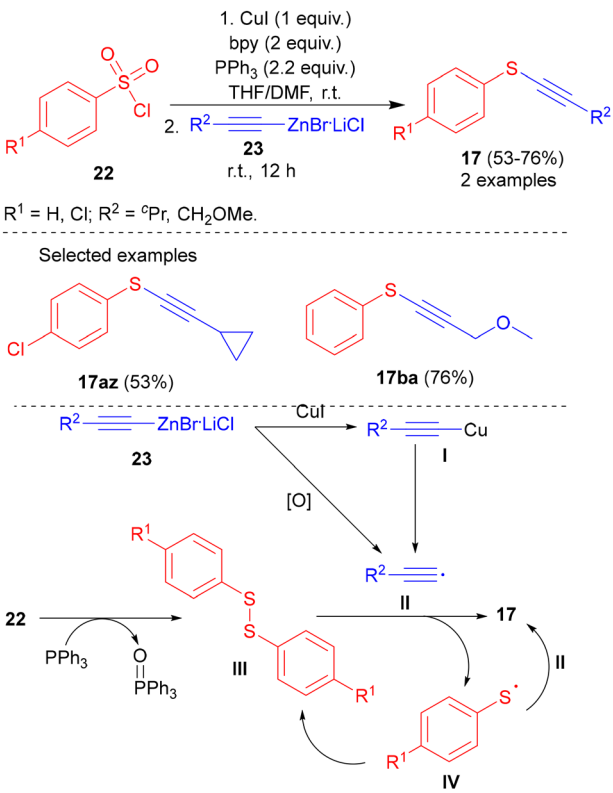
The authors proposed a mechanistic pathway in which the catalytic cycle begins with the excitation of the photocatalyst 4CzIPN under blue light, generating its excited state (4CzIPN*), which undergoes single-electron transfer to reduce the Ni(II) species to a Ni(I) intermediate (Scheme 34). Simultaneously, the thiol **18** is deprotonated by a base, forming a thiolate anion, which is then oxidized by the oxidized form of 4CzIPN to generate a thiyl radical **I**. This radical reacts with the Ni(I) species, forming a Ni(II)–S complex **II**. Subsequently, oxidative addition of the alkynyl bromide **13** to the nickel center affords a Ni(III) intermediate **III**. Finally, reductive elimination from this high-valent species forms the desired C(sp)–S bond, yielding the alkynyl sulfide product **17**



Scheme 33 Flow photochemistry for alkynyl sulfide **17** synthesis described by Collins and co-workers in 2017.[42]



Scheme 34 Mechanism of Ni/photoredox flow catalysis.[42]



Scheme 35 Cu-catalyzed synthesis of alkynyl sulfides **17** from sulfonyl chlorides **22** by Fu and co-workers in 2017.[43]

and regenerating the Ni(I) species (**IV**) within the catalytic cycle (Scheme 34).

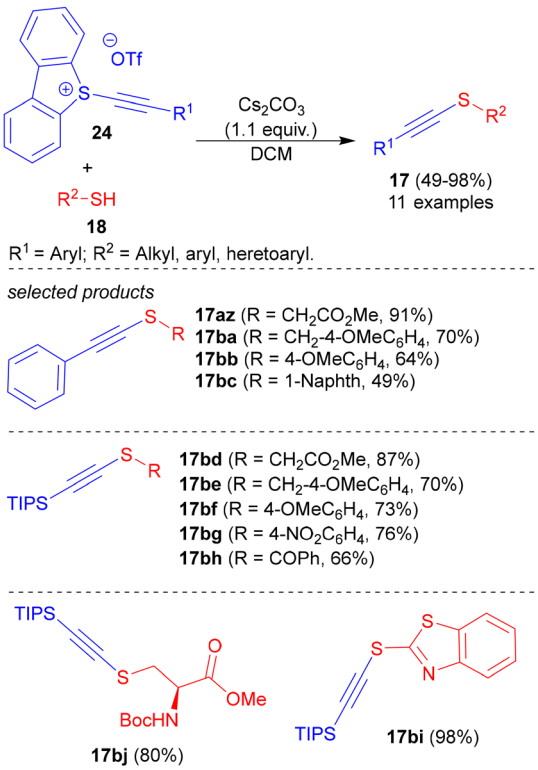
In 2017, Fu and co-workers[43] reported an efficient methodology for the synthesis of aromatic alkynyl sulfide **17** *via* the sulfenylation of organozinc reagents **23** with arylsulfonyl chlorides **22**. The transformation proceeds under mild conditions, employing 1 equiv. of CuI as the catalyst, 2 equiv. of 2,2′-bipyridine asa ligand, 2 equiv. of triphenylphosphine (PPh_3) as a reducing agent, and a THF/DMF mixture as the solvent at room temperature for 12 h (Scheme 35). A large scope of aromatic thioethers was reported. Among them, in particular, two examples of alkynyl sulfides **17** were synthesized in yields of 53% and 76% (**17az** and **17ba**, respectively). In the first example, the arylsulfonyl chloride **22** bearing a *para*-chloro substituent reacted with cyclopropylzinc bromide, leading to the formation of the corresponding alkynyl sulfide **17az** in 53% yield. This case highlights the reaction's tolerance for aryl halides, a valuable functionality in organic synthesis due to their potential for further transformations, such as cross-coupling reactions. In the second example, the arylsulfonyl chloride **22** lacking substituents was combined with an organozinc reagent **23** containing a methoxymethyl group (CH_2OMe),

affording the corresponding alkynyl sulfide **17ba** in a higher yield (76%). This result underscores the reaction's efficiency even with aliphatic chains bearing heteroatoms, such as oxygen. Therefore, the method demonstrated broad synthetic versatility, being applicable to a wide range of products, especially in the case of two examples of alkynyl sulfides, making it a valuable tool for C–S bond formation in organic synthesis.

With support from the experimental findings, the authors proposed a plausible reaction mechanism, illustrated in Scheme 35. In the initial step, the arylsulfonyl chloride **22** undergoes reduction by triphenylphosphine, yielding a diaryl disulfide intermediate **III**. The organozinc reagent **23** then engages in a transmetalation reaction with CuI, forming the corresponding organocopper species **I**. This intermediate subsequently undergoes homolytic bond cleavage to generate the alkynyl radical **II**. Alternatively, this radical can be generated directly from the organozinc precursor in the presence of trace oxygen. The disulfide species **III** intercepts this radical **II**, leading to the formation of the alkynyl sulfide **17**, while simultaneously producing a thiyl radical **IV**, which may either dimerize to regenerate the disulfide **III** or react with another alkynyl radical **II**, thereby forming an additional equivalent of the product **17** (Scheme 35).

In 2018, Alcarazo and co-workers[44] demonstrated the efficient electrophilic alkynylation of thiols **18** using 5-(alkynyl)dibenzothiophenium triflates **24**, obtaining 11 different alkynyl sulfides **17** in yields ranging from 49% to 98% (Scheme 36). The reactions were performed under mild conditions using 1.1 equiv. of Cs_2CO_3 as the base in DCM. The method showed broad substrate compatibility, including aryl, alkyl, and heteroaryl thiols. In general, aliphatic and electron-rich aryl thiols provided high yields, while substrates with higher steric hindrance or reduced nucleophilicity led to lower conversions. For example, the 1-naphthyl-substituted thiol gave the lowest yield at 49% (**17bc**), probably due to steric effects. In contrast, heteroaryl thiols showed excellent reactivity, with yields reaching up to 98% (**17bi**). These observations emphasize how electronic and steric factors influence reaction outcome. In general, the main contribution of the article was the synthesis and characterization of a new class of sulfur-based electrophilic alkynylation reagents: 5-(alkynyl)dibenzothiophenium triflates **24**. These compounds were obtained *via* oxidation of dibenzothiophene followed by reaction with trimethylsilyl-protected alkynes, and their structures were confirmed by X-ray crystallography. Their broad substrate scope and good functional group tolerance highlight their potential as versatile alternatives to traditional EBX reagents in electrophilic alkynylation (Scheme 36).

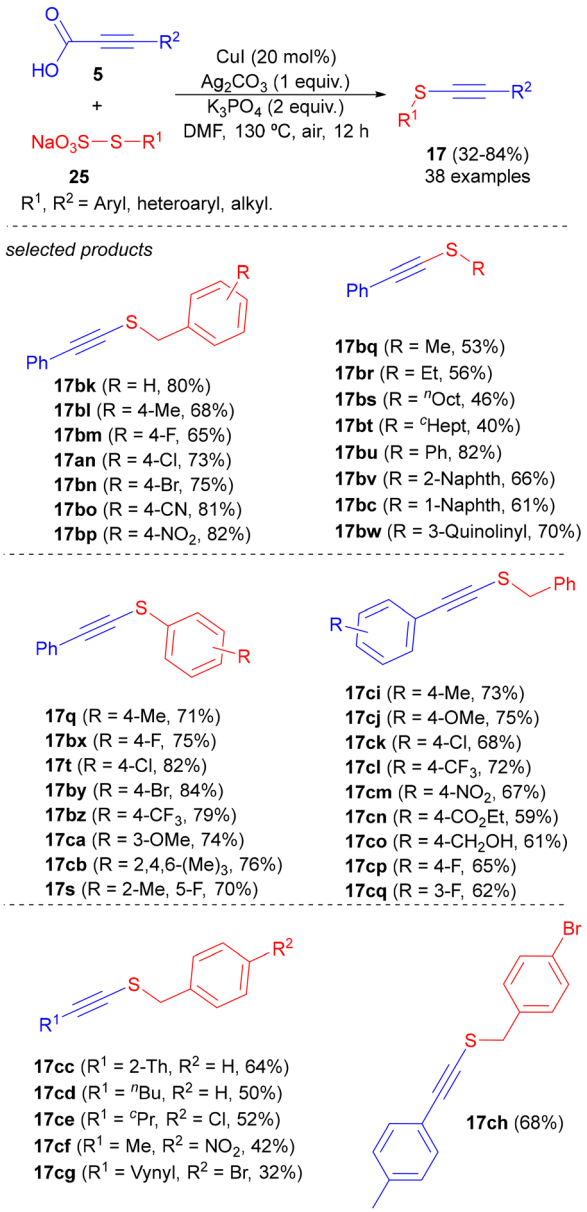
As described for the alkynyl selenides in section 4, Scheme 81, Liu and Yi[45] also proposed a thiol-free, copper-catalyzed decarboxylative cross-coupling method for the synthesis of alkynyl sulfides **17** using alkynyl carboxylic acids **5** and sulfur-based Bunte salts **25** (Scheme 37). The reaction was carried out under the same optimized conditions: CuI (20 mol%), Ag_2CO_3 (1 equiv.), and K_3PO_4 (2 equiv.) in DMF at



Scheme 36 Cs_2CO_3-mediated synthesis of alkynyl sulfides **17** described by Alcarazo and co-workers in 2018.[44]

130 °C for 12 h under air. This strategy led to the formation of 38 alkynyl sulfides **17** in moderate to very good yields (32–84%), highlighting the broad applicability and robustness of the methodology. The reaction exhibited wide functional group tolerance, efficiently accommodating a variety of aryl, heteroaryl, and alkyl substituents on both coupling partners with good to high efficiency. In contrast to some selenide examples, alkyl-substituted Bunte salts **17bq**, **17br**, **17bs**, and **17bt** gave moderate to low yields (40–56%), which may be attributed to the decreased stability or reactivity of the corresponding alkylthiosulfonate intermediates. Furthermore, the strategy demonstrates broad applicability and operational simplicity, offering a clean and efficient route to a wide variety of organosulfur compounds without depending on thiol reagents (Scheme 37).

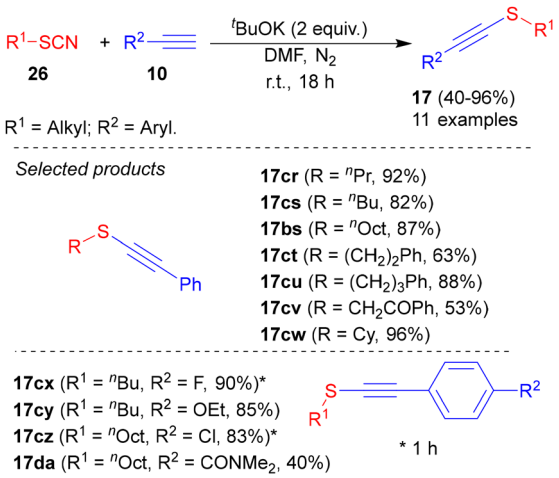
In 2019, Yang, Tian and Zhang[46] reported an efficient strategy for the synthesis of alkynyl sulfides **17** *via* the reaction between alkyl thiocyanates **26** and terminal alkynes **10**, using 2 equiv. of ^{t}BuOK as the base in DMF under a nitrogen atmosphere. The transformation proceeded at room temperature over 18 h, affording 11 products **17** in moderate to excellent yields (40–96%) (Scheme 38). The reaction demonstrated broad functional group tolerance, accommodating various substituents on the thiocyanate moiety, including linear, branched, and cyclic alkyl chains. Likewise, the substituents on the aromatic alkyne included both electron-donating and electron-withdrawing groups. Particularly, halogenated substi-



Scheme 37 Cu/Ag-catalyzed synthesis of alkynyl sulfides **17** from sodium sulfinates **25** described by Liu and Yi in 2018.[45]

tuents on the aromatic alkyne, such as fluoro and chloro groups led to excellent yields in just 1 h (**17cx** and **17cz**), thereby demonstrating the high reactivity of these substrates. Thus, this protocol stands out for its operational simplicity, broad substrate scope, and high efficiency under mild conditions (Scheme 38). The protocol was also extended to synthesis of alkynyl selenides (section 4, Scheme 83).

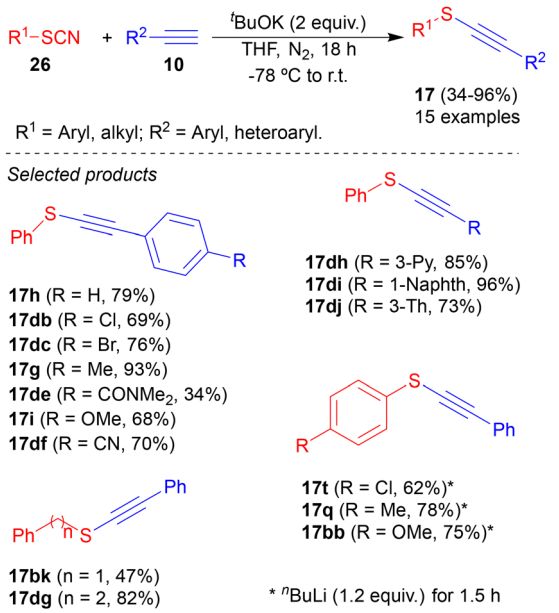
In the same work, the authors further demonstrated the generality of their approach by applying it to a broader set of aryl and alkyl thiocyanates **26** and a diverse range of terminal alkynes **10**, including aryl and heteroaryl derivatives. This extended protocol also employed 2 equiv. of ^{t}BuOK as the base in a THF solution under nitrogen, with temperatures ranging



Scheme 38 Synthesis of alkynyl sulfides **17** from thiocyanates **26** using DMF as solvent described by Yang, Tian and Zhang in 2019.[46]

from −78 °C to room temperature over 18 h. The reaction yielded 15 alkynyl sulfides **17** in moderate to excellent yields (34–96%) (Scheme 39). The methodology showed good tolerance for electron-rich, electron-deficient, and sterically hindered substituents on both the thiocyanate and alkyne partners. Moreover, for more challenging substrates, such as *ortho*-substituted alkynes, the authors successfully employed *n*-BuLi as the base at low temperature, achieving satisfactory yields after just 1.5 h (**17t**, **17q** and **17bb**). These results support the robustness and adaptability of the method for constructing C–S bonds across a wide substrate scope (Scheme 39).

Furthermore, the authors proposed a mechanism in which the reaction begins with the deprotonation of a terminal

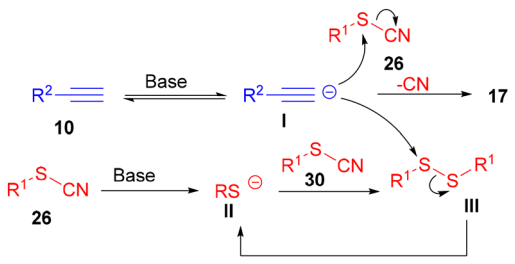


Scheme 39 Synthesis of alkynyl sulfides **17** from thiocyanates **26** using THF as solvent described by Yang, Tian and Zhang in 2019.[46]

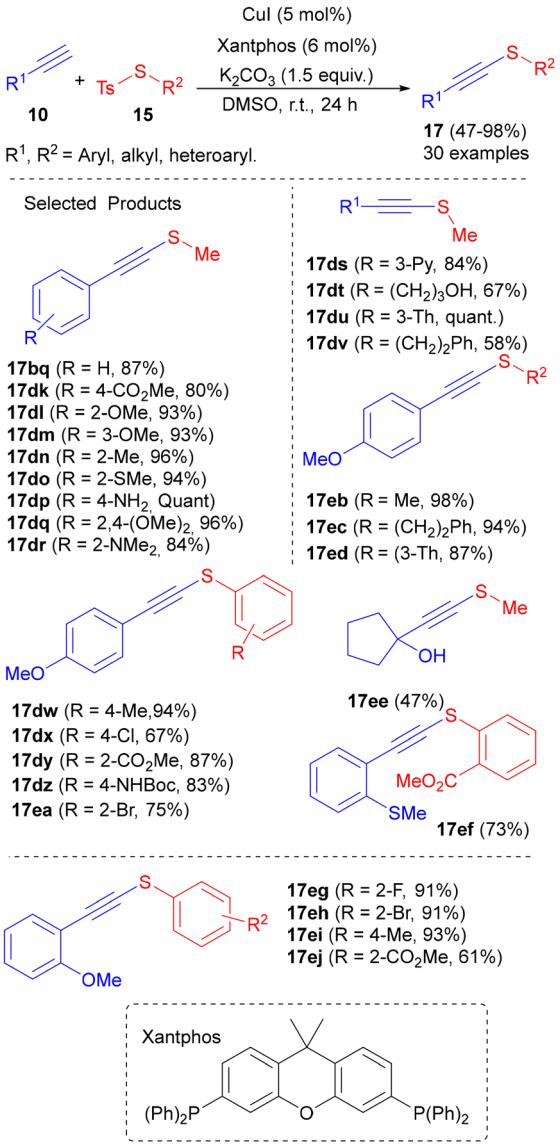
alkyne **10** by the base, leading to the formation of a nucleophilic acetylide anion **I**. This intermediate then attacks the electrophilic sulfur atom of the thiocyanate **26**, resulting in the displacement of the cyano group (–CN) and the formation of the corresponding alkynyl sulfide **17** (Scheme 40). The efficiency of this step is attributed to the excellent leaving group ability of the cyano moiety, which facilitates rapid nucleophilic substitution (Scheme 40).

In 2019, Kanemoto, Yoshida e Hosoya[47] described a protocol for the synthesis of a diverse scope of alkynyl sulfides using a copper catalyzed method. A total of 30 products **17** were synthesized in yields ranging from 47% to 98% from the reaction of thiosulfonates **15** with terminal alkynes **10** (Scheme 41). Under the reaction conditions, 5 mol% of CuI was used as the catalyst, 6 mol% of Xantphos as the ligand, and 1.5 equiv. of K_2CO_3 as the catalyst. The reaction was performed in a DMSO solution at room temperature in a reaction time of 24 h. In general, when present on the alkyne component, EDG groups, such as methyl, methoxy, amino and dimethylamino led to high yields. This suggests that electron-rich arylacetylenes may help stabilize copper intermediates or enhance reactivity during the coupling process. EWG and halogen substituents on the alkyne, such as CO_2Me, Cl, and Br, were also well tolerated, giving moderate to high yields depending on their position and electronic nature. On the thiosulfonate **15** side, a broad range of substituents was compatible, including alkyl and aryl groups such as substituted phenyl rings and thiophenes. Interestingly, even sterically hindered or potentially coordinating groups did not strongly interfere with the reaction, though a few cases showed slightly lower yields (*e.g.*, **17ee**, 47%). Overall, the method proved to be quite versatile, handling a wide range of functional groups with consistently good results (Scheme 41).

Based on control experiments, the authors described a catalytic mechanism (Scheme 42). They proposed that the process is initiated by the generation of a copper acetylide species **II** *via* ligand substitution between the terminal alkyne **10** and the Cu(I) complex bound to Xantphos, with the aid of a base. From there, two potential routes are considered. In route (**a**), the copper acetylide reacts with the thiosulfonate **15** through a σ-bond metathesis, producing the alkynyl sulfide **17** and restoring the catalyst. In route (**b**), the mechanism involves an oxidative addition of the thiosulfonate **15** to the copper complex,



Scheme 40 Proposed mechanism for the synthesis of alkynyl sulfides **17**.[46]

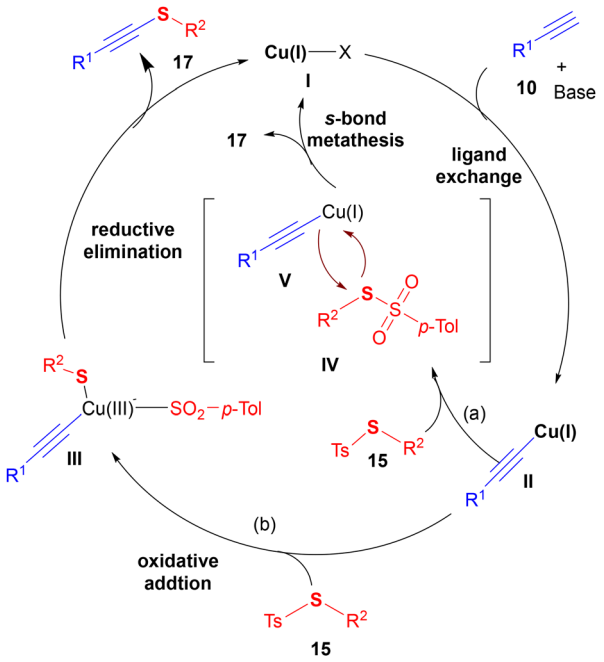


Scheme 41 Cu-catalyzed synthesis of alkynyl sulfides **17** by Kanemoto, Yoshida and Hosoya in 2019.[47]

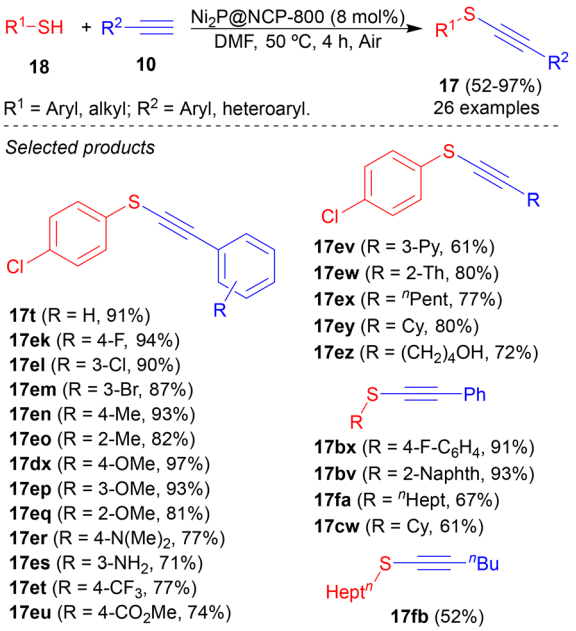
forming a Cu(III) intermediate **III**, which subsequently undergoes reductive elimination to yield the product **17** and reestablish the catalytic cycle (Scheme 42).

As described for selenium and tellurium derivatives (section 4, Scheme 88), Godoi and co-workers[48] also explored the cross-coupling reaction of the propynylbenzamide **27a** with bis(4-chlorophenyl) disulfide **16b**, using CuI as the catalyst (10 mol%) and 1 equiv. of $NaHCO_3$ as the base in DMSO at room temperature under an air atmosphere for 24 h. Under these conditions, the corresponding organosulfur compound **28a** was satisfactorily obtained in 75% yield, further demonstrating the method's broad applicability across different chalcogen sources (Scheme 43).

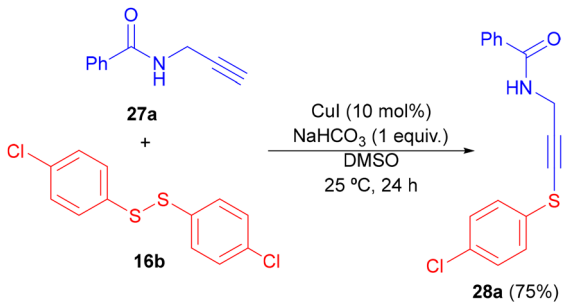
In 2020, Yang and co-workers[49] developed a method for the synthesis of new heterogeneous catalysts based on ultrafine Ni_2P nanoparticles, dispersed on N,P-codoped biomass-



Scheme 42 Proposed mechanism for the Cu-catalyzed synthesis of alkynyl sulfides **17**.[47]



Scheme 44 Ni-catalyzed synthesis of alkynyl sulfides **17** described by Yang and co-workers in 2020.[49]

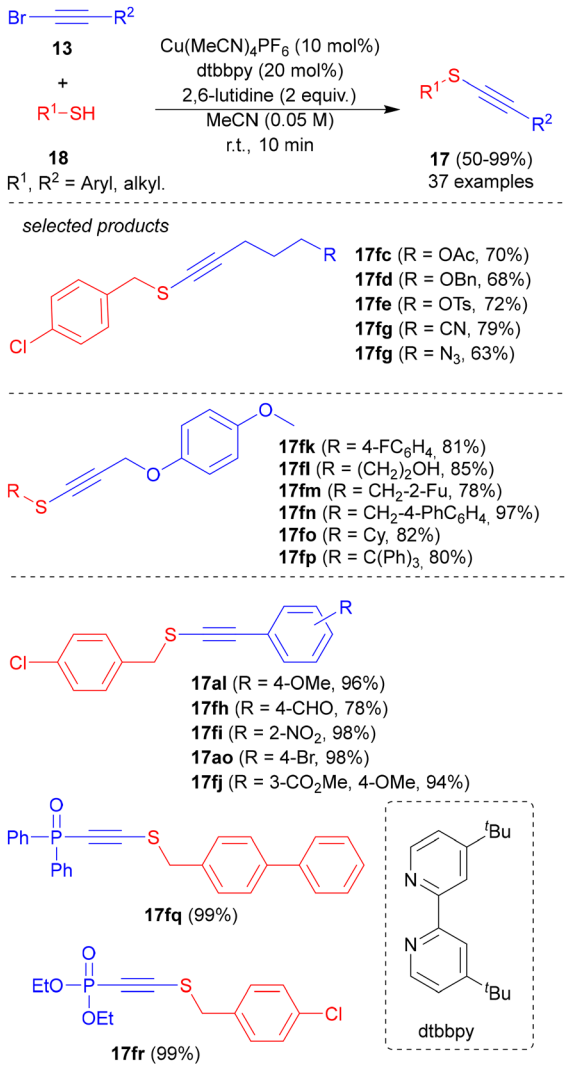


Scheme 43 CuI-catalyzed cross-coupling of propynylbenzamide **27a** and bis(4-chlorophenyl) disulfide **16b** described by Godoi and co-workers in 2019.[48]

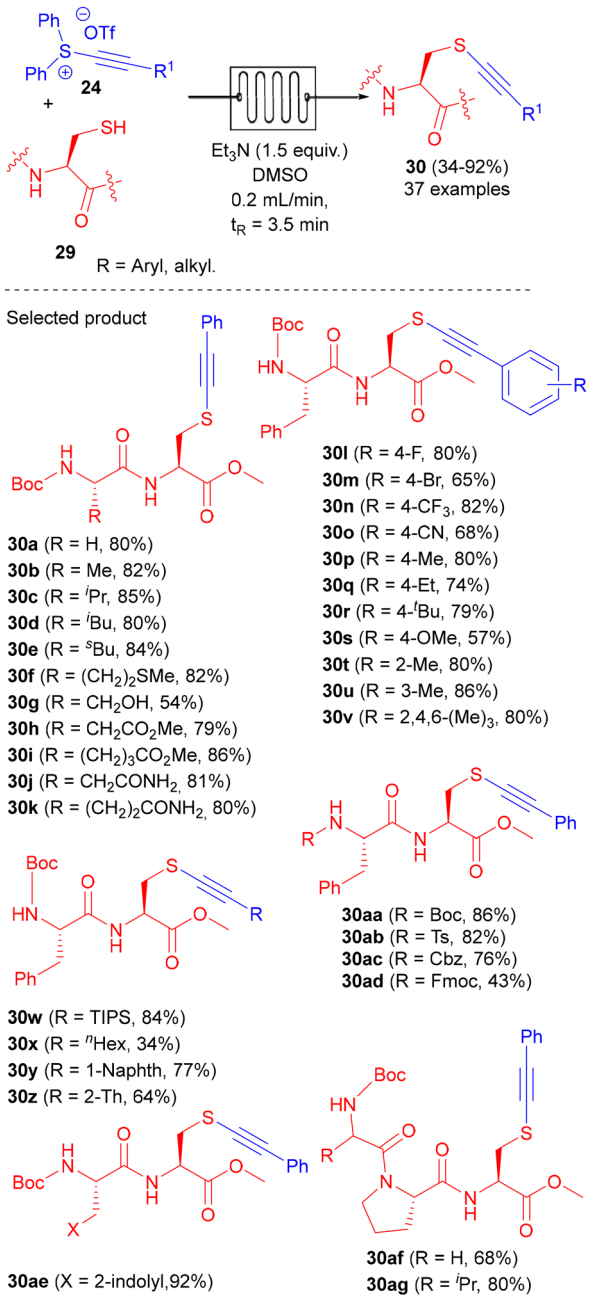
derived porous carbon. This efficient catalyst contains pyridinic units, which play a key role in reactions that involve hydrogen bonding interactions (Scheme 44). Based on these characteristics, this catalyst was applied to synthesize alkynyl sulfides **17** through a base- and ligand-free cross-dehydrogenative coupling reaction, providing a cost-effective and environmentally friendly method to obtain the target alkynyl sulfides **17** under mild conditions, using atmospheric air as the oxidant. The authors established the best conditions when terminal alkynes **10** and thiols **18** were reacted in the presence of 8 mol% Ni_2P@NCP-800 (heterogeneous catalyst), DMF as the solvent, at 50 °C for 4 h under an air atmosphere (Scheme 44). Under these conditions, several alkynyl sulfides **17** (26 examples) were obtained in yields ranging from moderate to excellent (52–97%). This approach tolerates both starting materials substituted with alkyl and heteroaryl groups, as well as aryl substrates containing EDG and EWG groups. However, the protocol was less effective when alkyl thiols **18** were reacted under standard conditions, affording poor yields of the target products **17fa**, **17cw** and **17fb**. To the best of our knowledge, this represents the first protocol for the synthesis of alkynyl sulfides (**17**) using a stable, heterogeneous Ni-based catalyst (Scheme 44).

In 2020, Collins and co-workers[50] developed a Cu-catalyzed protocol for the synthesis of alkynyl sulfides **17** *via* the cross-coupling of thiols **18** and bromoalkynes **13** through C_{sp}–S bond formation. This approach tolerated a wide range of functional groups attached to the alkyne substrate **13**. The standard conditions identified by the authors involved reacting thiols **18** were reacted with bromoalkynes **13** in the presence of 10 mol% $Cu(MeCN)_4PF_6$, 20 mol% of dtbbpy, 2 equiv. of 2,6-lutidine, in MeCN at r.t. for 10 min (Scheme 45). A total of 37 examples of fully decorated alkynyl sulfides **17** were synthesized under these conditions, in yields ranging from moderate to excellent (50–99%). This protocol was efficiently extended to both thiols **18** and bromoalkynes **13** containing fully functionalized aryl and alkyl groups. In addition, the protocol was applied to cysteine derivatives, as well as to obtain bis-heteroatom-substituted alkynes (S,S-, S,P- and S,N-). This method exhibited broad functional group tolerance, chemoselectivity, high reactivity, while employing commercially available catalysts and reagents. Overall, it represents an efficient strategy under mild conditions for accessing target alkynyl sulfides (**17**), which have broad potential as synthons (Scheme 45).

In 2021, Guo and co-workers[51] reported a continuous-flow approach for the selective S-alkynylation of cysteine-containing

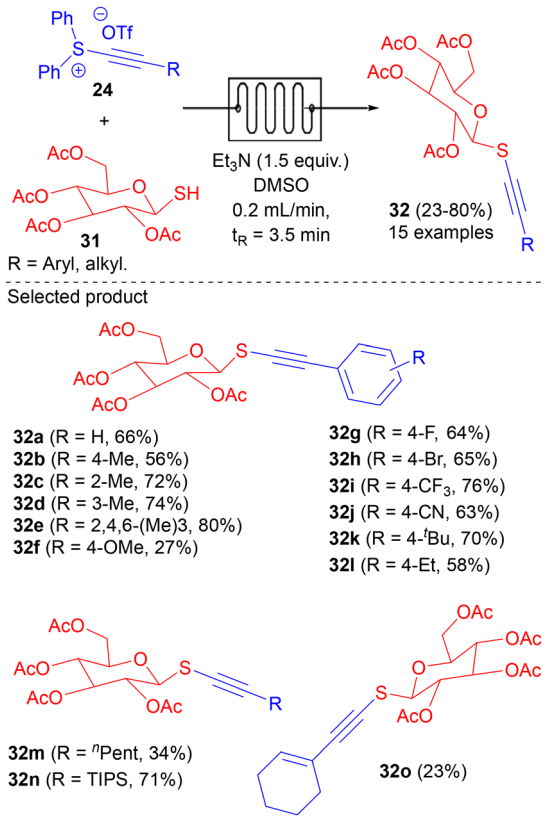


Scheme 45 Cu-catalyzed alkynyl sulfides **17** synthesis described by Collins and co-workers in 2020.[50]

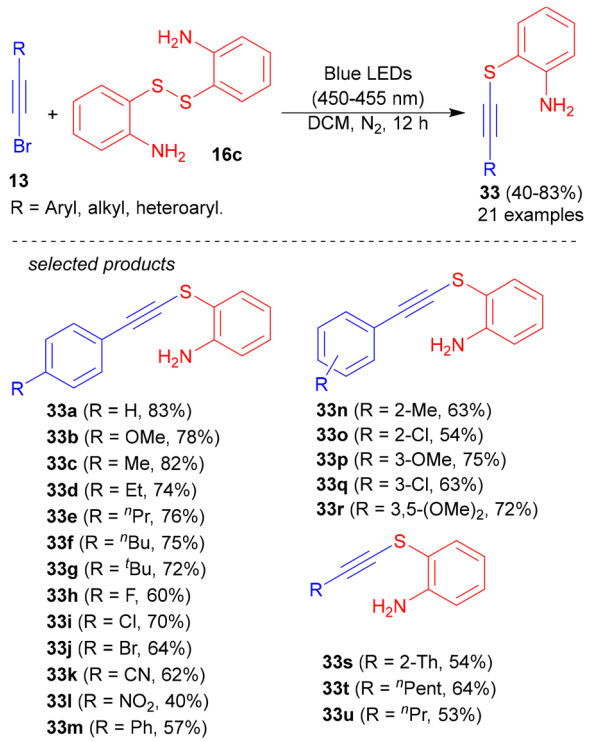


Scheme 46 Flow synthesis of amino acid-derived alkynyl sulfides **30** by Guo and co-workers in 2021.[51]

peptides **29** and 1-thioglycoside residues **31**, carried out under mild, metal-free, and oxidant-free conditions. Through the use of novel electrophilic alkynylation reagents, the reaction was completed in just 3–5 minutes, achieving high efficiency, broad substrate compatibility, and excellent functional group tolerance (Schemes 46 and 47). Compared to conventional batch processes, which can take several hours, the continuous-flow strategy significantly improved productivity while lowering costs and enhancing sustainability. In total, the research group reported over 50 examples, including structurally complex and biologically important derivatives, demonstrating the method's strong potential for peptide modification and bioconjugation applications. The continuous-flow S-alkynylation methodology was first evaluated with a broad range of cysteine-containing dipeptides and tripeptides **29**, demonstrating high efficiency, chemoselectivity, and functional group tolerance (Scheme 46). Using 1.5 equiv. of Et_3N in a DMSO flow of 0.2 mL min^{-1}, 37 alkynylated peptides **30** were obtained in yields ranging from 34% to 92% in only 3.5 minutes of residence time. The reaction proved compatible with various *N*-protecting groups (Boc, Cbz, Fmoc, Ts) and tolerated both polar and hydrophobic amino acid side chains. Even sterically hindered or less reactive substrates underwent successful alkynylation. In addition, a variation of the electrophilic alkynyl sulfonium reagent **24** revealed that electron-withdrawing, electron-donating, and neutral aromatic substituents all performed well, including hindered groups such as TIPS (**30w**). In contrast, alkyl-substituted reagents delivered



Scheme 47 Flow synthesis of glycosyl alkynyl sulfides **32** by Guo and co-workers in 2021.[51]



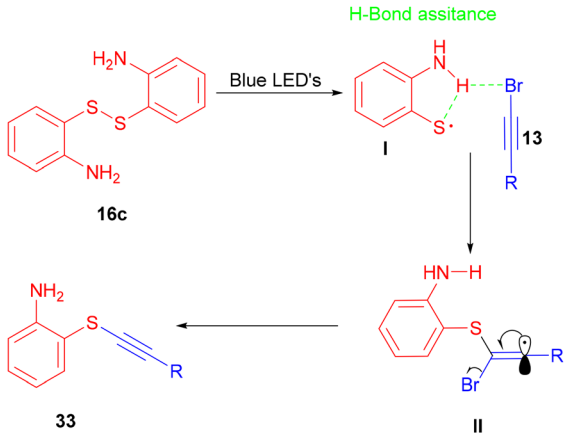
Scheme 48 Visible-light synthesis of thioalkynes **33** described by Wang and co-workers in 2021.[52]

lower yields (Ex: **30x**), though still producing the desired S-alkynylated products efficiently (Scheme 46).

Based on the performance of the reaction procedure with peptide substrates, the scope of the methodology was extended to the S-alkynylation of 1-thioglycosides **31** (Scheme 47), compounds of significant interest in pharmaceutical applications. A total of 15 phenylethynyl(diphenyl)sulfonium reagents **24**, bearing diverse electronic and steric profiles, were tested, delivering the corresponding alkynylated thioglycosides **32** in yields ranging from 23% to 80%. The reaction worked well with both electron-rich and electron-poor aryl groups was also able to modify hindered thioglycosides **31** in a residence time of only 3.5 minutes, demonstrating how versatile the continuous-flow system can be for quickly producing a wide variety of structures. Overall, these findings show that the method can be applied to different types of biologically relevant thiol compounds (Scheme 47).

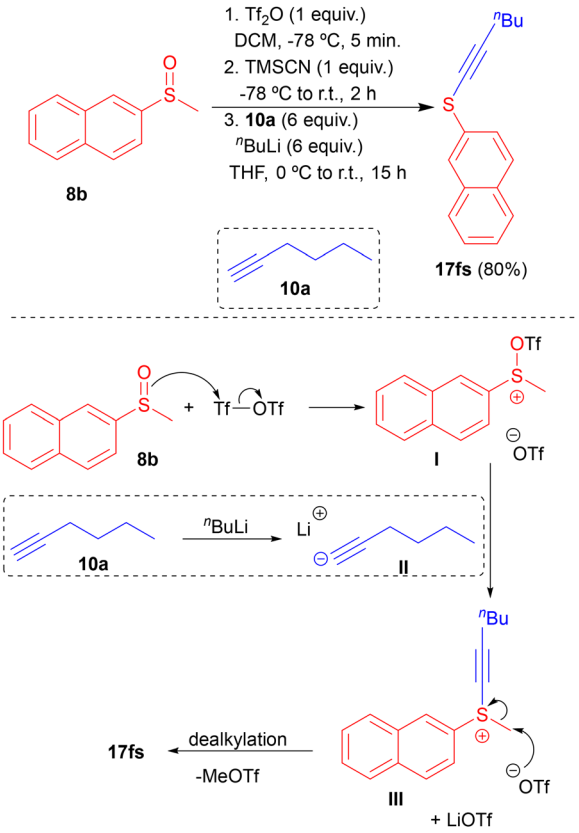
In 2021, Wang and co-workers[52] reported a visible-light-promoted coupling reaction to obtain the alkynyl sulfides **33** by reaction of bromoalkynes **13** with 2,2′-diaminodiaryldisulfides **16c** (Scheme 48). In this approach, the amino group present in the disulfides is essential to promote the reaction. Moreover, this method featured several advances, being metal-, additive-, and photocatalyst-free. The starting materials, bromoalkynes **13** with 2,2′-diaminodiaryldisulfides **16c** were reacted in the presence of blue LED's (450–455 nm) in DCM as solvent under an N_2 atmosphere for 12 h (Scheme 48). Under these conditions, several target alkynyl sulfide **33** (21 examples) were synthesized in yields ranging from moderate to good (40–83%) influenced by electronic effects. For example, aryl alkynes (**13**) substituted with EDGs at the *para* position of the aromatic ring gave the target products (**33c** and **33b**) in higher yields (R = Me, 82%; R = OMe, 78%) compared to those bearing EWGs. In these cases, the products **33k** and **33l** were obtained in slightly poor yields (R = CN, 62% and R = NO_2, 40%, respectively) (Scheme 48). Additionally, the method was also sensitive to steric effects: when *ortho*-substituted aryl alkynes were used, the desired products **33n** and **33o** were obtained in educed yields (R = 2-Me, 63% and R = 2-Cl, 54%, respectively) compared to their *para*-substituted analogues, which afforded the compounds **33c** and **33i** in 82% (R = 4-Me) and 70% (R = 4-Cl), respectively. Still, the influence of heteroaryl (2-Th) and alkyl (^{n}Pent and ^{n}Pr) alkynes in this method was checked, the alkynyl sulfides **33s**, **33t** and **33u** were obtained in 54%, 64% and 53%, respectively (Scheme 48).

The mechanism proposed by the authors to synthesize alkynyl sulfides **33** starts with the homolytic cleavage of 2,2′-diaminodiphenyl disulfide **16c** induced by visible light, affording intermediate **I**. Additionally, the authors noted that this free-radical intermediate **I** may be stabilized through a weak H-bond. Subsequently, the formation of a vinylic intermediate **II**, occurs after the addition of intermediate **I** to bromoalkyne **13**. Finally, the alkynyl sulfides **33** are formed after the elimination step of intermediate **II** (Scheme 49).



Scheme 49 Proposed mechanism for light-assisted thioalkyne **33** synthesis.[52]

In 2021, Maulide and co-workers[53] reported a protocol for the synthesis of thiocyanates *via* the dealkylative cyanation of sulfoxides. Among the various products obtained, the formation of the alkynyl sulfide, 2-(methylsulfinyl)naphthalene hex-1-yne **17fs** was particularly noteworthy, achieving 80% yield under mild conditions (Scheme 50). The reaction process involves three steps, beginning with the electrophilic activation of the sulfoxide by trifluoromethanesulfonic anhydride (Tf_2O) in DCM at −78 °C, followed by the addition of trimethylsilyl cyanide (TMSCN) as the temperature gradually rises to room temperature. Simultaneously, a solution of hex-1-yne **10a** in THF is cooled and treated with *n*-butyllithium to generate the corresponding alkynyl lithium species. This nucleophile then reacts with the activated sulfonium intermediate, forming a new C–S bond. Finally, dealkylation promoted by the triflate anion furnishes the thiolated product **17fs**, with methyl triflate as a byproduct (Scheme 50). Thus, the method is operationally simple and provides access to structurally diverse thiocyanates, including the highlighted alkynyl sulfide (Scheme 50).

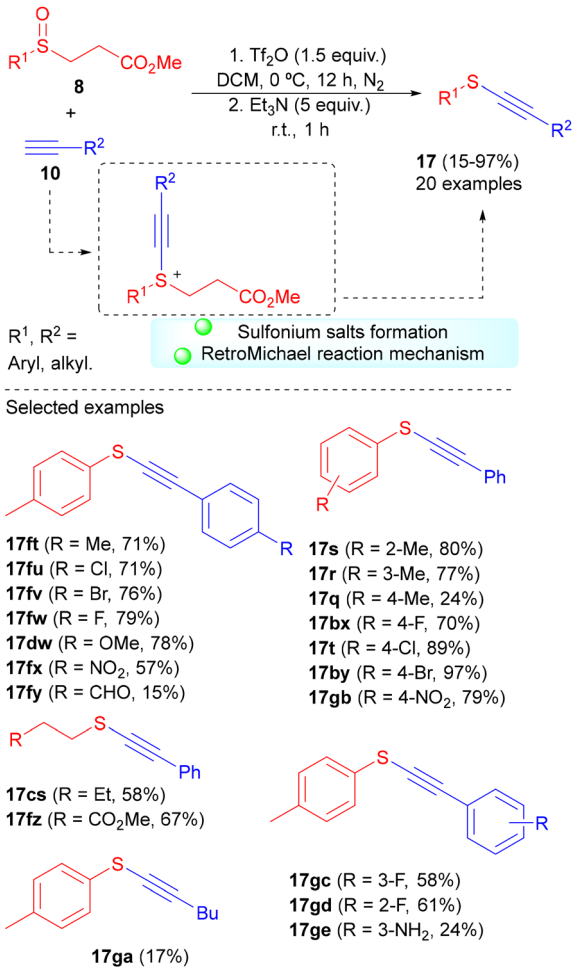


Scheme 50 Synthesis of the alkynyl sulfide **17fs** *via* triflate activation by Maulide and co-workers in 2021.[53]

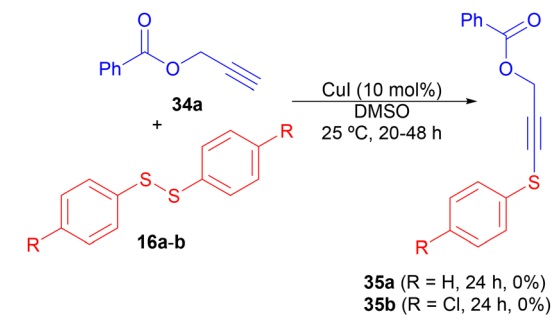
Cheng and co-workers, in 2021,[54] reported a metal-free protocol for the synthesis of alkynyl sulfides **17** using β-sulfinylesters **8** and terminal alkynes **10** by direct $C_{(sp)}$–H thiolation reaction (Scheme 51). In this approach, sulfinylesters **8** are used as a versatile sulfur source, affording sulfonium salts *in situ* after reaction with terminal alkynes **10**. The target products **17** are then formed through chemoselective C–S bond cleavage of the sulfonium salts, this being a key step in the formation of the desired product **17** (Scheme 51). Additionally, mechanistic studies revealed that the acrylate byproduct was captured, supporting a retro-Michael reaction mechanism. In this protocol, a wide range of both starting materials β-sulfinylesters **8** and terminal alkynes **10** were reacted in a two-step protocol, first, 1.5 equiv. of Tf_2O were added to the reaction medium in DCM as solvent at 0 °C, under N_2 atmosphere (Scheme 51). After 12 h of reaction, 5 equiv. of Et_3N are added to the reaction at r.t., and the reaction was stirred for an additional 1 h. Under these reactional conditions, several organyl alkynyl sulfides **17** (20 examples) were synthesized in yields ranging from lower to excellent yields (15–97%). This approach was efficient to a wide range of both starting materials substituted **8** and **10** with EDG and EWG attached in the aromatic ring, however, lower yields were obtained when the 3-ethynylaniline, 4-ethynylbenzaldehyde and hex-1-yne were reacted under standard conditions (Scheme 51). In these cases, the products **17ge**, **17fy** and **17ga** were obtained in only 24%, 15% and 17% of yield, respectively. A similar result was observed when methyl 3-(*p*-tolylsulfinyl) propanoate was reacted with phenylacetylene under standard conditions, giving the target alkynyl sulfide **17q** in 24% yield (Scheme 51).

The protocol described by Godoi and co-workers[55] in 2021 for the synthesis of alkynyl selenides (section 4, Scheme 94) was also tested with other dichalcogenide starting material, when **34a** was reacted with diaryl disulfide **16a–b** instead of diaryl diselenides or ditellurides, the protocol proved inefficient under the standard conditions, as the compounds **35a** and **35b** were not obtained (Scheme 52).

In 2022, Zhao and co-workers[56] reported the synthesis of alkynyl sulfides **17** from the reaction of terminal alkynes **10** with *N*-thiosuccinimides **36** in a Cu-catalyzed protocol. This efficient protocol offers the advantages of using odorless and bench-stable thiolating reagents and enables the synthesis of a

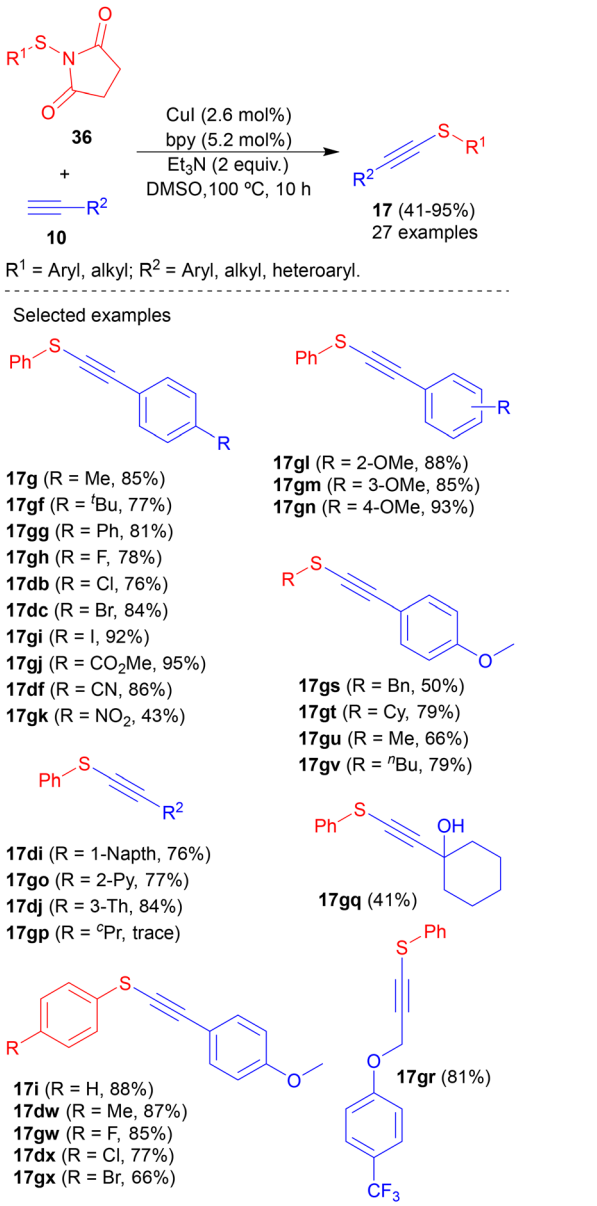


Scheme 51 Alkynyl sulfide **17** synthesis *via* sulfonium salts intermediates described by Cheng and co-workers 2021.[54]



Scheme 52 Cu-catalyzed extended trials for the synthesis of alkynyl sulfides **35a–b** described by Godoi and co-workers in 2021.[55]

broad scope of products **17** tolerating a wide range of functional groups (Scheme 53). The best conditions were established by the authors when several terminal alkynes **10** and *N*-thiosuccinimides **36** were reacted in the presence of 2.6 mol% CuI, 5.2 mol% Bpy, and 2 equiv. Et_3N in DMSO at 100 °C for 10 h. In general, this approach was not sensitive to the electronic effects of EDG and EWG attached to the aromatic ring of terminal alkynes **10**, with the exception of 1-ethynyl-4-nitrobenzene, which afforded the target product **17** in low yield (43%). Under these conditions, the method gave the target alkynyl sulfides **17** (containing both EWG and EDG) in comparable yields (76–92%) (Scheme 53). Similarly, the method was also not sensitive to steric effects: when substituted terminal alkyne **10** with a methoxy group attached at the *ortho*, *meta* and *para* positions of the aromatic ring were evaluated under standard conditions, the target products **17gl**, **17gm** and **17gn** were obtained in yields of 88%, 85% and 93%, respectively. Additionally, when terminal alkynes containing 1-naphthyl and heteroaryl (2-pyridinyl and 3-thienyl) were evaluated, the method was also efficient giving the alkynyl sulfides **17di**, **17go** and **17dj** in yields of 76%, 77% and 84%, respect-



Scheme 53 Cu/bpy-catalyzed alkynyl sulfide **17** synthesis described by Zhao and co-workers in 2022.[56]

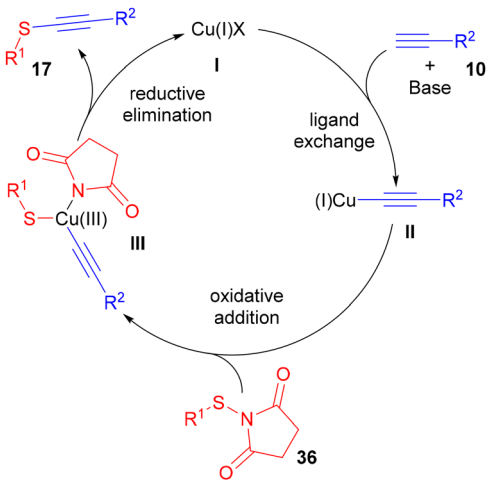
ively. Alkyl terminal alkynes were also tested, affording compounds (**17gq** and **17gr**) in 41% and 81% yield, respectively (Scheme 53). On the other hand, when ethynylcyclopropane was used, the desired product **17gp** was not formed. Gratifyingly, the authors extended the protocol to aryl and alkyl *N*-thiosuccinimides **36**, affording the alkynyl sulfides products S-Bn (**17gs**), S-Cy (**17gt**), S-Me (**17gu**) and S-Bu (**17gv**) in 50%, 79%, 66% and 79% yield, respectively, (Scheme 53).

The plausible mechanism proposed by the authors starts with the formation of an active copper acetylide **II** through the reaction of the Cu(I)X **I** catalyst with an alkyne **10** in the presence of a base *via* a ligand exchange step. Subsequently, this Cu-intermediate **II** undergoes an oxidative addition with *N*-thiosuccinimide **36**, forming to form the copper(III) intermediate **III**, which then undergoes reductive elimination to afford the target alkynyl sulfides **17** and the copper catalyst **I** is regenerated, initiating a new catalytic cycle (Scheme 54).

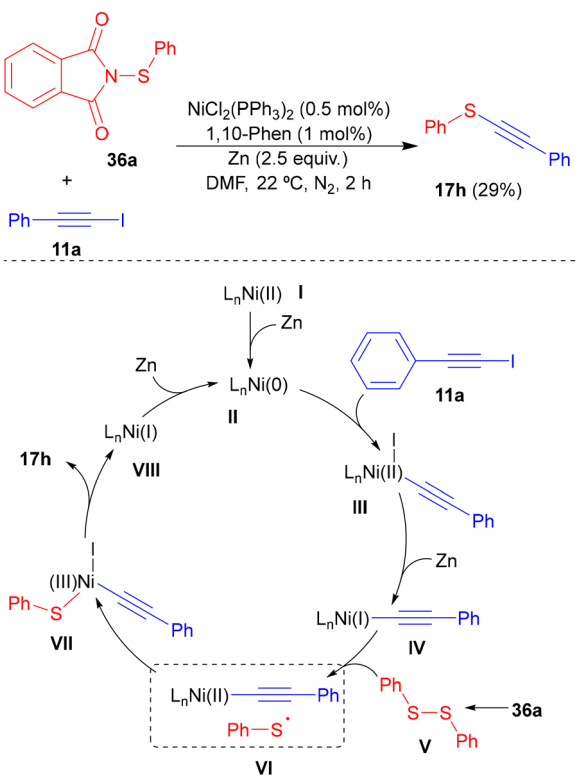
In 2022, Shao and co-workers[57] reported the thiolation reaction by $C_{(sp)}$–S bond formation between *N*-thiophthalimides **3a** with organic halides. In this protocol, the synthesis and application of efficient electrophilic sulfur transfer reagents were described, with the *N*-thiophthalimides **36** serving as direct thiolating surrogates (Scheme 52). In this method, a wide range of diorganyl sulfides were synthesized using organyl halides. For instance, when (iodoethynyl)benzene **11a** was reacted with 2-(phenylthio)isoindoline-1,3-dione **36a** (Scheme 52). Using 0.5 mol% of $NiCl_2(PPh_3)_2$ as the catalyst, 1 mol% of 1,10-phen as the ligand, 2.5 equiv. of Zn, DMF, at 22 °C under N_2 atmosphere for 2 h. The reductive cross-coupling product (**17h**) was obtained in low yield (29%) (Scheme 52). The plausible mechanism for the formation of alkynyl sulfide **17h** in the nickel-catalyzed reductive thiolation process was proposed by the authors. It starts with the reduction of LnNi(I) **I** to form the active catalyst species LnNi (0) **II**. Subsequently, this species **II** reacts with the (iodoethynyl)benzene **11a**, undergoing oxidative addition to give intermediate **III**, which, in the presence of Zn, is reduced to afford intermediate **IV**. In parallel, the corresponding *N*-thiophthalimides **36a** generate diphenyl disulfide **V**, which reacts with the previously formed intermediate **IV** to yield intermediate **VI**. Next, this intermediate **VI** generates the adduct intermediate **VII** which, after reductive elimination, produces the target alkynyl sulfide **17h** and regenerates the LnNi(I) **VIII** species. Finally, this species **VIII** is reduced in the presence of Zn to regenerate the active catalyst species **II**, completing a new catalytic cycle (Scheme 55).

In 2023, Saito and Euteneuer[58] reported the synthesis of alkynyl sulfides **17** in a one-pot, three-component protocol, starting from 2-((4-chlorobenzyl)sulfinyl)pyridine **8c**, two Grignard reagents and trimethylsilyl chloride **37a** (Scheme 56). This approach uses the 2-((4-chlorobenzyl)sulfinyl)pyridine **8c** as the sulfur source, which reacts with (3-methoxyphenyl)magnesium bromide **37a** in THF for 15 min. Subsequently, 1.5 equiv. of TMSCl is added to the reaction, which is maintained at −78 °C for 30 min. Finally, the (organylethynyl)lithium species **19′** is added at −78 °C and stirred for 1 h to give the target alkynyl sulfides **17** (Scheme 56). When the (phenylethynyl)lithium and (cyclopropylethynyl)lithium were used as starting materials under standard conditions, the target compounds **17ca** and **17gy** were synthesized in yields of 71% and 68%, respectively (Scheme 56).

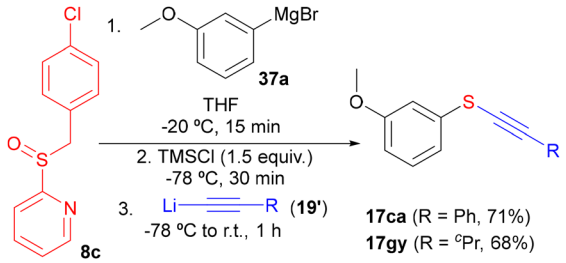
In 2023, Rong and co-workers[59] reported a metal-free protocol for the direct thiolation of terminal alkynes **10** using



Scheme 54 Proposed mechanism for the Cu-catalyzed synthesis of alkynyl sulfide **17**.[56]



Scheme 55 Ni-catalyzed alkynyl sulfide **17h** synthesis and mechanism described by Shao and co-workers in 2022.[57]



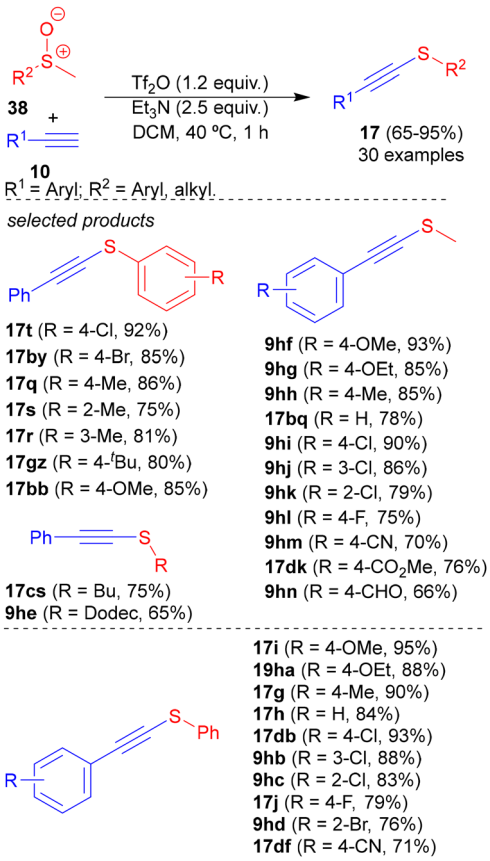
Scheme 56 Alkynyl sulfide **17ca** and **17gy** synthesis *via* organometallic route by Saito and Euteneuer in 2023.[58]

phenylacetylene derivatives **10** and either methyl sulfoxides **38**, affording alkynyl sulfides **17**. The transformation was carried out by reacting phenylacetylenes **10** with methyl sulfoxides **38** (1.2 equiv.) and trifluoromethanesulfonic anhydride (Tf_2O, 1.2 equiv.) in the presence of triethylamine (Et_3N, 2.5 equiv.). The reaction mixture was stirred at 40 °C, furnishing 30 target compounds **17** in isolated yields ranging from 65% to 95% (Scheme 57). The method also was extended to obtain alkynyl selenide using methyl phenyl selenoxides, which are described in section 4, Scheme 104.

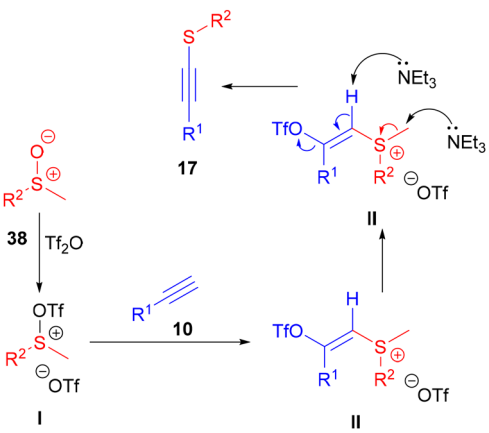
The proposed mechanism in this study involves a direct reaction between methyl sulfoxides **38** and alkynes **10**, leading to the formation of a vinyl intermediate **II**. Subsequently, deprotonation of the vinyl moiety by triethylamine (Et_3N) occurs, followed by the elimination of the triflate group (TfO) from the substrate. This sequence regenerates the carbon–carbon triple bond, affording the desired product **17** (Scheme 58).

In 2023, Xie and Liu[60] developed a new metal-free protocol to obtain alkynyl sulfides **17** using hexafluoroisopropanol (HFIP) a promoter for the reaction between *N*-thiosuccinimides **36** and silyl alkynes **39a**. This straightforward protocol to access alkynyl sulfides **17** involves reacting trimethyl(phenylethynyl)silane **39a** with *N*-arylthiosuccinimides **36** in the presence of 0.5 mL of HFIP per 0.1 mmol of alkyne, at 100 °C for 12 h (Scheme 59). A total of 3 examples of desired compound **17** were synthesized using these conditions, in which the target compounds (4-chlorophenyl)(phenylethynyl)sulfide **17t**, 1-(4-((phenylethynyl)thio)phenyl)ethan-1-one **17ho** and (2-fluorophenyl)(phenylethynyl)sulfide **17hp** were obtained in yields of 66%, 73% and 70%, respectively. It is important to emphasise that the silyl group is crucial for the success of the transformation (Scheme 59). Additionally, the authors extended the protocol to obtain (alkynyl)(trifluoromethyl)sulfides which are described in section 5.1, Scheme 110.

The proposed mechanism for the synthesis of alkynyl sulfides **17** promoted by HFIP, begins with the interaction of HFIP with the *N*-thiosuccinimides **36**, forming intermediate **I**, which is in resonance with the intermediate **II**. Subsequently, the active sulfenyl cation (RS+) **III** and hexafluoro alkoxy anion **IV** were formed. The hexafluoro alkoxy anion **IV** interacts with the silyl atom of the silyl alkynyl starting material **39a** to form the intermediate **V**, which reacts with the sulfenyl cation (RS+) **III** to afford the intermediate **VII** after the electrophilic cyclization step. Finally, the target product **17** is formed after desilicification of intermediate **VI** (Scheme 60).

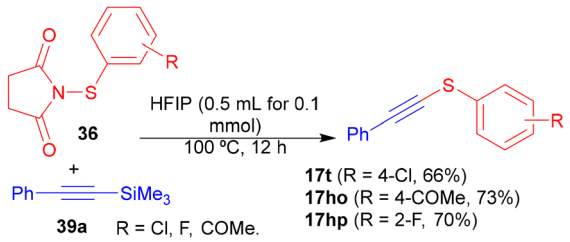


Scheme 57 Tf_2O-mediated alkynyl sulfide **17** synthesis developed by Rong and co-workers in 2023.[59]

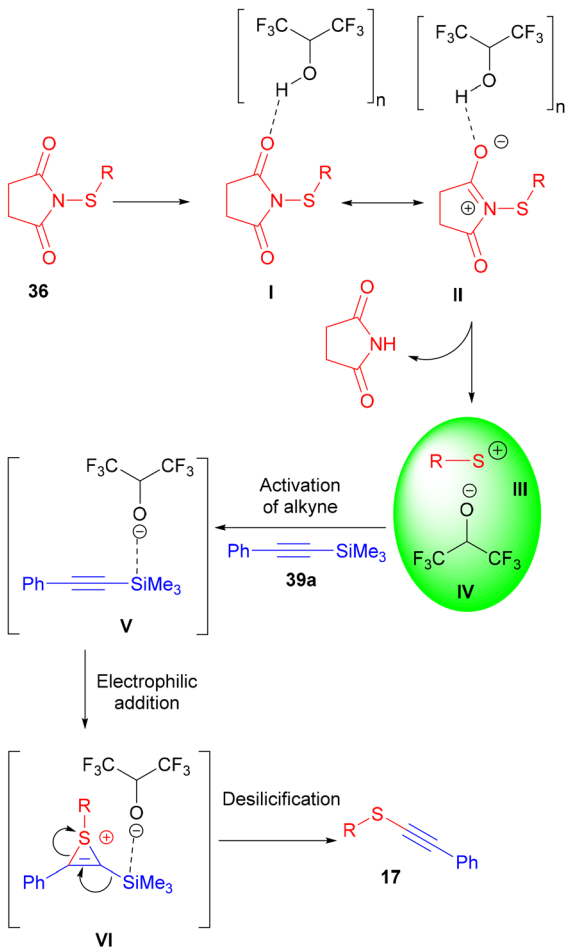


Scheme 58 Proposed mechanism for Tf_2O-mediated process.[59]

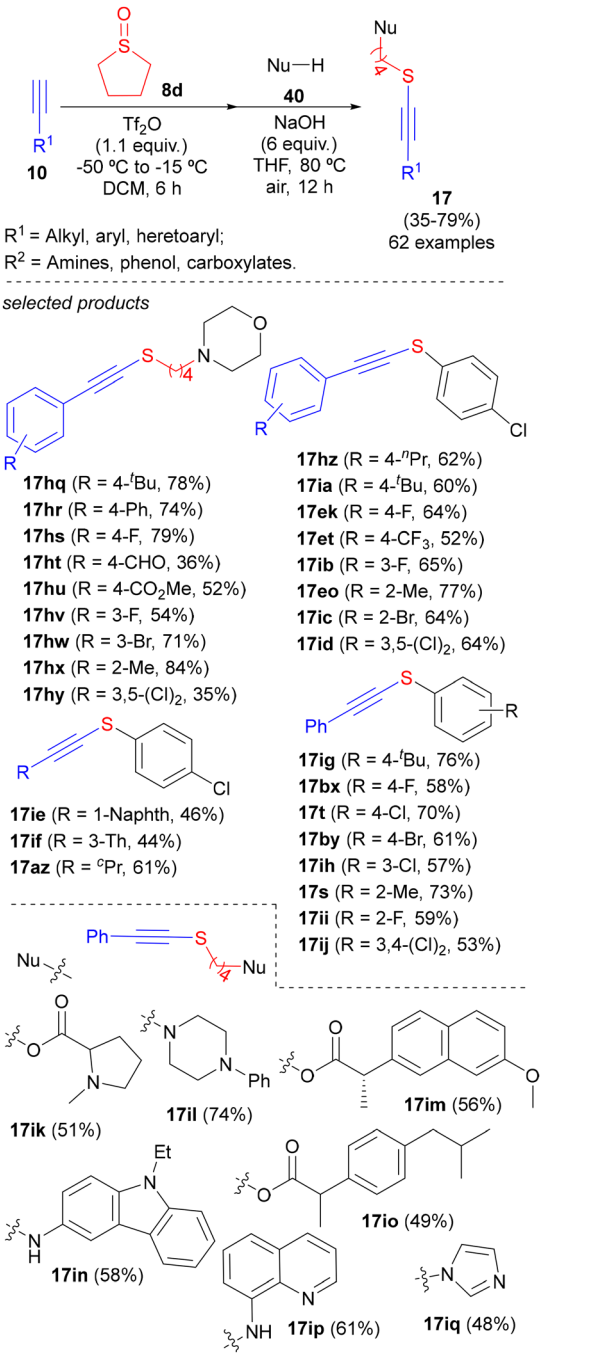
In 2024, Wen and co-workers[61] reported a practical and efficient strategy for the selective synthesis of alkynyl sulfides **17** through the cleavage of C–S bonds in alkynyl sulfonium salts. This one-pot, two-step process begins with the electrophilic activation of the alkyne **10** using 1.1 equiv. of trifluoromethanesulfonic anhydride (Tf_2O) in dichloromethane at low temperatures (−50 to −15 °C) to form the corresponding sulfonium salt,



Scheme 59 HFIP-promoted alkynyl sulfides (**17t**, **17ho** and **17hp**) synthesis described by Xie and Liu in 2023.[60]



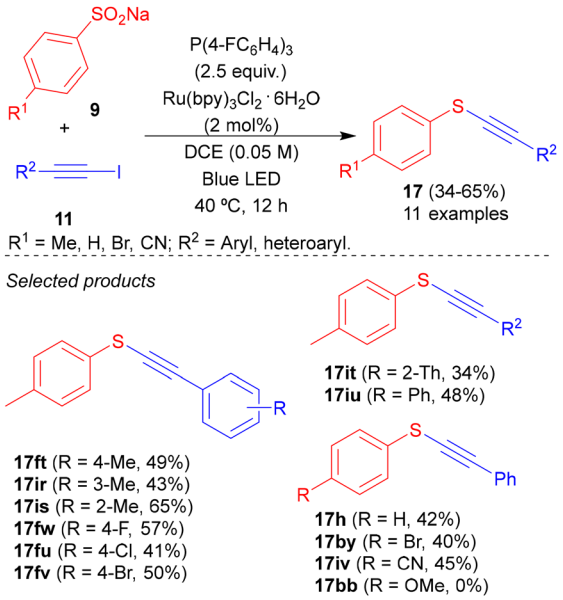
Scheme 60 Proposed mechanism for the HFIP-promoted alkynyl sulfides **17** synthesis.[60]



Scheme 61 Tf_2O-mediated synthesis of thioalkynes **17** with different nucleophiles **40** described by Wen and co-workers in 2024.[61]

followed by base-promoted C–S bond cleavage with 6 equiv. of NaOH in THF at 80 °C under air for 12 h. The method exhibits broad functional group tolerance, applying alkyl, aryl, and heteroaryl substituents, as well as different nucleophiles. A large scope of 62 products **17** were synthesized in yields ranging from 35% to 79% (Scheme 61). The methodology also proved suitable for the incorporation of more complex nucleophiles **40**, enabling the late-stage functionalization of bioactive molecules and pharmaceuticals, such as natural product derivatives, nitrogen-containing heterocycles, and drug-like scaffolds. These examples demonstrate the method's range and its value for bioactive and complex molecule modification, highlighting its versatility and practicality (Scheme 61).

In 2025, Chen, Yu and Chen[62] developed a visible-light phosphine-mediated deoxyfunctionalization protocol of sodium arylsulfinates **9** in reaction with several iodoalkynes **11**, affording the target alkynyl sulfides **17** (Scheme 62). This protocol is the first example of directly obtaining to obtain directly the target alkynyl sulfide **17** through the reaction of



Scheme 62 Visible-light Ru-catalyzed alkynyl sulfide **17** synthesis by Chen, Yu and Chen in 2025.[62]

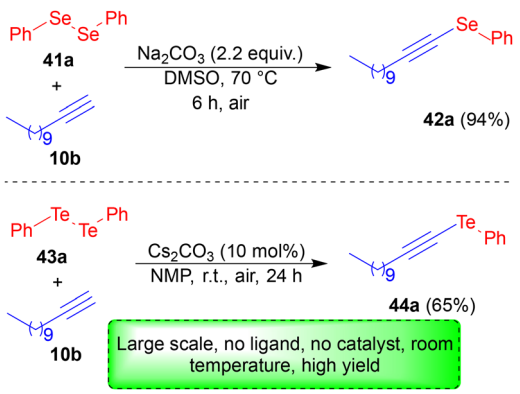
sulfinate salts **9** as starting materials. It is important to emphasize that the use of acidic additives (such as HCl) facilitates the generation of arylthiyl radicals thereby favoring thioesters while disfavoring the formation of alkynyl sulfides **17** (Scheme 62). The best conditions identified by the authors involved the reaction of sodium arylsulfinates **9** with iodoalkynes **11** in the presence of 2.5 equiv. of $P(4\text{-}FC_6H_4)_3$, 2 mol% $Ru(bpy)_3Cl_2{\cdot}6H_2O$, in dichloroethane (DCE, 0.05 M) under blue LED's irradiation at 40 °C for 12 h. Under these conditions, several alkynyl sulfides **17** (11 examples) were synthesized in yields ranging from low to good (34–65%). This protocol was not sensitive to electronic and steric effects of EWG and EDG attached to the aromatic ring of aryl iodoalkynes **11**; in these cases, the target compounds **17** were obtained in moderate yields (Scheme 62). On the other hand, the same effect was not observed when substituents bonded in the sulfinate salts **9** were evaluated. In this case, the presence of EWG attached to the aromatic ring of sulfinates salts afforded the desired alkynyl sulfides **17by** and **17iv** in moderate yields (R = Br, 40% and R = CN, 45%, respectively), while the presence of EDG ones no reaction was observed. Additionally, the protocol was extended to alkynyl substituted with heteroaryl groups under standard conditions, affording the desired alkynyl sulfide **17it** in low yield (34%) (Scheme 62).

4 Alkynyl selenides and tellurides: emerging chalcogen-containing alkyne

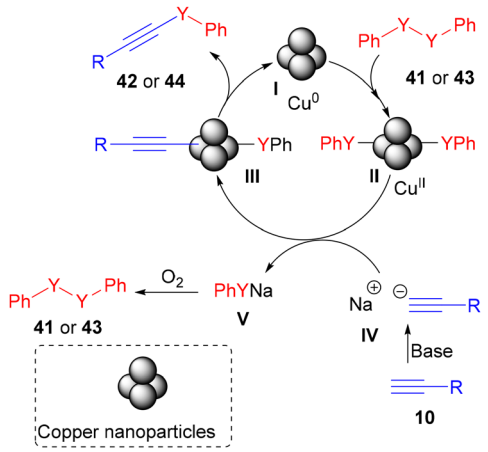
In contrast to the more extensively explored sulfur analogues, alkynyl selenides and tellurides represent a less common yet highly intriguing class of chalcogen-containing compounds. The presence of organic selenium or tellurium groups bonded with an alkyne unit imparts distinctive electronic and chemical properties, often translating into unique reactivity profiles. These features make them attractive intermediates in synthetic organic chemistry, particularly in the development of functionalized heterocycles, organometallic transformations, and materials-oriented applications. Although their synthesis has been historically less developed, recent years have witnessed significant advances, including transition-metal-catalyzed procedures and innovative coupling strategies that enable the efficient construction of these motifs. In this section, we summarize the principal methodologies reported for the preparation of alkynyl selenides and tellurides, with emphasis on their synthetic potential and emerging relevance.

In addition to the synthesis of alkynyl sulfides **17** (section 3, Scheme 29), Park and co-workers[39] also reported the synthesis of alkynylphenyl selenide **42** and telluride **44**. When the authors performed the reaction of diphenyl diselenide **41a** with 1-dodecyne **10b** under similar conditions, the target alkynyl selenide **42a** was obtained in excellent yield (94%) after a shorter reaction time (6 h) and under an air atmosphere, which served as the oxidant (Scheme 63). On the other hand, for the alkynyl telluride **44a**, the use of copper nanoparticles as a catalyst was not necessary. Diphenyl ditelluride **43a** reacted with 1-dodecyne **10b** in the presence of only 10 mol% Cs_2CO_3 as the base and *N*-methyl-2-pyrrolidone (NMP) as the solvent at room temperature. Under these mild conditions, the alkynyl telluride **44a** was formed in 65% yield after a reaction time of 1 day (Scheme 63).

The proposed mechanism described by the authors starts with the formation of intermediate **II** through the oxidative addition of Cu(0) **II** to diphenyl dichalcogenide **41** or **43** (Y = S, Se). In parallel, alkyne **10** reacts with the base to afford ionic intermediate **IV**, which then reacts with previously formed intermediate **II** to give intermediate **III**. Subsequently, the target alkynyl chalcogenide **42** or **44** is obtained *via* the reductive elimination step of intermediate **III**, regenerating catalyst **I** for a new catalytic cycle. In addition, the ionic species **V**



Scheme 63 Base-mediated synthesis of alkynyl selenides **42a** and **44a** and tellurides by Park and co-workers in 2015.[39]

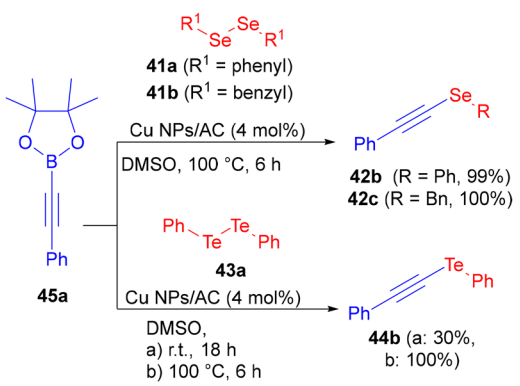


Scheme 64 Proposed mechanism for the synthesis of alkynyl chalcogenides **42** or **44**.[39]

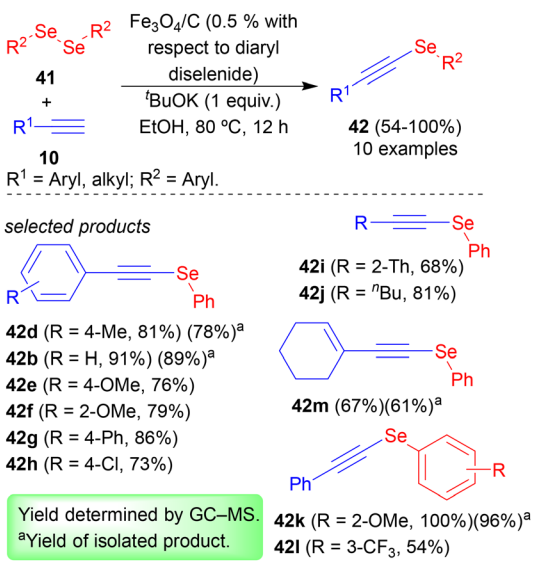
formed undergoes an oxidation step to regenerate the diphenyl dichalcogenide **41** or **43** within the reaction system (Scheme 64).

In 2015, Park and co-workers[63] reported the synthesis of organyl alkynyl selenides **42** and tellurides **44** from alkynylboronic acid **45a** derivatives and diorganyl dichalcogenides **41** or **43**, using copper nanoparticles as the catalyst. In their study, diaryl diselenide **41** and diphenyl ditelluride **41a–b** or **43a** were employed as selenium and tellurium sources, respectively (Scheme 65). The synthesis of organyl alkynyl selenides **42** was achieved through the reaction of diphenyl or dibenzyl diselenide **41a–b** with 2-phenyl-1-ethynylboronic acid pinacol ester **45a** (2.2 equiv.), catalyzed by supported copper nanoparticles (CuNPs/AC, 4 mol%) in DMSO at 100 °C for 6 h. Under these conditions, the desired products **42b** and **42c** were obtained in excellent yields (99% and 100%, respectively). For the synthesis of alkynyl tellurides **44b**, a similar protocol was employed (Scheme 65). The reaction between diphenyl ditelluride **43a** and 2-phenyl-1-ethynylboronic acid pinacol ester **45a** (2.2 equiv.), using CuNPs/AC (4 mol%) in DMSO at room temperature for 18 h, resulted in a moderate yield of the target compound **44b** (30%). However, when the temperature was increased to 100 °C and the reaction time reduced to 6 h, the yield improved dramatically, reaching 100%. This study highlights an efficient and sustainable approach for the preparation of alkynyl chalcogenides **42** or **44** from alkynylboronic acids **45**, employing copper nanoparticles as a reusable catalyst under mild and environmentally friendly conditions (Scheme 65).

Park and co-workers[64] reported in 2016 the synthesis and application of magnetite (Fe_3O_4) nanoparticles supported on charcoal as a heterogeneous catalyst for the formation of new C–Se bonds (Scheme 66). This catalyst was efficiently employed to promote C–H and Se–Se bond activation in the cross-coupling reaction of several terminal alkynes **10** with diaryl diselenide **41** (Scheme 66). The optimal conditions involved small amounts of Fe_3O_4/C catalyst (0.5% with respect to diaryl diselenide **41**), 1 equiv. of ^{t}BuOK in EtOH as solvent at 80 °C for 12 h to synthesize the desired alkynyl selenide **42** (10 examples) in yields ranging from moderate to quantitative (54–100%) (Scheme 66). This method proved efficient for several aryl terminal alkynes **10**, which provided the desired compounds **42** in generally good yields (73–91%). Furthermore, heteroaryl and alkyl terminal alkynes **10** were also tested, giving alkynyl selenide **42i**, **42j** and **42m** in yields of 68%, 81% and 67%, respectively (Scheme 66). The approach was found to be sensitive to the electronic effect of substituents attached to the aromatic ring of diaryl diselenides **41**. For example, when phenylacetylene was reacted under standard conditions with 1,2-bis(2-methoxyphenyl) diselenide (containing the EDG), the target product **42k** was obtained quantitative yield (100%, compound **42k**), compared with the reaction using 1,2-bis(3-(trifluoromethyl)phenyl) diselenide, which afforded alkynyl selenide **42l** in 54% yield (Scheme 66). Additionally, the authors evaluated the recyclability of the cata-



Scheme 65 Alkynyl chalcogenides (**42b**, **42c** and **44b**) synthesis described by Park and co-workers in 2015.[63]



Scheme 66 Fe_3O_4/C-catalyzed synthesis of alkynyl selenides **42** developed by Park and co-workers in 2016.[64]

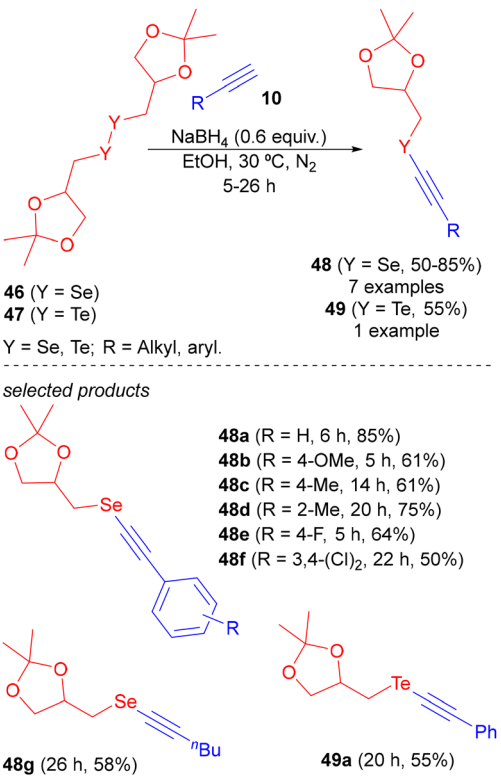
lyst, which retained excellent activity and could be reused up to five times without significant loss of efficiency.

Focused on the synthesis of water-soluble organochalcogen compounds, Perin and co-workers[65] reported in 2016 the preparation of alkynyl and vinyl chalcogenides. The reaction between terminal alkynes **10** and glycerol-derived dichalcogenides **46** or **47** is solvent-dependent and highly selective. When polyethylene glycol-400 (PEG-400) was used as the solvent, the reaction produces vinyl chalcogenides, whereas in EtOH the target glycerol-derived alkynyl selenide **48** was formed. The best conditions were established by the authors when several terminal alkynes **10** reacted with glycerol-derived diselenides **46** in the presence of 0.6 equiv. $NaBH_4$, with EtOH as the solvent at 30 °C under N_2 atmosphere (Scheme 67). After reactional times of 5–26 h, 7 examples of alkynyl selenides **48** were obtained in yields ranging from moderate to good (50–85%) (Scheme 67). This protocol was efficient for both aryl and alkyl terminal alkynes **10**. When 1-hexyne was employed as the starting material under standard conditions, the target product **48g** was obtained in a moderate yields (58%), after 26 h. Additionally, when glycerol-derived diselenides **46** were replaced by glycerol-derived ditelluride **47** in the reaction with phenylacetylene, the target alkynyl telluride **49a** was obtained in modest yield (55%) after a longer reaction time (20 h), compared with the corresponding alkynyl selenide **48a** (6 h, 85%) (Scheme 67). Finally, the authors perform the deprotection of the ketal unit of in alkynyl selenide **48a**, using the acidic cation-exchange resin Dowex-(H^+), afforded the water-soluble organochalcogen compounds (3-((phenylethynyl)selanyl) propane-1,2-diol) in moderate yield (60%).

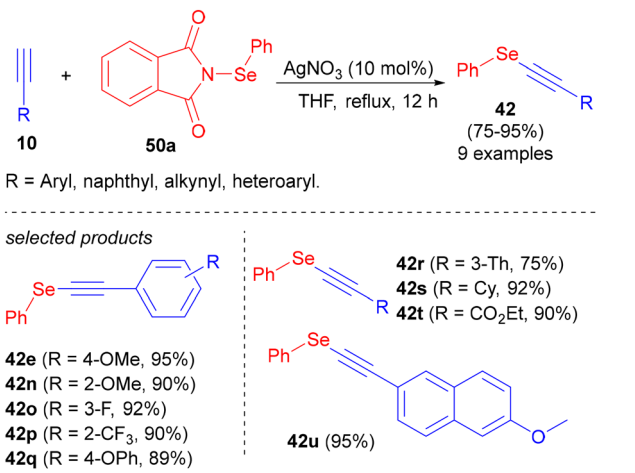
In 2017, Ranu and co-workers[66] described the first silver-catalyzed phenylselenylation using *N*-(phenylseleno)phthalimide **50a** as the selenium source (Scheme 68). Compared to the commonly used selenylating reagents (PhSeSePh, PhSeCl, PhSeBr, PhSeCN), this reagent represents an alternative and less explored selenium source. The optimal conditions consisted of refluxing a mixture of the terminal alkynes **10** and *N*-(phenylseleno)phthalimide **50a** in the presence of $AgNO_3$ (20 mol%) as the Lewis acid catalyst, using dry THF as the solvent for 12 h to afford the target compounds **42** (9 examples) in good yields (75–95%). This method was not sensitive to electronic effects, and was successfully to several aryl terminal alkynes **10** bearing different EDG and EWG substituents on the aromatic ring, affording the target alkynyl selenides **42** in excellent yields (89–95%). Alkynes **10** substituted with heteroaryl (thienyl), alkyl (cyclohexyl and ethyl carboxylate) and polyaromatic (5-acenaphthene) groups were also evaluated as starting materials; in these cases, compounds **42r**, **42s**, **42t** and **42u** were obtained in yields of 75%, 92%, 90% and 95%, respectively (Scheme 68).

The proposed mechanism reported by authors starts with the coordination of Ag^+ to the selenium atom of *N*-(phenylseleno)phthalimide **50a**, thereby increasing the electrophilicity of the –SePh fragment (intermediate **I**). In parallel, Ag^+ also coordinates with terminal alkyne **10**, which subsequently reacts with intermediate **I**, to afford alkynyl selenide **42**, along with *N–H* phthalimide **II** as a side product (Scheme 69).

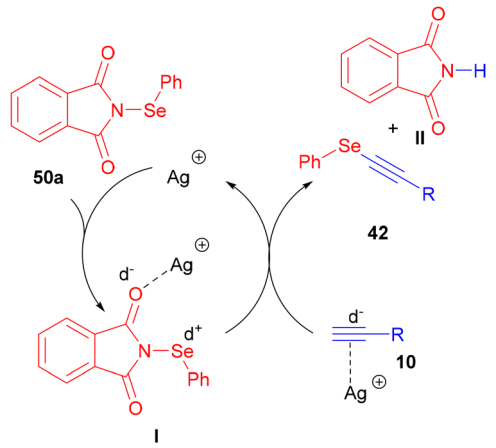
Organic selenocyanates represent a versatile and synthetically valuable class of organoselenium compounds. Numerous methodologies have been developed for their efficient preparation, and they serve as key intermediates in diverse organic transformations.[67] In 2017, Ranu and co-workers[68] reported the silver-catalyzed decyanative, non-conventional cross-coup-



Scheme 67 $NaBH_4$-mediated alkynyl seleinides **48** and telluride **49** synthesis described by Perin and co-workers in 2016.[65]

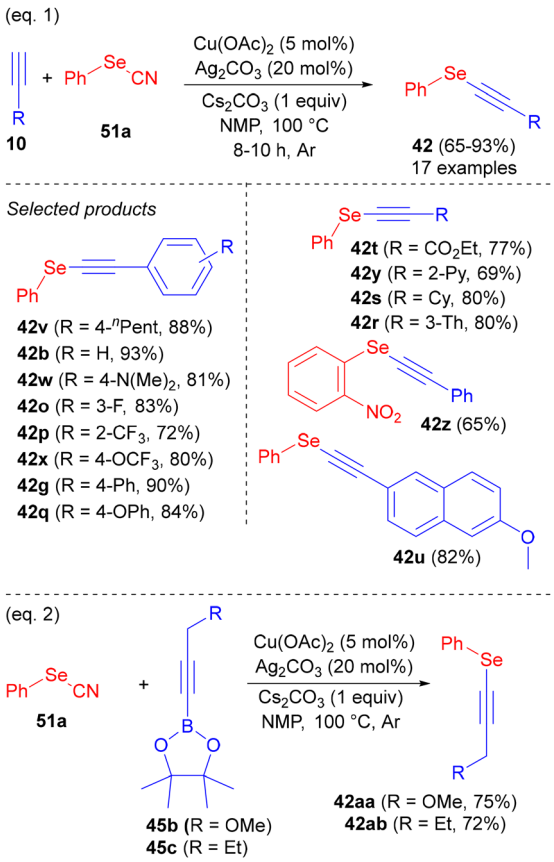


Scheme 68 Ag-catalyzed alkynyl selenides **42** synthesis by Ranu and co-workers in 2017.[66]



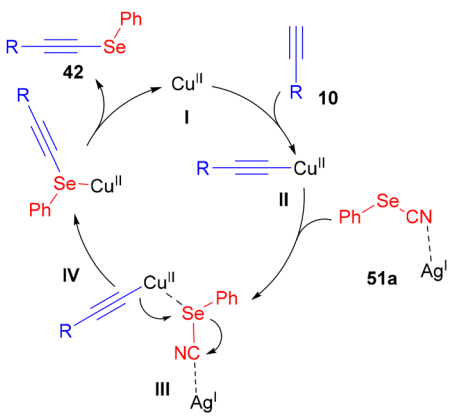
Scheme 69 Proposed mechanism for the Ag-catalyzed process for the synthesis of alkynyl selenide **42**.[66]

ling of terminal alkynes **10** with phenyl selenocyanates **51a** to afford alkynyl selenides **42** (Scheme 70, eqn (1)). The optimal conditions involved the reaction of a broad range of terminal alkynes **10** with phenylselenocyanate **51a** in the presence of 5 mol% of $Cu(OAc)_2$ as the catalyst, 20 mol% Ag_2CO_3, and 1.0 equiv. Cs_2CO_3 in *N*-methylpyrrolidinone (NMP) at 100 °C for 8–10 h. The alkynyl phenyl selenide **42** (17 examples) were obtained in good to excellent yield (65–93%) (Scheme 70, eqn (1)). This approach tolerated aryl alkynes bearing EDG and EWG substituents on the aromatic ring, as well as polyaromatic compounds; for example, naphthalene derivative product **42u** was obtained in 82% of yield. Additionally, alkynes containing heteroaryl groups (thiophene and pyridine), were also examined, affording compounds **42r** and **42y** in 80% and 69% yield, respectively (Scheme 70, eqn (1)). The use of an alkynyl pinacol ester **45b–c** instead of a terminal alkyne **10** was also evaluated under the standard conditions. In these cases, the target alkynyl phenyl selenides **42aa** and **42ab** were obtained in good yields (75% and 72%, respectively) (Scheme 70, eqn (2)).

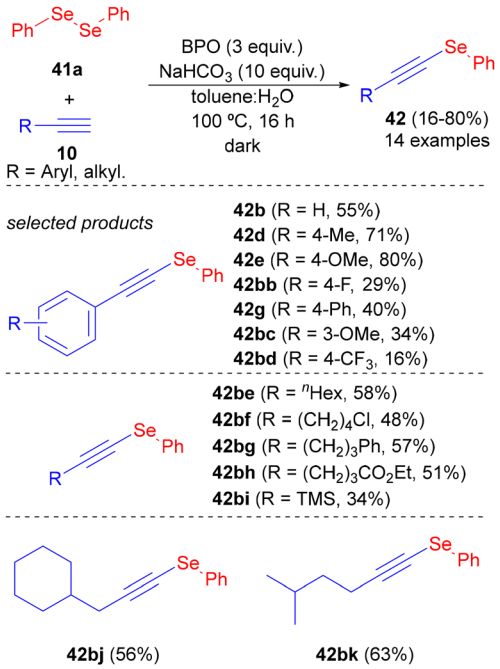


Scheme 70 Cu/Ag-catalyzed synthesis of alkynyl selenides **42** reported by Ranu and co-workers in 2017.[68]

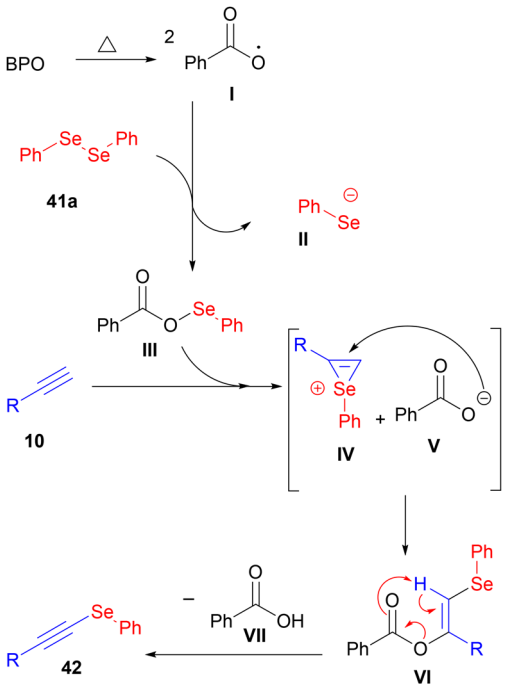
In 2017, Ogawa and co-workers,[69] developed a metal-free protocol based on binary systems composed of benzoyl peroxide (BPO) and diorganyl diselenide **41a** to promote the formation of C–Se bonds using alkynes. When internal alkynes were used, benzoyloxyselenation of the alkyne unit was observed. In contrast, when terminal alkynes **10** were used, the reaction was selective, affording the target alkynyl phenyl selenide **42** (Scheme 72). This approach involves the reaction of diphenyl diselenide **51a** with terminal alkynes **10** in the presence of 3 equiv. of BPO and 10 equiv. of $NaHCO_3$, in a toluene : H_2O solvent mixture at 100 °C for 16 h, in the dark. Under these conditions, several alkynyl phenyl selenides **42** (14 examples) were obtained in yields ranging from low to excellent (16–80%). The protocol was sensitive to electronic effects; when aryl terminal alkynes **10** bearing EWG substituents were used, the target products were formed in lower



Scheme 71 Proposed mechanism of Cu/Ag dual catalysis for the synthesis of alkynyl selenide **42**.[68]



Scheme 72 Alkynyl selenide **42** synthesis developed by Ogawa and co-workers in 2017.[69]

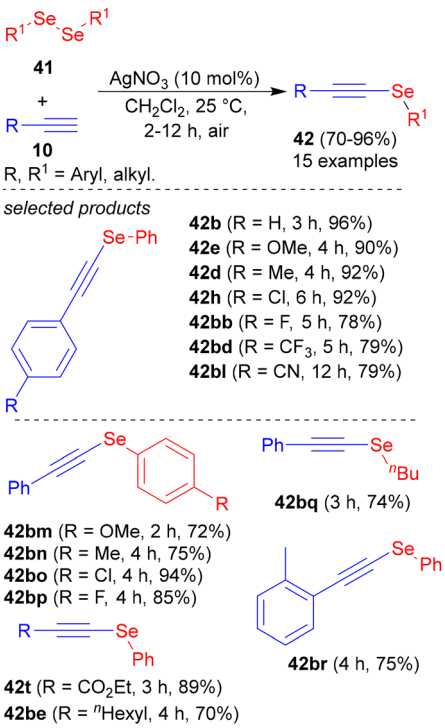


Scheme 73 Proposed mechanism of BPO-initiated selenylation for the synthesis of alkynyl selenide **42**.[69]

yields compared to those with EDG substituents. For example, the compounds **42bb** and **42bd** were formed in 29% (R = 4-F) and 16% (R = 4-CF_3) yields, respectively, whereas compounds **42d** (R = 4-Me) and **42e** (R = 4-OMe) were synthesized in 71% and 80% yield, respectively (Scheme 72). Additionally, this approach was efficiently extended to alkyl alkynes **10** under the standard conditions, where the target alkynyl selenides **42be–bk** were generally obtained in moderate yields (48–63%). Ethynyltrimethylsilane was also used as starting material; in this case, trimethyl((phenylselanyl)ethynyl)silane **42bi** was isolated in 34% yield (Scheme 72).

A plausible mechanism proposed by the authors begins with the formation of benzoyloxy radicals **I** through thermal decomposition of BPO. Subsequently, this radical intermediate **I** reacts with diphenyl diselenide **41a** to generate the key intermediate benzoyloxy phenyl selenide **III**. Next, the seleniranium ion **IV** is formed after the reaction terminal alkyne **10** with the intermediate **III**. This intermediate gives the intermediate **VI** after attack of benzoyloxy anion **V**. Finally, elimination of benzoic acid **VII** from the vinylic intermediate **VI** affords the target alkynyl selenide **42** (Scheme 73). The electrophilic selenium species is benzoyloxy selenide **III** (PhC(O)O-SeAr), which is the key intermediate in the reaction. It was isolated in 95% yield and characterized by ^{77}Se nuclear magnetic resonance (NMR) after several control experiments.

In 2017, Alves and co-workers[70] described the direct C–H functionalization of terminal alkynes using silver nitrate as a catalyst, to promote the new C–Se bond formation (Scheme 74). In this approach, a wide range of alkynyl selenides **42** (15 examples) were synthesized in yields ranging from



Scheme 74 Ag-catalyzed diselenide coupling with alkynes described by Alves and co-workers in 2017.[70]

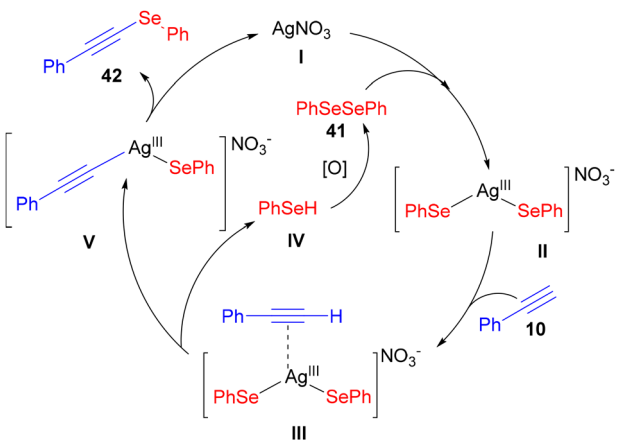
good to excellent (70–96%), with short reaction times. The optimal conditions were established by reacting several terminal alkynes **10** and diorganyl diselenides **41** in the presence of

10 mol% of $AgNO_3$ as the catalyst, in DCM at 25 °C. This cross-coupling protocol was sensitive to the electronic effects of substituents attached to the arylalkynes **10**, the presence of EWG afforded products in lower yields (**42bb**, R = 4-F, 78%–5 h; **42bl**, R = 4-CN, 79%–5 h; **42bd**, R = 4-CF_3, 79%–12 h and **42bh**, R = 4-Cl, 92%–6 h) when compared with EDG ones (**42e**, R = 4-OMe and **42d**, R = 4-Me, 90%–4 h and 92%–4 h, respectively). On the other hand, when diaryl diselenides bearing substituents **41** were evaluated, an opposite effect was observed. This approach was efficient for alkyl substituent in both starting materials, which yielded the products **42be** (R = ^{n}Hexyl) and **42bq** (R = ^{n}Bu) in 70% (4 h) and 74% (3 h), respectively (Scheme 74).

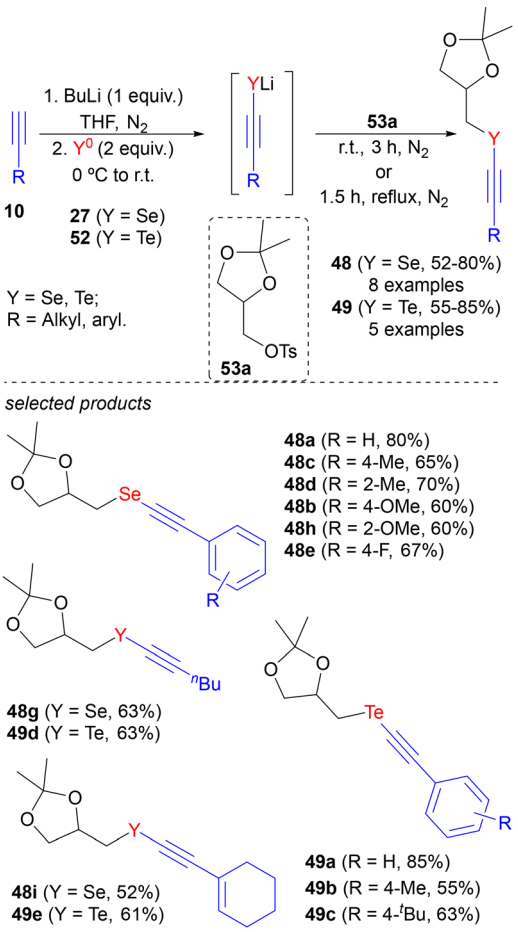
The mechanism proposed by the authors starts with an oxidative addition step, in which diorganyl diselenide **41a** reacts with the silver catalyst **I** ($AgNO_3$) to generate intermediate **II** (Scheme 75). Subsequently, intermediate **II** undergoes complexation with arylacetylene **10**, forming intermediate **III**. This species then evolves to generate intermediates **IV** and **V**. Intermediate **IV** is oxidized, regenerating the diorganyl diselenide **41a** for a new cycle, while silver nitrate **I** is also regenerated for the next catalytic cycle following the reductive elimination step of **V**, which yields the target alkynyl selenide **42** (Scheme 75). Additionally, further studies were conducted by the authors to gain deep insight into the reaction pathway. Intermediate **V** was identified by high-resolution mass spectrometry (HRMS) in ESI(+)-MS mode and confirmed by ^{77}Se NMR analysis.

Focused on obtaining water-soluble organochalcogen, in the following year (2017), the same research group[71] developed an alternative protocol to synthesize alkynyl tellurides **49**, overcoming the limitations of the previous study, in which only one example of an alkynyl telluride was synthesized **49** (Scheme 67, compound **49a**). This efficient protocol is based on the *in situ* formation of lithium alkynylchalcogenolate intermediates, which affords the target glycerol-derived alkynyl selenide **48** and telluride **49** *via* nucleophilic substitution on tosylated solketal **53a** (Scheme 76). The optimal conditions identified by the authors involved reacting aryl or alkyl terminal alkynyl with 1 equiv. of ^{n}BuLi in THF under a N_2 atmosphere, followed by the addition of 2 equiv. of elemental chalcogen (Y^0) at 0 °C to form the reactive alkynylchalcogenolate anion intermediates. Subsequently, the tosylated solketal **53a** was added to the reactional mixture to undergo nucleophilic substitution, promoting the synthesis of alkynyl chalcogenides **48** or **49** (13 examples) in good yields (52–85%) (Scheme 76). When elemental selenium **27** was used, 8 examples of alkynyl selenides **48** were formed in yields ranging from 52% to 80%. Additionally, the authors extended the protocol to elemental tellurium **52**, which afforded the target alkynyl tellurides **49** (5 examples) in comparable yields (55–85%) to those of the selenides. This protocol was not sensitive to the nature of the chalcogen atom, as both alkynyl selenides **48** and tellurides **49** were obtained in similar yields (Scheme 76).

In 2017, Peñéñory and co-workers[72] reported a practical and efficient approach to the synthesis of alkynyl selenides through a one-pot, three-step process. A key aspect of the method is that it avoids the need for diorganyl diselenides, organoselanyl halides, or selenolate anions as starting materials, using instead commercially available potassium



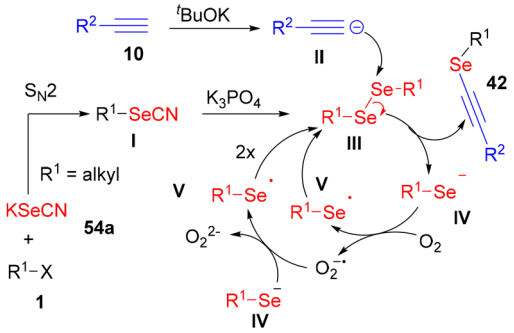
Scheme 75 Ag-mediated mechanism for Se-alkyne bond formation.[70]



Scheme 76 Synthesis of alkynyl selenides **48** and tellurides **49** described by Perin and co-workers in 2017.[71]

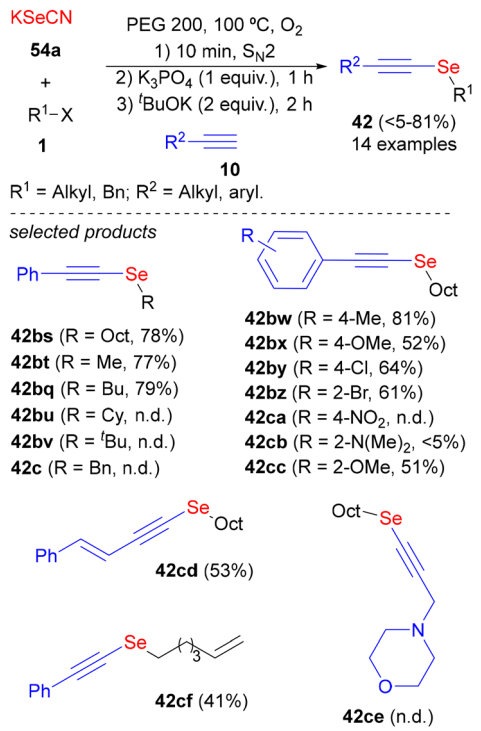
selenocyanate **54a** and alkyl halides **1**. The reaction is carried out in polyethylene glycol-200 (PEG-200) under an oxygen atmosphere in the presence of 1 equiv. of K_3PO_4 and 2 equiv. of *t*-BuOK. Under these conditions, diorganyl diselenides are generated *in situ via* nucleophilic substitution of alkyl halides, followed by their reaction with terminal alkynes **10** to afford the desired alkynyl selenides **42**. The method allowed the synthesis of 14 different compounds **42** with yields ranging from 5% to 81% (Scheme 77). The yields of the alkynyl selenide products vary significantly depending on the substituents present on the aryl ring **42**, for instance, *para*-substituted electron-donating groups such as 4-methyl (81%) **42bw** and 4-chloro (64%) **42by** lead to relatively good yields, indicating compatibility with the reaction conditions. Substituents in the *ortho* position, like 2-bromo (61%) **42bz** and 2-methoxy (51%) **42cc**, showed moderately reduced yields, likely due to steric hindrance affecting the reactivity of the arylacetylene **10**. On the other hand, strongly electron-donating groups like 2-dimethylamino (**42cb**) and electron-withdrawing groups like 4-nitro (**42ca**) afforded very low or undetectable yields, suggesting that both pronounced electronic effects and steric bulk can hinder the formation of the desired products. These results highlight the importance of considering both electronic and steric factors in determining the efficiency of the reaction (Scheme 77).

To account for the results obtained, the authors proposed a reaction mechanism for the formation of alkynyl selenides **42** (Scheme 78). The sequence begins with a nucleophilic substitution between an alkyl halide **1** and potassium selenocyanate **54a**, generating an alkyl selenocyanate **I**. Upon addition of K_3PO_4, this intermediate is efficiently converted to a dialkyl diselenide **III**. Next, the introduction of an arylacetylene **10** and ^{t}BuOK leads to the formation of the corresponding arylacetylide anion **II**, which then attacks the dialkyl diselenide **III**, yielding the target selenide and an alkyl selenolate species **IV**. Importantly, since the reaction is carried out under an oxygen atmosphere, molecular oxygen reoxidizes the selenolate **IV** back into the corresponding diselenide **III**, enabling a regenerative cycle that continues until complete consumption of the selenolate species **IV** (Scheme 78).

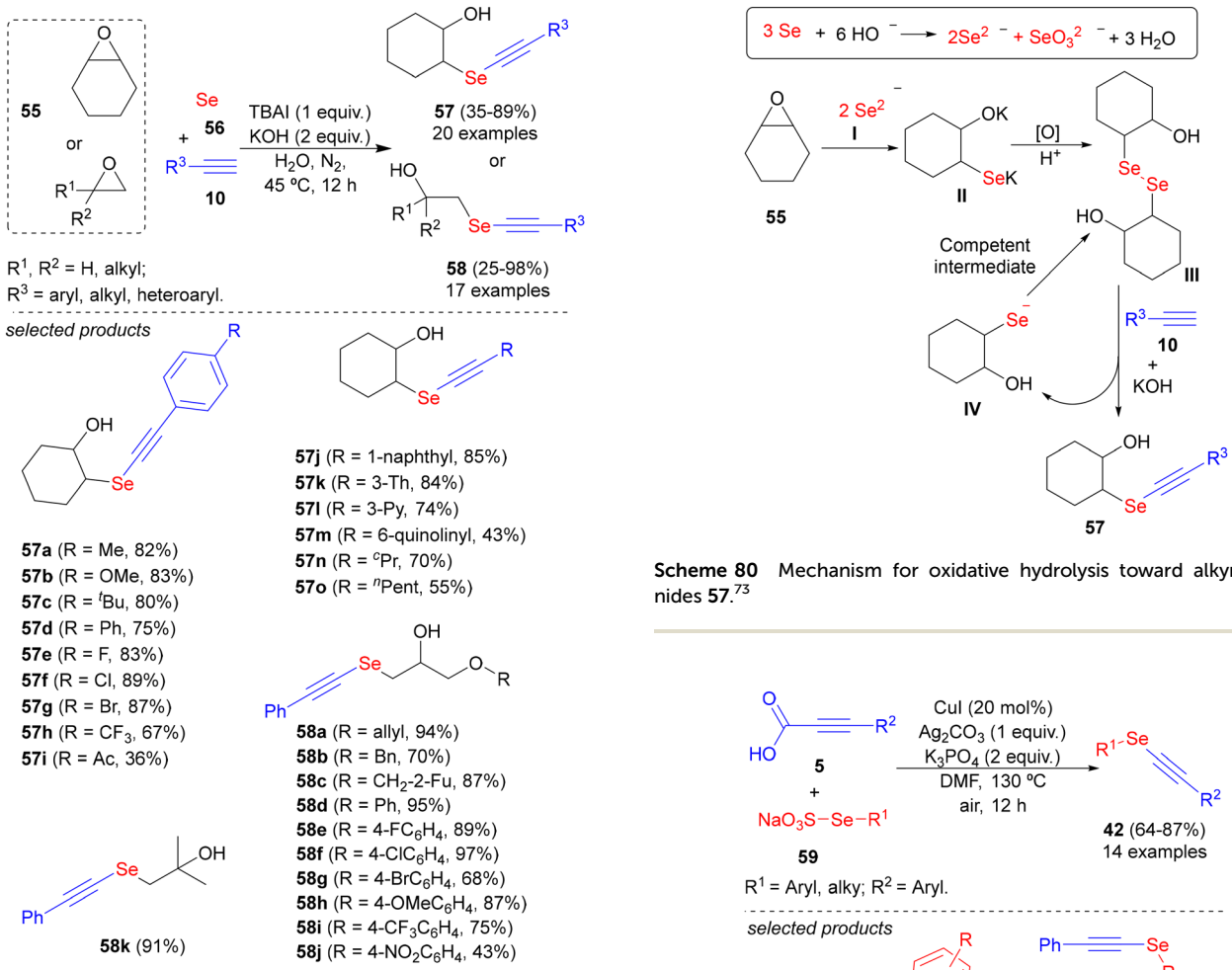


Scheme 78 Radical pathway leading to alkynyl selenides **42**.[72]

In 2018, Wu and co-workers[73] introduced a novel and eco-friendly approach for the synthesis of alkynyl alkyl selenides **57** or **58** through a metal-free three-component coupling reaction involving epoxides **55**, elemental selenium **56**, and terminal alkynes **10** (Scheme 79). A key feature of the methodology relies on the dual role of elemental selenium. Initially, selenium acts as an oxidant, facilitating the formation of selenide anions. These intermediates subsequently react with epoxides **55** to generate active dialkyl diselenide species, which then undergo coupling with terminal alkynes **10** to yield the desired selenides **57** or **58**. This tandem process highlights the operational simplicity of the transformation. Thus, using 2 equiv. of KOH as the base, 1 equiv. of TBAI as a phase transfer catalyst, H_2O as the solvent, at 45 °C for 12 h, total of 37 different molecules were synthesized (**57** and **58**), with yields ranging from 25% to 98%, by varying both the alkyne **10** and epoxide components **55**. The study also demonstrated the applicability of the methodology across a broad substrate scope, including the late-stage functionalization of bioactive compounds such as pargyline. Furthermore, gram-scale reactions confirmed the robustness and scalability of the process, key factors for future applications in organic synthesis and pharmaceutical development. From a green chemistry perspective, the method stands out for its use of water as a solvent, operational simplicity, low-cost reagents, and broad functional group tolerance. It offers a promising alternative to traditional methods by avoiding heavy metals or harsh conditions, representing a sustainable and versatile route for the integration of selenium-based units into organic molecules (Scheme 79).



Scheme 77 Synthesis of alkynyl selenides **42** from KSeCN **54a** developed by Peñéñory and co-workers in 2017.[72]

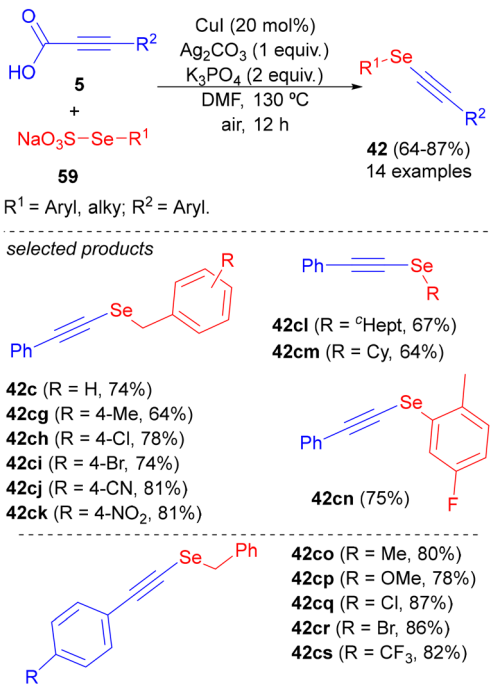


Scheme 79 Synthesis of alkynyl selenides **57** and **58** reported by Wu and co-workers in 2018.[73]

With support from both experimental data and previous literature, the authors proposed a plausible mechanism for the double C–Se bond formation observed in this transformation (Scheme 80). According to the proposed pathway (Scheme 80) elemental selenium **56** first undergoes disproportionation under basic conditions, generating a selenide anion **I**. This reactive species then attacks epoxide **55**, resulting in a ring-opening process that yields an alkylselenide anion **II**. Subsequent oxidative homo-coupling of this intermediate leads to the formation of diselenide **III**. Finally, in the presence of a base, the terminal alkyne **10** undergoes alkylselenation with diselenide to afford the desired alkynyl alkyl selenide product **57** (Scheme 80).

In 2018, Liu and Yi[45] reported a selenol-free, copper-catalyzed method for the synthesis of alkynyl selenides **42** by decarboxylative cross-coupling of alkynyl carboxylic acids **5** with selenium-based Bunte salts **59**. The reaction was performed using CuI (20 mol%) as the catalyst, Ag_2CO_3 (1 equiv.) as the oxidant, and K_3PO_4 (2 equiv.) as the base in DMF at 130 °C for 12 h under air, affording 14 alkynyl selenides **42** in yields ranging from64% to 87% yields (Scheme 81). A key strength of

Scheme 80 Mechanism for oxidative hydrolysis toward alkynyl selenides **57**.[73]



Scheme 81 Alkynyl selenides **42** synthesized by Cu/Ag dual catalysis developed by Liu and Yi in 2018.[45]

the method is its broad tolerance toward electronic and structural diversity in both coupling partners. The electronic effect was examined by the authors, who evaluated several EDG and EWG attached in the aromatic ring. In this regard, the reaction proceeded smoothly with electron-donating groups such as methyl (80%) **42co** and methoxy (78%) **42cp**, as well as with halogenated substituents like fluoro (75%) **42cn**, chloro (87%) **42cq** and bromo (86%) **42cr**. Similar results were observed for

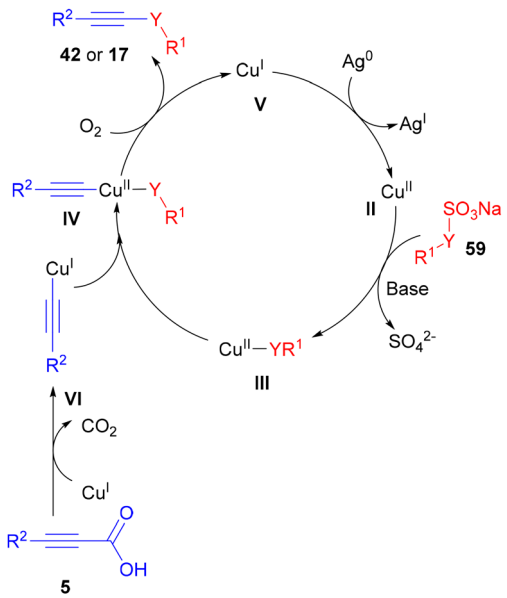
strongly EWG substituents such as trifluoromethyl (82%) **42cs**, cyano (81%) **42cj**, and nitro (81%) **42ck**. This highlights the robustness of the method across different electronic conditions, likely due to the resilience of the copper intermediate and the stable generation of the selenide nucleophile under oxidative conditions. Overall, the method stands out by enabling the construction of diverse organoselenium compounds using air-stable, inexpensive, and easily handled precursors, without relying on air-sensitive and malodorous selenol reagents (Scheme 81). These features make it a highly practical approach for the synthesis of bioactive organochalcogenides. In addition, this methodology was also applied to the synthesis of organosulfides, which are described in section 3, Scheme 37.

In the mechanism proposed by the authors, and supported bycontrol experiments showing that Ag_2CO_3 is essential for the oxidative step, that CuI is required for the reaction to proceed, and that a (phenylethynyl)copper species is likely generated during decarboxylation, the Bunte salt **59** initially reacts with a copper(II) intermediate to form a copper chalcogenide species **III**, releasing SO_3 from the Bunte salts, which is converted to a sulfate anion under basic conditions. This intermediate **III** then undergoes ligand exchange with the metal phenylacetylide **VI**, forming an alkynyl copper complex **IV**. A subsequent reductive elimination from this complex **IV** yields the desired alkynyl chalcogenide product **42** or **17** and regenerates the Cu(I) species. Finally, Cu(I) **V** is oxidized back to Cu(II) **I** by a silver species, thus completing the catalytic cycle (Scheme 82).

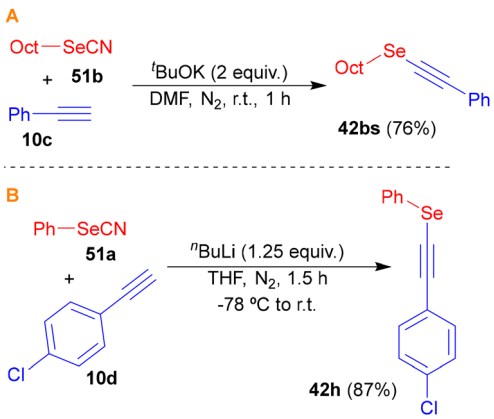
As a complementary extension of the work reported in 2019 by Yang, Tian, and Zhang[46] (discussed in section 3, Scheme 38), the authors expanded their methodology to the synthesis of alkynyl selenides **42**. In the first example, octyl selenocyanate **51b** was reacted with phenylacetylene **10c** under conditions analogous to those used for alkynyl sulfide formation, with ^{t}BuOK (2 equiv.) as the base in DMF under a nitrogen atmosphere at room temperature for 1 h. Using this protocol, the desired alkynyl selenide **42bs** was obtained in 76% yield after just 1 h (Scheme 83A). In a second approach, they employed ^{n}BuLi (1.25 equiv.) in THF at −78 °C to room temperature to promote the coupling between phenyl selenocyanate **51a** and the 4-chlorophenylacetylene **10d**, achieving the corresponding product **42h** in 87% yield in 1.5 h (Scheme 83B). Together, these results show the adaptability of the protocol to selenocyanates and the efficiency of both base-mediated and lithium-mediated strategies for C–Se bond formation (Scheme 83).

In 2019, Schneider and co-workers[74] developed a mild, and efficient synthetic protocol for the preparation of chalcogenoacetylenes *via* copper-selanylpyrazole catalysis (Scheme 84). The reaction involves the coupling of acetylenes **10** with diorganyl dichalcogenides **41** or **43**, using an equimolar mixture (5 mol%) of CuI and an arylselanylpyrazole **A** ligand as the catalytic system. The transformation proceeds smoothly at room temperature under aerobic conditions, employing 1 equiv. of Cs_2CO_3 as the base and DMSO as the solvent, with a short reaction time of just 25 minutes. A total of 13 selanylalkynes **42** were obtained, with yields ranging from low (14%, compound **42ct**) to very good (88%, compound **42cv**), demonstrating the catalyst's broad functional group tolerance. The scope was also extended to include a tellurium-substituted alkyne (**44b**, 38% yield) and a sulfur-containing alkyne (**17h**, 84% yield), using diphenyl ditelluride and thiophenol as the respective chalcogen sources (Scheme 84).

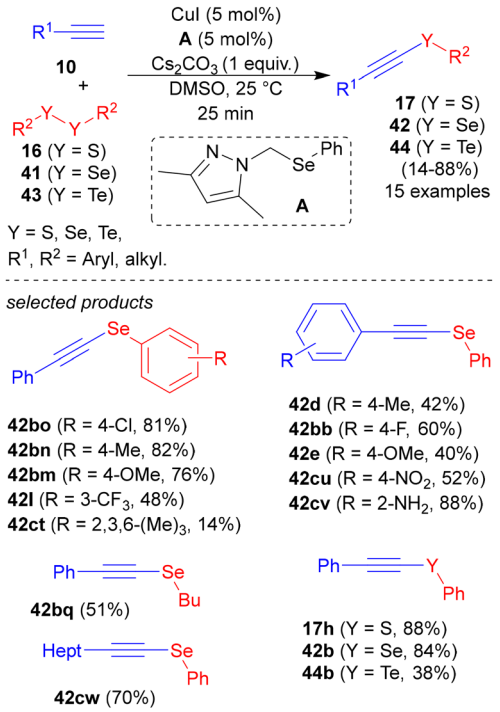
The authors proposed a mechanism in which the catalytic cycle begins with the oxidative addition of diaryl dichalcogenide **41** or **43** to the copper center, forming an intermediate complex **II**. The formation of this intermediate **II** was corroborated by ESI-HRMS and ^{77}Se NMR analyses. These results also support the behavior of the arylselanylpyrazole ligand, which plays a key role in facilitating the oxidative addition step by enabling flexible coordination to the metal center. In the next



Scheme 82 Proposed mechanism for the copper-mediated synthesis of alkynyl chalcogenides **42** or **17**.[45]

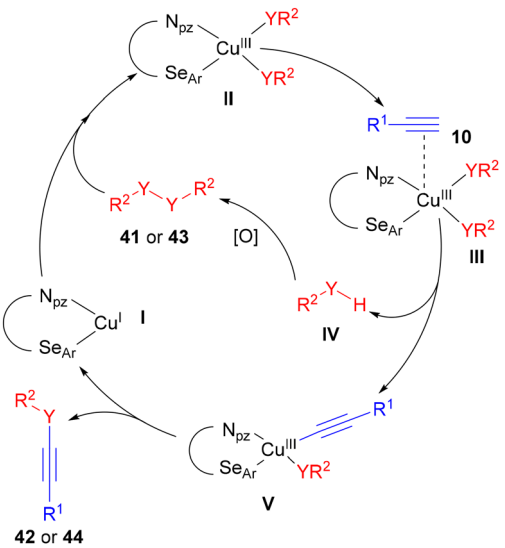


Scheme 83 Synthesis of alkynyl selenides **42bs** (A) and **42h** (B) reported by Yang, Tian, and Zhang in 2019.[46]



Scheme 84 Synthesis of alkynyl chalcogenides (**17**, **42** and **44**) *via* Cu-catalysis described by Schneider and co-workers in 2019.[74]

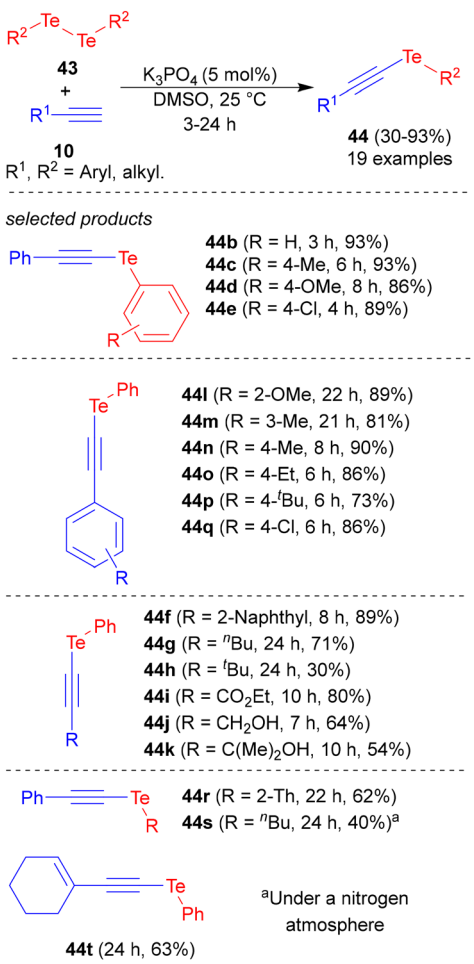
step, the terminal alkyne **10** coordinates to the copper complex **II** through a π-complex, forming another intermediate **V** and the selenochalcogenol **IV** (Scheme 85). This specie **IV** generates the diaryl dichalcogenide **41** or **43**. Finally, the intermediate **V** undergoes reductive elimination to yield the desired chalcogenoacetylene products **42** or **44** and regenerate the active catalyst (Scheme 85).



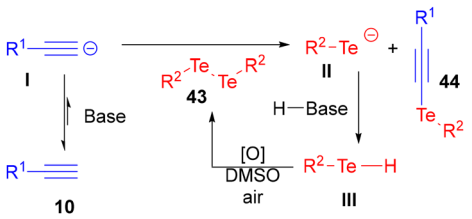
Scheme 85 Proposed mechanism for Cu-catalyzed chalcogen-alkyne **42** or **44** formation.[74]

In 2019, Alves and co-workers[75] reported a metal-free synthetic protocol for the synthesis of alkynyl tellurides **44** by reacting terminal alkynes **10** with diorganyl ditellurides **43**, using K_3PO_4 (5 mol%) as a base/catalyst in DMSO at room temperature under an air atmosphere. This methodology stands out for its mild conditions not requiring transition metal catalysts, which are commonly required in previous protocols (Scheme 86). A broad scope of 19 alkynyl telluride derivatives **43** were successfully synthesized, with isolated yields ranging from 30% to 93% and reaction times varying between 3 and 24 h depending on the substrate combination (Scheme 86). When dibutyl ditelluride was used as a starting material, the reaction had to be conducted under a nitrogen atmosphere, likely due to the air sensitivity of the product **44s**, which may undergo decomposition in the presence of oxygen. The method tolerated a variety of functional groups, including aryl, alkyl, alkenyl, and ester substituents, demonstrating both robustness and versatility under ambient conditions (Scheme 86).

Although the authors mention that the mechanistic pathway for the base-mediated synthesis of alkynyl tellurides



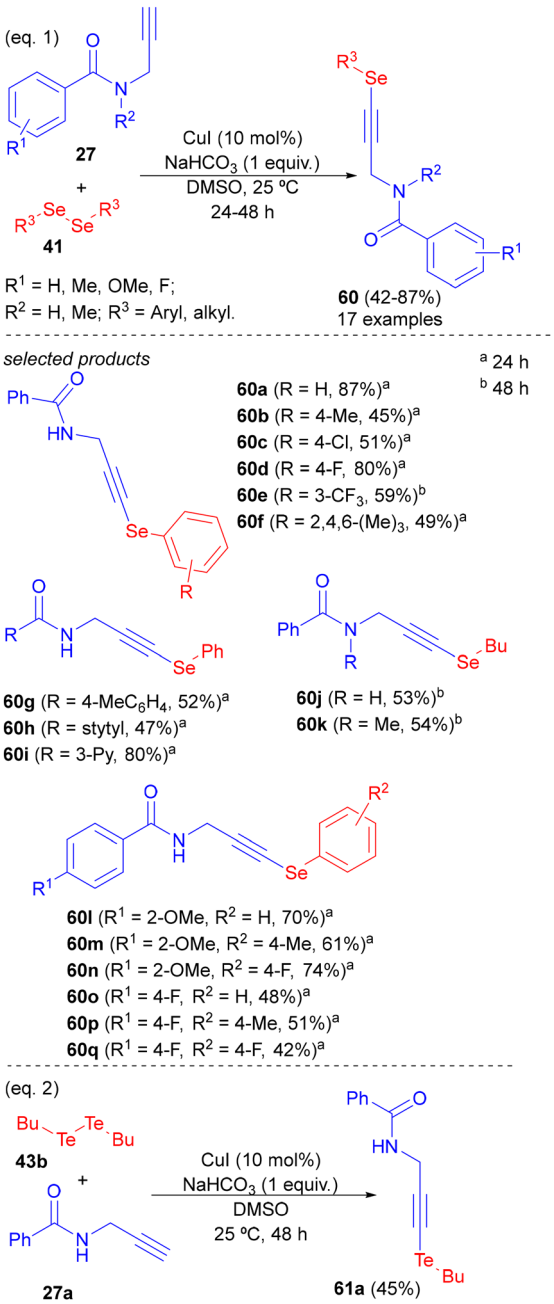
Scheme 86 Alkynyl tellurides **44** obtained through base-mediated coupling developed by Alves and co-workers in 2019.[75]



Scheme 87 Proposed mechanism for base-promoted the-alkynyl telluride **44** formation.[75]

in DMSO has not been fully elucidated, they propose a plausible anionic mechanism based on experimental evidence. In this mechanism, as shown in Scheme 87, the terminal alkyne **10** is reversibly deprotonated to form an acetylide intermediate **I**, which then attacks the tellurium atom of the diorganyl ditelluride **43**. This yields the corresponding alkynyl telluride **44** and a tellurolate species **II**. The tellurolate species **II** then undergoes proton exchange with the conjugate acid of the base to form the tellurol **III**, which is readily oxidized in the presence of air and DMSO, thus regenerating the ditelluride **43** and sustaining the catalytic cycle (Scheme 87). The necessity of an oxidizing atmosphere is supported by the diminished yield observed under nitrogen. Moreover, the reaction's insensitivity to the radical inhibitor TEMPO suggests that the transformation proceeds through an anionic rather than a radical pathway.

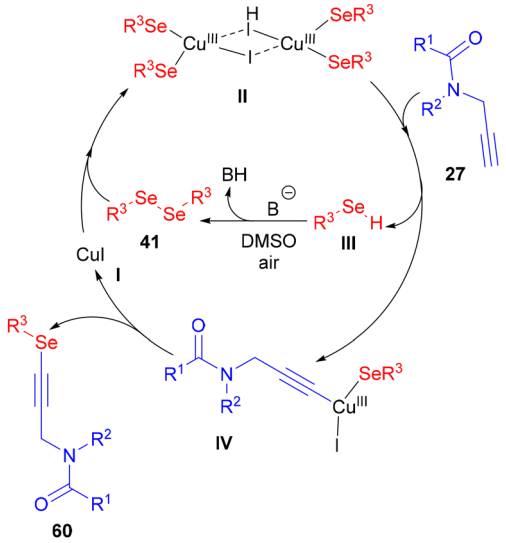
In 2019, Godoi and co-workers[48] proposed a method to synthesize a series of 17 *N*-(3-(organoselanyl)prop-2-yn-1-yl) amides **60** *via* a copper-catalyzed C_{sp}–Se bond formation. The products **60** were obtained in moderate to very good yields (42–87%) through cross-coupling reactions of propynylbenzamides **27** with diorganyl diselenides **41**. The reaction was carried out using CuI (10 mol%) as the catalyst and $NaHCO_3$ (1 equiv.) as the base in DMSO at room temperature under an air atmosphere (Scheme 88, eqn (1)). In general, the reactions were completed within 24 h. However, in the cases of **60j** and **60k**, where dibutyl diselenide was used as the selenium source, a reaction time of 48 h was required (Scheme 88). This methodology exhibited good functional group tolerance, accommodating both electron-donating and electron-withdrawing substituents on the phenylselanyl ring. Additionally, the amide moiety was compatible with various substituents such as –H, –Me, –OMe, and –F attached to the aromatic ring, as well as with styryl and pyridinyl groups. The best yields were achieved for compounds **60a**, **60d** and **60i**, which were obtained in 87%, 80%, and 80% yields, respectively (Scheme 88, eqn (1)). Moreover, the synthetic utility of the resulting selanyl derivatives was further explored, employing a synthesized molecule as a precursor in palladium-catalyzed Suzuki and Sonogashira reactions, demonstrating the versatility of the C_{sp}–Se bond as a reactive site for functionalizations, including the synthesis of unsymmetrical diynes and other π-conjugated systems with potential applications in medicinal chemistry. Finally, to reinforce the applicability and versatility



Scheme 88 Synthesis of alkynyl selenides **60** and telluride **61a** from amides **27** reported by Godoi and co-workers in 2019.[48]

of the method, an example of an organotellurium benzamide derivative was also described. The compound **61a** was obtained in 45% yield using dibutyl ditelluride **43b** as the tellurium source under the same reaction conditions employed for the selenium derivatives (Scheme 88, eqn (2)). This result highlights the potential extension of the protocol to other chalcogen elements, broadening its synthetic scope.

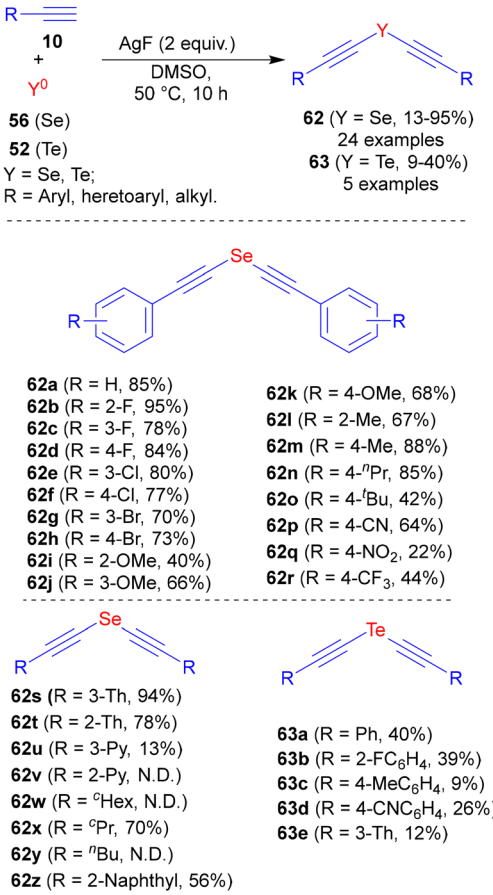
The authors also proposed a plausible reaction mechanism based on previous reports and their experimental trials (Scheme 89). Initially, the copper(I) salt **I** interacts with the



Scheme 89 Proposed mechanism for Cu-mediated alkynyl selenides **60** formation.[48]

diorganyl diselenide **41** to form a tetracoordinated Cu(III) complex **II**. This complex subsequently reacts with the terminal alkyne portion of the propynylbenzamide **27**, generating an intermediate **IV** and an organoselenol species **III**. The latter is easily reoxidized *in situ* to produce the corresponding diorganyl diselenide **41**, thus regenerating the copper catalyst (**I**). Finally, reductive elimination from the intermediate **IV** leads to the formation of the carbon–chalcogen (C_{sp}–Se) bond, affording the desired organoselanylbenzamide **60** and regenerating the Cu(I) **I** catalyst to complete the catalytic cycle (Scheme 89).

In 2020, Ji and co-workers[76] introduced a straightforward and efficient method to synthesize bis(arylethynyl)selenides **62** through the silver-mediated C–H activation of terminal alkynes **10**, using elemental selenium powder **56** as the selenium source. The reaction proceeds with 2 equiv. of AgF in DMSO at 50 °C for 10 h, yielding a wide variety of bis(arylethynyl)selenium compounds **62** in yields ranging from 13% to 95% (Scheme 90). This method stands out for its excellent chemoselectivity, broad substrate scope, and high atom economy, offering a valuable and sustainable alternative to existing strategies that often rely on prefunctionalized selenium reagents and require harsher conditions. Its versatility was demonstrated across a wide range of arylacetylenes bearing both electron-donating and electron-withdrawing groups. Moreover, the system tolerated heteroaryl alkynes **10** and even some aliphatic substrates, such as cyclopropylacetylene, although with slightly diminished efficiency. Furthermore, despite the decrease in yields with strongly electron-deficient alkynes, the method demonstrated good robustness and functional group tolerance. The scope was further expanded by replacing selenium powder with tellurium powder **52**, enabling access to bis(arylethynyl)tellurides **63** under the same conditions. However, these tellurium-based

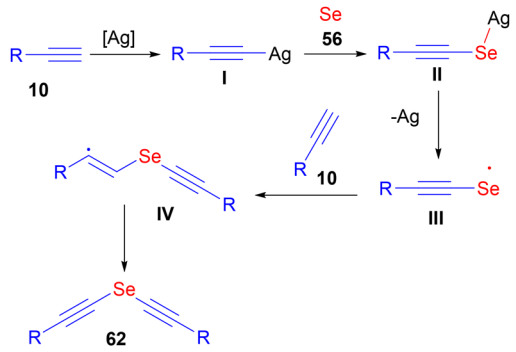


Scheme 90 AgF-mediated synthesis of symmetrical bis-alkynyl selenides **62** and tellurides **63** described by Ji and co-workers in 2020.[76]

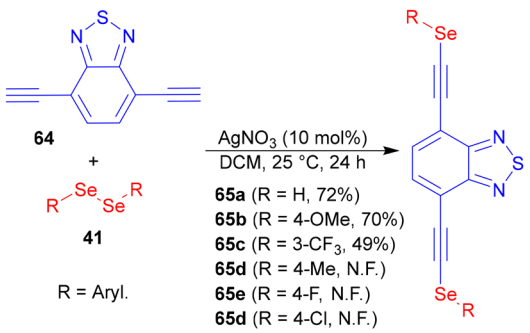
reactions generally afforded lower yields, with maximum isolated values around 40%, reflecting the lower reactivity of tellurium in this system. In general, this silver-mediated approach offers a valuable synthetic route to structurally diverse bis(alkynyl) selenium and tellurium compounds **62** and **63** from simple terminal alkynes **10** and elemental chalcogen sources **53** or **52** (Scheme 90).

The authors propose the following mechanism for the formation of the alkynylselenide **62**: the reaction begins with arylacetylene **10** interacting with the silver salt, leading to the formation of intermediate **I**. Subsequently, a selenium atom **56** inserts into the carbon–silver bond, giving rise to intermediate **II**. This step is followed by the generation of a selenium-centered radical **III**, which reacts with a second molecule of arylacetylene to form intermediate **10**. After undergoing dehydrogenation, this intermediate **IV** ultimately leads to the formation of the final product **62** (Scheme 91).

In 2021, Alves and co-workers[77] reported the synthesis of a set of bis-alkynylselanyl benzo[*c*][1,2,5]thiadiazoles (BTDs) **65a–d** through a silver-catalyzed direct selenylation approach. Using 4,7-diethynylbenzo[*c*][1,2,5]thiadiazole as the starting material **64**, they reacted it with various diaryl diselenides **41** under mild conditions (Scheme 92). Initial efforts employing



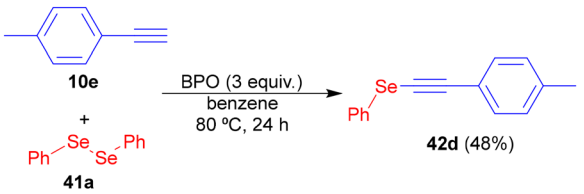
Scheme 91 Proposed mechanism for Ag-mediated synthesis of bis-alkynyl selenides **62**.[76]



Scheme 92 Bis-selenylated pyridines **65** synthesized *via* Ag-catalysis reported by Alves and co-workers in 2021.[77]

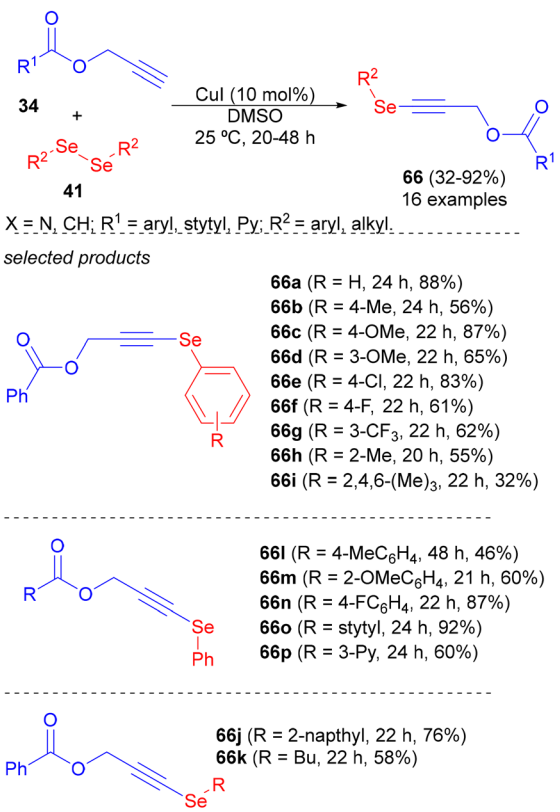
copper catalysis led predominantly to unwanted homocoupling side products. In contrast, the use of $AgNO_3$ (10 mol%) in DCM at room temperature successfully yielded the desired compound **65a** in 72% yield (Scheme 92). This strategy was further applied to diaryl diselenides substituted **41** with both electron-donating (OMe) and electron-withdrawing (CF_3) groups attached in the aromatic ring, delivering the corresponding products **65b** and **65c** from moderate to good yields (70% and 49%, respectively). However, attempts with specific aryl substituents such as 4-methyl, 4-fluoro, and 4-chloro resulted in complex reaction mixtures, suggesting a limitation in the substrate tolerance for these variants. Overall, the work showcases an efficient route to functionalized BTD derivatives using readily available reagents and mild reaction conditions (Scheme 92).

In a study conducted by Ogawa and co-workers,[78] a coupling reaction between *p*-tolylacetylene **10e**, diphenyl diselenide **41a**, and 3 equiv. of benzoyl peroxide (BPO) as an oxidant was carried out in benzene at 80 °C under atmospheric conditions. This reaction selectively produced the alkynyl selenide **42d** in a 48% yield, representing a direct C(sp)–H functionalization of the terminal alkyne **10** with a phenylselanyl group (Scheme 93). Based on a simple oxidizing system and avoiding the use of metal catalysts, the transformation stands out for its mild conditions and high selectivity. Overall, this study introduces an innovative and practical approach to the conversion of terminal alkynes **10** into geminal diorganoselanyl-substituted alkenes through a BPO/$(PhSe)_2$-mediated oxidative multicomponent reaction, offering an efficient route to synthetically valuable organochalcogen compounds (Scheme 93).



Scheme 93 Synthesis of the alkynyl selenide **42d** described by Ogawa and co-workers in 2021.[78]

In 2021, Godoi and co-workers[55] reported a base-free strategy for the synthesis of organochalcogen compounds *via* copper-catalyzed cross-coupling of diorganyl diselenide **41** with a series of prop-2-yn-1-yl esters **34** (Scheme 94). The transformation afforded alkynyl selenides **66** through selective Se–Se bond activation under ligand- and base-free conditions. The coupling reactions were conducted using 0.6 equivalent of diorganyl diselenide **41** with prop-2-yn-1-yl aryl esters **34**, CuI (10 mol%), under mild conditions (DMSO at 25 °C) under air atmosphere (Scheme 94). Under these conditions, the products

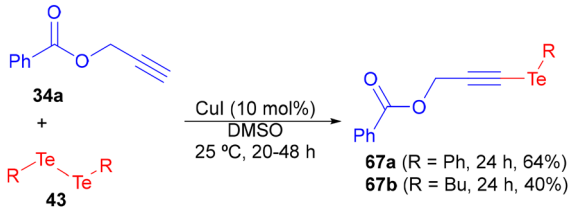


Scheme 94 Synthesis of alkynyl selenides **66** described by Godoi and co-workers in 2021.[55]

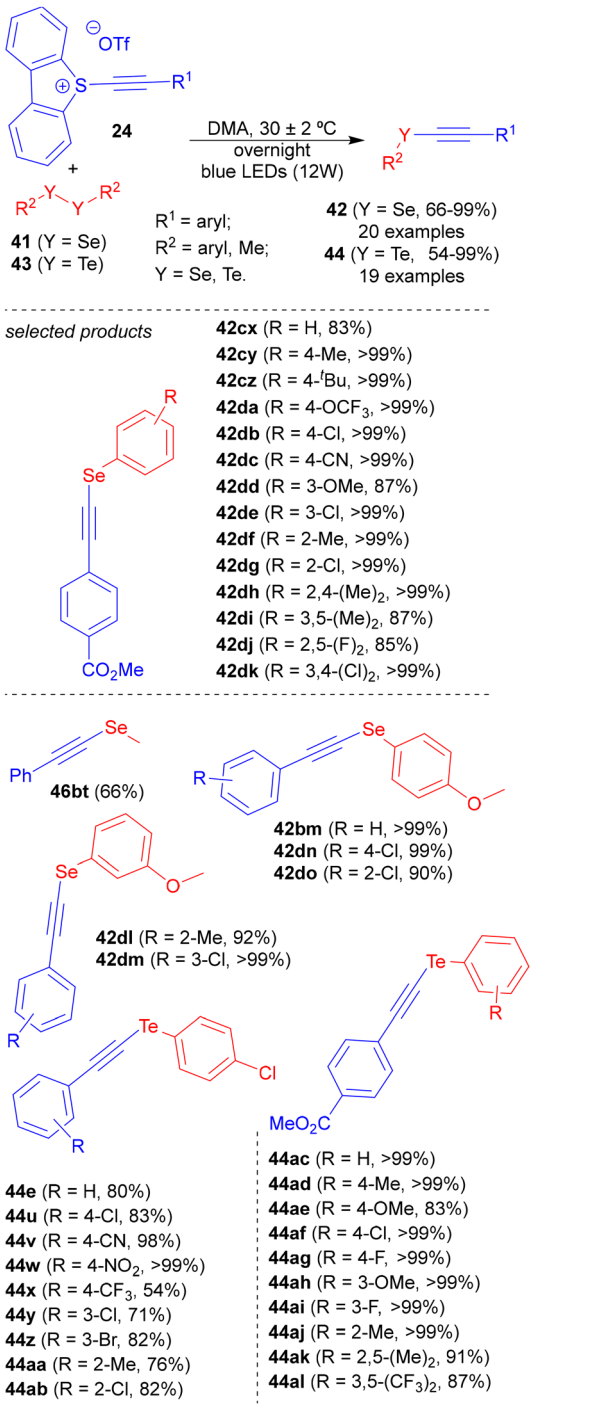
66 were obtained in yields ranging from 32% to 88%. Only a slight influence from electron-donating (EDG) and electron-withdrawing (EWG) groups on the aromatic ring of alkynyl ester was observed. In this case the target products **66** substituted with EWG were formed in better yields than EDG ones. The protocol was efficient for several substituted diaryl diselenides, as well as to 1,2-di(naphthalen-2-yl) diselenide and dibuthyl diselenide, in these cases the desired alkynyl selenide **66j** and **66k** were formed in 76% and 58% yield, respectively, both in 22 h of reaction (Scheme 94).

The authors also extended the scope to include diaryl and dialkyl ditellurides **43** in the reaction with prop-2-yn-1-yl ester **34a** under standard conditions (Scheme 95). When diphenyl and dibuthyl ditelluride were used as starting materials, the target products **67a** and **67b** were formed in 64% and 40% of yield, respectively. Overall, the work reported by the authors presented interesting results using different parameters to study of the compounds obtained in cross-coupling protocol applying CuI as the catalyst with diorganyl dichalcogenides as chalcogen sources and alkynyl esters in a base-free reaction process. In this case, 16 examples of alkynyl chalcogenides **66** were obtained, with yields ranging from 32% to 92% (Scheme 95).

In 2022, Chen and co-workers[79] reported an efficient, metal-free approach to access alkynyl selenium and tellurium compounds **42** and **44** *via* chalcogen-bonding (ChB) catalysis using alkynyl-sulfonium salts **24** under blue-light irradiation. The method relies on the generation of alkynyl radicals through single-electron transfer (SET) from a non-covalent charge-transfer complex formed between sulfonium salt **24** and diorganyl dichalcogenide **41** or **43**, representing a novel activation mode in radical chalcogenation chemistry. The key transformation involves the photochemical reaction of alkynyl-sulfonium salts **24** with diorganyl diselenides **41** or ditellurides **43** in *N*,*N*-dimethylacetamide (DMA) under blue LED irradiation at room temperature (Scheme 96). The protocol proved efficient for a variety of substituted starting materials **24** and **41**, giving a wide range of desired alkynyl selenides **42** (20 examples) in yields ranging from good to excellent (66–>99%). For instance, the reaction between dimethyl diselenide and the sulfonium salt provided alkynyl selenide **46bt** in 66% isolated yield (Scheme 96). The protocol showed broad applicability to a wide range of substituted diselenides and ditellurides **41** or **43**. Both diaryl diselenides **41** substituted with EDG and EWG delivered the corresponding alkynyl selenides **42** in 83–96% yield. The method also tolerated a variety of sulfonium



Scheme 95 Alkynyl tellurides **67a–b** obtained through Cu-catalyzed coupling reported by Godoi and co-workers in 2021.[55]

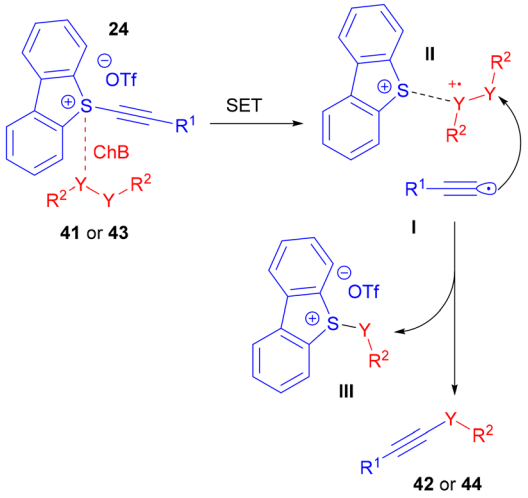


Scheme 96 Synthesis of alkynyl selenides **42** and alkynyl tellurides **44** under visible-light conditions reported by Chen and co-workers in 2022.[79]

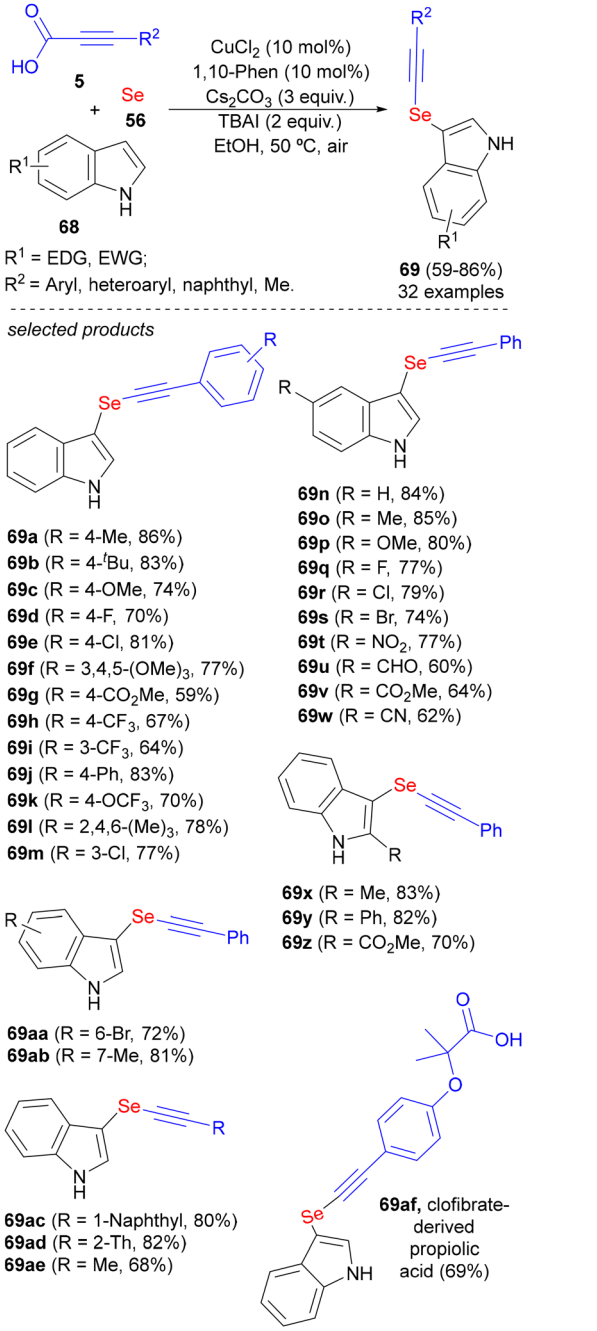
substrates **24** bearing different aryl substituents attached to the alkynyl unit (Scheme 96). Extension of the protocol to diorganyl ditellurides **43** furnished structurally diverse alkynyl tellurides **44** (19 examples) in moderate to excellent yields (54–>99%). Electronic variations on both the alkynyl-sulfonium and telluride moieties were well tolerated (Scheme 96).

Radical trapping and mechanistic studies, including UV-vis, ^{77}Se NMR titration, and Time-Dependent Density Functional Theory (TDDFT) simulations, confirmed the formation of an alkynyl radical intermediate from the photoactivated (ChB) complex, followed by direct reaction with the dichalcogenide to afford the desired products **42** or **44** (Scheme 97). This strategy provides a sustainable and operationally simple route to chalcogenoacetylenes **42** or **44** under additive-, photocatalyst-, and transition-metal-free conditions, expanding the synthetic utility of chalcogen bonding in radical chemistry.

In 2022, Wu and co-workers[80] reported a novel copper-catalyzed decarboxylative alkynylselenation of indoles **68** employing selenium powder **56** and propiolic acids **5** as coupling partners (Scheme 98). This method elegantly circumvents the need for prefabricated electrophilic arylselenation reagents, addressing common issues of over-selenation and reagent instability. The protocol proceeds *via in situ* generation of nucleophilic alkynylseleno copper intermediates through copper-catalyzed decarboxylation of propiolic acids **5**, which subsequently undergo Chan–Lam type coupling with indoles to synthesize alkynyl selenide **69** (Scheme 98). The optimized conditions involve $CuCl_2$ (10 mol%) as the catalyst, cesium carbonate (3 equiv.) as the base, and ethanol as a green solvent, operating efficiently under air atmosphere at 50 °C for 24 h (Scheme 98). This transformation tolerates a broad substrate scope, including various functional groups on both the indole ring and aryl-substituted propiolic acids **5**, affording the target product (32 examples) **69** in yields ranging from moderate to excellent (59–86%). The methodology also extends to late-stage functionalization of clofibrate-derived propiolic acid **5**, demonstrating potential pharmaceutical applications. In this case, the reaction of compound **5** under the standard conditions afforded the indolyl alkynyl selenide clofibrate-derived **69af** was formed in 69% of yield (Scheme 98). This copper-catalyzed decarboxylative alkynylselenation represents a significant advance in the synthesis of arylalkynyl selenides **69**, showcasing operational simplicity, broad functional group tolerance, and the use of stable, inexpensive selenium powder. The extension of this strategy to pyrroles and gram-scale synthesis under mild, environmentally friendly conditions further underscores its synthetic utility. This work paves the way for the development of selenium-containing bioactive molecules, highlighting the expanding chemical space accessible through innovative C–Se bond-forming methodologies (Scheme 98).



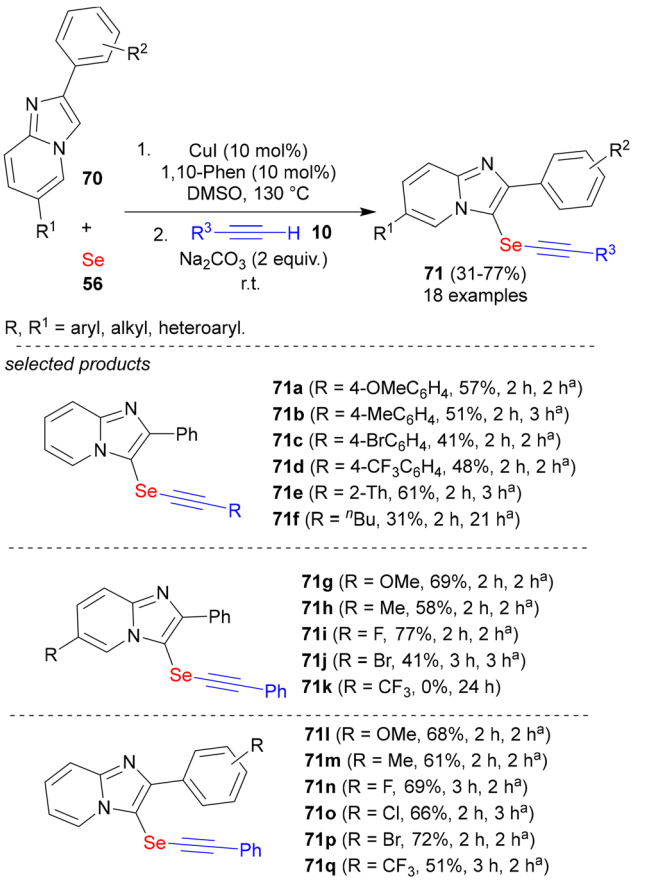
Scheme 97 Proposed mechanism for photoredox-mediated formation of alkynyl selenides/tellurides-alkynes **42/44**.[79]



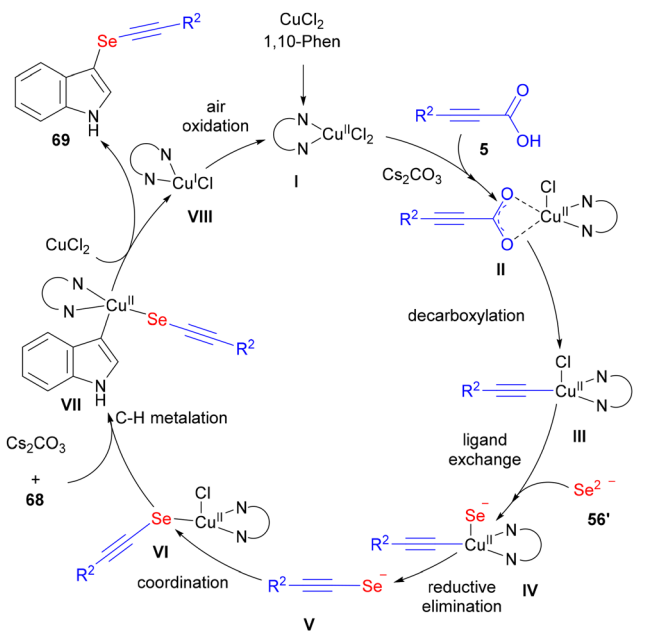
Scheme 98 Synthesis of alkynyl selenides **69** described by Wu and co-workers in 2022.[80]

The authors performed several control experiments to propose a plausible mechanism, which starts with copper-phenanthroline complex coordination **I** with the alkynyl carboxylic acid **5**, followed by decarboxylation to generate an alkynylcopper intermediate **III**. Simultaneously, selenium powder **56** is activated under basic conditions to yield selenium anions **56′** that insert into the copper-alkynyl species **III**, forming alkynylseleno copper intermediates **IV**. Subsequently, reductive elimination affords intermediate **V**, followed by coordination to give intermediate **VI**. Subsequent, the coupling of **VI** with indoles **68** delivers the alkynyl selenide **69** products *via* reductive elimination of **VII**, completing the catalytic cycle (Scheme 99). Based on control experiments, it is notable that *N*-unprotected indoles are essential, since *N*-substituted analogues fail to deliver the desired products **69**, underscoring the mechanistic requirement for carbanion formation.

In 2022, Yasuike and co-workers[81] reported the first protocol to obtain alkynyl selenides **71** from imidazopyridines **70** and alkynes **10** and powder selenium **56** as starting materials, promoting the formation of the new $C_{(sp2)}$–Se–$C_{(sp)}$ bond (Scheme 100). In this Cu-catalyzed approach, Se powder **56** is used as a selenium source to form the diimidazopyridinyl diselenides one-pot as the key intermediate. The standard conditions were established when several imidazo[1,2-*a*]pyridines **70** were reacted with selenium powder **56** in the 10 mol% CuI as the catalyst, 10 mol% of 1,10-phen as the ligand in DMSO as the solvent at 130 °C to form the diimidazopyridinyl diselenides *in situ* under aerobic conditions. Subsequently, Na_2CO_3 (2 equiv.) was added at room temperature to afford a wide range of target alkynyl imidazopyridinyl selenides **71** (18 examples) in yields ranging from moderate to good (31–77%). This method tolerates several imidazopyridines **70** and aryl



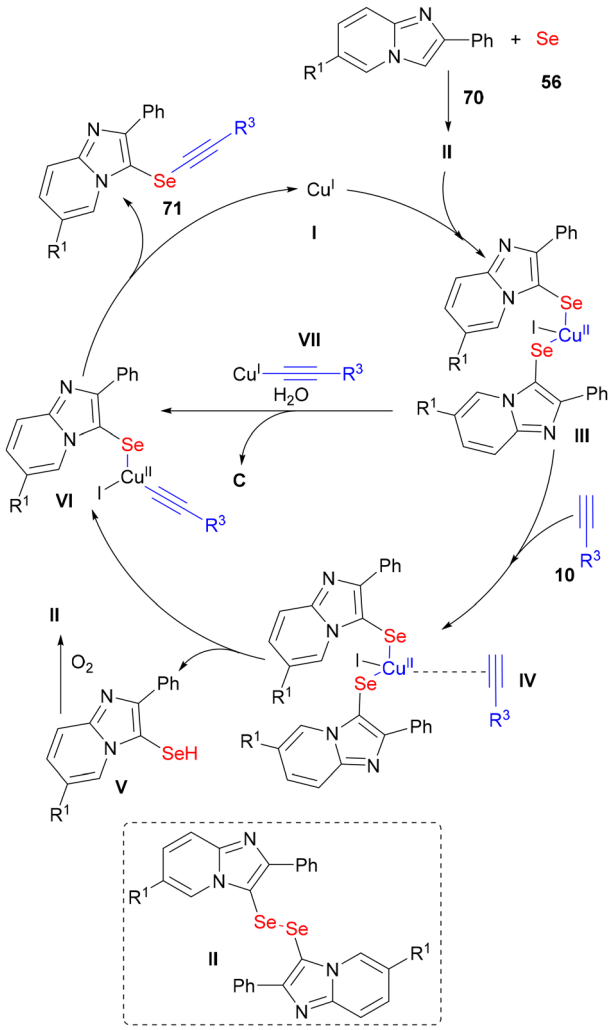
Scheme 100 Synthesis of alkynyl selenides **71** reported by Yasuike and co-workers in 2022.[81]



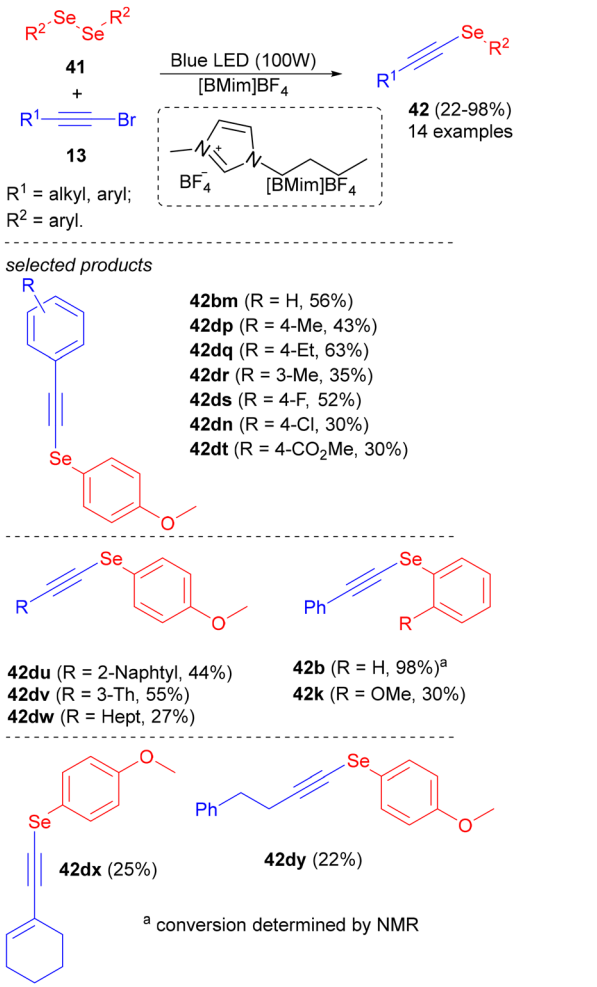
Scheme 99 Proposed mechanism for decarboxylative selenylation leading to alkynyl selenides **69**.[80]

alkynes **10** bearing EDG or EWG attached on the aromatic ring of either starting materials. Additionally, the heteroaryl alkyne was also checked, in this case, the compound **71e** was obtained in moderate yield. On the other hand, the presence of an alkyl group attached to the alkyne unit, afforded the desired alkynyl selenide in a low yield (compound **71f**, 31%) (Scheme 100).

The proposed mechanism (Scheme 101) starts with the formation of disselenide **II** from the reaction between selenium powder **56** and imidazo[1,2-*a*]pyridine **70**. Subsequently, the intermediate **III** is formed *via* oxidative addition of the Cu(I) catalyst **I** into **II**. Next, the terminal alkyne **10** coordinates with intermediate **III** to generate π-complex **IV**. Subsequent ligand exchange of **IV** affords intermediate **VI**, accompanied by the elimination of selenol **V**, which is further oxidized to diselenide **II**. Intermediate **VI** then undergoes reductive elimination to furnish the desired product **71** with concurrent regeneration of Cu(I) **I**. Alternatively, an alternative pathway involves Cu-acetylide **VII** directly engaging intermediate **III** to deliver **VI**, thereby affording the target product **71** (Scheme 101). Based on control experiment, the authors reported that although the transformation was carried out under aerobic conditions, no evidence of Glaser-type homocoupling was observed, and diynes were absent. Furthermore, the reaction between disele-



Scheme 101 Proposed mechanism for Cu-mediated C–H selenylation toward alkynyl selenides **71**.[81]



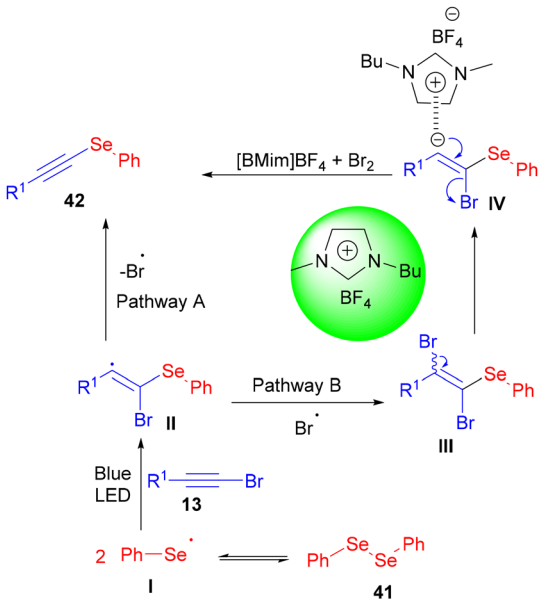
Scheme 102 Alkynyl selenides **42** synthesized *via* ionic liquid-assisted photoredox catalysis developed by Schneider and co-workers in 2023.[82]

nide **II** and **10** in the absence of base afforded product **71** in good yield. Collectively, these results suggest that the transformation predominantly proceeds through the pathway involving π-complex **IV**. The role of the base is most likely to neutralize the protons released during the initial step, wherein diselenide **II** is derived from imidazopyridine **70** and elemental selenium **56**.

In 2023, Schneider and co-workers[82] developed a visible-light-promoted, metal-free methodology for the synthesis of alkynylselenides **42** using 1-bromoalkynes **13** (3.0 equiv.) and diaryldiselenides **41** (1.0 equiv.) as substrates (Scheme 102). The reaction proceeded under blue LED irradiation (100 W) at room temperature in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIm]BF_4) as a green and sustainable solvent for 24 h (Scheme 102). Under these conditions, a wide range of alkynyl selenides **42** (14 examples) were synthesized. This protocol tolerated aryl, heteroaryl and alkyl groups attached to the bromoalkynes substrates **13**. Overall, this work demonstrates an environmentally benign, operationally simple protocol for C_{sp}–Se bond formation without transition metals, photosensitizers, or directing groups, using an ionic liquid solvent that also assists by suppressing side reactions. The findings offer new insights into the application of ionic liquids as sustainable media in organochalcogen chemistry, with reported yields for compounds **42** ranging from 22% to 98% (Scheme 102).

Mechanistic studies suggest that LED irradiation promotes the homolytic cleavage of the Se–Se bond in diaryl diselenide **41**, generating a selenyl radical **I** that subsequently reacts with bromoalkyne **13** to form a radical intermediate **II**. This intermediate **II** is stabilized by the ionic liquid [BMIm]BF_4, facilitating the elimination of bromide to form intermediate **IV**. The departure of the [BMIm]BF_4-stabilized leaving group ultimately furnishes the desired alkynyl selenide **42** (Scheme 103).

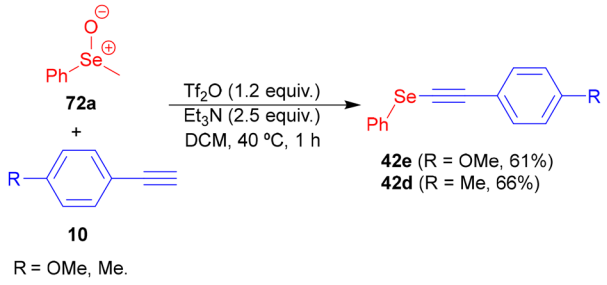
The method for the synthesis of alkynyl selenides **42** involves the reaction of phenylacetylenes **10** with methyl phenyl selenoxide **72a** (1.2 equiv.) under conditions similar to those used for the synthesis of alkynyl sulfide, as described by Rong and co-workers in 2023 [59] (section 3, Scheme 57). The



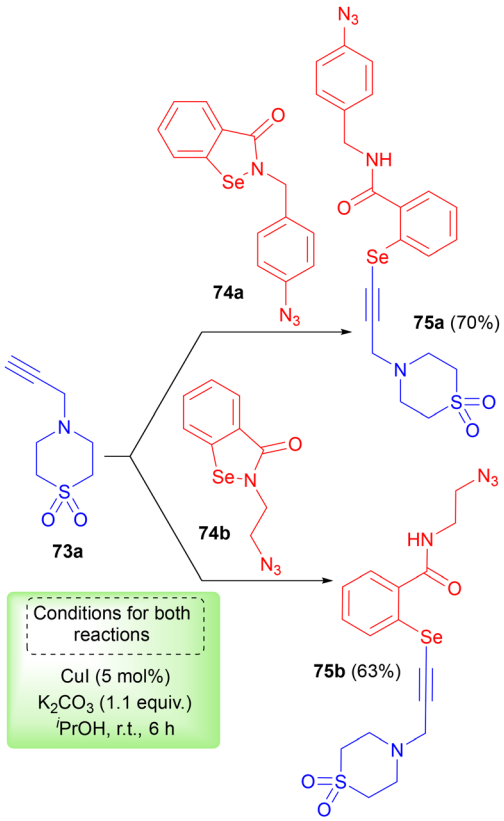
Scheme 103 Proposed mechanism for the synthesis of alkynyl selenides **42**.[82]

reaction was carried out in the presence of trifluoromethanesulfonic anhydride (Tf_2O, 1.2 equiv.) and triethylamine (Et_3N, 2.5 equiv.) at 40 °C for 1 h, affording two alkynyl selenide derivatives in 61% and 66% yields, respectively (Scheme 104). This work highlights a significant advancement in metal-free methodologies for the synthesis of diverse alkynyl selenides **42** (Scheme 104).

In 2025, Xu and co-workers[83] reported the uses of 2-(4-azidobenzyl)benzo[1,2]selenazol-3(2*H*)-ones (Selenium(II)–Nitrogen Exchange (SeNEx)) **74a** to react with 4-(prop-2-yn-1-yl) thiomorpholine 1,1-dioxide (alkyne) **73a** under alkaline conditions, to obtain a range of alkynyl selenides **75a**. The reaction proceeds through SeNEx **74a–b** with the alkyne **73a** in the presence of CuI (5 mol%) as catalyst, K_2CO_3 (1.1 equiv.) as base in a ^{i}PrOH solution for 6 h at room temperature. As a result, two compounds (**75b** and **75a**) were obtained in yields of 63% and 70%, respectively (Scheme 105). When the authors used DMSO, maintaining the same reaction conditions, and using the starting material **74c**, the product **75c** was obtained



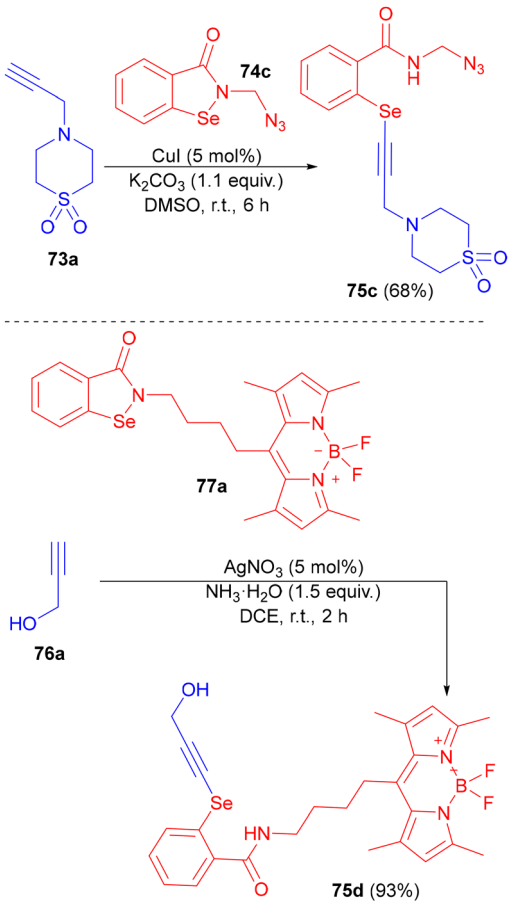
Scheme 104 Synthesis of the alkynyl selenides **42e** and **42d** reported by Rong and co-workers in 2023.[59]



Scheme 105 Functionalized alkynyl selenides **75a–b** obtained from azido derivatives **74a–b** described by Xu and co-workers in 2025.[83]

in 68% of yield. Furthermore, when the SeNEx substrate was changed from 2-(4-azidobenzyl)benzo[1,2] selenazol-3(2*H*)-one **74a** to 2-(4-(5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4l4,5l4-dipyrrolo[1,2-*c*:2′,1′-*f*][1,3,2]diazaborinin-10-yl)butyl)benzo[*d*][1,2] selenazol-3(2*H*)-one (Bodipy) **77a** was replaced by $AgNO_3$ (5 mol%) in combination with ammonia ($NH_3{\cdot}H_2O$) (1.5 equiv.), using DCE as solvent at room temperature by 2 h of reaction, the yield of the desire product **75d** was increased to 93% (Scheme 106). The change of catalyst can improve the product yield, but altering the precursor by introducing different substituent groups in the substrate can also influence reactivity. In this sense, this work presents a novel approach to obtaining alkynyl selenide compounds, using SeNEx as an efficient and effective synthetic route.

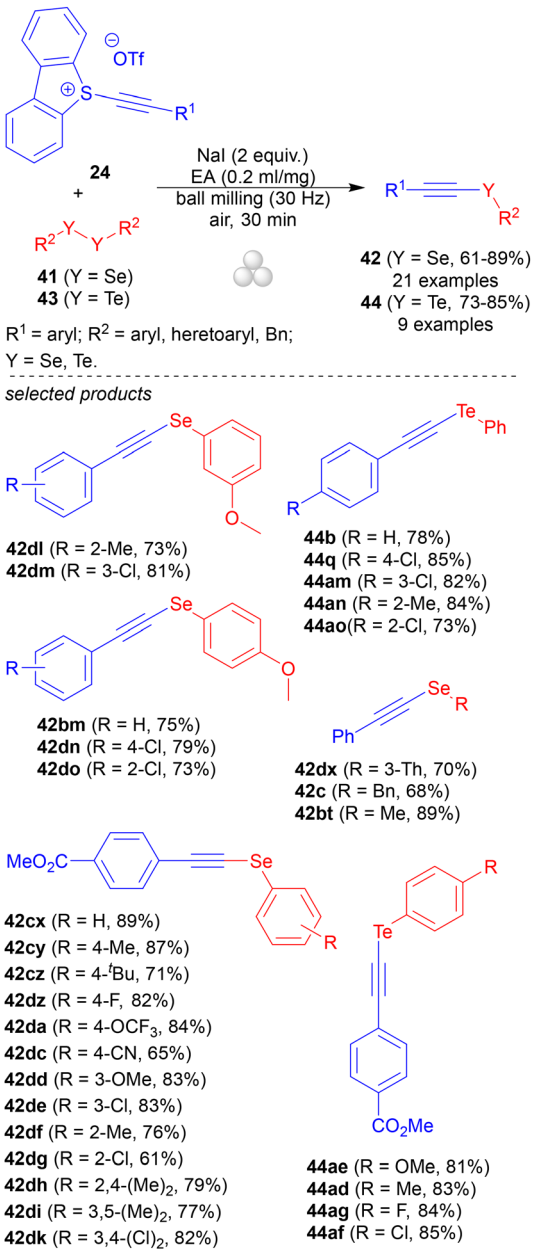
In 2025, Chen and co-workers[84] developed a mechanochemical approach for the synthesis of various alkynyl chalcogenides **42** or **44** *via* alkynyl radicals. The protocol involves the reaction between an alkynyl sulfonium salt **24** and diorganyl diselenides **41** in the presence of 2 equiv. of NaI as the electron donor and ethyl acetate (EA, 0.2 μL mg^{-1}) as a liquid-assisted grinding additive. The mixture was subjected to ball milling under air using nine stainless-steel balls at 30 Hz for 30 minutes. Under these conditions, 21 alkynyl selenide derivatives **42** were obtained in yields ranging from 61% to 89% (Scheme 107). In addition, the methodology was successfully applied to the synthesis of alkynyl tellurides **44** by repla-



Scheme 106 Alkynyl selenides incorporated into bioactive motifs **75c–d** synthetized by Xu and co-workers in 2025.[83]

cing diorganyl diselenide **41**with diorganyl ditelluride **43** under the same conditions established, affording nine alkynyl telluride derivatives **44** in yields ranging from 73% to 85% (Scheme 107). Thus, this work represents a sustainable mechanochemical protocol for the rapid synthesis of a range of (Se and Te) alkynyl chalcogenides **42** and **44**.

The proposed mechanism highlights the pivotal role of NaI as an electron donor in the activation of the alkynyl sulfonyl salt. In the initial step, electron transfer from NaI to the alkynyl sulfonyl salt **24** generates the radical anion intermediate **II**. This activated species **II** exhibits enhanced reactivity, enabling the cleavage of the Se–Se bond in the diorganyl dichalcogenides **41** or **43** and ultimately affording the formation of the desired products **42** or **44** (Scheme 108).

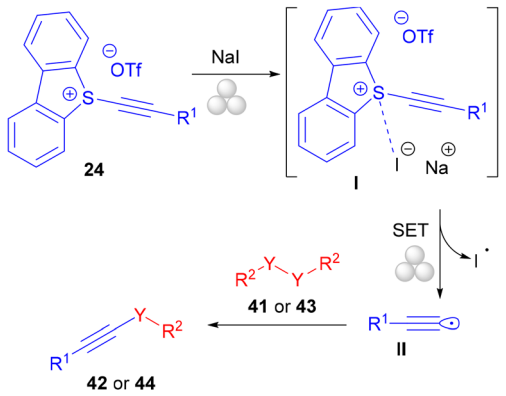


Scheme 107 Mechanochemical approach for the synthesis of alkynyl selenides **42** and tellurides **44** developed by Chen and co-workers in 2025.[84]

5 Trifluoromethyl-substituted alkynyl sulfides and selenides: scarce yet promising derivatives

5.1 Synthesis of trifluoromethyl-substituted alkynyl sulfides

Trifluoromethyl-substituted alkynyl sulfides and alkynyl selenides represent an even more restricted subclass within the family of chalcogen-alkynyl compounds. The introduction of the $-CF_3$ group dramatically enhances lipophilicity, metabolic stability, and electronic properties, features that are highly desirable in the design of bioactive molecules and advanced materials. Nevertheless, reports describing their synthesis remain extremely scarce, often relying on specialized electrophilic $-SCF_3$ or $-SeCF_3$ reagents.[85] Given that a comprehensive review already covered synthetic advances from 2015 to 2022, here we focus on developments reported since then to provide an up-to-date perspective.[86] In this section, we briefly outline the limited strategies reported for accessing these rare com-



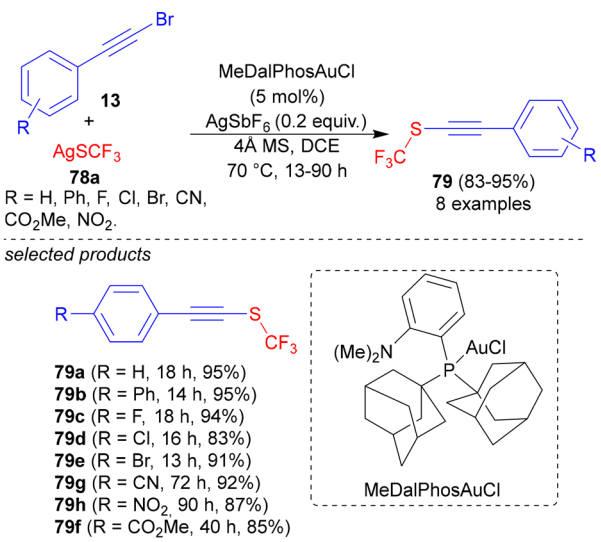
Scheme 108 Proposed mechanism for the synthesis of alkynyl selenides/tellurides **42**/**44**.[84]

pounds, while emphasizing their potential to expand the chemical space of fluorinated organochalcogen derivatives.

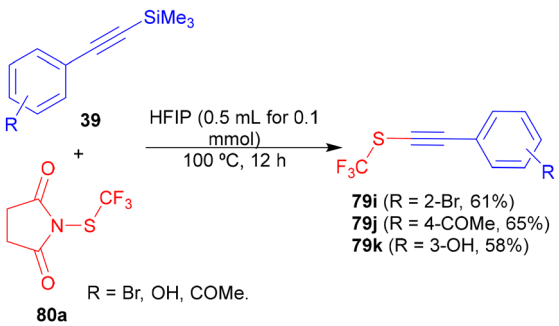
Lu and co-workers, in 2022,[87] developed an attractive and robust approach for the synthesis of trifluoromethyl alkynyl sulfides **79** *via* cross-coupling reactions employing gold redox catalysis [(MeDalPhos)AuCl], which can be applied to the late-stage functionalization of various bioactive molecules. In this protocol, several bromoacetylenes **13** were reacted with $AgSCF_3$ **78a** in the presence of 5 mol% MeDalPhosAuCl, 0.2 equiv. $AgSbF_6$, and 4 Å MS, using DCE as a solvent, at 70 °C for reaction times ranging from 13 h to 90 h. Under these conditions, 8 examples of target trifluoromethyl alkynyl sulfides **79** were obtained in good yields (83–95%) (Scheme 109). The presence of phenyl, bisphenyl and halogen atom (F, Cl and Br) substituents attached in the aryl bromo acetylenes afforded the target products **79a**, **79b**, **79c**, **79d** and **79e** in excellent yields (83–95%), 13–18 h with shorter reaction times than when the starting materials contained electron-withdrawing groups (EWGs). In the latter case, the desired products **79f–h** were obtained in comparable yields (85–92%) but required longer reaction times (40–72 h) (Scheme 109).

In 2023, Xie and Liu[60] extended their previously developed (section 3, Scheme 59) metal-free protocol for the synthesis of alkynyl sulfides **17** to also access synthesis (alkynyl)(trifluoromethyl)sulfides **79**. In this case, the *N*-(trifluoromethylthio) succinimide **80a** was reacted with different aryl silyl alkynes **39** under the same previously established reaction conditions (0.5 mL HFIP per 0.1 mmol of alkyne at 100 °C for 12 h). Three examples of (alkynyl)(trifluoromethyl)sulfides **79i–k** were obtained in moderate yields (58–65%) (Scheme 110).

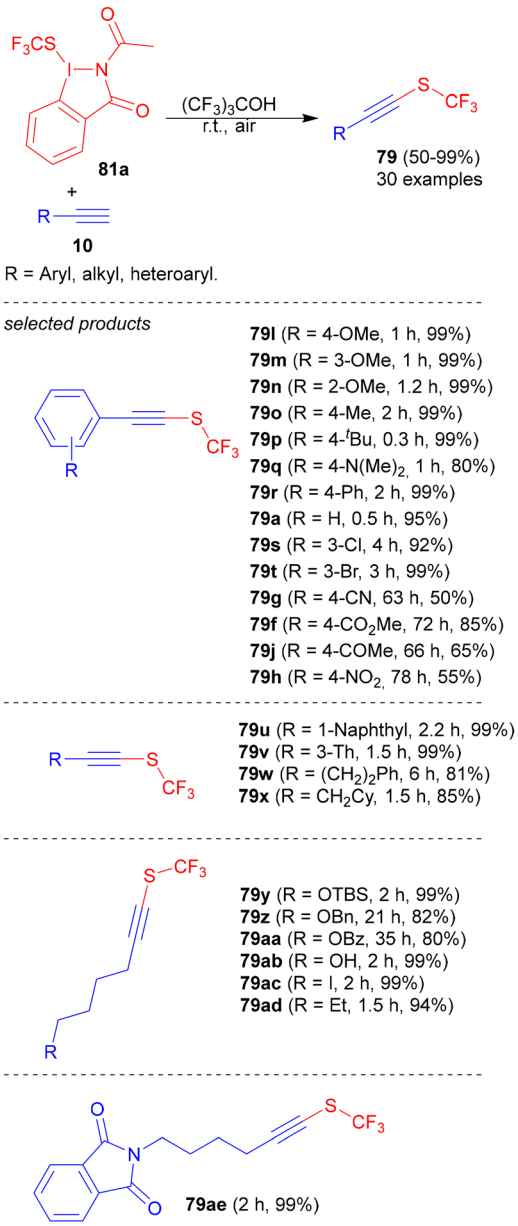
Zhang and co-workers, in 2024,[88] developed a simple and efficient protocol for the synthesis of alkynyl trifluoromethyl sulfides **79** through the reaction of terminal alkynes **10** using a hypervalent trifluoromethylthio-iodine(III) reagent **81a** as the SCF_3 source, in the presence of perfluoro-*tert*-butanol (PFTB) (Scheme 111). In this protocol, the authors used several terminal alkynes **10** in the presence of **81a** as (SCF_3 source), PFTB at room temperature under air, for reaction times ranging from 0.3 h to 78 h. A total of 30 examples of alkynyl trifluoromethyl sulfides **79** were synthesized in yields ranging from moderate to excellent (50–90%). This approach was sensitive to electronic effect; when terminal alkynes **10** containing EWG attached on the aromatic ring were evaluated, the target products were formed in poor yields compared to EDG ones. These were exemplified by compounds **79g**, **79j** and **79h**, which required longer reaction times and were formed in lower yields (**79g**, R = 4-CN, 63 h, 50%; **79j**, R = 4-COMe, 66 h, 65% and **79h**, R = 4-NO_2, 78 h, 55%, respectively), when compared to products **79l**, **79q** and **79o** (containing the EDG), which were formed in better yields and shorter reaction times (**79l**, R = 4-OMe, 1 h, 99%; **79q**, R = 4-$N(Me)_2$, 1 h, 80% and **79o**, R = 4-Me, 2 h, 99%, respectively) (Scheme 111). Additionally, the protocol was efficiently extended to terminal alkynes substituted with 1-naphthyl and 3-thienyl groups, which afforded the target alkynyl trifluoromethyl sulfides **79u** and **79v** in excellent yields (**79u**, 2.2 h, 99% and **79v**, 1.5 h, 99%, respectively). Furthermore, the authors explored a wide range of substituted alkyl alkynes **10**, affording the target products **79** in yields ranging from good to excellent



Scheme 109 Synthesis of trifluoromethylthio-alkynes **79** *via* Au catalysis reported by Lu and co-workers in 2022.[87]



Scheme 110 Trifluoromethylthio-alkynes **79i–k** described by Xie and Liu in 2023.[60]

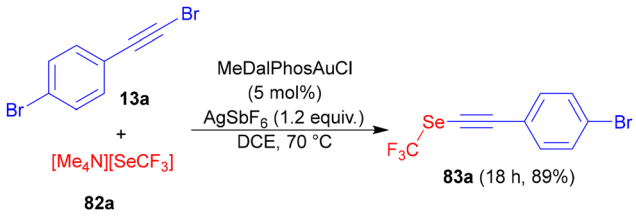


Scheme 111 Synthesis of trifluoromethylthio-alkynes **79** developed by Zhang and co-workers in 2024.[88]

(Scheme 111). The authors also evaluated the green chemistry profile of the method, and the EcoScale score indicated that the protocol should be considered excellent in the context of sustainable synthesis.

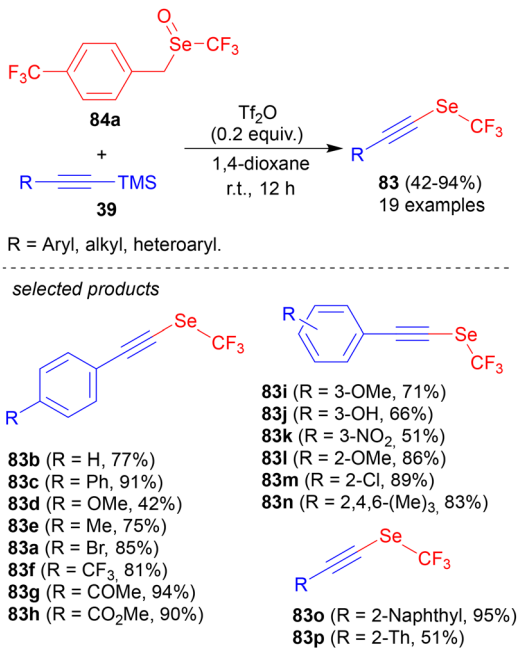
5.2 Synthesis of trifluoromethyl-substituted alkynyl selenides

The protocol previously reported by Lu and co-workers,[87] in 2022 for the synthesis of trifluoromethyl alkynyl sulfides **79** was efficiently extended to the synthesis of a trifluoromethyl alkynyl selenide **83** (Scheme 112). For this expansion of scope and to evaluate the versatility of the method, the authors applied the standard conditions, modifying the amount of $AgSbF_6$ from 0.2 equiv. to 1.2 equiv., as well as the trifluoromethyl chalcogen source. In this case, Me_4NSeCF_3 **82a** served as the starting material instead of $AgSCF_3$ **78a**, and was reacted with 1-bromo-4-(bromoethynyl)benzene **13a**, which afforded the target ((4-bromophenyl)ethynyl)(trifluoromethyl)selenide **83a** in excellent yield (89%) after 18 h (Scheme 112).



Scheme 112 Trifluoromethylseleno-alkyne **83a** synthesized *via* Au catalysis reported by Lu and co-workers in 2022.[87]

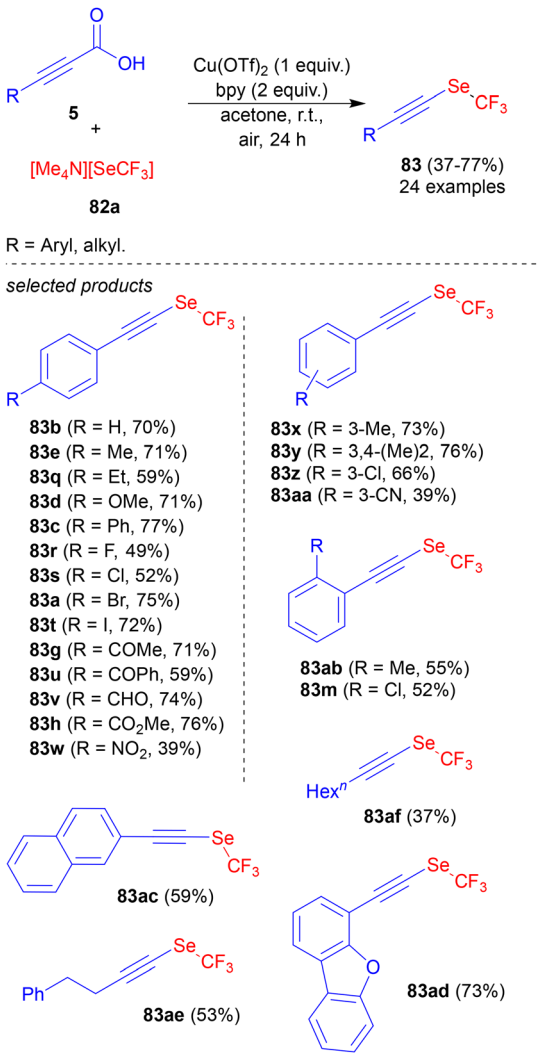
In 2023, Yuan and co-workers[89] developed a Lewis-acid-catalyzed divergent trifluoromethylselenolation of alkynes **83** using trifluoromethyl selenoxide **84a** as the electrophilic selenium source. Overall, the article described the synthesis of α-trifluoromethylselenylated ketones **84** and alkynes **39**. Specifically, for the preparation of the alkynyl trifluoromethylselenides **83**, different TMS-substituted alkynes **39** were reacted with trifluoromethyl selenoxide **84a** in the presence of 0.2 equiv. Tf_2O in 1,4-dioxane at room temperature for 12 h, providing 19 examples of trifluoromethylselenolated alkynes **83** in yields ranging from 42% to 92% (Scheme 113). In general, the method stands out for its broad substrate scope, demonstrating a good functional group tolerance and gram-scale applicability. Furthermore, the authors proposed an electrophilic selenolation mechanism, in which activation of tri-



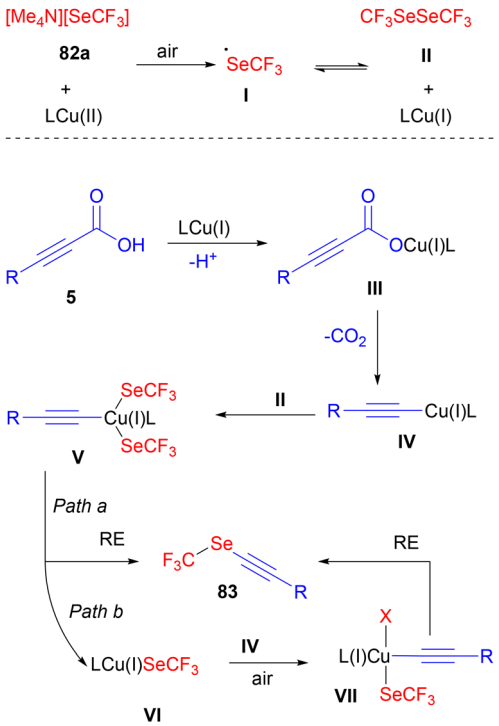
Scheme 113 Synthesis of trifluoromethylseleno-alkynes **83** described by Yuan and co-workers in 2023.[89]

fluoromethyl selenoxide **84a** by a Lewis acid generates a reactive species that reacts with the alkyne **39**, underscoring the versatility of trifluoromethyl selenoxide **84a** and its potential for broader applications in organic synthesis (Scheme 113).

In 2024, Zhang and co-workers[90] reported a copper-mediated aerobic decarboxylative trifluoromethylselenolation of alkynyl carboxylic acids **5** using $[Me_4N][SeCF_3]$ **82a** as the $SeCF_3$ source. The transformation was carried out under air atmosphere at room temperature in the presence of 1 equiv. $Cu(OTf)_2$ and 2 equiv. bpy in acetone, without requiring external oxidants or harsh conditions. Using this protocol, both aryl and alkyl alkynyl carboxylic acids **5** were smoothly converted into the corresponding alkynyl trifluoromethyl selenoethers **83** in yields ranging from 37% to 77% (Scheme 114). Thus, the methodology demonstrates a broad substrate scope, successfully tolerating electron-donating and electron-withdrawing substituents, as well as heteroaryl and aliphatic derivatives. Moreover, this approach is distinguished by



Scheme 114 Cu-catalyzed synthesis of trifluoromethylseleno-alkynes **83** reported by Zhang and co-workers in 2024.[90]



Scheme 115 Proposed mechanism for the Cu-mediated formation of alkynyl trifluoromethylselenides.[90]

employing stable and non-volatile alkynyl carboxylic acids **5** as starting materials and a readily accessible $SeCF_3$ reagent, being the first example of decarboxylative trifluoromethylselenolation of alkynyl carboxylic acids **5** with a $SeCF_3$ source (**82a**) (Scheme 114). Taken together, these findings underscore the synthetic utility and versatility of this oxidative strategy for future applications in organic chemistry.

The authors proposed a plausible mechanism supported by control experiments and ^{19}F NMR studies. They suggest that $[Me_4N][SeCF_3]$ **82a** is oxidized by Cu(II) salts under aerobic conditions to generate $CF_3SeSeCF_3$ **II** and Cu(I) species. The alkynyl carboxylic acid **5** subsequently undergoes decarboxylation to form an alkynyl-Cu(I) intermediate **IV**, which reacts with the *in situ* generated $CF_3SeSeCF_3$ **II**. From there, two mechanistic pathways were proposed: in pathway A, an oxidative addition affords an alkynyl-Cu(III)-$(SeCF_3)_2$ complex **V**, followed by reductive elimination to deliver the final product **83**. In pathway B, a Cu(I)-$SeCF_3$ complex **VI** is formed through ligand exchange and oxidation before reductive elimination, generating the desired product **83** (Scheme 115).

Beyond the trifluoromethylation of alkynes, some studies have also reported the monofluoromethylselenolation[91] and difluoromethylthiolation[92] of these substrates.

6 Conclusions

Alkynyl chalcogenides represent a significant class of compounds in organic chemistry, owing to their versatile reactivity

and structural features. These compounds have found broad application in diverse transformations, and their importance has been highlighted in numerous studies, particularly within the fields of biological and pharmacological research. This review has summarized recent advances in the synthesis of alkynyl chalcogenides, including sulfides, selenides, and tellurides, as well as alkynyl sulfones, and alkynyl trifluoromethyl chalcogenyl derivatives. Various methodologies developed over the past decade are discussed, which have provided powerful tools for the efficient construction of C(sp)–S, C(sp)–Se, and C(sp)–Te bonds. These methods have significantly expanded the structural diversity, functional group tolerance, and accessibility of sulfur-, selenium-, and tellurium-containing alkynes. By consolidating these approaches, this work aims to provide a useful reference for researchers and facilitate future studies in this area. Looking ahead, future research will likely focus on integrating these protocols with continuous-flow systems, biocatalytic strategies, and late-stage functionalization approaches. Such advances will not only enhance the synthetic utility of alkynyl chalcogenides but also foster their translation into practical applications, reinforcing their position as valuable building blocks in contemporary organic chemistry.

Author contributions

Conceptualisation, G. P. C. and A. F. C. F.; methodology, A. M. B., L. H. D. and R. C. B.; writing – original draft preparation, D. C. V., L. H. D. and R. C. B.; writing – review and editing, G. P. C., L. H. D., A. M. B. and A. F. C. F.; supervision, G. P. C. and A. F. C. F. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results and no new data were generated or analysed as part of this review.

Acknowledgements

The authors are grateful for the financial support and scholarships from the Brazilian agencies, Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq (310635/2022-5) and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul – FAPERGS (PDJ 23/2551-0001921-3 and ARD/ARC 23/2551-0000766-5). CNPq is also acknowledged for the fellowship for A. F. C. F. This study was partially financed by the Coordenação de Aperfeiçoamento de Pessoal de Nivel Superior-Brasil (CAPES)-finance code 001.

References

1 V. Lippolis, C. Santi, E. J. Lenardão and A. L. Braga, *Chalcogen Chemistry: Fundamentals and Applications*, RSC, Cambridge, 2023, DOI: 10.1039/9781839167386.
2 (*a*) R. C. Pinheiro, L. S. Marques, J. T. K. Jung, C. W. Nogueira and G. Zeni, Recent Progress in Synthetic and Biological Application of Diorganyl Diselenides, *Chem. Rec.*, 2024, **24**, e202400044; (*b*) J. Yu and X. Jiang, *Adv. Agrochem*, 2023, **2**, 3–14; (*c*) A. Henriquez-Figuereo, C. Moran-Serradilla, E. Angulo-Elizari, C. Sanmartín and D. Plano, Small molecules containing chalcogen elements (S, Se, Te) as new warhead to fight neglected tropical diseases, *Eur. J. Med. Chem.*, 2023, **246**, 115002; (*d*) F. Islam and Q. Zeng, Advances in Organosulfur-Based Polymers for Drug Delivery Systems, *Polymers*, 2024, **16**, 1207.
3 (*a*) M. Feng, B. Tang, S. H. Liang and X. Jiang, Sulfur Containing Scaffolds in Drugs: Synthesis and Application in Medicinal Chemistry, *Curr. Top. Med. Chem.*, 2016, **16**, 1200–1216; (*b*) C. Zhao, K. P. Rakesh, L. Ravidar, W.-Y. Fang and H.-L. Qin, Pharmaceutical and medicinal significance of sulfur (SVI)-Containing motifs for drug discovery: A critical review, *Eur. J. Med. Chem.*, 2019, **162**, 679–734.
4 (*a*) H. Yang, M.-Y. Wei, C.-Y. Wang, Y.-C. Gu and C.-L. Shao, The intriguing chemistry and biology of sulfur-containing natural products from marine microorganisms (1987–2020), *Mar. Life Sci. Technol.*, 2021, **3**, 488–518; (*b*) M. Mustafaa and J.-Y. Winum, The importance of sulfur-containing motifs in drug design and discovery, *Expert Opin. Drug Discovery*, 2022, **17**, 501–512.
5 E. J. Lenardão, C. Santi and L. Sancineto, *New Frontiers in Organoselenium Compounds*, Springer, Cham, Switzerland, 1st edn, 2018.
6 (*a*) C. W. Nogueira, G. Zeni and J. B. T. Rocha, Organoselenium and Organotellurium Compounds: Toxicology and Pharmacology, *Chem. Rev.*, 2004, **104**, 6255–6285; (*b*) C. W. Nogueira, N. V. Barbosa and J. B. T. Rocha, Toxicology and pharmacology of synthetic organoselenium compounds: an update, *Arch. Toxicol.*, 2021, **95**, 1179–1226; (*c*) A. Madabeni, M. Bortoli, P. A. Nogara, G. Ribaudo, M. D. Tiezza, L. Flohé, J. B. T. Rocha and L. Orian, 50 Years of Organoselenium Chemistry, Biochemistry and Reactivity: Mechanistic Understanding, Successful and Controversial Stories, *Chem. – Eur. J.*, 2024, **30**, e202403003; (*d*) C. Morán-Serradilla, D. Plano, C. Sanmartín and A. Sharma, Selenization of Small Molecule Drugs: A New Player on the Board, *J. Med. Chem.*, 2024, **67**, 7759–7787.
7 (*a*) S. Panda, A. Panda and S. S. Zade, Organoselenium compounds as fluorescent probes, *Coord. Chem. Rev.*, 2015, **300**, 86–100; (*b*) R. Mamgain and F. V. Singh, Selenium-Based Fluorescence Probes for the Detection of Bioactive Molecules, *ACS Org. Inorg. Au*, 2022, **2**, 262–288.
8 (*a*) G. da Costa, G. B. Blödorn, A. M. Barcellos and D. Alves, Recent Advances in the Use of Diorganyl Diselenides as Versatile Catalysts, *Molecules*, 2023, **28**, 6614; (*b*) P. Qu and G.-Q. Liu, Recent progress in the organoselenium-catalyzed

difunctionalization of alkenes, *Org. Biomol. Chem.*, 2025, **23**, 1552–1568.

9 (*a*) Q. Li, Y. Zhang, Z. Chen, X. Pan, Z. Zhang, J. Zhu and X. Zhu, Organoselenium chemistry-based polymer synthesis, *Org. Chem. Front.*, 2020, **7**, 2815–2841; (*b*) B. Fan, F. Lin, X. Wu, Z. Zhu and A. K.-Y. Jen, Selenium-Containing Organic Photovoltaic Materials, *Acc. Chem. Res.*, 2021, **54**, 3906–3916.

10 (*a*) T. Chivers and R. S. Laitinen, Tellurium: a maverick among the chalcogens, *Chem. Soc. Rev.*, 2015, **44**, 1725–1739; (*b*) R. L. O. R. Cunha, I. E. Gouvea and L. Juliano, A glimpse on biological activities of tellurium compounds, *An. Acad. Bras. Cienc.*, 2009, **81**, 393–407.

11 (*a*) P. Wonner, L. Vogel, M. Düser, L. Gomes, F. Kniep, B. Mallick, D. B. Werz and S. M. Huber, Carbon–Halogen Bond Activation by Selenium-Based Chalcogen Bonding, *Angew. Chem., Int. Ed.*, 2017, **56**, 12009–12012; (*b*) P. Wonner, L. Vogel, F. Kniep and S. M. Huber, Catalytic Carbon–Chlorine Bond Activation by Selenium-Based Chalcogen Bond Donors, *Chem. – Eur. J.*, 2017, **23**, 16972–16975.

12 (*a*) A. Capperucci and D. Tanini, Tellurium-containing Thiol-peroxidase-like Antioxidants and their Catalytic Mechanism, *Curr. Chem. Biol.*, 2023, **17**, 13–25; (*b*) A. Bhardwaj, A. Dubey, A. Ragusa, P. Alam, S. Garg and A. Bendi, Organotellurium(IV) Complexes as Potent Antimalarial and Antimicrobial Agents: Synthesis, Biological Evaluation, and Computational Insights, *Appl. Organomet. Chem.*, 2025, **39**, e70206; (*c*) F. F. M. Al-joborae, S. S. Al-Rawi, A. H. Ibrahim, A. W. Salman and M. Iqbal, Advances in synthesis and anticancer applications of organo-tellurium compounds, *Rev. Inorg. Chem.*, 2025, **45**, 337–358.

13 (*a*) P. Pale and V. Mamane, Chalcogen Bonding Catalysis: Tellurium, the Last Frontier?, *Chem. – Eur. J.*, 2023, **29**, e202302755; (*b*) S. Barata-Vallejo, M. del R. Torviso and A. Postigo, Unlocking Tellurium–Centered Radicals: From Intermediates in Total Organic Syntheses to Stable Organotellurides and Catalysts, *Asian J. Org. Chem.*, 2025, e00492; (*c*) G. Sekar, V. V. Naira and J. Zhu, Chalcogen bonding catalysis, *Chem. Soc. Rev.*, 2024, **53**, 586–605.

14 P. R. O. Campos, G. P. P. P. Silva, Y. Shibuya, S. Koguchi and E. E. Alberto, Oxidation Reactions Promoted or Catalyzed by Organotellurium Compounds, *ACS Omega*, 2025, **10**, 28691–28708.

15 A. M. Barcellos, M. Sacramento, G. P. da Costa, G. Perin, E. J. Lenardão and D. Alves, Organoboron compounds as versatile reagents in the transition metal-catalyzed C–S, C–Se and C–Te bond formation, *Coord. Chem. Rev.*, 2021, **442**, 214012.

16 J. Rafique, D. S. Rampon, J. B. Azeredo, F. L. Coelho, P. H. Schneider and A. L. Braga, Light-Mediated Seleno-Functionalization of Organic Molecules: Recent Advances, *Chem. Rec.*, 2021, **21**, 2739.

17 M. Sacramento, G. P. da Costa, A. M. Barcellos, G. Perin, E. J. Lenardão and D. Alves, Transition-Metal-Free C–S, C–Se, and C–Te Bond Formation from Organoboron Compounds, *Chem. Rec.*, 2021, **21**, 2855.

18 (*a*) B. Movassagh and E. Mohammadi, Green Trends in Synthesis of Alkenyl and Alkynyl Chalcogenides, *Curr. Green Chem.*, 2016, **3**, 18–35; (*b*) L. L. Baldassari, A. C. Mantovani, S. Senoner, B. Maryasin, N. Maulide and D. S. Lüdtke, Redox-Neutral Synthesis of Selenoesters by Oxyarylation of Selenoalkynes under Mild Conditions, *Org. Lett.*, 2018, **20**, 5881–5885; (*c*) A. D. Sonawane, R. A. Sonawane, M. Ninomiya and M. Koketsu, Synthesis of Seleno-Heterocycles via Electrophilic/Radical Cyclization of Alkyne Containing Heteroatoms, *Adv. Synth. Catal.*, 2020, **362**, 3485–3515; (*d*) Y. Xu, D. Huang, J. Wu and X. Wu, Recent Developments in Selenylation of Alkynes, *Adv. Synth. Catal.*, 2024, **366**, 3761–3789; (*e*) A. Temperini, G. Brufani, S. Santoro and L. Vaccaro, Alkynyl Phenyl Selenides as Intermediates in the Metal-Free Cyclisation of N-Tosyl Homopropargyl Amides to γ-Lactams, *Eur. J. Org. Chem.*, 2025, e202401248.

19 M. A. Guerrero-Robles, M. A. Vilchis-Reyes, E. M. Ramos-Rivera and C. Alvarado, Synthesis of Alkynyl Sulfones, *ChemistrySelect*, 2019, **4**, 13698–13708.

20 C. C. Chen and J. Waser, One-Pot, Three-Component Arylalkynyl Sulfone Synthesis, *Org. Lett.*, 2015, **17**, 736–739.

21 R. Singh, B. K. Allam, N. Singh, K. Kumari, S. K. Singh and K. N. Singh, A Direct Metal-Free Decarboxylative Sulfono Functionalization (DSF) of Cinnamic Acids to α,β-Unsaturated Phenyl Sulfones, *Org. Lett.*, 2015, **17**, 2656–2659.

22 S. Li, X. Li, F. Yang and Y. Wu, Copper-catalyzed direct decarboxylative hydrosulfonylation of aryl propiolic acids with sulfonylhydrazides leading to vinylsulfones, *Org. Chem. Front.*, 2015, **2**, 1076–1079.

23 J. Wei and Z. Sun, tert-Butyl Sulfoxide as a Starting Point for the Synthesis of Sulfinyl Containing Compounds, *Org. Lett.*, 2015, **17**, 5396–5399.

24 J. Meesin, P. Katrun, C. Pareseecharoen, M. Pohmakotr, V. Reutrakul, D. Soorukram and C. Kuhakarn, Iodine-catalyzed Sulfonylation of Arylacetylenic Acids and Arylacetylenes with Sodium Sulfinates: Synthesis of Arylacetylenic Sulfone, *J. Org. Chem.*, 2016, **81**, 2744–2752.

25 L. Wang, W. Wei, D. Yang, H. Cui, H. Yue and H. Wang, Direct cross-coupling of aryl alkynyliodines with arylsulfinic acids leading to alkynyl sulfones under catalyst-free conditions, *Tetrahedron Lett.*, 2017, **58**, 4799–4802.

26 P. Chen, C. Zhu, R. Zhu, W. Wu and H. Jiang, MnO_2-Promoted Oxidative Radical Sulfonylation of Haloalkynes with Sulfonyl Hydrazides: C(sp)-S Bond Formation towards Alkynyl Sulfones, *Chem. – Asian J.*, 2017, **12**, 1875–1878.

27 C. Dai, J. Wang, S. Deng, C. Zhou, W. Zhang, Q. Zhu and X. Tang, Acid-mediated sulfonylation of arylethynylene bromides with sodium arylsulfinates: synthesis of (E)-1,2-bis(arylsulfonyl)ethylenes and arylacetylenic sulfones, *RSC Adv.*, 2017, **7**, 36112–36116.

28 S. G. E. Amos, S. Nicolai, A. Gagnebin, F. Le Vaillant and J. Waser, Metal-Free Electrophilic Alkynylation of Sulfenate

Anions with Ethynylbenziodoxolone Reagents, *J. Org. Chem.*, 2019, **84**, 3687–3701.
29 Z.-Y. Mo, Y.-Z. Zhang, G.-B. Huang, X.-Y. Wang, Y.-M. Pan and H.-T. Tang, Electrochemical Sulfonylation of Alkynes with Sulfonyl Hydrazides: A Metal- and Oxidant-Free Protocol for the Synthesis of Alkynyl Sulfones, *Adv. Synth. Catal.*, 2020, **362**, 2160–2167.
30 X. Meng, H. Xu, X. Cao, X.-M. Cai, J. Luo, F. Wang and S. Huang, Electrochemically Enabled Sulfonylation of Alkynes with Sodium Sulfinates, *Org. Lett.*, 2020, **22**, 6827–6831.
31 Q. Zhong, Y. Zhao, S. Sheng and J. Chen, Electrochemical decarboxylative sulfonylation of arylacetylenic acids with sodium arylsulfinates: Access to arylacetylenic sulfones, *Synth. Commun.*, 2020, **50**, 161–167.
32 D. S. Raghuvanshi and N. Verma, An iodine-mediated new avenue to sulfonylation employing N-hydroxy aryl sulfonamide as a sulfonylating agent, *Org. Biomol. Chem.*, 2021, **19**, 4760–4767.
33 X. Gong, M. Yang, J.-B. Liu, F.-S. He and J. Wu, Photoinduced synthesis of alkylalkynyl sulfones through a reaction of potassium alkyltrifluoroborates, sulfur dioxide, and alkynyl bromides, *Org. Chem. Front.*, 2020, **7**, 938–943.
34 X. Yang, J. Yi, X. Li, Y. Wu, J. Dong, Z. He, G. Zeng, J. Xu and B. Fan, Photocatalytic synthesis of alkynylsulfones and alkenylsulfones using sulfonylhydrazides and alkynes, *Org. Biomol. Chem.*, 2023, **21**, 5747–5751.
35 K. Cao, N. Zhang, L. Lin, Q. Shen, H. Jiang and J. Li, The Synthesis of (E)-Vinyl and Alkynyl Sulfones by the Formation of an Electron Donor-Acceptor Complex Using Thiosulfonates and Sodium Iodide Under Visible Light, *Adv. Synth. Catal.*, 2024, **366**, 207–213.
36 W. Chen, Q. Zhang, S. Zhang, F. Huang, X. Zhang and J. Jia, Visible Light Promoted Coupling Reaction of Alkynyl Iodide and Sodium Sulphinate without Photocatalyst, *Chin. J. Org. Chem.*, 2024, **44**, 584–592.
37 D. Ge, X. Wang and X.-Q. Chu, SOMOphilic alkynylation using acetylenic sulfones as functional reagents, *Org. Chem. Front.*, 2021, **8**, 5145–5164.
38 W.-H. Tang, L.-Y. Wu, Q.-Q. Zhou and J.-P. Wan, Photoredox catalytic phosphine-mediated deoxygenative alkynylation of carboxylic acids with alkynyl sulfones for alkynone synthesis, *Org. Chem. Front.*, 2025, **12**, 2340–2345.
39 B. Mohan, S. Hwang, H. Woo and K. H. Park, Copper Nanoparticle Catalyzed Formation of C–S Bonds through Activation of S–S and C–H Bonds: An Easy Route to Alkynyl Sulfides, *Synthesis*, 2015, 3741–3745.
40 Z. Fang, W. He, M. Cai, Y. Lin and H. Zhao, A heterogeneous copper(I)-catalyzed aerobic oxidative cross-dehydrogenative coupling of terminal alkynes with thiols leading to alkynyl sulfides, *Tetrahedron Lett.*, 2015, **56**, 6463–6467.
41 J. Doroszuk, M. Musiejuk, S. Demkowicz, J. Rachon and D. Witt, Convenient and efficient synthesis of functionalized unsymmetrical alkynyl sulfides, *RSC Adv.*, 2016, **6**, 105449–105453.
42 J. Santandrea, C. Minozzi, C. Cruchø and S. K. Collins, Photochemical Dual-Catalytic Synthesis of Alkynyl Sulfides, *Angew. Chem., Int. Ed.*, 2017, **56**, 12255–12259.
43 Y. Fu, Y. Su, Q.-S. Xu, Z. Du, Y. Hu, K.-H. Wang and D. Huang, CuI promoted sulfenylation of organozinc reagents with arylsulfonyl chlorides, *RSC Adv.*, 2017, **7**, 6018–6022.
44 B. Waldecker, F. Kraft, C. Golz and M. Alcarazo, 5-(Alkynyl) dibenzothiophenium Triflates: Sulfur-Based Reagents for Electrophilic Alkynylation, *Angew. Chem., Int. Ed.*, 2018, **57**, 12538–12542.
45 F. Liu and W. Yi, A thiol-free synthesis of alkynyl chalcogenides by the copper-catalyzed C–X (X = S, Se) cross-coupling of alkynyl carboxylic acids with Bunte salts, *Org. Chem. Front.*, 2018, **5**, 428–433.
46 L. Yang, Z.-Y. Tian and C.-P. Zhang, Transition-Metal-Free Selective Synthesis of (Z)-1,2-Diarylthio-1-arylalkenes, (2-Arylethene-1,1,2-triyl)tris(arylsulfane)s and Alkynyl Sulfides from Thiocyanates and Terminal Arylalkynes, *ChemistrySelect*, 2019, **4**, 311–315.
47 K. Kanemoto, S. Yoshida and T. Hosoya, Synthesis of Alkynyl Sulfides by Copper-Catalyzed Thiolation of Terminal Alkynes Using Thiosulfonates, *Org. Lett.*, 2019, **21**, 3172–3177.
48 E. B. Balbom, F. Gritzenco, A. Sperança, M. Godoi, D. Alves, T. Barcellos and B. Godoi, Copper-catalyzed Csp-chalcogen bond formation: Versatile approach to N-(3-(organochalcogenyl)prop-2-yn-1-yl)amides, *Tetrahedron*, 2019, **75**, 4017–4023.
49 T. Song, P. Ren, J. Xiao, Y. Yuan and Y. Yang, Highly dispersed Ni2P nanoparticles on N,P-codoped carbon for efficient cross-dehydrogenative coupling to access alkynyl thioethers, *Green Chem.*, 2020, **22**, 651–656.
50 É. Godin, J. Santandrea, A. Caron and S. K. Collins, General Cu-Catalyzed Csp–S Coupling, *Org. Lett.*, 2020, **22**, 5905–5909.
51 L.-Z. Qin, X. Yuan, J. Liu, M.-Y. Wu, Q. Sun, X. Duan, X.-P. Zhang, J.-K. Qiu and K. Guo, Continuous-flow processes for the S-alkynylation of cysteine-containing peptides and thioglycosides under catalyst-free, oxidant-free and mild conditions, *Green Chem.*, 2021, **23**, 6598–6603.
52 R. Ye, H. Ruan, H. Xu, Z. Li, L.-G. Meng and L. Wang, Amino-assisted synthesis of alkynylthioethers via a visible-light-induced C(sp)–SII coupling between bromoalkynes and 2,2′-diaminodiaryldisulfides, *Org. Chem. Front.*, 2021, **8**, 5345–5351.
53 U. Todorović, I. Klose and N. Maulide, Straightforward Access to Thiocyanates via Dealkylative Cyanation of Sulfoxides, *Org. Lett.*, 2021, **23**, 2510–2513.
54 Y. Chen, S. Wen, Q. Tian, Y. Zhang and G. Cheng, Transition Metal-Free C–H Thiolation via Sulfonium Salts Using β-Sulfinylesters as the Sulfur Source, *Org. Lett.*, 2021, **23**, 7905–7909.
55 F. Gritzenco, J. C. Kazmierczak, T. Anjos, A. Sperança, M. L. B. Peixoto, M. Godoi, K. N. B. Ledeburh, C. A. Brüning, L. L. Zamin and B. Godoi, *Synthesis*, 2021, 2676–2688.

56 G.-Q. Hu, C. Wang, F. Zhao, Y.-W. Liu, J.-H. Liu and B. Zhao, Copper-Catalyzed Thiolation of Terminal Alkynes with N-Thiosuccinimides to Access Alkynyl Sulfides, *ChemistrySelect*, 2022, **7**, e202104380.
57 Y. Liu, Y. Xu, Y. Zhang, W.-C. Gao and X. Shao, Thiol-free synthesized" and sustainable thiolating synthons for nickel-catalyzed reductive assembly of sulfides with high efficiency, *Org. Chem. Front.*, 2022, **9**, 6490–6497.
58 F. Saito and S. Euteneuer, One-Pot, Three-Component Assembly of Sulfides Using a Sulfoxide Reagent as a Sulfur Dication Equivalent, *Org. Lett.*, 2023, **25**, 6057–6061.
59 C. Chen, L. Pan, J. Zhu, J. Shao, J. Dai, G. Qian and Z. Rong, Metal-free direct thiolation of terminal alkynes with methyl sulfoxides, *Tetrahedron Lett.*, 2023, **114**, 154275.
60 W. Xie and S. Liu, Access to derivatives of 4-(arylthio)isocoumarins via hydrogen bonding network assisted electrophilic cyclization, *New J. Chem.*, 2023, **47**, 20262–20265.
61 Z. Wang, M. Su, H. Xu, J. Zhou and J. Wen, Base–Promoted Selective Synthesis of Alkynyl Sulfides via C–S Bond Cleavage of Alkynyl Sulfonium Salts, *Adv. Synth. Catal.*, 2024, **366**, 2264–2269.
62 S. Chen, Y. Yu and M. Chen, Visible-light-promoted phosphine-mediated synthesis of thioesters and thioalkynes from sodium arylsulfinates, *Org. Biomol. Chem.*, 2025, **23**, 5174–5181.
63 B. Mohan, C. Yoon, S. Jang and K. H. Park, Copper Nanoparticles Catalyzed Se(Te)-Se(Te) Bond Activation: A Straightforward Route Towards Unsymmetrical Organochalcogenides from Boronic Acids, *ChemCatChem*, 2015, **7**, 405–412.
64 B. Mohan, J. C. Park and K. H. Park, Mechanochemical Synthesis of Active Magnetite Nanoparticles Supported on Charcoal for Facile Synthesis of Alkynyl Selenides by C–H Activation, *ChemCatChem*, 2016, **8**, 2345–2350.
65 L. K. Soares, R. B. Silva, T. J. Peglow, M. S. Silva, R. G. Jacob, D. Alves and G. Perin, Selective Synthesis of Vinyl- or Alkynyl Chalcogenides from Glycerol and their Water-Soluble Derivatives, *ChemistrySelect*, 2016, **1**, 2009–2013.
66 S. Mukherjee, A. Pal, B. Saha and B. C. Ranu, Silver-catalyzed carbon–selenium cross-coupling using N-(phenylseleno)phthalimide: an alternate approach to the synthesis of organoselenides, *Can. J. Chem.*, 2017, **95**, 51–56.
67 P. G. Karmaker and F. Huo, Organic Selenocyanates: Rapid Advancements and Applications in the Field of Organic Chemistry, *Asian J. Org. Chem.*, 2022, **11**, e202200226.
68 N. Mukherjee, D. Kundu and B. C. Ranu, Copper-Silver Dual Catalyzed Decyanative C–Se Cross-Coupling, *Adv. Synth. Catal.*, 2017, **359**, 329–338.
69 S. Kodama, T. Saeki, K. Mihara, S. Higashimae, S.-I. Kawaguchi, M. Sonoda, A. Nomoto and A. Ogawa, A Benzoyl Peroxide/Diphenyl Diselenide Binary System for Functionalization of Alkynes Leading to Alkenyl and Alkynyl Selenides, *J. Org. Chem.*, 2017, **82**, 12477–12484.
70 M. C. D. F. Xavier, B. Goldani, R. F. Schumacher, G. Perin, P. H. Schneider and D. Alves, Silver-catalyzed direct selenylation of terminal alkynes through C-H bond functionalization, *J. Mol. Catal. A: Chem.*, 2017, **427**, 73–79.
71 E. J. Lenardão, E. L. Borges, G. Stach, L. K. Soares, D. Alves, R. F. Schumacher, L. Bagnoli, F. Marini and G. Perin, Glycerol as Precursor of Organoselanyl and Organotellanyl Alkynes, *Molecules*, 2017, **22**, 391.
72 A. A. Heredia and A. B. Peñéñory, Transition-metal-free one-pot synthesis of alkynyl selenides from terminal alkynes under aerobic and sustainable conditions, *Beilstein J. Org. Chem.*, 2017, **13**, 910–918.
73 G. Wu, L. Min, H. Li, W. Gao, J. Ding, X. Huang, M. Liu and H. Wu, Metal-free synthesis of alkynyl alkyl selenides via three-component coupling of terminal alkynes, Se, and epoxides, *Green Chem.*, 2018, **20**, 1560–1563.
74 F. L. Coelho, L. C. Dresch, R. Stieler, L. F. Campo and P. H. Schneider, New arylselanylpyrazole-copper catalysts: Highly efficient catalytic system for C-Se and C-S coupling reactions, *Catal. Commun.*, 2019, **121**, 19–26.
75 M. Sacramento, L. Menezes, B. Goldani, G. Perin, M. S. Silva, T. Barcellos and D. Alves, Synthesis of alkynyltellurides mediated by K3PO4 and DMSO, *New J. Chem.*, 2019, **43**, 11091–11098.
76 D.-L. Wang, Y. Fang, S.-Y. Wang and S.-J. Ji, Silver-mediated activation of terminal alkynes: A strategy to construct bisethynynl selenides and tellurides, *Tetrahedron*, 2020, **76**, 131083.
77 C. H. Silveira, M. G. Fronza, R. A. Balaguez, A. M. E. Larroza, L. Savegnago, D. F. Back, B. A. Iglesias and D. Alves, Alkynylselenium-functionalized benzothiadiazoles: Synthesis, photophysics, electrochemistry, and biomolecular interaction studies, *Dyes Pigm.*, 2021, **185**, 108910.
78 S. Kodama, V. T. Hung, T. Saeki, K. Mihara, Y. Yamamoto, M. Sonoda, A. Nomoto and A. Ogawa, 2,2-Bis(phenylselanyl)-1-(p-tolyl)vinyl 2-Oxo-2-(p-tolyl)acetate, *Molbank*, 2021, **2021**, M1283.
79 Y. Lu, Q. Liu, Z.-X. Wang and X.-Y. Chen, Alkynyl Sulfonium Salts Can Be Employed as Chalcogen-Bonding Catalysts and Generate Alkynyl Radicals under Blue-Light Irradiation, *Angew. Chem., Int. Ed.*, 2022, **61**, e202116071.
80 G. Wu, X. Zhou and C. Wang, Copper-catalyzed decarboxylative Se insertion coupling of indoles and propiolic acids, *Chin. Chem. Lett.*, 2022, **33**, 4531–4535.
81 M. Matsumura, K. Tsukada, K. Sugimoto, Y. Murata and S. Yasuike, Synthesis of novel alkynyl imidazopyridinyl selenides: copper-catalyzed tandem selenation of selenium with 2-arylimidazo[1,2-a]pyridines and terminal alkynes, *Beilstein J. Org. Chem.*, 2022, **18**, 863–871.
82 E. G. O. Soares, D. B. Paixão, C. D. G. da Silva and P. H. Schneider, Synthesis of Alkynylselenides under Visible-Light Irradiation Using the Ionic Liquid [BMIm]BF4 as a Solvent, *J. Braz. Chem. Soc.*, 2023, **34**, 590–599.
83 W. Hou, X. Zhou, Z. Yang, H. Xia, Y. Wang, K. Xu, S. Hou, S. Zhang, D. Cui, P. Ma, W. Zhou and H. Xu, Multicomponent Reaction Integrating Selenium(II)–Nitrogen Exchange (SeNEx) Chemistry and Copper-

Catalyzed Azide–Alkyne Cycloaddition (CuAAC), *Angew. Chem., Int. Ed.*, 2025, **64**, e202500942.

84 F. Tan, C.-Z. Fang, B.-S. Qiu, H. Sheng, Y.-L. Tu and X.-Y. Chen, Charge transfer complex enabled mechanochemical synthesis of chalcogenoacetylenes via alkynyl radicals, *Org. Chem. Front.*, 2025, **12**, 649–654.

85 (*a*) D. Louvel, C. Ghiazza, V. Debrauwer, L. Khrouz, C. Monnereau and A. Tlili, Forging C-SeCF3 Bonds with Trifluoromethyl Tolueneselenosulfonate under Visible-Light, *Chem. Rec.*, 2021, **21**, 417–426; (*b*) F. Li, J.-W. Song, X. Han and C.-P. Zhang, Progress in Photocatalyzed Trifluoromethylthiolation and Trifluoromethylselenolation Reactions, *Synthesis*, 2025, 539–570; (*c*) Q. Shen, A Toolbox of Reagents for Trifluoromethylthiolation: From Serendipitous Findings to Rational Design, *J. Org. Chem.*, 2023, **88**, 3359–3333.

86 (*a*) M. Briand, E. Anselmi, G. Dagousset and E. Magnier, The Revival of Enantioselective Perfluoroalkylation – Update of New Synthetic Approaches from 2015–2022, *Chem. Rec.*, 2023, **23**, e202300114; (*b*) Y. Wang, Z. Ye, H. Zhang and Z. Yuan, Recent Advances in the Development of Direct Trifluoromethylselenolation Reagents and Methods, *Adv. Synth. Catal.*, 2021, **363**, 1835–1854.

87 S. R. Mudshinge, Y. Yang, B. Xu, G. B. Hammond and Z. Lu, Gold (I/III)-Catalyzed Trifluoromethylthiolation and Trifluoromethylselenolation of Organohalides, *Angew. Chem., Int. Ed.*, 2022, **61**, e202115687.

88 Y.-X. Cheng, X.-G. Yang, F.-H. Du and C. Zhang, Direct trifluoromethylthiolation of terminal alkynes mediated by a hypervalent trifluoromethylthio-iodine(III) reagent; boosting effect of fluorinated alcohol, *Green Chem.*, 2024, **26**, 5914–5920.

89 Y. Gao, R. Xiao, B. Feng, Z. Bian, H. Zhang, G. Zhu, Y. Wang and Z. Yuan, Metal-free Lewis-acid-catalyzed divergent trifluoromethylselenolation of alkynes: construction of α-trifluoromethylselenolated ketones and alkynes, *Org. Chem. Front.*, 2023, **10**, 4905–4911.

90 X. Ding, Y.-F. Yao, J.-Y. Li and C.-P. Zhang, Copper-Mediated Decarboxylative Trifluoromethylselenolation of Alkynyl Carboxylic Acids with [Me4N][SeCF3], *Eur. J. Org. Chem.*, 2024, e202400851.

91 R.-L. Guo, X.-L. Zhang, X.-P. Bu, M.-Y. Wang, B.-Y. Zhao, Y.-R. Gao, Q. Jia and Y.-Q. Wang, Se-(Fluoromethyl) Benzenesulfonoselenoates: Shelf-Stable, Easily Available Reagents for Monofluoromethylselenolation, *Chem. – Eur. J.*, 2022, **28**, e202200981.

92 D. Zhu, Y. Gu, L. Lu and Q. Shen, N-Difluoromethylthiophthalimide: A Shelf-Stable, Electrophilic Reagent for Difluoromethylthiolation, *J. Am. Chem. Soc.*, 2015, **137**, 10547–10553.