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Green Synthesis of Stereodefined Tri- and Tetrasubstituted Alkenes *via* 100% Atom-economic and Regio-, and Stereoselective Halo-chalcogenation and Sulfonylation of Alkynes

Appanapalli N. V. Satyanarayana and Tanmay Chatterjee*

Abstract: Achieving 100% atom economy in an organic transformation is a challenging task but it is always desirable in the context of green chemistry. Difunctionalization of alkynes using a bifunctional reagent is a useful strategy to achieve 100% atom economy, however, the challenge is to control the regio- and stereoselectivity of the reaction. In this article, we discuss the recent advances in developing 100% atom economic, highly regio- and stereoselective halo-chalcogenation and chlorosulfonylation strategies with alkynes for the green and sustainable synthesis of stereodefined tri- or tetrasubstituted alkenes, and its application in accessing valuable molecules including a marketed drug in a green and sustainable manner. The green chemistry metrics are presented to highlight the greenness of some of these protocols.

Keywords: 100% Atom-economy · Alkynes · Chlorosulfonylation · Halo-chalcogenation

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1. Introduction

The synthesis of stereodefined tri- or tetrasubstituted alkenes poses a significant challenge in organic synthesis, however, they have garnered considerable interest from organic chemists owing to their crucial importance. This class of alkenes is frequently found in life-saving pharmaceuticals, natural products, and biologically active compounds, including tamoxifen, brasilenol, isovirescenol A, and guadalupol, *etc.* (Fig. 1).[1] They also serve as useful building blocks in materials chemistry.[2] While various strategies exist for synthesizing stereodefined tetrasubstituted alkenes,[3] difunctionalization of alkynes is recognized as the most effective and widely employed approach owing to its high atom-economic feature. One of these processes involves the cleavage of a heteroatom-heteroatom bond in a species, followed by the addition of the two heteroatoms into a –C≡C– triple bond in a single step, thus making it a 100% atom-economic and effective process in the context of green chemistry.[4] Among all the heteroatom-heteroatom difunctionalizations of alkynes, the halo-chalcogenation is particularly noteworthy, as it provides a straightforward strategy for accessing stereodefined tetrasubstituted alkenes bearing useful functional groups such as halogen and chalcogen, which could be further utilized to install required functional groups *via* a cross-coupling reaction for synthesizing potential organic molecules, including drugs.[5] Moreover, alkenylchalcogenides are found in many biologically active molecules, including natural products and they are also found in many useful materials.[6] Consequently, several reports have been published on the synthesis of halochalcogenation of alkynes. However, they suffer from limitations such as the requirement for transition metals, harsh reaction conditions, selectivity issues, poor atom economy, generation of hazardous organic wastes, and the requirement for specially designed chalcogen precursors.[7–10]

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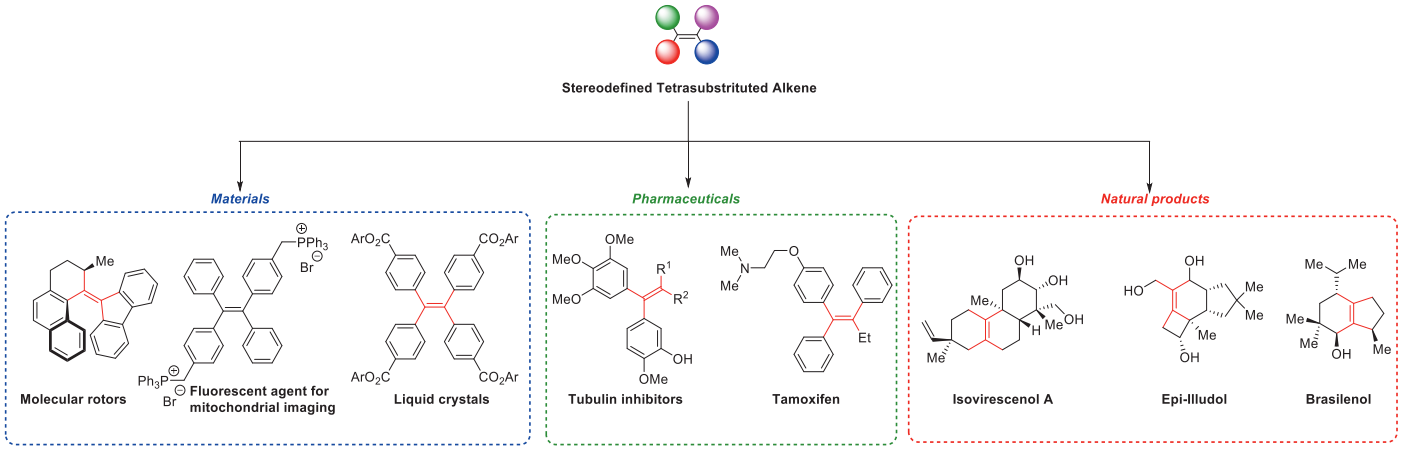


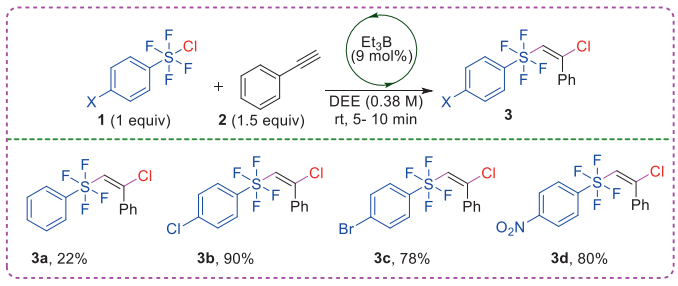
Fig. 1. Valuable stereodefined tetrasubstituted alkenes.

In the realm of environmental sustainability, the 12 principles of green chemistry highlight the significance of a reaction that achieves a 100% atom economy.

These reactions are particularly important in modern organic synthesis because they effectively reduce or sometimes eliminate the generation of hazardous wastes, which is the ultimate goal of green chemistry. Additionally, these practices promote sustainability, enhance resource efficiency, and improve cost-effectiveness.[11] In this review article, we present the recently developed 100% atom-economic, halo-chalcogenations and chlorosulfonylations of alkynes or ynamides for the synthesis of stereodefined tri- or tetrasubstituted alkenes.

1.1 Chlorosulfenylation of Alkynes

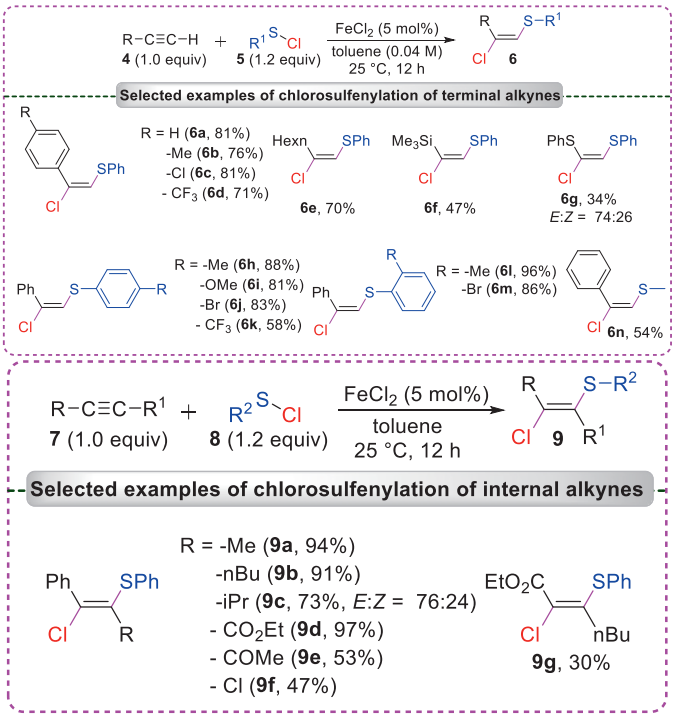
In 2014, Welch and coworkers[12] developed a triethyl boron (BEt_3) catalyzed direct radical addition of chlorotetrafluorosulfanyl arenes to terminal alkynes in a short reaction time with 100% atom-economy (Scheme 1). This protocol was efficient and furnished the desired products in a moderate to excellent yield. However, it was limited to the insertion of chloro and aryltetrafluorosulfanyl groups to the terminal alkynes only.



Scheme 1. Et_3B-catalyzed, 100% atom-economic addition of chlorotetrafluorosulfanylarenes to alkynes.

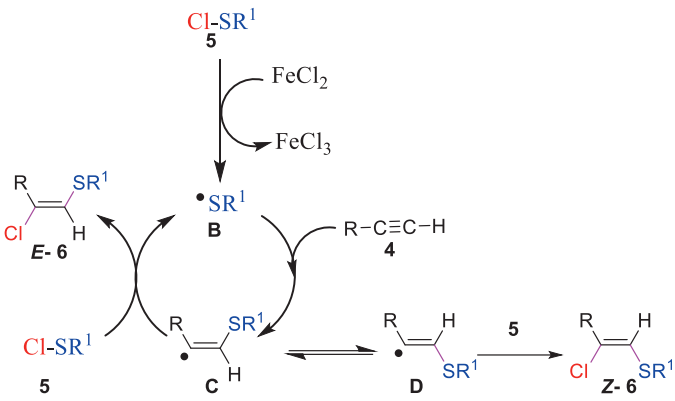
In 2014, Nishihara and coworkers[13] reported an Fe-induced 100% atom-economic anti-addition of sulfenyl chlorides to alkynes (Scheme 2). The S-Cl bond in the sulfenyl chlorides was effectively added to various –C≡C– triple bonds with impressive regio- and stereoselectivity, aided by a catalytic amount of $FeCl_2$.

This reaction is compatible with a wide range of functional groups and can be scaled up to gram quantities without any decrease in yield. Both terminal and internal alkynes have undergone stereospecific chlorosulfenylation, resulting in stereodefined tri- and tetrasubstituted alkenes in a 100% atom-economic fashion.



Scheme 2. Fe-induced 100% atom-economic anti-chlorosulfenylation of internal and terminal alkynes with sulfenyl chlorides.

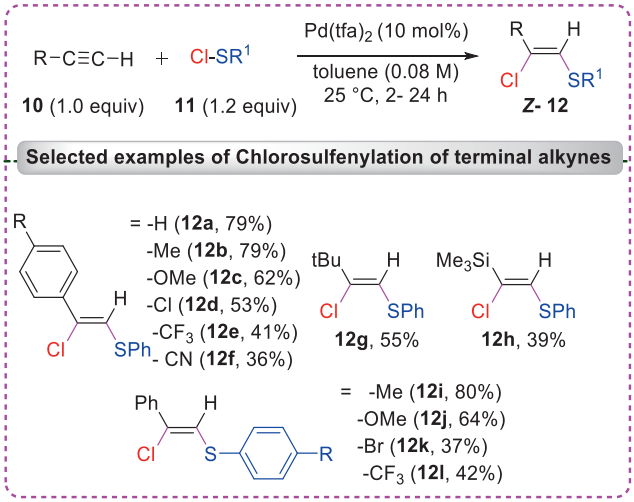
Initial mechanistic studies suggested that the reaction likely followed a radical pathway, involving a sulfur-centered radical intermediate formed through the iron-mediated homolysis of the S-Cl



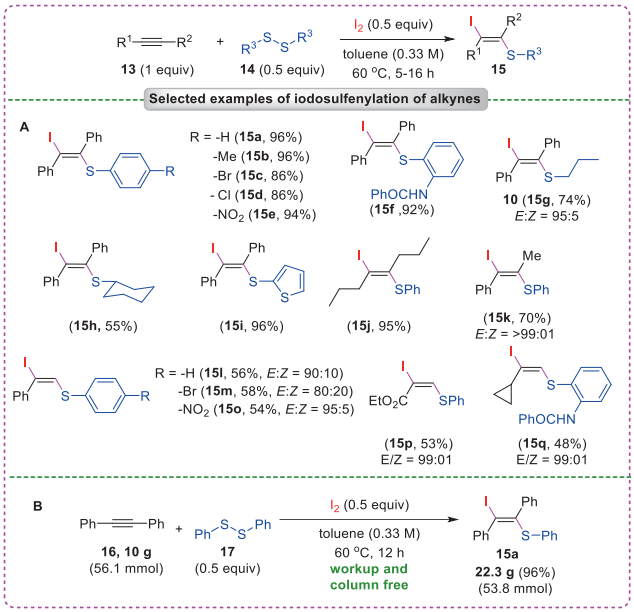
Scheme 3. Proposed reaction mechanism.

bond (Scheme 3). The synthesized product was successfully converted into other useful compounds *via* cross-coupling reactions.

In 2014, the same group[14] reported the *syn*-addition of sulfenyl chlorides to terminal alkynes in the presence of a catalytic amount of $Pd(tfa)_2$ (tfa = trifluoroacetate) at room temperature, which afforded other stereoisomeric products, *i.e.* chloroalkenyl sulfides (*Z*-isomer) as the major product in good to excellent yields along with the formation of the *E*-isomer as a minor product (1–9%) (Scheme 4). However, the method was limited to terminal alkynes.



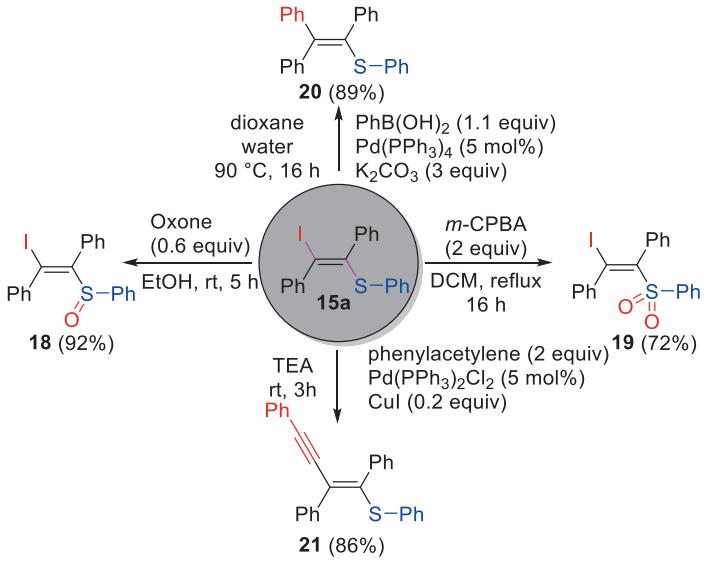
Scheme 4. Pd-catalysed *syn*-chlorosulfenylation of alkynes.



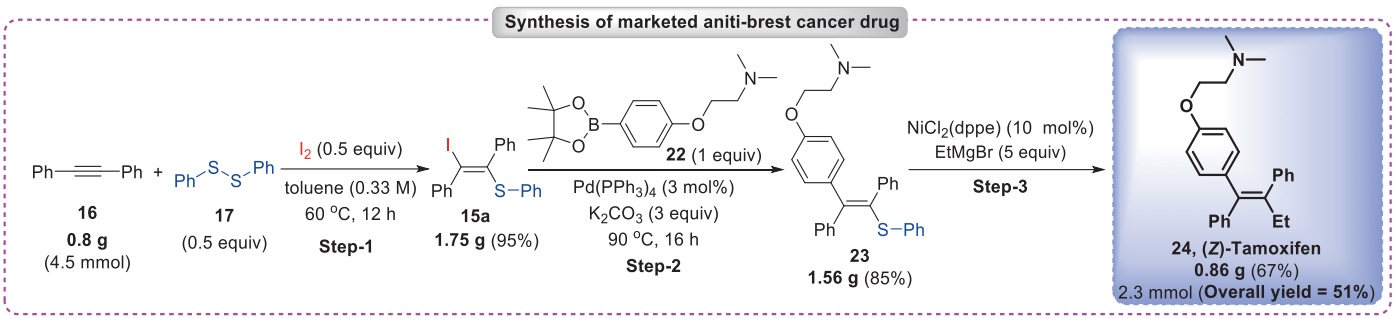
Scheme 5. Reagentless and 100% atom-economic iodosulfenylation of alkynes and multi-gram synthesis of **15a**.

1.2 *Iodosulfenylation of Alkynes*

Our group developed a reagentless and sustainable approach to access (*E*)-β-iodoalkenyl sulfides in a 100% atom-economic and highly regio- and stereoselective manner using commercially available starting materials,[15] such as alkynes (1 equiv.), iodine (0.5 equiv.), and disulfides (0.5 equiv.), in toluene at 60–120 °C (Scheme 5). This protocol was effective for both internal and terminal alkynes, yielding stereodefined tetra- and trisubstituted alkenes, in particular, (*E*)-β-iodoalkenyl sulfides in moderate to excellent yields with a broad substrate scope (Scheme 5A). Most reactions were clean and yielded the pure product from a simple cold pentane wash of the crude reaction mixture. The developed protocol was scalable up to a 10-gram scale without compromising the outcome and furnished the desired product in 96% yield (Scheme 5B). It exhibited high regio- and stereoselectivity, producing the anti-addition products, *i.e.* the *E*-isomer exclusively. (*E*)-(2-Iodo-1,2-diphenylvinyl)(phenyl)sulfane **15a** was synthetically diversified into other potential stereodefined tetrasubstituted alkenes (Scheme 6). Significantly, **15a** was converted to a marketed breast-cancer drug, *Z*-tamoxifen, in just three steps *via* cross-coupling reactions (overall three-step synthesis starting from commercially available feedstock materials, *i.e.* diphenyl acetylene, diphenyl disulfide, and iodine), with a good overall yield (51%) (Scheme 7). Our strategy for the synthesis of (*Z*)-tamoxifen could be considered as step-economic, sustainable, and practical as compared to several previously developed multi-step strategies.[16] These results demonstrated the practical application of the developed protocol. Significantly, this protocol achieved outstanding green metrics, such as 100% atom economy, 96% atom efficiency, 95.9% carbon efficiency, 95.93% reaction mass efficiency, and a low *E*-factor of 0.19 g waste/g product formation. Additionally, it attained an excellent EcoScale score of 84 (Fig. 2).



Scheme 6. Synthetic diversification of **15a**.



Scheme 7. Synthesis of *Z*-tamoxifen.

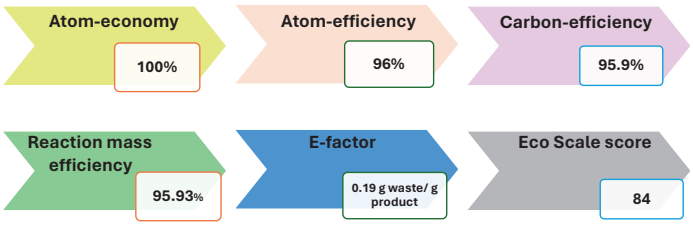
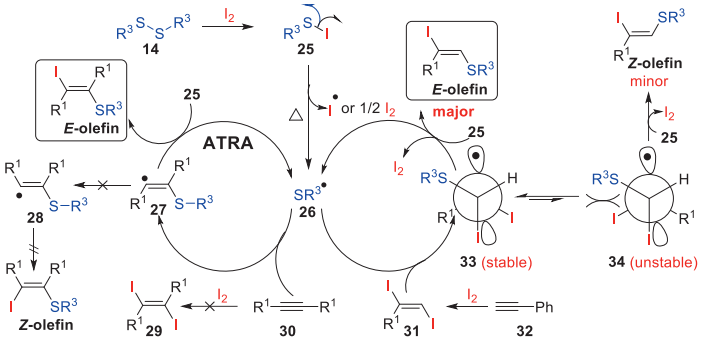


Fig. 2. Green chemistry metrics for the synthesis of **15a**.

Control experiments were conducted to demonstrate the underlying mechanism, and an atom transfer radical addition (ATRA) mechanism was proposed for both internal and terminal alkynes based on the experimental results (Scheme 8). First, iodine reacted with the disulfide, affording the corresponding sulfenyl-iodide **25** (R^3SI), which, after the homolytic cleavage of the S-I bond, generated a reactive thiyl radical (**26**). The addition of the thiyl radical to an internal alkyne forms the corresponding vinyl radical (**27**), which abstracts the iodine atom from **25** to furnish the *E*-alkene along with the regeneration of the thiyl radical. Under these conditions, isomerization of the vinyl radical did not occur; hence, the *Z*-olefin was not formed. Terminal alkynes first reacted with iodine to produce (*E*)-(1,2-diiodovinyl)aryl (**31**).



Scheme 8. Proposed reaction mechanism for the iodosulfenylation of alkynes.

Next, when the *in situ* generated thiyl radical was added to **26**, it formed two diiodo aryl radicals, *i.e.* **33** (stable) and **34** (unstable due to steric hindrance). Finally, these radicals reacted with **25** to form the *E*-alkene as the major product from **33** and the *Z*-alkene as the minor product from **34**, along with the regeneration of thiyl radical **26** and molecular iodine.

1.3 *Halochalcogenation of Ynamides*

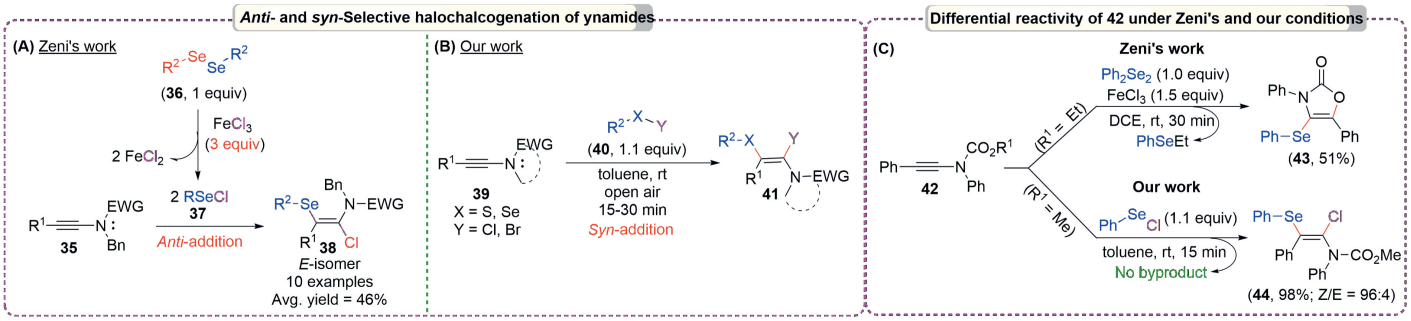
Ynamides, a special kind of alkynes, represent a compelling and rapidly advancing category of organic compounds that have attracted considerable interest in contemporary organic synthesis. Defined by a carbon–carbon triple bond adjacent to a nitrogen atom with an electron-withdrawing group (such as a sulfonyl or carbonyl), ynamides possess distinctive electronic properties that set them apart from other alkynes.[17] Their stability and versatile reactivity have facilitated new pathways in the synthesis of complex molecules, particularly in the fields of pharmaceutical development, natural product synthesis, and materials science. Due to the polarizability of the triple bond, ynamides readily undergo reactions with electrophiles. Numerous electrophilic difunctionalizations have been documented on ynamides, consistently yielding anti-addition products with selectivity in most cases. In the specific area of halochalcogenation of ynamides, two studies have been published so far.

In 2021, Zeni's group[18] and in 2024, our group[19] reported the 100% atom-economic halochalogenation of ynamides, independently, with completely opposite stereoselectivity (Scheme 9). While Zeni and coworkers (Scheme 9A) reported an *E*-selective *anti*-chloroselenylation of ynamides using only diaryl diselenide (1 equiv.) and an over-stoichiometric amount of $FeCl_3$ (3 equiv.), our group achieved a *Z*-selective *syn*-halochalcogenation of the same class of substrates using chalcogenyl halides such as selenyl chlorides, selenyl bromides, sulfenyl chlorides, and sulfenyl bromides without using any other reagent at room temperature (Scheme 9B). While Zeni's protocol suffered from some serious limitations, such as the requirement of over-stoichiometric amounts of a transition metal salt, limited substrate scope (only chloroselenylation), poor atom economy, generation of metal-based and organic wastes, *etc.*, our reagentless protocol overcame all these limitations.

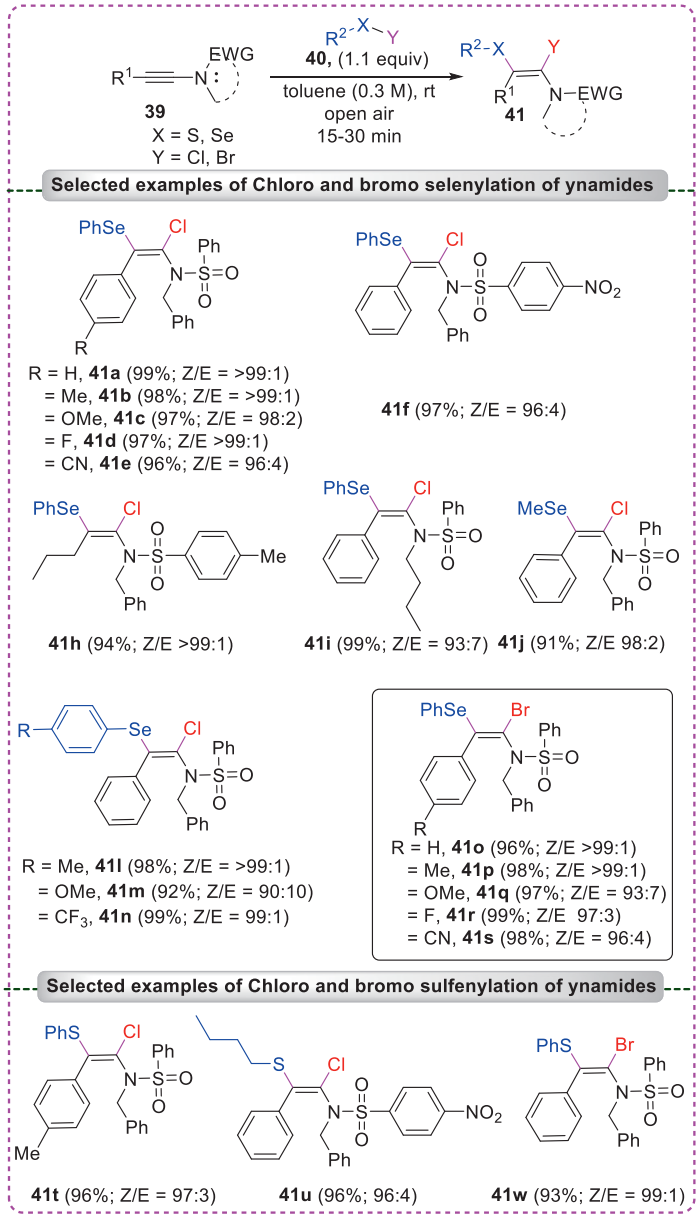
Our protocol demonstrated a solvent-controlled, highly regio- and stereoselective *syn*-halochalcogenation of ynamides using only chalcogenyl halides in toluene within a short reaction time (15–30 min) at room temperature. Our method consistently delivered a wide variety of stereodefined tetrasubstituted alkenes bearing four different but useful functional groups in excellent yield (average yield >96%). Remarkably, the protocol accomplished a wide range of halochalcogenation, *i.e.* chlorosulfenylation, bromosulfenylation, chloroselenylation, and bromoselenylation of ynamides with good to excellent selectivity (*Z*/*E* = 90:10 to >99:01) (Scheme 10). The transformation does not require any transition metal, catalyst, oxidising reagent, reducing reagent, or external energy.

The reaction was very clean, furnishing the pure products obtained *via* a simple washing of the crude with cold ethanol or cold pentane (column chromatography-free synthesis).

The solvent was recovered after the reaction *via* distillation and reused for subsequent reactions, which makes the protocol



Scheme 9. 100% Atom-economic (A) anti-chloroselenylation of ynamides (Zeni's work); (B) *Syn*-halo-chalcogenation of ynamides (our work); (C) Differential reactivity of an yne-carbamate under Zeni's conditions and our conditions.



Scheme 10. 100% atom economic halochalcogenation of ynamides.

highly sustainable. The protocol demonstrated efficient scalability, achieving a 96% yield on a gram scale. Notably, the products were synthetically diversified into novel classes of other stereodefined tetrasubstituted alkenes. Importantly, the green chemistry metrics of the protocol (Fig. 3) were found to be excellent, such as 100% atom economy, 96% atom efficiency, 93.1% carbon efficiency, 91.5% reaction mass efficiency, very low *E*-factor (0.31 g waste/g product formation), and excellent EcoScale score (78).

In this study, the stereoselectivity of the product was controlled by the polarity of the solvent, as illustrated in Fig. 4. Nonpolar solvents, such as toluene, xylene, CCl_4, and cyclohexane, demonstrated excellent (*Z*)-stereoselectivity, which gradually decreased with the increase in polarity of the solvent. Thus, polar aprotic solvents, including chlorobenzene, dichloroethane, dimethylformamide, and dimethylsulfoxide, facilitated the formation of the *E*-isomer.

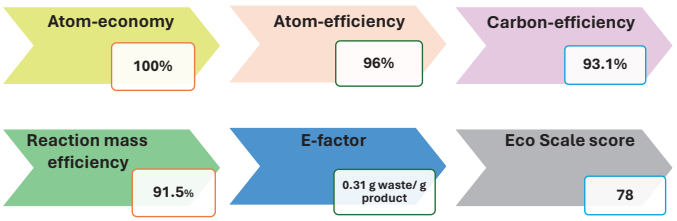


Fig. 3. Green chemistry metrics for the synthesis of **41o**.

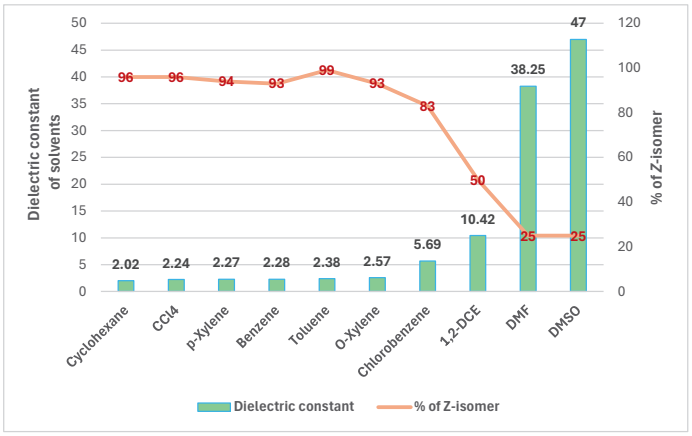
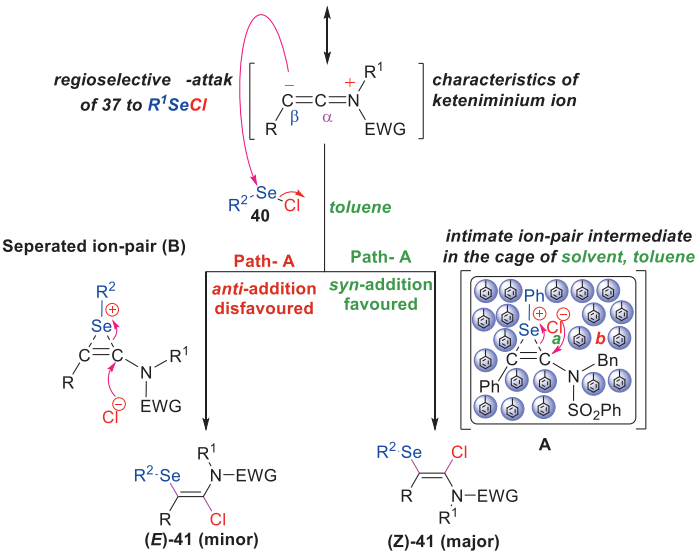


Fig. 4. Effect of solvent polarity on halochalcogenation of ynamides.

Based on the control experiments and literature reports, a reaction mechanism was proposed, which is presented in Scheme 11. Firstly, chalcogenyl halide reacts with ynamide to produce the reactive keteneiminium chloride intermediate. In non-polar solvents such as toluene, keteneiminium chloride will remain as an intimate ion pair in a solvent-cage, and thus, the nucleophilic quenching of the keteneiminium ion by the chloride anion will happen from the same side of the C=C double bond to which selenium is attached, resulting the formation of (*Z*)-**41** as the major product (Scheme 11).



Scheme 11. Proposed reaction mechanism of halochalcogenation of ynamides.

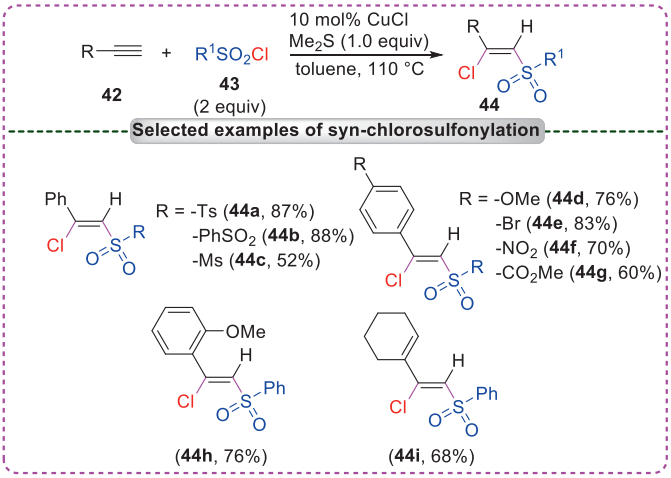
1.4 Chlorosulfonylation of Alkynes

Sulfones represent a crucial and dynamic class of compounds in the realm of bioactive molecules, playing an integral role in the design and effectiveness of many pharmaceutical compounds.[20,21] This versatile functional group is prevalent in a wide array of significant drugs, including apremilast, known for its innovative approach to treating inflammatory conditions; ceritinib, a targeted therapy in the battle against cancer; and chlormezanone, which aids in soothing the complexities of anxiety.

Among various classes of sulfones, vinyl sulfone has garnered significant interest in organic synthesis due to the presence of this motif in various bioactive molecules, pharmaceuticals, pesticides, and materials. For instance, rofecoxib is utilized to alleviate pain and inflammation, especially in cases of arthritis. Furthermore, oxycarboxin serves as a fungicide in agricultural applications.[22,23] Therefore, the development of sustainable synthetic methodologies is desirable for the synthesis of these classes of molecules. Notably, β-halo vinyl sulfones are particularly appealing, as they enable the synthetic creation of a variety of valuable bioactive molecules. Various synthetic methodologies have been developed; however, here we focus primarily on 100% atom-economic synthetic transformations.

1.5 Syn-Chlorosulfonylation of Alkynes

In 2005, Liu *et al*. developed a highly regio and stereoselective, metal-catalyzed, *syn*-selective chlorosulfonylation of terminal alkynes. This process utilized inexpensive CuCl as a catalyst, Me_2S as an additive, and sulfonyl chloride as the sulfonyl reagent, and the reactions were found to be efficient, furnishing the desired products with moderate to good yields (53–91%) (Scheme 12).[24] The reaction followed a radical mechanism, and Me_2S stabilized the intermediate to achieve the *syn* addition product.



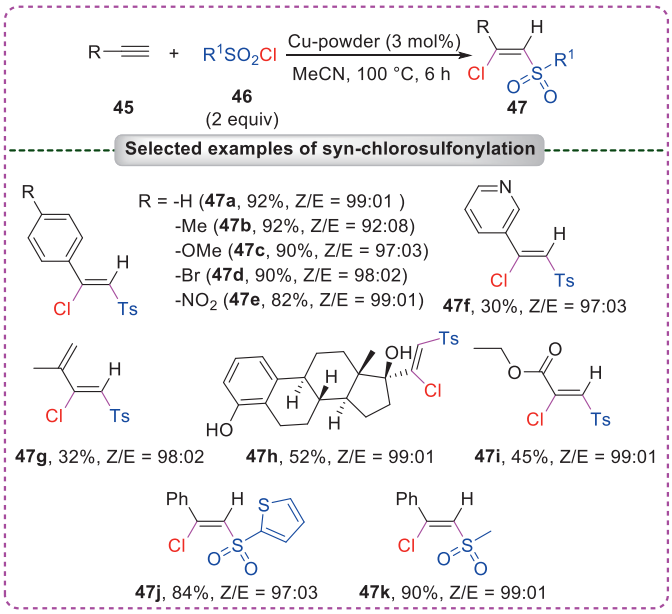
Scheme 12. CuCl-catalyzed *syn*-chlorosulfonylation of terminal alkynes.

In 2023, Shen and colleagues reported a copper powder-catalyzed 100% atom-economic *syn*-chlorosulfonylation of internal alkynes through an atom transfer radical addition (ATRA) process.[25] This method demonstrated high regio- and stereoselectivity. Radical quenching experiments confirmed that the reaction proceeded *via* radical formation, while DFT studies supported and corroborated the occurrence of *syn*-addition. Various functional groups were tolerated under these optimized conditions (Scheme 13).

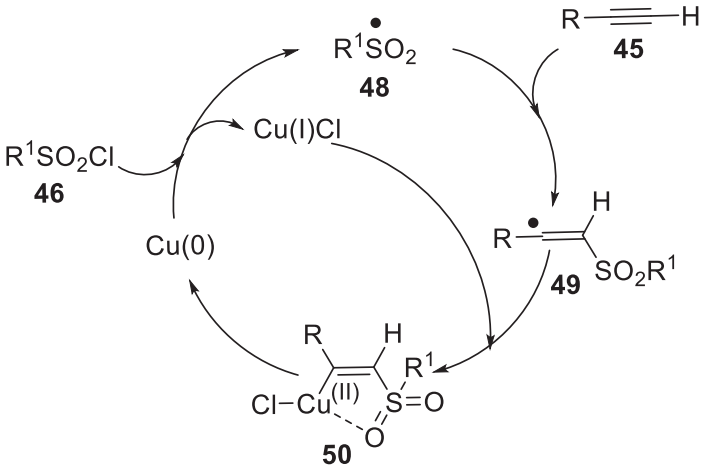
In the reaction mechanism (Scheme 14), first, Cu(0) reacted with sulfonyl chloride to generate a sulfonyl radical (**48**) and Cu-Cl. Subsequently, the radical was added to alkynes to produce a vinyl radical (**49**), which was added to the Cu-center oxidatively, leading to a five-membered ring transition state (**50**). Finally, the chlorine atom was exchanged, regenerating Cu(0).

1.6 Anti-Chlorosulfonylation of Alkynes

In 2012, Nakamura and colleagues reported an Fe(II), *i.e.* $Fe(acac)_2$ (acac = acetylacetonato)-catalyzed *anti*-chlorosulfonylation of alkynes, achieving 100% atom economy along with high regio- and stereoselectivity.[26] The reaction conditions were compatible with various functional groups, including halides, nitro groups, and carbonyls (Scheme 15). However, this method was limited to aromatic sulfonyl chlorides. The proposed mechanism involved an initial electron transfer from iron to sulfonyl chloride, generating a sulfonyl radical, which subsequently added to the alkyne to form a vinyl radical. Finally, the vinyl radical abstracted a chlorine atom from iron(III) chloride, yielding the final desired product.

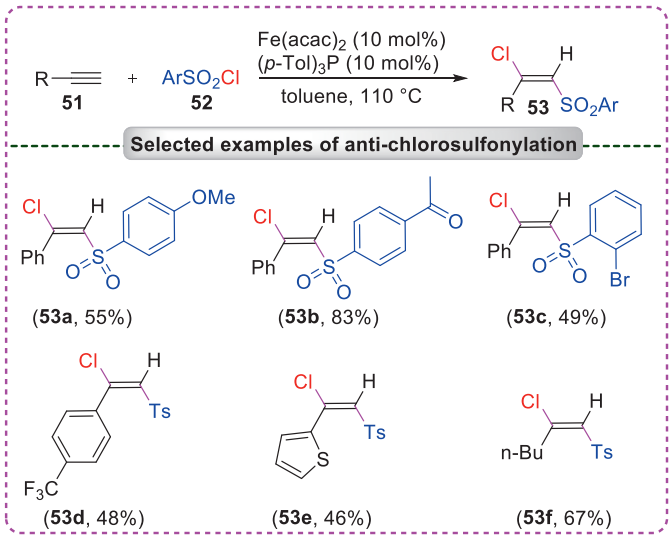


Scheme 13. Cu-powder catalyzed *syn*-chlorosulfonylation of terminal alkynes.

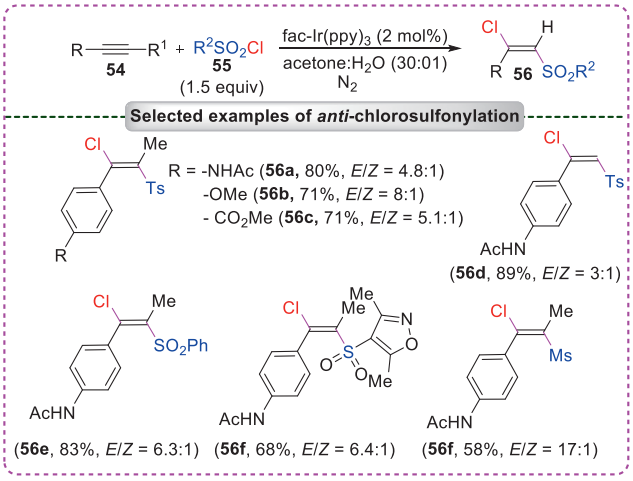


Scheme 14. Plausible reaction mechanism for *syn*-chlorosulfonylation of terminal alkynes.

In 2018, Han and coworkers reported a visible-light-mediated, photoredox-catalyzed process for the regio- and stereoselective chlorosulfonylation of alkynes (Scheme 16).[27] The method was successfully applied to both internal and terminal alkynes. Blue LEDs served as the light source, while an iridium catalyst (fac-$Ir(ppy)_3$), ppy = 2-phenylpyridine, was used as the photocatalyst, producing β-chlorovinyl sulfones. The reaction was proposed to be initiated by the excitation of the photocatalyst by the blue LEDs. In its excited state, the photocatalyst acted as a reductant, generating a sulfonyl radical, **57**, through a reductive single-electron transfer (SET) process from the photocatalyst (Scheme 17).



Scheme 15. Fe(II)-catalyzed anti-chlorosulfonylation of alkynes.



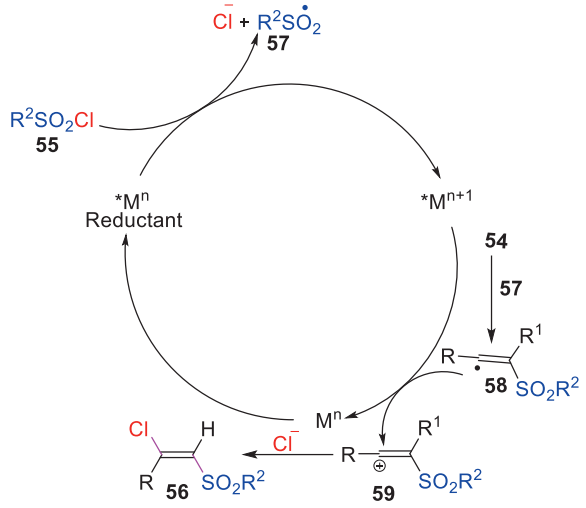
Scheme 16. Visible-light-mediated photoredox-catalyzed anti-chlorosulfonylation of alkynes.

The sulfonyl radical, **57**, then reacted with the alkyne **54**, forming a vinyl radical **58**, which underwent a SET process with the oxidized catalyst, thus regenerating the catalyst and forming a vinyl cation **59**. The process concluded with the trapping of **59** by a halide, leading to the synthesis of β-chlorovinyl sulfones.

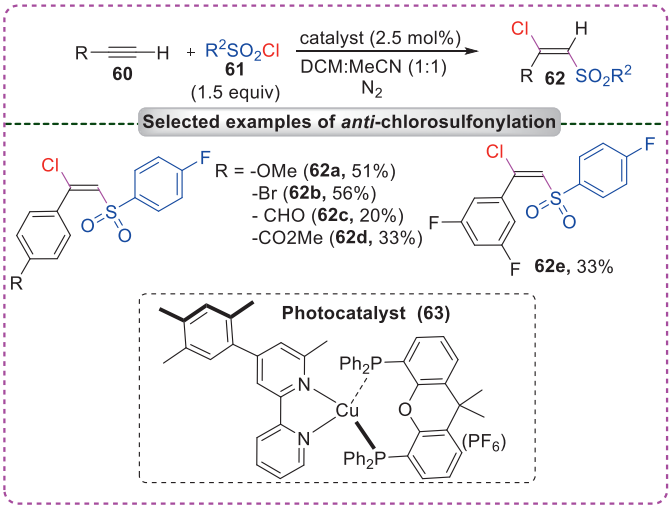
In 2019, Hu and Alkan-Zambada developed a highly regio- and stereoselective, copper-catalyzed photoredox chlorosulfonylation of alkenes and alkynes (Scheme 18).[28] However, the method was limited to terminal alkynes and yielded the desired product with an average yield of only 39.76%. The photocatalyst employed was specifically developed in their laboratory. In the presence of a copper catalyst and a 40W LED (450 nm), commercially available alkynes and sulfonyl chlorides reacted efficiently under a nitrogen atmosphere, producing β-chloro vinyl sulfones with high regio- and stereoselectivity. However, a glove box was required to conduct the reaction.

2. Conclusions

Developing completely atom-economic and highly regio- and stereoselective difunctionalization processes is crucial for the green synthesis of stereodefined tri- or tetrasubstituted alkenes, which could be further utilized for the cost-effective and sustainable synthesis of potential molecules, including a marketed drug like tamoxifen. Various synthetic strategies are described that achieved 100% atom-economic halo-chalcogenations and halo-sulfonylation of alkynes, including ynamides, along with high regio- and stereoselectivity. While most of the halo-chalcogenation and halo-sulfonylation reactions of alkynes are found to follow a radical pathway, this is not true for ynamides, which follow an ionic reaction mechanism. It was also found that the stereochemical outcome of the halochalcogenation of ynamides can be modulated by altering the reaction conditions. Hence, with a proper selection of reaction conditions, one can selectively synthesize two isomeric stereodefined tetrasubstituted alkenes. We believe that these synthetic strategies will be utilized further for developing other difunctionalization reactions with alkynes with 100% atom-economy to synthesize new classes of stereodefined tri- or tetrasubstituted alkenes bearing useful functional groups. We hope that this review will be useful to the scientific community working in the area of green organic synthesis.



Scheme 17. Plausible reaction mechanism.



Scheme 18. Visible-light-induced, copper-catalyzed chlorosulfonylation for alkynes.

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Author Contributions

A. N. V. Satyanarayana prepared the initial draft and T. Chatterjee edited the manuscript.

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[1] (a) W. Liu, W. Kong, *Org. Chem. Front*. **2020**, *7*, 3941, https://doi.org/10.1039/d0qo01097a; (b) A. B. Flynn, W. W. Ogilvie, *Chem. Rev*. **2007**, *107*, 4698, https://doi.org/10.1021/cr050051k.

[2] C. Lauterbach, J. Fabian, *Eur. J. Inorg. Chem*. **1999**, *11*, 1995, https://doi.org/10.1002/(SICI)1099-0682(199911)1999:11<1995::AID-EJIC1995>3.0.CO;2-E.

[3] (a) Y. Li, Q. Shao, H. He, C. Zhu, X. S. Xue, J. Xie, *Nat Commun*. **2022**, *13*, https://doi.org/10.1038/s41467-021-27507-x; (b) B. E. Maryanof, A. B. Reitz, *Chem. Rev*. **1989**, *89*, 863, https://doi.org/10.1021/cr00094a007; (c) D. J. Ager, 'The Peterson olefin reaction', *Org. React*. **1990**, *38*, 1; (d) S. Schreiber, 'Comprehensive Organic Synthesis', **1991**, *1*; (e) T. Takeda, 'Modern Carbonyl Olefination', **2004**, Wiley, https://doi.org/10.1002/3527601880.

[4] (a) P. Anastas, N. Eghbali, *Chem. Soc. Rev*. **2010**, *39*, 301312, https://doi.org/10.1039/B918763B; (b) A. N. V. Satyanarayana, P. Pattanayak, T. Chatterjee, *Org. Biomol. Chem*. **2025**, *23*, 2235, https://doi.org/10.1039/D4OB01984A; (c) A. N. V. Satyanarayana, T. Chatterjee, *J. Org. Chem*. **2024**, *89*, 12439, https://doi.org/10.1021/acs.joc.4c01373.

[5] (a) I. Shiina, M. Suzuki, K. Yokoyama, *Tetrahedron Lett.* **2004**, *45*, 965, https://doi.org/10.1016/j.tetlet.2003.11.119; (b) S. Zhouab, G. Huang, *RSC Adv*. **2020**, *10*, 5874, https://doi.org/10.1039/c9ra10659f.

[6] (a) T. Ogawa, K. Hayami, H. Suzuki, *Chem. Lett*. **1989**, *18*, 769, https://doi.org/10.1246/cl.1989.769; (b) N. Taniguchi, *Tetrahedron*. **2009**, *65*, 2782, https://doi.org/10.1016/j.tet.2009.01.094.

[7] N. Taniguchi, *Synlett*. **2008**, *6*, 849, https://doi.org/10.1055/s-2008-1042903.

[8] S. Liu, X. Zeng, B. Xu, *Org. Chem. Front*. **2020**, *7*, 1690, https://doi.org/10.1039/D0QO00367K.

[9] Y. Bao, X. Yang, Q. Zhou, F. Yang, *Org. Lett*. **2018**, *20*, 1966, https://doi.org/10.1021/acs.orglett.8b00511.

[10] Y.-M. Lin, G.-P. Lu, C. Cai, W.-B. Yi, *Org. Lett*. **2015**, *17*, 3310, https://doi.org/10.1021/acs.orglett.5b01488.

[11] J. Pandey, S. Singh, R. Dubey, *J. Chem. Pharm. Res*. **2025**, *17*, 01, https://doi.org/10.37532/0975-7384.2025.17(1).233; (b) A. Sáenz-Galindo, A. Facio, R. Rodriguez-Herrera, 'Green Chemistry and Applications', 1st Edn, Boca Raton, **2020**, https://doi.org/10.1201/9780429291166.

[12] L. Zhong, P. R. Savoie, A. S. Filatov, J. T. Welch, *Angew. Chem. Int. Ed*. **2014**, *53*, 526, https://doi.org/10.1002/anie.201306507.

[13] M. Iwasaki, T. Fujii, K. Nakajima, Y. Nishihara, *Angew. Chem. Int. Ed*. **2014**, *53*, 13880, https://doi.org/10.1002/anie.201408121.

[14] M. Iwasaki, T. Fujii, A. Yamamoto, K. Nakajima, Y. Nishihara, *Chem. Asian J.* **2014**, *9*, 58, https://doi.org/10.1002/asia.201301295.

[15] A. N. V. Satyanarayana, N. Mukherjee, T. Chatterjee, *Green Chem*. **2023**, *25*, 779, https://doi.org/10.1039/d2gc04101d.

[16] N. Tandon, V. Luxami, R. Tandon, K. Paul, *Asian J. Org. Chem*. **2020**, *9*, 1432, https://doi.org/10.1002/ajoc.202000308; (b) D. Heijnen, M. V. Zuijlen, F. Tosi, B. L. Feringa, *Org. Biomol. Chem*. **2019**, *17*, 2315, https://doi.org/10.1039/C8OB02977F. (c) K. M. Kasiotis, S. A. Haroutounian, *Curr. Org. Chem*. **2012**, *16*, 335, https://doi.org/10.2174/138527212799499886; (d) R. B. Miller, M. I. Al-Hassan, *J. Org. Chem*. **1985**, *50*, 2121, https://doi.org/10.1021/jo00212a023; (e) P. E. Tessier, A. J. Penwell, F. E. S. Souza, A. G. Fallis, *Org. Lett*. **2003**, *5*, 17, https://doi.org/10.1021/ol0347794.

[17] (a) G. Evano, J. Zhao, 'The Chemistry of Ynamides', 1st Edn, Jenny Stanford Publishing, New York, **2024**, https://doi.org/10.1201/9781032670997; (b) S. Dutta, R. K. Mallick, A. K. Sahoo, *Angew. Chem. Int. Ed.* **2023**, *62*, e202300816, https://doi.org/10.1002/anie.202300816.

[18] T. A. C. Goulart, D. F. Back, S. M. E. Silva, G. Zeni, *J. Org. Chem.* **2021**, *86*, 980, https://doi.org/10.1021/acs.joc.0c02480.

[19] A. N. V. Satyanarayana, P. Pattanayak, T. Chatterjee, *J. Org. Chem*. **2024**, *89*, 11455, https://doi.org/10.1021/acs.joc.4c01134.

[20] Y. Zhang, E. Vessally, *RSC Adv*. **2021**, *11*, 33447, https://doi.org/10.1039/d1ra03443j.

[21] D. C. Meadows, J. Gervay-Hague, *Med. Res. Rev*. **2006**, *26*, 793, https://doi.org/10.1002/med.20074.

[22] R. J. Reddy, J. J. Kumar, A. H. Kumari, *Org. Biomol. Chem*. **2024**, *22*, 2492, https://doi.org/10.1039/d3ob01980b.

[23] R. Yi, Q. Li, H. Liu, W. T. Wei, *Chem. Eur. J*. **2024**, *30*, e202401386, https://doi.org/10.1002/chem.202401386.

[24] X. Liu, X. Duan, Z. Pan, Y. Han, Y. Liang, *Synlett* **2005**, *11*, 1752, https://doi.org/10.1055/s-2005-869876.

[25] M. Zhang, W. Zhao, J. Ma, J. Li, Q. Meng, C. Shen, X. Zeng, *Org. Lett.* **2023**, *25*, 231, https://doi.org/10.1021/acs.orglett.2c04074.

[26] X. Zeng, L. Ilies, E. Nakamura, *Org. Lett*. **2012**, *14*, 955, https://doi.org/10.1021/ol203446t.

[27] P. Chakrasali, K. Kim, Y. S. Jung, H. Kim, S. B. Han, *Org. Lett*. **2018**, *20*, 7509, https://doi.org/10.1021/acs.orglett.8b03273.

[28] M. A. Zambada, X. Hu, *J. Org. Chem*. **2019**, *84*, 4525, https://doi.org/10.1021/acs.joc.9b00238.

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