Letter

Selenium-#-Acid Catalyzed Oxidative Functionalization of Alkynes: Facile Access to Ynones and Multisubstituted Oxazoles

Lihao Liao, Hang Zhang, and Xiaodan Zhao

ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.8b01595 • Publication Date (Web): 19 Jun 2018

Selenium-π-Acid Catalyzed Oxidative Functionalization of Alkynes: Facile Access to Ynones and Multisubstituted Oxazoles

Lihao Liao, Hang Zhang, and Xiaodan Zhao*

Institute of Organic Chemistry & MOE Key Laboratory of Bioinorganic and Synthetic Chemistry, School of Chemistry, Sun Yat-Sen University, Guangzhou 510275, P. R. China

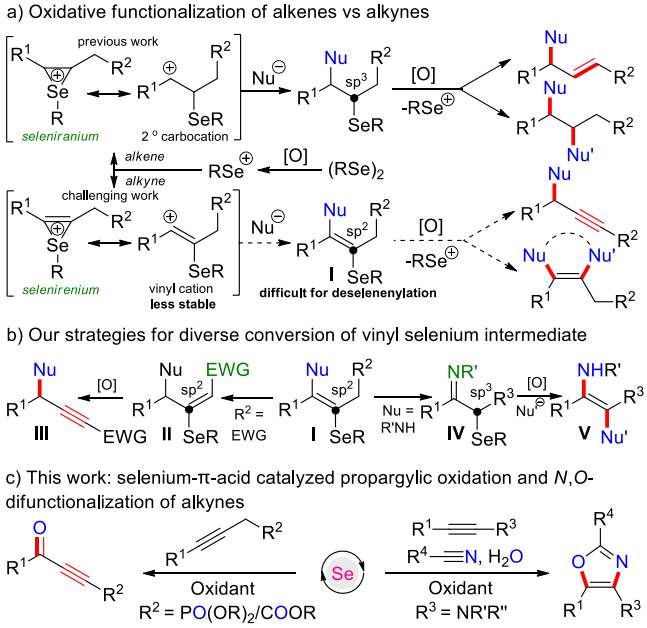
Supporting Information Placeholder

ABSTRACT: Unprecedented selenium-catalyzed propargylic oxidation of alkynes is disclosed. Various propargylphosphonates and 3-alkynoates were efficiently converted to valuable ynones via unusual C–C triple bond migration and deselenenylation at a vinyl carbon. By the strategies of tautomerization of enamine intermediate and S_N2 displacement, the similar conditions were effective for the oxidative difunctionalization of ynamides to afford multisubstituted oxazoles with high regioselectivity. Mechanistic studies revealed these detailed processes.

KEYWORDS: *selenium catalysis, π-activation, alkyne, propargylic oxidation, difunctionalization*

Alkynes are useful building blocks in organic synthesis owing to the versatile reactivities of C–C triple bonds.[1] They can be converted to a variety of compounds by the powerful strategy of catalytic π-activation.[2-5] In the past decades, alkyne π-activation has been dominated by metal catalysis.[2] Recently, the activation by organocatalysts such as Brønsted acids,[3] organoborons,[4] and organoiodides,[5] has been paid much attention since organocatalysis might enable new reactions.[6] Despite these efforts, approaches for organocatalytic challenging alkyne transformations are still limited. Thus, developing new methods of organocatalytic alkyne π-activation to meet the requirement of synthetic diversity is highly desirable.

Organoselenium catalysis has emerged as a powerful tool for the synthesis of various compounds.[7-11] As an important part in this field, selenium-π-acid catalysis through electrophilic interactions between selenenium and π bond is different with peroxyseleninic acid catalysis probably through oxygen transfer to π bond.[7a,7b,7f] This catalysis has garnered considerable attention in recent years since selenium-π-acid exhibits a distinct carbophilicity to alkene π bond.[8a] As a result, catalytic oxidative functionalization of alkenes has been well established.[9,10] Generally, this transformation goes through nucleophilic ring opening of *seleniranium* intermediate and then oxidation of alkyl selenium species followed by *syn*-H elimination or S_N2 displacement (Scheme 1a, top). Alkynes have similar π bonds to alkenes, which implies the potentiality of oxidative transformation by selenium-π-acid catalysis. However, selenium-π-acid catalyzed reactions of alkynes were considered to be challenging. Until now, only catalytic oxidation of alkynes to form protected and unprotected 1,2-diketones has been reported.[11] Important reactions such as selenium-π-acid catalyzed propargylic functionalization and difunctionalization of alkynes have not been developed (Scheme 1a, bottom).

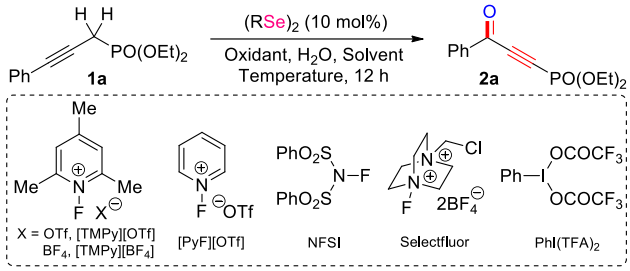


Scheme 1. Selenium-π-Acid Catalyzed Transformations of Alkenes and Alkynes

Restricting the development of this area might be ascribed to two issues: (i) vinyl cation, a resonance structure of *selenirenium*, is much less stable than a secondary carbocation from *seleniranium* resulting in a limited range of nucleophiles;[12] (ii) deselenenylation of vinyl selenium species requires harsh oxidative conditions in which substrates and products could not tolerate to lead to more side reactions.[12a,13] As our continuous interest in chalcogenide catalysis,[14] especially selenium-π-acid catalysis,[10] we would like to solve these issues by new strategies to pave a route for oxidative functionalization of alkynes. We hypothesized that the limited range of

nucleophiles resulted from the less stability of vinyl cation could be handled by using an intramolecular nucleophile to reduce the energy barrier or a heteroatom-substituted substrate to stabilize vinyl cation via p-π conjugation. Since N–F type oxidants were effective in mild deselenenylation of alkyl selenium species with good compatibility,[8b] it might be suitable for deselenenylation of vinyl selenium species, which is the most challenging step for alkyne functionalizations. By using N–F/diselenide system, we rationalized that challenging propargylic functionalization and difunctionalization of alkynes were feasible based on the diverse conversion of vinyl selenium intermediate in Scheme 1b. If R^2 on vinyl selenium intermediate **I** is an electron-withdrawing group, tautomerization becomes easier to give **II**. At the same time, the acidity of the vinyl proton increases, which could benefit the following *β*-H elimination to give the final product **III** (Scheme 1b, left). Furthermore, we envisioned that when **I** is an enamine, tautomerization occurs to generate alkyl selenium species **IV**. The following oxidative deselenenylation at the sp^3 carbon by S_N2 displacement is easier. Then, a second tautomerization forms C–C double bond to give a difunctionalization product **V** (Scheme 1b, right). Herein, we report our discovery that propargylphosphonates and 3-alkynoates could undergo unprecedented propargylic oxidation to afford ynones by selenium-π-acid catalysis (Scheme 1c, left). The similar conditions was effective for oxidative *N*,*O*-difunctionalization of ynamides to give oxazoles (Scheme 1c, right).

Table 1. Condition Evaluation[a]

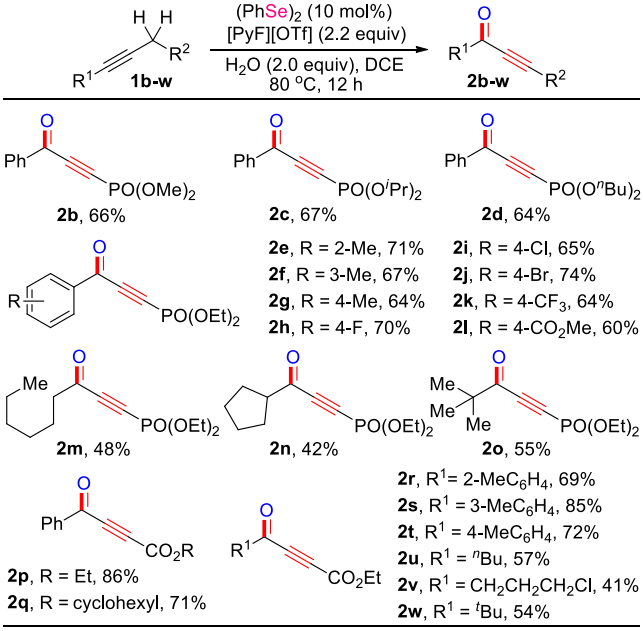


entry	R	oxidant	solvent	temp. (°C)	yield (%)[b]
1	Ph	[TMPy][OTf]	MeCN	RT	5
2	Ph	[TMPy][OTf]	MeCN	45	21
3	Ph	[TMPy][OTf]	MeCN	80	65
4	Ph	[TMPy][BF_4]	MeCN	80	61
5	Ph	[Py][OTf]	MeCN	80	69
6	Ph	NFSI	MeCN	80	49
7	Ph	Selectfluor	MeCN	80	51
8	Ph	$PhI(TFA)_2$	MeCN	80	24
9	Ph	[Py][OTf]	EtOAc	80	69
10	Ph	[Py][OTf]	DCE	80	72 (70)
11	*p*-$MeOC_6H_4$	[Py][OTf]	DCE	80	48
12	*p*-$CF_3C_6H_4$	[Py][OTf]	DCE	80	65
13	Bn	[Py][OTf]	DCE	80	46
14[c]	-	[Py][OTf]	DCE	80	0

[a]Conditions: **1a** (0.05 mmol), $(RSe)_2$ (10 mol%), oxidant (2.2 equiv), solvent (2 mL), H_2O (2.0 equiv), temp., 12 h. [b]Refers to NMR yield with BzOBn as the internal standard; isolated yield is in parentheses in 0.15 mmol scale. [c]No $(RSe)_2$.

Based on our assumption, placing phosphonate group, a class of important functional groups,[15] at the propargylic position of substrate could benefit tautomerization and deselenenylation to afford propargylic functionalization product. So we began our study with easily prepared diethyl (3-phenyl-2-propynyl)phosphonate (**1a**) as the model substrate using a N–F/diselenide system (Table 1). First, **1a** was treated with bulky N–F oxidant [TMPy][OTf] in the presence of PhSeSePh (10 mol%) at room temperature. H_2O was used as nucleophile to generate propargylic alcohol as expected product. Instead, a propargylic oxidation product **2a** was formed via triple bond migration and further oxidation of hydroxy group (entry 1). Although the yield was only 5%, this result reflected that deselenenylation of vinyl selenide could occur and propargylic functionalization was possible. To accelerate deselenenylation of intermediate, reaction temperature was elevated. When the reaction was carried out at 80 °C, **2a** was obtained in 65% yield (entry 3). Other oxidants were tested for the reaction (entries 4-8). [PyF][OTf] gave slightly better yield (entry 5) and NFSI led to moderate yield (entry 6). In both reactions, competitive byproducts that could be possibly formed by the addition of endogenous nitrogen nucleophiles to substrates were not observed.[9b,10d] Next, different solvents were tested (entries 9 and 10). DCE was found to be slightly more effective than MeCN and EtOAc, and led to 70% isolated yield of **2a** (entry 10). When water or ethanol was utilized as the solvent, ynone product was not observed and most of starting material remained after the reaction. Other catalyst precursors of diselenides were evaluated. None of them gave better results than $(PhSe)_2$ (entries 11-13). The reaction did not work in the absence of diselenides (entry 14). It is noteworthy that there are rare methods available for the synthesis of phosphonate-substituted ynones.[16] Our method is a significant supplement.

Table 2. Substrate Scope for Propargylic Oxidation[a]

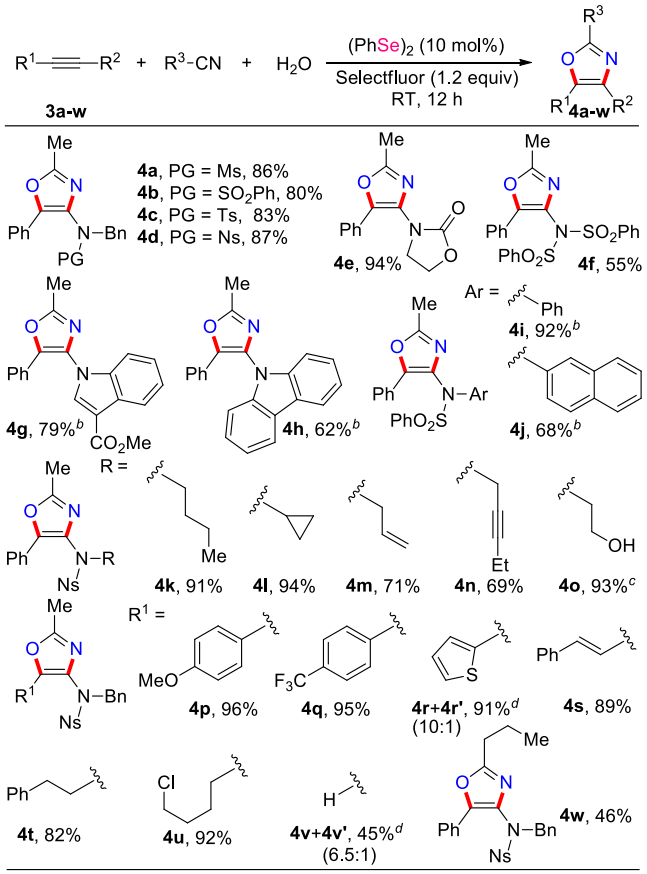


[a]Conditions: **1** (0.15 mmol), $(PhSe)_2$ (10 mol%), [PyF][OTf] (2.2 equiv), DCE (6 mL), H_2O (2.0 equiv), 80 °C, 12 h. For the reactions of 3-alkynoates, **1** (0.10 mmol) and [TMPyF][OTf] (2.2 equiv) were used.

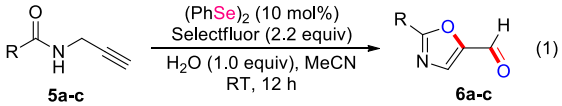
With the optimal conditions in hand, the scope of propargylphosphonates was evaluated (Table 2). Different dialkyl 3-phenylpropargylphosphonates efficiently underwent oxidative migration to afford ynones **2b-d** in good yields. Substituents such as Me–, F–, Cl–, Br–, CF_3–, and MeO_2C– at the para-, meta- or ortho-position of the phenyl group did not have a big impact on this transformation. The corresponding aryl-substituted ynones were obtained in good yields (**2e-l**, 60-

74%). 3-Alkylpropargylphosphonates including **1o** bearing a bulky tert-butyl group also underwent the same migration to form ynones **2m-o** in moderate yields. In comparison with aryl alkyne substrates, alkyl alkynes with less reactivities gave the products in lower yields. Although the yields are moderate, these results indicate the generality of this method. To the best of our knowledge, this work is the first example of catalytic conversion of sp^3 C–P to sp C–P bond. Besides, 3-alkynoates could also be transformed to the corresponding ester-substituted ynones under the similar conditions (**2p-w**, 41-85%). Similarly, the reactions worked better with aryl-substituted substrates (**1p-1t**) than alkyl-substituted those (**1u-1w**).

Table 3. Substrate Scope for *N,O*-Difunctionalization[a]

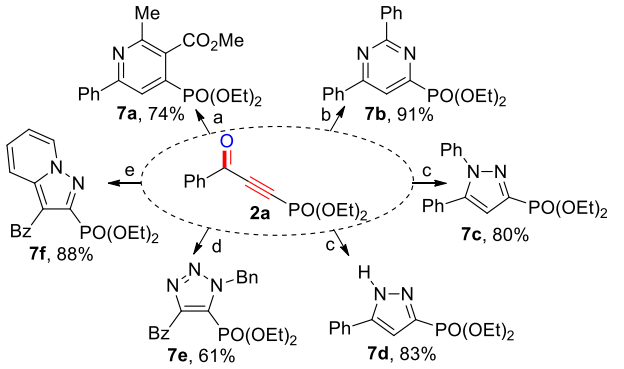


[a]Conditions: **3** (0.10 mmol), $(PhSe)_2$ (10 mol%), Selectfluor (1.2 equiv), H_2O (1.0 equiv), R^3CN (8 mL), RT, 12 h. [b][PyF][OTf] (1.2 equiv) was used as the oxidant; MeCN (4 mL). [c]TBDMS protected alcohol was utilized as the substrate. [d]Regioisomers were formed.



6a, R = Ph, 94%; **6b**, R = PhCH=CH, 90%; **6c**, R = Bn, 87%

To stabilize vinyl cation from *selenirenium* and promote tautomerization of enamine intermediate, ynamides were selected as substrates and acetonitrile was used as nucleophile and nitrogen source. To our delight, a formal difunctionalization product, polysubstituted oxazoles, was formed by this selenium-π-acid catalysis. The reactions could run with Selectfluor as the oxidant at room temperature (Table 3). It is well-known that oxazoles are privileged scaffolds in natural products and bioactive molecules.[17] Although cycloaddition of alkynes is a facile method to form oxazoles,[18,19] the known multicomponent cycloaddition of ynamides to substituted oxazoles suffered from limited substrate scope.[18f] In comparison, the scope of our reaction is relatively broad. In the reactions, a series of protecting groups, i.e., Ms–, $PhSO_2$–, Ts–, Ns–, and carbamate, on the nitrogen atom were well tolerated (**4a-e**, 80-94%). Ynimides and ynamines underwent the similar cycloaddition to give the products nicely (**4f-h**, 55-79%). When *N*-aryl and -alkyl ynamides even bearing a double bond or another triple bond that could be reactive in selenium catalysis were used, the reactions worked efficiently without the influence of the functional groups except that the reaction of TBDMS-protected ynamide **3o** gave the deprotecting product **4o** (**4i-o**, 68-94%). The effect of various substituents on the triple bonds was studied. It was found that electron-rich and -deficient aryl, heteroaryl, styryl, and functionalized alkyl groups were well tolerated (**4p-u**, 82-96%). It is noted that when terminal ynamide substrate was used, the reaction still worked well to give regioisomer oxazoles (**4v**+**4v'**, 45%, 6.5:1). When butyronitrile was used as solvent, the desired product could be obtained. In addition, the conditions were effective for the synthesis of oxazoles in an intramolecular way. When *N*-propargylamides **5** were utilized, cyclization gave oxazole aldehydes **5a-c** in excellent yields (eq. 1).



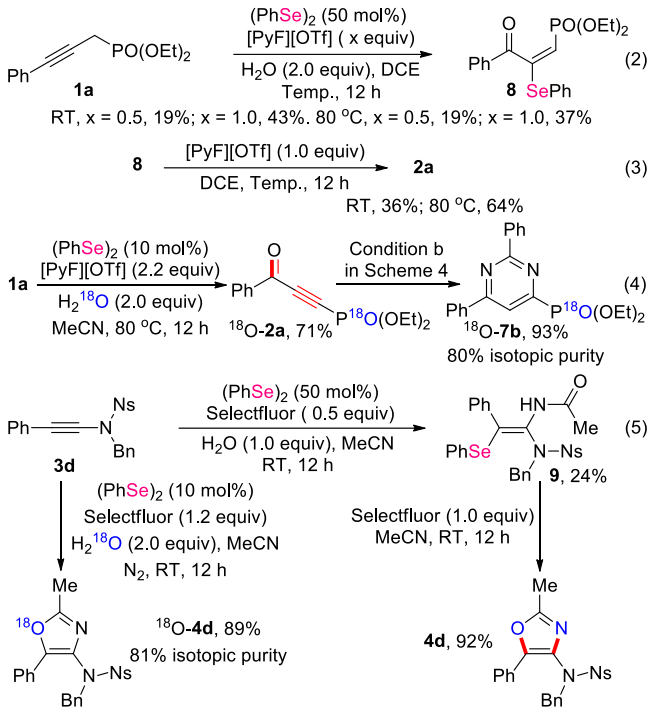
Conditions: (a) Methyl 3-aminocrotonate, EtOH, rt, 5 h. (b) Benzamidine-HCl, K_2CO_3, MeCN/H_2O, RT, 30 min. (c) $PhNHNH_2$ or H_2NNH_2-H_2O, EtOH, 0 °C, 10 min; then reflux, 1 h. (d) BnN_3, PhMe, 110 °C, overnight. (e) 1-Aminopyridinium iodide, K_2CO_3, DMF, RT, 1 h; then RT under air, 14 h.

Scheme 2. Further Transformations of Ynone 2a

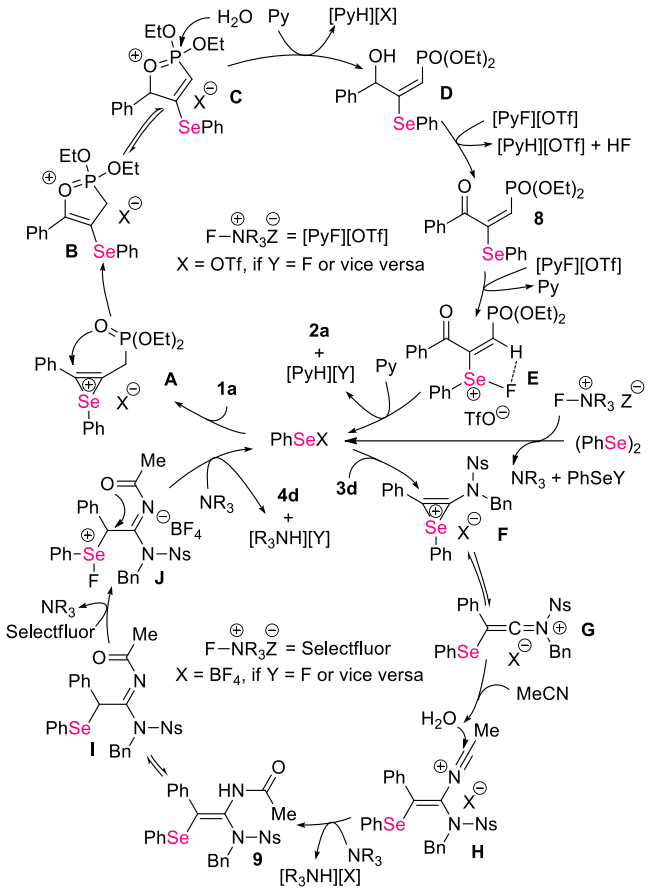
The obtained phosphonate ynones are good precursors for the synthesis of valuable heteroaryl phosphonates. For example, ynone **2a** could be easily converted into polysubstituted pyridines, pyrimidines and pyrazoles via condensation reactions (Scheme 2, **7a-d**). When it was treated with BnN_3 or 1-aminopyridinium iodide, the direct cycloaddition products, triazole **7e** and pyrazolo[1,5-a]pyridine **7f**, respectively, were efficiently formed in excellent regioselectivity.

To elucidate the reaction mechanisms, control experiments have been conducted. When **1a** was treated with 50 mol% of $(PhSe)_2$ in the presence of different amount of [PyF][OTf] at different temperature, a selenenylated intermediate **8** with single configuration was formed, and its yield relied on the amount of [PyF][OTf] and was slightly affected by temperature (eq. 2). The more the oxidant was added, the more **8** was formed. Intermediate **8** could be deselenenylated to give ynone **2a** by oxidation (eq. 3). Elevating temperature favored the

deselenenylation process, which is consistent with the results that higher yields were attained at 80 °C in Table 1. The ^{18}O labeling experiments were also conducted. The reaction of **1a** with $H_2{}^{18}O$ gave ^{18}O labeled pyrimidines, which indicates that the ^{18}O from $H_2{}^{18}O$ was transferred to the phosphonate group, not triple bond motif (eq. 4). This process offers a good route for the synthesis of aromatic compounds bearing an ^{18}O-labeled phosphonate group. Similarly, a selenenylated intermediate **9** was formed when ynamide **3d** was treated with 50 mol% of $(PhSe)_2$ and Selectfluor. As expected, oxazole **4d** was formed in high yield through the deselenenylation of **9** with equimolar Selectfluor. When $H_2{}^{18}O$ was used, ^{18}O labeled oxazole was generated, which indicates that the oxygen on oxazole comes from H_2O.



Based on the mechanistic studies and previous reports,[8] possible mechanisms for the formation of ynones and oxazoles are depicted in Scheme 3. First, PhSeSePh is oxidized by N–F reagent to give electrophilic species PhSeX. It reacts with alkyne **1a** to form *selenirenium* ion **A**,[20] followed by the attack of the phosphonate group in an intramolecular way to yield intermediate **B**. Equilibrium between **B** and **C** exists and can be broken by the nucleophilic attack of H_2O to form alcohol **D** with the aid of base.[21] Then, the oxidation of the hydroxy group on **D** towards carbonyl group gives intermediate **8**. After the oxidative *syn* elimination of selenium motif and hydrogen via intermediate **E**, ynone **2a** is formed and the catalyst is regenerated. It is noted that catalytic deselenenylation via sp^2 C–Se bond cleavage was realized for the first time.[8] The mechanism for the formation of oxazoles is somewhat different. **A** stable keteniminium ion **G** is first formed via *selenirenium* ion **F**. After the nucleophilic attack of acetonitrile and the hydrolysis, intermediate **9** is formed. Due to the tautomerization, intermediate **I** is generated. It can be further oxidized to species **J**. A S_N2 displacement of the selenium group by the carbonyl group and the isomerization with the aid of base leads to oxazoles **4** and the catalyst species. Interestingly, this S_N2 displacement is superior to the competitive β-H elimination in all the reactions of alkyl ynamides.



Scheme 3. Proposed Mechanism

In summary, we have developed an efficient method for selenium-π-acid catalyzed synthesis of ynones with propargylphosphonates and 3-alkynoates via oxidative triple bond migration. The similar conditions could be applied to the synthesis of multisubstituted oxazoles by an oxidative difunctionalization. Mechanistic studies revealed intramolecular oxygen transfer and oxidative elimination of PhSe group at the sp^2 carbon in the formation of ynones as well as the conversion of sp^2 C–Se to sp^3 C–Se bond and a S_N2 displacement in the formation of oxazoles. Our discovery enriched the mechanism of selenium catalysis and promoted further design of new reactions by selenium-π-acid catalysis.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: XXX

Experimental details, characterization data, mechanistic studies and NMR spectra of new compounds.

AUTHOR INFORMATION

Corresponding Author

*E-mail: zhaoxd3@mail.sysu.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We thank Sun Yat-Sen University, the "One Thousand Youth Talents" Program of China and the Natural Science Foundation of Guangdong Province (Grant No. 2014A030312018) for financial support.

REFERENCES

(1) For book, see: Trost, B. M.; Li, C.-J. *Modern Alkyne Chemistry: Catalytic and Atom-Economic Transformations*; Wiley-VCH: Weinheim, Germany, 2014. For selected reviews, see: (a) Hein, J. E.; Fokin, V. V. Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC) and Beyond: New Reactivity of Copper(I) Acetylides. *Chem. Soc. Rev*. **2010**, *39*, 1302-1315. (b) Godoi, B.; Schumacher, R. F.; Zeni, G. Synthesis of Heterocycles via Electrophilic Cyclization of Alkynes Containing Heteroatom. *Chem. Rev.* **2011**, *111*, 2937-2980.

(2) For selected reviews, see: (a) Fürstner, A. P.; Davies, W. Catalytic Carbophilic Activation: Catalysis by Platinum and Gold π Acids. *Angew. Chem. Int. Ed*. **2007**, *46*, 3410-3449. (b) Dorel, R.; Echavarren, A. M. Gold(I)-Catalyzed Activation of Alkynes for the Construction of Molecular Complexity. *Chem. Rev.* **2015**, *115*, 9028-9072. (c) Fang, G.; Bi, X. Silver-Catalysed Reactions of Alkynes: Recent Advances. *Chem. Soc. Rev.* **2015**, *44*, 8124-8173.

(3) (a) Peng, B.; Huang, X.; Xie, L.-G.; Maulide, N. A. Brønsted Acid Catalyzed Redox Arylation. *Angew. Chem. Int. Ed*. **2014**, *53*, 8718-8721. (b) Wang, Y.; Song, L.-J.; Zhang, X.; Sun, J. Metal-Free [2+2+2] Cycloaddition of Ynamides and Nitriles: Mild and Regioselective Synthesis of Fully Substituted Pyridines. *Angew. Chem. Int. Ed.* **2016**, *55*, 9704-9708. (c) Patil, D. V.; Kim, S. W.; Nguyen, Q. H.; Kim, H.; Wang, S.; Hoang, T.; Shin, S. Brønsted Acid Catalyzed Oxygenative Bimolecular Friedel-Crafts Type Coupling of Ynamides. *Angew. Chem. Int. Ed.* **2017**, *129*, 3724-3728. (d) Shibuya, M.; Fujita, S.; Abe, M.; Yamamoto, Y. Brønsted Acid/Silane Catalytic System for Intramolecular Hydroalkoxylation and Hydroamination of Unactivated Alkynes. *ACS Catal.* **2017**, *7*, 2848-2852.

(4) (a) Mahdi, T.; Stephan, D. W. Frustrated Lewis Pair Catalyzed Hydroamination of Terminal Alkynes. *Angew. Chem. Int. Ed*. **2013**, *52*, 12418-12421. (b) Tamke, S.; Qu, Z.-W.; Sitte, N. A.; Flörke, U.; Grimme, S.; Paradies, J. Frustrated Lewis Pair-Catalyzed Cycloisomerization of 1,5-Enynes via a 5-*endo*-dig Cyclization/Protodeborylation Sequence. *Angew. Chem. Int. Ed*. **2016**, *55*, 4336-4339. (c) Yuan, K.; Wang, S. *trans*-Aminoboration across Internal Alkynes Catalyzed by $B(C_6F_5)_3$ for the Synthesis of Borylated Indoles. *Org. Lett.* **2017**, *19*, 1462-1465. (d) Shibuya, M.; Okamoto, M.; Fujita, S.; Abe, M.; Yamamoto, Y. Boron-Catalyzed Double Hydrofunctionalization Reactions of Unactivated Alkynes. *ACS Catal.* **2018**, *8*, 4189-4193.

(5) (a) Rodríguez, A.; Moran, W. J. Iodobenzene-Catalyzed Intramolecular Oxidative Cyclization Reactions of *δ*-Alkynyl *β*-Ketoesters. *Org. Lett*. **2011**, *13*, 2220-2223. (b) Yagyu, T.; Takemoto, Y.; Yoshimura, A.; Zhdankin, V. V.; Saito A. Iodine(III)-Catalyzed Formal [2+2+1] Cycloaddition Reaction for Metal-Free Construction of Oxazoles. *Org. Lett*. **2017**, *19*, 10, 2506-2509. (c) Okamura, Y.; Sato, D.; Yoshimura, A.; Zhdankin, V. V.; Saito, A. Iodine(III)-Mediated/Catalyzed Cycloisomerization-Amination Sequence of *N*-Propargyl Carboxamides. *Adv. Synth. Catal*. **2017**, *359*, 18, 3243-3247.

(6) For selected reviews, see: (a) Flanigan, D. M.; Romanov-Michailidis, F.; White, N. A.; Rovis, T. Organocatalytic Reactions Enabled by N-Heterocyclic Carbenes. *Chem. Rev.* **2015**, *115*, 9307-9387. (b) Qin, Y.; Zhu, L.; Luo, S. Organocatalysis in Inert C-H Bond Functionalization. *Chem. Rev*. **2017**, *117*, 9433-9520. (c) Zou, Y.-Q.; Hormann, F. M.; Bach, T. Iminium and Enamine Catalysis in Enantioselective Photochemical Reactions. *Chem. Soc. Rev.* **2018**, *47*, 278-290.

(7) For selected examples, see: (a) Santoro, S.; Santi, C.; Sabatini, M.; Testaferri, L.; Tiecco, M. Eco-Friendly Olefin Dihydroxylation Catalyzed by Diphenyl Diselenide. *Adv. Synth. Catal*. **2008**, *350*, 2881-2884. (b) García-Marín, H.; van der Toorn, J. C.; Mayoral, J. A.; García, J. I.; Arends, I. W. C. E. Glycerol-Based Solvents as Green Reaction Media in Epoxidations with Hydrogen Peroxide Catalysed by Bis[3,5-bis(trifluoromethyl)-diphenyl]diselenide. *Green Chem.* **2009**, *11*, 1605-1609. (c) Chen, F.; Tan, C. K.; Yeung, Y.-Y. C_2-Symmetric Cyclic Selenium-Catalyzed Enantioselective Bromoaminocyclization. *J. Am. Chem. Soc.* **2013**, *135*, 1232-1235. (d) Yu, L.; Li, H.; Zhang, X.; Ye, J.; Liu, J.; Xu, Q.; Lautens, M. Organoselenium-Catalyzed Mild Dehydration of Aldoximes: An Unexpected Practical Method for Organonitrile Synthesis. *Org. Lett.* **2014**, *16*, 1346-1349. (e) Jin, W.; Zheng, P.; Wong, W.-T.; Lawa, G.-L. Efficient Selenium-Catalyzed Selective $C(sp^3)$−H Oxidation of Benzylpyridines with Molecular Oxygen. *Adv. Synth. Catal.* **2017**, *359*, 1588-1593. (f) Sancineto, L.; Mangiavacchi, F.; Tidei, C.; Bagnoli, L.; Marini, F.; Gioiello, A.; Scianowski, J.; Santi, C. Selenium-Catalyzed Oxacyclization of Alkenoic Acids and Alkenols. *Asian J. Org. Chem*. **2017**, *6*, 988-992. (g) Horibe, T.; Ohmura, S.; Ishihara, K. Selenium−Iodine Cooperative Catalyst for Chlorocyclization of Tryptamine Derivatives. *Org. Lett*. **2017**, *19*, 5525-5528. (h) Akondi, S. M.; Gangireddy, P.; Pickel, T. C.; Liebeskind, L. S. Aerobic, Diselenide-Catalyzed Redox Dehydration: Amides and Peptides. *Org. Lett*. **2018**, *20*, 538-541. (i) Tao, Z.; Robb, K. A.; Zhao, K.; Denmark, S. E. Enantioselective, Lewis Base-Catalyzed Sulfenocyclization of Polyenes. *J. Am. Chem. Soc*. **2018**, *140*, 3569-3573.

(8) For recent reviews, see: (a) Ortgies, S.; Breder, A. Oxidative Alkene Functionalizations via Selenium-π-Acid Catalysis. *ACS Catal*. **2017**, *7*, 5828-5840. (b) Guo, R.; Liao, L.; Zhao, X. Electrophilic Selenium Catalysis with Electrophilic N-F Reagents as the Oxidants. *Molecules* **2017**, *22*, 835-847.

(9) For selected examples, see: (a) Browne, D. M.; Niyomura, O.; Wirth, T. Catalytic Use of Selenium Electrophiles in Cyclizations. *Org. Lett.* **2007**, *9*, 3169-3171. (b) Trenner, J.; Depken, C.; Weber, T.; Breder, A. Direct Oxidative Allylic and Vinylic Amination of Alkenes through Selenium Catalysis. *Angew. Chem. Int. Ed*. **2013**, *52*, 8952-8956. (c) Cresswell, A. J.; Eey, S. T.-C.; Denmark, S. E. Catalytic, Stereospecific *syn*-Dichlorination of Alkenes. *Nat. Chem.* **2015**, *7*, 146-152. (d) Kawamata, Y.; Hashimoto, T.; Maruoka, K. A Chiral Electrophilic Selenium Catalyst for Highly Enantioselective Oxidative Cyclization. *J. Am. Chem. Soc.* **2016**, *138*, 5206-5209. (e) Depken, C.; Krätzschmar, F.; Rieger, R.; Rode, K.; Breder, A. Photocatalytic Aerobic Phosphatation of Alkenes. *Angew. Chem. Int. Ed.* **2018**, *57*, 2459-2463.

(10) (a) Deng, Z.; Wei, J.; Liao, L.; Huang, H.; Zhao, X. Organoselenium-Catalyzed, Hydroxy-Controlled Regio- and Stereoselective Amination of Terminal Alkenes: Efficient Synthesis of 3-Amino Allylic Alcohols. *Org. Lett.* **2015**, *17*, 1834-1837. (b) Zhang, X.; Guo, R.; Zhao, X. Organoselenium-Catalyzed Synthesis of Indoles through Intramolecular C-H Amination. *Org. Chem. Front.* **2015**, *2*, 1334-1337. (c) Guo, R.; Huang, J.; Huang, H.; Zhao, X. Organoselenium-Catalyzed Synthesis of Oxygen- and Nitrogen-Containing Heterocycles. *Org. Lett.* **2016**, *18*, 504-507. (d) Liao, L.; Guo, R.; Zhao, X. Organoselenium-Catalyzed Regioselective C–H Pyridination of 1,3-Dienes and Alkenes. *Angew. Chem. Int. Ed*. **2017**, *56*, 3201-3205. (e) Guo, R.; Huang, J.; Zhao, X. Organoselenium-Catalyzed Oxidative Allylic Fluorination with Electrophilic N−F Reagent. *ACS Catal.* **2018**, *8*, 926-930.

(11) (a) Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. Selenium-Mediated Conversion of Alkynes into *α*-Dicarbonyl Compounds. *J. Org. Chem*. **1991**, *56*, 4529-4534. (b) Santoro, S.; Battistelli, B.; Gjoka, B.; Si, C. S.; Testaferri, L.; Tiecco, M.; Santi, C. Oxidation of Alkynes in Aqueous Media Catalyzed by Diphenyl Diselenide. *Synlett* **2010**, 1402-1406.

(12) (a) Back, T. G.; Muralidharan, K. R. Formation and Electrophilic Reactions of Benzeneselenenyl *p*-Toluenesulfonate. Preparation and Properties of Addition Products with Acetylenes. *J. Org. Chem*. **1991**, *56*, 2781-2787. (b) Poleschner, H.; Seppelt, K. Selenirenium and Tellurirenium Ions. *Angew. Chem. Int. Ed.* **2008**, *47*, 6461-6464. (c) Zheng, G.; Zhao, J.; Li, Z.; Zhang, Q.; Sun, J.; Sun, H.;

Zhang, Q. Highly Regio- and Stereoselective Intermolecular Seleno- and Thioamination of Alkynes. *Chem. Eur. J.* **2016**, *22*, 3513-3518.

(13) (a) Reich, H. J.; Willis, Jr. W. W. Organoselenium Chemistry. Formation of Acetylenes and Allenes by Syn Elimination of Vinyl Selenoxides. *J. Am. Chem. Soc.* **1980**, *102*, 5967-5968. (b) Back, T. G.; Collins, S.; Kerr, R. G. Selenosulfonation of Acetylenes: Preparation of Novel *β*-(Phenylse1eno)vinyl Sulfones and Their Conversion to Acetylenic and *β*-Functionalized Sulfones. *J. Org. Chem.* **1983**, *48*, 3077-3084.

(14) (a) Liu, X.; An, R.; Zhang, X.; Luo, J.; Zhao, X. Enantioselective Trifluoromethylthiolating Lactonization Catalyzed by an Indane-Based Chiral Sulfide. *Angew. Chem. Int. Ed.* **2016**, *55*, 5846-5850. (b) Luo, J.; Cao, Q.; Cao, X.; Zhao, X. Selenide-Catalyzed Enantioselective Synthesis of Trifluoromethylthiolated Tetrahydronaphthalenes by Merging Desymmetrization and Trifluoromethylthiolation. *Nat. Commun.* **2018**, *9*, 527-535. (c) Liu, X.; Liang, Y.; Ji, J.; Luo, J.; Zhao, X. Chiral Selenide-Catalyzed Enantioselective Allylic Reaction and Intermolecular Difunctionalization of Alkenes: Efficient Construction of C-SCF_3 Stereogenic Molecules. *J. Am. Chem. Soc.* **2018**, *140*, 4782-4786.

(15) (a) Savignac, P.; Iorga, B. *Modern Phosphonate Chemistry*; CRC Press: Boca Raton, USA, 2003. (b) Horsman, G. P.; Zechel, D. L. Phosphonate Biochemistry. *Chem. Rev.* **2017**, *117*, 5704-5783.

(16) (a) Öhler, E.; Zbiral, E. Synthesis, Reactions and NMR Spectra of Dialkyl 2-Bromo-3-Oxo-1-Alkenylphosphonates and Dialkyl 3-Oxo-1-Alkynylphosphonates. *Monatsh. Chem.* **1984**, *115*, 493-508. (b) Moglie, Y.; Mascaró, E.; Gutierrez, V.; Alonso, F.; Radivoy, G. Base-Free Direct Synthesis of Alkynylphosphonates from Alkynes and *H*-Phosphonates Catalyzed by Cu_2O. *J. Org. Chem.* **2016**, *81*, 1813-1818. (c) Yu, Y.; Yang, W.; Pflästerer, D.; Hashmi, A. S. K. Dehydrogenative Meyer-Schuster-Like Rearrangement: A Gold-Catalyzed Reaction Generating an Alkyne. *Angew. Chem. Int. Ed.* **2014**, *53*, 1144-1147. (d) Shiroodi, R. K.; Soltani, M.; Gevorgyan, V. Gold-Catalyzed 1,3-Transposition of Ynones. *J. Am. Chem. Soc.* **2014**, *136*, 9882-9885.

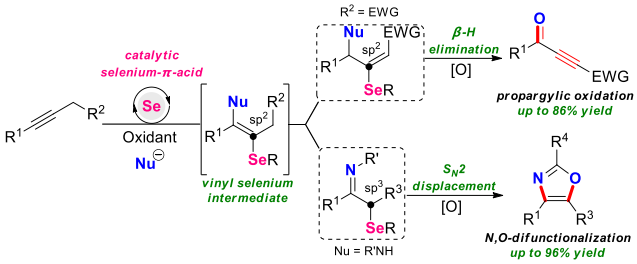
(17) (a) Yeh, V. S. C. Recent Advances in the Total Syntheses of Oxazole-Containing Natural Products. *Tetrahedron* **2004**, *60*, 11995-12042. (b) Davyt, D.; Serra, G. Thiazole and Oxazole Alkaloids: Isolation and Synthesis. *Mar. Drugs* **2010**, *8*, 2755-2780. (c) Jin, Z. Muscarine, Imidazole, Oxazole and Thiazole Alkaloids. *Nat. Prod. Rep.* **2016**, *33*, 1268-1317.

(18) (a) Davies, P. W.; Cremonesi, A.; Dumitrescu, L. Intermolecular and Selective Synthesis of 2,4,5-Trisubstituted Oxazoles by a Gold-Catalyzed Formal [3+2] Cycloaddition. *Angew. Chem. Int. Ed.* **2011**, *50*, 8931-8935. (b) He, W.; Li, C.; Zhang, L. An Efficient [2+2+1] Synthesis of 2,5-Disubstituted Oxazoles via Gold-Catalyzed Intermolecular Alkyne Oxidation. *J. Am. Chem. Soc.* **2011**, *133*, 8482-8485. c) Luo, Y.; Ji, K.; Li, Y.; Zhang, L. Tempering the Reactivities of Postulated *α*-Oxo Gold Carbenes Using Bidentate Ligands: Implication of Tricoordinated Gold Intermediates and the Development of an Expedient Bimolecular Assembly of 2,4-Disubstituted Oxazoles. *J. Am. Chem. Soc.* **2012**, *134*, 17412-17415. (d) Li, X.; Huang, L.; Chen, H.; Wu, W.; Huang, H.; Jiang, H. Copper-Catalyzed Oxidative [2+2+1] Cycloaddition: Regioselective Synthesis of 1,3-Oxazoles from Internal Alkynes and Nitriles. *Chem. Sci.* **2012**, *3*, 3463-3467. (e) Rassadin, V. A.; Boyarskiy, V. P.; Kukushkin, V. Yu. Facile Gold-Catalyzed Heterocyclization of Terminal Alkynes and Cyanamides Leading to Substituted 2-Amino-1,3-Oxazoles. *Org. Lett.* **2015**, *17*, 3502-3505. (f) Mallick, R. K.; Prabagar, B.; Sahoo, A. K. Regioselective Synthesis of 2,4,5-Trisubstituted Oxazoles and Ketene Aminals via Hydroamidation and Iodo-Imidation of Ynamides. *J. Org. Chem.* **2017**, *82*, 10583-10594.

(19) Oxazole was observed as a by-product in trace amounts. See: Tingoli, M.; Mazzella, M.; Panunzi, B.; Tuzi, A. Elemental Iodine or Diphenyl Diselenide in the [Bis(trifluoroacetoxy)-iodo]benzene-Mediated Conversion of Alkynes into 1,2-Diketones. *Eur. J. Org. Chem.* **2011**, 399-404.

(20) Our mechanistic studies did not support that the formation of ynones went through an allene intermediate with propargylphosphonates. For the reactions of 3-alkynoates, allene is possible as intermediate since ester-substituted allenes could give ynones (see Supporting Information).

(21) (a) He, G.; Guo, H.; Qian, R.; Guo, Y.; Fu, C.; Ma, S. Studies on Highly Regio- and Stereoselective Selenohydroxylation Reaction of 1,2-Allenyl Phosphine Oxides with PhSeCl. *Tetrahedron*, **2009**, *65*, 4877-4889. (b) Li, F.-H.; Cai, Z.-J.; Yin, L.; Li, J.; Wang, S.-Y.; Ji, S.-J. Silver-Catalyzed Regioselective Fluorination of Carbonyl Directed Alkynes: Synthesis of *α*-Fluoroketones. *Org. Lett.* **2017**, *19*, 1662-1665. (c) Yuan, S.-T.; Zhou, H.; Gao, L.; Liu, J.-B.; Qiu, G. Regioselective Neighboring-Group-Participated 2,4-Dibromohydration of Conjugated Enynes: Synthesis of 2 - (2,4-Dibromobut-2-enoyl)benzoate and Its Applications. *Org. Lett.* **2018**, *20*, 562-565.


catalytic
selenium-π-acid
Se
Oxidant
Nu⊖
vinyl selenium
intermediate
R² = EWG
β-H
elimination
[O]
propargylic oxidation
up to 86% yield
SN2
displacement
[O]
N,O-difunctionalization
up to 96% yield
Nu = R'NH