DOI: 10.1002/adsc.201900940
Advanced Synthesis & Catalysis

in situ Formation of RSCl/ArSeCl and Their Oxidative Coupling with Enaminone Derivatives Under Transition-metal Free Conditions

Zhenhua Shang,[a] Qingyu Chen,[a] Linlin Xing,[b,*] Yilin Zhang,[c] Laura Wait,[d] and Yunfei Du[b,*]

[a] College of Chemical and Pharmaceutical Engineering, Hebei University of Science and Technology; Hebei Research Center of Pharmaceutical and Chemical Engineering, Shijiazhuang 050018, People's Republic of China
[b] Tianjin Key Laboratory for Modern Drug Delivery & High-Efficiency, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, People's Republic of China
E-mail: duyunfeier@tju.edu.cn; xinglinlin@tju.edu.cn
[c] C. Eugene Bennett Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506-6045, United States
[d] School of Chemistry and Molecular Biosciences, The University of Queensland, St Lucia, Queensland 4068, Australia

Manuscript received: July 28, 2019; Revised manuscript received: September 1, 2019;
Version of record online: ■■, ■■

Supporting information for this article is available on the WWW under https://doi.org/10.1002/adsc.201900940

Abstract: The reaction of diorganyl disulfides or diselenides with $PhICl_2$ in DMF at room temperature led to the *in situ* formation of the reactive organosulfenyl chloride (RSCl) or selenenyl chloride (ArSeCl), which reacted with enaminone compounds to afford a series of α-thioenaminones or α-selenylenaminones, respectively, including the bioactive inhibitor for Cdc25B and its analogue, via the intermolecular oxidative C(sp^2)-S/Se cross coupling reactions under metal-free conditions.

Keywords: Diorganyl disulfide/diselenide; $PhICl_2$; Organosulfenyl/Organoselenenyl chloride; Enamine; Oxidative coupling

Enaminones and their analogues play important roles in numerous organic transformations due to the fact that this class of compounds possess both electrophilic and nucleophilic reactive sites in their structures, which enables the construction of various molecules with enriched structural diversity.[1] On the other hand, there has been long-standing interest in the construction of C–S/Se bonds because of their important applications in organic synthesis[2] and the broad biological properties associated with S or Se-containing compounds.[3] As a result, α-chalcogenylenaminone compounds and their analogues, known as significant and useful polyfunctionalized olefins, have attracted considerable attention from organic chemists to explore their synthetic method and application. This might also be attributed to the fact that they could be conveniently converted into multifunctional compounds through asymmetric hydrogenation.[4] Furthermore, α-thioenamine compounds are also potential scaffolds found in pharmaceutical and bioactive molecules.[5] For example, compound **I**,[5a,b] which is known as an inhibitor for Cdc25B dual specificity protein phosphatase, possesses a thioenamine scaffold in its structure. In addition, thioenamino peptide **II**,[5c] a potential new type of β-turn mimic, also bears a thioenamine moiety in its cyclic peptide molecule (Figure 1).

Hence, tremendous effort has been devoted to the construction of the α-thioenamine skeleton, which combines structural diversity with interesting biological activities.[4,6] Among these strategies, one of the most straightforward methods is by the means of direct C(sp^2)-S bond formation through C–H bond functionalization of the alkene moiety in the enamine substrates. The transition metal-free C–H bond func-

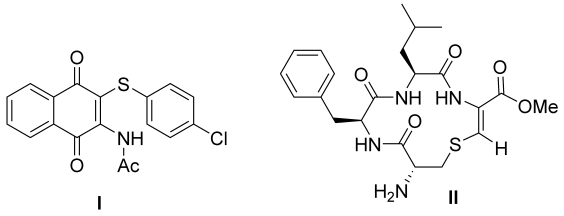
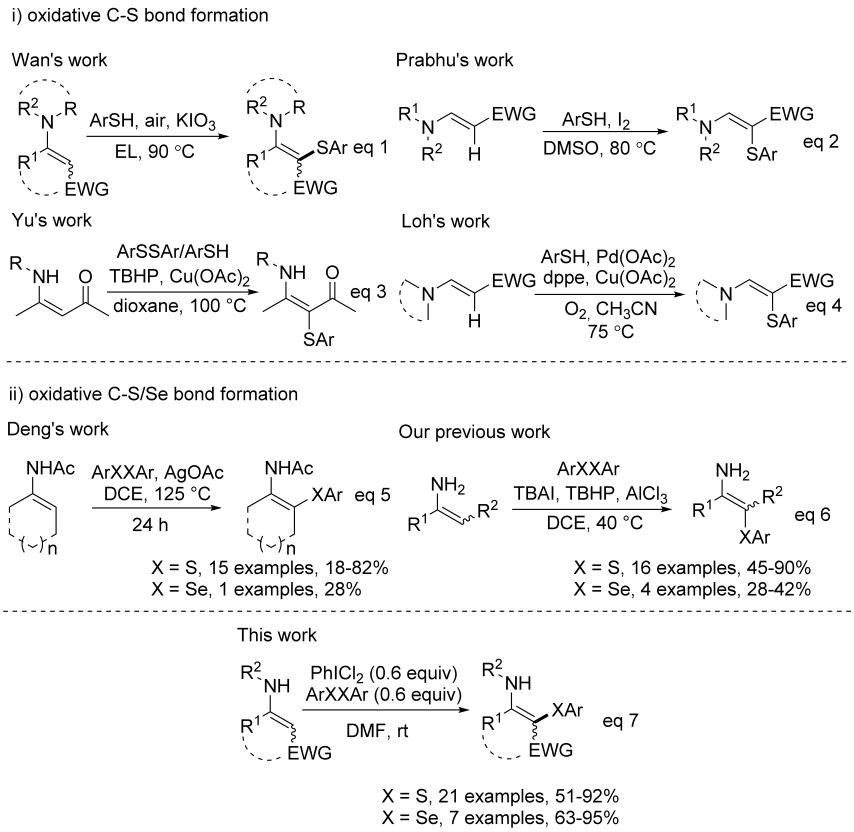


Figure 1. Representative Pharmaceutically Active Agents Possessing Thioenamine Scaffold



Scheme 1. Existing Strategies for Oxidative C–S/Se Bond Formation

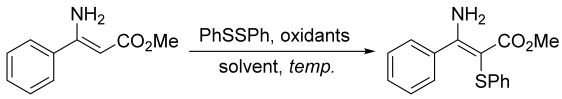
tionalization of enamines has recently witnessed notable advances.[7] In the last few decades, several delicate methods for the introduction of a thio group through direct C(sp^2)-S bond formation have been developed.[6a,c–f,i–r,7] For example, Kostyuk and co-workers[6q] reported their synthesis of sulfenylated enamine derivatives by treatment of enamines with arylsulfenyl chloride in the presence of Et_3N. Besides that, both arenethiols and disulfides have been widely employed as the thio source for this type of sulfenylation reactions. For instance, Lei group[6c] has demonstrated that the radical-radical cross coupling between enamines and thiophenols could be achieved under electrochemical oxidative conditions. In addition to electrochemical condition, conventional methodologies which use a variety of oxidants to achieve the oxidative coupling process have also been documented. For examples, Wan[6m] and Prabhu group[6i] revealed their metal-free cross coupling reactions of enaminones with arenethiols using air/KIO_3 or DMSO/I_2 system, respectively (Scheme 1, eq 1 & 2). Alternatively, Loh and coauthors[6d] developed a palladium-catalyzed C–S bond formation of enamines with thiols using Cu$(OAc)_2$ as an oxidant. When disulfides were used as reaction partners, both silver salts and TBHP could serve as oxidants (Scheme 1, eq 4). Deng and co-workers reported that stoichiometric AgOAc and 2 equiv. of disulfides were required for the radical coupling reaction to afford the sulfenylated enamide (Scheme 1, eq 5).[6k] By using TBHP as an oxidant, our group[6a] reported an oxidative coupling of enaminone and disulfides catalyzed by TBAI (Scheme 1, eq 6), while Yu group[6r] developed a similar protocol using $Cu(OAc)_2$ as the catalyst (Scheme 1, eq 3).

Although these reactions have their own merits, there are several problems that need to be addressed, such as the inevitable use of metal oxidants or catalyst, lack of atom economy, and the requirement of high reaction temperature or a relatively longer reaction time for almost all of these transformations. Furthermore, it is also known that organoselenium compounds are promising pharmaceutical reagents owing to their unique biological properties, specifically their anti-cancer and antitumor activity.[3d] However, these strategies were seldom feasible in the installation of selenyl group through C(sp^2)-Se bond formation to achieve these compounds. Although Deng[6k] and our group[6a] have realized the introduction of the selenyl group (Scheme 1, eq 5 & 6), the desired selenylation products were achieved in unsatisfactory yield (28% and 28–42% respectively).

Recently, we have successfully developed a one-pot protocol to achieve regioselective intramolecular chalcogenylacyloxylation of alkynes which is promoted by *in situ* generated organosulfenyl chloride (RSCl) or selenenyl chloride (RSeCl).[8] Inspired by this work, we are interested to understand whether this one-pot strategy could be applied in the introduction of thio and selenyl functional groups to enaminone and its analogues. Based on our findings, herein, we report a novel metal-free C–H bond functionalization of the enamine compounds to afford the α-chalcogenylenamines in good to excellent yields in the presence of the *in situ* generated ArSCl or ArSeCl from the reaction between the inactivated disulfides or diselenides and $PhICl_2$.

To test our hypothesis on the sulfenylation of enamine by the *in situ* generated organosulfenyl chloride, enamine **1a** was initially employed to react with PhSSPh and hypervalent iodine oxidant under various conditions (Table 1). To our delight, subjecting

Table 1. Optimization of the Reaction Conditions[a]



Entry	Oxidant (equiv)	Solvent	*Temp.* (°C)	Yield (%)[b]
1	$PhICl_2$ (1.0 equiv.)	CH_3CN	rt	46
2	$PhICl_2$ (0.8 equiv.)	CH_3CN	rt	65
3	$PhICl_2$ (0.6 equiv.)	CH_3CN	rt	81
4	$PhICl_2$ (0.5 equiv.)	CH_3CN	rt	59
5	$PhICl_2$ (0.6 equiv.)	DMF	rt	86
6	$PhICl_2$ (0.6 equiv.)	DCM	rt	80
7	$PhICl_2$ (0.6 equiv.)	CH_3OH	rt	ND
8	$PhICl_2$ (0.6 equiv.)	THF	rt	trace
9	$PhICl_2$ (0.6 equiv.)	CF_3CH_2OH	rt	NR
10	$PhICl_2$ (0.6 equiv.)	DMF	0	87
11	PIFA (0.6 equiv.)	DMF	rt	ND
12	PhIO (0.6 equiv.)	DMF	rt	15
13	PIDA (0.6 equiv.)	DMF	rt	NR

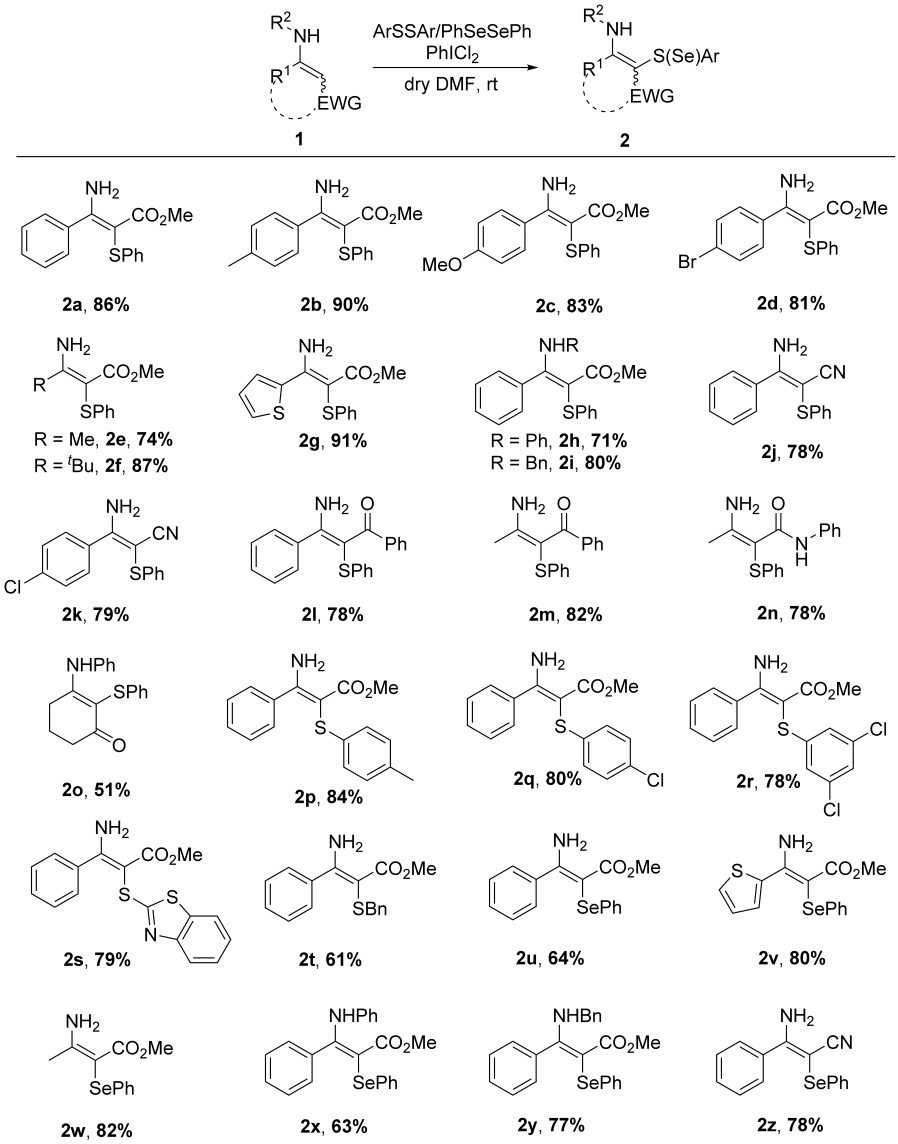
[a] Reaction conditions: **1a** (0.5 mmol), PhSSPh (0.3 mmol), and oxidant in dry solvent (5 mL) at rt for 30 min.
[b] Isolated yields based on the enamine substrates.

the solution resulting from the reaction of PhSSPh (0.6 equiv.) and $PhICl_2$ (1.0 equiv.) to enamine **1a** (1.0 equiv.) delivered the desired sulfenylated enamine **2a** in a yield of 46%. As we can see, loading a reduced amount of oxidant from 1.0 equiv. to 0.6 equiv. resulted in improved conversions (entries 1–3). However, further decrease in the oxidant amount led to a slight drop in the reaction yield (entry 4). Afterward, a series of solvents including DMF, DCM, methanol, THF, and CF_3CH_2OH were tested and only DMF provided superior result (entries 5–9). Conducting the reaction under an ice-bath rather than at room temperature gave similar results (entry 10). Additionally, the sources of hypervalent iodine(III) oxidants dramatically affected the outcome of the reaction, since other hypervalent iodine reagents including PIFA, PhIO and PIDA gave either poor or no conversion under otherwise identical conditions (entries 11–13).

Subsequently, to verify the broad substrate scope of the transformation, a variety of enamines were prepared and subjected to the optimized conditions. As shown in Table 2, all these enamines underwent smooth reactions at room temperature within 30 min to give the sulfenyl substituted products. Substrates **1b–d** with either an electron-donating or -withdrawing group including methyl, methoxy, and bromide on the aromatic ring of enamine **1**, proved to be well tolerated under the standard conditions, delivering the corresponding products in good yields. To our delight, the reaction worked equally well with both methyl and sterically hindered *tert*-butyl alkyl R^1 functional groups, leading to the desired products **2e–f** in 82% and 78% yield, respectively. In addition, the reaction could be further extended to substrate **1g** with a heteroaryl ring thiophene linked to the alkene moiety. The R^2 group substituted on the amine moiety was also investigated. Both enamines **1h** and **1i** containing a phenyl or benzyl protecting group on the amine were suitable for this C–S bond formation strategy. It was also found that not only esters, but also a wide range of electron-withdrawing groups such as cyano, ketone and amide substituted enamines, were all good reaction partners. All these enamines **1j-n** with R^1 group being phenyl, *p*-chlorophenyl or methyl were found to be tolerable under the standard conditions to furnish the corresponding products **2j–n** in 78–82% yield. Interestingly, cyclic enamine **1o** was still a facile substrate, albeit with lower efficiency (51%) when compared to the linear reactants.

After the thorough exploration of the reaction scope of enamines, we then came to investigate the reactivity of variously substituted diphenyl disulfides. The electronic nature of substituents on diphenyl disulfides did not have a great influence on the yields of the reaction. For instance, both disulfides bearing an electron-donating methyl group as well as an electron-withdrawing chloro-substituted phenyl ring exhibited high reactivity in this conversion, giving products **2p–r** in high yields. It is noteworthy that a heterocyclic disulfide underwent the sulfenylation process with a similar efficiency, affording product **2s** with 79% yield. In addition, the method was also applicable to alkyl disulfide, albeit the corresponding product **2t** was obtained in a slightly lower yield. Most strikingly, when we tried to install a selenyl group into the enamine skeleton, we found that the outcome of reactions was improved significantly under this method, despite the fact that initial attempts by other

Table 2. $PhICl_2$/PhSSPh-Mediated Synthesis of Chalcogenyl Enamine.[a]

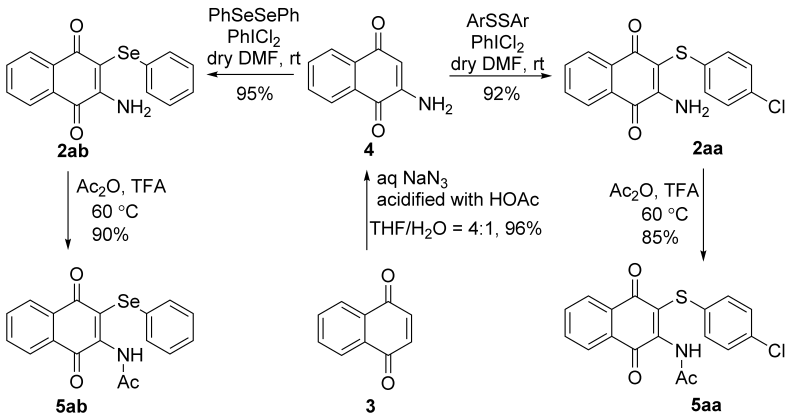


[a] Reaction conditions: **1** (0.5 mmol), PhSSPh (0.3 mmol), and $PhICl_2$ (0.3 mmol) in DMF (5 mL) at rt for 30 min.
[b] Isolated yields based on the enamine substrates.

researchers ended up with relatively low yields. When enamines with a phenyl, thiophene or a methyl R^1 group were applied in the selenylation procedure, the corresponding products **2u–w** were obtained in a yield of 64–82%. Furthermore, substrates bearing phenyl or benzyl protecting amine groups gave similar results to the substrates with free NH_2 group and were converted to selenyl products **2x** and **2y** in 63% and 77% yield, respectively. Moreover, the phenylselenyl group was successfully introduced to the cyano-substituted enamine **1z** as well in a yield of 78%.

To further demonstrate the practical use of this synthetic methodology, the bioactive molecule naphthoquinone **5aa** was synthesized in an overall yield of 75% in 3 steps (Scheme 2). To our delight, the enaminone skeleton **4**, prepared from commercial available naphthoquinone **3** according to literature procedure,[9] can be converted to sulfenylated enaminone **2aa** through this one-pot method in an excellent yield. The following NH_2 protection by acetic anhydride fulfilled the efficient synthesis of biologically active **5aa**. In addition, the selenyl analogue **5ab** was also achieved in the same route with a high overall yield of 85%.

Indole and its derivatives are important scaffolds that have been widely found in bioactive natural products, pharmaceuticals and functional materials.[10] Encouraged by the results above, we next turned our



Scheme 2. Application of the Synthetic Methodology to the Synthesis of Bioactive Molecule and Its Selenyl Analogue

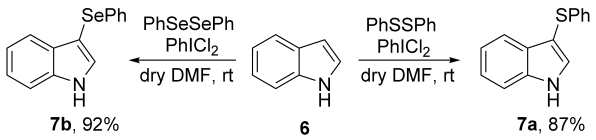
attention to the functionalization of indole compound, a particular type of enamine compound, by this approach (Scheme 3). To our delight, the desired sulfenylated and selenylated indole were delivered smoothly under the standard conditions in a yield of 87% and 92%, respectively.

The resulting sulfenylated enamine could be further converted to other building block by a known method.[11] For example, by treatment with I_2 and DBU, enamine **2 a** was conveniently converted to the sulfenylated azirine derivative **8** via intramolecular azirination (Scheme 4). Although azirines bearing various substitution pattern have been reported,[12] the synthesis of sulfenylated azirine from sulfenylated enamine has been seldom documented.

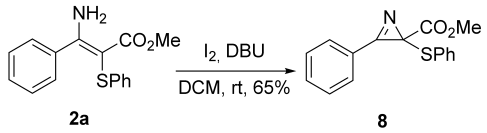
To probe the mechanism of the C–S(Se) formation process, a couple of control experiments were conducted (Scheme 5). First, the active species PhSeCl was isolated from the reaction of diphenyl diselenide and $PhICl_2$. Subsequently, the resulting PhSeCl solid was subjected to enamine solution in DMF at room temperature and the corresponding selenylated product **2 a** was obtained in 60% yield. The reaction of enamine **1 a** with disulfide in the presence of TEMPO or BHT under the standard conditions provided a good yield of the sulfenylated enamine **2 a**, which excluded a free-radical pathway for this reaction.

Based on the results from the control experiments as well as the previous report,[8] a plausible mechanism was put forward as depicted in Scheme 6. The whole process mainly consisted of two steps, the first of which was the formation of active species phenylsulfenyl chloride. The diphenyl disulfides reacted with $PhICl_2$ to form the sulfonium salt **B** through release of PhI from intermediate **A**, and the dissociation of intermediate **B** gave rise to 2 molecules PhSCl. The second step fulfilled the installation of sulfenyl group, which was initiated by the nucleophlic attack of the enamine electrons to the sulfonium center of the PhSCl to afford the intermediate **C**. The intermediate **C** tautomerized to give the final product **2 a**.

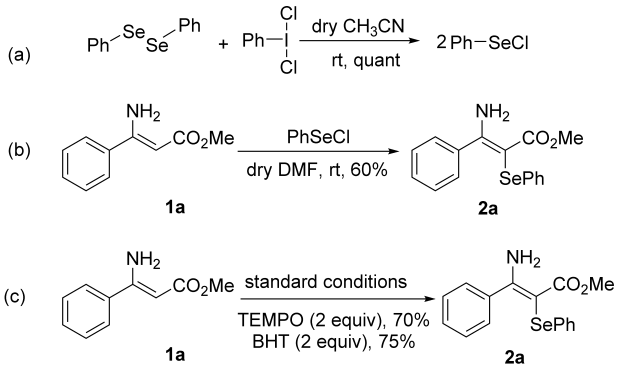
In summary, a new C–H functionalization of enamines involving *in situ* generation of organosulfenyl chloride (RSCl) or selenenyl chloride (ArSeCl) from the reaction between diorganyl disulfides or disele-



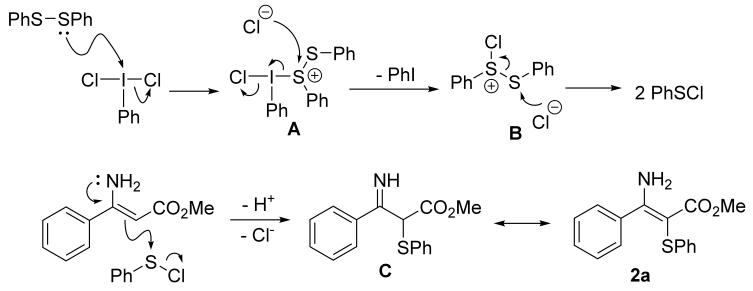
Scheme 3. Synthesis of Sulfenylated and Selenylated Indole



Scheme 4. Further Derivatization of Sulfenylated Enamine **2 a**



Scheme 5. Control Experiments



Scheme 6. Proposed Mechanism

nides and $PhICl_2$ was developed. This method not only provides an alternative approach that is simple and mild for the direct thiolation of enamines, but also achieves a significantly improved yield of selenation through C(sp^2)-Se bond formation, affording a variety of sulfenylated and selenenylated enamines including indole derivatives. Furthermore, the synthetic method was also applicable to a highly efficient synthesis of an inhibitor for Cdc25B dual specificity protein phosphatase and its selenyl analogue.

Experimental Section

To a solution of diorganyl disulfide/diselenide (0.6 mmol) in DMF (8 mL), was added $PhICl_2$ (0.6 mmol) at rt. The mixture was stirred in dark for 15 min to give an orange solution. Then the above solution was added dropwise to a solution of enamine **1** or iodole **6** (1.0 mmol) in DMF and stirred for another 30 min until complete consumption of the starting material (monitored by TLC). Then reaction mixture was treated with water (50 mL) and extracted with DCM (100 mL × 3). The organic phases was combined and washed with brine (50 mL), dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Then the residue was purified by flash column chromatography to afford the desired compound **2**/**7**.

Acknowledgements

We acknowledge the National Natural Science Foundation of China (#21472136) for financial support.

References

[1] a) J.-P. Wan, Y. Lin, X. Cao, Y. Liu, L. Wei, *Chem. Commun.* **2016**, *52*, 1270–1273; b) A.-Z. A. Elassar, A. A. El-Khair, *Tetrahedron* **2003**, *59*, 8463–8480; c) Z.-J. Zhang, Z.-H. Ren, Y.-Y. Wang, Z.-H. Guan, *Org. Lett.* **2013**, *15*, 4822–4825; d) B. Stanovnik, J. Svete, *Chem. Rev.* **2004**, *104*, 2433–2480; e) Y. Gao, Y. Liu, J.-P. Wan, *J. Org. Chem.* **2019**, *84*, 2243–2251; f) E. Karadeniz, M. Zora, *Synlett* **2019**, *30*, 1231–1236; g) J. D. White, D. C. Ihle, *Org. Lett.* **2006**, *8*, 1081–1084; h) G. Li, K. Watson, R. W. Buckheit, Y. Zhang, *Org. Lett.* **2007**, *9*, 2043–2046; i) P. Zhou, B. Hu, L. Li, K. Rao, J. Yang, F. Yu, *J. Org. Chem.* **2017**, *82*, 13268–13276; j) J.-P. Wan, Y. Gao, *Chem. Rec.* **2016**, *16*, 1164–1177.

[2] a) K. C. Nicolaou, D. J. Edmonds, P. G. Bulger, *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186; *Angew. Chem.* **2006**, *118*, 7292–7344; b) S. G. Modha, V. P. Mehta, E. V. Van der Eycken, *Chem. Soc. Rev.* **2013**, *42*, 5042–5055; c) F. Zhu, Z.-X. Wang, *Org. Lett.* **2015**, *17*, 1601–1604; d) H. J. Reich, R. J. Hondal, *ACS Chem. Biol.* **2016**, *11*, 821–841; e) D. M. Freudendahl, S. Santoro, S. A. Shahzad, C. Santi, T. Wirth, *Angew. Chem. Int. Ed.* **2009**, *48*, 8409–8411; *Angew. Chem.* **2009**, *121*, 8559–8562; f) P. C. Ho, J. Rafique, J. Lee, L. M. Lee, H. A. Jenkins, J. F. Britten, A. L. Braga, I. Vargas-Baca, *Dalton Trans.* **2017**, *46*, 6570–6579; g) T. E. Frizon, J. Rafique, S. Saba, I. H. Bechtold, H. Gallardo, A. L. Braga, *Eur. J. Org. Chem.* **2015**, *2015*, 3470–3476; h) K. B. Sharpless, R. F. Lauer, *J. Am. Chem. Soc.* **1972**, *94*, 7154–7155; i) J.-D. Yu, W. Ding, G.-Y. Lian, K.-S. Song, D.-W. Zhang, X. Gao, D. Yang, *J. Org. Chem.* **2010**, *75*, 3232–3239; j) B. Hu, Q. Zhang, S. Zhao, Y. Wang, L. Xu, S. Yan, F. Yu, *Adv. Synth. Catal.* **2019**, *361*, 49–54.

[3] a) D. Manna, G. Roy, G. Mugesh, *Acc. Chem. Res.* **2013**, *46*, 2706–2715; b) C. Jacob, G. I. Giles, N. M. Giles, H. Sies, *Angew. Chem. Int. Ed.* **2003**, *42*, 4742–4758; *Angew. Chem.* **2003**, *115*, 4890–4907; c) M. Doering, L. A. Ba, N. Lilienthal, C. Nicco, C. Scherer, M. Abbas, A. A. P. Zada, R. Coriat, T. Burkholz, L. Wessjohann, M. Diederich, F. Batteux, M. Herling, C. Jacob, *J. Med. Chem.* **2010**, *53*, 6954–6963; d) C. W. Nogueira, G. Zeni, J. B. T. Rocha, *Chem. Rev.* **2004**, *104*, 6255–6286; e) J. A. Woods, J. A. Hadfield, A. T. McGown, B. W. Fox, *Bioorg. Med. Chem.* **1993**, *1*, 333–340.

[4] P.-F. Yuan, Q.-B. Zhang, X.-L. Jin, W.-L. Lei, L.-Z. Wu, Q. Liu, *Green Chem.* **2018**, *20*, 5464–5468.

[5] a) A. Lavecchia, S. Cosconati, V. Limongelli, E. Novellino, *ChemMedChem* **2006**, *1*, 540–550; b) J. S. Lazo, K. Nemoto, K. E. Pestell, K. Cooley, E. C. Southwick, D. A. Mitchell, W. Furey, R. Gussio, D. W. Zaharevitz, B. Joo, P. Wipf, *Mol. Pharmacol.* **2002**, *61*, 720; c) D. Pappo, Y. Kashman, *Org. Lett.* **2006**, *8*, 1177–1179.

[6] a) J. Sun, D. Zhang-Negrerie, Y. Du, *Adv. Synth. Catal.* **2016**, *358*, 2035–2040; b) L. Jiang, J. Qian, W. Yi, G. Lu, C. Cai, W. Zhang, *Angew. Chem. Int. Ed.* **2015**, *54*, 14965–14969; *Angew. Chem.* **2015**, *127*, 15178–15182;

c) D. Li, S. Li, C. Peng, L. Lu, S. Wang, P. Wang, Y.-H. Chen, H. Cong, A. Lei, *Chem. Sci.* **2019**, *10*, 2791–2795; d) Y. Jiang, G. Liang, C. Zhang, T.-P. Loh, *Eur. J. Org. Chem.* **2016**, *2016*, 3326–3330; e) Y.-D. Yang, A. Azuma, E. Tokunaga, M. Yamasaki, M. Shiro, N. Shibata, *J. Am. Chem. Soc.* **2013**, *135*, 8782–8785; f) A. Kolasa, *J. Fluorine Chem.* **1987**, *36*, 29–40; g) S. Vijay Kumar, B. Saraiah, N. C. Misra, H. Ila, *J. Org. Chem.* **2012**, *77*, 10752–10763; h) S. Yugandar, A. Acharya, H. Ila, *J. Org. Chem.* **2013**, *78*, 3948–3960; i) Y. Siddaraju, K. R. Prabhu, *J. Org. Chem.* **2017**, *82*, 3084–3093; j) J. Wang, S. Jia, K. Okuyama, Z. Huang, E. Tokunaga, Y. Sumii, N. Shibata, *J. Org. Chem.* **2017**, *82*, 11939–11945; k) L. Yang, Q. Wen, F. Xiao, G.-J. Deng, *Org. Biomol. Chem.* **2014**, *12*, 9519–9523; l) M.-J. Bu, G.-P. Lu, C. Cai, *Org. Chem. Front.* **2017**, *4*, 266–270; m) J.-P. Wan, S. Zhong, L. Xie, X. Cao, Y. Liu, L. Wei, *Org. Lett.* **2016**, *18*, 584–587; n) H. Chachignon, M. Maeno, H. Kondo, N. Shibata, D. Cahard, *Org. Lett.* **2016**, *18*, 2467–2470; o) S. Arimori, O. Matsubara, M. Takada, M. Shiro, N. Shibata, *R. Soc. Open Sci.* **2016**, *3*, 160102; p) X. Zhao, X. Zheng, M. Tian, J. Sheng, Y. Tong, K. Lu, *Tetrahedron* **2017**, *73*, 7233–7238; q) A. N. Kostyuk, Y. V. Svyaschenko, D. M. Volochnyuk, N. V. Lysenko, A. A. Tolmachev, A. M. Pinchuk, *Tetrahedron Lett.* **2003**, *44*, 6487–6491; r) B. Hu, P. Zhou, K. Rao, J. Yang, L. Li, S. Yan, F. Yu, *Tetrahedron Lett.* **2018**, *59*, 1438–1442.

[7] a) L. Fu, J.-P. Wan, *Asian J. Org. Chem.* **2019**, *8*, 767–776; b) S. Zhong, Y. Liu, X. Cao, J.-P. Wan, *ChemCatChem* **2017**, *9*, 465–468; c) J.-P. Wan, S. Zhong, Y. Guo, L. Wei, *Eur. J. Org. Chem.* **2017**, *2017*, 4401–4404; d) Y. Guo, G. Wang, L. Wei, J.-P. Wan, *J. Org. Chem.* **2019**, *84*, 2984–2990.

[8] L. Xing, Y. Zhang, B. Li, Y. Du, *Org. Lett.* **2019**, *21*, 3620–3624.

[9] B. J. Josey, E. S. Inks, X. Wen, C. J. Chou, *J. Med. Chem.* **2013**, *56*, 1007–1022.

[10] a) A. Casapullo, G. Bifulco, I. Bruno, R. Riccio, *J. Nat. Prod.* **2000**, *63*, 447–451; b) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2005**, *105*, 2873–2920; c) R. Ragno, A. Coluccia, G. La Regina, G. De Martino, F. Piscitelli, A. Lavecchia, E. Novellino, A. Bergamini, C. Ciaprini, A. Sinistro, G. Maga, E. Crespan, M. Artico, R. Silvestri, *J. Med. Chem.* **2006**, *49*, 3172–3184; d) D. Crich, A. Banerjee, *Acc. Chem. Res.* **2007**, *40*, 151–161; e) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev.* **2010**, *110*, 4489–4497; f) M. Bandini, A. Eichholzer, *Angew. Chem. Int. Ed.* **2009**, *48*, 9608–9644; *Angew. Chem.* **2009**, *121*, 9786–9824; g) Y. Zhang, J. W. Hubbard, N. G. Akhmedov, J. L. Petersen, B. C. G. Söderberg, *J. Org. Chem.* **2015**, *80*, 4783–4790; h) Y. Zhang, I. W. McArdle, J. W. Hubbard, N. G. Akhmedov, B. C. G. Söderberg, *Tetrahedron Lett.* **2016**, *57*, 2865–2867; i) F. Bai, S. Zhang, L. Wei, Y. Liu, *Asian J. Org. Chem.* **2018**, *7*, 371–373.

[11] M. Wang, J. Hou, W. Yu, J. Chang, *J. Org. Chem.* **2018**, *83*, 14954–14961.

[12] A. F. Khlebnikov, M. S. Novikov, N. V. Rostovskii, *Tetrahedron* **2019**, *75*, 2555–2624.

in situ Formation of RSCl/ArSeCl and Their Oxidative Coupling with Enaminone Derivatives Under Transition-metal Free Conditions

Adv. Synth. Catal. **2019**, *361*, 1–8

Z. Shang, Q. Chen, L. Xing*, Y. Zhang, L. Wait, Y. Du*