Advanced Synthesis & Catalysis

Accepted Article

Title: Ag-Catalyzed Cyclization of Arylboronic Acids with Elemental Selenium for the Synthesis of Selenaheterocycles

Authors: Xue Zhang, Xiaobo Huang, Wenxia Gao, Yun-Bing Zhou, Miaochang Liu, and Huayue Wu

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.202001006

Link to VoR: https://doi.org/10.1002/adsc.202001006

10.1002/adsc.202001006

COMMUNICATION

DOI: 10.1002/adsc.202((will be filled in by the editorial staff))

Ag-Catalyzed Cyclization of Arylboronic Acids with Elemental Selenium for the Synthesis of Selenaheterocycles

Xue Zhang,[a] Xiao-Bo Huang,[a] Wen-Xia Gao,[a] Yun-Bing Zhou,[a,*] Miao-Chang Liu[a,*] and Hua-Yue Wu[a]

[a] *College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou 325035, People's Republic of China. E-mail: zyb@wzu.edu.cn; mcl@wzu.edu.cn*

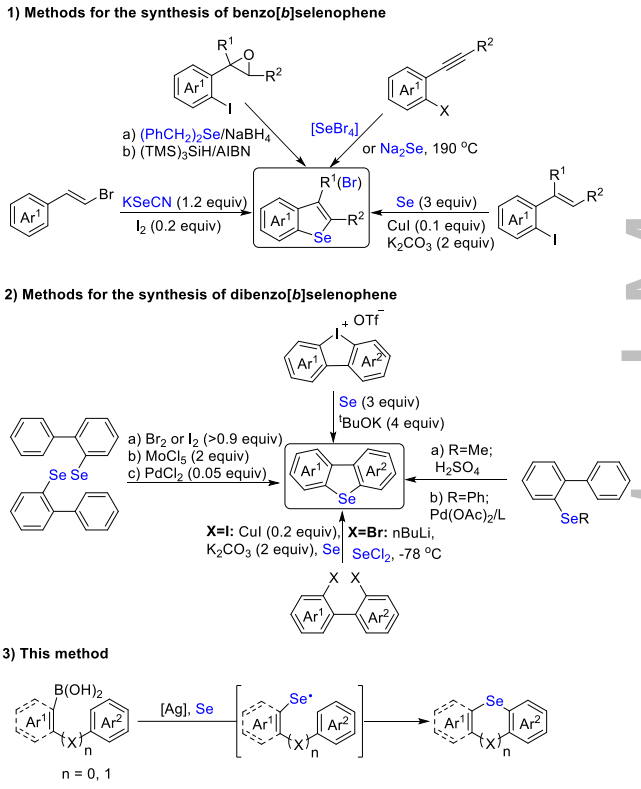
Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.

A general method for the synthesis of five-membered and six-membered selenaheterocycles through Ag-catalyzed C-Se bond-forming reaction. This reaction proceeds via intramolecular cyclization of arylboronic acids with selenium powder. Preliminary mechanism studies demonstrate that this transformation involves a selenium-centred radical intermediate.

Keywords: Cyclization; Arylboronic Acids; Elemental Selenium; Selenaheterocycles; Selenium-centred radical

The organoselenium compounds are of significant interest because they are widely used in numerous fields such as pharmaceutical, agrochemical, material, catalysis and ligand.[1] In particular, selenaheterocycles, representing an important class of heterocyclic compounds, attract growing attention. For example, the benzo[*b*]selenophene was considered to be a bioisoster of indole, benzofurane and benzothiophene though its core was not found in natural products.[2] Moreover, benzo[*b*]selenophene could serve as the key motif for thin film transistors,[3] as well as AT1 receptor antagonists which showed better activity than the corresponding benzo[*b*]thiophene analogues.[4] Traditional methods to synthesize benzo[*b*]selenophenes relied on the use of Na_2Se,[5] $SeBr_4$,[6] $(PhCH_2)_2Se$[7] or KSeCN[8] as a selenium source (Scheme 1.1). Yoshikai's group[9] disclosed an alternative synthetic route to benzoselenophenes through copper-catalyzed cyclization reactions between *ortho*-alkenylaryl iodines and elemental selenium. On the other hand, dibenzo[*b*]selenophenes could be accessed from cyclization reactions of diselenide[10] or monoselenide[11] as well as the reaction between 2,2'-dihalobiphenyls and $SeCl_2$ or selenium powder,[12] but the substrate scope of these reactions were not examined (Scheme 1.2). Remarkably, a smart synthetic route via elemental selenium−iodine exchange was reported by Jiang.[13] Regardless of their efficiency, these synthetic approaches were limited to the synthesis of only one type of selenaheterocycle, and usually suffered from narrow substrate scope, harsh reaction conditions and the need for unfavourable selenium sources. In this regard, the development of a general and facile method to synthesize various selenaheterocycles remained to be desirable.



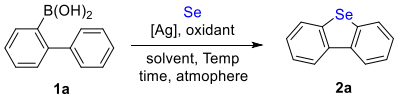
Scheme 1. The methods for the construction of selenaheterocycles.

Recently, our group[14] disclosed a concise synthetic route to selenated benzofurans (benzothiophenes) via Ag-catalyzed three-component radical cyclization, in which a selenium-centred radical acted as the key intermediate. Herein, we envisioned that in situ generated selenium-centred radical would undergo intramolecular radical cyclization which enables the direct construction of selenaheterocycles including benzo[*b*]selenophene,

10.1002/adsc.202001006

dibenzo[*b*]selenophenes and phenoxaselenine (Scheme 1.3).

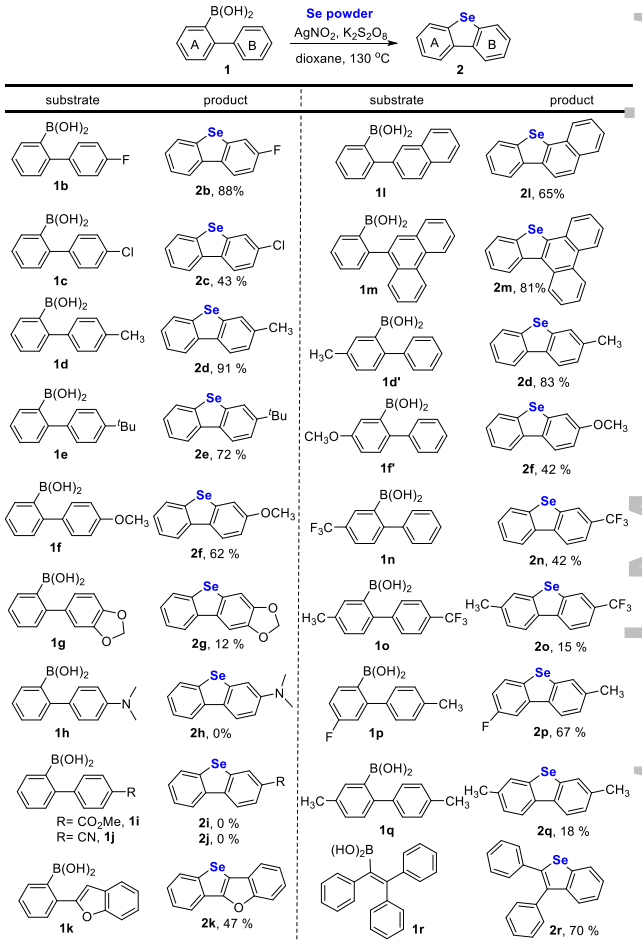
Table 1 Reaction optimization.[a]



entry	catalyst	solve	oxidant	yield(%)
1[b]	$AgNO_2$	DMSO	-	0
2	$AgNO_2$	DMSO	-	0
3	$AgNO_2$	dioxane	-	39
4	$AgNO_2$	dioxane	$K_2S_2O_8$	86
5	$AgNO_2$	dioxane	$Na_2S_2O_8$	0
6	$AgNO_2$	dioxane	$(NH_4)_2S_2O_8$	0
7	$AgNO_2$	dioxane	benzoquinone	29
8	$AgNO_2$	DMSO	$K_2S_2O_8$	0
9	$AgNO_2$	DMF	$K_2S_2O_8$	0
10	$AgNO_2$	$PhCH_3$	$K_2S_2O_8$	0
11	$AgNO_2$	CH_3CN	$K_2S_2O_8$	0
12	Ag_2O	dioxane	$K_2S_2O_8$	0
13	Ag_2CO_3	dioxane	$K_2S_2O_8$	0
14	AgOAc	dioxane	$K_2S_2O_8$	0
15	$AgNO_3$	dioxane	$K_2S_2O_8$	0
16	AgOTf	dioxane	$K_2S_2O_8$	0
17[c]	$AgNO_2$	dioxane	$K_2S_2O_8$	83
18[d]	$AgNO_2$	dioxane	$K_2S_2O_8$	52
19[b]	$AgNO_2$	dioxane	$K_2S_2O_8$	0
20[e]	$AgNO_2$	dioxane	$K_2S_2O_8$	85
21[f]	$AgNO_2$	dioxane	$K_2S_2O_8$	51

[a]Reaction conditions: **1a** (0.2 mmol), Se powder (0.4 mmol), Ag catalyst (0.02 mmol), oxidant (0.3 mmol), solvent (2.0 mL), 24 h, air atmosphere, 130 °C, isolated yields. [b]At 100 °C. [c]At 120 °C. [d]At 110 °C. [e]Under O_2 atmosphere. [f]Under N_2 atmosphere.

Along with the above idea, we commenced our study by submitting [1,1'-biphenyl]-2-ylboronic acid (**1a**) to our previous catalytic system which was used in the synthesis of selenated benzofurans (benzothiophenes) (Table 1). It was found that this catalytic system failed to enable the intramolecular radical cyclization of **1a** to provide the desired product **1b** (entry 1), even with the reaction temperature being increased to 130 °C (entry 2). We were pleased to find that the use of dioxane as a solvent successfully led to the desired product **1b** in 39% yield (entry 3). The addition of $Na_2S_2O_8$ as an oxidant resulted in a significant boost in the yield of **1b** (entry 4), but other oxidants including $K_2S_2O_8$ and $(NH_4)_2S_2O_8$ didn't give the desired product but generated large amount of 2-phenylphenol as the main byproduct (entries 5 and 6). The reaction with benzoquinone as an oxidant led to 29% yield of **2b** along with 58% yield of phenylphenol (entry 7). Systematical screening for solvents revealed that the intramolecular cyclization process did not occur in the solvents such as DMSO, DMF, $PhCH_3$, and CH_3CN (entries 8-11). It should be noted that a substantial amount of side product biphenyl could be observed when the reaction was performed in these poor solvents. Next, we turned to examine the effect of Ag catalysts on reaction efficiency. Surprisingly, the use of other Ag catalysts including Ag_2O, Ag_2CO_3, AgOAc, $AgNO_3$ and AgOTf did not promote this transformation at all (entries 12-16). Lowering the reaction temperature had a significantly negative impact on the reaction outcome (entries 17-19). The employment of the O_2 atmosphere gave a comparable yield to that under air atmosphere (entry 20). However, the reaction under N_2 atmosphere gave an inferior yield, demonstrating that the presence of oxygen could boost this transformation (entry 21).

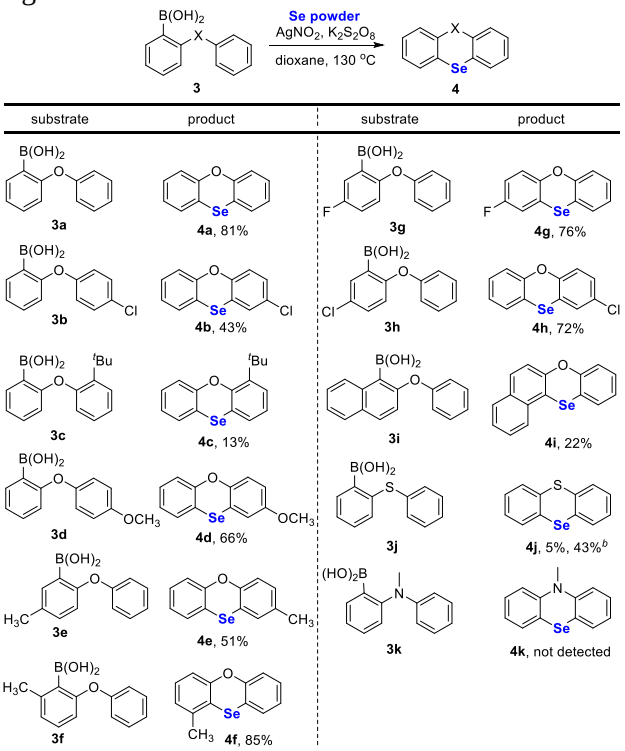


Scheme 2. The substrate scope for the synthesis of dibenzo[*b*]selenophene. Reaction conditions: **1** (0.2 mmol), Se powder (0.4 mmol), $AgNO_2$ (0.02 mmol), $K_2S_2O_8$ (0.3 mmol), 1,4-dioxane (2.0 mL), 24 h, air, isolated yields.

To test the substrate scope for the construction of dibenzo[*b*]selenophene, a range of arylboronic acids tethered an aromatic ring were examined (Scheme 2). These arylboronic acids were typically prepared by two synthetic steps involving Suzuki coupling reaction and the reaction of an aryllithium intermediate with a trialkylborate. The phenyl ring B of arylboronic acids could tolerate a range of substituents with diverse electronic properties, such as halogens (**1b** and **1c**), weakly electron-donating alkyl groups (**1d** and **1e**), and electron-donating groups (**1f** and **1g**). Unfortunately, the substrates

10.1002/adsc.202001006

bearing amino, cyano and ester groups on ring B failed to the desired products (**2h- 2j**). In addition, ring B could be an

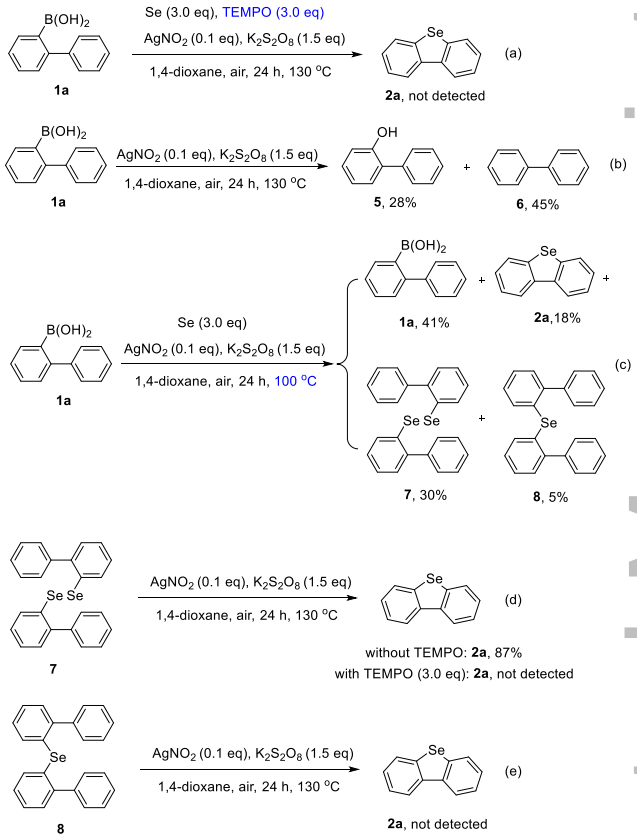


Scheme 3. The substrate scope for the synthesis of phenoxaselenines. Reaction conditions: **3** (0.2 mmol), Se powder (0.4 mmol), $AgNO_2$ (0.02 mmol), $K_2S_2O_8$ (0.3 mmol), 1,4-dioxane (2.0 mL), 24 h, air atmosphere, isolated yields. [b]50 mol% of $AgNO_2$ was used.

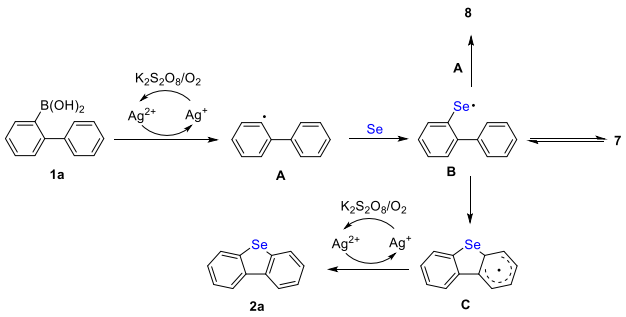
aromatic heterocycle (**1k**) or a fused ring (**1l** and **1m**). Significant differences in the yields were observed when the same group is located on a different ring (**1d** *vs* **1d'**, **1f** *vs* **1f'**). The present of trifluoromethyl group on ring A resulted in 42% yields (**2n**). Substrates with two substituted aromatic rings delivered the corresponding products in relatively low yields, which was attributed to the formation of biphenyl derivatives (**2o-2q**). Alkenylboronic acid proved to be a suited precursor to benzo[*b*]selenophene (**2r**).

Next, we intended to extend this synthetic approach to the synthesis of six-membered selenaheterocycles (Scheme 3). It was found that (2-phenoxyphenyl)boronic acid reacted well with Se powder to furnish phenoxaselenine with 81% yield (**4a**). The transformation was also operable with substrates bearing a halogen (**3b** and **3g**), an alkyl group (**3c**, **3e** and **3f**) or a methoxyl group (**3d**). Low yields (**4c** and **4i**) were observed under the standard conditions, which was attributed to the formation of diaryl ethers from the protonation of substrates. Dibenzo[*b*,*e*][1,4]thiaselenine (**4j**) was also obtained in 43% yield albeit with 50 mol% of $AgNO_2$. The attempt to synthesize 10-methyl-10*H*-phenoselenazine (**4k**) failed with the complete recovery of the starting materials.

To investigate how this C-Se forming reaction takes place, some control experiments were conducted (Scheme 4). The addition of TEMPO to the model reaction led to no formation of the desired product **2a** (Scheme 4a). The control reaction in the absence of Se powder afforded product **5** in 28% yield and product **6** in 45% yield (Scheme 4b). The reaction at a lower temperature (100 °C) gave a mixture that consists of starting material **1a** (41%), product **2a** (18%), diselenide **7** (30%), selenide **8** (5%) (Scheme 4c). The reaction of diselenide **7** under standard reaction conditions successfully offered product **2a** in 87% yield, but was inhibited in the presence of TEMPO (Scheme 4d). No corresponding product **2a** was detected when selenide **8** was exposed to standard reaction conditions (Scheme 4e).



Scheme 4. The control experiments.



Scheme 5. The possible mechanism.

In line with these results and previous references,[15] a possible mechanism for the Ag-catalyzed cyclization of arylboronic acids with elemental selenium is proposed (Scheme 5). The reaction is initiated by the oxidation of **1a** to afford

radical **A** in the presence of $AgNO_2/K_2S_2O_8/O_2$. The radical **A** was trapped by selenium powder to yield selenium-centred radical **B**, followed by intramolecular radical cyclization/oxidation to provide the final product **2a**. Alternatively, the in-situ generated **B** either undergoes homocoupling to give **7** in a reversible way, or reacts with radical A to furnish **8**.

In conclusion, we have developed an Ag-catalyzed C-Se bond-forming strategy, providing an efficient method for the synthesis of selenaheterocycles including benzo[*b*]selenophene, dibenzo[*b*]selenophenes and phenoxaselenines. The studies on the substrate scope showed a significant influence on the nature of the electron-rich group of arylboronic acids. We also demonstrated key mechanistic features of this C-Se bond-forming reaction by control experiments.

Experimental Section

Typical procedure for the synthesis of selenaheterocycles. A 10 mL Schlenk tube equipped with a stir bar was charged with arylboronic acid (0.2 mmol), Se (0.4 mmol), $AgNO_2$ (10 mol %) and $K_2S_2O_8$ (0.3 mmol). Then dioxane (2 mL) was added in the Schlenk tube through the rubber septum using syringes. The reaction mixture was stirred in a heating mantle preheated to 130 °C for 24 h. After cooling down, the reaction mixture was diluted with 10 mL of ethyl ether, filtered through a pad of silica gel and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

Acknowledgements

We are grateful for financial support from the National Natural Science Foundation of China (21901187, 21372177 and 21672164).

References

[1] a) S. T. Manjare, Y. Kim, D. G. Churchill, *Acc. Chem. Res.* **2014**, *47*, 2985-2998; b) T. G. Back, Z. Moussa, *J. Am. Chem. Soc.* **2003**, *125*, 13455-13460; c) L. Shao, Y. Li, J.-M. Lu, X. Jiang, *Org. Chem. Front.* **2019**, *6*, 2999-3041; d) L. Liao, R. Guo, X. Zhao. *Angew .Chem., Int. Ed.* 2**017**, *56*, 3201-3205; e) R. Guo, J. Huang, X. Zhao, *ACS Catal*. **2018**, *8*, 926-930; f) X. Liu, Y. Liang, J. Ji, J. Luo, X. Zhao. *J. Am. Chem. Soc*. **2018**, *140*, 4782-4786; g) H. Azuma, S. Tamagaki, K. Ogino, *J. Org. Chem.* **2000**, *65*, 3538-3541; h) E. M. Treadwell, J. D. Neighbors, D. F. Wiemer, *Org. Lett.* **2002**, *4*, 3639-3642; i) K. B. Sharpless, R. F. Lauer, *J. Am. Chem. Soc.* **1973**, *95*, 2697-2699; j) T. Hori, K. B. Sharpless, *J. Org. Chem.* **1978**, *43*, 1689-1697; k) M. Gruttadauria, C. Aprile, S. Riela, R. Noto, *Tetrahedron Lett.* **2001**, *42*, 2213-2215; l) T. S. Chisholm, S. S. Kulkarni, K. R. Hossain, F. Cornelius, R. J. Clarke, R. J. Payne, *J. Am. Chem. Soc.* **2020**, *142*, 1090-1100; m) H. Xu, W. Cao, X. Zhang, *Acc. Chem. Res.* **2013**, *46*, 1647-1658; n) S.-Y. Jang, I.-B. Kim, M. Kang, Z. Fei, E. Jung, T. McCarthy-Ward, J. Shaw, D.-H. Lim, Y.-J. Kim, S. Mathur, M. Heeney, D.-Y. Kim, *Adv. Sci.* **2019**, *6*, 1900245-1900251.

[2] R. Lisiak, J. Mochowski, *Synth. Commun.* **2009**, *39*, 4271-4281.

[3] a) T. Yamamoto, K. Takimiya, *J. Am. Chem. Soc.* **2007**, *129*, 2224-2225; b) H. Ebata, E. Miyazaki, T. Yamamoto, K. Takimiya, *Org. Lett.* **2007**, **9**, 4499-4502; c) T. Izawa, E. Miyazaki, K. Takimiya, *Adv. Mater.* **2008**, *20*, 3388-3392; d) K. Niimi, S. Shinamura, I. Osaka, E. Miyazaki, K. Takimiya, *J. Am. Chem. Soc.* **2011**, *133*, 8732-8739; e) T. Mori, T. Nishimura, T. Yamamoto, I. Doi, E. Miyazaki, I. Osaka, K. Takimiya, *J. Am. Chem. Soc.* **2013**, *135*, 13900-13913.

[4] M. K. Staples, R. L. Grange, J. A. Angus, J. Ziogas, N. P. H. Tan, M. K. Taylor, C. H. Schiesser, *Org. Biomol. Chem.* **2011**, *9*, 473-479.

[5] T. Kashiki, S. Shinamura, M. Kohara, E. Miyazaki, K. Takimiya, M. Ikeda, H. Kuwabara, *Org. Lett.* **2009**, *11*, 2473-2475.

[6] E. Paegle, S. Belyakov, P. Arsenyan, *Eur. J. Org. Chem.* **2014**, 3831-3840.

[7] J. E. Lyons, C. H. Schiesser, K. Sutej, *J. Org. Chem.* **1993**, *58*, 5632-5638.

[8] P. Maity, B. Paroi, B. C. Ranu, *Org. Lett.* **2017**, *19*, 5748-5751.

[9] B. Wu, N. Yoshikai, *Angew. Chem., Int. Ed.* **2013**, *52*, 10496-10499.

[10] a) J. D. McCullough, T. W. Campbell, E. S. Gould, *J. Am. Chem. Soc.* **1950**, *72*, 5753-5754; b) K. Nishino, Y. Ogiwara, N. Sakai, *Eur. J. Org. Chem.* **2017**, 5892-5895; c) P. Franzmann, S. B. Beil, D. Schollmeyer, S. R. Waldvogel, *Chem. Eur. J.* **2019**, *25*, 1936-1940; d) K. Nishino, Y. Ogiwara, N. Sakai, *Chem. Eur. J.* **2018**, *24*, 10971-10974.

[11] a) A. Daft, L. E. Christiaens, M. J. Renson, *Acta Chem. Scand*, **1993**, *47*, 208-211; b) M. Tobisu, Y. Masuya, K. Babaa, N. Chatani, *Chem. Sci.* **2016**, *7*, 2587-2591.

[12] a) T. Okamoto, M. Mitani, C. P. Yu, C. Mitsui, M. Yamagishi, H. Ishii, G. Watanabe, S. Kumagai, D. Hashizume, S. Tanaka, M. Yano, T. Kushida, H. Sato, K. Sugimoto, T. Kato, J. Takeya. *J. Am. Chem. Soc.* **2020**, 10.1021/jacs.0c05522; b) Wenguang Li, Genhua Xiao, Guobo Deng and Yun Liang. *Org. Chem. Front.* **2018**, *5*, 1488-1492.

[13] M. Wang, Q. Fan, X. Jiang, *Org. Lett.* **2016**, *18*, 5756-5759.

[14] C. An, C.-Y. Li, X.-B. Huang, W.-X. Gao, Y.-B. Zhou, M.-C. Liu, H.-Y. Wu, *Org. Lett.* **2019**, *21*, 6710-6714.

[15] Y.-F. Yang, C.-Y. Li, T. Leng, X.-B. Huang, W.-X. Gao, Y.-B. Zhou, M.-C. Liu, H.-Y. Wu, *Adv. Synth. Catal.* **2020**, *362*, 2168-2172.

10.1002/adsc.202001006

10.1002/adsc.202001006

COMMUNICATION

Ag-Catalyzed Cyclization of Arylboronic Acids with Elemental Selenium for the Synthesis of Selenaheterocycles

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Xue Zhang, Xiao-Bo Huang, Wen-Xia Gao, Yun-Bing Zhou,* Miao-Chang Liu* and Hua-Yue Wu