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Brønsted acid-catalyzed phenylselenenylation of internal olefins

Ping Wu, Fei Huang, Jiang Lou, Quannan Wang, Zhuqing Liu, Zhengkun Yu *

Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian, Liaoning 116023, China

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ABSTRACT

Brønsted acid *p*-TsOH·H_2O-catalyzed phenylselenenylation of α-oxo ketene dithioacetals was efficiently achieved by using *N*-phenylselenophthalimide (*N*-PSP) as the phenylseleno reagent. The resultant selenated ketene dithioacetals reacted with styrene in the presence of the same acid to undergo PhSe group transfer, regioselectively affording Markovnikov-type PhSe-alkylated olefins. Their further transformation with phenylboronic acid, guanidine, and hydrazine offers a promising route to access S,Se-incorporated organic compounds.

Functionalization of an internal olefinic C—H bond has been a challenging task in organic synthesis due to the intrinsic steric hindrance and electronic environment around the carbon–carbon double bond.[1] In order to activate an internal olefinic C—H bond, we previously developed a strategy to introduce a structural element, that is, electron-donating 1,2-dithiane functionality, at one end of a C=C bond, and an electron-withdrawing group such as carbonyl at the other end of this unsaturated carbon–carbon double bond to assemble a polarized olefin, achieving the direct oxidative cross-coupling of an internal olefin with a terminal olefin.[2] Such polarized olefins, that is, α-oxo ketene dithioacetals, have recently become attractive to be utilized as a class of useful synthetic building blocks.[3] However, their transformations were usually conducted under basic conditions[3a] or in the presence of a transition metal catalyst.[3b,4] Rare examples on the functionalization of α-oxo ketene dithioacetals at their terminal C—S bond(s) by indoles under Brønsted acid catalysis[5] and alkylation at their internal C—H bond by means of a Lewis acid catalyst[4b] have recently been documented.

N-Phenylselenophthalimide (*N*-PSP) has been known as a phenylseleno reagent for the preparation of bioactive organoselenium compounds[6] and also for versatile organic synthesis due to the removal property of the PhSe group.[7] Under Brønsted acid catalysis three-component alkylation of indoles with *N*-PSP and styrenes or the reactions of indoles with *N*-PSP occurred to afford phenylseleno-alkylated indole derivatives or phenylselenated indoles.[7b] Keeping these results in mind, we reasonably envisioned that the internal C—H bond in polarized α-oxo ketene dithioacetals might be functionalized with *N*-PSP by means of a Brønsted acid catalyst.[8] Herein, we report *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H_2O)-catalyzed phenylselenenylation of internal olefins α-oxo ketene dithioacetals as well as PhSe group transfer of the resultant selenated olefins (Scheme 1).

Initially, the reaction of α-(4-bromobenzoyl) ketene dithioacetal (**1a**) with *N*-PSP (**2**) was performed to optimize the reaction conditions (Table 1). In the presence of 5 mol % *p*-TsOH·H_2O as the catalyst in dichloromethane at 0 °C, the target product **3a** was obtained in 83% yield (Table 1, entry 1). Testing the reaction at 0–40 °C reveals that ambient temperature was suitable for the desired transformation (Table 1, entries 1–3). 1,2-Dichloroethane (DCE) also acted as the effective reaction solvent, but using toluene or THF led to lower product yields (Table 1, entries 4–7). In hexane, the reaction did not occur due to the insolubility of both *N*-PSP and the catalyst. Increasing the loading of *N*-PSP to 1.1 equiv in DCE led to **3a** in 92% isolated yield, whereas further increasing the amount of *N*-PSP to 1.2 equiv or using 10 mol % *p*-TsOH·H_2O did not further improve the reaction efficiency (Table 1, entries 9–10). Extending the reaction time to 5 h reached the best yield (96%) for **3a** (Table 1, entries 11–13).

Next, the substrate scope of α-oxo ketene dithioacetals **1** was explored under the optimal conditions (Table 2). α-Acetyl, aroyl, and cinnamoyl-functionalized ketene dithioacetals reacted with **2** to give the target products **3** in 60–99% yields. Methyl, chloro, bromo, fluoro, and trifluoromethyl were tolerated on the aroyl moieties of substrates **1**. 2-Thienoyl and furoyl-functionalized

* Corresponding author. Tel./fax: +86 411 8437 9227.
E-mail address: zkyu@dicp.ac.cn (Z. Yu).

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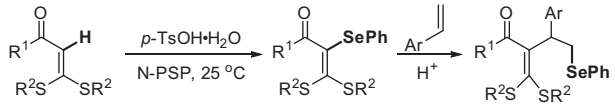
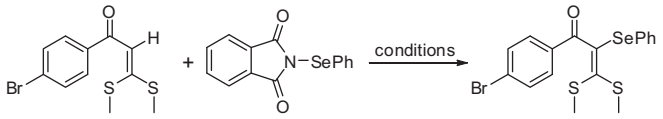


Scheme 1. Phenylselenenylation of α-oxo ketene dithioacetals and PhSe transfer.

Table 1
Screening of reaction conditions[a]



1a **2** (N-PSP) **3a**

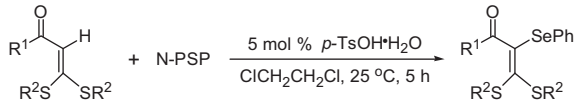
Entry	Solvent	**1a**/**2**[b]	Catalyst[c] (mol %)	Temp. (°C)	Time (h)	Yield[d] (%)
1	CH_2Cl_2	1:1	5	0	4	83
2	CH_2Cl_2	1:1	5	25	4	92
3	CH_2Cl_2	1:1	5	40	4	92
4	DCE	1:1	5	25	4	93
5	Toluene	1:1	5	25	4	20
6	THF	1:1	5	25	4	79
7	Hexane	1:1	5	25	4	0
8	DCE	1:1.1	5	25	4	94 (92)[e]
9	DCE	1:1.2	5	25	4	94
10	DCE	1:1.1	10	25	4	94
11	DCE	1:1.1	5	25	3	87
12	DCE	1:1.1	5	25	5	98 (96)[e]
13	DCE	1:1.1	5	25	6	95

[a] Conditions: **1a** (0.3 mmol), solvent (3 mL).
[b] Molar ratio.
[c] Catalyst = *p*-TsOH·H_2O.
[d] Determined by GC analysis.
[e] Isolated yield in parentheses. DCE = 1,2-dichloroethane.

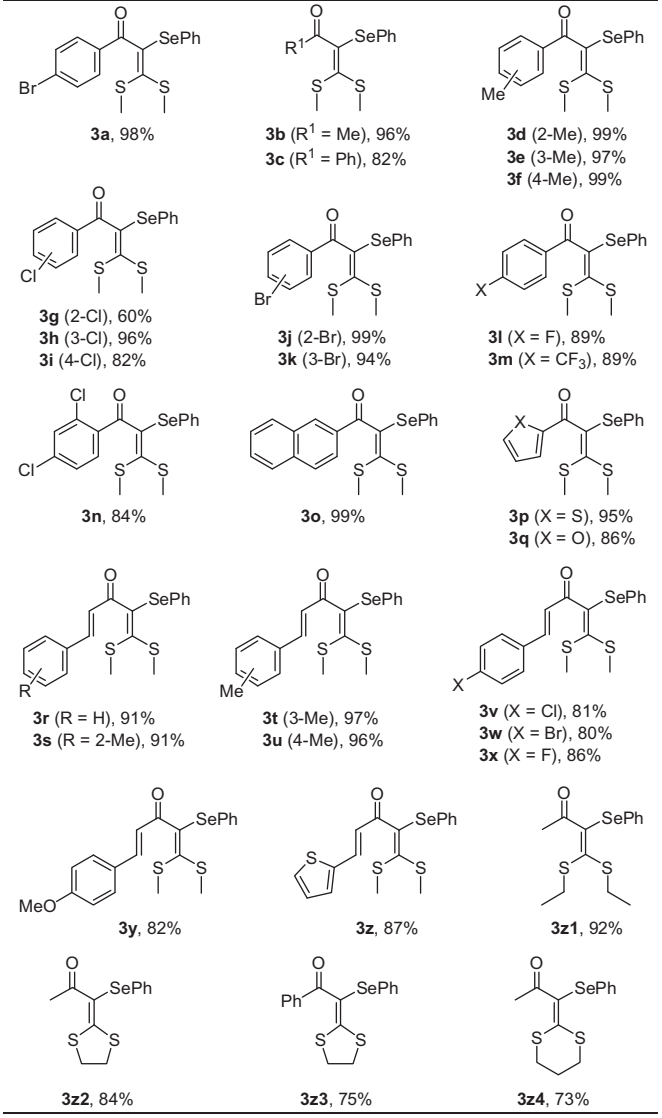
ketene dithioacetals also underwent the reactions efficiently, giving **3p** (95%) and **3q** (86%), respectively. Although the α-cinnamoyl ketene dithioacetals have two reactive C—H sites α-adjacent to the carbonyl functionality, the phenylselenation reaction regioselectively occurred at the C—H site of the dithio-ketene moiety, which is attributed to the push–pull effect between the two thioalkyls and the α-oxo functionality on the internal C—H bond activation.[3b] The dithioethyl substrate underwent the reaction to afford **3z1** (92%), while the cyclic 1,2- or 1,3-dithiane-functionalized substrates exhibited a lower reactivity to form **3z2–3z4** (73–84%). It is noteworthy that the molecular structure of **3a** was confirmed by X-ray crystallographic analysis (Fig. 1).

Lewis acid $TiCl_4$-mediated or photochemical PhSe transfer has been reported to functionalize organic compounds,[9] but Brønsted acids were seldom reported as the sole catalysts for such reactions.[7b] To our delight, Brønsted acid *p*-TsOH·H_2O promoted the reactions of PhSe-substituted olefins **3** with styrene (**4**) in 1,2-dichloroethane at ambient temperature (Scheme 2). A variety of compounds **3** were treated with styrene, undergoing Brønsted acid-catalyzed PhSe transfer, regioselectively forming Markovnikov-type PhSe-alkylated olefins **5**. α-Acetyl, aroyl, and cinnamoyl-functionalized substrates reacted to give the target products **5** in 48–79% isolated yields within 0.5 h. Substituents such as methyl, bromo, and trifluoromethyl were tolerant on the aroyl groups of substrates **3**. In such a fashion, the carbon—carbon double bond of styrene was inserted into the C—Se bond of **3**, furnishing a regioselective PhSe group transfer process. It is noted

Table 2
Brønsted acid-catalyzed phenylselenenylation of α-oxo ketene dithioacetals (**1**) with *N*-PSP (**2**)[a,b].



1 **2** **3**



[a] Conditions: **1** (0.5 mmol), **2** (0.55 mmol), *p*-TsOH·H_2O (5 mg, 0.025 mmol), solvent (5 mL), 25 °C.
[b] Isolated yields based on **1**.

that compounds **3** are stable under neutral conditions at ambient temperature, but some of them could slowly decompose in an acidic solution.

Further transformations of the phenylselenenylation product **3b** were carried out to demonstrate the potential application of the phenylselenated compounds by means of Liebeskind–Srogl cross-coupling reaction[10] or condensation with *N*-nucleophiles (Eqs. 1–3). Compound **3b** reacted with phenylboronic acid to form the copper-mediated mono-desulfurative cross-coupling product **6** (68%) with a (*Z*)/(*E*) ratio of 1:1 (Eq. 1).[4d,11] Condensation of **3b** with

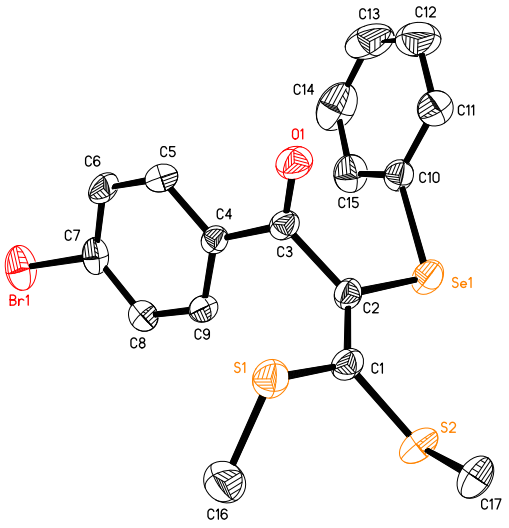
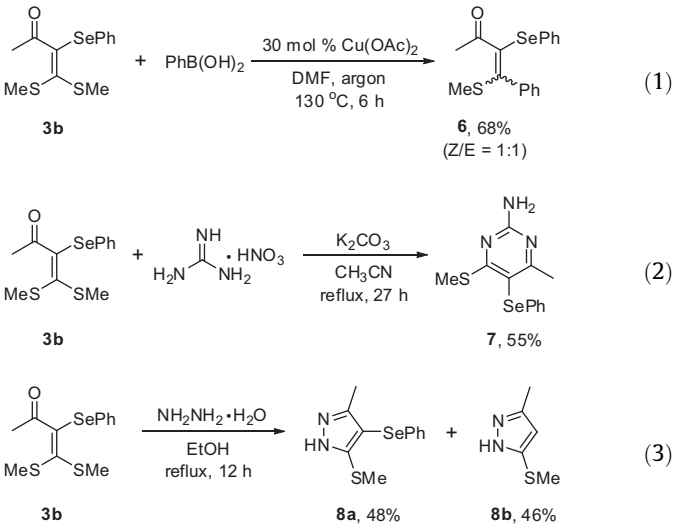
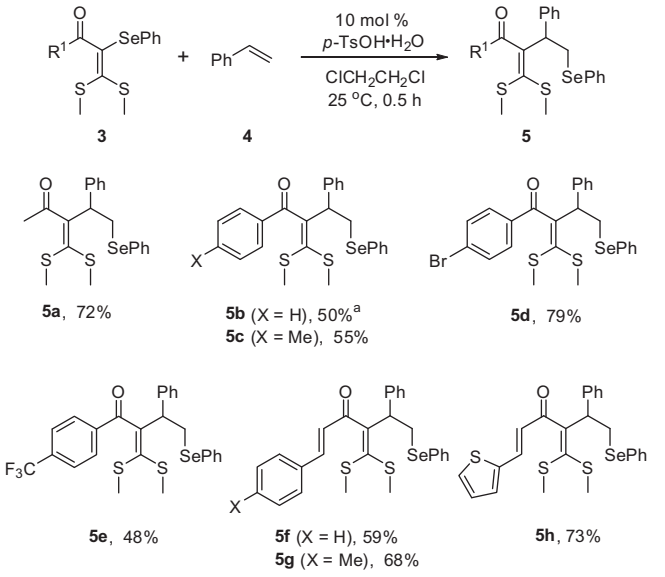


Figure 1. Molecular structure of **3a**.



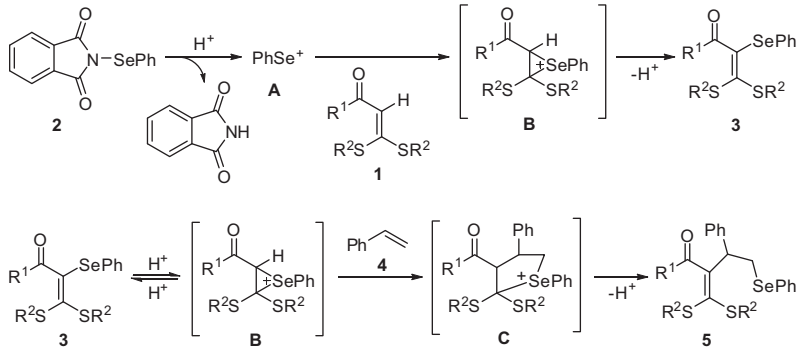


Scheme 2. Brønsted acid-catalyzed PhSe group transfer. Reagents and conditions: **3** (0.3 mmol), **4** (0.6 mmol), *p*-TsOH·H_2O (6 mg, 0.03 mmol), solvent (3 mL), 25 °C. Isolated yields based on **3**. [a]3 h.

guanidine afforded S-, Se-, N-, and alkyl-substituted pyrimidine **7** (55%) (Eq. 2), and with hydrazine hydrate formed the target pyrazole **8a** (48%) as well as the hydrodeselenated pyrazole **8b**[12] (46%) (Eq. 3). Although the results have demonstrated a promising route to access diverse S,Se-incorporated organic compounds,[13] these PhSe-containing compounds exhibited lower reactivity than the corresponding Se-free ketene dithioacetals.[5,14,15]

A plausible mechanism is proposed for the formation of **3** and **5** as shown in Scheme 3. The Brønsted acid initiates generation of cation $PhSe^+$ (**A**) from *N*-PSP (**2**), which electrophilically attacks the electron-rich vinylic carbon α adjacent to the carbonyl in **1**, forming episelenonium ion **B**.[7b,d,16] Subsequent proton release from species **B** affords the phenylselenative products **3**. Proton may also assist the generation of **B** from **3**. Thus, the in situ generated species **B** from **3** in the presence of the Brønsted acid catalyst interacts with styrene (**4**) to form cation **C** via regioselective insertion of the vinylic C=C bond of **4** into the C—Se bond in **B**. Regeneration of the acid catalyst produces the target product **5**. It cannot be excluded that phthalimide was involved in the deprotonation of intermediate species **B** and **C**.

In summary, Brønsted acid *p*-TsOH·H_2O-catalyzed phenylselenylation of internal olefins α-oxo ketene dithioacetals with *N*-PSP efficiently afforded phenylseleno-substituted olefins, which further react with styrene to form Markovnikov-type phenylselenative codimerization products of the two olefins through PhSe group transfer. The present protocol provides a promising route to access potentially bioactive S,Se-incorporated organic compounds.



Scheme 3. Proposed mechanisms.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.03.096.

References and notes

1. (a) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215; (b) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068.
2. Yu, H. F.; Jin, W. W.; Sun, C. L.; Chen, J. P.; Du, W. M.; He, S. B.; Yu, Z. K. *Angew. Chem. Int. Ed.* **2010**, *49*, 5792.
3. (a) Pan, L.; Bi, X. H.; Liu, Q. *Chem. Soc. Rev.* **2013**, *42*, 1251; (b) Wang, L. D.; He, W.; Yu, Z. K. *Chem. Soc. Rev.* **2013**, *42*, 599.
4. (a) Mao, Z. F.; Huang, F.; Yu, H. F.; Chen, J. P.; Yu, Z. K.; Xu, Z. Q. *Chem. Eur. J.* **2014**, *20*, 3439; (b) Yang, Q.; Wu, P.; Chen, J. P.; Yu, Z. K. *Chem. Commun.* **2014**, 6337; (c) Liu, B. Y.; Zheng, G.; Liu, X. C.; Xu, C.; Liu, J. X.; Wang, M. *Chem. Commun.* **2013**, 2201; (d) Jin, W. W.; Yang, Q.; Wu, P.; Chen, J. P.; Yu, Z. K. *Adv. Synth. Catal.* **2014**, *356*, 2097; (e) Dong, Y.; Liu, B.; Chen, P.; Liu, Q.; Wang, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 3442; (f) Liang, D.; Wang, M.; Dong, Y.; Guo, Y.; Liu, Q. *RSC Adv.* **2014**, *4*, 6564.
5. Yu, H. F.; Yu, Z. K. *Angew. Chem. Int. Ed.* **2009**, *48*, 2929.
6. (a) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* **2014**, *104*, 6255; (b) Freudendahl, D. M.; Shahzad, S. A.; Wirth, T. *Eur. J. Org. Chem.* **2009**, 1649; (c) Mukherjee, A. J.; Zade, S. S.; Singh, H. B.; Sunoj, R. B. *Chem. Rev.* **2010**, *110*, 4357; (d) Santoro, S.; Azeredo, J. B.; Nascimento, V.; Sancineto, L.; Braga, A. L.; Santi, C. *RCS Adv.* **2014**, *4*, 31521.
7. Selected recent reports, see: (a) Clive, D. L. J.; Pham, M. P.; Subedi, R. *J. Am. Chem. Soc.* **2007**, *129*, 2713; (b) Zhao, X. D.; Yu, Z. K.; Xu, T. Y.; Wu, P.; Yu, H. F. *Org. Lett.* **2007**, *9*, 5263; (c) Lim, H. J.; RajanBabu, T. V. *Org. Lett.* **2009**, *11*, 2924; (d) Denmark, S. E.; Kalyani, D.; Collins, W. R. *J. Am. Chem. Soc.* **2010**, *132*, 15752; (e) Sahu, P. K.; Kim, G.; Yu, K.; Ahn, J. Y.; Song, J.; Choi, Y.; Jin, X.; Kim, J. H.; Lee, S. K.; Park, S.; Jeong, L. S. *Org. Lett.* **2014**, *16*, 5796.
8. Wu, P.; Wang, L. D.; Wu, K. K.; Yu, Z. K. *Org. Lett.* **2015**, *17*, 868.
9. (a) Toru, T.; Kawai, S.; Ueno, Y. *Synlett* **1996**, 539; (b) Curran, D. P.; Eichenberger, E.; Collis, M.; Roepel, M. G.; Thoma, G. *J. Am. Chem. Soc.* **1994**, *116*, 4279; (c) Ryu, I.; Muraoka, H.; Kambe, N.; Komatsu, M.; Sonoda, N. *J. Org. Chem.* **1996**, *61*, 6396; (d) Yang, D.; Gao, Q.; Lee, O.-Y. *Org. Lett.* **2002**, *4*, 1239.
10. Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260.
11. Dong, Y.; Wang, M.; Liu, J.; Ma, W.; Liu, Q. *Chem. Commun.* **2011**, 7380.
12. Abdel-Ghany, H.; El-Saghier, A. M. M.; El-Sayed, A. M. *Synth. Commun.* **1996**, *26*, 4289.
13. Iqbal, I.; Imran, M.; Langer, P. *Helv. Chim. Acta* **2010**, *93*, 1779.
14. Jin, W. W.; Du, W. M.; Yang, Q.; Yu, H. F.; Chen, J. P.; Yu, Z. K. *Org. Lett.* **2011**, *13*, 4272.
15. Jin, W. W.; Yu, H. F.; Yu, Z. K. *Tetrahedron Lett.* **2011**, *52*, 5884.
16. (a) Liotta, D. *Acc. Chem. Res.* **1984**, *17*, 28; (b) Toshimitsu, A.; Nakano, K.; Mukai, T.; Tamao, K. *J. Am. Chem. Soc.* **1996**, *118*, 2756.