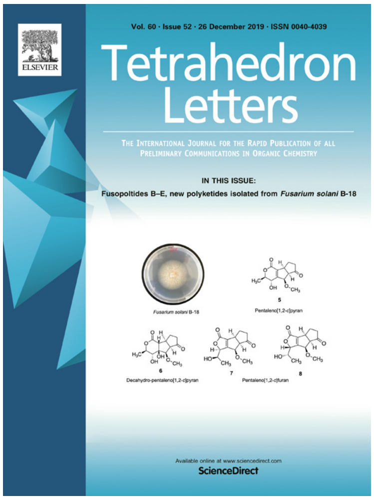

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# Electrochemical Selenation of Phosphonates and Phosphine Oxides

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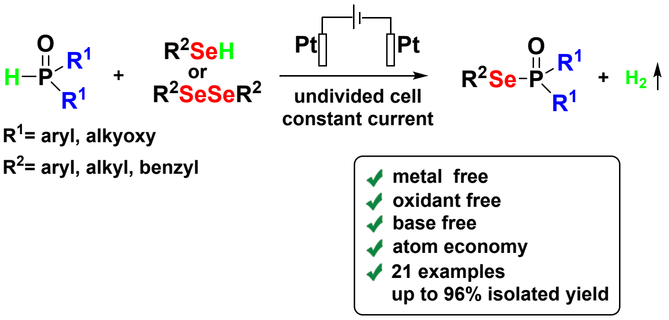
ABSTRACT

An environmentally friendly electrocatalytic strategy for the synthesis of organoselenophosphorus between phosphonates /phosphine oxides and selenols/diselenides is reported. The reaction was performed with metal-, base- and oxidant-free at room temperature, and affords the selenophosphorus products in good to excellent yields. The good tolerance of substituents enables the reaction more attractive in the preparation of organoselenophosphorus compounds.

## Introduction

Organoselenophosphorus are crucial structural motifs in various organic molecules[1] and natural products[2], which possess special chemical and biological properties, thus are used in many areas such as organic synthesis, biochemistry[3] and pesticide chemistry.[4] Therefore, the synthesis of such compounds has attracted continuous interest.[5] Traditionally, the approach for the formation selenophosphorus compounds often relies on the substitution reaction of $R_2P(O)X$ or RSeX (X = RSe, Cl, Br, I, etc.).[6] While, these methodologies needed the use of toxic and unstable reagents,[7] and required harsh reaction measures, leading to inconvenient procedures, low functional groups tolerance and unsatisfactory yield.[8] To overcome upon drawbacks, recently, efforts have been made to realize the conversion. Zhao's group and other groups[9] separately developed a metal-catalyzed phosphonation of phenyldiselenide. While Qiu[10] reported the synthesis of selenophosphorus promoted by phase transfer catalyst (PTC) under KOH. Huang[11] and Chen[12] independently disclosed ways for the Se-P bond formation of phenyl diselenide and organophosphorus by using AIBN or $NaN_3/PhI(OAc)_2$ as radical initiators. Yan[13] used equivalent amounts of iodine to enable the construction P-Se bonds. Xu[14] and Han[15] found that alkaline could efficiently allow for the construction of P-Se bonds. Besides these, Saha[16] developed a strategy for the formation of organoselenophosphates through appealing the pre-functionalized RSeH compounds. In addition, Jana[17] revealed a method for the synthesis of such compounds under $O_2$ conditions. Despite significant progress, those reactions still needed transition-metal, PTC, strong base, AIBN or oxidant, which might cause environmental issue, the substrate limitation or other. Thus, a convenient, practical, efficient, green and atom economical synthesis methodology under mild conditions is desirable.

Regarding the global environment problem, environmentally friendly strategies for the synthesis organic molecules in organic chemistry community are highly urgent. Electrochemical organic synthesis has been considered as one of the convenient, environmentally friendly and mild organic synthesis methods, which do not need oxidants, transition-metal catalysts comparing to traditional oxidative reactions and has attracted continuous attention.[18] Here, we reported a metal-, oxidant- and base-free strategy for the synthesis of organoselenophosphorus under electrochemical conditions (Scheme 1).

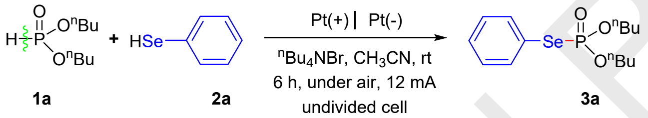


**Scheme 1.** Selenation of phosphonates

Re

With our ongoing interest in the phosphonation reactions[19], we initiated our investigation with the reaction of dibutyl-phosphonate (**1a**, 0.5 mmol) and benzeneselenol (**2a**, 0.6 mmol) as model to identify the optimal reaction conditions (Table 1). When the reaction was performed in $^nBu_4NBr/CH_3CN$ at room temperature in air atmosphere by conducting a platinum anode and a platinum cathode with constant current electrolysis at 12 mA, the expected product was obtained in a high yield (86%, entry 1). We found that when the $^nBu_4NBr$ was replaced by $^nBu_4NI$, the reaction gave the corresponding product in 46% yield (entry 2). However, no product was formed when other electrolytes such as $^nBu_4NF$ and $LiClO_4$ displacing the $^nBu_4NBr$ (entries 3-4). The reaction was detected that no expected product without electrolytes or constant current (entries 5-6). The screening of current density found that electric current of 10 mA or 14 mA could enable the desired product of **3a** in 75% and 68% respectively (entries 7-8). Other solvents such as $CH_3OH$, DCM ($CH_2Cl_2$), DCE($ClCH_2CH_2Cl$), DMF failed to promote the reactions (entries 9-12). Reducing or increasing the reaction time, the reaction yields were slightly decreased (entries 13-14). When we used the graphite rod as anode, the reaction resulted in the product **3a** in 60% yield (entry 15). Besides, operating the reaction under a nitrogen atmosphere, only a lowered yield was detected (entry 16).

**Table 1** Optimization of reaction conditions [a]

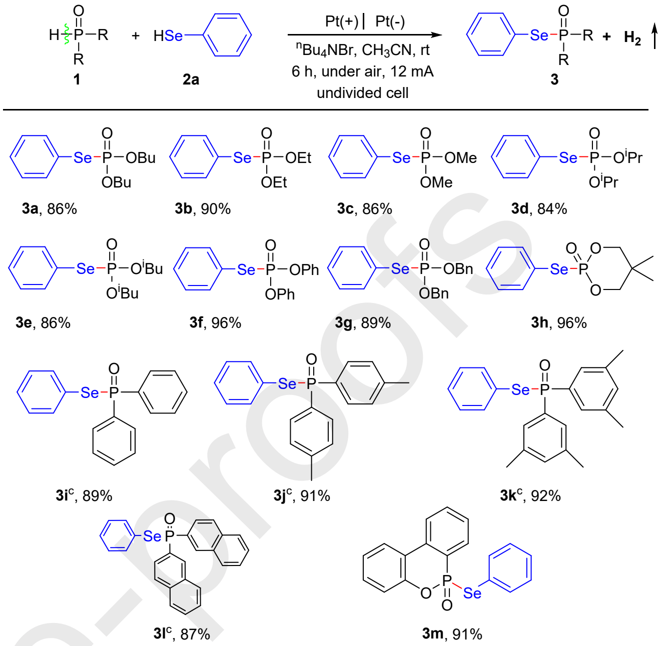


| Entry | Deviation from standard conditions | Yield[b] (%) |
|---|---|---|
| 1 | none | 86 |
| 2 | $^nBu_4NI$ instead of $^nBu_4NBr$ | 46 |
| 3 | $^nBu_4NF$ instead of $^nBu_4NBr$ | ND |
| 4 | $LiClO_4$ instead of $^nBu_4NBr$ | ND |
| 5 | no $^nBu_4NBr$ | ND |
| 6 | no electricity | ND |
| 7 | 10 mA instead of 12 mA | 75 |
| 8 | 14 mA instead of 12 mA | 68 |
| 9 | $CH_3OH$ instead of $CH_3CN$ | 29 |
| 10 | DCM instead of $CH_3CN$ | 75 |
| 11 | DCE instead of $CH_3CN$ | 51 |
| 12 | DMF instead of $CH_3CN$ | 31 |
| 13 | 4 h of reaction time | 70 |
| 14 | 8 h of reaction time | 78 |
| 15 | graphite rod as anode | 60 |
| 16 | under $N_2$ | 69 |

[a]Reaction conditions: **1a** (0.50 mmol), **2a** (0.60 mmol), electroyte (1.0 equiv), solvent (8 mL), air, Pt anode in an undivided cell at room temperature for 6 h; [b]Isolated yields.

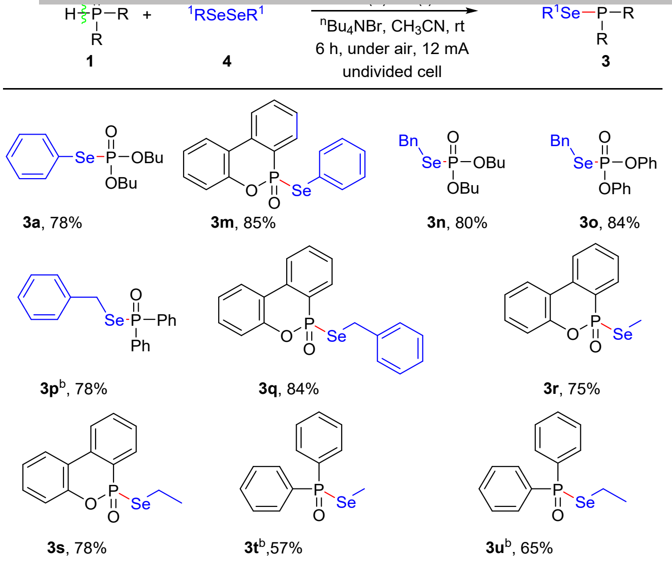
After the optimized reaction conditions were established, we first explored the substrates scope of this electrochemical reaction between phosphates/phosphine oxides and selenols (Scheme 2). Various phosphates were first investigated.

iver the corresponding products successfully with good yields respectively (**3a-3e**), and the electron effect of the substrates on the reaction was small. Aryl phosphonates such as diphenyl phosphonate furnished the desired product in 96% yield (**3f**), and dibenzyl phosphonate led the selenation product in 89% yield (**3g**). When 5,5-dimethyl-1,3,2-dioxaphosphinane 2-oxide was severed as a reaction partner, the selenation product was obtained in 96% yield (**3h**). Interestingly, the reaction of diarylphosphine oxides with selenols gave the desired products in moderate yield. The yields were increased to excellent, when they were performed in DCM (8 mL) with electric current of 10 mA for 4 hours (**3i-3l**). Finally, the dibenzo *[c, e]* [1,2]oxaphosphinine 6-oxide also delivered the desired product in 91% yield (**3m**).



[a] Reaction conditions: constant current = 12.0 mA, **1** (0.5 mmol), **2a** (0.6 mmol), $^nBu_4NBr$ (0.5 mmol), $CH_3CN$ (8 mL), air atmosphere, room temperature, 6 h; [b] Isolated yield; [c] DCM (8 mL), 10 mA, 4 h.

**Scheme 2.** The scope of the reactions.

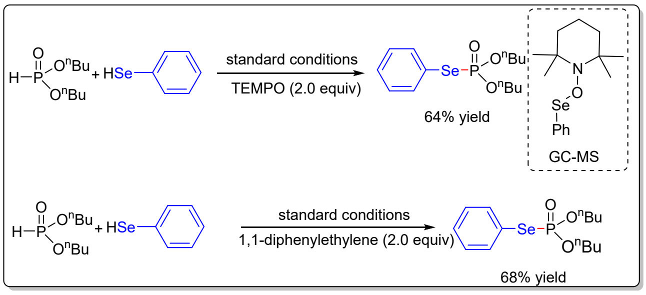


$^a$ Reaction conditions: **1** (0.5 mmol), **4** (0.3 mmol), $^n$Bu$_4$NBr (0.5 mmol), CH$_3$CN (8 mL), room temperature, 6 h. isolated yield; $^b$ DCM (8 mL), 10 mA, 4h.

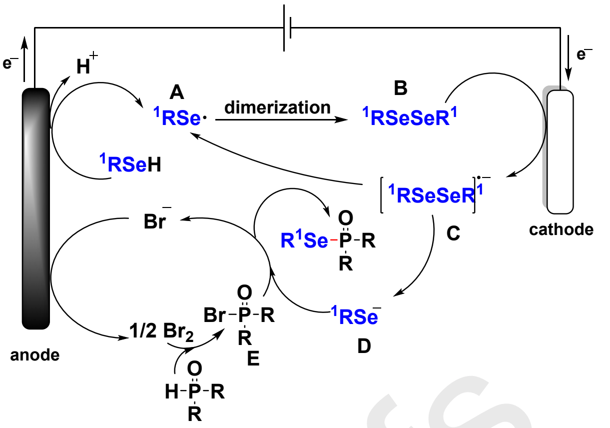
**Scheme 3.** The scope of the reactions.

The determination of reaction solution by GC-MS showed that there exists diselenides. So, we wondered that the diselenides might be the reaction intermediates. Then the scope of diselenides was subsequently studied with phosphonates /phosphine oxides (Scheme 3). 1,2-Diphenyldiselane was treated with dialkyl phosphates, and the reaction proceeded well, leading to **3a** and **3m** in 78% and 85% yields, respectively. The dibenzyl diselenide performed well in the reaction systems, resulting the corresponding products of **3n**, **3o**, **3p** and **3q** in 80%, 84%, 78% and 84% yield. Moreover, the reaction of dialkyldiselenides with dibenzo *[c, e]* [1,2] oxaphosphinine 6-oxide also proceeded smoothly, yielding the desired products in 75–78% (**3r-3s**). Finally, when the diphenylphosphine oxide was subjected to dialkyldiselenides, the product was isolated in 57% and 65% yield (**3t-3u**).

Two control experiments were conducted to clarify the reaction mechanism (Scheme 4). To explore whether the reaction occurs through a radical procedure, we used TEMPO (2.0 equiv.) as radical scavenger, and the desired product **3a** was decreased 64% yield, along with the radical product of TEMPO with benzeneselenol (detected by GC-MS). Next, 1,1-diphenylethylene (2.0 equiv.) instead of TEMPO was used, and the desired product **3a** was isolated in 68% yield. It means that the reaction is might undergo a radical process.



**Scheme 4.** Control experiments.



**Scheme 5.** The plausible mechanism.

On the basis of the above results and the previous reports[17,20], a proposed reaction pathway of selenation phosphonates and phosphine oxides is depicted in Scheme 5. Firstly, at the anode, selenol was oxidized to generate selenium radical **A**, followed by a dimerization to form diselenide **B**. This intermediator was then reduced at the cathode to generate **C**, which was composed to lead **A** and selenium anion **D**. On the other hand, Br$^-$ was oxidized to form Br$_2$, in the presence of phosphonate, the phosphorobromidate **E** was obtained. Finally, **E** was attacked by **D** to afford the desired selenation product.

## Conclusions

In summary, a concise, convenient, environmentally friendly and efficient electrocatalytic-mediated selenation of phosphates/ phosphine oxides was developed. The substrates scope was broad, and products were obtained in good to excellent yields under mild conditions. The use of electrocatalytic strategy avoids the use of metal catalyst, oxidant, base, thus reduced formation of organic wastes. These features enable the method more useful in organic synthesis.

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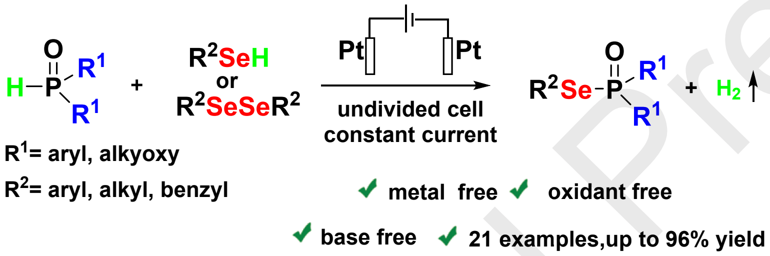
## Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.



Our work has below advantages:

(1) Metal-, oxidant-, and base free in this transformation
(2) The Scope of substrate are broad
(3) The reaction is atom economy with high yield