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Versatile electrooxidative amino- and oxyselenation of alkenes†

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Herein, we describe a general and eco-friendly electrochemical methodology for amino- and oxyselenation of alkenes under transition-metal catalyst- and additional-oxidant-free conditions. This electrocatalytic difunctionalisation reaction exhibits excellent chemoselectivity, ample substrate scope, and high functional group tolerance. To our delight, the selenation products (118 examples, up to 99% yield) were constructed from various alkenes including the challenging 1-aryl-1,3-dienes, unactivated aliphatic alkenes, and various N- or O-centered nucleophiles. Preliminary mechanistic studies were conducted. The practical utility of this protocol is highlighted by the gram-scale synthesis and late-stage modification of bioactive molecules.

Introduction

Alkenes are important bulk chemicals which can be produced from the traditional petrochemical industry and emerging coal chemical industry. The difunctionalisation of accessible alkene feedstocks into varied highly value-added fine chemicals with increased molecular complexity is a cutting-edge research hotspot in synthetic chemistry.[1,2] During the past few years, a wide spectrum of elegant alkene oxidative difunctionalisation reactions,[3] which can concurrently introduce two vicinal C–C/C–C, C–hetero/C–hetero, or C–C/C–hetero bonds to multiple bonds, have been well established with the strategies of transition-metal catalysis,[4–6] visible-light catalysis,[7] and organocatalysis.[8] Meanwhile, the asymmetric version of the alkene difunctionalisation reactions as a much more challenging topic has also achieved rapid progress.[9,10]

Organoselenium compounds are widespread in the areas of the pharmaceutical industry,[11,12] polymer chemistry,[13] and advanced organic functional materials[14] due to their abundant biological activities and specific photophysical and photochemistry properties. They are also exploited as small molecule catalysts[15,16] and polydentate ligands[17] in organic synthesis. The direct selenofunctionalisation of alkene skeletons with the formation of adjacent C–Se and C–X (X = carbon and heteroatoms) bonds has been proved to be a straightforward and powerful protocols for synthesising organic selenium-containing products.[18–30] However, the use of transition-metal catalysts, excessive chemical oxidants, various reaction additives, and harsh reaction conditions of some of the methods mentioned above usually result in unwanted byproducts and large amounts of waste, thus increasing the difficulties of the workup procedure and bringing the risk of environmental pollution.

In recent years, electrochemical organic synthesis[31,32] and the merging of electrosynthesis with transition-metal catalysis[33] or visible-light photoredox catalysis[34,35] have achieved remarkable advances in the functionalisation of olefins. Among them, tandem electrochemical oxidative inter- or intramolecular carbonselenation,[36–38] aminoselenation,[39] oxyselenation,[39–50] selenosulfonylation,[51] and fluoroselenation[52] of alkene derivatives with C–X (X = C, N, O, S, F) and C–Se bonds formation have been successfully reported. Lei's group described an efficient electrooxidative amino- and oxyselenation of styrenes with benzotriazoles, carboxylic acids, and alcohols as the nucleophiles.[39] However, only 35% of the target product is obtained when saccharin is used as the nitrogen source. In contrast, other electrochemical oxyselenation processes are mainly confined to the intramolecular annula-

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tion reactions of unactivated alkenes, such as olefinic carbonyl, olefinic alcohols, alkenoic acids, allylphenol, β,γ-unsaturated amides, and olefinic amides. Notably, some electrooxidative carbonselenation,[53,54] oxyselenation,[55,56] and diselenylation[57] of alkynes have also been realised.

Compared with the extensively studied difunctionalisation of activated alkenes, the conversion of inactive aliphatic olefins has rarely been researched and the general and green protocol for the difunctionalisation of activated alkenes[58–63] and challenging 1-aryl-1,3-dienes[64,65] is far from established. Based on our previous work on the electrooxidative trifunctionalisation of styrenes,[66] we herein present a universal methodology for the regioselective aminoselenation reaction of alkenes including activated arylalkenes, challenging 1-aryl-1,3-dienes, and non-activated aliphatic alkenes, and excitingly the oxyselenation of inert alkenes was also successful from diversified carboxylic acids (Scheme 1).

Results and discussion

After the systematic screening of reaction parameters (see Tables S1–S3 in the ESI† for details), the reaction conditions for the aminoselenation of activated alkenes were optimised as follows: in an undivided cell with C(+)/Ni(−) electrodes, constant current electrolysis was performed at 10 mA with Et$_4$BrN as the electrolyte in CH$_3$CN at room temperature for 2 h. With optimized reaction conditions in hand, the scope for the aminoselenation of activated alkenes **1** was primarily studied (Scheme 2). Generally, under standard conditions, a wide variety of substituted styrenes with varied electron-donating and -withdrawing groups can be conveniently transformed into their corresponding products **4a–4p** in moderate to excellent yields (53–93%). Moreover, 2-vinylnaphthalene, 2-vinylthiophene, and vinyl ferrocene also delivered their respective aminoselenation products **4q–4s** in 94%, 84%, and 45% yields. Even substrates containing steric hindrance, such as 1H-indene, α-methlystyrene, and β-methlystyrene, smoothly produce the target products **4t–4v** with good yields.

1,3-Dienes often function as versatile feedstocks to assemble structurally diverse, complex molecular architectures by way of transition-metal- or visible-light photoredox-catalyzed alkene-functionalization reactions. In light of 1,3-dienes containing multiple reaction sites, the regioselective alkene functionalisation of 1,3-dienes is a challenging research topic. Delightfully, this methodology was successfully expanded to 1-aryl-1,3-dienes under standard electrolytic conditions with
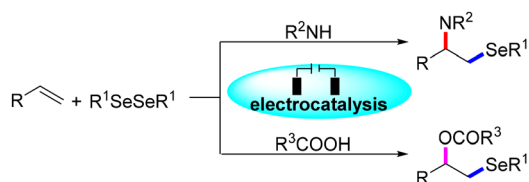
Scheme 1 Electrooxidative amino- and oxyselenation of alkenes.
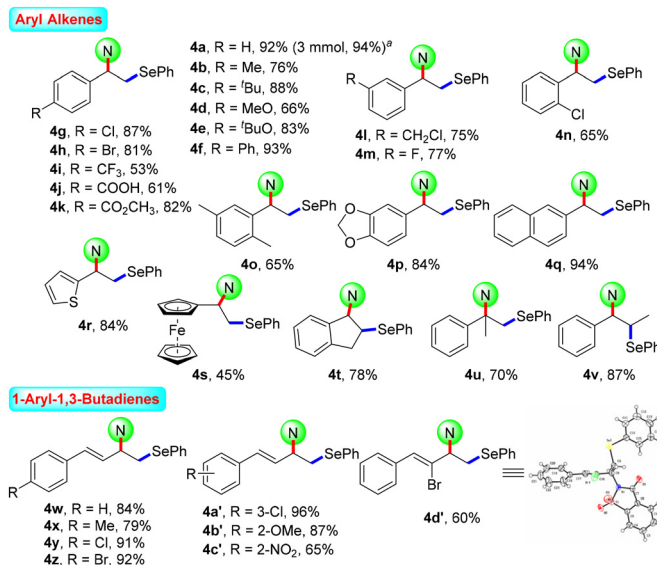
Scheme 2 Substrate scope for the aminoselenation of activated alkenes. Reaction conditions: **1** (0.3 mmol), **2a** (0.2 mmol), **3a** (0.15 mmol), Et$_4$NBr (0.2 mmol), CH$_3$CN (4.0 mL), C anode, Ni cathode, 10 mA, 2 h, r.t., undivided cell. Isolated yields. [a] Gram-scale reaction.

exclusive 1,2-regio- and stereoselectivity. The substituent effects of the aromatic ring had little influence on the reaction efficiency. A series of functional groups, including −Me, −MeO, −Cl, −Br, and even strongly deactivated −NO$_2$, were well tolerated, forming the products **4w–4c′** in good to excellent yields. Notably, the reaction of (Z)-(2-bromobuta-1,3-dien-1-yl)benzene with saccharin (**2a**) and diphenyl diselenide (**3a**) proceeded well to result in the target product **4d′** in 60% yield. The molecular structure of **4d′** was determined by single-crystal X-ray diffractometry.

Aliphatic alkenes usually have lower reaction activity and are difficult to activate. The functionalisation of this kind of skeleton is a promising and cutting-edge research field, and has attracted much attention from synthetic chemists all over the world. Various non-activated aliphatic olefins were selected to probe the generality and limitations of this catalytic system. As shown in Scheme 3, a wide range of substituted allylbenzenes were selected as substrates, furnishing the corresponding products **5a–5g** in 44–79% yields. Using homoallylbenzene as the starting material, the desired aminoselenation product **5h** was also generated in moderate yield. In the same fashion, unactivated propylenes with attached useful synthetic functional groups such as phenol oxygen, ester, carbonate, amide, and phthalimide were suitable substrates, producing the difunctionalisation products **5i–5o** in acceptable yields. Moreover, diselenide substrate scope was also investigated using allylbenzene as the olefin source. Under optimal electrolytic conditions, substituted diaryl- and dibenzyl diselenides were subjected to this reaction, showing moderate reaction efficiencies for the generation of the corresponding products **5p–5x**.

Scheme 3 Substrate scope for the aminoselenation of unactivated alkenes. Reaction conditions: **1** (0.3 mmol), **2a** (0.2 mmol), **3** (0.15 mmol), r.t., undivided cell. Conditions A: Et₄NBr (0.2 mmol), CH₃CN (4.0 mL), C anode, Ni cathode, 10 mA, 3 h; conditions B: VBImBr (0.2 mmol), CH₃CN/TFE (4 mL, v : v = 1 : 3), C anode, C cathode, 5 mA, 2 h. Isolated yields. [a] Gram-scale reaction. [b] Under conditions A. VBImBr = 1-butyl-3-vinylimidazolium bromide. TFE = 2,2,2-trifluoroethanol.

For cyclohexene, a moderate isolated yield (66%) of the target product **5y** was obtained under the current standard conditions A, as shown in Scheme 3. Under modified electrolysis conditions (conditions B in Scheme 3, see Tables S4–S11† for details), the desired product **5y** was formed with up to a quantitative yield. Furthermore, a suite of symmetric diselenides containing diaryl, diheteroaryl, and dialkyl diselenides were well involved in this electrochemical reaction system to assemble the expected disubstituted products **5z–5h′** in moderate to excellent yields (52–97%). In addition, 5-/7-membered cyclic and long chain aliphatic alkenes were proved to be good starting materials and led to the desired aminoselenation products **5i′–5q′** in satisfactory yields. Unfortunately, due to the relatively poor nucleophilic ability, other amine sources as nucleophiles only presented lower reaction activities (**5r′–5t′**). The possible reason may be the smaller reduction current of saccharin than other N-centered nucleophiles; this gives it a higher nucleophilicity by smoothly losing the protons (see Fig. S4 in the ESI† for details).

Inspired by the good performance of the electrooxidative aminoselenation of various alkenes, we envisioned that this protocol may be qualified to realise the oxyselenation of inert olefins with similar electrolytic processes. Pleasingly, under the slightly altered reaction conditions of Scheme 3, B (see Tables S12–S15† for details), the electrochemical oxyselenation of unactivated alkenes proved to be feasible and the desired product **7a** was produced in 90% yield (Scheme 4). Benzoic acids decorated with electron-rich (–Me, –Et, –ᵗBu, –MeO, –MeS, and –PPh₂) and -deficient groups (–F, –Cl, –Br, –I, –CF₃, –CN, and –NO₂) on the phenyl ring were compatible to give rise to **7b–7p** in 71–97% yields. Other analogues of carboxylic acid, such as condensed, polyhalogenated, and aryl alkynyl carboxylic acid reacted well with saccharin and diphenyl diselenide to generate the corresponding products **7q–7t** in moderate to good yields. Importantly, the treatment of aliphatic carboxylic acids formed the oxyselenation products **7u–7y** in good yields. In the cases of 5-, 7-, 8-membered cyclic alkenes and the linear aliphatic alkenes, the desired products **7z–7d′** were obtained with up to 99% yield. It should be pointed out that these oxyselenation products substituted with plenty of easily modified function groups can be transformed for the further production of synthetically useful organic molecules. The structures of products **5y** and **7m** were finally determined by X-ray single crystal analysis (Fig. 1). Unfortunately, no desired difunctionalization products were formed when aliphatic alcohols such as methanol and ethanol were used as nucleophiles.
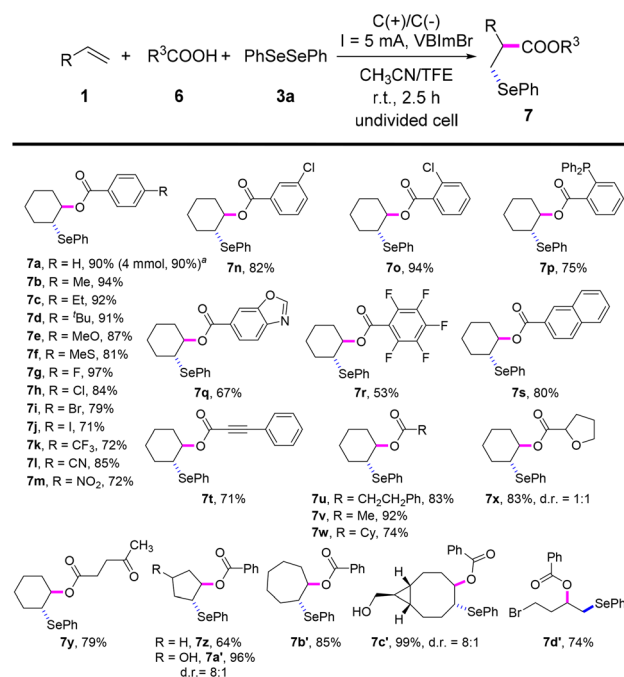
Scheme 4 Substrate scope for the oxyselenation of unactivated alkenes. Reaction conditions: **1** (0.2 mmol), **6** (0.4 mmol), **3a** (0.15 mmol), VBImBr (0.2 mmol), CH₃CN/TFE (4 mL, v : v = 2 : 2), C anode, C cathode, 5 mA, 2.5 h, r.t., undivided cell. Isolated yields. [a] Gram-scale reaction.
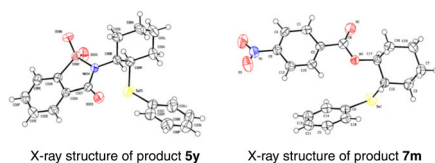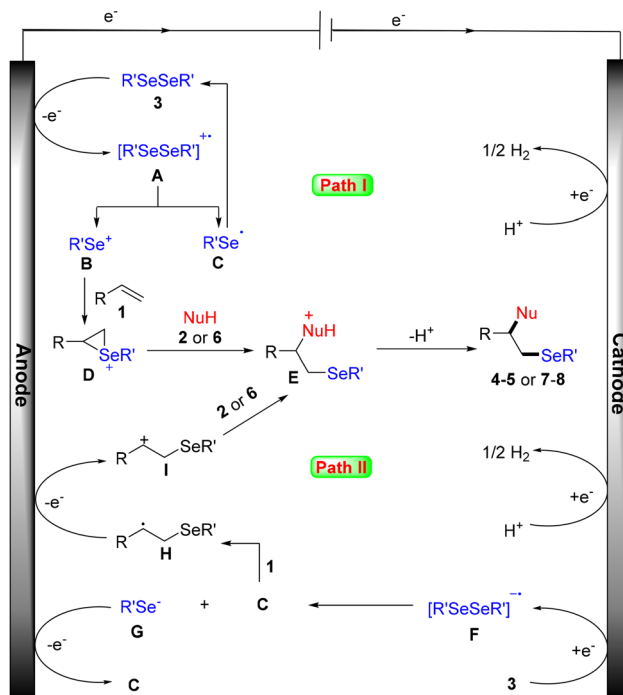
whole experiment. All the authors discussed and approved the final manuscript.

Conflicts of interest

There are no conflicts to declare.

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